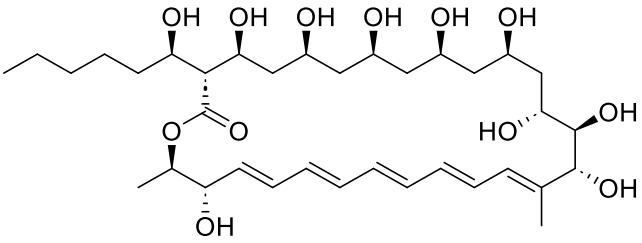
UNIVERSITÄT BONN

# Totalsynthesis of Pentamycin




## Dissertation

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## Eidesstattliche Erklärung

Hiermit versichere ich an Eides statt, dass ich die vorliegende Arbeit unter Einhaltung der Regeln guter wissenschaftlicher Praxis selbständig verfasst, keine anderen als die angegebenen Quellen und Hilfsmittel benutzt und die Zitate kenntlich gemacht habe.

Bonn, den 17.04.2024

Alexander Babczyk

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# Table of Contents

## List of Abbreviations

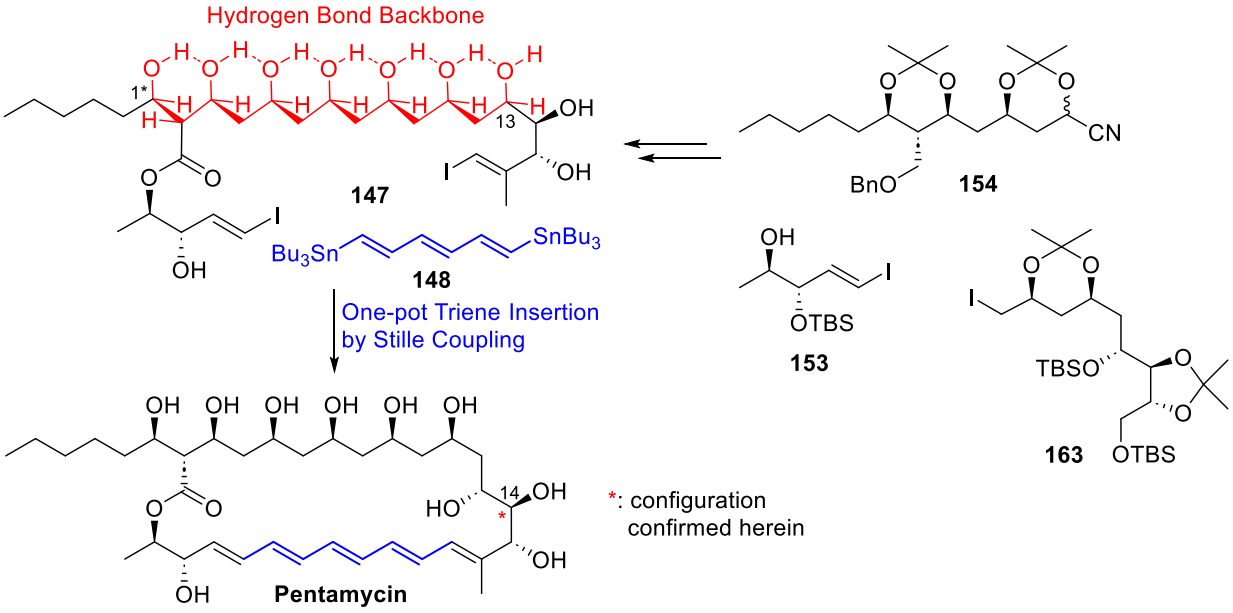
| | |
|---|---|
| **18-C-6** | 18-crown-6 |
| **2,2-DMP** | 2,2-dimethoxypropane |
| **9-BBN** | 9-borabicyclo[3.3.1]nonane |
| **ACP** | acyl carrier protein |
| **AIBN** | azobisisobutyronitrile |
| **AT** | acyltransferase |
| **BAIB** | (diacetoxyiodo)benzene |
| **Bn** | benzyl |
| **Boc** | *tert*-butyloxycarbonyl |
| **Bu** | butyl |
| **calcd.** | calculated |
| **CoA** | coenzyme A |
| **COSY** | correlation spectroscopy |
| **Cp** | cyclopentadienyl |
| **CSA** | camphorsulfonic acid |
| **CYP** | cytochrome P450 |
| **DCC** | *N*,*N*′-dicyclohexyl-carbodiimide |
| **DCM** | dichloromethane |
| **DDQ** | 2,3-dichloro-5,6-dicyano-1,4-benzoquinone |
| **DET** | diethyltartrate |
| **DH** | dehydrogenase |
| **DIAD** | diisopropyl azodicarboxylate |
| **DIBAL-H** | diisobutylaluminium hydride |
| **DIPA** | diisopropylamine |
| **DIPEA** | diisopropylethylamine |
| **DIPT** | diisopropyltartrate |
| **DMF** | dimethylformamide |
| **DMP** | dess-Martin periodinane |
| **DMPU** | *N*,*N*′-dimethylpropyleneurea |
| **DMSO** | dimethyl sulfoxide |
| ***dr*** | diastereomeric ratio |
| **EDC** | 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide |
| **EI** | electron ionization |
| **equiv** | equivalents |
| **ESI** | electrospray ionization |
| **Et** | ethyl |
| **HMBC** | heteronuclear multiple bond correlation |
| **HMPA** | hexamethylphosphoramide |
| **HPLC** | high-performance liquid chromatography |
| **HRMS** | high resolution mass spectrometry |
| **HSQC** | heteronuclear single quantum coherence |
| **HWE** | Horner-Wadsworth-Emmons |
| **IBX** | 2-iodoxybenzoic acid |
| **Ipc** | isopinocampheyl |
| **KR** | ketoreductase |
| **KS** | ketosynthase |
| **LDA** | lithium diisopropylamide |
| **LLS** | longest linear sequence |
| **MALDI** | matrix assisted laser desorption ionization |
| **MAO** | methylaluminoxane |
| **Me** | methyl |
| **MIDA** | *N*-methyliminodiacetic acid |
| **MOM** | methoxymethyl |
| **MS** | mass spectrometry |
| **MTPA** | *α*-methoxy-*α*-trifluoromethylphenylacetic acid |
| **NIS** | *N*-iodosuccinimide |

| | |
|---|---|
| **NMO** | *N*-methylmorpholine *N*-oxide |
| **NMR** | nuclear magnetic resonance |
| **NOESY** | nuclear Overhauser enhancement spectroscopy |
| **OTf** | triflate |
| **Ph** | phenyl |
| **PMB** | *para*-Methoxybenzyl |
| **PPTS** | pyridinium *para*-toluene-sulfonate |
| **Pr** | propyl |
| ***p*-TsOH** | *para*-toluenesulfonic acid |
| **RCM** | ring closing metathesis |
| **rt** | room temperature |
| **SAD** | Sharpless asymmetric dihydroxylation |
| **SAE** | Sharpless asymmetric epoxidation |
| **SEM** | 2-(trimethylsilyl)-ethoxymethyl |
| **SET** | single electron transfer |
| **TBAF** | tetra-*n*-butylammonium fluoride |
| **TBDPS** | *tert*-butyldiphenylsilyl |
| **TBS** | *tert*-butyldimethylsilyl |
| **TCA** | trichloroacetimidate |
| **TCBC** | 2,4,6-trichlorobenzoyl chloride |
| **TE** | thioesterase |
| **TEMPO** | 2,2,6,6-tetra-methylpiperidinyloxy |
| **TES** | triethylsilyl |
| **TFA** | trifluoroacetic acid |
| **THF** | tetrahydrofuran |
| **THP** | tetrahydropyran |
| **TIPS** | triisopropylsilyl |
| **TLC** | thin layer chromatography |
| **TMS** | trimethylsilyl |
| **TOF** | time-of-flight |

## Abstract

The polyene macrolide pentamycin (**10**), first isolated from *Streptomyces penticus* in 1958,[1] displays impressive biological activities against various pathogens, including *Trichomonas vaginalis* or *Candida albicans*, and can be used clinically to treat vaginal candidiasis, trichomoniasis, and other mixed infections.[2] Its powerful biological properties combined with its unique 3D structure have attracted considerable interest from the synthetic community.[3] However, a total synthesis has remained elusive, mainly due to the notorious instability caused by the pentaene fragment.

In this work, the first total synthesis of pentamycin was accomplished by a modular strategy in 25 steps (longest linear sequence) in an overall yield of 1.5%. The key step was a final Stille-type ring closure that circumvented any stability problems during the synthesis, which proved essential for the realization of this total synthesis. This linchpin insertion of protective group free *bis*-vinyl iodide **147** and trienyl-*bis*-stannane **148** concomitantly closed the macrocycle and installed the sensitive pentaene fragment in the very last step (Scheme 1). Presumably, a linear hydrogen bonding network of the polyol substrate, enabled by the 1,3-*syn* polyol moiety between C1* and C13, facilitates ring closure.


Scheme 1: Overview of the total synthesis of pentamycin.

*Bis*-vinyl iodide **147** was obtained from northern **154**, eastern **163**, and western fragment **153** after coupling, modification, and global deprotection (Scheme 1). Further key steps were the Rychnovsky coupling between cyanohydrin acetonides and alkyl iodides, the Krische carbonyl allylation, and Carreira's stereoselective addition of alkynes to aldehydes.[4] The total synthesis unequivocally confirms the full relative and absolute stereochemistry of this polyketide,

including the previously uncertain hydroxyl bearing center at C14. Furthermore, it represents one of the first examples of an extended hydrogen bond network being designed as a conformational template for complex macrocyclization and documents the importance of conformational design in total synthesis of complex natural products.

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# 1 Introduction

Natural products are small molecules produced by biological sources like plants, bacteria, or fungi, as a result of secondary metabolism.[1,2] Unlike primary metabolites, found in most organisms, secondary metabolites are unique to individual species and are not crucial for their survival.[2] However, since secondary metabolites are often cytotoxic, they equip organisms with specific advantages over other, competing species.[3] Harnessing the resulting biological activities like anticancer or antibiotic effects of many natural products, humans were able to develop cures for major diseases.[4] Beside remarkable biological activities, highly complex architectures are a further motivation for organic chemists to engage in total synthesis of natural products.[5–7]

According to K. C. Nicolaou, total synthesis can be defined as the “art and science” of making natural products and its analogues in the laboratory.[7] The first synthesized molecule was urea in 1828 by F. Wöhler which can be considered as the birth of total synthesis.[6,8] E. Fischer (1890) synthesized the first chiral molecule, (+)-glucose, containing four controllable stereogenic centers.[6,9] At the beginning of the twentieth century complexity of synthetic targets increased, especially the contributions of R. B. Woodward, since 1937 professor in Harvard, shaped the field of organic chemistry and total synthesis.[6] Molecules like quinine (**1**),[10] strychnine (**2**),[11] reserpine (**3**)[12] and steroids like cortisone (**4**),[13] with highly complex structures were synthesized during this time (Figure 1.1).

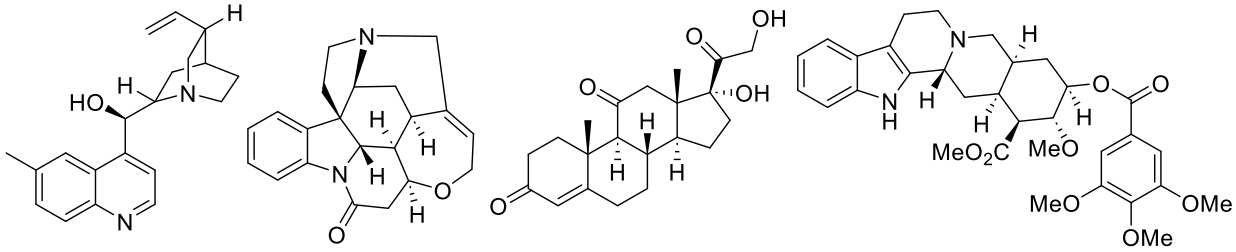



Figure 1.1: Structures of quinine (**1**), strychnine (**2**), reserpine (**3**), and cortisone (**4**), synthesized by R. B. Woodward.

In addition to Woodward, another pioneer of modern total synthesis was E. J. Corey, who has been a professor at Harvard since 1959. He established an organized and systematic approach to total synthesis and introduced the concept of retrosynthetic analysis and the development of new synthetic methods as integral part of total synthesis.[6]

Total synthesis provides various benefits to science and society.[14] Molecules isolated in nature can be replicated in the laboratory using novel synthetic strategies. These strategies can be used for design and synthesis of analogues which can then further be evaluated regarding

their usefulness in biology and medicine. Another important motivation for total synthesis is the possibility to finally confirm or revise structures as well as relative and absolute configuration.

## 1.1 Polyene Macrolide Antibiotics

Polyene macrolide antibiotics are macrocyclic natural products characterized by a conjugated polyene moiety and a lactone motif. Additionally, a polyol section is included typically made up of 1,2-, 1,3- or 1,4-diols with 1,3-diols being the most common.[15] Some polyene macrolides additionally contain attached sugar moieties such as mycosamine (Figure 1.2).[16,17]

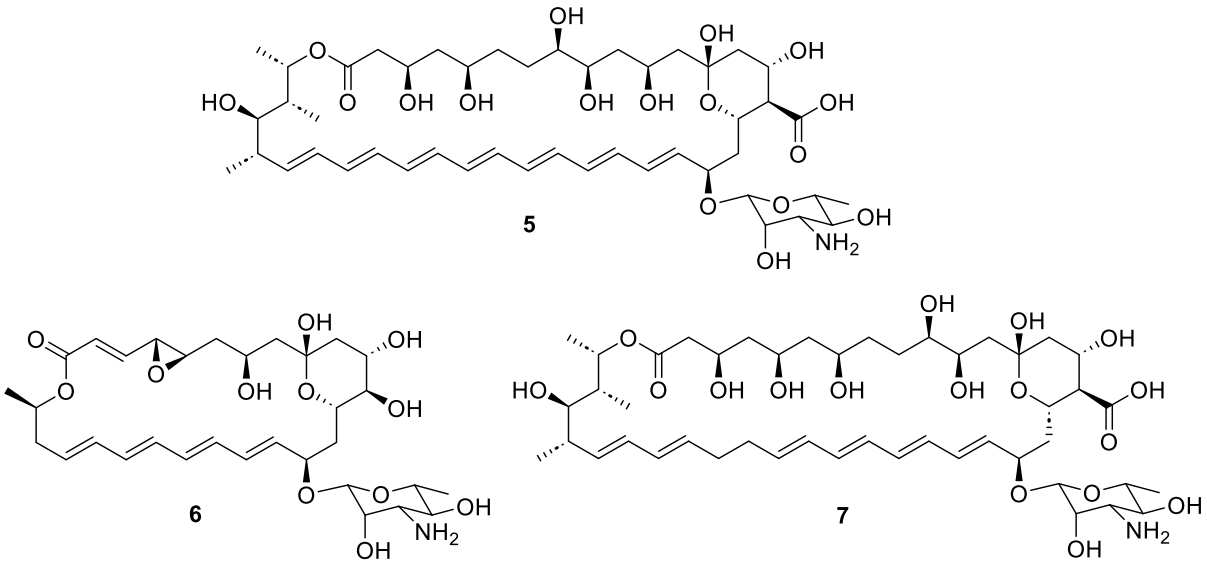


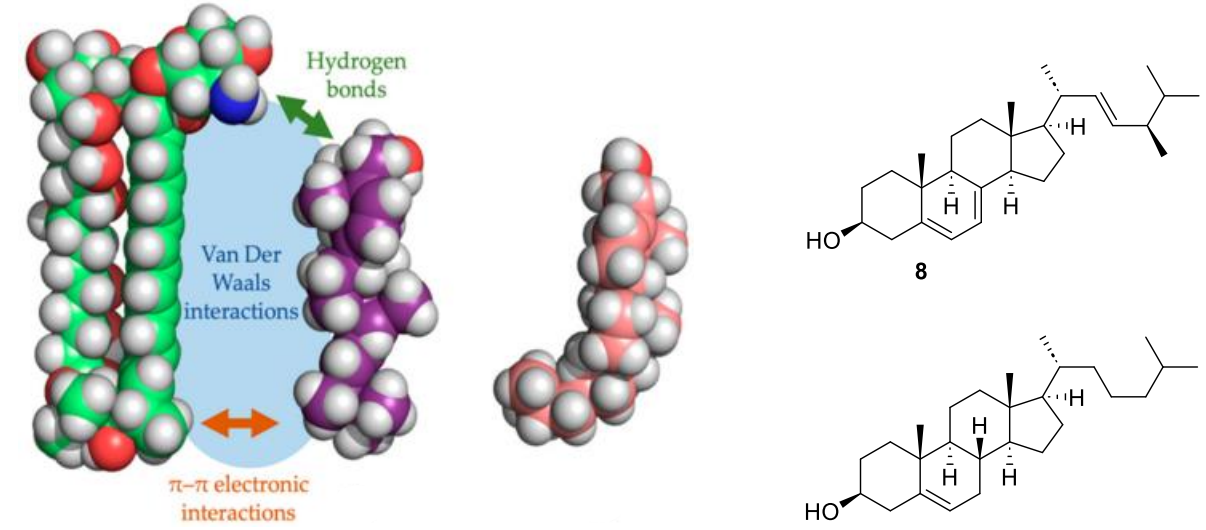

Figure 1.2: Structures of amphotericin B (**5**), natamycin (**6**), and nystatin (**7**).

This class of compounds shows activity towards various bacteria but mainly towards mycopathological species like yeasts, dermatophytes, and molds.[16,18] Especially since the 1970s and 1980s, the increased use of immunosuppressants and the raising number of AIDS cases have led to a massive incidence of fungal diseases requiring effective remedy.[19] Although many polyene macrolide antibiotics are quite toxic and consequently cannot be used to treat diseases in humans, some less toxic ones are useful because of their broad spectrum of activity against many fungal infections.[20,21] Today, mainly the three polyene macrolide antibiotics amphotericin B (**5**), natamycin (**6**), and nystatin (**7**) are still used clinically (Figure 1.2).[22]

### 1.1.1 Mode of Action

In contrast to many other secondary metabolites, polyene macrolides usually do not target a specific enzyme but bind to ergosterol (**8**) the primary sterol in the fungal cell membrane.[19] Figure 1.3 shows the three types of interactions between polyene macrolides on the example of amphotericin B (**5**) and ergosterol (**8**) which consist of hydrogen bonds between the sugar

moiety of the polyene macrolide and the hydroxy function of ergosterol (**8**), van der Waals forces between the non-polar parts of both molecules and *π-π* interactions between the double bond of the sterol side chain and the polyene part of the macrolide.[21]




Amphotericin B (**5**) | Ergosterol (**8**) | Cholesterol (**9**)

Figure 1.3: Interactions between amphotericin B (**5**) and ergosterol (**8**) consisting of hydrogen bonds, van der Waals forces and *π-π* interactions. The sigmoidal conformation of cholesterol (**9**) leads to weaker interactions.[21]

The primary sterol in mammalian cells is cholesterol (**9**) which possesses a sigmoidal conformation leading to weaker van der Waals interactions between sterol and polyene macrolide than in case of ergosterol (**8**) which has a rod-like conformation. Furthermore, the lacking double bond in the sterol tail of cholesterol (**9**) prevents *π-π* interactions which results in selective activity of polyene macrolides towards fungal cells.[23]

Depending on the respective molecules there are different conceivable mechanisms of action between polyene macrolides and fungal cells. Mainly distortion and destabilization of the cell membrane by interacting with ergosterol (**8**) leads to malfunction of the cell.[16,24] Amphotericin B (**5**) for instance can build pores along the cell membrane leading to a disbalance of $K^+$ ions and other small organic molecules necessary for cell function. Smaller compounds like natamycin (**6**) cannot build pores, but they can extract ergosterol (**8**) from the cell membrane acting like a sponge (Figure 1.4).[25]

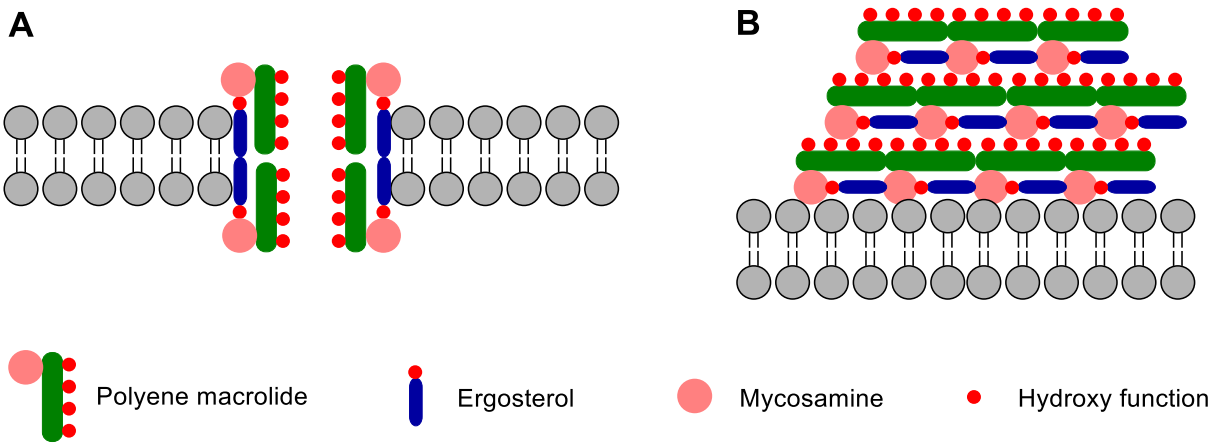



Figure 1.4: Two possible mechanisms of action of polyene macrolide antibiotics. **A**: Ion channel or pore forming model. **B**: Sterol sponge model.[21,25]

### 1.1.2 Pentamycin and Filipin III – Two Closely Related Polyene Macrolides

Pentamycin (**10**) and filipin III (**11**) are structurally related to amphotericin B (**5**) and other polyene macrolide antibiotics introduced above, although the mycosamine unit is missing.[26] Pentamycin (**10**) was first isolated from *Streptomyces penticus* in 1958[27] three years after the first isolation of a compound named filipin, isolated from *Streptomyces filipinensis*.[28] Both compounds are built by a 28-membered macrolactone core and contain five conjugated double bonds. The polyol part of filipin III (**11**) contains eight 1,3-*syn* hydroxy functions, pentamycin (**10**) contains an additional one at C14, which is the only difference between both molecules (Figure 1.5).[24]

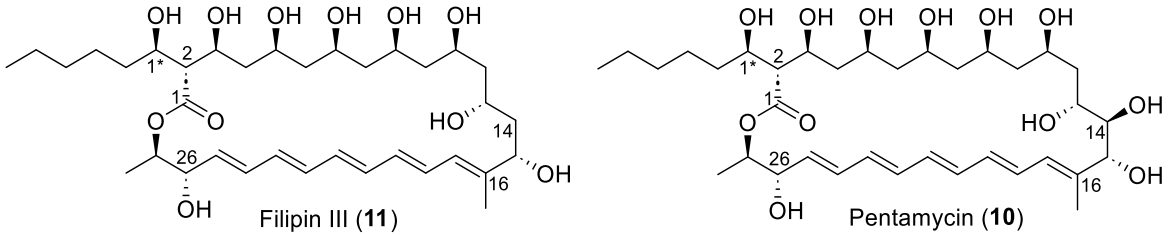



Figure 1.5: Structures of filipin III (**11**) and pentamycin (**10**).

Filipin III (**11**) is the main compound of a mixture containing various related compounds, called the filipin complex (see pp. 6–7).[29] First structure elucidation experiments were performed by Golding *et al*. (1964)[30] and Dhar *et al*. (1964).[31] Rychnovsky & Richardson (1995) performed an NMR-based structure elucidation of filipin III (**11**) supported by acetonide formation and acetylation, as well as degradation and hydrogenation reactions of the natural product.[32] The structure was finally confirmed by the first total synthesis of filipin III (**11**) in 1997.[33] The structure of pentamycin (**10**), although closely related to filipin III (**11**) was not fully confirmed at the beginning of this work. Similar to filipin III (**11**) various NMR-experiments of the acetonide and

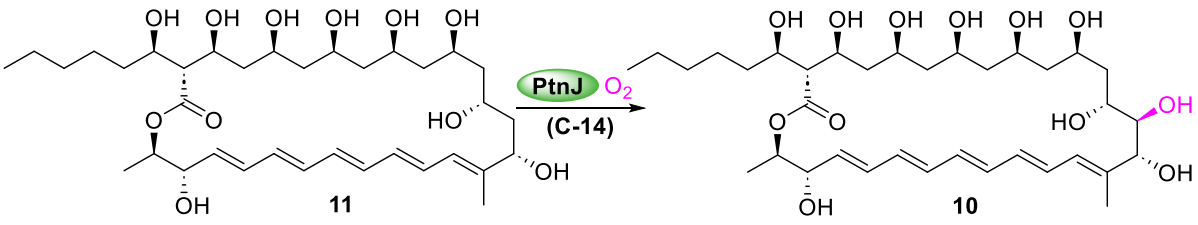
acetyl protected and degraded natural product were conducted, however, while a *trans*-configuration of the C14 and C15 hydroxy moieties is very likely, the absolute stereochemistry has not been rigorously assigned.[34]

Pentamycin (**10**) shows activity against various fungal and bacterial pathogens like *Candida albicans* and *Trichomonas vaginalis* and is registered in Switzerland for treatment of vaginal candidiasis, trichomoniasis, and mixed infections.[35] Furthermore, it acts as an adjuvant of the anticancer drug bleomycin by increasing its efficacy *in vitro*.[36] Although pentamycin (**10**) has attractive biological activities, its widespread pharmaceutical application is prevented by chemical instability.[24]

In contrast to clinically useful polyene macrolides, filipin III (**11**) shows similar affinity to ergosterol (**8**) and cholesterol (**9**) making it useless for selectively targeting fungal cell membranes and thus toxic for mammalian cells.[16,24] Although filipin III (**11**) cannot be used as a drug, its high intrinsic fluorescence and the affinity to cholesterol can be exploited by using it as diagnostic agent for type C Niemann-Pick disease, a progressive storage disorder of cholesterol resulting in accumulation of cholesterol (**9**) in the lysosome.[37]

### 1.1.3 Biosynthesis of Pentamycin

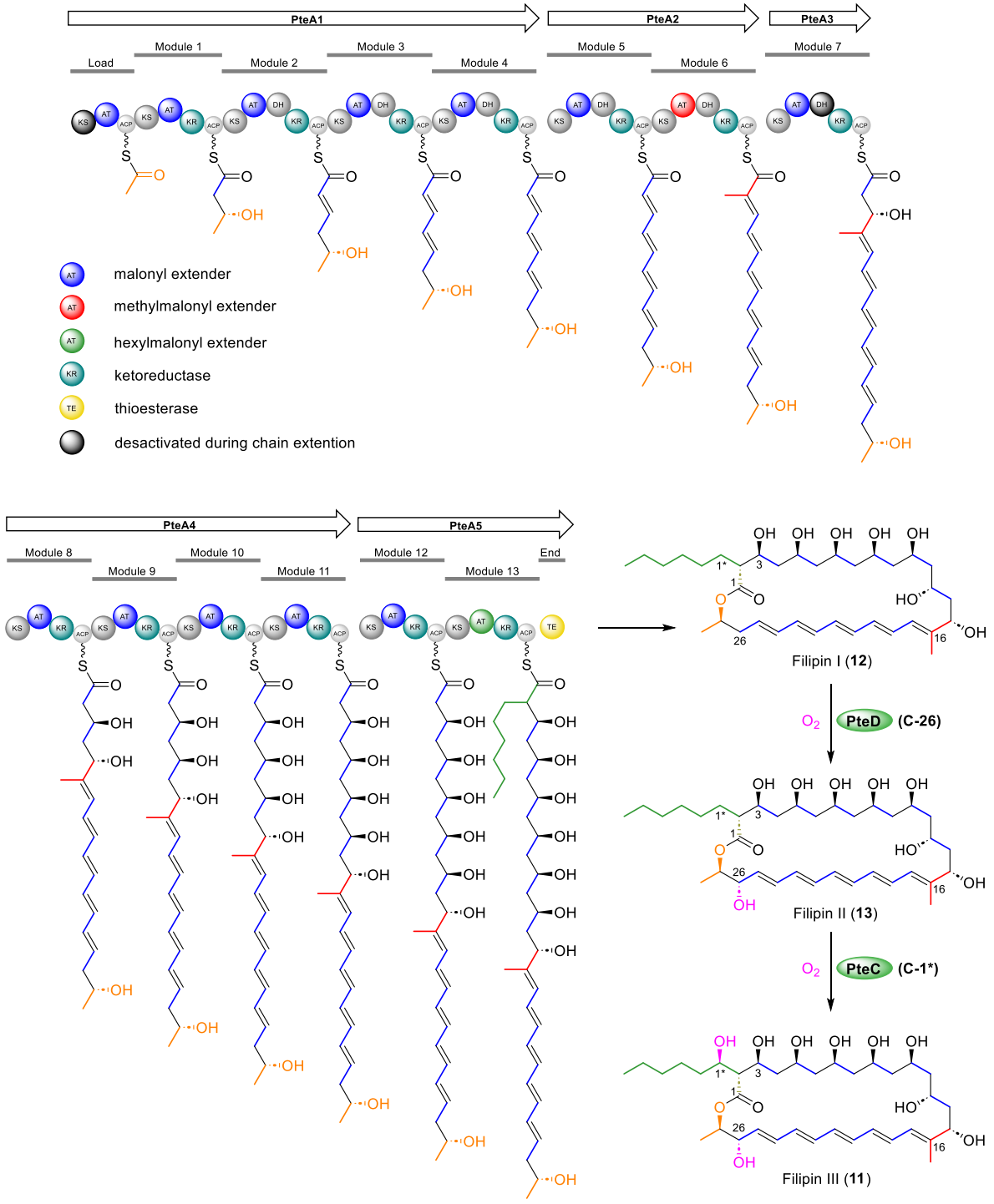
The close structural similarity of pentamycin (**10**) and filipin III (**11**) leads to the assumption that the biosynthetic pathways must be closely related. In fact, the biosynthetic gene clusters of pentamycin (**10**) in *Streptomyces* sp. S816 and filipin III (**11**) in *Streptomyces avermitilis* MA-4680 are very similar. However, the pentamycin cluster encodes an additional cytochrome P450 monooxygenase (CYP) and ferredoxin (Fd/Fr) PtnJ, catalyzing the hydroxylation at C14 (Scheme 1.1).[24]




Scheme 1.1: Transformation of filipin III (**11**) to pentamycin (**10**) in *Streptomyces* sp. S816 through hydroxylation of C14 by PtnJ.[24]

Since filipin III (**11**) can be viewed as the precursor of pentamycin (1**0**) the biosynthetic pathway is discussed in the following. The polyketide framework is assembled by type I modular polyketide synthases (type I PKS). The gene cluster contains 13 protein-coding genes, five of which encode multifunctional type I PKS enzyme complexes (PteA1–PteA5) with a total of 14 modules responsible for formation the polyketide framework of filipin III (**11**).[38] The resulting

product of these five PKSs is filipin I (**12**) the non-oxidized precursor of filipin III and pentamycin (Scheme 1.2).

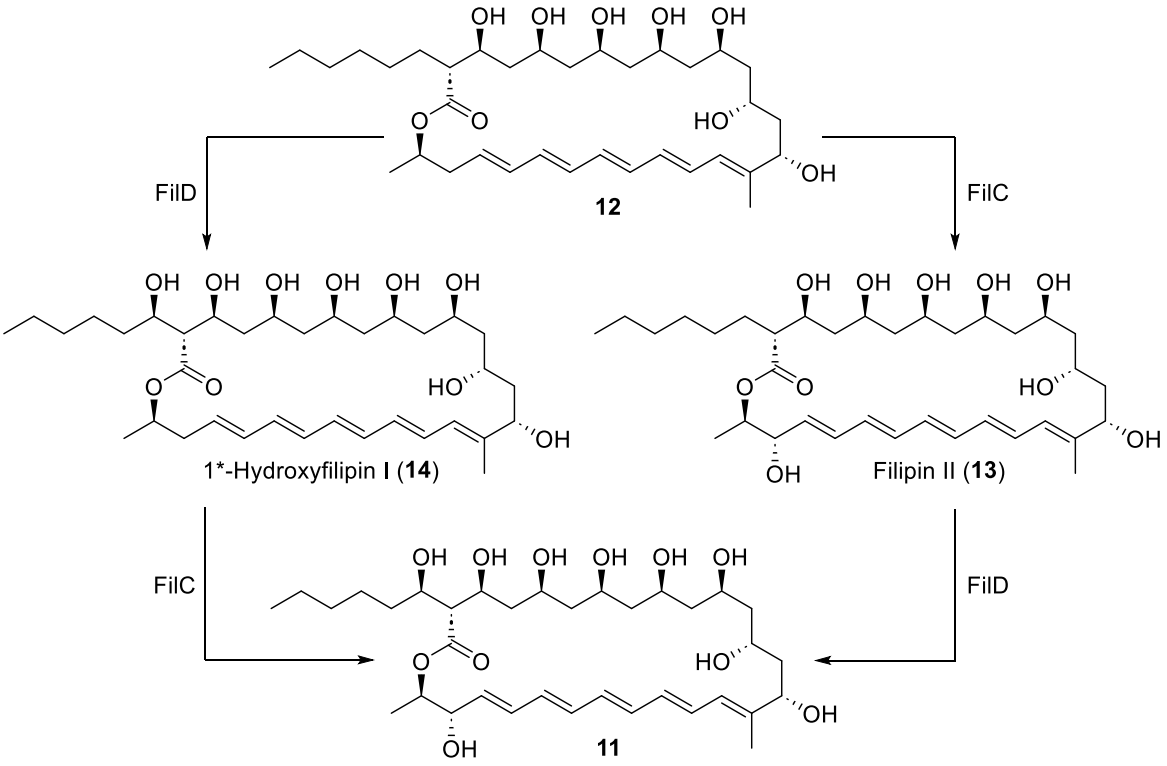



Scheme 1.2: Biosynthetic pathway of filipin III (**11**), the precursor of pentamycin (**10**) in *Streptomyces avermitilis*.[39]

The starter unit acetyl-CoA is elongated with five malonyl extender-units until a methyl malonyl extender unit is introduced by PteA2 resulting in the methyl group at C16. Whereas the starter unit is reduced to the secondary alcohol, the extender units are reduced and dehydrated to generate the polyene part. The following six malonyl extender units (PteA4 and PteA5) are just

reduced to the alcohol to create the polyol part of the filipins (**11**–**13**) and pentamycin (**10**). Finally, a hexyl malonyl-CoA extender unit is introduced by PteA5 leading to the pentyl side chain before the thioesterase closes the macrolactone affording filipin I (**12**) (Scheme 1.2).[39]

Post-PKS modifications of polyene macrolides by CYP are common and provide molecular diversity.[40] The two genes PteD and PteC are located downstream the PKS genes and encode CYP responsible for hydroxylation at C1* and C26.[39,41] The oxidation product of PteD is filipin II (**13**), additional oxidation by PteC at C1* leads to filipin III (**11**) the biosynthetic precursor of pentamycin (**10**). However, the suggested biosynthetic pathway of filipin III (**11**) in *Streptomyces avermitilis* is only one possible route to convert filipin I (**12**) to filipin III (**11**). A specific mutant of *Streptomyces filipinensis* also produces large amounts of 1*-hydroxyfilipin I (**14**), leading to the assumption that filipin III (**11**) is not necessarily produced via filipin II (**13**) but the order of oxidizing C26 and C1* depends on the respective rate of the enzymes[a] in different organisms or mutants (Scheme 1.3).[42]




Scheme 1.3: Two different pathways of oxidizing filipin I (**12**) to filipin III (**11**).[42]

What nature does with high efficiency has always been a motivation for chemists to achieve in the laboratory. The following section will formulate the objective of this work before the already published synthetic studies on both molecules, pentamycin (**10**) and filipin III (**11**) are discussed in Chapter 2.

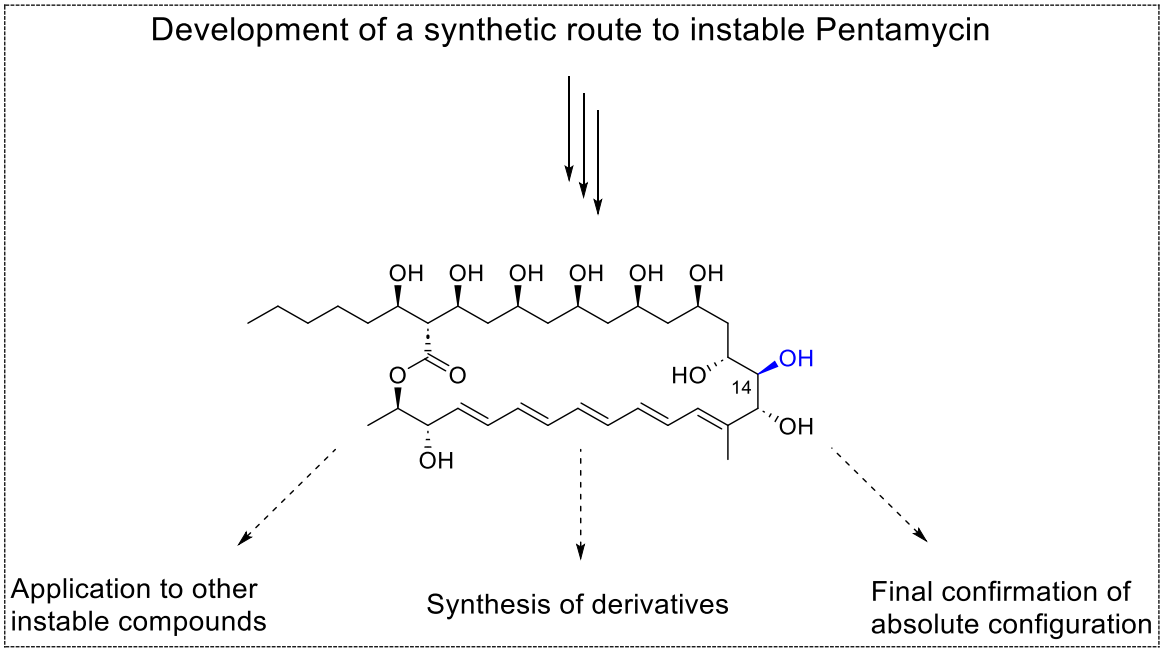
[a] PteC and PteD in *Streptomyces avermitilis* or analog FilC and FilD in *Streptomyces filipinensis*.[42]

## 1.2 Aim of this Project

Whereas a total synthesis of filipin III (**11**) has already been published by Richardson & Rychnovsky in 1997,[33] a first total synthesis of the closely related pentamycin (**10**) is still missing. Various attempts, synthetic studies and fragments on both molecules were published during the last decades. While an attempt by Oishi *et al*. (1990) was close, other publications only discuss fragment syntheses.[43–45]

The main goal of this work is to develop a strategy for the first total synthesis of the unstable polyene macrolide pentamycin (**10**). It is believed that the instability is caused by the pentaene moiety and the adjacent allylic alcohols. Therefore, the core of the strategy should focus on how to address and prevent stability issues during the synthetic process. Chapter 2 analyzes multiple published attempts for the synthesis of pentamycin (**10**) and the closely related polyene macrolide filipin III (**11**). In particular, the unsuccessful syntheses should help to develop a suitable strategy. Chapter 3 then presents a new strategy developed on the basis of previous problems.

As already discussed in the very beginning, total synthesis provides various benefits to the scientific community. One important point is the final confirmation of the structure and absolute configuration of natural products. Although isolated more than 60 years ago, the absolute configuration of C14 of pentamycin (**10**) is not clear yet and should ultimately be confirmed by total synthesis of and NMR comparison.




Scheme 1.4: Schematic overview of the goals of this work.

Not pursued in this work but a secondary objective resulting from the development of a synthetic method to access pentamycin (**10**) is the possibility to make derivatives. The notorious

instability of pentamycin (**10**) prevents extensive pharmaceutical application so far, however, derivatives with similar bioactivity and higher stability may be attractive synthetic targets. In addition, the developed method potentially offers the opportunity to establish synthetic routes to other highly unstable polyene macrolides, thereby creating added value for the synthetic community.

# 2 State of the Knowledge

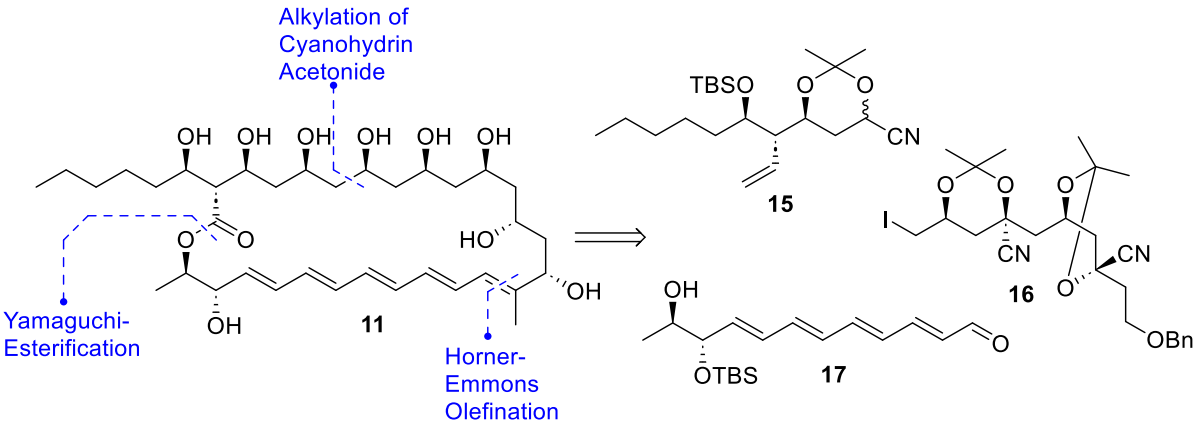
During the last three decades several publications addressing synthetic work on filipin III (**11**) and pentamycin (**10**) have been published. This chapter provides an overview and analyzes the synthetic strategies. Due to the close structural similarity of both molecules not only the published synthetic studies on pentamycin (**10**) are taken into account, but also successful and unsuccessful results towards filipin III (**11**) are used for the development of a new synthetic strategy for a first total synthesis of pentamycin (**10**).

## 2.1 Previous Work on Filipin III

Filipin III (**11**) is the less complex molecule as one hydroxy function in missing in contrast to pentamycin (**10**). The first total synthesis was published by Richardson & Rychnovsky in 1997.[33] Kiyooka *et al*. (1999 and 2000) provided interesting results for the synthesis of the polyol part suitable for a total synthesis of the molecule.[46,47] The third approach discussed here was published by the group of Cossy (2016) and contains an almost complete synthesis of filipin III (**11**), which could however not be finalized due to problems in one of the very last steps.[48]

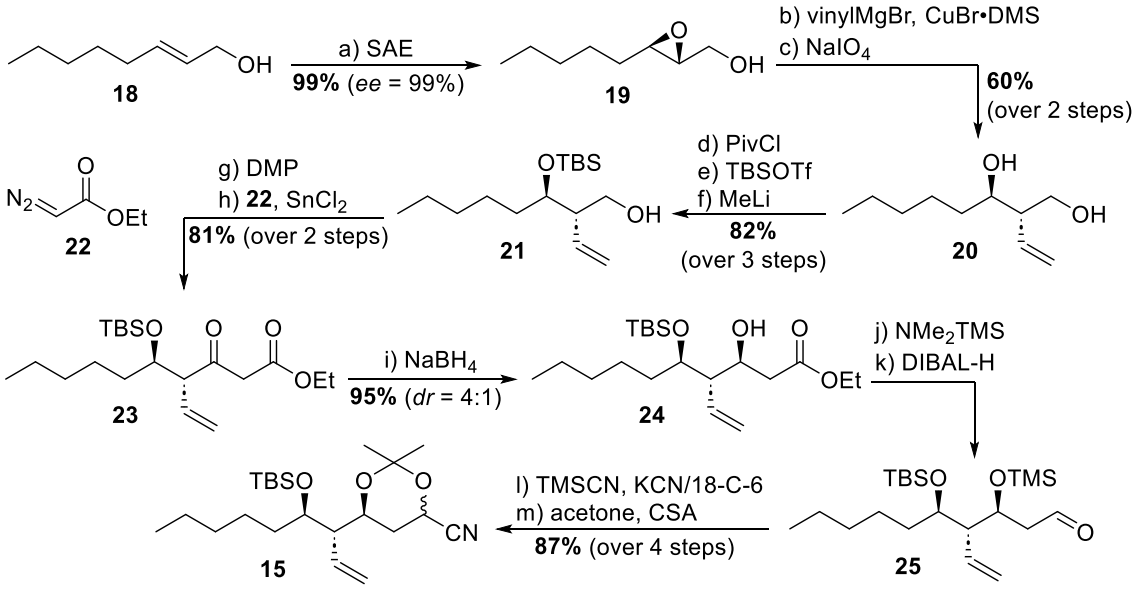
### 2.1.1 First Total Synthesis of Filipin III by Richardson & Rychnovsky

The key steps in this synthesis were an alkylation reaction of cyanohydrin acetonides to establish the characteristic 1,3-*syn* configuration of the polyol chain. The lactone was obtained by Yamaguchi esterification and final ring closure was achieved via Horner-Emmons cyclization (Scheme 2.1). Retrosynthetic analysis led to three central fragments,[33] the synthesis of which is discussed in more detail below.



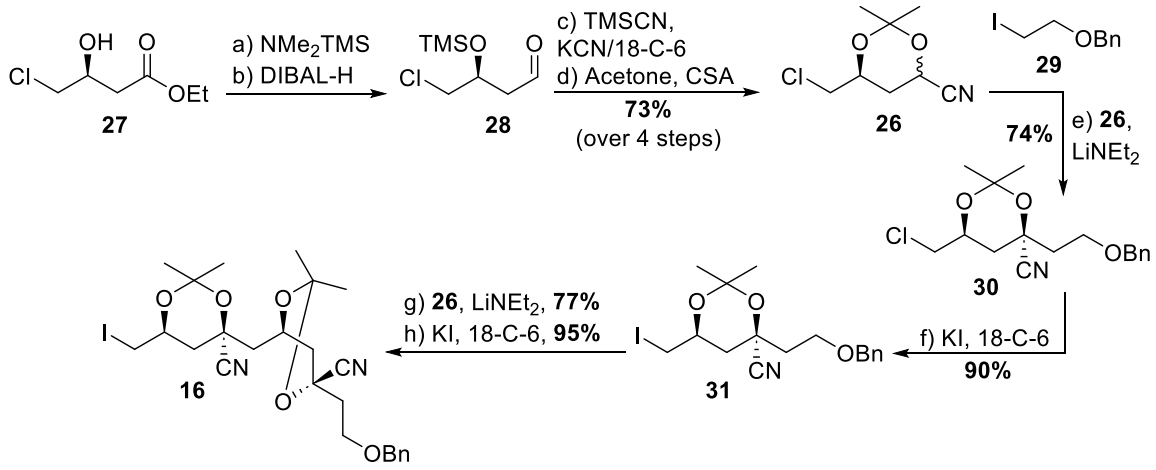

Scheme 2.1: Retrosynthetic analysis of filipin III (**11**) by Richardson & Rychnovsky.[33,49]

Synthesis of the northwestern part containing the pentyl chain started with a Sharpless asymmetric epoxidation of allylic alcohol **18** to obtain epoxide **19** followed by a copper catalyzed nucleophilic epoxide opening setting the first two stereocenters (Scheme 2.2). As the regioselectivity of this reaction was not optimal and the ratio of the 1,3- and 1,2-diol was only 2:1, the undesired minor 1,2-isomer was oxidatively cleaved using $NaIO_4$ which simplified purification of the desired 1,3-isomer **20**.[49] Protection of the secondary alcohol was achieved through a three-step protection/deprotection sequence affording mono-protected diol **21** which was oxidized to the aldehyde. Roskamp conditions,[50] i.e. ethyl diazoacetate (**22**) and $SnCl_2$ yielded *β*-ketoester **23** which was reduced by $NaBH_4$ generating protected 1,3-*syn* diol **24**. A four step sequence containing protection, reduction, addition of cyanide, and acetonide protection yielded cyanohydrin acetonide **15**.[33,49]



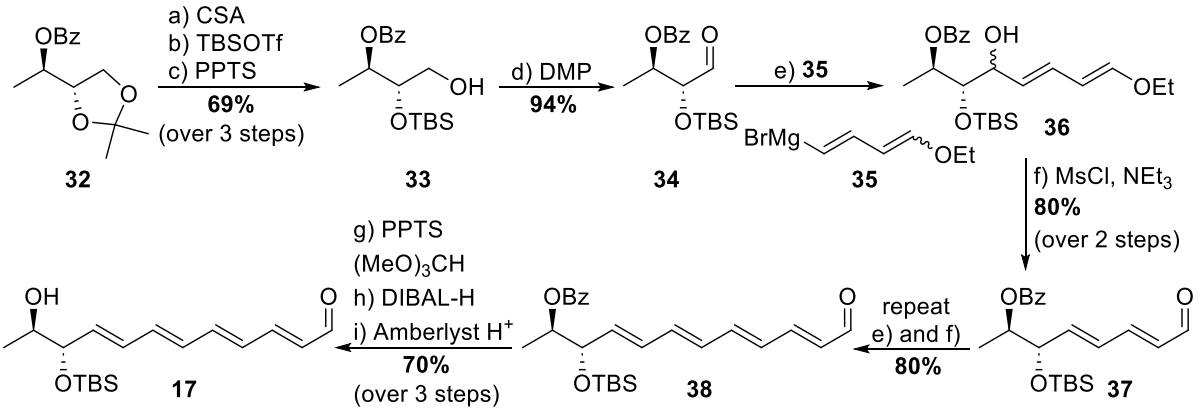

Scheme 2.2: Synthesis of cyanohydrin acetonide **15** by Richardson & Rychnovsky.[33,49]
Reaction conditions: a) Ti(O*i*-Pr)$_4$, D-(−)-DET, *tert*-BuOOH, DCM, −25 °C, 3 h, **99%** (*ee* = 99%); b) CuBr·DMS, $Et_2O$, −25 °C, then DMS, vinylMgBr, 15 min, then **19**, −20 °C, 16 h, then rt, 6 h; c) $NaIO_4$, THF:$H_2O$ (3:2), 90 min, **60%** (over 2 steps); d) PivCl, DMAP, $NEt_3$, DCM, rt, 4 h; e) TBSOTf, 2,6-lutidine, DCM, 0 °C to rt, overnight; f) MeLi, THF, 0 °C, 1 h, **82%** (over 3 steps); g) DMP, $NaHCO_3$, DCM, rt, 1 h; h), **22**, $SnCl_2$, DCM, rt, 22 h, **81%** (over 2 steps); i) $NaBH_4$, MeOH, 0 °C, 10 min, **95%** (*dr* = 4:1); j) $NMe_2TMS$, 0 °C to rt, overnight; k) DIBAL-H, $Et_2O$, −78 °C, 1 h; l) TMSCN, KCN/18-C-6 complex, 0 °C, 2 h; m) 2,2-DMP, acetone, CSA, rt, 14 h, **87%** (over 4 steps).

Northeastern fragment **16** was synthesized in an iterative manner using building block **26** which could be obtained in a four step sequence starting from *β*-hydroxyester **27** (Scheme 2.3).[51] $LiNEt_2$-mediated coupling of iodide **29** to cyanohydrin acetonide **26** afforded 1,3-*syn* acetonide **30** and a subsequent Finkelstein reaction generated alkyl iodide **31** which was again coupled with building block **26**. A second Finkelstein reaction exchanged chlorine to iodine and resulting compound **16** was used later for coupling to cyanohydrin acetonide **15**.[33,49]




Scheme 2.3: Synthesis of alkyl iodide **16** by Richardson & Rychnovsky.[33,49]
Reaction conditions: a) $NMe_2TMS$, rt, 16 h; b) DIBAL-H, $Et_2O$, −78 °C, 1.5 h; c) TMSCN, KCN/18-C-6 complex, 0 °C to rt , 1 h; d) acetone:2,2-DMP (4:1), CSA, rt, 48 h, **73%** (over 4 steps); e) $LiNEt_2$, **26**, DMPU, THF, −78 °C to −30 °C to rt, 15 h, **74%**; f) KI, 18-C-6, xylenes, reflux, 48 h, **90%**; g) $LiNEt_2$, **26**, DMPU, THF, −78 °C to −25 °C, 16 h, **77%**; h) KI, 18-C-6, xylenes, reflux, 48 h, **95%**.

Synthesis of southern fragment **17** started from protected butane triol **32** which could be obtained from L-ascorbic acid (Scheme 2.4).[52] Deprotection of the acetonide, TBS-protection of both hydroxy functions and cleavage of the primary TBS-group led to primary alcohol **33**. Oxidation with DMP yielded aldehyde **34** which was treated with Wollenberg's reagent **35**.[53] Mesylation of resulting secondary alcohol **36** and subsequent elimination afforded aldehyde **37** which could be homologated to aldehyde **38** by repeating this procedure.

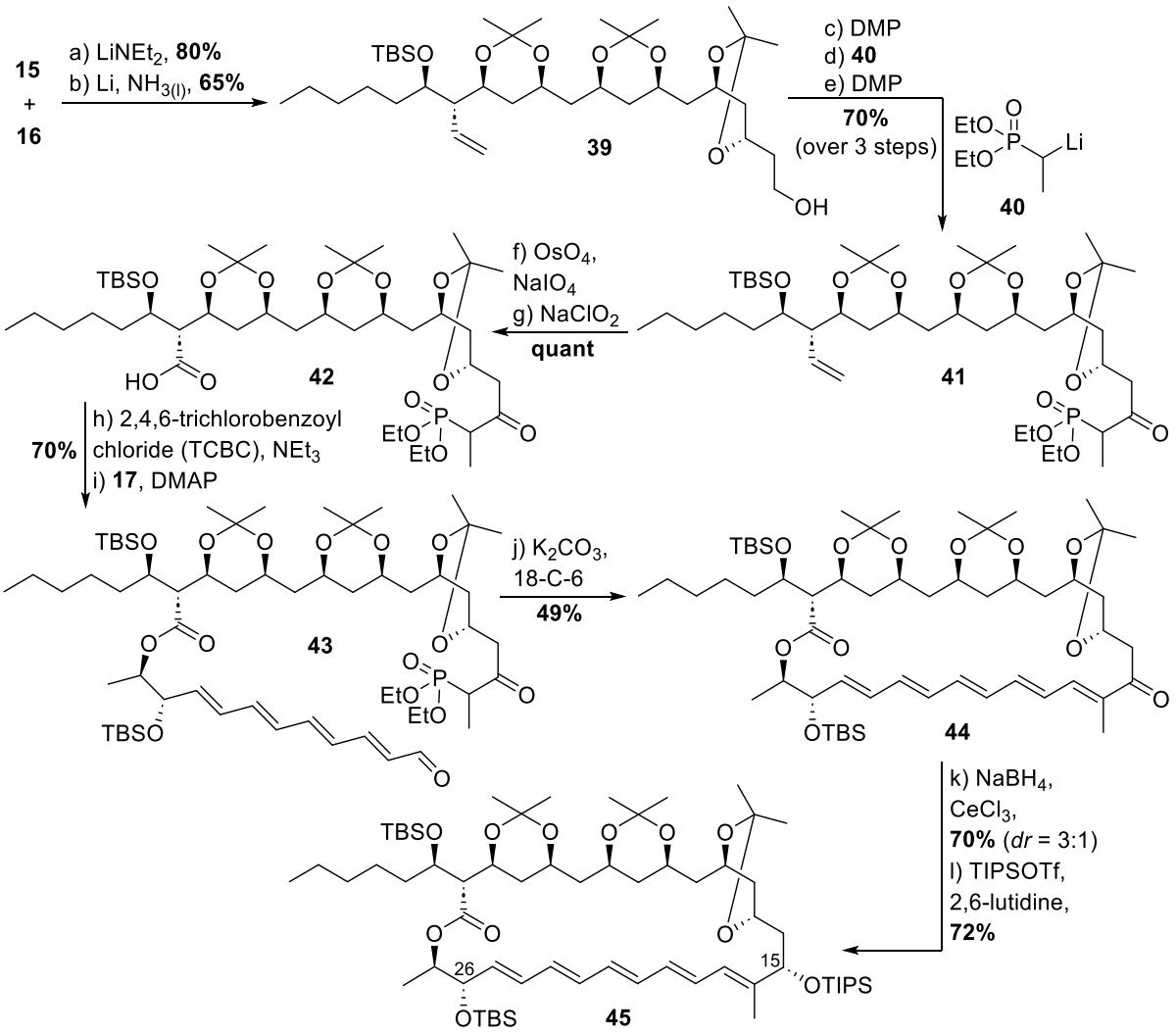



Scheme 2.4: Synthesis of the southern fragment **17** by Richardson & Rychnovsky.[33,49]
Reaction conditions: a) CSA, MeOH, rt, 16 h; b) TBSOTf, 2,6-lutidine, DCM, 0 °C, 1 h; c) PPTS, MeOH, 50 °C, 8 h, then rt, 16 h, **69%** (over 3 steps); d) DMP, $NaHCO_3$, rt, 1 h, **94%**; e) 1-(4-ethoxybutadienyl)tributylstannane, *n*-BuLi, THF, −78 °C, 10 min, then $MgBr_2$, 10 min, then **34**, −78 °C, 1 h; f) MsCl, $NEt_3$, DCM, −40 °C, 45 min, then 0 °C, THF, pH 7 buffer, 45 min, **80%** (over 2 steps); g) PPTS, $(MeO)_3CH$, MeOH, rt, 1 h; h) DIBAL-H, $Et_2O$, −78 °C, 10 min; i) amberlyst-15 acidic ion exchange resin, THF:$H_2O$ (25:1), rt, 2 h, **70%** (over 3 steps).

Finally, protection of the aldehyde function of **38**, reductive cleavage of the benzoyl group and deprotection of the aldehyde yielded polyene fragment **17** (Scheme 2.4).[33,49] However, it

should be mentioned that compound **17** is prone to degradation due to light sensitivity and must be used immediately after preparation.

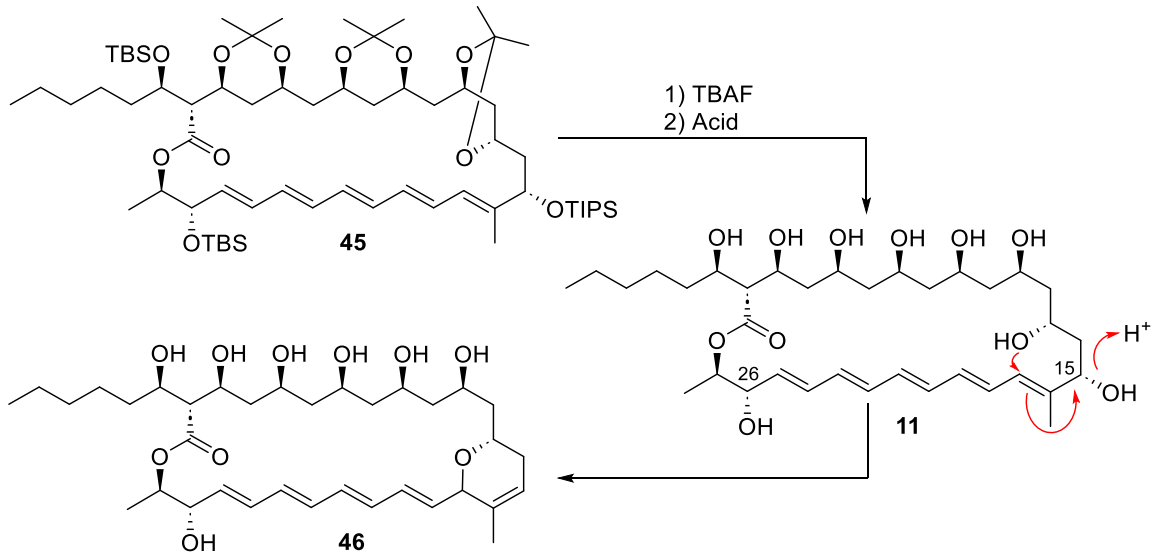
Scheme 2.5 shows the coupling of the northwestern **15** and the northeastern fragment **16** which was achieved through $LiNEt_2$-mediated coupling of the iodide function of **16** to cyanohydrin acetonide **15**, the same method that was used to assemble northeastern fragment **16**. Birch reduction removed the nitrile groups and simultaneously cleaved the benzyl protection group to generate coupling product **39**. Coupling occurs in such a way that 1,3-*syn*-acetonides are formed although the starting materials are diastereomeric mixtures.[51] The exact mechanism is discussed in detail in Chapter 3.2.5 (pp. 50–52).




Scheme 2.5: Synthetic pathway to protected filipin III (**45**) by Richardson & Rychnovsky.[33,49]
Reaction conditions: a) $LiNEt_2$, DMPU, THF, −78 °C to −30 °C to rt, 16 h, **80%**; b) Li, liquid $NH_3$, THF, *tert*-butanol, −78 °C, 1 h, **65%**; c) DMP, $NaHCO_3$, rt, 1 h; d) **40**, *n*-BuLi, THF, −78 °C, 15 min, then **39**, THF, −78 °C, 1 h; e) DMP, $NaHCO_3$, rt, 1 h, **70%** (over 3 steps); f) $OsO_4$, NMO, *tert*-butanol, THF, $H_2O$, rt, 16 h, then $NaIO_4$, rt, 1 h; g) $NaClO_2$, $KH_2PO_4$, 2-methyl-2-butene, THF, rt, 1 h, **95%** (over 2 steps); h) TCBC, $NEt_3$, **17**, THF, rt, 16 h; i) **42**, DMAP, toluene, rt, 2 h, **70%** (over 2 steps); j) $K_2CO_3$, 18-C-6, toluene, 60 °C, 20 h, **49%**; k) $NaBH_4$, MeOH, −78 °C, 20 min, **70%** (*dr* = 3:1); l) TIPSOTf, 2,6-lutidine, DCM, 0 °C, **72%**.

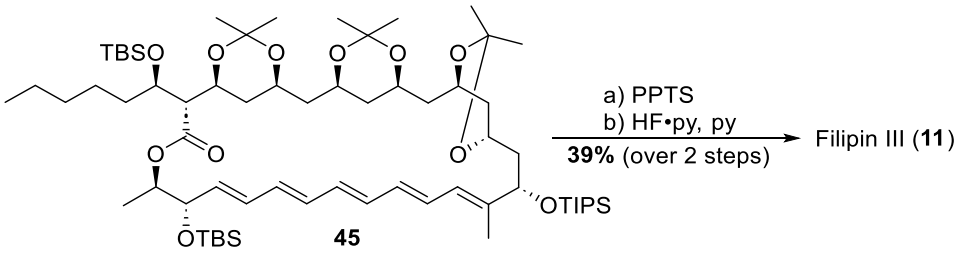
Oxidation to the aldehyde, addition of the lithium salt of ethyl diethyl phosphonate (**40**) and again oxidation of the resulting secondary hydroxy function afforded a 1:1 diastereomeric mixture of *β*-keto phosphonate **41**, however, the stereoinformation of the methyl bearing center is lost after ring closure (Scheme 2.5). The next steps transformed the terminal olefin of compound **41** to carboxylic acid **42** by dihydroxylation of the double bond, diol cleavage with $NaIO_4$, and Pinnick oxidation. The carboxylic acid function was coupled to polyene segment **17** under Yamaguchi conditions after other esterification methods proved to be difficult.[54] Ring closure of phosphonate **43** to macrocycle **44** was achieved by Horner-Emmons olefination with $K_2CO_3$ and 18-C-6 since a macrolactonization was anticipated to be difficult due to steric hinderance of C1.[55] The stereocenter at C15 was introduced by reduction under Luche conditions and a 3:1 mixture of diastereomers was obtained. Due to the acid lability of the C15 and C26 allylic alcohols, the newly generated free hydroxy function at C15 was protected with TIPS before acid catalyzed cleavage of the acetonides of fully protected filipin III **45** was conducted.[33,49]

If the silyl protecting groups of compound **45** were removed using TBAF and hydrolysis of the acetonides was conducted under acetic conditions, a degradation product less polar than filipin III (**11**) was detected and a blue shift in the UV-Vis spectrum occurred. Consequently, one double bond must have moved out of conjugation as proposed in Scheme 2.6.[49]




Scheme 2.6: Solvolysis of the alcohol at C15 by an intramolecular attack.[49]

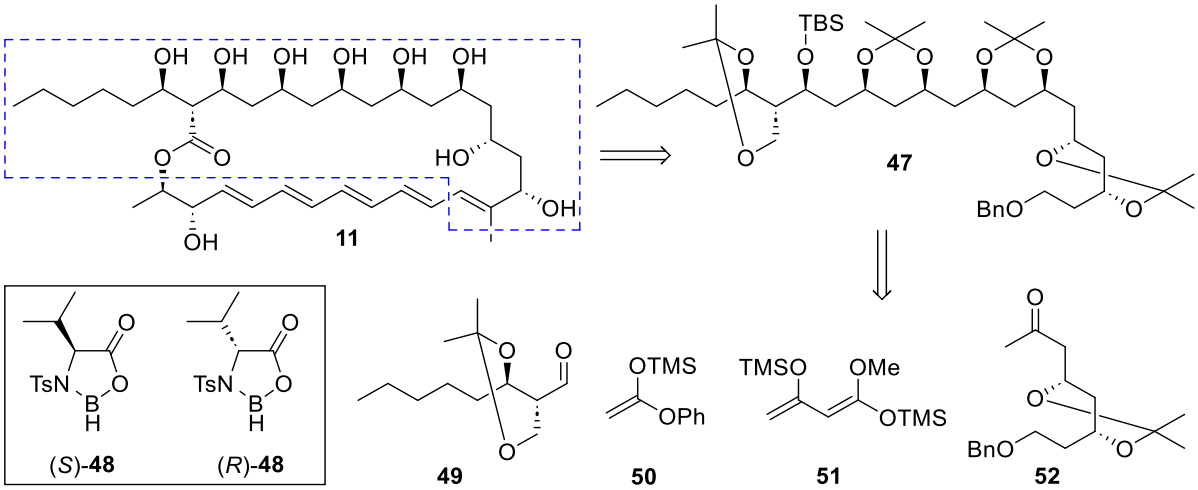
Instead of first deprotecting the silyl groups, cleavage of the acetonides with PPTS in warm methanol was done first which resulted in a product mixture with some of the silyl groups cleaved too. Finally, the remaining silyl protecting groups were cleaved using HF·py buffered with additional pyridine obtaining filipin III (**11**) in 39% yield over two steps (Scheme 2.7).[33,49]




Scheme 2.7: Final deprotection in the synthesis of filipin III (**11**) by Richardson & Rychnovsky.[33,49] Reaction conditions: a) PPTS, MeOH/THF/ethylene glycol (5:1:1), 60 °C, 3 h; b) HF·py, pyridine, THF, 0 °C to rt, 12 h.

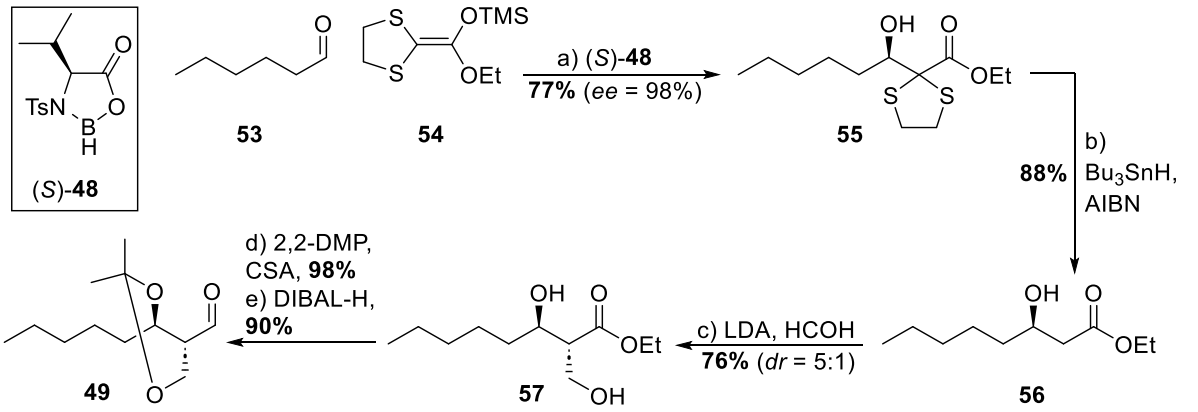
## 2.1.2 Synthesis of the Polyol Part by Kiyooka *et al.*

The synthesis of the polyol segment of filipin III (**11**) is based on an asymmetric aldol reaction to assemble the iterative 1,3-*syn* polyol unit **47**. Nucleophiles in this strategy were silyl enol ethers that were added to aldehydes in a stereospecific manner using Lewis-acidic, chiral oxazaborolidinone (*S*)-**48** or (*R*)-**48** to induce stereochemistry. Four fragments **49**, **50**, **51**, and **52** resulted from retrosynthetic analysis (Scheme 2.8).[47]



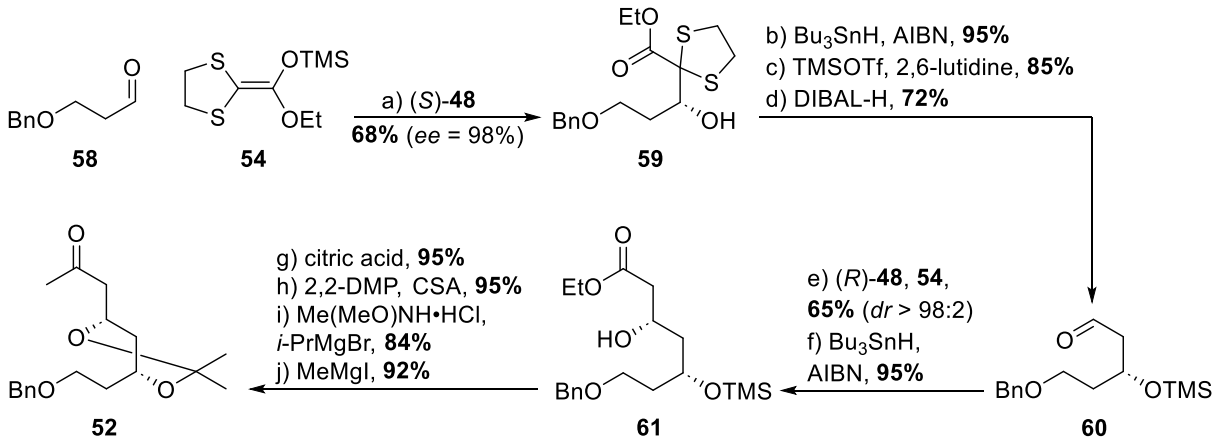

Scheme 2.8: Retrosynthetic analysis of polyol fragment **47** of filipin III (**11**) by Kiyooka *et al*.[46,47]

Western fragment **49** containing the pentyl side chain was obtained using the same aldol strategy starting from hexanal (**53**) and dithiolane silyl nucleophile **54** in presence of borane (*S*)-**48** (Scheme 2.9). Dithiolane aldol product **55** was obtained in good yield and excellent selectivity, before radical desulfurization with $Bu_3SnH$ and AIBN produced *β*-hydroxyester **56**.[46] Formation of the dianion of **56** using two equivalents of LDA and subsequent addition of the generated enolate to formaldehyde led to a diastereomeric mixture of aldol products with the favored 1,2-*anti* diastereomer **57** as main product.[56] Subsequent acetonide formation and reduction of the ester to the aldehyde afforded fragment **49**, the starting material for the next aldol reaction.[46]




Scheme 2.9: Synthesis of western fragment **49** by Kiyooka *et al*.[46]
Reaction conditions: a) (*S*)-**48** ($BH_3$·THF, *N*-Ts-L-valine), DCM, −78 °C, 20 h, **77%** (*ee* = 98%); b) $Bu_3SnH$, AIBN, benzene, 80 °C, 1.5 h, **88%**; c) LDA, HCOH, THF, −20 °C, 1 h, **76%** (*dr* = 5:1); d) 2,2-DMP, CSA, acetone, rt, 20 min, **98%**; e) DIBAL-H, DCM, −78 °C, 2 h, **90%**.

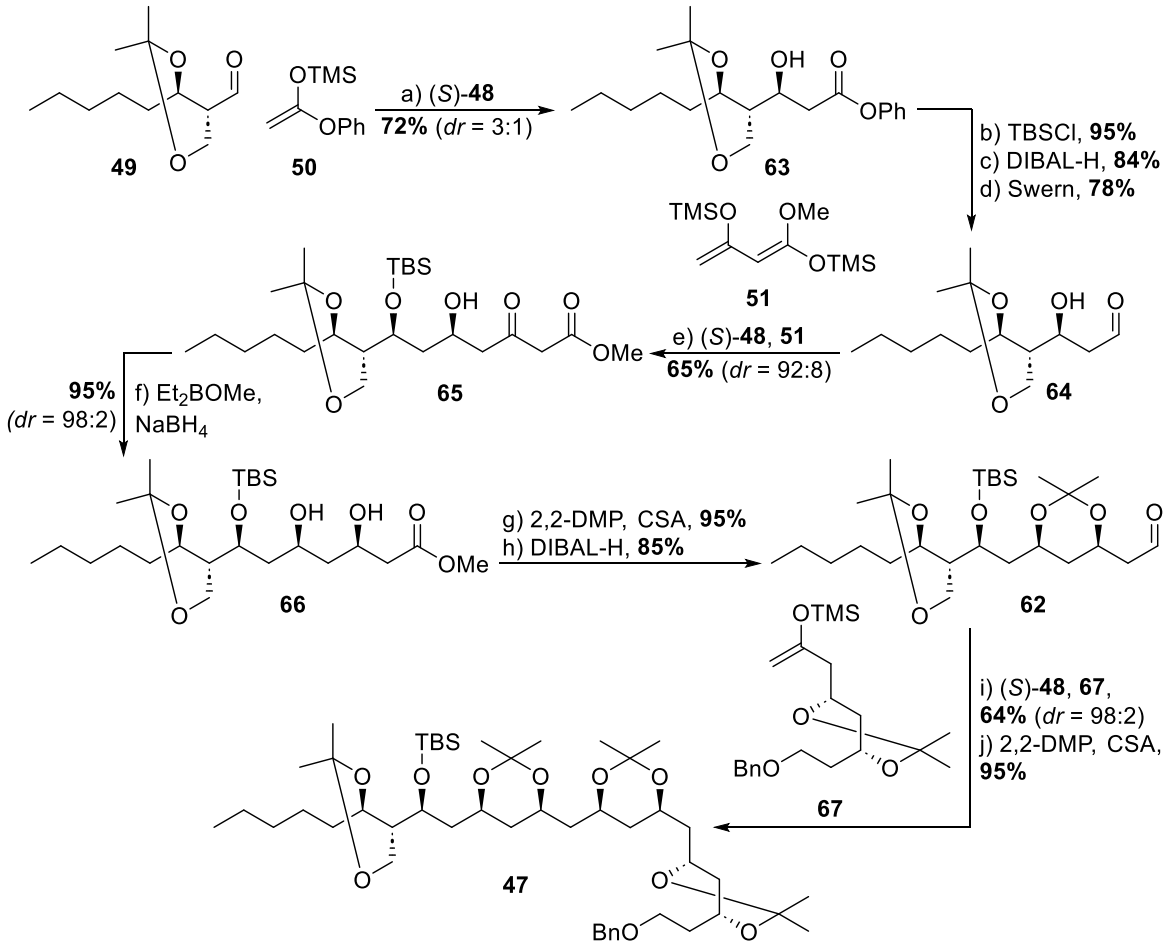
Synthesis of the eastern part **52** of polyol segment **47** was accomplished in a very similar way. Again, borane (*S*)-**48** promoted the addition of dithiolane silyl nucleophile **54** to the aldehyde function of **58** to obtain dithiolane aldol **59**, and subsequent radical desulfurization, TMS-protection, and reduction by DIBAL-H led to aldehyde **60** (Scheme 2.10). A second aldol reaction-desulfurization sequence with borane (*R*)-**48** afforded *β*-hydroxyester **61** that could be transformed to acetonide protected methyl ketone **52** by reprotection with 2,2-DMP, formation of the Weinreb amide[57] and subsequent treatment with MeMgI.[47]




Scheme 2.10: Synthesis of eastern fragment **52** by Kiyooka *et al*.[47]
Reaction conditions: a) (*S*)-**48** ($BH_3$·THF, *N*-Ts-D-valine), **54**, DCM, −78 °C, 20 h, **68%** (*ee* = 98%); b) $Bu_3SnH$, AIBN, benzene, 80 °C, 1.5 h, **95%**; c) TMSOTf, 2,6-lutidine, **85%**; d) DIBAL-H, DCM, −78 °C, **72%**; e) (*R*)-**48** ($BH_3$·THF, *N*-Ts-D-valine), **54**, DCM, −78 °C, 20 h, **65%** (*dr* > 98:2); f) $Bu_3SnH$, AIBN, benzene, 80 °C, 1.5 h, **95%**; g) citric acid, MeOH, **95%**; h) 2,2-DMP, CSA, acetone, **95%**; i) Me(MeO)NH·HCl, *i*-PrMgBr, **84%**; MeMgI, **92%**. Some reaction conditions, solvents, and reaction times are not stated in the publication.[47]

To assemble the complete polyol part of filipin III (**11**) western part **49** was elongated in a linear manner to aldehyde **62** by two further aldol reactions coupling fragments **50** and **51** each. First,

enol ether **50** was coupled in the presence of borane (*S*)-**48**, however, *β*-hydroxy phenyl ester **63** was obtained with a moderate diastereoselectivity of only 3:1. The free hydroxy function was protected with TBS, the ester function was reduced with DIBAL-H and the obtained alcohol was oxidized to aldehyde **64** by Swern oxidation (Scheme 2.11).[47]

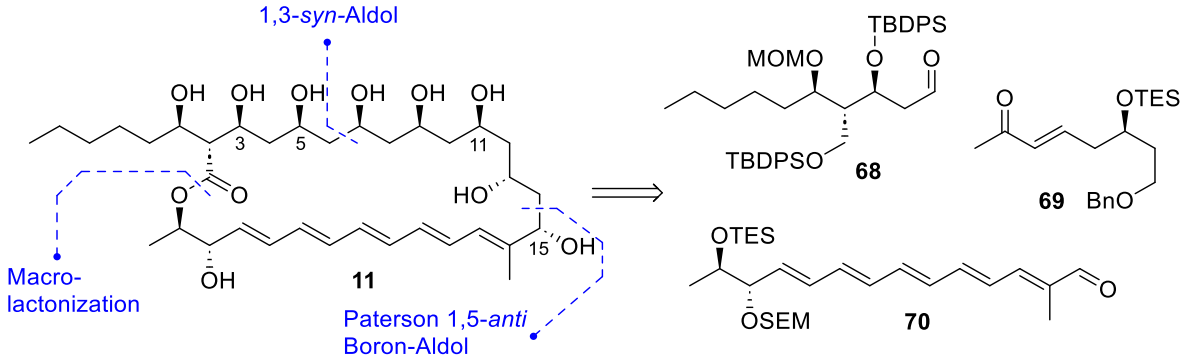



Scheme 2.11: Assembly of polyol part **47** by Kiyooka *et al*.[47]
Reaction conditions: a) (*S*)-**48** ($BH_3$·THF, *N*-Ts-L-valine), **50**, DCM, −78 °C, 3 h, **72%** (*dr* = 3:1); b) TBSCl, DMF, **95%**; c) DIBAL-H, DCM, −78 °C to rt, **84%**; d) Swern, **78%**; e) (*S*)-**48** ($BH_3$·THF, *N*-Ts-L-valine), **51**, DCM, −78 °C, 6 h, **65%** (*dr* = 92:8), f) $Et_2BOMe$, $NaBH_4$, MeOH, **95%** (*dr* = 98:2); g) 2,2-DMP, CSA, acetone, **95%**; h) DIBAL-H, DCM, −78 °C, **85%**; i) (*S*)-**48** ($BH_3$·THF, *N*-Ts-L-valine), **67**, EtCN, −78 °C, 5 h, **64%** (*dr* = 98:2); j) 2,2-DMP, CSA, acetone, **95%**. Some reaction conditions, solvents, and reaction times are not stated in the publication.[47]

The second aldol reaction proceeded with much better selectivity and the keto function of resulting *β*-keto ester **65** was reduced in a 1,3-*syn* manner under Narasaka-Prasad conditions.[58] Acetonide protection of 1,3-*syn* diol **66** followed by reduction of the ester function with DIBAL-H led to aldehyde **62** which could be coupled with silyl enol ether **67** derived from eastern fragment **52**. The aldol reaction was accompanied by direct 1,3-*syn* reduction of the intermediate aldol product through borane (*S*)-**48** making this reaction highly efficient. Final acetonide protection yielded polyol part **47** (Scheme 2.11).[47]

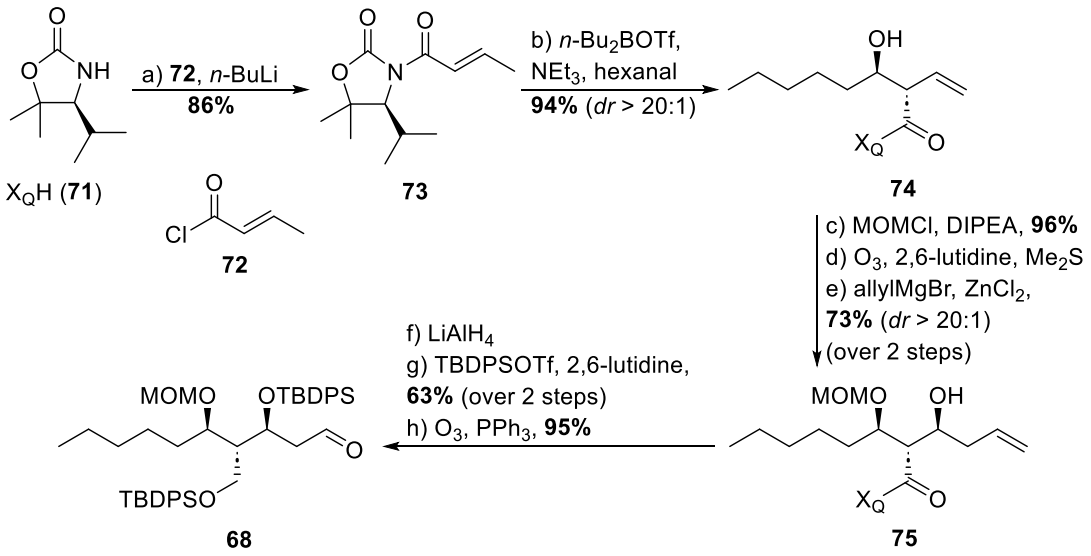
### 2.1.3 Studies Towards a Total Synthesis of Filipin III by Cossy *et al.*

The retrosynthetic analysis of this approach towards filipin III (**11**) strived to assemble the molecule by different aldol reactions with a final macrolactonization. Three main fragments resulted, a northwestern fragment **68** and an eastern fragment **69** forming the polyol part, and a southern fragment **70** making up the polyene part. Coupling of **68** and **69** was accomplished by a 1,3-*syn* aldol reaction with stereogenic control of the hydroxy function at C5 by the hydroxy function at C3. Coupling of southern polyene fragment **70** with the polyol part occurred under creation of the stereogenic center at C15, which is controlled by the stereochemistry of C11 (Scheme 2.12).[48]



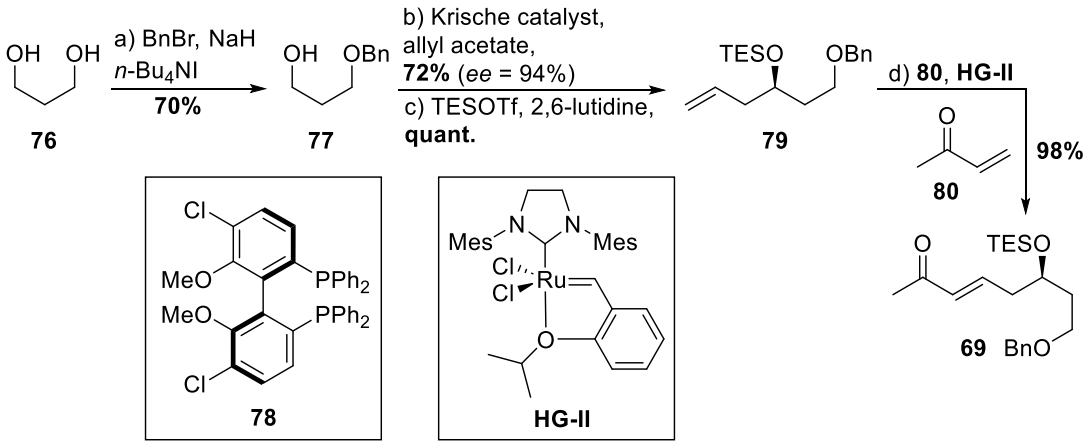

Scheme 2.12: Retrosynthetic analysis of filipin III (**11**) by Cossy *et. al*.[48]

Synthesis of northwestern fragment **68** started from chiral auxiliary (*S*)-4-isopropyl-5,5-dimethyloxazolidin-2-one ($X_QH$, **71**), which was acylated with (*E*)-crotonyl chloride (**72**) (Scheme 2.13). Enolization of **73** under Evans conditions[59] and subsequent treatment with hexanal afforded aldol product **74** as a single diastereomer. The free hydroxy function was MOM-protected, and the terminal olefin was cleaved by an ozonolysis to create the corresponding aldehyde. Immediate addition of allylMgBr in the presence of $ZnCl_2$ generated homoallylic alcohol **75**, which was stated to be the only detected diastereomer.[60] The synthesis of northwestern fragment **68** was completed by reductive cleavage of the auxiliary, TBDPS-protection of the secondary hydroxy group, and again, ozonolysis of the terminal olefin.[48]




Scheme 2.13: Synthesis of northwestern fragment **68** by Cossy *et. al*.[48]
Reaction conditions: a) **72**, *n*-BuLi, THF, −78 °C to 0 °C, 2.5 h, **86%**; b) *n*-$Bu_2BOTf$, $NEt_3$, hexanal, DCM, −78 °C to 0 °C, 5 h, **94%** (*dr* > 20:1); c) MOMCl, DIPEA, DCM, rt, 18 h, **96%**; d) $O_3$, 2,6-lutidine, $Me_2S$, DCM/MeOH, −78 °C; e) allylMgBr, $ZnCl_2$, THF, −78 °C to −40 °C, 3.5 h, **73%** (over 3 steps, *dr* > 20:1); f) $LiAlH_4$, toluene, −30 °C to −15 °C, 1 h; g) TBDPSCl, 2,6-lutidine, DCM, 0 °C to rt, 18 h, **63%** (over 2 steps); h) $O_3$, $PPh_3$, DCM, −78 °C, **95%**.

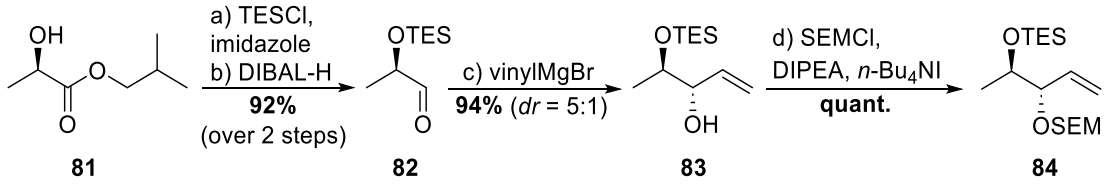
Eastern fragment **69** was obtained in four steps from 1,3-propanediol (**76**) which was first mono benzylated generating compound **77** (Scheme 2.14). Enantioselective Krische allylation with chiral phospine ligand **78** afforded the homoallylic alcohol with a selectivity of 94%. The free hydroxy function was protected with the TES protection group to obtain **79** and cross metathesis with methyl vinyl ketone (**80**) afforded methyl ketone **69** as the eastern fragment.[48]




Scheme 2.14: Synthesis of eastern fragment **69** by Cossy *et. al*.[48]
Reaction conditions: a) BnBr, NaH, *n*-$Bu_4NI$, THF, rt, 7 h, **70%**, b) Krische catalyst: $[Ir(COD)Cl]_2$, (*R*)-Cl,MeO-BIPHEP (**78**), dinitrobenzoic acid, $Cs_2CO_3$; allyl acetate, THF, 120 °C, 15 h, **72%** (*ee* = 94%); c) TESOTf, 2,6-lutidine, DCM, −78 °C, 1.5 h, **quant.**; d) **80**, **HG-II**, DCM, 45 °C, 2 h, **98%**.

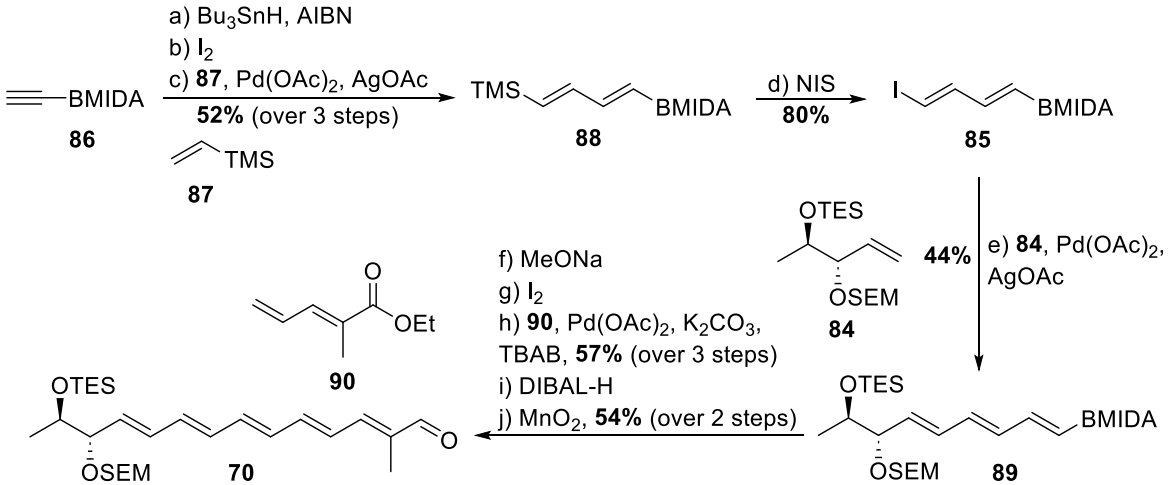
The southern fragment **70** representing the polyene part was further divided into two sub fragments which were coupled by a Heck reaction later. The left part of the molecule was derived

from lactic acid with (*R*)-isobutyl lactate (**81**) being the starting material (Scheme 2.15). TES-protection and reduction with DIBAL-H provided aldehyde **82** which was treated with vinylMgBr to yield allylic alcohol **83** as the Felkin-Anh product in excellent yield and good selectivity. The free hydroxy function was protected as a SEM ether to obtain fragment **84** in a four step sequence.[48]



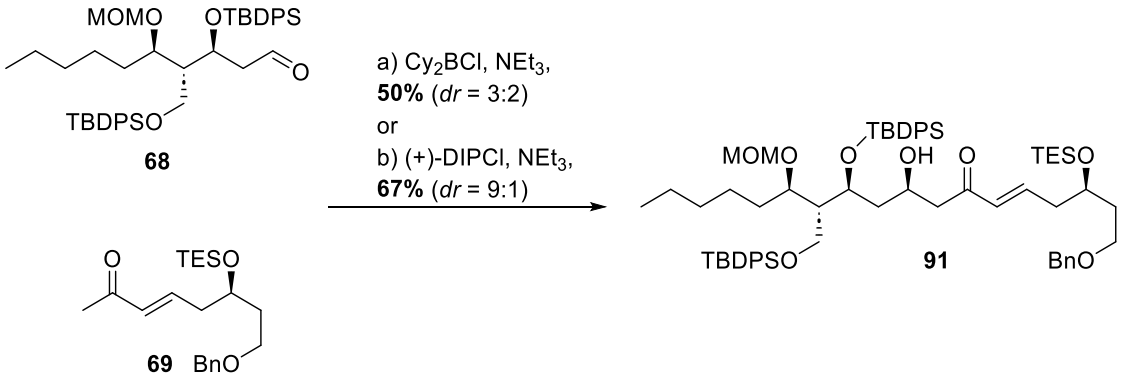

Scheme 2.15: Synthesis of the left part of southern fragment **70** by Cossy *et. al*.[48]
Reaction conditions: a) TESCl, imidazole, DMF, rt, 4.5 h; b) DIBAL-H, $Et_2O$, −78 °C, 3 h, **92%** (over 2 steps); c) vinylMgBr, THF, −60 °C to rt, 3.5 h, **94%** (*dr* = 5:1); d) SEMCl, DIPEA, *n*-$Bu_4NI$, DCM, rt, 16 h, **quant**.

Vinyl iodide **85** was obtained from alkyne **86** by hydrostannylation, followed by iodo-destannylation, subsequent Heck reaction with vinyl trimethylsilane (**87**), and finally iodo-desilylation of compound **88** with NIS (Scheme 2.16). The compound was then coupled to above described fragment **84** in a second Heck reaction to yield triene **89**. The MIDA boronate function of **89** was hydrolyzed by sodium methoxide and the resulting boronic acid underwent iodo-deborylation by treatment with iodine. The obtained vinyl iodide was coupled to dienic ester **90** in a third Heck coupling using Jeffrey's conditions,[61] and final reduction with DIBAL-H followed by oxidation of the allylic alcohol provided pentaene **70** as the southern fragment. Since the compound is prone to degradation it must be used immediately once prepared.[48]




Scheme 2.16: Synthesis of southern fragment **70** by Cossy *et. al*.[48]
Reaction conditions: a) $Bu_3SnH$, AIBN, THF, reflux, 24 h; b) $I_2$, THF, −78 °C to rt, 14 h; c) **87**, $Pd(OAc)_2$, AgOAc, MeCN, 80 °C, 14 h, **52%** (over 3 steps); d) NIS, MeCN, 0 °C, 6 h, **80%**; e) **84**, $Pd(OAc)_2$, AgOAc, MeCN, 50 °C, 14 h, **44%**; f) MeONa, MeOH/THF, rt, 1 h; g) $I_2$, THF, rt, 2.5 h; h) **90**, $Pd(OAc)_2$, $K_2CO_3$, TBAB, DMF, 50 °C, 16 h, **57%** (over 3 steps); i) DIBAL-H, DCM, −78 °C, 20 min; j) $MnO_2$, DCM, rt, 2.5 h, **54%** (over 2 steps).

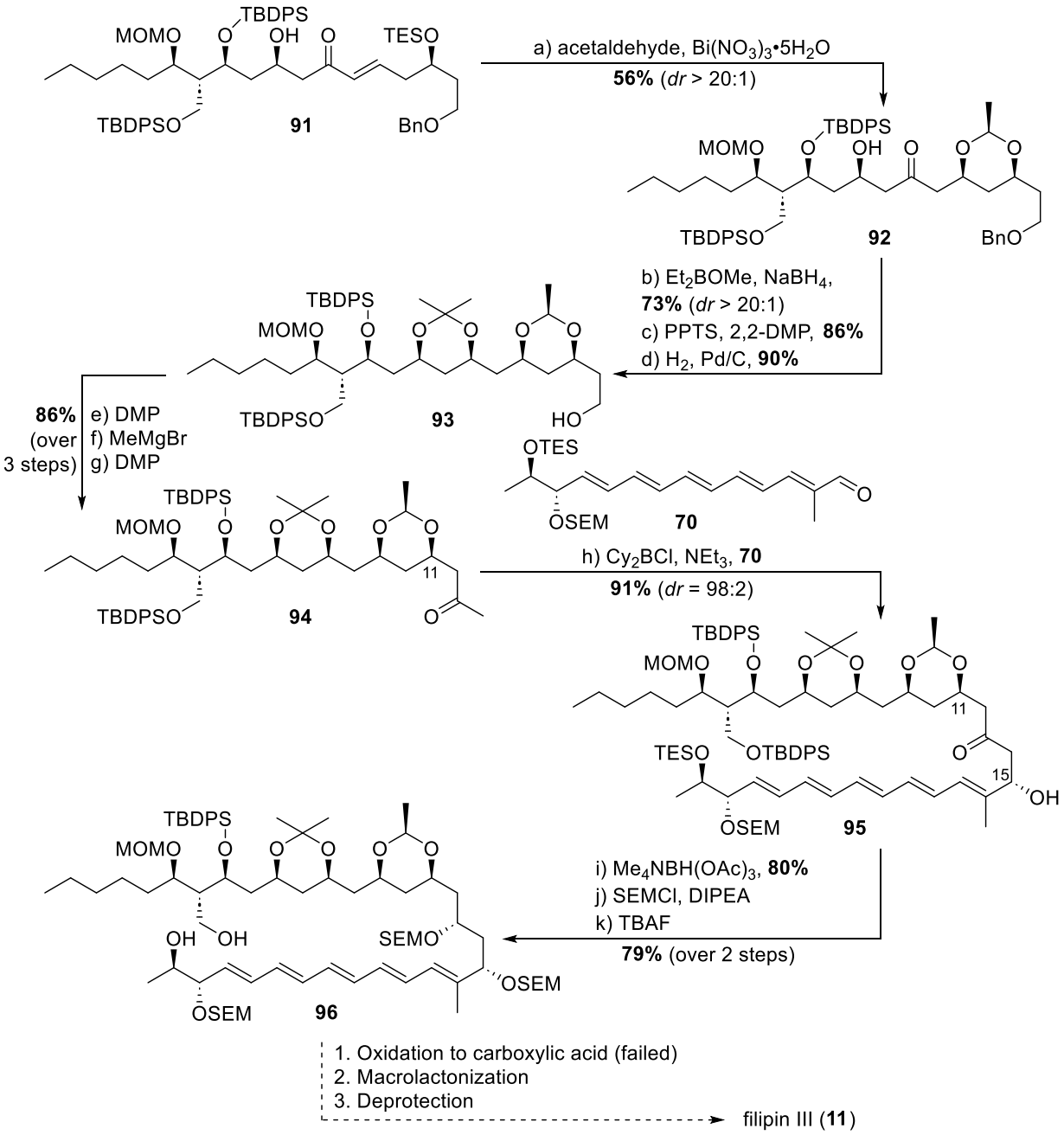
The northwestern and the eastern fragments **68** and **69** were coupled by a 1,3-*syn* aldol reaction as already mentioned above (Scheme 2.17). Stereochemistry was induced by the TBDPS-protected hydroxy function in *β*-position to the aldehyde of northwestern fragment **68**. Two attempts are stated based on Paterson's conditions, i.e. dialkyl borane reagents and $NEt_3$ as a base with low steric bulk.[62] Whereas the selectivity was unsatisfactory with $Cy_2BCl$, chiral boron reagent (+)-DIPCl furnished **91** in better yield and much better selectivity.[48]




Scheme 2.17: Coupling of northwestern fragment **68** and eastern fragment **69** to **91** by a Paterson 1,3-*syn* aldol reaction.[48]
Reaction conditions: a) $Cy_2BCl$, $NEt_3$, $Et_2O$, −78 °C to −20 °C, 5.5 h, **50%** (*dr* = 3:2); b) (+)-DIPCl, $NEt_3$, $Et_2O$, −78 °C to −20 °C, 5.5 h, **67%** (*dr* = 9:1).

The coupling product was modified before final coupling with the southern fragment was accomplished (Scheme 2.18). Therefore, two more stereogenic centers had to be controlled, the first of which was accomplished by a hemi acetalization/1,4-addition sequence applied to the *α*,*β*-unsaturated ketone of compound **91**, catalyzed by the pentahydrate of $Bi(NO_3)_3$. The TES protection group was directly cleaved under these conditions and acetal **92** was obtained as the only detectable isomer. The second remaining stereocenter was generated by a 1,3-*syn* diastereoselective reduction of *β*-hydroxyketone **92** and the product could also be isolated as a single diastereomer.[58] The resulting 1,3-*syn* diol was protected as acetonide and the benzyl protection group was cleaved with hydrogen in the presence of Pd/C to generate primary alcohol **93**. A three-step sequence consisting of oxidation of the primary alcohol to the aldehyde, addition of the Grignard reagent MeMgBr, and again oxidation of the resulting secondary alcohol to the corresponding ketone afforded methyl ketone **94** as starting material for a 1,5-*anti* aldol reaction with southern fragment **70**. Again, Paterson's conditions were used and the stereochemistry at C15 was controlled by the stereochemistry at C11, thus *β*-hydroxy ketone **95** was obtained in very good yield and selectivity.[63] The stereochemistry at C13 was induced by a 1,3-*anti* reduction[64] of the keto function and this time the stereo information was induced by the newly generated stereocenter at C15. Both reactions proceeded in excellent stereoselectivity, so only one single diastereomer was isolated in both cases. The two secondary hydroxy functions of the obtained 1,3-*anti* diol were protected with SEM before the primary TBDPS-

group and the TES-group were cleaved by treatment with TBAF to furnish protected, non-cyclized filipin III **96**.




Scheme 2.18: Modification of coupling product **91** and coupling with southern fragment **70** to synthesize protected, non-cyclized filipin III **96**.[48]
Reaction conditions: a) acetaldehyde, $Bi(NO_3)_3 \cdot 5H_2O$, DCM, rt, 15 h, **56%** (*dr* > 20:1); b) $Et_2BOMe$, $NaBH_4$, THF/MeOH, −78 °C to 0 °C, 5 h, **73%** (*dr* > 20:1); c) PPTS, 2,2-DMP, acetone, rt, 14 h, **86%**; d) $H_2$, Pd/C, MeOH, rt, 24 h, **90%**; e) DMP, $NaHCO_3$, DCM, 0 °C to rt, 2 h; f) MeMgBr, $Et_2O$, 0 °C, 1 h; g) DMP, $NaHCO_3$, DCM, 0 °C to rt, 14 h, **86%** (over 3 steps); h) $Cy_2BCl$, $NEt_3$, $Et_2O$, 0 °C, 2 h, then **70**, −78 °C to −20 °C, 14 h, **91%** (*dr* = 98:2); i) $Me_4NBH(OAc)_3$, MeCN/AcOH, −20 °C, 14 h, **80%**; j) SEMCl, DIPEA, DCM, rt, 14 h; k) TBAF, THF, rt, 4 d, **79%** (over 2 steps).

However, oxidation at C1 to the carboxylic acid could not be achieved under various conditions and consequently, macrolactonization was not possible. While oxidation to the corresponding

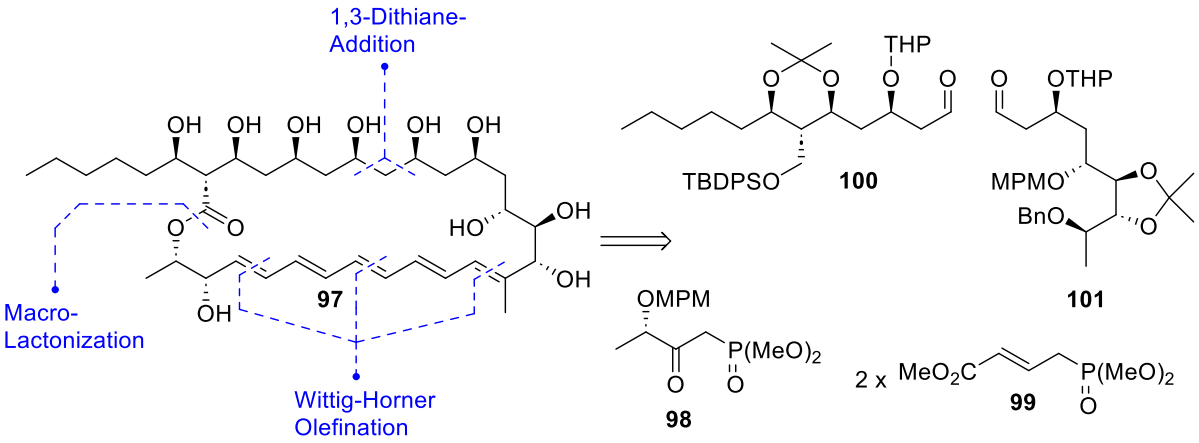
aldehyde was possible under Epp-Widlanski conditions (TEMPO/BAIB), further oxidation to the carboxylic acid led to degradation of the sensitive polyene part of the molecule and the total synthesis could not be finalized.[48]

## 2.2 Previous Work on Pentamycin

The closest attempt for a first total synthesis of pentamycin (**10**) was published by Oishi *et al*. in 1990.[45] Their targeted structure, however, is not completely correct since the stereocenter at C27 was assigned wrong. Similar to the attempt of Cossy *et al*.[48] for a total synthesis of filipin III (**11**) no ring closure was achieved. Two further publications are discussed here, one by Walleser & Brückner (2014)[44] and the most current publication about synthetic work on pentamycin (**10**) by Bali & Prasad (2020).[43]

### 2.2.1 Studies Towards a Total Synthesis of 27-*epi*-Pentamycin by Oishi *et. al.*

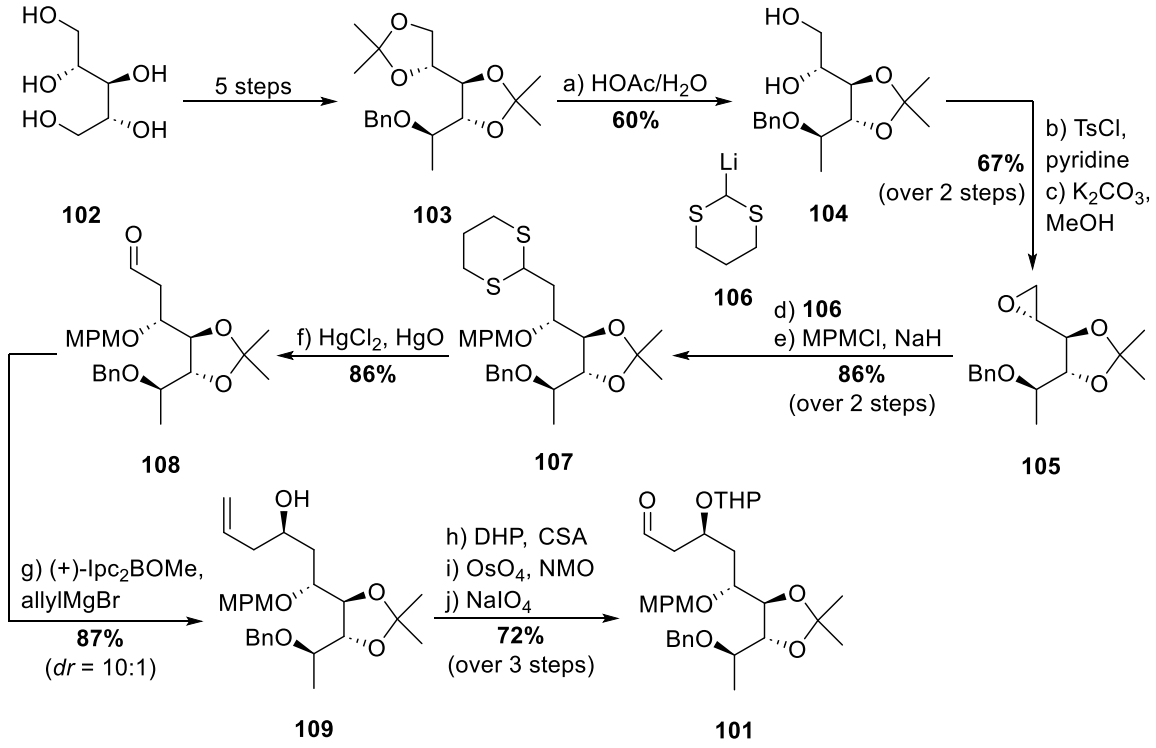
The key step in this synthetic approach of 27-*epi*-pentamycin (**97**) was a macrolactonization in the very end of the synthesis. The polyene moiety was built up by Wittig-Horner olefinations with phosphonates **98** and **99** and the polyol part was assembled by two fragments, a north-western fragment **100**, and an eastern fragment **101**. Coupling of these two fragments was achieved by a 1,3-dithiane addition (Scheme 2.19).




Scheme 2.19: Retrosynthetic analysis of 27-*epi*-pentamycin (**97**) by Oishi *et al*.[45]

Synthesis of the eastern fragment started from D-mannitol (**102**) which was converted to compound **103** in five steps (Scheme 2.20). Treatment with a mixture of acetic acid and water cleaved the acetonide leading to diol **104**. Tosylation of the primary hydroxy function and subsequent basic conditions formed epoxide **105** which was opened with the lithium anion of 1,3-dithiane **106**. The secondary hydroxy function was protected with the MPM-protecting group to yield compound **107** which was transferred to aldehyde **108** by cleavage of the dithiane

moiety with mercury(II). Brown allylation provided homoallylic alcohol **109** in good yield and selectivity and protection of the free hydroxy function as well as cleavage of the terminal olefin afforded aldehyde **101** as the eastern fragment.[45]

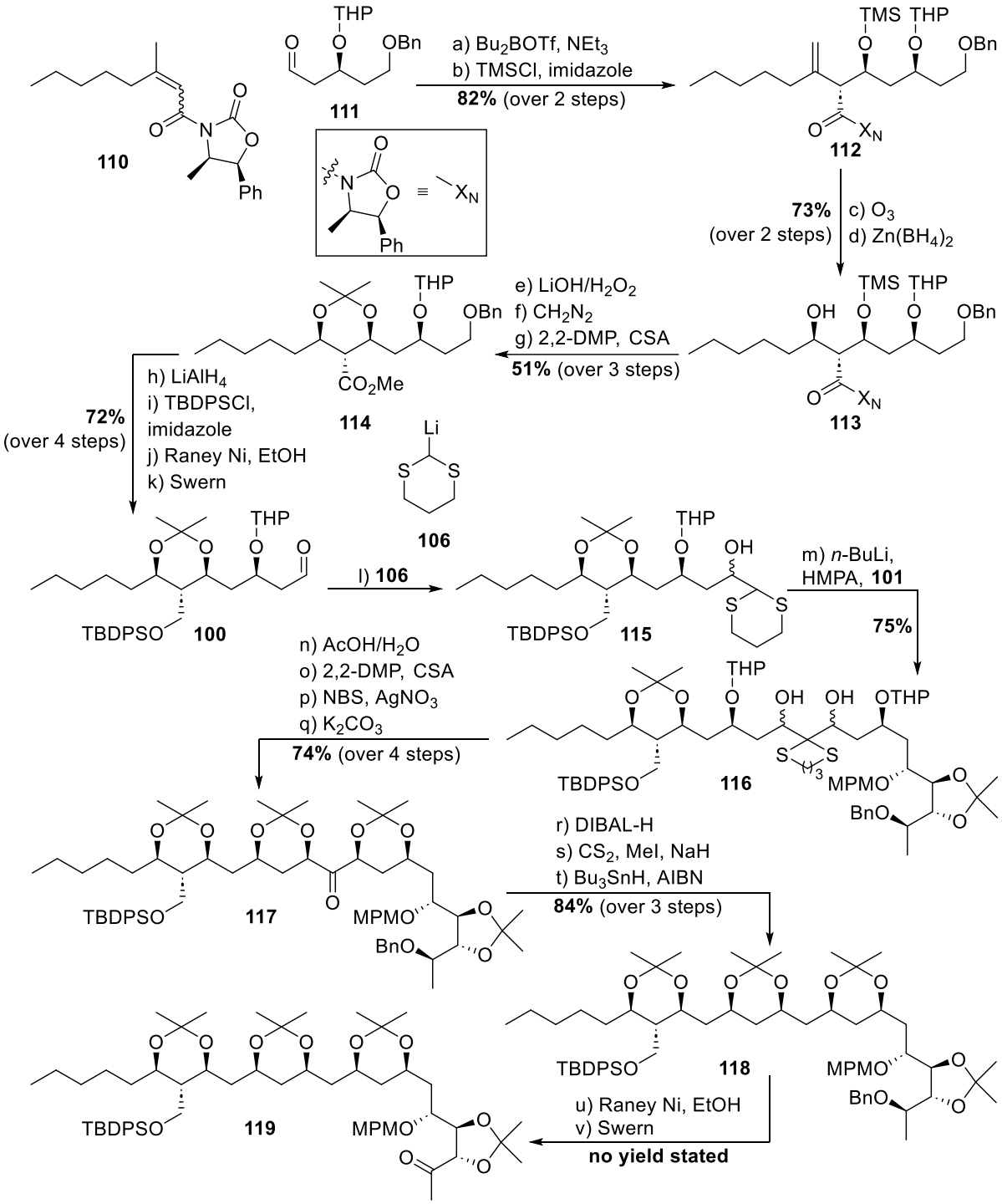



Scheme 2.20: Synthesis of eastern fragment **101** by Oishi *et. al*.
Reaction conditions: Reaction conditions, solvents, and reaction times are not stated in the publication.[45]

Auxiliary-bound pentyl chain-containing compound **110** and aldehyde **111** were coupled in an Evans' asymmetric aldol reaction and the arising free hydroxy function was protected with TMS to afford protected aldol product **112** (Scheme 2.21).[65] The terminal olefin was converted to the ketone and stereoselective reduction with $Zn(BH_4)_2$ generated secondary alcohol **113**. The auxiliary was cleaved under basic conditions and the carboxylic acid was esterified with diazomethane. These conditions also cleaved the TMS-protecting group, and the resulting 1,3-diol was reprotected to obtain acetonide **114**. Reduction of the methyl ester with $LiAlH_4$ produced the primary alcohol, which was protected with TBDPS before the benzyl group was cleaved and the primary alcohol was oxidized to aldehyde **100** using Swern-conditions.[45]

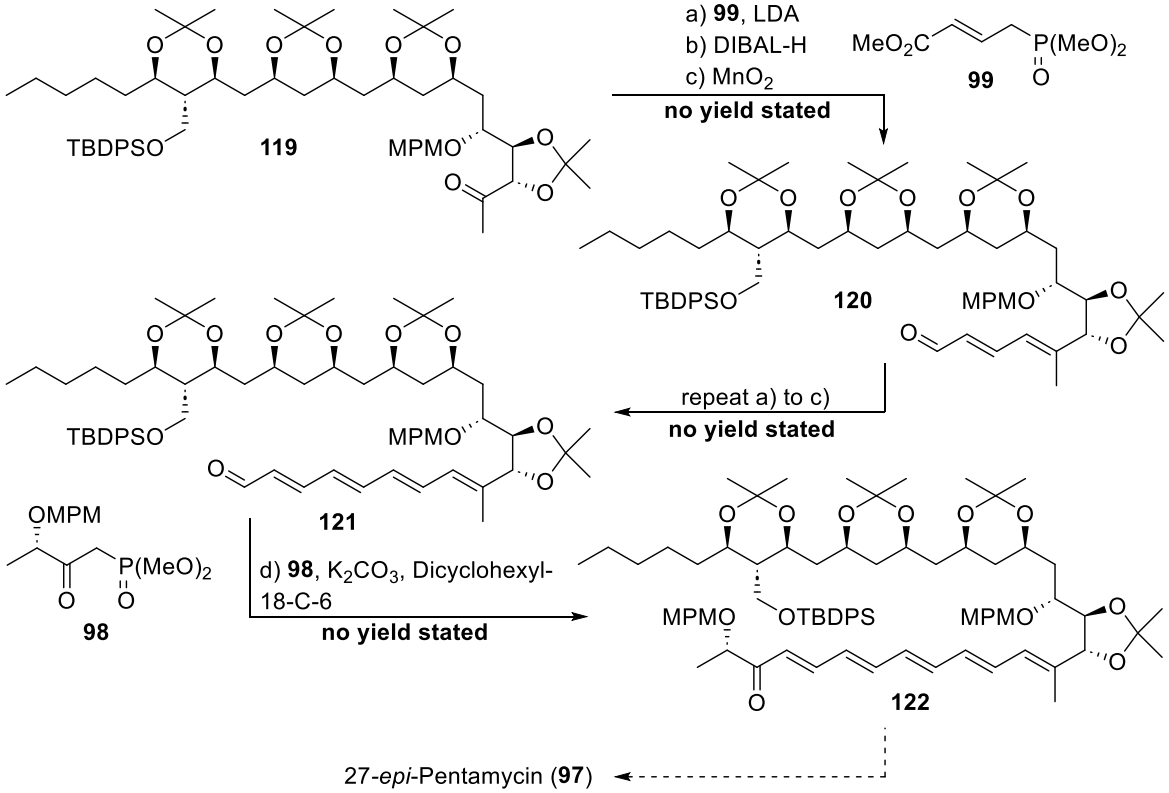
In the following the aldehyde functions of both, the northwestern **100** and the eastern fragment **101** were condensed by the usage of the lithium anion of 1,3-dithiane **106** to obtain coupling product **116** *via* **115** (Scheme 2.21). The THP-protecting groups of the coupling product were cleaved under acidic conditions and the resulting 1,3-diols were protected as acetonides. Cleavage of the dithioacetal released the ketone whose *α*-acidity could be exploited to create 1,3-*syn* acetonides by treatment with $K_2CO_3$. Afterwards, the keto function of compound **117**

was removed by reduction to the secondary alcohol followed by Barton-McCombie deoxygenation to obtain protected polyol segment **118**.[66] Cleavage of the benzyl group and subsequent oxidation furnished methyl ketone **119** which is used as starting material for the Wittig-Horner reaction (Scheme 2.21).[45]




Scheme 2.21: Synthesis of northwestern fragment **100**, coupling with eastern fragment **101**, and modification by Oishi *et al*.
Reaction conditions: Reaction conditions, solvents, and reaction times are not stated in the publication.[45]

Methyl ketone **119** was homologated with phosphonate **99** and after reduction of the methyl ester and oxidation of the resulting allylic alcohol with $MnO_2$, aldehyde **120** was obtained (Scheme 2.22). The reaction sequence consisting of Wittig-Horner reaction, DIBAL-H reduction, and oxidation of the allylic alcohol was repeated to yield aldehyde **121**. Another Wittig-Horner olefination with phosphonate **98** was conducted furnishing protected, non-cyclized 27-*epi*-pentamycin **122**.[45]

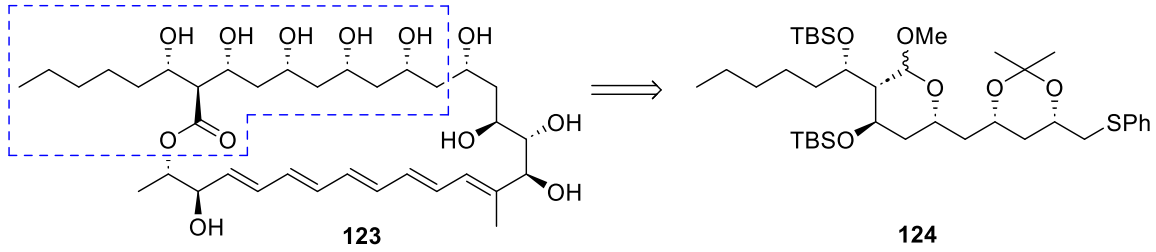



Scheme 2.22: Construction of the polyene part by Wittig-Horner reactions by Oishi *et al*.
Reaction conditions: Reaction conditions, solvents, and reaction times are not stated in the publication.[45]

It was not stated in the publication, why the synthesis could not be finalized. However, similar to the discussed approach of filipin III (**11**) by Cossy *et al*. the remaining steps are deprotection of the TBDPS group at C1, oxidation to the carboxylic acid, macrolactonization, and final deprotection. Additionally, it is required to reduce the keto function at C26 selectively. It is likely, that the oxidation failed in a similar way than in the synthesis of filipin III (**11**) by Cossy *et al*. Since pentamycin (**10**) is known to be more instable than filipin III (**11**),[24] the sensitive pentaene fragment of non-cyclized 27-*epi*-pentamycin **122** may decompose during oxidation or cyclization attempts.

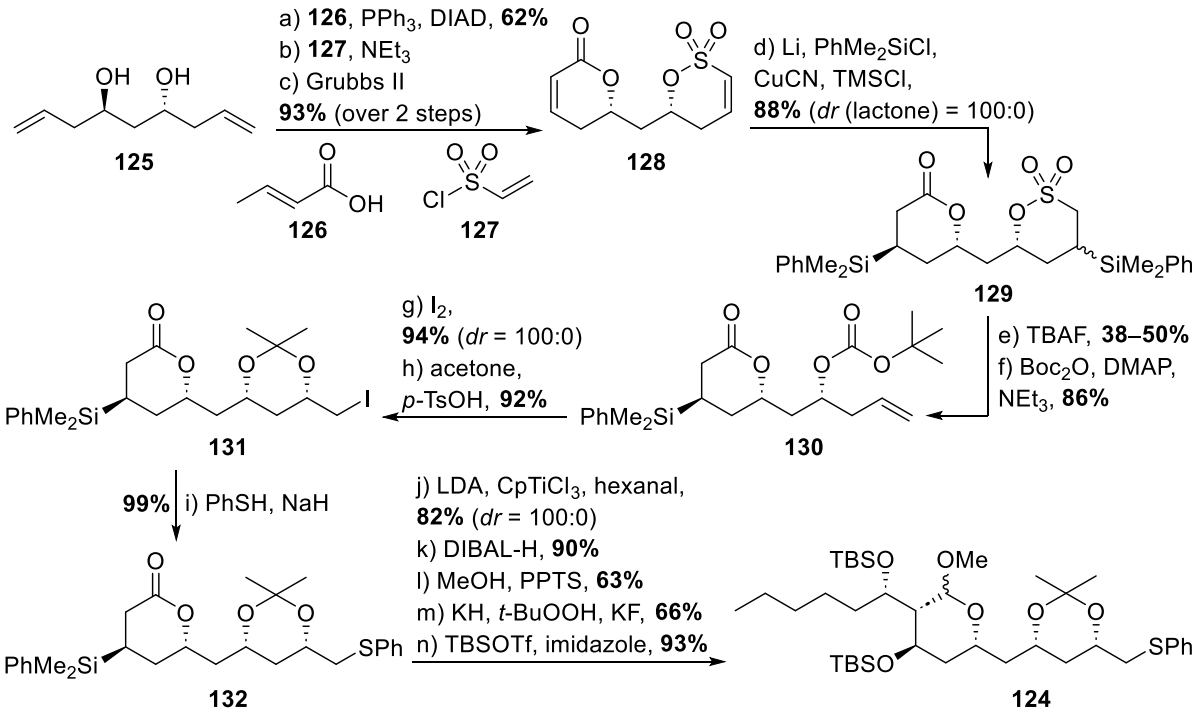
## 2.2.2 Synthesis of a Polyol Building Block by Walleser & Brückner

The synthetic approach focused on the unnatural enantiomers of filipin III (**11**) and pentamycin (**10**). Although the goal was to suggest a common strategy to enable the synthesis of both molecules, only a segment of the polyol part suitable for a further synthesis of both molecules was published to date. Retrosynthetic analysis of *ent*-pentamycin (**123**) resulted in northwestern fragment **124** containing six relevant stereocenters (Scheme 2.23).[44]




Scheme 2.23: Retrosynthetic analysis of *ent*-pentamycin (**123**) by Walleser & Brückner.[44]

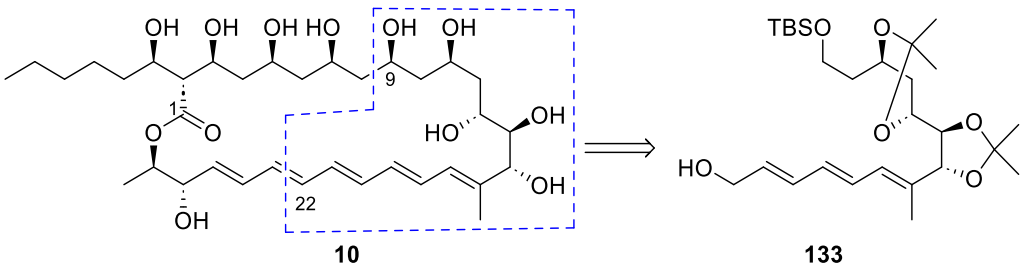
*Bis*-homoallylic alcohol **125** was mono esterified with crotonic acid (**126**) and inverted under standard Mitsunobu conditions (Scheme 2.24).[67] The free hydroxy function was esterified with ethene sulfonyl chloride (**127**) and Grubbs metathesis closed both rings to generate bicycle **128**. In the next step, a silicon nucleophile in form of the higher-order cyanocuprate $Li_2(PhMe_2Si)_2Cu(CN)$ was generated which added to both, the lactone and the sulfone moiety of bicycle **128**. The addition to the lactone moiety was highly stereoselective and resulted in *trans*-configuration, whereas the sulfone moiety was attacked unselectively. However, disubstituted bicycle **129** could be transformed to a homoallylic alcohol with TBAF[68] and subsequently, the free hydroxy function was protected with the Boc-protecting group to afford mixed carbonate **130**. Acetonide **131** was obtained by reprotection of the iodocarbonate which was generated by treatment of carbonate **130** with iodine. The selectivity of this transformation was excellent with the 1,3-*syn* diastereomer being the only detected isomer. In an $S_N2$ reaction, the primary iodide of **131** was replaced with PhSH to produce mixed sulfide **132**. Deprotonation with LDA generated the lithium lactone enolate of **132**, which could be transmetalated with $CpTiCl_3$ to give the respective titanium enolate. Aldol reaction with hexanal provided the corresponding aldol product in good yield and excellent selectivity. Reduction of the lactone with DIBAL-H generated the lactol which formed a mixed acetal with MeOH. Finally, the $PhMe_2Si$-group was oxidatively replaced by a hydroxy function under basic conditions[69] before the free hydroxy functions were protected with TBS to afford northwestern building block **124** in 14 steps.[44]




Scheme 2.24: Synthesis of fragment **124** of *ent*-pentamycin (**123**) by Walleser & Brückner.[44] Reaction conditions: a) **126**, $PPh_3$, toluene, rt, 10 min, then −30 °C, DIAD, rt, overnight, **62%**; b) $NEt_3$, **127**, THF, −15 °C, 30 min; c) Grubbs II, toluene, 100 °C, 3 h, **93%** (over 2 steps); d) Li, $PhMe_2SiCl$, THF, −10 °C, 18 h, then CuCN, 2 h, then −78 °C, TMSCl, addition of **128**, −50 °C, 1 h, **88%** (*dr* (lactone) = 100:0; *dr* (sulfone moiety) = 68:32); e) TBAF, THF, 0 °C to rt, 3 h, **38–50%**; f) $Boc_2O$, DMAP, $NEt_3$, DCM, 0 °C to rt, overnight, **86%**; g) $I_2$, MeCN, −20 °C, 16 h, **94%** (*dr* = 100:0); h) acetone, *p*-TsOH, rt, 4 d, **92%**; i) NaH, PhSH, rt to 50 °C, 2 h, **99%**; j) LDA, **132**, $Et_2O$, 2 h, then $CpTiCl_3$, 24 h, then hexanal, 24 h, **82%** (*dr* = 100:0), k) DIBAL-H, toluene/hexane, −78 °C, 3 h, **90%**; l) MeOH, PPTS, rt, 2.5 h, **63%**; m) KH, N-methylpyrrolidone, *t*-BuOOH, 0 °C to rt, 10 min, KF, 60 °C, 1.5 h, **66%**; n) TBSOTf, imidazole, DMF, 0 °C to rt, 60 min, **93%**. The expression "*dr* = 100:0" was reproduces from the original publication.

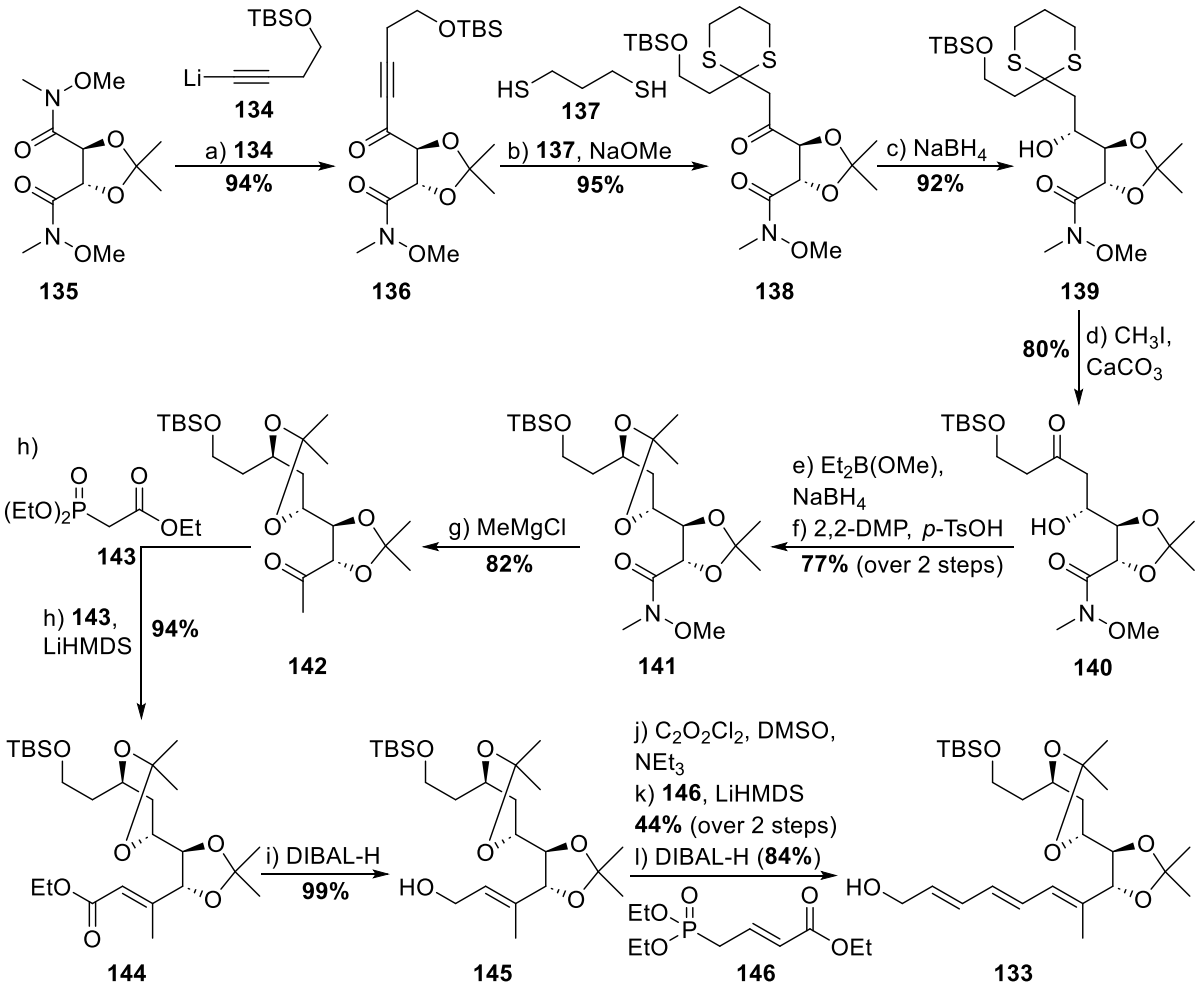
## 2.2.3 Fragment Synthesis of Pentamycin by Bali & Prasad

In 2020, Bali & Prasad described the stereoselective synthesis of the C9-C22 building block of pentamycin (**10**). In contrast to other approaches for both, pentamycin (**10**) and filipin III (**11**), the molecule was not separated in polyol- and polyene fragments but was divided in a building block **133** containing half of the polyene and half of the polyol part (Scheme 2.25). The fragment was derived from tartaric acid providing both stereocenters at C14 and C15.[43]




Scheme 2.25: Retrosynthetic analysis of pentamycin (**10**) by Bali & Prasad.[43]

The synthesis started with the addition of alkyne **134** to *bis*-Weinreb amide **135** and propargylic ketone **136** was obtained (Scheme 2.26). The alkyne function reacted in a double conjugate addition with propane-1,3-dithiol (**137**) under basic conditions and furnished 1,3-dithianyl ketone **138**.[70] In the next step, the ketone was reduced selectively to the secondary alcohol **139**, however, detailed information about the exact selectivity were not available. Deprotection of the dithiane was accomplished using methyl iodide and calcium carbonate and resulting *β*-hydroxy ketone **140** was reduced to the 1,3-*syn* diol under Narasaka-Prasad conditions. After acetonide protection compound **141** was transformed to methyl ketone **142** by Grignard addition of MeMgBr to the Weinreb amide, thus, generating the starting material for a Horner-Wadsworth-Emmons reaction (HWE) with triethyl phosphonoacetate (**143**) resulting in *α*,*β*-unsaturated ester **144**.[43]




Scheme 2.26: Synthesis of southwestern part **133** of pentamycin **10** by Bali & Prasad.[43]
Reaction conditions: a) **134**, THF, −78 °C, 1.5 h, **94%**; b) **137**, NaOMe, MeOH:DCM (4:1), −10 °C to rt, 1.5 h, **95%**; c) $NaBH_4$, MeOH, −78 °C, 2 h, **92%**; d) $CH_3I$, $CaCO_3$, MeCN:$H_2O$ (2:1), 45 °C, 7 h, **80%**; e) $Et_2B(OMe)$, $NaBH_4$, THF:MeOH (4:1), −78 °C, 3 h; f) 2,2-DMP, *p*-TsOH, DCM, 0 °C to 10 °C, 30 min, **77%** (over 2 steps); g) MeMgCl, THF, 0 °C to rt, 2 h, **82%**; h) **143**, LiHMDS, THF, −78 °C to rt, 5 h, **94%**; i) DIBAL-H, DCM, −78 °C, 3 h, **99%**; j) $C_2O_2Cl_2$, DMSO, $NEt_3$, DCM, −78 °C, 20 min; k) **146**, LiHMDS, THF, −78 °C, to −45 °C, 2 h, **44%** (over 2 steps); l) DIBAL-H, DCM, −78 °C, 1 h, **84%**. No exact selectivity was stated in the original publication.[43]

Reduction with DIBAL-H afforded allylic alcohol **145** which was oxidized to the aldehyde by Swern oxidation. The aldehyde was starting material for a second HWE reaction with phosphonate **146** which yielded again an *α*,*β*-unsaturated ester. Reduction with DIBAL-H provided allylic alcohol **133** which represents the C9-C22 fragment of pentamycin (**10**) (Scheme 2.26).[43]

## 2.3 Implications for a First Total Synthesis of Pentamycin

The different publications about synthetic studies on both molecules, filipin III (**11**) and pentamycin (**10**) used completely different approaches. Mainly aldol reactions, selective 1,3-*syn* reductions and Rychnovsky's coupling were used to construct the polyol part. The polyene part was mainly assembled by Wittig-type olefination reactions or by Heck-couplings.

It is noticeable, that the two advanced synthetic studies by Oishi *et al*. and Cossy *et al*. which could not yet finalize the total synthesis chose a macrolactonization as final cyclization reaction. However, it was not possible to oxidize the alcohol at C1 to the carboxylic acid due to instability of the already attached, highly sensitive polyene part (Figure 2.1). Richardson & Rychnovsky chose a HWE mediated ring closure in their successful total synthesis, but they also mentioned the high sensitivity of their polyene fragment.[33,45,48]

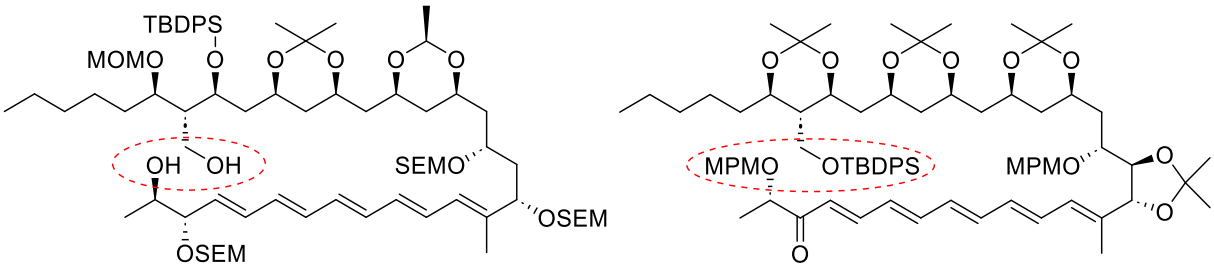



Figure 2.1: Critical steps in the unsuccessful attempts of a total synthesis of filipin III (**11**) by Cossy *et al*. and of pentamycin (**10**) by Oishi *et al*.[45,48]

It may be helpful to oxidize C1 to the carboxylic acid before the polyene segment is coupled with the rest of the molecule to circumvent these problems. Since the final deprotection after ring closure also proofed to be very challenging in the successful total synthesis of filipin III (**11**) by Richardson & Rychnovsky, the attempt to introduce the polyene part in the very last step of the synthesis, even after global deprotection, may be an option.

Beside these unsuccessful points some very useful lessons can be learned from the above discussed synthetic approaches. Rychnovsky's addition of alkyl iodides to a diastereomeric mixture of cyanohydrin acetonides is an excellent method to generate 1,3-*syn* polyols and could find application in the anticipated synthesis of the polyol part of pentamycin (**10**).[33,51]

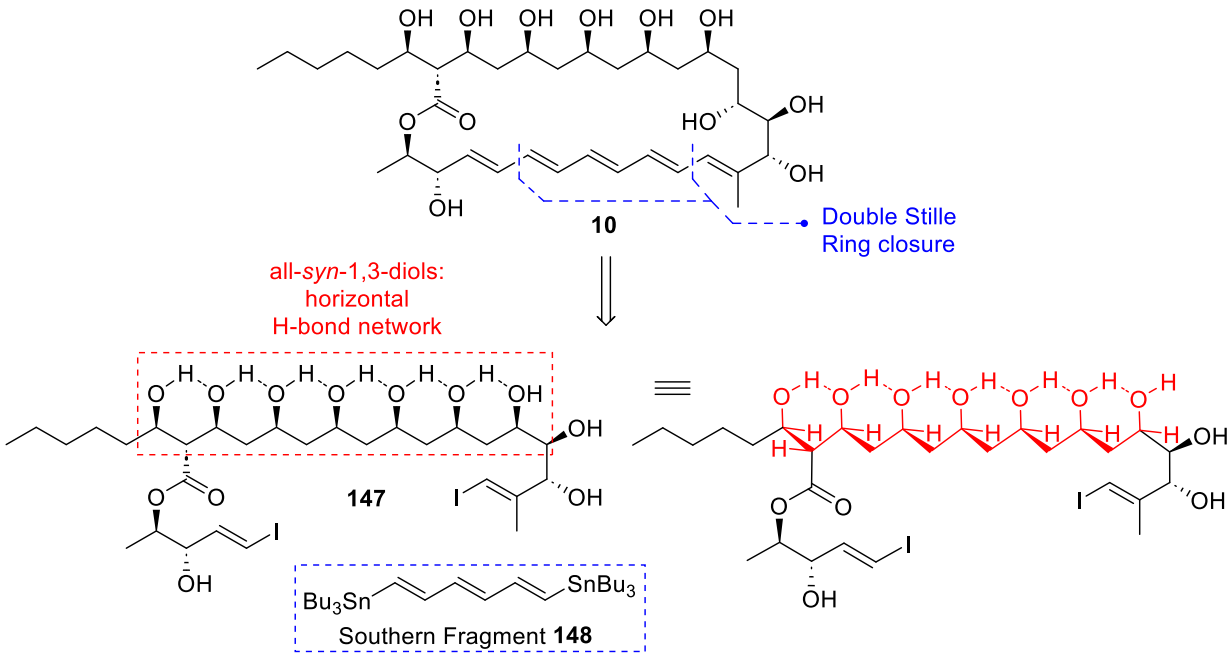
Furthermore, a total synthesis can always be simplified by exploiting nature's chiral pool. The southwestern part of pentamycin (**10**) can be derived from lactic acid as described in the synthesis of Cossy *et al*. Additionally, the use of tartaric acid by Bali & Prasad to generate the stereocenters at C14 and C15 is quite interesting. These points and the above discussed thoughts were included in the development of a retrosynthetic analysis for the first successful total synthesis of pentamycin (**10**) which is discussed in the next chapter.[43,48]

# 3 Synthetic Work on Pentamycin

This section discusses the overall synthetic work conducted towards the first total synthesis of pentamycin. It begins with a retrosynthetic analysis of the molecule and a derived protective group concept. Next, it presents the key reactions used to assemble the molecule and create the stereocenters. The third chapter covers the development of synthetic routes towards the fragments and how they are coupled and modified to assemble the overall molecule. The ultimate total synthesis of pentamycin is then discussed in detail in the next section (Chapter 4).

## 3.1 Retrosynthetic Analysis of Pentamycin

The general idea for a retrosynthetic analysis of pentamycin (**10**) was the complete separation of polyol and polyene part. The pentaene segment was planned to be installed in the last step on protective group free precursor **147**. This should be achieved by a double Stille cross coupling with concomitant macrocyclization using linear trienyl-*bis*-stannane **148** (Scheme 3.1).

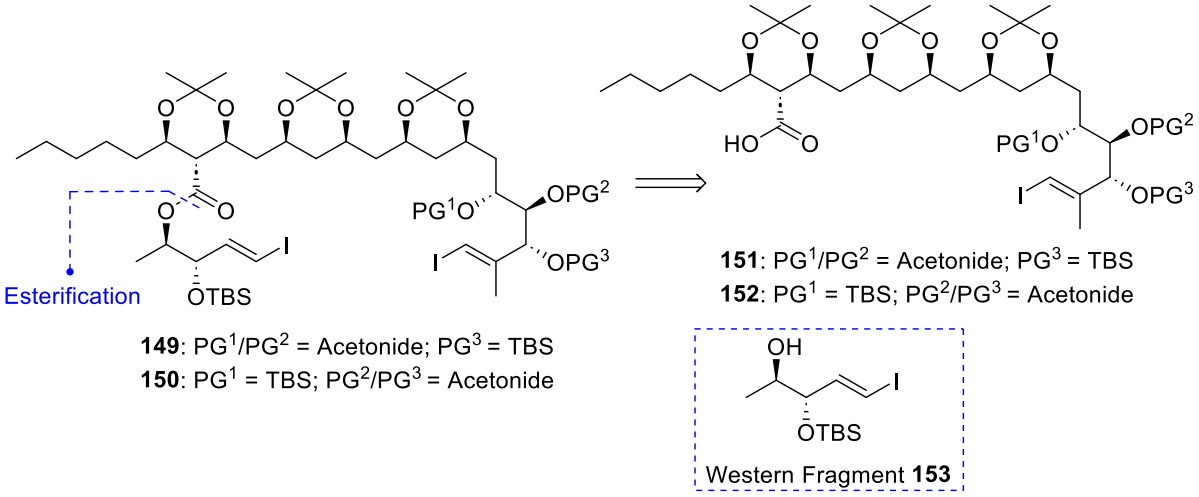



Scheme 3.1: Retrosynthetic analysis of pentamycin (**10**). The labile polyene part was planned to be inserted into protective group free polyene part **147** in the last step, supported by an extended hydrogen bond network.

It was expected that this strategy would have two major advantages. Firstly, the coupling of two protective group-free fragments would lead directly to the final product pentamycin (**10**), and the deprotection of the labile compound could be circumvented. Secondly, it was anticipated that this challenging coupling would be enhanced by a conformational bias of the polyol part of *bis*-vinyl iodide **147**. Specifically, it was assumed that this all-*syn*-1,3-hydroxy polyol motif would reside in a staggered horizontal skeleton, based on an extended hydrogen bond

network (Scheme 3.1).[71] This matrix would perfectly serve as a template to enable the ambitious insertion of the straight triene subunit **148**.

*Bis*-vinyl iodide **147** was derived from its protected precursors **149** or **150** depending on the protective groups at C13, C14, and C15 (Scheme 3.2). The different protective group pattern resulted from different approaches toward the eastern fragment (*vide infra*). Protected *bis*-vinyl iodides **149** and **150** were derived from carboxylic acids **151** and **152** which could be coupled with the western fragment **153** by esterification before final ring closure, since macrolactonization was not possible in the syntheses of Cossy *et al*. and Oishi *et al*, as discussed above.[45,48]

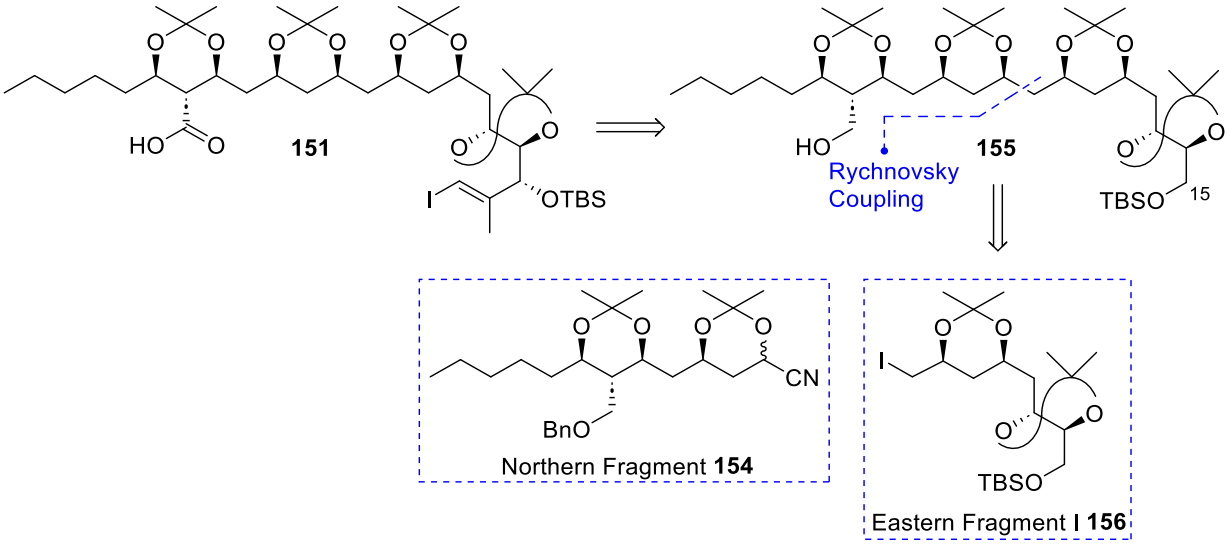



Scheme 3.2: Retrosynthetic analysis of *bis*-vinyl iodides **149** and **150**, which could be obtained by esterification of carboxylic acids **151** and **152** with western fragment **153**.

While the structures of northern **154**, western **153** and southern fragment **148** remained the same during retrosynthetic analysis and development of a synthetic route towards pentamycin (**10**), two structures for an eastern fragment were suggested. The resulting different ways to access carboxylic acids **151** and **152** as the polyol part of pentamycin (**10**), are elaborated in the following two sections of this chapter.

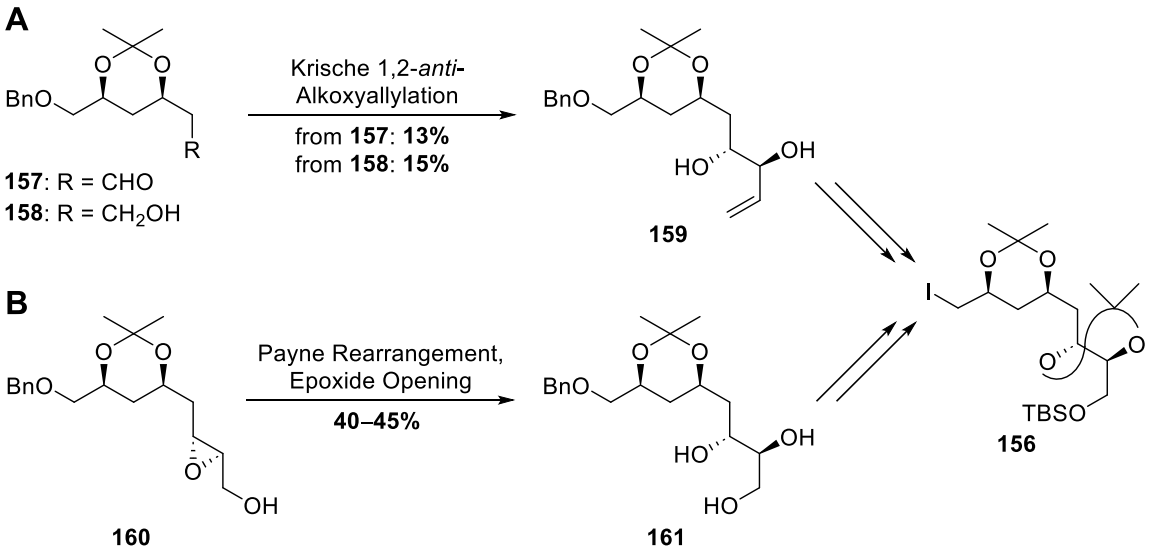
### 3.1.1 First Generation Retrosynthetic Analysis of the Polyol Part

The first plan to obtain carboxylic acid **151** as coupling partner for western fragment **153** was the modification of coupling product **155** (Scheme 3.3). Deprotection of the hydroxy function at C15 and oxidation would generate the aldehyde which could be the starting material for a stereoselective addition of an acetylene equivalent according to Carreira's protocol.[72] This transformation would create the required stereocenter at C15 and provide the substrate for creation of the *α*-methyl vinyl iodide. Oxidation at C1 would afford carboxylic acid **151**. Coupling product **155** could be obtained from northern fragment **154** and eastern fragment I **156** by Rychnovsky coupling with subsequent Birch reduction to cleave the nitrile function.



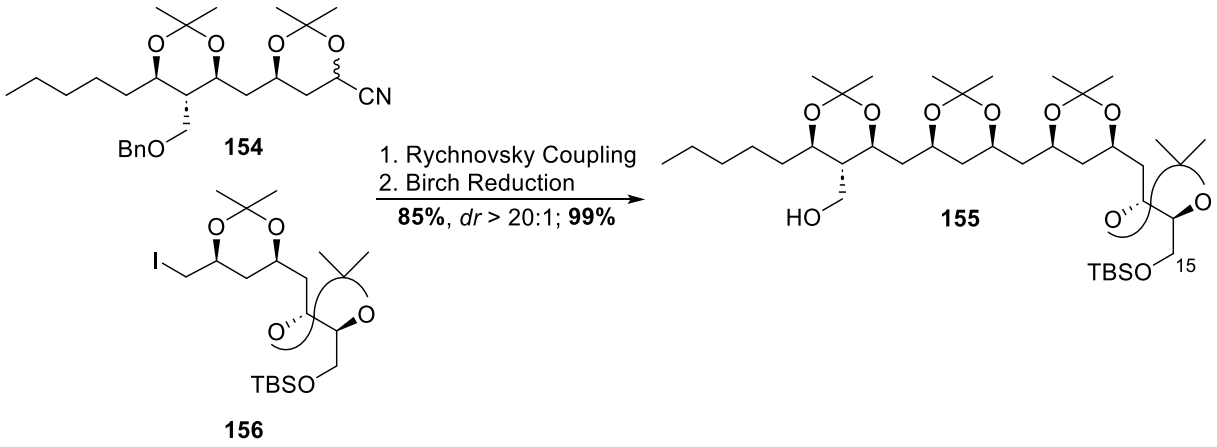

Scheme 3.3: First generation retrosynthetic analysis of the polyol part by modification of coupling product **155** which could be obtained by Rychnovsky coupling of northern fragment **154** and eastern fragment I **156**.

However, synthetic work on the planned route towards the eastern fragment I **156** revealed some problems (for details, see Chapter 3.3.5). The creation of the 1,2-*anti* diol moiety of C13-C14 was attempted using Krische's 1,2-*anti*-alkoxyallylation[73] of aldehyde **157** or primary alcohol **158**, but the reaction did not give a desirable yield of compound **159** (Scheme 3.4 **A**). A second strategy was implemented that used Sharpless asymmetric epoxidation, followed by Payne rearrangement of Sharpless epoxide **160** and nucleophilic epoxide opening (Scheme 3.4 **B**).[74] However, the yields of compound **161** achieved *via* Payne rearrangement only reached a maximum of 45%, which is insufficient to support a multistep sequence.




Scheme 3.4: Attempts to create the 1,2-*anti* diol of the C13-C14 moiety in the eastern region of pentamycin (discussed in detail in Chapter 3.3.4). **A**: *Via* Krische 1,2-*anti*-alkyxyallylation.[73] **B**: *Via* Payne rearrangement and epoxide opening.[74] Poor yields led to the rejection of these routes.

Another problematic issue is the late stage introduction of the stereocenter at C15 which increases synthetic complexity. In combination with the bad yields obtained in the previous steps towards eastern fragment I **156** it was decided to proceed in a different way. Since a test of Rychnovsky's alkylation of the cyanohydrin acetonide function of northern fragment **154** and eastern fragment I **156** relinquished excellent results (Scheme 3.5), the coupling reaction was integrated in the synthetic pathway of the eastern part of pentamycin.[51] A convergent route instead of a linear approach was the result of a second retrosynthetic analysis discussed in the next chapter.

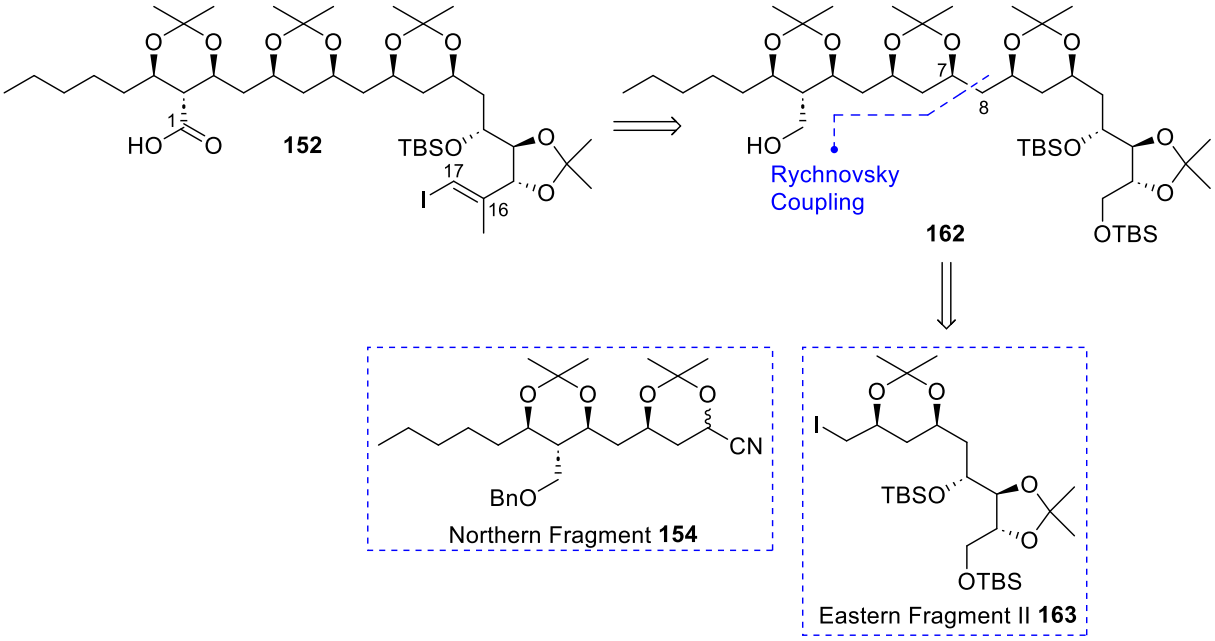



Scheme 3.5: Test coupling of northern fragment **154** and eastern fragment I **156** by Rychnovsky coupling with subsequent Birch reduction to remove the nitrile substituent (discussed in detail in Chapter 3.3.4).

## 3.1.2 Second Generation Retrosynthetic Analysis of the Polyol Part

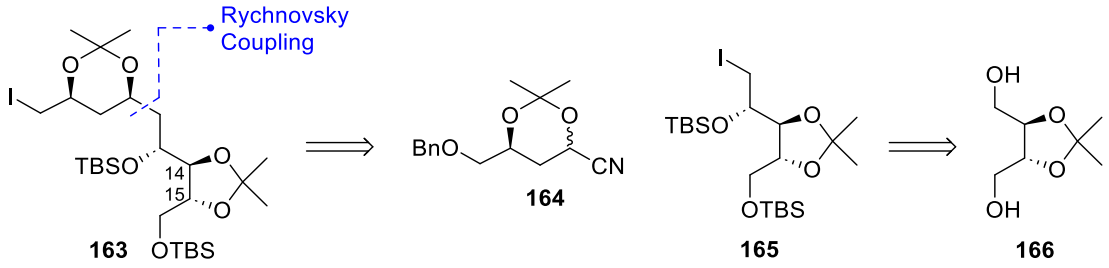
The different strategy to access the eastern fragment of pentamycin (**10**) resulted in a slightly different protecting group pattern of carboxylic acid **152** compared to the previously discussed strategy. The coupling between C7 and C8, and the coupling procedure remained the same, as well as the northern fragment **154** (Scheme 3.6). However, coupling product **162** with a different eastern part could be derived from eastern fragment II **163**.

In contrast to the first generation retrosynthetic analysis, this approach does not require the introduction of the C15 stereocenter after coupling. All stereocenters were already installed, and the only remaining challenge would be the installation of the *α*-methyl vinyl iodide at the C16-C17 moiety. It was useful that various ideas and reactions established during the first approach could also be applied in this second approach. The coupling between the northern and eastern parts remained unchanged, as did the plan to produce *α*-methyl vinyl iodide at the C16-C17 moiety and the carboxylic acid at C1.




Scheme 3.6: Second generation retrosynthetic analysis of the polyol part by modification of coupling product **162** which could be obtained by Rychnovsky coupling of northern fragment **154** and eastern fragment II **163**.

The selected strategy presents two additional benefits. The first one is the modular approach towards the eastern part of pentamycin (**10**). Eastern fragment II **163** was further divided into two smaller fragments, cyanohydrin acetonide **164** and alkyl iodide **165** (Scheme 3.7), both of which were easily accessible in a few steps. The second advantage is the natural origin of the C14 and C15 stereocenters in this approach. Instead of creating them through stereoselective reactions, the precursor of the alkyl iodide fragment **165** is a tartaric acid derivative **166**. This would avoid the highly demanding steps required to introduce the necessary stereocenters.




Scheme 3.7: Retrosynthetic analysis of eastern fragment II **163**, which is further divided into cyanohydrin acetonide **164** and alkyl iodide **165**.

Efficient synthetic planning always requires a well-designed protective group strategy to minimize the number of protection and deprotection steps and maximize the benefits of using protective groups. As seen in the discussed retrosynthetic analyses, mainly two types of protective groups, i.e., acetonides, and silyl protecting groups were utilized for the polyol part of pentamycin. The following chapter discusses the advantages of these protecting groups for the

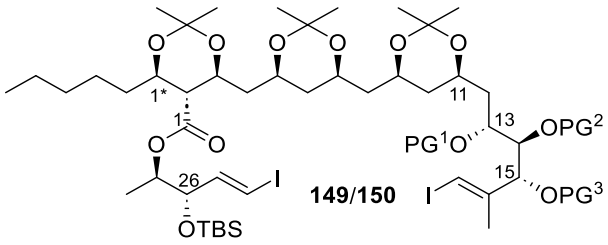
successful total synthesis of pentamycin and other benefits that can be exploited by using these groups.

### 3.1.3 General Protective Group Concept

In most total syntheses, the last step involves a global deprotection.[75] However, for pentamycin, final global deprotection poses a problem due to its notorious instability. To tackle this challenge, the final step was planned to be the key insertion of the polyene part into protective group-free precursor **147** by a double Stille cross coupling, instead of global deprotection. Thus, the labile pentaene motif would be generated immediately after deprotection to prevent its decomposition during the process.

Protected pentamycin precursors **149** or **150**, derived from the two retrosynthetic approaches, display a very similar pattern of protective groups (Table 3.1). The only difference between the first and second generation retrosynthetic analyses is the eastern part of the molecule, which results in a different pattern of protective groups in this region. The aim during retrosynthetic analysis was to maintain a simple and minimally orthogonal concept of protective groups. The 1,3-*syn* diols between C1* and C11 were planned to be protected as six-membered acetonides, and the 1,2,3-triol (C13-C15) as a five-membered acetonide. The remaining hydroxy function should be protected as TBS ethers. To enable global deprotection in as few steps as possible, the hydroxy function at C26 should also be protected as a TBS-ether during synthesis of western fragment **153**. Acetonides and TBS groups can be cleaved under slightly acidic or Lewis acidic conditions.[76,77] Additionally, TBS-ethers can be cleaved with fluoride-containing reagents such as TBAF or HF·pyridine.[78]

Table 3.1: Protecting group concept in the first and second generation retrosynthetic analyses.




| PG | 1st Generation 149 | 2nd Generation 150 |
|---|---|---|
| $PG^1$ | Acetonide | TBS |
| $PG^2$ | Acetonide | Acetonide |
| $PG^3$ | TBS | Acetonide |

The acetonide protecting group is the major protecting group used in the overall synthesis. This group is advantageous in the total synthesis of polyols because it is easy to introduce and protects two hydroxy functions simultaneously. Additionally, it has a lower molecular weight compared to other protective groups such as silyl or benzyl groups, resulting in less mass loss after deprotection in the final steps of the total synthesis.[79] Another highly beneficial feature is the ability to determine the relative configuration of a 1,3-diol.[80]

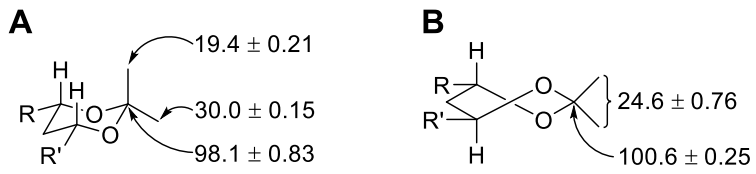



Figure 3.1: Chemical shifts of the carbon atoms contained in the acetonide protection group. **A**: 1,3-syn acetonide (chair conformation), **B**: 1,3-anti acetonide (twist-boat conformation).[81]

By comparing the chemical shift of the $^{13}$C-NMR signals, it is possible to predict whether the acetonide has a 1,3-*syn*- or 1,3-*anti* configuration. In case of a 1,3-*syn* configuration, the acetonide adopts a chair conformation with one methyl group in the axial position and one in the equatorial position, resulting in different chemical shifts in the $^{13}$C-NMR spectra (Figure 3.1 **A**). On the other hand, 1,3-*anti* acetonides adopt the twist boat conformation, resulting in equal shifts for the methyl groups (Figure 3.1 **B**). Hence, acetonides fulfil two functions in the total synthesis of pentamycin: They protect the hydroxy functions and confirm the 1,3-*syn* configuration of the polyol part.

## 3.2 Key Reactions and Concepts in the Total Synthesis of Pentamycin

This section provides a concise overview of the key concepts and reactions utilized during the project (Figure 3.2). As indicated by the retrosynthetic analysis, the primary coupling reactions employed to connect the fragments are a double Stille coupling and Rychnovsky's coupling of alkyl iodides to cyanohydrin acetonides with subsequent Birch reduction.[51] Allylation reactions are crucial in constructing 1,3-polyols and are an integral part of pentamycin synthesis.[82–84] Other methods for creating hydroxy centers with high stereoselectivity include SAE[85] and Carreira's addition of alkynes to aldehydes,[72] both of which are commonly used in total syntheses. The polyene part of pentamycin is created by a Ramberg-Bäcklund rearrangement.[86]

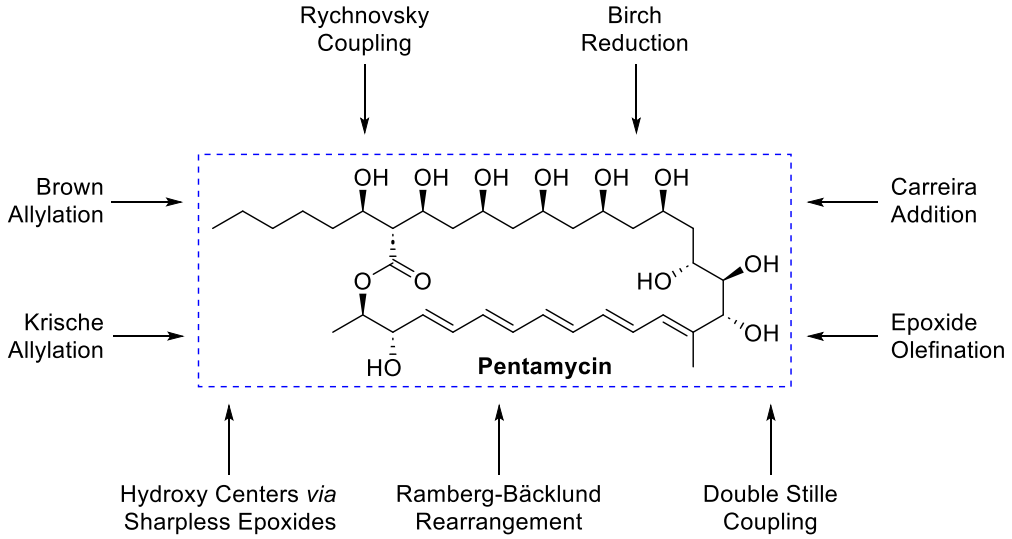



Figure 3.2: Key Reactions used in the proposed total synthesis of pentamycin.

The upcoming sections will cover the mechanisms of the key reactions and how stereoselectivity is induced. Each chapter begins by highlighting the relevant hydroxy centers and carbon atoms incorporated by each reaction, with a dashed box. It is important to note that not every highlighted region is used in the ultimate synthetic route towards pentamycin discussed in Chapter 4 but may belong to different routes. Therefore, specific positions will be referred to multiple times throughout the following chapters.

### 3.2.1 Stereoselective Carbonyl Allylation Reactions

Stereoselective carbonyl allylation reactions in form of Brown and Krische allylation were used to build up the northern fragment **154** of pentamycin (**10**) and found application in an attempt of a route to access the eastern fragment I **156** (Figure 3.3).

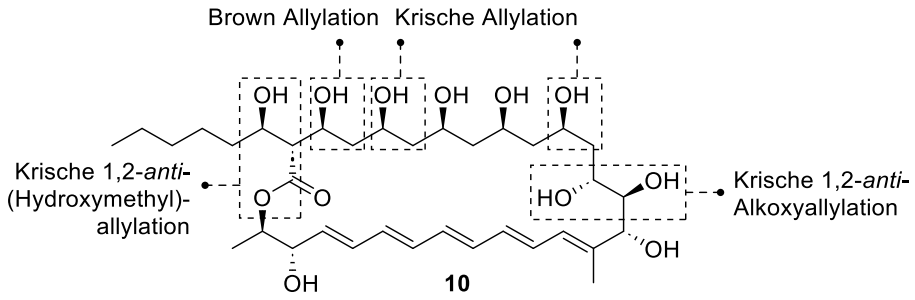
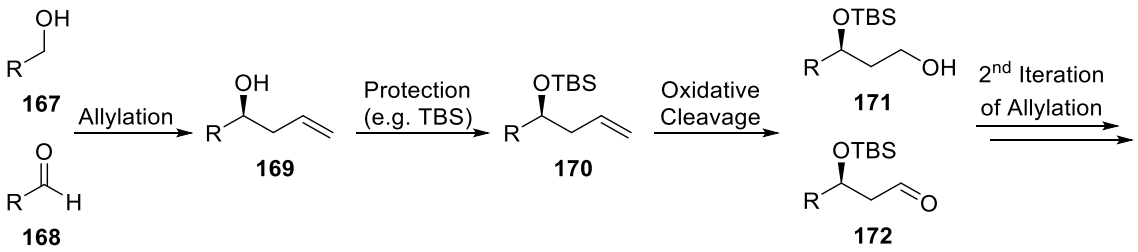



Figure 3.3: Areas in the target molecule pentamycin (**10**) created by allylation reactions.

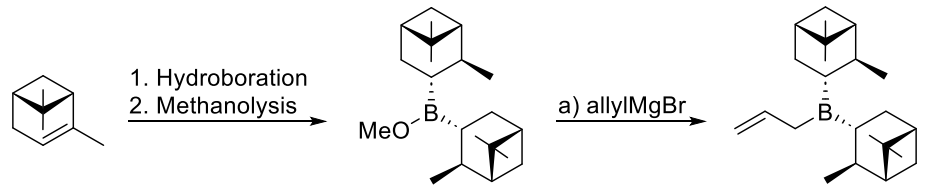
Allylation reactions are a valuable method in polyketide natural product total synthesis.[87] Beside the stereoselective generation of secondary hydroxy centers from primary alcohols **167** or aldehydes **168**, a new carbon-carbon bond is formed which enables the construction of a polyketide scaffold.[88] Allylation reactions are particularly useful to create 1,3-polyol fragments since their products, homoallylic alcohols **169**, contain a masked hydroxy or aldehyde function (see **171** or **172**) in form of a terminal olefin in a 1,3-distance to the newly generated hydroxy center. The hydroxy or aldehyde function is easily accessible by oxidative cleavage of the double bond, e.g. of protected homoallylic alcohols like **170** and therefore enables an iterative use of these reactions (Scheme 3.8).[89]




Scheme 3.8: Possible strategy to access 1,3-polyols by stereoselective allylation reactions.

The Brown allylation is a condensation reaction between the chiral reagent (−)-$(Ipc)_2$B-allyl (**175**, Brown's reagent)[b] and aldehydes to form homoallylic alcohols. (−)-$(Ipc)_2$B-allyl (**177**) is derived from the monoterpene (+)-*α*-pinene **173** which is hydroborated, followed by methanolysis and subsequent reaction with allylMgBr (Scheme 3.9).[90–92] The intermediate (−)-$(Ipc)_2$BOMe (**174**) is commercially available and mostly used as the starting material for generation of allyl donor **175**.

[b] With (−)-α-pinene (+)-$(Ipc)_2$B-allyl is obtained *via* (+)-$(Ipc)_2$BOMe. To increase clarity only (−)-$(Ipc)_2$B-allyl is stated here.

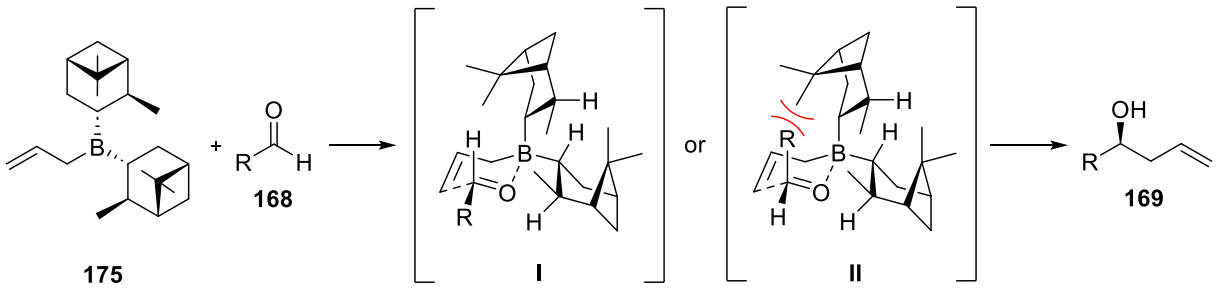



(1*R*)-(+)-α-pinene (**173**) (–)-$(Ipc)_2BOMe$ (**174**) (–)-$(Ipc)_2B$-allyl (**175**)

Scheme 3.9: Generation of Brown's reagent (−)-**175**, the allyl donor for the Brown allylation used herein.[92] Reaction conditions: a) **174**, allylMgBr, $Et_2O$, 0 °C, 1 h.

To increase stereoselectivity, the reaction is typically carried out at a low temperature of −78 °C, higher temperatures lead to a loss of stereoselectivity. The classic solvents used in this reaction are THF and $Et_2O$, both of which give best results in terms of reactivity and stereoselectivity.[88]

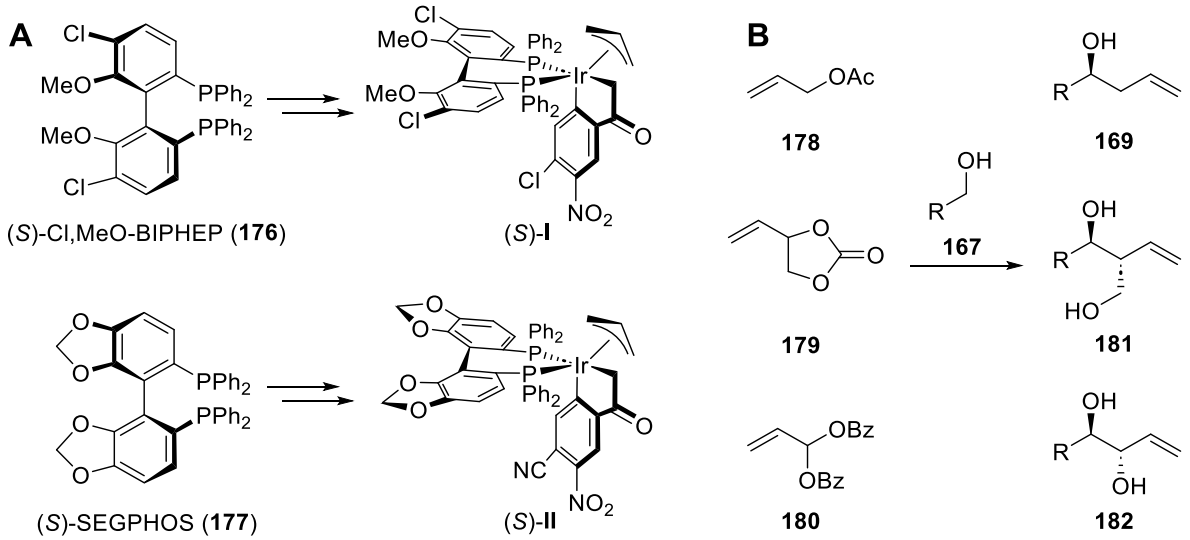
The Brown allylation belongs to type I allylation reactions proceeding *via* Zimmermann-Traxler transition states (Scheme 3.10), in contrast to type II allylations proceeding *via* open transition states.[93,94] The aldehyde is activated by the boron and the nucleophile attacks in a way that the residue of the aldehyde occupies the equatorial position of the chair, preventing 1,3-diaxial interactions caused by steric clash between the Ipc-ligand and the substituent of the aldehyde (**II**). Scheme 3.10 displays the *Si*-face attack (**I**) occurring if (−)-$(Ipc)_2B$-allyl **175** is used as allyl donor like in the discussed total synthesis of pentamycin.[91,92,95]




Scheme 3.10: Possible transition states and favored *Si*-face attack for the stereoselective allylation of aldehydes with (−)-$(Ipc)_2B$-allyl **175**.

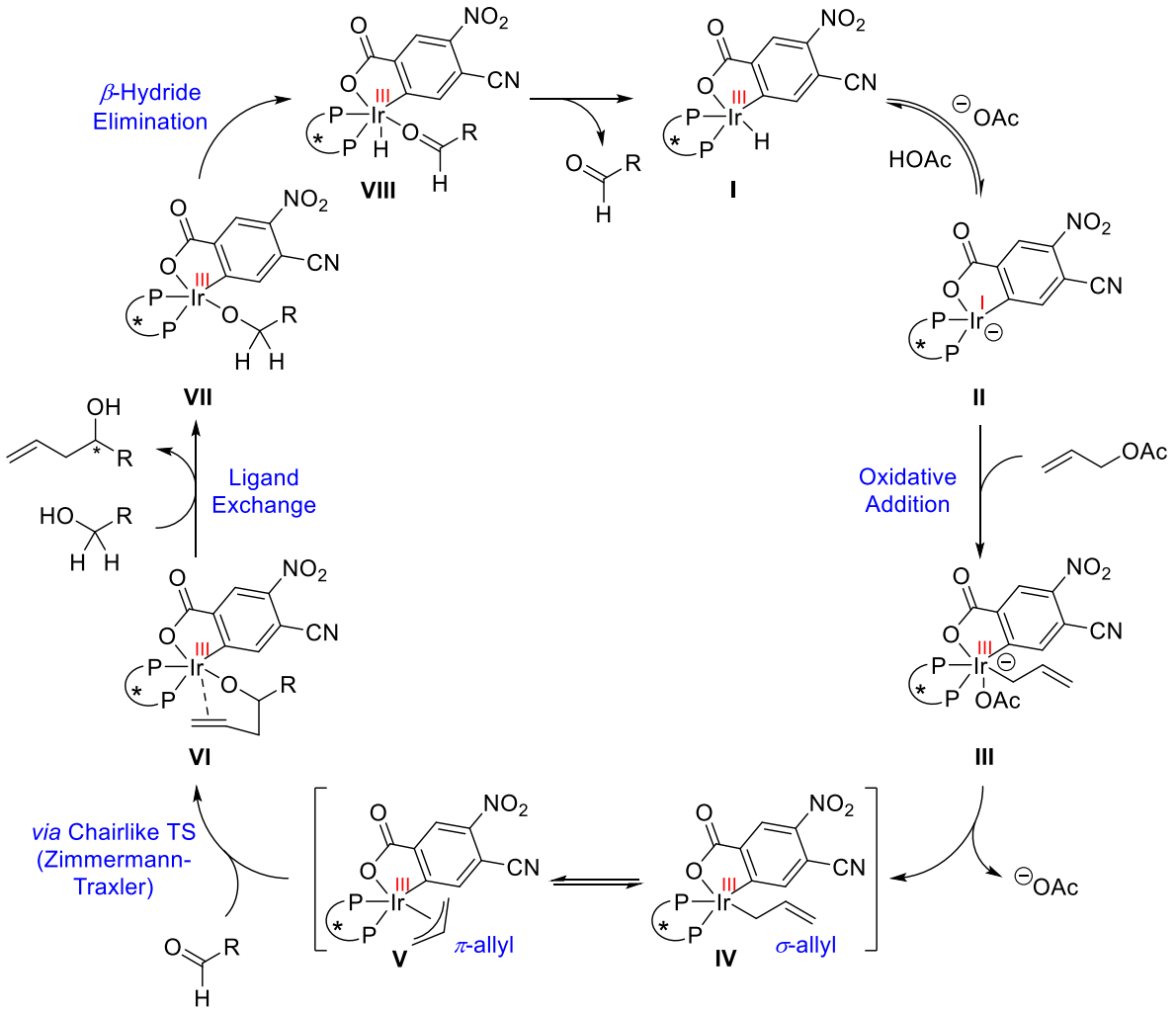
The Krische allylation is a stereoselective, catalytic, transfer hydrogenative carbonyl allylation and thus proceeding in the absence of stoichiometric preformed organometallic reagents. The iridium catalyst is generated from $[Ir(cod)Cl]_2$, a chiral, chelating triarylphosphine ligand like (*S*)-Cl,MeO-BIPHEP (**176**) or (*S*)-SEGPHOS (**177**) and the additives $CsCO_3$ and a substituted nitrobenzoic acid (Scheme 3.11 **A**). The catalysts can either be prepared *in situ* like (*S*)-**I**, or precipitated, isolated, and stored like (*S*)-**II**.[82] Various non-metallic allyl donors can be used to increase the diversity of structural motifs accessible by this reaction.[73,83,96] Scheme 3.11 **B** shows the three different transformations performed with the different allyl donors on the

journey to provide a route for the total synthesis of pentamycin (**10**). Allyl acetate (**178**) is used to create chiral, homoallylic alcohols like **169**. With modified allyl donors like cyclic carbonate **179** or allylic-*gem*-dicarboxylate **180** homoallylic alcohols substituted by a hydroxymethyl (**181**), or just a hydroxy group in *α*-position (**182**) are accessible.




Scheme 3.11: **A**: Catalysts used in the total synthesis of pentamycin. **B**: Possible allyl donors and structural motifs employed in the development of a synthetic route towards pentamycin.[73,82,83,96]

Scheme 3.12 presents a possible catalytic cycle for the Krische allylation.[83] The presence of acetic acid and acetate leads to an equilibrium between *ortho*-cyclometalated Ir(III) complex **I** and anionic Ir(I) complex **II**. Deprotonation is facilitated by the stabilization of the anion by the electron withdrawing effect of the *ortho*-carboxy and the *para*-nitro moieties of the benzoate. Oxidative addition of allyl acetate (**178**) furnishes anionic Ir(III) complex **III** which forms neutral *σ*-allyl complex **IV** and rapidly equilibrates with the respective *π*-allyl haptomer **V**. Like the Brown allylation, the Krische allylation belongs to type I allylation reactions since allyl transfer to the aldehyde occurs through a closed chair-like Zimmermann-Traxler transition state to yield homoallyl iridium alkoxide **VI**.[93,94] The free coordination side of Ir(III) in complex **VI** is occupied by the terminal olefin of the homoallylic alcohol which prevents *β*-hydride elimination and is therefore the reason for conformational stability of the homoallylic alcohol. Subsequent ligand exchange between the homoallylic alcohol and the substrate alcohol releases a free coordination site and *β*-hydride elimination can occur leading to complex **VIII**. Dissociation of the generated aldehyde regenerates *ortho*-cyclometalated Ir(III) complex **I** and closes the catalytic cycle. In contrast to Brown allylation, which uses aldehydes as a substrate, both aldehydes and alcohols are suitable for this reaction. If the allylation substrate is an aldehyde, isopropanol as hydrogen donor is added to facilitate the formation of complexes **VIII** and **I**.[82]




Scheme 3.12: Catalytic cycle of the Krische allylation.[83]

The stereochemical course of the Krische allylation can be explained by the coordination mode during the six-membered transition state between σ-allyl haptomer **IV** and complex **VI** (Figure 3.4).

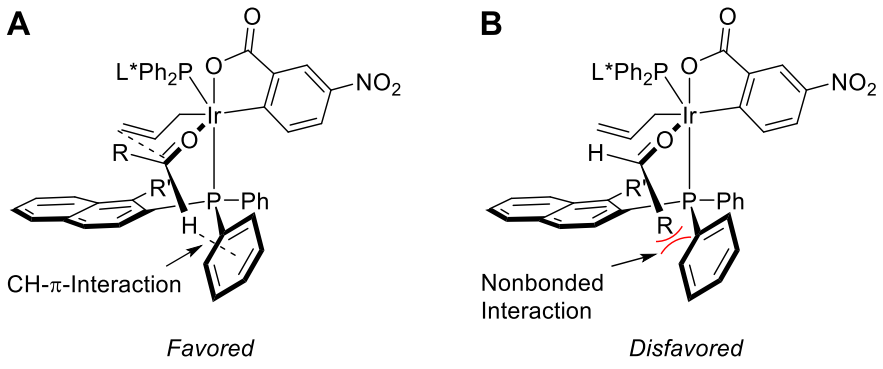



Figure 3.4: Proposed model of stereoinduction by the binding of the aldehyde to σ-allyl haptomer **IV** (L*: chiral ligand, here BINAP; R': second part of the BINAP ligand).[83]

The sterically less demanding allyl moiety is placed between the sterically demanding chiral aromatic (here naphtyl) and phenyl moieties of the ligand. Consequently, the aldehyde shows to the front to reside in a more open environment and is bound in a way that the aldehydic C-H bond interacts with the *π*-face of the phenyl ring leading to weak C-H-*π* interactions (Figure 3.4 **A**). Steric clash between the residue of the aldehyde and the phenyl moiety prevent the other possible bonding mode of the aldehyde leading to the high selectivity (Figure 3.4 **B**).[83]

The Krische allylation has several advantages over the Brown allylation. Since both, aldehydes and alcohols are suitable substrates for allylation, often one step in a multi-step sequence can be saved. The catalytic course of the reaction prevents the stoichiometric formation of byproducts and therefore facilitates the workup. However, the Krische allylation requires high reaction temperatures between 90 °C and 120 °C and long reaction times of about 48 h, and thus, thermically stable substrates are required. The Brown allylation typically proceeds at −78 °C and takes about 1 h, so less stable substrates which decompose under Krische conditions may be successfully allylated under Brown conditions.

### 3.2.2 Creation of Hydroxy Centers *via* Sharpless Epoxides

The development of a successful synthetic route for the macrolide pentamycin (**10**) relies heavily on the stereoselective introduction of its ten hydroxy centers. In addition to the allylation reactions discussed above, the Sharpless asymmetric epoxidation (SAE) is a valuable, catalytic method for creating epoxides with highly predictable stereoselectivity, which can then be converted into hydroxy functions.[97] Figure 3.5 displays the hydroxy functions introduced *via* SAE during synthetic studies towards pentamycin (**10**).

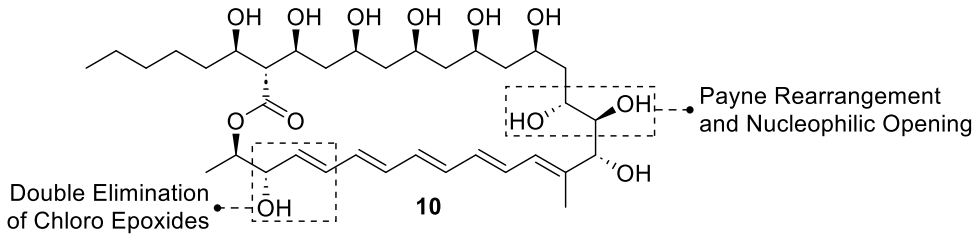
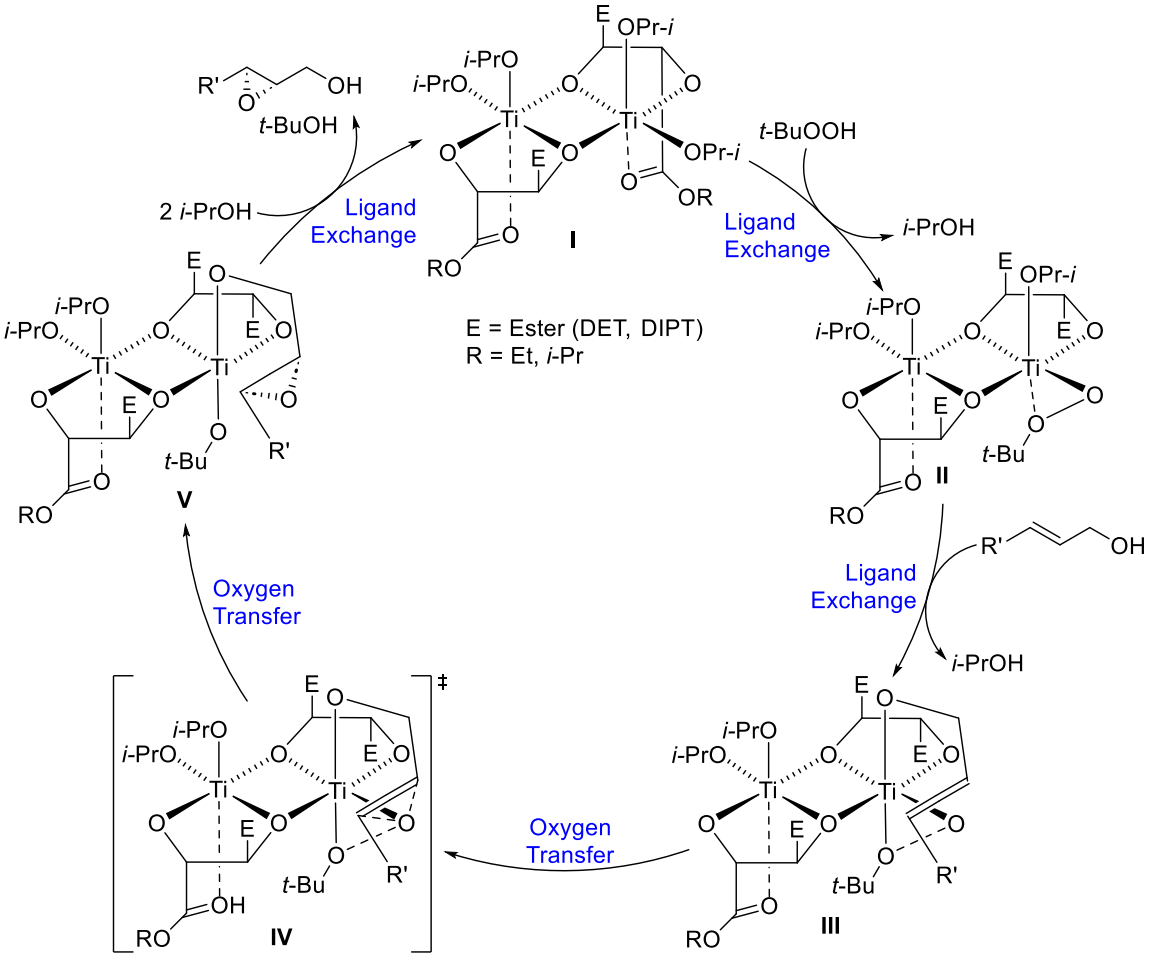



Figure 3.5: Areas in the target molecule pentamycin (**10**) created by processing Sharpless epoxides.

The SAE is a catalytic reaction with an active titanium-tartrate catalyst responsible for asymmetric epoxidation of allylic alcohols. The catalyst is formed from titanium isopropoxide (Ti(*i*-OPr)$_4$), and a tartrate derivative. The oxygen donating species is *tert*-butyl hydroperoxide (*t*-BuOOH).[97] Allylic alcohols are easily accessible since there is a myriad of published literature for synthesis, like for instance cross metathesis, Julia- or Wittig olefinations, or reductive couplings of alkynes and aldehydes.[98]

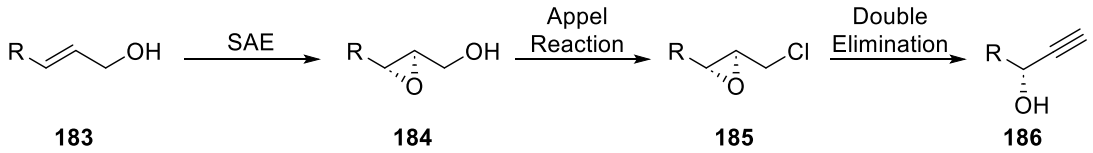
Scheme 3.13 shows the mechanism of oxygen transfer during SAE. The active catalyst is believed to be a bimetallic complex with two Ti-centers bridged by two of the tartrate ligands, such as diethyl tartrate (DET). The Ti-source in the reaction is Ti(*i*-OPr)$_4$, however, ligand exchange occurs, and the Ti-atoms are coordinated by the chelating tartrate ligands in addition to the isopropoxide-ligands (**I**). Epoxidation most probably takes place at one Ti-atom, the other Ti-atom may have a cooperative effect.[99] First two ligand exchanges take place. The *t*-BuOOH substitutes the equatorial isopropoxide group forming a bidentate, triangular dioxametallacycle (**II**), the allylic alcohol substitutes the remaining isopropoxide and occupies the axial position of the Ti-complex (**III**).[100] Oxygen transfer then takes place from the lower face (**IV**) and ligand exchange from complex **V** releases the epoxide and *t*-BuOH in exchange for two isopropanol ligands.[85,99]




Scheme 3.13: Catalytic cycle and mechanism of oxygen transfer of the SAE.[99,101]

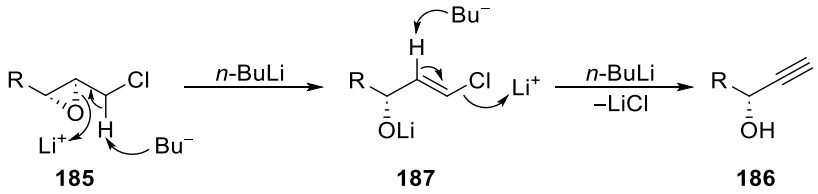
Sharpless epoxides can be used to create hydroxyl centers. A possible sequence to create chiral propargylic alcohols like **186** consists of SAE, Appel reaction, and double elimination. (Scheme 3.14). After SAE of allylic alcohol **183**, the primary hydroxyl function of Sharpless epoxide **184** is exchanged by a chlorine using Appel conditions. The key step in this sequence

is the double elimination of substituted epichlorohydrin **185** which has found application in some natural product total syntheses.[102,103]



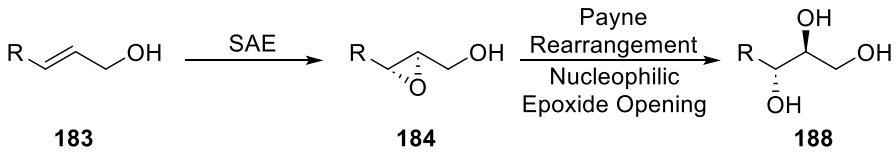

Scheme 3.14: Sequence to create chiral propargylic alcohols by SAE, Appel reaction, double elimination.

Double elimination is usually induced by a strong base such as *n*-BuLi. The first step in the reaction involves the abstraction of the acidic proton of *α*,*β*-epoxy chloride **185** at the chlorinated carbon by *n*-BuLi, leading to epoxide opening and formation of vinyl chloride **187** (Scheme 3.15).[104] The second step involves the deprotonation at the vinylogous carbon, in *α*-position to the newly generated hydroxy function, resulting in the final extrusion of LiCl and the formation of chiral propargylic alcohol **186**. The selectivity introduced by the SAE is preserved in the corresponding propargylic alcohols.[105]




Scheme 3.15: Mechanism of the double elimination of *α*,*β*-epoxy alcohols by *n*-BuLi.[104,105]

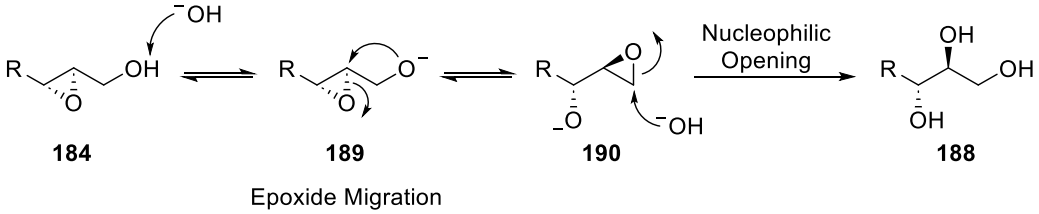
Another, highly useful reaction to create 1,2-*anti* diols is the Payne rearrangement with subsequent nucleophilic epoxide trapping (Scheme 3.16). This reaction also proceeds from Sharpless epoxides and relies on epoxide migration, specifically the migration of 2,3-epoxy alcohols to 1,2-epoxy alcohols under basic conditions, resulting in inversion of the configuration at C2 (Scheme 3.17).[106]




Scheme 3.16: Sequence of SAE, Payne rearrangement, and nucleophilic epoxide opening to access 1,2-*anti* diols form Sharpless epoxides.

The mechanism of epoxide migration involves deprotonation of 2,3-epoxy alcohol **184**, followed by intramolecular nucleophilic epoxide opening by alkoxide **189** with simultaneous formation of 1,2-epoxy alcohol **190** (Scheme 3.17).[107] The two epoxides **184** and **190** are in

equilibrium, and their isomerization is highly dependent on the solvent. Epoxide migration occurs in aqueous solution, i.e., aqueous NaOH, while aprotic conditions, such as NaH in THF, prevent isomerization. Under protic conditions, the free anion is believed to be formed, while aprotic conditions lead to the formation of a tight ion pair between alkoxide **189** and sodium, preventing any nucleophilic attack.[108]




Scheme 3.17: Mechanism of the Payne rearrangement with subsequent nucleophilic epoxide opening by $OH^-$.[106,108]

Sharpless epoxides can be used to create 1,2- or 1,3-diols with various stereochemical relationships.[109] This is particularly the case if the epoxides are substituted. In the case discussed here, the migrated epoxide is a terminal epoxide directing nucleophilic opening by $OH^-$ to that position since an $S_N2$-reaction is favored at the primary carbon. Therefore, triol **188** which contains the 1,2-*anti* diol motif is the final product. The powerful combination of the SAE and Payne rearrangement is demonstrated in the total synthesis of the L-hexoses by Masamune & Sharpless.[110]

### 3.2.3 Cobalt-Catalyzed Epoxide Olefination

An important substrate to build up of the C8-C11 moiety in the eastern part of pentamycin (**10**) is homoallylic alcohol **191** (Scheme 3.18). A cobalt-catalyzed epoxide olefination was used to synthesize compound **191** on large scale (Figure 3.6).

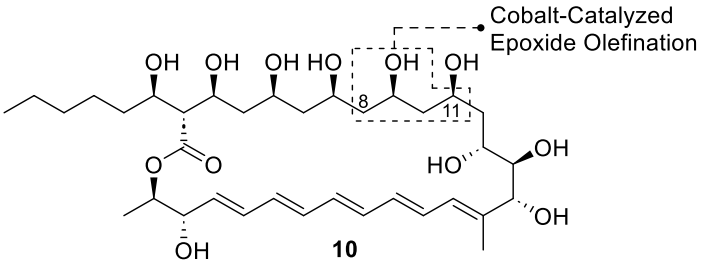
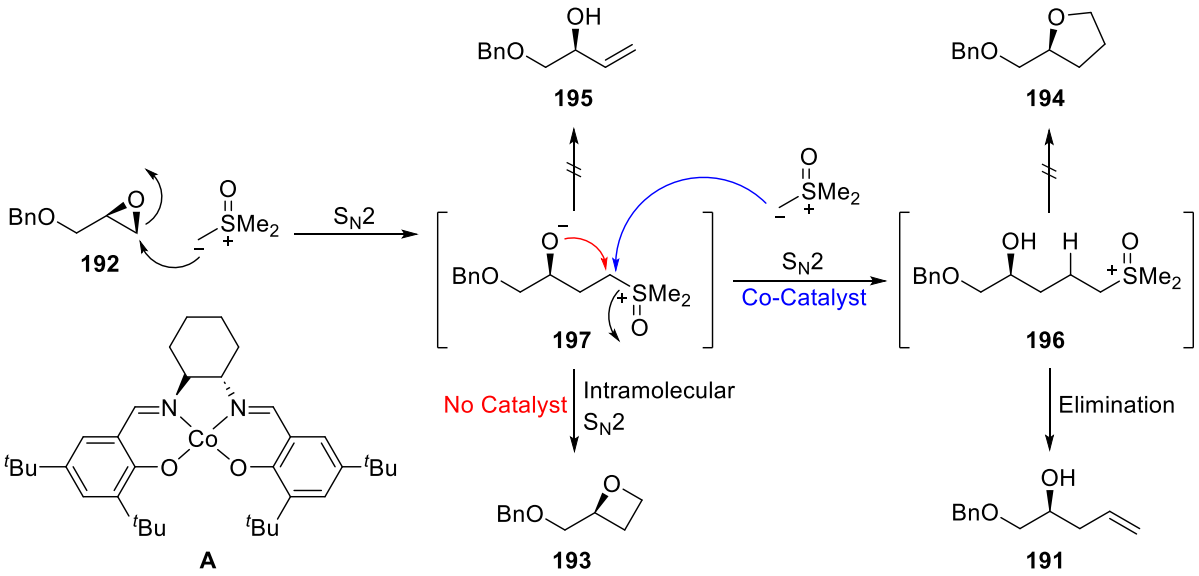



Figure 3.6: Area in the target molecule pentamycin (**10**) created by the cobalt-catalyzed epoxide olefination.

The presence of Jacobsen's cobalt(III) salen catalyst **A** has an unexpected influence on the reactivity of epoxides with dimethylsulfoxonium methylide ($Me_3SOI$).[111] Without a cobalt

catalyst, epoxides such as **192** can be converted to oxetanes **193** in the presence of potassium *tert*-butoxide and further ring expansion leads to oxolanes such as **194**.[112]

Although the exact mechanism is unclear, it is assumed that betaine cyclization theoretically competes with *β*-deprotonation and elimination of DMSO. If Jacobsen's catalyst is added to the reaction mixture, cyclization and ring expansion are prevented but elimination to homoallylic alcohol **191** occurs (Scheme 3.18). Interestingly, no allylic alcohols like **195** are formed so addition of two $Me_3SO^-$ units takes place to form homologated betaine **196** from betaine **197**.




Scheme 3.18: Proposed mechanism for cobalt-catalyzed epoxide olefination.[111]

### 3.2.4 Carreira Addition

The C12-C13 moiety of pentamycin (**10**), including the stereocenter at C13 was introduced by a stereoselective alkyne addition to the aldehyde function at C13 (Figure 3.7). A procedure reported by Carreira was used which employs $Zn(OTf)_2$ and *N*-methylephedrine under basic conditions to create chiral propargylic alcohols.[72]

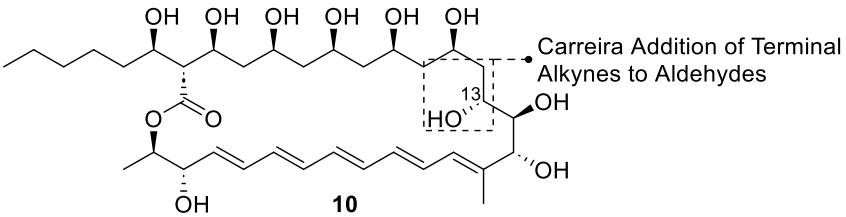
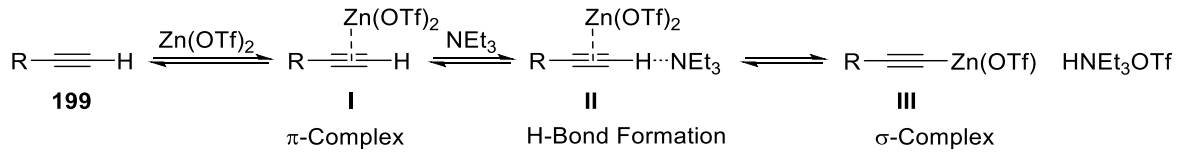



Figure 3.7: Area in the target molecule pentamycin (**10**) created by Carreira's stereoselective addition of alkynes to aldehydes.

Chiral secondary propargylic alcohols are highly useful building blocks in synthetic organic chemistry. The stereoselective addition of alkylzinc reagents to aldehydes has already been

published by Noyori *et al*. in 1986,[113] however, a method with comparable stereoselectivity for the addition of alkynes to aldehydes remained elusive. In 1990, Soai *et al*. published a method to produce alkynylzinc reagents which could be added to aldehydes in high yields but rather low stereoselectivity.[114] Carreira *et al*. developed a mild method for *in situ* generation of zinc alkynylides from $Zn(OTf)_2$ and an amine base like $NEt_3$. The presence of the chiral amino alcohol (−)-*N*-methylephedrine[c] (**198**) makes this reaction highly stereoselective and leads to chiral propargylic alcohols.[72]

To generate nucleophiles from alkynes deprotonation is necessary, which typically requires strong basic conditions. In case of this reaction however, a weak base like $NEt_3$ is sufficient due to the formation of a *π*-complex (**I**) between the Lewis acidic $Zn(OTf)_2$ and alkyne **199** (Scheme 3.19). The acidity of the terminal hydrogen is strongly increased and hydrogen bond formation between the alkyne and the amine base occurs (**II**), ultimately leading to deprotonation.[115] Deprotonation is accompanied by formation of a *σ*-complex (**III**), the reactive alkynyl zinc species which is in equilibrium with the respective *π*-complex (**I**), so the whole metalation process is reversible.[116]

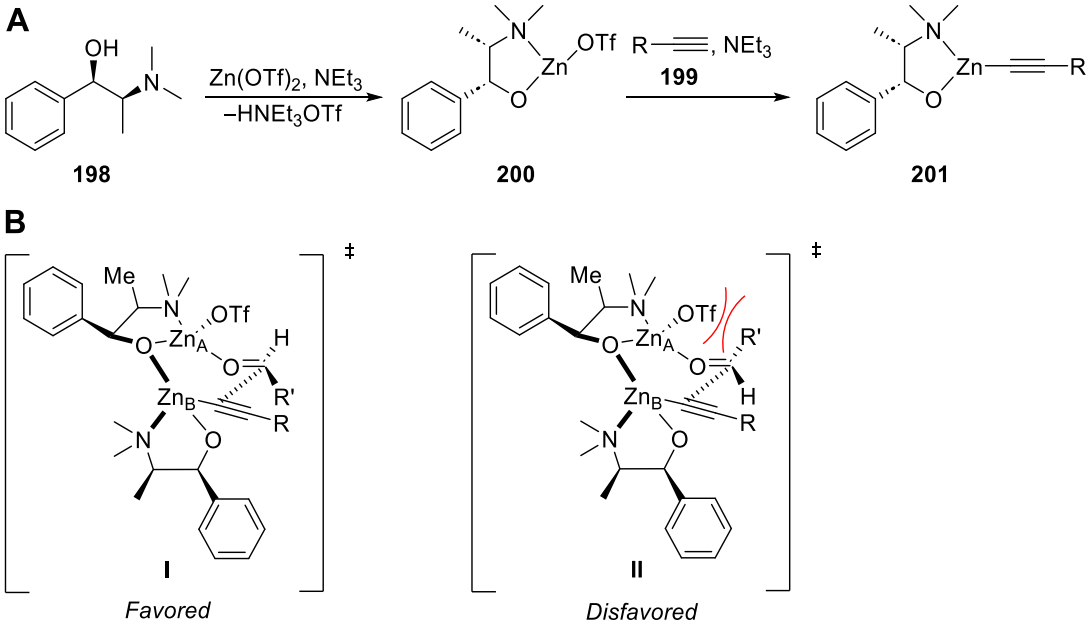



Scheme 3.19: Generation of the zinc alkynylide.[115,116]

Stereoselectivity of the reaction can be explained by analyzing two possible diastereomeric transition states according to the transition state model by Noyori, for the addition of alkyl groups from dialkylzinc compounds to aldehydes (Scheme 3.20 **B**).[117] Scheme 3.20 **A** displays the formation of the respective zinc species **200** and **201**, generated from $Zn(OTf)_2$ and (−)-*N*-methylephedrine (**198**) which combine to a bimetallic transition state, containing two zinc atoms per aldehyde. The electronic properties of the two zinc atoms $Zn_A$ and $Zn_B$ differ, since $Zn_A$ is more Lewis acidic due to the electron withdrawing triflate group, whereas $Zn_B$ is more electron rich due to its interaction with the alkyne. The more electrophilic zinc atom $Zn_A$ is responsible for activating the aldehyde, the nucleophilic zinc atom $Zn_B$ transfers the alkyne to the carbonyl function (Scheme 3.20 **B**).[118] Depending on which of the two lone pairs of the aldehyde binds to the zinc, either the aldehydic hydrogen atom, or the residue R' of the aldehyde show to the same side than the triflate bound to $Zn_A$. In case of the disfavored transition state **II** steric clash between the residue R' of the aldehyde and the triflate at $Zn_A$ leads to an

[c] Both enantiomers (+)- and (−)-*N*-methylephedrine are available.

unfavorable binding event. In transition state **I** this unfavorable steric interaction is prevented since the smaller hydrogen atom takes the position of R'.[117]




Scheme 3.20: **A**: Formation of the two relevant zinc species **200** and **201**. **B**: The two diastereomeric, bimetallic transition states **I** and **II** according to Noyori, explaining the stereoselectivity of the alkyne addition.[117,118]

### 3.2.5 Rychnovsky Coupling and Birch Reduction

A central coupling reaction in the total synthesis of pentamycin (**10**) is the coupling of alkyl iodides to cyanohydrin acetonides, a reaction developed by Rychnovsky and coworkers.[51] The reaction is used to couple northern fragment **154** to eastern fragments **156** and **163**, and to assemble the two subunits **164** and **165** of eastern fragment II **163**, the ultimately developed eastern part of pentamycin. These coupling reactions concomitantly create the stereocenters at C7 and C11 (Figure 3.8).

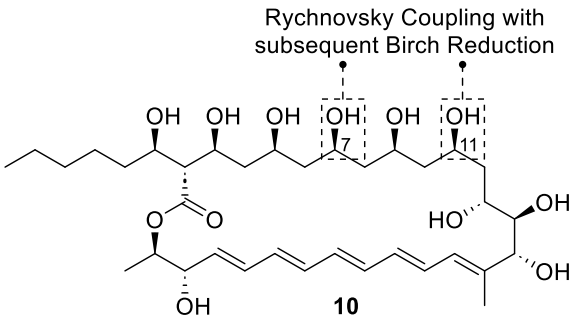
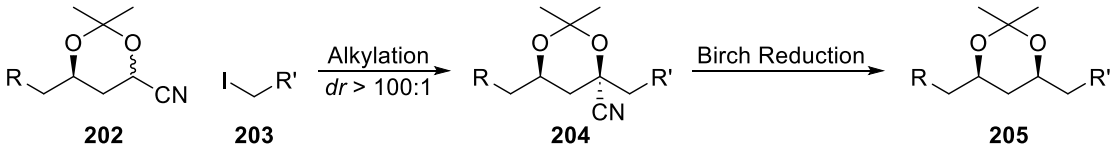


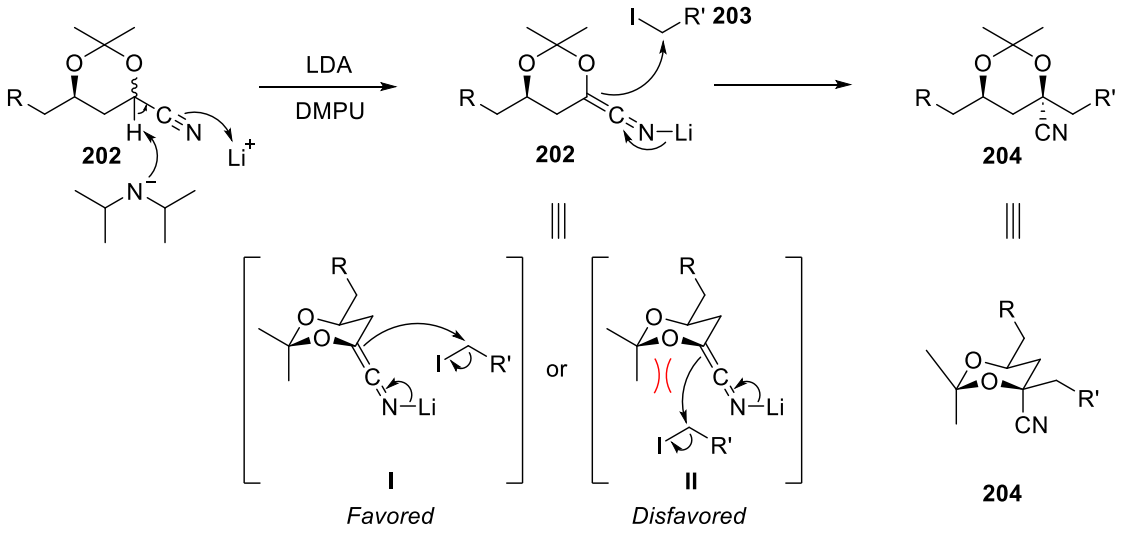

Figure 3.8: Areas in the target molecule pentamycin (**10**) created by the Rychnovsky coupling and subsequent Birch reduction.

Based on Stork's cyanohydrin alkylation which uses LDA and HMPA to nucleophilically activate a cyanohydrin and then couple it with an alkylhalide,[119] Rychnovsky developed a method to selectively couple alkyliodides **203** to cyanohydrin acetonides **202** in a 1,3-*syn* manner.[51] This overall coupling consists of two reactions, first the alkylation itself to obtain **204** and second the reductive decyanation under Birch conditions to yield the 1,3-*syn* acetonide **205** (Scheme 3.21).[120]




Scheme 3.21: Schematic overview of the Rychnovsky coupling consisting of alkylation of a cyanohydrin acetonide and reductive decyanation.[120]

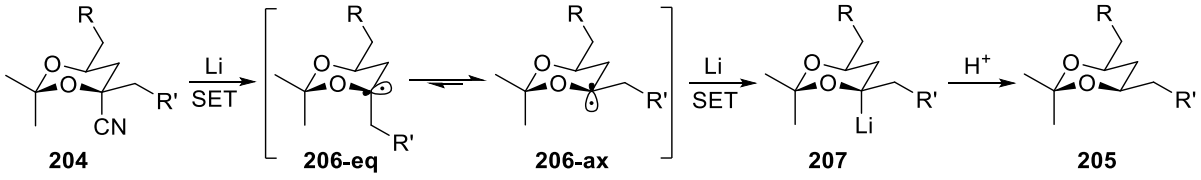
The alkylation exhibits a very high 1,3-*syn* selectivity of typically greater than 100:1 in favor of the axial nitrile.[120] Scheme 3.22 shows the mechanism of nucleophilic activation by LDA in **202** with subsequent attack of the alkyl iodide **203** by the nucleophilic carbon in intermediate **202**. The 1,3-*syn* selectivity during alkylation is caused by favorable steric interactions when the smaller nitrile substituent occupies the axial position and accordingly, the residue of the alkyl iodide occupies the equatorial position (**I**). 1,3-Diaxial interactions between the axial methyl group of the acetonide and the residue of the alkyl iodide, in case of an axial occupation, prevent a 1,3-*anti* configuration (**II**).[120]




Scheme 3.22: Mechanism and stereochemical explanation of the alkylation of the cyanohydrin acetonide.[120]

Cleavage of the nitrile substituent finally establishes the 1,3-*syn* acetonide (Scheme 3.23). Reductive decyanation of **204** under Birch conditions yields product **205** also with selectivities up to 100:1. The cyanide anion is eliminated with concomitant formation of a radical

intermediate **206**.[121] The selectivity could arise either from the previous reaction by retention of configuration, or from axial protonation. Indeed, the second explanation reflects reality since the Birch reduction proceeds *via* two single electron transfers (SET) and the pyramidal radical, the intermediate after the first SET, equilibrates between **206-eq** and **206-ax**.[120] Calculations have shown that the axial radical **206-ax** is more stable than the equatorial radical **206-eq**.[122] The stabilization is caused by overlap with the oxygen lone pair, similar to the hyperconjugative interaction-hypothesis of the anomeric effect which suggests electron delocalization of the 2p-type lone pair of oxygen to the adjacent antibonding σ*-orbital at the anomeric carbon.[122,123] A second SET leads to axial carbanion or *α*-alkoxylithium reagent **207** which is conformationally stable at −78 °C, the temperature which is also required to keep the ammonia liquid during the reaction. Protonation of the axial anion ultimately furnishes the 1,3-*syn* acetonide **205**.




Scheme 3.23: Mechanism and stereochemical course of the reductive decyanation under Birch conditions.[122]

It can be concluded that although the selectivity of the alkylation is already very high, the ultimate stereoselectivity of the Rychnovsky coupling is established during the reductive decyanation under Birch conditions. Consequently, the high selectivity of the nitrile substituent occupying the axial position plays a minor role for synthesizing 1,3-*syn* acetonides.

### 3.2.6 Ramberg-Bäcklund Rearrangement

The southern part of pentamycin, containing the pentaene fragment should be built up by a Ramberg-Bäcklund rearrangement. Proceeding from sulfones, this reaction enables the synthesis of olefins, in case of pentamycin of the C20-C21 double bond (Figure 3.9).[124]

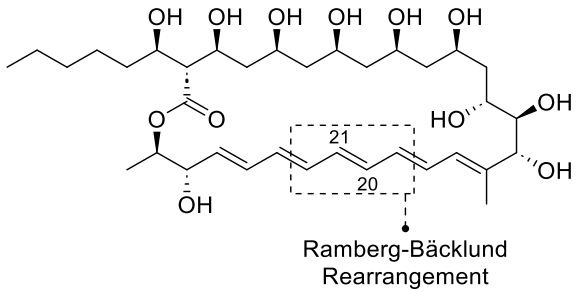
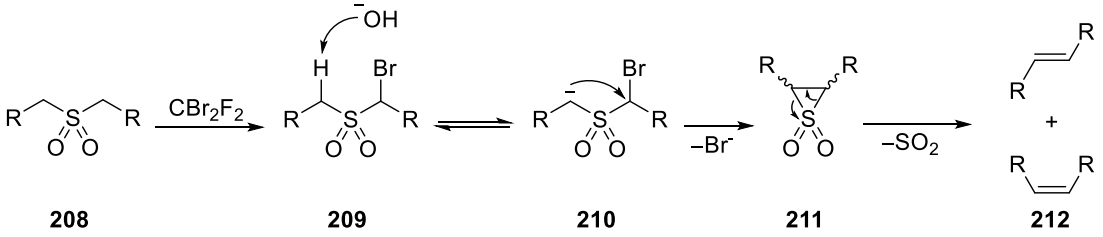


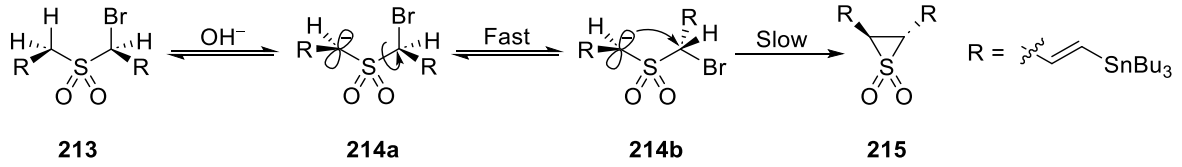

Figure 3.9: Area in the target molecule pentamycin (**10**) created by a Ramberg-Bäcklund rearrangement.

The Ramberg-Bäcklund rearrangement occurs from *α*-halo sulfone **209**, which can be produced *in situ* by reaction of sulfone **208** with $CCl_4$ or $CBr_2F_2$ (Scheme 3.24).[124,125] Deprotonation of the *α*-hydrogen in **209** generates carbanion **210** which can undergo an intramolecular $S_N2$-reaction leading to cyclic sulfone **211**. A cheletropic extrusion of $SO_2$ finally takes place and furnishes olefins **212**-(*E*) and **212**-(*Z*).[86]




Scheme 3.24: Proposed mechanism of the Ramberg-Bäcklund reaction.[86,124]

The reaction's stereochemical course is complex, and predicting the stereochemical outcome is difficult. Generally mild bases lead to (*Z*)-olefins, stronger bases favor (*E*)-olefins.[86] In case of the substrate synthesized for the total synthesis of pentamycin, high (*E*)-selectivity was observed.[126] The following mechanistic analysis proposes an explanation for this high selectivity.




Scheme 3.25: Proposed mechanistic model to explain the observed high (*E*)-selectivity of the Ramberg-Bäcklund reaction used in the synthesis of the polyene part of pentamycin.[127]

The deprotonation of **213** is assumed to be reversible and conformers **214a** and **214b** equilibrate very fast due to the possible rotation around the C-S bond (Scheme 3.25).[127] Due to the very large $Bu_3Sn$-residues it is assumed that a *trans*-configuration of the residues is favored in **215**. Since $S_N2$-attack occurs from the backside, structure **214b** is the relevant structure in this mechanism.[128] Typically, $SO_2$-extrusion occurs highly stereospecific, meaning that configuration of the olefin is determined at the stage of formation of cyclic sulfone **215**. These conclusions lead to high (*E*)-selectivity for the discussed example.[127,129]

### 3.2.7 Double Stille Coupling

The Stille coupling is a palladium-catalyzed cross coupling reaction that forms carbon-carbon bonds between organotin compounds and organohalides, mainly organoiodides.[130] The pentaene moiety C17-C25 (Figure 3.10) of pentamycin (**10**) should be introduced in the final step

of the overall synthesis by a double Stille cross coupling reaction between *bis*-vinyl iodide **147** and *bis*-stannane **148** (Scheme 3.27 **A**).

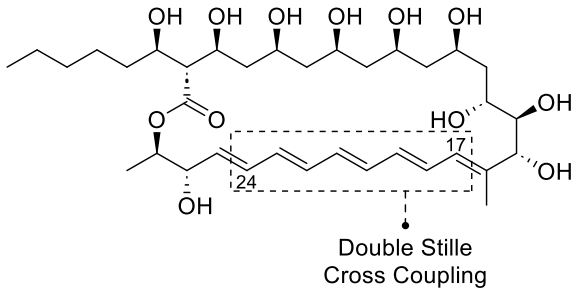
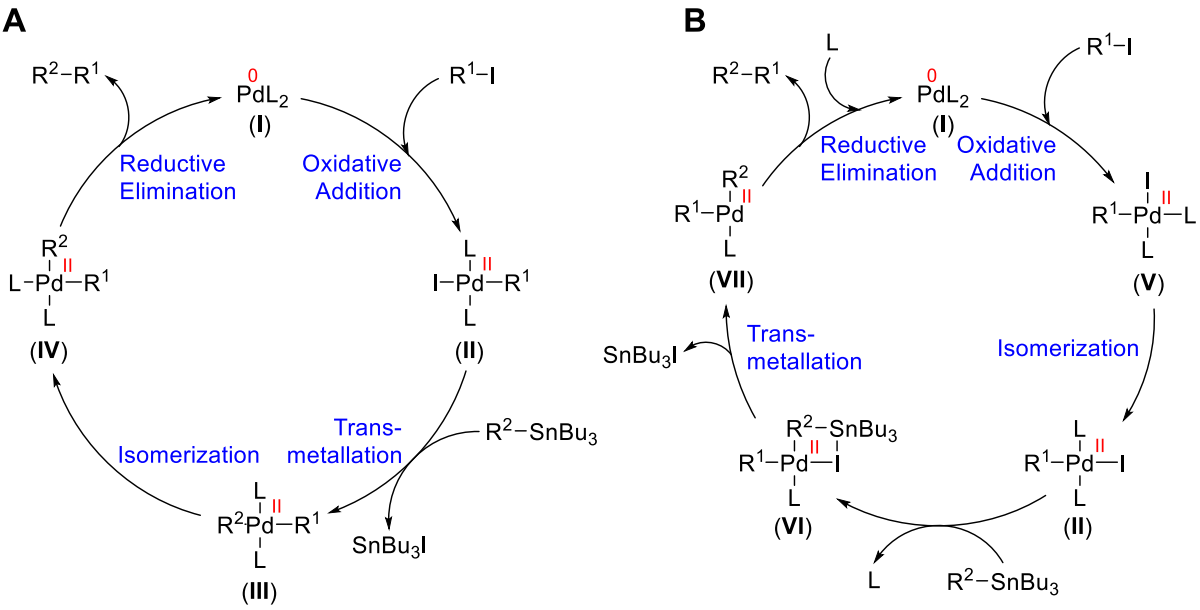



Figure 3.10: Area in the target molecule pentamycin (**10**) created by a double Stille cross coupling.

The Stille coupling is a commonly employed reaction in the total synthesis of complex natural products.[131] Organostannanes are advantageous due to their air and moisture stability, making them easy to store and use.[132] Additionally, the Stille coupling is highly tolerant to various functional groups, including free hydroxy functions.[133]

The mechanism of the Stille coupling is intricate, and multiple pathways for each step in the catalytic cycle are conceivable. Scheme 3.26 displays two potential catalytic cycles: the general catalytic cycle proposed by J. K. Stille (**A**) and a revised catalytic cycle suggested by Casado & Espinet (**B**).[134,135]



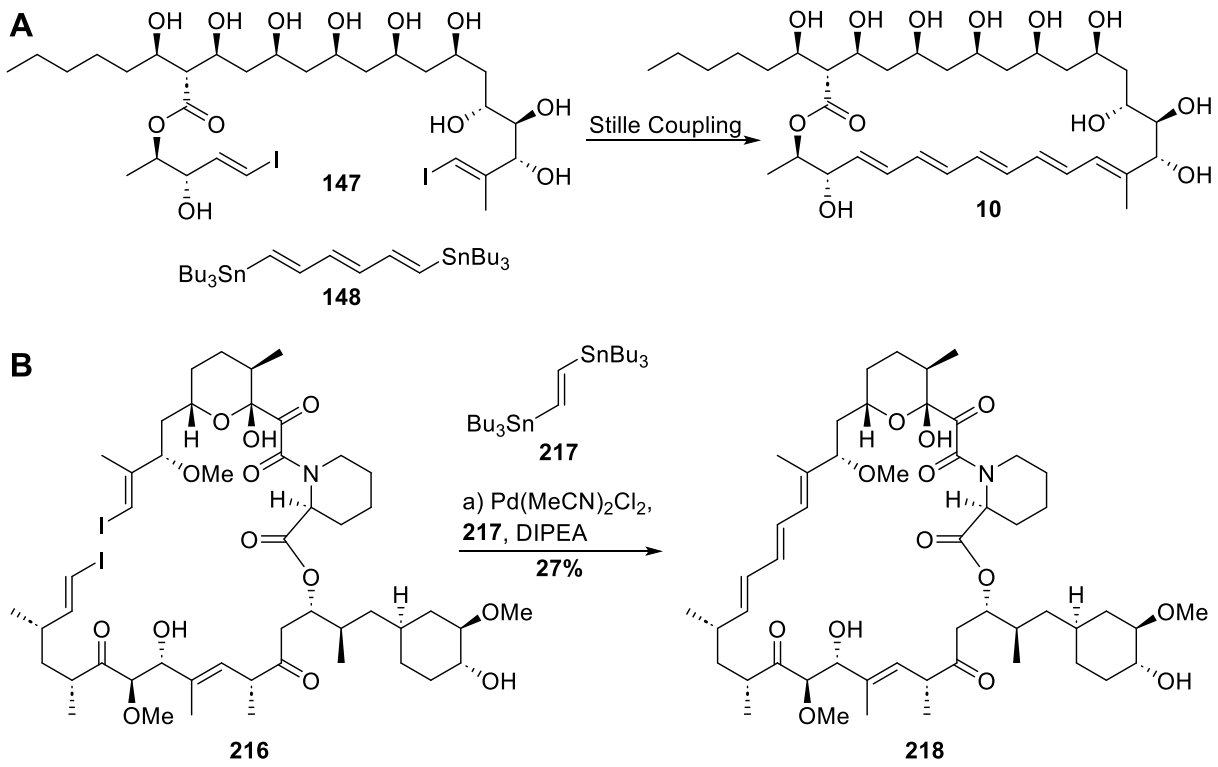

Scheme 3.26: Proposed catalytic cycles for the Stille coupling. **A**: By J. K. Stille (1986); **B**: By Casado & Espinet (1998).[134,135]

The simplified catalytic cycle shown in Scheme 3.26 **A** involves an oxidative addition of an organohalide to the Pd(0)-center (**I**) resulting in Pd(II)-complex (**II**). Transmetalation with an organotin reagent leads to complex (**III**) and isomerization furnishes complex (**IV**) with $R^1$ and

$R^2$ in *cis*-configuration. Ultimately, reductive elimination releases the coupling product and regenerates Pd(0)-catalyst (**I**).[134]

The catalytic cycle depicted in Schem 3.26 **B** incorporates the results of research conducted by Casado & Espinet. It is stated that the oxidative addition does not directly result in the more stable *trans*-configurated complex (**II**). Instead, it first forms the *cis*-Pd(II) complex (**V**), which then isomerizes to the *trans*-Pd(II) complex (**II**).[136] It is widely recognized that the reductive elimination can only occur on *cis*-complexes like (**IV**).[137] In contrast, the suggested *trans*-to-*cis* isomerization in cycle **A** is known to be very slow,[138] so *trans*-isomer (**III**) should be observable under catalytic conditions which is however, not the case. The process of transmetallation occurs through an associative L-for-$R^2$ substitution, leading directly to the $R^1/R^2$-*cis* complex (**VI**) instead of $R^1/R^2$-*trans* complex (**III**) like in cycle **A**. After dissociation of $Bu_3SnI$, the *cis*-T-shaped complex (**VII**) can undergo reductive elimination by releasing the coupling product of $R^1$ and $R^2$, and association of L closes the catalytic cycle.[135]

Due to its functional group tolerance, the Stille coupling is highly suited for the problem at hand (Scheme 3.27 **A**). Since all protecting groups should be removed before that step, to prevent decomposition of the sensitive polyene part during deprotection, the polyol backbone of pentamycin (**10**) contains ten free hydroxy functions.




Scheme 3.27: **A**: Final Stille coupling to introduce the pentaene moiety and concomitantly close the macrocycle. **B**: Finalization of the total synthesis of rapamycin (**218**) by a double Stille coupling bis vinyl iodide **216** and bis stannane **217**.[139,140]
Reaction conditions: a) $Pd(MeCN)_2Cl_2$, **217**, DIPEA, DMF/THF (2:1), 25 °C, 48 h, **27%**.

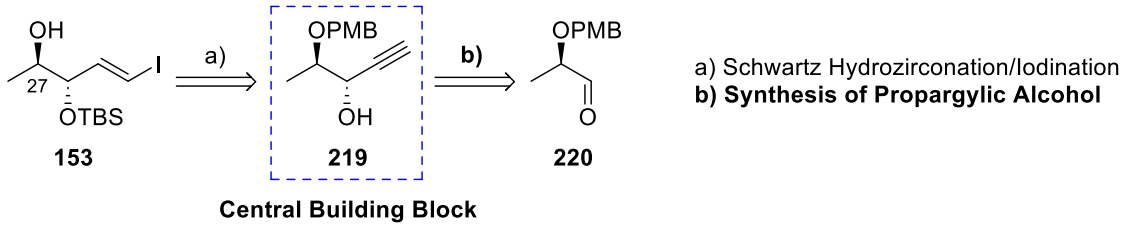
A double Stille coupling in the very end of the synthesis would be highly beneficial since it would accomplish two complex coupling reactions in a one-pot procedure. A similar reaction on protective group-free *bis*-vinyl iodide **216** was already performed by K. C. Nicolaou in the total synthesis of rapamycin (**218**) to simultaneously introduce the triene moiety and close the macrocycle (Scheme 3.27 **B**).[139,140] However, the fragments of pentamycin are very different from those used by Nicolaou. Polyol fragment **147** contains ten free hydroxy functions, resulting in a much more polar molecule. Trienyl-*bis*-stannane **148** contains three instead of one double bond and is highly unpolar, so solubility of both substrates may be more challenging.

## 3.3 Development of a Synthetic Route towards Pentamycin

This chapter presents the detailed development of synthetic routes for the four fragments and their coupling to ultimately create an efficient route to pentamycin. Furthermore, the appropriateness of certain reactions for particular problems is discussed, as well as dead ends during synthetic work and reaction optimization. Importantly, conditions of most of the reactions used in the final, successful synthetic route are not discussed in detail within this chapter, they are presented in Chapter 4.

### 3.3.1 Western Fragment

Western fragment **153** is rather small; however, it brings certain synthetic complexity. One challenge to address here is the orthogonal protection of the two hydroxy functions which enables selective cleavage of the protecting group at C27 before coupling of the western fragment to the rest of the molecule. This can be accomplished by the PMB protective group which could be cleaved in the last step of the fragment synthesis with DDQ in the presence of a vinyl iodide. Since the general protecting group concept requires an exclusively acetonide and TBS-protected molecule at the end (Chapter 3.1.3, pp. 37–38), TBS was set as the protecting group on the hydroxy function of C26.

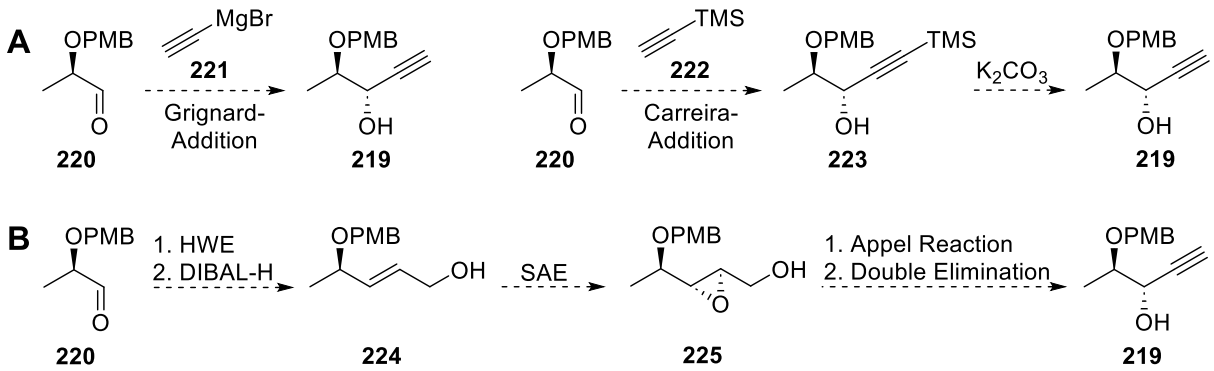



Scheme 3.28: Retrosynthetic analysis of western fragment **153.**

The vinyl iodide was introduced by hydrozirconation of the alkyne of propargylic alcohol **219** after TBS-protection using Schwartz reagent with subsequent iodination of the organozirconium intermediate (Scheme 3.28).[141] Another challenge was the creation of the propargylic alcohol motif in a 1,2-*anti*-fashion related to the PMB-protected hydroxy function at C27. Thus, compound **219** serves as the central building block, with three steps left, i.e., TBS-protection, hydrozirconation/iodination, and PMB-deprotection to obtain western fragment **153**.

Two paths are available to access propargylic alcohol **219** from aldehyde **220**. The first method involves adding a nucleophile, containing the alkyne moiety to the aldehyde, which can achieve the desired transformation in one or two steps. The simplest reaction is a Grignard addition of ethynylmagnesium bromide (**221**). Another possibility is the above discussed (Chapter 3.2.4, pp. 48–50) Carreira addition which is assumed to enable stereoselective addition of TMS-acetylene (**222**) to aldehyde **220** leading to alcohol **219** after deprotection of alkyne **223** (Scheme

3.29 **A**). The second method is the synthesis of propargylic alcohols from Sharpless epoxides, as discussed earlier (Chapter 3.2.2, pp. 44–46). However, this sequence requires more steps. Aldehyde **220** can be converted into propargylic alcohol **219** through a five-step process involving HWE reaction and DIBAL-H reduction to obtain allylic alcohol **224**, SAE to produce Sharpless epoxide **225**, and finally Appel reaction, and double elimination (Scheme 3.29 **B**).




Scheme 3.29: Possible paths to access propargylic alcohol **219**. **A**: Carbonyl addition reactions. **B**: Five-step sequence consisting of HWE-reaction, DIBAL-H reduction, SAE, Appel reaction, and double elimination.

At first glance, Grignard addition should be the most efficient method due to less steps for achieving the desired transformation, but stereoselectivity is problematic here. The desired 1,2-*anti* motif reflects the Felkin-Anh product **226** of carbonyl addition (Figure 3.11 **A**). However, Grignard conditions will lead to the 1,2-*syn* motif, i.e., the *anti*-Felkin-Ahn product **227** or Cram-chelate, for given substrate **220**. (Figure 3.11 **B**).[142] Figure 3.11 shows the transition states of both, the Felkin-Anh product (**I**) and the Cram-chelate (**II**). For both models, the aldehyde function is approached by the nucleophile according to the Bürgi-Dunitz angle of about 107° from the less hindered site.[143]

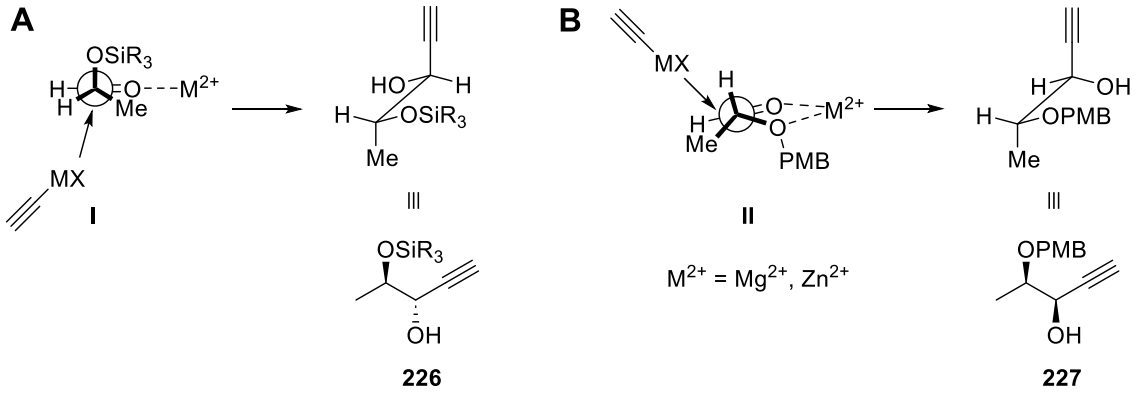
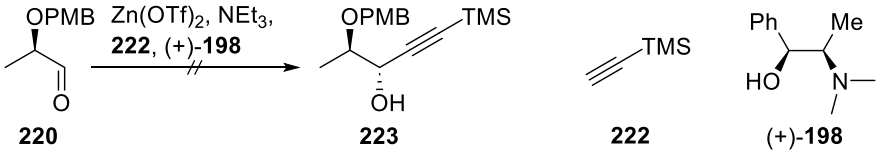



Figure 3.11: Possible carbonyl additions depending on the protective group. **A**: Felkin-Anh transition state in case of a bulky, non-coordinating silyl protective group; **B**: Cram-chelate transition state in case of a coordinating PMB-group.[144]

In case of a bulky silyl protective group (Figure 3.11 **A**) Felkin-Anh product **226** would be the major product of the Grignard addition. However, the necessity of PMB-protection at the hydroxy function of C27 due to required orthogonal protection leads to coordination of $Mg^{2+}$-ions between the PMB-ether and the carbonyl function.[145] The corresponding transition state would be a Cram-chelate and the anti-Felkin-Anh **227** product would be the major product (Figure 3.11 **B**).[144]

The thorough analysis of the stereochemical course of this Grignard addition to aldehyde **220** revealed that the desired transformation would not be achieved. Since the wrong diastereomer **227** is the expected product, the reaction was not conducted. However, it was thought that a chiral ligand could solve this problem, so Carreira addition of TMS-acetylene **222** to aldehyde **220** with chiral ligand (+)-*N*-methylephedrine (+)-(**198**) was considered (Scheme 3.30). Nevertheless, the reaction led to a mixture of diastereomers, so most probably formation of the required transition state discussed in Chapter 3.2.4 (pp. 49–50) competes with formation of a Cram-chelate, since $Zn^{2+}$ has a strong tendency to do so.[142] Furthermore, weakly coordinating solvents such as toluene, required for the Carreira addition, promote the chelation of $Zn^{2+}$ and the OPMB and aldehyde function of substrate **220**, leading to a product mixture.[144]

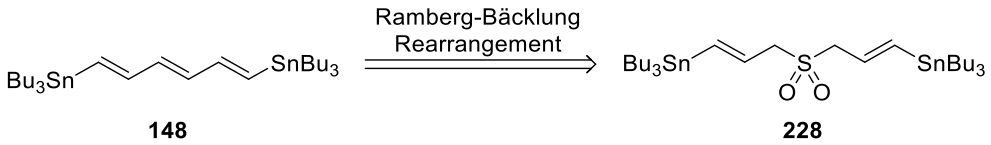



Scheme 3.30: Attempted Carreira addition of TMS-acetylene (**222**) to aldehyde **220**.
Reaction conditions: $Zn(OTf)_2$, (+)-**198**, $NEt_3$, toluene, rt, 2 h, then **222**, rt, 15 min, then **220**, rt, 5 h, no product isolated.

The unsuccessful Carreira addition and the Grignard addition unsuitable for the given substrate necessitated the use of the second strategy presented above although it consists of more steps. This sequence could be successfully used to synthesize propargyl alcohol **219** as the central building block (discussed in detail in Chapter 4).

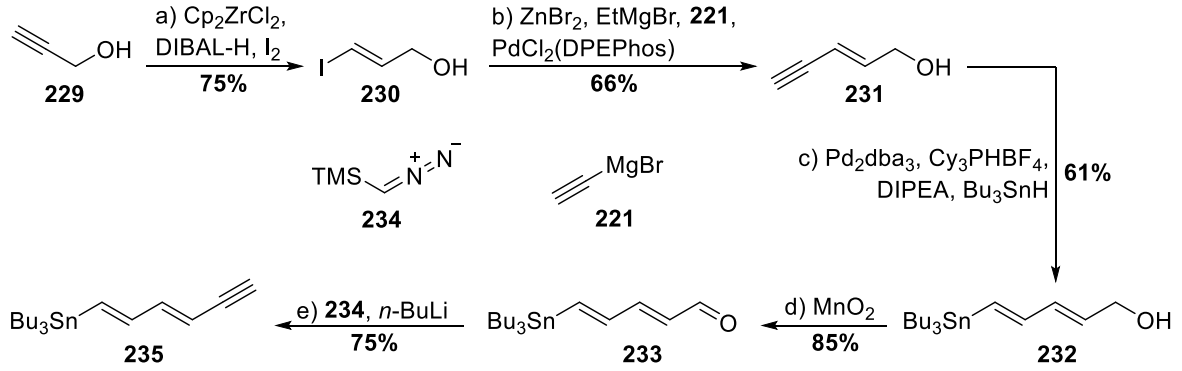
### 3.3.2 Southern Fragment

The southern fragment should introduce the polyene part of pentamycin to the polyol framework, as discussed in the retrosynthetic analysis (Chapter 3.1, p. 32). Trienyl-*bis*-stannane **148** as the southern fragment was synthesized by a procedure reported by Brückner (Scheme 3.31),[126] with the key step being a Ramberg-Bäcklund rearrangement of sulfone **228** (Chapter 3.2.6, pp. 52–53). The detailed synthesis is discussed in Chapter 4.



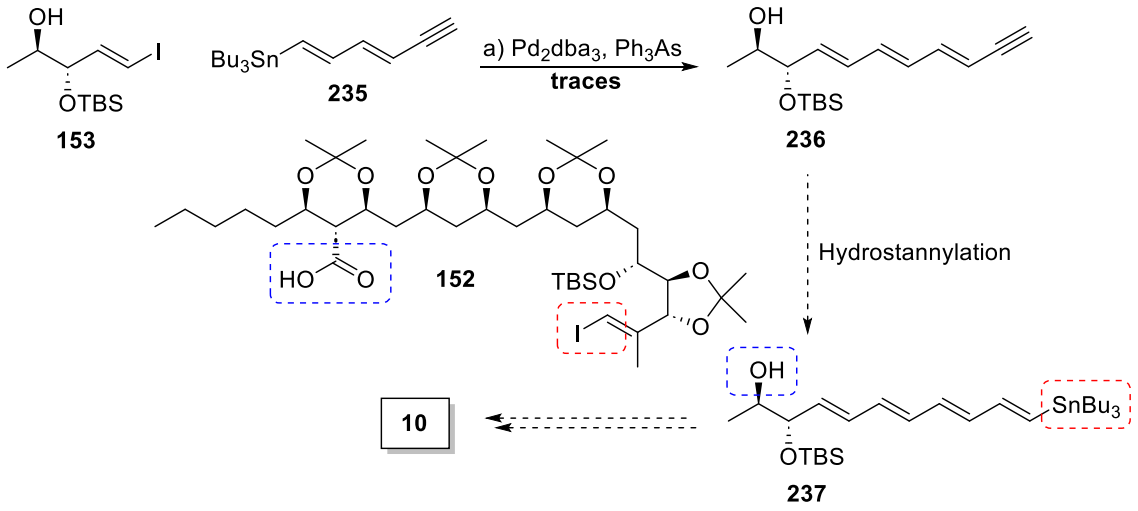

Scheme 3.31: Ramberg-Bäcklund rearrangement of sulfone **228** as key step in the synthesis of trienyl-*bis*-stannane **148** as the southern fragment of pentamycin.

Another approach was tested in parallel, which was not discussed in the retrosynthesis chapter above. The objective was to connect western fragment **153** with a fragment containing the polyene moiety of pentamycin as an alternative in case the double Stille coupling at the end would not succeed. Therefore, vinyl stannane **235** was synthesized starting from propargylic alcohol (**229**). Hydrozirconation with *in situ* generated Schwartz' reagent afforded vinyl iodide **230** and Negishi conditions led to terminal alkyne **231** (Scheme 3.32).[146] Palladium-catalyzed hydrostannylation gave vinyl stannane **232** and the allylic alcohol could be oxidized with $MnO_2$.[147] Aldehyde **233** was then homologated using the lithium salt of trimethylsilyl diazomethane (**234**) to generate the terminal alkyne of vinyl stannane **235**.[148]




Scheme 3.32: Synthesis of vinyl stannane **235**, representing an alternative polyene fragment of pentamycin.
Reaction conditions: a) 1st flask: $Cp_2ZrCl_2$, DIBAL-H, THF, 0 °C, 30 min, 2nd flask: **229**, DIBAL-H, −78 °C, then rt, 30 min, then 2nd flask in 1st flask, rt, 2 h, then −78 °C, $I_2$, 30 min, **75%**; b) 1st flask: $ZnBr_2$, EtMgBr, THF, 0 °C, 30 min, then **230**, 0 °C, 30 min, 2nd flask: $ZnBr_2$, **221**, THF, 0 °C, 30 min, then 2nd flask in 1st flask, $PdCl_2$(DPEphos), DMF, rt, 12 h, **66%**; c) $Pd_2dba_3$, $Cy_3PHBF_4$, DIPEA, DCM, rt, 10 min, then **231**, 0 °C, $Bu_3SnH$, 2 h, then rt, 2 h, **61%**; d) $MnO_2$, DCM, rt, 5 h, **85%**; e) **234**, *n*-BuLi, THF, −78 °C, 30 min, then **233**, −78 °C, 1 h, then 0 °C, 1 h, **75%**.

The vinyl stannane function of compound **235** was then attempted to be coupled to the vinyl iodide of western fragment **153** by a Stille coupling (Scheme 3.33).[149] The consumption of vinyl iodide **153** and formation of a new compound was observed by TLC analysis. Mass spectrometric analysis confirmed the presence of coupling product **236**, which was the only compound present detected by TLC after 4 h. However, workup and purification led to degradation of the product, so NMR analysis to ultimately confirm the structure of **236** was not possible.

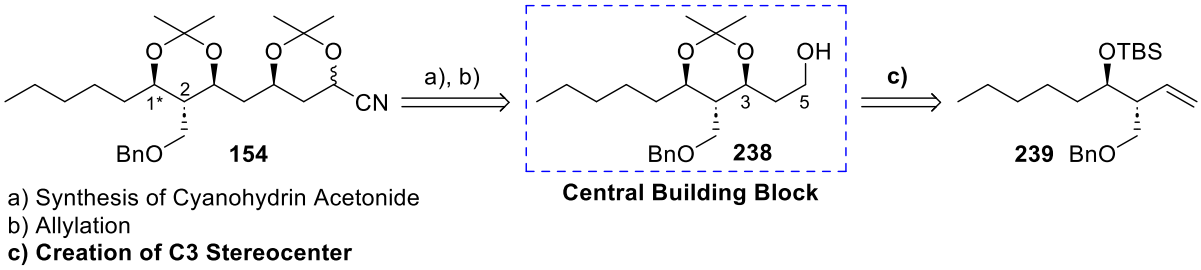



Scheme 3.33: Coupling of western fragment **153** to vinyl stannane **235**, and potential further steps towards pentamycin (**10**).
Reaction conditions: a) $Pd_2dba_3$, $Ph_3As$, DMF, rt, 4 h, no product isolated, detection by MS.

In the case of a stable compound **236**, its alkyne function was planned to be hydrostannylated to form vinyl stannane **237**. Coupling could then occur either through the secondary hydroxy function to the carboxylic acid of **152** by esterification (marked in blue), or by Stille coupling of the vinyl stannane to the vinyl iodide moiety (marked in red). The respective other step would then accomplish ring closure and global deprotection would be the final step in this route. However, the instability of compound **236** precludes this approach and supports the idea that the double Stille coupling might be the most expedient solution.

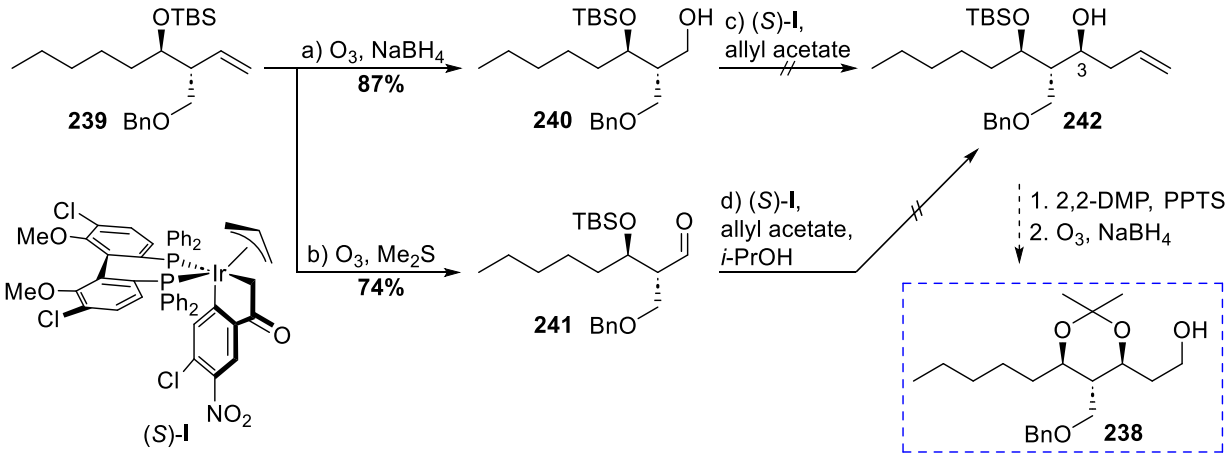
### 3.3.3 Northern Fragment

The northern fragment **154** contains the pentyl side chain of pentamycin and incorporates five stereocenters. Four of them are set during fragment synthesis while the fifth is created during coupling to eastern fragment **163**. Scheme 3.34 shows the key steps in the synthesis of northern fragment **154**. Synthesis of protected 1,3-diol **239** can be accomplished by Krische chemistry (Chapter 3.2.1, pp. 41–44) to create the stereocenters at C1* and C2 and thus a suitable substrate for the creation of the stereocenters at C3.[96]




Scheme 3.34: Retrosynthetic analysis of northern fragment **154**.

During synthesis of the northern fragment **154**, the main challenge was the synthesis of primary alcohol **238** as the central building block in the route from protected 1,3-diol **239**. Four routes were tested to create the stereocenter at C3 and access central building block **238** from protected 1,3-diol **239**. Key steps include a Sharpless asymmetric dihydroxylation (SAD), a Krische allylation, a Carreira addition, or a Brown allylation.[72,82,84,150]

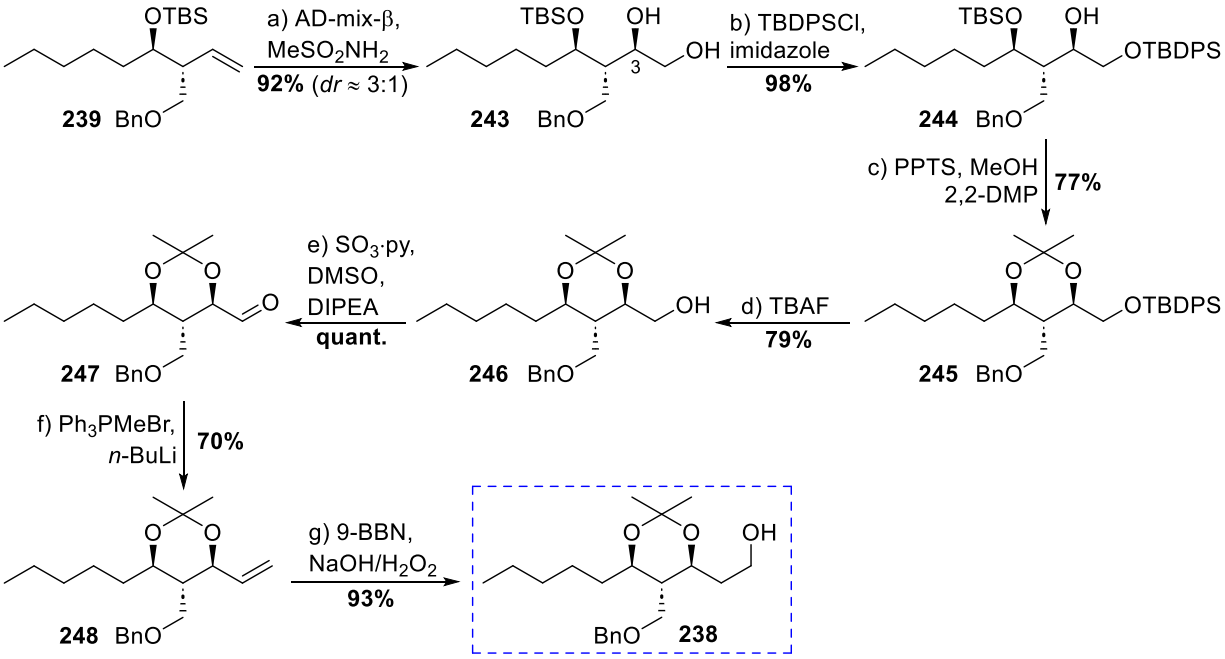



Scheme 3.35: Attempt to access central building block **238** by Krische allylation.
Reaction conditions: a) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 16 h, **87%**; b) $O_3$, DCM/MeOH (1:1), −78 °C, then $Me_2S$, −78 °C, 2.5 h, **74%**; c) (*S*)-**I**: $[Ir(COD)Cl]_2$, (*S*)-Cl,MeO-BIPHEP (**176**), 4-chloro-3-nitrobenzoic acid, $Cs_2CO_3$; allyl acetate, THF, 110 °C, 48 h, decomposition; d) (*S*)-**I**: $[Ir(COD)Cl]_2$, (*S*)-Cl,MeO-BIPHEP (**176**), 4-chloro-3-nitrobenzoic acid, $Cs_2CO_3$; allyl acetate, *i*-PrOH, THF, 110 °C, 48 h, decomposition.

The initial attempt to generate homoallylic alcohol **242** involved Krische allylation with *in situ* generated catalyst (*S*)-**I** and with allyl acetate (**178**) as the allyl donor (Scheme 3.35).[82] However, primary alcohol **240**, obtained from protected diol **239** by ozonolysis with subsequent $NaBH_4$-reduction, proved to be unstable under the required conditions. Just a significant amount of degradation products was detected during reaction control by TLC. The same was observed for the corresponding aldehyde **241**, so neither alcohol **240** nor aldehyde **241** were considered as starting materials for accessing central building block **238**.

The second approach utilized the terminal olefin of protected diol **239** as a reactive group for an SAD with AD-mix-*β* to create the C3 stereocenter through stereoselective dihydroxylation (Scheme 3.36). Despite the excellent yield of 92%, the selectivity of only 3:1 in favor of the desired isomer **243** was deemed insufficient. However, the route was pursued as the isomers were easily separable by flush chromatography. The primary hydroxy function of diol **243** was protected by using the bulky TBDPS protective group, resulting in the silyl ether **244**. Acetonide **245** was obtained in good yield over two steps by cleaving the secondary TBS group in the presence of the primary TBDPS group with PPTS and direct acetonide protection. The TBDPS group was then cleaved with TBAF, and the resulting primary alcohol **246** was oxidized under Parikh-Doering conditions to furnish aldehyde **247**. The aldehyde was transformed to terminal

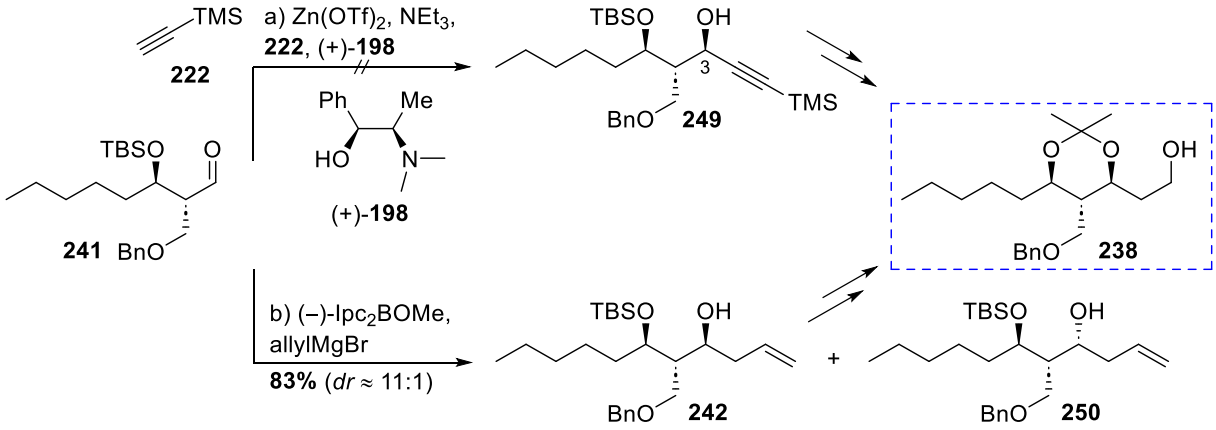
olefin **248** by a Wittig reaction[151] and the central building block **238** was finally obtained by hydroboration with 9-BBN.[152]




Scheme 3.36: Synthesis of central building block **238** by SAD.
Reaction conditions: a) AD-mix-*β*, $MeSO_2NH_2$, *t*-BuOH/$H_2O$ (1:1), rt, 48 h, **92%** (*dr* ≈ 3:1); b) TBDPSCl, imidazole, DCM, 0 °C, 30 min, **98%**; c) PPTS, MeOH, rt, 22 h, then 2,2-DMP, DCM, rt, 40 °C to rt, 1 h, **77%**; d) TBAF, THF, 0 °C, 2 h, **79%**; e) $SO_3$·py, DMSO, DIPEA, DCM, 0 °C, 20 min, **quant.**; f) $Ph_3PMeBr$, *n*-BuLi, THF, −78 °C, then 0 °C, 30 min, then **257**, 0 °C, 1 h, **70%**; g) 9-BBN, THF, 0 °C, 90 min, then rt, 2.5 h, then 0 °C, NaOH, $H_2O_2$, 20 min, **93%**.

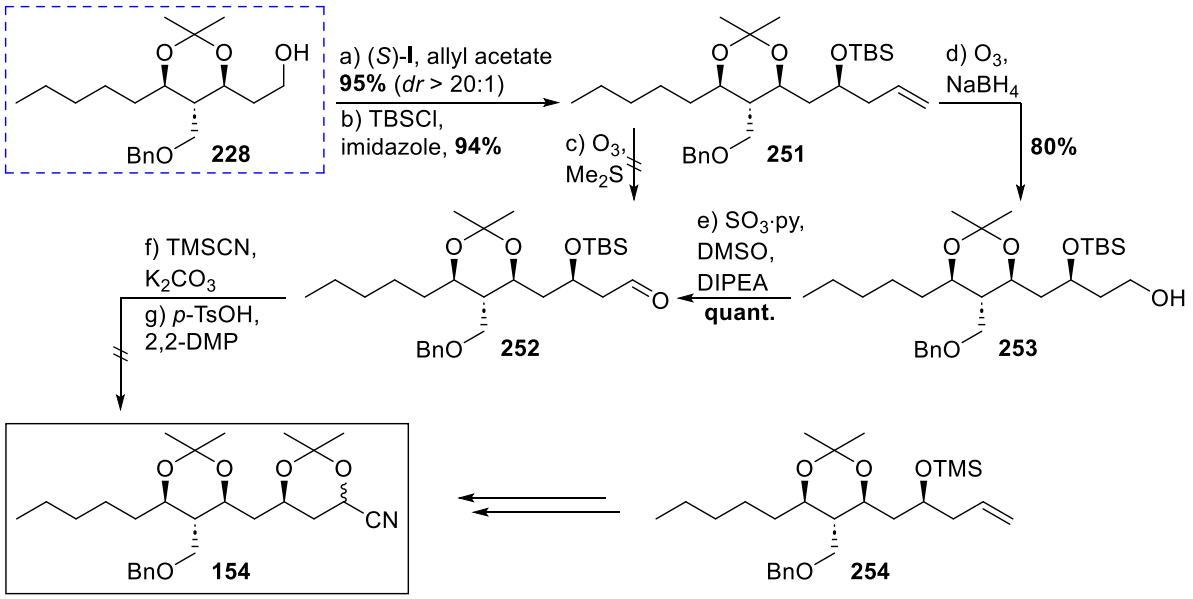
However, the sequence of seven steps to convert protected diol **239** into central building block **238** is rather lengthy. Additionally, due to the poor selectivity of the SAD, it was decided that this route was not suitable for further conversion. As aldehyde **241** appears to be thermally unstable, two alternative reactions were tested that operate at lower temperatures than the Krische allylation (Scheme 3.37). The first reaction used aldehyde **241** as a substrate for a Carreira addition of TMS-acetylene (**222**) to create the C3 stereocenter.[72] The propargylic alcohol **249** was intended to be protected as an acetonide after combined cleavage of the silyl protecting groups at the hydroxy function at C1* and the alkyne. Lindlar-hydrogenation of the alkyne would yield terminal olefin **248** which was already generated by Wittig reaction earlier. As demonstrated in Scheme 3.36, hydroboration with 9-BBN would yield central building block **238**. However, no conversion of aldehyde **241** was observed under the stated conditions (Scheme 3.37), and the substrate was reisolated. Finally, Brown allylation was successful which provided homoallylic alcohol **242** in a good yield of 83% and a good selectivity (Scheme 3.37).[84] The corresponding 1,3-*anti* diastereomer **250** could be separated by flush chromatography so 1,3-*syn* isomer **242** was accessible in high purity. Cleavage of the TBS group

under slightly acidic conditions with simultaneous acetonide protection and subsequent ozonolysis furnished central building block in just three steps.




Scheme 3.37: Attempted generation of propargylic alcohol **249** by Carreira addition and finally successful synthesis of central building block **238** by Brown allylation.
Reaction conditions: a) $Zn(OTf)_2$, (+)-**198**, $NEt_3$, toluene, rt, 2 h, then **222**, rt, 15 min, then **241**, rt, 14 h, no conversion; b) (−)-Ipc2BOMe, allylMgBr, $Et_2O$, 0 °C, 1 h, then **241**, −78 °C, 1 h, then $NaOH/H_2O_2$, **83%** (*dr* ≈ 11:1).

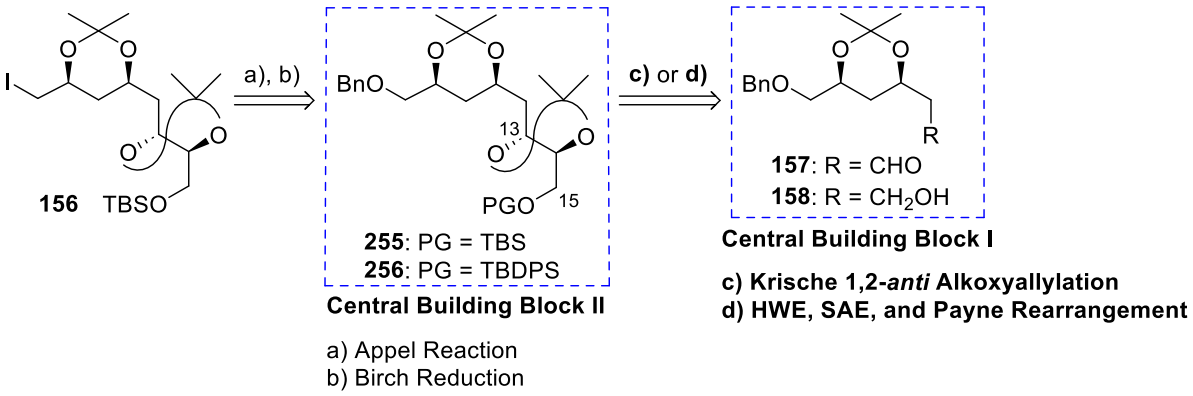
Proceeding from central building block **238**, two key steps remained: creating the stereocenter at C5 and synthesizing the cyanohydrin acetonide (Scheme 3.34). To achieve this, the primary alcohol **238** was allylated under Krische conditions with allyl acetate (**178**), and the resulting homoallylic alcohol was protected as a TBS-ether **251** (Scheme 3.38).[153] The terminal double bond should be oxidatively cleaved to obtain an aldehyde. However, ozonolysis and subsequent treatment with $Me_2S$ did not yield the desired aldehyde **252**. Various degradation products, most likely ozonides, were detected on the TLC even after stirring overnight. The solution was then treated with $NaBH_4$ to obtain the primary alcohol **253**, which was subsequently oxidized to aldehyde **252** under Parikh-Doering conditions. Finally, TMSCN was successfully added to the aldehyde as reaction monitoring by TLC indicated, but the formation of the acetonide was not possible.[154] The TBS group could not be cleaved under the required conditions, and treatment with TBAF led to substrate decomposition. A different protective group strategy was employed, with TMS-protection of the hydroxy function at C5. Starting from the TMS-ether **254**, the northern fragment **154** was obtained in three steps, as detailed in Chapter 4.




Scheme 3.38: Problems in the final steps of the synthesis of northern fragment **154**.
Reaction conditions: a) (*S*)-**I**: $[Ir(COD)Cl]_2$, (*S*)-Cl,MeO-BIPHEP (**176**), 4-chloro-3-nitrobenzoic acid, $Cs_2CO_3$; allyl acetate, THF, 110 °C, 48 h, **95%** (*dr* > 20:1); b) TBSCl, imidazole, DCM, rt, 6 h, **94%**; c) $O_3$, DCM/MeOH (1:1), −78 °C, then $Me_2S$, −78 °C to rt, 16 h, no product isolated; d) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 16 h, **80%**; e) $SO_3$·py, DMSO, DIPEA, DCM, 0 °C, 20 min, **quant.**; f) TMSCN, $K_2CO_3$, DMF, rt, 30 min; g) PPTS, MeOH, rt, 24 h, no deprotection.

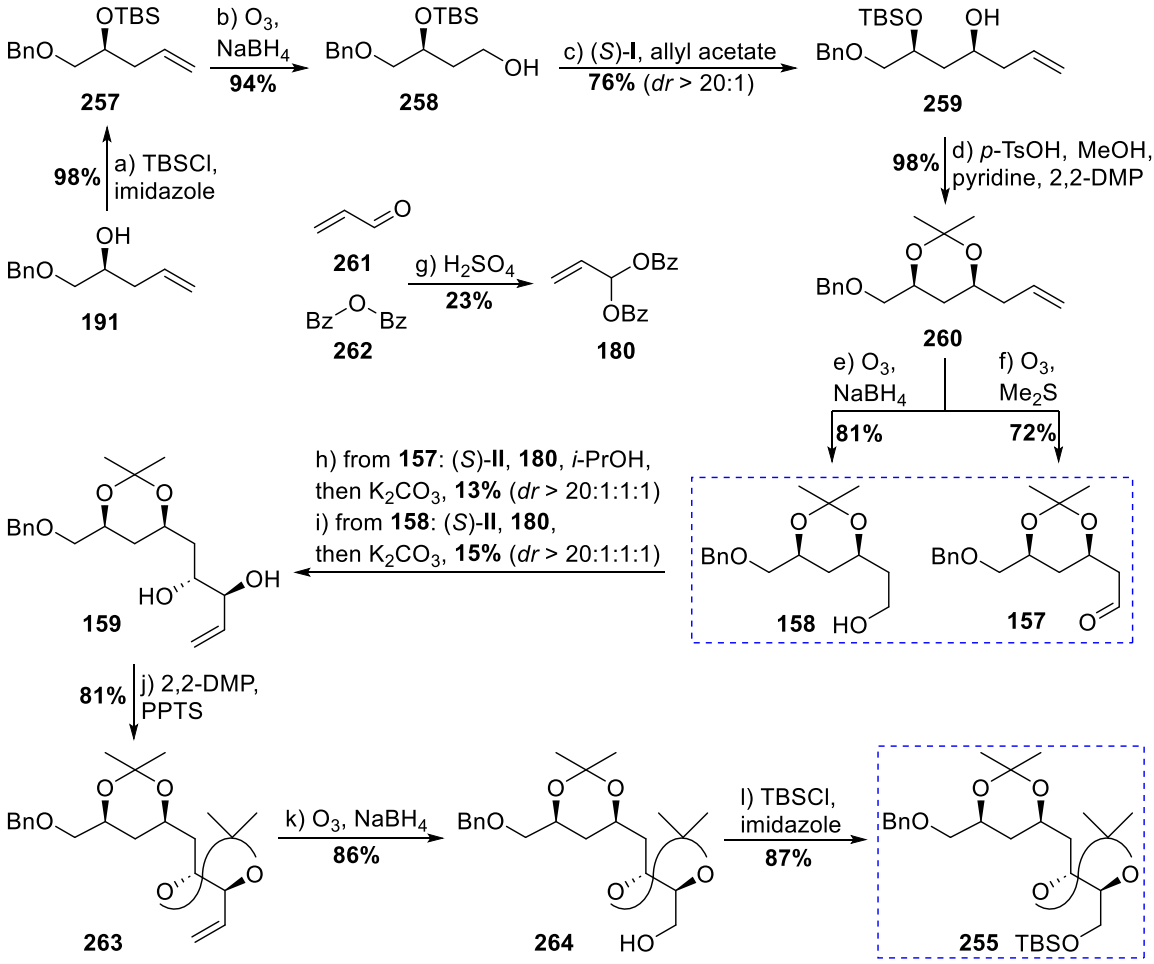
## 3.3.4 Eastern Fragment and Coupling with the Northern Fragment

The significant structural motif of the eastern part of pentamycin is the 1,2,3-triol moiety of C13-C15. First, the linear approach towards eastern fragment I **156** is discussed, which is later rejected in favor of the convergent approach to eastern fragment II **163**. The retrosynthetic analysis of eastern fragment I **156** results in two central building blocks (Scheme 3.39). Central building block I **157** or **158** is the starting material for either a Krische 1,2-*anti* alkoxyallylation or for a sequence consisting of HWE-reaction, SAE, and Payne rearrangement leading to central building block II **255** or **256**.[73,74,155]




Scheme 3.39: Retrosynthetic analysis of eastern fragment I **156**.

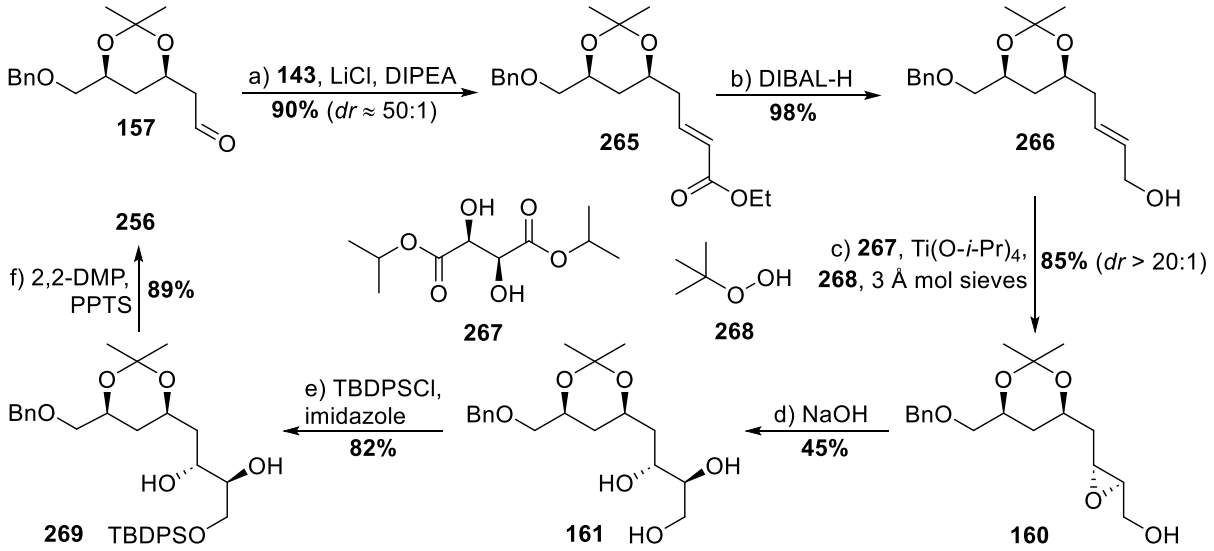
The synthesis of central building block I started from homoallylic alcohol **191** which was obtained from the above discussed cobalt-catalyzed epoxide olefination (Chapter 3.2.3, pp. 47–48).[111] TBS-protection gave TBS ether **257** and ozonolysis cleaved the terminal double bond to obtain primary alcohol **258** (Scheme 3.40). A Krische allylation was then used to generate homoallylic alcohol **259** with moderate yield and excellent selectivity. In a one-pot procedure, TBS deprotection with *p*-TsOH took place, which was followed by acetonide formation of **260** after buffering with pyridine and addition of 2,2-DMP. Subsequent ozonolysis cleaved the terminal olefin and depending on the reduction agent either alcohol **158** or aldehyde **157** were obtained as central building block I.[153]




Scheme 3.40: Synthesis of aldehyde **157** and alcohol **158** as central building block I and their transformation to central building block II **255** by Krische's 1,2-*anti* alkoxyallylation.
Reaction conditions: a) TBSCl, imidazole, DCM, rt, 6 h, **98%**; b) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 16 h, **94%**; c) (*S*)-**I**: $[Ir(COD)Cl]_2$, (*S*)-Cl,MeO-BIPHEP (**176**), 4-chloro-3-nitrobenzoic acid, $Cs_2CO_3$; allyl acetate, THF, 110 °C, 48 h, **76%** (*dr* > 20:1); d) *p*-TsOH, MeOH, rt, 90 min, then 2,2-DMP, rt, 1 h, then evaporation, 2,2-DMP, pyridine, **98%**; e) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 3 h, **81%**; f) $O_3$, DCM/MeOH (1:1), −78 °C, then $Me_2S$, −78 °C, 2.5 h, **72%**; g) **262**, conc. $H_2SO_4$, DCM, then **261**, rt, 24 h, **23%**; h) (*S*)-**II**, **180**, $K_3PO_4$, *i*-PrOH, THF, 60 °C, 48 h, then MeOH, $K_2CO_3$, rt, 20 h, **13%** (*dr* > 20:1:1:1); i) (*S*)-**II**, **180**, THF, 90 °C, 48 h, then MeOH, $K_2CO_3$, rt, 20 h, **15%** (*dr* > 20:1:1:1); j) 2,2-DMP, PPTS, rt, 30 min, **81%**; k) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 3 h, **86%**; l) TBSCl, imidazole, DCM, rt, 5 h, **87%**.

Both compounds **157** and **158** were used in a Krische 1,2-*anti* alkoxyallylation with catalyst (*S*)-**II** (see Scheme 3.11) and allylic-*gem*-dicarboxylate **180** as allyl donor (Scheme 3.40).[73] Compound **180** was synthesized from benzoic anhydride (**262**) and acrolein (**261**) by treatment with concentrated sulfuric acid. The poor yield of only 23% wasn't an issue here since both compounds are cheap commodity chemicals. However, both substrates, aldehyde **157** and alcohol 1**58** gave poor yields of 13 and 15% respectively. Nevertheless, compound **159** was the only isolated product, so the selectivity was considered to be very good. Next, the 1,2-*anti* diol was protected as acetonide **263**, followed by ozonolysis of the terminal olefin with reductive workup to afford primary alcohol **264**. After TBS protection, central building block II **255** was obtained in four steps from central building block I, but the yield of the overall sequence, especially of the 1,2-*anti* alkoxyallylation was not sufficient for continuing with that route.

Instead, another strategy was tested, with aldehyde **157** being transformed to *α*,*β*-unsaturated ester **265** by HWE reaction under Masamune-Roush conditions (Scheme 3.41).[156] Reduction with DIBAL-H produced allylic alcohol **266** which was utilized as starting material for an SAE. Sharpless epoxide **160** was obtained in good yield and selectivity and was subjected to undergo a Payne rearrangement induced by aqueous NaOH (Chapter 3.2.2, pp. 46–47).[74,155] The yield was rather low, with 45% being the best result achieved by heating the reaction mixture to 70 °C for 40 h. Nevertheless, enough material could be synthesized to protect the primary hydroxyl function of triol **161** with the bulky TBDPS protective group to obtain diol **269**, and acetonide formation of the 1,2-*anti* diol gave central building block II **256**.

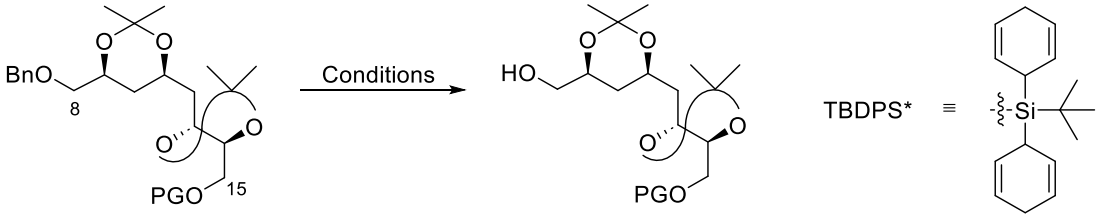



Scheme 3.41: Synthesis of central building block II **256** from aldehyde **157** by Payne rearrangement of Sharpless epoxide **160**.
Reaction conditions: a) **143**, LiCl, DIPEA, MeCN, 0 °C to rt, 3 h, **90%** (*dr* ≈ 50:1); b) DIBAL-H, DCM, −78 °C, 30 min, **98%**; c) (−)-DIPT (**267**), 3 Å molecular sieves, DCM, 30 min, then Ti(O-*i*-Pr)$_4$, *t*-BuOOH (**268**), −30 °C, 30 min, then **266**, 16 h, **85%** (*dr* > 20:1); d) aqueous NaOH, dioxane, 70 °C, 40 h, **45%**; e) TBDPSCl, imidazole, 0 °C, 1 h, **82%**; f) 2,2-DMP, PPTS, rt, 1 h, **89%**.

The relatively low yield of the Payne rearrangement also does not make this route the ideal strategy to produce the eastern fragment on a large scale for the multi-step synthesis of pentamycin. However, once the central building blocks II **255** and **256**, depending on the protecting group at C15, were available, the final steps to produce eastern fragment I **156** were initiated. First, the benzyl group at the C8 hydroxy function had to be cleaved before the resulting alcohol could be converted to the alkyl iodide and thus to the eastern fragment I **156**.

Various conditions for benzyl cleavage were tested (Table 3.2). Hydrogenolysis with catalytic palladium on charcoal led to decomposition of both molecules **255** and **256**, before benzyl cleavage was completed (entries 1 and 4). Lewis acidic cleavage with $BCl_3$-dimethyl sulfide complex also cleaved the acetonides and the silyl ether beside the benzyl protective group (entries 2 and 5).[157] Since the molecule was to be exposed to Birch conditions after coupling with the northern fragment **154** later in the synthesis, the benzyl cleavage under these conditions was already taken into account in the current step.[51] Since benzyl cleavage under Birch conditions relies on partial hydrogenation of the aromatic system, the phenyl rings of the TBDPS group were also reduced and unusual silyl ether **270** was generated in 70% yield (entry 3). However, benzyl deprotection of both substrates worked quite well, for the TBS-protected substrate **255** even in a quantitative yield of compound **271** (entry 6).

Table 3.2: Screening of conditions for the cleavage of the benzyl group at the C8 hydroxy function of central building blocks II **255** and **256** in the synthesis of eastern fragment I **156**.



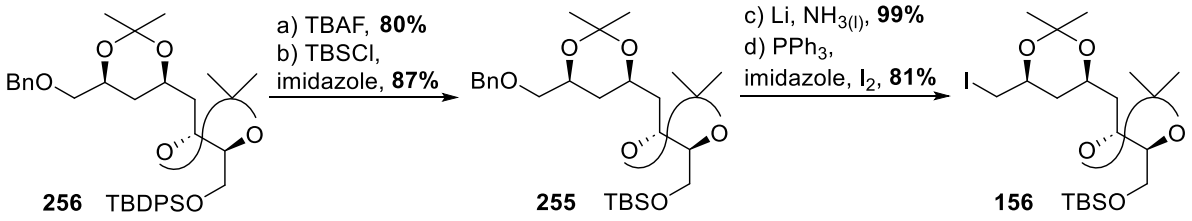

**256**: PG = TBDPS
**255**: PG = TBS

**270**: PG = TBDPS*
**271**: PG = TBS

| # | Conditions | Compound | Result/Yield |
|---|---|---|---|
| **1** | $H_2$, Pd/C, MeOH, rt, 3 h | **256** | Decomposition |
| **2** | $BCl_3 \cdot Me_2S$, DCM, 0 °C, 30 min | | Complete deprotection |
| **3** | Li, $NH_{3(l)}$, THF, −78 °C, 1 h | | **70%** of **270** |
| **4** | $H_2$, Pd/C, MeOH, rt, 3 h | **255** | Decomposition |
| **5** | $BCl_3 \cdot Me_2S$, DCM, 0 °C, 30 min | | Complete deprotection |
| **6** | Li, $NH_{3(l)}$, THF, −78 °C, 1 h | | **99%** of **271** |

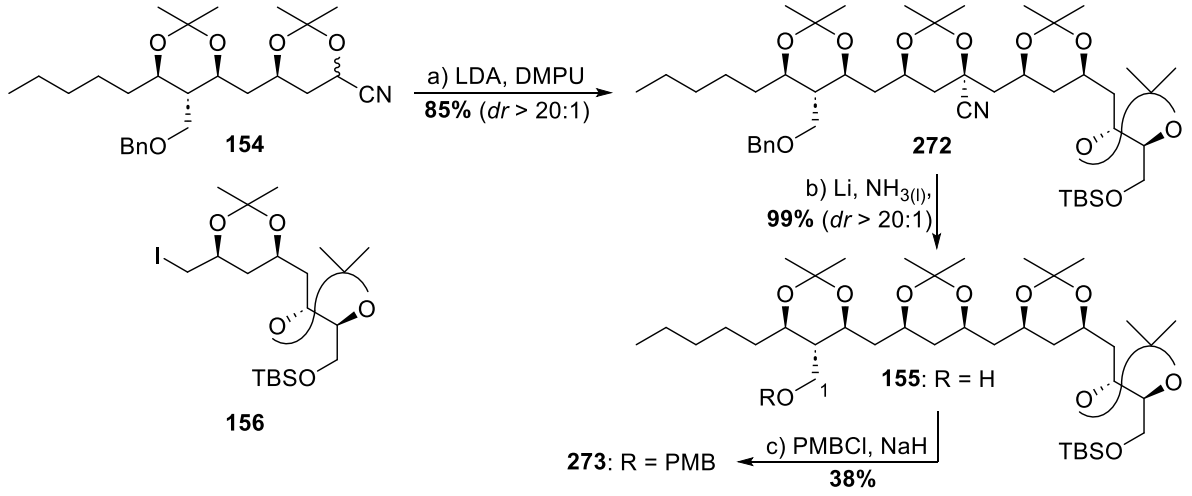
The reduced phenyl rings make the NMR spectra of compound **270** very confusing and lead to the overlap of signals. Thus, the TBDPS group was changed to a TBS group to facilitate

NMR-analysis of the following compounds, furthermore, the yield of the Birch reduction was better for the TBS protected substrate **255**. Therefore, compound **256** was treated with TBAF and resulting primary alcohol **264** was protected as TBS ether **255** (Scheme 3.42). After benzyl cleavage the primary hydroxy function was exchanged to an iodine by Appel reaction and eastern fragment I **156** was obtained.



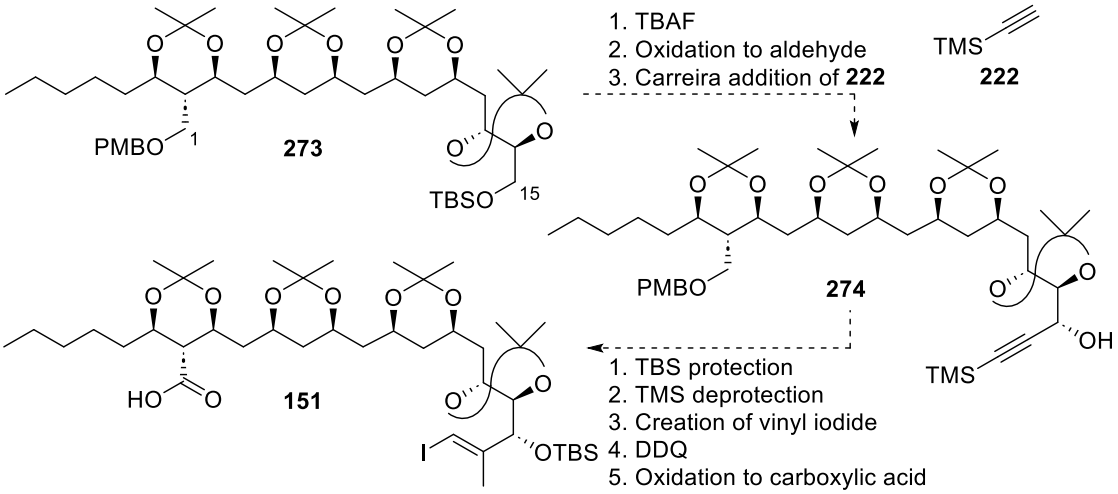

Scheme 3.42: Protective group exchange of **256** to **255** and finalization of the synthesis of the eastern fragment I **156**.
Reaction conditions: a) TBAF, THF, 0 °C to rt, 2 h, **80%**; b) TBSCl, imidazole, DCM, rt, 5 h, **87%**; c) Li, liquid $NH_3$, THF, −78 °C, 1 h, **99%**; d) $PPh_3$, imidazole, $I_2$, benzene, rt, 1 h, **81%**.

Although that route is still not good enough to prepare the eastern fragment of pentamycin in a reliable manner, due to the bad yield of the Payne rearrangement, Rychnovsky coupling of eastern fragment I **156** to northern fragment **154** was tested (Scheme 3.43).[51] A mixture of both fragments was treated with freshly prepared LDA in THF with DMPU as co-solvent at −40 °C and coupling product **272** was obtained in good yield and selectivity. Birch reduction to afford **155** proceeded in quantitative yield and the above discussed excellent selectivity (Chapter 3.2.5, pp. 50–52). To continue the synthesis towards carboxylic acid **151** the free hydroxy function at C1 had to be protected. Formation of a PMB ether was attempted, but the formation of several side products led to a poor yield of 38% for the desired product **273** (Scheme 3.43).



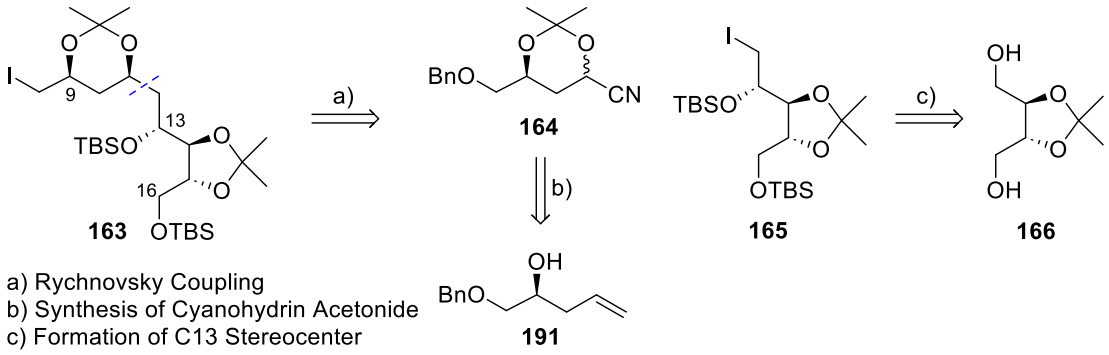

Scheme 3.43: Test coupling of eastern fragment I **156** to northern fragment **154** by Rychnovsky coupling. Reaction conditions:
a) LDA, DMPU, THF, −40 °C, 1 h, **85%** (*dr* > 20:1); e) Li, liquid $NH_3$, THF, −78 °C, 1 h, **99%** (*dr* > 20:1); c) PMBCl, NaH, DMF, 0 °C, 2 h, **38%**.

Future steps in this route could include cleavage of the TBS ether at the C15 hydroxy function, oxidation to the aldehyde, and Carreira addition of TMS acetylene (**222**) to afford the propargylic alcohol **274** (Scheme 3.44). Subsequent TBS protection and deprotection of the alkyne would provide a substrate for the formation of an *α*-methyl vinyl iodide motif. Deprotection of the PMB group at C1 and oxidation of the primary hydroxy function to the carboxylic acid would afford carboxylic acid **151**.




Schem 3.44: Further steps if the route with eastern fragment I **156** had been pursued further.

The yield issues discussed above and the small amount of material remaining after Birch reduction (54 mg of alcohol **155**) and PMB protection (20 mg of compound **273**) led to the rejection of this route and the development of a new one. However, several ideas and compounds developed yet were integrated into the new strategy. Since the Rychnovsky coupling between the northern **154** and the eastern fragment I **156** gave excellent results, it was decided to integrate this coupling as a key step in the new, convergent route towards the eastern part of pentamycin (Scheme 3.45).

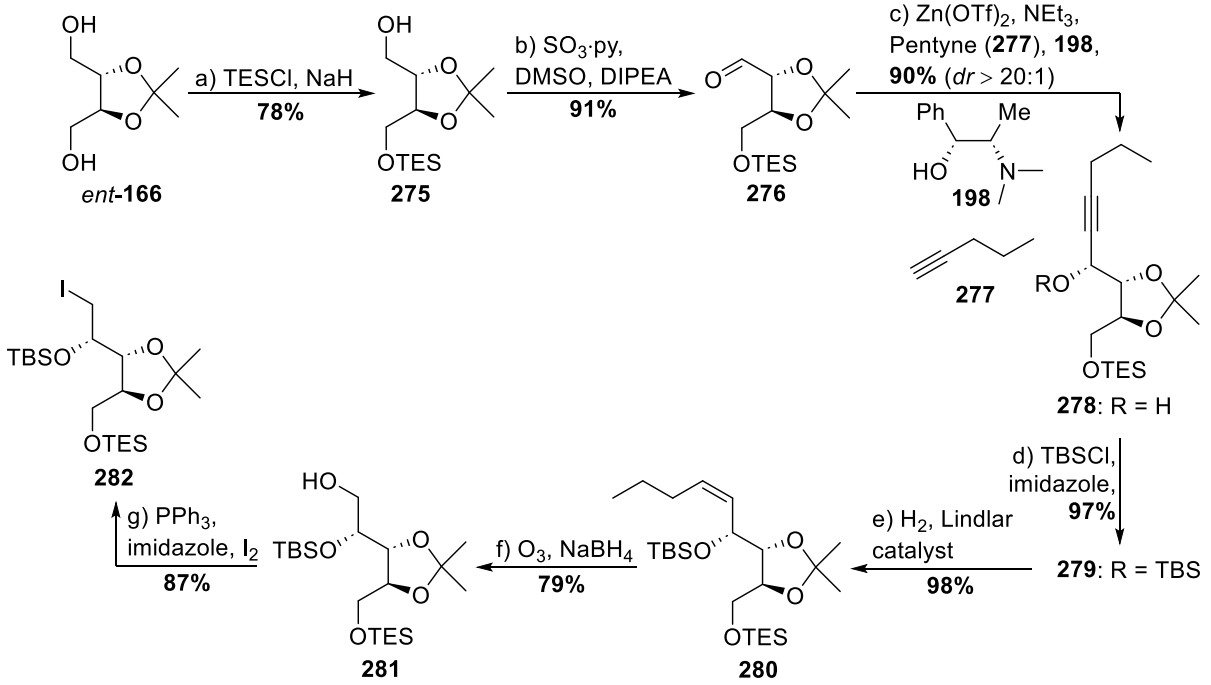



Scheme 3.45: Retrosynthetic analysis of eastern fragment II **163**.

Eastern fragment II **163** is the coupling product of the two subunits **164** and **165**. Cyanohydrin acetonide **164** containing the C9 stereocenter was synthesized from homoallylic alcohol **191**

which in turn was accessible from the cobalt-catalyzed epoxide olefination.[111] Oxidative cleavage of the terminal olefin and addition of cyanide to the corresponding aldehyde led to **164** after acetonide formation (synthesis discussed in detail in Chapter 4).

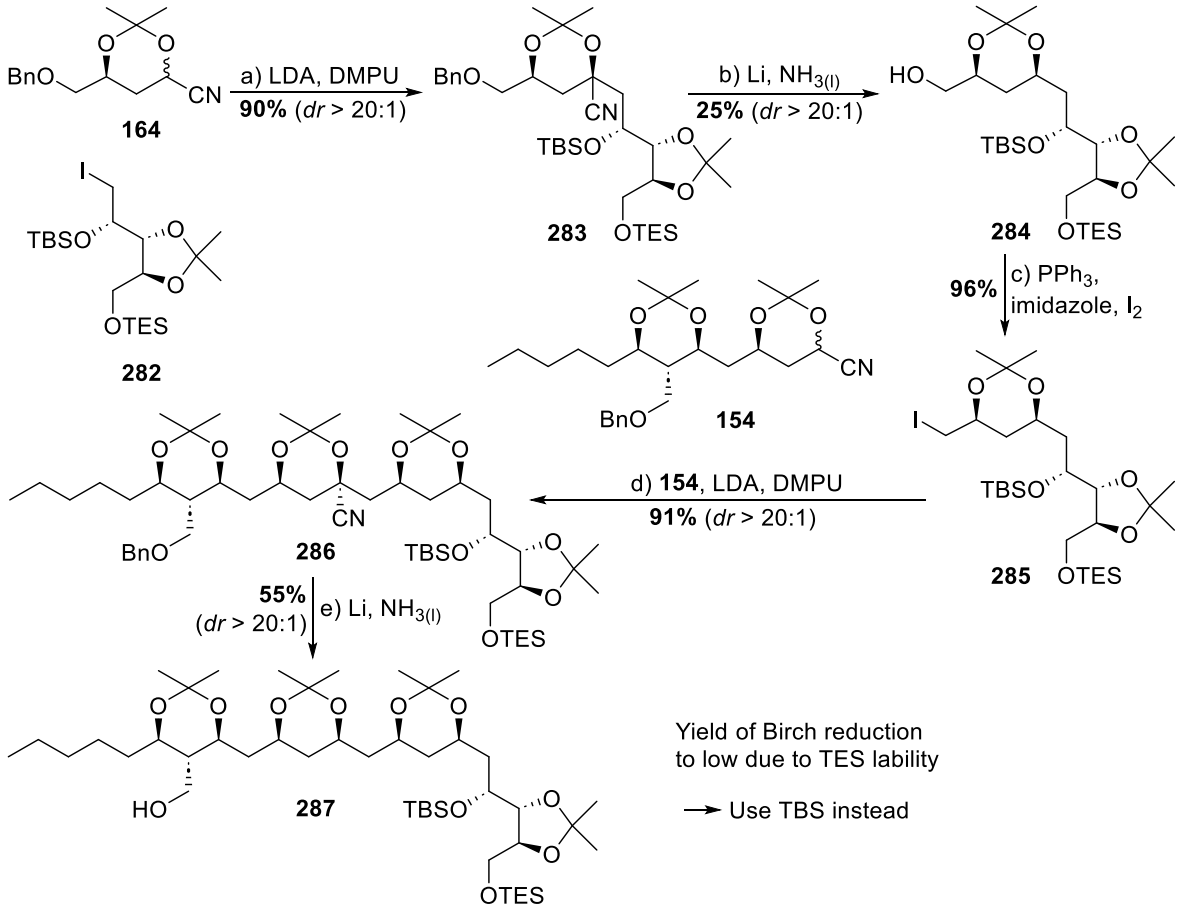
Both, the hydroxy functions at C13 and C16 were intended to be protected with a silyl protective group. Compound **163** in Scheme 3.45 is shown with two TBS ethers, but to facilitate later selective cleavage of the C16 silyl ether, a TES group was considered first. Alkyl iodide **165** is derived from protected (D)-threitol **166**, but due to supply problems a test route with the cheaper enantiomer *ent*-**166** and a TES group at C16 was carried out first. Therefore, protected (L)-threitol *ent*-**166** was monoprotected using NaH and TESCl, and the remaining hydroxy function of **275** was oxidized to the aldehyde by Parikh-Doering oxidation (Scheme 3.46).[158] Resulting aldehyde **276** was treated with $Zn(OTf)_2$, (−)-*N*-methylephedrine (**198**), and $NEt_3$ to conduct the stereoselective Carreira addition of pentyne (**277**).[72] Pentyne was used here as an affordable and easy-to-handle tool to introduce the necessary stereoinformation with high yield and excellent selectivity in a reliable manner. The propargylic hydroxy function of **278** was protected as TBS ether **279** before the alkyne was reduced to the olefin using the Lindlar catalyst.[159] Ozonolysis of the double bond of olefin **280** and reductive workup gave primary alcohol **281** which was transformed to the required alkyl iodide **282** by Appel conditions.[160,161]




Scheme 3.46: Test route towards alkyl iodide **282**, the TES protected stereoisomer of subunit **165**. Reaction conditions: a) *ent*-**166**, NaH, THF, 0 °C, 1 h, then TESCl, 0 °C, 3 h, **78%**; b) $SO_3$·py, DMSO, DIPEA, DCM, rt, 2 h, **91%**; c) $Zn(OTf)_2$, **198**, $NEt_3$, toluene, rt, 2 h, then **277**, **276**, rt, 2 h, **90%** (*dr* > 20:1); d) TBSCl, imidazole, DCM, rt, 24 h, **97%**; e) $H_2$ (1 atm), Lindlar catalyst (Pd, $CaCO_3$, quinoline), hexane, rt, 1 h, **98**; f) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 30 min, **79%**; g) $PPh_3$, imidazole, $I_2$, benzene, rt, 20 min, **87%**.

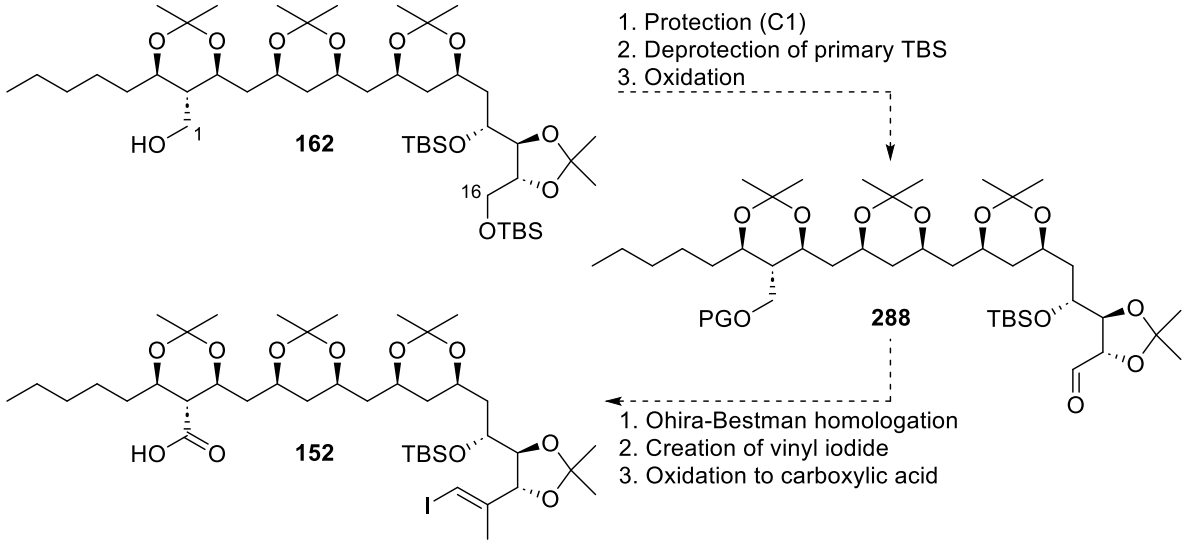
Alkyl iodide **282** was then used for a test coupling to cyanohydrin acetonide **164** to check the stability of the terminal TES ether (Scheme 3.47). While the LDA-mediated coupling provided compound **283** in a very good yield and selectivity, Birch reduction for cyanide and benzyl cleavage gave only 25% of coupling product **284**. The reason for this was the concomitant cleavage of the TES ether during quenching of the lithium metal despite consistent cooling. In the case of TES cleavage, two similar primary hydroxy functions are present in the molecule, which prevents selective reprotection and thus, further use.

Nevertheless, primary alcohol **284** was converted to alkyl iodide **285** and coupling to the northern fragment **154** was tested to establish the route for a later synthesis of authentic coupling product **162** (Scheme 3.47). Again, Rychnovsky coupling to produce compound **286** gave excellent results, but the Birch reduction resulted in a poor yield of 55% of product **287**, although it worked better than before. The cleavage of the TES ether during Birch reduction required the use of a TBS group at C16, accepting that selective cleavage in presence of the secondary TBS group at C13 may be more challenging (*vide infra*).




Scheme 3.47: Test coupling of **282** to **164** to generate eastern test fragment **283**, which is then coupled to the northern fragment **154**.
Reaction conditions: a) LDA, DMPU, THF, −40 °C, 1 h, **90%** (*dr* > 20:1); b) Li, liquid $NH_3$, THF, −78 °C, 1 h, **25%** (*dr* > 20:1); c) $PPh_3$, imidazole, $I_2$, benzene, rt, 1 h, **96%**; d) LDA, DMPU, THF, −40 °C, 1 h, **91%** (*dr* > 20:1); e) Li, liquid $NH_3$, THF, −78 °C, 1 h, **55%** (*dr* > 20:1).

The synthesis of the authentic eastern fragment **163** with the correct threitol derivative **166** as staring material for alkyl iodide **165** is presented in Chapter 4. Scheme 3.48 gives an overview of the transformations still required. After protection at C1, the primary TBS group at C16 must be cleaved before the resulting primary alcohol could be oxidized to produce aldehyde **288**. Ohira-Bestman homologation will provide the alkyne which could be used to create the *α*-methyl vinyl iodide. Deprotection at C1 will then enable the oxidation to carboxylic acid **152**.

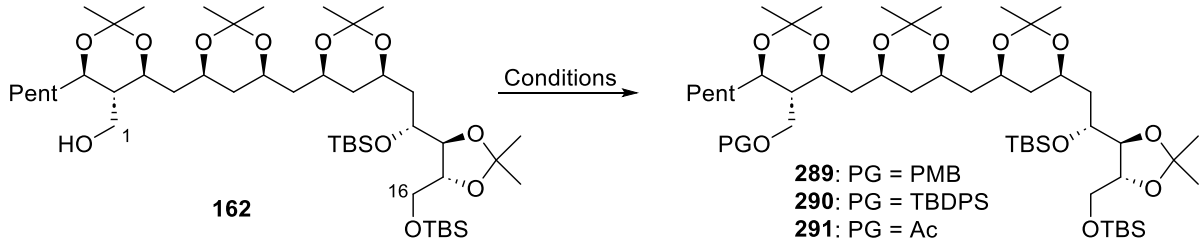



Scheme 3.48: Further steps required to generate carboxylic acid **152** from coupling product **162**.

### 3.3.5 Fragment Coupling and Completion of the Total Synthesis

After Rychnovsky coupling of northern fragment **154** and eastern fragment **163** followed by Birch reduction, coupling product **162** was obtained with a free primary hydroxy function at C1. Since it was planned to first modify the region around C16, the C1 hydroxy function had to be protected with a suitable protecting group that would allow selective cleavage of the primary TBS group at C16. Three protective groups were considered, the PMB group, the TBDPS group and the acetyl group (Table 3.3).

Table 3.3: Tested conditions for protection of the C1 hydroxy function.



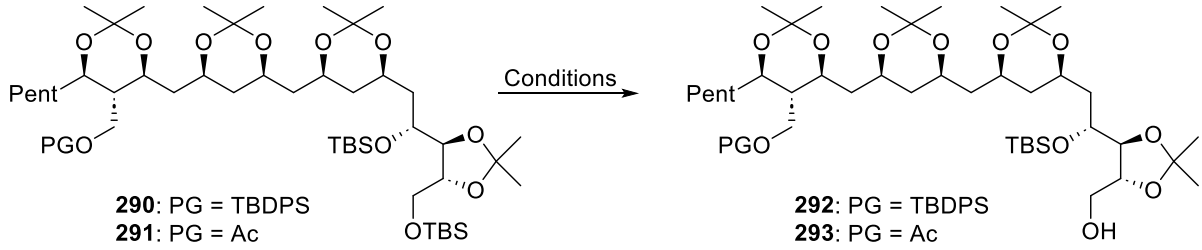

**162**

| # | Conditions | Result/Yield |
|---|---|---|
| **1** | PMBCl, NaH, DMF, rt, 3 h | Decomposition |
| **2** | PMBTCA, $TrBF_4$, $Et_2O$, rt, 5 h | Decomposition |
| **3** | PMBCl, $Ag_2O$, DCM, rt, 16 h | No conversion |
| **4** | TBDPSCl, imidazole, DCM, rt, 6 h | Crude **290** (contaminated with TBDPSOH) |
| **5** | AcCl, DIPEA, −78 °C to 0 °C, 5 h | 99% of **291** |

For the similar coupling product **155** PMB protection was already difficult at only 38% (Scheme 3.43, p. 69), but a new attempt was made because the cleavage with DDQ in the presence of vinyl iodides worked very well, as deprotection of the western fragment showed. Three conditions for formation of PMB ether **289** were tested. However, both basic conditions with NaH and PMBCl (entry 1) and Lewis acidic conditions with PMB-TCA and $TrBF_4$ (entry 2) led to decomposition of substrate **162**.[162] A method typically used for benzyl protection with $Ag_2O$ and BnBr was tested with PMBCl instead, but no conversion was observed (entry 3).[163]

No further effort was made to introduce a PMB group, but TBDPS protection was attempted (entry 4) since it is possible to selectively cleave a TBDPS ether in the presence of TBS ethers, which would be important later.[164] The reaction worked well, and TLC analysis showed complete conversion of substrate **162**, but it was difficult to purify the product to give a clean NMR of **290**. It was not possible to separate the byproduct TBDPSOH by column chromatography, but it was assumed that its presence would not affect the screening of deprotection conditions for the primary TBS ether at C16.

Table 3.4: Screening of conditions for selective cleavage of the primary TBS ether at C16.




**290**: PG = TBDPS
**291**: PG = Ac

**292**: PG = TBDPS
**293**: PG = Ac

| # | Conditions | Compound | Result/Yield |
|---|---|---|---|
| **1** | PPTS, MeOH, −10 °C, 1–8 h | **290** | Unselective deprotection[d] |
| **2** | CSA, MeOH/DCM (1:1), rt, 1–8 h | | Unselective deprotection |
| **3** | Oxone, MeOH/$H_2O$ (1:1), rt, 2 h | | Decomposition[e] |
| **4** | Formic acid, MeOH/DCM (1:1), 0 °C, 2 h | | Decomposition |
| **5** | TFA, THF/$H_2O$ (10:1), 0 °C, 3 h | | Decomposition |
| **6** | TBAF (1 equiv), THF, −10 °C, 1 h | | Unselective deprotection |
| **7** | PPTS, MeOH, −10 °C, 1–8 h | **291** | Unselective deprotection |
| **8** | TBAF (1 equiv), THF, −10 °C, 1 h | | Unselective deprotection |
| **9** | HF·py, pyridine, THF, 0 °C, 15 h | | 89% |

Entries 1–6 in Table 3.4 show the screening of conditions for selective TBS cleavage at the C16 hydroxy function using crude TBDPS ether **290** to generate alcohol **292**. Acidic conditions using PPTS or CSA resulted in nonselective deprotection of the silyl groups. The reactions were carried out at room temperature and at lower temperatures, as exemplified in entries 1 and 2. The use of oxone,[165] formic acid or TFA caused decomposition of the substrate (entries 3–5), the use of TBAF also cleaved the silyl groups unselectively (entry 6).

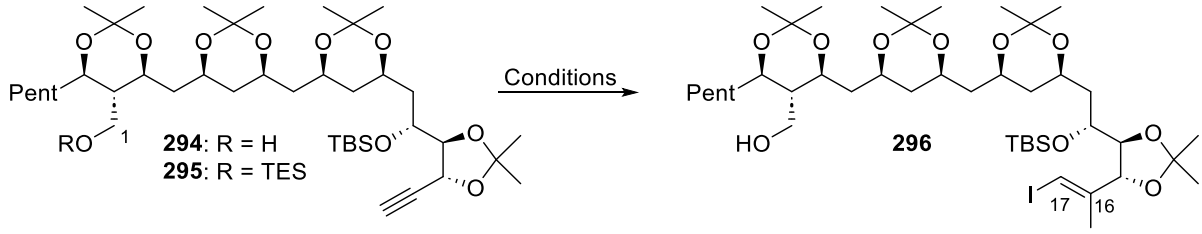
Acetyl protection with AcCl and DIPEA was performed without any problems to afford acetate **291** in quantitative yield (Table 3.3, entry 5). Again, acidic conditions with PPTS showed non-selective deprotection as did TBAF (Table 3.4, entry 7–8). A procedure using HF·py, buffered with additional pyridine afforded primary alcohol **293** in a very good yield of 89% after 15 h at 0 °C (Table 3.4, entry 9).[166]

The next challenge in modifying the polyol fragment of pentamycin was the formation of an *α*-methyl vinyl iodide in the C16/C17 region. Therefore, the C16 hydroxy function of primary alcohol **293** was oxidized to the aldehyde and Ohira-Bestmann homologation provided the

[d] Unselective deprotection refers to observation of two to three spots on TLC that can be assigned to double TBS cleavage and/or TBDPS cleavage under the respective conditions.
[e] Decomposition refers to observation of more spots on the TLC, most probably caused by additional unselective acetonide cleavage under the respective conditions.

terminal alkyne **294**.[167] The homologation reaction, which occurred in basic MeOH, also removed the acetyl function at the C1 hydroxy group. Different conditions for the conversion of the terminal alkyne to the *α*-methylvinyl iodide without a protecting group on the C1 hydroxyl function and of the TES ether **295** were investigated (Table 3.5).

Table 3.5: Screening of conditions for creation of the C16-C17 *α*-methyl vinyl iodide moiety by carbometalation and stannylcupration.




| # | Conditions | Compound | Result/Yield |
|---|---|---|---|
| **1** | $Cp_2ZrCl_2$, $AlMe_3$, DCM, 0 °C to rt, 3 h, then $I_2$, −78 °C, 1 h | **294** | No conversion |
| **2** | $Cp_2ZrCl_2$, $AlMe_3$, DCM, 0 °C to rt, 24 h, then $I_2$, −78 °C, 1 h | | Decomposition |
| **3** | $Cp_2ZrCl_2$, $AlMe_3$, MAO, DCM, rt, 10 h, then $I_2$, −78 °C, 1 h | | Decomposition |
| **4** | $SnCl_2$, *n*-BuLi, MeMgBr, CuCN, THF, 0 °C, 2 h, then MeI, 0 °C, 2 h, then $I_2$, 0 °C, 12 h | | Decomposition |
| **5** | $Cp_2ZrCl_2$, $AlMe_3$, DCM, 0 °C to rt, 24 h, then $I_2$, −78 °C, 1 h | **295** | Decomposition |
| **6** | $Cp_2ZrCl_2$, $AlMe_3$, MAO, DCM, rt, 10 h, then $I_2$, −78 °C, 1 h | | Decomposition |
| **7** | $SnCl_2$, *n*-BuLi, MeMgBr, CuCN, THF, 0 °C, 2 h, then MeI, 0 °C, 2 h, then $I_2$, 0 °C, 12 h | | Decomposition |
| **8** | CuCN, *n*-BuLi, $Bu_3SnH$, THF, −78 °C, 1 h, then MeI, DMPU, −78 °C to rt, 30 min, then $I_2$, DCM, −78 °C to 0 °C, 30 min then HF·py, pyridine, THF, 0 °C, 1h | | 57% (over 3 steps) |

First, Negishi's carbometalation conditions using $Cp_2ZrCl_2$ and $AlMe_3$ followed by iodination was tested.[168] A reaction time of 3 hours for carbometalation led to no conversion of substrate **294** (entry 1). However, longer reaction times resulted in a complex mixture of degradation products for both substrates, the free alcohol **294** and TES ether **295** (entries 2 and 5), which was also observed for a similar substrate by Ishihara *et al*. during the total synthesis of thuggacin.[169] Since the presence of methylaluminoxane (MAO) is known to accelerate the reaction, it was included as an additive for both substrates **294** and **295**.[170] The reaction time was shortened with the idea of reducing decomposition, but also a complex mixture of compounds was observed by TLC analysis after 10 h (entries 3 and 6).

In another attempt, a procedure developed by Uenishi and Nozaki which uses *in situ* generated $Bu_3SnMgMe$ in the presence of a catalytic amount of CuCN was performed (entries 4 and 7).[171] After stirring for two hours, MeI was added as the methyl source for C16 methylation. The method is known to work on substrates with free hydroxy functions, so again both substrates **294**, with the free C1 hydroxy function, and TES ether **295** were tested.[169] However, both reactions were unsuccessful and again, a complex mixture of compounds was observed during TLC analysis.

A third method was a sequence developed by Lipshutz, consisting of stannylcupration with subsequent iodination.[172] The complex stannylcuprate $Bu_3Sn(Bu)Cu(CN)Li_2$ was generated *in situ* from CuCN, *n*-BuLi, and $Bu_3SnH$, and as above, methylation was accomplished by the addition of MeI and in this case with DMPU as a co-solvent.[173] The most promising results for the required transformation were achieved by this reaction, but practical implementation was challenging since any proton source resulted in a mixture of the 16-demethyl compound **297** and the desired product **296**. Figure 3.12 shows the olefinic region of the $^1$H-NMR spectra of the crude mixtures of three exemplary attempts of this reaction. The two dd from about 6.68–6.60 ppm ($^3J$ = 14.5 Hz, $^3J$ = 6.2 Hz) and from 6.50–6.46 ppm ($^3J$ = 14.5 Hz, $^3J$ = 1.1 Hz) belong to the C16 and C17 hydrogen atoms of byproduct **297** since a typical olefinic *trans*-coupling is observed. The signal at 6.44–6.40 ppm belongs to the C17 hydrogen of compound **296**, since only $^4J$ coupling to the C16 methyl group and to C15 is possible.

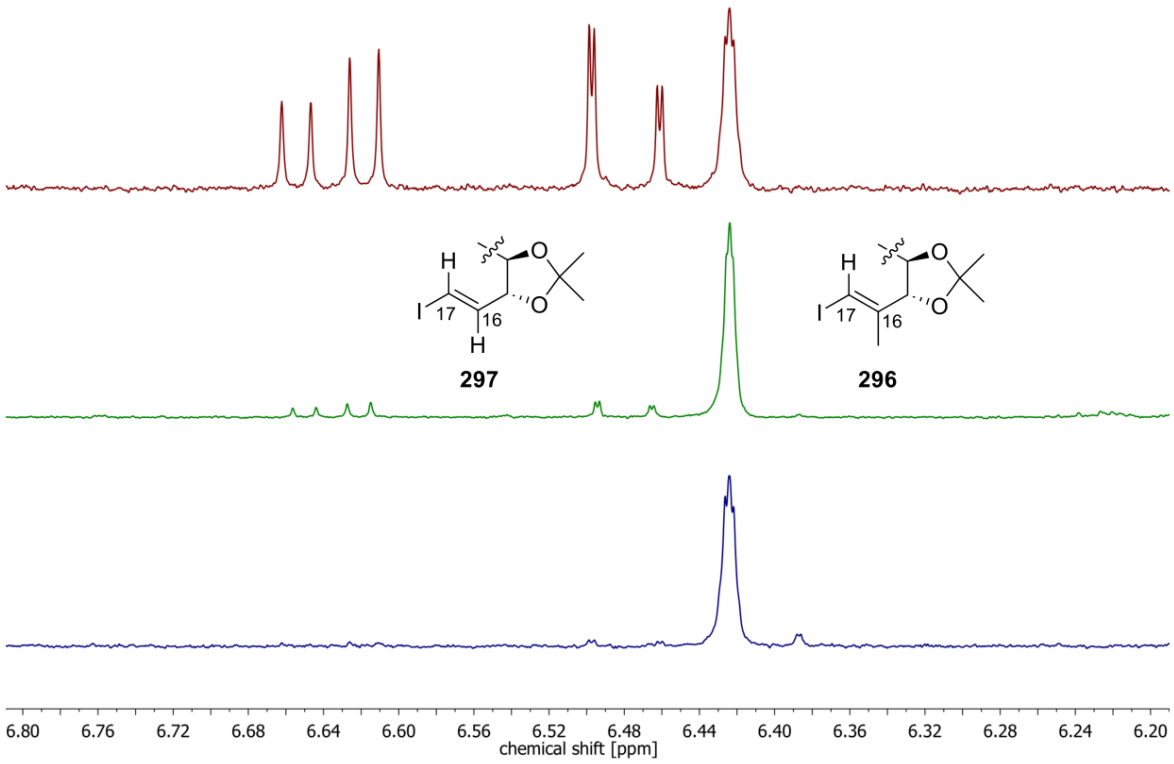
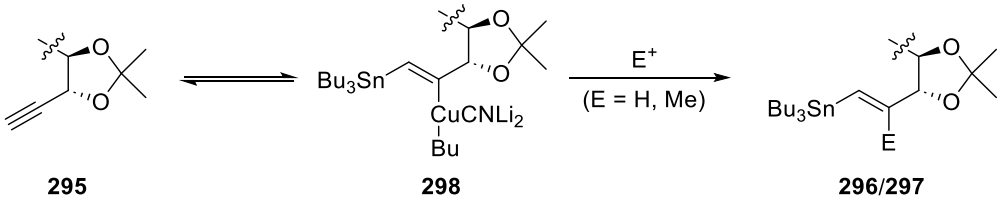



Figure 3.12: $^1$H-NMR spectra of the olefinic region of compounds **296** (desired) and **297** (undesired). The product ratio depends on the water content of the reactants and solvents.

Depending on the water content of the reaction, undesired byproduct **297** is formed to a higher extent. Since the two compounds cannot be separated by conventional normal or reversed-phase column chromatography or HPLC, it is essential to prevent the formation of 16-demethyl compound **297**. Therefore, the presence of water in the reaction had to be strictly avoided. The THF used in the reaction was freshly distilled over sodium, and solid reagents were taken from the glovebox, so the only critical substances were MeI and DMPU. The first spectrum in Figure 3.12 shows an approximate 1:1 mixture of the two compounds **297** and **296** (red). The DMPU used in this reaction was reagent grade but not stored over mol sieves or sealed with a septum. As a consequence, the DMPU was lyophilized three times and subsequently stored over mol sieves, resulting in the second spectrum (green) with much less byproduct **297** of about 1:10. A completely clean spectrum (blue) with no detectable byproduct formation was obtained by using a freshly opened bottle of MeI. The reason of the high water sensitivity during stannylcupration is intermediate **298** which is highly susceptible to hydrolysis (Scheme 3.49). It is assumed that protonation at C16 occurs faster than methylation, leading to formation of 16-demethyl compound **297** even in the presence of trace amounts of water, although MeI is added in large excess.[174,175]

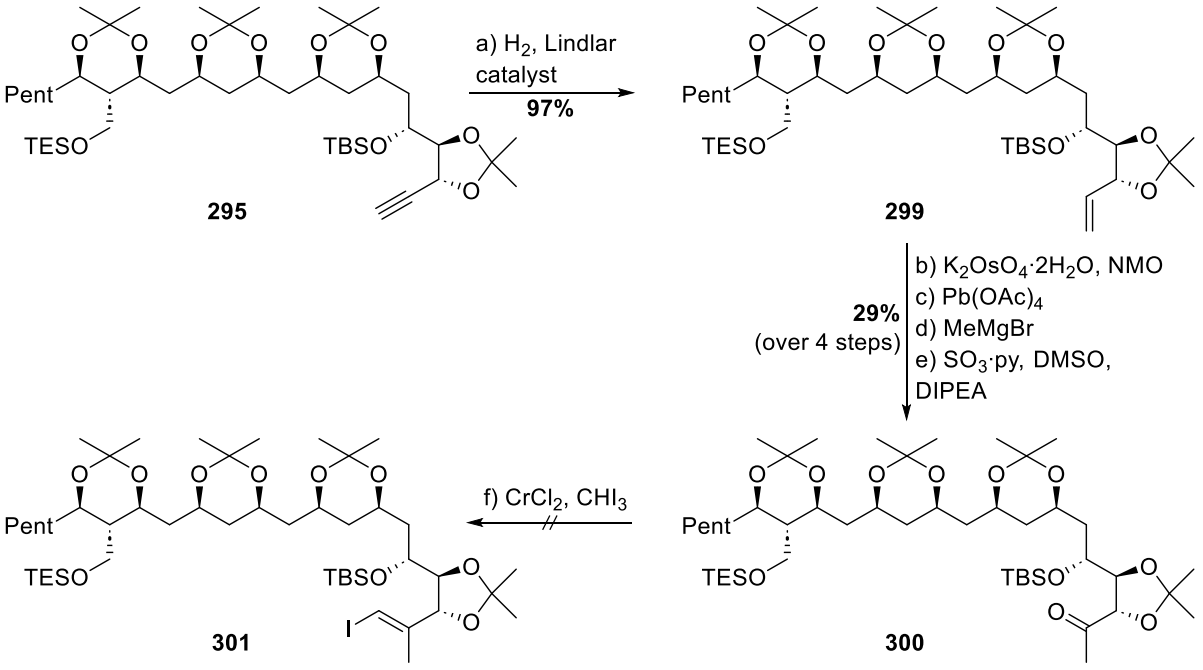



Scheme 3.49: Pathway of stannylcupration by complex stannylcuprate $Bu_3Sn(Bu)Cu(CN)Li_2$.[174,175]

Since the purification of the TES protected product of the reaction was very tedious due to a large amount of tin byproducts, it was decided to expose the crude product directly to a mixture of HF·py buffered with pyridine in THF. The goal was to increase the polarity of the product by generating the free alcohol and thus the difference in $R_f$ value between the product and non-polar byproducts to facilitate purification by column chromatography. At the same time, the liquid $Bu_3SnI$ was converted to the poorly soluble $Bu_3SnF$, an off-white solid that precipitated and could be filtered off. Finally, the desired product **296** could be obtained in a moderate yield of 57% over three steps consisting of stannylcupration, iodination, and deprotection of the TES ether at C1.

Due to the high complexity of successfully producing pure *α*-methyl vinyl iodide **296** under the discussed conditions, another approach consisting of a Takai olefination as the key step was tested in parallel (Scheme 3.50).[176] First, partial hydrogenation of the terminal alkyne **295** under Lindlar conditions generated terminal olefin **299**,[159] which was to be converted to the methyl ketone **300**. Therefore, the terminal double bond was cleaved using a dihydroxylation/diol

cleavage sequence with $OsO_4$/NMO and $Pb(OAc)_4$.[177] The instability of the resulting aldehyde required direct performance of a Grignard addition with MeMgBr and subsequent oxidation of the crude secondary alcohol to methyl ketone **300** without purification and characterization of the intermediates. However, the synthesis of TES protected vinyl iodide **301** by iodoolefination under Takai conditions with $CHI_3$ and $CrCl_2$ was not successful.[178] No conversion of the substrate was observed, probably due to steric hindrance.




Scheme 3.50: Attempt for an alternative route to vinyl iodide **301** by Takai iodoolefination.[176,178] Reaction conditions: a) $H_2$ (1 atm), Lindlar catalyst (Pd, $CaCO_3$, quinoline), hexane, rt, 1 h, **97%**; b) $K_2OsO_4{\cdot}H_2O$, NMO, acetone/$H_2O$ (10:1), rt, 20 h; c) $Pb(OAc)_4$, toluene, rt, 10 min; d) MeMgBr, $Et_2O$, rt, 1 h; e) $SO_3{\cdot}$py, DMSO, DIPEA, DCM, rt, 2 h, **29%** (over 4 steps); f) $CrCl_2$, THF, −10 °C, then **300**, $CHI_3$, rt, 24 h, no conversion.

After finding appropriate conditions for creating the C16/C17 *α*-methyl vinyl iodide moiety with direct deprotection of the C1 TES ether, the resulting free hydroxy function was oxidized to carboxylic acid **152** in two steps with IBX, followed by Pinnick reaction. The carboxylic acid was the starting material for coupling the western fragment **153** to the polyol part of pentamycin with the goal of creating *bis*-vinyl iodide **150**. As previously reported by Rychnovsky for the total synthesis of filipin III (**11**), esterification at C1 proved to be very challenging due to steric hinderance of the carboxylic acid.[33,49] Various reagents and conditions to achieve the desired transformation were tested (Figure 3.13, Table 3.6). Under Steglich conditions, i.e. a carbodiimide and DMAP (**302**), no conversion was observed for DCC (**303**), whereas a modified procedure using EDC·HCl (**304**) instead of DCC resulted in the decomposition of carboxylic acid **152** (entries 1 and 2).[179] The peptide coupling reagent COMU (**305**) which is also suitable

to prepare carboxylic acid esters was used next, but no conversion of the carboxylic acid was observed (entry 3).[180]

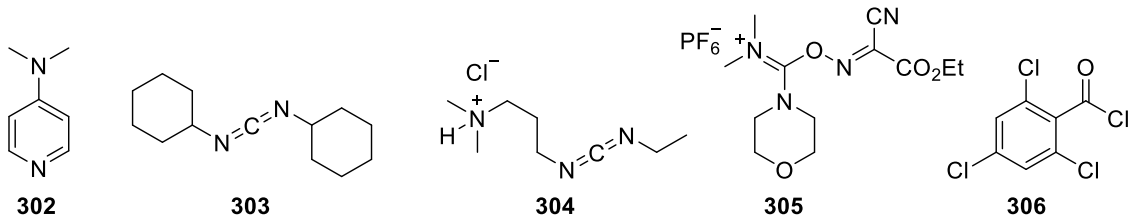
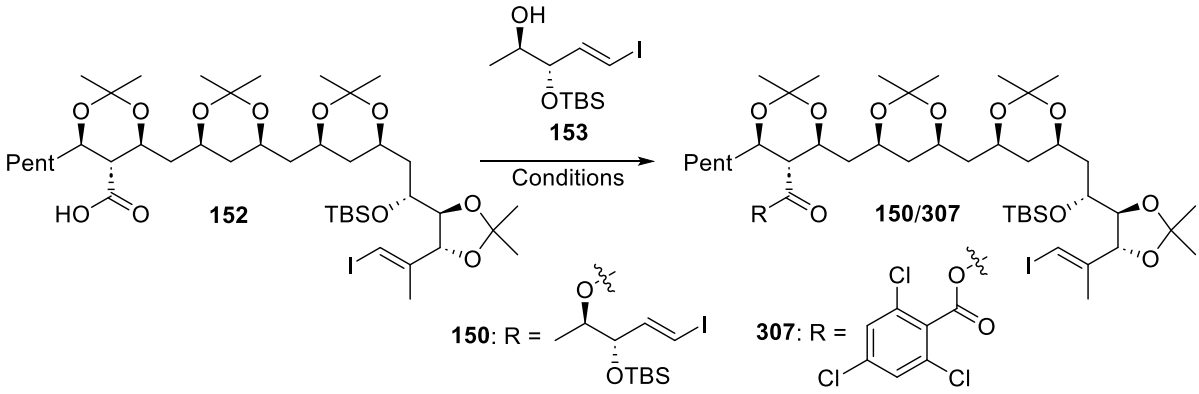



Figure 3.13: Coupling reagents screened for coupling carboxylic acid **152** with western fragment **153**.

Finally, Yamaguchi conditions, already used by Rychnovsky in the total synthesis of filipin III (**11**) were successful.[33] The final product **150** was isolated in a yield of 84% when the two steps, i.e., formation of the mixed anhydride **307** by TCBC (**306**) and $NEt_3$, and coupling of the mixed anhydride to western fragment with DMAP (**302**), were performed sequentially (entry 5). After stirring for 5 h in toluene, the white precipitate of $HNEt_3Cl$ had to be removed by filtration and coupling ran in THF for 48 h.[54] Mixed anhydride **307** was accidently isolated after column chromatography in case of the one-pot procedure (entry 4) and could be fully characterized (pp. 229–230).

Table 3.6: Screening of reagents for esterification of carboxylic acid **152** and western fragment **153**.

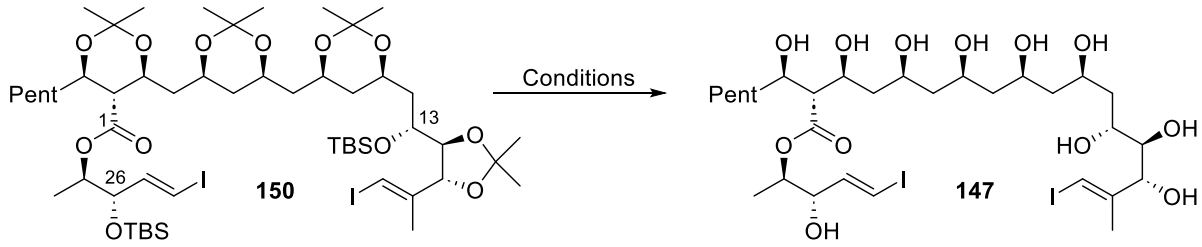



| # | Conditions | Result/Yield |
|---|---|---|
| **1** | DCC (**303**), DMAP (**302**), DCM, rt, 48 h | No conversion |
| **2** | EDC·HCl (**304**), DIPEA, DMAP (**302**), DCM, rt, 48 h | Decomposition |
| **3** | COMU (**305**), DIPEA, DMF, rt, 24 h | No conversion |
| **4** | TCBC (**306**), DMAP (**302**), $NEt_3$, toluene, rt, 5 h | 58% of **307** |
| **5** | 1. **152**, TCBC (**306**), $NEt_3$, THF, rt, 5 h, filtered, evap.<br>2. DMAP (**302**), **153**, toluene, rt, 48 h | 84% of **150** |

The penultimate challenge was global deprotection, i.e. cleavage of the TBS ethers at C13 and C26 and hydrolysis of the acetonides of *bis*-vinyl iodide **150**. The initial aim was to remove all

protecting groups simultaneously in a single step. Various conditions were investigated, in particular the use of Dowex acidic resign (Table 3.7), which had already been used by Krische *et al*. for the global deprotection, i.e., of one TES group and three six-membered acetonides in the total synthesis of (+)-roxaticin.[153] However, this method was not successful for compound **150**. Stirring in MeOH for one week resulted in only partial deprotection as observed by TLC (entry 1). Analysis by MS showed no desired product **147**, but the presence of several compounds with up to three acetonides and one or both TBS groups still attached. Heating to 50 °C did not improve the results after 10 h, but partial and complete decomposition occurred after 24 and 48 h (entries 2–4). Decomposition in this case refers to the cleavage of the ester bond at C1.

Table 3.7: Screening of conditions for global deprotection of *bis*-vinyl iodide **150**.



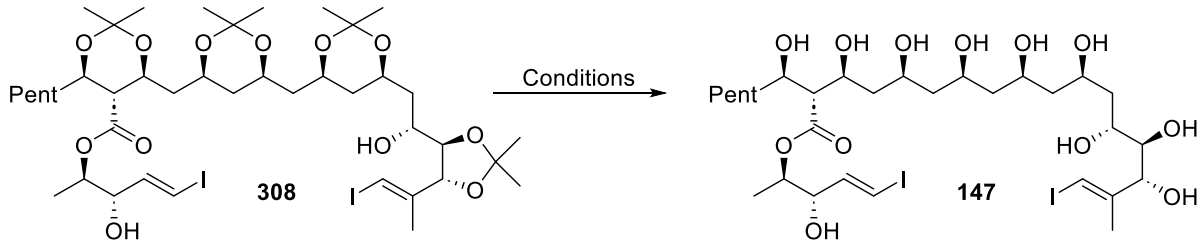

| # | Conditions | Result/Yield |
|---|---|---|
| **1** | Dowex acidic resign, MeOH, rt, 1 week | Partial deprotection |
| **2** | Dowex acidic resign, MeOH, 50 °C, 10 h | Partial deprotection |
| **3** | Dowex acidic resign, MeOH, 50 °C, 24 h | Partial deprotection, decomposition |
| **4** | Dowex acidic resign, MeOH, 50 °C, 48 h | Decomposition |
| **5** | 0.1M aqueous HCl, MeOH, rt, 2 h | Decomposition |
| **6** | 4M HCl in dioxane, rt, 1 h | Decomposition |
| **7** | $InCl_3$, wet MeCN, rt, 5 days | Partial deprotection |

Consequently, deprotection with stronger acids was tested at room temperature. However, both 0.1M aqueous HCl in MeOH and 4M HCl in dioxane led to decomposition of the molecule (entries 5 and 6). The most promising results were accomplished using a procedure reported by Reissig *et al*. for the cleavage of five- and six-membered acetonides with $InCl_3$ in wet MeCN.[77] After stirring for 5 days under these conditions, only partial deprotection was detected. Silyl groups are generally stable under these conditions, but also one acetonide, most likely the more stable, five-membered one, was still attached to the molecule as monitored by MS.

Separate deprotection of the TBS groups and screening of the course of acetonide cleavage by different temperatures should finally accomplish the preparation of compound **147**. First, the TBS groups were cleaved with TBAF to give diol **308**. By exposing this compound to the

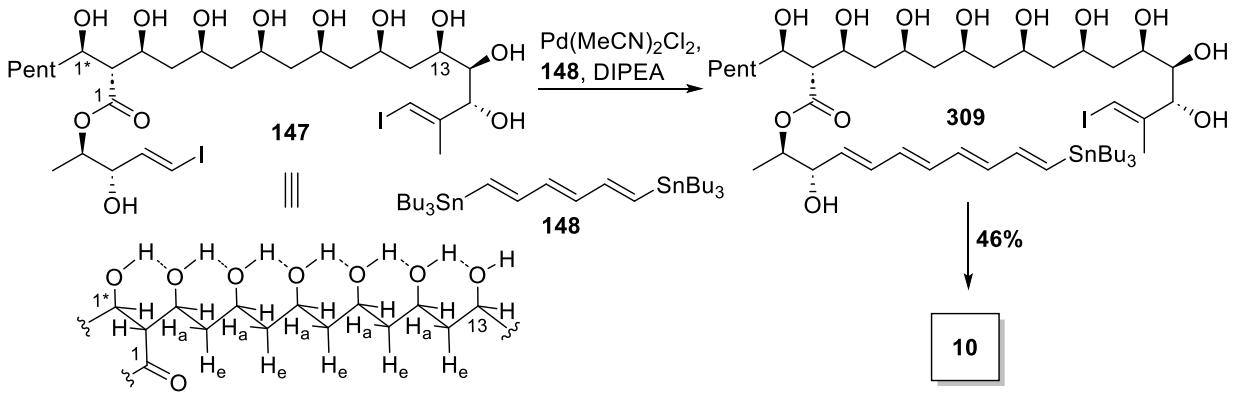
above mentioned conditions, i.e., $InCl_3$ in wet MeCN, again only partial deprotection was achieved by stirring at room temperature for 5 days (Table 3.8). One acetonide was still attached to the molecule as detected by MS (entry 1). Increasing the temperature to 40 °C and shortening the reaction time to 48 h showed an increased amount of **147** but also more degradation as observed by TLC (entry 2). Increasing the temperature to 70 °C showed an approximately 1:1 mixture of desired product and decomposition products (entry 3). The best results were obtained by stirring **308** for 10 h at 50 °C with 20 equiv of $InCl_3$ in HPLC grade MeCN (entry 4). Complete deprotection was not yet observed and some degradation products were still detectable, but *bis*-vinyl iodide **147** was obtained in 70% yield and these conditions were deemed good enough to produce enough material for the final step in the total synthesis.

Table 3.8: Screening of conditions for global deprotection of *bis*-vinyl iodide **308**.




| # | Conditions | Result/Yield |
|---|---|---|
| **1** | $InCl_3$, wet MeCN, rt, 5 days | Partial deprotection (one acetonide left) |
| **2** | $InCl_3$, wet MeCN, 40 °C, 48 h | **147** (traces), partial deprotection, decomposition |
| **3** | $InCl_3$, wet MeCN, 70 °C, 3 h | **147** (traces), decomposition |
| **4** | $InCl_3$, wet MeCN, 50 °C, 10 h | Deprotection, partial decomposition, 70% of **147** |

Polyol fragment **147** is characterized by large $^3J$ coupling constants between the protons of the hydroxyl-bearing centers and the vicinal, axial protons $H_a$ (Scheme 3.51). Remarkably, these data are also observed in protic solvents such as methanol, further confirming this strong conformational bias of the C1*-C13 polyol moiety of **147** and thus, the synthetic design.




Scheme 3.51: Proposed pathway of the employed double Stille ring closure to afford pentamycin (**10**).

The last step was accomplished by adopting the conditions of Nicolaou *et al*. reported for the total synthesis of rapamycin (**218**), i.e., $Pd(MeCN)_2Cl_2$ and DIPEA in a mixture of DMF and THF.[139,140] Since the formation of pentamycin (**10**) could be directly detected by MS (*m/z* [M+$Na^+$] = 693.382), no further conditions were explored. The focus was on determining the ideal reaction time to avoid degradation of the sensitive natural product. Therefore, the progress of the reaction was monitored by MS (Figure 3.14).

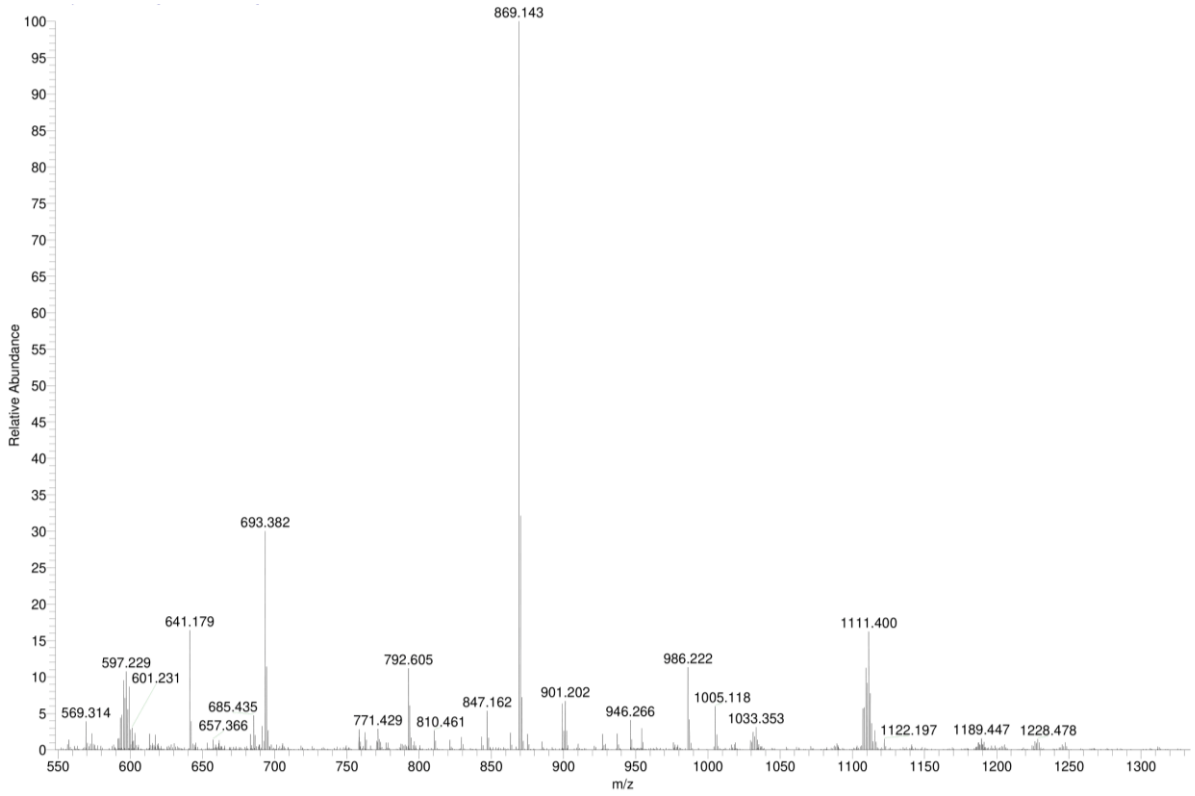


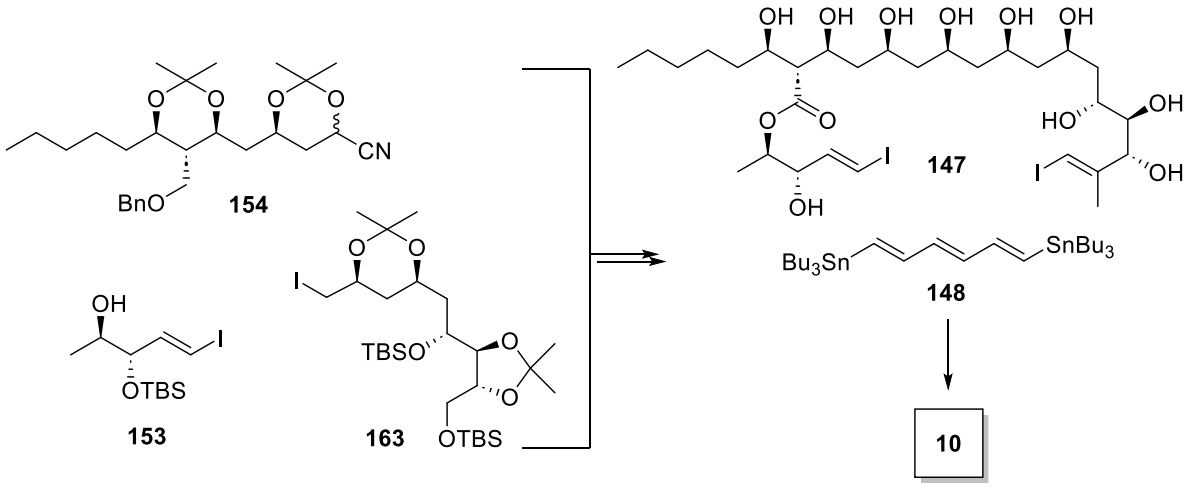

Figure 3.14: Mass spectrum of the crude mixture of the Stille reaction after 3 h to detect intermediate **309** (*m/z*: [**309**+$Na^+$] = 1111.400), pentamycin (*m/z*: [**10**+$Na^+$] = 693.382) and *bis*-vinyl iodide **147** (*m/z*: [**147**+$Na^+$] = 869.143).

After 3 h, substrate **147** was still detectable (*m/z* [M+$Na^+$] = 896.143) and the presence of the putative *seco*-vinyl iodide intermediate **309** was also demonstrated. It was assumed that the less hindered vinyl iodide at C24 reacted first, so the peak at *m/z* [M+$Na^+$] = 1111.400 was proposed to belong to structure **309**. However, the compound was not isolated, and no NMR-based structure elucidation was performed. After 24 h, substrate **147** and intermediate **309** were no longer detected, so this was assumed to be the ideal reaction time.

# 4 Total Synthesis of Pentamycin

After discussing the synthetic strategies for accessing the fragments and achieving the required couplings, as well as optimizing the reaction conditions for the key steps (Chapter 3.3), this chapter finally presents the first successful total synthesis of pentamycin based on these results.

According to the second generation retrosynthetic analysis, four fragments, i.e., western fragment **153**, northern fragment **154**, eastern fragment **163**, and southern fragment **148** were synthesized (Scheme 4.1). After modification of the coupling product of northern and eastern fragment, esterification with the western fragment was accomplished before the double Stille coupling of *bis*-vinyl iodide **147** and trienyl-*bis*-stannane **148** closed the macrocycle and established the pentaene part at the same time.

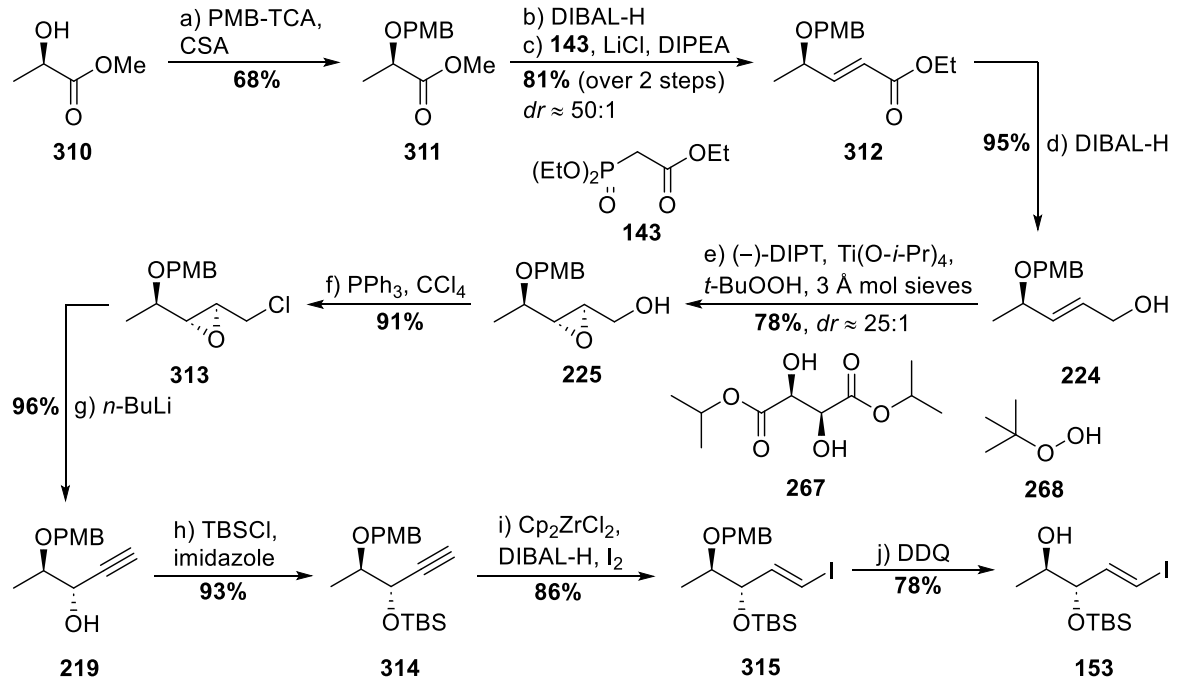



Scheme 4.1: Synthetic plan to access pentamycin (**10**).

## 4.1 Polyol Fragment Synthesis and Iterative Rychnovsky Coupling

Synthesis of western fragment **153** started with the PMB-protection of methyl D-lactate (**310**) using PMB-TCA under slightly acidic conditions (Scheme 4.2). The ester function of protected methyl lactate **311** was then reduced with DIBAL-H (1 equiv, −78 °C, DCM) to selectively access the corresponding aldehyde. An HWE reaction with Masamune Roush conditions using triethylphosphono acetate (**143**) in the presence of LiCl and DIPEA gave *α*,*β*-unsaturated ester **312** with high (*E*)-selectivity of 50:1.[156,181] Reduction with DIBAL-H afforded allylic alcohol **224** which was converted to Sharpless epoxide **225** with a good selectivity of 25:1.[182] The primary hydroxy function of **225** was then exchanged to a chlorine under Appel conditions and a double-elimination reaction of chloride **313** using *n*-BuLi afforded propargylic alcohol **219** in excellent yield.[102,103] After protection of the secondary hydroxyl function as TBS-ether **314**, the alkyne was converted to vinyl iodide **315** using $Cp_2ZrCl_2$-DIBAL-H according to a procedure of

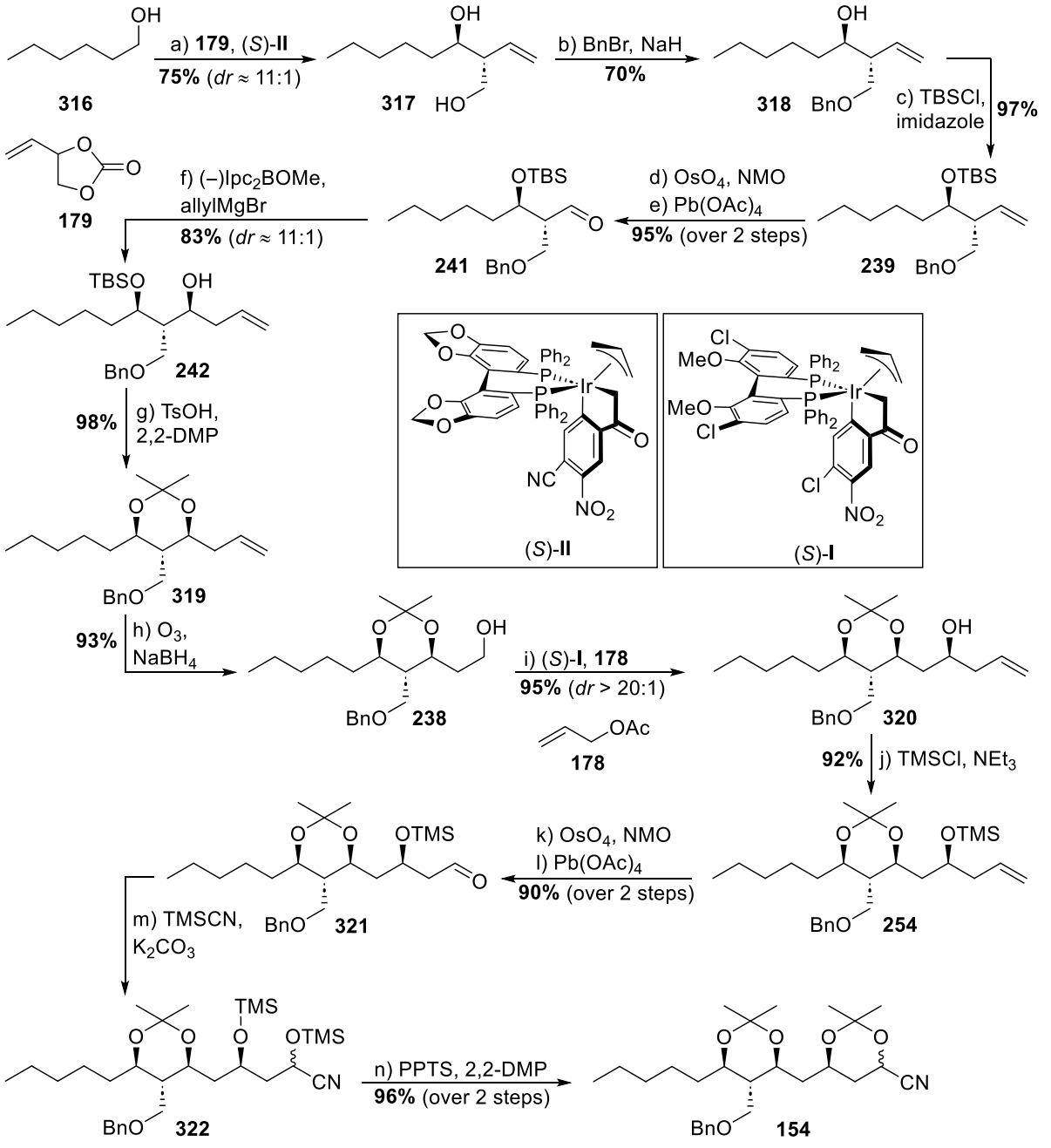
Huang & Negishi.[141] Finally, treatment with DDQ to remove the PMB protecting group yielded the desired western fragment **153**.[181]




Scheme 4.2: Synthesis of western fragment **153** of pentamycin (**10**).
Reaction conditions: a) PMB-TCA, CSA, DCM, rt, 16 h, **68%**; b) DIBAL-H (1 equiv), DCM, −78 °C, 30 min; c) **143**, LiCl, DIPEA, MeCN, 0 °C to rt, 90 min, **81%** (over 2 steps; *dr* ≈ 50:1); d) DIBAL-H, DCM, −78 °C, 90 min, **90%**; e) (−)-DIPT (**267**), 3 Å molecular sieves, DCM, 30 min, then Ti(O-*i*-Pr)$_4$, *t*-BuOOH (**268**), −30 °C, 30 min, then **224**, 44 h, **78%** (*dr* ≈ 25:1); f) $PPh_3$, $CCl_4$, 100 °C, 2.5 h, **91%**; g) *n*-BuLi, THF, −78 °C, 30 min, **96%**; h) TBSCl, imidazole, DCM, 0 °C, 4 h, **93%**; i) $Cp_2ZrCl_2$, DIBAL-H, THF, 0 °C, 45 min, then **434**, rt, 2 h, then $I_2$, −78 °C, 30 min, **86%**; j) DDQ, DCM/ pH = 7 buffer (10:1), rt, 90 min, **78%**.

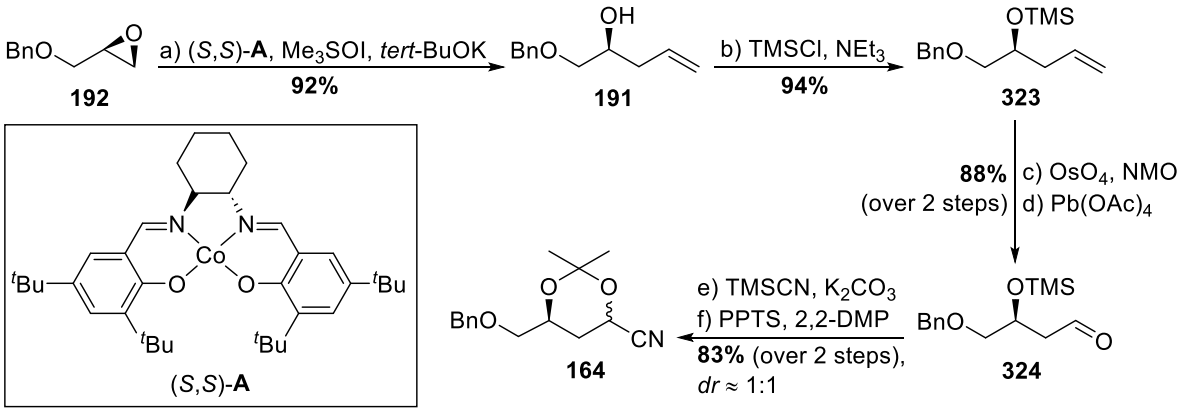
Northern fragment **154** was synthesized from hexanol (**316**) which was converted to diol **317** using Krische's 1,2-*anti* carbonyl (hydroxymethyl)allylation with freshly prepared catalyst (*S*)-**II** and allyl donor **179** (Scheme 4.3).[96] The reaction proceeded with good yield and selectivity of 11:1 and resulting diol **317** could be produced in large quantities (12.7 g). The primary and secondary hydroxy functions were then sequentially protected, first as benzyl ether, to obtain secondary alcohol **318**, and then as TBS ether to produce fully protected diol **239**. The double bond was cleaved using a dihydroxylation/diol-cleavage-sequence to obtain aldehyde **241**. For cleavage, $Pb(OAc)_4$ was used to achieve high yield with simple workup.[177] Aldehyde **241** was converted to homoallylic alcohol **242** through Brown allylation with (−)-$Ipc_2$B-allyl, achieving good degrees of conversion and selectivity.[84] Acetonide protection then yielded acetonide **319** and ozonolysis of the double bond with reductive workup afforded corresponding primary alcohol **238** which could be efficiently allylated using Krische's method.[153] For this purpose, catalyst (*S*)-**I** was prepared *in situ* and used to obtain homoallylic alcohol **320** with excellent yield and selectivity. Finally, the free hydroxy function of **320** was protected as TMS ether to obtain **254** and the double bond was cleaved oxidatively. Obtained aldehyde **321** was treated

with TMSCN, and addition of cyanide to the aldehyde gave TMS-cyanohydrin **322** which was immediately converted to an epimeric mixture of northern fragment **154** by acetonide protection.[154]



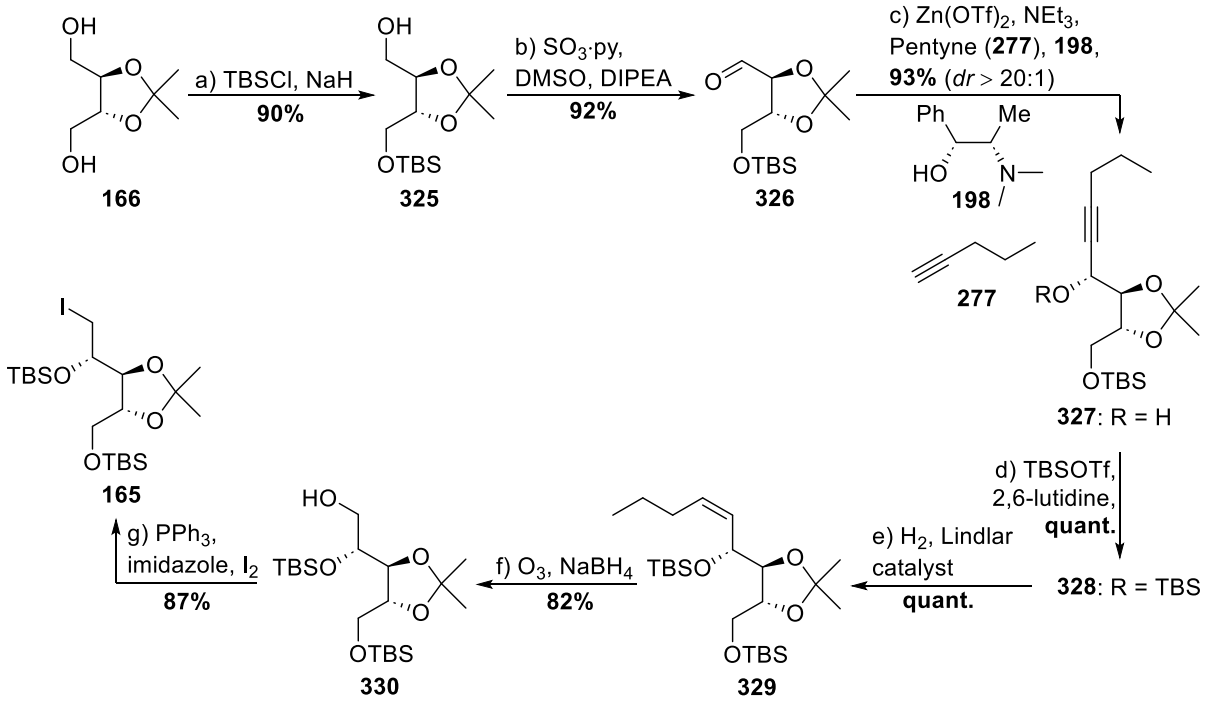

Scheme 4.3: Synthesis of northern fragment **154** of pentamycin (**10**).
Reaction conditions: a) (*S*)-**II**, **179**, THF, 90 °C, 48 h, **75%** (*dr* ≈ 11:1); b) BnBr, NaH, DMF, −10 °C, 90 min, **70%**; c) TBSCl, imidazole, DCM, rt, 48 h, **97%**; d) $OsO_4$, NMO, acetone/$H_2O$ (10:1), rt, 36 h; e) $Pb(OAc)_4$, toluene, rt, 20 min, **95%** (over 2 steps); f) (−)-$Ipc_2BOMe$, allylMgBr, $Et_2O$, 0 °C, 1 h, then **241**, −78 °C, 1 h, **83%** (*dr* ≈ 11:1); g) TsOH, MeOH, rt, 3 h, then 2,2-DMP, rt, 30 min, **98%**; h) $O_3$, DCM/MeOH (10:1), −78 °C, then $NaBH_4$, −78 °C, 30 min, **93%**; i) (*S*)-**I**: $[Ir(COD)Cl]_2$, (*S*)-Cl,MeO-BIPHEP (**176**), 4-chloro-3-nitrobenzoic acid, $Cs_2CO_3$; allyl acetate, THF, 110 °C, 48 h, **95%** (*dr* > 20:1); j) TMSCl, $NEt_3$, DCM, rt, 4 h, **92%**; k) $OsO_4$, NMO, acetone/$H_2O$ (10:1), rt, 20 h; l) $Pb(OAc)_4$, toluene, rt, 10 min, **90%** (over 2 steps); m) TMSCN, $K_2CO_3$, DMF, rt, 30 min; n) PPTS, MeOH, rt, 15 min, then 2,2-DMP, DCM, rt, 16 h, **96%** (over 2 steps; *dr* ≈ 1:1).

The eastern fragment was synthesized in a convergent manner from cyanohydrin acetonide **164** and alkyl iodide **165** which were coupled according to Rychnovsky's method.[51] Cyanohydrin acetonide **164** was derived from benzyl-(*S*)-glycidyl ether (**192**) which was transformed to homoallylic alcohol **191** by the cobalt-catalyzed epoxide olefination with cobalt-salen complex **A** and $Me_3SOI$ as discussed in Chapter 3.2.3 (Scheme 4.4).[111] The reaction proceeded with a very good yield, and the free hydroxy function was protected by treatment with TMSCl and $NEt_3$ to obtain TMS ether **323**. Oxidative cleavage of the terminal olefin gave aldehyde **324** which was transformed to an epimeric mixture of cyanohydrin acetonide **164** under the same conditions as the above discussed northern fragment **154**.



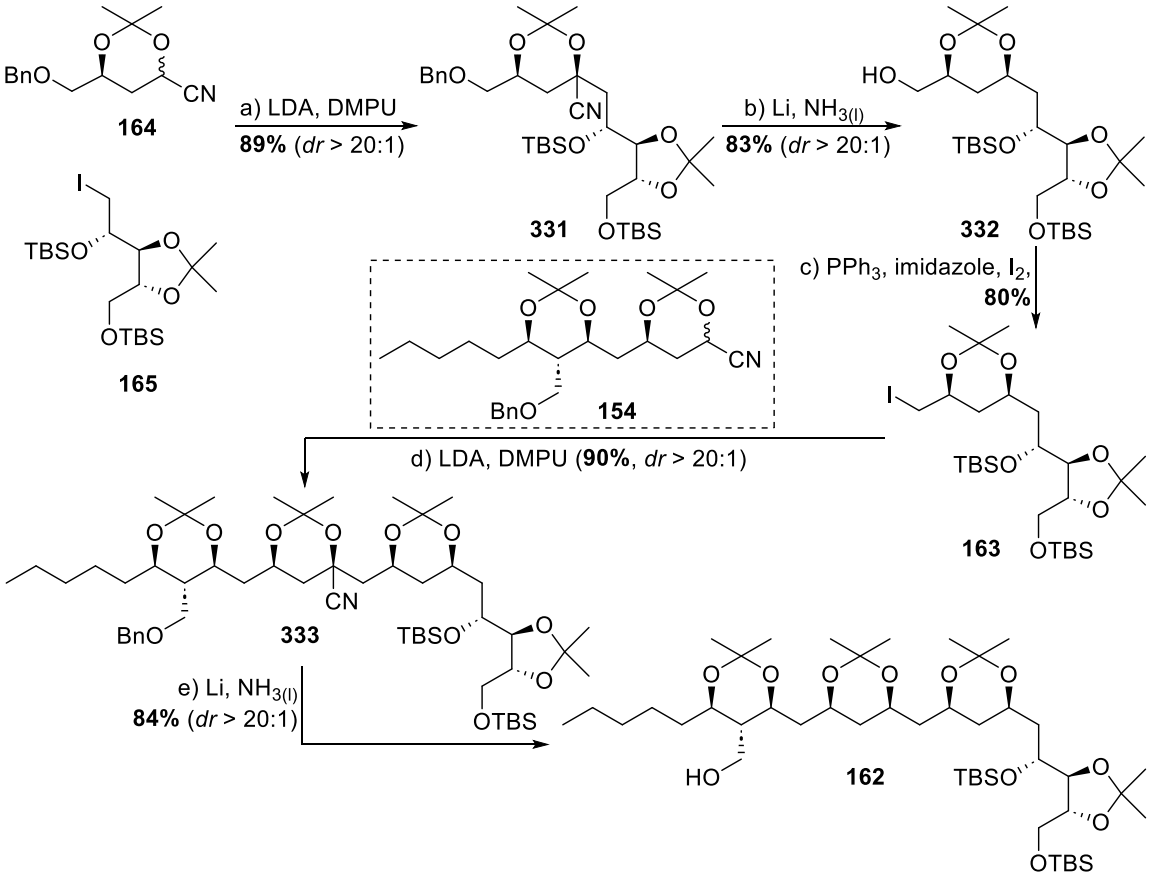

Scheme 4.4: Synthesis of cyanohydrin acetonide **164** as subunit of eastern fragment **163**.
Reaction conditions: a) (*S,S*)-**A**, $Me_3SOI$, *t*-BuOK, *t*-BuOH, 60 °C, 16 h, **91%**; b) TMSCl, $NEt_3$, DCM, rt, 2 h, **94%**; c) $OsO_4$, NMO, acetone/$H_2O$ (10:1), rt, 20 h; d) $Pb(OAc)_4$, benzene, rt, 10 min, **88%** (over 2 steps); e) TMSCN, $K_2CO_3$, DMF, rt, 20 min; f) PPTS, MeOH, rt, 15 min, then 2,2-DMP, DCM, rt, 16 h, **83%** (over 2 steps; *dr* ≈ 1:1).

As already discussed in Chapter 3.3.5 for the wrong isomer *ent*-**166**, alkyl iodide **165** was derived from acetonide protected (D)-threitol **166** which was monoprotected using NaH and TBSCl to give TBS ether **325** (Scheme 4.5).[158] The remaining free hydroxy function was oxidized under Parikh-Doering conditions and resulting aldehyde **326** was treated with $Zn(OTf)_2$, (−)-*N*-methylephedrine (**198**), and $NEt_3$ to add pentyne (**277**) in a stereoselective manner according to Carreira's protocol.[72] The propargylic hydroxy function of **327** was protected as TBS ether **328** before the alkyne was reduced to the olefin using Lindlar's catalyst.[159] Ozonolysis of the double bond of olefin **329** and reductive workup gave primary alcohol **330** which was transformed to required alkyl iodide **165** using Appel conditions.[160,161]




Scheme 4.5: Synthesis of alkyl iodide **165** as subunit of eastern fragment **163**.
Reaction conditions: a) **166**, NaH, THF, 0 °C, 1 h, then TBSCl, 0 °C, 3 h, **90%**; b) $SO_3$·py, DMSO, DIPEA, DCM, rt, 2 h, **92%**; c) $Zn(OTf)_2$, **198**, $NEt_3$, toluene, rt, 2 h, then **277**, **326**, rt, 2 h, **93%** (*dr* > 20:1); d) TBSOTf, 2,2-lutidine, DCM, 0 °C, 1 h, **quant.**; e) $H_2$ (1 atm), Lindlar catalyst (Pd, $CaCO_3$, quinoline), hexane, rt, 1 h, **quant.**; f) $O_3$, DCM/MeOH (1:1), −78 °C, then $NaBH_4$, −78 °C, 30 min, **82%**; g) $PPh_3$, imidazole, $I_2$, benzene, rt, 90 min, **87%**.

For coupling of subunits **164** and **165** of eastern fragment **163** Rychnovsky's conditions were applied, therefore both fragments were treated with freshly prepared LDA in THF/DMPU to get coupling product **331** in very good yield (Scheme 4.6).[51] Subsequent reductive cyanation under Birch conditions, employing lithium metal in liquid ammonia cleaved the nitrile substituent and the benzyl function to furnish primary alcohol **332**. As discussed in Chapter 3.2.5, although the coupling is often highly selective, the Birch reduction determines the selectivity of the overall sequence. No other diastereomer was detectable either on the TLC or in the NMR so it was assumed the selectivity is greater than 20:1. The primary hydroxy function of compound **332** was transformed to the alkyl iodide under Appel conditions to get eastern fragment **163** which is the starting material for the next coupling reaction with northern fragment **154**. Again, both fragments were treated with freshly prepared LDA in THF/DMPU to obtain coupling product **333** which contains the complete polyol backbone of pentamycin (**10**). Birch conditions again cleaved the nitrile substituent and the benzyl protection group and provided compound **162** in good yield and excellent selectivity.

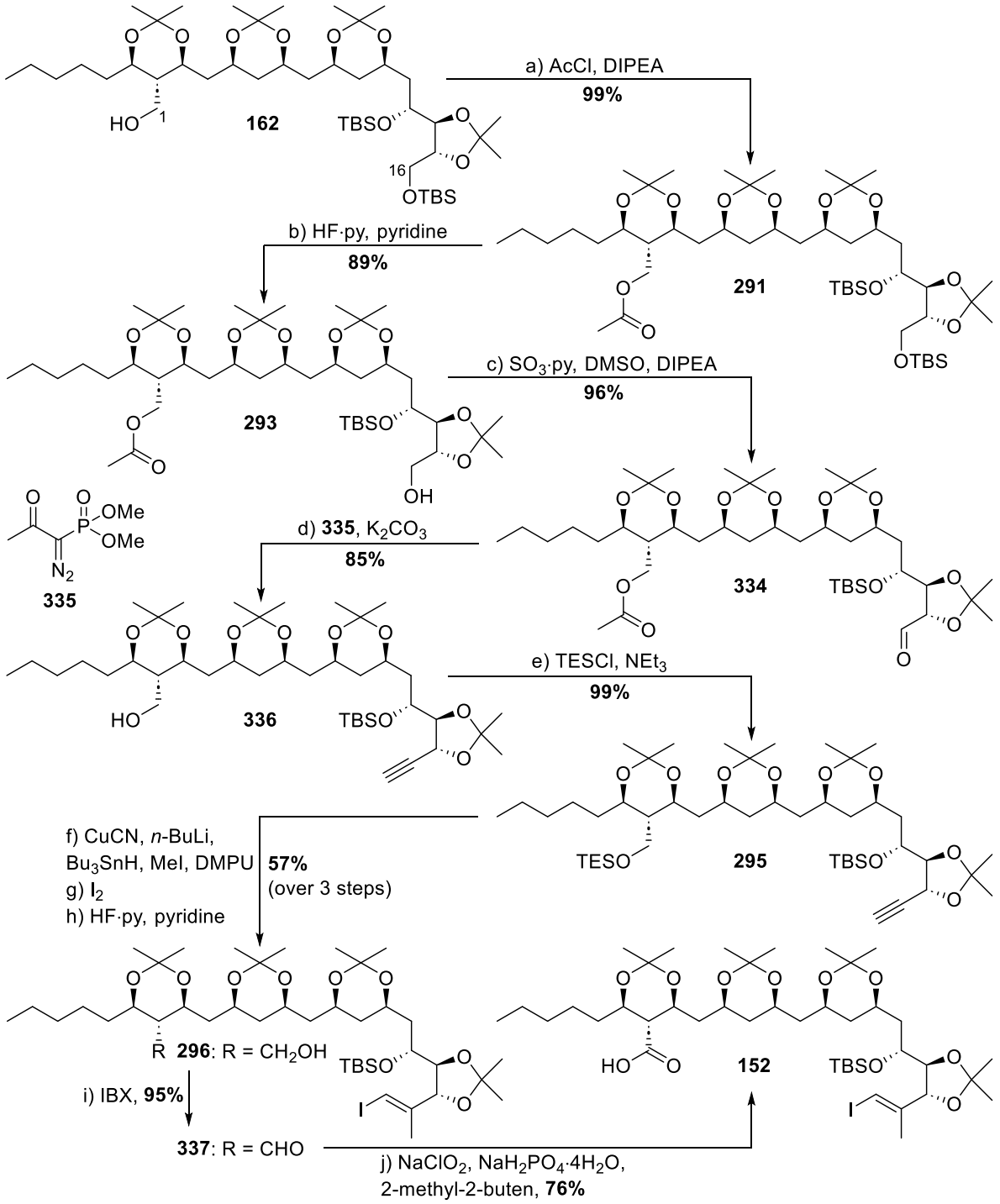



Scheme 4.6: Coupling of the subunits **164** and **165** of eastern fragment **163** and subsequent coupling of eastern and northern fragment **154** of pentamycin (**10**).
Reaction conditions: a) LDA, DMPU, THF, −40 °C, 1 h, **89%** (*dr* > 20:1); b) Li, liquid $NH_3$, THF, −78 °C, 1 h, **83%** (*dr* > 20:1); c) $PPh_3$, imidazole, $I_2$, benzene, rt, 1 h, **80%**; d) LDA, DMPU, THF, −40 °C, 1 h, **90%** (*dr* > 20:1); e) Li, liquid $NH_3$, THF, −78 °C, 1 h, **84%** (*dr* > 20:1).

## 4.2 Modification of the Polyol Part

Coupling product **162** of northern **154** and eastern fragment **163** was further modified, before the total synthesis could be finalized (Scheme 4.7). The free hydroxy function at C1 was protected with acetyl chloride to get acetate **291** before the primary TBS function at C16 was selectively cleaved in presence of a secondary TBS ether. A pyridine-buffered solution of HF·pyridine was used to accomplish excellent yield for primary deprotection.[166] The hydroxy function of primary alcohol **293** was oxidized to aldehyde **334** using Parikh-Doering conditions and Ohira-Bestmann homologation with reagent **335** and $K_2CO_3$ furnished terminal alkyne **336**.[167] Since the acetyl protecting group was also cleaved under the basic conditions, the hydroxy function at C1 was reprotected as TES ether **295**. The terminal alkyne of **295** served as starting material to introduce the *α*-methyl vinyl iodide of **296** by stannylcupration with subsequent methylation, iodination, and final deprotection of the TES group.[173] A moderate yield of 57% over three steps could be achieved for this preparatively challenging sequence. The final modification steps were oxidation at C1, first to aldehyde **337** using IBX, then to carboxylic

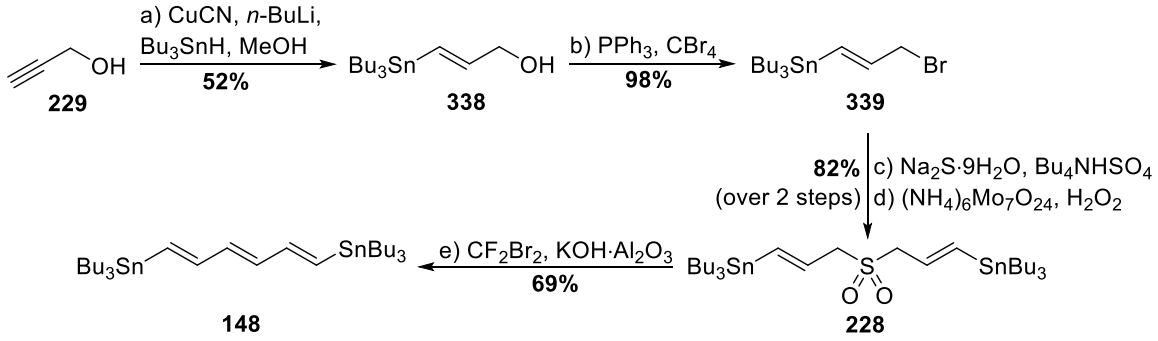
acid **152**, the starting material for esterification with western fragment **153**, under Pinnick conditions.[183]




Scheme 4.7: Modification of coupling product **162** to carboxylic acid **152**.
Reaction conditions: a) AcCl, DIPEA, DCM, −78 °C, 2.5 h, then 0 °C, 2.5 h, **99%**; b) HF·py, pyridine, THF, 0 °C, 15 h, then rt, 45 min, **89%**; c) $SO_3$·py, DMSO, DIPEA, DCM, 0 °C, 90 min, **96%**; d) **335**, $K_2CO_3$, MeOH, rt, 4 h, **85%**; e) TESCl, $NEt_3$, DCM, rt, 6 h, **99%**; f) CuCN, *n*-BuLi, THF, −78 °C to rt, 20 min, then $Bu_3SnH$, −78 °C, 10 min, then **295**, −78 °C, 1 h, then MeI, DMPU, −78 °C to rt, 30 min; g) $I_2$, DCM, −78 °C, then 0 °C, 30 min; h) HF·py, pyridine, THF, 0 °C, 90 min, **57%** (over 3 steps); i) IBX, DMSO, rt, 90 min, **95%**; j) $NaClO_2$, $NaH_2PO_4·4H_2O$, 2-methyl-2-buten, *t*-BuOH/$H_2O$ (10:1), rt, 2 h, **76%**.

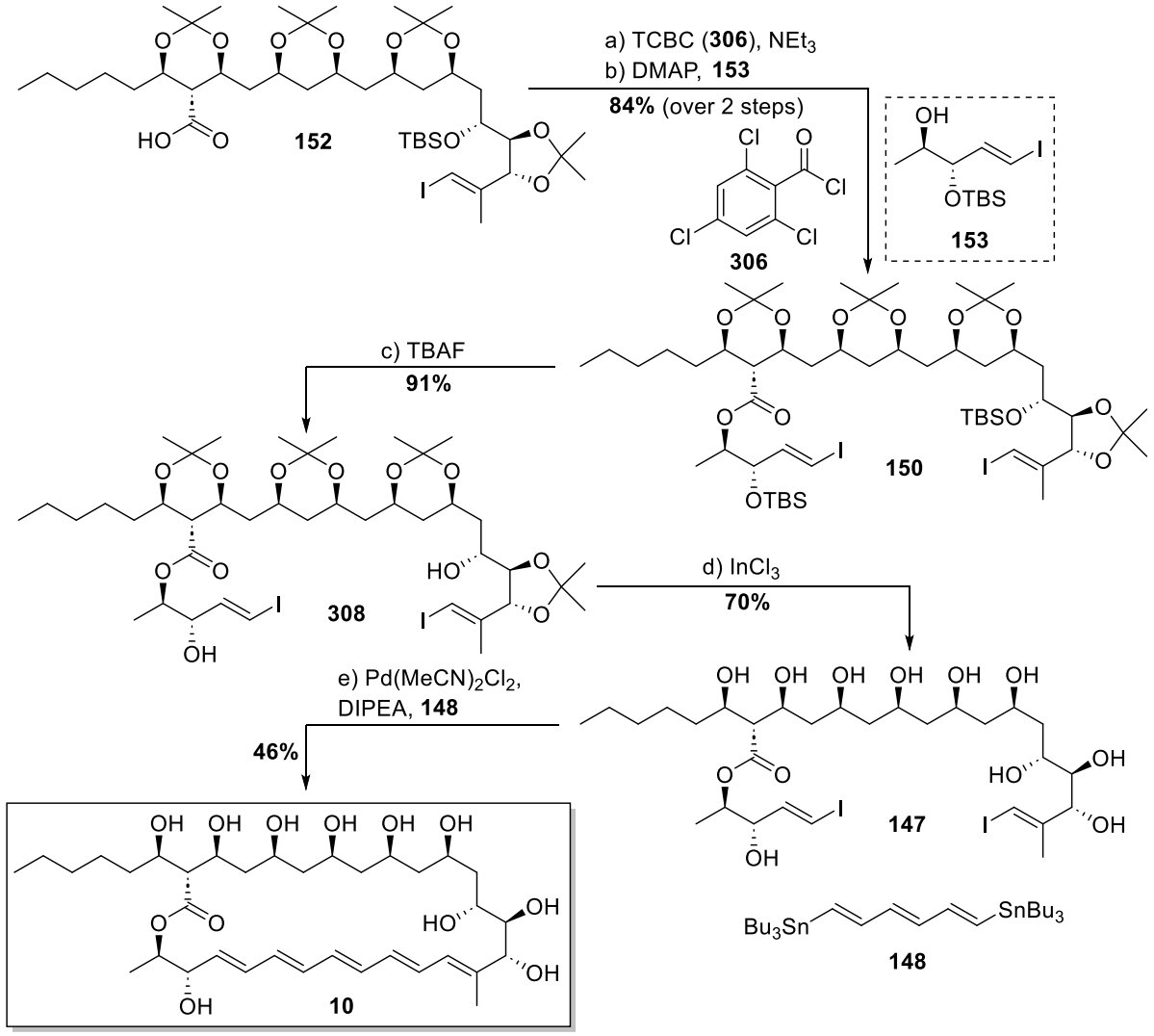
## 4.3 Synthesis of the Polyene Part and Endgame

The southern fragment, representing the polyene part of pentamycin (**10**) was synthesized by a procedure reported by Brückner (Scheme 4.8).[126] Therefore, allylic alcohol **338** was synthesized from propargylic alcohol (**229**) by stannylcupration.[174] An Appel reaction with $CBr_4$ as bromine source transferred the primary hydroxy function to the alkyl bromide **339**.[184] Nucleophilic substitution of the bromine with $Na_2S$ and subsequent oxidation gave sulfone **228** *via* the corresponding thioether as intermediate.[185] Final Ramberg-Bäcklund reaction with $CBr_2F_2$ and $Al_2O_3$-supported KOH for deprotonation furnished trienyl-*bis*-stannane **148** providing the starting material for the final Stille coupling (**10**).[124,127]




Scheme 4.8: Synthesis of southern fragment **148** by a procedure reported by Brückner.[126]
Reaction conditions: a) CuCN, *n*-BuLi, THF, −78 °C to rt, 20 min, then $Bu_3SnH$, −78 °C, 10 min, then **229**, −78 °C, 1 h, then MeOH, −78 °C to rt, **52%**; b) $PPh_3$, $CBr_4$, DCM, 0 °C to rt, 1 h, **98%**; c) $Na_2S{\cdot}9H_2O$, $Bu_4NHSO_4$, THF/$H_2O$ (1:1), rt, 18 h; d) $(NH_4)_6Mo_7O_{24}$, $H_2O_2$ (30% in $H_2O$), EtOH, 0 °C, 15 min, then rt, 1 h, **82%** (over 2 steps); e) $CF_2Br_2$, KOH (30% on $Al_2O_3$), THF, 0 °C, 30 min, **69%**.

Finally, western fragment **153** was coupled to carboxylic acid **152** and thus the second vinyl iodide moiety required for the final Stille coupling was attached to the molecule (Scheme 4.9). Coupling was achieved through esterification of the secondary hydroxy function of western fragment **153** under Yamaguchi conditions with TCBC (**306**) and DMAP.[54] Protected *bis*-vinyl iodide **150** was deprotected in a two-step sequence, first the TBS ethers were cleaved with TBAF to obtain diol **308**, second, the acetonides were deprotected using $InCl_3$ in wet MeCN.[77] Fully deprotected bis vinyl iodide **147** served as starting material for the ultimate linchpin insertion. $Pd(MeCN)_2Cl_2$ and DIPEA were used in a 5:1 mixture of DMF and THF.[139] This mixture was crucial to ensure the solubility of highly polar polyol fragment **147** dissolved in DMF and completely unpolar trienyl-*bis*-stannane **148** dissolved in THF. Pentamycin (**10**) was obtained after flush chromatography on reversed phase silica gel in good yield of 46% considering the complexity and high conformational challenge of this conversion. Although freshly prepared synthetic pentamycin (**10**) was obtained in high purity, the final compound proved to be delicate. HPLC purification with UV detection led to partial double bond isomerization and decomposition, as observed in the respective regions of the $^1$H-NMR spectrum (Figure 6.10, p. 170).




Scheme 4.9: Coupling of western fragment **153** to carboxylic acid **152**, deprotection, and double Stille ring closure with bis stannane **148**.
Reaction conditions: a) TCBC (**306**), $NEt_3$, THF, rt, 6 h; b) DMAP, toluene, rt, 10 min, then **153**, rt, 48 h, **84%** (over 2 steps); c) TBAF, THF, 0 °C, 4 h, **91%**; d) $InCl_3$, wet MeCN, 50 °C, 5 h, then evaporation, then wet MeCN, 50 °C, 5 h, **70%**; e) $Pd(MeCN)_2Cl_2$, DIPEA, DMF/THF (5:1), rt, dark, 24 h, **46%**.

The spectroscopic data ($^1$H- and $^{13}$C-NMR) of synthetic pentamycin (**10**) were in agreement with those published for an authentic sample of the natural product, thus confirming the relative and absolute configuration as shown in this work (Tables 6.6 and 7.7, pp. 170–172).[186] Figure 4.1 shows the $^1$H-NMR spectrum of synthetic pentamycin (**10**). The nine olefinic hydrogen atoms of the polyene moiety are located between 6.50 and 6.02 ppm. The hydrogen atom at C27 is overlapped by the water signal at 4.84 ppm, the ten protons at the hydroxy substituted carbon atoms have a chemical shift between 4.19 and 3.27. The hydrogen atom at C2 shows an isolated signal at 2.56 ppm. Except one of the C12 hydrogen atoms, which shows an isolated signal at 1.76 ppm, the remaining 17 methylene hydrogens located at the carbon atoms between the hydroxy substituted carbons, as well in the pentyl side chain show a chemical shift between 1.56 and 1.31 ppm. The three characteristic methyl signals of C6*, C28, and C29

are located at 0.92 (triplet), 1.30 (doublet), and 1.79 (doublet). The protons of the ten hydroxy functions are not visible in $CD_3OD$.

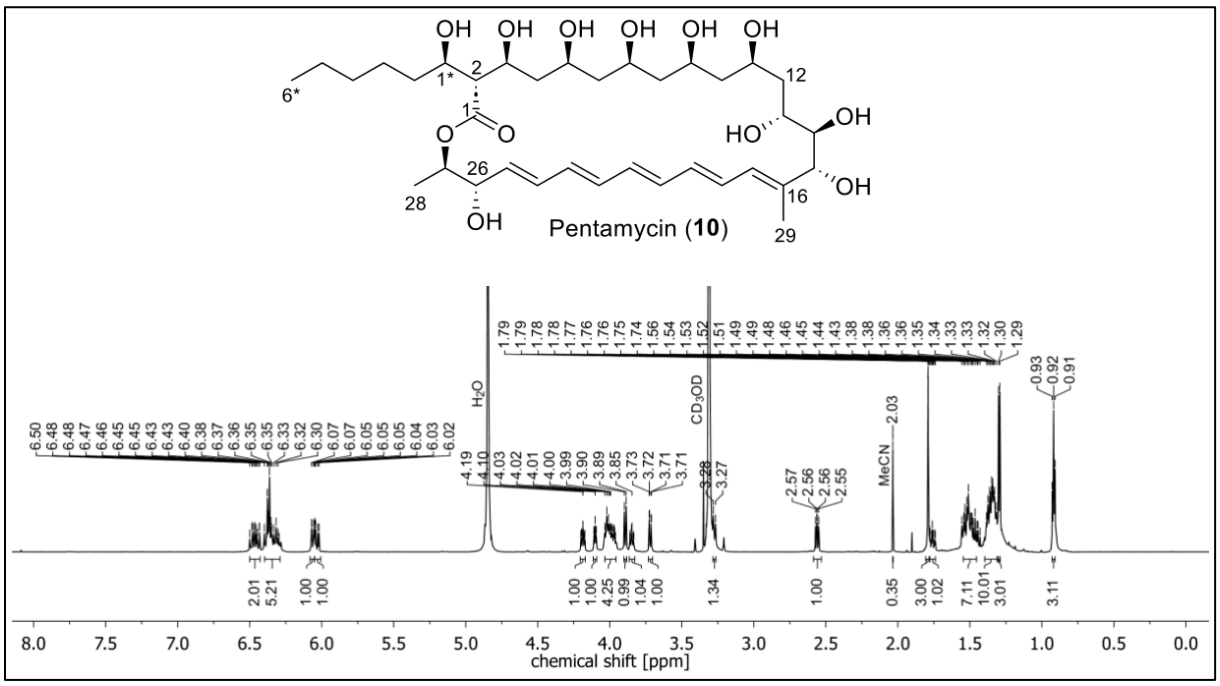
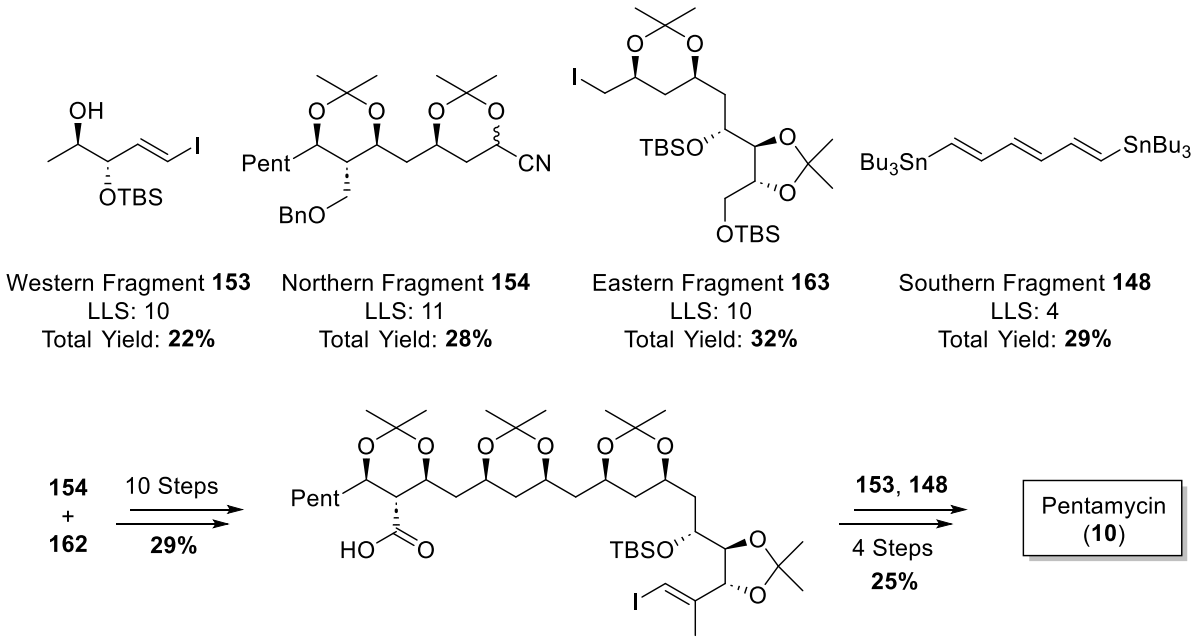



Figure 4.1: $^1$H-NMR-spectrum of synthetic pentamycin (**10**).

# 5 Summary and Outlook

## 5.1 Summary

The first total synthesis of pentamycin (**10**) was accomplished by a modular strategy from western fragment **153**, northern fragment **155**, eastern fragment **163**, and southern fragment **153**. The fragments were synthesized with longest linear sequences (LLS) between 11 and 4 steps and yields between 22 and 32% (Scheme 5.1). The overall synthesis contains a total of 55 steps and an LLS of 25 steps with an overall yield of 1.5%.

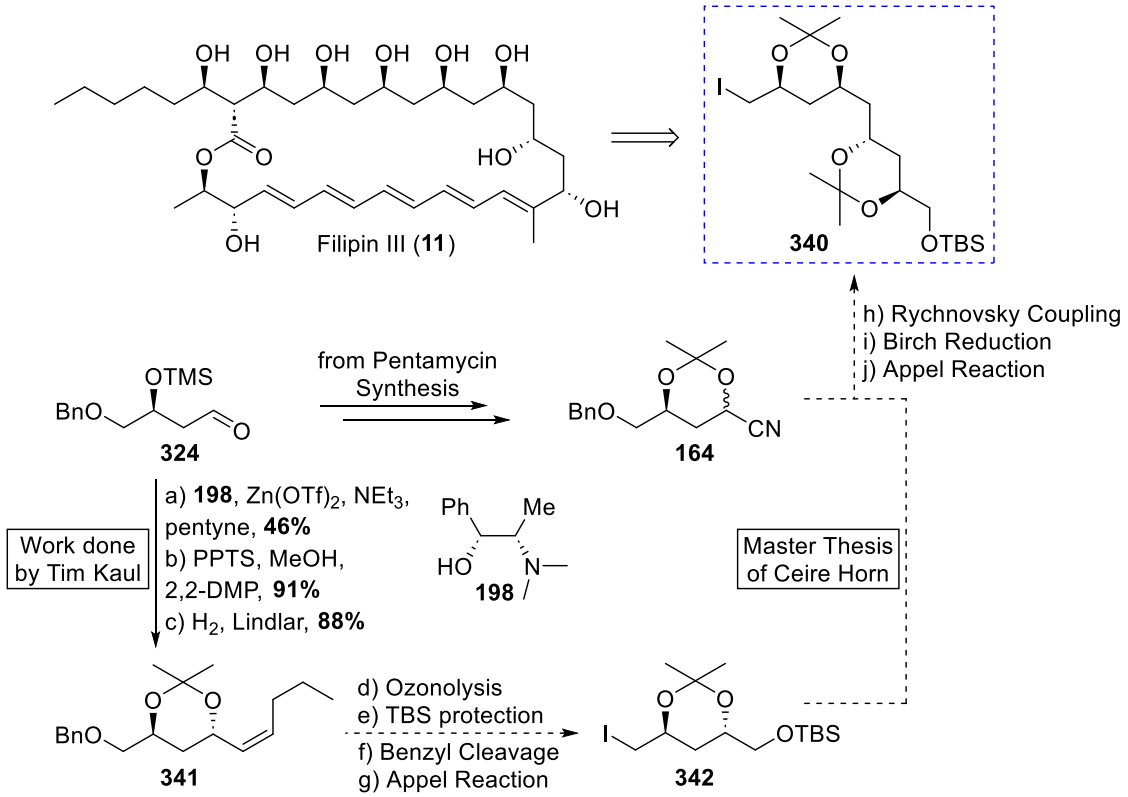



Scheme 5.1: Overview of the synthesized fragments utilized in the ultimate total synthesis of pentamycin, with LLSs and yields.

Key step of the total synthesis was an ultimate Stille-type ring closure, circumventing any stability issues during the synthesis which proved essential for realization of this sequence. Further key reactions were the Rychnovsky coupling with subsequent Birch reduction, several types of Kirsche allylations, the Sharpless asymmetric epoxidation and Carreira's zinc-mediated addition of alkynes to aldehydes. This total synthesis unequivocally confirms the complete relative and absolute configuration of pentamycin (**10**), which had never been definitively confirmed before. Moreover, the strategy adopted underlines the usefulness of conformational control in the synthesis of complex polyketides (Scheme 3.51). It represents one of the first examples where an extended hydrogen bonding network has been designed as a conformational template for a complex macrocyclization and may provide an alternative to macrolactonizations or HWE-mediated as well as RCM ring closure approaches.

## 5.2 Outlook

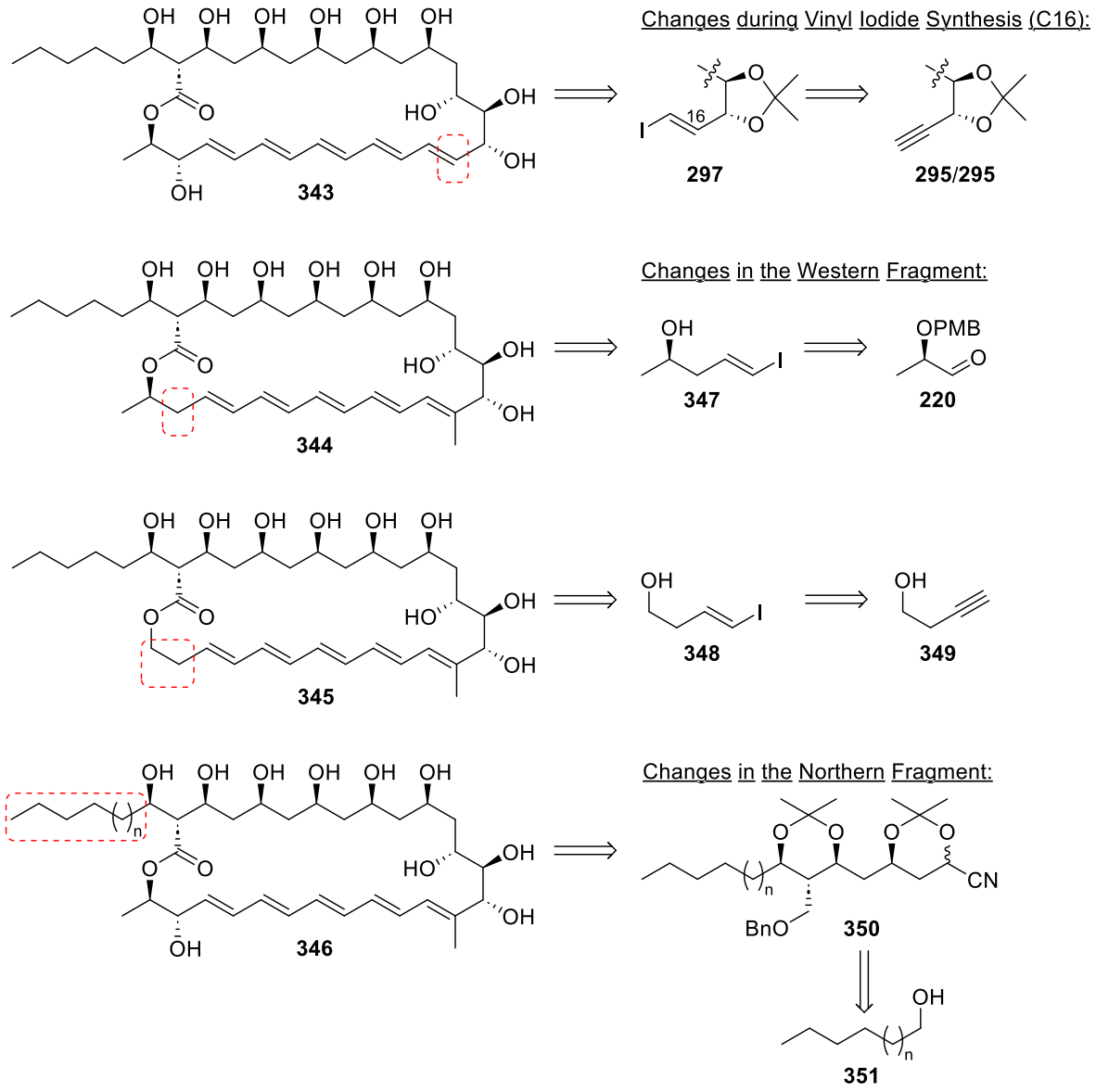
The established sequence should be applicable to designed analogs of pentamycin, as well as to its biosynthetic precursor filipin III (**11**). To prove the robustness of the route, its application to the very similar molecule filipin III (**11**) is a topic for current master theses in our group. Since the only difference between pentamycin and filipin III is the hydroxy group at C14, just the eastern part has to be redesigned, resulting in eastern fragment **340** (Scheme 5.2). Aldehyde **324** is a compound already prepared and used in the route towards pentamycin. Based on this, Tim Kaul was previously able to establish the three steps, i.e. Carreira addition, acetonide formation of the resulting 1,3-*anti* diol, and hydrogenation under Lindlar conditions to produce olefin **341** as part of his master thesis (April to October 2023). An integral part of Ceire Horn's master's thesis (April to September 2024) will be the synthesis of alkyl iodide **342**, which should be coupled to cyanohydrin acetonide **164** to synthesize the novel eastern fragment **340** towards filipin III (**11**).




Scheme 5.2: Synthetic plan for filipin III (**11**) based on the established strategy for the total synthesis of pentamycin (**10**).

Other derivatives as potential targets for synthesis are shown in Scheme 5.3. 16-Demethylpentamycin (**343**) might be accessible by modifying the procedure of *α*-methylvinyl iodide formation. During the discussed stannylcupration, quenching of the stannylcuprate could occur with MeOH instead of MeI, to introduce a hydrogen atom instead of the C29 methyl group to C16 and produce the byproduct **297** observed during production of **296** as the desired product.

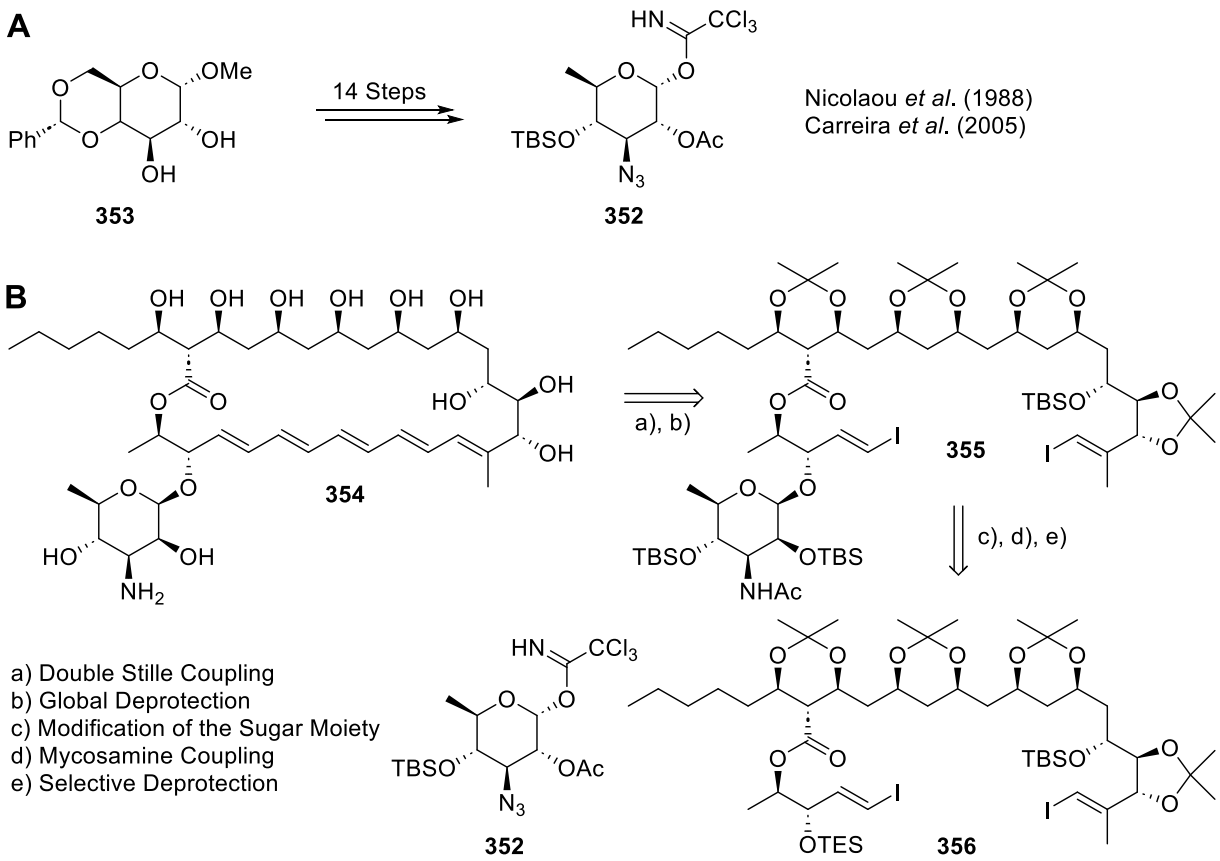
Another possibility could be Schwartz hydrozirconation followed by iodination to produce the vinyl iodide. Derivatives **344** and **345** could be obtained by coupling a simplified western fragment to carboxylic acid **152**. Fragment **347** could be obtained from aldehyde **220**, used for the synthesis of authentic western fragment **153**, by enol-ether Wittig reaction to homologate the aldehyde, Ohira-Bestmann homologation, Schwartz hydrozirconation with iodination and final cleavage of the PMB ether. Fragment **348** is accessible by hydrozirconation/iodination of 3-butyn-1-ol (**349**) in a single step. The fourth proposed derivative **346** contains a longer side chain. Therefore, the northern fragment must be modified, by starting the synthesis with a higher homologue from hexanol **351**. A derivative with a longer side chain would increase lipophilicity by the longer non-polar residue which could have a significant influence on its bioactivity.




Scheme 5.3: Structures of suggested derivatives **343**–**346** of pentamycin with highlighted modified regions (red dashed box) and brief retrosynthetic analysis of the modified fragments.

The derivatives could be tested in microbiological assays to further explore their bioactivity. In this context, it may be attractive to introduce the mycosamine moiety, which is typical for many macrolide antibiotics such as amphotericin B (**5**) and nystatin (**7**), as discussed in Chapter 1 (Figure 1.2). The mycosamine moiety is known to play an important role in the mode of action of macrolides (Figures 1.3 and 1.4).

Mycosamine donor **352** has been synthesized by Nicolaou *et al*. and by Carreira *et al*. Both routes involve 14 steps starting from **353** (Scheme 5.4 **A**).[187,188] A potential coupling position on the pentamycin core could be the hydroxy group at C26, located in the western part of pentamycin. Scheme 5.4 **B** shows a retrosynthetic analysis for accessing pentamycin glycone **354**. The double Stille coupling would again be the last step in the proposed pathway. Prior to global deprotection, mycosamine donor **352** is coupled to the C26 hydroxy function and modified. Selective deprotection of the C26 hydroxy function might be possible, e.g. by introducing a TES group during the synthesis of the western fragment.




Scheme 5.4: **A**: Overview of existing pathways to mycosamine donor **352**. **B**: Retrosynthetic analysis of proposed pentamycin glycone **354**.[187,188]

The established strategy may also be applied to the total synthesis of other polyene macrolides. In particular, molecules that have not yet been synthesized due to instability are attractive targets.

# 6 Experimental Part

## 6.1 Material and Methods

### 6.1.1 Reaction Conditions

All reagents were purchased from commercial suppliers (Sigma Aldrich, TCI, Acros, Alfa Aesar, abcr, Carbolution) in the highest purity grade available and used without further purification. Anhydrous solvents (THF, toluene, $CH_2Cl_2$, MeCN, $Et_2O$) were obtained from a solvent drying system MB SPS-800 (MBraun) and stored over molecular sieves (4 Å).

The reactions in which dry solvents were used were performed under an argon atmosphere in flame-dried glassware, which had been flushed with argon unless stated otherwise. The reactants were handled using standard Schlenk techniques. Temperatures above rt (23 °C) refer to oil bath temperatures which were controlled by a temperature modulator. For cooling, the following baths were used: acetone/dry ice (−78 °C), acetonitrile/dry ice (−40 °C), water/ice (0 °C). For cooling overnight an immersion cooler was used (huber, TC100E-F).

TLC monitoring was performed with silica gel $60_{F254}$ pre-coated polyester sheets (0.2 mm silica gel, *Macherey-Nagel*) and for reversed phase TLC silica gel 60 RP-18 $F_{254}S$ pre-coated aluminum sheets (*Merck*). For highly acid sensitive compounds TLC sheets coated with Alox (*Macherey-Nagel*) were used. The spots were visualized using UV light and stained with a solution of CAM (1.0 g $Ce(SO_4)_2$), 2.5 g $(NH_4)_6Mo_7O_{24}$, 8 mL conc. $H_2SO_4$ in 100 mL $H_2O$) and subsequent heating.

### 6.1.2 Purification Methods

For column chromatography, silica gel (pore size 60 Å, 40-63 µm) obtained from *Merck* or *Sigma Aldrich* was used. For reversed phase column chromatography $C_{18}$-reversed phase silica gel (pore size 90 Å) from *Sigma Aldrich* or *Carl Roth* was used. Compounds were eluted using the stated mixtures under a positive pressure of argon or air. Solvents for column chromatography were distilled prior to use.

Semi-preparative and analytical HPLC analyzes were performed on *Knauer Wissenschaftliche Geräte GmbH* systems by Andreas J. Schneider. The solvents for HPLC were purchased in HPLC grade. The chromatograms were recorded by UV-detection.

### 6.1.3 Analytical Methods

All NMR spectra were recorded on Bruker spectrometers at the University Bonn under supervision of Dr. Senada Nozinovic with operating frequencies of 100 ($^{13}C$), 125 ($^{13}C$), 175 ($^{13}C$), 400 ($^{1}H$), 500 ($^{1}H$), and 700 MHz ($^{1}H$) in deuterated solvents obtained from *Deutero*, *Carl Roth*

or *Sigma Aldrich*. Spectra were measured at room temperature unless stated otherwise and chemical shifts are reported in ppm relative to $(Me)_4Si$ ($\delta$ = 0.00 ppm) and were calibrated to the residual signal of undeuterated solvents.[189] Data for $^1$H-NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogens, assignment). Abbreviations used are: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad).

Mass spectra (MS) and High-resolution-mass spectra (HRMS) were recorded on the documented systems in Table 6.1 at the University Bonn under supervision of Dr. Marianne Engeser.

Table 6.1: Used MS systems for MS and HRMS.

| System | Manufacturer | Measurements |
|---|---|---|
| **micrOTOF-Q** | Bruker Daltonik (Bremen) | ESI, APCI, nano-ESI, MS/MS |
| **Orbitrap XL** | Thermo Fisher Scientific (Bremen) | ESI, APCI, APPI, nano-ESI |
| **Apex IV FT-ICR** | Bruker Daltonik (Bremen) | ESI, nano-ESI, MALDI, EI, CI |

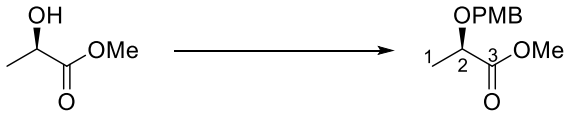
## 6.2 Total Synthesis of Pentamycin

The numbering of the atoms in this section does not necessarily correspond to the numbering in the main body. In the official numbering of pentamycin (**10**) and its derivatives, the atoms are identified as HX and CX. The experimental part uses a different numbering for the atoms, which is defined in the respective structure of the target molecule at the beginning of each procedure, since not all atoms introduced into the molecule during the synthetic routes are included in the final molecule. The atoms in the experimental part are numbered H-X and C-X to avoid confusion with the numbering in the main section.

### 6.2.1 Synthesis of the Western Fragment

#### Synthesis of Compound 311

**Methyl (*R*)-2-((4-methoxybenzyl)oxy)propanoate**




**310** **311**

$C_{12}H_{16}O_4$
M = 224.26 g/mol

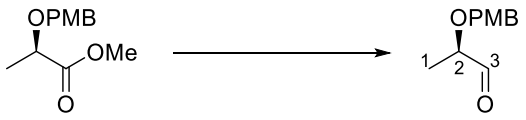
To a stirred solution of methyl D-lactate (**310**) (1.28 g, 13.5 mmol, 1 equiv) in DCM (25 mL) were added 4-methoxybenzyl-2,2,2-trichloroacetimidate (3.63 mL, 17.5 mmol, 1.3 equiv) and

CSA (0.62 g, 2.69 mmol, 0.2 equiv) at room temperature. The mixture was stirred for 16 h at room temperature and was then quenched with saturated $NaHCO_3$ solution (25 mL). After separation of the organic phase, the aqueous phase was extracted with DCM (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 9:1). The pure product was obtained as a yellowish oil (2.04 g, 9.10 mmol, 68%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.22. $[\alpha]_D^{20}$ = +50.0° (c = 1.14, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.28–7.25 (m, 2H, 2xCH-PMB), 6.88–6.86 (m, 2H, 2xCH-PMB), 4.55 (d, $^2J$ = 11.1 Hz, 1H, $CH_2$-PMB), 4.35 (d, $^2J$ = 11.1 Hz, 1H, $CH_2$-PMB´), 4.04 (q, $^3J_{H\text{-}2,\,H\text{-}1}$ = 6.9 Hz, 1H, H-2), 3.79 (s, 3H, OMe), 3.72 (s, 3H, OMe), 1.38 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 6.9 Hz, 3H, H-3). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 174.2 (C-3), 160.0 ($C_q$-PMB), 130.5 ($C_q$-PMB), 130.1 (2xCH-PMB), 114.2 (2xCH-PMB), 74.4 (C-2), 72.1 ($CH_2$-PMB), 55.8 (OMe), 52.2 (OMe), 19.1 (C-1). **MS (ESI-TOF)** *m/z*: $[M+K]^+$ Calcd for $C_{12}H_{16}O_4K^+$ 263.068, found 263.068. For NMR-spectra see p. 231.

**Synthesis of Compound 220**

**(*R*)-2-((4-methoxybenzyl)oxy)propanal**




**311** **220**

$C_{11}H_{14}O_3$
M = 194.23 g/mol

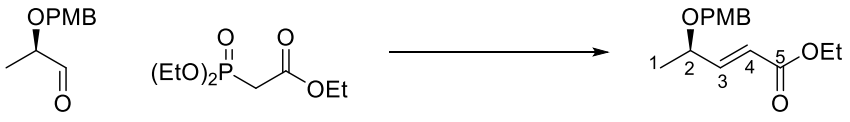
A stirred solution of protected methyl D-lactate **311** (1.13 g, 5.04 mmol, 1 equiv) in DCM (12 mL) was cooled to −78 °C. A solution of DIBAL-H (1M in hexane, 5.04 mL, 5.04 mmol, 1 equiv) was added dropwise and the mixture was stirred for 30 min at −78 °C. The reaction mixture was quenched with a saturated solution of Rochelle salt (15 mL) and was stirred for 2 h. After that, the organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure to obtain crude aldehyde **220** as a clear, yellow oil which was used immediately in the next reaction.

**TLC** (silica, CyHex:EtOAc = 8:1): $R_f$ = 0.16. $[\alpha]_D^{20}$ = +9.7° (c = 1.76, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.62 (d, $^3J_{H\text{-}3,\,H\text{-}2}$ = 1.7 Hz, 1H, H-3), 7.31–7.25 (m, 2H, 2xCH-PMB), 6.90–6.86 (m, 2H, 2xCH-PMB), 4.55 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB), 4.52 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB´), 3.87 (qd, $^3J_{H\text{-}2,\,H\text{-}1}$ = 7.0 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 1.7 Hz, 1H, H-2), 3.80 (s,

3H, OMe), 1.28 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 7.0 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 204.0 (C-3), 160.1 ($C_q$-PMB), 130.3 ($C_q$-PMB), 130.1 (2xCH-PMB), 114.3 (2xCH-PMB) 79.9 (C-2), 72.2 ($CH_2$-PMB), 55.8 (OMe), 15.6 (C-1). **MS (EI, 70.0 eV)** *m/z*: [$M^{\cdot+}$] Calcd for $C_{11}H_{14}O_3^{\cdot+}$ 194.09, found 194.1. For NMR-spectra see p. 233.

**Synthesis of Compound 312**

**Ethyl (4*R*,2*E*)-4-((4-methoxybenzyl)oxy)pent-2-enoate**




**220** **143** **312**

$C_{15}H_{20}O_4$
M = 264.32 g/mol

A stirred solution of crude aldehyde **220** in MeCN (10 mL) was cooled to 0 °C. LiCl (0.38 g, 9.07 mmol, 1.8 equiv), triethyl phosphonoacetate (1.75 mL, 8.82 mmol, 1.75 equiv) and DIPEA (1.50 mL, 8.82 mmol, 1.75 equiv) were added and the mixture was warmed to room temperature. After stirring for 1.5 h at room temperature the reaction mixture was quenched with saturated $NH_4Cl$ solution (20 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (2 x 30 mL). The combined organic layers were washed with water (50 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a slightly yellow oil (1.08 g, 4.09 mmol, 81% over two steps, (1.06 g (*E*); 22 mg (*Z*)) *dr* ≈ 50:1).

(*E*)-Isomer:

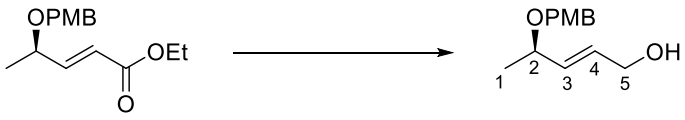
**TLC** (silica, CyHex:EtOAc = 8:1): $R_f$ = 0.29. $[\alpha]_D^{20}$ = +39.1° (c = 0.92, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.27–7.24 (m, 2H, 2xCH-PMB), 6.90–6.83 (m, 3H, 2xCH-PMB, H-3), 5.99 (dd, $^3J_{H\text{-}4,\,H\text{-}3}$ = 15.8 Hz, $^4J_{H\text{-}4,\,H\text{-}2}$ = 1.0 Hz, 1H, H-4), 4.47 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB), 4.36 (d, $^2J$ = 11.4 Hz, 1H, $CH_2$-PMB´), 4.18 (q, $^3J$ = 7.1 Hz, 2H, $CH_2$-Et), 4.13–4.08 (m, 1H, H-2), 3.79 (s, 3H, OMe), 1.30–1.26 (m, 6H, H-1, $CH_3$-Et). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.7 (C-5), 159.8 ($C_q$-PMB), 149.8 (C-3), 131.1 ($C_q$-PMB), 129.7 (2xCH-PMB), 121.8 (C-4), 114.2 (2xCH-PMB), 74.3 (C-2), 70.9 ($CH_2$-PMB), 60.9 ($CH_2$-Et), 55.8 (OMe), 21.0 ($CH_3$-Et), 14.6 (C-1). **MS (EI, 70.0 eV)** *m/z*: [$M^{\cdot+}$] Calcd for $C_{15}H_{20}O_4^{\cdot+}$ 264.14, found 264.1. For NMR-spectra see p. 235.

(*Z*)-Isomer:

**TLC** (silica, CyHex:EtOAc = 8:1): $R_f$ = 0.35. $[\alpha]_D^{20}$ = +45.2° (c = 1.24, DCM). **$^1$H-NMR** (400 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.28–7.18 (m, 2H, 2xCH-PMB), 6.90–6.82 (m, 2H, 2xCH-PMB), 6.19 (dd, $^3J_{H\text{-}3,\ H\text{-}4}$ = 11.8 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 8.2 Hz, 1H, H-3), 5.83 (dd, $^3J_{H\text{-}4,\ H\text{-}3}$ = 11.7 Hz, $^4J_{H\text{-}4,\ H\text{-}2}$ = 1.3 Hz, 1H, H-4), 5.09 (m, 1H, H-2), 4.42 (d, $^2J$ = 11.2 Hz, 1H, 1x$CH_2$-PMB), 4.33 (d, $^2J$ = 11.2 Hz, 1H, 1x$CH_2$-PMB), 4.14 (q, $^3J$ = 7.1 Hz, 2H, $CH_2$-Et), 3.78 (s, 3H, OMe), 1.28–1.24 (m, 6H, H-1, $CH_3$-Et). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.3 (C-5), 159.8 ($C_q$-PMB), 152.5 (C-3), 131.4 ($C_q$-PMB), 129.8 (2xCH-PMB), 120.8 (C-4), 114.1 (2xCH-PMB), 71.7 (C-2), 71.2 ($CH_2$-PMB), 60.7 ($CH_2$-Et), 55.8 (OMe), 20.8 ($CH_3$-Et), 14.6 (C-1). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{20}O_4H^+$ 265.1434, found 265.1443. For NMR-spectra see p. 237.

**Synthesis of Compound 224**

**(4*R*,2*E*)-4-((4-methoxybenzyl)oxy)pent-2-en-1-ol**




**312** **224**

$C_{13}H_{18}O_3$
M = 222.28 g/mol

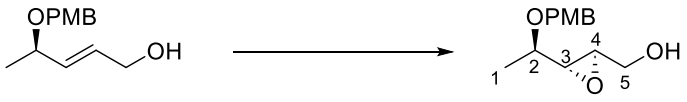
A stirred solution of α,β-unsaturated ester **312** (0.98 g, 3.71 mmol, 1 equiv) in DCM (10 mL) was cooled to −78°C. A solution of DIBAL-H (1M in hexane, 9.30 mL, 9.30 mmol, 2.5 equiv) was added dropwise and the mixture was stirred for 1.5 h at −78 °C. The reaction mixture was quenched with a saturated solution of Rochelle salt (10 mL) and stirred for 2 h. After that, the organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 7:3) and the pure product was obtained as a colorless liquid (0.78 g, 3.52 mmol, 95%).

**TLC** (silica, CyHex:EtOAc = 7:3): $R_f$ = 0.21. $[\alpha]_D^{20}$ = +29.7° (c = 0.74, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.26–7.21 (m, 2H, 2xCH-PMB), 6.88–6.84 (m, 2H, 2xCH-PMB), 5.81 (dtd, $^3J_{H\text{-}4,\ H\text{-}3}$ = 15.5 Hz, $^3J_{H\text{-}4,\ H\text{-}1}$ = 5.4 Hz, $^4J_{H\text{-}4,\ H\text{-}2}$ = 0.9 Hz, 1H, H-4), 5.64 (ddt, $^3J_{H\text{-}3,\ H\text{-}4}$ = 15.6 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.3 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 1.6 Hz, 1H, H-3), 4.45 (d, $^2J$ = 11.4 Hz, 1H, $CH_2$-PMB), 4.30 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB´), 4.16–4.10 (m, 2H, H-5), 3.98–3.92 (m, 1H, H-2), 3.79 (s, 3H, OMe), 1.24 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.7 ($C_q$-PMB), 133.8 (C-4), 131.7 ($C_q$-PMB), 131.6 (C-3), 129.7

(2xCH-PMB), 114.1 (2xCH-PMB), 75.5 (C-2), 70.1 ($CH_2$-PMB), 63.4 (C-5), 55.8 (OMe), 21.8 (C-1). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{18}O_3H^+$ 223.1329, found 223.1327. For NMR-spectra see p. 239.

**Synthesis of Compound 225**

**((2*R*,3*R*,)-3-((*R*)-1-((4-methoxybenzyl)oxy)ethyl)oxiran-2-yl)methanol**




**224** **225**

$C_{13}H_{18}O_4$
M = 238.28 g/mol

A stirred solution of (−)-DIPT (0.24 g, 1.04 mmol, 0.3 equiv) in DCM (15 mL) containing 3 Å molecular sieves (2 g) was stirred for 30 min at room temperature. Subsequently, the mixture was cooled to −30 °C and titanium tetraisopropoxide (0.41 mL, 1.39 mmol, 0.4 equiv) as well as *tert*-butyl hydroperoxide (5.5M in decane, 4.1 mL, 22.5 mmol, 6.5 equiv) were added sequentially. The mixture was stirred for another 30 min and a solution of allylic alcohol **224** (0.77 g, 3.46 mmol, 1 equiv) in DCM (8 mL) was added. The reaction mixture was stirred for 44 h and the temperature was kept between −30 °C and −20 °C. After that, the molecular sieves were removed by filtration over celite, and the filtrate was diluted with DCM (50 mL) and quenched with 2M NaOH (20 mL). After stirring for 1 h at room temperature, the organic phase was separated, and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 2:1) and the pure product was obtained as a colorless liquid (0.65 g, 2.72 mmol, 78%, (623 mg (2*R*3*R*); 24.1 mg (2*S*3*S*)) *dr* ≈ 25:1).

(2*R*3*R*)-Isomer (desired):

**TLC** (silica, CyHex:EtOAc = 1:1): $R_f$ = 0.37. $[\alpha]_D^{20}$ = +17.9° (c = 1.12, DCM). **$^1$H-NMR** (400 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.27–7.22 (m, 2H, 2xCH-PMB), 6.89–6.84 (m, 2H, 2xCH-PMB), 4.52–4.45 (m, 2H, $CH_2$-PMB), 3.86 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}5,\ OH}$ = 5.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 2.6 Hz, 1H, H-5), 3.79 (s, 3H, OMe) 3.56 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}5',\ OH}$ = 7.1 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 4.6 Hz, 1H, H-5´), 3.46 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 5.1 Hz, 1H, H-2), 3.07 (ddd, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 4.7 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 2.4 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.4 Hz, 1H, H-4), 2.91 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 5.1 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.3 Hz, 1H, H-3), 1.67 (dd, $^3J_{OH,\ H\text{-}5'}$ = 7.1 Hz, $^3J_{OH,\ H\text{-}5}$ = 5.6 Hz, 1H, OH), 1.24 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.8 ($C_q$-PMB), 131.4 ($C_q$-PMB), 129.7 (2xCH-PMB), 114.2 (2xCH-PMB), 74.1 (C-2), 71.6 ($CH_2$-PMB), 62.2 (C-5),

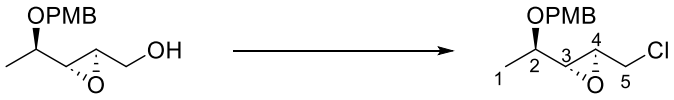
58.2 (C-3), 57.5 (C-4), 55.8 (OMe), 17.8 (C-1). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{18}O_4Na^+$ 261.1097, found 261.1093. For NMR-spectra see p. 241.

(2*S*3*S*)-Isomer:

**TLC** (silica, CyHex:EtOAc = 1:1): $R_f$ = 0.27. $[\alpha]_D^{20}$ = −7.1° (c = 1.5, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.30–7.25 (m, 2H, 2xCH-PMB), 6.90–6.83 (m, 2H, 2xCH-PMB), 4.61 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB), 4.50 (d, $^2J$ = 11.4 Hz, 1H, $CH_2$-PMB´), 3.90 (m, 1H, H-5), 3.79 (s, 3H, OMe) 3.59 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}5´,\ OH}$ = 6.8 Hz, $^3J_{H\text{-}5´,\ H\text{-}4}$ = 4.5 Hz, 1H, H-5´), 3.34 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.5 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 6.5 Hz, 1H, H-2), 3.01 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 6.6 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.3 Hz, 1H, H-3), 2.94 (ddd, $^3J_{H\text{-}4,\ H\text{-}5´}$ = 4.7 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 2.4 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.4 Hz, 1H, H-4), 1.76 (m, 1H, OH), 1.22 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.5 Hz, 3H, H-1). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.8 ($C_q$-PMB), 131.4 ($C_q$-PMB), 129.8 (2xCH-PMB), 114.2 (2xCH-PMB), 74.1 (C-2), 71.3 ($CH_2$-PMB), 62.1 (C-5), 59.4 (C-3), 55.8 (OMe), 55.3 (C-4), 17.6 (C-1). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{18}O_4Na^+$ 261.1097, found 261.1110. For NMR-spectra see p. 243.

**Synthesis of Compound 313**

**(2*S*,3*R*)-2-(chloromethyl)-3-((*R*)-1-((4-methoxybenzyl)oxy)ethyl)oxirane**




**225** **313**

$C_{13}H_{17}ClO_3$
M = 256.73 g/mol

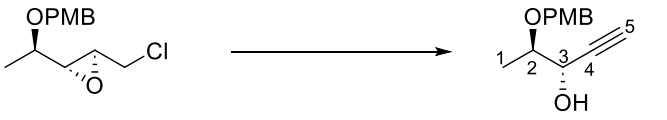
To a stirred solution of epoxide **225** (0.41 g, 1.72 mmol, 1 equiv) in $CCl_4$ (5 mL) was added $PPh_3$ (0.54 g, 2.06 mmol, 1.2 equiv) and the mixture was heated to 100 °C and refluxed for 2.5 h. After complete conversion of the starting material, the mixture was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was dissolved in DCM (20 mL) and applied on silica. After purification by flash chromatography (silica, CyHex:EtOAc = 7:1) the pure product was obtained as a white solid (0.40 g, 1.56 mmol, 91%).

**TLC** (silica, CyHex:EtOAc = 7:1): $R_f$ = 0.29. $[\alpha]_D^{20}$ = +21.4° (c = 0.98, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.27–7.23 (m, 2H, 2xCH-PMB), 6.89–6.86 (m, 2H, 2xCH-PMB), 4.52 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB), 4.47 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB´), 3.79 (s, 3H, OMe), 3.58 (dd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 4.8 Hz, 1H, H-5), 3.52 (dd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}5´,\ H\text{-}4}$ = 6.2 Hz, 1H, H-5´), 3.44 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 5.1 Hz, 1H, H-2), 3.18 (ddd, $^3J_{H\text{-}4,\ H\text{-}5´}$ = 6.0 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 4.8 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.0 Hz, 1H, H-4), 2.87 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 5.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.0 Hz, 1H, H-3), 1.25 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.9 ($C_q$-PMB), 131.3 ($C_q$-PMB), 129.7 (2xCH-PMB), 114.2 (2xCH-PMB),

73.7 (C-2), 71.7 ($CH_2$-PMB), 61.2 (C-3), 56.3 (C-4), 55.8 (OMe), 45.4 (C-5), 17.9 (C-1). **HRMS (ESI-TOF)** *m/z*: $[M+NH_4]^+$ Calcd for $C_{13}H_{17}ClO_3(NH_4)^+$ 274.1204, found 274.1205. For NMR-spectra see p. 245.

**Synthesis of Compound 219**

**(3*S*,4*R*)-4-((4-methoxybenzyl)oxy)pent-1-yn-3-ol**




**313** **219**

$C_{13}H_{16}O_3$
M = 220.27 g/mol

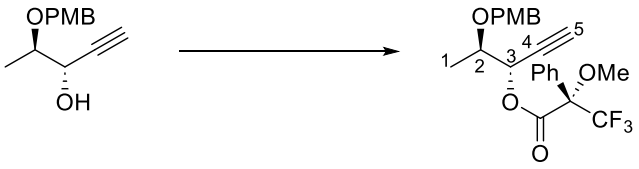
A stirred solution of chloro epoxide **313** (0.38 g, 1.48 mmol, 1 equiv) in THF (5 mL) was cooled to −78 °C. A solution of *n*-BuLi (2.5M in hexane, 1.80 mL, 4.44 mmol, 3 equiv) was added dropwise and the mixture was stirred for 30 min at −78 °C. The reaction mixture was quenched with a saturated $NH_4Cl$-solution (10 mL), diluted with DCM (15 mL) and warmed to room temperature. The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1) and the pure product was obtained as a colorless liquid (0.31 g, 1.42 mmol, 96%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.27. $[\alpha]_D^{20}$ = −6.7° (c = 1.34, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.28–7.26 (m, 2H, 2xCH-PMB), 6.90–6.87 (m, 2H, 2xCH-PMB), 4.57 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB), 4.44 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB´), 4.37 (ddd, $^3J_{H\text{-}3,\ OH}$ = 7.0 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 3.6 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 2.2 Hz, 1H, H-3), 3.79 (s, 3H, OMe), 3.66 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 3.6 Hz, 1H, H-2), 2.48 (d, $^4J_{H\text{-}5,\ H\text{-}3}$ = 2.3 Hz, 1H, H-5), 2.45 (d, $^3J_{OH,\ H\text{-}3}$ = 7.0 Hz, 1H, OH), 1.25 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.3 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 160.0 ($C_q$-PMB), 130.8 ($C_q$-PMB), 130.0 (2xCH-PMB), 114.3 (2xCH-PMB), 82.6 (C-4), 77.1 (C-2), 74.3 (C-5), 71.4 ($CH_2$-PMB), 65.6 (C-3), 55.8 (OMe), 15.1 (C-1). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{16}O_3H^+$ 221.1172, found 221.1175. For NMR-spectra see p. 247.

**Mosher's Ester Analysis of Propargylic Alcohol 219**

**Synthesis of Compound 357-(*S*)**

**(3*S*,4*R*)-4-((4-methoxybenzyl)oxy)pent-1-yn-3-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**219** **357-(*S*)**

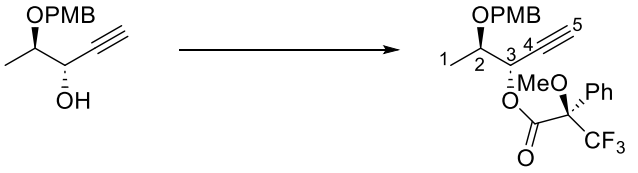
$C_{23}H_{23}F_3O_5$
M = 436.43 g/mol

To a stirred solution of propargylic alcohol **219** (10.3 mg, 46.8 µmol, 1 equiv) in DCM (1 mL) was added pyridine (38.0 µL, 468 µmol, 10 equiv) and (*R*)-MTPA-Cl (35.0 µL, 187 µmol, 4 equiv) and the mixture was stirred for 2 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The phases were separated, and the aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by preparative HPLC (column: KNAUER Eurospher II 100-5 C18; 5 µm; 250 x 16 mm, eluent: MeCN/$H_2O$ = 3:1) to obtain the pure ester as a colorless oil (11.7 mg, 26.8 µmol, 57%).

**TLC** (silica, CyHex:EtOAc = 7:1): $R_f$ = 0.29. $[\alpha]_D^{20}$ = +24.1° (c = 1.34, $CH_2Cl_2$). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.56–7.53 (m, 2H, 2xCH-Ph), 7.43–7.40 (m, 1H, CH-Ph), 7.37–7.34 (m, 2H, 2xCH-Ph), 7.24–7.21 (m, 2H, 2xCH-PMB), 6.87–6.84 (m, 2H, 2xCH-PMB), 5.80 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 3.1 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 2.3 Hz, 1H, H-3), 4.53 (d, $^2J$ = 11.1 Hz, 1H, $CH_2$-PMB), 4.47 (d, $^2J$ = 11.1 Hz, 1H, $CH_2$-PMB), 3.83 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.4 Hz, $^4J_{H\text{-}2,\ H\text{-}3}$ = 3.1 Hz, H-2), 3.79 (s, 3H, OMe-PMB), 3.55–3.54 (m, 3H, OMe), 2.60 (d, $^4J_{H\text{-}5,\ H\text{-}3}$ = 2.3 Hz, 1H, H-5), 1.31 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.2 (C=O), 159.9 ($C_q$-PMB), 132.6 ($C_q$-Ph), 130.5 ($C_q$-PMB), 130.2 (CH-Ph), 129.9 (2xCH-PMB), 128.9 (2xCH-Ph), 128.1 (2xCH-Ph), 123.9 (q, $^1J$ = 288.2 Hz, $CF_3$), 114.2 (2xCH-PMB), 85.4 (q, $^2J$ = 27.8 Hz, $C_q$-Mosher), 77.9 (C-4), 76.4 (C-5), 75.8 (C-2), 71.6 ($CH_2$-PMB), 67.8 (C-3), 56.1 (OMe), 55.8 (OMe-PMB), 15.4 (C-1). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K) $\delta$ (ppm) = −72.2. **HRMS (ESI-TOF)** *m/z*: $[M+NH_4]^+$ Calcd for $C_{23}H_{23}F_3O_5(NH_4)^+$ 454.1836, found 454.1836. For NMR-spectra see p. 249.

**Synthesis of Compound 357-(*R*)**

**(3*S*,4*R*)-4-((4-methoxybenzyl)oxy)pent-1-yn-3-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**219** **357-(*R*)**

$C_{23}H_{23}F_3O_5$
M = 436.43 g/mol

To a stirred solution of propargylic alcohol **219** (11.0 mg, 49.9 µmol, 1 equiv) in DCM (1 mL) was added pyridine (40 µL, 499 µmol, 10 equiv) and (*S*)-MTPA-Cl (37.4 µL, 200 µmol, 4 equiv) and the mixture was stirred for 2 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The phases were separated, and the aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by preparative HPLC (column: KNAUER Eurospher II 100-5 C18; 5 µm; 250 x 16 mm, eluent: MeCN/$H_2O$ = 3:1) to obtain the pure ester as a colorless oil (15.3 mg, 35.1 µmol, 70%).

**TLC** (silica, CyHex:EtOAc = 7:1): $R_f$ = 0.28. $[\alpha]_D^{20}$ = +78.9° (c = 1.23, $CH_2Cl_2$). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.56–7.53 (m, 2H, 2xCH-Ph), 7.44–7.40 (m, 1H, CH-Ph), 7.40–7.36 (m, 2H, 2xCH-Ph), 7.19–7.16 (m, 2H, 2xCH-PMB), 6.85–6.82 (m, 2H, 2xCH-PMB), 5.76 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 3.4 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 2.2 Hz, 1H, H-3), 4.48 (d, $^2J$ = 11.1 Hz, 1H, $CH_2$-PMB), 4.39 (d, $^2J$ = 11.1 Hz, 1H, $CH_2$-PMB), 3.75 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 3.4 Hz, 1H, H-2), 3.78 (s, 3H, OMe-PMB), 3.58–3.57 (m, 3H, OMe), 2.65 (d, $^4J_{H\text{-}5,\ H\text{-}3}$ = 2.2 Hz, 1H, H-5), 1.20 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 3H, H-1). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.1 (C=O), 159.9 ($C_q$-PMB), 132.7 ($C_q$-Ph), 130.6 ($C_q$-PMB), 130.3 (CH-Ph), 129.9 (2xCH-PMB), 128.9 (2xCH-Ph), 128.0 (2xCH-Ph), 123.9 (q, $^1J$ = 288.4 Hz, $CF_3$), 114.2 (2xCH-PMB), 85.1 (q, $^2J$ = 27.8 Hz, $C_q$-Mosher), 78.1 (C-4), 76.6 (C-5), 75.8 (C-2), 71.7 ($CH_2$-PMB), 68.0 (C-3), 56.1 (OMe), 55.8 (OMe-PMB), 15.8 (C-1). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K) $\delta$ (ppm) = −72.2. **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{23}F_3O_5Na^+$ 459.1390, found 459.1388. For NMR-spectra see p. 251.

**Mosher's Ester Analysis for Confirmation of the Absolute Configuration at C-3**

The determination of the absolute configuration was confirmed by the model for the analysis of the Mosher ester. Therefore, the $^1$H-NMR data of both esters were collected and analyzed

as shown in Table 6.2.[190] The difference between each signal led to the absolute configuration showed in Figure 6.1.

Table 6.2: NMR-data for Mosher's ester analysis of propargylic alcohol **219**.

| Position | δ (*S*)-Ester 357-(*S*) | δ (*R*)-Ester 357-(*R*) | $\Delta\delta^{SR}$ |
|---|---|---|---|
| **H-5** | 2.60 | 2.65 | –0.05 |
| **H-3** | 5.80 | 5.76 | +0.04 |
| **H-2** | 3.83 | 3.75 | +0.08 |
| **H-1** | 1.31 | 1.20 | +0.11 |
| **$CH_2$-PMB** | 4.53 | 4.48 | +0.05 |
| **$CH_2$-PMB´** | 4.47 | 4.39 | +0.08 |
| ***m*-PMB** | 7.22 | 7.17 | +0.05 |
| ***o*-PMB** | 6.86 | 6.84 | +0.02 |
| **OMe-PMB** | 3.79 | 3.78 | +0.01 |

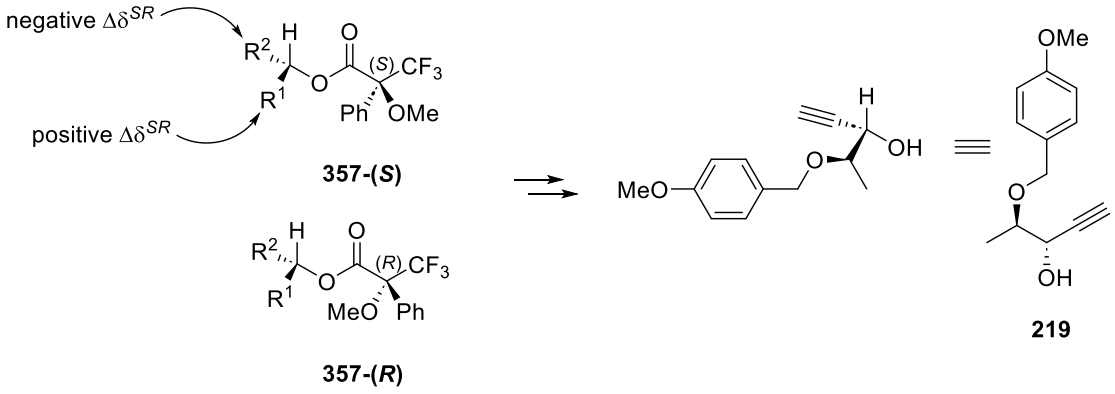
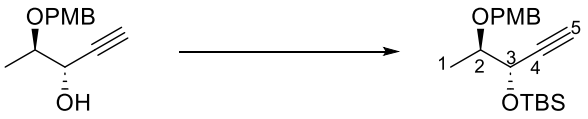



Figure 6.1: Proposed conformation according to the Mosher's ester analysis.

### Synthesis of Compound 314

**_tert_-butyl(((3*S*,4*R*)-4-((4-methoxybenzyl)oxy)pent-1-yn-3-yl)oxy)dimethylsilane**




**219** **314**

$C_{19}H_{30}O_3Si$
M = 334.53 g/mol

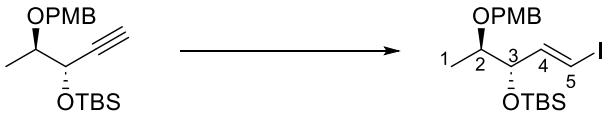
A stirred solution of propargylic alcohol **219** (270 mg, 1.23 mmol, 1 equiv) in DCM (3 mL) was treated with imidazole (125 g, 1.84 mmol, 1.5 equiv) and cooled to 0 °C. TBSCl (277 mg, 1.84 mmol, 1.5 equiv) was added and the mixture was stirred for 4 h at 0 °C. Subsequently, DCM (10 mL) and water (10 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 15 mL) and the combined organic layers were

dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 33:1) and the pure product was obtained as a colorless oil (382 mg, 1.44 mmol, 93%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.30. $[\alpha]_D^{20}$ = +40.0° (c = 1.30, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.29–7.25 (m, 2H, 2xCH-PMB), 6.88–6.84 (m, 2H, 2xCH-PMB), 4.58 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB), 4.52 (d, $^2J$ = 11.3 Hz, 1H, $CH_2$-PMB´), 4.34 (dd, $^3J_{H\text{-}3,\,H\text{-}2}$ = 4.7 Hz, $^4J_{H\text{-}3,\,H\text{-}5}$ = 2.2 Hz, 1H, H-3), 3.79 (s, 3H, OMe), 3.58 (qd, $^3J_{H\text{-}2,\,H\text{-}1}$ = 6.3 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 4.7 Hz, 1H, H-2), 2.45 (d, $^4J_{H\text{-}5,\,H\text{-}3}$ = 2.1 Hz, 1H, H-5), 1.20 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 6.3 Hz, 3H, H-1), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.15 (s, 3H, $CH_3$-TBS), 0.12 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.7 ($C_q$-PMB), 131.5 ($C_q$-PMB), 129.8 (2xCH-PMB), 114.1 (2xCH-PMB), 84.4 (C-4), 78.6 (C-2), 73.4 (C-5), 71.9 ($CH_2$-PMB), 66.9 (C-3), 55.8 (OMe), 26.1 (3x$CH_3$-TBS), 18.6 ($C_q$-TBS), 16.2 (C-1), −4.4 ($CH_3$-TBS), −4.8 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+NH_4]^+$ Calcd for $C_{19}H_{30}SiO_3(NH_4)^+$ 352.2302, found 352.2301. For NMR-spectra see p. 253.

### Synthesis of Compound 315

***tert*-butyl(((3*S*,4*R*,*E*)-1-iodo-4-((4-methoxybenzyl)oxy)pent-1-en-3-yl)oxy)dimethylsilane**




**314** **315**

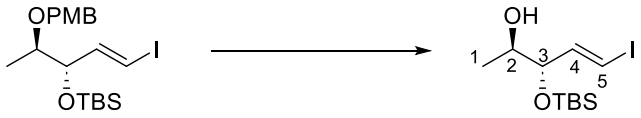
$C_{19}H_{31}IO_3Si$
M = 462.44 g/mol

A suspension of $Cp_2ZrCl_2$ (419 mg, 1.20 mmol, 1.3 equiv) in THF (2.8 mL) was cooled to 0 °C and a solution of DIBAL-H (1M in THF, 1.43 mL, 1.43 mmol, 1.3 equiv) was added dropwise. The white suspension was stirred for 45 min at 0 °C and a solution of alkyne **314** (400 mg, 1.20 mmol, 1 equiv) in THF (0.6 mL) was added. The reaction mixture was warmed to room temperature and stirred for 2 h, until a clear yellow solution was visible. The mixture was cooled to −78 °C and a solution of iodine (395 mg, 1.55 mmol, 1.3 equiv) in THF (1.8 mL) was added dropwise. After stirring for another 30 min, the dark-brown solution was diluted with DCM (20 mL) and quenched with a saturated solution of $NH_4Cl$ (20 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$-solution (20 mL) and were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica RP-18, MeCN:$H_2O$ = 10:1). The pure product was obtained as a slightly yellow liquid (474 mg, 1.02 mmol, 86%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.38. $[\alpha]_D^{20}$ = +18.1° (c = 1.16, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.25–7.23 (m, 2H, 2xCH-PMB), 6.89–6.84 (m, 2H, 2xCH-PMB), 6.60 (dd, $^3J_{H\text{-}4,\ H\text{-}5}$ = 14.4 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 6.2 Hz, 1H, H-4), 6.29 (dd, $^3J_{H\text{-}5,\ H\text{-}4}$ = 14.4 Hz, $^4J_{H\text{-}5,\ H\text{-}3}$ = 1.1 Hz, 1H, H-5), 4.49 (d, $^2J$ = 11.4 Hz, 1H, $CH_2$-PMB), 4.46 (d, $^2J$ = 11.4 Hz, 1H, $CH_2$-PMB´), 4.04 (ddd, $^3J_{H\text{-}3,\ H\text{-}4}$ = 6.1 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 4.7 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 1.3 Hz, 1H, H-3), 3.79 (s, 3H, OMe), 3.42 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 4.7 Hz, 1H, H-2), 1.12 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.3 Hz, 3H, H-1), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS), 0.04 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.7 ($C_q$-PMB), 147.4 (C-4), 131.5 ($C_q$-PMB), 129.8 (2xCH-PMB), 114.1 (2xCH-PMB), 78.9 (C-3), 78.3 (C-2), 77.6 (C-5), 71.6 ($CH_2$-PMB), 55.8 (OMe), 26.1 (3x$CH_3$-TBS), 18.6 ($C_q$-TBS), 16.1 (C-1), −4.3 ($CH_3$-TBS), −4.5 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+NH_4]^+$ Calcd for $C_{19}H_{31}IO_3Si(NH_4)^+$ 480.1425, found 480.1424. For NMR-spectra see p. 255.

**Synthesis of Compound 153**

**(2*R*,3*S*,4*E*)-3-((*tert*-butyldimethylsilyl)oxy)-5-iodopent-4-en-2-ol**




**315** **153**

$C_{11}H_{23}IO_2Si$
M = 342.29 g/mol

To a stirred solution of PMB-ether **315** (540 mg, 1.17 mmol, 1 equiv) in DCM (30 mL) and pH 7 buffer (3 mL) was added DDQ (292 mg, 1.28 mmol, 1.3 equiv). The reaction mixture was stirred for 90 min at room temperature and was then quenched with water (50 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (silica RP-18, MeCN:$H_2O$ = 2:1) and the pure product was obtained as a dark yellow oil (310 mg, 0.91 mmol, 78%).

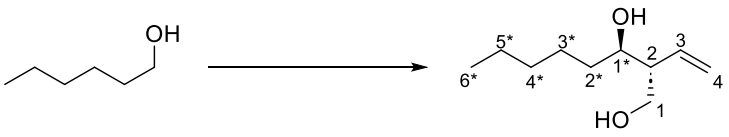
**TLC** (silica RP-18, MeCN:$H_2O$ = 2:1): $R_f$ = 0.19. $[\alpha]_D^{20}$ = +59.0° (c = 1.22, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.57 (dd, $^3J_{H\text{-}4,\ H\text{-}5}$ = 14.5 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 6.9 Hz, 1H, H-4), 6.32 (dd, $^3J_{H\text{-}5,\ H\text{-}4}$ = 14.5 Hz, $^4J_{H\text{-}5,\ H\text{-}3}$ = 1.1 Hz, 1H, H-5), 3.98 (ddd, $^3J_{H\text{-}3,\ H\text{-}4}$ = 6.9 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 3.9 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 1.1 Hz, 1H, H-3), 3.71 (qd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 3.9 Hz, 1H, H-2), 2.17–1.91 (br s, 1H, OH), 1.08 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 3H, H-1), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 145.7 (C-4), 79.7 (C-3), 78.6 (C-5), 70.8 (C-2), 26.1 (3x$CH_3$-TBS), 18.6 ($C_q$-TBS), 18.0 (C-1), −4.2

($CH_3$-TBS), −4.7 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{23}IO_2SiH^+$ 343.0585, found 343.0586. For NMR-spectra see p. 257.

## 6.2.2 Synthesis of the Northern Fragment

### Synthesis of Compound 317

**(2*R*,3*R*)-2-vinyloctane-1,3-diol**




**316** **317**

$C_{10}H_{20}O_2$
M = 172.27 g/mol

A screw cap reaction vessel was charged with hexanol (**316**) (12.2 mL, 97.9 mmol, 1 equiv), 4-vinyl-1,3-dioxolan-2-one (18.8 mL, 196 mmol, 2 equiv) and (*S*)-**II*** (5.06 g, 4.89 mmol, 0.05 equiv) before THF (100 mL) was added. The tube was closed, and the mixture was heated to 90 °C for 48 h. After that, the mixture was cooled to room temperature and evaporated into silica. Purification by flash chromatography (silica, CyHex:EtOAc = 3:1) yielded diol **16** as a colorless oil and an inseparable mixture of diastereomers. (12.7 g, 73.7 mmol, 75%, *dr* ≈ 11:1, *ee* > 95%, determined by Mosher´s ester analysis).

*(*S*)-**II** was prepared by a procedure reported by Krische.[96]

**TLC** (silica, CyHex:EtOAc = 2:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = −6.3° (c = 1.12, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 5.86 (ddd, $^3J_{H\text{-}3,\ H\text{-}4\text{-}E}$ = 17.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4\text{-}Z}$ = 10.5 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 8.9 Hz, 1H, H-3), 5.23 (dd, $^3J_{H\text{-}4\text{-}Z,\ H\text{-}3}$ = 10.4 Hz, $^2J$ = 2.0 Hz, 1H, H-4-*Z*), 5.17 (ddd, $^3J_{H\text{-}4\text{-}E,\ H\text{-}3}$ = 17.4 Hz, $^2J$ = 2.0 Hz, $^4J_{H\text{-}4\text{-}E,\ H\text{-}2}$ = 1.0 Hz, 1H, H-4-*E*), 3.81–3.74 (m, 2H, H-1*, H-1), 3.71 (dd, $^2J$ = 10.5, $^3J_{H\text{-}1',\ H\text{-}2}$ = 5.9 Hz, 1H, H-1´), 2.31–2.25 (m, 1H, H-2), 2.00–1.93 (m, 2H, OH-1, OH-1*), 1.47–1.39 (m, 2H, H-2*), 1.36–1.24 (m, 6H, H-5*, H-4*, H-3*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 135.8 (C-3), 119.0 (C-3), 73.3 (C-1*), 65.3 (C-1), 51.6 (C-2), 35.6 (C-2*), 32.4 (C-4*), 26.0 (C-3*), 23.2 (C-5*), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{10}H_{20}O_2Na^+$ 195.1356, found 195.1359. For NMR-spectra see p. 259.

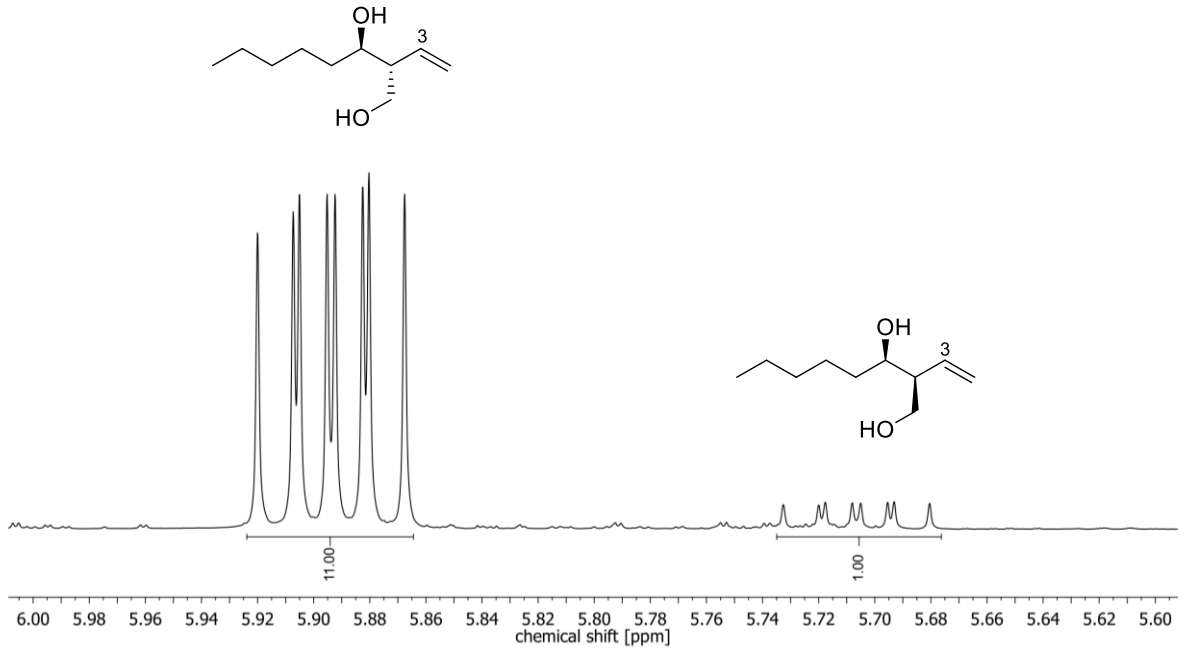


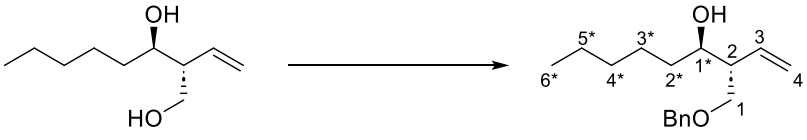

Figure 6.2: Determination of the diastereoselectivity by $^{1}$H-NMR spectroscopy by comparison of the integrals of H-3.

The absolute configuration at C-1* was confirmed after benzyl protection at OH-1 and subsequent Mosher ester analysis (p. 115). Since no further set of signals was visible in the $^{1}$H-NMR-spectra of the respective Mosher esters (pp. 263–266), it was assumed that the enantioselectivity of this reaction is larger than 95%.

The configuration of the stereocenter at C-2 will be confirmed after the 6-membered acetonide is formed and a well resolved NMR-Spectrum is available (compound **238**, pp. 120–121).

**Synthesis of Compound 318**

**(3*R*,4*R*)-3-((benzyloxy)methyl)non-1-en-4-ol**




**317** **318**

$C_{17}H_{26}O_2$
M = 262.39 g/mol

A suspension of NaH (60% in mineral oil, 3.83 g, 95.7 mmol, 2 equiv) in DMF (220 mL) was cooled to −10 °C before BnBr (6.25 mL, 52.6 mmol, 1.1 equiv) was added dropwise. Subsequently, a solution of diol **317** (8.24 g, 47.8 mmol, 1 equiv) in DMF (20 mL) was added dropwise and the reaction mixture was stirred at −10 °C for 90 min. The mixture was quenched by

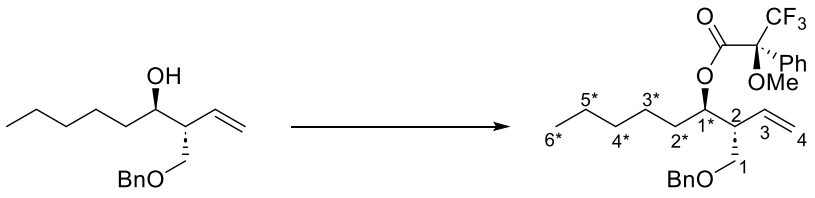
slow addition of water (200 mL). DCM (300 mL) was added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 300 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless highly viscous oil (8.40 g, 32.0 mmol, 67%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.2. $[\alpha]_D^{20}$ = −9.8° (c = 0.92, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 5.87 (ddd, $^3J_{H\text{-}3,\ H\text{-}4\text{-}E}$ = 17.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4\text{-}Z}$ = 10.4 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 8.7 Hz, 1H, H-3), 5.17 (ddd, $^3J_{H\text{-}4\text{-}Z,\ H\text{-}3}$ = 10.4 Hz, $^2J$ = 2.0 Hz, $^4J_{H\text{-}4\text{-}Z,\ H\text{-}2}$ = 0.6 Hz, 1H, H-4-*Z*), 5.12 (ddd, $^3J_{H\text{-}4\text{-}E,\ H\text{-}3}$ = 17.3 Hz, $^2J$ = 2.0 Hz, $^4J_{H\text{-}4\text{-}E,\ H\text{-}2}$ = 1.0 Hz, 1H, H-4-*E*), 4.51–4.50 (m, 2H, $CH_2$-Bn), 3.78–3.73 (m, 1H, H-1*), 3.65 (dd, $^2J$ = 9.2 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.4 Hz, 1H, H-1), 3.60 (dd, $^2J$ = 9.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 5.1 Hz, 1H, H-1´), 2.42–2.37 (m, 1H, H-2), 2.24 (d, $^3J_{OH,\ H\text{-}1*}$ = 4.6 Hz, 1H, OH), 1.42–1.37 (m, 2H, H-2*), 1.34–1.22 (m, 6H, H-3*, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6*,\ H\text{-}5*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.9 ($C_q$-Bn), 136.2 (C-3), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn), 128.2 (CH-Bn), 118.1 (C-4), 73.9 ($CH_2$-Bn), 73.2 (C-1), 72.9 (C-1*), 46.9 (C-2), 35.2 (C-2*), 32.4 (C-4*), 26.2 (C-3*), 23.2 (C-5*), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{26}O_2H^+$ 263.2006, found 263.2007. For NMR-spectra see p. 261.

**Mosher's Ester Analysis of Secondary Alcohol 318**

**Synthesis of Compound 358-(*S*)**

**(3*R*,4*R*)-3-((benzyloxy)methyl)non-1-en-4-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**318** **358-(*S*)**

$C_{27}H_{33}F_3O_4$
M = 428.55 g/mol

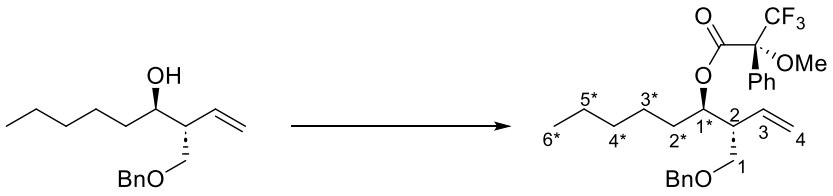
To a stirred solution of secondary alcohol **318** (6.00 mg, 22.9 µmol, 1 equiv) in DCM (0.5 mL) was added pyridine (18.5 µL, 229 µmol, 10 equiv) and (*R*)-MTPA-Cl (17.1 µL, 91.5 µmol, 4 equiv) and the mixture was stirred for 6 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The

crude product was purified by flash chromatography (silica, CyHex:EtOAc = 30:1) to obtain the pure ester as a colorless oil (6.5 mg, 13.6 µmol, 59%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.14. $[\alpha]_D^{20}$ = −46.5° (c = 0.86, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.57–7.51 (m, 2H, 2xCH-Ph), 7.46–7.24 (m, 8H, 3xCH-Ph, 5xCH-Bn), 5.63 (ddd, $^3J_{H\text{-}3,\ H\text{-}4\text{-}E}$ = 17.1 Hz, $^3J_{H\text{-}3,\ H\text{-}4\text{-}Z}$ = 10.5 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 9.0 Hz, 1H, H-3), 5.39–5.34 (m, 1H, H-1*), 5.18–5.10 (m, 2H, H-4-*Z*, H-4-*E*), 4.41 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.36 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 3.54–3.51 (m, 3H, OMe), 3.33–3.23 (m, 2H, H-1, H-1´), 2.67–2.59 (m, 1H, H-2), 1.75–1.56 (m, 2H, H-2*), 1.37–1.22 (m, 6H, H-3*, H-4*, H-5*), 0.87 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.4 (C=O), 139.0 ($C_q$-Bn), 134.5 (C-3), 133.1 ($C_q$-Ph), 130.1–127.9 (5xCH-Ph, 5xCH-Bn), 124.1 (q, $^1J$ = 288.4 Hz, $CF_3$), 119.5 (C-4), 84.9 (q, $^2J$ = 27.5 Hz, $C_q$-Mosher), 76.8 (C-1*), 73.6 ($CH_2$-Bn), 70.7 (C-1), 56.0 (OMe), 47.7 (C-2), 32.4 (C-2*), 32.1 (C-4*), 25.5 (C-3*), 23.0 (C-5*), 14.3 (C-6*). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K) $\delta$ (ppm) = −71.8. **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{27}H_{33}F_3O_4Na^+$ 501.2223, found 501.2226. For NMR-spectra see p. 263.

**Synthesis of Compound 358-(*R*)**

**(3*R*,4*R*)-3-((benzyloxy)methyl)non-1-en-4-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**318** **358-(*R*)**

$C_{27}H_{33}F_3O_4$
M = 428.55 g/mol

To a stirred solution of secondary alcohol **318** (6.00 mg, 22.9 µmol, 1 equiv) in DCM (0.5 mL) was added pyridine (18.5 µL, 229 µmol, 10 equiv) and (*S*)-MTPA-Cl (17.1 µL, 91.5 µmol, 4 equiv) and the mixture was stirred for 6 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 30:1) to obtain the pure ester as a colorless oil (6.7 mg, 14.0 µmol, 61%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.14. $[\alpha]_D^{20}$ = +26.8° (c = 0.82, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.55–7.51 (m, 2H, 2xCH-Ph), 7.43–7.26 (m, 8H,

3xCH-Ph, 5xCH-Bn), 5.71 (ddd, $^3J_{H\text{-}3,\ H\text{-}4\text{-}E}$ = 17.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4\text{-}Z}$ = 10.4 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 8.9 Hz, 1H, H-3), 5.37–5.34 (m, 1H, H-1*), 5.20–5.14 (m, 2H, H-4-*Z*, H-4-*E*), 4.47 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn), 4.44 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 3.49–3.47 (m, 3H, OMe), 3.45–3.39 (m, 2H, H-1, H-1´), 2.68–2.63 (m, 1H, H-2), 1.64–1.50 (m, 2H, H-2*), 1.29–1.15 (m, 6H, H-3*, H-4*, H-5*), 0.85 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.6 (C=O), 139.0 ($C_q$-Bn), 135.0 (C-3), 132.9 ($C_q$-Ph), 130.1–128.1 (5xCH-Ph, 5xCH-Bn), 124.1 (q, $^1J$ = 288.9 Hz, $CF_3$), 119.4 (C-4), 85.2 (q, $^2J$ = 27.9 Hz, $C_q$-Mosher), 77.0 (C-1*), 73.7 ($CH_2$-Bn), 70.9 (C-1), 55.9 (OMe), 47.8 (C-2), 32.1 (C-2*), 32.0 (C-4*), 25.3 (C-3*), 23.0 (C-5*), 14.3 (C-6*). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K) $\delta$ (ppm) = −72.0. **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{27}H_{33}F_3O_4Na^+$ 501.2223, found 501.2221. For NMR-spectra see p. 265.

### Mosher's Ester Analysis for Confirmation of the Absolute Configuration at C-1*

The determination of the absolute configuration was confirmed by the model for the analysis of the Mosher ester. Therefore, the $^1$H-NMR data of both esters were collected and analyzed as shown in Table 6.3.[190] The difference between each signal led to the absolute configuration showed in Figure 6.3.

Table 6.3: NMR-data for Mosher's ester analysis of alcohol **318**.

| Position | δ (*S*)-Ester 358-(*S*) | δ (*R*)-Ester 358-(*R*) | $\Delta\delta^{SR}$ |
|---|---|---|---|
| **H-4** | 5.14 | 5.17 | −0.03 |
| **H-3** | 5.63 | 5.71 | −0.08 |
| **H-2** | 2.63 | 2.66 | −0.03 |
| **H-1** | 3.28 | 3.42 | −0.14 |
| **$CH_2$-Bn** | 4.41 | 4.47 | −0.06 |
| **$CH_2$-Bn´** | 4.36 | 4.44 | −0.08 |
| **H-1*** | 5.37 | 5.36 | +0.01 |
| **H-2*** | 1.70 | 1.57 | +0.13 |
| **H-3*, H-4*, H-5*** | 1.30 | 1.22 | +0.08 |
| **H-6*** | 0.87 | 0.85 | +0.02 |

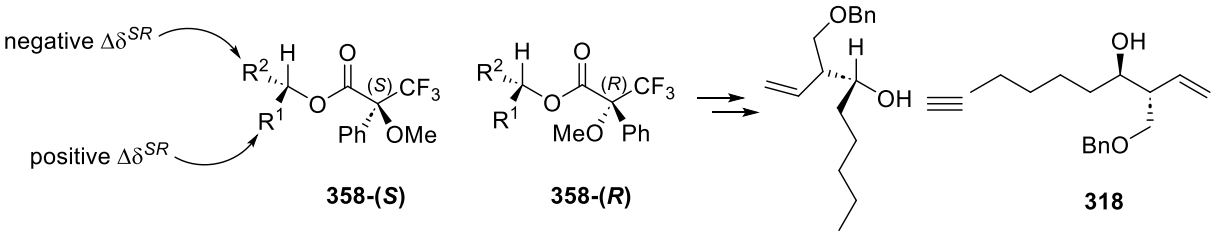
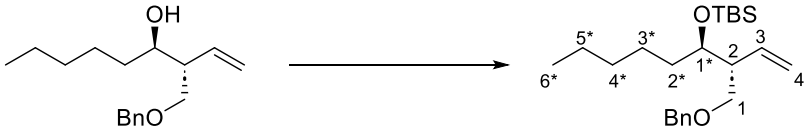



Figure 6.3: Proposed conformation according to the Mosher's ester analysis.

**Synthesis of Compound 239**

**(((3*R*,4*R*)-3-((benzyloxy)methyl)non-1-en-4-yl)oxy)(*tert*-butyl)dimethylsilane**




**318** **239**

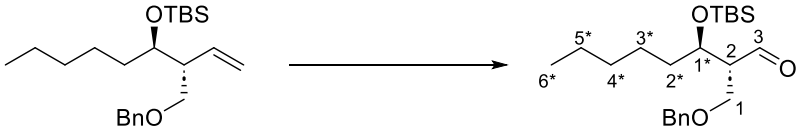
$C_{23}H_{40}SiO_2$
M = 376.66 g/mol

To a stirred solution of alcohol **318** (8.30 g, 31.6 mmol, 1 equiv) in DCM (60 mL) were added imidazole (6.46 g, 94.9 mmol, 3 equiv) and TBSCl (14.3 g, 94.9 mmol, 3 equiv). The mixture was stirred for 48 h at room temperature and was then quenched with water (100 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 100 mL). The combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 50:1) and the pure product was obtained as a colorless oil (11.8 g, 31.3 mmol, 99%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.37. $[\alpha]_D^{20}$ = +7.4° (c = 1.08, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.35–7.31 (m, 4H, 4xCH-Bn), 7.29–7.25 (m, 1H, CH-Bn), 5.80 (ddd, $^3J_{H\text{-}3,\ H\text{-}4\text{-}E}$ = 17.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4\text{-}Z}$ = 10.5 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 8.8 Hz, 1H, H-3), 5.14–5.08 (m, 2H, H-4-*Z*, H-4-*E*), 4.49 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn), 4.44 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 3.84 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.5 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 5.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 2.6 Hz, 1H, H-1*), 3.60 (dd, $^2J$ = 9.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 7.1 Hz, 1H, H-1), 3.40 (dd, $^2J$ = 9.1 Hz, $^3J_{H\text{-}1^{\prime},\ H\text{-}2}$ = 6.9 Hz, 1H, H-1´), 2.50–2.45 (m, 1H, H-2), 1.50–1.44 (m, 1H, H-2*), 1.41–1.33 (m, 1H, H-2*´), 1.32–1.21 (m, 6H, H-3*, H-4*, H-5*), 0.90–0.86 (m, 12H, H-6*, 3x$CH_3$-TBS), 0.05 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.5 ($C_q$-Bn), 137.0 (C-3), 128.8 (2xCH-Bn), 128.2 (2xCH-Bn), 127.9 (CH-Bn), 117.6 (C-4), 73.4 ($CH_2$-Bn), 72.4 (C-1*), 71.8 (C-1), 49.4 (C-2), 35.5 (C-2*), 32.5 (C-4*), 26.3 (3x$CH_3$-TBS), 25.9 (C-3*), 23.2 (C-5*), 18.6 ($C_q$-TBS), 14.4 (C-6*), −3.9 ($CH_3$-TBS), −4.4 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{40}SiO_2H^+$ 377.2870, found 377.2872. For NMR-spectra see p. 267.

**Synthesis of Compound 241**

**(2*R*,3*R*)-2-((benzyloxy)methyl)-3-((*tert*-butyldimethylsilyl)oxy)octanal**




**239** **241**

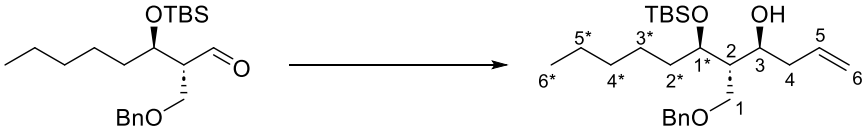
$C_{22}H_{38}SiO_3$
M = 378.63 g/mol

To a solution of alkene **239** (10.3 g, 27.4 mmol, 1 equiv) in acetone/$H_2O$ (10:1; 300 mL) was added NMO·$H_2O$ (7.39 g, 54.7 mmol, 2 equiv) and a solution of $OsO_4$ (4% in $H_2O$, 8.69 mL, 1.37 mmol, 0.05 equiv). The mixture was stirred for 36 h at room temperature. The reaction mixture was quenched with saturated $Na_2S_2O_3$-solution (200 mL) and diluted with DCM (200 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was redissolved in a solution of $Pb(OAc)_4$ (13.9 g, 31.5 mmol, 1.15 equiv) in toluene (350 mL) and stirred for 20 min before it was filtered through a glass filter frit. The solvent was evaporated *in vacuo* and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure aldehyde was obtained as a colorless oil (9.80 g, 25.9 mmol, 95%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.41. $[\alpha]_D^{20}$ = −7.4° (c = 1.56, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.75 (d, $^3J_{H\text{-}3,\ H\text{-}2}$ = 2.7 Hz, 1H, H-3), 7.40–7.22 (m, 5H, 5xCH-Bn), ), 4.51 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.47 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 4.08 (td, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 6.2 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 3.9 Hz, 1H, H-1*), 3.85 (dd, $^2J$ = 9.4 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 7.6 Hz, 1H, H-1), 3.65 (dd, $^2J$ = 9.5 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 5.7 Hz, 1H, H-1´), 2.66 (dddd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 7.6 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 3.9 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 2.7 Hz, 1H, H-2), 1.62–1.49 (m, 2H, H-2*), 1.39–1.20 (m, 6H, H-3*, H-4*, H-5*), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*), 0.86 (s, 9H, 3x$CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS), 0.04 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 204.1 (C-3), 138.8 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.2 (CH-Bn), 73.8 ($CH_2$-Bn), 71.4 (C-1*), 67.5 (C-1), 57.1 (C-2), 36.1 (C-2*), 32.4 (C-4*), 26.1 (3x$CH_3$-TBS), 25.3 (C-3*), 23.1 (C-5*), 18.5 ($C_q$-TBS), 14.3 (C-6*), −4.0 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** ***m/z***: $[M+H]^+$ Calcd for $C_{22}H_{38}SiO_3H^+$ 379.2663, found 379.2662. For NMR-spectra see p. 269

**Synthesis of Compound 242**

**(4*S*,5*S*,6*R*)-5-((benzyloxy)methyl)-6-((*tert*-butyldimethylsilyl)oxy)undec-1-en-4-ol**




**241** **242**

$C_{25}H_{44}SiO_3$
M = 420.71 g/mol

A solution of (−)-Ipc$_2$BOMe (9.25 g, 29.3 mmol, 1.25 equiv) in $Et_2O$ (30 mL) was cooled to 0 °C and allylMgBr (1M in $Et_2O$, 28.1 mL, 28.1 mmol, 1.2 equiv) was added dropwise over 5 min. The mixture was stirred for 1 h at room temperature before it was cooled to −78 °C. A solution of aldehyde **241** (8.86 g, 23.4 mmol, 1 equiv) in $Et_2O$ (15 mL) was added dropwise and the reaction mixture was stirred for 1 h at −78 °C. The white suspension was filtered through a glas filter frit and was washed with THF (100 mL). The resulting solution was again cooled to −78 °C and treated with aqueous NaOH (30 mL) and $H_2O_2$ (35% in $H_2O$, 20 mL) before it was warmed to room temperature and then refluxed for 2 h at 70 °C. The reaction mixture was cooled to room temperature and saturated $Na_2S_2O_3$-solution (100 mL) was added. $Et_2O$ (200 mL) was added, and the organic phase was separated. The aqueous phase was extracted with $Et_2O$ (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product, a separable mixture of diastereomers was purified by flash chromatography (two columns, silica; 1. CyHex:EtOAc = 20:1; 2. CyHex:EtOAc = 30:1) and the pure product was obtained as a colorless oil (8.20 g, 19.5 mmol, 83%, (7.49 g (1,3-syn); 710 mg (1,3-anti)) *dr* ≈ 11:1).

1,3-*syn*-isomer:

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.25. $[\alpha]_D^{20}$ = −5.1° (c = 0.78, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.31 (m, 4H, 4xCH-Bn), 7.30–7.26 (m, 1H, CH-Bn), 5.91 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}E}$ = 16.8 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 7.4 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 6.4 Hz 1H, H-5), 5.11–5.04 (m, 2H, H-6-*Z*, H-6-*E*), 4.46 (s, 2H, $CH_2$-Bn), 4.00 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 6.1 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 6.1 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 4.4 Hz, 1H, H-1*), 3.81 (dddd, $^3J_{H\text{-}3,\ H\text{-}4}$ = 9.2 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 6.0 Hz, $^3J_{H\text{-}3,\ OH}$ = 4.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 3.3 Hz, 1H, H-3), 3.57 (dd, $^2J$ = 9.4 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.3 Hz, 1H, H-1), 3.54 (dd, $^2J$ = 9.4 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 6.1 Hz, 1H, H-1´), 2.81 (d, $^3J_{OH,\ H\text{-}3}$ = 4.7 Hz, 1H, OH), 2.45 (ddddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 6.4 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 3.2 Hz, $^4J_{H\text{-}4',\ H\text{-}6\text{-}E}$ = 1.5 Hz, $^3J_{H\text{-}4',\ H\text{-}6\text{-}Z}$ = 1.5 Hz, 1H, H-4´), 2.18 (ddddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 9.0 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 7.5 Hz, $^4J_{H\text{-}4,\ H\text{-}6\text{-}E}$ = 1.2 Hz, $^3J_{H\text{-}4,\ H\text{-}6\text{-}Z}$ = 1.2 Hz, 1H, H-4), 1.91 (dddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 6.1 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 6.1 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 4.3 Hz, 1H, H-2), 1.65–1.59 (m, 1H, H-2*), 1.49–1.43 (m, 1H,

H-2*´), 1.38–1.22 (m, 6H, H-3*, H-4*, H-5*), 0.90–0.87 (m, 13H, H-6*, 3x$CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.05 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 136.9 (C-5), 128.8 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 117.1 (C-6), 73.8 ($CH_2$-Bn), 73.1 (C-1*), 71.4 (C-3), 69.8 (C-1), 48.5 (C-2), 40.1 (C-4), 35.8 (C-2*), 32.5 (C-4*), 26.2 (3x$CH_3$-TBS), 25.6 (C-3*), 23.2 (C-5*), 18.5 ($C_q$-TBS), 14.4 (C-6*), −4.0 ($CH_3$-TBS), −4.4 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{44}SiO_3H^+$ 421.3132, found 421.3133. For NMR-spectra see p. 271.

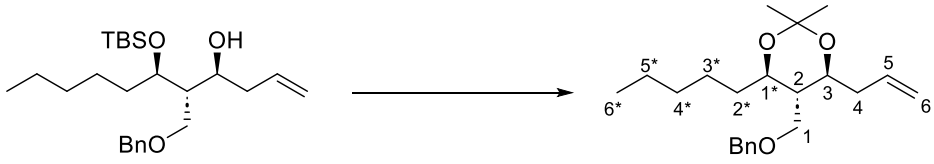
1,3-*anti*-isomer:

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −2.4° (c = 0.84, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.26 (m, 1H, CH-Bn), 5.83 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}E}$ = 16.9 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}Z}$ = 10.3 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 7.4 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 6.6 Hz 1H, H-5), 5.10–5.01 (m, 2H, H-6-*Z*, H-6-*E*), 4.49 (s, 2H, $CH_2$-Bn), 4.14 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.3 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 5.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 2.6 Hz, 1H, H-1*), 4.09 (m, 1H, H-3), 3.75–3.66 (m, 2H, H-1, H-1´), 3.60 (d, $^3J_{OH,\ H\text{-}3}$ = 1.1 Hz, 1H, OH), 2.33 (ddddd, $^2J$ = 14.1 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 7.9 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 6.7 Hz, $^4J_{H\text{-}4',\ H\text{-}6\text{-}E}$ = 1.5 Hz, $^3J_{H\text{-}4',\ H\text{-}6\text{-}Z}$ = 1.5 Hz, 1H, H-4´), 2.22 –2.14 (m, 1H, H-4), 1.91 (dddd, $^3J_{H\text{-}2,\ H\text{-}1}$ = 7.6 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.0 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 2.5 Hz, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 2.5 Hz, 1H, H-2), 1.71–1.60 (m, 1H, H-2*), 1.59–1.49 (m, 1H, H-2*´), 1.35–1.18 (m, 6H, H-3*, H-4*, H-5*), 0.91–0.86 (m, 13H, H-6*, 3x$CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.2 ($C_q$-Bn), 136.4 (C-5), 128.8 (2xCH-Bn), 128.2 (2xCH-Bn), 128.0 (CH-Bn), 117.0 (C-6), 74.0 (C-1*), 73.6 ($CH_2$-Bn), 70.2 (C-3), 67.9 (C-1), 44.7 (C-2), 40.0 (C-4) 35.1 (C-2*), 32.4 (C-4*), 26.2 (3x$CH_3$-TBS), 25.8 (C-3*), 23.1 (C-5*), 18.4 ($C_q$-TBS), 14.3 (C-6*), −4.1 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{25}H_{44}SiO_3H^+$ 421.3132, found 421.3133. For NMR-spectra see p. 273.

The configuration of the stereocenter at C-3 will be confirmed after the 6-membered acetonide is formed (compound **319**, next page).

### Synthesis of Compound 319

**(4*S*,5*R*,6*R*)-4-allyl-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane**




**242** **319**

$C_{22}H_{34}O_3$
M = 346.51 g/mol

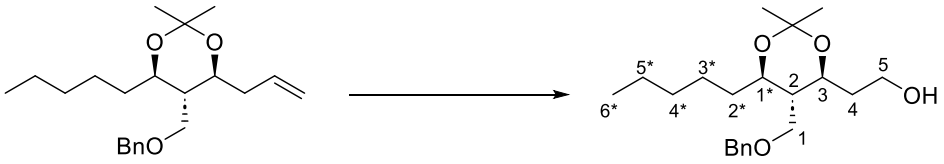
A stirred solution of TBS ether **242** (4.80 g, 11.4 mmol, 1 equiv) in MeOH (110 mL) was treated with *p*-TsOH (0.20 g, 1.14 mmol, 0.1 equiv). The mixture was stirred for 3 h at room temperature before 2,2 -dimethoxypropane (70 mL, 570 mmol, 50 equiv) was added and was stirred for another 30 min at room temperature. The reaction mixture was quenched with saturated $NaHCO_3$-solution and the aqueous phase was extracted with DCM (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 50:1) and the pure product was obtained as a colorless oil (3.88 g, 11.2 mmol, 98%).

**TLC** (silica, CyHex:EtOAc = 50:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +21.2° (c = 0.52, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.38–7.26 (m, 5H, 5xCH-Bn), 5.96–5.83 (m, 1H, H-5), 5.06–4.98 (m, 2H, H-6-*E*, H-6-*Z*), 4.64–4.39 (m, 2H, $CH_2$-Bn), 4.02 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 7.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 3.2 Hz, 1H, H-3), 3.91 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.5 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.0 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.7 Hz, 1H, H-1*), 3.43 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.0 Hz, 2H, H-1), 2.40 (ddddd, $^2J$ = 14.8 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 6.4 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 3.2 Hz, $^4J_{H\text{-}4',\ H\text{-}6\text{-}E}$ = 1.6 Hz, $^3J_{H\text{-}4',\ H\text{-}6\text{-}Z}$ = 1.6 Hz, 1H, H-4´), 2.15 (ddddd, $^2J$ = 14.6 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 7.2 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 7.2 Hz, $^4J_{H\text{-}4,\ H\text{-}6\text{-}E}$ = 1.3 Hz, $^3J_{H\text{-}4,\ H\text{-}6\text{-}Z}$ = 1.3 Hz, 1H, H-4), 1.64–1.56 (m, 1H, H-2*), 1.48–1.39 (m, 4H, H-3*, $CH_3$), 1.36–1.20 (m, 10H, H-2, H-2*´, H-3*´, H-4*, H-5*, $CH_3$), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 136.0 (C-5), 128.9 (2xCH-Bn), 128.1 (2xCH-Bn), 128.1 (CH-Bn), 116.5 (C-6), 98.2 ($C_q$), 73.7 ($CH_2$-Bn), 70.3 (C-1*, C-3), 67.5 (C-1), 44.6 (C-2), 38.2 (C-4), 33.7 (C-2*), 32.4 (C-4*), 30.4 ($CH_3$), 25.3 (C-3*), 23.3 (C-5*), 20.2 ($CH_3$), 14.5 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{34}O_3H^+$ 347.2581, found 347.2580. For NMR-spectra see p. 275

The 1,3-*syn* configuration was confirmed by the $^{13}$C-signals (30.4 and 20.2 ppm) of the methyl groups of the acetonide.[81]

### Synthesis of Compound 238

**2-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)ethan-1-ol**



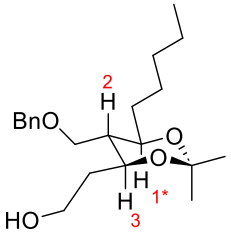

**319** **238**

$C_{21}H_{34}O_4$
M = 350.50 g/mol

A stirred solution of alkene **319** (3.80 g, 11.0 mmol, 1 equiv) in MeOH/DCM (1:1, 55 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 20 min until a slightly blue color persisted. The excess ozone was then purged with argon for 5 min and $NaBH_4$ (2.07 g, 54.8 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 30 min at room temperature. $NH_4Cl$-solution (100 mL) and DCM (100 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 100 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:1). The pure product was obtained as a colorless oil (3.58 g, 10.2 mmol, 93%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +13.6° (c = 1.32, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 4.43 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.41 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn´), 4.18 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 8.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 2.8 Hz, 1H, H-3), 3.92 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.5 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.1 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.5 Hz, 1H, H-1*), 3.73–3.67 (m, 2H, H-5), 3.44 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.4 Hz, 1H, H-1), 3.41 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 3.2 Hz, 1H, H-1´) 2.53 (t, $^3J_{OH,\ H\text{-}5}$ = 5.7 Hz, 1H, OH), 1.89 (dtd, $^2J$ = 14.5 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 5.0 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 2.8 Hz, 1H, H-4´), 1.65–1.56 (m, 2H, H-2*, H-4), 1.50–1.43 (m, 1H, H-3*), 1.45 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.39 (dddd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.5 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 3.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 3.1 Hz, 1H, H-2), 1.32 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.32–1.19 (m, 6H, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (CH-Bn), 128.1 (2xCH-Bn), 98.4 ($C_q$), 73.7 ($CH_2$-Bn), 71.8 (C-3), 70.3 (C-1*), 67.5 (C-1), 61.6 (C-5), 45.1 (C-2), 35.7 (C-4), 33.6 (C-2*), 32.4 (C-4*), 30.5 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 20.2 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{34}O_4H^+$ 351.2530, found 351.2538. For NMR-spectra see p. 277.

The relative configuration of the 1,3-diol and the benzyloxymethyl group was confirmed by NMR-analysis of the acetonide (Figure 6.4). The large coupling constants indicate the *trans*-coupling of H-2 and H-1* or H-3 in the armchair conformation of the six-membered ring.




$^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.5 Hz

$^3J_{H\text{-}3,\ H\text{-}2}$ = 10.4 Hz

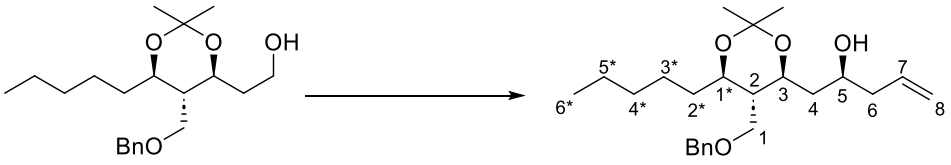
$^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.5 Hz

$^3J_{H\text{-}2,\ H\text{-}3}$ = 10.4 Hz

Figure 6.4: Confirmation of the given configuration by the $^1$H-$^1$H-coupling constants.

**Synthesis of Compound 320**

**(*S*)-1-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)-pent-4-en-2-ol**




**238** **320**

$C_{24}H_{38}O_4$
M = 390.56 g/mol

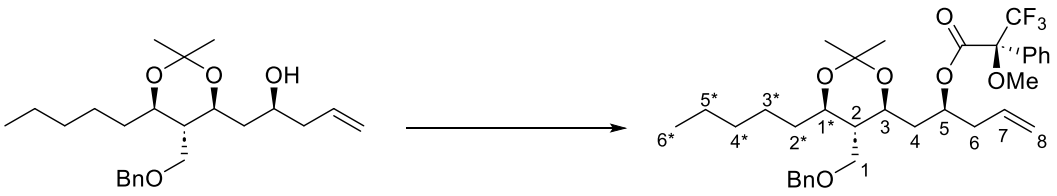
To an oven-dried pressure tube charged with $[Ir(cod)Cl]_2$ (168 mg, 0.25 mmol, 0.025 equiv), (*S*)-Cl,MeO-BIPHEP (326 mg, 0.50 mmol, 0.05 equiv), $Cs_2CO_3$ (651 mg, 2.00 mmol, 0.2 equiv) and 4-chloro-3-nitrobenzoic acid (201 mg, 1.00 mmol, 0.1 equiv) were added THF (20 mL) and allyl acetate (10.8 mL, 100 mmol, 10 equiv). The mixture was heated to 90 °C and stirred for 30 min before a solution of alcohol **238** (3.51 g, 10.0 mmol, 1 equiv) in THF (30 mL) was added. The tube was closed with a screw cap and stirred at 110 °C for 48 h. After completion of the reaction, the reaction mixture was filtered through a pad of celite and then evaporated onto silica gel. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a yellowish oil (3.71 g, 9.50 mmol, 95%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.19. $[\alpha]_D^{20}$ = −3.7° (c = 1.08, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 7.37–7.27 (m, 5H, 5xCH-Bn), 5.83 (dddd, $^3J_{H\text{-}7,\ H\text{-}8\text{-}E}$ = 17.2 Hz, $^3J_{H\text{-}7,\ H\text{-}8\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 7.0 Hz, $^3J_{H\text{-}7,\ H\text{-}6'}$ = 7.0 Hz, 1H, H-7), 5.10–5.00 (m, 2H, H-8-*E*, H-8-*Z*), 4.43 (d, $^2J$ = 12.2 Hz, 1H, $CH_2$-Bn), 4.39 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn´), 4.19 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 10.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.4 Hz, 1H, H-3), 3.93 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.5 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 8.0 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 2.5 Hz, 1H, H-1*), 3.85–3.77 (m, 1H, H-5), 3.50 (br s, 1H, OH), 3.44–3.36 (m, 2H, H-1, H-1´), 2.22–2.09 (m, 2H, H-6, H-6´), 1.83 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.4 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 2.4 Hz, 1H, H-4), 1.62–1.55 (m, 1H, H-2*), 1.47 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.45–1.42 (m, 1H, H-3*), 1.41–1.35 (m, 1H, H-4´), 1.33 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.34–1.31 (m, 1H, H-2), 1.31–1.19 (m, 6H, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 138.9 ($C_q$-Bn), 136.1 (C-7), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn, CH-Bn), 117.0 (C-8), 98.5 ($C_q$), 73.7 ($CH_2$-Bn), 72.5 (C-3), 71.7 (C-5), 70.2 (C-1*), 67.3 (C-1), 45.7 (C-2), 42.5 (C-6), 39.9 (C-4), 33.6 (C-2*), 32.4 (C-4*), 30.4 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 20.3 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{38}O_4H^+$ 391.2843, found 391.2838. For NMR-spectra see p. 279.

**Mosher's Ester Analysis of Secondary Alcohol 320**

**Synthesis of Compound 359-(*S*)**

**(*S*)-1-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)pent-4-en-2-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**320** **359-(*S*)**

$C_{34}H_{45}F_3O_6$
M = 606.72 g/mol

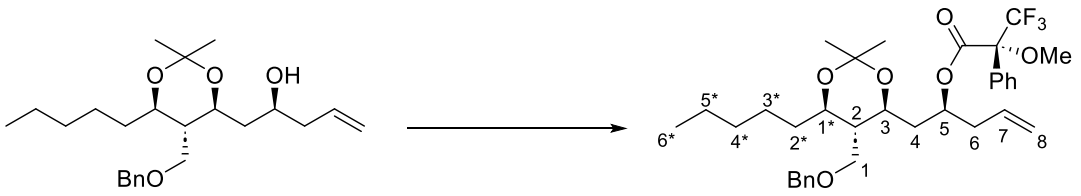
To a stirred solution of secondary alcohol **320** (11.5 mg, 29.4 µmol, 1 equiv) in DCM (0.5 mL) was added pyridine (24.0 µL, 294 µmol, 10 equiv) and (*R*)-MTPA-Cl (22.0 µL, 118 µmol, 4 equiv) and the mixture was stirred for 6 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 20:1) to obtain the pure ester as a colorless oil (14.7 mg, 24.2 µmol, 82%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +21.4° (c = 1.40, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.55–7.49 (m, 2H, 2xCH-Ph), 7.44–7.23 (m, 8H, 3xCH-Ph, 5xCH-Bn), 5.61 (dddd, $^3J_{H\text{-}7,\ H\text{-}8\text{-}E}$ = 17.5 Hz, $^3J_{H\text{-}7,\ H\text{-}8\text{-}Z}$ = 9.7 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 7.8 Hz, $^3J_{H\text{-}7,\ H\text{-}6'}$ = 6.4 Hz, 1H, H-7), 5.38–5.33 (m, 1H, H-5), 5.01–4.94 (m, 2H, H-8-*E*, H-8-*Z*), 4.43 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.38 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.07 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 9.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 9.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.8 Hz, 1H, H-3), 3.90 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 2.6 Hz, 1H, H-1*), 3.54–3.51 (m, 3H, OMe), 3.41–3.39 (m, 2H, H-1, H-1´), 2.46 (ddddd, $^2J$ = 14.9 Hz, $^3J_{H\text{-}6',\ H\text{-}7}$ = 6.1 Hz, $^3J_{H\text{-}6',\ H\text{-}5}$ = 4.5 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}E}$ = 1.5 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}E}$ = 1.5 Hz, 1H, H-6´), 2.32–2.25 (m, 1H, H-6), 2.02 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 8.5 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.8 Hz, 1H, H-4), 1.76 (ddd, $^2J$ = 13.9 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 9.5 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 5.0 Hz, 1H, H-4´), 1.62–1.55 (m, 1H, H-2*), 1.49–1.42 (m, 1H, H-3*), 1.42 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.32 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.31–1.20 (m, 7H, H-2, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.2 (C=O), 138.9 ($C_q$-Bn), 133.4 (C-7), 133.0 ($C_q$-Ph), 130.1–128.0 (5xCH-Ph, 5xCH-Bn), 124.0 (q, $^1J$ = 288.3 Hz, $CF_3$), 118.8 (C-8), 98.4 ($C_q$), 85.1 (q, $^2J$ = 27.3 Hz, $C_q$-Mosher), 74.8 (C-5), 73.8 ($CH_2$-Bn), 70.2 (C-1*), 68.1 (C-3), 67.4 (C-1), 56.0 (OMe), 45.6 (C-2), 37.7 (C-6), 37.1 (C-4), 33.7 (C-2*), 32.4 (C-4*), 30.3 ($CH_3$),

25.2 (C-3*), 23.2 (C-5*), 20.0 ($CH_3$), 14.4 (C-6*). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = −72.1. **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{34}H_{45}F_3O_6H^+$ 607.3241, found 607.3238. For NMR-spectra see p. 281.

**Synthesis of Compound 359-(*R*)**

**(*S*)-1-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)pent-4-en-2-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**320** **359-(*R*)**

$C_{34}H_{45}F_3O_6$
M = 606.72 g/mol

To a stirred solution of secondary alcohol **320** (11.5 mg, 29.4 µmol, 1 equiv) in DCM (0.5 mL) was added pyridine (24.0 µL, 294 µmol, 10 equiv) and (*S*)-MTPA-Cl (22.0 µL, 118 µmol, 4 equiv) and the mixture was stirred for 6 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 20:1) to obtain the pure ester as a colorless oil (12.1 mg, 19.9 µmol, 68%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +43.8° (c = 1.30, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.55–7.51 (m, 2H, 2xCH-Ph), 7.44–7.25 (m, 8H, 3xCH-Ph, 5xCH-Bn), 5.83 (dddd, $^3J_{H\text{-}7,\ H\text{-}8\text{-}E}$ = 16.7 Hz, $^3J_{H\text{-}7,\ H\text{-}8\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 7.8 Hz, $^3J_{H\text{-}7,\ H\text{-}6'}$ = 6.2 Hz, 1H, H-7), 5.37–5.33 (m, 1H, H-5), 5.16–5.06 (m, 2H, H-8-*E*, H-8-*Z*), 4.41 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.35 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.01 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 9.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 3.0 Hz, 1H, H-3), 3.87 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 2.7 Hz, 1H, H-1*), 3.53–3.51 (m, 3H, OMe), 3.36–3.33 (m, 2H, H-1, H-1´), 2.55 (ddddd, $^2J$ = 14.9 Hz, $^3J_{H\text{-}6',\ H\text{-}7}$ = 6.2 Hz, $^3J_{H\text{-}6',\ H\text{-}5}$ = 4.6 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}E}$ = 1.6 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}E}$ = 1.6 Hz, 1H, H-6´), 2.37 (ddddd, $^2J$ = 14.6 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 7.8 Hz, $^3J_{H\text{-}6,\ H\text{-}5}$ = 6.6 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}E}$ = 1.2 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}E}$ = 1.2 Hz, 1H, H-6), 1.93 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 8.5 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 3.0 Hz, 1H, H-4), 1.71 (ddd, $^2J$ = 13.9 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 9.1 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 4.9 Hz, 1H, H-4´), 1.57–1.52 (m, 1H, H-2*), 1.47–1.39 (m, 1H, H-3*), 1.36 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.30 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.33–1.18 (m, 7H, H-2, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H,

H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.3 (C=O), 138.9 ($C_q$-Bn), 133.9 (C-7), 132.9 ($C_q$-Ph), 130.1–128.1 (5xCH-Ph, 5xCH-Bn), 124.0 (q, $^1J$ = 288.3 Hz, $CF_3$), 118.8 (C-8), 98.3 ($C_q$), 85.1 (q, $^2J$ = 27.3 Hz, $C_q$-Mosher), 75.0 (C-5), 73.7 ($CH_2$-Bn), 70.2 (C-1*), 67.8 (C-3), 67.3 (C-1), 56.0 (OMe), 45.5 (C-2), 37.8 (C-6), 36.9 (C-4), 33.6 (C-2*), 32.4 (C-4*), 30.3 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 20.0 ($CH_3$), 14.4 (C-6*). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = −72.1. **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{34}H_{45}F_3O_6H^+$ 607.3241, found 607.3241. For NMR-spectra see p. 283.

### Mosher's Ester Analysis for Confirmation of the Absolute Configuration at C-5

The determination of the absolute configuration was confirmed by the model for the analysis of the Mosher ester. Therefore, the $^1$H-NMR data of both esters were collected and analyzed as shown in Table 6.4.[190] The difference between each signal led to the absolute configuration showed in Figure 6.5.

Table 6.4: NMR-data for Mosher's ester analysis of alcohol **320**.

| Position | δ (*S*)-Ester 359-(*S*) | δ (*R*)-Ester 359-(*R*) | $\Delta\delta^{SR}$ |
|---|---|---|---|
| **H-8** | 4.97 | 5.11 | −0.14 |
| **H-7** | 5.61 | 5.83 | −0.22 |
| **H-6** | 2.28 | 2.37 | −0.09 |
| **H-6´** | 2.46 | 2.55 | −0.09 |
| **H-5** | 5.35 | 5.35 | - |
| **H-4** | 2.02 | 1.93 | +0.09 |
| **H-4´** | 1.76 | 1.71 | +0.05 |
| **H-3** | 4.07 | 4.01 | +0.06 |
| **H-1*** | 3.90 | 3.87 | +0.03 |
| **$CH_3$-acetonide** | 1.42 | 1.36 | +0.06 |
| **$CH_3$´-acetonide** | 1.32 | 1.30 | +0.02 |
| **H-1/H-1´** | 3.40 | 3.34 | +0.06 |
| **H-2*** | 1.59 | 1.55 | +0.04 |
| **H-3*** | 1.46 | 1.43 | +0.03 |
| **H-2, H-2*´, H-3*´, H-4*, H-5*** | 1.26 | 1.26 | - |
| **H-6*** | 0.89 | 0.89 | - |

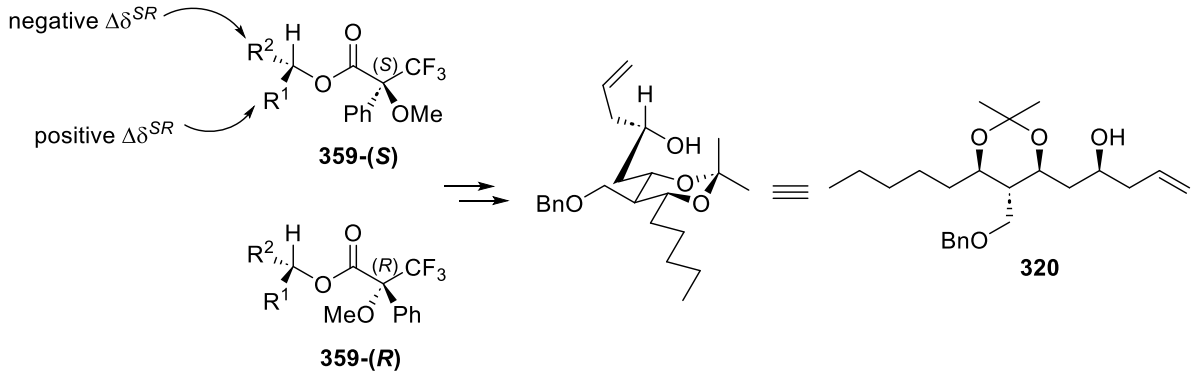
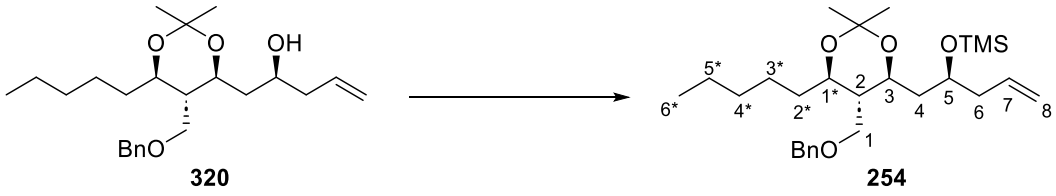



Figure 6.5: Proposed conformation according to the Mosher's ester analysis.

### Synthesis of Compound 254

**(((*S*)-1-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)pent-4-en-2-yl)oxy)trimethylsilane**




$C_{27}H_{46}SiO_4$
M = 462.75 g/mol

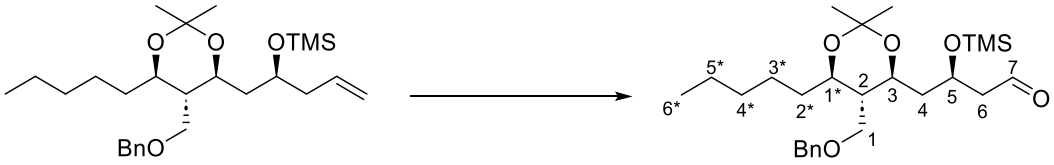
To a stirred solution of secondary alcohol **320** (3.85 g, 9.86 mmol, 1 equiv) in DCM (100 mL) was added $NEt_3$ (6.18 mL, 44.3 mmol, 4.5 equiv) and TMSCl (3.75 mL, 29.6 mmol, 3 equiv). The mixture was stirred for 4 h at room temperature before saturated $NaHCO_3$-solution (100 mL) was added. The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 30:1) and the pure product was obtained as a colorless oil (4.20 g, 9.08 mmol, 92%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.43. $[\alpha]_D^{20}$ = +5.2° (c = 1.34, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.25 (m, 5H, 5xCH-Bn), 5.91–5.78 (m, 1H, H-7), 5.05–4.99 (m, 2H, H-8-*E*, H-8-*Z*), 4.44 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.38 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.01–3.93 (m, 2H, H-3, H-5), 3.90 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 2.7 Hz, 1H, H-1*), 3.42 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.0 Hz, 2H, H-1), 2.28 (ddddd, $^2J$ = 14.1 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 7.1 Hz, $^3J_{H\text{-}6,\ H\text{-}5}$ = 4.6 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}E}$ = 1.3 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}Z}$ = 1.3 Hz, 1H, H-6), 2.12 (ddddd, $^2J$ = 13.9 Hz, $^3J_{H\text{-}6',\ H\text{-}7}$ = 7.5 Hz, $^3J_{H\text{-}6',\ H\text{-}5}$ = 6.6 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}E}$ = 1.2 Hz, $^4J_{H\text{-}6',\ H\text{-}8\text{-}Z}$ = 1.2 Hz, 1H, H-6´), 1.82 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 8.4 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 2.6 Hz, 1H, H-4), 1.61–1.55 (m, 1H, H-2*), 1.53–1.49 (m, 1H, H-4´), 1.48–1.42 (m, 1H, H-3*), 1.41 (s, 3H, $CH_3$), 1.30

(s, 3H, $CH_3$), 1.29–1.20 (m, 7H, H-2, H-2*´, H-3*´, H-4*, H-5*), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*), 0.09 (s, 9H, 3x$CH_3$-TMS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 136.3 (C-7), 128.8 (2xCH-Bn), 128.1 (2xCH-Bn), 128.1 (CH-Bn), 116.9 (C-8), 98.1 ($C_q$), 73.8 ($CH_2$-Bn), 70.5 (C-1*), 69.4 (C-5), 67.9 (C-3), 67.7 (C-1), 45.6 (C-2), 41.6 (C-4), 41.4 (C-6), 33.7 (C-2*), 32.4 (C-4*), 30.4 ($CH_3$), 25.3 (C-3*), 23.3 (C-5*), 20.1 ($CH_3$), 14.5 (C-6*), 0.5 (3x$CH_3$-TMS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{46}SiO_4H^+$ 463.3238, found 463.3235. For NMR-spectra see p. 285.

### Synthesis of Compound 321

**(*R*)-4-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)-3-((trimethylsilyl)oxy)butanal**




$C_{26}H_{44}SiO_5$
M = 464.72 g/mol

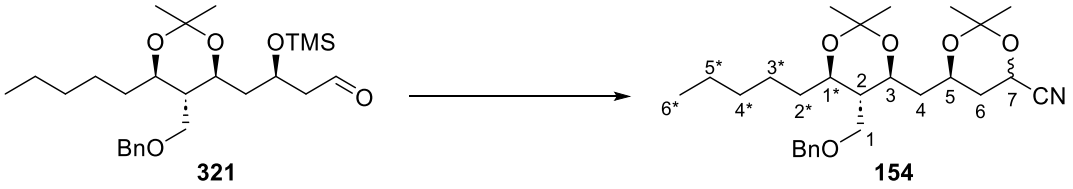
To a solution of alkene **254** (4.10 g, 8.86 mmol, 1 equiv) in acetone/$H_2O$ (10:1; 100 mL) was added NMO·$H_2O$ (2.40 g, 17.7 mmol, 2 equiv) and a solution of $OsO_4$ (4% in $H_2O$, 2.82 mL, 0.44 mmol, 0.05 equiv). The mixture was stirred for 20 h at room temperature. The reaction mixture was quenched with saturated $Na_2S_2O_3$-solution (100 mL) and diluted with DCM (100 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was redissolved in a solution of $Pb(OAc)_4$ (4.50 g, 10.2 mmol, 1.15 equiv) in toluene (100 mL) and stirred for 10 min before it was filtered through a glass filter frit. The solvent was evaporated *in vacuo* and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure aldehyde was obtained as a colorless oil (3.69 g, 7.94 mmol, 90%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −5.0° (c = 1.80, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.72 (dd, $^3J_{H\text{-}7,\ H\text{-}6}$ = 3.2 Hz, $^3J_{H\text{-}7,\ H\text{-}6´}$ = 1.8 Hz, 1H, H-7), 7.39–7.26 (m, 5H, 5xCH-Bn), 4.48–4.37 (m, 3H, H-5, $CH_2$-Bn, $CH_2$-Bn´), 3.97 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4´}$ = 9.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.4 Hz, 1H, H-3), 3.89 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*´}}$ = 2.6 Hz, 1H, H-1*), 3.41 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.0 Hz, 2H, H-1), 2.55 (ddd, $^2J$ = 15.7 Hz, $^3J_{H\text{-}6´,\ H\text{-}5}$ = 4.2 Hz, $^3J_{H\text{-}6´,\ H\text{-}7}$ = 1.9 Hz, 1H, H-6´), 2.42 (ddd, $^2J$ = 15.7 Hz, $^3J_{H\text{-}6,\ H\text{-}5}$ = 7.8 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 3.2 Hz, 1H, H-6), 1.87 (ddd, $^2J$ = 13.9 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 8.7 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.4 Hz,

1H, H-4), 1.67 (ddd, $^{2}J$ = 13.7 Hz, $^{3}J_{\text{H-4´, H-3}}$ = 9.5 Hz, $^{3}J_{\text{H-4´, H-5}}$ = 3.9 Hz, 1H, H-4´), 1.62–1.55 (m, 1H, H-2*), 1.48–1.42 (m, 1H, H-3*), 1.40 (d, $^{4}J$ = 0.9 Hz, 3H, $CH_3$), 1.30 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.29–1.19 (m, 7H, H-2, H-2*´, H-3*´, H-4*, H-5*), 0.88 (t, $^{3}J_{\text{H-6*, H-5*}}$ = 7.1 Hz, 3H, H-6*), 0.10 (s, 9H, 3x$CH_3$-TMS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 202.8 (C-7), 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn), 128.2 (CH-Bn), 98.2 ($C_q$), 73.8 ($CH_2$-Bn), 70.3 (C-1*), 67.6 (C-3), 67.6 (C-1), 65.8 (C-5), 50.7 (C-6), 45.4 (C-2), 42.0 (C-4), 33.7 (C-2*), 32.4 (C-4*), 30.3 ($CH_3$), 25.3 (C-3*), 23.2 (C-5*), 20.1 ($CH_3$), 14.4 (C-6*), 0.4 (3x$CH_3$-TMS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{44}SiO_5H^+$ 465.3031, found 465.3036. For NMR-spectra see p. 287.

### Synthesis of Compound 154

**(4*R*/4*S*,6*R*)-6-(((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




$C_{27}H_{41}NO_5$
M = 459.63 g/mol

A flame dried Schlenk flask was charged with anhydrous $K_2CO_3$ (55.0 mg, 0.40 mmol, 0.05 equiv) and a solution of aldehyde **321** (3.69 g, 7.94 mmol, 1 equiv) in DMF (40 mL) was added. TMSCN (1.10 mL, 8.73 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 30 min at room temperature. The reaction mixture was quenched with saturated NaCl-solution (50 mL) and diluted with DCM (100 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure.

The crude, double TMS-protected cyanohydrin was dissolved in MeOH (80 mL) and PPTS (200 mg, 0.79 mmol, 0.1 equiv) was added. The mixture was stirred for 15 min at room temperature and evaporated *in vacuo*. The residue was redissolved in DCM (100 mL) and 2,2-DMP (97.3 mL, 794 mmol, 100 equiv) was added. The mixture was stirred for 16 h at room temperature. After complete conversion of the starting material, the mixture was quenched with saturated $NaHCO_3$-solution (100 mL) and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 100 mL), the combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1) and the pure cyanohydrin acetonide

**154** was obtained as a yellowish highly viscous oil and a 1:1 mixture of diastereomers (3.51 g, 7.64 mmol, 96%).

An analytic sample was separated by HPLC for a separate NMR analysis of the diastereomers. (column: DAICEL Chiralpak IA; 5 µm; 250 x 20 mm, eluent: MeCN:$H_2O$ = 65:35). However, the mixture of the diastereomers is used for the next reaction.

1,3-*syn*-isomer:

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.48. $[\alpha]_D^{20}$ = +1.9° (c = 1.06, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.41–7.26 (m, 5H, 5xCH-Bn), 4.77 (dd, $^3J_{H\text{-}7,\ H\text{-}6\text{-}ax}$ = 12.1 Hz, $^3J_{H\text{-}7,\ H\text{-}6\text{-}eq}$ = 2.9 Hz, 1H, H-7), 4.44 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.40 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn´), 4.11 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}ax}$ = 11.4 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 7.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 5.8 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}eq}$ = 2.6 Hz, 1H, H-5), 4.02 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 7.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 4.5 Hz, 1H, H-3), 3.91 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.7 Hz, 1H, H-1*), 3.43 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 2.9 Hz, 2H, H-1), 1.86 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}7}$ = 2.8 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}5}$ = 2.6 Hz, 1H, H-6-eq), 1.74–1.62 (m, 3H, H-4, H-4´, H-6-ax), 1.61–1.55 (m, 1H, H-2*), 1.47–1.40 (m, 7H, H-3*, 2x$CH_3$), 1.38 (s, 3H, $CH_3$), 1.33 (ddt, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 3.0 Hz, 1H, H-2), 1.31–1.19 (m, 9H, H-2*´, H-3*´, H-4*, H-5*, $CH_3$), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn, CH-Bn), 118.7 (CN), 100.4 ($C_q$), 98.3 ($C_q$), 73.8 ($CH_2$-Bn), 70.3 (C-1*), 67.3 (C-1), 66.9 (C-3), 65.5 (C-5), 59.8 (C-7), 45.2 (C-2), 39.7 (C-4), 34.5 (C-6), 33.6 (C-2*), 32.4 (C-4*), 30.4 ($CH_3$), 30.0 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 20.1 ($CH_3$), 19.6 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{41}NO_5H^+$ 460.3057, found 460.3055. For NMR-spectra see p. 289.

The configuration of the 1,3-*syn* isomer is confirmed by the coupling constants between H-7 and H-6 which are typical for the axial and equatorial coupling in the chair conformation.

1,3-*anti*-isomer:

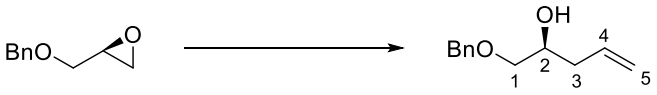
**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.50. $[\alpha]_D^{20}$ = +25.9° (c = 1.08, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.27 (m, 5H, 5xCH-Bn), 4.83 (dd, $^3J_{H\text{-}7,\ H\text{-}6}$ = 6.0 Hz, $^3J_{H\text{-}7,\ H\text{-}6'}$ = 3.4 Hz, 1H, H-7), 4.46–4.35 (m, 3H, H-5, $CH_2$-Bn, $CH_2$-Bn´), 4.05 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 7.1 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 4.4 Hz, 1H, H-3), 3.91 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.6 Hz, 1H, H-1*), 3.44 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.0 Hz, 2H, H-1), 1.90–1.79 (m, 2H, H-6, H-6´), 1.76–1.69 (m, 2H, H-4, H-4´), 1.63 (s, 3H, $CH_3$), 1.61–1.56 (m, 1H, H-2*), 1.49–1.42 (m, 1H, H-3*), 1.42 (s, 3H, $CH_3$), 1.37 (ddt, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 3.0 Hz, 1H, H-2), 1.33 (s, 3H, $CH_3$), 1.32 (s, 3H, $CH_3$), 1.31–1.20 (m, 6H, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn, CH-Bn), 120.5 (CN),

101.3 ($C_q$), 98.3 ($C_q$), 73.7 ($CH_2$-Bn), 70.4 (C-1*), 67.4 (C-1), 67.1 (C-3), 63.4 (C-5), 59.3 (C-7), 45.1 (C-2), 39.3 (C-4), 33.6 (C-2*, C-6), 32.4 (C-4*), 30.4 ($CH_3$), 29.9 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 22.3 ($CH_3$), 20.1 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{41}NO_5H^+$ 460.3057, found 460.3059. For NMR-spectra see p. 291.

## 6.2.3 Synthesis of the Eastern Fragment

### Synthesis of Compound 191

**(2*S*)-1-(benzyloxy)pent-4-en-2-ol**




**192** **191**

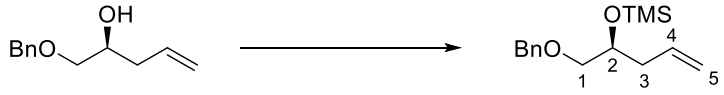
$C_{12}H_{16}O_2$
M = 192.26 g/mol

To a mixture of (*S*)-glycidyl benzyl ether (**192**) (5.00 g, 30.5 mmol, 1 equiv), (*S*,*S*)-*N*,*N*'-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (0.92 g, 1.52 mmol, 0.05 equiv), trimethylsulfoxonium iodide (26.8 g, 122 mmol, 4 equiv) and *t*-BuOK (1M in *t*-BuOH, 122 mL, 122 mmol, 4 equiv) was added *t*-BuOH (180 mL) and the suspension was heated to 60 °C. After stirring for 16 h, the mixture was quenched with $NaHCO_3$-solution (400 mL) and $Et_2O$ (500 mL) was added. The organic phase was separated, and the aqueous phase was extracted with $Et_2O$ (3 x 500 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 8:1) and the pure product was obtained as a yellow liquid (5.41 g, 28.2 mmol, 92%).

**TLC** (silica, CyHex:EtOAc = 7:1): $R_f$ = 0.16. $[\alpha]_D^{20}$ = −7.3° (c = 1.10, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.39–7.26 (m, 5H, 5xCH-Bn), 5.84 (ddt, $^3J_{H\text{-}4,\ H\text{-}5\text{-}E}$ = 17.2 Hz, $^3J_{H\text{-}4,\ H\text{-}5\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 7.1 Hz, 1H, H-4), 5.14–5.04 (m, 2H, H-5-*Z*, H-5-*E*), 4.54 (br s, 2H, $CH_2$-Bn), 3.87–3.81 (m, 1H, H-2), 3.50 (dd, $^2J$ = 9.5 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.4 Hz, 1H, H-1), 3.36 (dd, $^2J$ = 9.5 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 7.3 Hz, 1H, H-1´), 2.28 (d, $^3J_{OH,\ H\text{-}2}$ = 3.7 Hz, 1H, OH), 2.24 (m, 2H, H-3, H-3´). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.9 ($C_q$-Bn), 135.2 (C-4), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.2 (CH-Bn), 117.7 (C-5), 74.6 (C-1), 73.8 ($CH_2$-Bn), 70.3 (C-2), 38.5 (C-3). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{16}O_2Na^+$ 215.1043, found 215.1046. For NMR-spectra see p. 293.

**Synthesis of Compound 323**

**(*S*)-((1-(benzyloxy)pent-4-en-2-yl)oxy)trimethylsilane**




**191** **323**

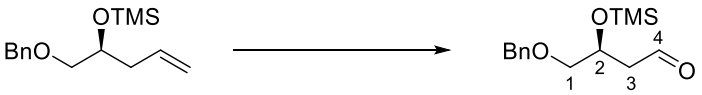
$C_{15}H_{24}SiO_2$
M = 264.44 g/mol

To a stirred solution of secondary alcohol **191** (3.50 g, 18.2 mmol, 1 equiv) in DCM (180 mL) was added $NEt_3$ (11.4 mL, 81.9 mmol, 4 equiv) and TMSCl (6.93 mL, 54.6 mmol, 3 equiv). The mixture was stirred for 2 h at room temperature before it was quenched with saturated Na-$HCO_3$-solution. The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 150 mL). The combined organic layers were dried over $MgSO_4$ , and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1) and the pure product was obtained as a yellow liquid (4.54 g, 17.2 mmol, 94%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −5.5° (c = 2.00, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.31 (m, 4H, 4xCH-Bn), 7.31–7.25 (m, 1H, CH-Bn), 5.82 (ddt, $^3J_{H\text{-}4,\ H\text{-}5\text{-}E}$ = 17.3 Hz, $^3J_{H\text{-}4,\ H\text{-}5\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 7.1 Hz, 1H, H-4), 5.09–5.00 (m, 2H, H-5-Z, H-5-*E*), 4.51 (br s, 2H, $CH_2$-Bn), 3.90–3.84 (m, 1H, H-2), 3.41–3.35 (m, 2H, H-1, H-1´), 2.35–2.28 (m, 1H, H-3), 2.19 (dddt, $^2J$ = 14.0 Hz, $^3J_{H\text{-}3',\ H\text{-}4}$ = 7.0 Hz, $^3J_{H\text{-}3',\ H\text{-}2}$ = 7.0 Hz, $^4J_{H\text{-}3',\ H\text{-}5}$ = 1.2 Hz, 1H, H-3´), 0.10 (s, 9H, 3x$CH_3$-TMS). **$^{13}$C-NMR** (125 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.3 ($C_q$-Bn), 135.8 (C-4), 128.8 (2xCH-Bn), 128.1 (2xCH-Bn), 128.0 (CH-Bn), 117.2 (C-5), 74.9 (C-1), 73.7 ($CH_2$-Bn), 71.8 (C-2), 39.7 (C-3), 0.5 (3x$CH_3$-TMS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{24}SiO2H^+$ 265.1618, found 265.1618. For NMR-spectra see p. 295.

**Synthesis of Compound 324**

**(*S*)-4-(benzyloxy)-3-((trimethylsilyl)oxy)butanal**




**323** **324**

$C_{14}H_{22}SiO_3$
M = 266.41 g/mol

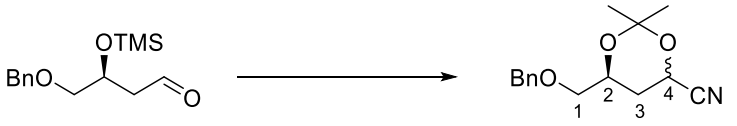
To a solution of alkene **323** (4.50 g, 17.0 mmol, 1 equiv) in acetone/$H_2O$ (10:1; 190 mL) was added NMO (3.99 g, 34.0 mmol, 2 equiv) and a solution of $OsO_4$ (4% in $H_2O$, 5.41 mL,

0.85 mmol, 0.05 equiv). The mixture was stirred for 20 h at room temperature. The reaction mixture was quenched with saturated $Na_2S_2O_3$-solution (200 mL) and diluted with DCM (100 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 200 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was redissolved in a solution of $Pb(OAc)_4$ (8.68 g, 19.6 mmol, 1.15 equiv) in benzene (400 mL) and stirred for 10 min before it was filtered through a glass filter frit. The solvent was evaporated *in vacuo* and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure aldehyde was obtained as a colorless oil (3.99 g, 15.0 mmol, 88%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.46. $[\alpha]_D^{20}$ = −13.0° (c = 1.08, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.75 (dd, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.7 Hz, $^3J_{H\text{-}4,\ H\text{-}3'}$ = 1.9 Hz, 1H, H-4), 7.38–7.26 (m, 5H, 5xCH-Bn), 4.52 (br s, 2H, $CH_2$-Bn), 4.40–4.32 (m, 1H, H-2), 3.48 (dd, $^2J$ = 9.6 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.3 Hz, 1H, H-1), 3.40 (dd, $^2J$ = 9.6 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.7 Hz, 1H, H-1´), 2.61 (ddd, $^2J$ = 16.0 Hz, $^3J_{H\text{-}3',\ H\text{-}2}$ = 4.9 Hz, $^3J_{H\text{-}3',\ H\text{-}4}$ = 1.9 Hz, 1H, H-3´), 2.54 (ddd, $^2J$ = 16.0 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.7 Hz, 1H, H-3), 0.11 (s, 9H, 3x$CH_3$-TMS). **$^{13}$C-NMR** (125 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 201.7 (C-4), 138.9 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 74.7 (C-1), 73.8 ($CH_2$-Bn), 67.6 (C-2), 49.3 (C-3), 0.4 (3x$CH_3$-TMS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{22}SiO_3Na^+$ 289.1230, found 289.1225. For NMR-spectra see p. 297.

### Synthesis of Compound 164

**(4*R*/*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




**324** **164**

$C_{15}H_{19}NO_3$
M = 261.32 g/mol

A flame dried Schlenk flask was charged with anhydrous $K_2CO_3$ (103 mg, 0.75 mmol, 0.05 equiv) and a solution of aldehyde **324** (3.95 g, 14.9 mmol, 1 equiv) in DMF (75 mL) was added. TMSCN (2.06 mL, 16.4 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 20 min at room temperature. The reaction mixture was quenched with saturated NaCl-solution (100 mL) and diluted with DCM (200 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure.

The crude, double TMS-protected cyanohydrin was dissolved in MeOH (150 mL) and PPTS (375 mg, 1.49 mmol, 0.1 equiv) was added. The mixture was stirred for 15 min at room temperature and evaporated *in vacuo*. The residue was redissolved in DCM (180 mL) and 2,2-DMP (180 mL, 1.49 mol, 100 equiv) was added. The mixture was stirred for 16 h at room temperature. After complete conversion of the starting material, the mixture was quenched with saturated $NaHCO_3$-solution (200 mL) and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 200 mL), the combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 6:1) and the pure cyanohydrin acetonide **21** was obtained as a yellowish oil and a 1:1 mixture of diastereomers (3.24 g, 12.4 mmol, 83%).

1,3-*syn*-isomer:

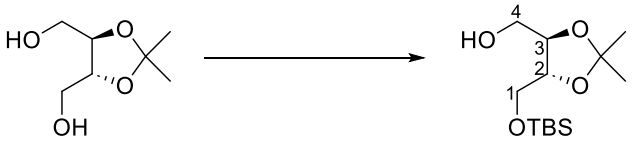
**TLC** (silica, CyHex:EtOAc = 6:1): $R_f$ = 0.39. $[\alpha]_D^{20}$ = +36.6° (c = 1.22, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.28 (m, 5H, 5xCH-Bn), 4.88 (dd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 6.6 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.8 Hz, 1H, H-4), 4.55 (br s, 2H, $CH_2$-Bn), 4.37–4.32 (m, 1H, H-2), 3.55 (dd, $^2J$ = 10.3 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.4 Hz, 1H, H-1), 3.47 (dd, $^2J$ = 10.3 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H, H-1´), 2.02 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.4 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 6.5 Hz, 1H, H-3-ax), 1.86 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 3.0 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 3.0 Hz, 1H, H-3-eq), 1.66 (d, $^4J$ = 0.9 Hz, 3H, $CH_3$), 1.38 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.8 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.2 (CH-Bn), 120.4 (CN), 101.4 ($C_q$), 74.0 ($CH_2$-Bn), 73.0 (C-1), 65.8 (C-2), 59.1 (C-4), 30.7 (C-3), 29.8 ($CH_3$), 22.2 ($CH_3$). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{19}NO_3H^+$ 262.1438, found 262.1437. For NMR-spectra see p. 299.

1,3-*anti*-isomer:

**TLC** (silica, CyHex:EtOAc = 6:1): $R_f$ = 0.25. $[\alpha]_D^{20}$ = +5.80° (c = 1.04, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.28 (m, 5H, 5xCH-Bn), 4.81–4.79 (m, 1H, H-4), 4.53 (br s, 2H, $CH_2$-Bn), 4.09 (dddd, 1H, H-2), 3.52 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.4 Hz, 1H, H-1), 3.42 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.8 Hz, 1H, H-1´), 1.90–1.84 (m, 2H, H-3, H-3´), 1.45 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.43 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.7 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.3 (CH-Bn), 118.5 (CN), 100.6 ($C_q$), 74.0 ($CH_2$-Bn), 73.2 (C-1), 68.0 (C-2), 59.6 (C-4), 32.0 (C-3), 29.8 ($CH_3$), 19.5 ($CH_3$). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{19}NO_3H^+$ 262.1438, found 262.1440. For NMR-spectra see p. 301.

**Synthesis of Compound 325**

**((4*R*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-methanol**




**166** **325**

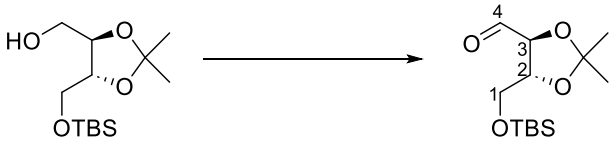
$C_{13}H_{28}SiO_4$
M = 276.45 g/mol

To a stirred suspension of NaH (60% in mineral oil; 2.10 g, 35.0 mmol, 1.6 equiv) in THF (140 mL) was added a solution of diol **166** (5.20 g, 32.0 mmol, 1.1 equiv) in THF (10 mL) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C before TBSCl (4.39 g, 29.1 mmol, 1 equiv) was added in portions. The mixture was stirred for 3 h at 0 °C. Subsequently, the reaction mixture was quenched with $H_2O$ (150 mL) and DCM (150 mL) and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 150 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless liquid (7.25 g, 26.2 mmol, 90%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −19.0° (c = 1.42, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 3.94 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.8 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 4.5 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 4.5 Hz, 1H, H-3), 3.88–3.81 (m, 2H, H-1, H-2), 3.73 (ddd, $^2J$ = 11.6 Hz, $^3J_{H\text{-}4,\ OH}$ = 4.5 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 4.5 Hz, 1H, H-4), 3.69–3.61 (m, 2H, H-1´, H-4´), 2.25–2.20 (m, 1H, OH), 1.38 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.9 Hz, 3H, $CH_3$), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.08 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.6 ($C_q$), 80.5 (C-3), 78.6 (C-2), 64.4 (C-1), 63.2 (C-4), 27.4 ($CH_3$), 27.3 ($CH_3$), 26.2 (3x$CH_3$-TBS), 18.8 ($C_q$-TBS), −5.2 ($CH_3$-TBS), −5.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{28}SiO_4H^+$ 277.1830, found 277.1830. For NMR-spectra see p. 303.

**Synthesis of Compound 326**

**(4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde**




**325** **326**

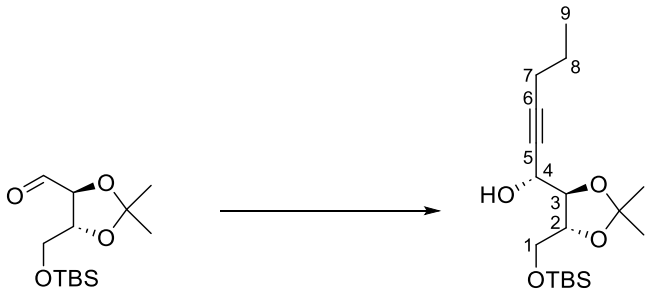
$C_{13}H_{26}SiO_4$
M = 274.43 g/mol

To a Schlenk flask charged with sulfur trioxide pyridine complex (12.4 g, 78.1 mmol, 3 equiv) were added DCM (200 mL), DMSO (18.5 mL, 260 mmol, 10 equiv) and DIPEA (18.2 mL, 104 mmol, 4 equiv). A solution of alcohol **325** (7.20 g, 26.0 mmol, 1 equiv) in DCM (60 mL) was added and the mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was washed with saturated $NaHCO_3$-solution (100 mL). The organic phase was further washed with saturated $CuSO_4$-solution (2 x 50 mL) before it was finally washed with saturated $NH_4Cl$-solution (100 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless liquid (6.55 g, 23.9 mmol, 92%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −4.5° (c = 1.34, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.74 (d, $^3J_{H\text{-}4,\ H\text{-}3}$ = 1.7 Hz, 1H, H-4), 4.28 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 1.7 Hz, 1H, H-3), 4.11 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.2 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.5 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.5 Hz, 1H, H-2), 3.82–3.76 (m, 2H, H-1, H-1´), 1.45 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.39 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.08 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 201.4 (C-4), 111.9 ($C_q$), 82.6 (C-3), 78.2 (C-2), 63.6 (C-1), 27.2 ($CH_3$), 26.7 ($CH_3$), 26.2 (3x$CH_3$-TBS), 18.7 ($C_q$-TBS), −5.1 ($CH_3$-TBS), −5.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{26}SiO_4H^+$ 275.1673, found 275.1678. For NMR-spectra see p. 305.

**Synthesis of Compound 327**

**(*R*)-1-((4*R*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-hex-2-yn-1-ol**




**326** **327**

$C_{18}H_{34}SiO_4$
M = 342.55 g/mol

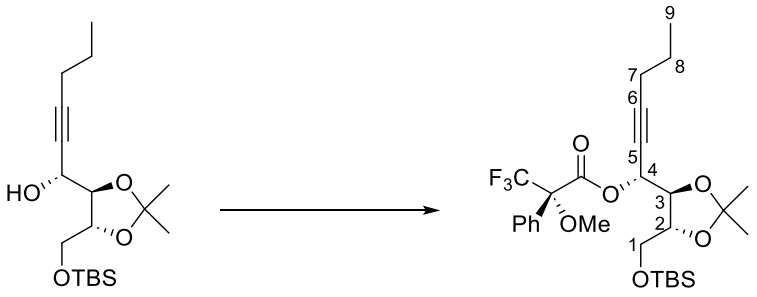
To an oven-dried Schlenk tube charged with $Zn(OTf)_2$ (9.47 g, 26.1 mmol, 1.1 equiv) and (1*R*,2*S*)-(−)-*N*-methylephedrine (5.10 g, 28.4 mmol, 1.2 equiv) were added toluene (60 mL) and $NEt_3$ (3.90 mL, 28.4 mmol, 1.2 equiv). The mixture was stirred for 2 h at room temperature before pentyne (2.80 mL, 28.4 mmol, 1.2 equiv) was added. After stirring for another 15 min at room temperature aldehyde **326** (6.50 g, 23.7 mmol, 1 equiv) in toluene (12 mL) was added. The mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was quenched with $NH_4Cl$-solution and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 100 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless liquid (7.51 g, 21.9 mmol, 93%, *dr* > 20:1). No other isomer was detected and isolated.

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.19. $[\alpha]_D^{20}$ = +8.0° (c = 1.76, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.48 (ddt, $^3J_{H\text{-}4,\ OH}$ = 4.4 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 4.4 Hz, $^5J_{H\text{-}4,\ H\text{-}7}$ = 2.0 Hz, 1H, H-4), 4.05 (dt, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.5 Hz, 1H, H-2), 3.97 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 4.3 Hz, 1H, H-3), 3.81 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.5 Hz, 2H, H-1), 2.56 (d, $^3J_{OH,\ H\text{-}4}$ = 4.7 Hz, 1H, OH), 2.20 (td, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.1 Hz, $^5J_{H\text{-}7,\ H\text{-}4}$ = 2.1 Hz, 2H, H-7), 1.58–1.50 (m, 2H, H-8), 1.41 (d, $^4J$ = 0.9 Hz, 3H, $CH_3$), 1.39 (d, $^4J$ = 0.9 Hz, 3H, $CH_3$), 0.98 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.09 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 110.0 ($C_q$), 87.5 (C-6), 80.8 (C-3), 78.8 (C-2), 78.2 (C-5), 64.6 (C-1), 63.3 (C-4), 27.5 ($CH_3$), 27.4 ($CH_3$), 26.2 (3x$CH_3$-TBS), 22.6 (C-8), 21.2 (C-7), 18.8($C_q$-TBS), 13.8 (C-9), −5.1 ($CH_3$-TBS), −5.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{34}SiO_4Na^+$ 365.2119, found 365.2125. For NMR-spectra see p. 307

**Mosher's Ester Analysis of Propargylic Alcohol 327**

**Synthesis of Compound 360-(*S*)**

**(*R*)-1-((4*R*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-hex-2-yn-1-yl-(*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**327** **360-(*S*)**

$C_{28}H_{41}F_3SiO_6$
M = 558.71 g/mol

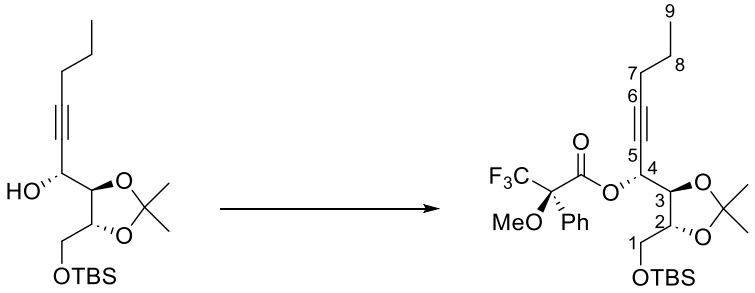
To a stirred solution of propargylic alcohol **327** (10.0 mg, 29.2 µmol, 1 equiv) in DCM (0.5 mL) was added pyridine (23.5 µL, 292 µmol, 10 equiv) and (*R*)-MTPA-Cl (21.9 µL, 117 µmol, 4 equiv) and the mixture was stirred for 6 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The phases were separated, and the aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by preparative HPLC (Column: KNAUER Eurospher II 100-5 C18; 5 µm; 250 x 16 mm, eluent: MeCN/$H_2O$ = 4:1) to obtain the pure ester as a colorless oil (12.1 mg, 21.7 µmol, 74%).

**TLC** (silica, CyHex:EtOAc = 30:1): $R_f$ = 0.19. $[\alpha]_D^{20}$ = −25.6° (c = 2.14, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.55–7.52 (m, 2H, 2xCH-Ph), 7.44–7.39 (m, 3H, 3xCH-Ph), 5.74 (dt, $^3J_{H\text{-}4,\ H\text{-}3}$ = 3.4 Hz, $^5J_{H\text{-}4,\ H\text{-}7}$ = 2.1 Hz, 1H, H-4), 4.11 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 3.4 Hz, 1H, H-3), 3.99 (dt, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.0 Hz, 1H, H-2), 3.76 (dd, $^2J$ = 11.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.9 Hz, 1H, H-1), 3.65 (dd, $^2J$ = 11.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.1 Hz, 1H, H-1´), 3.61–3.59 (m, 3H, OMe), 2.23 (td, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.0 Hz, $^5J_{H\text{-}7,\ H\text{-}4}$ = 2.1 Hz, 2H, H-7), 1.58–1.51 (m, 2H, H-8), 1.33 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.20 (d, $^4J$ = 0.9 Hz, 3H, $CH_3$), 0.98 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.07 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.1 (C=O), 132.9 ($C_q$-Ph), 130.3 (CH-Ph), 129.0 (2xCH-Ph), 127.8 (2xCH-Ph), 123.9 (q, $^1J$ = 288.5 Hz, $CF_3$), 110.5 ($C_q$), 90.1 (C-6), 84.9 (q, $^2J$ = 27.6 Hz, $C_q$-Mosher), 78.5 (C-2), 77.9 (C-3), 73.8 (C-5), 66.6 (C-4), 63.9 (C-1), 56.1 (OMe), 27.5 ($CH_3$), 27.0 ($CH_3$), 26.2 (3x$CH_3$-TBS), 22.3 (C-8), 21.1 (C-7), 18.8 ($C_q$-TBS), 13.8 (C-9), −5.1 ($CH_3$-TBS), −5.2 ($CH_3$-TBS). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = −72.0.

**HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{28}H_{41}F_3SiO_6Na^+$ 581.2517, found 581.2516. For NMR-spectra see p. 309.

**Synthesis of Compound 360-(*R*)**

**(*R*)-1-((4*R*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)hex-2-yn-1-yl-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate**




**327** **360-(*R*)**

$C_{28}H_{41}F_3SiO_6$
M = 558.71 g/mol

To a stirred solution of propargylic alcohol **327** (10.0 mg, 29.2 µmol, 1 equiv) in DCM (0.5 mL) was added pyridine (23.5 µL, 292 µmol, 10 equiv) and (*S*)-MTPA-Cl (21.9 µL, 117 µmol, 4 equiv) and the mixture was stirred for 6 h at room temperature. Subsequently, the mixture was diluted with DCM (5 mL) and quenched with water (5 mL). The phases were separated, and the aqueous phase was extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by preparative HPLC (Column: KNAUER Eurospher II 100-5 C18; 5 µm; 250 x 16 mm, eluent: MeCN/$H_2O$ = 4:1) to obtain the pure ester as a colorless oil (7.30 mg, 13.1 µmol, 45%).

**TLC** (silica, CyHex:EtOAc = 30:1): $R_f$ = 0.19. $[\alpha]_D^{20}$ = +24.3° (c = 2.18, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 7.55–7.53 (m, 2H, 2xCH-Ph), 7.46–7.40 (m, 3H, 3xCH-Ph), 5.77 (dt, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.9 Hz, $^5J_{H\text{-}4,\ H\text{-}7}$ = 2.1 Hz, 1H, H-4), 4.18 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 8.1 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.9 Hz, 1H, H-3), 4.04 (dt, $^3J_{H\text{-}2,\ H\text{-}3}$ = 8.2 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.2 Hz, 1H, H-2), 3.82 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.1 Hz, 1H, H-1), 3.78 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H, H-1´), 3.56–3.55 (m, 3H, OMe), 2.20 (td, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.2 Hz, $^5J_{H\text{-}7,\ H\text{-}4}$ = 2.1 Hz, 2H, H-7), 1.57–1.48 (m, 2H, H-8), 1.39 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 0.96 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.07 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 166.0 (C=O), 132.5 ($C_q$-Ph), 130.3 (CH-Ph), 129.0 (2xCH-Ph), 128.1 (2xCH-Ph), 123.9 (q, $^1J$ = 288.4 Hz, $CF_3$), 110.5 ($C_q$), 90.1 (C-6), 85.3 (q, $^2J$ = 27.5 Hz, $C_q$-Mosher), 78.3 (C-2), 78.1 (C-3), 73.4 (C-5), 66.7 (C-4), 64.1 (C-1), 56.1 (OMe), 27.5 ($CH_3$), 27.2 ($CH_3$), 26.2 (3x$CH_3$-TBS), 22.3 (C-8), 21.1 (C-7), 18.8 ($C_q$-TBS), 13.8

(C-9), −5.1 ($CH_3$-TBS), −5.2 ($CH_3$-TBS). **$^{19}$F-NMR** (470 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = −72.2. **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{28}H_{41}F_3SiO_6Na^+$ 581.2517, found 581.2522. For NMR-spectra see p. 311.

### Mosher's Ester Analysis for Confirmation of the Absolute Configuration at C-3

The determination of the absolute configuration was confirmed by the model for the analysis of the Mosher ester. Therefore, the $^1$H-NMR data of both esters were collected and analyzed as shown in Table 6.5. The difference between each signal led to the absolute configuration showed in Figure 6.6.

Table 6.5: NMR-data for Mosher's ester analysis of alcohol **S17**.

| Position | δ (*S*)-Ester 360-(*S*) | δ (*R*)-Ester 360-(*R*) | $\Delta\delta^{SR}$ |
|---|---|---|---|
| **$CH_3$-TBS** | 0.07 | 0.07 | 0 |
| **3x$CH_3$-TBS** | 0.90 | 0.90 | 0 |
| **H-1** | 3.75 | 3.82 | −0.07 |
| **H-1´** | 3.65 | 3.78 | −0.13 |
| **H-2** | 3.99 | 4.04 | −0.05 |
| **H-3** | 4.11 | 4.18 | −0.07 |
| **$CH_3$-acetonide** | 1.33 | 1.39 | −0.06 |
| **$CH_3$´-acetonide** | 1.20 | 1.37 | −0.17 |
| **H-7** | 2.23 | 2.20 | 0.03 |
| **H-8** | 1.55 | 1.53 | 0.02 |
| **H-9** | 0.98 | 0.96 | 0.02 |

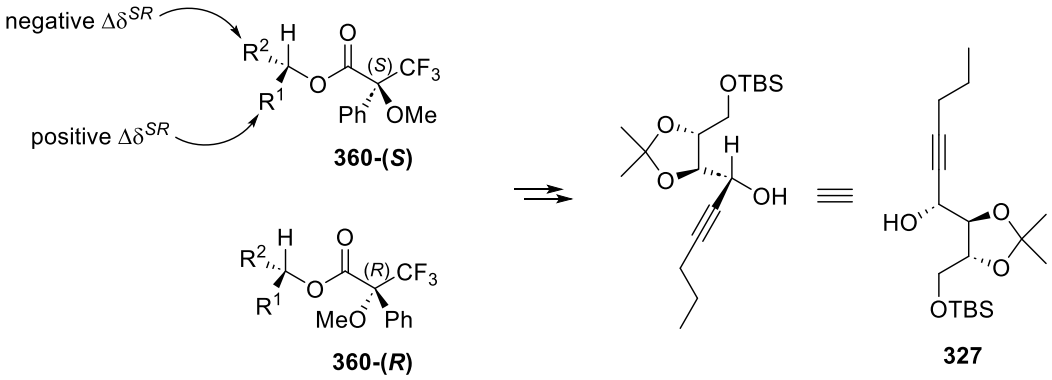
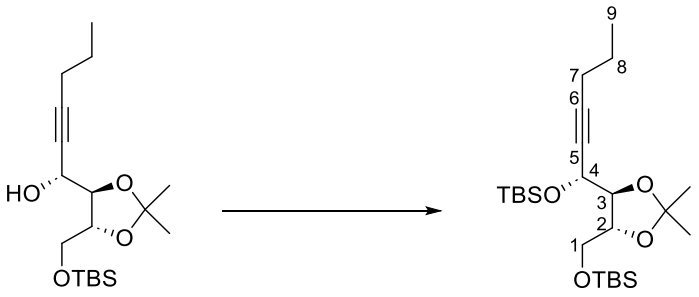



Figure 6.6: Proposed conformation according to the Mosher's ester analysis.

**Synthesis of Compound 328**

***tert*-butyl(((4*R*,5*S*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)hex-2-yn-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)-dimethylsilane**




**327** **328**

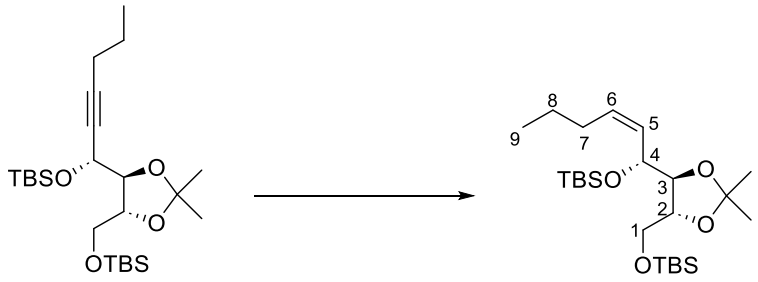
$C_{24}H_{48}Si_2O_4$
M = 456.81 g/mol

A stirred solution of propargylic alcohol **327** (7.00 g, 20.4 mmol, 1 equiv) in DCM (40 mL) was treated with 2,6-lutidine (4.73 mL, 40.9 mmol, 2 equiv) and cooled to 0 °C. TBSOTf (7.00 mL, 30.7 mmol, 1.5 equiv) was added and the mixture was stirred for 1 h at 0 °C. Subsequently, DCM (50 mL) and water (100 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 100 mL) and the combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1) and the pure product was obtained as a colorless oil (9.33 g, 20.4 mmol, quant.).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.25. $[\alpha]_D^{20}$ = −14.5° (c = 1.24, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.50 (dt, $^3J_{H\text{-}4,\ H\text{-}3}$ = 4.2 Hz, $^5J_{H\text{-}4,\ H\text{-}7}$ = 2.0 Hz, 1H, H-4), 4.09 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.0 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 3.0 Hz, 1H, H-2), 3.90–3.86 (m, 2H, H-3, H-1´), 3.73 (dd, $^2J$ = 11.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.0 Hz, 1H, H-1), 2.18 (td, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.1 Hz, $^5J_{H\text{-}7,\ H\text{-}4}$ = 2.0 Hz, 2H, H-7), 1.58–1.47 (m, 2H, H-8), 1.38 (s, 3H, $CH_3$), 1.38 (s, 3H, $CH_3$), 0.97 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.15 (s, 3H, $CH_3$-TBS), 0.12 (s, 3H, $CH_3$-TBS), 0.08 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.8 ($C_q$), 86.9 (C-6), 80.6 (C-3), 79.6 (C-5), 79.1 (C-2), 65.0 (C-1), 64.4 (C-4), 27.7 ($CH_3$), 27.6 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.2 (3x$CH_3$-TBS), 22.6 (C-8), 21.2 (C-7), 18.9 ($C_q$-TBS), 18.7 ($C_q$-TBS), 13.9 (C-9), −4.3 ($CH_3$-TBS), −4.6 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{48}Si_2O_4H^+$ 457.3164, found 457.3173. For NMR-spectra see p. 313.

**Synthesis of Compound 329**

***tert*-butyl(((4*R*,5*S*)-5-((*R*,*Z*)-1-((*tert*-butyldimethylsilyl)oxy)hex-2-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)-dimethylsilane**




**328** **329**

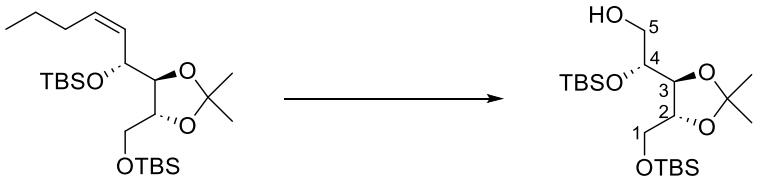
$C_{24}H_{50}Si_2O_4$
M = 458.83 g/mol

To a stirred solution of alkyne **328** (9.30 g, 20.4 mmol, 1 equiv) in hexane (200 mL) was added Lindlar catalyst consisting of Pd/$CaCO_3$ (5% Pd, 2.17 g, 1.02 mmol, 0.05 equiv, with respect to Pd) and quinoline (0.12 mL, 1.02 mmol, 0.05 equiv). The reaction mixture was stirred under a hydrogen atmosphere (1 atm) for 1 h at room temperature. Subsequently, the mixture was purged with argon and filtered over a pad of celite. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1). The pure product was obtained as a colorless liquid (9.33 g, 20.3 mmol, quant.).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.39. $[\alpha]_D^{20}$ = +4.4° (c = 1.58, DCM). **$^1$H-NMR** (700 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 5.49 (dtd, $^3J_{H\text{-}6,\,H\text{-}5}$ = 11.2 Hz, $^3J_{H\text{-}6,\,H\text{-}7}$ = 7.4 Hz, $^4J_{H\text{-}6,\,H\text{-}4}$ = 1.2 Hz, 1H, H-6), 5.36–5.29 (m, 1H, H-5), 4.50 (ddd, $^3J_{H\text{-}4,\,H\text{-}5}$ = 8.9 Hz, $^3J_{H\text{-}4,\,H\text{-}3}$ = 5.0 Hz, $^4J_{H\text{-}4,\,H\text{-}6}$ = 1.2 Hz, 1H, H-4), 4.07 (ddd, $^3J_{H\text{-}2,\,H\text{-}3}$ = 7.5 Hz, $^3J_{H\text{-}2,\,H\text{-}1}$ = 4.4 Hz, $^3J_{H\text{-}2,\,H\text{-}1'}$ = 3.0 Hz, 1H, H-2), 3.84–3.81 (m, 2H, H-3, H-1´), 3.67 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1,\,H\text{-}2}$ = 4.4 Hz, 1H, H-1), 2.09–2.02 (m, 2H, H-7), 1.44–1.38 (m, 2H, H-8), 1.39 (s, 6H, 2x$CH_3$), 0.92 (t, $^3J_{H\text{-}9,\,H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.88 (s, 9H, 3x$CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS), 0.04 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 132.1 (C-6), 130.4 (C-5), 109.1 ($C_q$), 80.2 (C-3), 79.1 (C-2), 69.9 (C-4), 64.4 (C-1), 30.4 (C-7), 27.4 ($CH_3$), 27.3 ($CH_3$), 26.1 (3x$CH_3$-TBS), 26.0 (3x$CH_3$-TBS), 22.8 (C-8), 18.6 ($C_q$-TBS), 18.3 ($C_q$-TBS), 14.1 (C-9), −4.1 ($CH_3$-TBS), −4.5 ($CH_3$-TBS), −5.1 ($CH_3$-TBS), −5.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{50}Si_2O_4Na^+$ 481.3140, found 481.3142. For NMR-spectra see p. 315.

**Synthesis of Compound 330**

**(*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-ethan-1-ol**




**329** **330**

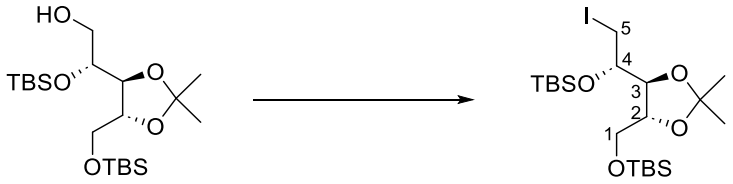
$C_{20}H_{44}Si_2O_5$
M = 420.74 g/mol

A stirred solution of alkene **329** (8.90 g, 19.4 mmol, 1 equiv) in MeOH/DCM (1:1, 100 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 70 min until a slightly blue color persisted. The excess ozone was then purged with argon for 5 min and $NaBH_4$ (3.67 g, 97.0 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 30 min at room temperature. $NH_4Cl$-solution (100 mL) and DCM (100 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 150 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless liquid (6.67 g, 15.9 mmol, 82%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.26. $[\alpha]_D^{20}$ = +5.1° (c = 1.36, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.01 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 3.2 Hz, 1H, H-2), 3.95 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 6.2 Hz, 1H, H-3), 3.82 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 3.2 Hz, 1H, H-1´), 3.81–3.78 (m, 1H, H-4), 3.70 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.8 Hz, 1H, H-1), 3.66–3.62 (m, 2H, H-5, H-5´), 2.08 (dd, $^3J_{OH,\ H\text{-}5}$ = 7.1 Hz, $^3J_{OH,\ H\text{-}5'}$ = 5.5 Hz, 1H, OH), 1.37 (s, 6H, 2x$CH_3$), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.12 (s, 3H, $CH_3$-TBS), 0.11 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.6 ($C_q$), 80.5 (C-2). 78.3 (C-3), 74.3 (C-4), 65.1 (C-5), 65.0 (C-1), 27.6 ($CH_3$), 27.4 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.2 (3x$CH_3$-TBS), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), −4.2 (2x$CH_3$-TBS), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{44}Si_2O_5H^+$ 421.2800, found 421.2804. For NMR-spectra see p. 317.

**Synthesis of Compound 165**

***tert*-butyl(((4*R*,5*S*)-5-((*S*)-1-((*tert*-butyldimethylsilyl)oxy)-2-iodoethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)-dimethylsilane**




**330** **165**

$C_{20}H_{43}ISi_2O_4$
M = 530.63 g/mol

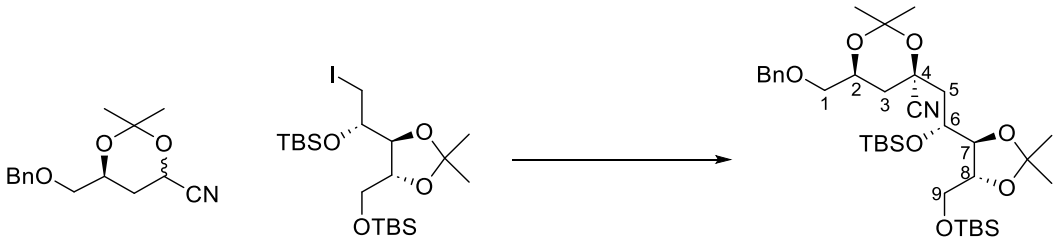
To a stirred solution of alcohol **330** (2.50 g, 5.94 mmol, 1 equiv) in benzene (12 mL) were added $PPh_3$ (3.12 g, 11.9 mmol, 2 equiv) and imidazole (0.81 g, 11.9 mmol, 2 equiv). Iodine (2.26 g, 8.91 mmol, 1.5 equiv) was added and the reaction mixture was stirred for 90 min at room temperature. The mixture was filtered over a pad of celite, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 70:1) and the pure product was obtained as a colorless viscous liquid (3.10 g, 5.84 mmol, 98%).

Traces of $PPh_3$ could not be removed via column chromatography so the product was used for the next reaction without further purification.

**TLC** (silica, CyHex:EtOAc = 70:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = −14.2° (c = 1.06, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.03 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.0 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 3.2 Hz, 1H, H-2), 3.96–3.91 (m, 1H, H-3), 3.80 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 3.2 Hz, 1H, H-1´), 3.67 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.9 Hz, 1H, H-1), 3.54–3.48 (m, 1H, H-5), 3.35–3.28 (m, 2H, H-4, H-5´), 1.37 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 0.93 (s, 9H, 3x$CH_3$-TBS), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.14 (s, 3H, $CH_3$-TBS), 0.11 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.9 ($C_q$), 80.7(C-2), 79.4 (C-3), 72.5 (C-4), 65.0 (C-1), 27.8 ($CH_3$), 27.5 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.2 (3x$CH_3$-TBS), 18.8 ($C_q$-TBS), 18.5 ($C_q$-TBS), 13.7 (C-5), −4.0 ($CH_3$-TBS), −4.1 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.0 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{43}ISi_2O_4H^+$ 531.1817, found 531.1811. For NMR-spectra see p. 319.

**Synthesis of Compound 331**

**(4*S*,6*S*)-6-((benzyloxy)methyl)-4-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




**164** **165** **331**

$C_{35}H_{61}NSi_2O_7$
M = 664.04 g/mol

A mixture of iodide **165** (2.50 g, 4.71 mmol, 1 equiv) and cyanohydrin acetonide **164** (1.85 g, 7.07 mmol, 1.5 equiv) in THF (47 mL) was cooled to −40 °C. DMPU (3.42 mL, 28.3 mmol, 6 equiv) and freshly prepared LDA* (0.5M, 19.8 mL, 9.89 mmol, 2 equiv) were added sequentially, and the mixture was stirred for 1 h at −40 °C. After quenching with saturated $NH_4Cl$-solution (100 mL) DCM (100 mL) was added and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 150 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 15:1). The pure product was obtained as a colorless highly viscous oil (2.77 g, 4.17 mmol, 89%, *dr* > 20:1).

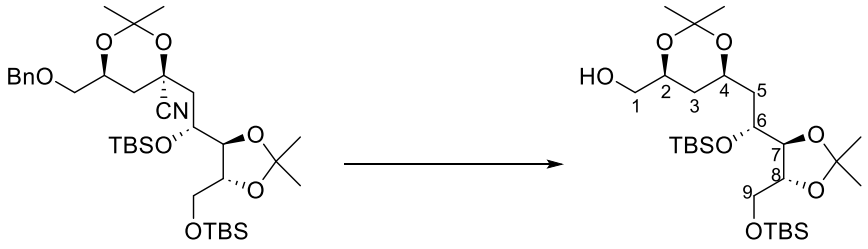
**n*-BuLi (2.5M in hexane, 4.26 mL, 10.7 mmol, 1 equiv) was added to a solution of DIPA (1.80 mL, 12.8 mmol, 1.2 equiv) in THF (15.3 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 15:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +27.2° (c = 1.14, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.38–7.27 (m, 5H, 5xCH-Ph), 4.54 (s, 2H, $CH_2$-Bn), 4.38 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.6 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 3.1 Hz, 1H, H-2), 4.22–4.14 (m, 2H, H-6, H-7), 3.85 (ddd, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.8 Hz, $^3J_{H\text{-}8,\ H\text{-}9}$ = 4.3 Hz, $^3J_{H\text{-}8,\ H\text{-}9'}$ = 4.3 Hz, 1H, H-8), 3.79 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}9,\ H\text{-}8}$ = 4.5 Hz, 1H, H-9), 3.72 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}9',\ H\text{-}8}$ = 4.0 Hz, 1H, H-9´), 3.56 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.4 Hz, 1H, H-1), 3.45 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.6 Hz, 1H, H-1´), 2.21 (dd, $^2J$ = 15.2 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 4.6 Hz, 1H, H-5), 2.01 (dd, $^2J$ = 15.1 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.2 Hz, 1H, H-5´), 1.88–1.76 (m, 2H, H-3-ax, H-3-eq), 1.70 (s, 3H, $CH_3$), 1.40 (s, 3H, $CH_3$), 1.39 (s, 3H, $CH_3$), 1.33 (s, 3H, $CH_3$), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.13 (s, 3H, $CH_3$-TBS), 0.12 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.8

($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.2 (CH-Bn), 122.5 (C-4), 109.1 ($C_q$), 101.8 ($C_q$), 82.0 (C-7), 78.1 (C-8), 74.0 ($CH_2$-Bn), 73.2 (C-1), 69.1 (CN), 68.4 (C-6), 66.6 (C-2), 64.4 (C-9), 45.7 (C-5), 36.5 (C-3), 31.2 ($CH_3$), 27.5 ($CH_3$), 27.1 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 21.8 ($CH_3$), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), −3.6 ($CH_3$-TBS), −4.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{35}H_{61}NSi_2O_7H^+$ 664.4059, found 664.4064. For NMR-spectra see p. 321.

**Synthesis of Compound 332**

**((4*S*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methanol**




**331** **332**

$C_{27}H_{56}Si_2O_7$
M = 548.91 g/mol

Lithium metal (1.15 g, 166 mmol, 50 equiv) was dissolved in liquid ammonia (30 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of cyanohydrin acetonide **331** (2.20 g, 3.31 mmol, 1 equiv) in THF (10 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched with solid $NH_4Cl$ (17.7 g, 331 mmol, 100 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (20 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 50 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless highly viscous liquid (1.51 g, 2.75 mmol, 83%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = +6.2° (c = 0.80, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 4.15 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.7 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 8.2 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 4.5 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-4), 3.98–3.90 (m, 4H, H-2, H-6, H-7, H-8), 3.83–3.78 (m, 1H, H-9), 3.68–3.64 (m, 1H, H-9´), 3.54 (ddd, $^2J$ = 11.3 Hz, $^3J_{H\text{-}1,\ OH}$ = 6.3 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.1 Hz, 1H, H-1), 3.43 (ddd, $^2J$ = 11.2 Hz, $^3J_{H\text{-}1',\ OH}$ = 6.2 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 1.92 (dd, $^3J_{OH,\ H\text{-}1}$ = 6.3 Hz, $^3J_{OH,\ H\text{-}1'}$ = 6.2 Hz 1H, OH), 1.82–1.77 (m, 1H, H-5), 1.64–

1.59 (m, 1H, H-5´), 1.43 (s, 3H, $CH_3$), 1.38 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.36 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 1.22 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.1 ($C_q$), 99.1 ($C_q$), 80.3 (C-8), 80.2 (C-7), 70.3 (C-2, C-6), 66.6 (C-1), 65.8 (C-4), 64.9 (C-9), 42.3 (C-5), 33.3 (C-3), 30.4 ($CH_3$), 27.7 ($CH_3$), 27.4 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 20.3 ($CH_3$), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), −4.0 ($CH_3$-TBS), −4.1 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{56}Si_2O_7H^+$ 549.3637, found 549.3636. For NMR-spectra see p. 323.

The 1,3-*syn* configuration was confirmed by the $^{13}$C-signals (30.4 and 20.3 ppm) of the methyl groups of the six-membered acetonide.[81] The NOESY correlation between H-2 and H-4 is an additional prove (Figure 6.7).

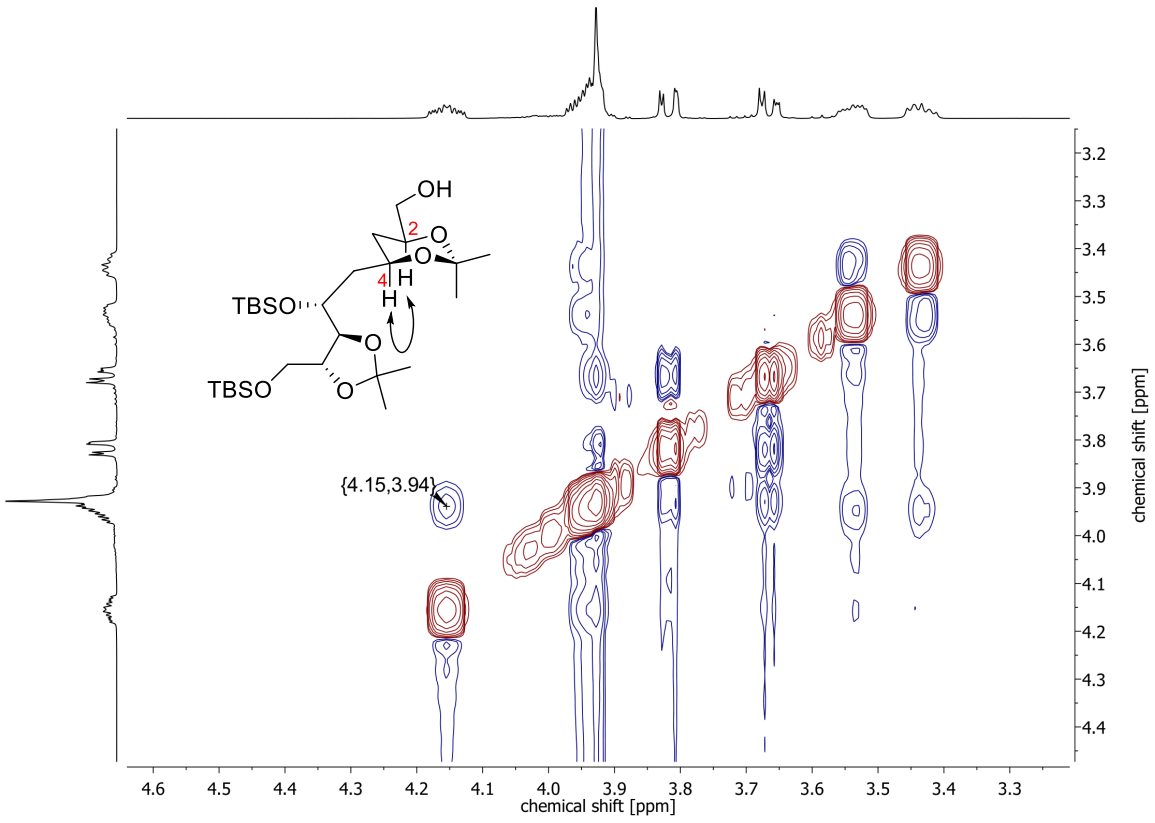
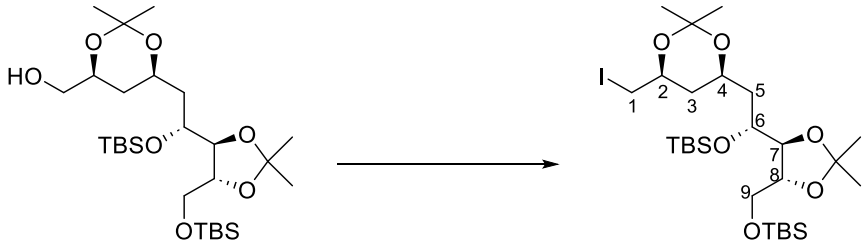



Figure 6.7: NOESY-spectrum of acetonide **332** to confirm the given configuration.

**Synthesis of Compound 163**

***tert*-butyl(((4*R*,5*S*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,6*S*)-6-(iodomethyl)-2,2-dimethyl-1,3-dioxan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane**




**332** **163**

$C_{27}H_{55}ISi_2O_6$
M = 658.81 g/mol

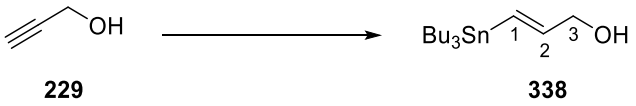
To a stirred solution of alcohol **332** (1.45 g, 2.64 mmol, 1 equiv) in benzene (5.5 mL) were added $PPh_3$ (1.04 g, 3.96 mmol, 1.5 equiv) and imidazole (0.27 g, 3.96 mmol, 1.5 equiv). Iodine (1.01 g, 3.96 mmol, 1.5 equiv) was added and the reaction mixture was stirred for 90 min at room temperature. The mixture was filtered over a pad of celite, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1) and the pure product was obtained as a colorless viscous liquid (1.39 g, 2.11 mmol, 80%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.13. $[\alpha]_D^{20}$ = +10.8° (c = 1.02, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.13 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 8.2 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 4.6 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.4 Hz, 1H, H-4), 3.96–3.93 (m, 1H, H-6), 3.93–3.91 (m, 2H, H-7, H-8), 3.85 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.0 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.4 Hz, 1H, H-2), 3.83–3.80 (m, 1H, H-9), 3.69–3.66 (m, 1H, H-9´), 3.14 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.0 Hz, 1H, H-1), 3.11 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 5.7 Hz, 1H, H-1´), 1.81 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 8.1 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 4.3 Hz, 1H, H-5), 1.75 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.5 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.5 Hz, 1H, H-3-eq), 1.62 (ddd, $^2J$ = 14.2 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 6.5 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 4.5 Hz, 1H, H-5´) 1.41 (s, 3H, $CH_3$), 1.36 (s, 3H, $CH_3$), 1.36 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 1.07 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.4 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.4 Hz, 1H, H-3-ax), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.2 ($C_q$), 99.8 ($C_q$), 80.4 (C-7), 80.2 (C-8), 70.3 (C-6), 69.8 (C-2), 66.1 (C-4), 64.9 (C-9), 42.0 (C-5), 37.7 (C-3), 30.2 ($CH_3$), 27.7 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 20.2 ($CH_3$), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), 10.3 (C-1), −4.0 ($CH_3$-TBS), −4.1 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{55}ISi_2O_6H^+$ 659.2655, found 659.2648. For NMR-spectra see p. 325.

## 6.2.4 Synthesis of the Southern Fragment

### Synthesis of Compound 338

***trans*-3-(Tributylstannyl)-2-propen-1-ol**




**229** **338**

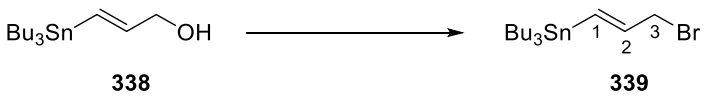
$C_{15}H_{32}SnO$
M = 347.13 g/mol

A suspension of CuCN (240 mg, 2.68 mmol, 1 equiv) in THF (8 mL) was cooled to −78 °C and *n*-BuLi (2.5 M in hexane, 2.14 mL, 5.35 mmol, 2 equiv) was added dropwise. The mixture was removed from the cooling bath and stirred for 20 min at room temperature. Afterwards the mixture was again cooled to −78 °C and $Bu_3SnH$ (1.42 mL, 5.35 mmol, 2 equiv) was added dropwise. After stirring for another 10 min at −78 °C propargylic alcohol (**229**) (0.15 mL, 2.68 mmol, 1 equiv) was added and the mixture was stirred 1 h at −78 °C. MeOH (2 mL) was added dropwise, and the mixture was warmed to room temperature. Water (10 mL) was added, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1) and the pure product was obtained as a colorless oil (481 mg, 1.39 mmol, 52%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.33. **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.26–6.10 (m, 2H, H-1, H-2), 4.16–4.08 (m, 2H, H-3), 1.62–1.41 (m, 6H, 3x$CH_2$), 1.36–1.27 (m, 6H, 3x$CH_2$), 0.99–0.82 (m, 15H, 3x$CH_2$, 3x$CH_3$). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 148.0 (C-1), 128.3 (C-2), 66.7 (C-3), 29.6 (3x$CH_2$), 27.9 (3x$CH_2$), 14.0 (3x$CH_3$), 9.9 (3x$CH_2$). **MS (EI, 70.0 eV)** *m/z*: [$M^{\cdot+}$] Calcd for $C_{15}H_{32}SnO^{\cdot+}$ 348.1, found 348.2. For NMR-spectra see p. 327.

### Synthesis of Compound 339

***trans*-3-Bromo-1-(tributylstannyl)propene**




**338** **339**

$C_{15}H_{31}BrSn$
M = 410.03 g/mol

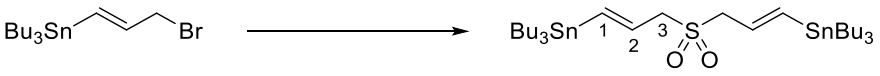
A solution of allylic alcohol **338** (1.06 g, 3.05 mmol, 1 equiv) in DCM (10 mL) was cooled to 0 °C and $CBr_4$ (1.22 g, 3.66 mmol, 1.2 equiv) was added. A solution of $PPh_3$ (0.88 g, 3.36 mmol, 1.1 equiv) in DCM (5 mL) was added dropwise at 0 °C and the mixture was stirred

for 1 h at room temperature. Subsequently, the mixture was reduced by half of the volume and pentane (10 mL) was added. The yellow precipitate was filtered off and the remaining solution was evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex) and the pure product was obtained as a colorless oil (1.23 g, 3.00 mmol, 98%).

**TLC** (silica, CyHex): $R_f$ = 0.80. **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.31 (dt, $^3J_{H\text{-}1,\ H\text{-}2}$ = 18.6 Hz, $^4J_{H\text{-}1,\ H\text{-}3}$ = 1.0 Hz, 1H, H-1), 6.15 (dt, $^3J_{H\text{-}2,\ H\text{-}1}$ = 18.6 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 6.8 Hz, 1H, H-2), 3.97 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 6.8 Hz, $^3J_{H\text{-}3,\ H\text{-}1}$ = 1.1 Hz, 2H, H-3), 1.59–1.43 (m, 6H, 3x$CH_2$), 1.36–1.25 (m, 6H, 3x$CH_2$), 0.95–0.91 (m, 6H, 3x$CH_2$), 0.89 (t, $^3J$ = 7.3 Hz, 9H, 3x$CH_3$). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 143.7 (C-1), 135.7 (C-2), 36.6 (C-3), 29.6 (3x$CH_2$), 27.8 (3x$CH_2$), 14.0 (3x$CH_3$), 10.1 (3x$CH_2$). **MS (EI, 70.0 eV)** *m/z*: [$M^{\cdot+}$] Calcd for $C_{15}H_{31}BrSn^{\cdot+}$ 410.1, found 410.2. For NMR-spectra see p. 329.

**Synthesis of Compound 228**

**Bis(trans-3-(tributylstannyl)-2.propenyl)sulfone**




**339** **228**

$C_{30}H_{62}O_2SSn_2$
M = 724.30 g/mol

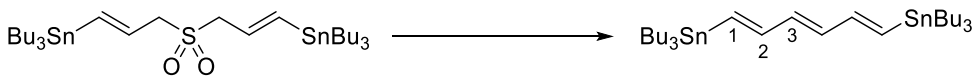
A solution of bromide **339** (1.20 g, 2.93 mmol, 1 equiv) in THF (5.5 mL) was added a solution of $Na_2S{\cdot}9H_2O$ (352 mg, 1.47 mmol, 0.5 equiv) and $Bu_4NHSO_4$ (7.00 mg, 20.5 µmol, 0.007 equiv) in $H_2O$ (5.5 mL). After stirring at room temperature for 18 h the aqueous mixture was extracted with pentane (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting crude sulfide was dissolved in EtOH (6 mL). The ethanolic mixture was cooled to 0 °C and a solution of $(NH_4)_6Mo_7O_{24}$ (210 mg, 306 µmol, 0.2 equiv) in $H_2O_2$ (30% in $H_2O$, 1.56 mL, 13.8 mmol, 9 equiv) was added dropwise. After 15 min at 0 °C the mixture was warmed to room temperature and stirred for 1 h. $H_2O$ (10 mL) was added, and the aqueous mixture was extracted with pentane (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 25:1) and the pure product was obtained as a colorless oil (905 mg, 1.25 mmol, 82% over 2 steps).

**TLC** (silica, CyHex:EtOAc = 25:1): $R_f$ = 0.43. **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.42 (dt, $^3J_{H\text{-}1,\ H\text{-}2}$ = 18.9 Hz, $^4J_{H\text{-}1,\ H\text{-}3}$ = 1.2 Hz, 2H, 2xH-1), 6.01 (dt, $^3J_{H\text{-}2,\ H\text{-}1}$ = 19.0 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 6.9 Hz, 2H, 2xH-2), 3.72 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.0 Hz, $^4J_{H\text{-}3,\ H\text{-}1}$ = 1.1 Hz, 4H, 2xH-3), 1.59–1.46 (m, 12H, 6x$CH_2$), 1.38–1.25 (m, 12H, 6x$CH_2$), 1.01–0.93 (m, 12H, 6x$CH_2$), 0.90 (t, $^3J$ = 7.3 Hz,

18H, 6xCH$_3$). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 142.9 (C-1), 134.4 (C-2), 59.6 (C-3), 29.7 (6xCH$_2$), 27.8 (6xCH$_2$), 14.0 (6xCH$_3$), 10.1 (6xCH$_2$). **MS (EI, 70.0 eV)** *m/z*: [M$^{\cdot+}$] Calcd for $C_{30}H_{62}O_2SSn_2^{\cdot+}$ 726.3, found 726.2. For NMR-spectra see p. 331.

**Synthesis of Compound 148**

**all-*trans*-1,6-Bis(tributylstannyl)-1,3,5-hexatriene**




**228** **148**

$C_{30}H_{60}Sn_2$
M = 658.23 g/mol

A stirred solution of sulfone **228** (113 mg, 156 µmol, 1 equiv) in THF (1.5 mL) was cooled to 0 °C. Precooled $CF_2Br_2$ (57.0 µL, 624 µmol, 4 equiv) and KOH* (30% on Alox, 523 mg, 3.12 mmol, 20 equiv) were added and the suspension was stirred at 0 °C. After 30 min the mixture was filtered through a pad of celite which was washed with pentane (10 mL) and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (Alox N (desactivated with 3% $H_2O$), CyHex:EtOAc = 50:1) and the pure product was obtained as a slightly yellow oil (71.0 mg, 108 µmol, 69%).

*Alox N (612 mg) was desactivated with 3% $H_2O$ and subsequently suspended in dry MeOH (3 mL). KOH (315 mg) was added, and the mixture was shaken until the KOH plates dissolved completely. The solvent was evaporated *in vacuo* and the white solid was grinded under argon.

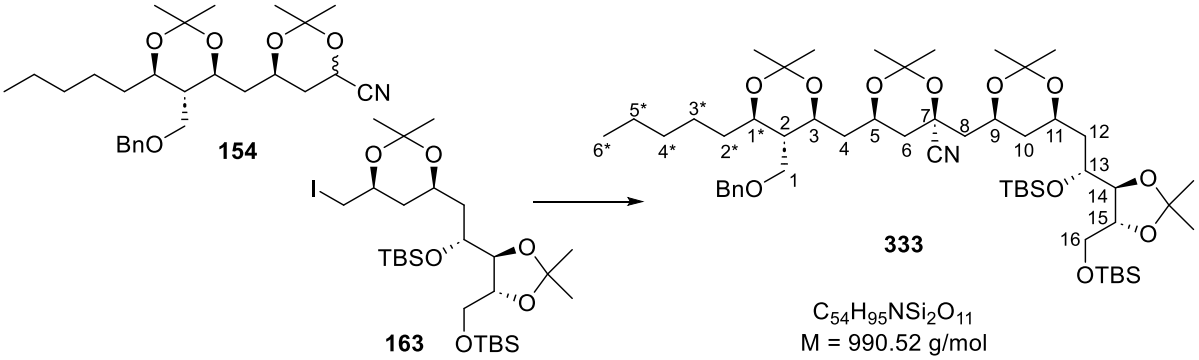
**TLC** (Alox N (deactivated with 3% $H_2O$), CyHex:EtOAc = 50:1): $R_f$ = 0.90. **$^1$H-NMR*** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.55 (m, 2H, 2xH-2), 6.30 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 18.7 Hz, 2H, 2xH-1), 6.17–6.13 (m, 2H, 2xH-3), 1.53–1.46 (m, 12H, 6xCH$_2$), 1.34–1.27 (m, 12H, 6xCH$_2$), 0.94–0.86 (m, 30H, 6xCH$_2$, 6xCH$_3$). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 147.0 (C-2), 135.7 (C-1), 134.6 (C-3), 29.3 (6xCH$_2$), 27.4 (6xCH$_2$), 13.9 (6xCH$_3$), 9.7 (6xCH$_2$). **MS** No mass spectrum could be measured due to decomposition and a high Sn proportion. For NMR-spectra see p. 333.

*Sn isotope satellites made it difficult to interpret the $^1$H-signals.

## 6.2.5 Coupling of Northern and Eastern Fragment and Modification

### Synthesis of Compound 333

**(4*R*,6*R*)-6-(((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)methyl)-4-(((4*S*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




A mixture of iodide **163** (2.10 g, 3.19 mmol, 1 equiv) and cyanohydrin acetonide **154** (2.20 g, 4.78 mmol, 1.5 equiv) in THF (32 mL) was cooled to −40 °C. DMPU (2.31 mL, 19.1 mmol, 6 equiv) and freshly prepared LDA* (0.5M, 13.4 mL, 6.69 mmol, 2.1 equiv) were added sequentially, and the mixture was stirred for 1 h at −40 °C. After quenching with saturated $NH_4Cl$-solution (50 mL) DCM (50 mL) was added and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 50 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless highly viscous oil (2.85 g, 2.88 mmol, 90%, *dr* > 20:1).

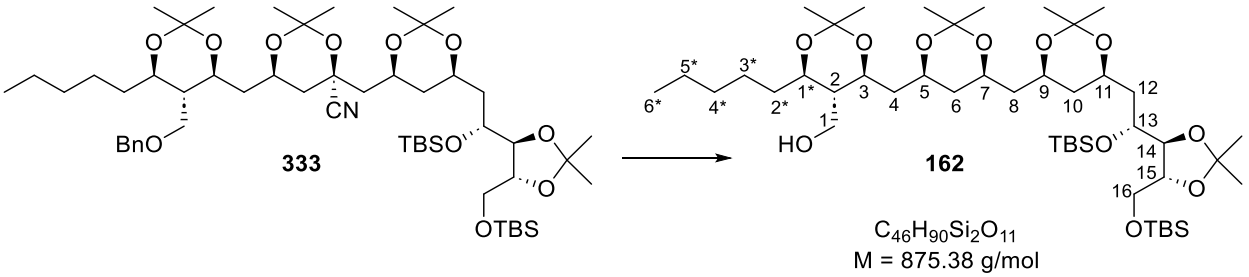
**n*-BuLi (2.5M in hexane, 4.26 mL, 10.7 mmol, 1 equiv) was added to a solution of DIPA (1.80 mL, 12.8 mmol, 1.2 equiv) in THF (15.3 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.30. $[\alpha]_D^{20}$ = +50.0° (c = 0.88, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.27 (m, 5H, 5xCH-Bn), 4.46 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.43–4.36 (m, 2H, H-5, $CH_2$-Bn´), 4.19–4.10 (m, 2H, H-9, H-11), 4.07 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.8 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 7.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 3.5 Hz, 1H, H-3), 3.97–3.90 (m, 4H, H-1*, H-13, H-14, H-15), 3.82 (dd, $^2J$ = 11.1 Hz, $^3J_{H\text{-}16,\ H\text{-}15}$ = 2.7 Hz, 1H, H-16), 3.66 (dd, $^2J$ = 11.1 Hz, $^3J_{H\text{-}16',\ H\text{-}15}$ = 3.9 Hz, 1H, H-16´), 3.47–3.42 (m, 2H, H-1, H-1´), 2.00 (dd, $^2J$ = 14.5 Hz, $^3J_{H\text{-}8,\ H\text{-}9}$ = 7.4 Hz, 1H, H-8), 1.85 (dd, $^2J$ = 14.5 Hz, $^3J_{H\text{-}8',\ H\text{-}9}$ = 3.6 Hz, 1H, H-8´), 1.81 (dd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}5}$ = 2.1 Hz, 1H, H-6-eq), 1.79–1.76 (m, 1H, H-12), 1.75–1.69 (m, 3H, H-6-ax, H-4, H-4´), 1.66 (s, 3H, $CH_3$), 1.63–1.55 (m, 2H, H-2*, H-12´), 1.53 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}10\text{-}eq,\ H\text{-}9}$ = 2.5 Hz, $^3J_{H\text{-}10\text{-}eq,\ H\text{-}11}$ = 2.5 Hz, 1H, H-10-eq), 1.45–1.40 (m, 7H, H-3*, 2x$CH_3$), 1.41–1.37 (m, 1H, H-2),

1.36 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 1.34 (s, 3H, $CH_3$), 1.33 (s, 3H, $CH_3$), 1.31–1.26 (m, 7H, C-2*´, C-3*´, C-5*, $CH_3$), 1.26–1.22 (m, 2H, H-4*), 1.20 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}9}$ = 11.5 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}11}$ = 11.5 Hz, 1H, H-10-ax), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.3 Hz, 3H, H-6*), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.1 (CH-Bn), 128.1 (2xCH-Bn), 122.8 (C-7), 109.1 ($C_q$), 101.4 ($C_q$), 99.0 ($C_q$), 98.3 ($C_q$), 80.3 (C-14), 80.0 (C-15), 73.8 ($CH_2$-Bn), 70.4 (C-1*), 70.1 (C-13), 68.7 (CN), 67.5 (C-1), 67.3 (C-3), 66.3 (C-11), 64.9 (C-9, C-16), 64.2 (C-5), 48.4 (C-8), 45.2 (C-2), 42.3 (C-12), 39.4 (C-4), 38.6 (C-6), 38.3 (C-10), 33.6 (C-2*), 32.4 (C-4*), 31.3 ($CH_3$), 30.4 ($CH_3$), 30.4 ($CH_3$), 27.7 ($CH_3$), 27.4 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 25.2 (C-3*), 23.3 (C-5*), 22.0 ($CH_3$), 20.1 ($CH_3$), 20.1 ($CH_3$), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), 14.5 (C-6*), −3.9 ($CH_3$-TBS), −4.1 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{54}H_{95}NSi_2O_{11}H^+$ 990.6516, found 990.6510. For NMR-spectra see p. 335.

**Synthesis of Compound 162**

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methanol**




Lithium metal (0.95 g, 136 mmol, 50 equiv) was dissolved in liquid ammonia (30 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of cyanohydrin acetonide **333** (2.70 g, 2.73 mmol, 1 equiv) in THF (13 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched with solid $NH_4Cl$ (14.6 g, 273 mmol, 100 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (20 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 50 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash

chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a white solid (2.00 g, 2.28 mmol, 84%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.20. $[\alpha]_D^{20}$ = +4.6° (c = 1.52, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.18 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.7 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 5.7 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}eq}$ = 2.5 Hz, 1H, H-5), 4.13–4.07 (m, 1H, H-11), 4.04–3.99 (m, 1H, H-7), 3.99–3.94 (m, 3H, H-3, H-9, H-13), 3.94–3.91 (m, 2H, H-14, H-15), 3.84–3.80 (m, 1H, H-16), 3.74 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 8.2 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2'}$ = 2.5 Hz, 1H, H-1*), 3.69–3.65 (m, 1H, H-16´), 3.65–3.63 (m, 1H, H-1), 3.51 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}1',\ OH}$ = 5.5 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H, H-1´), 2.14 (dd, $^3J_{OH,\ H\text{-}1}$ = 5.3 Hz, $^3J_{OH,\ H\text{-}1'}$ = 5.5 Hz, 1H, OH), 1.82–1.73 (m, 3H, H-4, H-4´, H-12), 1.73–1.70 (m, 1H, H-8), 1.69–1.64 (m, 1H, H-2*), 1.58 (ddd, $^2J$ = 14.2 Hz, $^3J_{H\text{-}12',\ H\text{-}13}$ = 6.4 Hz, $^3J_{H\text{-}12',\ H\text{-}11}$ = 4.7 Hz, 1H, H-12´), 1.53–1.47 (m, 2H, H-6-eq, H-10-eq), 1.48–1.43 (m, 4H, H-3*, $CH_3$), 1.42–1.37 (m, 9H, H-2, H-2*´, H-8´, 2x$CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.33–1.23 (m, 14H, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.18 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}5}$ = 11.5 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}7}$ = 11.5 Hz, 1H, H-6-ax), 1.10 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}9}$ = 11.4 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}11}$ = 11.4 Hz, 1H, H-10-ax), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.1 ($C_q$), 99.0 ($C_q$), 98.8 ($C_q$), 98.2 ($C_q$), 80.3 (C-14), 79.9 (C-15), 70.4 (C-1*), 70.1 (C-13), 68.1 (C-3), 66.3 (C-5), 66.1 (C-11), 65.8 (C-7), 65.8 (C-9), 64.9 (C-16), 60.5 (C-1), 46.2 (C-2), 43.7 (C-8), 42.2 (C-12), 40.2 (C-4), 37.8 (C-10), 36.9 (C-6), 33.8 (C-2*), 32.5 (C-4*), 30.5 ($CH_3$), 30.5 ($CH_3$), 30.5 ($CH_3$), 27.6 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 25.3 (C-3*), 23.3 (C-5*), 20.3 ($CH_3$), 20.2 ($CH_3$), 20.1 ($CH_3$), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), 14.4 (C-6*), −3.9 ($CH_3$-TBS), −4.1 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{46}H_{90}Si_2O_{11}H^+$ 875.6094, found 875.6094. For NMR-spectra see p. 337.

The 1,3-*syn* configuration was confirmed by the $^{13}$C-signals (30.5, 30.5, 30.5 and 20.3, 20.2, 20.1 ppm) of the methyl groups of the six-membered acetonides.[81] The NOESY correlation between H-5 and H-7 is an additional prove (Figure 6.8).

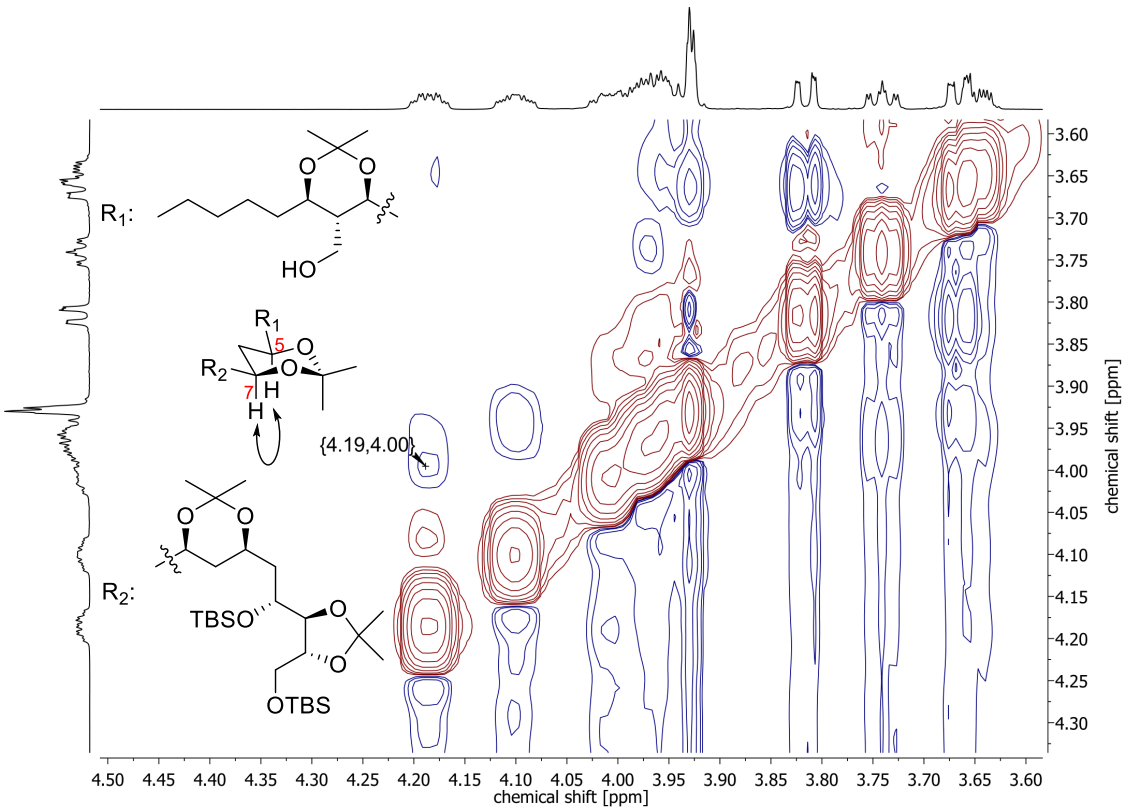
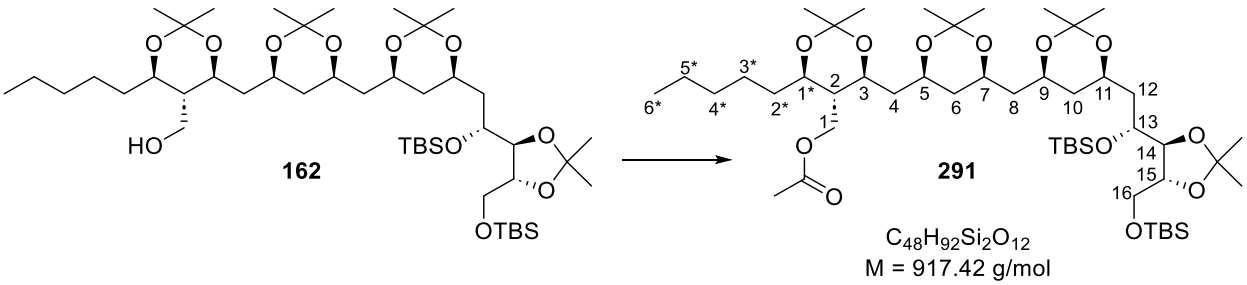



Figure 6.8: NOESY-spectrum of acetonide **162** to confirm the given configuration.

### Synthesis of Compound 291

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methyl acetate**



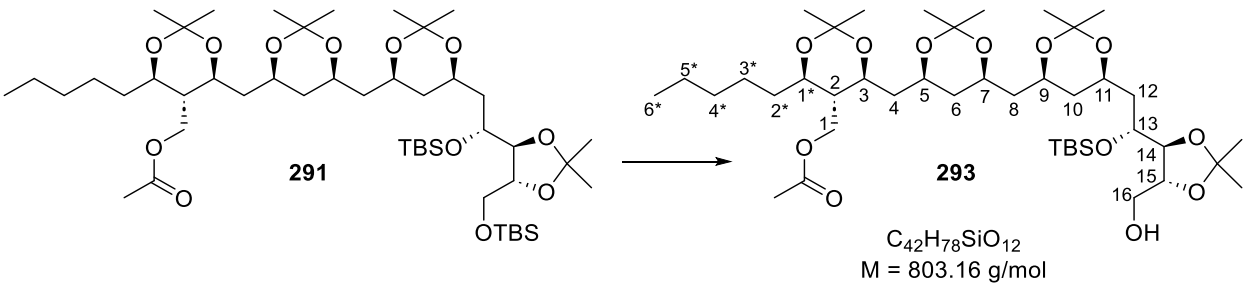

A stirred solution of alcohol **162** (2.00 g, 2.28 mmol, 1 equiv) in DCM (23 mL) was cooled to −78 °C. DIPEA (3.19 mL, 18.3 mmol, 8 equiv) and acetyl chloride (0.65 mL, 9.14 mmol, 4 equiv) were added sequentially and the mixture was stirred for 2.5 h at −78 °C. After that it was stirred for another 2.5 h at 0 °C before it was quenched with water (20 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced

pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 8:1). The pure product was obtained as a colorless highly viscous oil (2.08 g, 2.27 mmol, 99%).

**TLC** (silica, CyHex:EtOAc = 8:1): $R_f$ = 0.24. $[\alpha]_D^{20}$ = −0.9° (c = 1.17, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.14–4.09 (m, 2H, H-5, H-11), 4.09–4.04 (m, 2H, H-1, H-1´), 4.01–3.95 (m, 3H, H-7, H-9, H-13), 3.95–3.89 (m, 3H, H-3, H-14, H-15), 3.83–3.80 (m, 1H, H-16), 3.78 (ddd, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 8.2 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2'}$ = 2.6 Hz, 1H, H-1*), 3.69–3.65 (m, 1H, H-16´), 2.02 (s, 3H, $CH_3$-Ac), 1.78 (ddd, $^2J$ = 14.2 Hz, $^3J_{H\text{-}12,\,H\text{-}11}$ = 7.9 Hz, $^3J_{H\text{-}12,\,H\text{-}13}$ = 4.7 Hz, 1H, H-12), 1.75–1.69 (m, 2H, H-4, H-8), 1.67–1.61 (m, 2H, H-4, H-2*), 1.58 (ddd, $^2J$ = 14.2 Hz, $^3J_{H\text{-}12',\,H\text{-}13}$ = 6.3 Hz, $^3J_{H\text{-}12',\,H\text{-}11}$ = 4.8 Hz, 1H, H-12´), 1.54–1.49 (m, 3H, H-2, H-6-eq, H-10-eq), 1.48–1.42 (m, 1H, H-3*), 1.42–1.39 (m, 10H, H-8´, 3x$CH_3$), 1.38–1.37 (m, 1H, H-2*´), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.33–1.30 (m, 8H, H-5*, 2x$CH_3$), 1.30–1.23 (m, 6H, H-3*´, H-4*, $CH_3$), 1.14–1.05 (m, 2H, H-6-ax, H-10-ax), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\,H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 171.1 (C=O-Ac), 109.1 ($C_q$), 98.8 ($C_q$), 98.7 ($C_q$), 98.2 ($C_q$), 80.3 (C-14), 79.9 (C-15), 70.3 (C-1*), 70.2 (C-13), 67.2 (C-3), 66.1 (C-11), 66.0 (C-5), 65.8 (C-7), 65.6 (C-9), 64.9 (C-16), 61.8 (C-1), 43.7 (C-8), 43.5 (C-2), 42.2 (C-12), 40.1 (C-4), 37.7 (C-10), 37.0 (C-6), 33.6 (C-2*), 32.4 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 27.6 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 25.0 (C-3*), 23.2 (C-5*), 21.1 ($CH_3$-Ac), 20.2 ($CH_3$), 20.2 ($CH_3$), 19.9 ($CH_3$), 18.9 ($C_q$-TBS), 18.5 ($C_q$-TBS), 14.4 (C-6*), −3.9 ($CH_3$-TBS), −4.1 ($CH_3$-TBS), −5.0 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{48}H_{92}Si_2O_{12}Na^+$ 939.6020, found 939.6020. For NMR-spectra see p. 339.

### Synthesis of Compound 293

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methyl acetate**



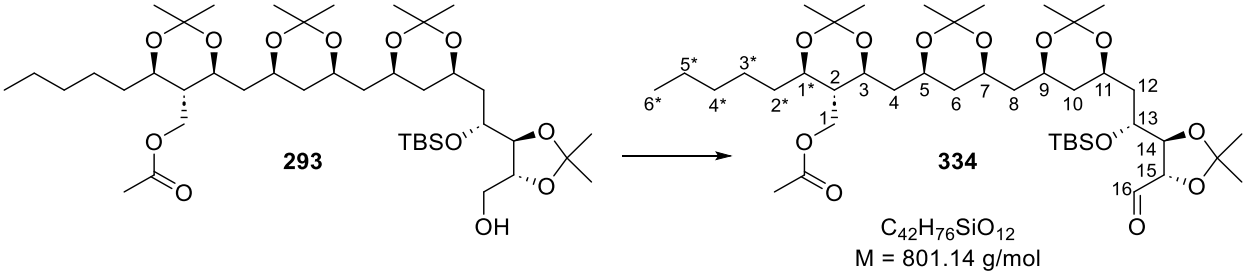
A solution of TBS-ether **291** (2.08 g, 2.27 mmol, 1 equiv) in THF (16 mL) was cooled to 0 °C. Freshly prepared HF·py stock solution* (31 mL) was added slowly and the mixture was stirred for 15 h at 0 °C. The mixture was warmed to room temperature and was stirred for another 45 min until TLC showed complete consumption of the starting material. Water (50 mL) and DCM (100 mL) were added to the mixture and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 50 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:1). The pure product was obtained as a white foamy solid (1.62 g, 2.02 mmol, 89%).

*A solution of pyridine (15 mL) in THF (26 mL) was cooled to 0 °C and HF·py (70% HF, 5 mL) was added dropwise. The mixture was stirred for 2 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.26. $[\alpha]_D^{20}$ = −9.4° (c = 0.74, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.17–4.09 (m, 2H, H-5, H-11), 4.09–4.04 (m, 2H, H-1, H-1´), 4.02–3.96 (m, 3H, H-7, H-9, H-15), 3.95–3.89 (m, 2H, H-3, H-13), 3.87 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 7.7 Hz, $^3J_{H\text{-}14,\ H\text{-}13}$ = 6.5 Hz, 1H, H-14), 3.81–3.75 (m, 2H, H-1*, H-16), 3.60 (ddd, $^2J$ = 11.9 Hz, $^3J_{H\text{-}16´,\ H\text{-}15}$ = 7.1 Hz, $^3J_{H\text{-}16´,\ OH}$ = 5.0 Hz, 1H, H-16´), 2.02 (s, 3H, $CH_3$-Ac), 1.96 (dd, $^3J_{OH,\ H\text{-}16}$ = 7.3 Hz, $^3J_{OH,\ H\text{-}16´}$ = 5.1 Hz, 1H, OH), 1.77 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}12,\ H\text{-}11}$ = 8.4 Hz, $^3J_{H\text{-}12,\ H\text{-}13}$ = 3.8 Hz, 1H, H-12), 1.75–1.69 (m, 2H, H-4, H-8), 1.67–1.60 (m, 3H, H-2*, H-4´, H-12´), 1.53–1.47 (m, 3H, H-2, H-6-eq, H-10-eq), 1.47–1.43 (m, 1H, H-3*), 1.43–1.39 (m, 10H, H-8´, 3x$CH_3$), 1.38–1.35 (m, 7H, H-2*´, 2x$CH_3$), 1.33–1.31 (m, 6H, 2x$CH_3$), 1.31–1.22 (m, 8H, H-3*´, H-4*, H-5*, $CH_3$), 1.13 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}9}$ = 11.5 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}11}$ = 11.5 Hz, 1H, H-10-ax), 1.09 (ddd, $^2J$ = 12.5 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}5}$ = 11.4 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}7}$ = 11.4 Hz, 1H, H-6-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6*,\ H\text{-}5*}$ = 7.2 Hz, 3H, H-6*), 0.11 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 171.1 (C=O-Ac), 109.4 ($C_q$), 98.8 ($C_q$), 98.7 ($C_q$), 98.2 ($C_q$), 80.4 (C-14), 80.3 (C-15), 70.7 (C-13), 70.3 (C-1*), 67.1 (C-3), 66.0 (C-11), 66.0 (C-5), 65.9 (C-7), 65.7 (C-9), 64.1 (C-16), 61.8 (C-1), 43.6 (C-8), 43.5 (C-2), 43.0 (C-12), 40.2 (C-4), 37.8 (C-10), 36.9 (C-6), 33.6 (C-2*), 32.4 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 27.5 ($CH_3$), 27.4 ($CH_3$), 26.2 (3x$CH_3$-TBS), 25.0 (C-3*), 23.2 (C-5*), 21.1 ($CH_3$-Ac), 20.2 ($CH_3$), 20.2 ($CH_3$), 19.9 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), −4.0 ($CH_3$-TBS), −4.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{42}H_{78}SiO_{12}Na^+$ 825.5155, found 825.5152. For NMR-spectra see p. 341.

**Synthesis of Compound 334**

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*S*)-5-formyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methyl acetate**



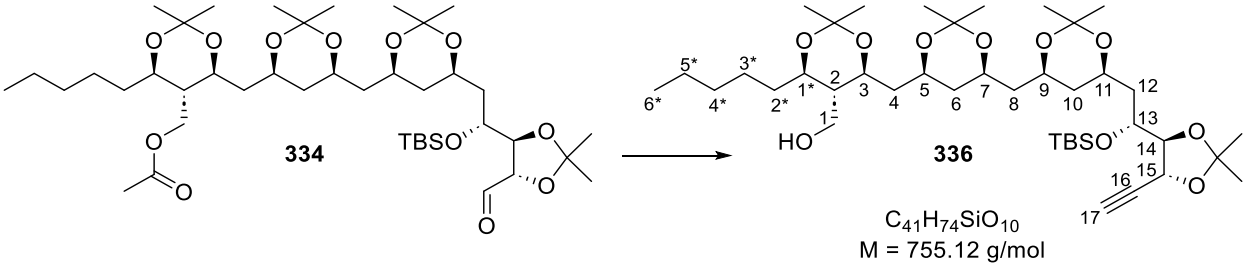

To a Schlenk flask charged with sulfur trioxide pyridine complex (0.65 g, 4.11 mmol, 3 equiv) were added DCM (10 mL) and pyridine (0.33 mL, 4.11 mmol, 3 equiv). The suspension was stirred for 10 min at room temperature before DMSO (0.97 mL, 13.7 mmol, 10 equiv) and DIPEA (0.96 mL, 5.48 mmol, 4 equiv) were added. The mixture was cooled to 0 °C and a solution of alcohol **293** (1.10 g, 1.37 mmol, 1 equiv) in DCM (4 mL) was added and the mixture was stirred for 90 min at 0 °C. After completion of the reaction, the reaction mixture was diluted with DCM (20 mL) and washed with saturated $NaHCO_3$-solution (30 mL). The organic phase was washed with saturated $CuSO_4$-solution (2 x 10 mL) before it was finally washed with saturated $NH_4Cl$-solution (20 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The pure product was obtained without further purification as a white foamy solid (1.05 g, 1.31 mmol, 96%).

**TLC** (silica, CyHex:EtOAc = 4:1): $R_f$ = 0.20. $[\alpha]_D^{20}$ = −8.1° (c = 1.16, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.76 (d, $^3J_{H\text{-}16,\ H\text{-}15}$ = 1.6 Hz, 1H, H-16), 4.35 (dd, $^3J_{H\text{-}15,\ H\text{-}14}$ = 6.7 Hz, $^3J_{H\text{-}15,\ H\text{-}16}$ = 1.7 Hz, 1H, H-15), 4.16 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 6.7 Hz, $^3J_{H\text{-}14,\ H\text{-}13}$ = 4.2 Hz, 1H, H-14), 4.13–4.09 (m, 1H, H-11), 4.09–4.04 (m, 3H, H-1, H-1´, H-13), 4.03–3.96 (m, 3H, H-5, H-7, H-9), 3.91 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 7.8 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 3.0 Hz, 1H, H-3), 3.78 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.2 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 2.6 Hz, 1H, H-1*), 2.02 (s, 3H, $CH_3$-Ac), 1.75–1.69 (m, 3H, H-4, H-8, H-12), 1.66–1.58 (m, 3H, H-2*, H-4´, H-12´), 1.54–1.50 (m, 3H, H-2, H-6-eq, H-10-eq), 1.48 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.46–1.43 (m, 1H, H-3*), 1.43–1.41 (m, 4H, H-8´, $CH_3$), 1.41–1.39 (m, 6H, 2x$CH_3$), 1.38–1.35 (m, 1H, H-2*´), 1.34–1.31 (m, 9H, 3x$CH_3$), 1.30–1.21 (m, 8H, H-3*´, H-4*, H-5*, $CH_3$), 1.16–1.05 (m, 2H, H-6-ax, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.11 (s, 3H, $CH_3$-TBS), 0.10 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 202.4 (C-16), 171.1 (C=O-Ac), 111.4 ($C_q$), 98.8 ($C_q$), 98.7 ($C_q$), 98.2 ($C_q$), 81.9 (C-15), 80.4 (C-14), 70.3 (C-1*), 68.9 (C-13), 67.1 (C-3), 66.0 (C-11), 65.9 (C-5), 65.8 (C-7), 65.7 (C-9), 61.8 (C-1), 43.6 (C-8), 43.5 (C-2), 42.1 (C-12), 40.2 (C-4), 37.5 (C-10), 36.9 (C-6), 33.6 (C-2*), 32.4 (C-4*), 30.6 ($CH_3$), 30.5

($CH_3$), 30.4 ($CH_3$), 27.0 ($CH_3$), 26.2 (3x$CH_3$-TBS), 26.1 ($CH_3$), 25.0 (C-3*), 23.2 (C-5*), 21.1 ($CH_3$-Ac), 20.2 ($CH_3$), 20.2 ($CH_3$), 19.9 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), −4.0 ($CH_3$-TBS), −4.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{42}H_{76}SiO_{12}Na^+$ 823.4998, found 823.5001. For NMR-spectra see p. 343.

**Synthesis of Compound 336**

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-ethynyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methanol**



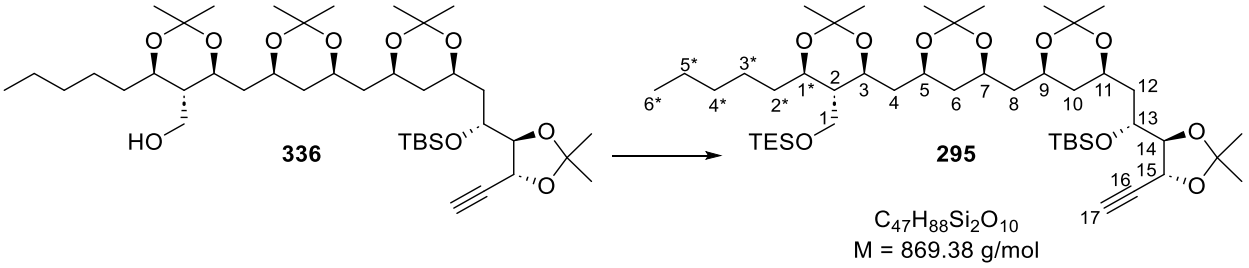

To a stirred solution of aldehyde **334** (1.05 g, 1.31 mmol, 1 equiv) in MeOH (26) was added $K_2CO_3$ (0.36 g, 2.62 mmol, 2 equiv). Ohira-Bestmann reagent **335** (0.24 mL, 1.57 mmol, 1.2 equiv) was added dropwise and the mixture was stirred for 4 h at room temperature before it was quenched with saturated $NaHCO_3$-solution (30 mL) and DCM (30 mL). The organic phase was separated and the aqueous phase was extracted with DCM (3 x 50 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a white solid foam (844 mg, 1.12 mmol, 85%)

**TLC** (silica, CyHex:EtOAc = 4:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = −5.2° (c = 1.08, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.59 (dd, $^3J_{H\text{-}15,\ H\text{-}14}$ = 7.1 Hz, $^4J_{H\text{-}15,\ H\text{-}17}$ = 2.1 Hz, 1H, H-15), 4.18 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 5.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.9 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}eq}$ = 2.4 Hz, 1H, H-5), 4.14 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 7.1 Hz, $^4J_{H\text{-}14,\ H\text{-}13}$ = 3.9 Hz, 1H, H-14), 4.08–4.03 (m, 2H, H-7, H-13), 4.03–3.95 (m, 3H, H-3, H-9, H-11), 3.74 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.2 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.5 Hz, 1H, H-1*), 3.65 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}1,\ OH}$ = 4.8 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 2.7 Hz, 1H, H-1), 3.52 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}1',\ OH}$ = 4.6 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.6 Hz, 1H, H-1´), 2.56 (d, $^4J_{H\text{-}17,\ H\text{-}15}$ = 2.1 Hz, 1H, H-17), 2.14 (m, 1H, OH), 1.79 (ddd, $^2J$ = 14.6 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 6.0 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 6.0 Hz, 1H, H-4), 1.76–1.69 (m, 3H, H-4´, H-8, H-12), 1.70–1.61 (m, 2H, H-2*, H-12´), 1.53–1.48 (m, 2H, H-6-eq, H-10-eq), 1.48–1.45 (m, 1H, H-3*), 1.45–1.43 (m, 6H, 2x$CH_3$), 1.42–1.39 (m, 10H, H-8´, 3x$CH_3$), 1.38–1.35 (m, 2H, H-2, H-2*´), 1.34–1.24 (m, 14H, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.18 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}5}$ = 11.5 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}7}$ = 11.5 Hz, 1H, H-6-ax),

1.11 (ddd, $^{2}J$ = 12.9 Hz, $^{3}J_{\text{H-10-ax, H-9}}$ = 11.4 Hz, $^{3}J_{\text{H-10-ax, H-11}}$ = 11.4 Hz, 1H, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^{3}J_{\text{H-6*, H-5*}}$ = 7.2 Hz, 3H, H-6*), 0.09 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 110.7 ($C_q$), 99.0 ($C_q$), 98.9 ($C_q$), 98.2 ($C_q$), 84.6 (C-14), 83.4 (C-16), 74.5 (C-17), 70.4 (C-1*), 68.4 (C-13), 68.1 (C-3), 66.4 (C-5), 66.4 (C-15), 66.1 (C-7), 65.8 (C-11), 65.8 (C-9), 60.5 (C-1), 46.2 (C-2), 43.5 (C-8), 42.3 (C-12), 40.2 (C-4), 37.6 (C-10), 36.9 (C-6), 33.8 (C-2*), 32.5 (C-4*), 30.5 ($CH_3$), 30.5 ($CH_3$), 30.5 ($CH_3$), 27.0 ($CH_3$), 26.2 (3x$CH_3$-TBS), 25.9 ($CH_3$), 25.3 (C-3*), 23.3 (C-5*), 20.3 ($CH_3$), 20.2 ($CH_3$), 20.1 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), −4.1 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{41}H_{74}SiO_{10}H^+$ 755.5124, found 755.5121. For NMR-spectra see p. 345.

### Synthesis of Compound 295

***tert*-butyl((*R*)-2-((4*R*,6*R*)-6-(((4*S*,6*S*)-6-(((4*S*,5*R*,6*R*)-2,2-dimethyl-6-pentyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)-1-((4*S*,5*R*)-5-ethynyl-2,2-dimethyl-1,3-dioxolan-4-yl)ethoxy)dimethylsilane**



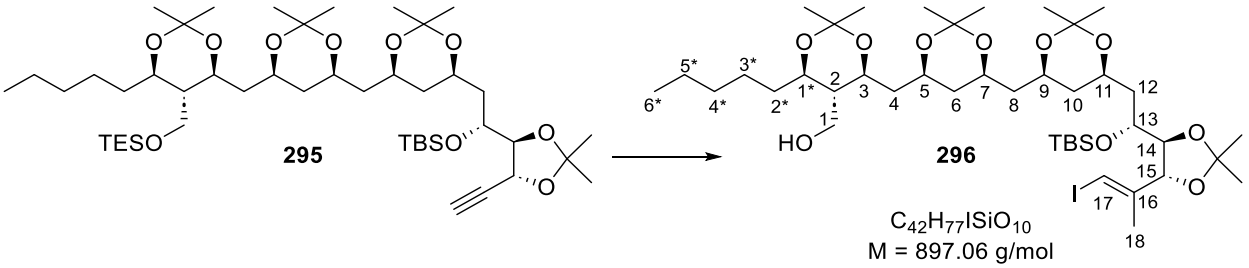

To a stirred solution of alcohol **336** (840 mg, 1.11 mmol, 1 equiv) in DCM (11 mL) were added TESCl (0.37 mL, 2.22 mmol, 2 equiv) and $NEt_3$ (0.62 mL, 4.45 mmol, 4 equiv). The mixture was stirred for 6 h at room temperature before it was quenched with water (10 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a white sticky foam (960 mg, 1.10 mmol, 99%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −3.1° (c = 1.04, DCM). **$^{1}$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.59 (dd, $^{3}J_{\text{H-15, H-14}}$ = 7.1 Hz, $^{4}J_{\text{H-15, H-17}}$ = 2.1 Hz, 1H, H-15), 4.14 (dd, $^{3}J_{\text{H-14, H-15}}$ = 7.1 Hz, $^{4}J_{\text{H-14, H-13}}$ = 4.0 Hz, 1H, H-14), 4.12–4.03 (m, 4H, H-3, H-5, H-7, H-13), 4.02–3.94 (m, 3H, H-1*, H-9, H-11), 3.69–3.64 (m, 2H, H-1, H-1´), 2.54 (d, $^{4}J_{\text{H-17, H-15}}$ = 2.1 Hz, 1H, H-17), 1.77–1.69 (m, 2H, H-8, H-12), 1.64–1.61 (m, 4H, H-2*, H-4, H-4´, H-12´), 1.57 (ddd, $^{2}J$ = 12.6 Hz, $^{3}J_{\text{H-6-eq, H-5}}$ = 2.5 Hz, $^{3}J_{\text{H-6-eq, H-7}}$ = 2.5 Hz, 1H, H-6-eq), 1.51 (ddd, $^{2}J$ = 12.8 Hz, $^{3}J_{\text{H-10-eq, H-9}}$ = 2.5 Hz, $^{3}J_{\text{H-10-eq, H-11}}$ = 2.5 Hz, 1H, H-10-eq), 1.48–1.45 (m, 1H,

H-3*), 1.44 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.41 (br s, 3H, $CH_3$), 1.40 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.40–1.39 (m, 7H, H-8´, 2x$CH_3$), 1.34–1.26 (m, 15H, H-2*´, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.20 (dddd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 2.5 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 2.6 Hz, 1H, H-2), 1.11 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}9}$ = 11.4 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}11}$ = 11.4 Hz, 1H, H-10-ax), 1.04 (ddd, $^2J$ = 12.5 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}5}$ = 11.4 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}7}$ = 11.4 Hz, 1H, H-6-ax), 0.96 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.59 (q, $^3J$ = 7.9 Hz, 6H, 3x$CH_2$-TBS), 0.09 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 110.7 ($C_q$), 98.9 ($C_q$), 98.7 ($C_q$), 98.0 ($C_q$), 84.6 (C-14), 83.4 (C-16), 74.5 (C-17), 69.7 (C-1*), 68.5 (C-13), 66.4 (C-5), 66.3 (C-15), 66.3 (C-3), 66.2 (C-7), 65.8 (C-11), 65.6 (C-9), 59.7 (C-1), 46.2 (C-2), 43.6 (C-8), 42.3 (C-12), 40.5 (C-4), 37.6 (C-10), 36.9 (C-6), 33.7 (C-2*), 32.5 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 27.0 ($CH_3$), 26.2 (3x$CH_3$-TBS), 25.9 ($CH_3$), 25.3 (C-3*), 23.2 (C-5*), 20.3 ($CH_3$), 20.1 ($CH_3$), 20.1 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), 7.2 ($CH_3$-TES), 4.8 ($CH_2$-TES), −4.1 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{47}H_{88}Si_2O_{10}H^+$ 869.5989, found 869.5987. For NMR-spectra see p. 347.

**Synthesis of Compound 296**

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-((*E*)-1-iodoprop-1-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methanol**




A suspension of CuCN (35.5 mg, 0.40 mmol, 3 equiv) in THF (1 mL) was cooled to −78 °C and *n*-BuLi (2.5M in hexane, 0.32 mL, 0.79 mmol, 6 equiv) was added dropwise. The mixture was stirred for 20 min at room temperature and was again cooled to −78 °C. $Bu_3SnH$ (0.21 mL, 0.79 mmol, 6 equiv) was added and the mixture was stirred for 10 min at −78 °C before a solution of alkyne **295** (115 mg, 0.13 mmol, 1 equiv) in THF (1 mL) was added. The mixture was stirred for 1 h at −78 °C and MeI (85.4 µL, 1.32 mmol, 10 equiv) as well as DMPU (48.0 µL, 0.40 mmol, 3 equiv) were added. After 5 min at −78 °C the mixture was slowly warmed to room temperature over a period of 30 min. Subsequently, the mixture was quenched with saturated $NH_4Cl$-solution (2 mL) and the aqueous phase was extracted with

DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure.

The crude vinyl stannane was dissolved in DCM (1 mL) and cooled to −78 °C. A solution of iodine (67.2 mg, 0.27 mmol, 2 equiv) in DCM (2 mL) was added dropwise and the mixture was stirred for 30 min at 0 °C. The organic phase was washed with water (2 mL), dried over $MgSO_4$, and evaporated *in vacuo*.

The crude vinyl iodide was dissolved in THF (1 mL) and cooled to 0 °C. Freshly prepared HF·py stock solution* (2 mL) was added dropwise and the mixture was stirred for 90 min at 0 °C. Water (5 mL) and DCM (5 mL) were added to the mixture and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a highly viscous, sticky liquid (68 mg, 75.8 µmol, 57%, over 3 steps).

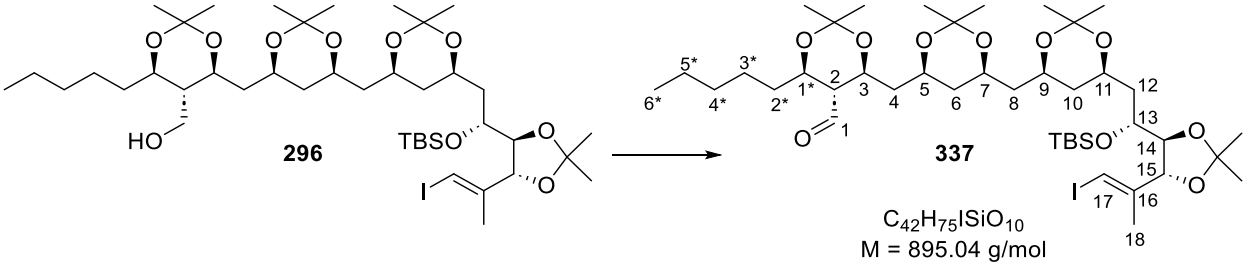
*A solution of pyridine (1.00 mL) in THF (1.73 mL) was cooled to 0 °C and HF·py (70% HF, 0.33 mL) was added dropwise. The mixture was stirred for 2 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.15. $[\alpha]_D^{20}$ = +12.5° (c = 0.40, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.42 (qd, $^4J_{H\text{-}17,\,H\text{-}18}$ = 1.1 Hz, $^4J_{H\text{-}17,\,H\text{-}15}$ = 1.1 Hz, 1H, H-17), 4.48 (d, $^3J_{H\text{-}15,\,H\text{-}14}$ = 7.9 Hz, 1H, H-15), 4.19 (dddd, $^3J_{H\text{-}5,\,H\text{-}6\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}5,\,H\text{-}4}$ = 5.6 Hz, $^3J_{H\text{-}5,\,H\text{-}4'}$ = 5.7 Hz, $^3J_{H\text{-}5,\,H\text{-}6\text{-}eq}$ = 2.5 Hz, 1H, H-5), 4.04–3.99 (m, 2H, H-7, H-13), 3.99–3.95 (m, 3H, H-3, H-9, H-11), 3.93 (dd, $^3J_{H\text{-}14,\,H\text{-}15}$ = 7.9 Hz, $^3J_{H\text{-}14,\,H\text{-}13}$ = 4.2 Hz, 1H, H-14), 3.74 (ddd, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^{*'}}$ = 8.2 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^*}$ = 2.6 Hz, 1H, H-1*), 3.65 (ddd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}1,\,OH}$ = 5.3 Hz, $^3J_{H\text{-}1,\,H\text{-}2}$ = 2.7 Hz, 1H, H-1), 3.55–3.48 (m, 1H, H-1´), 2.14 (t, $^3J_{OH,\,H\text{-}1}$ = 5.3 Hz, 1H, OH), 1.87 (d, $^4J_{H\text{-}18,\,H\text{-}17}$ = 1.1 Hz, 3H, H-18), 1.83–1.77 (m, 1H, H-4), 1.76–1.69 (m, 3H, H-4´, H-8, H-12), 1.68–1.63 (m, 1H, H-2*), 1.57–1.52 (m, 1H, H-12´), 1.52–1.48 (m, 1H, H-6-eq), 1.47–1.41 (m, 6H, H-3*, H-8´, H-10-eq, $CH_3$), 1.41–1.35 (m, 14H, H-2, H-2*´, 4x$CH_3$), 1.34–1.24 (m, 14H, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.18 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}6\text{-}ax,\,H\text{-}5}$ = 11.5 Hz, $^3J_{H\text{-}6\text{-}ax,\,H\text{-}7}$ = 11.5 Hz, 1H, H-6-ax), 1.10 (ddd, $^2J$ = 12.4 Hz, $^3J_{H\text{-}10\text{-}ax,\,H\text{-}9}$ = 11.3 Hz, $^3J_{H\text{-}10\text{-}ax,\,H\text{-}11}$ = 11.3 Hz, 1H, H-10-ax), 0.92–0.86 (m, 12H, H-6*, 3x$CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 146.2 (C-16), 109.3 ($C_q$), 99.0 ($C_q$), 98.8 ($C_q$), 98.2 ($C_q$), 82.2 (C-17), 81.7 (C-15), 81.1 (C-14), 70.4 (C-1*), 69.0 (C-13), 68.1 (C-3), 66.4 (C-5), 66.2 (C-7), 65.8 (C-11), 65.8 (C-9), 60.5 (C-1), 46.2 (C-2), 43.6 (C-8), 41.8 (C-12), 40.2 (C-4), 37.6 (C-10), 36.9 (C-6), 33.8 (C-2*), 32.5 (C-4*), 30.5 ($CH_3$), 30.5 ($CH_3$), 30.5 ($CH_3$), 27.8 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.3 (C-3*), 23.3 (C-5*), 20.4 ($CH_3$), 20.3 (C-18), 20.2 ($CH_3$), 20.1 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), −3.9

($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{42}H_{77}ISiO_{10}H^+$ 897.4403, found 897.4404. For NMR-spectra see p. 349.

**Synthesis of Compound 337**

**(4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-((*E*)-1-iodoprop-1-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane-5-carbaldehyde**



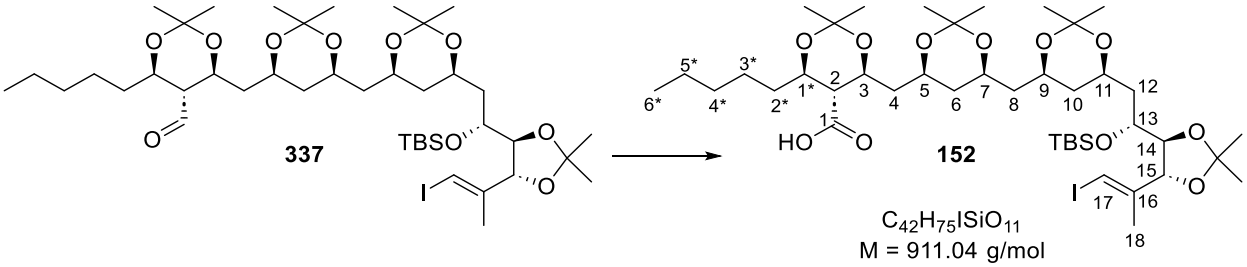

To a stirred solution of alcohol **296** (42.0 mg, 46.8 µmol, 1 equiv) in DMSO (1 mL) was added IBX (39.3 mg, 140 µmol, 3 equiv) at room temperature. The mixture was stirred for 90 min at room temperature and was then quenched with water (2 mL). DCM (5 mL) was added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 8:1). The pure product was obtained as a white solid foam (40 mg, 44.7 µmol, 95%).

**TLC** (silica, CyHex:EtOAc = 8:1): $R_f$ = 0.25. $[\alpha]_D^{20}$ = +9.1° (c = 0.44, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.76 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.1 Hz ,1H, H-1), 6.43–6.42 (m, 1H, H-17), 4.47 (d, $^3J_{H\text{-}15,\ H\text{-}14}$ = 8.0 Hz, 1H, H-15), 4.16 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.5 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 6.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 3.6 Hz, 1H, H-3), 4.07 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}ax}$ = 12.1 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 6.3 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 6.2 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}eq}$ = 2.5 Hz, 1H, H-5), 4.04–4.00 (m, 1H, H-13), 3.99–3.95 (m, 4H, H-1*, H-7, H-9, H-11), 3.93 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 7.9 Hz, $^3J_{H\text{-}14,\ H\text{-}13}$ = 4.2 Hz, 1H, H-14), 2.55 (ddd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 3.1 Hz, 1H, H-2), 1.87 (d, $^3J_{H\text{-}18,\ H\text{-}17}$ = 1.2 Hz, 3H, H-18), 1.76–1.66 (m, 3H, H-4, H-8, H-12), 1.57–1.49 (m, 2H, H-4´, H-12´), 1.48–1.43 (m, 8H, H-2*, H-2*´, H-3*, H-6-eq, H-10-eq, $CH_3$), 1.42 (s, 3H, $CH_3$), 1.41–1.37 (m, 10H, H-8´, 3x$CH_3$), 1.35 (s, 3H, $CH_3$), 1.32 (s, 3H, $CH_3$), 1.31–1.20 (m, 8H, H-3*´, H-4*, H-5*, $CH_3$), 1.14–1.05 (m, 2H, H-6-ax, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 203.4 (C-1), 146.2 (C-16), 109.3 ($C_q$), 98.9 ($C_q$), 98.8 ($C_q$), 98.8 ($C_q$), 82.2 (C-17), 81.7 (C-15), 81.1 (C-14), 69.9 (C-1*), 69.0 (C-13), 66.5 (C-3), 66.2 (C-7), 65.8 (C-11), 65.6 (C-9), 65.4 (C-5), 58.8 (C-2),

43.5 (C-8), 41.8 (C-12), 41.3 (C-4), 37.6 (C-10), 37.1 (C-6), 35.0 (C-2*), 32.2 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.2 ($CH_3$), 27.8 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.2 (C-3*), 23.1 (C-5*), 20.3 ($CH_3$), 20.3 ($CH_3$), 20.2 (C-18), 19.8 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), −3.9 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{42}H_{75}ISiO_{10}H^+$ 895.4247, found 895.4245. For NMR-spectra see p. 351.

**Synthesis of Compound 152**

**(4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-((*E*)-1-iodoprop-1-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane-5-carboxylic acid**




To a stirred solution of aldehyde **337** (40.0 mg, 44.7 µmol, 1 equiv) in *t*-BuOH (5 mL) was added 2-methyl-2-butene (40.0 µL, 0.36 mmol, 8 equiv). Sodium chlorite (36.4 mg, 0.40 mmol, 9 equiv) and Sodium dihydrogenphosphate dihydrate (48.8 mg, 0.31 mmol, 7 equiv) were dissolved in water (0.5 mL) and the solution was added to the reaction mixture. After stirring 2 h at room temperature the reaction mixture was quenched with saturated $NH_4Cl$-solution. DCM (10 mL) was added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1). The pure product was obtained as a white solid foam (31.0 mg, 34.0 µmol, 76%).

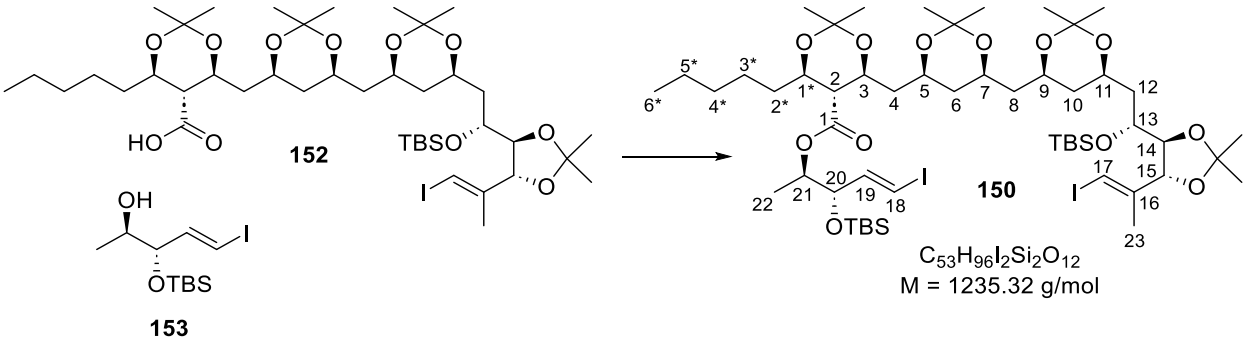
**TLC** (silica, CyHex:EtOAc = 4:1): $R_f$ = 0.27. $[\alpha]_D^{20}$ = +14.3° (c = 0.42, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.43 (br s, 1H, H-17), 4.48 (d, $^3J_{H\text{-}15,\ H\text{-}14}$ = 7.9 Hz, 1H, H-15), 4.38–4.32 (m, 1H, H-5), 4.09–4.04 (m, 2H, H-3, H-7), 4.04–3.99 (m, 2H, H-1*, H-13), 3.98–3.96 (m, 2H, H-9, H-11), 3.94 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 7.8 Hz, $^3J_{H\text{-}14,\ H\text{-}13}$ = 4.1 Hz, 1H, H-14), 2.40 (dd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.3 Hz, 1H, H-2), 1.87 (d, $^4J_{H\text{-}18,\ H\text{-}17}$ = 1.2 Hz, 3H, H-18), 1.88–1.82 (m, 1H, H-4), 1.76–1.69 (m, 2H, H-8, H-12), 1.65 (ddd, $^2J$ = 15.2 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 3.3 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 3.3 Hz, 1H, H-4´), 1.58–1.50 (m, 5H, H-2*, H-12´, $CH_3$), 1.50–1.47 (m, 1H, H-6-eq), 1.47–1.42 (m, 6H, H-3*, H-8´, H-10-eq, $CH_3$), 1.41–1.38 (m, 12H, 4x$CH_3$), 1.38–1.34 (m, 4H, H-2*´, $CH_3$), 1.34–1.31 (m, 4H, H-3*´, $CH_3$), 1.31–1.20 (m, 5H, H-4*, H-5*, H-6-ax),

1.15–1.07 (m, 1H, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 172.3 (C-1), 146.2 (C-16), 109.3 ($C_q$), 99.7 ($C_q$), 99.0 ($C_q$), 98.9 ($C_q$), 82.2 (C-17), 81.7 (C-15), 81.1 (C-14), 70.5 (C-1*), 69.0 (C-13), 68.3 (C-3), 66.3 (C-5), 66.2 (C-9), 66.0 (C-7), 65.7 (C-11), 51.6 (C-2), 43.3 (C-8), 41.8 (C-12), 40.3 (C-4), 37.6 (C-10), 37.3 (C-6), 34.7 (C-2*), 32.2 (C-4*), 30.5 ($CH_3$), 30.3 ($CH_3$), 30.1 ($CH_3$), 27.8 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.1 (C-3*), 23.2 (C-5*), 20.5 ($CH_3$), 20.3 (C-18), 20.1 ($CH_3$), 19.9 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), −3.9 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{42}H_{75}ISiO_{11}Na^+$ 933.4016, found 933.4013. For NMR-spectra see p. 353.

### 6.2.6 Coupling with the Western Fragment and Endgame

**Synthesis of Compound 150**

**(2*R*,3*S*,*E*)-3-((tert-butyldimethylsilyl)oxy)-5-iodopent-4-en-2-yl (4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((tert-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-((*E*)-1-iodoprop-1-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane-5-carboxylate**

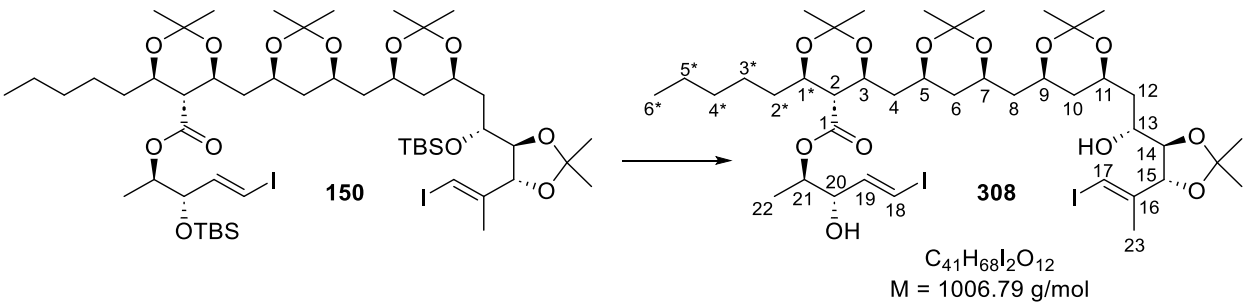



To a stirred solution of carboxylic acid **152** (30 mg, 32.9 µmol, 1 equiv) in THF (1 mL) was added $NEt_3$ (13.7 µL, 98.8 µmol, 3 equiv) and 2,4,6-trichlorobenzoyl chloride (**306**, 15.5 µL, 98.8 µmol, 3 equiv). The mixture was stirred for 6 h at room temperature before it was filtered through a glass filter frit and washed with THF (3 mL). The solvent was evaporated, and the residue was purged through a short pad of silica and eluted with CyHex:EtOAc = 15:1. After evaporation of the solvent the residue was redissolved in toluene (2 mL) and DMAP (16.1 mg, 132 µmol, 4 equiv) was added. The mixture was stirred for 10 min at room temperature and a solution of the western fragment **153** (12.4 mg, 36.2 µmol, 1.1 equiv) in toluene (0.1 mL) was added. The mixture was stirred for 48 h at room temperature. Afterwards, the mixture was filtered through a pad of celite, and the solvent was evaporated. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 15:1) and the pure product was obtained as a colorless highly viscous oil (34.0 mg, 27.5 µmol, 84%).

**TLC** (silica, CyHex:EtOAc = 15:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = +16.1° (c = 0.64, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.55 (dd, $^3J_{H\text{-}19,\,H\text{-}18}$ = 14.5 Hz, $^3J_{H\text{-}19,\,H\text{-}20}$ = 6.1 Hz, 1H, H-19), 6.43 (dq, $^4J_{H\text{-}17,\,H\text{-}23}$ = 1.1 Hz, $^3J_{H\text{-}17,\,H\text{-}15}$ = 1.0 Hz, 1H, H-17), 6.40 (dd, $^3J_{H\text{-}18,\,H\text{-}19}$ = 14.5 Hz, $^4J_{H\text{-}18,\,H\text{-}20}$ = 1.2 Hz, 1H, H-18), 4.86 (qd, $^3J_{H\text{-}21,\,H\text{-}22}$ = 6.4 Hz, $^3J_{H\text{-}21,\,H\text{-}20}$ = 3.9 Hz, 1H, H-21), 4.48 (dd, $^3J_{H\text{-}15,\,H\text{-}14}$ = 7.9 Hz, $^4J_{H\text{-}15,\,H\text{-}18}$ = 0.9 Hz, 1H, H-15), 4.11 (ddd, $^3J_{H\text{-}20,\,H\text{-}19}$ = 6.1 Hz, $^3J_{H\text{-}20,\,H\text{-}21}$ = 3.8 Hz, $^4J_{H\text{-}20,\,H\text{-}18}$ = 1.3 Hz, 1H, H-20), 4.09–4.04 (m, 2H, H-3, H-5), 4.03–4.00 (m, 1H, H-13), 4.00–3.95 (m, 2H, H-7, H-9), 3.93 (dd, $^3J_{H\text{-}14,\,H\text{-}15}$ = 7.9 Hz, $^4J_{H\text{-}14,\,H\text{-}13}$ = 4.2 Hz, 1H, H-14), 3.94–3.90 (m, 2H, H-1*, H-11), 2.20 (dd, $^3J_{H\text{-}2,\,H\text{-}1^*}$ = 10.2 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 10.2 Hz, 1H, H-2), 1.88 (d, $^3J_{H\text{-}23,\,H\text{-}17}$ = 1.1 Hz, 3H, H-23), 1.74–1.66 (m, 3H, H-4, H-8, H-12), 1.57–1.53 (m, 1H, H-12´), 1.51–1.49 (m, 1H, H-6-eq), 1.46–1.42 (m, 6H, H-3*, H-4´, H-10-eq, $CH_3$), 1.42–1.40 (m, 4H, H-8´, $CH_3$), 1.40–1.37 (m, 11H, H-2*, H-2*´, 3x$CH_3$), 1.35 (br s, 3H, $CH_3$), 1.32 (br s, 3H, $CH_3$), 1.30 (br s, 3H, $CH_3$), 1.29–1.23 (m, 5H, H-3*´, H-4*, H-5*), 1.16 (d, $^3J_{H\text{-}22,\,H\text{-}21}$ = 6.4 Hz, 3H, H-22), 1.13–1.06 (m, 2H, H-6-ax, H-10-ax), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.88 (t, $^3J_{H\text{-}6^*,\,H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*), 0.10 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 171.3 (C-1), 146.2 (C-16), 145.4 (C-19), 109.3 ($C_q$), 98.9 ($C_q$), 98.8 ($C_q$), 98.8 ($C_q$), 82.2 (C-17), 81.7 (C-15), 81.1 (C-14), 79.3 (C-18), 77.6 (C-20), 73.5 (C-21), 71.3 (C-1*), 69.0 (C-13), 67.5 (C-3), 66.2 (C-9), 65.9 (C-5), 65.8 (C-7), 65.6 (C-11), 53.5 (C-2), 43.6 (C-8), 41.8 (C-12), 41.2 (C-4), 37.6 (C-10), 36.6 (C-6), 34.8 (C-2*), 32.3 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.1 ($CH_3$), 27.8 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.1 (3x$CH_3$-TBS), 24.9 (C-3*), 23.2 (C-5*), 20.3 (C-23), 20.3 ($CH_3$), 20.2 ($CH_3$), 19.9 ($CH_3$), 18.7 ($C_q$-TBS), 18.5 ($C_q$-TBS), 15.3 (C-22), 14.4 (C-6*), −3.9 ($CH_3$-TBS), −4.2 ($CH_3$-TBS), −4.2 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{53}H_{96}I_2Si_2O_{12}H^+$ 1235.4602, found 1235.4608. For NMR-spectra see p. 355.

**Synthesis of Compound 308**

**(2*R*,3*S*,*E*)-3-hydroxy-5-iodopent-4-en-2-yl (4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*S*,6*S*)-6-((*R*)-2-hydroxy-2-((4*R*,5*R*)-5-((*E*)-1-iodoprop-1-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane-5-carboxylate**

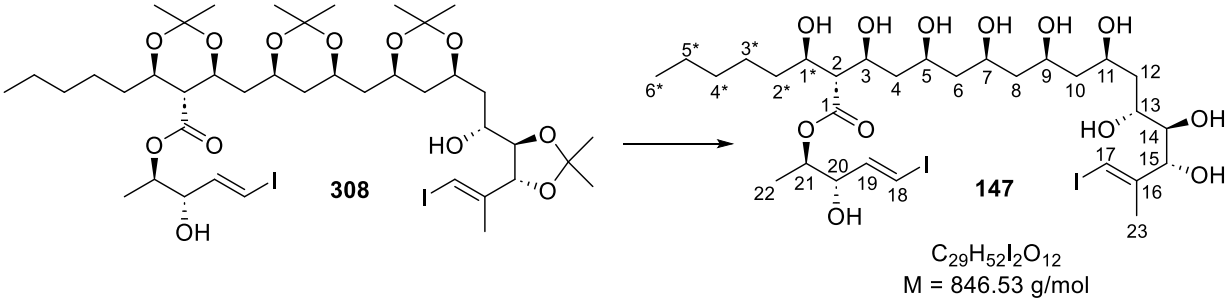


A stirred solution of TBS-ether **150** (23.0 mg, 18.6 µmol, 1 equiv) in THF (1 mL) was cooled to 0 °C. TBAF (1M in THF, 60.0 µL, 60.0 µmol, 3 equiv) was added at 0 °C and the mixture was stirred for 4 h at room temperature. Subsequently, the mixture was quenched with water (2 mL) and DCM (2 mL) and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1). The pure product was obtained as a white solid foam (17 mg, 16.9 µmol, 91%).

**TLC** (silica, CyHex:EtOAc = 4:1): $R_f$ = 0.18. $[\alpha]_D^{20}$ = +8.8° (c = 0.34, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.57 (dd, $^3J_{H\text{-}19,\,H\text{-}18}$ = 14.5 Hz, $^3J_{H\text{-}19,\,H\text{-}20}$ = 5.7 Hz, 1H, H-19), 6.51 (dd, $^3J_{H\text{-}18,\,H\text{-}19}$ = 14.4 Hz, $^4J_{H\text{-}18,\,H\text{-}20}$ = 1.2 Hz, 1H, H-18), 6.44 (dq, $^4J_{H\text{-}17,\,H\text{-}23}$ = 1.0 Hz, $^3J_{H\text{-}17,\,H\text{-}15}$ = 1.0 Hz, 1H, H-17), 4.96 (qd, $^3J_{H\text{-}21,\,H\text{-}22}$ = 6.5 Hz, $^3J_{H\text{-}21,\,H\text{-}20}$ = 3.2 Hz, 1H, H-21), 4.52 (dd, $^3J_{H\text{-}15,\,H\text{-}14}$ = 7.5 Hz, $^4J_{H\text{-}15,\,H\text{-}18}$ = 0.9 Hz, 1H, H-15), 4.22–4.19 (m, 1H, H-20), 4.16 (dddd, $^3J_{H\text{-}5,\,H\text{-}6ax}$ = 12.0 Hz, $^3J_{H\text{-}5,\,H\text{-}4}$ = 6.0 Hz, $^3J_{H\text{-}5,\,H\text{-}4'}$ = 5.9 Hz, $^3J_{H\text{-}5,\,H\text{-}6eq}$ = 2.5 Hz, 1H, H-5), 4.12 (dddd, $^3J_{H\text{-}11,\,H\text{-}10ax}$ = 12.2 Hz, $^3J_{H\text{-}11,\,H\text{-}12'}$ = 9.6 Hz, $^3J_{H\text{-}11,\,H\text{-}10eq}$ = 2.7 Hz, $^3J_{H\text{-}11,\,H\text{-}12}$ = 2.6 Hz, 1H, H-11), 4.08 (ddd, $^3J_{H\text{-}3,\,H\text{-}2}$ = 10.1 Hz, $^3J_{H\text{-}3,\,H\text{-}4}$ = 6.0 Hz, $^3J_{H\text{-}3,\,H\text{-}4'}$ = 3.8 Hz, 1H, H-3), 4.05–4.02 (m, 1H, H-9), 4.01–3.97 (m, 1H, H-7), 3.97–3.91 (m, 1H, H-1*), 3.89–3.84 (m, 1H, H-13), 3.67 (dd, $^3J_{H\text{-}14,\,H\text{-}15}$ = 7.3 Hz, $^3J_{H\text{-}14,\,H\text{-}13}$ = 6.5 Hz, 1H, H-14), 3.47 (d, $^3J$ = 1.2 Hz, 1H, OH-13), 2.76 (d, $^3J$ = 4.6 Hz, 1H, OH-20), 2.39 (dd, $^3J_{H\text{-}2,\,H\text{-}1*}$ = 10.3 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 10.3 Hz, 1H, H-2), 1.87 (d, $^3J_{H\text{-}23,\,H\text{-}17}$ = 1.1 Hz, 3H, H-23), 1.79 (ddd, $^2J$ = 14.4 Hz, $^3J_{H\text{-}12,\,H\text{-}11}$ = 2.5 Hz, $^3J_{H\text{-}12,\,H\text{-}13}$ = 2.5 Hz, 1H, H-12), 1.71 (ddd, $^2J$ = 14.0 Hz, $^3J_{H\text{-}8,\,H\text{-}7}$ = 7.1 Hz, $^3J_{H\text{-}8,\,H\text{-}9}$ = 7.1 Hz, 1H, H-8), 1.62–1.58 (m, 2H, H-4, H-4´), 1.57–1.54 (m, 1H, H-12´), 1.52–1.49 (m, 2H, H-6-eq, H-10-eq), 1.47–1.43 (m, 10H, H-3*, 3x$CH_3$), 1.43–1.39 (m, 6H, H-2*, H-2*´, H-8´, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (br s, 3H, $CH_3$), 1.35–1.32 (m, 6H, 2x$CH_3$), 1.32–1.25 (m, 5H, H-3*´, H-4*, H-5*), 1.24–1.22 (m, 1H, H-10-ax), 1.18 (d, $^3J_{H\text{-}22,\,H\text{-}21}$ = 6.6 Hz, 3H, H-22), 1.15–1.11 (m, 1H, H-6-ax), 0.88 (t, $^3J_{H\text{-}6*,\,H\text{-}5*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 172.0 (C-1), 146.3 (C-16), 143.8 (C-19), 109.8 ($C_q$), 99.2 ($C_q$), 99.2 ($C_q$), 99.0 ($C_q$), 83.2 (C-15), 81.8 (C-14), 81.4 (C-17), 80.0 (C-18), 75.9 (C-20), 73.6 (C-13), 73.2 (C-21), 71.2 (C-1*), 71.0 (C-11), 68.4 (C-3), 65.9 (C-5), 65.8 (C-9), 65.7 (C-7), 52.3 (C-2), 43.2 (C-8), 40.7 (C-4), 40.1 (C-12), 37.4 (C-10), 37.3 (C-6), 34.9 (C-2*), 32.2 (C-4*), 30.5 ($CH_3$), 30.5 ($CH_3$), 30.1 ($CH_3$), 27.6 ($CH_3$), 27.4 ($CH_3$), 24.9 (C-3*), 23.1 (C-5*), 20.4 (C-23), 20.3 ($CH_3$), 20.3 ($CH_3$), 19.8 ($CH_3$), 14.6 (C-22), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{41}H_{68}I_2O_{12}H^+$ 1007.2873, found 1007.2874. For NMR-spectra see p. 357.

**Synthesis of Compound 147**

**(2*R*,3*S*,*E*)-3-hydroxy-5-iodopent-4-en-2-yl (2*R*,3*S*,5*S*,7*S*,9*R*,11*R*,13*R*,14*R*,15*R*,*E*)-3,5,7,9,11,13,14,15-octahydroxy-2-((*R*)-1-hydroxyhexyl)-17-iodo-16-methylheptadec-16-enoate**



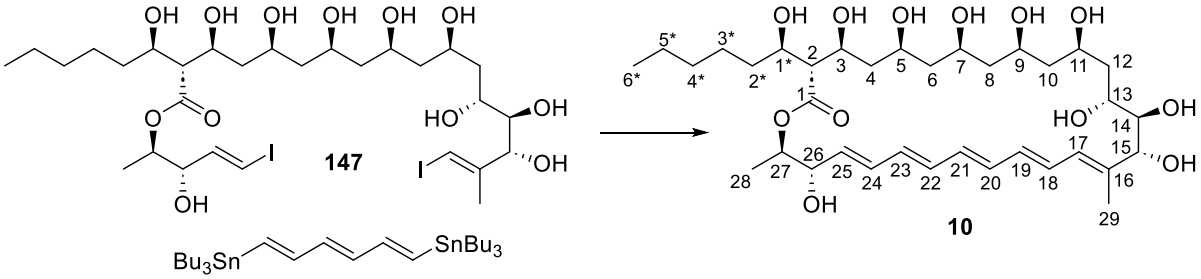

To a stirred solution of acetonide **308** (12.0 mg, 11.9 µmol, 1 equiv) in wet MeCN (1 mL) was added $InCl_3$ (52.7 mg, 0.24 mmol, 20 equiv). The mixture was heated to 50 °C and was stirred for 5 h before it was evaporated *in vacuo*. The residue was dissolved again in MeCN (1 mL) and stirred for another 5 h at 50 °C. After evaporation of the solvent the crude product was purified by flash chromatography (silica RP-18, MeCN:$H_2O$ = 2:3) and the pure product was obtained as a white solid after lyophilization (7.10 mg, 8.39 µmol, 70%).

**TLC** (silica RP-18, MeCN:$H_2O$ = 2:3): $R_f$ = 0.19. $[\alpha]_D^{20}$ = +20.0° (c = 0.20, MeOH). **$^1$H-NMR** (700 MHz, $CD_3OD$, 298 K): $\delta$ (ppm) = 6.66 (dd, $^3J_{H\text{-}19,\ H\text{-}18}$ = 14.5 Hz, $^3J_{H\text{-}19,\ H\text{-}20}$ = 6.5 Hz, 1H, H-19), 6.56 (dd, $^3J_{H\text{-}18,\ H\text{-}19}$ = 14.5 Hz, $^4J_{H\text{-}18,\ H\text{-}20}$ = 1.1 Hz, 1H, H-18), 6.39 (qd, $^4J_{H\text{-}17,\ H\text{-}23}$ = 1.2 Hz, $^3J_{H\text{-}17,\ H\text{-}15}$ = 1.2 Hz, 1H, H-17), 4.92 (qd, $^3J_{H\text{-}21,\ H\text{-}22}$ = 6.4 Hz, $^3J_{H\text{-}21,\ H\text{-}20}$ = 4.5 Hz, 1H, H-21), 4.38 (dd, $^3J_{H\text{-}15,\ H\text{-}14}$ = 3.1 Hz, $^4J_{H\text{-}15,\ H\text{-}17}$ = 1.2 Hz, 1H, H-15), 4.21 (ddd, $^3J_{H\text{-}3,\ H\text{-}4}$ = 9.9 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.4 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 2.5 Hz, 1H, H-3), 4.10 (ddd, $^3J_{H\text{-}20,\ H\text{-}19}$ = 6.5 Hz, $^3J_{H\text{-}20,\ H\text{-}21}$ = 4.5 Hz, $^4J_{H\text{-}20,\ H\text{-}18}$ = 1.2 Hz, 1H, H-20), 4.09–4.05 (m, 2H, H-5, H-11), 4.05–4.01 (m, 2H, H-7, H-9), 3.93 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 8.8 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 2.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.6 Hz, 1H, H-1*), 3.78 (ddd, $^3J_{H\text{-}13,\ H\text{-}12}$ = 9.6 Hz, $^3J_{H\text{-}13,\ H\text{-}14}$ = 6.9 Hz, $^3J_{H\text{-}13,\ H\text{-}12'}$ = 2.8 Hz, 1H, H-13), 3.44 (dd, $^3J_{H\text{-}14,\ H\text{-}13}$ = 7.0 Hz, $^3J_{H\text{-}14,\ H\text{-}15}$ = 3.0 Hz, 1H, H-14), 2.65 (dd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 9.0 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.4 Hz, 1H, H-2), 1.94 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}12',\ H\text{-}11}$ = 5.4 Hz, $^3J_{H\text{-}12',\ H\text{-}13}$ = 2.8 Hz, 1H, H-12´), 1.87 (d, $^4J_{H\text{-}23,\ H\text{-}17}$ = 1.1 Hz, 3H, H-23), 1.79–1.67 (m, 5H, H-4, H-4´, H-6, H-8, H-10), 1.66–1.59 (m, 4H, H-6´, H-8´, H-10´, H-12), 1.58–1.54 (m, 1H, H-3*), 1.54–1.48 (m, 1H, H-2*), 1.47–1.40 (m, 1H, H-2*´), 1.40–1.28 (m, 5H, H-3*´, H-4*, H-5*), 1.22 (d, $^3J_{H\text{-}22,\ H\text{-}21}$ = 6.5 Hz, 3H, H-22), 0.94 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_3OD$, 298 K): $\delta$ (ppm) = 173.0 (C-1), 149.6 (C-16), 145.9 (C-19), 79.6 (C-18), 78.5 (C-17), 76.8 (C-20), 76.0 (C-14), 75.7 (C-15), 74.0 (C-21), 72.4 (C-1*), 72.1 (C-3), 71.6 (C-13), 70.6 (C-5), 70.6 (C-11), 70.3 (C-7), 70.1 (C-9), 59.8 (C-2), 45.3 (C-8), 45.1 (C-6), 45.0 (C-10), 41.8 (C-4), 41.4 (C-12), 36.4 (C-2*), 33.0 (C-4*), 26.0 (C-3*), 23.7 (C-5*), 21.6 (C-23), 15.7 (C-22),

14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{52}I_2O_{12}H^+$ 847.1621, found 847.1625. For NMR-spectra see p. 359.

**Synthesis of Pentamycin (10)**

**(3*R*,4*S*,6*S*,8*S*,10*R*,12*R*,14*R*,15*R*,16*R*,17*E*,19*E*,21*E*,23*E*,25*E*,27*S*,28*R*)-4,6,8,10,12,14,15,16,27-nonahydroxy-3-((*R*)-1-hydroxyhexyl)-17,28-dimethyloxacyclooctacosa-17,19,21,23,25-pentaen-2-one**




To a solution of bisvinyl iodide **147** (3.00 mg, 3.54 µmol, 1 equiv) in DMF (1 mL) was added $Pd(MeCN)_2Cl_2$-stock solution (1.83 mg in 1 mL DMF; 100 µL, 0.71 µmol, 0.20 equiv). A separate reaction tube was charged with trienyl-*bis*-stannane **148** (2.92 mg, 4.43 µmol, 1.25 equiv), THF (200 µL) and DIPEA (3.10 µL, 17.7 µmol, 5 equiv). Both solutions were degassed using the freeze-pump-thaw method (4 cycles). The solution of the bisvinyl stannane was added to the solution of the bisvinyl iodide and the mixture was stirred in the dark for 24 h. The DMF was evaporated using high vacuum and the crude product was purified by flash chromatography (silica RP-18, MeCN:$H_2O$ = 2:3). Pure pentamycin (**10**) was obtained as an off-white solid after lyophilization (1.1 mg, 1.64 µmol, 46%).

**TLC** (silica RP-18, MeCN:$H_2O$ = 2:3): $R_f$ = 0.30. $[\alpha]_D^{20}$ = −115.0° (c = 0.20, MeOH). **$^1$H-NMR** (700 MHz, $CD_3OD$, 298 K): $\delta$(ppm) = 6.48 (dd, $^3J_{H\text{-}18,\,H\text{-}19}$ = 14.0 Hz, $^3J_{H\text{-}18,\,H\text{-}17}$ = 11.2 Hz, 1H, H-18), 6.45 (ddd, $^3J_{H\text{-}24,\,H\text{-}25}$ = 15.3 Hz, $^3J_{H\text{-}24,\,H\text{-}23}$ = 10.5 Hz, $^4J_{H\text{-}24,\,H\text{-}26}$ = 1.3 Hz, 1H, H-24), 6.40–6.36 (m, 3H, H-20, H-21, H-23), 6.36–6.33 (m, 1H, H-19), 6.32–6.28 (m, 1H, H-22), 6.06 (dd, $^3J_{H\text{-}17,\,H\text{-}18}$ = 11.3 Hz, $^4J_{H\text{-}17,\,H\text{-}29}$ = 1.3 Hz, 1H, H-17), 6.03 (dd, $^3J_{H\text{-}25,\,H\text{-}24}$ = 15.2, $^3J_{H\text{-}25,\,H\text{-}26}$ = 5.0 Hz, 1H, H-25), 4.84–4.83[1] (m, 1H, H-27), 4.19 (ddd, $^3J_{H\text{-}3,\,H\text{-}4}$ = 9.6 Hz, $^3J_{H\text{-}3,\,H\text{-}2}$ = 7.2 Hz, $^3J_{H\text{-}3,\,H\text{-}4'}$ = 3.1 Hz, 1H, H-3), 4.10 (ddd, $^3J_{H\text{-}26,\,H\text{-}27}$ = 6.7 Hz, $^3J_{H\text{-}26,\,H\text{-}25}$ = 5.1 Hz, $^4J_{H\text{-}26,\,H\text{-}24}$ = 1.3 Hz, 1H H-26), 4.05–3.99 (m, 3H, H-5, H-7, H-9), 3.98–3.95 (m, 1H, H-11) 3.89 (d, $^3J_{H\text{-}15,\,H\text{-}14}$ = 9.0 Hz, 1H, H-15), 3.85 (ddd, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 8.8 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^*}$ = 8.8 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^{*\prime}}$ = 2.4 Hz, 1H, H-1*), 3.72 (dd, $^3J_{H\text{-}14,\,H\text{-}15}$ = 9.1 Hz, $^3J_{H\text{-}14,\,H\text{-}13}$ = 1.9 Hz, 1H, H-14), 3.29–3.26[2] (m, 1H, H-13), 2.56 (dd, $^3J_{H\text{-}2,\,H\text{-}1^*}$ = 9.0 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 7.2 Hz, 1H, H-2), 1.79 (d, $^4J_{H\text{-}29,\,H\text{-}17}$ = 1.3 Hz, 3H, H-29), 1.76 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}12,\,H\text{-}13}$ = 11.0 Hz, $^3J_{H\text{-}12,\,H\text{-}11}$ = 3.7 Hz, 1H, H-12), 1.56–1.48 (m, 5H, H-2*, H-3*, H-4, H-4´,

H-10), 1.47–1.42 (m, 2H, H-8, H-6), 1.39–1.31 (m, 10H, H-2*´, H-3*´, H-4*, H-5*, H-6´, H-8´, H-10´, H-12´), 1.30 (d, $^{3}J_{\text{H-28, H-27}}$ = 6.4 Hz, 3H, H-28), 0.92 (t, $^{3}J_{\text{H-6*, H-5*}}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_3OD$, 298 K): $\delta$ (ppm) = 173.0 (C-1), 138.5 (C-16), 135.4 (C-19), 134.9 (C-21), 134.3 (C-20), 134.2 (C-23), 134.1 (C-25), 133.6 (C-22), 132.0 (C-24), 129.9 (C-17), 129.0 (C-18), 80.5 (C-15), 78.3 (C-14), 75.2 (C-27), 74.2 (C-9), 74.1 (C-5), 73.9 (C-7), 73.3 (C-3), 73.2 (C-26), 72.4 (C-1*), 71.4 (C-11), 70.3 (C-13), 60.5 (C-2), 45.3 (C-8), 45.2 (C-6), 44.3 (C-10), 41.2 (C-4), 39.5 (C-12), 36.2 (C-2*), 32.9 (C-4*), 26.1 (C-3*), 23.7 (C-5*), 17.9 (C-28), 14.4 (C-6*), 11.7 (C-29). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{35}H_{58}O_{12}Na^+$ 693.3820, found 693.3816. For NMR-spectra see p. 361.

[1]overlapping with the $^{1}$H-signal of water (assigned via HSQC, Figure 6.9).

[2]overlapping with the $CD_3OD$-signal (assigned via HSQC, Figure 6.9).

Traces of MeCN are visible in the $^{1}$H-spectrum as drying the compound overnight at the high vacuum is not possible due to instability.

Traces of deuterated ethanol, visible in the $^{13}$C-spectrum are present in the deuterated methanol purchased from deutero.

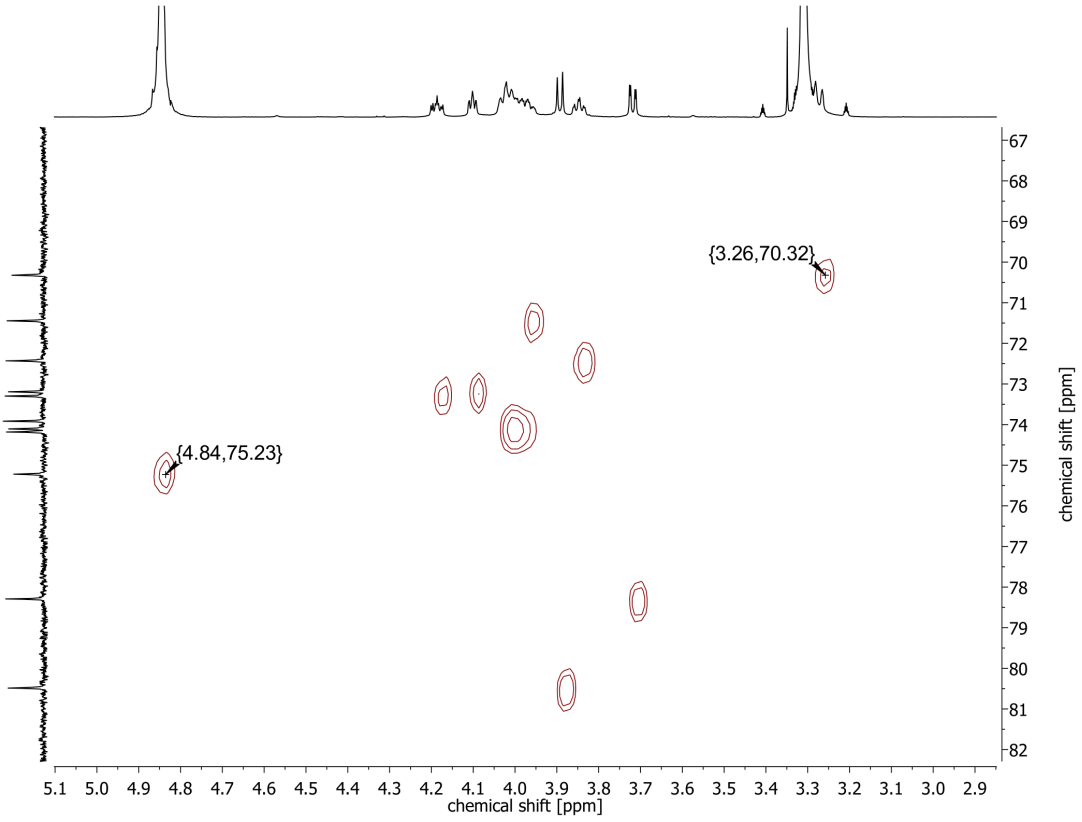



Figure 6.9: $^{1}$H-$^{13}$C-HSQC spectrum to show the assignment of H-13/C-13 and H-27/C-27.

Pentamycin (**10**) is instable in the presence of UV light. Purification via HPLC with UV detection leads to decomposition which is visible in the $^{1}$H-NMR between 3.90 and 3.50 ppm (Figure 6.10).

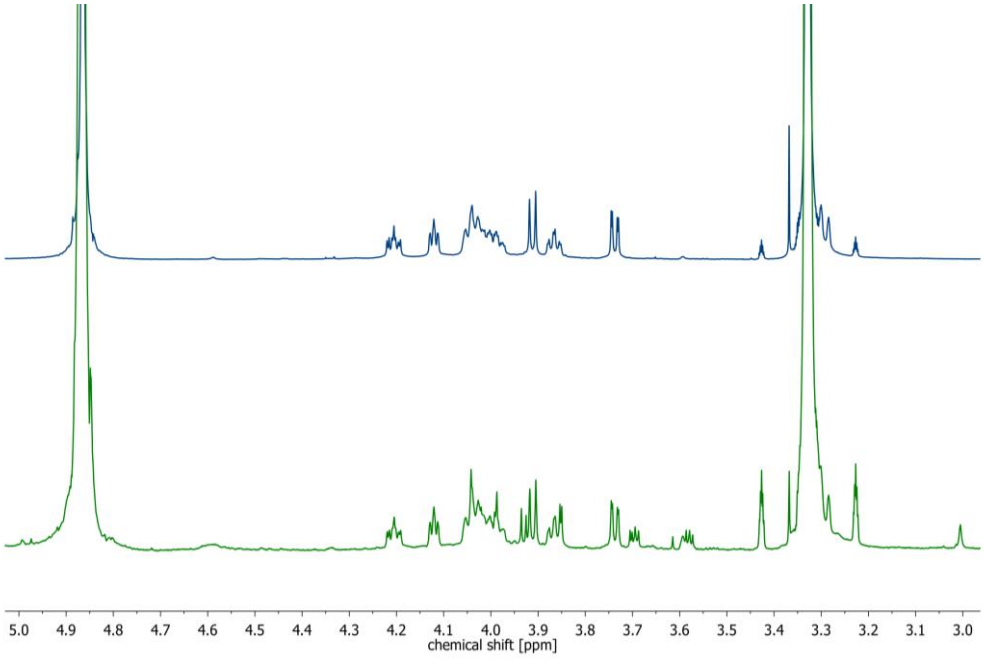
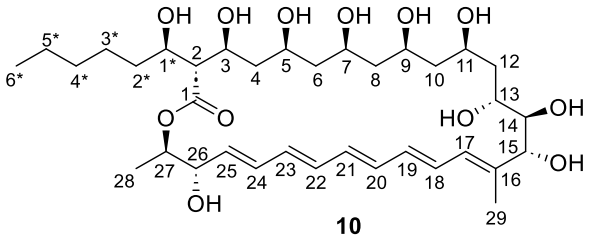



Figure 6.10: $^{1}$H-NMR-spectra of pentamycin (**10**) without HPLC purification and immediate NMR measurement (blue) and with HPLC purification and lyophilization overnight (green).

Table 6.6: Comparison of the $^{1}$H-NMR data of synthetic pentamycin (**10**) with the reported data.[186] The coupling constants are given in Hz.

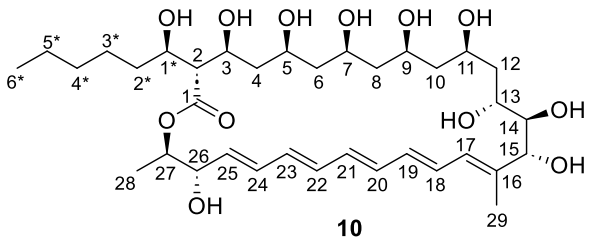



**10**

| **Atom** | Chemical Shift ($\delta$ in ppm), reported $^{1}$H-data[5] ($CD_3OD$, 500 MHz) | Chemical Shift ($\delta$ in ppm), $^{1}$H-data of synthesized pentamycin ($CD_3OD$, 700 MHz) |
|---|---|---|
| **1** | - | - |
| **2** | 2.55 (dd, 8.8, 7.3) | 2.56 (dd, 9.0, 7.2) |
| **1*** | 3.82–3.85 (m) | 3.85 (ddd, 8.8, 8.8, 2.4) |
| **2*** | 1.33 (m), 1.51 (m) | 1.56–1.48 (m), 1.39–1.31 (m) |
| **3*** | 1.33 (m), 1.51 (m) | 1.56–1.48 (m), 1.39–1.31 (m) |
| **4*** | 1.33 (m) | 1.39–1.31 (m) |
| **5*** | 1.33 (m) | 1.39–1.31 (m) |
| **6*** | 0.90 (t, 6.7) | 0.92 (t, 7.1) |
| **3** | 4.18 (m) | 4.19 (ddd, 9.6, 7.2, 3.1) |

| | | |
|---|---|---|
| **4** | 1.51 (m) | 1.56–1.48 (m) |
| **5** | 3.95–4.03 (m) | 4.05–3.99 (m) |
| **6** | 1.33 (m), 1.44 (m) | 1.47–1.42 (m), 1.39–1.31 (m) |
| **7** | 3.95–4.03 (m) | 4.05–3.99 (m) |
| **8** | 1.33 (m), 1.44 (m) | 1.47–1.42 (m), 1.39–1.31 (m) |
| **9** | 3.95–4.03 (m) | 4.05–3.99 (m) |
| **10** | 1.51 (m) | 1.56–1.48 (m), 1.39–1.31 (m) |
| **11** | 3.95–4.00 (m) | 3.98–3.95 (m) |
| **12** | 1.33 (m), 1.73 (m) | 1.39–1.31 (m), 1.76 (ddd, 14.3, 11.0, 3.7) |
| **13** | 3.26 (d, 11) | 3.29–3.26 (m) |
| **14** | 3.71 (dd, 9.0, 2.0) | 3.72 (dd, 9.1, 1.9) |
| **15** | 3.88 (d, 9.2) | 3.89 (d, 9.0) |
| **16** | - | - |
| **17** | 6.05 (d, 11) | 6.06 (dd, 11.3, 1.3) |
| **18** | 6.50 (dd, 14, 11) | 6.48 (dd, 14.0, 11.2) |
| **19** | 6.32–6.37 (m) | 6.36–6.33 (m) |
| **20** | 6.30–6.35 (m) | 6.40–6.36 (m) |
| **21** | 6.32–6.37 (m) | 6.40–6.36 (m) |
| **22** | 6.28 (m) | 6.32–6.28 (m) |
| **23** | 6.34–6.37 (m) | 6.40–6.36 (m) |
| **24** | 6.39–6.45 (m) | 6.45 (ddd, 15.3, 10.5, 1.3) |
| **25** | 6.02 (dd, 15, 4.9) | 6.03 (dd, 15.2, 5.0) |
| **26** | 4.09 (dd, 6.1, 5.2) | 4.10 (ddd, 6.7, 5.1, 1.3) |
| **27** | 4.86 (d, 7.3) | 4.84–4.83 (m) |
| **28** | 1.20 (d, 6.1) | 1.30 (d, 6.4) |
| **29** | 1.77 (s) | 1.79 (d, 1.3) |

Table 6.7: Comparison of the $^{13}$C-NMR data of synthetic pentamycin (**10**) with the reported data.[186]




**10**

| **Posi-tion** | Chemical Shift (δ in ppm), reported $^{1}$H-data[5] ($CD_3OD$, 125 MHz) | Chemical Shift (δ in ppm), $^{1}$H-data of synthesized pentamycin ($CD_3OD$, 175 MHz) |
|---|---|---|
| **1** | 173.0 | 173.0 |
| **2** | 60.4 | 60.5 |
| **1*** | 72.5 | 72.4 |
| **2*** | 36.2 | 36.2 |
| **3*** | 26.1 | 26.1 |
| **4*** | 32.9 | 32.9 |

| | | |
|---|---|---|
| **5*** | 23.7 | 23.7 |
| **6*** | 14.4 | 14.4 |
| **3** | 73.4 | 73.3 |
| **4** | 41.2 | 41.2 |
| **5** | 74.1 | 74.1 |
| **6** | 45.2 | 45.2 |
| **7** | 73.9 | 73.9 |
| **8** | 45.3 | 45.3 |
| **9** | 74.2 | 74.2 |
| **10** | 44.3 | 44.3 |
| **11** | 71.4 | 71.4 |
| **12** | 39.5 | 39.5 |
| **13** | 70.3 | 70.3 |
| **14** | 78.3 | 78.3 |
| **15** | 80.5 | 80.5 |
| **16** | 138.5 | 138.5 |
| **17** | 129.9 | 129.9 |
| **18** | 129.1 | 129.0 |
| **19** | 135.4 | 135.4 |
| **20** | 134.1 | 134.3[#] |
| **21** | 134.9 | 134.9 |
| **22** | 133.7 | 133.6 |
| **23** | 134.2 | 134.2 |
| **24** | 132.0 | 132.0 |
| **25** | 134.3 | 134.1[#] |
| **26** | 73.2 | 73.2 |
| **27** | 75.2 | 75.2 |
| **28** | 17.9 | 17.9 |
| **29** | 11.7 | 11.7 |

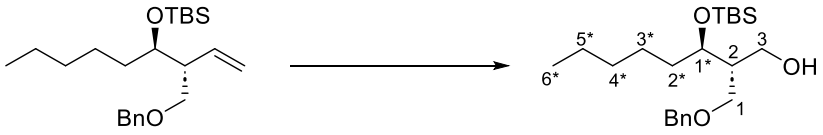
[#]The carbon atoms C20 and C25 were reassigned using H,H-COSY and HMBC NMR-data.

## 6.3 Contributions to the Total Synthesis of Pentamycin

### 6.3.1 Contributions to the Northern Fragment

#### Synthesis of Compound 240

**(2*R*,3*R*)-2-((benzyloxy)methyl)-3-((*tert*-butyldimethylsilyl)oxy)octan-1-ol**




**239** **240**

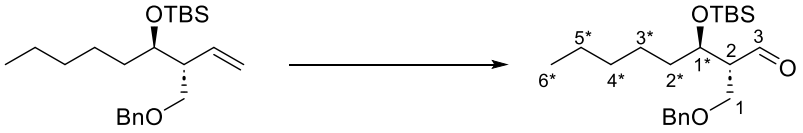
$C_{22}H_{40}O_3Si$
M = 380.64 g/mol

A stirred solution of alkene **239** (230 mg, 0.61 mmol, 1 equiv) in MeOH/DCM (1:1, 3 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 8 min until a slightly blue color persisted. The excess ozone was then purged with argon for 5 min and $NaBH_4$ (116 mg, 3.05 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 16 h at room temperature. $NH_4Cl$-solution (10 mL) and DCM (10 mL) was added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 8:1). The pure product was obtained as a colorless liquid (203 g, 0.53 mmol, 87%).

**TLC** (silica, CyHex:EtOAc = 6:1): $R_f$ = 0.35. $[\alpha]_D^{20}$ = −2.1° (c = 0.96, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.27 (m, 1H, CH-Bn), 4.52 (d, $^2J$ = 11.8 Hz, 1H, $CH_2$-Bn), 4.50 (d, $^2J$ = 11.8 Hz, 1H, $CH_2$-Bn´), 3.95 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 5.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 3.4 Hz, 1H, H-1*), 3.88 (ddd, $^2J$ = 11.2 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 4.6 Hz, $^3J_{H\text{-}3,\ OH}$ = 2.9 Hz, 1H, H-3), 3.69–3.62 (m, 3H, H-3´, H-1, H-1´), 2.80 (dd, $^3J_{OH,\ H\text{-}3'}$ = 8.4 Hz, $^3J_{OH,\ H\text{-}3}$ = 2.9 Hz, 1H, OH), 1.91–1.87 (m, 1H, H-2), 1.64–1.58 (m, 1H, H-2*), 1.55–1.48 (m, 1H, H-2*´), 1.32–1.21 (m, 6H, H-3*, H-4*, H-5*), 0.91–0.86 (m, 12H, H-6*, 3x$CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.2 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 73.8 ($CH_2$-Bn), 73.6 (C-1*), 71.4 (C-1), 62.5 (C-3), 44.3 (C-2), 35.6 (C-2*), 32.5 (C-4*), 26.2 (3x$CH_3$-TBS), 25.6 (C-3*), 23.2 (C-5*), 18.4 ($C_q$-TBS), 14.4 (C-6*), −4.1 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{40}O_3SiH^+$ 381.2819, found 381.2826. For NMR-spectra see p. 363.

**Synthesis of Compound 241**

**(2*R*,3*R*)-2-((benzyloxy)methyl)-3-((*tert*-butyldimethylsilyl)oxy)octanal**




**239** **241**

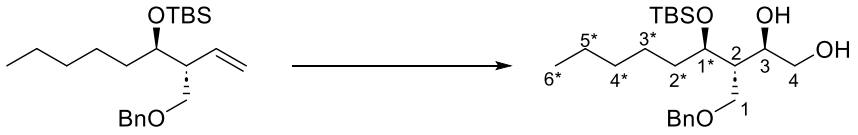
$C_{22}H_{38}SiO_3$
M = 378.63 g/mol

A stirred solution of alkene **239** (103 mg, 0.27 mmol, 1 equiv) in MeOH/DCM (1:1, 2 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 2 min until a slightly blue color persisted. The excess ozone was then purged with argon for 5 min and $Me_2S$ (100 µL, 1.35 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 2.5 h at room temperature. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1). The pure product was obtained as a colorless liquid (76.0 mg, 0.20 mmol, 74%).

For analytical data see p. 117.

**Synthesis of Compound 243**

**(2*R*,3*S*,4*R*)-3-((benzyloxy)methyl)-4-((*tert*-butyldimethylsilyl)oxy)nonane-1,2-diol**




**239** **243**

$C_{23}H_{42}SiO_4$
M = 410.67 g/mol

A solution of terminal olefin **239** (1.37 g, 3.64 mmol, 1 equiv) in *t*-BuOH (3 mL) was added to a mixture of AD-mix-β (5.84 g; 1.6 g/mmol) and $MeSO_2NH_2$ (0.35 g, 3.64 mmol, 1 equiv) in *t*-BuOH/$H_2O$ (1:1; 36 mL). The biphasic mixture was stirred for 48 h at room temperature before saturated $Na_2SO_3$-solution (20 mL) was added. After 30 min at room temperature the mixture was extracted with DCM (4 x 30 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtaines as a colorless highly viscous oil (1.37 g, 3.34 mmol, 92%, (1.01 g (1,3-syn); 0.36 g (1,3-anti)) *dr* ≈ 3:1).

1,3-*syn*-isomer:

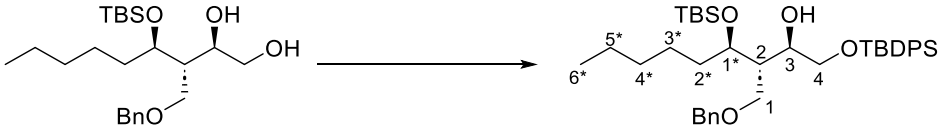
**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +6.4° (c = 0.94, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.28 (m, 5H, 5xCH-Bn), 4.49 (d, $^2J$ = 11.6 Hz, 1H, $CH_2$-Bn), 4.47 (d, $^2J$ = 11.7 Hz, 1H, $CH_2$-Bn´), 3.98 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 6.2 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 4.3 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 4.3 Hz, 1H, H-1*), 3.74 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 9.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 7.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4^{\prime}}$ = 5.0 Hz, 1H, H-3), 3.67–3.62 (m, 1H, H-4), 3.60 (dd, $^2J$ = 9.4 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.2 Hz, 1H, H-1), 3.58–3.56 (m, 1H, H-4´), 3.48 (dd, $^2J$ = 9.4 Hz, $^3J_{H\text{-}1^{\prime},\ H\text{-}2}$ = 7.5 Hz, 1H, H-1´), 3.02 (d, $^3J_{OH\text{-}3,\ H\text{-}3}$ = 6.2 Hz, 1H, OH-3), 2.61 (t, $^3J_{OH\text{-}4,\ H\text{-}4}$ = 6.4 Hz, 1H, OH-4), 2.06–2.00 (m, 1H, H-2), 1.60–1.56 (m, 1H, H-2*), 1.43–1.37 (m, 1H, H-2*´), 1.35–1.23 (m, 6H, H-3*, H-4*, H-5*), 0.90–0.87 (m, 12H, H-6*, 3x$CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.5 ($C_q$-Bn), 129.0 (2xCH-Bn), 128.4 (2xCH-Bn), 128.3 (CH-Bn), 74.0 ($CH_2$-Bn), 73.0 (C-1*), 72.6 (C-3), 69.7 (C-1), 65.3 (C-4), 47.2 (C-2), 35.1 (C-2*), 32.5 (C-4*), 26.2 (3x$CH_3$-TBS), 25.7 (C-3*), 23.2 (C-5*), 18.5 ($C_q$-TBS), 14.4 (C-6*), −4.1 ($CH_3$-TBS), −4.4 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{42}O_4SiH^+$ 411.2925, found 411.2915. For NMR-spectra see p. 365.

1,3-*anti*-isomer:

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.36. $[\alpha]_D^{20}$ = +12.3° (c = 0.92, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.31 (m, 4H, 4xCH-Bn), 7.31–7.28 (m, 1H, 1xCH-Bn), 4.51 (d, $^2J$ = 11.7 Hz, 1H, $CH_2$-Bn), 4.49 (d, $^2J$ = 11.6 Hz, 1H, $CH_2$-Bn´), 4.09–4.06 (m, 1H, H-3), 4.04 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.7 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 5.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 2.9 Hz, 1H, H-1*), 3.76 (dd, $^2J$ = 9.3 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 6.8 Hz, 1H, H-1), 3.67 (d, $^3J_{OH\text{-}3,\ H\text{-}3}$ = 2.1 Hz, 1H, OH-3), 3.63 (dd, $^2J$ = 9.4 Hz, $^3J_{H\text{-}1,\ H\text{-}2^{\prime}}$ = 5.5 Hz, 1H, H-1´), 3.62–3.58 (m, 1H, H-4), 3.53–3.49 (m, 1H, H-4´), 2.34–2.29 (m, 1H, OH-4), 1.89–1.85 (m, 1H, H-2), 1.68–1.61 (m, 1H, H-2*), 1.54–1.49 (m, 1H, H-2*´), 1.32–1.22 (m, 6H, H-3*, H-4*, H-5*), 0.90–0.87 (m, 12H, H-6*, 3x$CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.7 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.4 (2xCH-Bn), 128.2 (CH-Bn), 74.6 (C-1*), 73.9 ($CH_2$-Bn), 71.4 (C-3), 69.2 (C-1), 65.8 (C-4), 44.1 (C-2), 35.1 (C-2*), 32.4 (C-4*), 26.1 (3x$CH_3$-TBS), 25.9 (C-3*), 23.2 (C-5*), 18.4 ($C_q$-TBS), 14.3 (C-6*), −4.1 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{23}H_{42}O_4SiH^+$ 411.2925, found 411.2923. For NMR-spectra see p. 367.

**Synthesis of Compound 244**

**(6*R*,7*S*,8*R*)-7-((benzyloxy)methyl)-2,2,10,10,11,11-hexamethyl-8-pentyl-3,3-diphenyl-4,9-dioxa-3,10-disiladodecan-6-ol**




**243** **244**

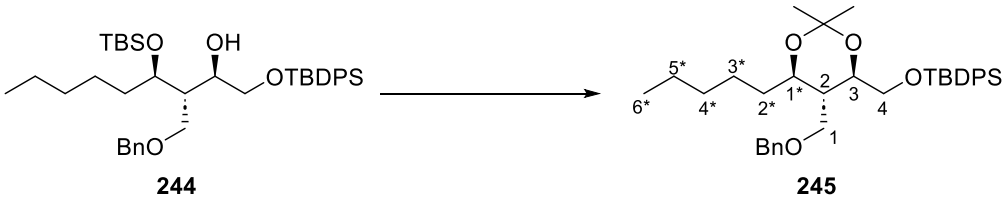
$C_{39}H_{60}Si_2O_4$
M = 649.07 g/mol

A solution of diol **243** (0.80 g, 1.95 mmol, 1 equiv) in DCM (4 mL) was cooled to 0 °C. Imidazole (0.20 g, 2.92 mmol, 1.5 equiv) and TBDPSCl (0.56 mL, 2.14 mmol, 1.1 equiv) were added sequentially and the mixture was stirred at 0 °C for 30 min. Subsequently, DCM (10 mL) and water (10 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 30:1) and the pure product was obtained as a colorless oil (1.24 g, 1.91 mmol, 98%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.43. $[\alpha]_D^{20}$ = +4.3° (c = 1.88, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.68–7.64 (m, 4H, 4xCH-Ar), 7.46–7.39 (m, 2H, 2xCH-Ar), 7.39–7.34 (m, 5H, 5xCH-Ar), 7.27–7.22 (m, 2H, 2xCH-Ar), 7.19–7.15 (m, 2H, 2xCH-Ar), 4.30 (br s, 2H, $CH_2$-Bn) 4.04 (ddd, $^3J_{H\text{-}1^*,\,H\text{-}2^*}$ = 7.1 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^{*\prime}}$ = 5.1 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 3.6 Hz, 1H, H-1*), 3.91 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}4,\,H\text{-}3}$ = 3.4 Hz, 1H, H-4), 3.87–3.78 (m, 1H, H-3), 3.61 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}4',\,H\text{-}3}$ = 7.8 Hz, 1H, H-4´), 3.51 (dd, $^2J$ = 9.3 Hz, $^3J_{H\text{-}1,\,H\text{-}2}$ = 3.4 Hz, 1H, H-1), 3.40 (dd, $^2J$ = 9.3 Hz, $^3J_{H\text{-}1',\,H\text{-}2}$ = 5.9 Hz, 1H, H-1´), 2.92 (d, $^3J_{OH,\,H\text{-}3}$ = 3.4 Hz, 1H, OH), 2.01–1.96 (m, 1H, H-2), 1.52–1.46 (m, 1H, H-2*), 1.37–1.21 (m, 7H, H-2*´, H-3*, H-4*, H-5*), 1.06 (s, 9H, 3x$CH_3$-TBDPS), 0.89 (t, $^3J_{H\text{-}6^*,\,H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*), 0.82 (s, 9H, 3x$CH_3$-TBS), 0.02 (s, 3H, $CH_3$-TBS), 0.01 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (125 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.2–127.9 (15xCH-Ar, 3x$C_q$-Ar), 73.5 ($CH_2$-Bn), 72.4 (C-3), 72.0 (C-1*), 68.3 (C-1), 67.6 (C-4), 46.9 (C-2), 34.5 (C-2*), 32.5 (C-4*), 27.2 (3x$CH_3$-TBDPS), 26.4 (C-3*), 26.2 (3x$CH_3$-TBS), 23.2 (C-5*), 19.6 ($C_q$-TBDPS), 18.4 ($C_q$-TBS), 14.4 (C-6*), −4.1 ($CH_3$-TBS), −4.4 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{39}H_{60}O_4Si_2Na^+$ 671.3922, found 671.3913. For NMR-spectra see p. 369.

**Synthesis of Compound 245**

**(((4*R*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)methoxy)(*tert*-butyl)diphenylsilane**



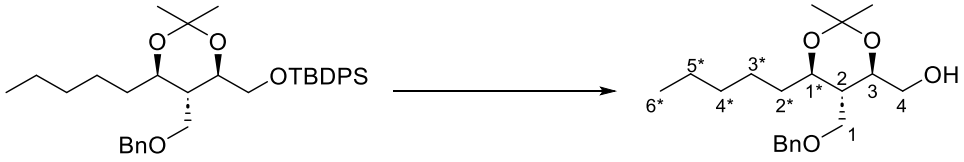

$C_{36}H_{50}SiO_4$
M = 574.88 g/mol

To a solution of TBS ether **244** (1.00 g, 1.54 mmol, 1 equiv) in MeOH (15 mL) was added PPTS (77.1 mg, 0.31 mmol, 0.2 equiv) at room temperature and the mixture was stirred for 22 h. 2,2-DMP (10 mL) was added, and the mixture was stirred for 15 min before the solvent was evaporated with a rotary evaporator (40 °C bath temperature). The residue was redissolved in DCM (5 mL) and 2,2-DMP (10 mL) and stirred for 1 h at room temperature. Afterwards, the mixture was quenched with saturated $NaHCO_3$ solution (10 mL) and DCM (15 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 50:1) and the pure product was obtained as a colorless oil (0.68 g, 1.18 mmol, 77%).

**TLC** (silica, CyHex:EtOAc = 50:1): $R_f$ = 0.22. $[\alpha]_D^{20}$ = +4.0° (c = 1.00, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.74–7.65 (m, 5H, 5xCH-Ar), 7.46–7.24 (m, 10H, 10xCH-Ar), 4.38 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.34 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn´), 4.05–4.01 (m, 1H, H-3), 3.95–3.90 (m, 1H, H-1*), 3.81 (dd, $^2J$ = 11.3 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.4 Hz, 1H, H-4), 3.76 (dd, $^2J$ = 11.3 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 4.6 Hz, 1H, H-4´), 3.44–3.38 (m, 2H, H-1, H-1´), 1.68–1.64 (m, 1H, H-2), 1.63–1.58 (m, 1H, H-2*), 1.49–1.44 (m, 1H, H-3*), 1.42 (s, 3H, $CH_3$), 1.37 (s, 3H, $CH_3$), 1.33–1.25 (m, 6H, H-2*´, H-3*´, H-4*, H-5*), 1.04 (s, 9H, 3x$CH_3$-TBDPS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1–128.0 (15xCH-Ar, 3x$C_q$-Ar), 98.2 ($C_q$), 73.6 ($CH_2$-Bn), 72.0 (C-3), 70.1 (C-1*), 67.7 (C-1), 66.2 (C-4), 41.0 (C-2), 33.8 (C-2*), 32.5 (C-4*), 30.3 ($CH_3$), 27.2 (3x$CH_3$-TBDPS), 25.3 (C-3*), 23.3 (C-5*), 20.2 ($CH_3$), 19.8 ($C_q$-TBDPS), 14.5 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{36}H_{50}O_4SiH^+$ 575.3551, found 575.3546. For NMR-spectra see p. 371.

**Synthesis of Compound 246**

**((4*R*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)-methanol**




**245** **246**

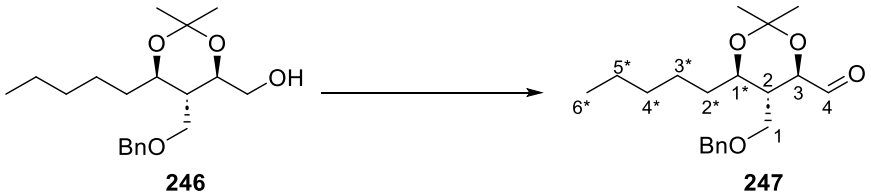
$C_{20}H_{32}O_4$
M = 336.47 g/mol

A solution of TBDPS ether **245** (0.68 g, 1.18 mmol, 1 equiv) in THF (20 mL) was cooled to 0 °C. TBAF (1M in THF; 3.54 mL, 3.54 mmol, 3 equiv) was added dropwise, and the mixture was stirred for 2 h at room temperature. Subsequently, the mixture was quenched with saturated $NH_4Cl$-solution (10 mL) and DCM (20 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 6:1) and the pure product was obtained as a colorless oil (0.31 g, 0.93 mmol, 79%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.18. $[\alpha]_D^{20}$ = +25.0° (c = 0.56, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.39–7.26 (m, 5H, 5xCH-Bn), 4.46 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.42 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 3.98 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.5 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 5.2 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 2.9 Hz, 1H, H-3), 3.86 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.5 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.1 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.5 Hz, 1H, H-1*), 3.68 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}4',\ OH}$ = 6.6 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 3.0 Hz, 1H, H-4´), 3.53 (ddd, $^2J$ = 11.6 Hz, $^3J_{H\text{-}4,\ OH}$ = 6.2 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 5.1 Hz, 1H, H-4), 3.44–3.40 (m, 2H, H-1, H-1´), 2.14 (dd, $^3J_{OH,\ H\text{-}4}$ = 6.2 Hz, $^3J_{OH,\ H\text{-}4'}$ = 6.6 Hz, 1H, OH), 1.64–1.51 (m, 2H, H-2, H-2*), 1.48–1.40 (m, 4H, H-3*, $CH_3$), 1.34 (s, 3H, $CH_3$), 1.33–1.15 (m, 6H, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (125 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.8 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (CH-Bn), 128.2 (2xCH-Bn), 98.5 ($C_q$), 73.8 ($CH_2$-Bn), 72.1 (C-3), 69.8 (C-1*), 67.8 (C-1), 64.4 (C-4), 41.0 (C-2), 33.8 (C-2*), 32.4 (C-4*), 30.2 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 20.2 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{20}H_{32}O_4Na^+$ 359.2193, found 359.2192. For NMR-spectra see p. 373.

**Synthesis of Compound 247**

**(4*R*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane-4-carbaldehyde**




**246** **247**

$C_{20}H_{30}O_4$
M = 334.46 g/mol

To a Schlenk flask charged with sulfur trioxide pyridine complex (0.47 g, 2.94 mmol, 3 equiv) were added DCM (6 mL), DMSO (0.70 mL, 9.81 mmol, 10 equiv) and DIPEA (0.67 mL, 3.92 mmol, 4 equiv). The mixture was cooled to 0 °C and a solution of alcohol **246** (0.33 g, 0.98 mmol, 1 equiv) in DCM (4 mL) was added. After stirring for 20 min at 0 °C the reaction mixture was washed with saturated $NaHCO_3$-solution (15 mL). The organic phase was further washed with saturated $CuSO_4$-solution (2 x 10 mL) before it was finally washed with saturated $NH_4Cl$-solution (10 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless liquid (0.32 g, 0.98 mmol, quant.).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.44. $[\alpha]_D^{20}$ = +60.2° (c = 1.08, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.53 (d, $^3J_{H\text{-}4,\ H\text{-}3}$ = 2.0 Hz, 1H, H-4), 7.37–7.26 (m, 5H, 5xCH-Bn), 4.49 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.41 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.34 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 2.0 Hz, 1H, H-3), 3.95 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.3 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.5 Hz, 1H, H-1*), 3.55 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.3 Hz, 1H, H-1), 3.48 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 1.70 (dddd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 3.3 Hz, 1H, H-2), 1.65–1.56 (m, 1H, H-2*), 1.49–1.42 (m, 1H, H-3*), 1.45 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.40 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.34–1.23 (m, 6H, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*). **$^{13}$C-NMR** (125 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 200.6 (C-4), 138.8 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (CH-Bn), 128.1 (2xCH-Bn), 98.9 ($C_q$), 75.4 (C-3), 73.8 ($CH_2$-Bn), 69.4 (C-1*), 66.8 (C-1), 40.2 (C-2), 33.7 (C-2*), 32.3 (C-4*), 30.0 ($CH_3$), 25.1 (C-3*), 23.2 (C-5*), 20.3 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{30}O_4H^+$ 335.2217, found 335.2213. For NMR-spectra see p. 375.

**Synthesis of Compound 248**

**(4*R*,5*R*,6*S*)-5-((benzyloxy)methyl)-2,2-dimethyl-4-pentyl-6-vinyl-1,3-dioxane**


**247** **248**

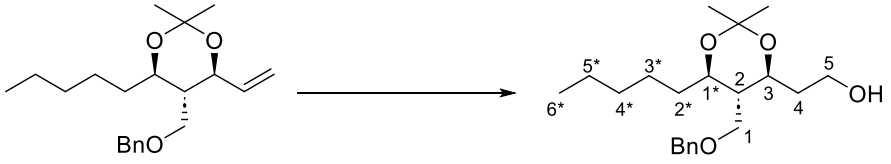
$C_{21}H_{32}O_3$
M = 332.48 g/mol

A mixture of $Ph_3PMeBr$ (489 mg, 1.37 mmol, 1.5 equiv) in THF (12 mL) was cooled to −78 °C and *n*-BuLi (2.5M in hexane; 0.55 mL, 1.37 mmol, 1.5 equiv) was added dropwise. The mixture was stirred for 30 min at 0 °C before a solution of aldehyde **247** (305 mg, 0.91 mmol, 1 equiv) in THF (6 mL) was added. After stirring for 1 h at 0 °C the reaction was quenched with saturated $NH_4Cl$-solution (15 mL). DCM (20 mL) was added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 20 mL), the combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 30:1) and the pure product was obtained as a colorless oil (212 mg, 0.64 mmol, 70%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.28. $[\alpha]_D^{20}$ = +25.5° (c = 1.02, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 5.72 (ddd, $^3J_{H\text{-}4,\ H\text{-}5\text{-}E}$ = 17.5 Hz, $^3J_{H\text{-}4,\ H\text{-}5\text{-}Z}$ = 10.3 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 7.4 Hz, 1H, H-4), 5.22 (ddd, $^3J_{H\text{-}5\text{-}E,\ H\text{-}4}$ = 17.2 Hz, $^2J_{H\text{-}5\text{-}E,\ H\text{-}5\text{-}Z}$ = 1.8 Hz, $^3J_{H\text{-}5\text{-}E,\ H\text{-}3}$ = 0.9 Hz, 1H, H-5-*E*), 5.16 (ddd, $^3J_{H\text{-}5\text{-}Z,\ H\text{-}4}$ = 10.3 Hz, $^2J_{H\text{-}5\text{-}E,\ H\text{-}5\text{-}Z}$ = 1.9 Hz, $^3J_{H\text{-}5\text{-}Z,\ H\text{-}3}$ = 0.7 Hz, 1H, H-5-*Z*), 4.43–4.37 (m, 3H, H-3, 2x $CH_2$-Bn), 4.01 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.1 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 2.5 Hz, 1H, H-1*), 3.46 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 2.8 Hz, 1H, H-1), 3.39 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 3.0 Hz, 1H, H-1´), 1.65–1.60 (m, 1H, H-2*), 1.49–1.42 (m, 1H, H-3*), 1.46 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.33 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.32–1.20 (m, 7H, H-2, H-2*´, H-3*´, H-4*, H-5*), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$(ppm) = 139.2 ($C_q$-Bn), 138.2 (C-4), 128.8 (2xCH-Bn), 128.1 (2xCH-Bn), 128.1 (CH-Bn), 118.0 (C-5), 98.4 ($C_q$), 73.7 ($CH_2$-Bn), 73.0 (C-3), 70.1 (C-1*), 67.4 (C-1), 45.0 (C-2), 33.7 (C-2*), 32.4 (C-4*), 30.4 ($CH_3$), 25.2 (C-3*), 23.2 (C-5*), 20.3 ($CH_3$), 14.4 (C-6*). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{32}O_3Na^+$ 355.2244, found 355.2216. For NMR-spectra see p. 377.

**Synthesis of Compound 238**

**2-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)ethan-1-ol**




**248** **238**

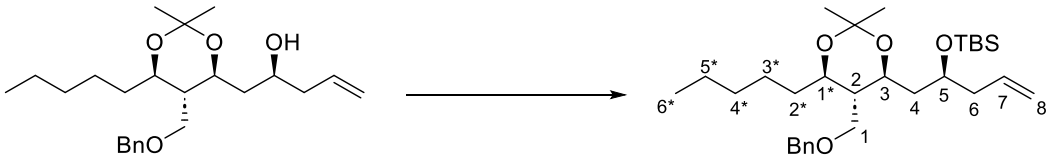
$C_{21}H_{34}O_4$
M = 350.50 g/mol

A stirred solution of 9-BBN (0.5M in THF, 0.85 mL, 0.42 mmol, 2 equiv) was cooled to 0 °C. Terminal olefin **248** (70.0 mg, 0.21 mmol, 1 equiv) in THF (1 mL) was added dropwise at 0 °C and the mixture was stirred at this temperature for 90 min. Afterwards, the reaction mixture was warmed to room temperature and stirring was continued for 2.5 h. The mixture was again cooled to 0 °C and aqueous NaOH (6M, 0.42 mL) and $H_2O_2$ (35% in $H_2O$, 0.18 mL) were added. After stirring for 20 min at 0 °C, the aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless oil (69.0 mg, 0.20 mmol, 93%).

For analytical data see p. 121.

**Synthesis of Compound 251**

**(((*S*)-1-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)pent-4-en-2-yl)oxy)(*tert*-butyl)dimethylsilane**




**320** **251**

$C_{30}H_{52}SiO_4$
M = 504.83 g/mol

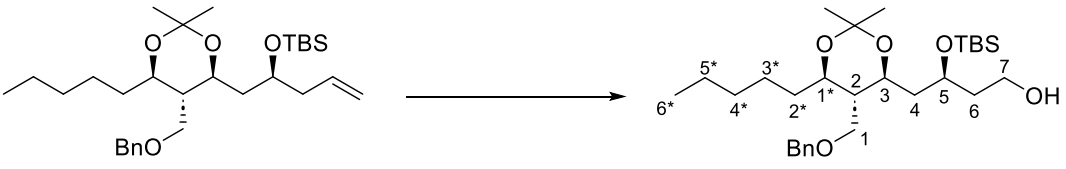
To a stirred solution of secondary alcohol **320** (110 mg, 0.28 mmol, 1 equiv) in DCM (1 mL) was added imidazole (58.0 mg, 0.85 mmol, 3 equiv) and TBSCl (127 mg, 0.85 mmol, 3 equiv). The mixture was stirred for 6 h at room temperature before water (5 mL) and DCM (5 mL) were added. The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica,

CyHex:EtOAc = 40:1) and the pure product was obtained as a colorless oil (133 mg, 0.26 mmol, 94%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.29. $[\alpha]_D^{20}$ = +5.1° (c = 0.98, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.26 (m, 5H, 5xCH-Bn), 5.88 (dddd, $^3J_{H\text{-}7,\ H\text{-}8\text{-}E}$ = 17.0 Hz, $^3J_{H\text{-}7,\ H\text{-}8\text{-}Z}$ = 10.5 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 7.7 Hz, $^3J_{H\text{-}7,\ H\text{-}6'}$ = 6.5 Hz, 1H, H-7), 5.06–4.99 (m, 2H, H-8-*E*, H-8-*Z*), 4.44 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.37 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.01–3.94 (m, 2H, H-3, H-5), 3.90 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*\prime}}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 2.6 Hz, 1H, H-1*), 3.41 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.0 Hz, 2H, H-1), 2.31 (ddddd, $^2J$ = 14.0 Hz, $^3J_{H\text{-}6',\ H\text{-}7}$ = 6.2 Hz, $^3J_{H\text{-}6',\ H\text{-}5}$ = 4.6 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}E}$ = 1.5 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}Z}$ = 1.5 Hz, 1H, H-6´), 2.12 (ddddd, $^2J$ = 13.9 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 8.0 Hz, $^3J_{H\text{-}6,\ H\text{-}5}$ = 5.9 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}E}$ = 1.1 Hz, $^4J_{H\text{-}6,\ H\text{-}8\text{-}Z}$ = 1.1 Hz, 1H, H-6), 1.84 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 9.0 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 2.4 Hz, 1H, H-4), 1.62–1.56 (m, 1H, H-2*), 1.56–1.49 (m, 1H, H-4´), 1.49–1.38 (m, 4H, H-3*, $CH_3$), 1.36–1.16 (m, 10H, H-2, H-2*´, H-3*´, H-4*, H-5*, $CH_3$), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.0 Hz, 3H, H-6*), 0.88 (s, 9H, 3x$CH_3$-TBS), 0.05 (s, 3H, $CH_3$-TBS), 0.05 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 136.3 (C-7), 128.8 (2xCH-Bn), 128.1 (2xCH-Bn), 128.0 (CH-Bn), 116.9 (C-8), 98.0 ($C_q$), 73.8 ($CH_2$-Bn), 70.5 (C-1*), 69.3 (C-5), 67.8 (C-3), 67.8 (C-1), 45.7 (C-2), 41.4 (C-4), 41.3 (C-6), 33.8 (C-2*), 32.5 (C-4*), 30.4 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.3 (C-3*), 23.3 (C-5*), 20.1 ($CH_3$), 18.5 ($C_q$-TBS), 14.5 (C-6*), −4.2 ($CH_3$-TBS), −4.3 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{30}H_{52}SiO_4H^+$ 505.3708, found 505.3702. For NMR-spectra see p. 379.

### Synthesis of Compound 253

**(*S*)-4-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)-3-((*tert*-butyldimethylsilyl)oxy)butan-1-ol**




**251** **253**

$C_{29}H_{52}SiO_5$
M = 508.81 g/mol

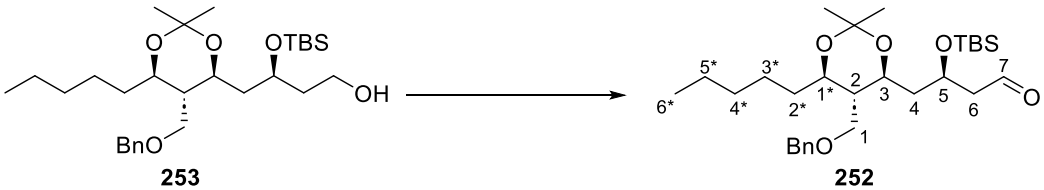
A stirred solution of alkene **251** (120 mg, 0.23 mmol, 1 equiv) in MeOH/DCM (1:1, 1.6 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 2 min until a slightly blue color persisted. The excess ozone was then purged with argon for 2 min and $NaBH_4$ (44.0 mg, 1.15 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 15 h at room temperature. $NH_4Cl$-solution (5 mL) and DCM (5 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM

(3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless liquid (94 mg, 0.18 mmol, 80%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.33. $[\alpha]_D^{20}$ = −37.0° (c = 0.54, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 4.45 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.40 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.17–4.11 (m, 1H, H-5), 3.94 (ddd, $^3J_{H\text{-}3,\,H\text{-}2}$ = 10.2 Hz, $^3J_{H\text{-}3,\,H\text{-}4}$ = 10.2 Hz, $^3J_{H\text{-}3,\,H\text{-}4'}$ = 2.2 Hz, 1H, H-3), 3.89 (ddd, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^{*'}}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^*}$ = 2.6 Hz, 1H, H-1*), 3.74 (dddd, $^2J$ = 12.3 Hz, $^3J_{H\text{-}7,\,H\text{-}6}$ = 8.3 Hz, $^3J_{H\text{-}7,\,H\text{-}6'}$ = 4.1 Hz, $^3J_{H\text{-}7,\,OH}$ = 4.1 Hz, 1H, H-7), 3.70–3.63 (m, 1H, H-7´), 3.43 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 3.2 Hz, 2H, H-1), 2.42 (d, $^3J_{OH,\,H\text{-}7}$ = 4.1 Hz, 1H, OH), 1.93 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}4',\,H\text{-}5}$ = 9.5 Hz, $^3J_{H\text{-}4',\,H\text{-}3}$ = 2.2 Hz, 1H, H-4´), 1.84 (dddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}6,\,H\text{-}7}$ = 8.1 Hz, $^3J_{H\text{-}6,\,H\text{-}5}$ = 4.5 Hz, $^3J_{H\text{-}6,\,H\text{-}7'}$ = 4.5 Hz, 1H, H-6), 1.66–1.54 (m, 3H, H-2*, H-4´, H-6´), 1.47–1.41 (m, 1H, H-3*), 1.39 (s, 3H, $CH_3$), 1.34–1.20 (m, 10H, H-2, H-2*´, H-3*´, H-4*, H-5*, $CH_3$), 0.92–0.85 (m, 12H, H-6*, 3x$CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 98.1 ($C_q$), 73.8 ($CH_2$-Bn), 70.4 (C-1*), 69.6 (C-5), 67.8 (C-3), 67.7 (C-1), 60.6 (C-7), 45.6 (C-2), 41.2 (C-4), 37.7 (C-6), 33.8 (C-2*), 32.4 (C-4*), 30.3 ($CH_3$), 26.2 (3x$CH_3$-TBS), 25.3 (C-3*), 23.2 (C-5*), 20.1 ($CH_3$), 18.4 ($C_q$-TBS), 14.4 (C-6*), −4.2 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{29}H_{52}SiO_5H^+$ 509.3657, found 509.3659. For NMR-spectra see p. 381.

### Synthesis of Compound 252

**(*R*)-4-((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)-3-((*tert*-butyldimethylsilyl)oxy)butanal**




$C_{29}H_{50}SiO_5$
M = 506.80 g/mol

To a Schlenk flask charged with sulfur trioxide pyridine complex (75.0 mg, 0.47 mmol, 3 equiv) were added DCM (1 mL), DMSO (0.11 mL, 1.57 mmol, 10 equiv) and DIPEA (0.11 mL, 0.63 mmol, 4 equiv). The mixture was cooled to 0 °C and a solution of alcohol **253** (80.0 mg, 0.16 mmol, 1 equiv) in DCM (1 mL) was added. After stirring for 20 min at 0 °C the reaction mixture was washed with saturated $NaHCO_3$-solution (2 mL). The organic phase was further

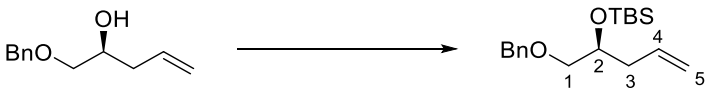
washed with saturated $CuSO_4$-solution (2 x 1 mL) before it was finally washed with saturated $NH_4Cl$-solution (2 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless liquid (79.0 mg, 0.16 mmol, quant.).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.43. $[\alpha]_D^{20}$ = −6.7° (c = 0.90, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.75 (dd, $^3J_{H\text{-}7,\ H\text{-}6}$ = 3.3 Hz, $^3J_{H\text{-}7,\ H\text{-}6'}$ = 1.8 Hz, 1H, H-7), 7.36–7.27 (m, 5H, 5xCH-Bn), 4.46–4.41 (m, 2H, H-5, $CH_2$-Bn), 4.39 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 3.98 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 10.1 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 10.1 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 2.3 Hz, 1H, H-3), 3.88 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.0 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 2.5 Hz, 1H, H-1*), 3.40 (d, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.1 Hz, 2H, H-1), 2.57 (ddd, $^2J$ = 15.6 Hz, $^3J_{H\text{-}6',\ H\text{-}5}$ = 4.4 Hz, $^3J_{H\text{-}6',\ H\text{-}7}$ = 1.9 Hz, 1H, H-6´), 2.43 (ddd, $^2J$ = 15.6 Hz, $^3J_{H\text{-}6,\ H\text{-}5}$ = 7.3 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 3.3 Hz, 1H, H-6), 1.88 (ddd, $^2J$ = 13.9 Hz, $^3J_{H\text{-}4',\ H\text{-}5}$ = 8.9 Hz, $^3J_{H\text{-}4',\ H\text{-}3}$ = 2.3 Hz, 1H, H-4´), 1.67 (ddd, $^2J$ = 13.7 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 9.8 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 3.6 Hz, 1H, H-4), 1.60–1.55 (m, 1H, H-2*), 1.47–1.41 (m, 1H, H-3*), 1.40 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.33–1.20 (m, 10H, H-2, H-2*´, H-3*´, H-4*, H-5*, $CH_3$), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.86 (s, 9H, 3x$CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.05 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 203.0 (C-7), 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 98.1 ($C_q$), 73.8 ($CH_2$-Bn), 70.4 (C-1*), 67.6 (C-1), 67.6 (C-3), 66.1 (C-5), 50.6 (C-6), 45.5 (C-2), 41.9 (C-4), 33.8 (C-2*), 32.4 (C-4*), 30.3 ($CH_3$), 26.1 (3x$CH_3$-TBS), 25.3 (C-3*), 23.2 (C-5*), 20.1 ($CH_3$), 18.4 ($C_q$-TBS), 14.4 (C-6*), −4.1 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{29}H_{50}SiO_5Na^+$ 529.3320, found 529.3326. For NMR-spectra see p. 383.

## 6.3.2 Contributions to the Eastern Fragment

### Synthesis of Compound 257

**(2*S*)-((1-(benzyloxy)pent-4-en-2-yl)oxy)(*tert*-butyl)dimethylsilane**




**191** **257**

$C_{18}H_{30}O_2Si$
M = 306.52 g/mol

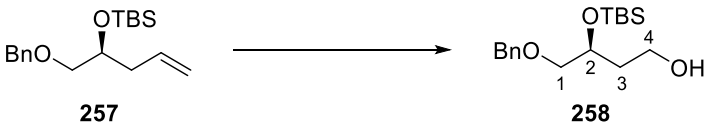
To a stirred solution of alcohol **191** (4.33 g, 22.5 mmol, 1 equiv) in DCM (45 mL) were added imidazole (3.07 g, 45.0 mmol, 2 equiv) and TBSCl (6.79 g, 45.0 mmol, 2 equiv). The mixture was stirred for 6 h at room temperature and was then quenched with water (40 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 40 mL). The

combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1) and the pure product was obtained as a colorless liquid (6.76 g, 22.0 mmol, 98%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.32. $[\alpha]_D^{20}$ = +0.7° (c = 1.5, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.25 (m, 1H, CH-Bn), 5.84 (ddt, $^3J_{H\text{-}4,\ H\text{-}5\text{-}E}$ = 17.3 Hz, $^3J_{H\text{-}4,\ H\text{-}5\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 7.2 Hz, 1H, H-4), 5.08–5.01 (m, 2H, H-5-*Z*, H-5-*E*), 4.50 (br s, 2H, $CH_2$-Bn), 3.91–3.86 (m, 1H, H-2), 3.40 (br s, 1H, H-1), 3.39 (br s, 1H, H-1´), 2.34 (dddt, $^2J$ = 13.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 6.8 Hz, $^3J_{H\text{-}3,\ H\text{-}2}$ = 5.4 Hz, $^4J_{H\text{-}3,\ H\text{-}5}$ = 1.4 Hz, 1H, H-3), 2.22 (dddt, $^2J$ = 13.9 Hz, $^3J_{H\text{-}3',\ H\text{-}4}$ = 7.5 Hz, $^3J_{H\text{-}3',\ H\text{-}2}$ = 6.2 Hz, $^4J_{H\text{-}3',\ H\text{-}5}$ = 1.2 Hz, 1H, H-3´), 0.88 (s, 9H, 3x$CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS), 0.05 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.3 ($C_q$-Bn), 135.7 (C-4), 128.8 (2xCH-Bn), 128.1 (2xCH-Bn), 128.0 (CH-Bn), 117.2 (C-5), 74.9 (C-1), 73.8 ($CH_2$-Bn), 71.8 (C-2), 39.9 (C-3), 26.2 (3x$CH_3$-TBS), 18.6 ($C_q$-TBS), −4.2 ($CH_3$-TBS), −4.4 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{30}SiO_2H^+$ 307.2088, found 307.2090. For NMR-spectra see p. 385.

**Synthesis of Compound 258**

**(3*S*)-4-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)butan-1-ol**




**257** **258**

$C_{17}H_{30}O_3Si$
M = 310.51 g/mol

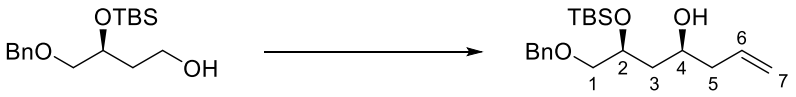
A stirred solution of alkene **257** (6.70 g, 21.9 mmol, 1 equiv) in MeOH/DCM (1:1, 110 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 25 min until a slightly blue color persisted. The excess ozone was then purged with argon for 5 min and $NaBH_4$ (4.13 g, 109 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 16 h at room temperature. $NH_4Cl$-solution (100 mL) and DCM (100 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 150 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 6:1). The pure product was obtained as a colorless liquid (6.38 g, 20.6 mmol, 94%).

**TLC** (silica, CyHex:EtOAc = 6:1): $R_f$ = 0.17. $[\alpha]_D^{20}$ = −17.5° (c = 1.26, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 4.52 (br s, 2H, $CH_2$-Bn), 4.08–4.02 (m, 1H, H-2), 3.74–3.66 (m, 2H, H-4, H-4´), 3.48 (dd, $^2J$ = 9.6 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.3 Hz,

1H, H-1), 3.43 (dd, $^2J$ = 9.6 Hz, $^3J_{H\text{-}1',\,H\text{-}2}$ = 5.9 Hz, 1H, H-1´), 2.13 (t, $^3J_{OH,\,H\text{-}4}$ = 5.3 Hz, 1H, OH), 1.84 (dddd, $^2J$ = 14.3 Hz, , $^3J_{H\text{-}3,\,H\text{-}2}$ = 7.5 Hz, $^3J_{H\text{-}3,\,H\text{-}4}$ = 5.6 Hz, $^3J_{H\text{-}3,\,H\text{-}4'}$ = 4.6 Hz, 1H, H-3), 1.72 (dddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}3',\,H\text{-}2}$ = 6.6 Hz, $^3J_{H\text{-}3',\,H\text{-}4}$ = 5.6 Hz, $^3J_{H\text{-}3',\,H\text{-}4'}$ = 4.9 Hz, 1H, H-3´), 0.88 (s, 9H, 3x$CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 75.0 (C-1), 73.9 ($CH_2$-Bn), 70.8 (C-2), 60.1 (C-4), 37.6 (C-3), 26.1 (3x$CH_3$-TBS), 18.5 ($C_q$-TBS), −4.2 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{31}SiO_3H^+$ 311.2037, found 311.2034. For NMR-spectra see p. 387.

**Synthesis of Compound 259**

**(4*S*,6*S*)-7-(benzyloxy)-6-((*tert*-butyldimethylsilyl)oxy)hept-1-en-4-ol**




**258** **259**

$C_{20}H_{34}SiO_3$
M = 350.57 g/mol

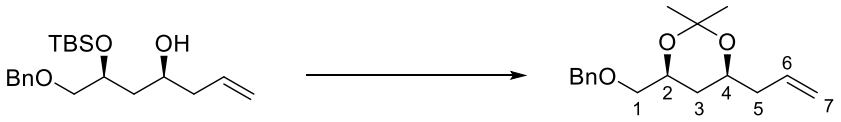
To an oven-dried pressure tube charged with $[Ir(cod)Cl]_2$ (0.34 g, 0.51 mmol, 0.025 equiv), (*S*)-Cl,MeO-BIPHEP (0.66 g, 1.01 mol, 0.05 equiv), $Cs_2CO_3$ (1.32 g, 4.06 mmol, 0.2 equiv) and 4-chloro-3-nitrobenzoic acid (0.41 g, 2.03 mmol, 0.1 equiv) were added THF (50 mL) and ally acetate (22 mL, 203 mmol, 10 equiv). The mixture was heated to 90 °C and stirred for 30 min before a solution of alcohol **258** (6.30 g, 20.3 mmol, 1 equiv) in THF (50 mL) was added. The tube was closed with a screw cap and stirred at 110 °C for 48 h. After completion of the reaction, the reaction mixture was evaporated onto silica gel and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a yellowish oil (5.41 g, 15.4 mmol, 76%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 6:1): $R_f$ = 0.34. $[\alpha]_D^{20}$ = −16.1 (c = 1.18, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 5.84 (ddt, $^3J_{H\text{-}6,\,H\text{-}7\text{-}E}$ = 17.3 Hz, $^3J_{H\text{-}6,\,H\text{-}7\text{-}Z}$ = 10.2 Hz, $^3J_{H\text{-}6,\,H\text{-}5}$ = 7.1 Hz, 1H, H-6), 5.13–5.04 (m, 2H, H-7-*Z*, H-7-*E*), 4.54–4.48 (m, 2H, $CH_2$-Bn), 4.06 (dddd, $^3J_{H\text{-}2,\,H\text{-}3}$ = 7.7 Hz, $^3J_{H\text{-}2,\,H\text{-}3'}$ = 5.1 Hz, $^3J_{H\text{-}2,\,H\text{-}1}$ = 5.1 Hz, $^3J_{H\text{-}2,\,H\text{-}1'}$ = 5.1 Hz, 1H, H-2), 3.83 (m, 1H, H-4), 3.47 (dd, $^2J$ = 9.7 Hz, $^3J_{H\text{-}1,\,H\text{-}2}$ = 5.0 Hz, 1H, H-1), 3.41 (dd, $^2J$ = 9.7 Hz, $^3J_{H\text{-}1',\,H\text{-}2}$ = 5.3 Hz, 1H, H-1´), 2.80 (d, $^3J_{OH,\,H\text{-}4}$ = 2.6 Hz, 1H, OH), 2.26–2.14 (m, 2H, H-5), 1.76 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}3',\,H\text{-}2}$ = 5.0 Hz, $^3J_{H\text{-}3',\,H\text{-}4}$ = 2.9 Hz, 1H, H-3´), 1.58 (ddd, $^2J$ = 14.2 Hz, $^3J_{H\text{-}3,\,H\text{-}4}$ = 8.9 Hz, $^3J_{H\text{-}3,\,H\text{-}2}$ = 7.7 Hz, 1H, H-3), 0.89 (s, 9H, 3x$CH_3$-TBS), 0.10 (s, 3H, $CH_3$-TBS), 0.08 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.9 ($C_q$-Bn), 135.9 (C-6), 128.8 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 117.5 (C-7), 75.4 (C-1), 73.9 ($CH_2$-Bn), 71.7 (C-2), 69.4 (C-4), 42.7 (C-5), 41.8 (C-3), 26.2 (3x$CH_3$-TBS),

18.5 ($C_q$-TBS), −4.0 ($CH_3$-TBS), −4.6 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{34}SiO_3H^+$ 351.2350, found 351.2351. For NMR-spectra see p. 389.

**Synthesis of Compound 260**

**(4*S*,6*S*)-4-Allyl-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxane**




**259** **260**

$C_{17}H_{24}O_3$
M = 276.38 g/mol

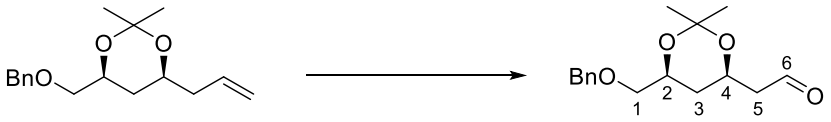
To a solution of secondary alcohol **259** (5.40 g, 15.4 mmol, 1 equiv) in MeOH (155 mL) was added *p*-toluenesulfonic acid monohydrate (290 mg, 1.54 mmol, 0.1 equiv) and the mixture was stirred for 90 min at room temperature. The mixture was diluted with 2,2-dimethoxypropane (28 mL, 231 mmol, 15 equiv) and was stirred for 60 min at room temperature. Subsequently, the mixture was evaporated *in vacuo* and the residue was dissolved in 2,2-dimethoxypropane (93 mL, 769 mmol, 50 equiv) again. After stirring another 2 h, pyridine (124 µL, 1.54 mmol, 0.1 equiv) was added and the mixture was stirred for another 20 min. After that, the mixture was diluted with DCM (300 mL) and quenched with $NaHCO_3$-solution (200 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 150 mL). The combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1) and the pure product was obtained as a yellowish oil (4.16 g, 15.1 mmol, 98%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.35. $[\alpha]_D^{20}$ = −7.3° (c = 1.11, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.25 (m, 5H, 5xCH-Bn), 5.86–5.76 (m, 1H, H-6), 5.11–5.02 (m, 2H, H-7-*Z*, H-7-*E*), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.07 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.6 Hz, 1H, H-2), 3.91 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.6 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 6.3 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 6.3 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-4), 3.47 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.9 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 2.27 (ddddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 6.5 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 6.5 Hz, $^4J_{H\text{-}5,\ H\text{-}7\text{-}Z}$ = 1.5 Hz, $^4J_{H\text{-}5,\ H\text{-}7\text{-}E}$ = 1.5 Hz, 1H, H-5), 2.18–2.11 (m, 1H, H-5´), 1.52 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.44 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.18 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 135.0 (C-6), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 117.2 (C-7), 99.0 ($C_q$), 74.4 (C-1), 73.8 ($CH_2$-Bn), 69.0 (C-2), 68.8 (C-4), 41.4 (C-5), 33.6 (C-3), 30.4 ($CH_3$), 20.1 ($CH_3$). **HRMS**

**(ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}O_3H^+$ 277.1798, found 277.1799. For NMR-spectra see p. 391.

**Synthesis of Compound 157**

**2-((4*R*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)acetaldehyde**




**260** **157**

$C_{16}H_{22}O_4$
M = 278.35 g/mol

Procedure 1:

A stirred solution of alkene **260** (440 mg, 1.59 mmol, 1 equiv) in MeOH/DCM (1:1, 3 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 8 min until a slightly blue color persisted. The excess ozone was then purged with argon for 5 min and $Me_2S$ (0.58 mL, 7.96 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 2.5 h at room temperature. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1). The pure product was obtained as a colorless liquid (319 mg, 1.15 mmol, 72%).

Procedure 2:

To a solution of alkene **260** (1.00 g, 3.26 mmol, 1 equiv) in acetone/$H_2O$ (10:1; 40 mL) was added NMO (0.85 g, 7.24 mmol, 2 equiv) and a solution of $OsO_4$ (4% in $H_2O$, 1.15 mL, 0.18 mmol, 0.05 equiv). The mixture was stirred for 24 h at room temperature. The reaction mixture was quenched with saturated $Na_2S_2O_3$-solution (50 mL) and diluted with DCM (50 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was redissolved in a solution of $Pb(OAc)_4$ (1.84 g, 4.16 mmol, 1.15 equiv) in benzene (50 mL) and stirred for 10 min before it was filtered through a glass filter frit. The solvent was evaporated *in vacuo* and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1). The pure aldehyde was obtained as a colorless oil (0.87 g, 3.13 mmol, 86%).

**TLC** (silica, CyHex:EtOAc = 4:1): $R_f$ = 0.20. $[\alpha]_D^{20}$ = −3.9° (c = 1.02, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.73 (dd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 2.6 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 1.6 Hz, 1H, H-6), 7.37–7.27 (m, 5H, 5xCH-Bn), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.52 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 4.44 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.9 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 7.4 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 4.7 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ =

2.6 Hz, 1H, H-4), 4.13 (dddd, $^{3}J_{\text{H-2, H-3-ax}}$ = 11.7 Hz, $^{3}J_{\text{H-2, H-1}}$ = 5.7 Hz, $^{3}J_{\text{H-2, H-1´}}$ = 4.4 Hz, $^{3}J_{\text{H-2, H-3-eq}}$ = 2.5 Hz, 1H, H-2), 3.49 (dd, $^{2}J$ = 10.1 Hz, $^{3}J_{\text{H-1, H-2}}$ = 5.7 Hz, 1H, H-1), 3.40 (dd, $^{2}J$ = 10.1 Hz, $^{3}J_{\text{H-1´, H-2}}$ = 4.5 Hz, 1H, H-1´), 2.55 (ddd, $^{2}J$ = 16.5 Hz, $^{3}J_{\text{H-5, H-4}}$ = 7.7 Hz, $^{3}J_{\text{H-5, H-6}}$ = 2.6 Hz, 1H, H-5), 2.46 (ddd, $^{2}J$ = 16.6 Hz, $^{3}J_{\text{H-5´, H-4}}$ = 4.7 Hz, $^{3}J_{\text{H-5´, H-6}}$ = 1.6 Hz, 1H, H-5´), 1.59 (ddd, $^{2}J$ = 12.8 Hz, $^{3}J_{\text{H-3-eq, H-2}}$ = 2.6 Hz, $^{3}J_{\text{H-3-eq, H-4}}$ = 2.6 Hz, 1H, H-3-eq), 1.47 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.30 (ddd, $^{2}J$ = 12.8 Hz, $^{3}J_{\text{H-3-ax, H-2}}$ = 11.7 Hz, $^{3}J_{\text{H-3-ax, H-4}}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 201.6 (C-6), 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 99.4 ($C_q$), 74.1 (C-1), 73.9 ($CH_2$-Bn), 68.9 (C-2), 65.0 (C-4), 50.5 (C-5), 33.8 (C-3), 30.3 ($CH_3$), 20.0 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{22}O_4Na^+$ 301.1410, found 301.1412. For NMR-spectra see p. 393.

**Synthesis of Compound 158**

**2-((4*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)ethan-1-ol**


**260** **158**

$C_{16}H_{24}O_4$
M = 280.36 g/mol

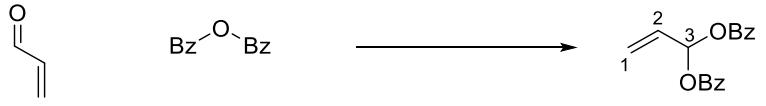
A stirred solution of alkene **260** (1.00 g, 3.62 mmol, 1 equiv) in MeOH/DCM (1:1, 45 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 10 min. The excess ozone was then purged with argon for 3 min and $NaBH_4$ (0.68 g, 18.1 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 3 h at room temperature. $NH_4Cl$-solution (50 mL) and DCM (50 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 50 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 2:1). The pure product was obtained as a colorless viscous liquid (0.82 mg, 2.92 mmol, 81%).

**TLC** (silica, CyHex:EtOAc = 1:1): $R_f$ = 0.38. $[\alpha]_D^{20}$ = −14.3° (c = 1.12, DCM). **$^{1}$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.38–7.32 (m, 4H, 4xCH-Bn), 7.32–7.27 (m, 1H, CH-Bn), 4.55 (d, $^{2}J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.52 (d, $^{2}J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.15–4.08 (m, 2H, H-2, H-4), 3.74–3.68 (m, 2H, H-6, H-6´), 3.49 (dd, $^{2}J$ = 10.1 Hz, $^{3}J_{\text{H-1, H-2}}$ = 5.8 Hz, 1H, H-1), 3.39 (dd, $^{2}J$ = 10.0 Hz, $^{3}J_{\text{H-1´, H-2}}$ = 4.4 Hz, 1H, H-1´), 2.35 (t, $^{3}J_{\text{OH, H-6}}$ = 5.3 Hz, 1H, OH), 1.73–1.66 (m, 2H, H-5, H-5´), 1.50 (ddd, $^{2}J$ = 12.9 Hz, $^{3}J_{\text{H-3-eq, H-2}}$ = 2.6 Hz, $^{3}J_{\text{H-3-eq, H-4}}$ = 2.6 Hz, 1H, H-3-eq), 1.47 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.37 (d, $^{4}J$ = 0.9 Hz, 3H, $CH_3$), 1.31 (ddd, $^{2}J$ = 12.9 Hz,

$^{3}J_{\text{H-3-ax, H-2}}$ = 11.7 Hz, $^{3}J_{\text{H-3-ax, H-4}}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 99.2 ($C_q$), 74.3 (C-1), 73.8 ($CH_2$-Bn), 69.1 (C-4), 69.0 (C-2), 60.8 (C-6), 39.1 (C-5), 33.9 (C-3), 30.5 ($CH_3$), 20.1 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{24}O_4H^+$ 281.1747, found 281.1750. For NMR-spectra see p. 395.

**Synthesis of Compound 180**

**prop-2-ene-1,1-diyl dibenzoate**




**261** **262** **180**

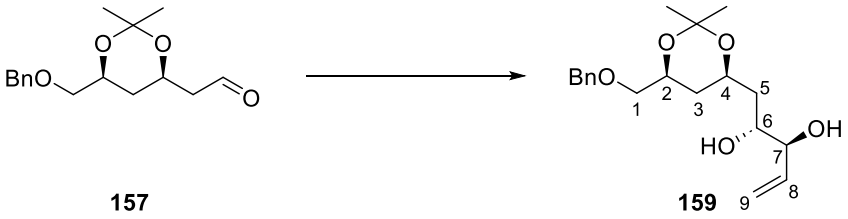
$C_{17}H_{14}O_4$
M = 282.29 g/mol

To a solution of benzoic acid anhydride (12.0 g, 53.0 mmol, 1 equiv) in DCM (55 mL) was added concentrated sulfuric acid (85 µL, 1.59 mmol, 0.03 equiv). Acrolein (5.3 mL, 79.6 mmol, 1.5 equiv) in DCM (5 mL) was added over 5 min and the mixture was stirred for 24 h at room temperature. Subsequently, the mixture was filtered through a short pad of $K_2CO_3$, and the solvent was removed under reduced pressure. The crude mixture was purified by flash chromatography (silica, CyHex:EtOAc = 15:1) and the pure product was obtained as a colorless oil (3.48 g, 12.3 mmol, 23%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.34. **$^{1}$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 8.09–8.06 (m, 4H, 4xCH-Bz), 7.64–7.59 (m, 3H, H-3, 2xCH-Bz), 7.49–7.45 (m, 4H, 4xCH-Bz), 6.19 (ddd, $^{3}J_{\text{H-2, H-1-}E}$ = 17.3 Hz, $^{3}J_{\text{H-2, H-1-}Z}$ = 10.6 Hz, $^{3}J_{\text{H-2, H-3}}$ = 5.3 Hz, 1H, H-2), 5.75 (ddd, $^{3}J_{\text{H-1-}E\text{, H-2}}$ = 17.3 Hz, $^{2}J$ = 1.0 Hz, $^{3}J_{\text{H-1-}E\text{, H-3}}$ = 1.0 Hz, 1H, H-1-*E*), 5.53 (ddd, $^{3}J_{\text{H-1-}Z\text{, H-2}}$ = 10.6 Hz, $^{2}J$ = 1.0 Hz, $^{3}J_{\text{H-1-}Z\text{, H-3}}$ = 1.0 Hz, 1H, H-1-*Z*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 164.9 (2xC=O-Bz), 134.2 (2xCH-Bz), 132.1 (C-2), 130.4 (4xCH-Bz), 129.8 (2x$C_q$-Bz), 129.1 (4xCH-Bz), 121.0 (C-1), 90.5 (C-3). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{14}O_4Na^+$ 305.0784, found 305.0784. For NMR-spectra see p. 397.

**Synthesis of Compound 159**

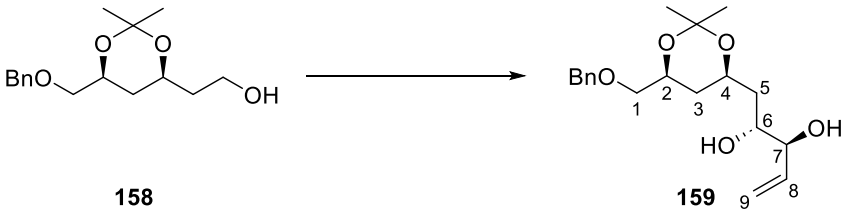
**(2*R*,3*S*)-1-((4*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)pent-4-ene-2,3-diol**




**157** **159**

$C_{19}H_{28}O_5$
M = 336.43 g/mol

A mixture of aldehyde **157** (0.28 g, 1.01 mmol, 1 equiv), acetal **180** (0.57 g, 2.01 mmol, 2 equiv), $K_3PO_4$ (0.21 g, 1.01 mmol, 1 equiv), isopropanol (0.15 mL, 2.01 mmol, 2 equiv), and (*S*)-**II** (52.0 mg, 50.3 µmol, 0.05 equiv) in THF (1 mL) was heated to 60 °C and stirred for 48 h. Subsequently, MeOH (10 mL) and $K_2CO_3$ (0.28 g, 2.01 mmol, 2 equiv) were added and the mixture was stirred for another 20 h at room temperature. The mixture was quenched with saturated $NH_4Cl$ solution (10 mL) and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1) to obtain the pure product as a colorless, highly viscous oil (45.0 mg, 0.13 mmol, 13%, *dr* > 20:1:1:1, no other stereoisomer detected by NMR).




**158** **159**

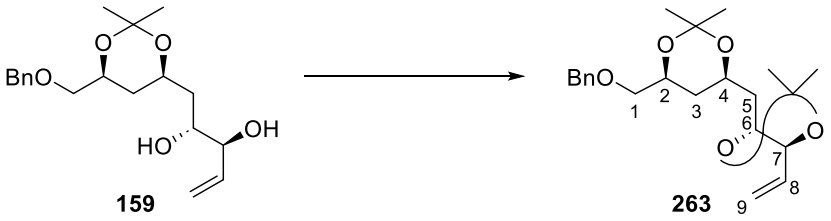
$C_{19}H_{28}O_5$
M = 336.43 g/mol

A mixture of alcohol **158** (0.20 g, 0.71 mmol, 1 equiv), acetal **180** (0.40 g, 1.43 mmol, 2 equiv), $K_3PO_4$ (0.15 g, 0.71 mmol, 1 equiv), and (*S*)-**II** (36.8 mg, 35.0 µmol, 0.05 equiv) in THF (1 mL) was heated to 90 °C and stirred for 48 h. Subsequently, MeOH (5 mL) and $K_2CO_3$ (0.20 g, 1.43 mmol, 2 equiv) were added and the mixture was stirred for another 20 h at room temperature. The mixture was quenched with saturated $NH_4Cl$ solution (5 mL) and the aqueous phase was extracted with DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 4:1) to obtain the pure product as a colorless, highly viscous oil (35.8 mg, 0.11 mmol, 15%, *dr* > 20:1:1:1, no other stereoisomer detected by NMR).

**TLC** (silica, CyHex:EtOAc = 1:1): $R_f$ = 0.28. $[\alpha]_D^{20}$ = −44.2° (c = 0.52, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.27 (m, 5H, 5xCH-Bn), 5.86 (ddd, $^3J_{H\text{-}8,\ H\text{-}9\text{-}E}$ = 17.3 Hz, $^3J_{H\text{-}8,\ H\text{-}9\text{-}Z}$ = 10.6 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 5.7 Hz, 1H, H-8), 5.30 (ddd, $^3J_{H\text{-}9\text{-}E,\ H\text{-}8}$ = 17.3 Hz, $^2J$ = 1.7 Hz, $^4J_{H\text{-}9\text{-}E,\ H\text{-}7}$ = 1.7 Hz, 1H, H-9-*E*), 5.20 (ddd, $^3J_{H\text{-}9\text{-}Z,\ H\text{-}8}$ = 10.6 Hz, $^2J$ = 1.6 Hz, $^4J_{H\text{-}9\text{-}Z,\ H\text{-}7}$ = 1.6 Hz, 1H, H-9-*Z*), 4.53 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 4.18–4.14 (m, 1H, H-4), 4.11 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1´}$ = 4.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.6 Hz, 1H, H-2), 4.06 (ddddd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 5.8, $^3J_{H\text{-}7,\ H\text{-}6}$ = 4.4 Hz, $^3J_{H\text{-}7,\ OH\text{-}7}$ = 4.4 Hz, $^4J_{H\text{-}7,\ H\text{-}9\text{-}E}$ = 1.5 Hz, $^4J_{H\text{-}7,\ H\text{-}9\text{-}Z}$ = 1.5 Hz, 1H, H-7), 3.82–3.78 (m, 1H, H-6), 3.47 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1´,\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 3.36 (br s, 1H, H-6), 2.47 (br s, 1H, H-7), 1.65–1.60 (m, 2H, H-5, H-5´), 1.52 (ddd, $^2J$ = 13.0 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.49 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.38 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.30 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 137.5 (C-8), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 116.6 (C-9), 99.3 ($C_q$), 75.8 (C-7), 74.4 (C-6), 74.1 (C-1), 73.9 ($CH_2$-Bn), 69.8 (C-4), 69.0 (C-2), 37.8 (C-5), 34.3 (C-3), 30.4 ($CH_3$), 20.2 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{28}O_5H^+$ 337.2010, found 337.2010. For NMR-spectra see p. 399.

**Synthesis of Compound 263**

**(4*S*,6*R*)-4-((benzyloxy)methyl)-6-(((4*R*,5*S*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane**



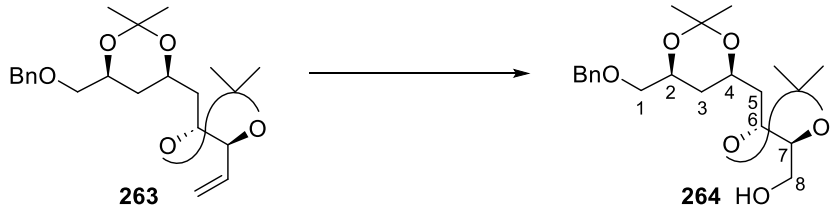

$C_{22}H_{32}O_5$
M = 376.49 g/mol

To a stirred solution of diol **159** (42.0 mg, 0.13 mmol, 1 equiv) in DCM (6 mL) was added 2,2-DMP (1.5 mL, 12.5 mmol, 100 equiv) and PPTS (3.10 mg, 12.5 µmol, 0.1 equiv). The mixture was stirred for 30 min at room temperature before it was quenched with saturated $NaHCO_3$ solution (10 mL) and DCM (20 mL). The organic phase was washed with $NaHCO_3$ solution (1 x 20 mL) and water (1 x 20 mL) and was dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the pure product was obtained without further purification (38.0 mg, 0.10 mmol, 81%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.16. $[\alpha]_D^{20}$ = +2.6° (c = 0.76, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.27 (m, 1H, CH-Bn), 5.80 (ddd, $^3J_{H\text{-}8,\ H\text{-}9\text{-}E}$ = 17.1 Hz, $^3J_{H\text{-}8,\ H\text{-}9\text{-}Z}$ = 10.3 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.8 Hz, 1H, H-8), 5.27 (ddd, $^3J_{H\text{-}9\text{-}E,\ H\text{-}8}$ = 17.1 Hz, $^2J$ = 1.7 Hz, $^4J_{H\text{-}9\text{-}E,\ H\text{-}7}$ = 1.0 Hz, 1H, H-9-*E*), 5.21 (ddd, $^3J_{H\text{-}9\text{-}Z,\ H\text{-}8}$ = 10.3 Hz, $^2J$ = 1.8 Hz, $^4J_{H\text{-}9\text{-}Z,\ H\text{-}7}$ = 0.9 Hz, 1H, H-9-*Z*), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn´), 4.47 (dddd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.7 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 6.1 Hz, $^4J_{H\text{-}7,\ H\text{-}9\text{-}E}$ = 1.0 Hz, $^4J_{H\text{-}7,\ H\text{-}9\text{-}Z}$ = 1.0 Hz H-7), 4.27 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 8.8 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 6.1 Hz, $^3J_{H\text{-}6,\ H\text{-}5´}$ = 5.3 Hz, 1H, H-6), 4.07 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1´}$ = 4.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.6 Hz, 1H, H-2), 4.00 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}4,\ H\text{-}5´}$ = 7.0 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 5.9 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-2), 3.47 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1´,\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 1.74 (ddd, $^2J$ = 13.7 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 8.8 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.9 Hz 1H, H-5), 1.58 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.5 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.5 Hz, 1H, H-3-eq), 1.48 (ddd, $^2J$ = 13.7 Hz, $^3J_{H\text{-}5´,\ H\text{-}4}$ = 7.1 Hz, $^3J_{H\text{-}5´,\ H\text{-}6}$ = 5.3 Hz, 1H, H-5´), 1.44 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.43 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.34 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.32 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.19 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.6 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 135.5 (C-8), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 118.4 (C-9), 108.7 ($C_q$), 99.1 ($C_q$), 80.2 (C-7), 74.4 (C-1), 74.4 (C-6), 73.8 ($CH_2$-Bn), 69.0 (C-2), 66.6 (C-4), 37.5 (C-5), 33.6 (C-3), 30.4 ($CH_3$), 28.6 ($CH_3$), 26.0 ($CH_3$), 20.1 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+NH_4]^+$ Calcd for $C_{22}H_{32}O_5NH_4^+$ 394.2588, found 394.2588. For NMR-spectra see p. 401.

### Synthesis of Compound 264

**((4*S*,5*R*)-5-(((4*R*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol**




$C_{21}H_{32}O_6$
M = 380.48 g/mol

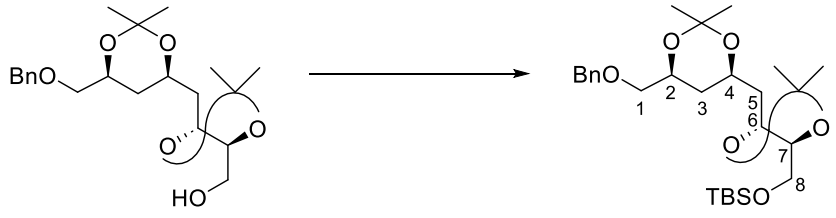
A stirred solution of alkene **263** (38.0 mg, 0.10 mmol, 1 equiv) in MeOH/DCM (1:1, 1 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 1 min. The excess ozone was then purged with argon for 3 min and $NaBH_4$ (19.0 mg, 0.50 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 3 h at room temperature. $NH_4Cl$-solution (2 mL) and DCM (5 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic

layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 2:1). The pure product was obtained as a colorless viscous liquid (32.0 mg, 86.0 µmol, 86%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.15. $[\alpha]_D^{20}$ = −8.8° (c = 0.80, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.38–7.31 (m, 4H, 4xCH-Bn), 7.31–7.26 (m, 1H, CH-Bn), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.29 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 8.4 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 5.8 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 5.8 Hz, 1H, H-6), 4.15–4.02 (m, 3H, H-2, H-4, H-7), 3.62–3.51 (m, 2H, H-8, H-8´), 3.49 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.40 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 1.95 (dd, $^3J_{OH,\ H\text{-}8}$ = 7.3 Hz, $^3J_{OH,\ H\text{-}8'}$ = 4.8 Hz, 1H, OH), 1.84 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 8.4 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.1 Hz, 1H, H-5), 1.65 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 7.1 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.6 Hz, 1H, H-5´), 1.59 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}3\text{eq},\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{eq},\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.44 (s, 3H, $CH_3$), 1.42 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 1.33 (s, 3H, $CH_3$), 1.27 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{ax},\ H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{ax},\ H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 108.4 ($C_q$), 99.2 ($C_q$), 78.5 (C-7), 74.3 (C-1), 73.9 ($CH_2$-Bn), 73.1 (C-6), 69.0 (C-2), 66.8 (C-4), 62.2 (C-8), 35.8 (C-5), 33.2 (C-3), 30.4 ($CH_3$), 28.5 ($CH_3$), 25.8 ($CH_3$), 20.1 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{32}O_6H^+$ 381.2272, found 381.2271. For NMR-spectra see p. 403.

### Synthesis of Compound 255

**(((4*S*,5*R*)-5-(((4*R*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)(*tert*-butyl)dimethylsilane**




**264** **255**

$C_{27}H_{46}SiO_6$
M = 494.74 g/mol

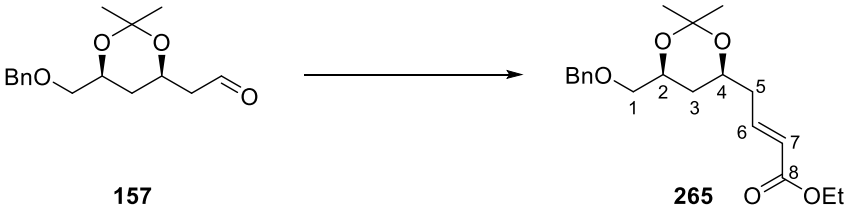
To a stirred solution of primary alcohol **264** (30.0 mg, 77.4 µmol, 1 equiv) in DCM (0.5 mL) was added imidazole (10.0 mg, 0.16 mmol, 2 equiv) and TBSCl (24.0 mg, 0.16 mmol, 2 equiv). The mixture was stirred for 5 h at room temperature before water (1 mL) and DCM (2 mL) were added. The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica,

CyHex:EtOAc = 10:1) and the pure product was obtained as a colorless oil (34.0 mg, 67.7 µmol, 87%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.28. $[\alpha]_D^{20}$ = +3.8° (c = 0.80, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.31–7.26 (m, 1H, CH-Bn), 4.54 (d, $^2J$ = 12.1 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.27 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 8.5 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 5.6 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 5.6 Hz, 1H, H-6), 4.10–4.03 (m, 3H, H-7, H-4, H-2), 3.66 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.3 Hz, 1H, H-8), 3.57 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}8',\ H\text{-}7}$ = 5.2 Hz, 1H, H-8´), 3.47 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.39 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H, H-1´), 1.79 (ddd, $^2J$ = 13.5 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 8.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 6.0 Hz, 1H, H-5), 1.67 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 6.8 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.5 Hz, 1H, H-5´), 1.59 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.5 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.5 Hz, 1H, H-3-eq), 1.44 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.30 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.19 (ddd, $^2J$ = 12.5 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.6 Hz, 1H, H-3-ax), 0.89 (s, 9H, 3x$CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.06 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.2 (2xCH-Bn), 128.1 (CH-Bn), 108.2 ($C_q$), 99.0 ($C_q$), 78.5 (C-7), 74.4 (C-1), 73.8 ($CH_2$-Bn), 73.7 (C-6), 69.0 (C-2), 66.8 (C-4), 62.7 (C-8), 36.3 (C-5), 33.6 (C-3), 30.4 ($CH_3$), 28.6 ($CH_3$), 26.2 (3x$CH_3$-TBS), 25.9 ($CH_3$), 20.2 ($CH_3$), 18.8 ($C_q$-TBS), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{46}SiO_6H^+$ 495.3136, found 495.3134. For NMR-spectra see p. 405.

### Synthesis of Compound 265

**ethyl (*E*)-4-((4*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)but-2-enoate**




**157** **265**

$C_{20}H_{28}O_5$
M = 348.44 g/mol

A stirred solution of aldehyde **157** (0.86 g, 3.09 mmol, 1 equiv) in MeCN (6 mL) was cooled to 0 °C. LiCl (0.24 g, 5.56 mmol, 1.8 equiv), triethyl phosphonoacetate (**143**) (1.08 mL, 5.41 mmol, 1.75 equiv) and DIPEA (0.94 mL, 5.41 mmol, 1.75 equiv) were added and the mixture was warmed to room temperature. After stirring for 3 h at room temperature the reaction mixture was quenched with saturated $NH_4Cl$ solution (10 mL) and DCM (20 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (2 x 20 mL). The combined organic layers were washed with water (10 mL) and dried over $MgSO_4$. The solvent was

removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless oil (970 mg, 2.78 mmol, 90% (950 mg (*E*); 20 mg (*Z*)) *dr* ≈ 50:1).

(*E*)-Isomer:

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.21. $[\alpha]_D^{20}$ = −5.5° (c = 1.10, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.27 (m, 1H, CH-Bn), 6.90 (ddd, $^3J_{H\text{-}6,\,H\text{-}7}$ = 15.6 Hz, $^3J_{H\text{-}6,\,H\text{-}5'}$ = 7.2 Hz, $^3J_{H\text{-}6,\,H\text{-}5}$ = 7.0 Hz, 1H, H-6), 5.86 (ddd, $^3J_{H\text{-}7,\,H\text{-}6}$ = 15.7 Hz, $^4J_{H\text{-}7,\,H\text{-}5}$ = 1.6 Hz, $^4J_{H\text{-}7,\,H\text{-}5'}$ = 1.5 Hz, 1H, H-7), 4.53 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.15 (q, $^3J$ = 7.1 Hz, 2H, $CH_2$-OEt), 4.08 (dddd, $^3J_{H\text{-}2,\,H\text{-}3\text{-}ax}$ = 11.8 Hz, $^3J_{H\text{-}2,\,H\text{-}1}$ = 5.8 Hz, $^3J_{H\text{-}2,\,H\text{-}1'}$ = 4.4 Hz, $^3J_{H\text{-}2,\,H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-2), 4.00 (dddd, $^3J_{H\text{-}4,\,H\text{-}3\text{-}ax}$ = 11.9 Hz, $^3J_{H\text{-}4,\,H\text{-}5}$ = 6.8 Hz, $^3J_{H\text{-}4,\,H\text{-}5'}$ = 5.5 Hz, $^3J_{H\text{-}4,\,H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-4), 3.47 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\,H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1',\,H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 2.39 (dddd, $^2J$ = 15.1 Hz, $^3J_{H\text{-}5,\,H\text{-}6}$ = 6.9 Hz, $^3J_{H\text{-}5,\,H\text{-}4}$ = 6.9 Hz, $^4J_{H\text{-}5,\,H\text{-}7}$ = 1.6 Hz, 1H, H-5), 2.31 (dddd, $^2J$ = 14.9 Hz, $^3J_{H\text{-}5',\,H\text{-}6}$ = 7.2 Hz, $^3J_{H\text{-}5',\,H\text{-}4}$ = 5.5 Hz, $^4J_{H\text{-}5',\,H\text{-}7}$ = 1.5 Hz, 1H, H-5´), 1.52 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}eq,\,H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\,H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.44 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.27 (t, $^3J$ = 7.1 Hz, 3H, $CH_3$-OEt), 1.22 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}ax,\,H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\,H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.7 (C-8), 145.0 (C-6), 139.1 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 124.1 (C-7), 99.3 ($C_q$), 74.3 (C-1), 73.9 ($CH_2$-Bn), 68.9 (C-2), 68.1 (C-4), 60.7 ($CH_2$-OEt), 39.6 (C-5), 33.8 (C-3), 30.3 ($CH_3$), 20.1 ($CH_3$), 14.6 ($CH_3$-OEt). **HRMS (ESI-TOF)** *m/z*: $[M+NH_4]^+$ Calcd for $C_{20}H_{28}O_5NH_4^+$ 366.2257, found 366.2276. For NMR-spectra see p. 407.

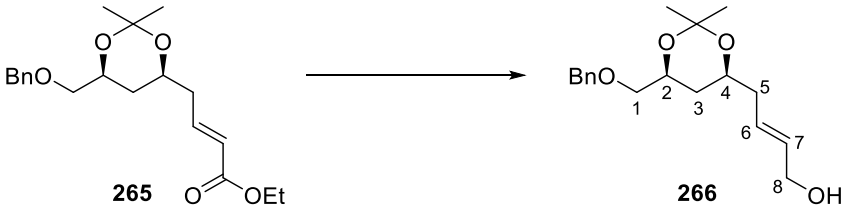
(*Z*)-Isomer:

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.27. $[\alpha]_D^{20}$ = −12.5° (c = 1.28, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.27 (m, 1H, CH-Bn), 6.32 (ddd, $^3J_{H\text{-}6,\,H\text{-}7}$ = 11.6 Hz, $^3J_{H\text{-}6,\,H\text{-}5'}$ = 7.1 Hz, $^3J_{H\text{-}6,\,H\text{-}5}$ = 7.1 Hz, 1H, H-6), 5.83 (ddd, $^3J_{H\text{-}7,\,H\text{-}6}$ = 11.6 Hz, $^4J_{H\text{-}7,\,H\text{-}5}$ = 1.9 Hz, $^4J_{H\text{-}7,\,H\text{-}5'}$ = 1.9 Hz, 1H, H-7), 4.53 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.52 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.14 (q, $^3J$ = 7.1 Hz, 2H, $CH_2$-OEt), 4.08 (dddd, $^3J_{H\text{-}2,\,H\text{-}3\text{-}ax}$ = 11.8 Hz, $^3J_{H\text{-}2,\,H\text{-}1}$ = 5.9 Hz, $^3J_{H\text{-}2,\,H\text{-}1'}$ = 4.4 Hz, $^3J_{H\text{-}2,\,H\text{-}3\text{-}eq}$ = 2.6 Hz, 1H, H-2), 3.98 (dddd, $^3J_{H\text{-}4,\,H\text{-}3\text{-}ax}$ = 11.9 Hz, $^3J_{H\text{-}4,\,H\text{-}5'}$ = 7.3 Hz, $^3J_{H\text{-}4,\,H\text{-}5}$ = 4.8 Hz, $^3J_{H\text{-}4,\,H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-4), 3.47 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1,\,H\text{-}2}$ = 5.9 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\,H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 2.86 (dddd, $^2J$ = 15.8 Hz, $^3J_{H\text{-}5,\,H\text{-}6}$ = 7.3 Hz, $^3J_{H\text{-}5,\,H\text{-}4}$ = 4.8 Hz, $^4J_{H\text{-}5,\,H\text{-}7}$ = 1.9 Hz, 1H, H-5), 2.74 (dddd, $^2J$ = 16.0 Hz, $^3J_{H\text{-}5',\,H\text{-}6}$ = 7.1 Hz, $^3J_{H\text{-}5',\,H\text{-}4}$ = 7.1 Hz, $^4J_{H\text{-}5',\,H\text{-}7}$ = 1.9 Hz, 1H, H-5´), 1.52 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}eq,\,H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\,H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.44 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.26 (t, $^3J$ = 7.1 Hz, 3H, $CH_3$-OEt), 1.25 (ddd, $^2J$ = 13.0 Hz, $^3J_{H\text{-}3\text{-}ax,\,H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\,H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz,

$CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.7 (C-8), 146.0 (C-6), 139.1 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 121.7 (C-7), 99.2 ($C_q$), 74.4 (C-1), 73.8 ($CH_2$-Bn), 69.0 (C-2), 68.7 (C-4), 60.4 ($CH_2$-OEt), 36.2 (C-5), 33.7 (C-3), 30.4 ($CH_3$), 20.1 ($CH_3$), 14.6 ($CH_3$-OEt). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{28}O_5H^+$ 349.2010, found 349.2009. For NMR-spectra see p. 409.

**Synthesis of Compound 266**

**(*E*)-4-((4*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)but-2-en-1-ol**




$C_{18}H_{26}O_4$
M = 306.40 g/mol

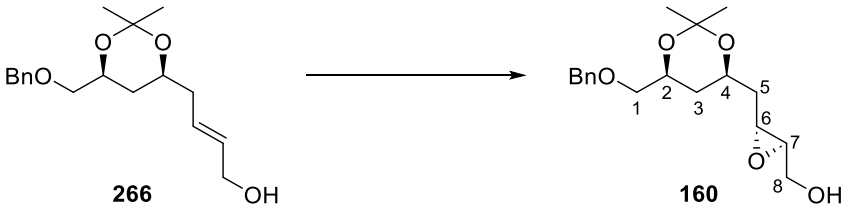
A stirred solution of α,β-unsaturated ester **265** (0.92 g, 2.64 mmol, 1 equiv) in DCM (5 mL) was cooled to −78°C. A solution of DIBAL-H (1M in hexane, 6.60 mL, 6.60 mmol, 2.5 equiv) was added dropwise and the mixture was stirred for 30 min at −78 °C. The reaction mixture was quenched with a saturated solution of Rochelle salt (5 mL) and stirred for 2 h. After that, the organic phase was separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:2) and the pure product was obtained as a colorless liquid (0.79 g, 2.58 mmol, 98%).

**TLC** (silica, CyHex:EtOAc = 1:1): $R_f$ = 0.48. $[\alpha]_D^{20}$ = −3.8° (c = 1.06, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.31 (m, 4H, 4xCH-Bn), 7.31–7.26 (m, 1H, CH-Bn), 5.73–5.63 (m, 2H, H-6, H-7), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.11–4.03 (m, 3H, H-2, H-8, H-8´), 3.90 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.6 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 6.2 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 6.2 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-4), 3.47 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 2.30–2.21 (m, 1H, H-5), 2.19–2.09 (m, 1H, H-5´), 1.51 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.44 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 1.17 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 132.4 (C-6), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.2 (C-7), 128.1 (CH-Bn), 99.1 ($C_q$), 74.4 (C-1), 73.8 ($CH_2$-Bn), 69.0 (C-2), 68.9 (C-4), 63.9 (C-8), 39.8 (C-5), 33.7 (C-3), 30.4 ($CH_3$), 20.1

($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{26}O_4Na^+$ 329.1723, found 329.1716. For NMR-spectra see p. 411.

### Synthesis of Compound 160

**((2*R*,3*R*)-3-(((4*R*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)oxiran-2-yl)methanol**




$C_{18}H_{26}O_5$
M = 322.40 g/mol

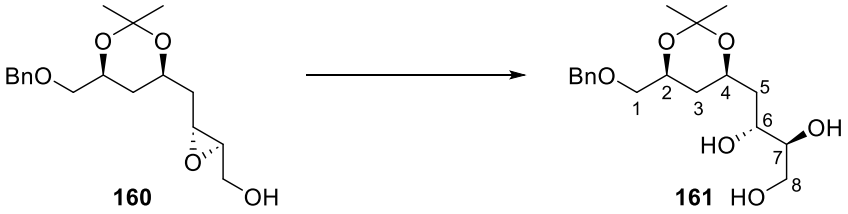
A stirred solution of (−)-DIPT (0.16 mL, 0.75 mmol, 0.3 equiv) in DCM (12 mL) containing 3 Å molecular sieves (1 g) was stirred for 30 min at room temperature. Subsequently, the mixture was cooled to −30 °C and titanium tetraisopropoxide (0.30 mL, 1.01 mmol, 0.4 equiv) as well as *tert*-butyl hydroperoxide (5.5M in decane, 2.97 mL, 16.3 mmol, 6.5 equiv) were added sequentially. The mixture was stirred for another 30 min and a solution of allylic alcohol **266** (0.77 g, 2.51 mmol, 1 equiv) in DCM (5 mL) was added. The reaction mixture was stirred for 16 h and the temperature was kept between −30 °C and −20 °C. After that, the molecular sieves were removed by filtration over celite, and the filtrate was diluted with DCM (20 mL) and quenched with 2M NaOH (20 mL). After stirring for 1 h at room temperature, the organic phase was separated, and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 1:1) and the pure product was obtained as a colorless liquid (0.69 g, 2.15 mmol, 85%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 1:1): $R_f$ = 0.25. $[\alpha]_D^{20}$ = +12.8° (c = 1.48, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.31–7.27 (m, 1H, CH-Bn), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.09 (dddd, $^3J_{H\text{-}2,\ H\text{-}3ax}$ = 11.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3ax}$ = 2.5 Hz, 1H, H-2), 4.04 (dddd, $^3J_{H\text{-}4,\ H\text{-}3ax}$ = 11.8 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 6.3 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 5.4 Hz, $^3J_{H\text{-}4,\ H\text{-}3ax}$ = 2.5 Hz, 1H, H-4), 3.86 (ddd, $^2J$ = 12.5 Hz, $^3J_{H\text{-}8,\ OH\text{-}8}$ = 5.5 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 2.7 Hz, 1H, H-8), 3.56 (ddd, $^2J$ = 12.5 Hz, $^3J_{H\text{-}8',\ OH\text{-}8}$ = 7.1 Hz, $^3J_{H\text{-}8',\ H\text{-}7}$ = 4.6 Hz, 1H, H-8´), 3.48 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.39 (dd, $^2J$ = 10.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.4 Hz, 1H, H-1´), 3.01 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 6.0 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 4.9 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 2.3 Hz, 1H, H-6), 2.91 (ddd, $^3J_{H\text{-}7,\ H\text{-}8'}$ = 4.8 Hz, $^3J_{H\text{-}7,\ H\text{-}8'}$ = 2.5 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 2.3 Hz, 1H, H-7), 1.76 (ddd, $^2J$ = 14.3 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 6.2 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 6.2 Hz, 1H,

H-5), 1.71 (ddd, $^2J$ = 14.3 Hz, $^3J_{\text{H-5´, H-4}}$ = 5.2 Hz, $^3J_{\text{H-5´, H-6}}$ = 5.2 Hz, 1H, H-5´), 1.63 (dd, $^3J_{\text{OH-8, H-8´}}$ = 6.9 Hz, $^3J_{\text{OH-8, H-8}}$ = 5.7 Hz, 1H, OH-8), 1.58–1.53 (m, 1H, H-3-eq), 1.45 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.31 (ddd, $^2J$ = 12.8 Hz, $^3J_{\text{H-3-ax, H-2}}$ = 11.7 Hz, $^3J_{\text{H-3-ax, H-4}}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 128.8 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 99.1 ($C_q$), 74.3 (C-1), 73.9 ($CH_2$-Bn), 69.0 (C-2), 66.8 (C-4), 62.2 (C-8), 58.4 (C-7), 52.8 (C-6), 38.6 (C-5), 33.7 (C-3), 30.4 ($CH_3$), 20.1 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{26}O_5Na^+$ 345.1672, found 345.1671. For NMR-spectra see p. 413.

**Synthesis of Compound 161**

**(2*S*,3*R*)-4-((4*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)butane-1,2,3-triol**




$C_{18}H_{28}O_6$
M = 340.42 g/mol

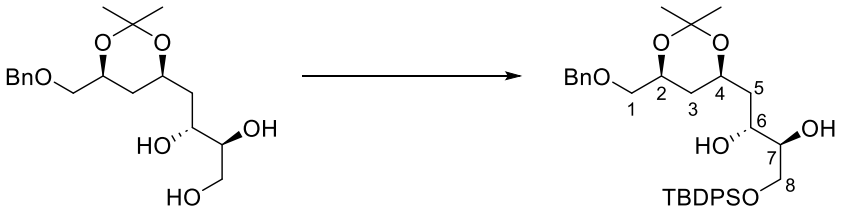
A solution of epoxide **160** (0.44 g, 1.36 mmol, 1 equiv) in dioxane (2.5 mL) was treated with NaOH (0.5M, 8 mL) and was stirred at 70 °C for 40 h. The reaction mixture was cooled to room temperature before saturated $NH_4Cl$ solution (10 mL) was added. The aqueous phase was extracted with $CHCl_3$ (5 x 10 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, $CHCl_3$:MeOH = 20:1). The pure product was obtained as a colorless liquid (0.21 g, 0.62 mmol, 45%).

**TLC** (silica, $CHCl_3$:MeOH = 20:1): $R_f$ = 0.17. $[\alpha]_D^{20}$ = −12.7° (c = 1.50, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.27 (m, 1H, CH-Bn), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.20 (dddd, $^3J_{\text{H-4, H-3-ax}}$ = 12.1 Hz, $^3J_{\text{H-4, H-5´}}$ = 9.8 Hz, $^3J_{\text{H-4, H-5}}$ = 2.6 Hz, $^3J_{\text{H-4, H-3-ax}}$ = 2.6 Hz, 1H, H-4), 4.12 (dddd, $^3J_{\text{H-2, H-3-ax}}$ = 11.8 Hz, $^3J_{\text{H-2, H-1}}$ = 5.8 Hz, $^3J_{\text{H-2, H-1´}}$ = 4.4 Hz, $^3J_{\text{H-2, H-3-ax}}$ = 2.6 Hz, 1H, H-2), 3.85 (dddd, $^3J_{\text{H-6, H-5´}}$ = 9.5 Hz, $^3J_{\text{H-6, H-7}}$ = 6.0 Hz, $^3J_{\text{H-6, H-5}}$ = 2.4 Hz, $^3J_{\text{H-6, OH-6}}$ = 1.8 Hz, 1H, H-6), 3.73–3.66 (m, 2H, H-8, H-8´), 3.51–3.44 (m, 3H, H-1, H-7, OH-6), 3.39 (dd, $^2J$ = 10.1 Hz, $^3J_{\text{H-1´, H-2}}$ = 4.4 Hz, 1H, H-1´), 2.70 (d, $^3J_{\text{OH-7, H-7}}$ = 5.3 Hz, 1H, OH-7), 2.25 (dd, $^3J_{\text{OH-8, H-8}}$ = 5.6 Hz, $^3J_{\text{OH-8, H-8}}$ = 5.6 Hz, 1H, OH-8), 1.78 (ddd, $^2J$ = 14.5 Hz, $^3J_{\text{H-5, H-4}}$ = 2.4 Hz, $^3J_{\text{H-5, H-6}}$ = 2.4 Hz, 1H, H-5), 1.64 (ddd, $^2J$ = 14.6 Hz, $^3J_{\text{H-5´, H-4}}$ = 9.5 Hz, $^3J_{\text{H-5´, H-6}}$ = 9.5 Hz, 1H, H-5´), 1.53 (ddd, $^2J$ = 13.0 Hz, $^3J_{\text{H-3-eq, H-2}}$ = 2.6 Hz, $^3J_{\text{H-3-eq, H-4}}$ = 2.6 Hz, 1H, H-3-eq), 1.49 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$),

1.38 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.32 (ddd, $^2J$ = 12.9 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.7 Hz, 1H, H-3-ax). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.1 (CH-Bn), 99.4 ($C_q$), 74.4 (C-7), 74.1 (C-1), 73.9 (C-6), 73.9 ($CH_2$-Bn), 70.1 (C-4), 69.0 (C-2), 64.3 (C-8), 39.7 (C-5), 34.3 (C-3), 30.4 ($CH_3$), 20.2 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{28}O_6Na^+$ 363.1778, found 363.1776. For NMR-spectra see p. 415.

### Synthesis of Compound 269

**(2*R*,3*S*)-1-((4*S*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)-4-((*tert*-butyldiphenylsilyl)oxy)butane-2,3-diol**




**161** **269**

$C_{34}H_{46}SiO_6$
M = 578.82 g/mol

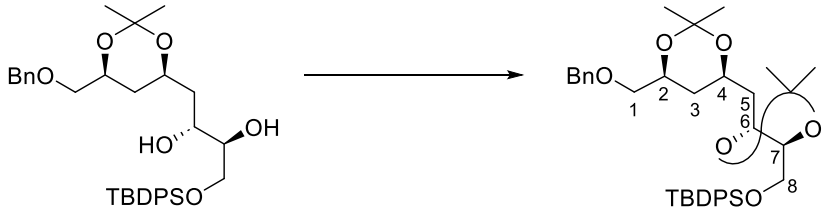
A solution of triol **161** (85.0 mg, 0.25 mmol, 1 equiv) in DCM (0.5 mL) was cooled to 0 °C. Imidazole (25.5 mg, 0.38 mmol, 1.5 equiv) and TBDPSCl (71.0 µL, 0.28 mmol, 1.1 equiv) were added sequentially and the mixture was stirred at 0 °C for 1 h. Subsequently, DCM (2 mL) and water (2 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 2 mL) and the combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:1) and the pure product was obtained as a colorless oil (119 mg, 0.21 mmol, 82%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.33. $[\alpha]_D^{20}$ = −5.0° (c = 0.60, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.69–7.65 (m, 4H, 4xCH-TBDPS), 7.46–7.42 (m, 2H, 2xCH-TBDPS), 7.42–7.38 (m, 4H, 4xCH-TBDPS), 7.36–7.31 (m, 4H, 4xCH-Bn), 7.30–7.26 (m, 1H, CH-Bn), 4.53 (d, $^2J$ = 11.9 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.16 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 12.0 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 9.6 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 2.8 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 2.8 Hz, 1H, H-4), 4.11 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 2.6 Hz, 1H, H-2), 3.79 (dd, $^2J$ = 10.3 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 4.6 Hz, 1H, H-8), 3.80–3.77 (m, 1H, H-6), 3.75 (dd, $^2J$ = 10.3 Hz, $^3J_{H\text{-}8',\ H\text{-}7}$ = 6.3 Hz, 1H, H-8´), 3.54 (dddd, $^3J_{H\text{-}7,\ H\text{-}8'}$ = 6.4 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 6.4 Hz, $^3J_{H\text{-}7,\ OH\text{-}7}$ = 4.5 Hz, $^3J_{H\text{-}7,\ H\text{-}8}$ = 4.5 Hz, 1H, H-7), 3.47 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.8 Hz, 1H, H-1), 3.38 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H, H-1´), 3.35 (d, $^3J_{OH\text{-}6,\ H\text{-}6}$ = 1.7 Hz, 1H, OH-6),

2.70 (d, $^3J_{OH\text{-}7,\ H\text{-}7}$ = 4.5 Hz, 1H, OH-7), 1.82 (ddd, $^2J$ = 14.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 2.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 2.6 Hz, 1H, H-5), 1.58 (ddd, $^2J$ = 14.6 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 9.3 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 9.3 Hz, 1H, H-5´), 1.51 (ddd, $^2J$ = 13.0 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.47 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.32–1.25 (m, 1H, H-3-ax), 1.06 (s, 9H, 3x$CH_3$-TBDPS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1–128.1 (15xCH-Ar, 3x$C_q$-Ar), 99.3 ($C_q$), 74.4 (C-7), 74.2 (C-1), 73.8 ($CH_2$-Bn), 72.9 (C-6), 70.0 (C-4), 69.0 (C-2), 65.9 (C-8), 39.4 (C-5), 34.3 (C-3), 30.4 ($CH_3$), 27.2 (3x$CH_3$-TBDPS), 20.2 ($CH_3$), 19.7 ($C_q$-TBDPS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{34}H_{46}SiO_6H^+$ 579.3136, found 579.3142. For NMR-spectra see p. 417.

### Synthesis of Compound 256

**(((4*S*,5*S*)-5-(((4*R*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)(*tert*-butyl)diphenylsilane**




**269** **256**

$C_{37}H_{50}SiO_6$
M = 618.89 g/mol

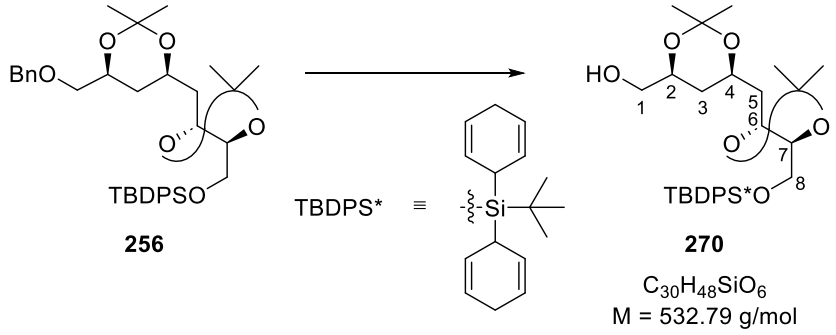
To a stirred solution of diol **269** (110 mg, 0.19 mmol, 1 equiv) in DCM (2 mL) was added 2,2-DMP (2.30 mL, 19.0 mmol, 100 equiv) and PPTS (4.50 mg, 19.0 µmol, 0.1 equiv). The mixture was stirred for 1 h at room temperature before saturated $NaHCO_3$ solution (2 mL) was added. The organic phase was separated, the aqueous phase was extracted with DCM (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1) and the pure product was obtained as a colorless oil (105 mg, 0.17 mmol, 89%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.30. $[\alpha]_D^{20}$ = −3.8° (c = 0.52, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.68–7.66 (m, 4H, 4xCH-TBDPS), 7.45–7.41 (m, 2H, 2xCH-TBDPS), 7.41–7.37 (m, 4H, 4xCH-TBDPS), 7.36–7.32 (m, 4H, 4xCH-Bn), 7.30–7.27 (m, 1H, CH-Bn), 4.54 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.51 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn´), 4.29 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 8.9 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 5.8 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 5.0 Hz, 1H, H-6), 4.16 (ddd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 6.7 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 5.5 Hz, $^3J_{H\text{-}7,\ H\text{-}8'}$ = 5.5 Hz, 1H, H-7), 4.07–4.00 (m, 2H, H-2, H-4), 3.74 (dd, $^2J$ = 10.7 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 6.8 Hz, 1H, H-8), 3.62 (dd, $^2J$ = 10.7 Hz, $^3J_{H\text{-}8',\ H\text{-}7}$ = 5.3 Hz, 1H, H-8´), 3.46 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.9 Hz, 1H, H-1), 3.37 (dd, $^2J$ = 10.1 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H,

H-1´), 1.80 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 8.9 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.7 Hz, 1H, H-5), 1.58 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 7.1 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.0 Hz, 1H, H-5´), 1.55 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.5 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.5 Hz, 1H, H-3-eq), 1.41 (s, 3H, $CH_3$), 1.34 (s, 3H, $CH_3$), 1.34 (s, 3H, $CH_3$), 1.29 (s, 3H, $CH_3$), 1.19 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.6 Hz, 1H, H-3-ax), 1.05 (s, 9H, 3x$CH_3$-TBDPS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.1–128.1 (15xCH-Ar, 3x$C_q$-Ar), 108.3 ($C_q$), 99.0 ($C_q$), 78.4 (C-7), 74.4 (C-1), 73.8 ($CH_2$-Bn), 73.6 (C-6), 68.9 (C-2), 66.8 (C-4), 63.6 (C-8), 36.3 (C-5), 33.5 (C-3), 30.4 ($CH_3$), 28.5 ($CH_3$), 27.2 (3x$CH_3$-TBDPS), 25.9 ($CH_3$), 20.2 ($CH_3$), 19.6 ($C_q$-TBDPS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{37}H_{50}SiO_6Na^+$ 641.3269, found 641.3263. For NMR-spectra see p. 419.

**Synthesis of Compound 270**

**((4*S*,6*R*)-6-(((4*S*,5*S*)-5-(((*tert*-butyldi(cyclohexa-2,5-dien-1-yl)silyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methanol**



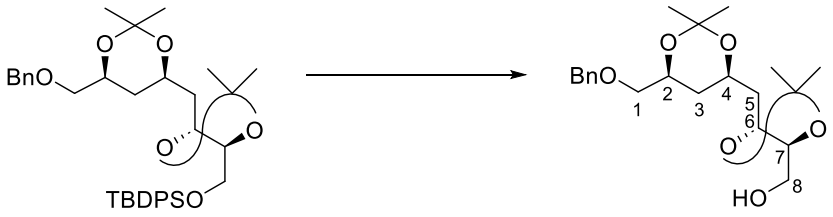

Lithium metal (27.0 mg, 3.88 mmol, 120 equiv) was dissolved in liquid ammonia (1.6 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of benzyl ether **256** (20.0 mg, 32.3 µmol, 1 equiv) in THF (1 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched with solid $NH_4Cl$ (0.36 g, 6.46 mmol, 200 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (1 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:1). The pure product was obtained as a colorless oil (12 mg, 22.5 µmol, 70%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = +10.0° (c = 0.80, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 5.84–5.80 (m, 4H, 4xCH-TBDPS*), 5.58–5.52 (m, 4H, 4xCH-TBDPS*), 4.27 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 9.3 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 5.8 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 4.7 Hz, 1H, H-6), 4.12 (ddd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.1 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 5.4 Hz, $^3J_{H\text{-}7,\ H\text{-}8'}$ = 5.4 Hz, 1H, H-7), 4.08 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 7.7 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 5.5 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 2.6 Hz, 1H, H-4), 3.96

(dddd, $^{3}J_{\text{H-2, H-3-ax}}$ = 12.0 Hz, $^{3}J_{\text{H-2, H-1}}$ = 6.0 Hz, $^{3}J_{\text{H-2, H-1´}}$ = 3.0 Hz, $^{3}J_{\text{H-2, H-3-ax}}$ = 3.0 Hz, 1H, H-2), 3.87 (dd, $^{2}J$ = 10.5 Hz, $^{3}J_{\text{H-8, H-7}}$ = 7.1 Hz, 1H, H-8), 3.82 (dd, $^{2}J$ = 10.5 Hz, $^{3}J_{\text{H-8´, H-7}}$ = 5.1 Hz, 1H, H-8´), 3.58–3.53 (m, 1H, H-1), 3.48–3.42 (m, 1H, H-1´), 2.81–2.68 (m, 6H, 2x$CH_2$-TBDPS*, 2xCH-TBDPS*), 1.93 (t, $^{3}J_{\text{OH, H-1}}$ = 6.4 Hz), 1.84 (ddd, $^{2}J$ = 13.6 Hz, $^{3}J_{\text{H-5, H-6}}$ = 9.3 Hz, $^{3}J_{\text{H-5, H-4}}$ = 5.5 Hz, 1H, H-5), 1.70 (ddd, $^{2}J$ = 13.6 Hz, $^{3}J_{\text{H-5´, H-4}}$ = 7.4 Hz, $^{3}J_{\text{H-5´, H-6}}$ = 4.7 Hz, 1H, H-5´), 1.51 (ddd, $^{2}J$ = 12.7 Hz, $^{3}J_{\text{H-3-eq, H-2}}$ = 2.6 Hz, $^{3}J_{\text{H-3-eq, H-4}}$ = 2.6 Hz, 1H, H-3-eq), 1.45 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.38 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.36 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.31 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.25 (ddd, $^{2}J$ = 12.7 Hz, $^{3}J_{\text{H-3-ax, H-2}}$ = 11.6 Hz, $^{3}J_{\text{H-3-ax, H-4}}$ = 11.6 Hz, 1H, H-3-ax), 1.05 (s, 9H, 3x$CH_3$-TBDPS*). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 126.4 (CH-TBDPS*), 126.4 (CH-TBDPS*), 126.3 (CH-TBDPS*), 126.3 (CH-TBDPS*), 122.6 (CH-TBDPS*), 122.6 (2xCH-TBDPS*), 122.5 (CH-TBDPS*), 108.4 ($C_q$), 99.2 ($C_q$), 78.5 (C-7), 73.6 (C-6), 70.2 (C-2), 66.7 (C-4), 66.6 (C-1), 63.6 (C-8), 36.2 (C-5), 32.3 (C-3), 30.4 ($CH_3$), 29.5 (CH-TBDPS*), 29.4 (CH-TBDPS*), 28.5 ($CH_3$), 28.0 (3x$CH_3$-TBDPS*), 26.6 ($CH_2$-TBDPS*), 26.6 ($CH_2$-TBDPS*), 25.9 ($CH_3$), 22.2 ($C_q$-TBDPS*), 20.3 ($CH_3$). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{30}H_{48}SiO_6Na^+$ 555.3112, found 555.3109. For NMR-spectra see p. 421.

**Synthesis of Compound 264**

**((4*S*,5*R*)-5-(((4*R*,6*S*)-6-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol**




**256** **264**

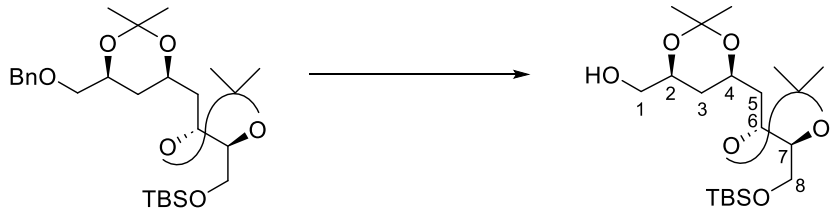
$C_{21}H_{32}O_6$
M = 380.48 g/mol

A solution of TBDPS ether **256** (188 mg, 0.30 mmol, 1 equiv) in THF (3 mL) was cooled to 0 °C. TBAF (1M in THF; 0.91 mL, 0.91 mmol, 3 equiv) was added dropwise, and the mixture was stirred for 2 h at room temperature. Subsequently, the mixture was quenched with saturated $NH_4Cl$-solution (5 mL) and DCM (10 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:1) and the pure product was obtained as a colorless oil (93.0 mg, 0.24 mmol, 80%).

For analytical data see p. 194

**Synthesis of Compound 271**

**((4*S*,6*R*)-6-(((4*R*,5*S*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methanol**




**255** **271**

$C_{20}H_{40}SiO_6$
M = 404.62 g/mol

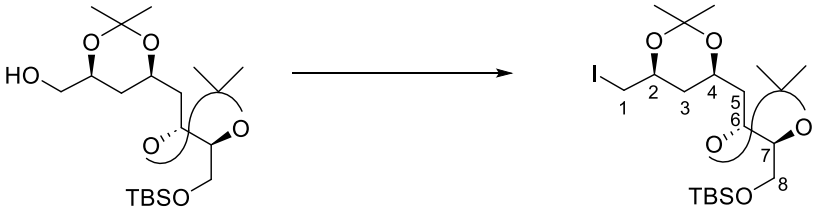
Lithium metal (140 mg, 20.2 mmol, 100 equiv) was dissolved in liquid ammonia (10 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of benzyl ether **255** (100 mg, 0.20 mmol, 1 equiv) in THF (4 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched with solid $NH_4Cl$ (2.16 g, 40.4 mmol, 200 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (10 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 3:1). The pure product was obtained as a colorless oil (81.0 mg, 0.20 mmol, 99%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.24. $[\alpha]_D^{20}$ = +10.5° (c = 0.76, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.27 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 8.6 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 5.6 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 5.6 Hz, 1H, H-6), 4.08 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.4 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 6.6 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 6.1 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.4 Hz, 1H, H-2), 4.06 (ddd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.4 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 5.4 Hz, $^3J_{H\text{-}7,\ H\text{-}8'}$ = 5.4 Hz, 1H, H-7), 3.99–3.92 (m, 1H, H-2), 3.66 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.4 Hz, 1H, H-8), 3.57 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}8',\ H\text{-}7}$ = 5.1 Hz, 1H, H-8´), 3.58–3.53 (m, 1H, H-1), 3-48–3.42 (m, 1H, H-1´), 1.90 (br s, 1H, OH), 1.80 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 8.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 6.1 Hz, 1H, H-5), 1.68 (ddd, $^2J$ = 13.5 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 6.8 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.5 Hz, 1H, H-5´), 1.49 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}2}$ = 2.6 Hz, $^3J_{H\text{-}3\text{-}eq,\ H\text{-}4}$ = 2.6 Hz, 1H, H-3-eq), 1.44 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.30 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.24 (ddd, $^2J$ = 12.5 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.6 Hz, 1H, H-3-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 108.2 ($C_q$), 99.2 ($C_q$), 78.5 (C-7), 73.7 (C-6), 70.2 (C-2), 66.7 (C-4), 66.6 (C-1), 62.7 (C-8), 36.2 (C-5), 32.4 (C-3), 30.4 ($CH_3$), 28.6 ($CH_3$), 26.2 (3x$CH_3$-TBS), 25.9 ($CH_3$), 20.3 ($CH_3$), 18.8

($C_q$-TBS), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{40}SiO_6H^+$ 405.2667, found 405.2662. For NMR-spectra see p. 423.

### Synthesis of Compound 156

***tert*-butyl(((4*S*,5*R*)-5-(((4*S*,6*S*)-6-(iodomethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane**




**271** **156**

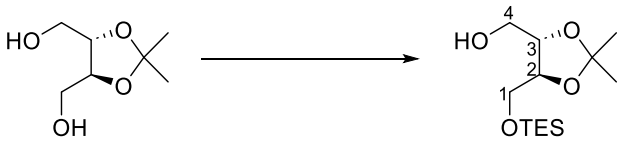
$C_{20}H_{39}ISiO_5$
M = 514.52 g/mol

To a stirred solution of alcohol **271** (76.0 g, 0.19 mmol, 1 equiv) in benzene (1 mL) were added $PPh_3$ (99.0 g, 0.38 mmol, 2 equiv) and imidazole (26.0 mg, 0.38 mmol, 2 equiv). Iodine (72.0 mg, 0.28 mmol, 1.5 equiv) was added and the reaction mixture was stirred for 1 h at room temperature. The mixture was filtered over a pad of celite, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 20:1) and the pure product was obtained as a colorless viscous liquid (78.0 mg, 0.15 mmol, 81%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.20. $[\alpha]_D^{20}$ = +1.1° (c = 0.90, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.28 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 8.4 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 5.7 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 5.7 Hz, 1H, H-6), 4.09–4.02 (m, 2H, H-4, H-7), 3.85 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-2), 3.66 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.5 Hz, 1H, H-8), 3.57 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}8',\ H\text{-}7}$ = 5.1 Hz, 1H, H-8´), 3.18–3.11 (m, 2H, H-1, H-1´), 1.86–1.77 (m, 2H, H-3-eq, H-5), 1.70 (ddd, $^2J$ = 13.6 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 6.6 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.6 Hz, 1H, H-5´), 1.42 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.30 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.11 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.4 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.4 Hz, 1H, H-3-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 108.2 ($C_q$), 99.8 ($C_q$), 78.4 (C-7), 73.7 (C-6), 69.6 (C-2), 67.0 (C-4), 62.7 (C-8), 36.8 (C-3), 36.0 (C-5), 30.3 ($CH_3$), 28.6 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.9 ($CH_3$), 20.3 ($CH_3$), 18.8 ($C_q$-TBS), 10.4 (C-1), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{39}ISiO_5H^+$ 515.1684, found 515.1677. For NMR-spectra see p. 425.

**Synthesis of Compound 275**

**((4*S*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)methanol**



*ent*-**166** **275**

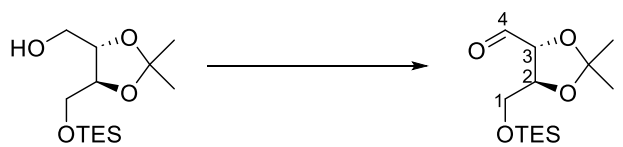
$C_{13}H_{28}SiO_4$
M = 276.45 g/mol

To a stirred suspension of NaH (60% in mineral oil; 0.60 g, 25.0 mmol, 1.6 equiv) in THF (68 mL) was added a solution of diol *ent*-**166** (3.79 g, 23.4 mmol, 1.5 equiv) in THF (10 mL) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C before TESCl (2.62 mL, 15.6 mmol, 1 equiv) was added dropwise. The mixture was warmed to room temperature and stirred for 3 h. Subsequently, the reaction mixture was quenched with $H_2O$ (100 mL) and DCM (100 mL) and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 150 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless liquid (3.36 g, 12.2 mmol, 78%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = +10.7° (c = 1.40, DCM). **$^1$H-NMR** (400 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 3.93 (ddd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 4.5 Hz, $^3J_{H\text{-}3,\ H\text{-}4'}$ = 4.5 Hz, 1H, H-3), 3.89–3.80 (m, 2H, H-1, H-2), 3.75–3.61 (m, 3H, H-4, H-4´, H-1´), 2.31 (dd, $^3J_{OH,\ H\text{-}4}$ = 8.2 Hz, $^3J_{OH,\ H\text{-}4'}$ = 4.5 Hz, 1H, OH), 1.38 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 0.96 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.63 (q, $^3J$ = 7.9 Hz, 6H, 3x$CH_2$-TES). **$^{13}$C-NMR** (100 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.6 ($C_q$), 80.7 (C-3), 78.9 (C-2), 64.1 (C-1), 63.3 (C-4), 27.4 ($CH_3$), 27.3 ($CH_3$), 7.0 (3x$CH_3$-TES), 4.7 (3x$CH_2$-TES). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{28}SiO_4H^+$ 277.1830, found 277.1830. For NMR-spectra see p. 427.

**Synthesis of Compound 276**

**(4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolane-4-carbaldehyde**



**275** **276**

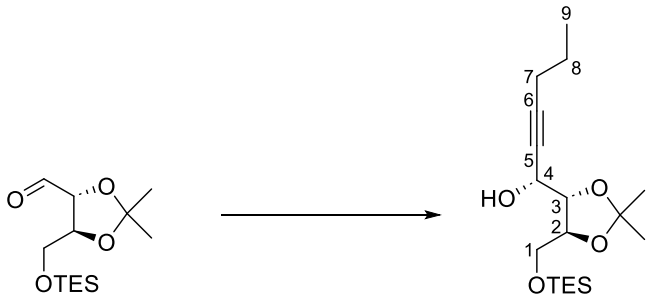
$C_{13}H_{26}SiO_4$
M = 274.43 g/mol

To a Schlenk flask charged with sulfur trioxide pyridine complex (6.91 g, 43.4 mmol, 3 equiv) were added DCM (130 mL), DMSO (10.3 mL, 145 mmol, 10 equiv) and DIPEA (10.1 mL, 57.9 mmol, 4 equiv). A solution of alcohol **275** (4.00 g, 14.5 mmol, 1 equiv) in DCM (15 mL) was added and the mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was quenched with $NH_4Cl$-solution and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 150 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless liquid (3.63 g, 13.2 mmol, 91%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.34. $[\alpha]_D^{20}$ = +5.4° (c = 1.68, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 9.74 (d, $^3J_{H\text{-}4,\ H\text{-}3}$ = 1.7 Hz, 1H, H-4), 4.26 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.3 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 1.7 Hz, 1H, H-3), 4.11 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.6 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.6 Hz, 1H, H-2), 3.80 (dd, $^2J$ = 10.9 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.7 Hz, 1H, H-1), 3.77 (dd, $^2J$ = 10.9 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.7 Hz, 1H, H-1´), 1.45 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.40 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 0.96 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.63 (q, $^3J$ = 7.9 Hz, 6H, 3x$CH_2$-TES). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 201.3 (C-4), 112.0 ($C_q$), 82.6 (C-3), 78.3 (C-2), 63.5 (C-1), 27.2 ($CH_3$), 26.7 ($CH_3$), 7.0 (3x$CH_3$-TES), 4.8 (3x$CH_2$-TES). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{26}SiO_4H^+$ 275.1673, found 275.1672. For NMR-spectra see p. 429.

### Synthesis of Compound 278

**(*R*)-1-((4*S*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)hex-2-yn-1-ol**




**276** **278**

$C_{18}H_{34}SiO_4$
M = 342.55 g/mol

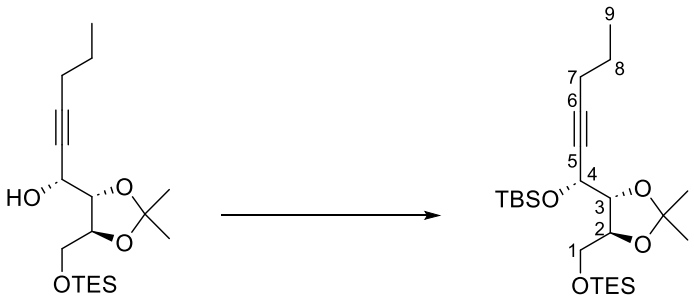
To an oven-dried Schlenk tube charged with $Zn(OTf)_2$ (0.53 g, 1.46 mmol, 1.1 equiv) and (1*R*,2*S*)-(−)-*N*-methylephedrine (0.29 g, 1.59 mmol, 1.2 equiv) were added toluene (4 mL) and $NEt_3$ (0.22 mL, 1.59 mmol, 1.2 equiv). The mixture was stirred for 2.5 h at room temperature before pentyne (0.16 mL, 1.59 mmol, 1.2 equiv) was added. After stirring for another 15 min at room temperature aldehyde **276** (0.36 g, 1.32 mmol, 1 equiv) in toluene (0.4 mL) was added.

The mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was quenched with $NH_4Cl$-solution and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 15:1). The pure product was obtained as a colorless liquid (0.41 g, 1.19 mmol, 90%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.21. $[\alpha]_D^{20}$ = +18.4° (c = 1.36, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.42 (ddt, $^3J_{H\text{-}4,\ OH}$ = 7.9 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 4.9 Hz, $^4J_{H\text{-}4,\ H\text{-}7}$ = 2.0 Hz, 1H, H-4), 4.09 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 6.0 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.7 Hz, 1H, H-2), 3.87 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 4.9 Hz, 1H, H-3), 3.83 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.7 Hz, 1H, H-1), 3.72 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 6.1 Hz, 1H, H-1´), 2.98 (d, $^3J_{OH,\ H\text{-}4}$ = 7.9 Hz, 1H, OH), 2.20 (td, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.1 Hz, $^4J_{H\text{-}7,\ H\text{-}4}$ = 2.0 Hz, 2H, H-7), 1.56–1.51 (m, 2H, H-8), 1.40 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.38 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 0.98 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.97 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES) 0.64 (q, $^3J$ = 7.9 Hz, 6H, 3x$CH_2$-TES). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 110.1 ($C_q$), 87.3 (C-6), 82.2 (C-3), 78.8 (C-5), 78.6 (C-2), 64.2 (C-1), 63.6 (C-4), 27.5 ($CH_3$), 27.4 ($CH_3$), 22.6 (C-8), 21.2 (C-7), 13.8 (C-9), 7.0 (3x$CH_3$-TES), 4.7 (3x$CH_2$-TES). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{34}SiO_4H^+$ 343.2299, found 343.2298. For NMR-spectra see p. 431.

### Synthesis of Compound 279

***tert*-butyl(((*R*)-1-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)hex-2-yn-1-yl)oxy)dimethylsilane**




**278** **279**

$C_{24}H_{48}Si_2O_4$
M = 456.81 g/mol

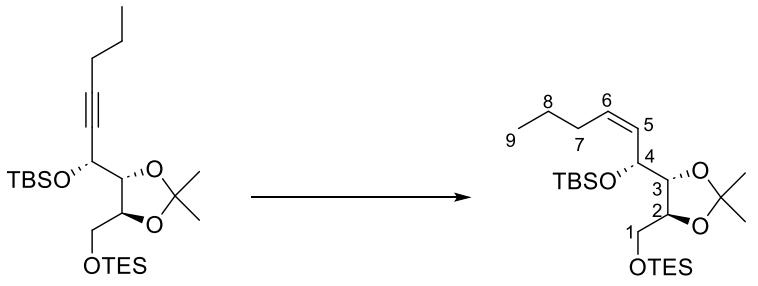
A stirred solution of propargylic alcohol **278** (0.34 g, 1.00 mmol, 1 equiv) in DCM (2 mL) was treated with imidazole (0.14 g, 2.00 mmol, 2 equiv) and TBSCl (0.30 g, 2.00 mmol, 2 equiv). The mixture was stirred for 24 h at room temperature and subsequently, DCM (10 mL) and water (5 mL) were added. The organic phase was separated, and the aqueous phase was

extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under removed pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1) and the pure product was obtained as a colorless oil (0.45 g, 0.97 mmol, 97%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.26. $[\alpha]_D^{20}$ = −33.3° (c = 1.56, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.54 (dt, $^3J_{H\text{-}4,\ H\text{-}3}$ = 5.1 Hz, $^5J_{H\text{-}4,\ H\text{-}7}$ = 2.0 Hz, 1H, H-4), 4.14 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 6.0 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 2.8 Hz, 1H, H-2), 3.86 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 2.8 Hz, 1H, H-1), 3.79 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 5.1 Hz, 1H, H-3), 3.68 (dd, $^2J$ = 11.0 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 6.0 Hz, 1H, H-1´), 2.19 (td, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.1 Hz, $^5J_{H\text{-}7,\ H\text{-}4}$ = 2.0 Hz, 2H, H-7), 1.58–1.48 (m, 2H, H-8), 1.39 (d, $^4J$ = 0.8 Hz 3H, $CH_3$), 1.38 (d, $^4J$ = 0.8 Hz 3H, $CH_3$), 0.98 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.97 (t, $^3J$ = 7.9 Hz, 9H, 3x$CH_3$-TES), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.62 (q, $^3J$ = 7.9 Hz, 6H, 3x$CH_2$-TES), 0.14 (s, 3H, $CH_3$-TBS), 0.12 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 110.1 ($C_q$), 87.1 (C-6), 80.1 (C-3), 79.8 (C-5), 79.2 (C-2), 65.3 (C-1), 64.9 (C-4), 27.7 ($CH_3$), 27.6 ($CH_3$), 26.1 (3x$CH_3$-TBS), 22.6 (C-8), 21.2 (C-7), 18.7 ($C_q$-TBS), 13.9 (C-9), 7.1 (3x$CH_3$-TES), 4.9 (3x$CH_2$-TES), −4.3 ($CH_3$-TBS), −4.8 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{48}Si_2O_4H^+$ 457.3164, found 457.3162. For NMR-spectra see p. 433.

**Synthesis of Compound 280**

***tert*-butyl(((*R*,*Z*)-1-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)hex-2-en-1-yl)oxy)dimethylsilane**




**279** **280**

$C_{24}H_{50}Si_2O_4$
M = 458.83 g/mol

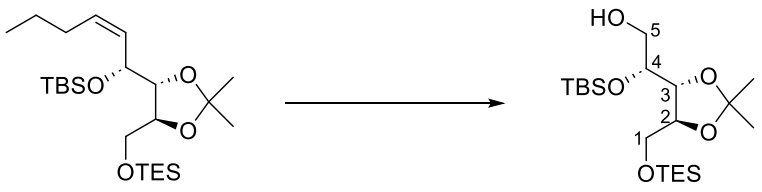
To a stirred solution of alkyne **279** (1.00 g, 2.19 mmol, 1 equiv) in hexane (20 mL) was added Lindlar catalyst consisting of Pd/$CaCO_3$ (5% Pd, 0.23 g, 0.11 mmol, 0.05 equiv, with respect to Pd) and quinoline (13.0 µL, 0.11 mmol, 0.05 equiv). The reaction mixture was stirred under a hydrogen atmosphere (1 atm) for 1 h at room temperature. Subsequently, the mixture was purged with argon and filtered over a pad of celite. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica,

CyHex:EtOAc = 40:1). The pure product was obtained as a colorless liquid (0.98 g, 2.16 mmol, 98%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.34. $[\alpha]_D^{20}$ = −19.9° (c = 1.56, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 5.52–5.46 (m, 1H, H-6), 5.42–5.34 (m, 1H, H-5), 4.56 (ddd, $^3J_{H\text{-}4,\ H\text{-}5}$ = 8.9 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 4.4 Hz, $^4J_{H\text{-}4,\ H\text{-}6}$ = 1.1 Hz, 1H, H-4), 3.97 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.8 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.6 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.2 Hz, 1H, H-2), 3.77–3.70 (m, 2H, H-1, H-3), 3.68 (dd, $^2J$ = 10.6 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.6 Hz, 1H, H-1´), 2.14–1.98 (m, 2H, H-7), 1.45–1.36 (m, 2H, H-8), 1.36 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 0.96 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.92 (t, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, 3H, H-9), 0.89 (s, 9H, 3x$CH_3$-TBS), 0.62 (q, $^3J$ = 7.8 Hz, 6H, 3x$CH_2$-TES), 0.07 (s, 3H, $CH_3$-TBS), 0.05 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 132.3 (C-6), 130.3 (C-5), 109.5 ($C_q$), 82.5 (C-3), 78.2 (C-2), 69.6 (C-4), 65.0 (C-1), 30.8 (C-7), 27.7 ($CH_3$), 27.5 ($CH_3$), 26.2 (3x$CH_3$-TBS), 23.3 (C-8), 18.7 ($C_q$-TBS), 14.3 (C-9), 7.1 (3x$CH_3$-TES), 4.8 (3x$CH_2$-TES), −4.1 ($CH_3$-TBS), −4.5 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{50}Si_2O_4Na^+$ 481.3140, found 481.3137. For NMR-spectra see p. 435.

**Synthesis of Compound 281**

**(*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)ethan-1-ol**




**280** **281**

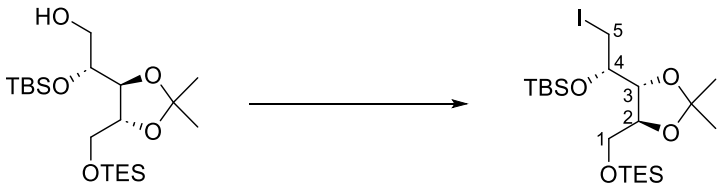
$C_{20}H_{44}Si_2O_5$
M = 420.74 g/mol

A stirred solution of alkene **280** (0.98 g, 2.14 mmol, 1 equiv) in MeOH/DCM (1:1, 10 mL) was cooled to −78 °C and stirred under an atmosphere of ozone for 15 min until a slightly blue color persisted. The excess ozone was then purged with argon for 2 min and $NaBH_4$ (0.40 g, 10.7 mmol, 5 equiv) was added at −78 °C. The reaction mixture was warmed to room temperature and stirred for 90 min at room temperature. $NH_4Cl$-solution (10 mL) and DCM (10 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless liquid (0.71 g, 1.69 mmol, 79%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.27. $[\alpha]_D^{20}$ = −7.0° (c = 1.42, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.08 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.0 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.4 Hz, 1H, H-2), 3.95 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.9 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 4.6 Hz, 1H, H-3), 3.83 (ddd, $^3J_{H\text{-}4,\ H\text{-}5}$ = 5.2 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 4.4 Hz, $^3J_{H\text{-}5,\ H\text{-}5'}$ = 4.4 Hz, 1H, H-4), 3.77–3.70 (m, 2H, H-1, H-1´), 3.67 (ddd, $^2J$ = 11.3 Hz, $^3J_{H\text{-}5,\ OH}$ = 6.0 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.3 Hz, 1H, H-5), 3.61 (ddd, $^2J$ = 11.4 Hz, $^3J_{H\text{-}5',\ OH}$ = 6.7 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 4.3 Hz, 1H, H-5´), 2.30 (dd, $^3J_{OH,\ H\text{-}5'}$ = 6.7 Hz, $^3J_{OH,\ H\text{-}5}$ = 5.9 Hz, 1H, OH), 1.38 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 0.96 (t, $^3J$ = 7.9 Hz, 9H, 3x$CH_3$-TES), 0.91 (s, 9H, 3x$CH_3$-TBS), 0.63 (q, $^3J$ = 7.7 Hz, 6H, 3x$CH_2$-TES), 0.11 (br s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.5 ($C_q$), 80.8 (C-2). 77.9 (C-3), 73.2 (C-4), 64.8 (C-5), 64.8 (C-1), 27.4 ($CH_3$), 27.4 ($CH_3$), 26.2 (3x$CH_3$-TBS), 18.7 ($C_q$-TBS), 7.0 (3x$CH_3$-TES), 4.7 (3x$CH_2$-TES), −4.3 ($CH_3$-TBS), −4.4 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{44}Si_2O_5H^+$ 421.2800, found 421.2798. For NMR-spectra see p. 437.

### Synthesis of Compound 282

***tert*-butyl((*S*)-1-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)-2-iodoethoxy)dimethylsilane**




**281** **282**

$C_{20}H_{43}ISi_2O_4$
M = 530.63 g/mol

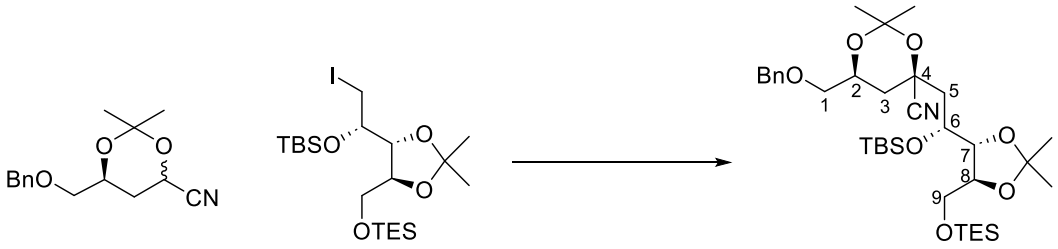
To a stirred solution of alcohol **281** (0.42 g, 1.00 mmol, 1 equiv) in benzene (2 mL) were added $PPh_3$ (0.29 g, 1.10 mmol, 1.1 equiv) and imidazole (74.8 mg, 1.10 mmol, 1.1 equiv). The mixture was cooled to 0 °C and iodine (0.28 g, 1.10 mmol, 1.1 equiv) was added. The reaction mixture was stirred for 20 min at room temperature and was filtered over a pad of celite. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 70:1). The pure product was obtained as a colorless viscous liquid (0.46 g, 0.87 mmol, 87%).

**TLC** (silica, CyHex:EtOAc = 70:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = −1.3° (c = 1.50, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.17 (dd, $^3J_{H\text{-}3,\ H\text{-}2}$ = 7.7 Hz, $^3J_{H\text{-}3,\ H\text{-}4}$ = 3.3 Hz, 1H, H-3), 4.01 (ddd, $^3J_{H\text{-}2,\ H\text{-}3}$ = 7.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 4.9 Hz, 1H, H-2), 3.86 (ddd, $^3J_{H\text{-}4,\ H\text{-}5}$ = 7.6 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 5.0 Hz, $^3J_{H\text{-}4,\ H\text{-}3}$ = 3.2 Hz, 1H, H-4), 3.77 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 4.9 Hz, 1H, H-1), 3.71 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 5.5 Hz, 1H, H-1´), 3.40 (dd,

$^2J$ = 9.8 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 7.7 Hz, 1H, H-5), 3.14 (dd, $^2J$ = 9.8 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 5.0 Hz, 1H, H-5´), 1.37 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 0.97 (t, $^3J$ = 7.9 Hz, 9H, 3x$CH_3$-TES), 0.92 (s, 9H, 3x$CH_3$-TBS), 0.63 (q, $^3J$ = 8.1 Hz, 6H, 3x$CH_2$-TES), 0.14 (s, 3H, $CH_3$-TBS), 0.11 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.7 ($C_q$), 80.1 (C-2), 77.7 (C-3), 72.8 (C-4), 64.7 (C-1), 27.6 ($CH_3$), 27.4 ($CH_3$), 26.2 (3x$CH_3$-TBS), 18.6 ($C_q$-TBS), 7.9 (C-5), 7.1 (3x$CH_3$-TES), 4.8 (3x$CH_2$-TES), −4.1 ($CH_3$-TBS), −4.1 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{43}ISi_2O_4H^+$ 531.1817, found 531.1811. For NMR-spectra see p. 439.

**Synthesis of Compound 283**

**(4*S*,6*S*)-6-((benzyloxy)methyl)-4-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




**164** **282** **283**

$C_{35}H_{61}NSi_2O_7$
M = 664.04 g/mol

A mixture of iodide **282** (0.59 g, 1.11 mmol, 1 equiv) and cyanohydrin acetonide **164** (0.58 g, 2.22 mmol, 2 equiv) in THF (11 mL) was cooled to −40 °C. DMPU (0.81 mL, 6.66 mmol, 6 equiv) and freshly prepared LDA* (0.5M, 4.66 mL, 2.33 mmol, 2.1 equiv) were added sequentially, and the mixture was stirred for 1 h at −40 °C. After quenching with saturated $NH_4Cl$-solution (10 mL) DCM (20 mL) was added and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 15:1). The pure product was obtained as a colorless highly viscous oil (0.66 g, 1.00 mmol, 90%, *dr* > 20:1).

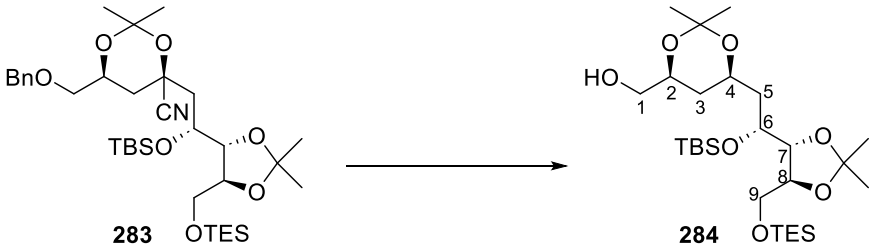
**n*-BuLi (2.5M, 1.07 mL, 2.68 mmol, 1 equiv) was added to a solution of DIPA (0.45 mL, 3.20 mmol, 1.2 equiv) in THF (3.83 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 15:1): $R_f$ = 0.23. $[\alpha]_D^{20}$ = +13.4° (c = 1.86, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.32 (m, 4H, 4xCH-Bn), 7.32–7.28 (m, 1H, 1xCH-Bn), 4.55 (s, 2H, $CH_2$-Bn), 4.39 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.3 Hz,

$^3J_{H\text{-}2,\ H\text{-}1'}$ = 4.9 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.3 Hz, 1H, H-2), 4.21–4.16 (m, 1H, H-6), 4.09 (dd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.7 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 3.1 Hz, 1H, H-7), 4.03 (ddd, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.7 Hz, $^3J_{H\text{-}8,\ H\text{-}9}$ = 5.1 Hz, $^3J_{H\text{-}8,\ H\text{-}9'}$ = 5.1 Hz, 1H, H-8), 3.76 (dd, $^2J$ = 10.4 Hz, $^3J_{H\text{-}9,\ H\text{-}8}$ = 5.0 Hz, 1H, H-9), 3.71 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}9',\ H\text{-}8}$ = 5.2 Hz, 1H, H-9´), 3.55 (dd, $^2J$ = 10.2 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 5.4 Hz, 1H, H-1), 3.46 (dd, $^2J$ = 10.2 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.5 Hz, 1H, H-1´), 2.42 (dd, $^2J$ = 14.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 6.3 Hz, 1H, H-5), 1.92–1.85 (m, 2H, H-5´, H-3-eq), 1.72–1.69 (m, 4H, H-3-ax, $CH_3$), 1.40 (s, 3H, $CH_3$), 1.39 (s, 3H, $CH_3$), 1.36 (s, 3H, $CH_3$), 0.97 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.63 (q, $^3J$ = 8.1 Hz, 6H, 3x$CH_2$-TES), 0.14 (s, 3H, $CH_3$-TBS), 0.12 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.8 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.3 (2xCH-Bn), 128.2 (CH-Bn), 122.1 (C-4), 109.4 ($C_q$), 101.8 ($C_q$), 80.9 (C-7), 77.7 (C-8), 74.0 ($CH_2$-Bn), 73.1 (C-1), 68.8 (CN), 67.7 (C-6), 66.5 (C-2), 64.9 (C-9), 46.6 (C-5), 37.5 (C-3), 31.2 ($CH_3$), 27.6 (2x$CH_3$), 26.3 (3x$CH_3$-TBS), 21.8 ($CH_3$), 18.5 ($C_q$-TBS), 7.1 (3x$CH_3$-TES), 4.8 (3x$CH_2$-TES), −3.6 ($CH_3$-TBS), −4.0 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{35}H_{61}NSi_2O_7H^+$ 664.4059, found 664.4055. For NMR-spectra see p. 441.

**Synthesis of Compound 284**

**((4*S*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methanol**



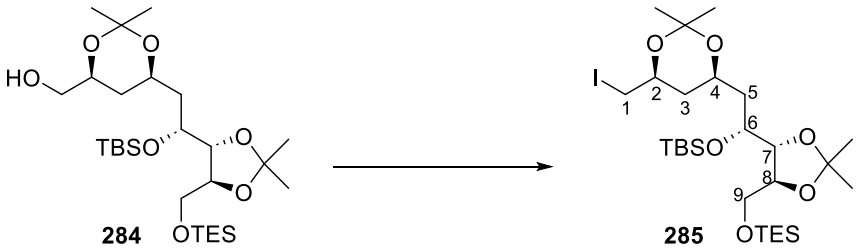

$C_{27}H_{56}Si_2O_7$
M = 548.91 g/mol

Lithium metal (0.33 g, 47.4 mmol, 50 equiv) was dissolved in liquid ammonia (10 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of cyanohydrin acetonide **283** (0.63 g, 0.95 mmol, 1 equiv) in THF (5 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched with solid $NH_4Cl$ (7.61 g, 142 mmol, 150 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (10 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a colorless highly viscous liquid (0.13 g, 0.24 mmol, 25%, *dr* > 20:1).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.24. $[\alpha]_D^{20}$ = −11.7° (c = 1.80, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.08 (dddd, $^3J_{H\text{-}4,\ H\text{-}3\text{-}ax}$ = 11.6 Hz, $^3J_{H\text{-}4,\ H\text{-}5'}$ = 7.7 Hz, $^3J_{H\text{-}4,\ H\text{-}5}$ = 4.9 Hz, $^3J_{H\text{-}4,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-4), 3.99 (ddd, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.7 Hz, $^3J_{H\text{-}8,\ H\text{-}9'}$ = 5.4 Hz, $^3J_{H\text{-}8,\ H\text{-}9}$ = 4.0 Hz, 1H, H-8), 3.97–3.91 (m, 2H, H-2, H-6), 3.88 (dd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.8 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 4.0 Hz, 1H, H-7), 3.76 (dd, $^2J$ = 10.8 Hz, $^3J_{H\text{-}9,\ H\text{-}8}$ = 4.0 Hz, 1H, H-9), 3.68 (dd, $^2J$ = 10.8 Hz, $^3J_{H\text{-}9',\ H\text{-}8}$ = 5.4 Hz, 1H, H-9´), 3.55 (ddd, $^2J$ = 11.3 Hz, $^3J_{H\text{-}1,\ OH}$ = 7.2 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.2 Hz, 1H, H-1), 3.44 (ddd, $^2J$ = 11.5 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 6.2 Hz, $^3J_{H\text{-}1',\ OH}$ = 5.4 Hz, 1H, H-1´), 1.92 (dd, $^3J_{OH,\ H\text{-}1}$ = 7.2 Hz, $^3J_{OH,\ H\text{-}1'}$ = 5.4 Hz 1H, OH), 1.76 (ddd, $^2J$ = 13.7 Hz, $^3J_{H\text{-}5,\ H\text{-}6}$ = 7.1 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 4.8 Hz, 1H, H-5), 1.64 (ddd, $^2J$ = 13.7 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 7.9 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.5 Hz, 1H, H-5´), 1.44–1.41 (m, 4H, H-3-eq, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.22 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.6 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.6 Hz, 1H, H-3-ax), 0.97 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.62 (q, $^3J$ = 7.8 Hz, 6H, 3x$CH_2$-TES), 0.09 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.3 ($C_q$), 99.1 ($C_q$), 80.3 (C-7), 78.3 (C-8), 70.3 (C-2), 69.2 (C-6), 66.6 (C-1), 66.1 (C-4), 64.8 (C-9), 41.2 (C-5), 33.2 (C-3), 30.4 ($CH_3$), 27.6 ($CH_3$), 27.5 ($CH_3$), 26.3 (3x$CH_3$-TBS), 20.2 ($CH_3$), 18.6 ($C_q$-TBS), 7.1 (3x$CH_3$-TES), 4.9 (3x$CH_2$-TES), −4.0 ($CH_3$-TBS), −4.3 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{56}Si_2O_7H^+$ 549.3637, found 549.3637. For NMR-spectra see p. 443.

### Synthesis of Compound 285

***tert*-butyl((*R*)-1-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)-2-((4*R*,6*S*)-6-(iodomethyl)-2,2-dimethyl-1,3-dioxan-4-yl)ethoxy)dimethylsilane**




$C_{27}H_{55}ISi_2O_6$
M = 658.81 g/mol

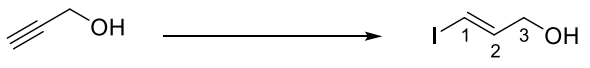
To a stirred solution of alcohol **284** (110 mg, 0.20 mmol, 1 equiv) in benzene (0.4 mL) were added $PPh_3$ (78.8 mg, 0.30 mmol, 1.5 equiv) and imidazole (20.5 mg, 0.30 mmol, 1.5 equiv). Iodine (76.3 mg, 0.30 mmol, 1.5 equiv) was added and the reaction mixture was stirred for 1 h at room temperature. The mixture was filtered over a pad of celite, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 40:1) and the pure product was obtained as a colorless viscous liquid (127 mg, 0.19 mmol, 96%).

**TLC** (silica, CyHex:EtOAc = 40:1): $R_f$ = 0.13. $[\alpha]_D^{20}$ = −5.0° (c = 1.00, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.08–4.03 (m, 1H, H-4), 3.99 (ddd, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.7 Hz, $^3J_{H\text{-}8,\ H\text{-}9'}$ = 5.3 Hz, $^3J_{H\text{-}8,\ H\text{-}9}$ = 4.1 Hz, 1H, H-8), 3.93 (ddd, $^3J_{H\text{-}6,\ H\text{-}5}$ = 7.0 Hz, $^3J_{H\text{-}6,\ H\text{-}5'}$ = 5.6 Hz, $^3J_{H\text{-}6,\ H\text{-}7}$ = 4.1 Hz, 1H, H-6), 3.88 (dd, $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.8 Hz, $^3J_{H\text{-}7,\ H\text{-}6}$ = 4.0 Hz, 1H, H-7), 3.85 (dddd, $^3J_{H\text{-}2,\ H\text{-}3\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 5.9 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 5.8 Hz, $^3J_{H\text{-}2,\ H\text{-}3\text{-}eq}$ = 2.5 Hz, 1H, H-2), 3.76 (dd, $^2J$ = 10.8 Hz, $^3J_{H\text{-}9,\ H\text{-}8}$ = 4.1 Hz, 1H, H-9), 3.68 (dd, $^2J$ = 10.8 Hz, $^3J_{H\text{-}9',\ H\text{-}8}$ = 5.4 Hz, 1H, H-9´), 3.16–3.11 (m, 2H, H-1, H-1´), 1.81–1.74 (m, 2H, H-3-eq, H-5), 1.66 (ddd, $^2J$ = 13.7 Hz, $^3J_{H\text{-}5',\ H\text{-}4}$ = 8.1 Hz, $^3J_{H\text{-}5',\ H\text{-}6}$ = 5.6 Hz, 1H, H-5´), 1.40 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.35 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.07 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}2}$ = 11.4 Hz, $^3J_{H\text{-}3\text{-}ax,\ H\text{-}4}$ = 11.4 Hz, 1H, H-3-ax), 0.97 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.62 (q, $^3J$ = 7.8 Hz, 6H, 3x$CH_2$-TES), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.3 ($C_q$), 99.7 ($C_q$), 80.3 (C-7), 78.3 (C-8), 69.7 (C-2), 69.2 (C-6), 66.4 (C-4), 64.7 (C-9), 40.9 (C-5), 37.6 (C-3), 30.2 ($CH_3$), 27.6 ($CH_3$), 27.5 ($CH_3$), 26.3 (3x$CH_3$-TBS), 20.2 ($CH_3$), 18.6 ($C_q$-TBS), 10.3 (C-1), 7.1 (3x$CH_3$-TES), 4.9 (3x$CH_2$-TES), −4.0 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{27}H_{55}ISi_2O_6H^+$ 659.2655, found 659.2653. For NMR-spectra see p. 445.

## 6.3.3 Contributions to the Southern Fragment

### Synthesis of Compound 230

**(*E*)-3-iodoprop-2-en-1-ol**




**229** **230**

$C_3H_5IO$
M = 183.98 g/mol

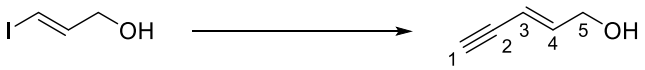
A Schlenk flask was charged with $Cp_2ZrCl_2$ (7.02 g, 24.0 mmol, 1.2 equiv) and THF (90 mL) and the suspension was cooled to 0 °C. For light exclusion the flask was wrapped with aluminum foil and DIBAL-H (1M in THF, 22.1 mL, 22.1 mmol, 1.1 equiv) was added dropwise. The mixture was stirred for 30 min at 0 °C. Meanwhile, another Schlenk flask was charged with propargylic alcohol (**229**, 1.16 mL, 20.1 mmol, 1 equiv) and the solution was cooled to −78 °C before DIBAL-H (1M in THF, 24.1 mL, 24.1 mmol, 1.2 equiv) was added dropwise. After stirring for 30 min at 0 °C, the mixture of the second flask was added to the first flask by a syringe. The combined mixture was stirred for 2 h at room temperature before it was cooled to −78 °C. A solution of iodine (7.60 g, 30.2 mmol, 1.5 equiv) in THF (20 mL) was added and the mixture was stirred for 30 min at −78 °C. Afterwards, the mixture was quenched with 1M HCl (50 mL) and the aqueous phase was extracted with $Et_2O$ (3 x 100 mL). The combined organic layers

were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, Pentane:$Et_2O$ = 3:1) and the pure product was obtained as a colorless oil (2.78 g, 15.1 mmol, 75%).

**TLC** (silica, Pentane:$Et_2O$ = 3:1): $R_f$ = 0.32. **$^1$H-NMR** (700 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 6.70 (dt, $^3J_{H\text{-}2,\,H\text{-}1}$ = 14.5 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 5.5 Hz, 1H, H-2), 6.40 (dt, $^3J_{H\text{-}1,\,H\text{-}2}$ = 14.5 Hz, $^4J_{H\text{-}1,\,H\text{-}3}$ = 1.6 Hz, 1H, H-1), 4.10 (dt, $^3J_{H\text{-}3,\,H\text{-}2}$ = 5.5 Hz, $^4J_{H\text{-}3,\,H\text{-}1}$ = 1.6 Hz, 1H, H-3). **$^{13}$C-NMR** (176 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 144.9 (C-2), 77.9 (C-1), 65.3 (C-3). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_3H_5IOH^+$ 184.9458, found 184.9456. For NMR-spectra see p. 447.

**Synthesis of Compound 231**

**(*E*)-pent-2-en-4-yn-1-ol**




**230** **231**

$C_5H_6O$
M = 82.10 g/mol

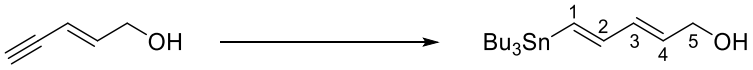
A Schlenk flask was charged with $ZnBr_2$ (1.53 g, 6.78 mmol, 0.6 equiv) and THF (55 mL) and the suspension was cooled to 0 °C. EtMgBr (1M in THF, 12.4 mL, 12.4 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 30 min at 0 °C before vinyl iodide **230** (2.08 g, 11.3 mmol, 1 equiv) in THF (2 mL) was added. The mixture was stirred for another 30 min at 0 °C. Meanwhile, another Schlenk flask was charged with $ZnBr_2$ (1.78 g, 7.19 mmol, 0.7 equiv) and THF (38 mL) and this mixture was also cooled to 0 °C. A solution of ethynyl magnesium bromide (0.5M in THF, 29.4 mL, 14.7 mmol, 1.3 equiv) was added and the mixture was stirred for 30 min at 0 °C. Subsequently, the mixture of the second flask was added to the first flask by a syringe. A solution of $PdCl_2$(DPEphos) (405 mg, 0.57 mmol, 0.05 equiv) in DMF (20 mL) was added and the mixture was stirred overnight at room temperature. Afterwards, the mixture was quenched with 1M HCl (50 mL) and the aqueous phase was extracted with $Et_2O$ (3 x 150 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, Pentane:$Et_2O$ = 3:1) and the pure product was obtained as a colorless oil (610 mg, 7.40 mmol, 66%).

**TLC** (silica, Pentane:$Et_2O$ = 3:1): $R_f$ = 0.32. **$^1$H-NMR** (700 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 6.36 (dt, $^3J_{H\text{-}4,\,H\text{-}3}$ = 16.0 Hz, $^3J_{H\text{-}4,\,H\text{-}5}$ = 5.0 Hz, 1H, H-4), 5.75 (ddd, $^3J_{H\text{-}3,\,H\text{-}4}$ = 16.0 Hz, $^4J_{H\text{-}3,\,H\text{-}1}$ = 2.1 Hz, $^4J_{H\text{-}3,\,H\text{-}5}$ = 1.8 Hz 1H, H-3), 4.23 (dd, $^3J_{H\text{-}5,\,H\text{-}4}$ = 5.1 Hz, $^4J_{H\text{-}5,\,H\text{-}3}$ = 1.9 Hz, 1H, H-3), 2.89 (d, $^4J_{H\text{-}1,\,H\text{-}3}$ = 2.2 Hz, 1H, H-1). **$^{13}$C-NMR** (176 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 143.9 (C-4),

109.3 (C-3), 81.7 (C-2), 78.1 (C-1), 62.9 (C-5). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_5H_6OH^+$ 83.0491, found 83.0494. For NMR-spectra see p. 449.

### Synthesis of Compound 232

**(2*E*,4*E*)-5-(tributylstannyl)penta-2,4-dien-1-ol**




**231** **232**

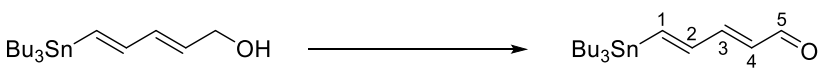
$C_{17}H_{34}SnO$
M = 373.17 g/mol

A Schlenk tube was charged with $Pd_2dba_3$ (10.0 mg, 11.0 µmol, 0.005 equiv) and $Cy_3PHBF_4$ (16.2 mg, 43.9 µmol, 0.02 equiv) and DCM (12 mL) as well as DIPEA (15.3 µL, 87.7 µmol, 0.04 equiv) were added. The mixture was stirred for 10 min at room temperature before alkyne **231** (180 mg, 2.19 mmol, 1 equiv) in DCM (1.5 mL) was added. The mixture was cooled to 0 °C and $Bu_3SnH$ (0.70 mL, 2.63 mmol, 1.2 equiv) in DCM (7 mL) was added dropwise over 5 min. The mixture was first stirred for 2 h at 0 °C and then for 2 h at room temperature. After complete conversion of the starting material the solvent was evaporated under reduced pressure and the crude mixture was purified by flash chromatography (silica, CyHex:EtOAc = 9:1). The pure product was obtained as a colorless oil (498 mg, 1.33 mmol, 61%).

**TLC** (silica, CyHex:EtOAc = 9:1): $R_f$ = 0.23. **$^1$H-NMR** (700 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 6.54 (ddd, $^3J_{H\text{-}2,\,H\text{-}1}$ = 18.7 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 9.9 Hz, $^4J_{H\text{-}2,\,H\text{-}4}$ = 0.8 Hz, 1H, H-2), 6.26 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 18.8 Hz, 1H, H-1), 6.26–6.21 (m, 1H, H-3), 5.82–5.77 (m, 1H, H-4), 4.20 (br s, 2H, H-5), 1.53–1.46 (m, 6H, 3x$CH_2$), 1.34–1.28 (m, 6H, 3x$CH_2$), 0.92–0.88 (m, 6H, 3x$CH_2$), 0.89 (t, $^3J$ = 7.4 Hz, 9H, 3x$CH_3$). **$^{13}$C-NMR** (176 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 146.0 (C-1), 109.3 (C-2), 81.7 (C-4), 78.1 (C-3), 62.9 (C-5), 29.2 (3x$CH_2$), 27.4 (3x$CH_2$), 13.8 (3x$CH_3$), 9.7 (3x$CH_2$). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{34}SnOH^+$ 375.1704, found 375.1706. For NMR-spectra see p. 451.

### Synthesis of Compound 233

**(2*E*,4*E*)-5-(tributylstannyl)penta-2,4-dienal**




**232** **233**

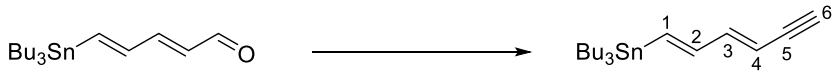
$C_{17}H_{32}SnO$
M = 371.15 g/mol

To a solution of primary alcohol **232** (0.60 g, 1.61 mmol, 1 equiv) in DCM (20 mL) was added $MnO_2$ (heated overnight to 80 °C, 2.38 g, 27.4 mmol, 17 equiv) and the suspension was stirred for 5 h at room temperature. The mixture was filtered through a pad of celite, and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 20:1) and the pure product was obtained as a colorless oil (0.51 g, 1.37 mmol, 85%).

**TLC** (silica, CyHex:EtOAc = 20:1): $R_f$ = 0.28. **$^1$H-NMR** (700 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 9.55 (d, $^3J_{H\text{-}5,\,H\text{-}4}$ = 8.0 Hz, 1H, H-5), 7.05 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 18.8 Hz, 1H, H-1), 7.04–7.00 (m, 1H, H-3), 6.84 (dd, $^3J_{H\text{-}2,\,H\text{-}1}$ = 18.7 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 10.2 Hz, 1H, H-2), 6.03 (dd, $^3J_{H\text{-}4,\,H\text{-}3}$ = 15.3 Hz, $^3J_{H\text{-}4,\,H\text{-}5}$ = 7.9 Hz, 1H, H-4), 1.59–1.48 (m, 6H, 3x$CH_2$), 1.35–1.28 (m, 6H, 3x$CH_2$), 1.04–0.94 (m, 6H, 3x$CH_2$), 0.90 (t, $^3J$ = 7.3 Hz, 9H, 3x$CH_3$). **$^{13}$C-NMR** (176 MHz, $CDCl_3$, 298 K): $\delta$ (ppm) = 194.7 (C-5), 154.0 (C-3), 151.8 (C-1), 144.8 (C-2), 130.6 (C-4), 29.6 (3x$CH_2$), 27.8 (3x$CH_2$), 14.0 (3x$CH_3$), 10.2 (3x$CH_2$). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{32}SnOH^+$ 373.1548, found 373.1542. For NMR-spectra see p. 453.

**Synthesis of Compound 235**

**tributyl((1*E*,3*E*)-hexa-1,3-dien-5-yn-1-yl)stannane**




**233** **235**

$C_{18}H_{32}Sn$
M = 367.16 g/mol

A solution of trimethylsilyl diazomethane (**234**, 2M in hexane, 0.30 mL, 0.61 mmol, 1.5 equiv) in THF (1 mL) was cooled to −78 °C and *n*-BuLi (2.5M in hexane, 0.21 mL, 0.53 mmol, 1.3 equiv) was added dropwise. The mixture was stirred for 30 min at −78 °C before a solution of aldehyde **233** (150 mg, 0.40 mmol, 1 equiv) in THF (2 mL) was added. After stirring 1 h at −78 °C the mixture was warmed to 0 °C and stirred for another 60 min at 0 °C. The mixture was quenched with saturated $NH_4Cl$-solution (3 mL) and extracted with pentane (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, Pentane) and the pure product was obtained as a colorless oil (110 mg, 0.30 mmol, 75%).

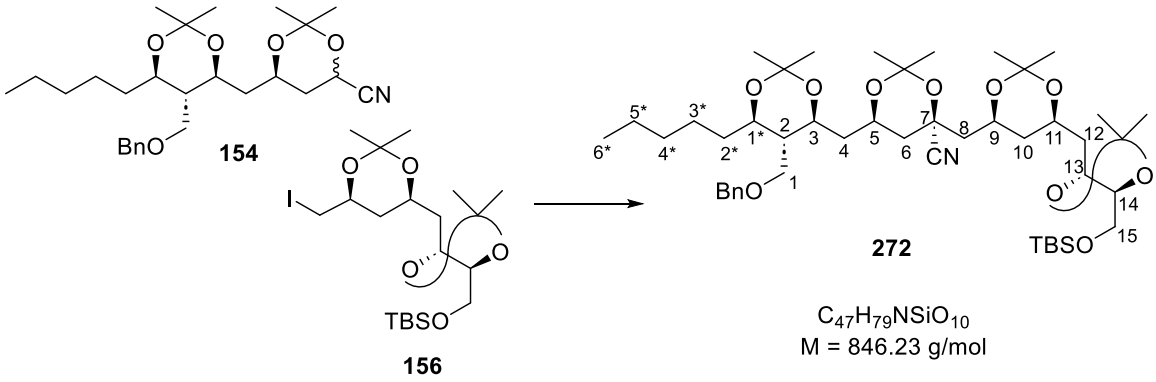
**TLC** (silica, Pentane): $R_f$ = 0.85. **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 6.66–6.55 (m, 2H, H-2, H-3), 6.47 (d, $^3J_{H\text{-}1,\,H\text{-}2}$ = 18.1 Hz, 1H, H-1), 5.53 (dd, $^3J_{H\text{-}4,\,H\text{-}3}$ = 15.4 Hz, $^4J_{H\text{-}4,\,H\text{-}6}$ = 2.2 Hz, 1H, H-4), 3.08 (d, $^3J_{H\text{-}6,\,H\text{-}4}$ = 2.3 Hz, 1H, H-6), 1.55–1.46 (m, 6H, 3x$CH_2$), 1.35–1.27 (m, 6H, 3x$CH_2$), 1.01–0.92 (m, 6H, 3x$CH_2$), 0.89 (t, $^3J$ = 7.3 Hz, 9H, 3x$CH_3$). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 146.6 (C-3), 145.8 (C-2), 140.9 (C-1), 109.1 (C-4), 83.4 (C-5), 80.2

(C-6), 29.6 (3x$CH_2$), 27.8 (3x$CH_2$), 14.0 (3x$CH_3$), 10.1 (3x$CH_2$). **MS (EI, 70.0 eV)** *m/z*: [$M^{\cdot+}$] Calcd for $C_{18}H_{32}Sn^{\cdot+}$ 368.2, found 368.2. For NMR-spectra see p. 455.

## 6.3.4 Contributions to Fragment Coupling

### Synthesis of Compound 272

**(4*R*,6*R*)-6-(((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)methyl)-4-(((4*S*,6*R*)-6-(((4*S*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




$C_{47}H_{79}NSiO_{10}$
M = 846.23 g/mol

A mixture of iodide **156** (40.0 mg, 77.7 µmol, 1 equiv) and cyanohydrin acetonide **154** (71.5 mg, 156 µmol, 1.5 equiv) in THF (0.8 mL) was cooled to −40 °C. DMPU (56.4 µL, 0.47 mmol, 6 equiv) and freshly prepared LDA* (0.5M, 0.33 mL, 163 µmol, 2.1 equiv) were added sequentially, and the mixture was stirred for 1 h at −40 °C. After quenching with saturated $NH_4Cl$-solution (2 mL) DCM (5 mL) was added and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless highly viscous oil (56 mg, 66.2 µmol, 85%).

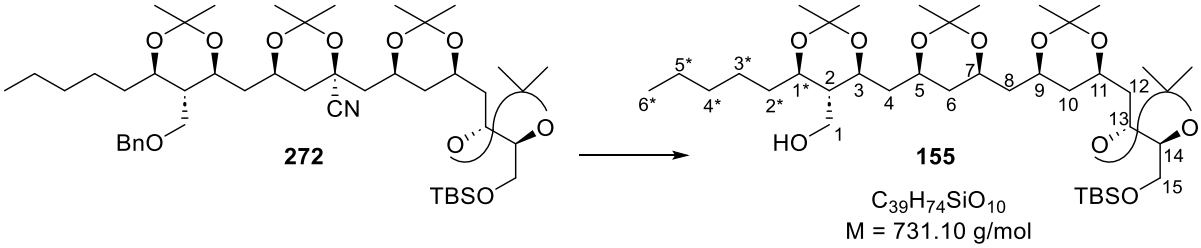
**n*-BuLi (2.5M in hexane, 0.14 mL, 0.36 mmol, 1 equiv) was added to a solution of DIPA (60.0 µL, 0.43 mmol, 1.2 equiv) in THF (0.51 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.20. $[\alpha]_D^{20}$ = +20.0° (c = 1.00, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.37–7.26 (m, 5H, 5xCH-Bn), 4.46 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.43–4.37 (m, 2H, H-5, $CH_2$-Bn´), 4.27 (ddd, $^3J_{H\text{-}13,\ H\text{-}12}$ = 8.5 Hz, $^3J_{H\text{-}13,\ H\text{-}14}$ = 5.6 Hz, $^3J_{H\text{-}13,\ H\text{-}12'}$ = 5.6 Hz, 1H, H-13), 4.17 (dddd, $^3J_{H\text{-}9,\ H\text{-}10\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.7 Hz, $^3J_{H\text{-}9,\ H\text{-}8'}$ = 3.7 Hz, $^3J_{H\text{-}9,\ H\text{-}10\text{-}eq}$ = 2.5 Hz, 1H, H-9), 4.10–4.03 (m, 3H, H-3, H-11, H-14), 3.92 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 2.5 Hz, 1H, H-1*), 3.66 (dd, $^2J$ = 10.5 Hz,

$^{3}J_{\text{H-15, H-14}}$ = 7.4 Hz, 1H, H-15), 3.57 (dd, $^{2}J$ = 10.4 Hz, $^{3}J_{\text{H-15´, H-14}}$ = 5.1 Hz, 1H, H-15´), 3.48–3.43 (m, 2H, H-1, H-1´), 2.01 (dd, $^{2}J$ = 14.5 Hz, $^{3}J_{\text{H-8, H-9}}$ = 7.6 Hz, 1H, H-8), 1.87 (dd, $^{2}J$ = 14.5 Hz, $^{3}J_{\text{H-8´, H-9}}$ = 3.6 Hz, 1H, H-8´), 1.82–1.77 (m, 2H, H-6, H-12), 1.77–1.70 (m, 3H, H-4, H-4´, H-12´), 1.69–1.65 (m, 4H, H-6´, $CH_3$), 1.63 (ddd, $^{2}J$ = 12.7 Hz, $^{3}J_{\text{H-10-eq, H-9}}$ = 2.5 Hz, $^{3}J_{\text{H-10-eq, H-11}}$ = 2.5 Hz, 1H, H-10-eq), 1.60–1.55 (m, 1H, H-2*), 1.47–1.43 (m, 1H, H-3*), 1.42 (s, 3H, $CH_3$), 1.42 (s, 3H, $CH_3$), 1.41–1.38 (m, 1H, H-2), 1.38 (s, 3H, $CH_3$), 1.34 (d, $^{4}J$ = 0.9 Hz, 3H, $CH_3$), 1.33–1.31 (m, 3H, $CH_3$), 1.31–1.28 (m, 9H, H-2*´, H-5*, 2x$CH_3$), 1.27–1.19 (m, 4H, H-3*´, H-4*, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^{3}J_{\text{H-6*, H-5*}}$ = 7.3 Hz, 3H, H-6*), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.2 (CH-Bn), 128.1 (2xCH-Bn), 122.8 (C-7), 108.2 ($C_q$), 101.4 ($C_q$), 99.0 ($C_q$), 98.3 ($C_q$), 78.5 (C-14), 73.8 ($CH_2$-Bn), 73.7 (C-13), 70.4 (C-1*), 68.7 (CN), 67.5 (C-1), 67.2 (C-3), 67.1 (C-11), 64.8 (C-9), 64.2 (C-5), 62.7 (C-15), 48.4 (C-8), 45.2 (C-2), 39.5 (C-4), 38.5 (C-12), 37.3 (C-10), 36.1 (C-6), 33.6 (C-2*), 32.4 (C-4*), 31.3 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 28.6 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.9 ($CH_3$), 25.2 (C-3*), 23.3 (C-5*), 22.0 ($CH_3$), 20.2 ($CH_3$), 20.1 ($CH_3$), 18.8 ($C_q$-TBS), 14.4 (C-6*), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (MALDI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{47}H_{79}NSiO_{10}Na^+$ 868.5365, found 868.5343. For NMR-spectra see p. 457.

### Synthesis of Compound 155

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-(((4*R*,5*S*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methanol**



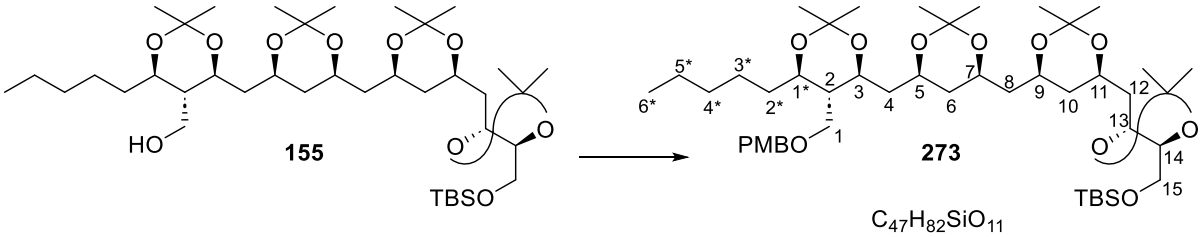

Lithium metal (52.0 mg, 6.94 mmol, 100 equiv) was dissolved in liquid ammonia (3.7 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of cyanohydrin acetonide **272** (63.0 mg, 75.5 µmol, 1 equiv) in THF (1.5 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched with solid $NH_4Cl$ (0.80 g, 14.9 mmol, 200 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (10 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash

chromatography (silica, CyHex:EtOAc = 3:1). The pure product was obtained as a white solid (54 mg, 73.7 µmol, 99%).

**TLC** (silica, CyHex:EtOAc = 3:1): $R_f$ = 0.30. $[\alpha]_D^{20}$ = +20.0° (c = 0.32, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.28 (ddd, $^3J_{H\text{-}13,\ H\text{-}12'}$ = 8.3 Hz, $^3J_{H\text{-}13,\ H\text{-}12'}$ = 5.7 Hz, $^3J_{H\text{-}13,\ H\text{-}14}$ = 5.7 Hz, 1H, H-13), 4.19 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 5.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}eq}$ = 2.4 Hz, 1H, H-5), 4.07–4.01 (m, 3H, H-7, H-11, H-14), 4.00–3.94 (m, 2H, H-3, H-9), 3.74 (ddd, $^3J_{H\text{-}1^*,\ H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^*}$ = 8.2 Hz, $^3J_{H\text{-}1^*,\ H\text{-}2^{*'}}$ = 2.5 Hz, 1H, H-1*), 3.66 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}15,\ H\text{-}14}$ = 7.4 Hz, 1H, H-15), 3.67–3.63 (m, 1H, H-1), 3.57 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}15',\ H\text{-}14}$ = 5.1 Hz, 1H, H-15´), 3.51 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}1',\ OH}$ = 5.5 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.2 Hz, 1H, H-1´), 2.14 (t, $^3J_{OH,\ H\text{-}2}$ = 5.3 Hz, 1H, OH), 1.82–1.76 (m, 2H, H-4, H-12), 1.76–1.70 (m, 2H, H-4´, H-8), 1.69–1.64 (m, 2H, H-2*, H-12´), 1.58 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}10\text{-}eq,\ H\text{-}9}$ = 2.5 Hz, $^3J_{H\text{-}10\text{-}eq,\ H\text{-}11}$ = 2.5 Hz, 1H, H-10-eq), 1.50 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}5}$ = 2.5 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}7}$ = 2.5 Hz, 1H, H-6-eq), 1.48–1.45 (m, 1H, H-3*), 1.44 (d, $^4J$ = 0.7 Hz, 3H, $CH_3$), 1.44–1.41 (m, 1H, H-8´), 1.41 (s, 3H, $CH_3$), 1.40 (s, 3H, $CH_3$), 1.39–1.35 (m, 5H, H-2, H-2*´, $CH_3$), 1.34–1.31 (m, 11H, H-5*, 3x$CH_3$), 1.30–1.24 (m, 6H, H-3*´, H-4*, $CH_3$), 1.18 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}5}$ = 11.6 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}7}$ = 11.6 Hz, 1H, H-6-ax), 1.13 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}9}$ = 11.5 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}11}$ = 11.5 Hz, 1H, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 108.1 ($C_q$), 99.0 ($C_q$), 98.9 ($C_q$), 98.2 ($C_q$), 78.5 (C-14), 73.8 (C-13), 70.4 (C-1*), 68.1 (C-3), 67.0 (C-11), 66.3 (C-5), 65.8 (C-7), 65.7 (C-9), 62.7 (C-15), 60.5 (C-1), 46.2 (C-2), 43.7 (C-8), 40.3 (C-4), 37.0 (C-10), 36.8 (C-6), 36.2 (C-12), 33.8 (C-2*), 32.5 (C-4*), 30.5 ($CH_3$), 30.5 ($CH_3$), 30.5 ($CH_3$), 28.6 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.9 ($CH_3$), 25.3 (C-3*), 23.3 (C-5*), 20.3 (2x$CH_3$), 20.1 ($CH_3$), 18.8 ($C_q$-TBS), 14.4 (C-6*), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (MALDI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{39}H_{74}SiO_{10}Na^+$ 753.4943, found 753.4927. For NMR-spectra see p. 459.

**Synthesis of Compound 273**

***tert*-butyl(((4*S*,5*R*)-5-(((4*R*,6*R*)-6-(((4*S*,6*S*)-6-(((4*S*,5*R*,6*R*)-5-(((4-methoxybenzyl)oxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methoxy)dimethylsilane**




$C_{47}H_{82}SiO_{11}$
M = 851.25 g/mol

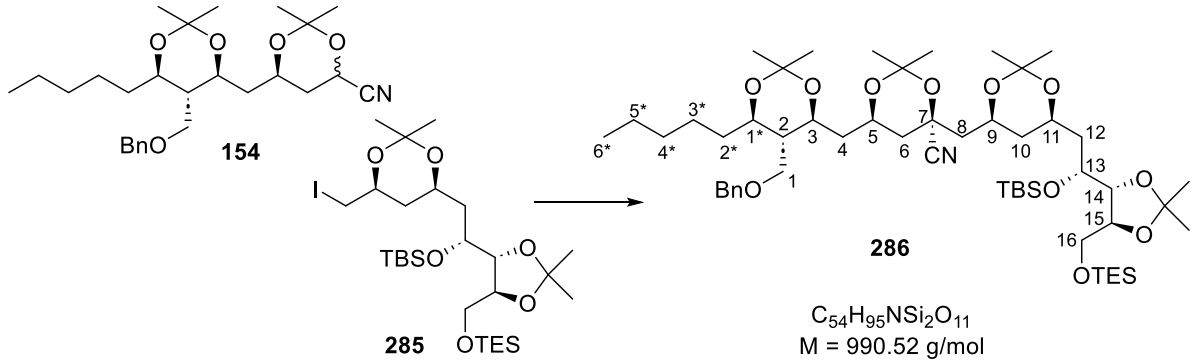
A solution of primary alcohol **155** (46.0 mg, 62.9 µmol, 1 equiv) in DMF (0.6 mL) was cooled to 0 °C and NaH (60% in mineral oil, 5.00 mg, 126 µmol, 2 equiv) was added. PMBCl (17.0 µL, 126 µmol, 2 equiv) was added and the mixture was stirred for 2 h at 0 °C. Subsequently, the mixture was quenched by slow addition of water (2 mL) and DCM (5 mL), and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 6:1). The pure product was obtained as a colorless highly viscous oil (20 mg, 23.5 µmol, 38%).

**TLC** (silica, CyHex:EtOAc = 6:1): $R_f$ = 0.26. $[\alpha]_D^{20}$ = +1.20° (c = 0.85, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.24–7.20 (m, 2H, 2xCH-PMB), 6.89–6.85 (m, 2H, 2xCH-PMB), 4.37 (d, $^2J$ = 11.7 Hz, 1H, $CH_2$-PMB), 4.31 (d, $^2J$ = 11.6 Hz, 1H, $CH_2$-PMB´), 4.29–4.26 (m, 1H, H-13), 4.11–3.95 (m, 6H, H-3, H-5, H-7, H-9, H-11, H-14), 3.88 (ddd, $^3J_{H\text{-}1^*,\,H\text{-}2}$ = 10.4 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^*}$ = 7.9 Hz, $^3J_{H\text{-}1^*,\,H\text{-}2^{*\prime}}$ = 2.6 Hz, 1H, H-1*), 3.79 (s, 3H, OMe), 3.67 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}15,\,H\text{-}14}$ = 7.3 Hz, 1H, H-15), 3.57 (dd, $^2J$ = 10.5 Hz, $^3J_{H\text{-}15',\,H\text{-}14}$ = 5.1 Hz, 1H, H-15´), 3.44–3.37 (m, 2H, H-1, H-1´), 1.79 (ddd, $^2J$ = 13.5 Hz, $^3J_{H\text{-}12,\,H\text{-}13}$ = 8.4 Hz, $^3J_{H\text{-}12,\,H\text{-}11}$ = 6.2 Hz, 1H, H-12), 1.74–1.69 (m, 1H, H-8), 1.69–1.65 (m, 1H, H-12´), 1.65–1.60 (m, 2H, H-4, H-4´), 1.60–1.54 (m, 2H, H-6-eq, H-10-eq), 1.53–1.51 (m, 1H, H-2*), 1.46–1.42 (m, 1H, H-3*´), 1.42–1.39 (m, 7H, H-8´, 2x$CH_3$), 1.38 (s, 3H, $CH_3$), 1.37 (s, 3H, $CH_3$), 1.34–1.31 (m, 4H, H-2, $CH_3$), 1.31–1.20 (m, 15H, H-2*´, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.13 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}10\text{-}ax,\,H\text{-}9}$ = 11.4 Hz, $^3J_{H\text{-}10\text{-}ax,\,H\text{-}11}$ = 11.4 Hz, 1H, H-10-ax), 1.03 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}6\text{-}ax,\,H\text{-}5}$ = 11.7 Hz, $^3J_{H\text{-}6\text{-}ax,\,H\text{-}7}$ = 11.7 Hz, 1H, H-6-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\,H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.07 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 159.8 ($C_q$-PMB), 131.7 ($C_q$-PMB), 129.7 (2xCH-PMB), 114.2 (2xCH-PMB), 108.1 ($C_q$), 98.8 ($C_q$), 98.7 ($C_q$), 98.1 ($C_q$), 78.5 (C-14), 73.8 (C-13), 73.3 ($CH_2$-PMB), 70.5 (C-1*), 67.1 (C-3), 67.1 (C-1), 67.0 (C-11), 66.3 (C-5), 65.7 (C-7), 65.6 (C-9), 62.8 (C-15), 55.8 (OMe),

45.3 (C-2), 43.8 (C-8), 40.3 (C-4), 36.9 (C-10), 36.8 (C-6), 36.2 (C-12), 33.6 (C-2*), 32.5 (C-4*), 30.6 ($CH_3$), 30.6 ($CH_3$), 30.4 ($CH_3$), 28.6 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.9 ($CH_3$), 25.3 (C-3*), 23.3 (C-5*), 20.3 ($CH_3$), 20.3 ($CH_3$), 20.2 ($CH_3$), 18.8 ($C_q$-TBS), 14.5 (C-6*), −5.1 ($CH_3$-TBS), −5.1 ($CH_3$-TBS). **HRMS (MALDI-TOF)** *m/z*: $[M+Ag]^+$ Calcd for $C_{47}H_{82}SiO_{11}Ag^+$ 957.4672, found 957.4655. For NMR-spectra see p. 461.

**Synthesis of Compound 286**

**(4*R*,6*R*)-6-(((4*S*,5*R*,6*R*)-5-((benzyloxy)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-4-yl)methyl)-4-(((4*S*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane-4-carbonitrile**




A mixture of iodide **285** (114 mg, 0.17 mmol, 1 equiv) and cyanohydrin acetonide **154** (119 mg, 0.26 mmol, 1.5 equiv) in THF (1.7 mL) was cooled to −40 °C. DMPU (130 µL, 1.04 mmol, 6 equiv) and freshly prepared LDA* (0.5M, 0.73 mL, 0.36 mmol, 2.1 equiv) were added sequentially, and the mixture was stirred for 1 h at −40 °C. After quenching with saturated $NH_4Cl$-solution (2 mL) DCM (5 mL) was added and the organic phase was separated. The aqueous phase was extracted with DCM (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless highly viscous oil (156 mg, 0.16 mmol, 91%).

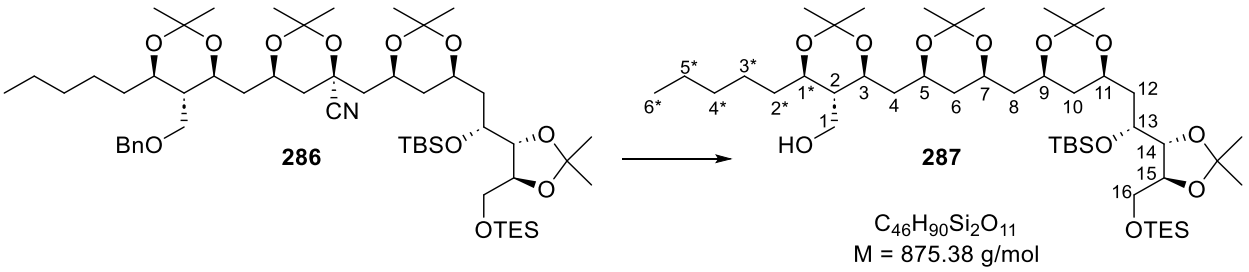
**n*-BuLi (2.5M in hexane, 0.43 mL, 1.07 mmol, 1 equiv) was added to a solution of DIPA (0.18 mL, 1.28 mmol, 1.2 equiv) in THF (1.53 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C before it was used for the reaction.

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.28. $[\alpha]_D^{20}$ = +6.8° (c = 1.46, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.36–7.27 (m, 5H, 5xCH-Bn), 4.46 (d, $^2J$ = 12.0 Hz, 1H, $CH_2$-Bn), 4.43–4.38 (m, 2H, H-5, $CH_2$-Bn´), 4.16 (dddd, $^3J_{H\text{-}9,\ H\text{-}10\text{-}ax}$ = 11.4 Hz, $^3J_{H\text{-}9,\ H\text{-}8}$ = 7.4 Hz, $^3J_{H\text{-}9,\ H\text{-}8'}$ = 3.8 Hz, $^3J_{H\text{-}9,\ H\text{-}10\text{-}eq}$ = 2.4 Hz, 1H, H-9), 4.09–4.03 (m, 2H, H-3, H-11), 4.00 (ddd, $^3J_{H\text{-}15,\ H\text{-}14}$ = 7.7 Hz, $^3J_{H\text{-}15,\ H\text{-}16'}$ = 5.3 Hz, $^3J_{H\text{-}15,\ H\text{-}16}$ = 4.1 Hz, 1H, H-15), 3.95–3.90 (m, 2H, H-1*,

H-13), 3.88 (dd, $^{3}J_{\text{H-14, H-15}}$ = 7.7 Hz, $^{3}J_{\text{H-14, H-13}}$ = 4.0 Hz, 1H, H-14), 3.76 (dd, $^{2}J$ = 10.8 Hz, $^{3}J_{\text{H-16, H-15}}$ = 4.1 Hz, 1H, H-16), 3.68 (dd, $^{2}J$ = 10.8 Hz, $^{3}J_{\text{H-16´, H-15}}$ = 5.1 Hz, 1H, H-16´), 3.48–3.42 (m, 2H, H-1, H-1´), 2.01 (dd, $^{2}J$ = 14.5 Hz, $^{3}J_{\text{H-8, H-9}}$ = 7.3 Hz, 1H, H-8), 1.86 (dd, $^{2}J$ = 14.5 Hz, $^{3}J_{\text{H-8´, H-9}}$ = 3.8 Hz, 1H, H-8´), 1.81 (dd, $^{2}J$ = 13.6 Hz, $^{3}J_{\text{H-6-eq, H-5}}$ = 2.1 Hz, 1H, H-6-eq), 1.78–1.69 (m, 4H, H-4, H-4´, H-6-ax, H-12), 1.66 (s, 3H, $CH_3$), 1.63 (ddd, $^{2}J$ = 13.7 Hz, $^{3}J_{\text{H-12´, H-13}}$ = 8.1 Hz, $^{3}J_{\text{H-12´, H-11}}$ = 5.6 Hz, 1H, H-12´), 1.60–1.55 (m, 2H, H-2*, H-10-eq), 1.47–1.43 (m, 1H, H-3*), 1.42 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$), 1.40–1.38 (m, 1H, H-2), 1.37 (s, 3H, $CH_3$), 1.36 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.34 (d, $^{4}J$ = 0.8 Hz, 3H, $CH_3$), 1.32 (d, $^{4}J$ = 0.7 Hz, 3H, $CH_3$), 1.32–1.25 (m, 9H, H-2*´, H-3*´, H-4*, H-5*, $CH_3$), 1.25–1.17 (m, 2H, H-6-eq, H-10-eq), 0.97 (t, $^{3}J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^{3}J_{\text{H-6*, H-5*}}$ = 7.2 Hz, 3H, H-6*), 0.62 (q, $^{3}J$ = 7.8 Hz, 6H, 3x$CH_2$-TES), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 139.0 ($C_q$-Bn), 128.9 (2xCH-Bn), 128.1 (CH-Bn), 128.1 (2xCH-Bn), 122.7 (C-7), 109.3 ($C_q$), 101.4 ($C_q$), 99.0 ($C_q$), 98.3 ($C_q$), 80.3 (C-14), 80.0 (C-15), 73.8 ($CH_2$-Bn), 70.4 (C-1*), 70.1 (C-13), 68.7 (CN), 67.5 (C-1), 67.2 (C-3), 66.6 (C-11), 64.9 (C-9), 64.7 (C-16), 64.2 (C-5), 48.4 (C-8), 45.2 (C-2), 41.1 (C-12), 39.4 (C-4), 38.6 (C-6), 38.1 (C-10), 33.6 (C-2*), 32.4 (C-4*), 31.3 ($CH_3$), 30.4 ($CH_3$), 30.4 ($CH_3$), 27.6 ($CH_3$), 27.5 ($CH_3$), 26.3 (3x$CH_3$-TBS), 26.3 (3x$CH_3$-TBS), 25.2 (C-3*), 23.3 (C-5*), 22.0 ($CH_3$), 20.1 ($CH_3$), 20.0 ($CH_3$), 18.6 ($C_q$-TBS), 14.4 (C-6*), 7.1 (3x$CH_3$-TES), 4.9 (3x$CH_2$-TES), −4.1 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+Na]^+$ Calcd for $C_{54}H_{95}NSi_2O_{11}Na^+$ 1012.6336, found 1012.6344. For NMR-spectra see p. 463.

**Synthesis of Compound 287**

**((4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,5*S*)-2,2-dimethyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxan-5-yl)methanol**



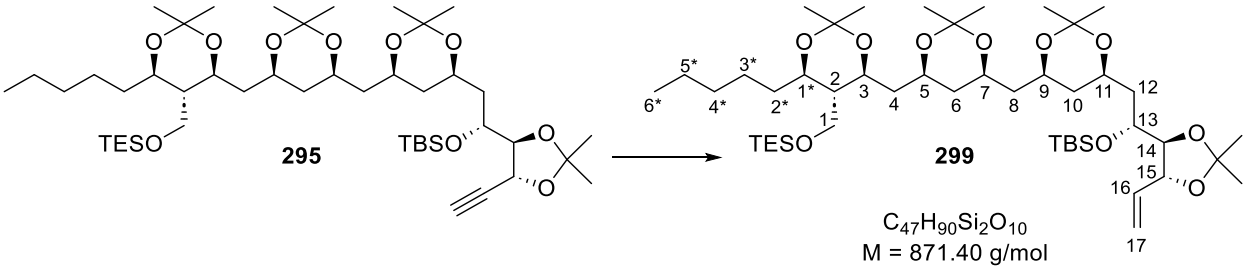

Lithium metal (46.0 mg, 6.65 mmol, 50 equiv) was dissolved in liquid ammonia (6.5 mL) which was condensed in a reaction tube before at −78 °C. The resulting blue solution was stirred for 5 min before a solution of cyanohydrin acetonide **286** (130 mg, 0.13 mmol, 1 equiv) in THF (3 mL) was added. The reaction mixture was stirred for 1 h at −78 °C and was then quenched

with solid $NH_4Cl$ (0.70 g, 13.3 mmol, 100 equiv). The mixture was slowly warmed to room temperature over 2 h and the ammonia was evaporated. The residue was again cooled to −78 °C and water (10 mL) was added slowly. After warming to room temperature, the residue was extracted with DCM (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 5:1). The pure product was obtained as a white solid (63.0 mg, 72.0 µmol, 55%).

**TLC** (silica, CyHex:EtOAc = 5:1): $R_f$ = 0.21. $[\alpha]_D^{20}$ = −7.7° (c = 0.52, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.19 (dddd, $^3J_{H\text{-}5,\ H\text{-}6\text{-}ax}$ = 11.5 Hz, $^3J_{H\text{-}5,\ H\text{-}4}$ = 5.6 Hz, $^3J_{H\text{-}5,\ H\text{-}4'}$ = 5.6 Hz, $^3J_{H\text{-}5,\ H\text{-}6\text{-}eq}$ = 2.5 Hz, 1H, H-5), 4.07–3.94 (m, 5H, H-3, H-7, H-9, H-11, H-15), 3.92 (ddd, $^3J_{H\text{-}13,\ H\text{-}12}$ = 6.7 Hz, $^3J_{H\text{-}13,\ H\text{-}12'}$ = 5.7 Hz, $^3J_{H\text{-}13,\ H\text{-}14}$ = 4.1 Hz, 1H, H-13), 3.88 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 7.8 Hz, $^3J_{H\text{-}14,\ H\text{-}13}$ = 4.1 Hz, 1H, H-14), 3.76 (dd, $^2J$ = 10.8 Hz, $^3J_{H\text{-}16,\ H\text{-}15}$ = 3.9 Hz, 1H, H-16), 3.76–3.72 (m, 1H, H-1*), 3.67 (dd, $^2J$ = 10.9 Hz, $^3J_{H\text{-}16',\ H\text{-}15}$ = 5.4 Hz, 1H, H-16´), 3.65 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}1,\ OH}$ = 5.5 Hz, $^3J_{H\text{-}1,\ H\text{-}2}$ = 3.1 Hz, 1H, H-1), 3.51 (ddd, $^2J$ = 11.7 Hz, $^3J_{H\text{-}1',\ OH}$ = 5.5 Hz, $^3J_{H\text{-}1',\ H\text{-}2}$ = 4.3 Hz, 1H, H-1´), 2.14 (dd, $^3J_{OH,\ H\text{-}1}$ = 5.4 Hz, $^3J_{OH,\ H\text{-}1'}$ = 5.5 Hz, 1H, OH), 1.81–1.77 (m, 1H, H-4), 1.76–1.70 (m, 3H, H-4´, H-8, H-12), 1.69–1.60 (m, 2H, H-2*, H-12´), 1.59–1.55 (m, 1H, H-10-eq), 1.50 (ddd, $^2J$ = 12.8 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}5}$ = 2.5 Hz, $^3J_{H\text{-}6\text{-}eq,\ H\text{-}7}$ = 2.5 Hz, 1H, H-6-eq), 1.48–1.45 (m, 1H, H-3*), 1.44 (s, 3H, $CH_3$), 1.43–1.41 (m, 1H, H-8´), 1.40–1.39 (m, 6H, 2x$CH_3$), 1.38–1.37 (m, 4H, H-2, $CH_3$), 1.36–1.35 (m, 4H, H-2*´, $CH_3$), 1.33–1.24 (m, 14H, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.18 (ddd, $^2J$ = 12.6 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}5}$ = 11.5 Hz, $^3J_{H\text{-}6\text{-}ax,\ H\text{-}7}$ = 11.5 Hz, 1H, H-6-ax), 1.10 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}9}$ = 11.3 Hz, $^3J_{H\text{-}10\text{-}ax,\ H\text{-}11}$ = 11.3 Hz, 1H, H-10-ax), 0.96 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TES), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.62 (q, $^3J$ = 7.8 Hz, 6H, 3x$CH_2$-TES), 0.09 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 109.3 ($C_q$), 99.0 ($C_q$), 98.8 ($C_q$), 98.2 ($C_q$), 80.2 (C-14), 78.3 (C-15), 70.4 (C-1*), 69.3 (C-13), 68.1 (C-3), 66.4 (C-5), 66.3 (C-11), 65.8 (C-7, C-9), 64.7 (C-16), 60.5 (C-1), 46.2 (C-2), 43.7 (C-8), 41.2 (C-12), 40.2 (C-4), 37.6 (C-10), 36.9 (C-6), 33.8 (C-2*), 32.5 (C-4*), 30.5 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 27.6 ($CH_3$), 27.6 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.3 (C-3*), 23.3 (C-5*), 20.3 ($CH_3$), 20.1 ($CH_3$), 20.1 ($CH_3$), 18.6 ($C_q$-TBS), 14.4 (C-6*), 7.1 (3x$CH_3$-TES), 4.9 (3x$CH_2$-TES), −4.0 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (APCI)** *m/z*: $[M+H]^+$ Calcd for $C_{46}H_{90}Si_2O_{11}H^+$ 875.6094, found 875.6096. For NMR-spectra see p. 465.

**Synthesis of Compound 299**

***tert*-butyl((*R*)-1-((4*S*,5*R*)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)-2-((4*R*,6*R*)-6-(((4*S*,6*S*)-6-(((4*S*,5*R*,6*R*)-2,2-dimethyl-6-pentyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)ethoxy)dimethylsilane**



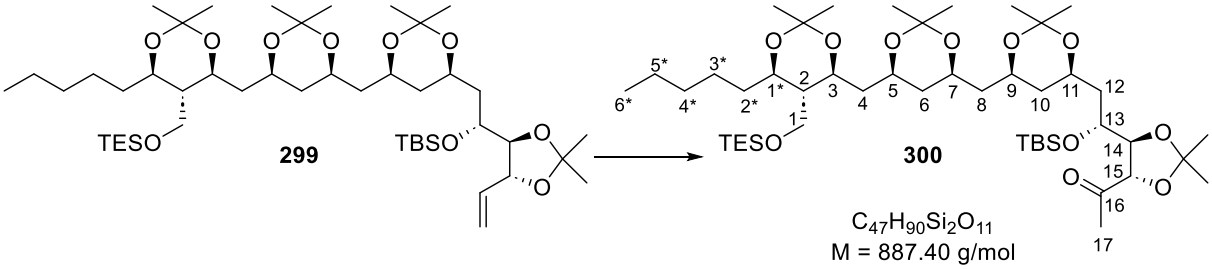

To a stirred solution of alkyne **295** (165 mg, 0.19 mmol, 1 equiv) in hexane (2 mL) was added Lindlar catalyst consisting of Pd/$CaCO_3$ (5% Pd, 20.1 mg, 9.50 µmol, 0.05 equiv, with respect to Pd) and quinoline (1.1 µL, 9.50 µmol, 0.05 equiv). The reaction mixture was stirred under a hydrogen atmosphere (1 atm) for 1 h at room temperature. Subsequently, the mixture was purged with argon and filtered over a pad of celite. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure product was obtained as a colorless liquid (160 mg, 0.18 mmol, 97%).

**TLC** (silica, CyHex:EtOAc = 10:1): $R_f$ = 0.31. $[\alpha]_D^{20}$ = −4.2° (c = 0.96, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 5.89 (ddd, $^3J_{H\text{-}16,\ H\text{-}17\text{-}E}$ = 17.0 Hz, $^3J_{H\text{-}16,\ H\text{-}17\text{-}Z}$ = 10.4 Hz, $^3J_{H\text{-}16,\ H\text{-}15}$ = 6.6 Hz, 1H, H-16), 5.35 (ddd, $^3J_{H\text{-}17\text{-}E,\ H\text{-}16}$ = 17.2 Hz, $^2J$ = 1.7 Hz, $^4J_{H\text{-}17\text{-}E,\ H\text{-}15}$ = 1.2 Hz, 1H, H-17-E), 5.18 (ddd, $^3J_{H\text{-}17\text{-}Z,\ H\text{-}16}$ = 10.4 Hz, $^2J$ = 1.7 Hz, $^4J_{H\text{-}17\text{-}Z,\ H\text{-}15}$ = 1.0 Hz, 1H, H-17-Z), 4.35 (dddd, $^3J_{H\text{-}15,\ H\text{-}14}$ = 7.7 Hz, $^3J_{H\text{-}15,\ H\text{-}16}$ = 6.6 Hz, $^4J_{H\text{-}15,\ H\text{-}17\text{-}E}$ = 1.1 Hz, $^4J_{H\text{-}15,\ H\text{-}17\text{-}Z}$ = 1.1 Hz 1H, H-15), 4.12–4.05 (m, 2H, H-3, H-7), 4.04–3.94 (m, 5H, H-1*, H-5, H-9, H-11, H-13), 3.78 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 7.8 Hz, $^4J_{H\text{-}14,\ H\text{-}13}$ = 4.2 Hz, 1H, H-14), 3.69–3.63 (m, 2H, H-1, H-1´), 1.76–1.69 (m, 2H, H-8, H-12), 1.68–1.61 (m, 3H, H-4, H-4´, H-2*), 1.60–1.54 (m, 2H, H-6, H-12´), 1.49 (ddd, $^2J$ = 12.7 Hz, $^3J_{H\text{-}10\text{-}eq,\ H\text{-}9}$ = 2.5 Hz, $^3J_{H\text{-}10\text{-}eq,\ H\text{-}11}$ = 2.5 Hz, 1H, H-10-eq), 1.47–1.42 (m, 1H, H-3*), 1.41 (s, 3H, $CH_3$), 1.40–1.37 (m, 10H, H-8, 3x$CH_3$), 1.36 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.34–1.24 (m, 15H, H-2*´, H-3*´, H-4*, H-5*, 3x$CH_3$), 1.20 (dddd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.3 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 2.6 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 2.6 Hz, 1H, H-2), 1.12–1.00 (m, 2H, H-6-ax, H-10-ax), 0.96 (t, $^3J$ = 8.0 Hz, 9H, 3x$CH_3$-TBS), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.89 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.2 Hz, 3H, H-6*), 0.59 (q, $^3J$ = 7.9 Hz, 6H, 3x$CH_2$-TBS), 0.09 (s, 6H, 2x$CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 138.0 (C-16), 117.6 (C-17), 109.2 ($C_q$), 98.8 ($C_q$), 98.7 ($C_q$), 98.0 ($C_q$), 83.9 (C-14), 79.0 (C-15), 69.7 (C-1*), 69.0 (C-13), 66.3 (C-5), 66.3 (C-3), 66.2 (C-7), 65.8 (C-11), 65.6 (C-9), 59.7 (C-1), 46.2 (C-2), 43.6 (C-8), 42.1 (C-12), 40.5 (C-4), 37.6 (C-10), 36.9

(C-6), 33.7 (C-2*), 32.5 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 27.4 ($CH_3$), 27.1 ($CH_3$), 26.3 (3x$CH_3$-TBS), 25.3 (C-3*), 23.2 (C-5*), 20.3 ($CH_3$), 20.1 ($CH_3$), 20.1 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), 7.2 ($CH_3$-TES), 4.8 ($CH_2$-TES), −3.9 ($CH_3$-TBS), −4.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{47}H_{90}Si_2O_{10}H^+$ 871.6145, found 871.6142. For NMR-spectra see p. 467.

**Synthesis of Compound 300**

**1-((4*S*,5*S*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)-2-((4*R*,6*R*)-6-(((4*S*,6*S*)-6-(((4*S*,5*R*,6*R*)-2,2-dimethyl-6-pentyl-5-(((triethylsilyl)oxy)methyl)-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethan-1-one**




To a solution of alkene **299** (150 mg, 0.17 mmol, 1 equiv) in acetone/$H_2O$ (10:1; 2 mL) was added NMO·$H_2O$ (69.8 mg, 0.52 mmol, 3 equiv) and a solution of $K_2OsO_4$·$H_2O$ (3.20 mg, 8.61 µmol, 0.05 equiv). The mixture was stirred for 20 h at room temperature. The reaction mixture was quenched with saturated $Na_2S_2O_3$-solution (2 mL) and diluted with DCM (5 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was redissolved in a solution of $Pb(OAc)_4$ (88.0 mg, 0.20 mmol, 1.15 equiv) in toluene (4 mL) and stirred for 10 min before it was filtered through a glass filter frit. The solvent was evaporated *in vacuo* and the crude product was purified by flash chromatography (silica, CyHex:EtOAc = 10:1). The pure aldehyde was obtained as a colorless oil (135 mg, 0.16 mmol, 90%) and was immediately used for the next reaction due to instability.

To a solution of the crude aldehyde (135 mg, 0.16 mmol, 1 equiv) in $Et_2O$ (1.5 mL) was added MeMgBr (1M in $Et_2O$, 100 µL, 0.31 mmol, 2 equiv) and the mixture was stirred for 1 h at room temperature. The reaction mixture was quenched with saturated $NH_4Cl$-solution (2 mL) and diluted with DCM (5 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude secondary alcohol was directly used for the next reaction.

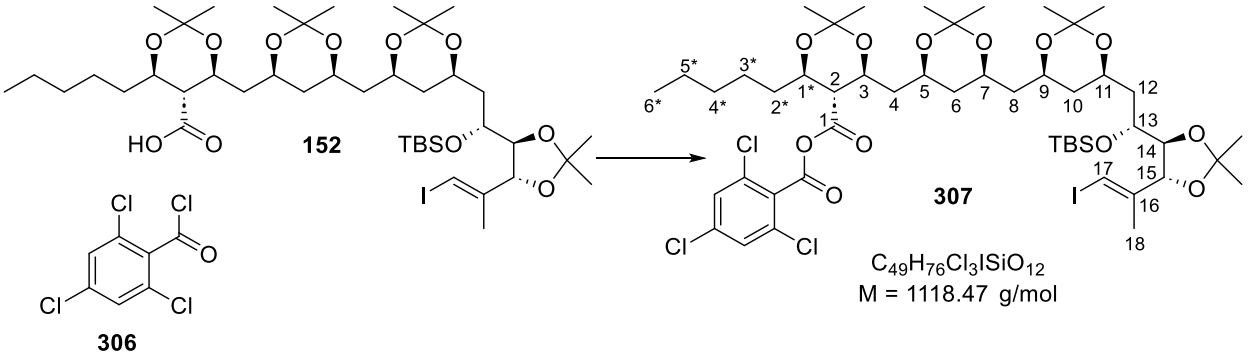
To a Schlenk flask charged with sulfur trioxide pyridine complex (76.5 mg, 0.48 mmol, 3 equiv) were added DCM (1 mL), DMSO (114 µL, 1.60 mmol, 10 equiv) and DIPEA (109 µL,

0.64 mmol, 4 equiv). A solution of the crude alcohol in DCM (1 mL) was added and the mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was washed with saturated $NaHCO_3$-solution (2 mL). The organic phase was further washed with saturated $CuSO_4$-solution (2 x 2 mL) before it was finally washed with saturated $NH_4Cl$-solution (3 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 8:1). The pure product was obtained as a colorless liquid (33 mg, 37.2 µmol, 29% over 4 steps).

**TLC** (silica, CyHex:EtOAc = 8:1): $R_f$ = 0.29. $[\alpha]_D^{20}$ = −8.4° (c = 1.04, DCM). **$^1$H-NMR** (500 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 4.28 (d, $^3J_{H\text{-}15,\ H\text{-}14}$ = 6.3 Hz, 1H, H-15), 4.23 (dd, $^3J_{H\text{-}14,\ H\text{-}15}$ = 6.3 Hz, $^3J_{H\text{-}14,\ H\text{-}13}$ = 3.4 Hz, 1H, H-14), 4.13–3.94 (m, 7H, H-1*, H-3, H-5, H-7, H-9, H-11, H-13), 3.69–3.62 (m, 2H, H-1, H-1´), 2.26 (s, 3H, H-17), 1.72 (ddd, $^2J$ = 14.1 Hz, $^3J_{H\text{-}8,\ H\text{-}7}$ = 7.2 Hz, $^3J_{H\text{-}8,\ H\text{-}9}$ = 7.2 Hz, 1H, H-8), 1.68–1.63 (m, 4H, H-2*, H-4, H-4´, H-12), 1.61–1.54 (m, 3H, H-6-eq, H-10-eq, H-12´), 1.48–1.44 (m, 4H, H-3*, $CH_3$), 1.43–1.41 (m, 4H, H-8´, $CH_3$), 1.41–1.37 (m, 6H, 2x$CH_3$), 1.35–1.25 (m, 18H, H-2*´, H-3*´, H-4*, H-5*, 4x$CH_3$), 1.20 (dddd, $^3J_{H\text{-}2,\ H\text{-}1^*}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}3}$ = 10.4 Hz, $^3J_{H\text{-}2,\ H\text{-}1}$ = 2.7 Hz, $^3J_{H\text{-}2,\ H\text{-}1'}$ = 2.7 Hz, 1H, H-2), 1.15–1.00 (m, 2H, H-6-ax, H-10-ax), 0.96 (t, $^3J$ = 7.9 Hz, 9H, 3x$CH_3$-TBS), 0.89 (s, 9H, 3x$CH_3$-TBS), 0.88 (t, $^3J_{H\text{-}6^*,\ H\text{-}5^*}$ = 7.3 Hz, 3H, H-6*), 0.59 (q, $^3J$ = 8.1 Hz, 6H, 3x$CH_2$-TBS), 0.10 (s, 3H, $CH_3$-TBS), 0.09 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (126 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 209.9 (C-16), 110.7 ($C_q$), 98.8 ($C_q$), 98.7 ($C_q$), 98.0 ($C_q$), 81.8 (C-15), 80.7 (C-14), 69.7 (C-1*), 68.8 (C-13), 66.3 (C-3, C-5), 66.2 (C-7), 65.8 (C-11), 65.7 (C-9), 59.7 (C-1), 46.2 (C-2), 43.6 (C-8), 41.8 (C-12), 40.5 (C-4), 37.6 (C-10), 36.9 (C-6), 33.7 (C-2*), 32.5 (C-4*), 30.6 ($CH_3$), 30.5 ($CH_3$), 30.4 ($CH_3$), 27.2 ($CH_3$), 27.1 ($CH_3$), 26.2 (3x$CH_3$-TBS), 26.0 (C-17), 25.3 (C-3*), 23.2 (C-5*), 20.3 ($CH_3$), 20.2 ($CH_3$), 20.1 ($CH_3$), 18.5 ($C_q$-TBS), 14.4 (C-6*), 7.2 ($CH_3$-TES), 4.8 ($CH_2$-TES), −4.0 ($CH_3$-TBS), −4.1 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{47}H_{90}Si_2O_{11}H^+$ 887.6094, found 887.6091. For NMR-spectra see p. 469.

**Synthesis of Compound 307**

**(4*S*,5*R*,6*R*)-4-(((4*S*,6*S*)-6-(((4*R*,6*R*)-6-((*R*)-2-((*tert*-butyldimethylsilyl)oxy)-2-((4*S*,5*R*)-5-((*E*)-1-iodoprop-1-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-6-pentyl-1,3-dioxane-5-carboxylic 2,4,6-trichlorobenzoic anhydride**




To a stirred solution of carboxylic acid **152** (16.7 mg, 18.3 µmol, 1 equiv) in THF (0.5 mL) was added $NEt_3$ (7.61 µL, 54.9 µmol, 3 equiv) and 2,4,6-trichlorobenzoyl chloride (**306**, 8.61 µL, 54.9 µmol, 3 equiv). The mixture was stirred for 6 h at room temperature before it was filtered through a glass filter frit and washed with THF (1 mL). After evaporation of the solvent the residue was redissolved in toluene (1 mL) and DMAP (8.94 mg, 73.3 µmol, 4 equiv) was added. The mixture was stirred for 10 min at room temperature and a solution of the western fragment **153** (6.89 mg, 20.1 µmol, 1.1 equiv) in toluene (0.1 mL) was added. The mixture was stirred for 48 h at room temperature. Afterwards, the mixture was filtered through a pad of celite, and the solvent was evaporated. The crude product was purified by flash chromatography (silica, CyHex:EtOAc = 15:1) and the mixed anhydride **307** (12.0 mg, 10.7 µmol, 58%) was obtained instead of the coupling product of western fragment **153** and carboxylic acid **152**.

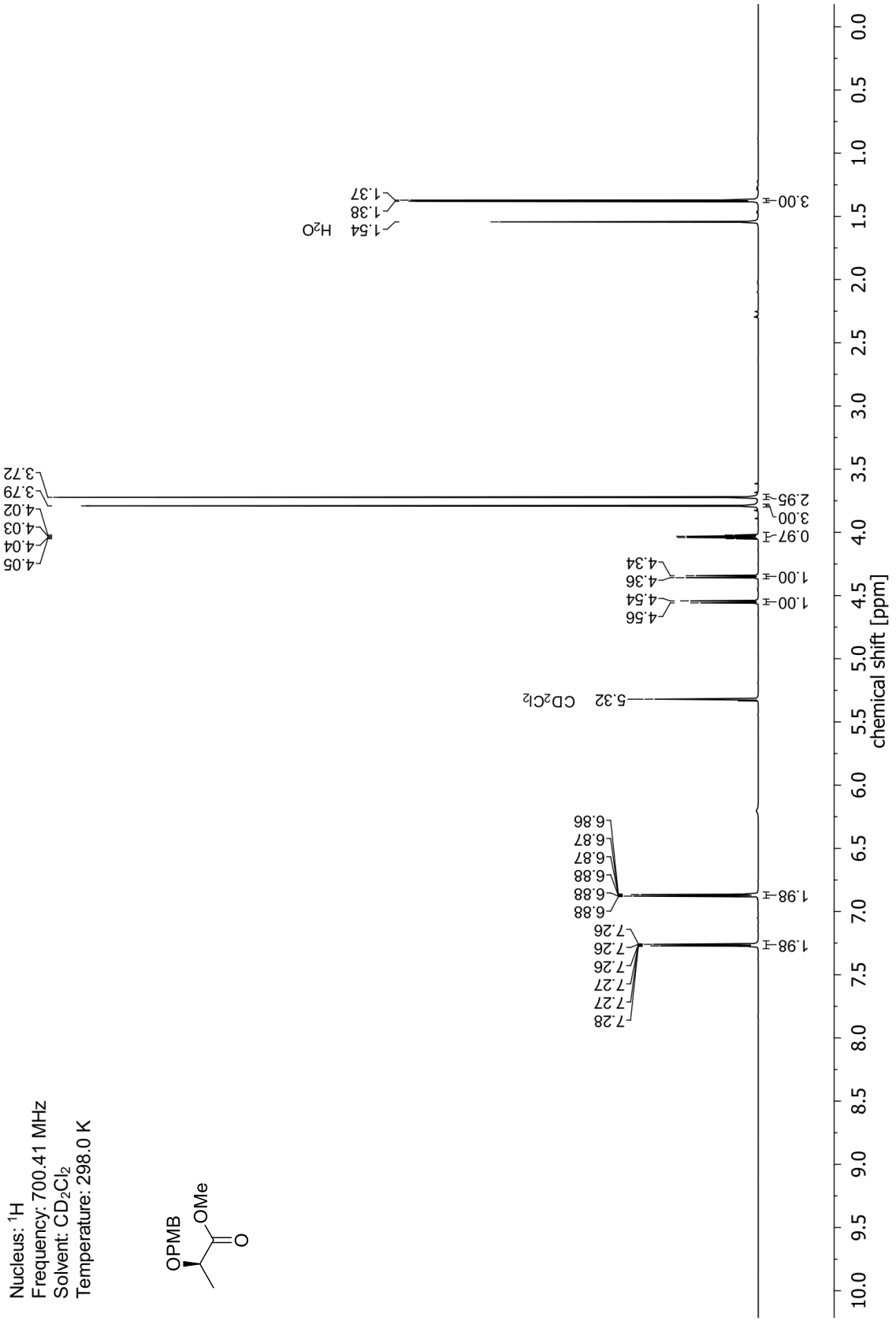
**TLC** (silica, CyHex:EtOAc = 15:1): $R_f$ = 0.28. $[\alpha]_D^{20}$ = +11.6° (c = 0.94, DCM). **$^1$H-NMR** (700 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 7.44 (s, 2H, 2xCH-TCBC), 6.43–6.42 (m, 1H, H-17), 4.48 (dd, $^3J_{H\text{-}15,\,H\text{-}14}$ = 7.9 Hz, $^4J_{H\text{-}15,\,H\text{-}18}$ = 0.8 Hz, 1H, H-15), 4.17 (ddd, $^3J_{H\text{-}3,\,H\text{-}2}$ = 10.6 Hz, $^3J_{H\text{-}3,\,H\text{-}4}$ = 7.7 Hz, $^3J_{H\text{-}3,\,H\text{-}4'}$ = 3.3 Hz, 1H, H-3), 4.10–4.05 (m, 1H, H-5), 4.04–4.00 (m, 2H, H-1*, H-13), 3.99–3.95 (m, 3H, H-7, H-9, H-11), 3.94 (dd, $^3J_{H\text{-}14,\,H\text{-}15}$ = 7.9 Hz, $^4J_{H\text{-}14,\,H\text{-}13}$ = 4.2 Hz, 1H, H-14), 2.47 (dd, $^3J_{H\text{-}2,\,H\text{-}1^*}$ = 10.2 Hz, $^3J_{H\text{-}2,\,H\text{-}3}$ = 10.2 Hz, 1H, H-2), 1.87 (d, $^4J_{H\text{-}18,\,H\text{-}17}$ = 1.1 Hz, 3H, H-18), 1.77 (ddd, $^2J$ = 13.8 Hz, $^3J_{H\text{-}4,\,H\text{-}3}$ = 7.7 Hz, $^3J_{H\text{-}4,\,H\text{-}5}$ = 5.9 Hz, 1H, H-4), 1.73–1.67 (m, 2H, H-8, H-12), 1.61–1.52 (m, 4H, H-4´, H-2*, H-2*´, H-12´), 1.49–1.43 (m, 6H, H-3*, H-6-eq, H-10-eq, $CH_3$), 1.41–1.38 (m, 13H, H-8´, 4x$CH_3$), 1.37 (d, $^4J$ = 0.8 Hz, 3H, $CH_3$), 1.33–1.31 (m, 4H, H-3*´, $CH_3$), 1.28–1.26 (m, 4H, H-4*, H-5*), 1.25–1.24 (m, 3H, $CH_3$), 1.13–1.06 (m, 2H, H-6-ax, H-10-ax), 0.90 (s, 9H, 3x$CH_3$-TBS), 0.87 (t, $^3J_{H\text{-}6^*,\,H\text{-}5^*}$ = 7.1 Hz, 3H, H-6*), 0.08 (s, 3H, $CH_3$-TBS), 0.07 (s, 3H, $CH_3$-TBS). **$^{13}$C-NMR** (176 MHz, $CD_2Cl_2$, 298 K): $\delta$ (ppm) = 166.8 (C-1),

158.9 (C=O-TCBC), 146.2 (C-16), 137.9 ($C_q$-TCBC), 133.3 (2xC-Cl-TCBC), 130.9 (C-Cl-TCBC), 129.0 (2xCH-TCBC), 109.3 ($C_q$), 99.3 ($C_q$), 98.8 ($C_q$), 98.8 ($C_q$), 82.2 (C-17), 81.7 (C-15), 81.1 (C-14), 71.2 (C-1*), 69.0 (C-13), 67.8 (C-3), 66.2 (C-9), 65.8 (C-7), 65.6 (C-11), 65.5 (C-5), 53.8 (C-2), 43.5 (C-8), 41.8 (C-12), 41.3 (C-4), 37.6 (C-10), 36.9 (C-6), 35.0 (C-2*), 32.1 (C-4*), 30.5 ($CH_3$), 30.4 ($CH_3$), 30.0 ($CH_3$), 27.8 ($CH_3$), 27.3 ($CH_3$), 26.3 (3x$CH_3$-TBS), 24.8 (C-3*), 23.1 (C-5*), 20.3 (C-18), 20.3 ($CH_3$), 20.2 ($CH_3$), 19.7 ($CH_3$), 18.5 ($C_q$-TBS), 14.3 (C-6*), −3.9 ($CH_3$-TBS), −4.2 ($CH_3$-TBS). **HRMS (ESI-TOF)** *m/z*: $[M+H]^+$ Calcd for $C_{49}H_{76}Cl_3ISiO_{12}H^+$ 1117.3289, found 1117.3285. For NMR-spectra see p. 471.

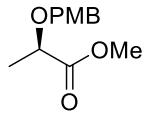
# 7 Experimental Spectra

– The NMR spectra of all compounds are shown on the following pages –

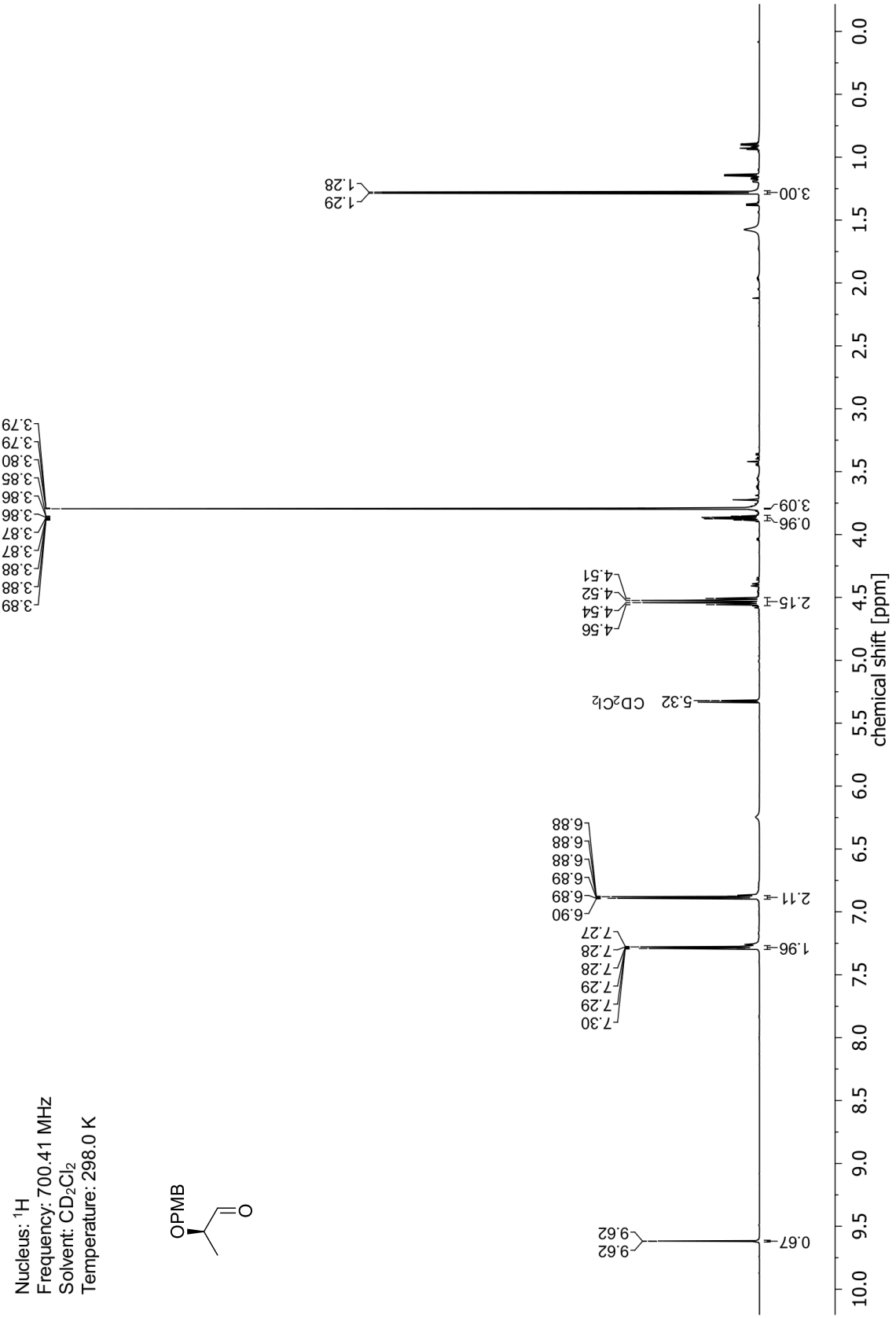
NMR-Spectra of Compound **311**:

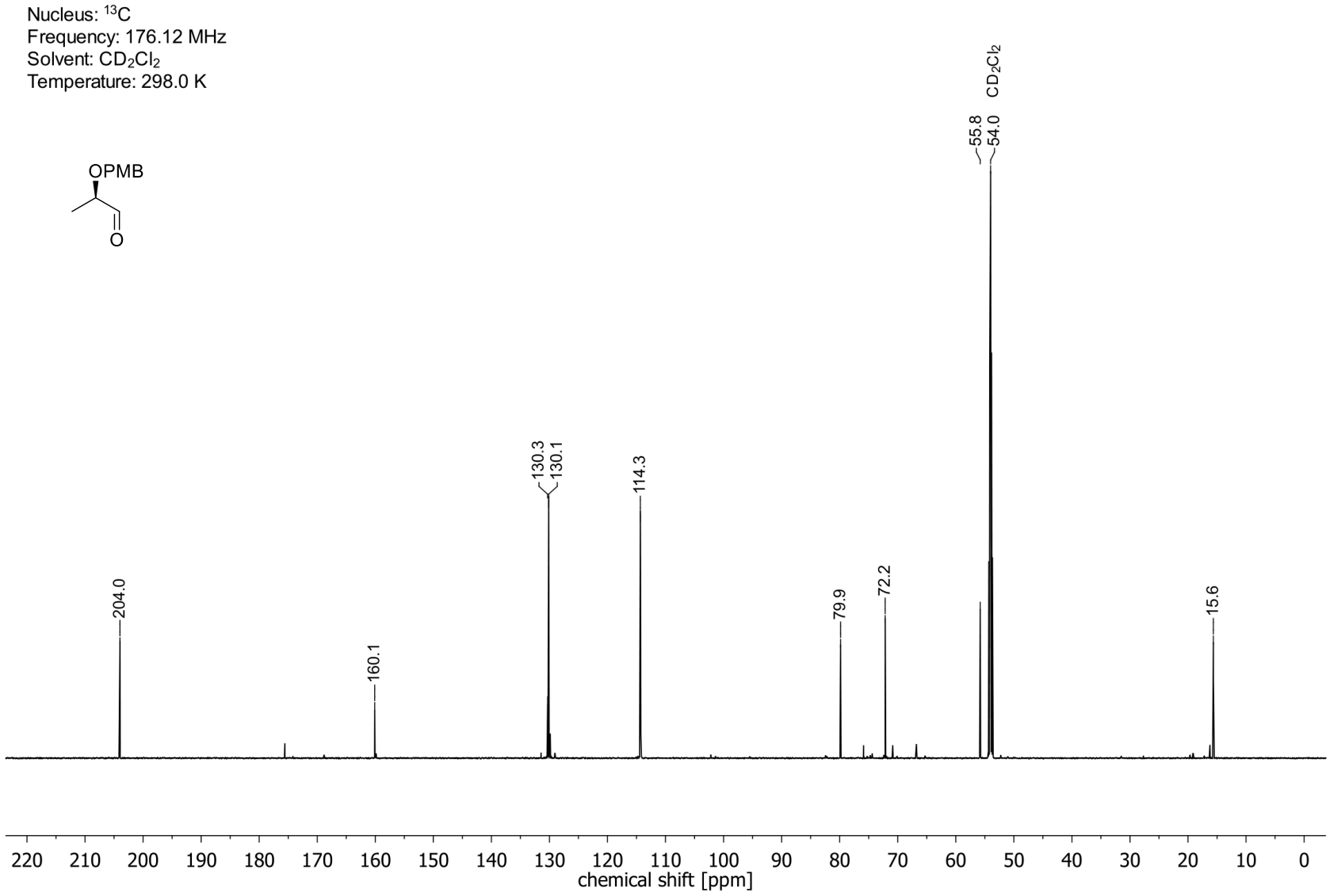


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

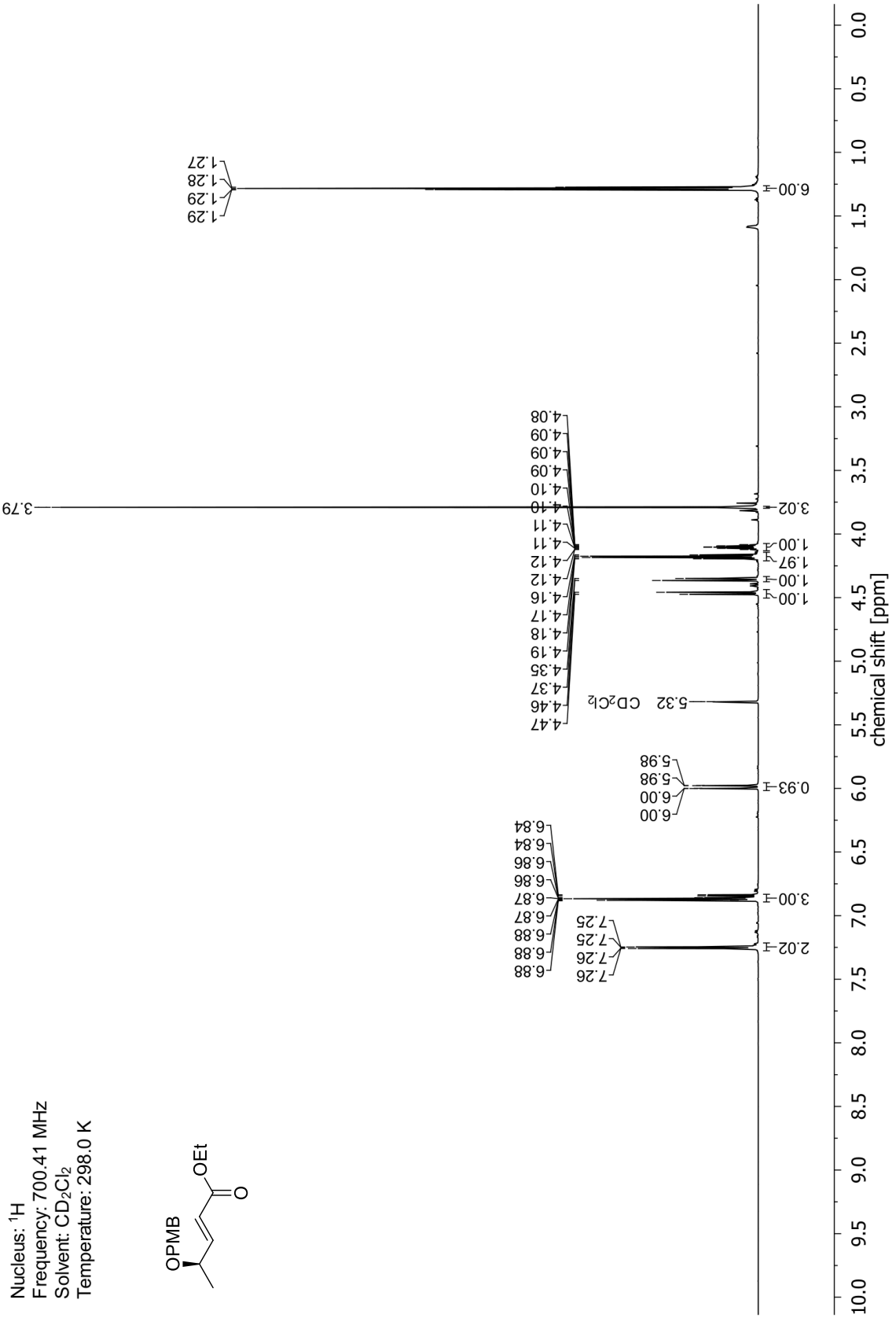


NMR-Spectra of Compound **220**:

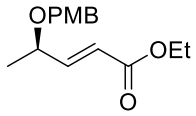


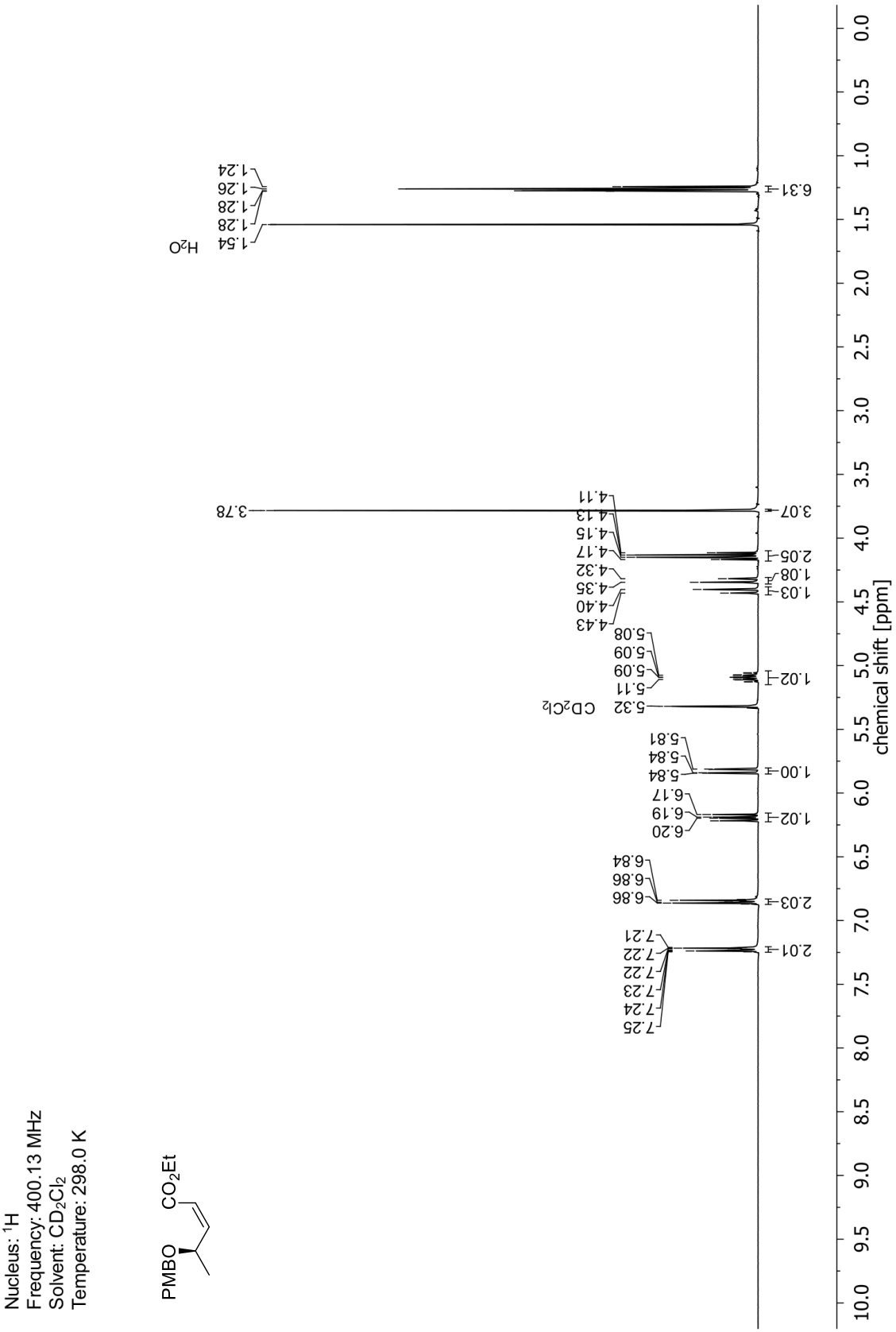

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OPMB
O
204.0
160.1
130.3
130.1
114.3
79.9
72.2
55.8
54.0
CD2Cl2
15.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

NMR-Spectra of Compound **312**:

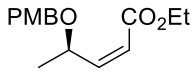


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

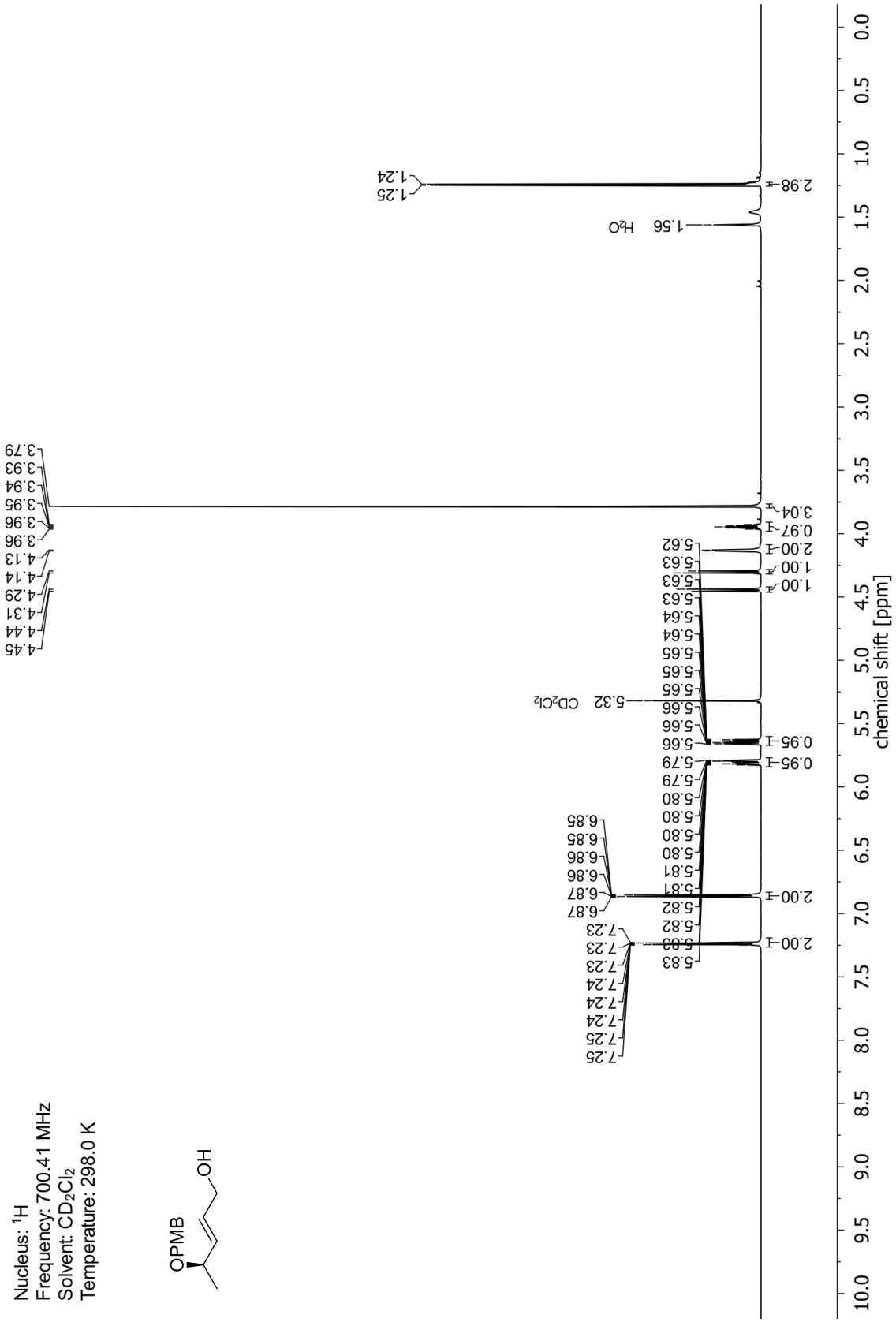



Nucleus: 1H
Frequency: 400.13 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
PMBO
CO2Et
chemical shift [ppm]
CD2Cl2
H2O

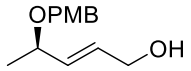
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



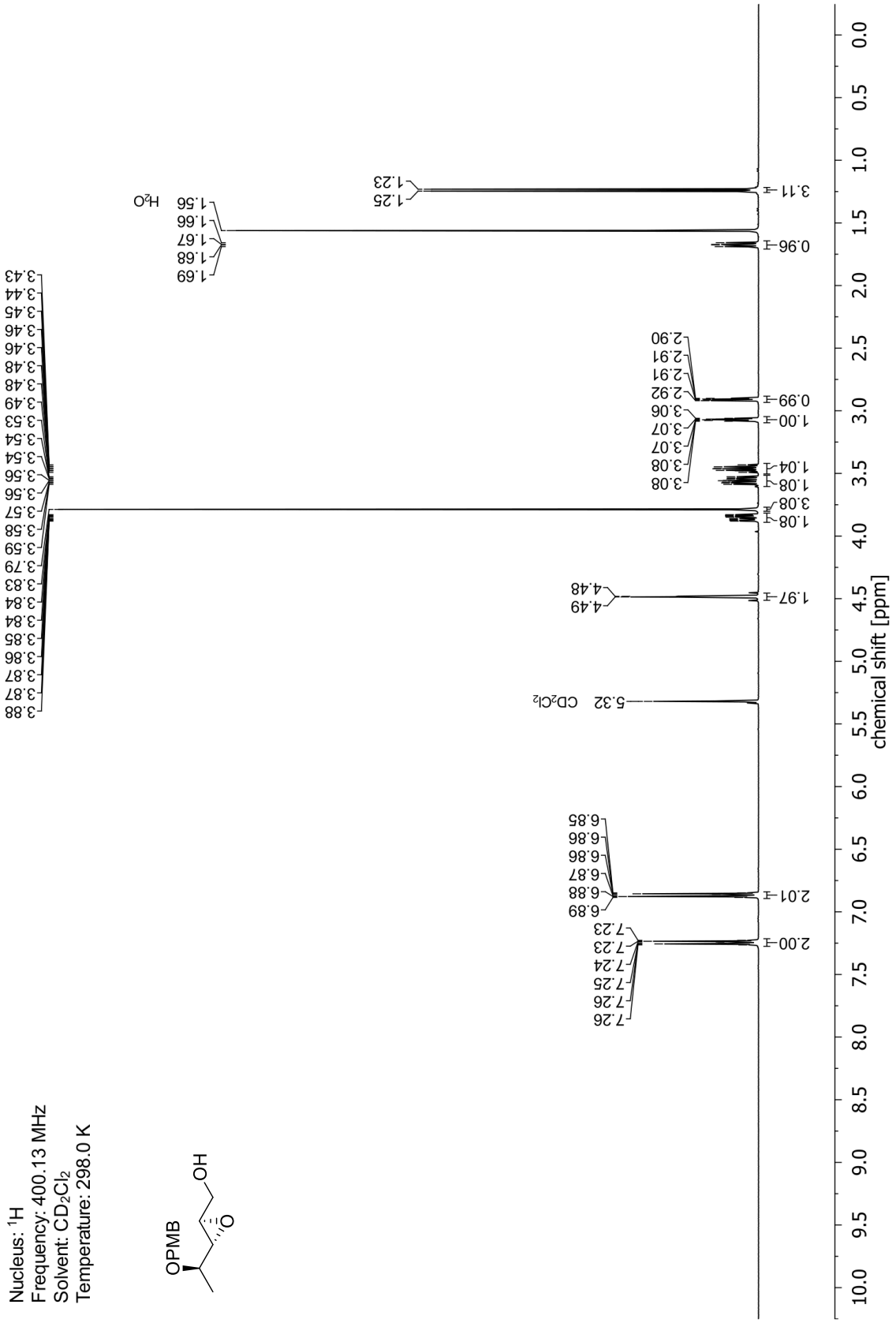
NMR-Spectra of Compound **224**:



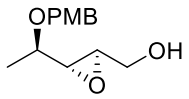
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

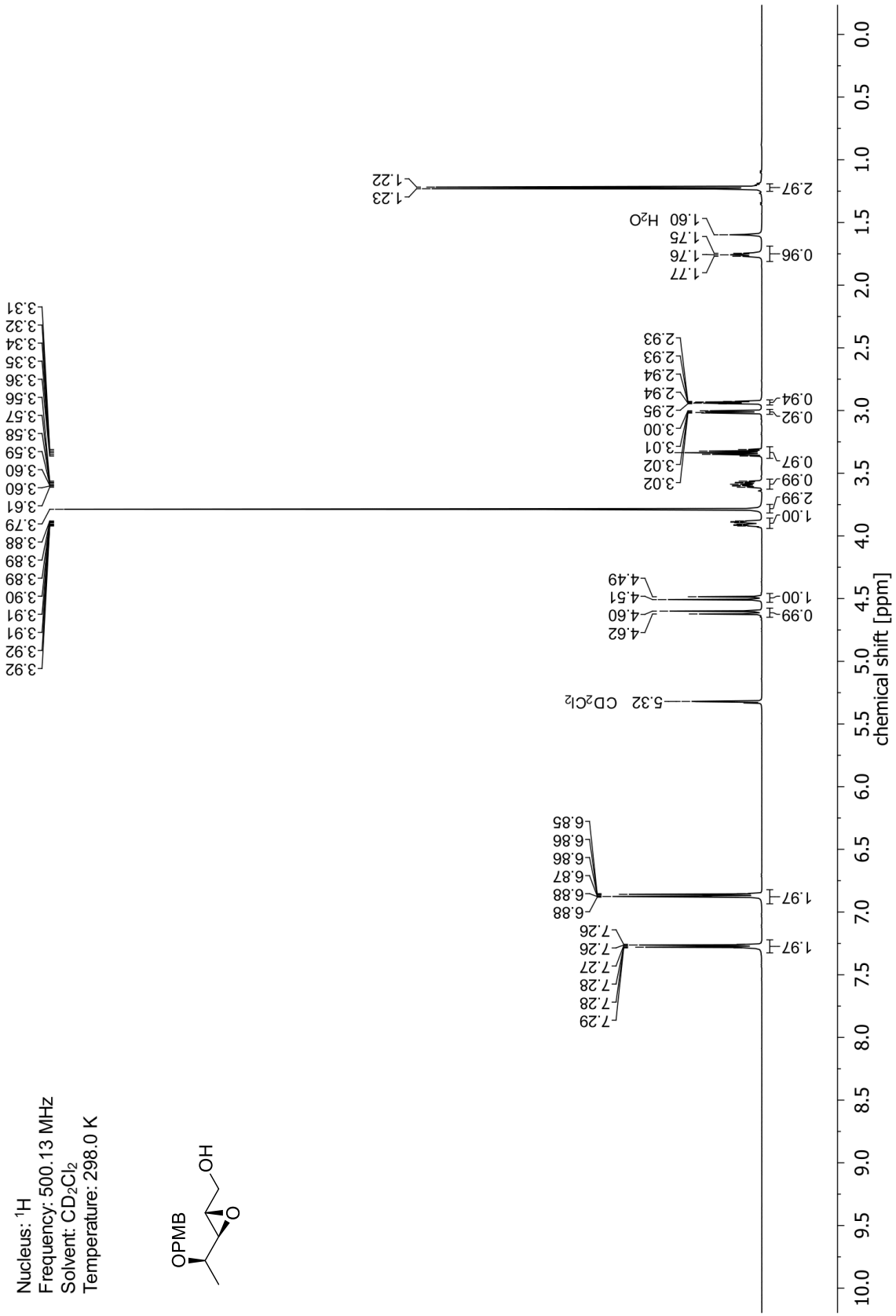


NMR-Spectra of Compound **225**:

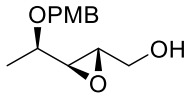


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

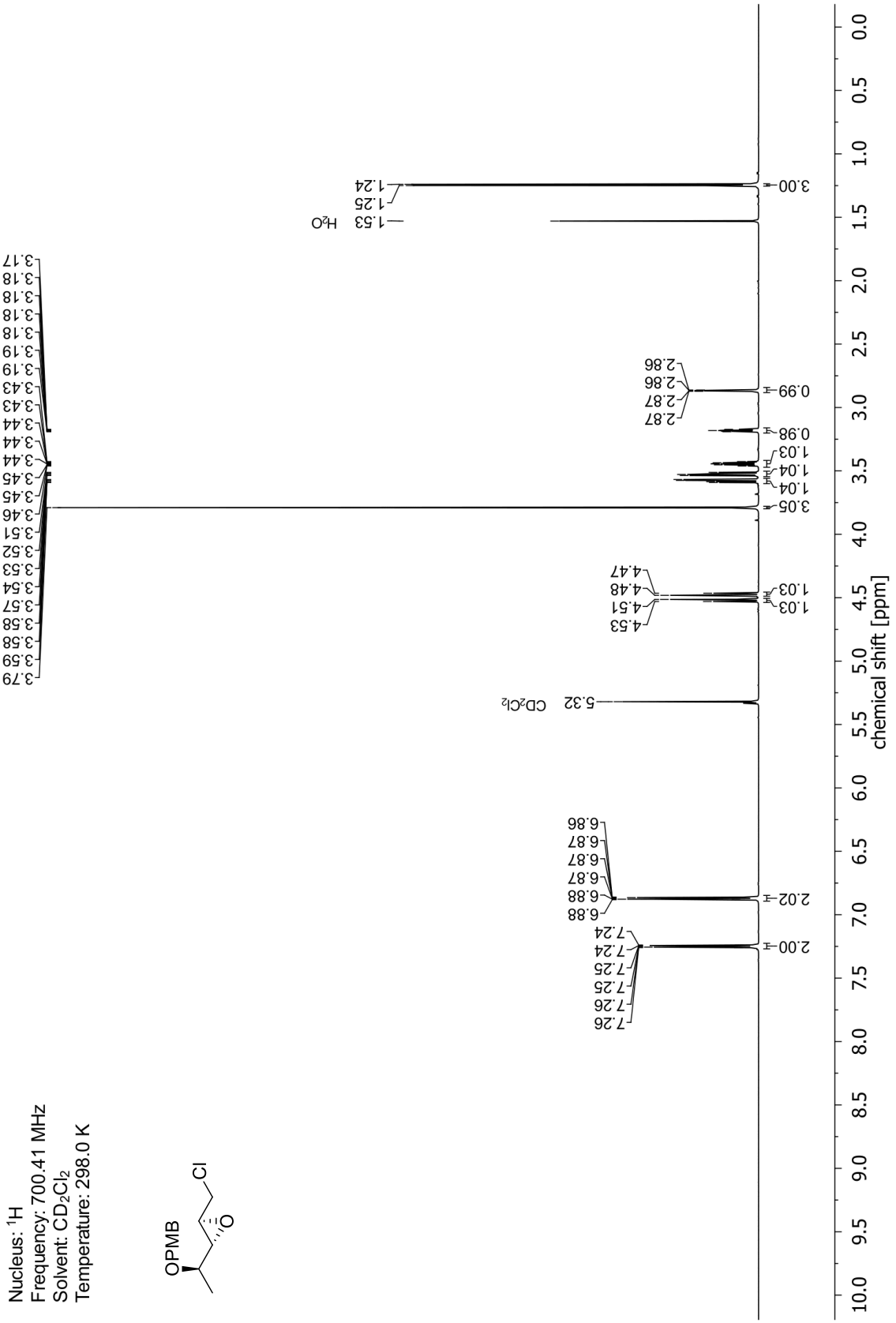



Nucleus: 1H
Frequency: 500.13 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OPMB
OH
O
chemical shift [ppm]
CD2Cl2
H2O

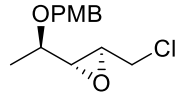
Nucleus: $^{13}C$
Frequency: 125.76 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



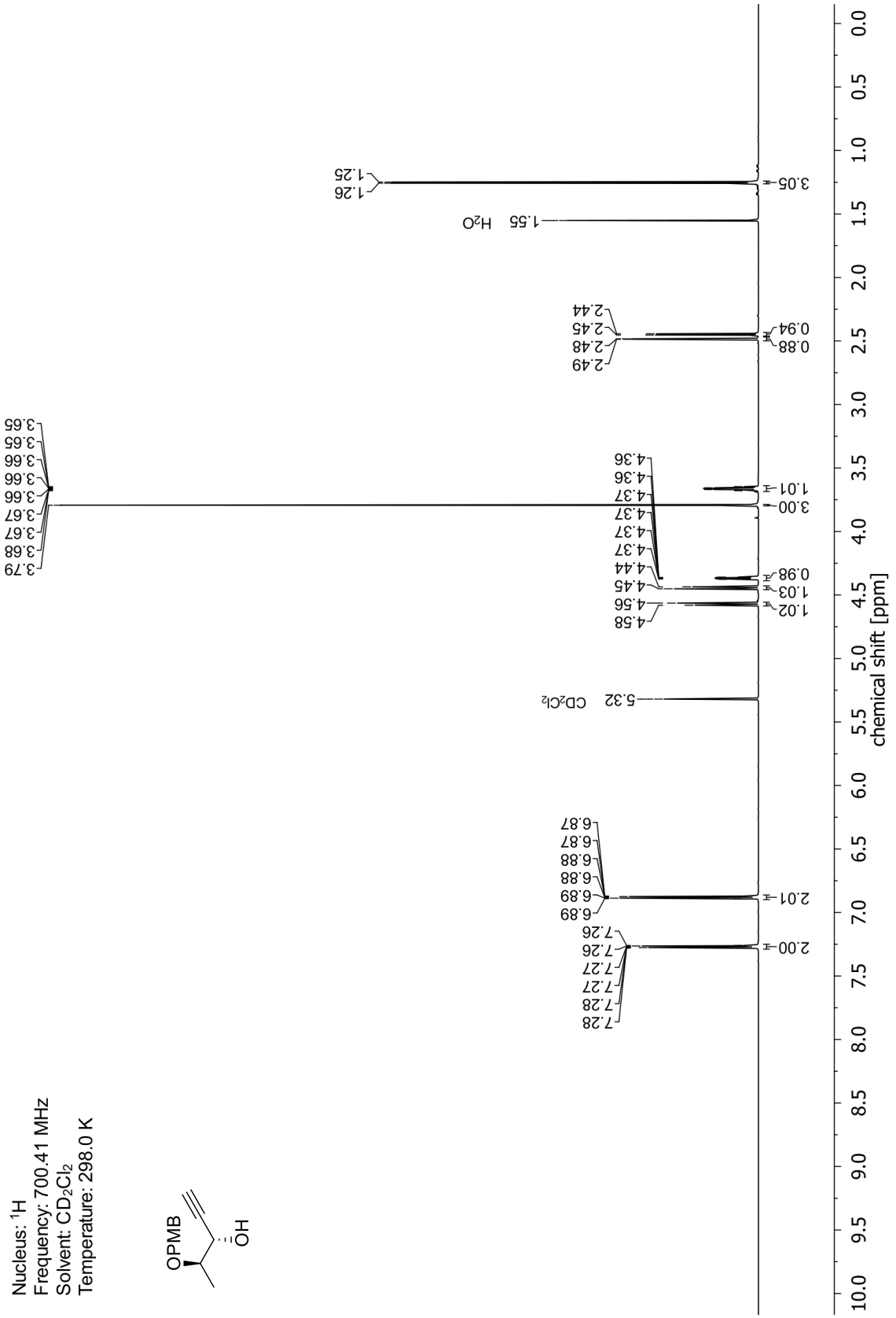
NMR-Spectra of Compound **313**:



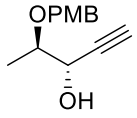
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



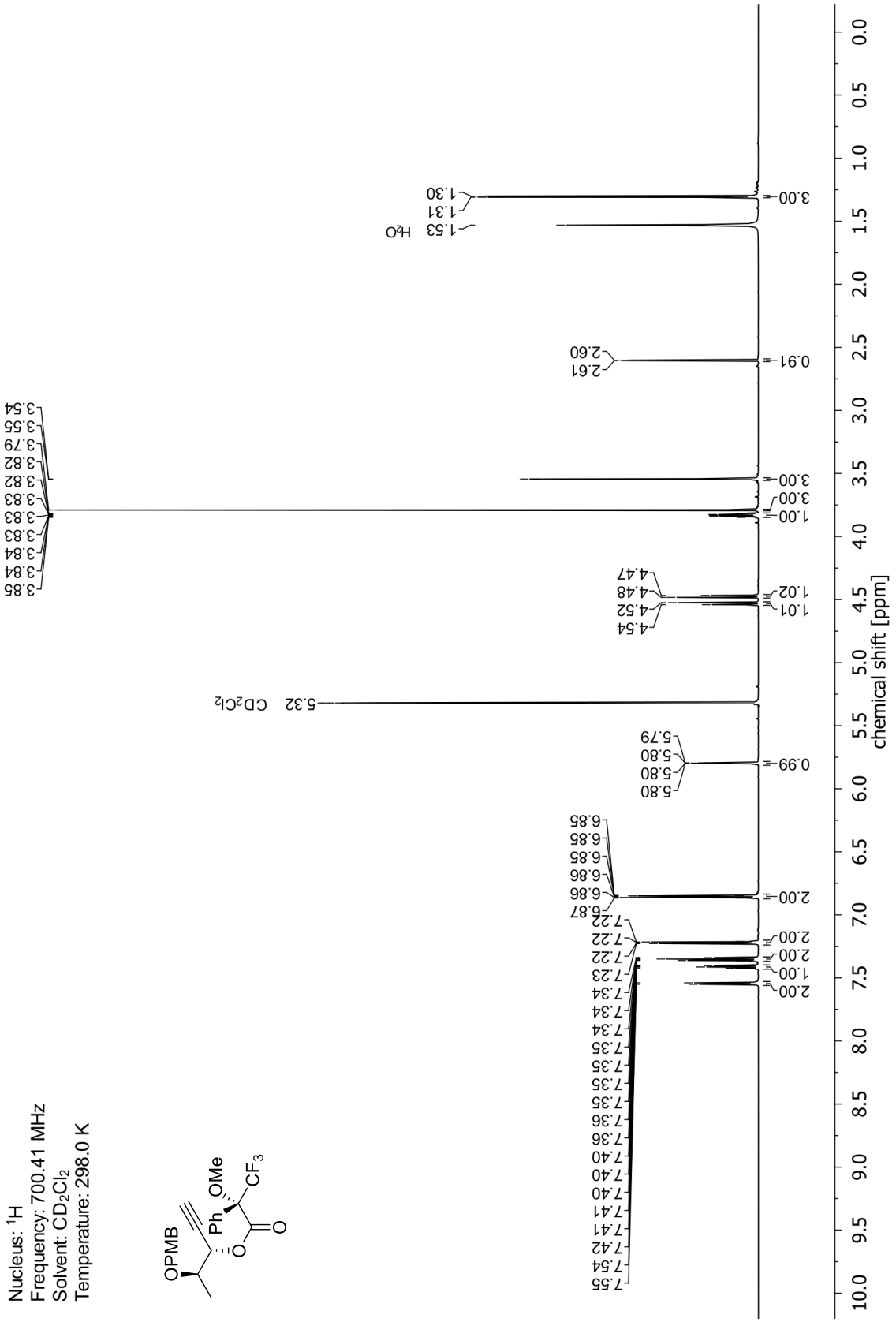
NMR-Spectra of Compound **219**:

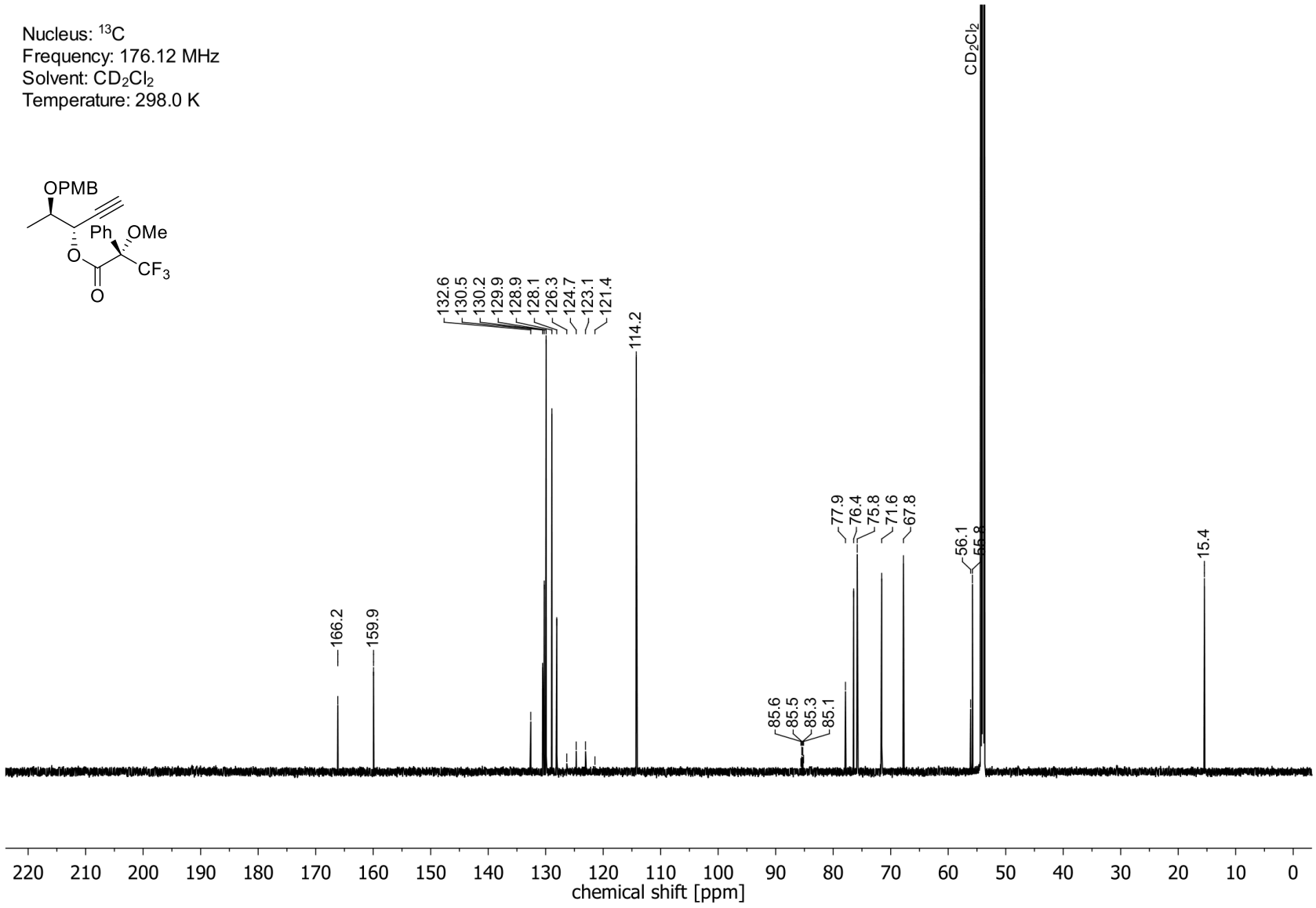


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

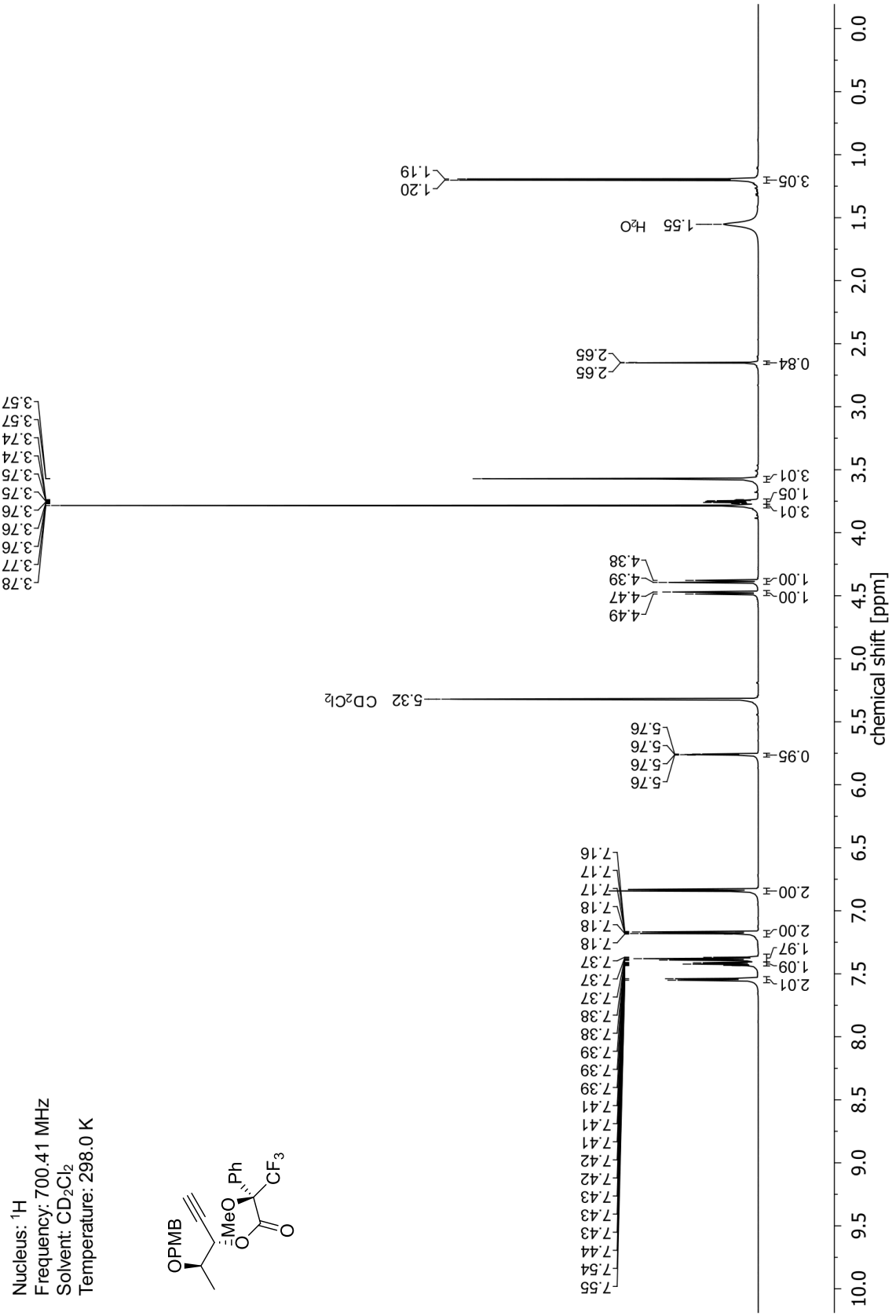


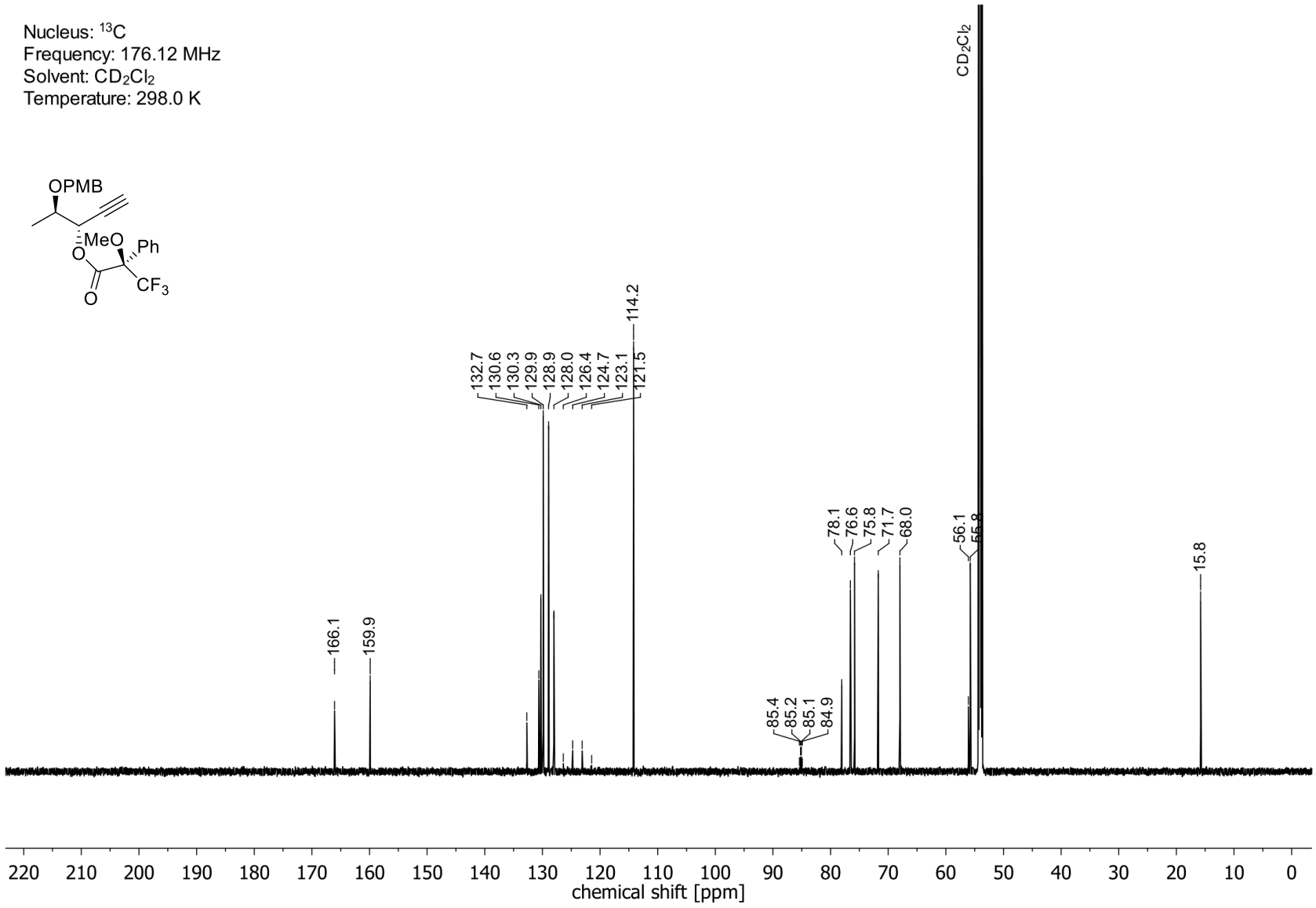
NMR-Spectra of Compound **357-(*S*)**:



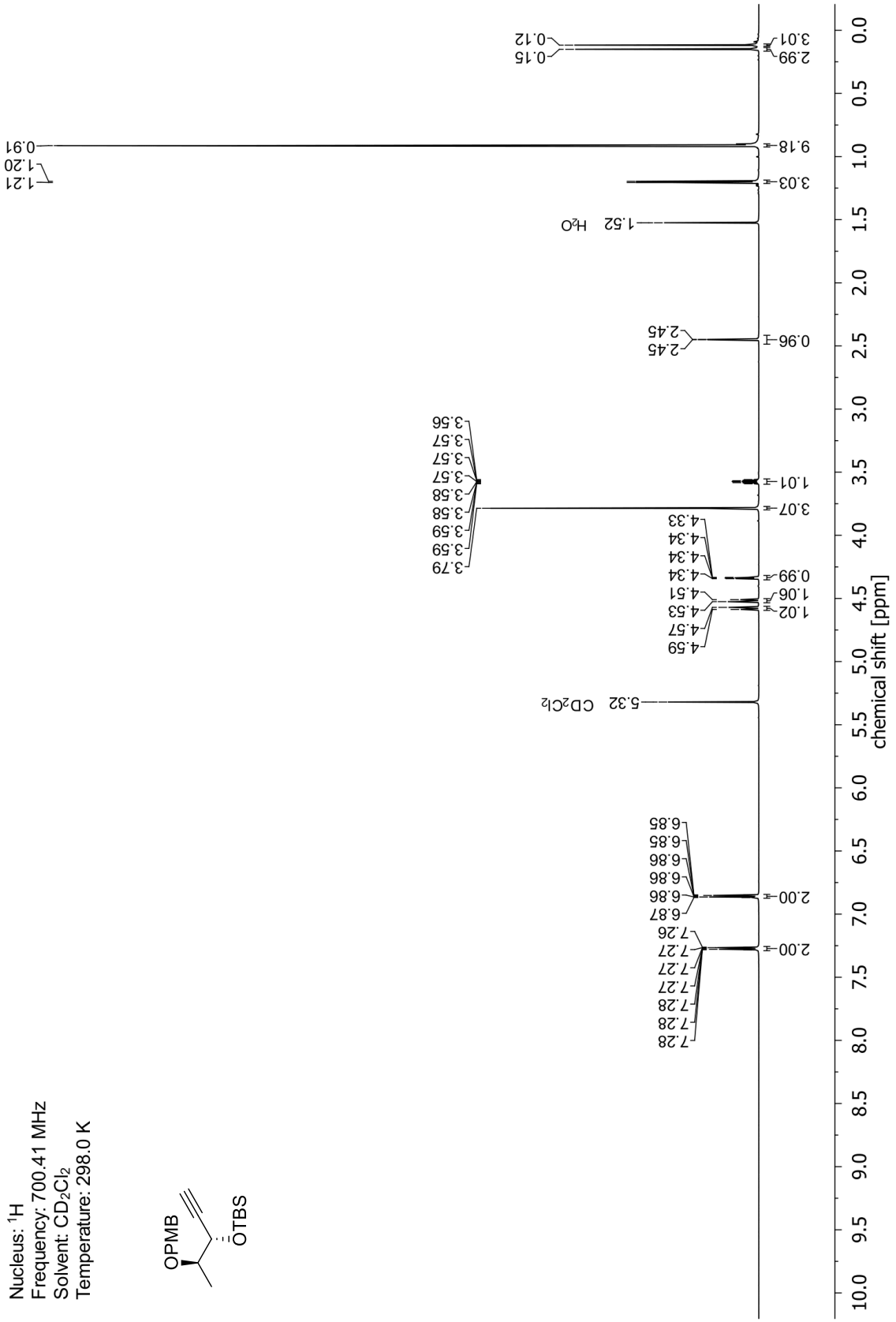

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OPMB
Ph
OMe
CF3
O
O
CD2Cl2
132.6
130.5
130.2
129.9
128.9
128.1
126.3
124.7
123.1
121.4
114.2
166.2
159.9
85.6
85.5
85.3
85.1
77.9
76.4
75.8
71.6
67.8
56.1
55.8
15.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

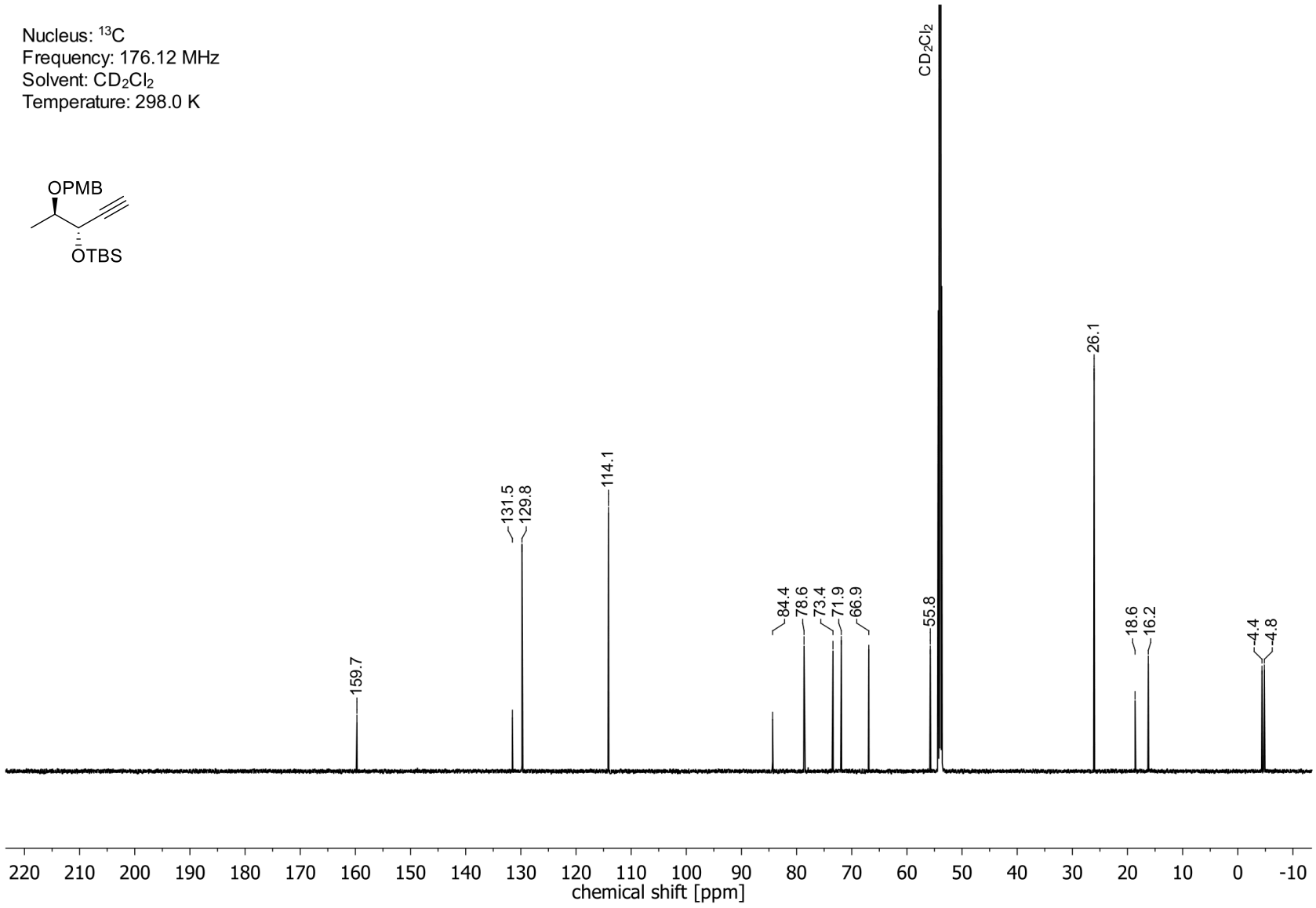
NMR-Spectra of Compound **357-(*R*)**:



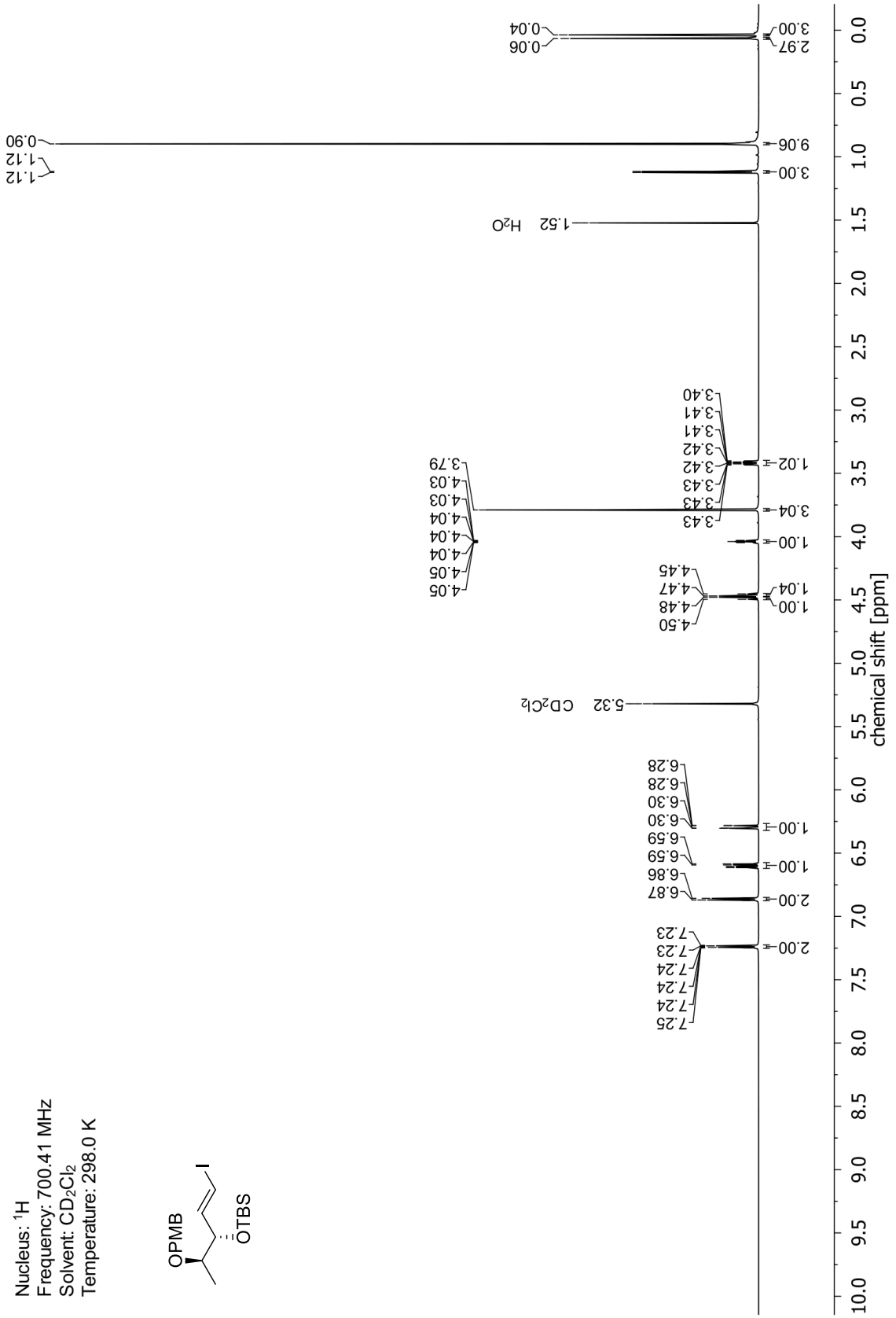

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OPMB
MeO
Ph
CF3
O
O
CD2Cl2
166.1
159.9
132.7
130.6
130.3
129.9
128.9
128.0
126.4
124.7
123.1
121.5
114.2
85.4
85.2
85.1
84.9
78.1
76.6
75.8
71.7
68.0
56.1
55.8
15.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

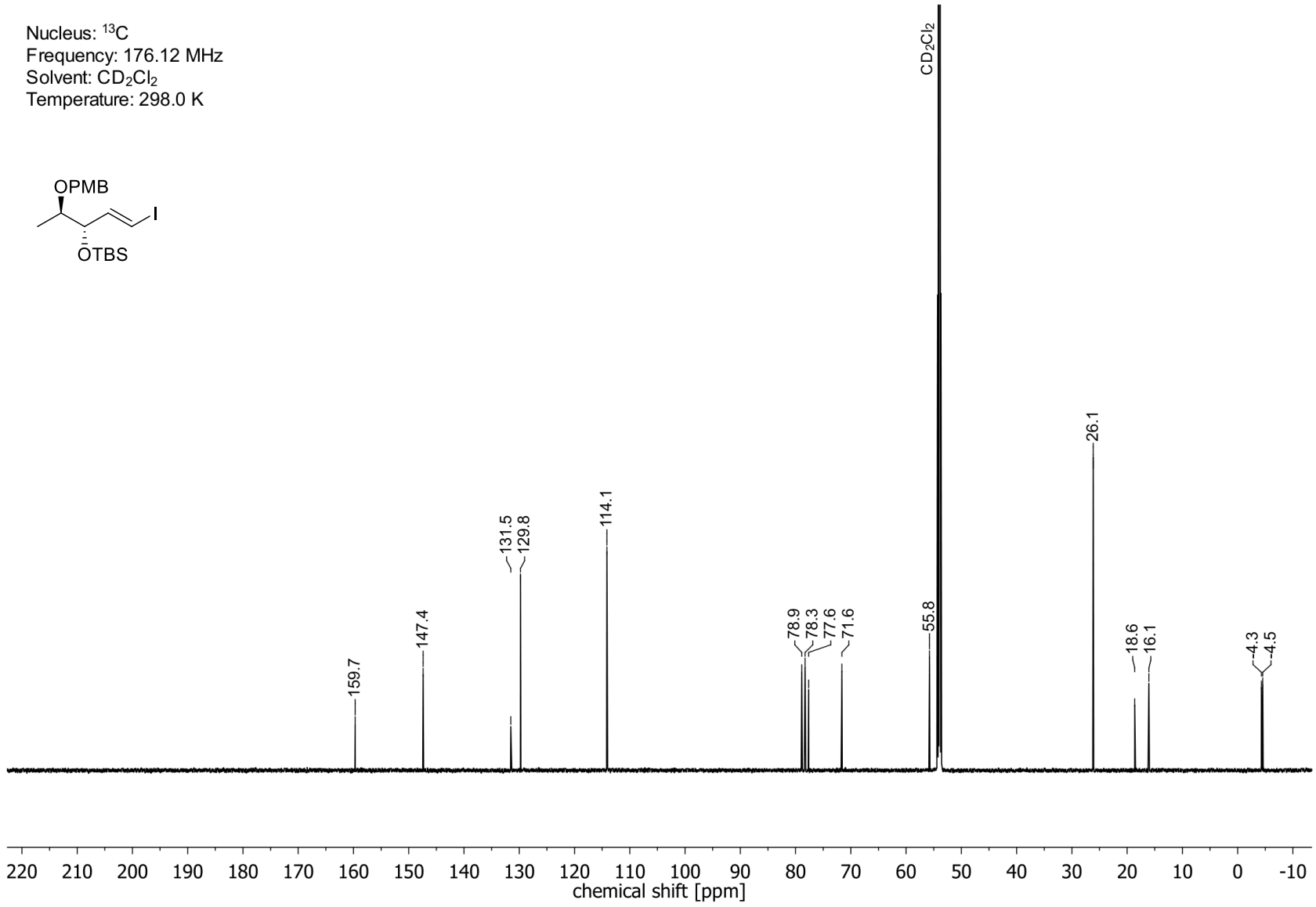
NMR-Spectra of Compound **314**:



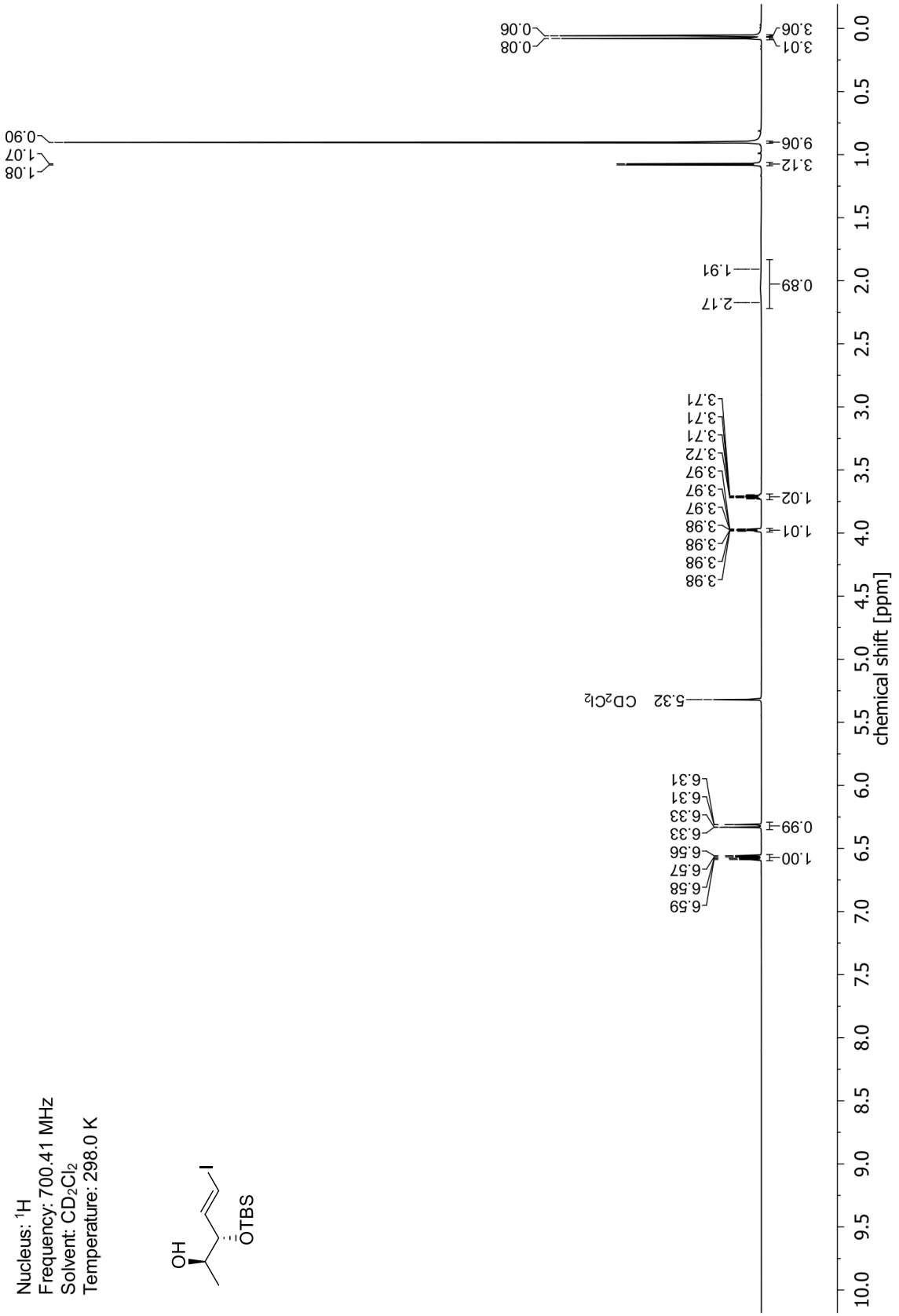

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OPMB
OTBS
CD2Cl2
159.7
131.5
129.8
114.1
84.4
78.6
73.4
71.9
66.9
55.8
26.1
18.6
16.2
-4.4
-4.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **315**:

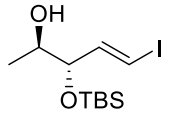



Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OPMB
I
OTBS
CD2Cl2
159.7
147.4
131.5
129.8
114.1
78.9
78.3
77.6
71.6
55.8
26.1
18.6
16.1
-4.3
-4.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

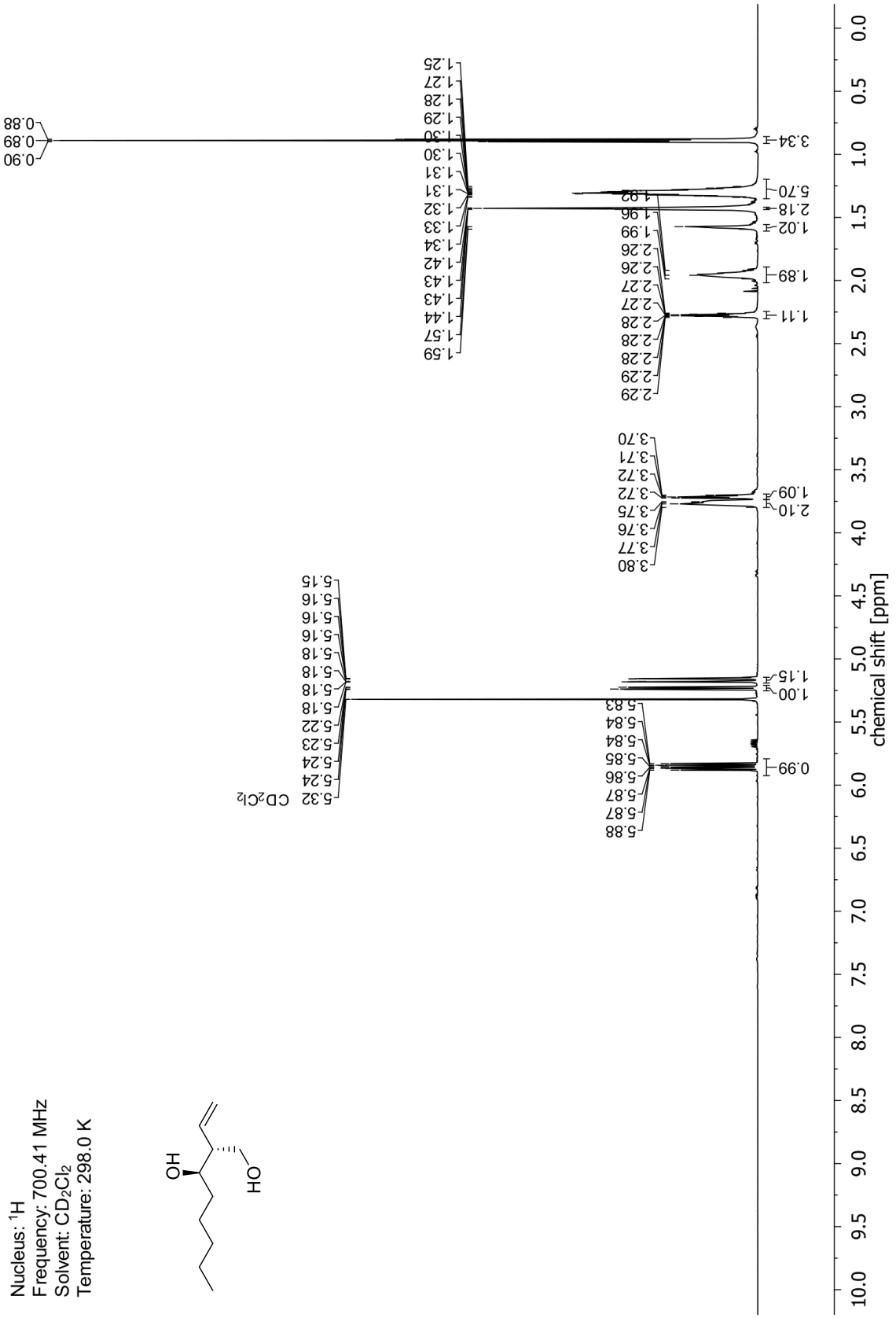
NMR-Spectra of Compound **153**:



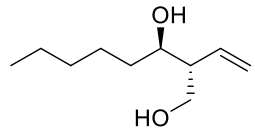
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



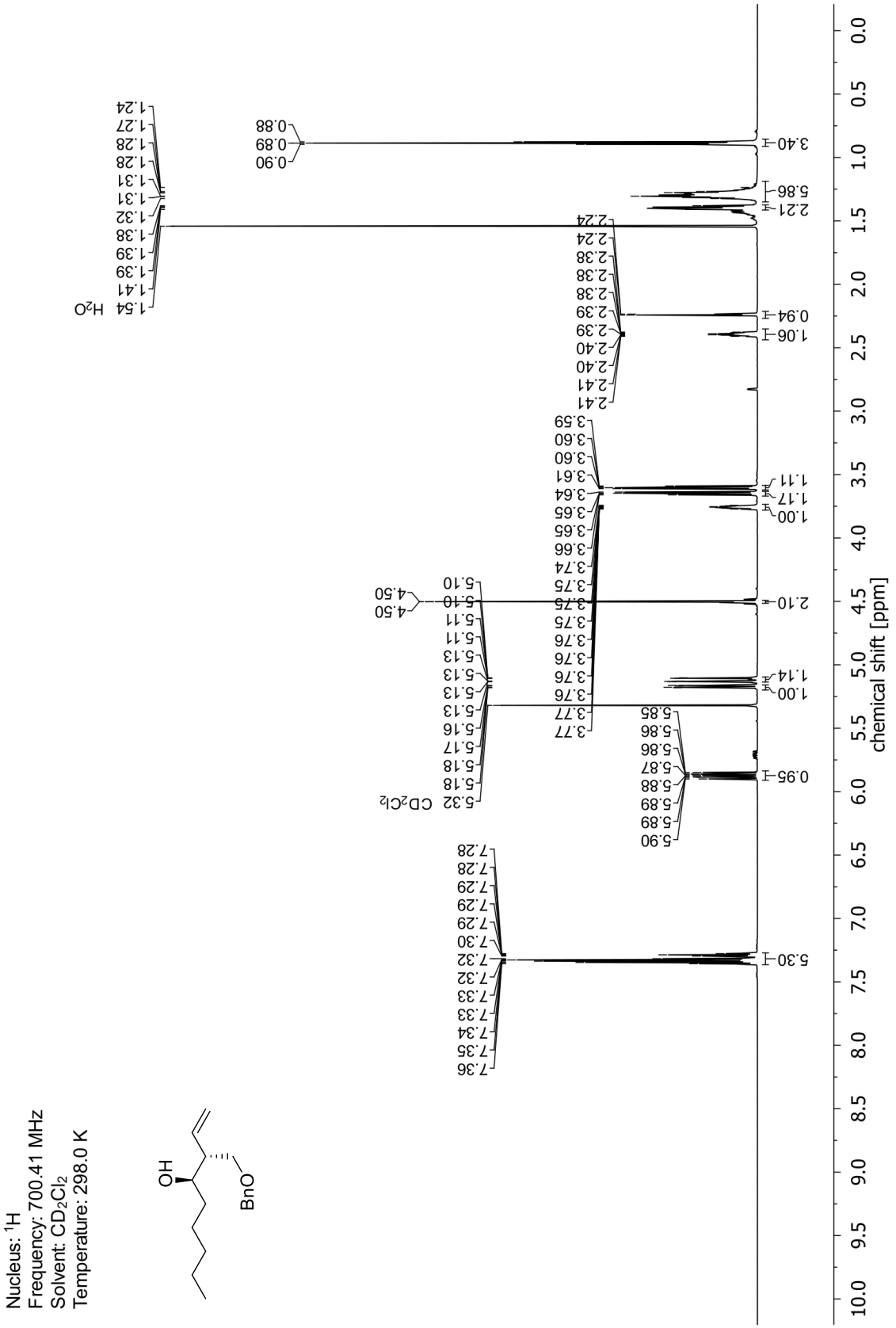
NMR-Spectra of Compound **317**:



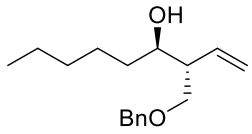
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



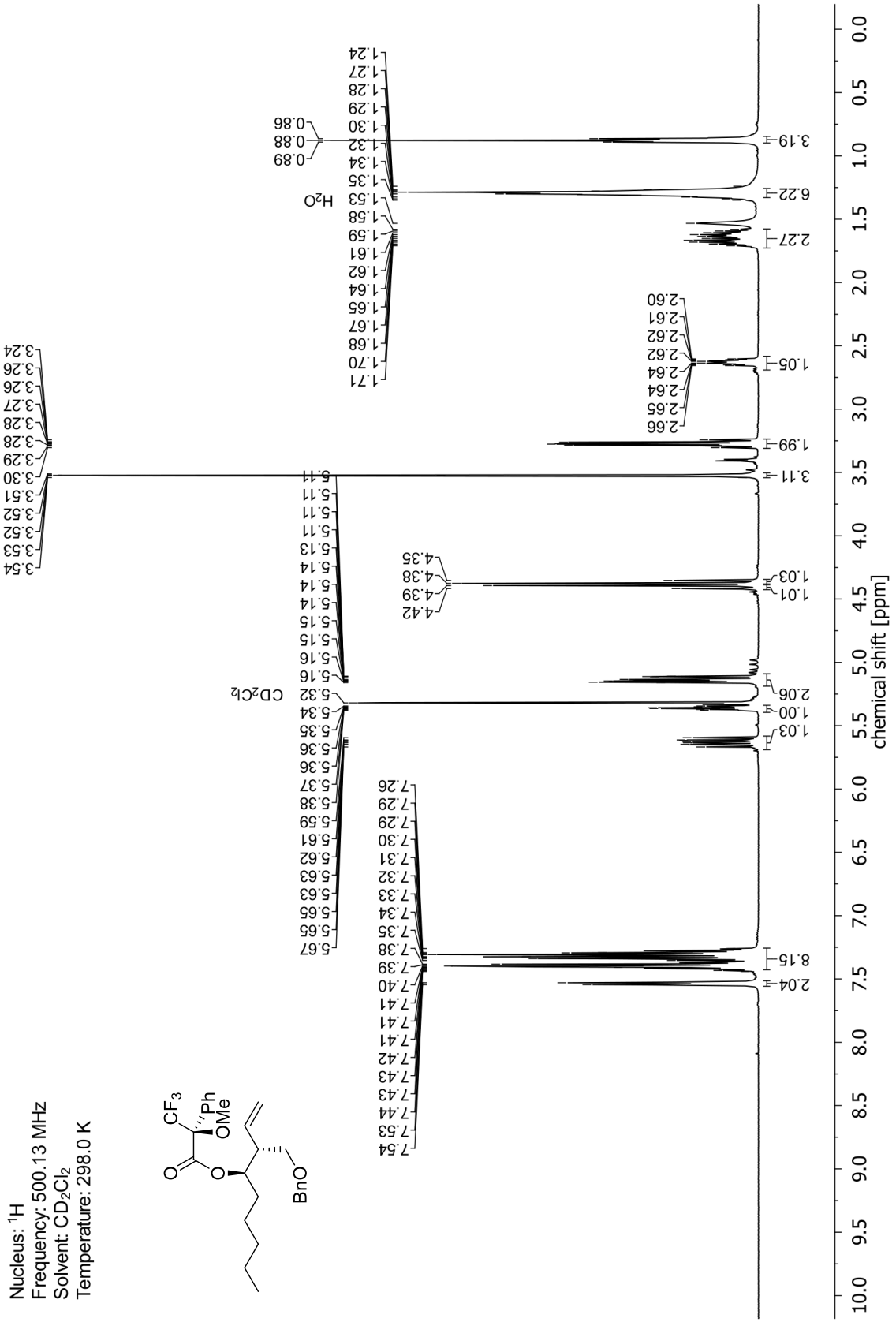
NMR-Spectra of Compound **318**:

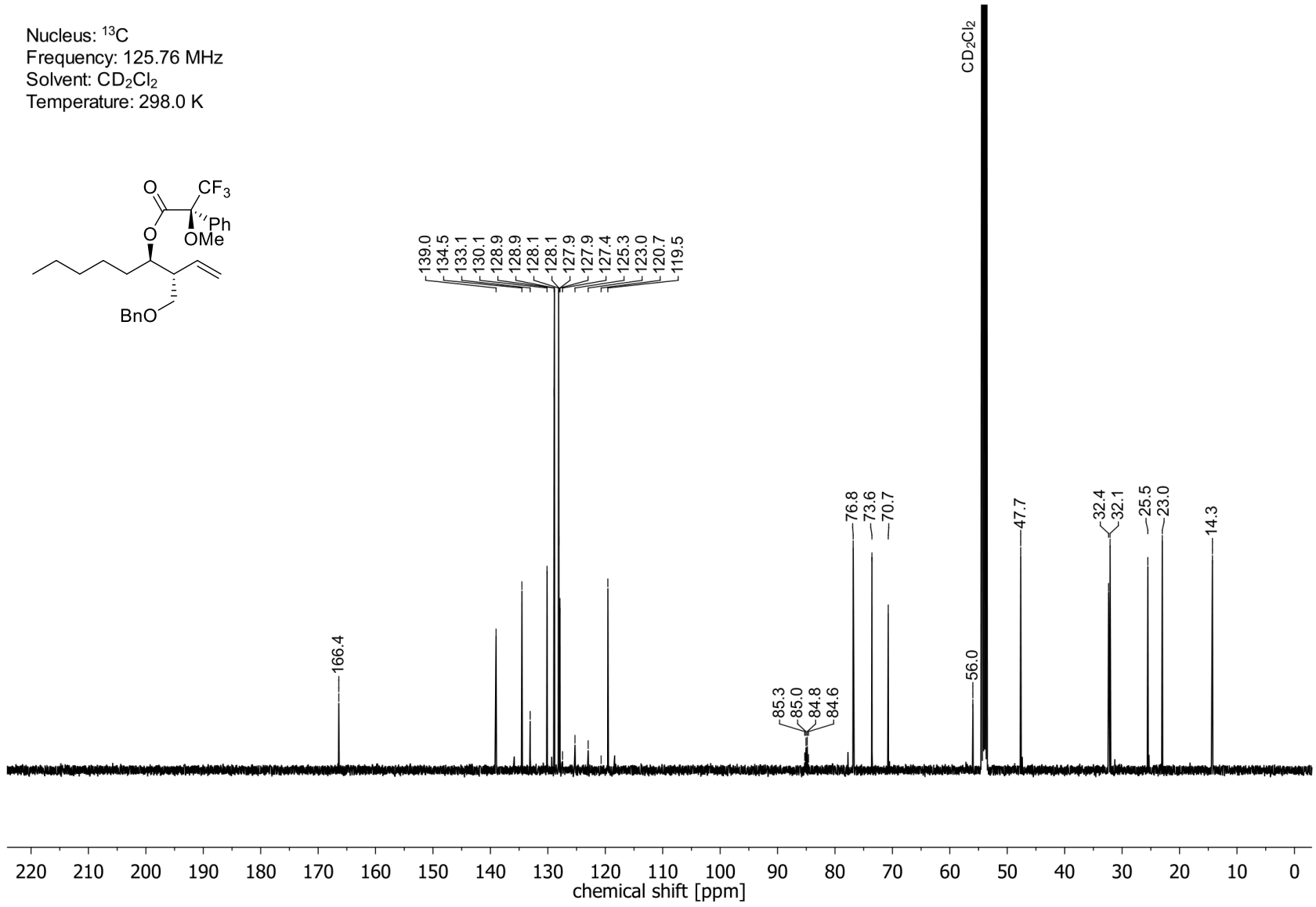


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

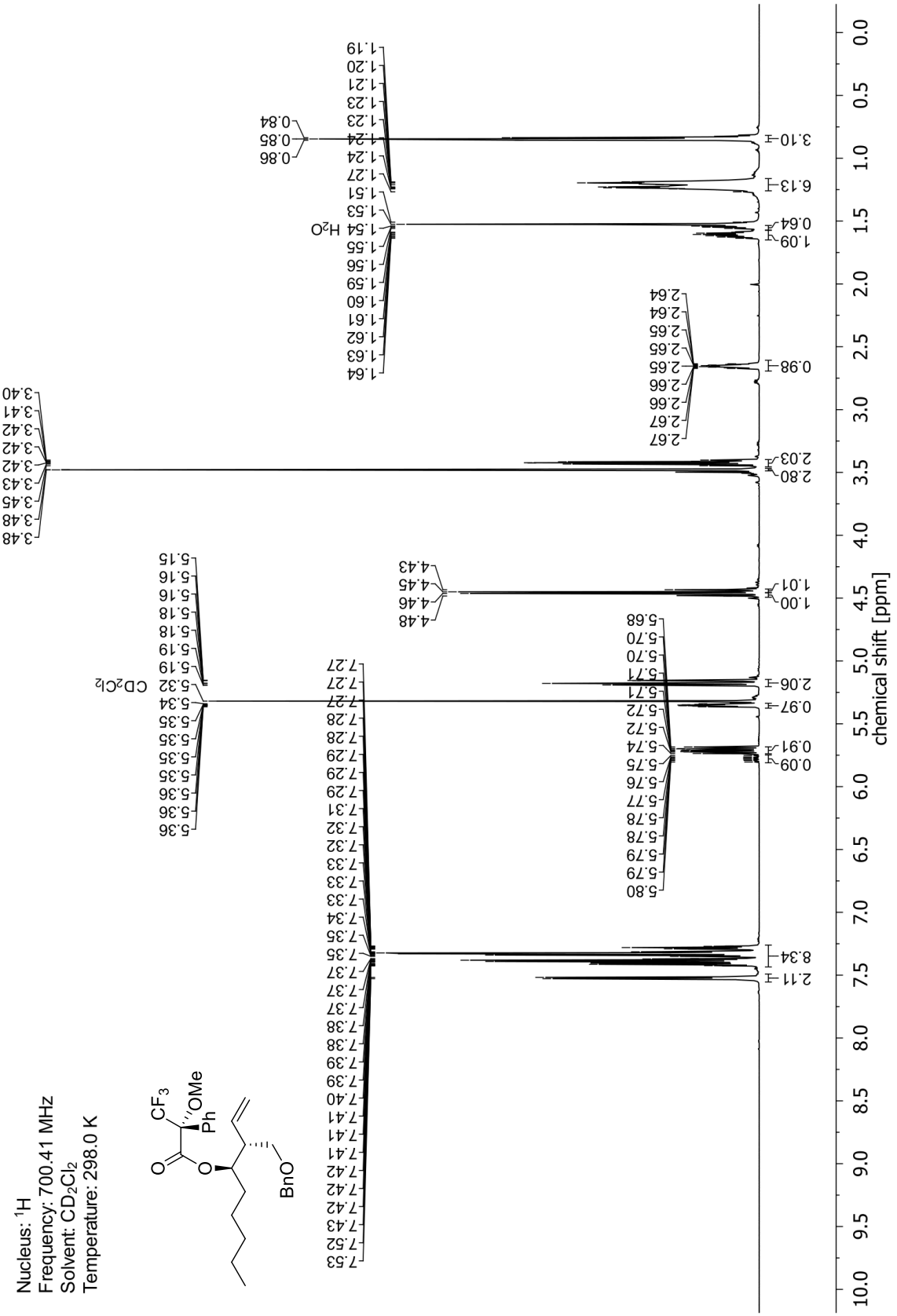


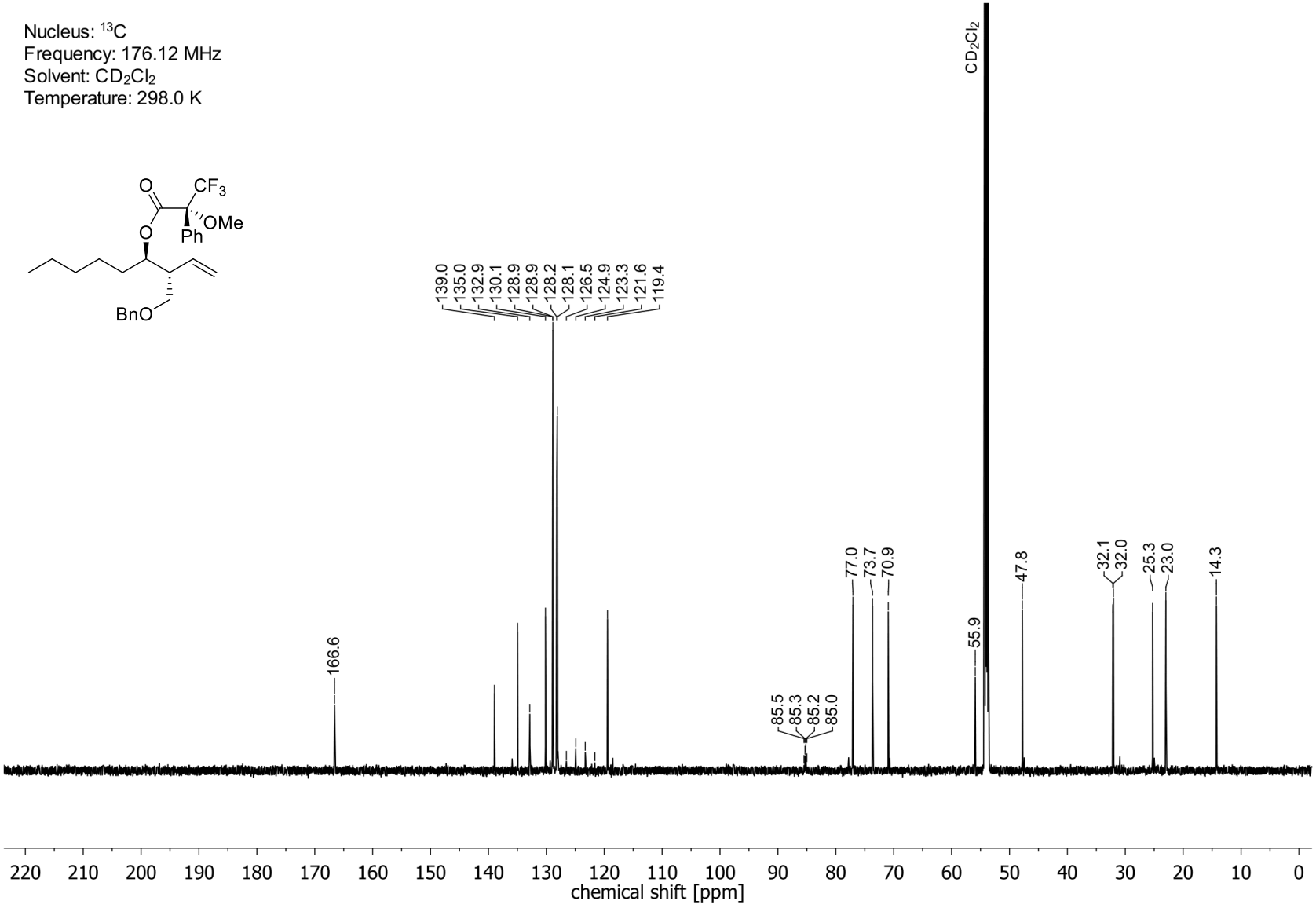
NMR-Spectra of Compound **358-(*S*)**:



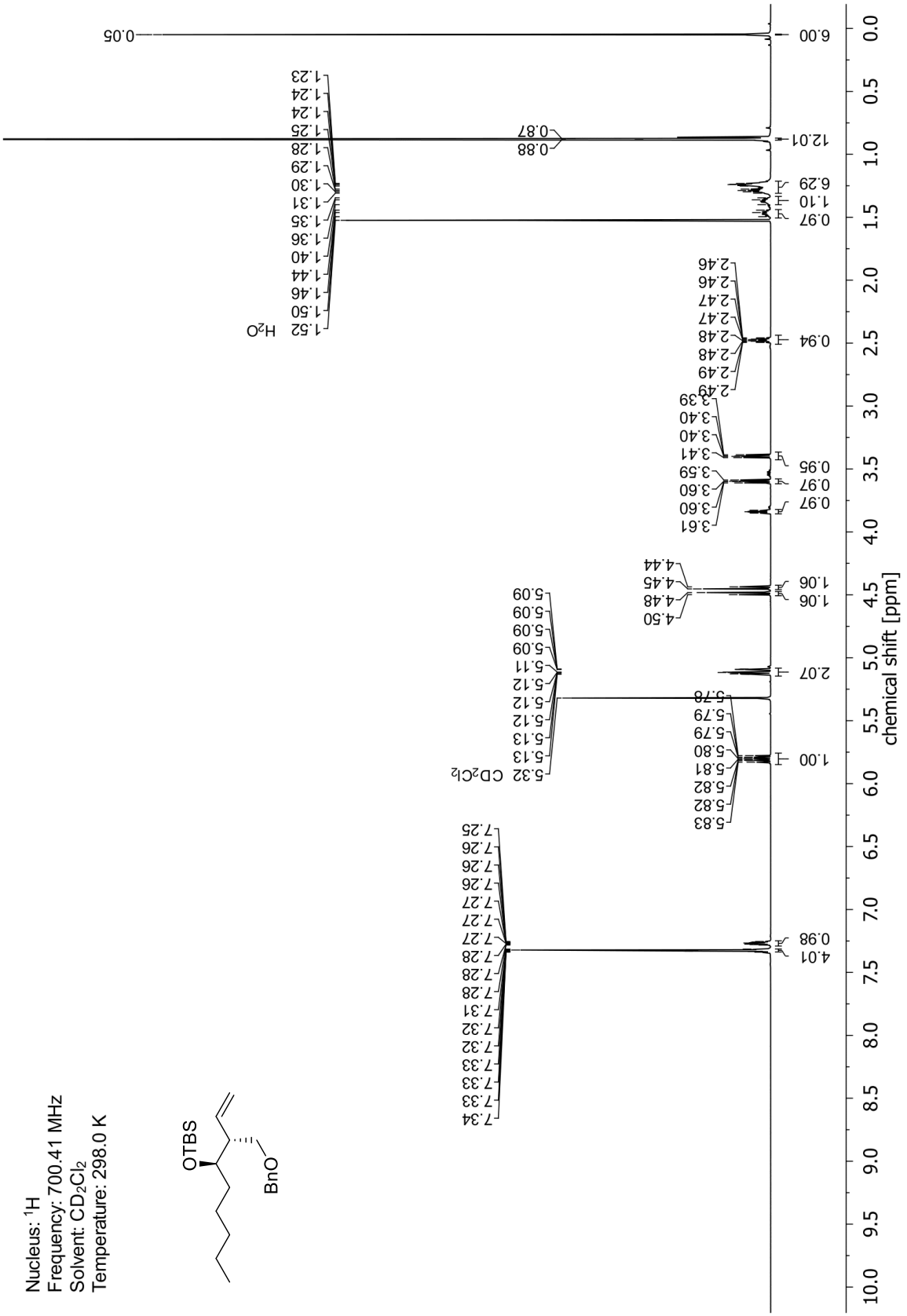

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
CF3
Ph
OMe
O
BnO
139.0
134.5
133.1
130.1
128.9
128.9
128.1
128.1
127.9
127.9
127.4
125.3
123.0
120.7
119.5
CD2Cl2
166.4
85.3
85.0
84.8
84.6
76.8
73.6
70.7
56.0
47.7
32.4
32.1
25.5
23.0
14.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

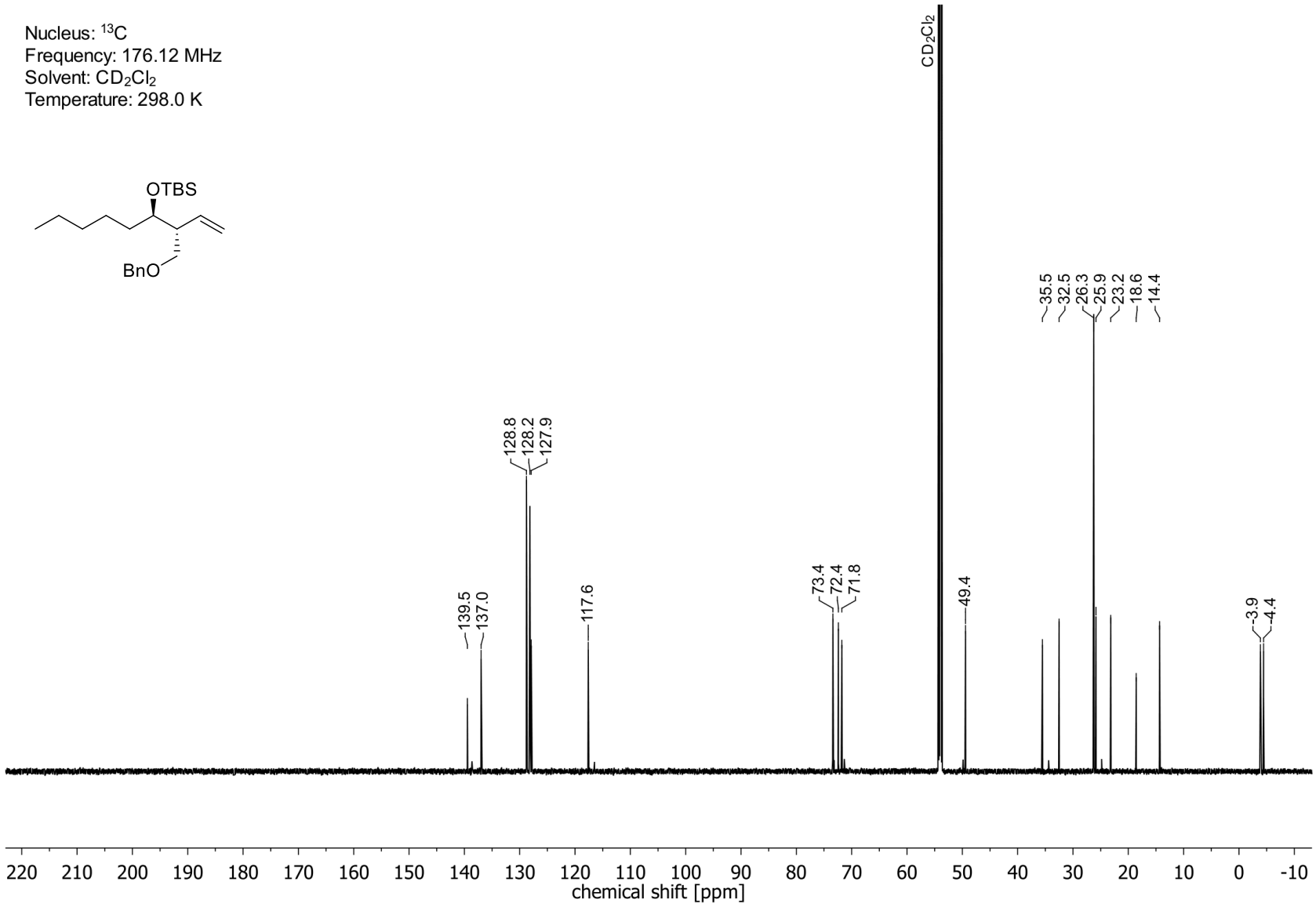
NMR-Spectra of Compound **358-(*R*)**:



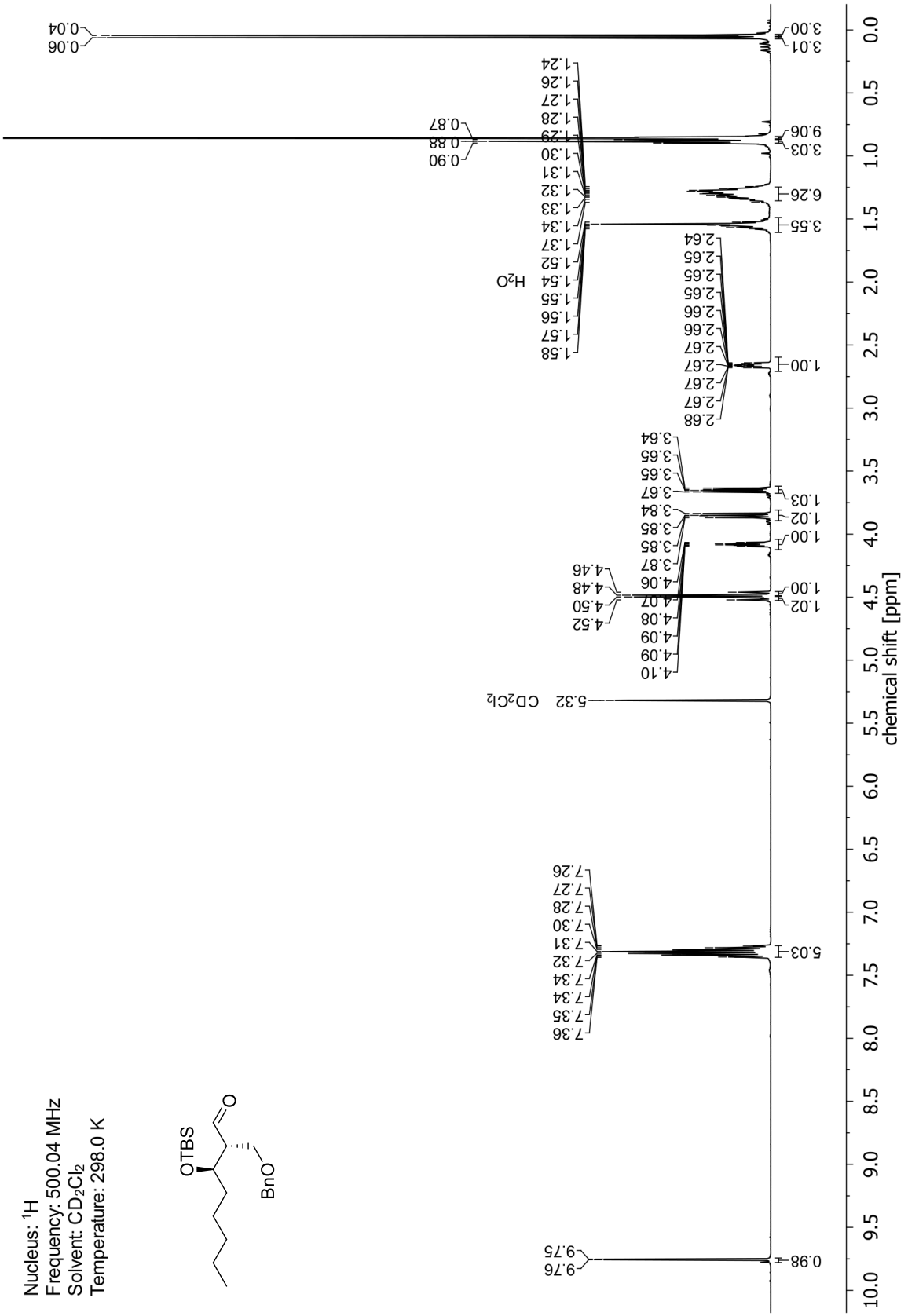

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
CF3
OMe
Ph
O
BnO
139.0
135.0
132.9
130.1
128.9
128.9
128.2
128.1
126.5
124.9
123.3
121.6
119.4
CD2Cl2
166.6
85.5
85.3
85.2
85.0
77.0
73.7
70.9
55.9
47.8
32.1
32.0
25.3
23.0
14.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

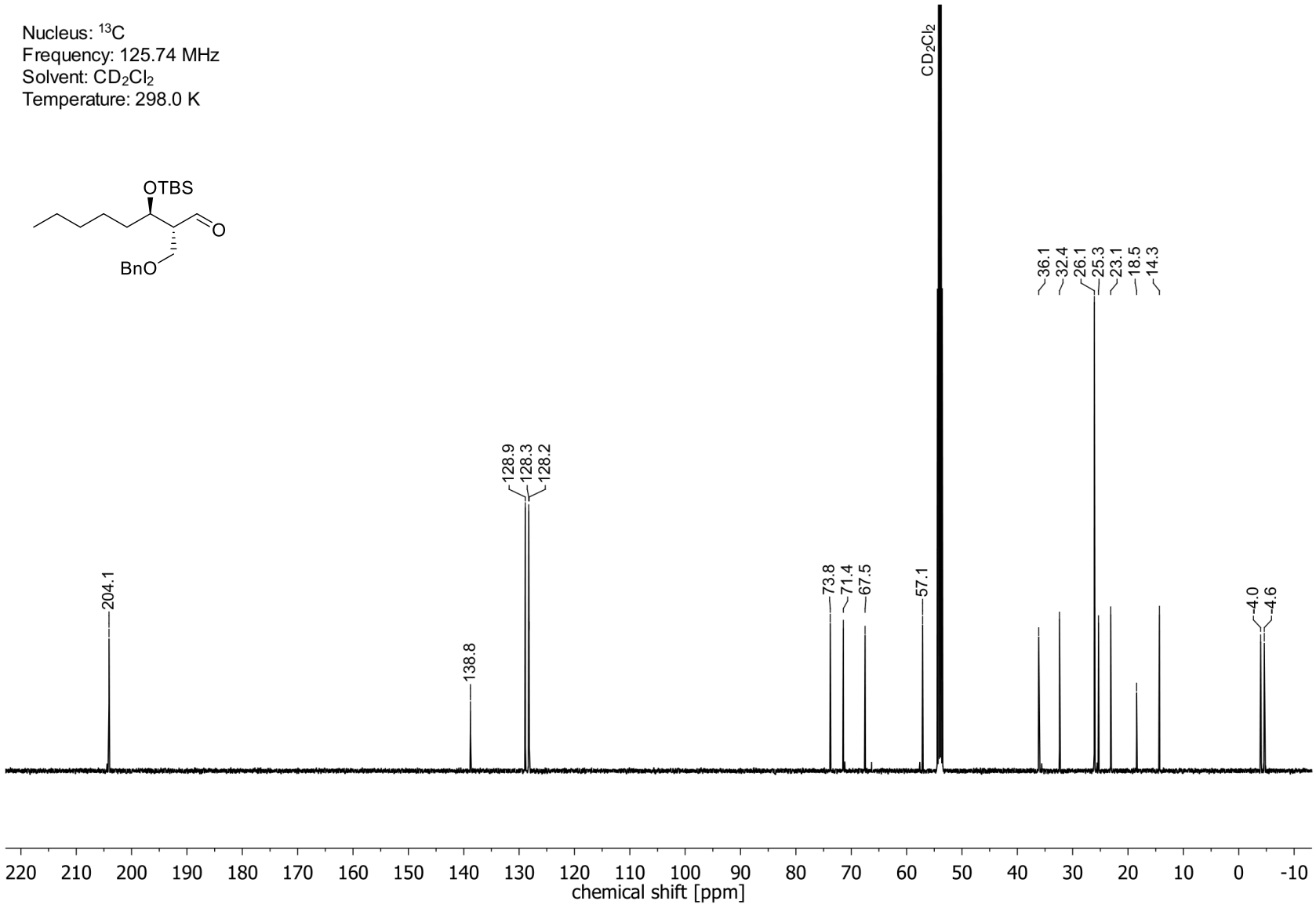
NMR-Spectra of Compound **239**:



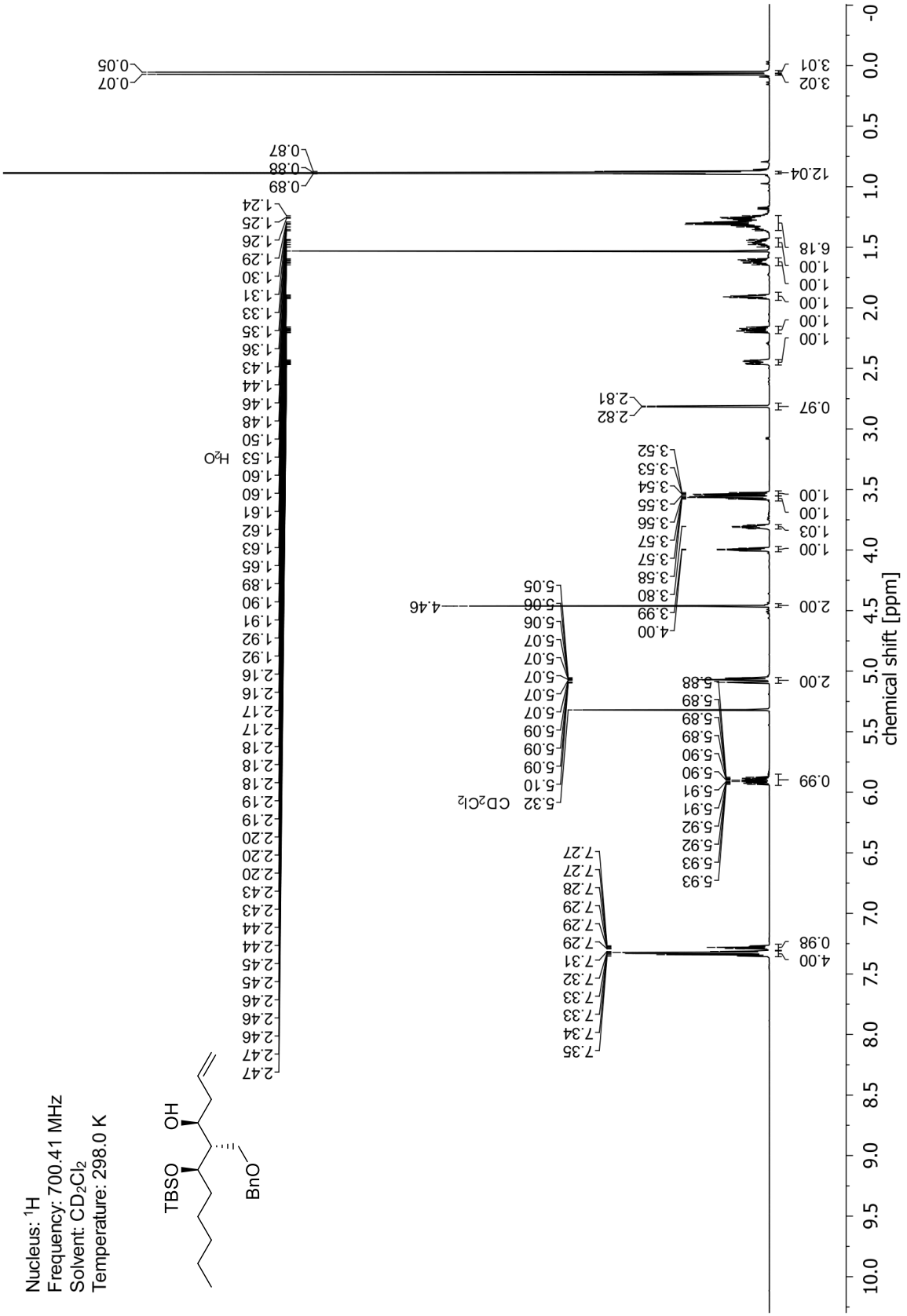

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OTBS
BnO
CD2Cl2
35.5
32.5
26.3
25.9
23.2
18.6
14.4
128.8
128.2
127.9
139.5
137.0
117.6
73.4
72.4
71.8
49.4
-3.9
-4.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

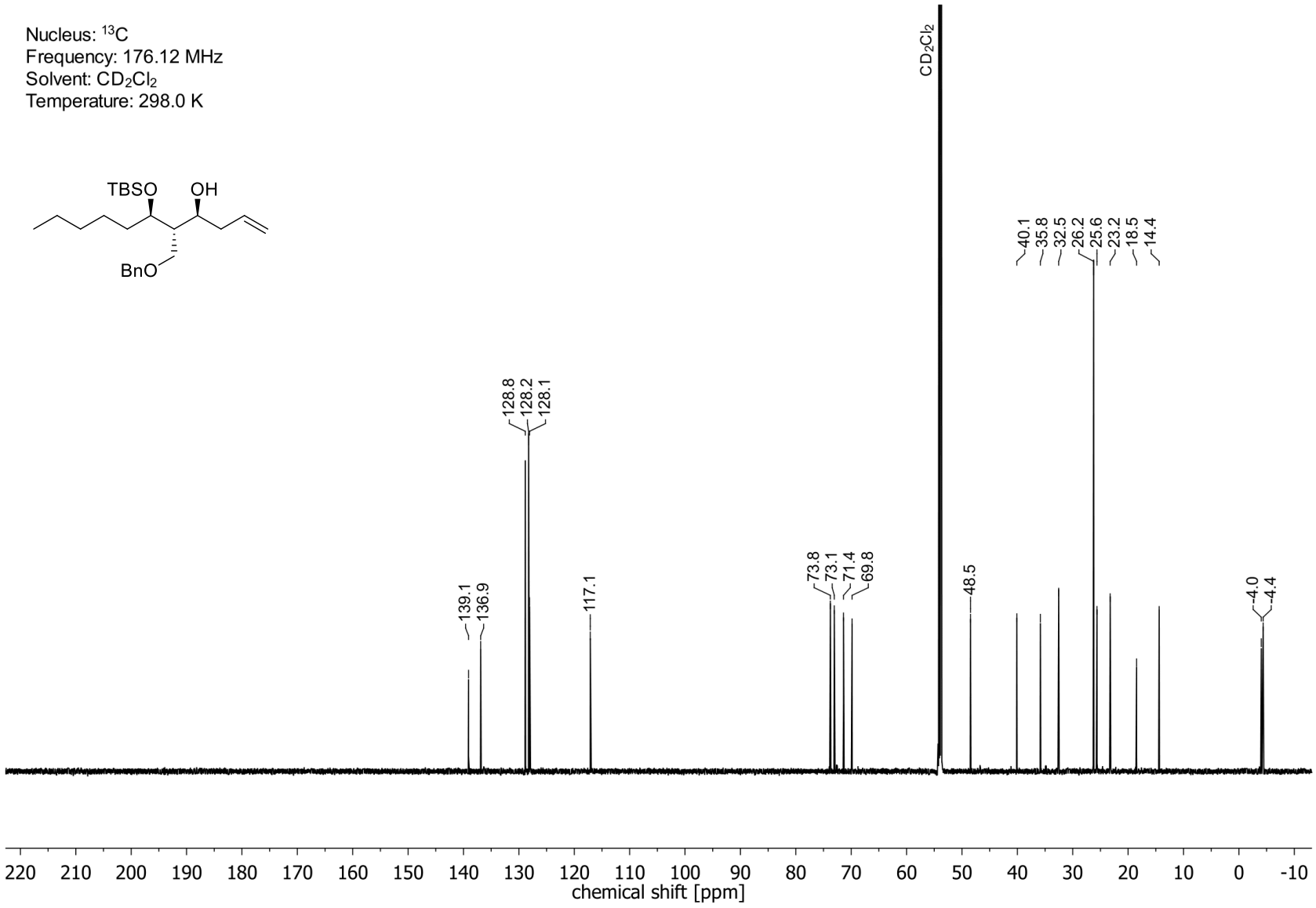
NMR-Spectra of Compound **241**:



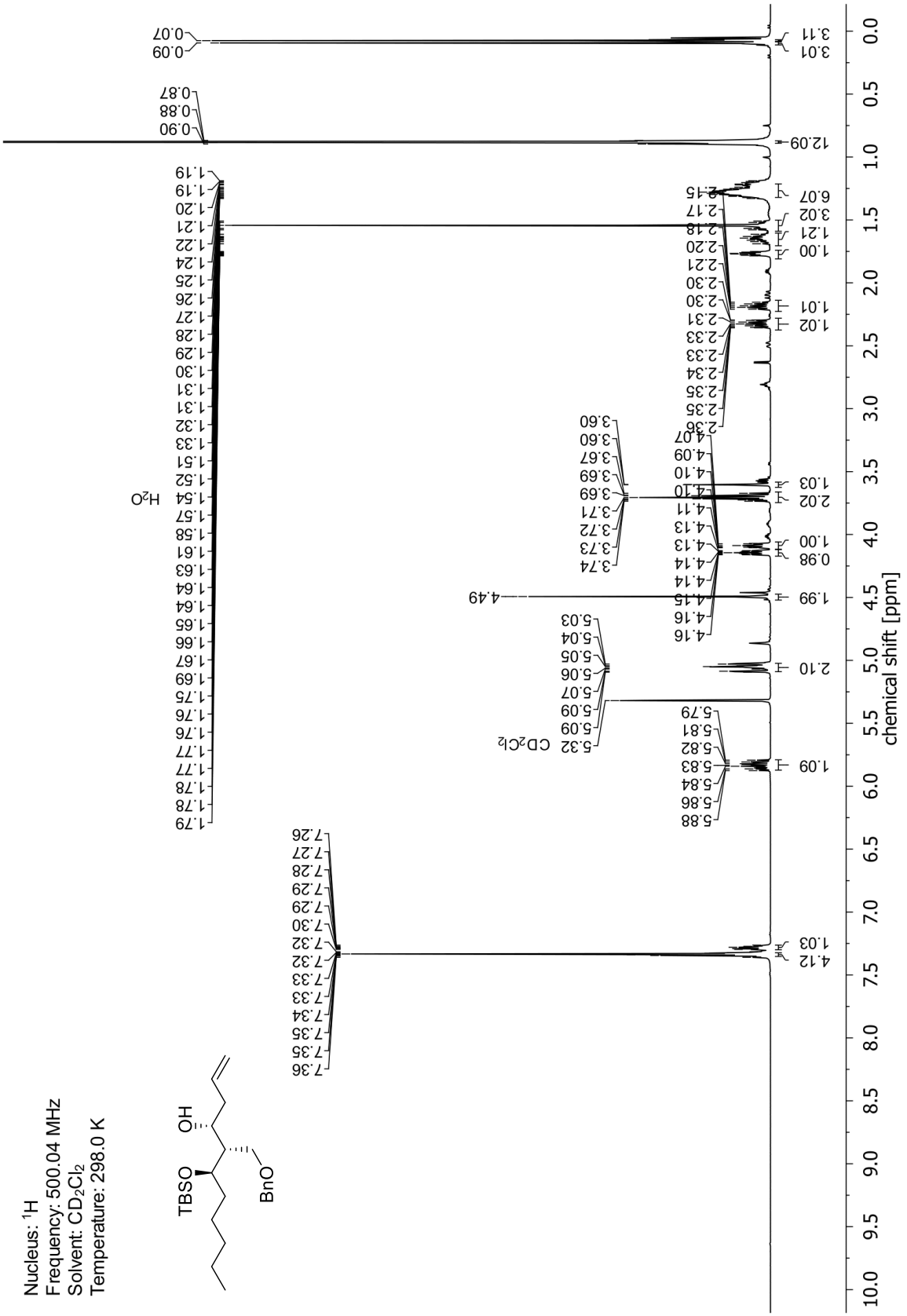

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OTBS
O
BnO
CD2Cl2
36.1
32.4
26.1
25.3
23.1
18.5
14.3
128.9
128.3
128.2
204.1
138.8
73.8
71.4
67.5
57.1
-4.0
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

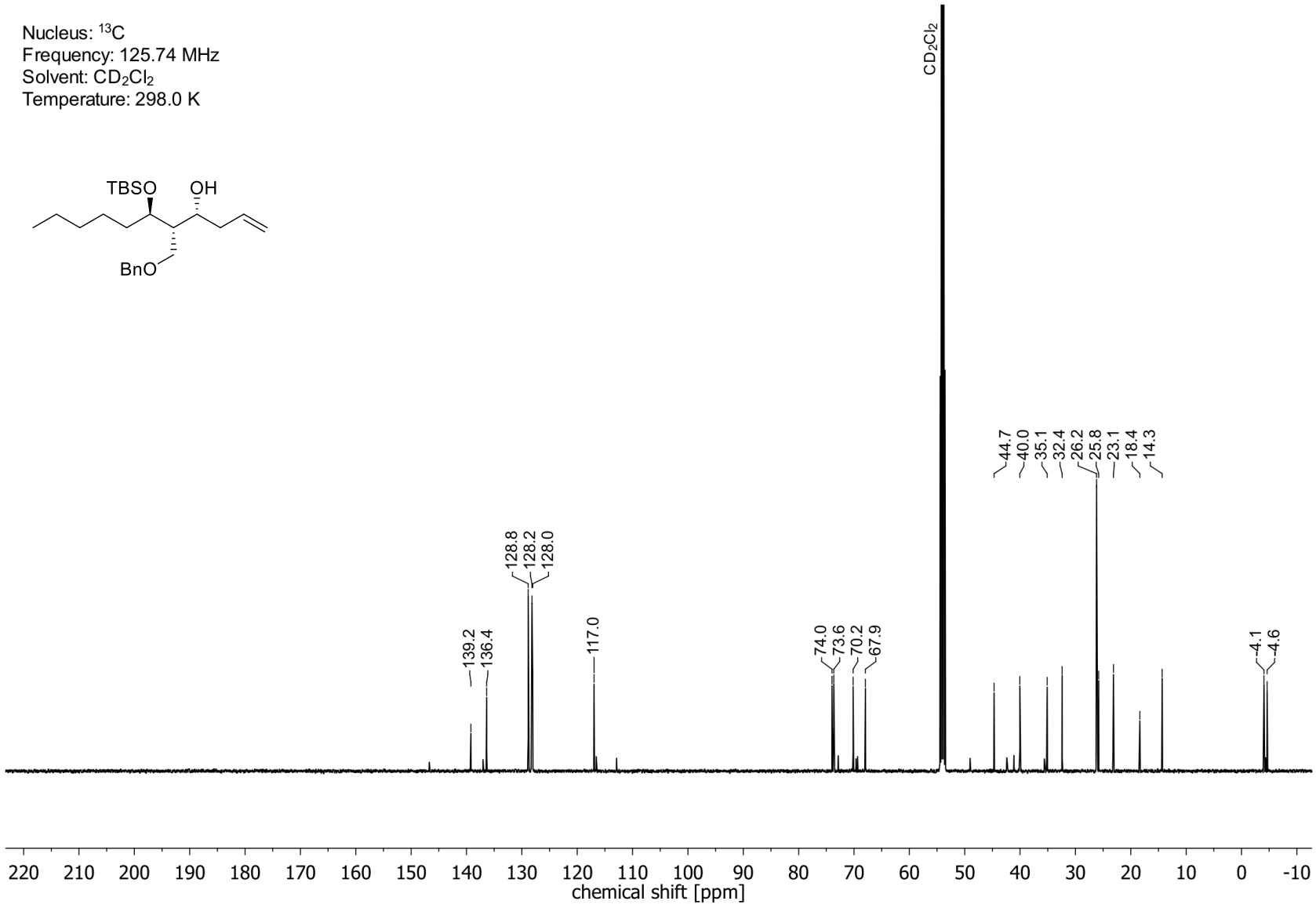
NMR-Spectra of Compound **242**:



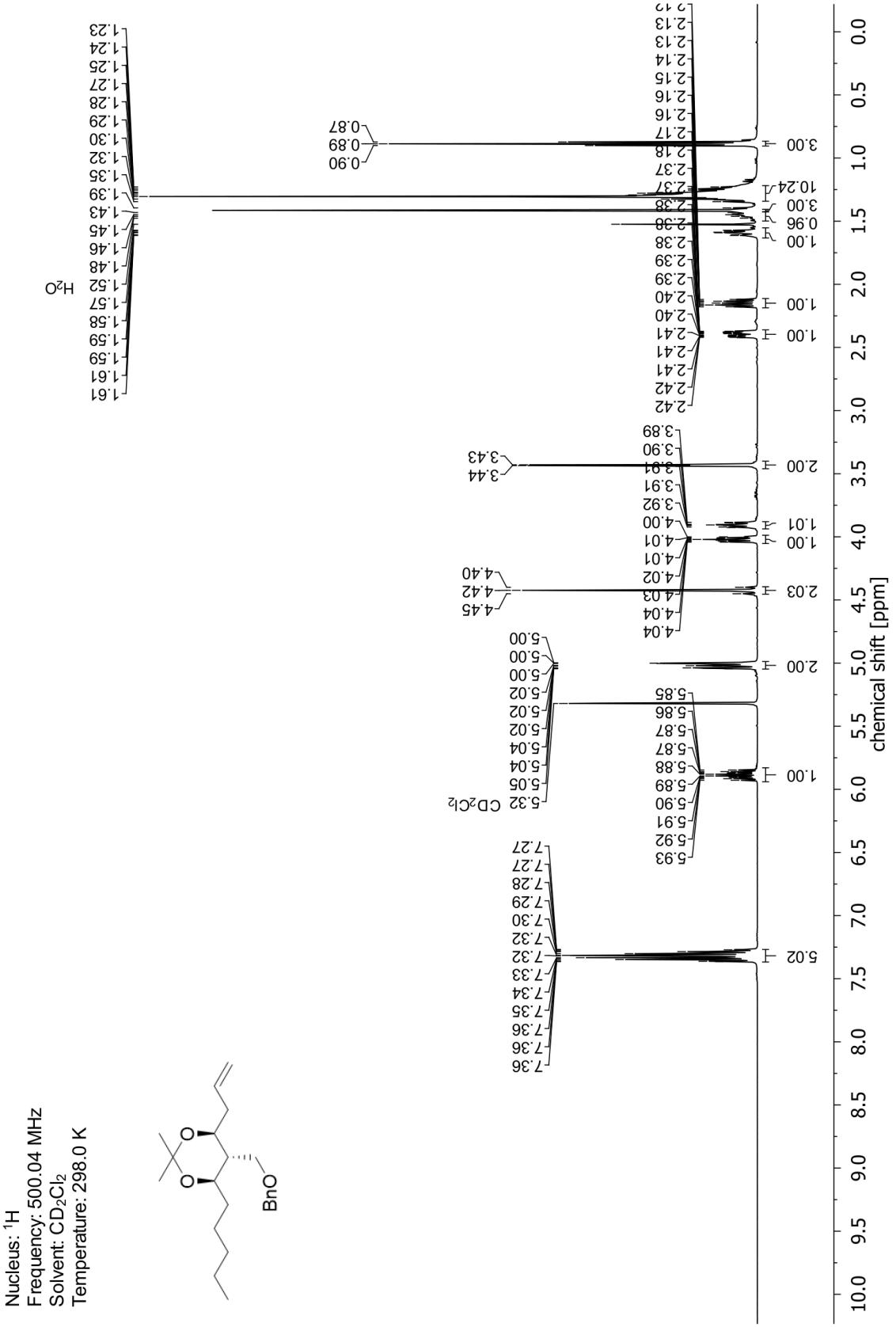

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
BnO
CD2Cl2
40.1
35.8
32.5
26.2
25.6
23.2
18.5
14.4
128.8
128.2
128.1
139.1
136.9
117.1
73.8
73.1
71.4
69.8
48.5
-4.0
-4.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

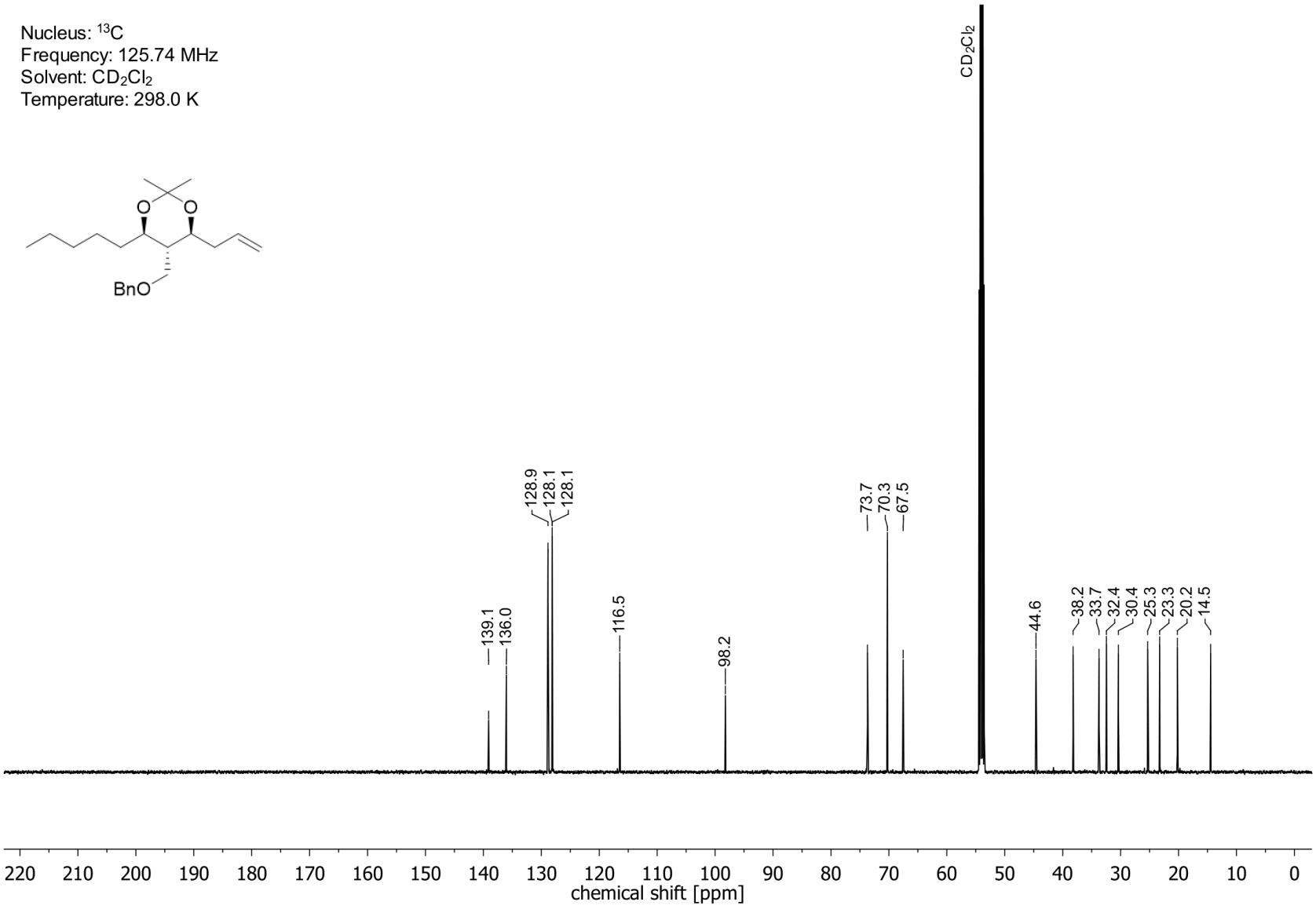
NMR-Spectra of Compound **250**:



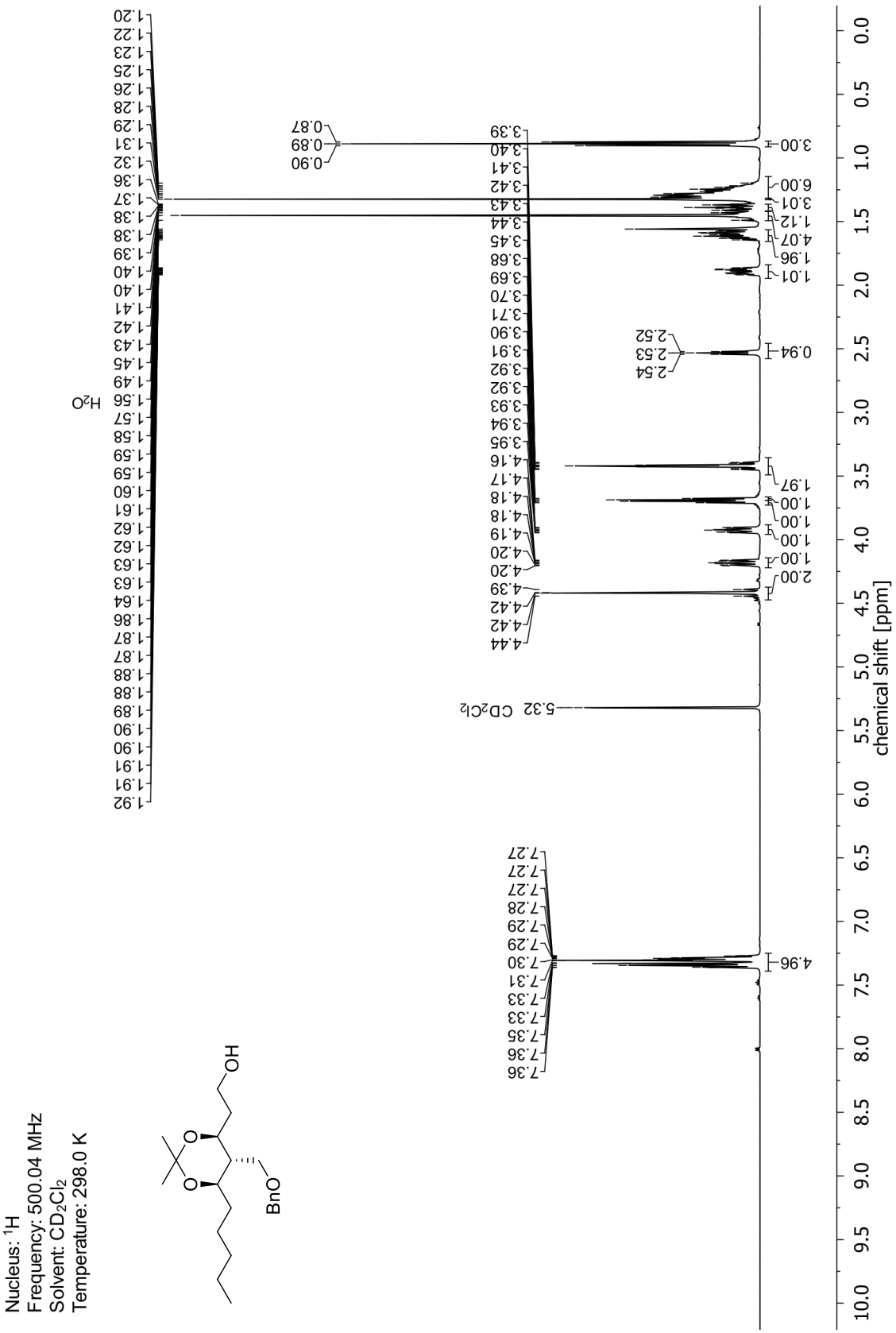

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
BnO
CD2Cl2
44.7
40.0
35.1
32.4
26.2
25.8
23.1
18.4
14.3
128.8
128.2
128.0
139.2
136.4
117.0
74.0
73.6
70.2
67.9
-4.1
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

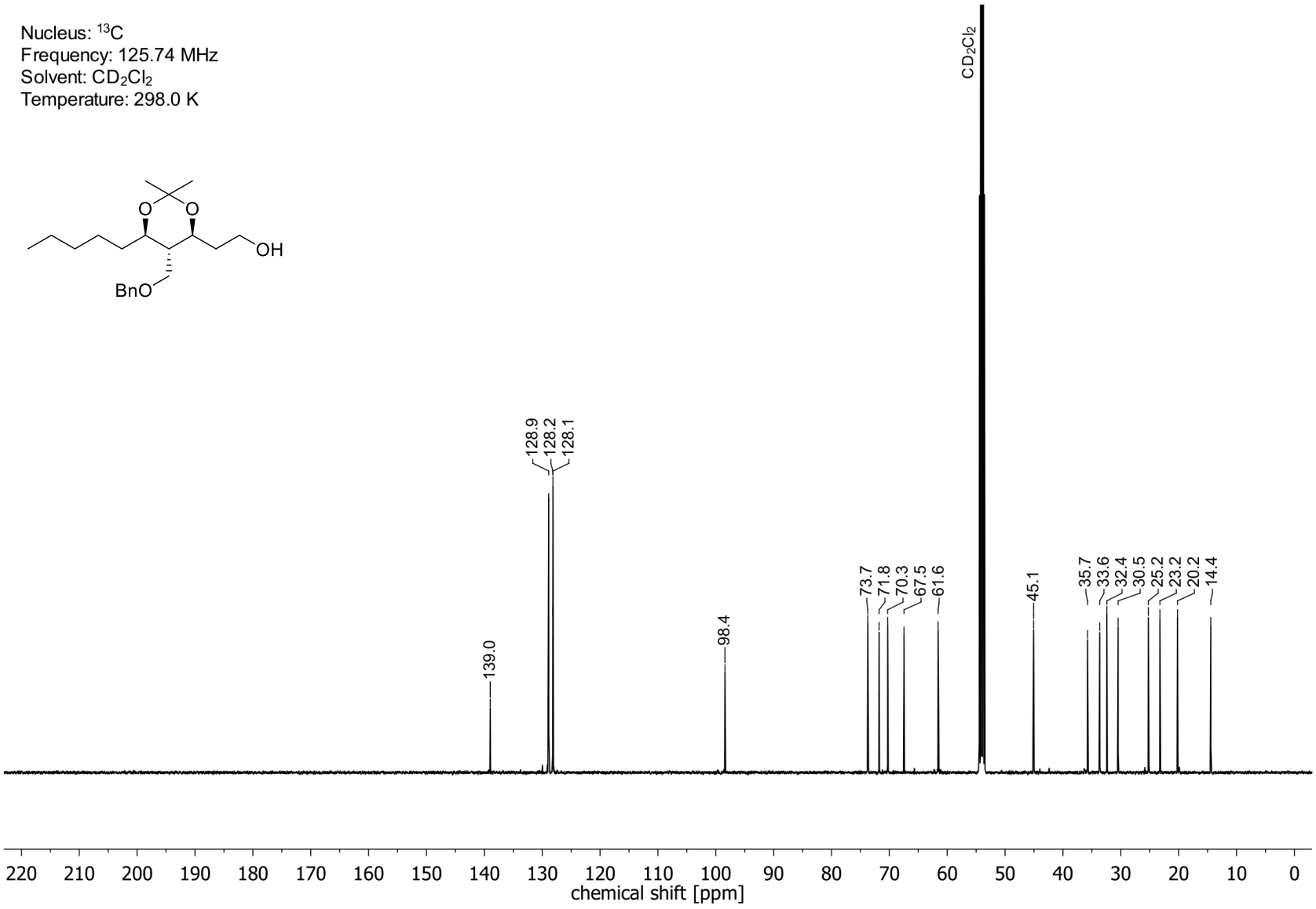
NMR-Spectra of Compound **319**:



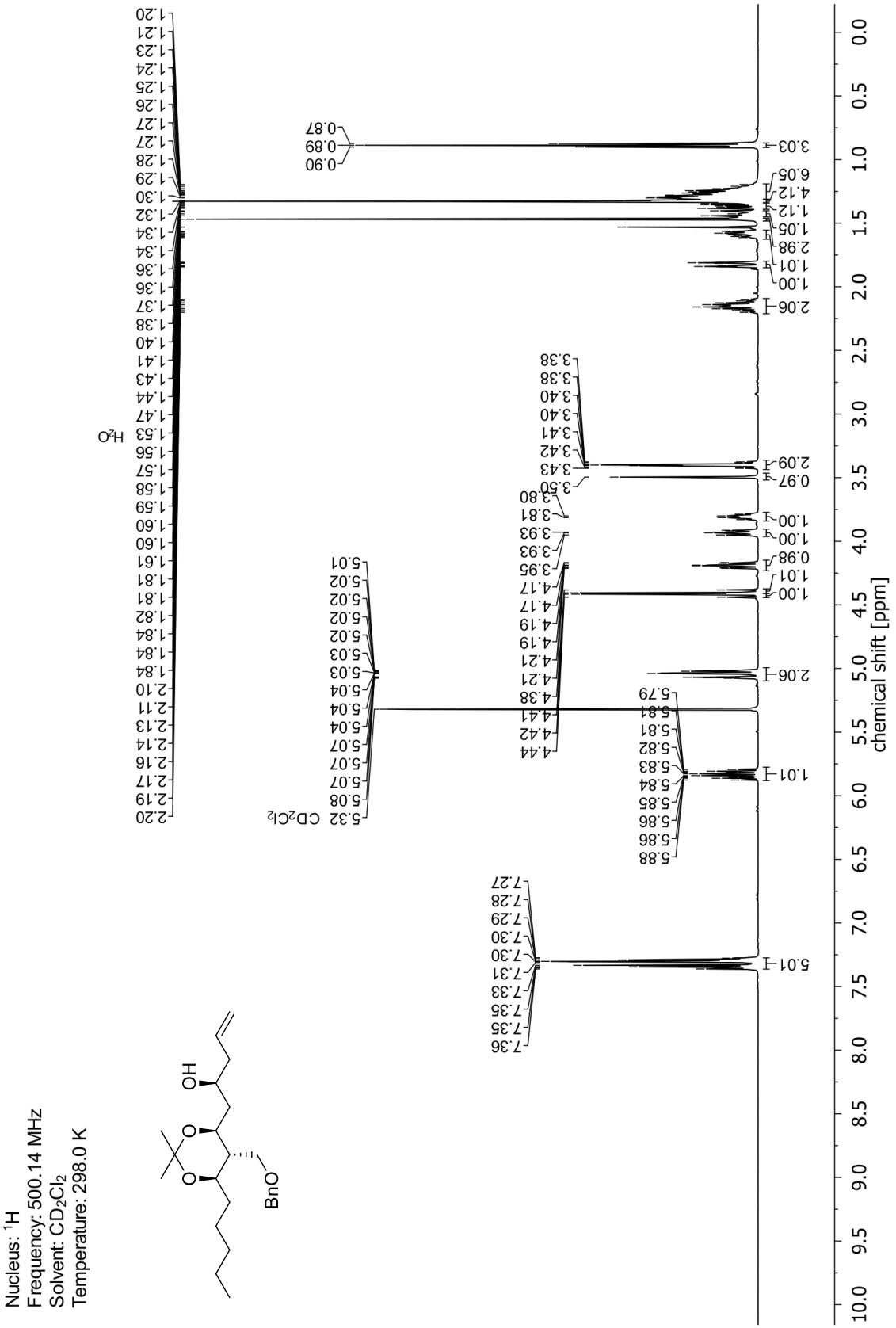

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CD2Cl2
139.1
136.0
128.9
128.1
128.1
116.5
98.2
73.7
70.3
67.5
44.6
38.2
33.7
32.4
30.4
25.3
23.3
20.2
14.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

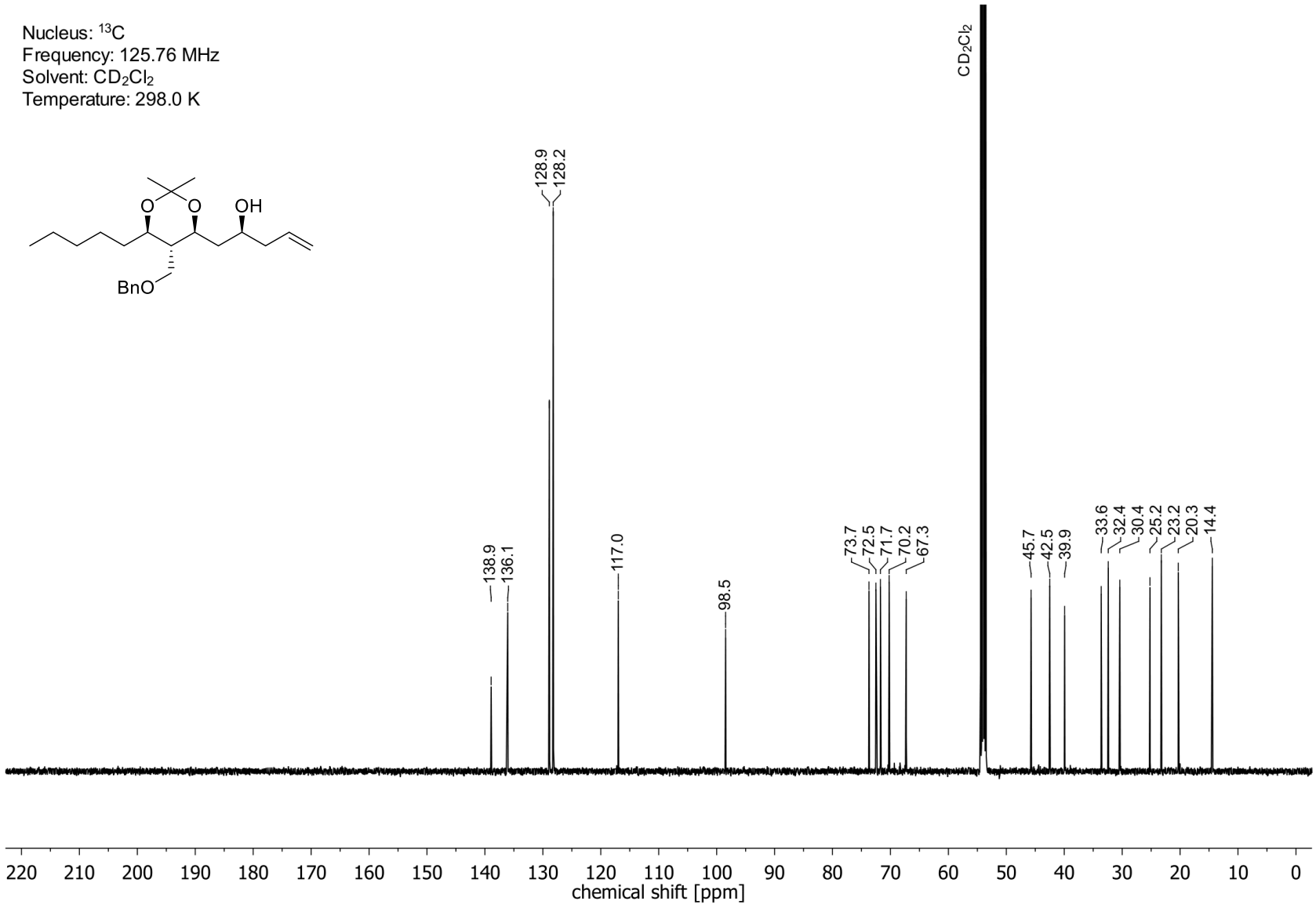
NMR-Spectra of Compound **238**:



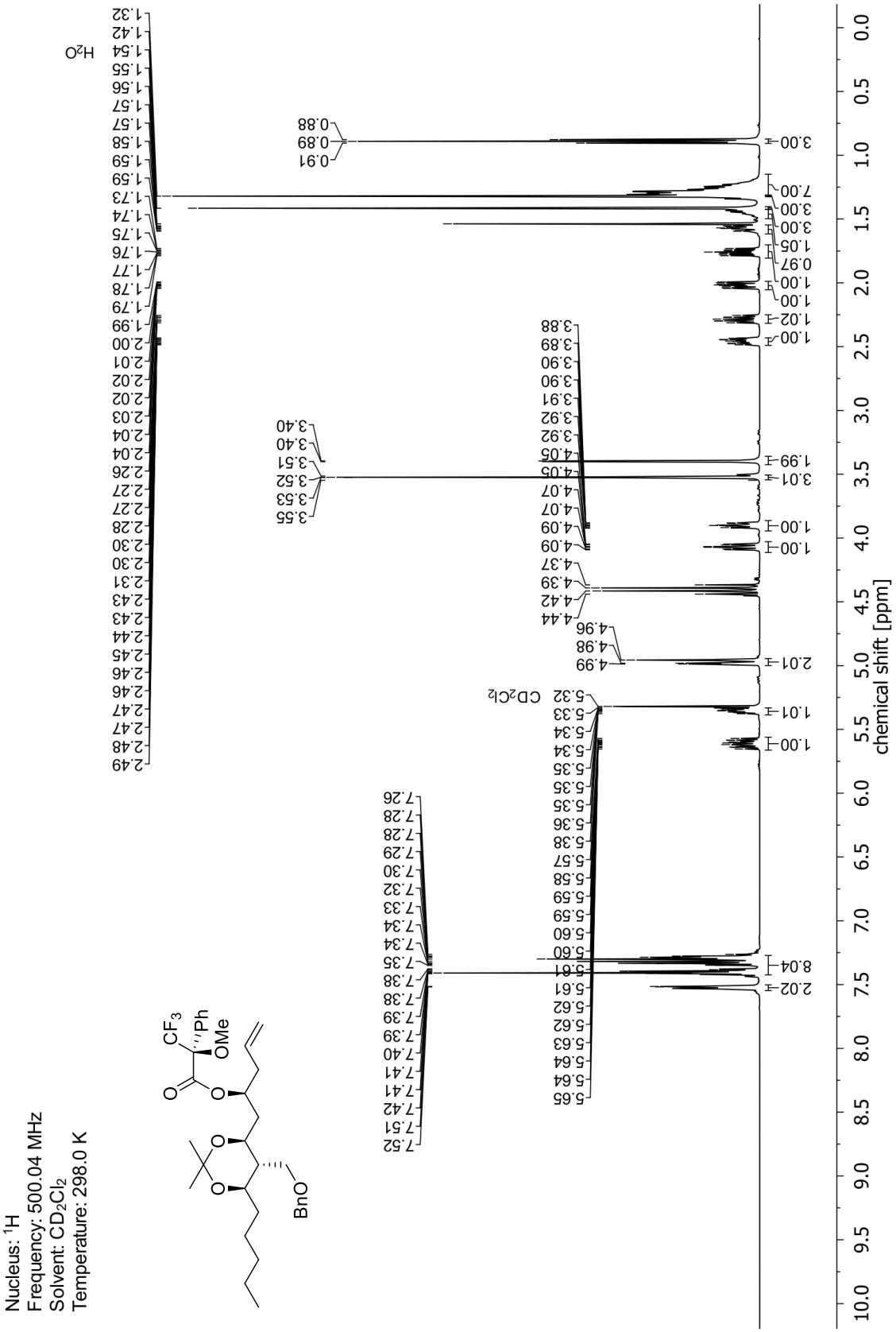

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OH
BnO
CD2Cl2
128.9
128.2
128.1
139.0
98.4
73.7
71.8
70.3
67.5
61.6
45.1
35.7
33.6
32.4
30.5
25.2
23.2
20.2
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

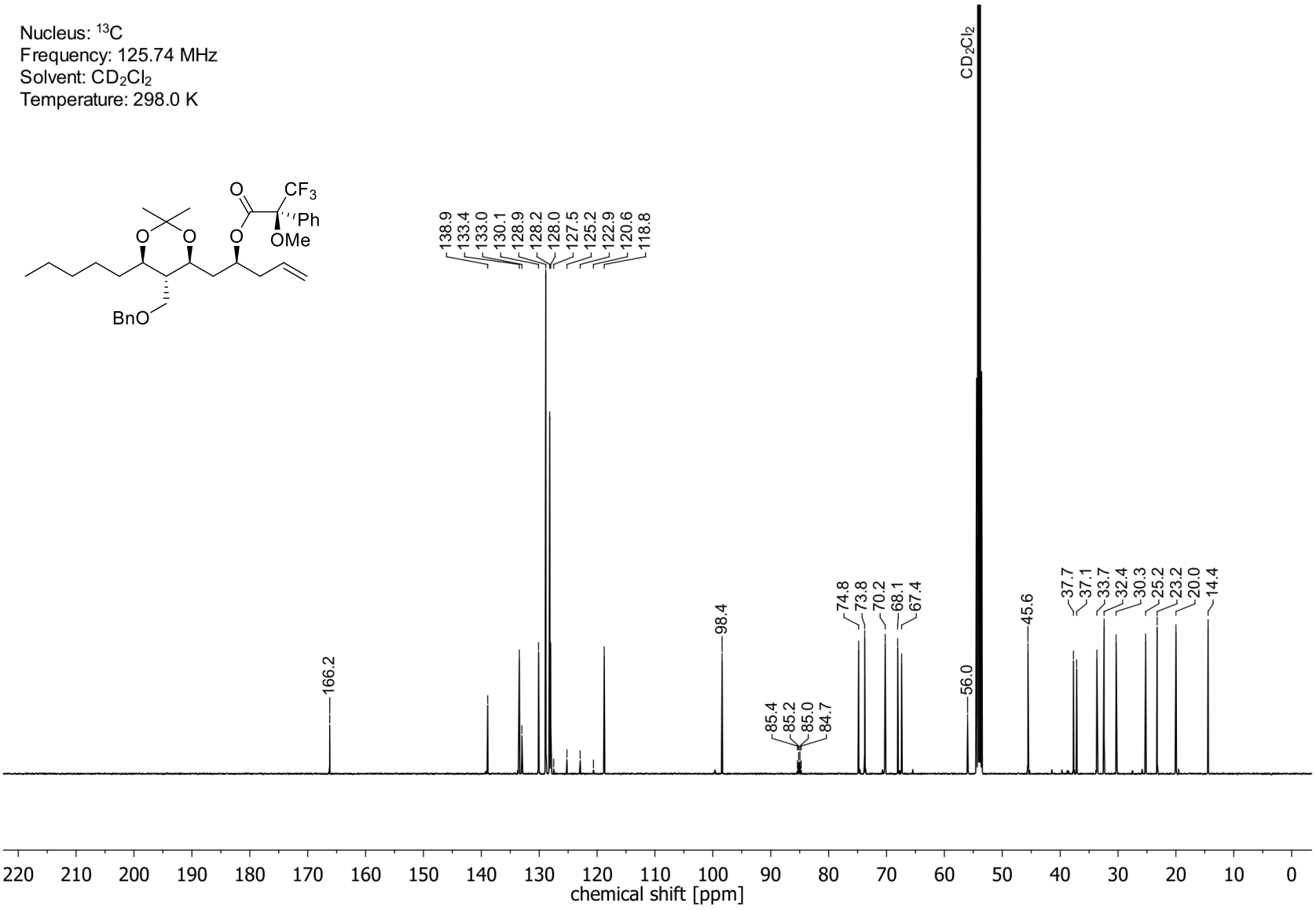
NMR-Spectra of Compound **320**:



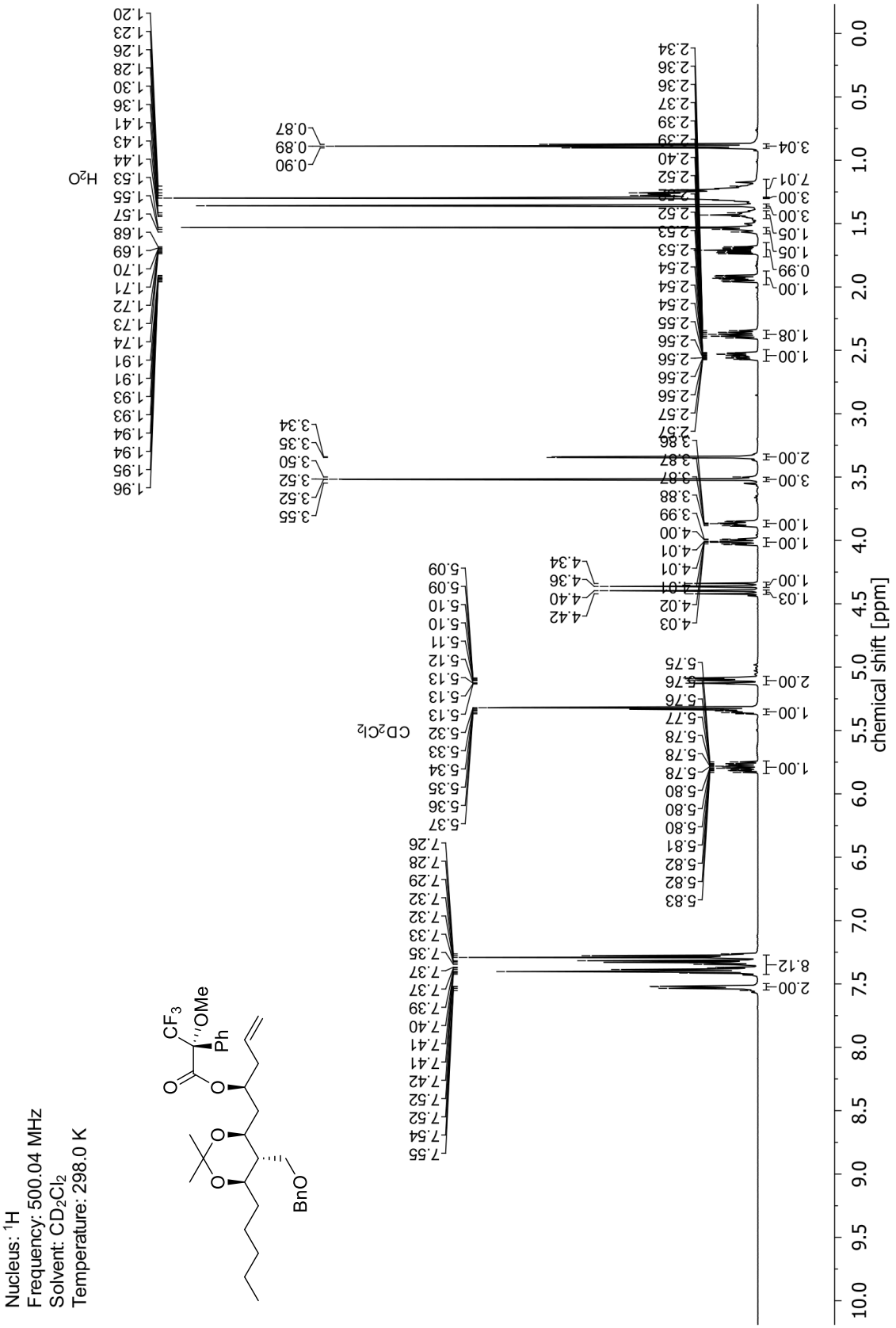

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OH
BnO
CD2Cl2
128.9
128.2
138.9
136.1
117.0
98.5
73.7
72.5
71.7
70.2
67.3
45.7
42.5
39.9
33.6
32.4
30.4
25.2
23.2
20.3
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

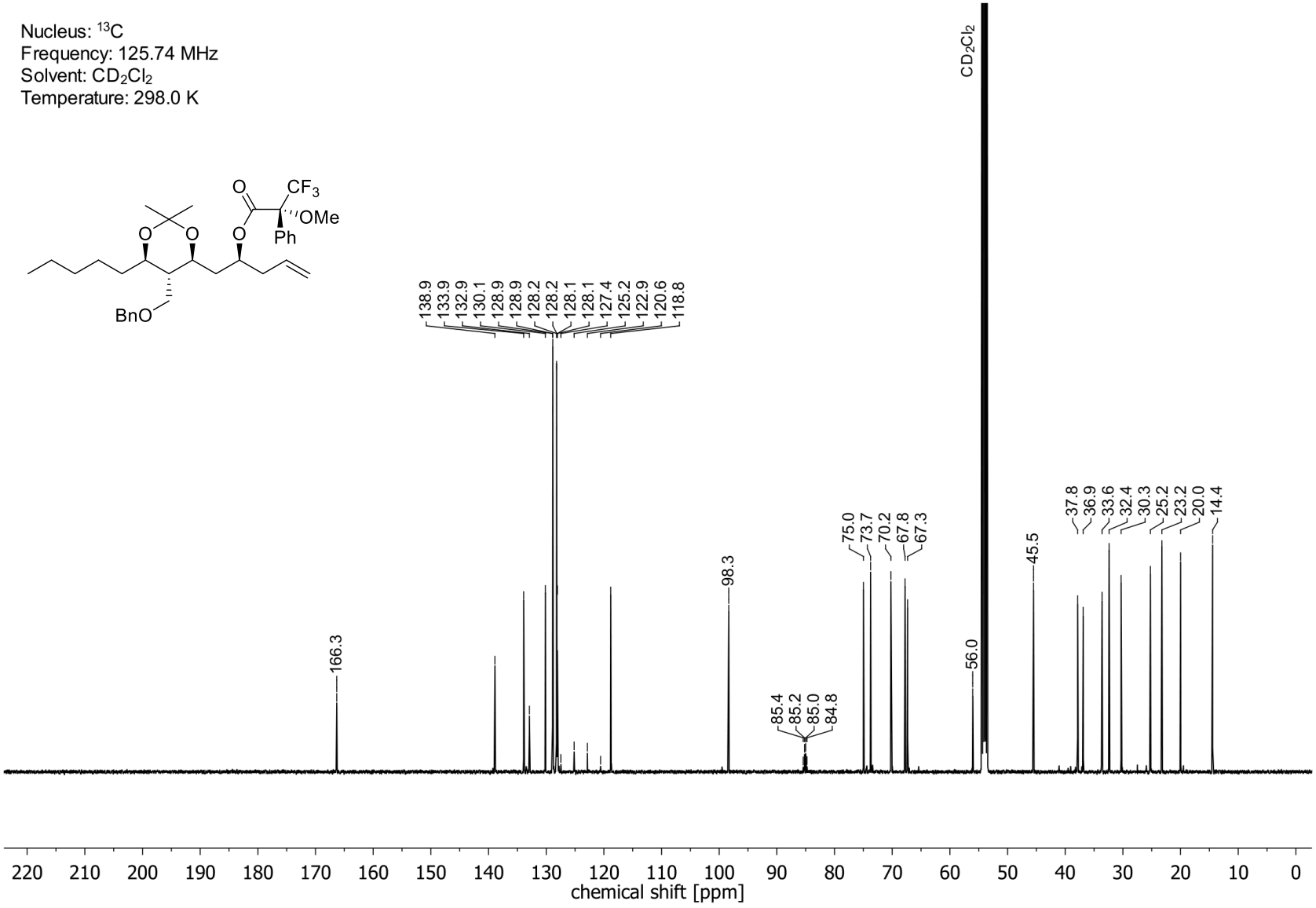
NMR-Spectra of Compound **359-(*S*)**:



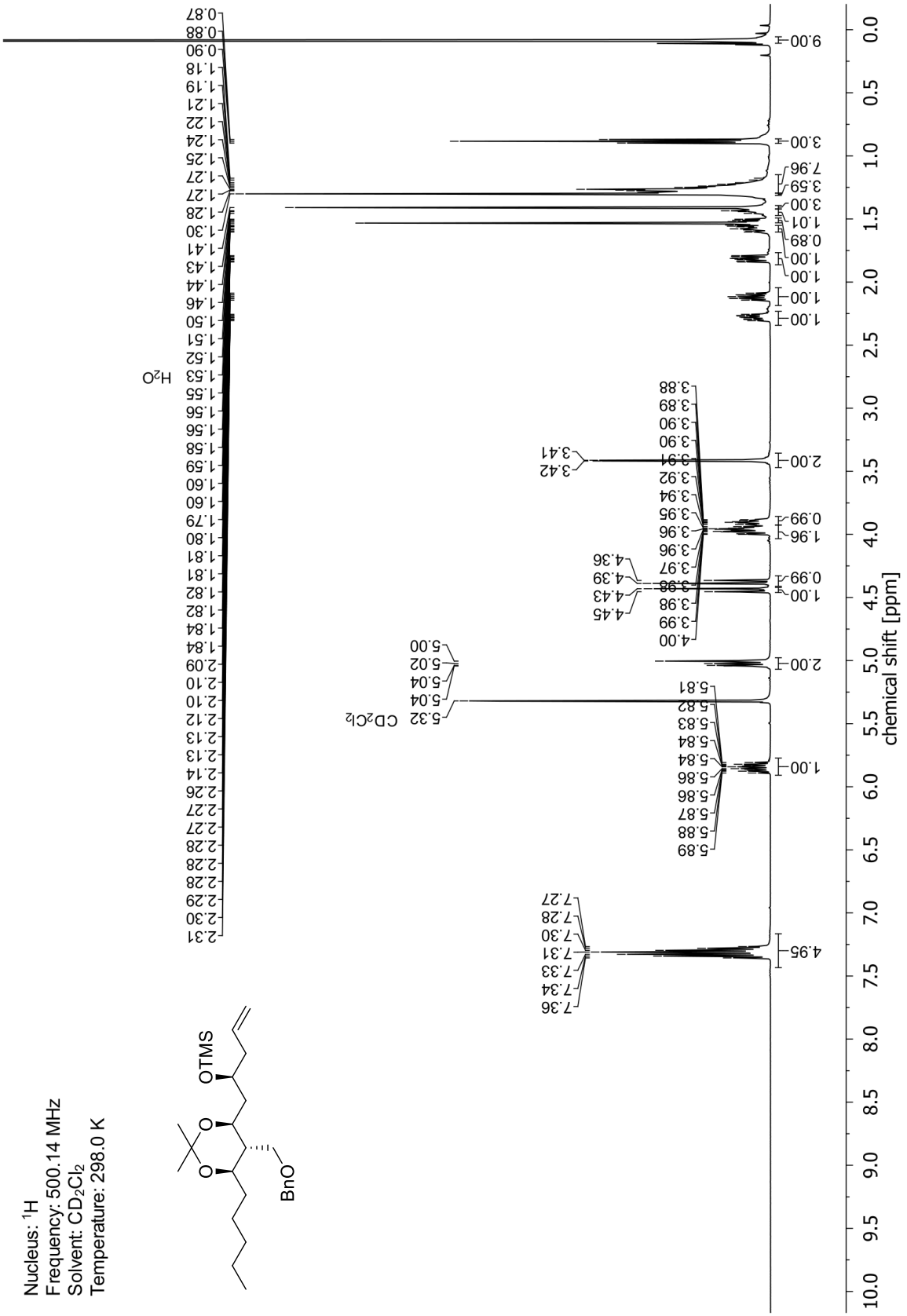

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
CF3
Ph
OMe
O
O
O
BnO
138.9
133.4
133.0
130.1
128.9
128.2
128.0
127.5
125.2
122.9
120.6
118.8
CD2Cl2
166.2
98.4
85.4
85.2
85.0
84.7
74.8
73.8
70.2
68.1
67.4
56.0
45.6
37.7
37.1
33.7
32.4
30.3
25.2
23.2
20.0
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

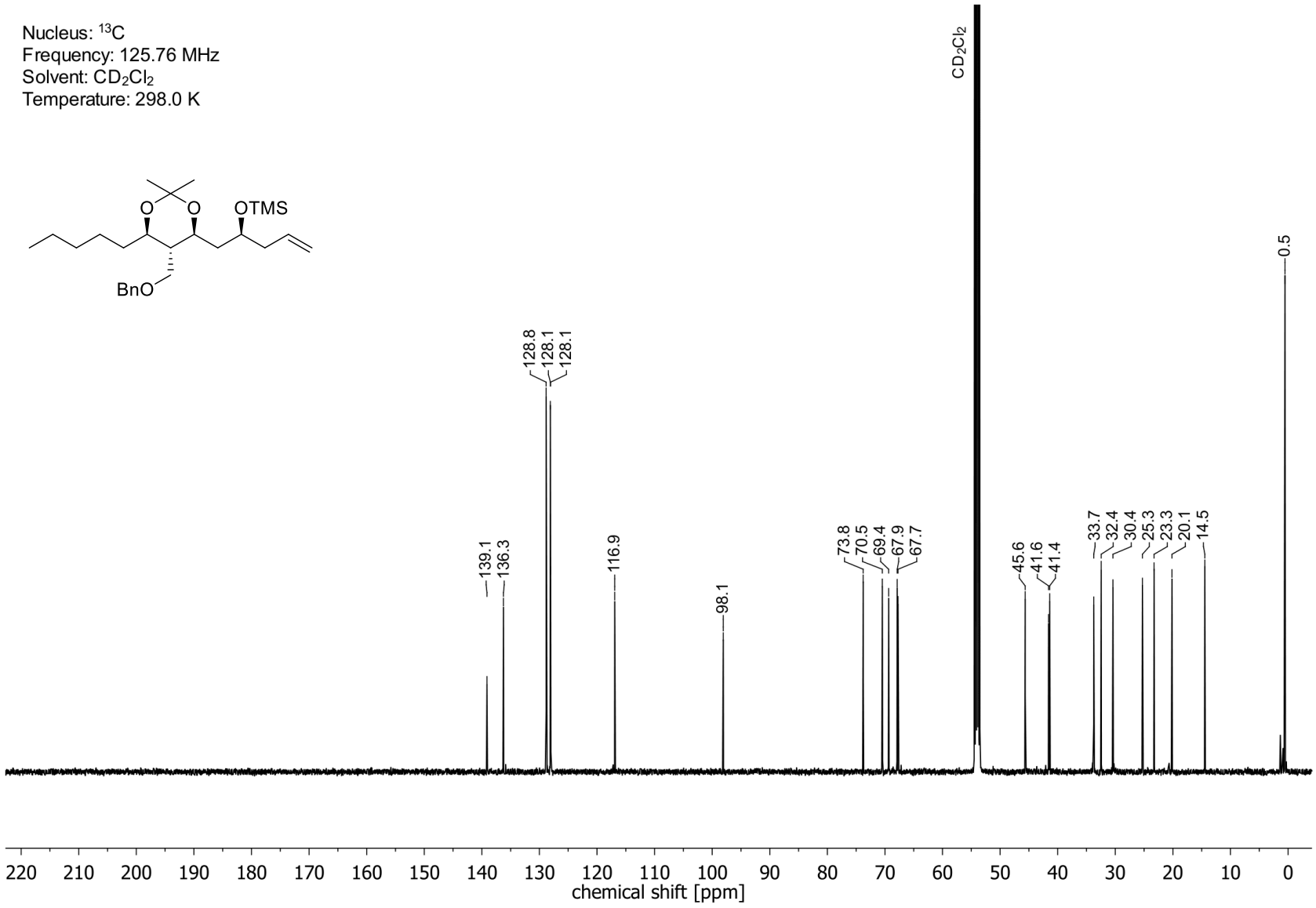
NMR-Spectra of Compound **359-(*R*)**:



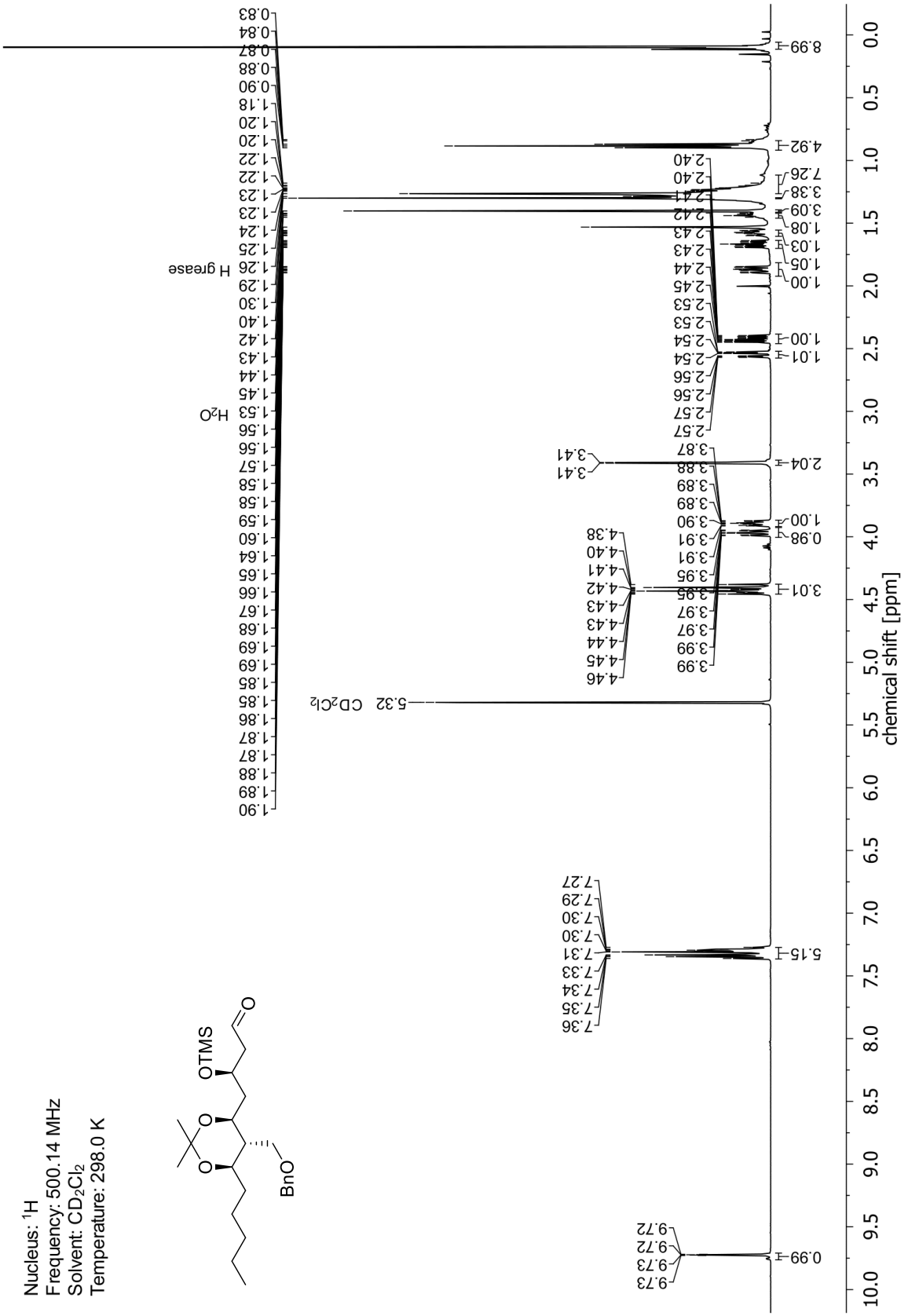

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
CF3
OMe
Ph
O
O
O
BnO
138.9
133.9
132.9
130.1
128.9
128.9
128.2
128.2
128.1
128.1
127.4
125.2
122.9
120.6
118.8
CD2Cl2
166.3
98.3
85.4
85.2
85.0
84.8
75.0
73.7
70.2
67.8
67.3
56.0
45.5
37.8
36.9
33.6
32.4
30.3
25.2
23.2
20.0
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

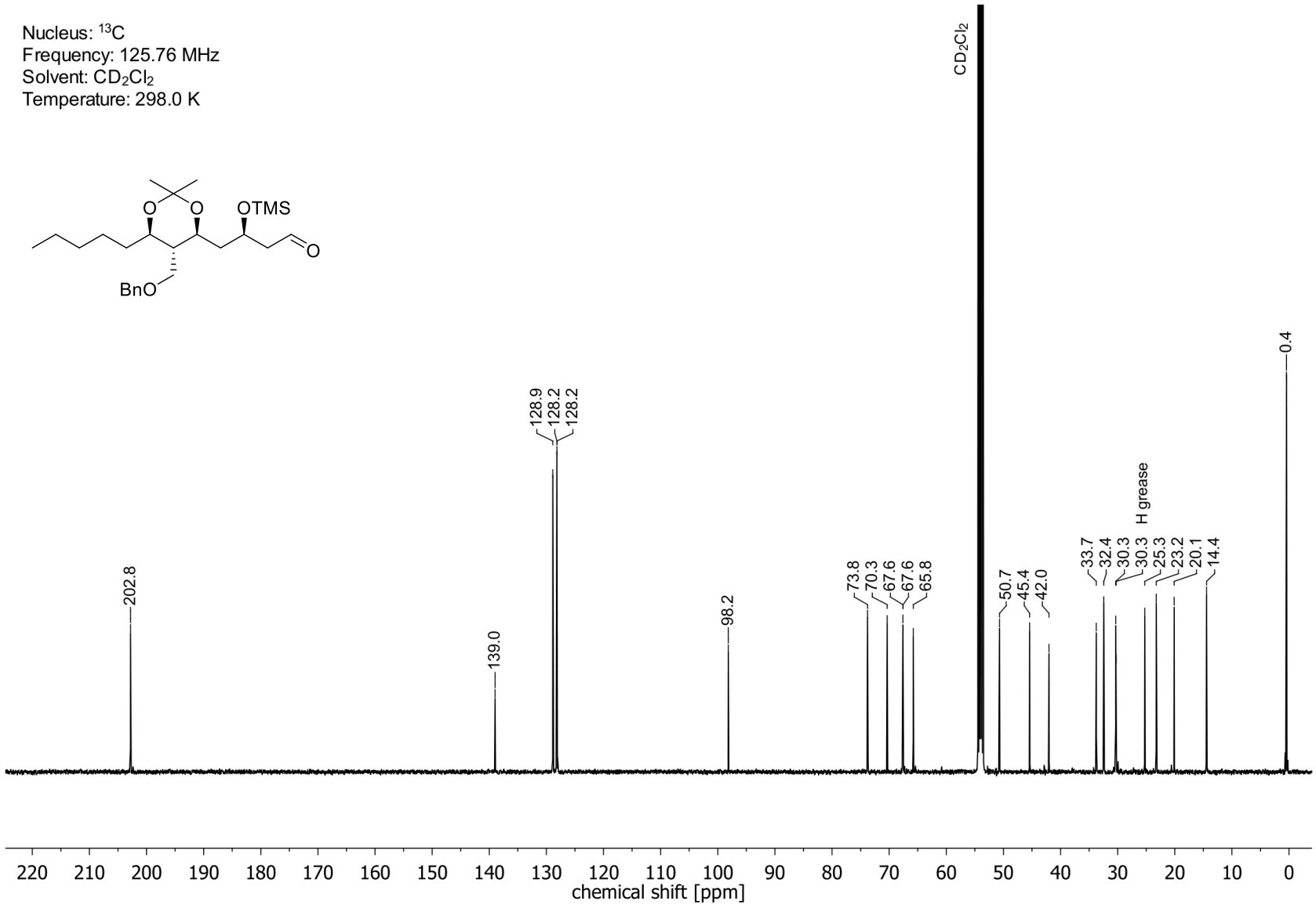
NMR-Spectra of Compound **254**:



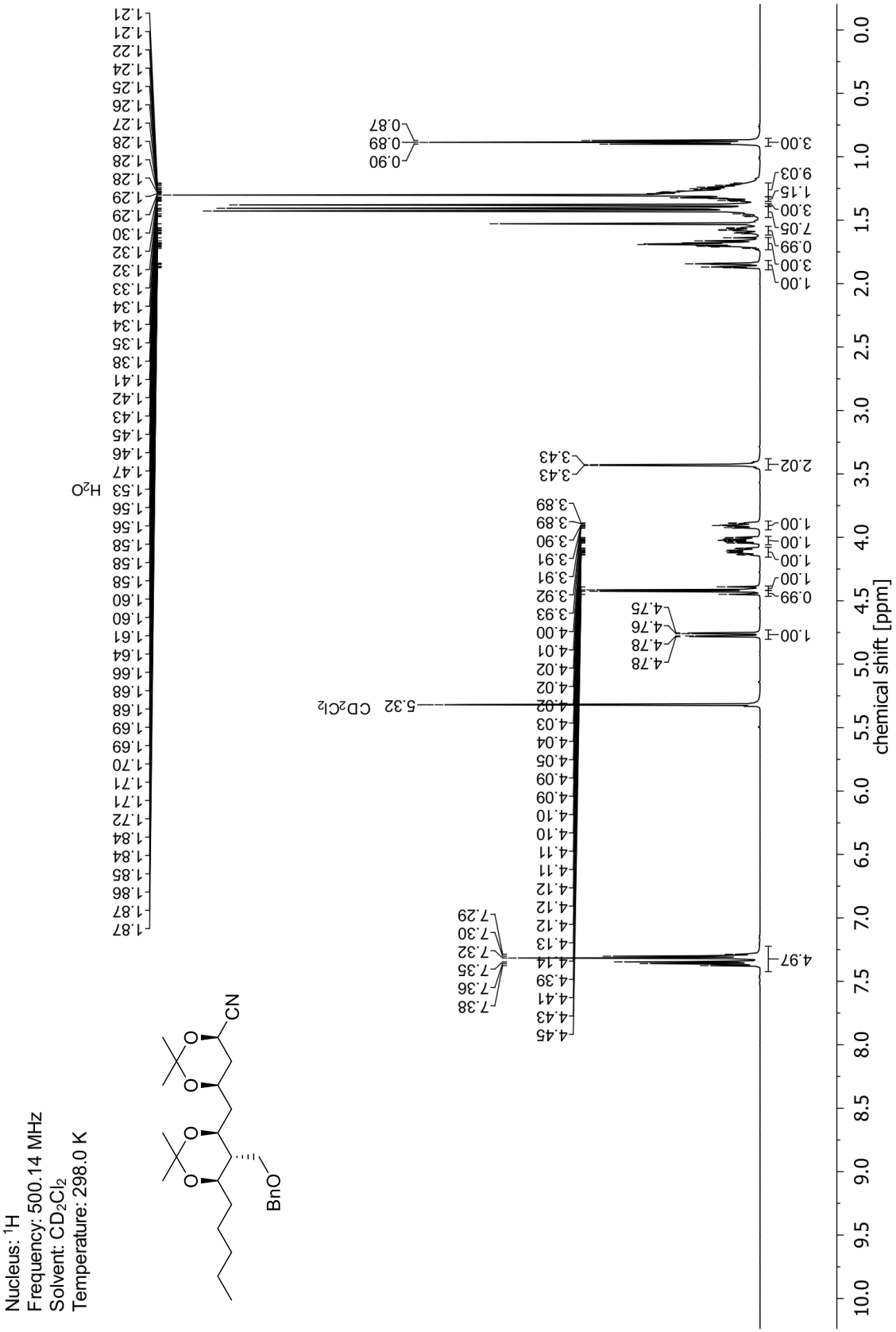

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OTMS
BnO
CD2Cl2
0.5
128.8
128.1
128.1
139.1
136.3
116.9
98.1
73.8
70.5
69.4
67.9
67.7
45.6
41.6
41.4
33.7
32.4
30.4
25.3
23.3
20.1
14.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

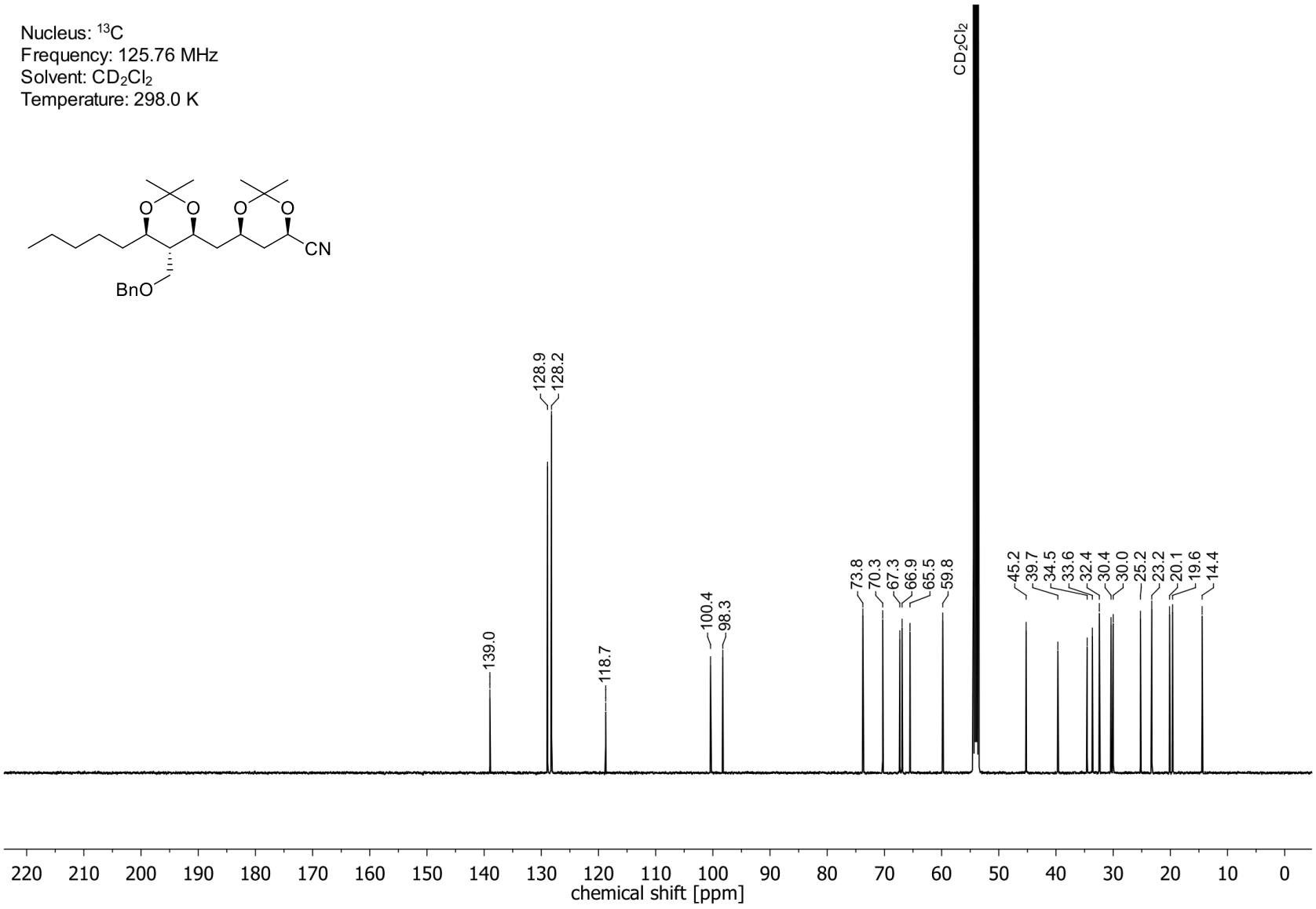
NMR-Spectra of Compound **321**:

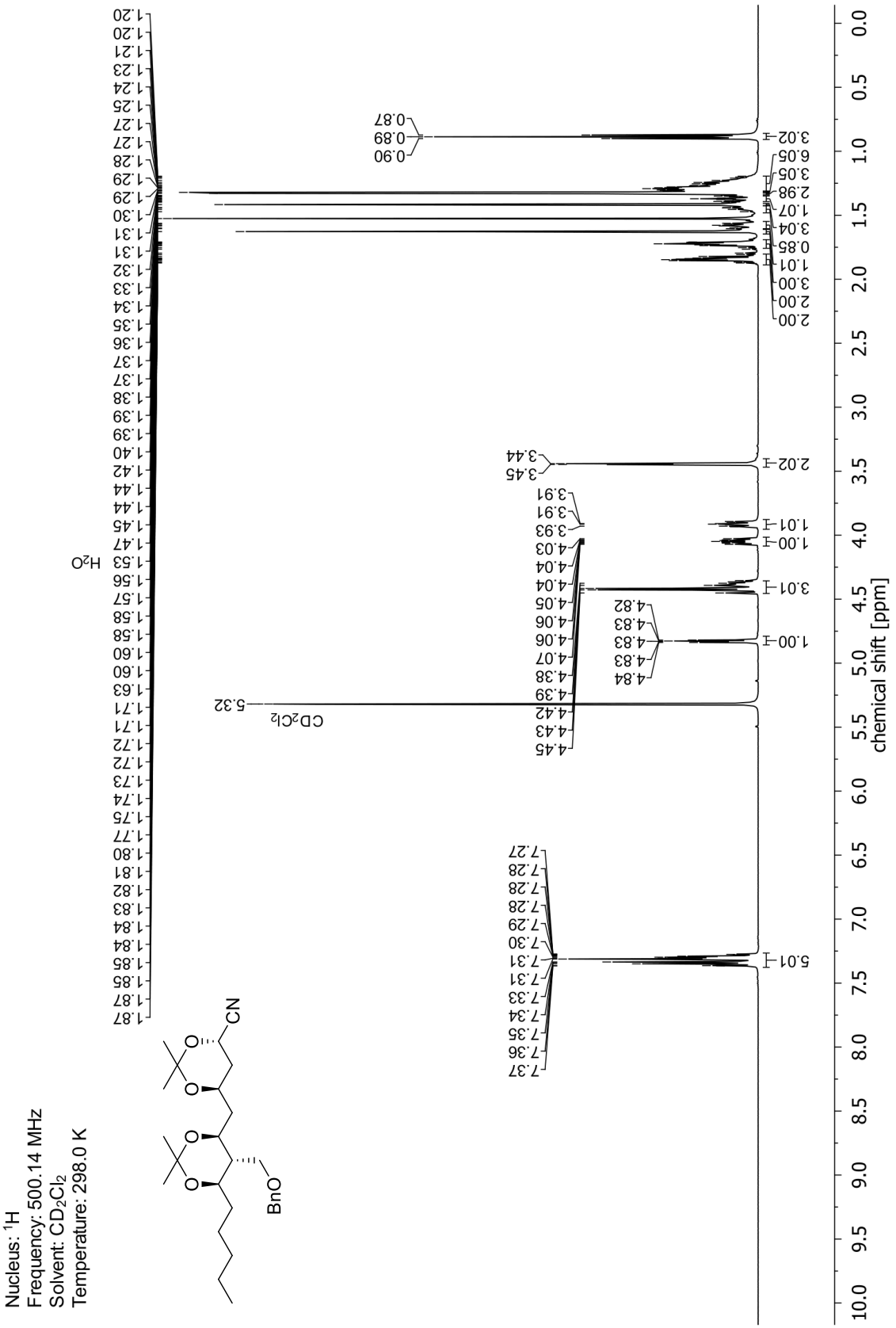


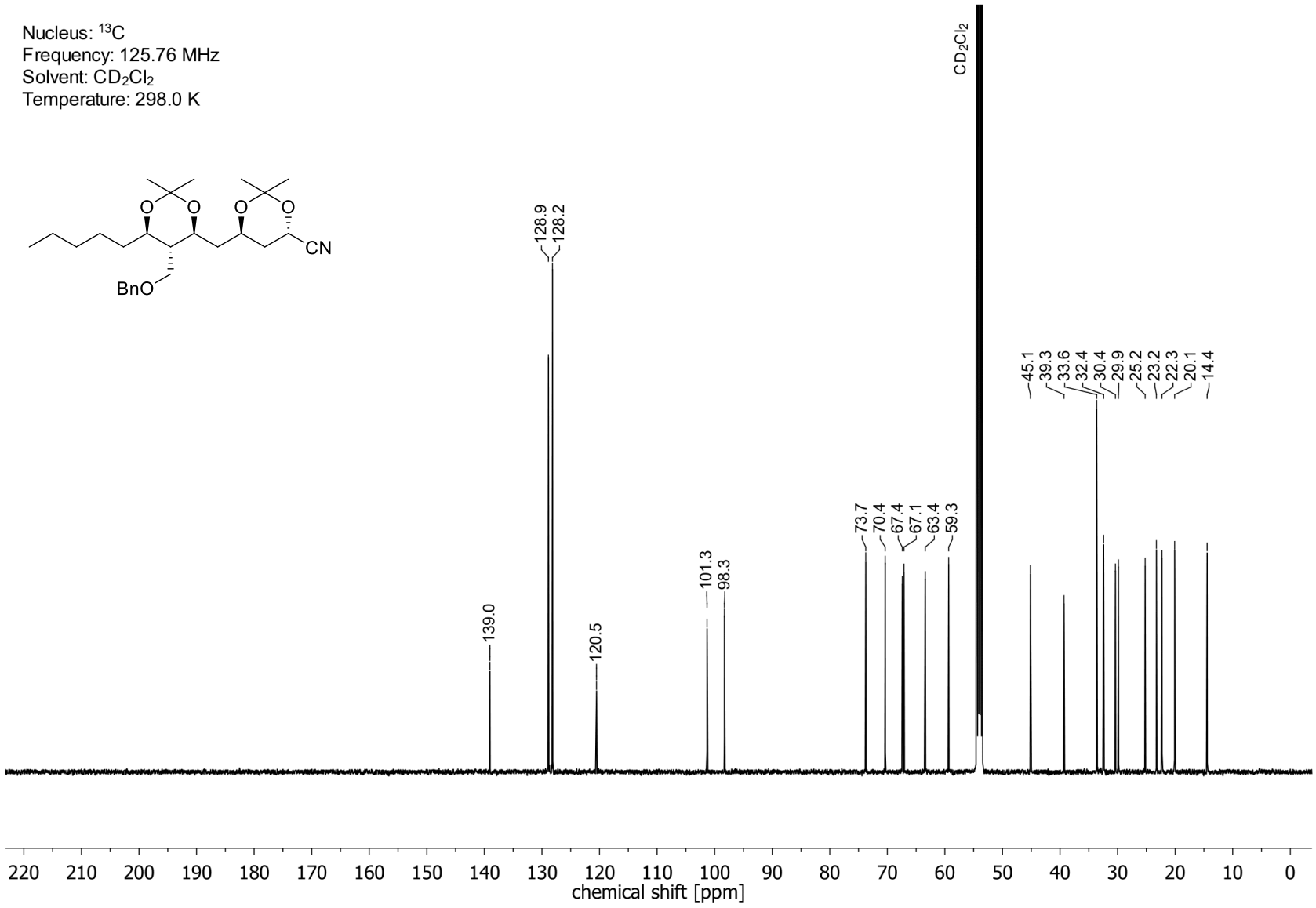

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OTMS
O
BnO
CD2Cl2
202.8
139.0
128.9
128.2
128.2
98.2
73.8
70.3
67.6
67.6
65.8
50.7
45.4
42.0
33.7
32.4
30.3
30.3
H grease
25.3
23.2
20.1
14.4
0.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

NMR-Spectra of Compound **154**:

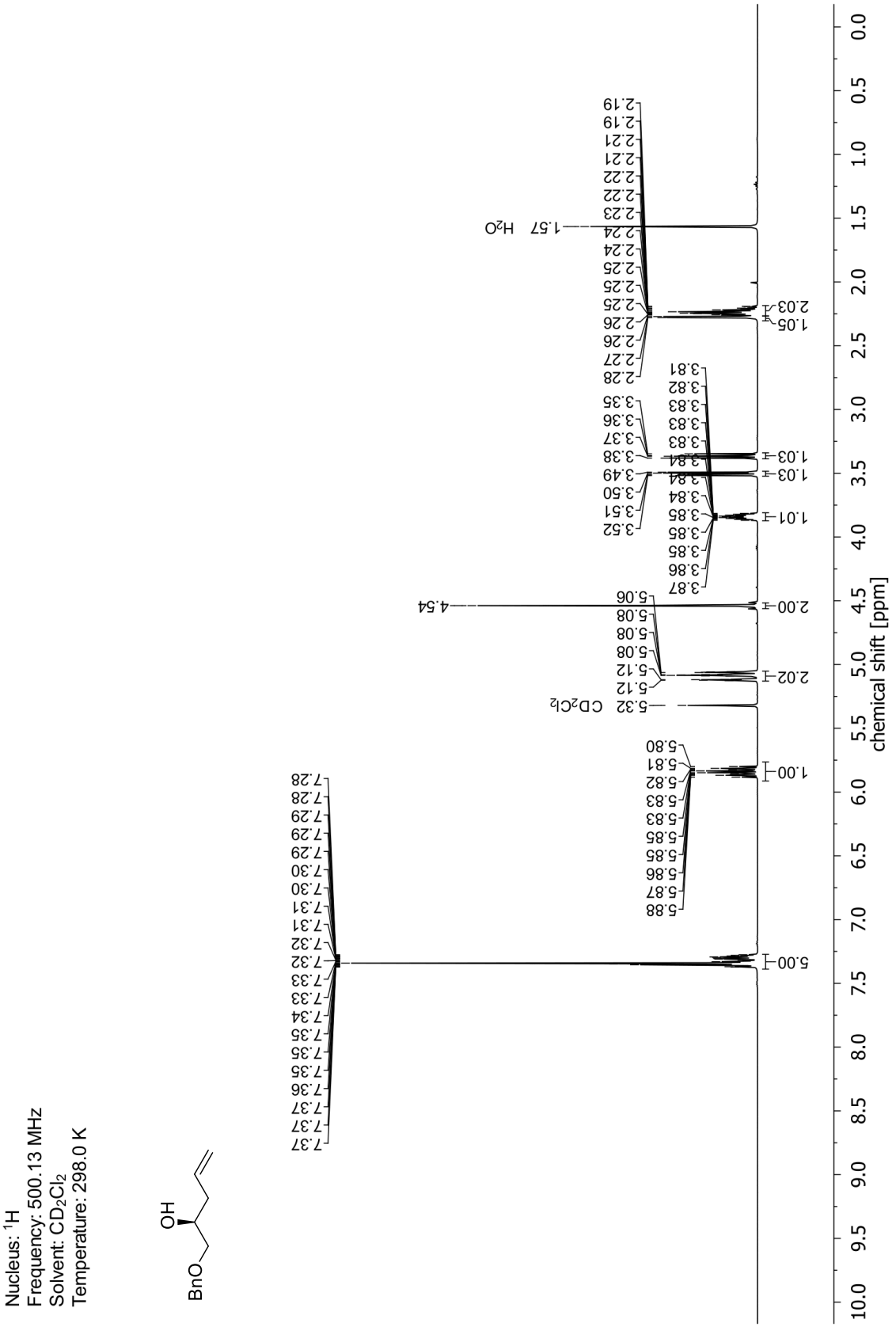



Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
O
O
CN
BnO
CD2Cl2
128.9
128.2
139.0
118.7
100.4
98.3
73.8
70.3
67.3
66.9
65.5
59.8
45.2
39.7
34.5
33.6
32.4
30.4
30.0
25.2
23.2
20.1
19.6
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

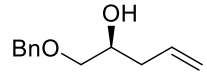

Nucleus: 1H
Frequency: 500.14 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
CN
BnO
H2O
CD2Cl2
chemical shift [ppm]


Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CN
CD2Cl2
128.9
128.2
139.0
120.5
101.3
98.3
73.7
70.4
67.4
67.1
63.4
59.3
45.1
39.3
33.6
32.4
30.4
29.9
25.2
23.2
22.3
20.1
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

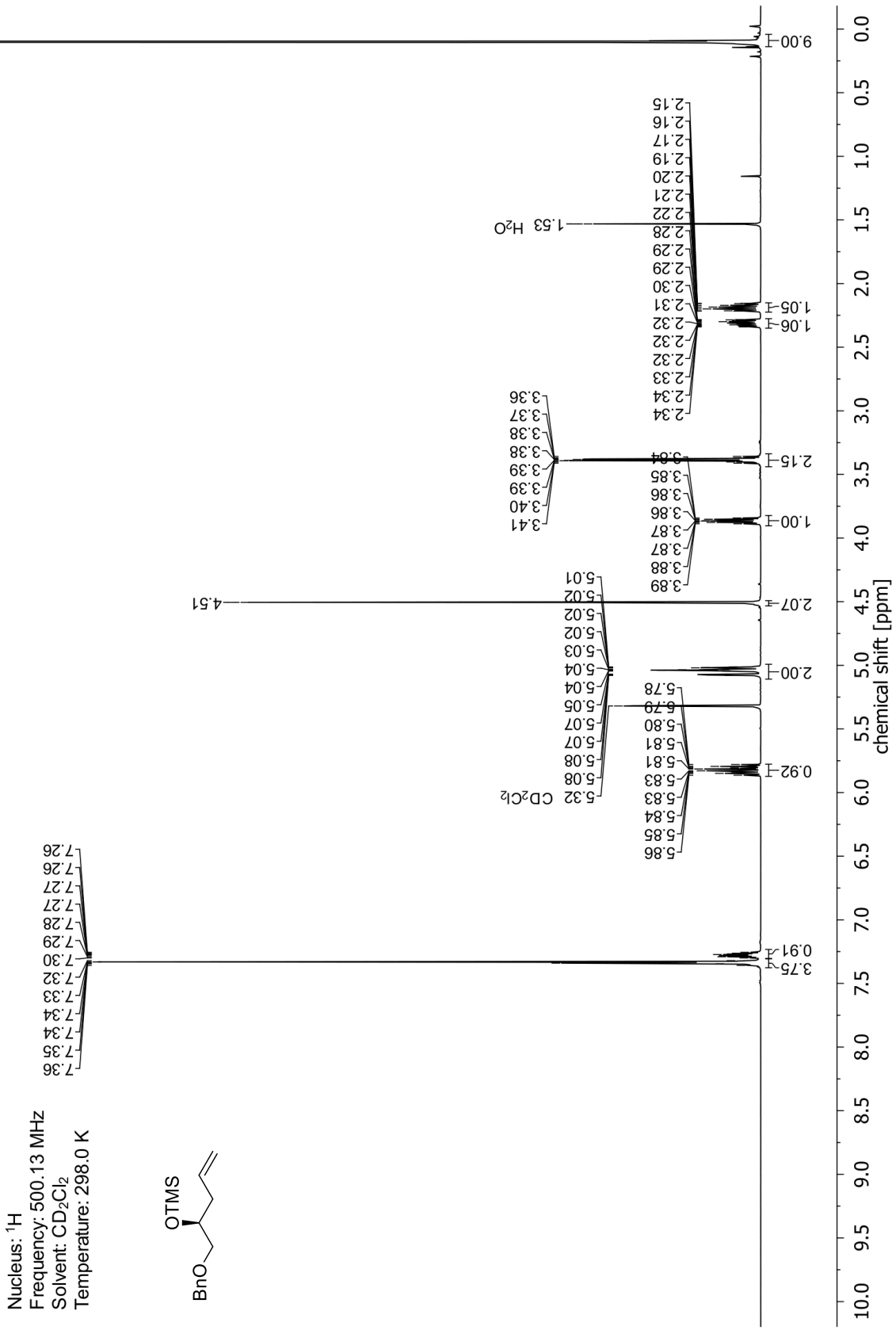
NMR-Spectra of Compound **191**:

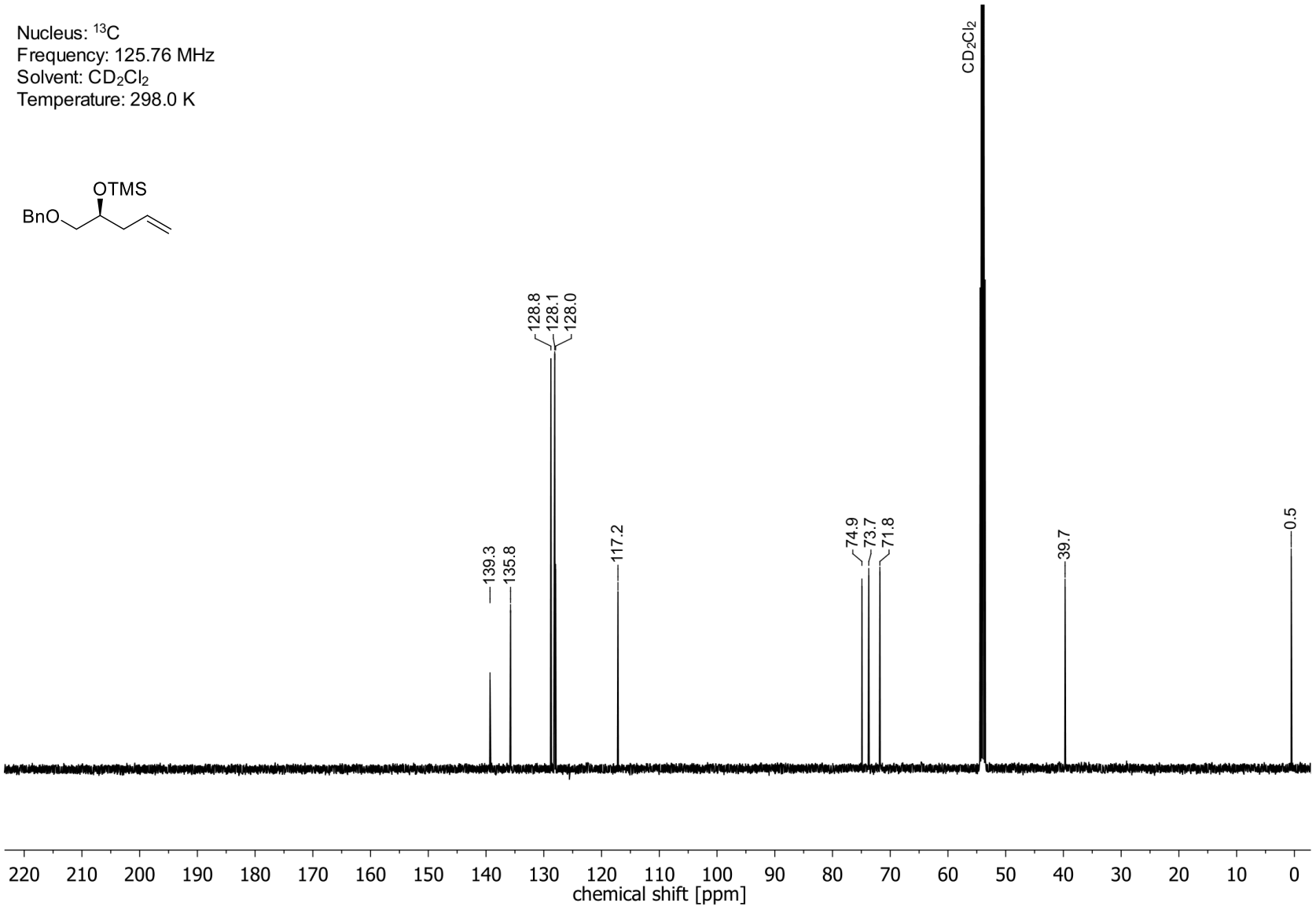


Nucleus: $^{13}C$
Frequency: 125.76 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

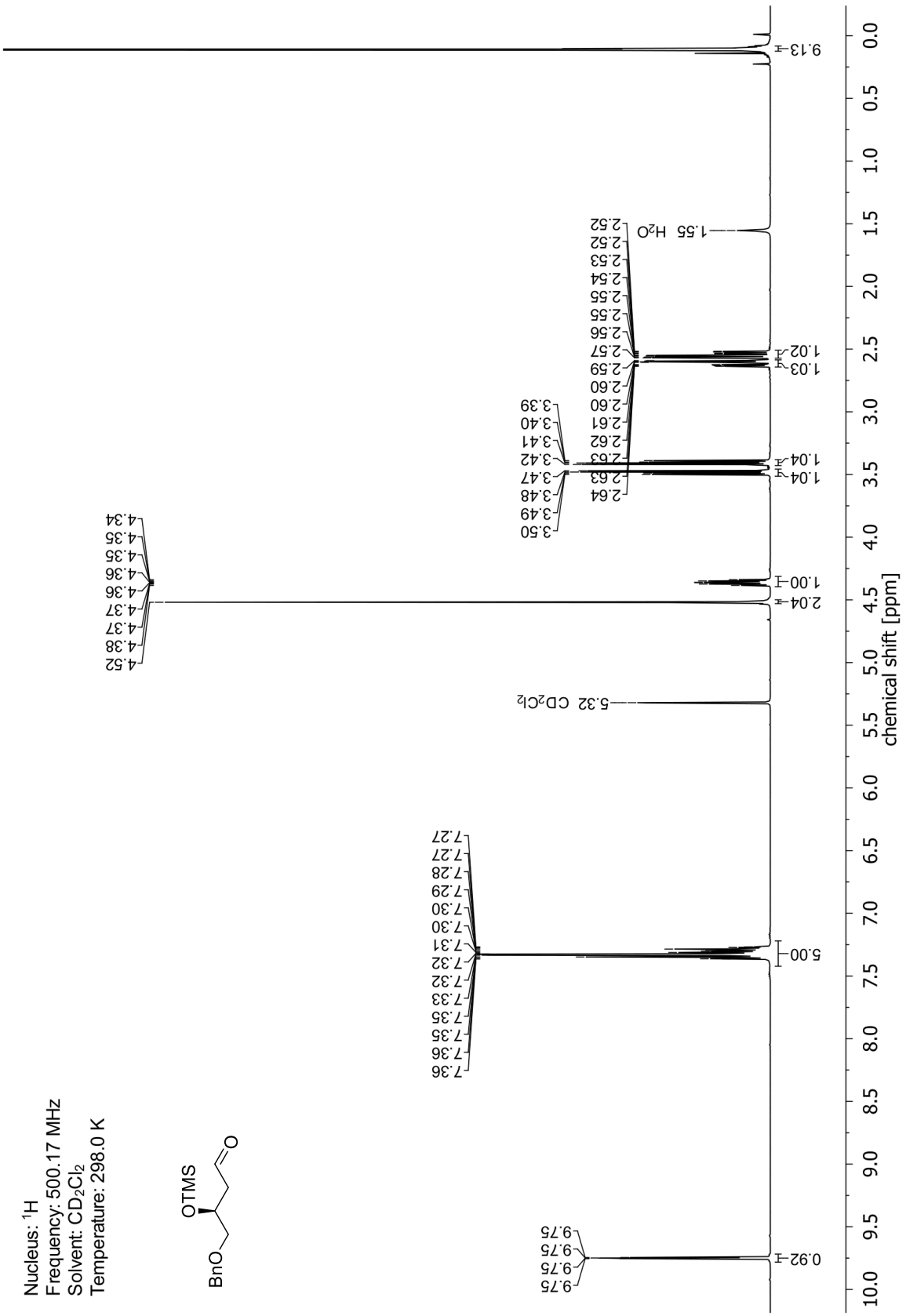


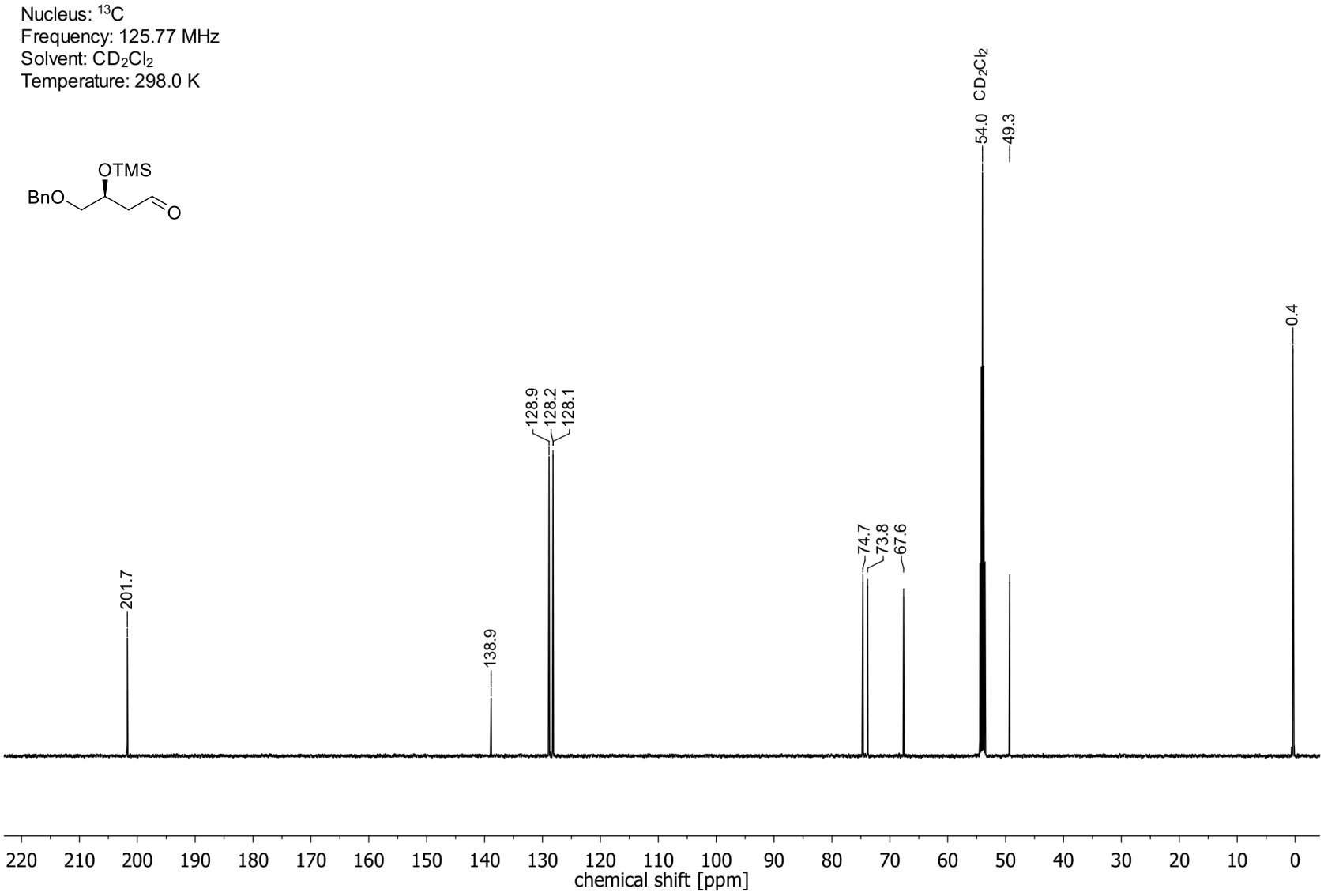
NMR-Spectra of Compound **323**:



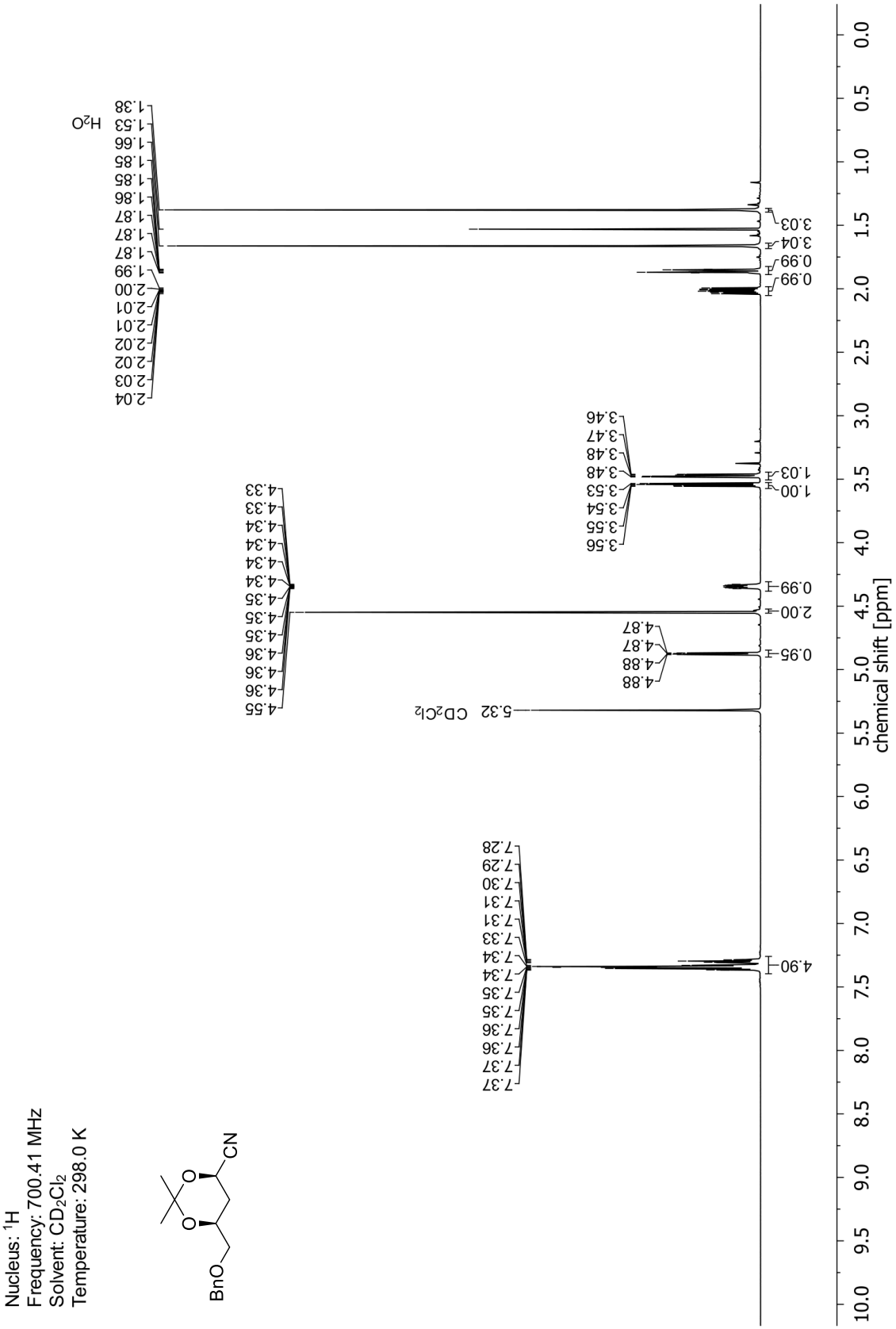

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OTMS
BnO
CD2Cl2
128.8
128.1
128.0
139.3
135.8
117.2
74.9
73.7
71.8
39.7
0.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

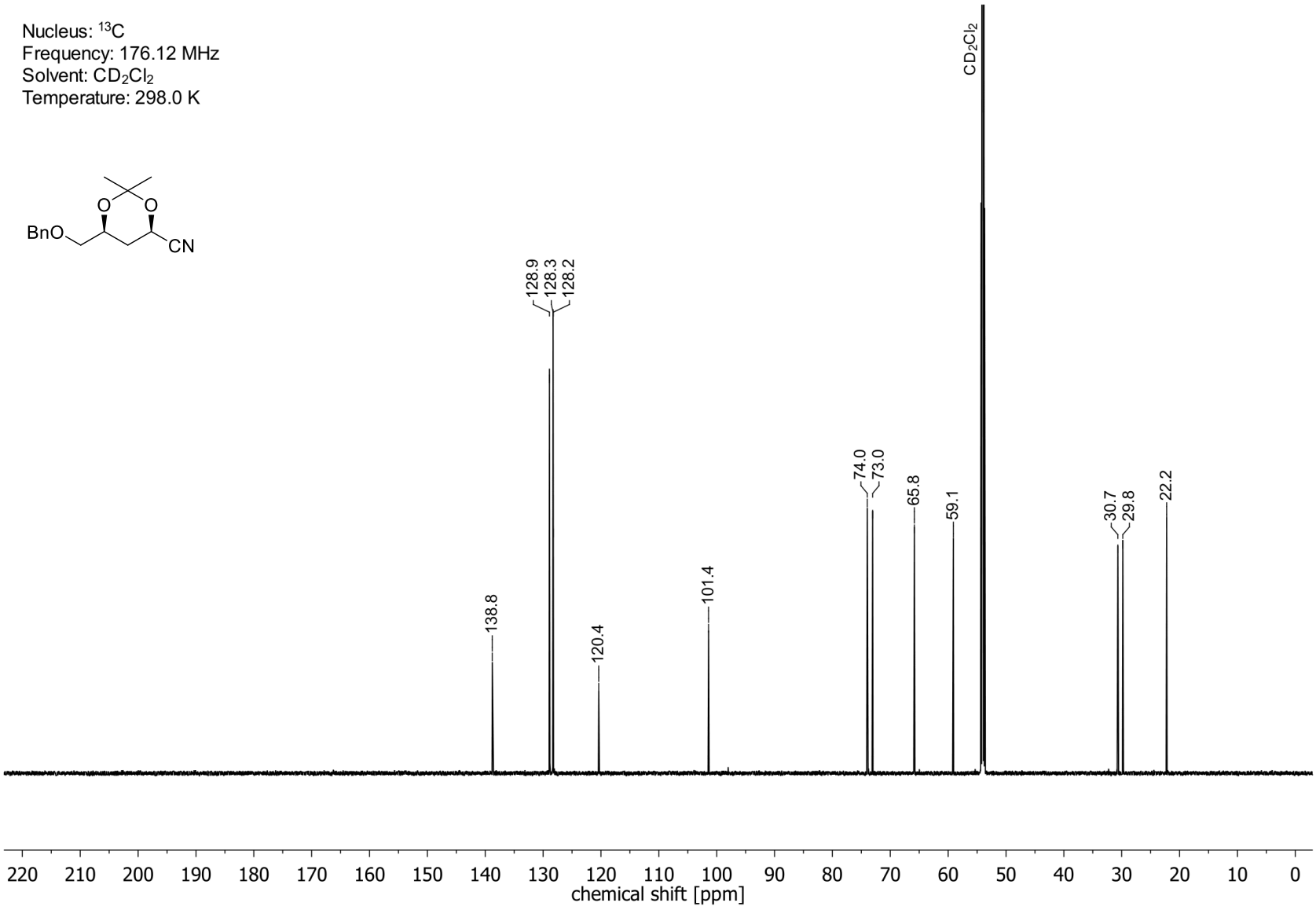
NMR-Spectra of Compound **324**:

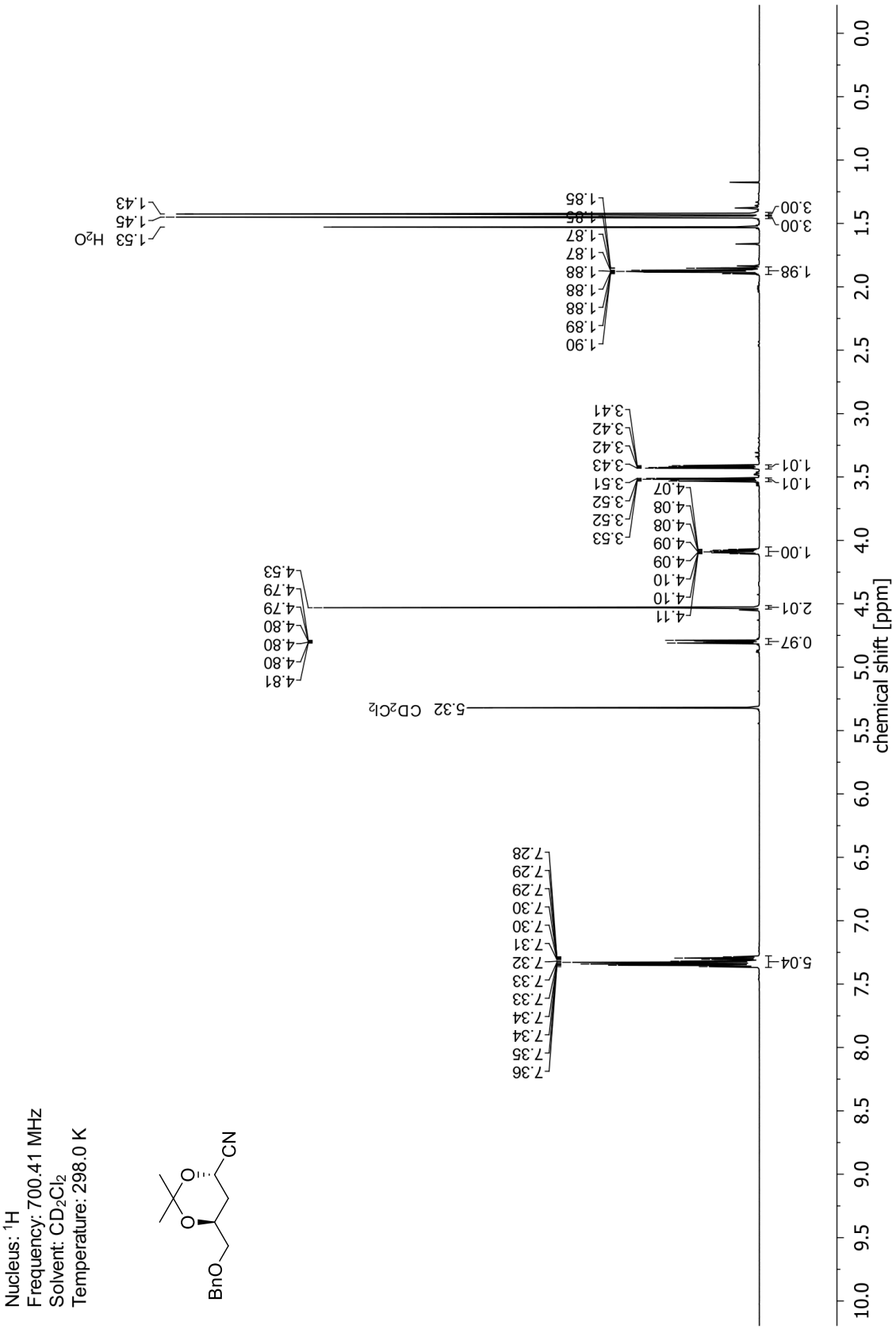


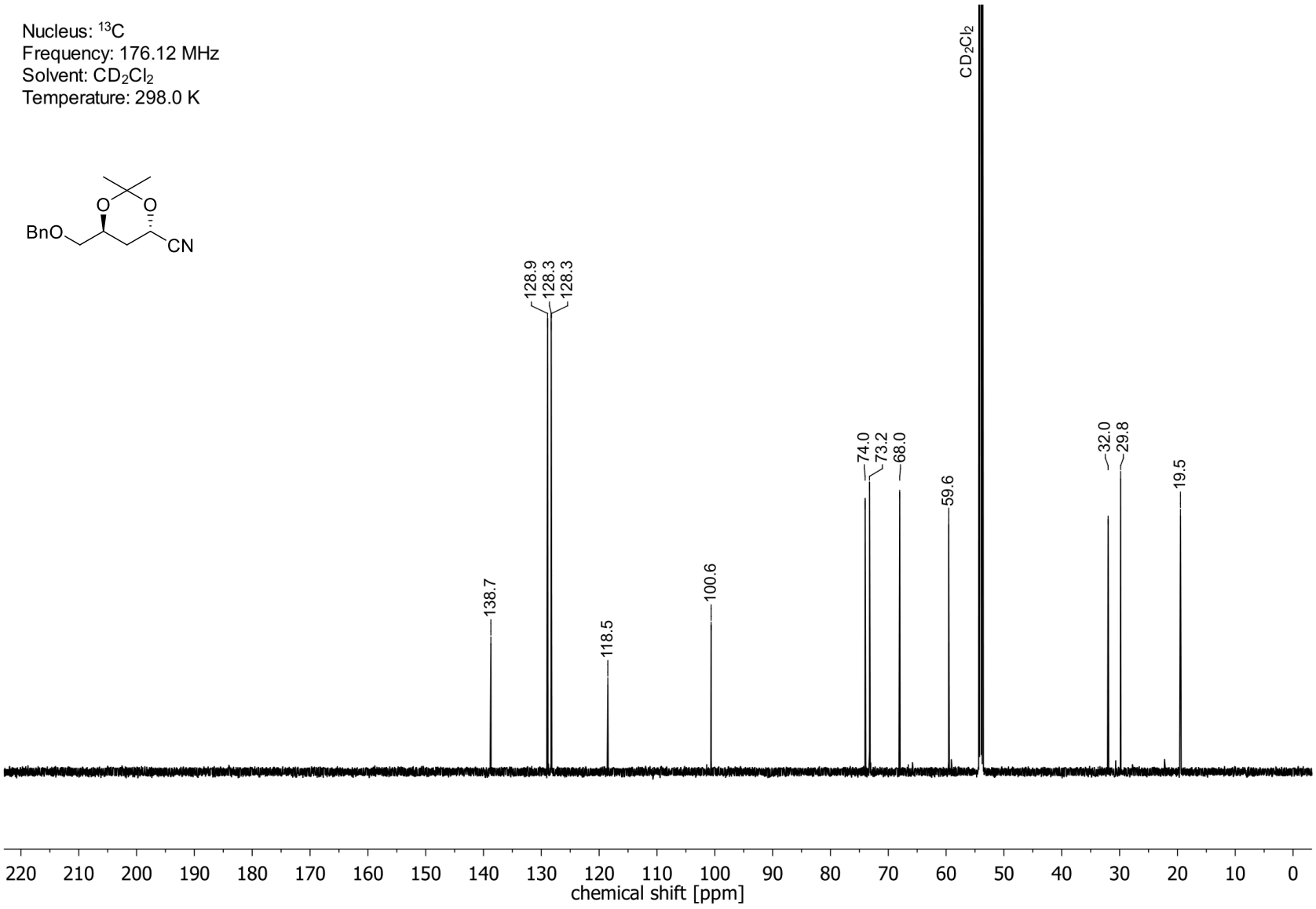

Nucleus: 13C
Frequency: 125.77 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OTMS
BnO
O
201.7
138.9
128.9
128.2
128.1
74.7
73.8
67.6
54.0
CD2Cl2
49.3
0.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

NMR-Spectra of Compound **164**:

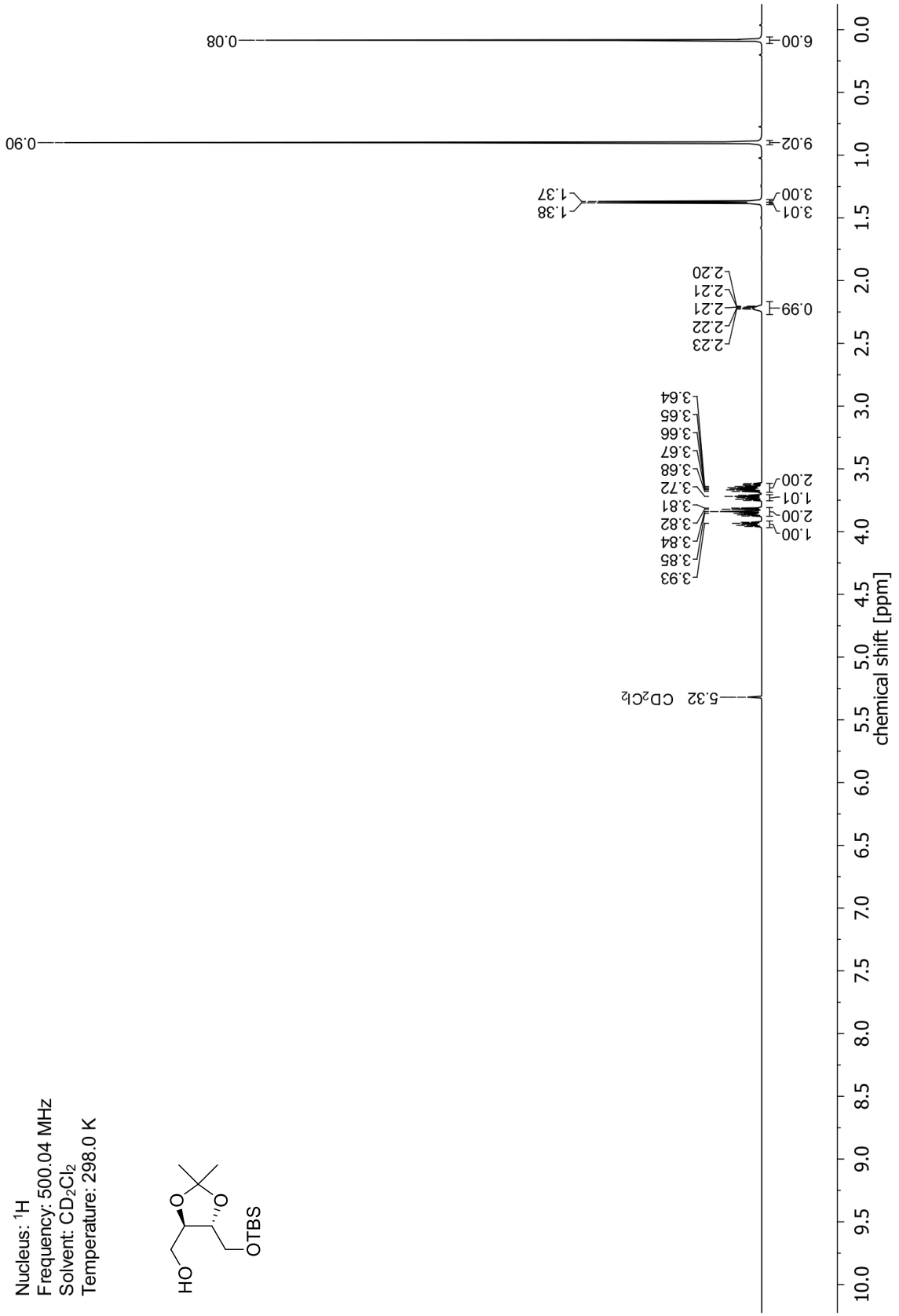



Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
CN
CD2Cl2
128.9
128.3
128.2
138.8
120.4
101.4
74.0
73.0
65.8
59.1
30.7
29.8
22.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

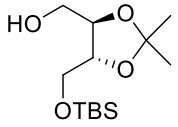

Nucleus: 1H
Frequency: 700.41 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
CN
chemical shift [ppm]
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
5.32 CD2Cl2
1.53 H2O
5.04
2.01
1.98
3.00
3.00
1.00
1.01
1.01
0.97


Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
CN
CD2Cl2
128.9
128.3
128.3
74.0
73.2
68.0
59.6
32.0
29.8
19.5
138.7
118.5
100.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

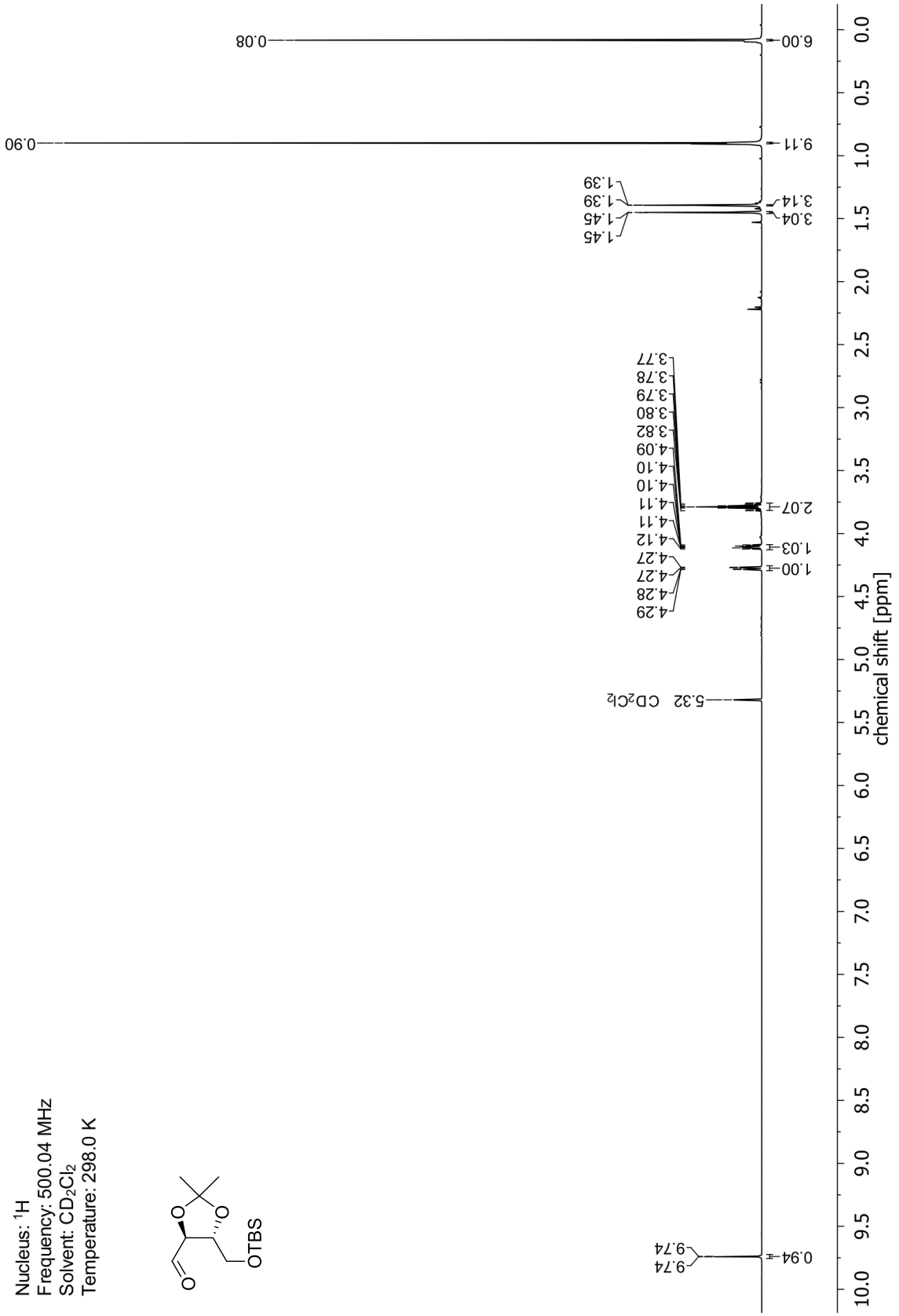
NMR-Spectra of Compound **325**:



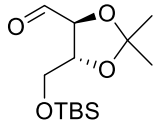
Nucleus: $^{13}C$
Frequency: 125.74 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



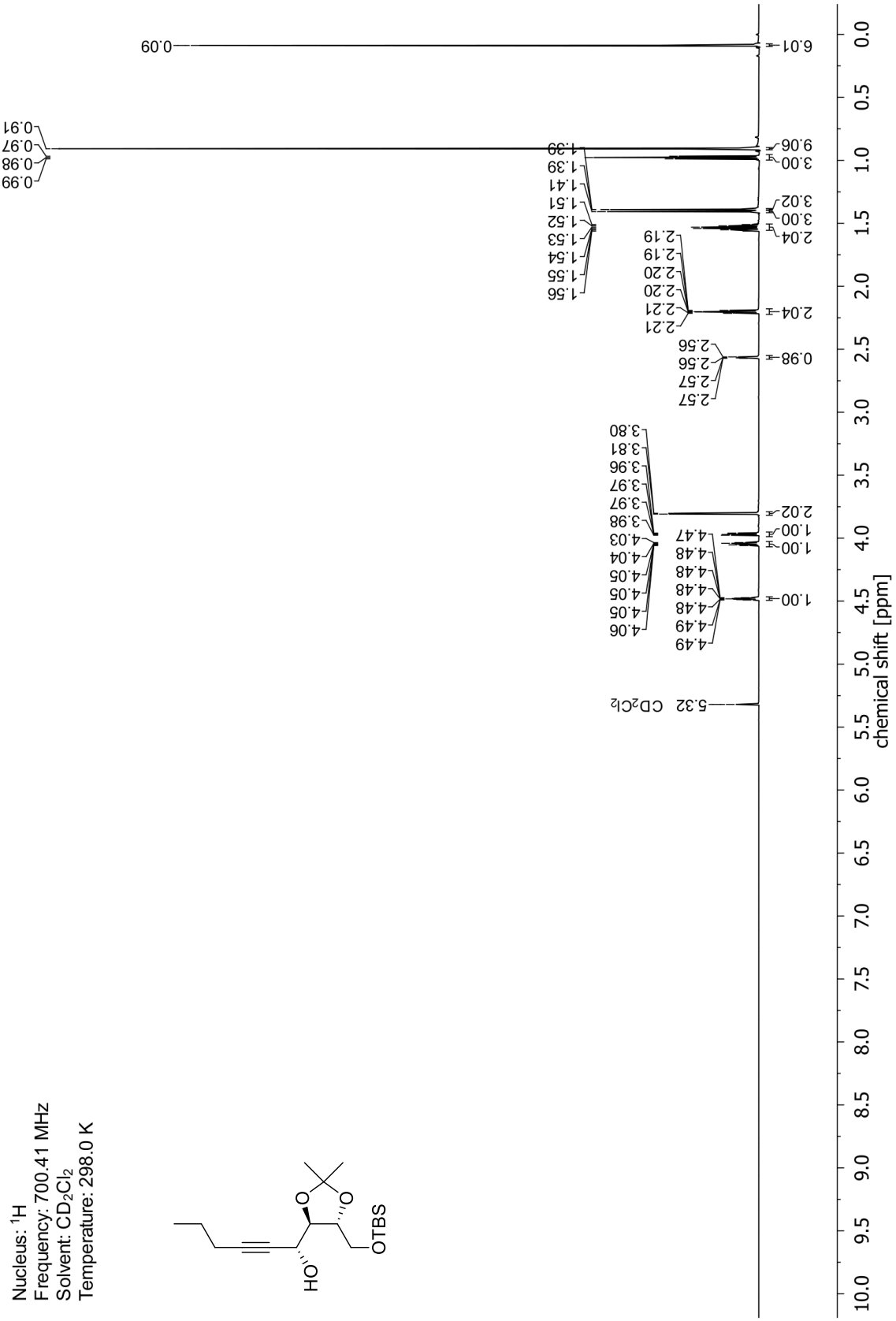
NMR-Spectra of Compound **326**:

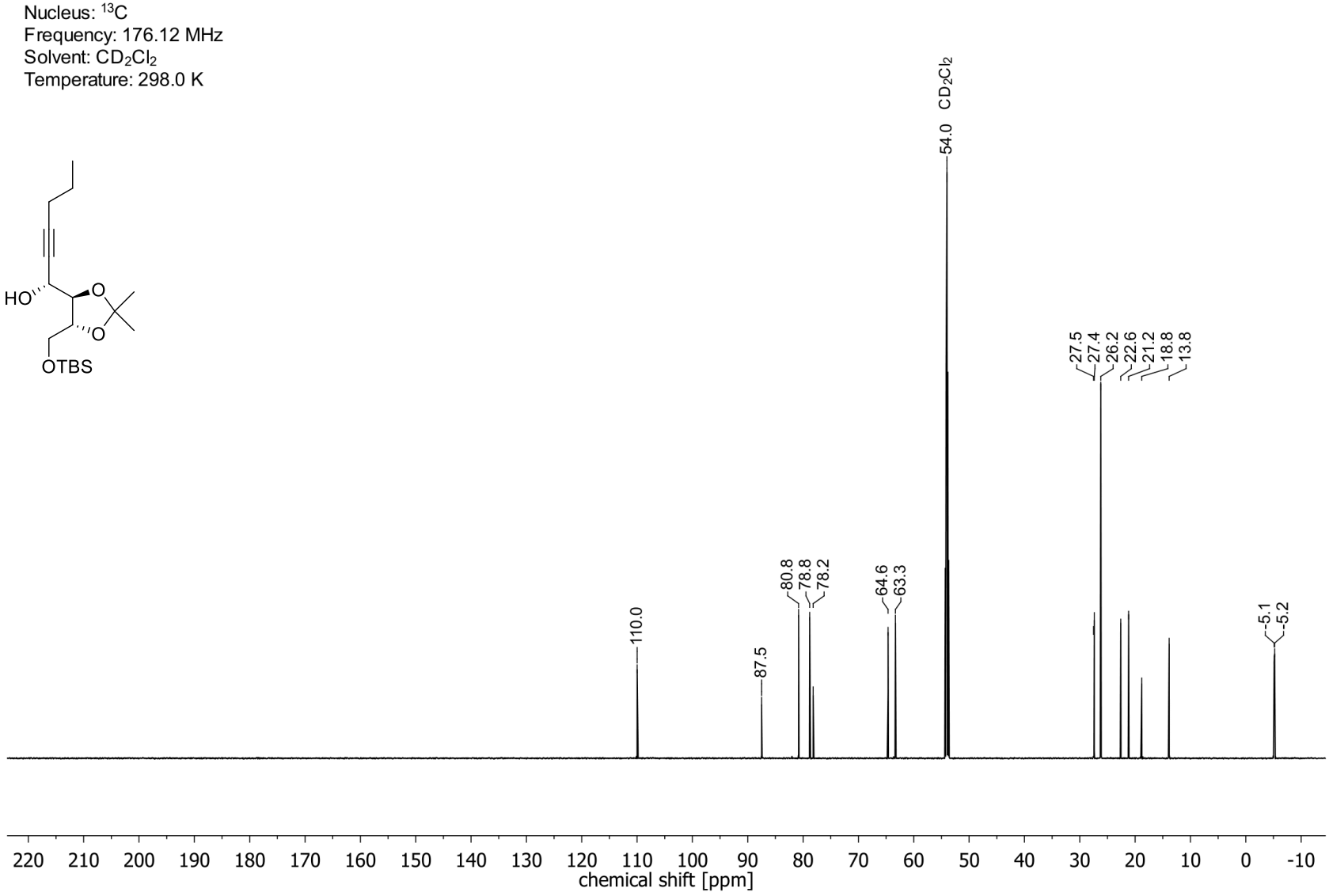


Nucleus: $^{13}C$
Frequency: 125.74 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

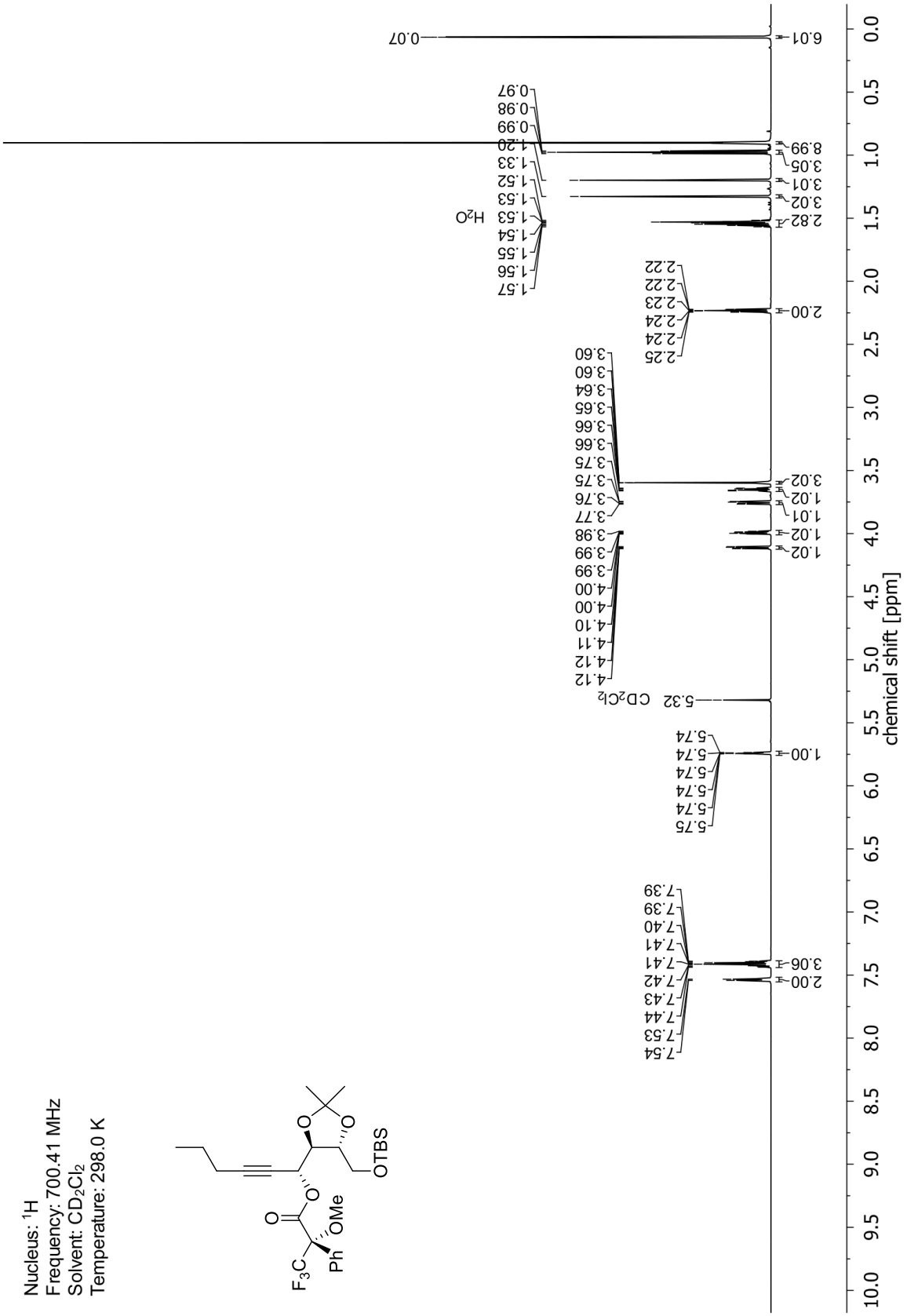


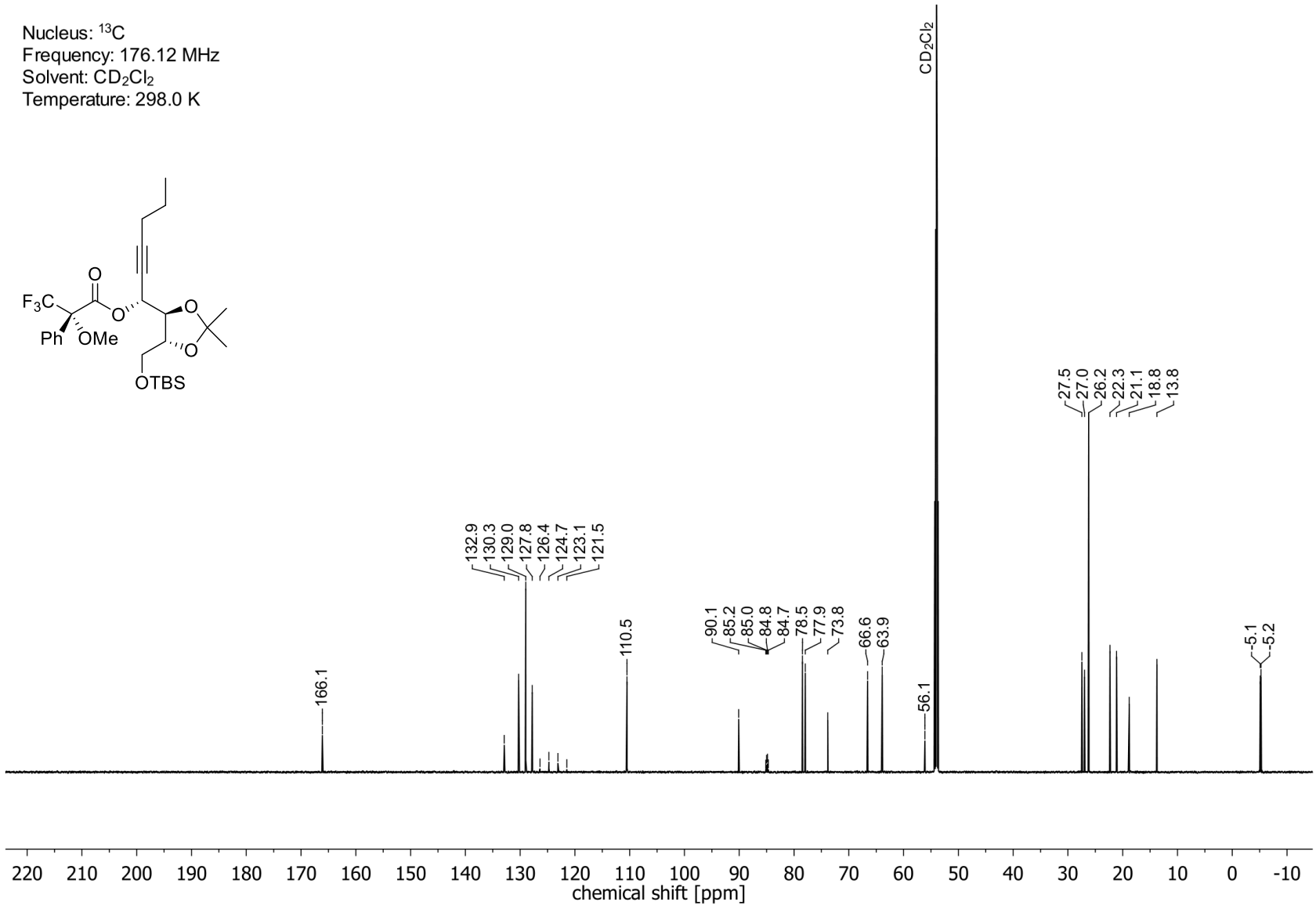
NMR-Spectra of Compound **327**:



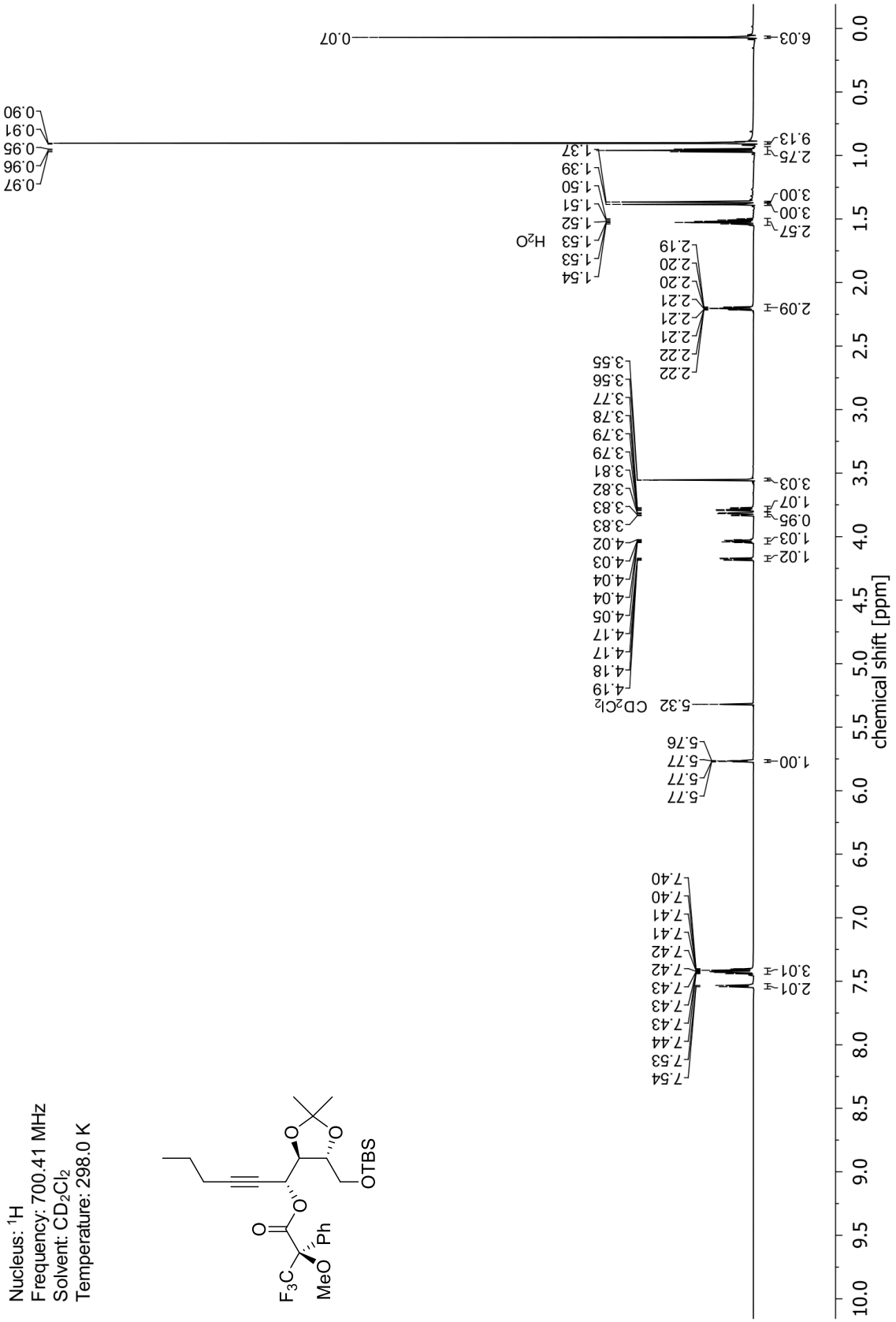

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
O
O
OTBS
54.0
CD2Cl2
27.5
27.4
26.2
22.6
21.2
18.8
13.8
110.0
87.5
80.8
78.8
78.2
64.6
63.3
-5.1
-5.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

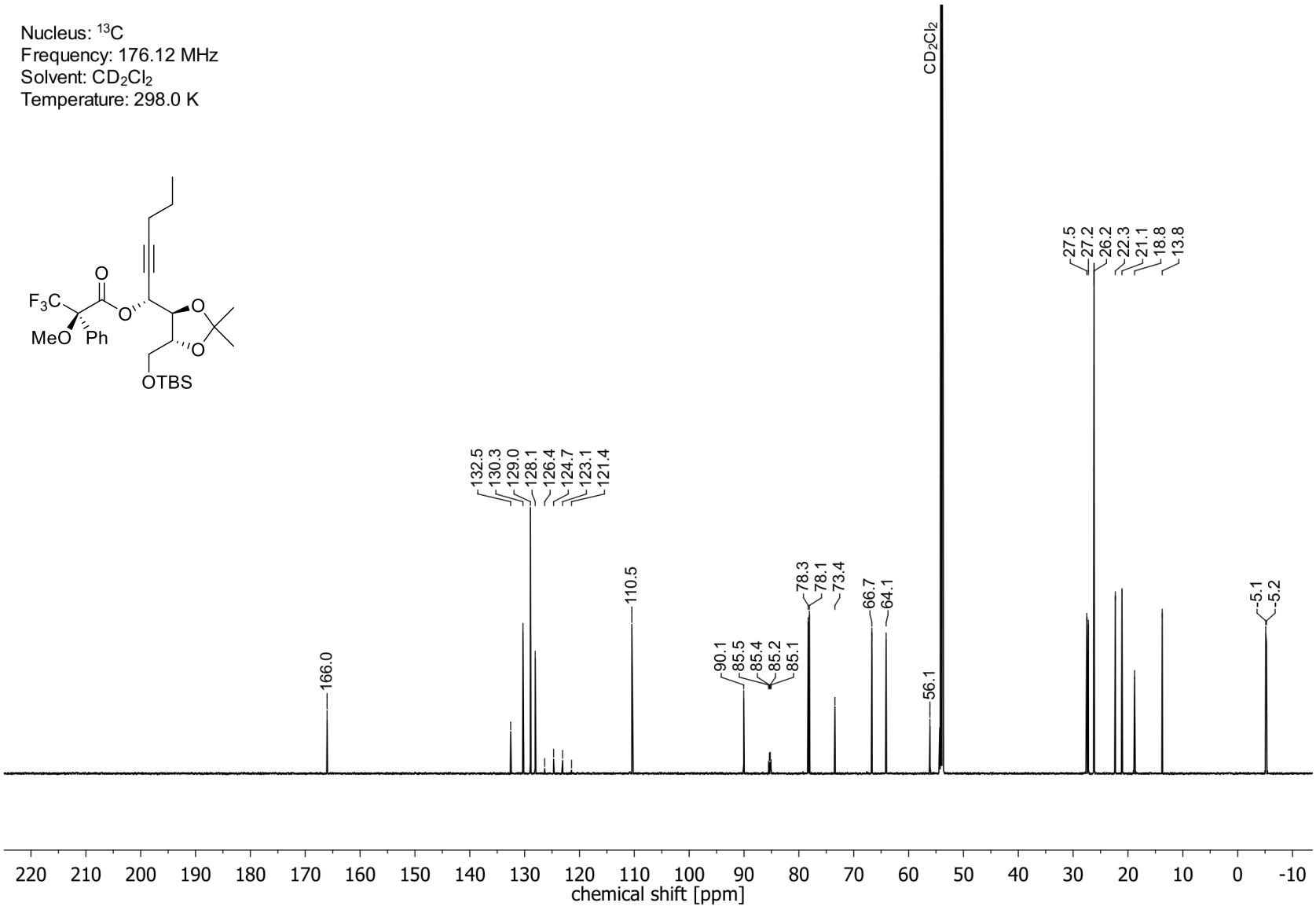
NMR-Spectra of Compound **360-(*S*)**:



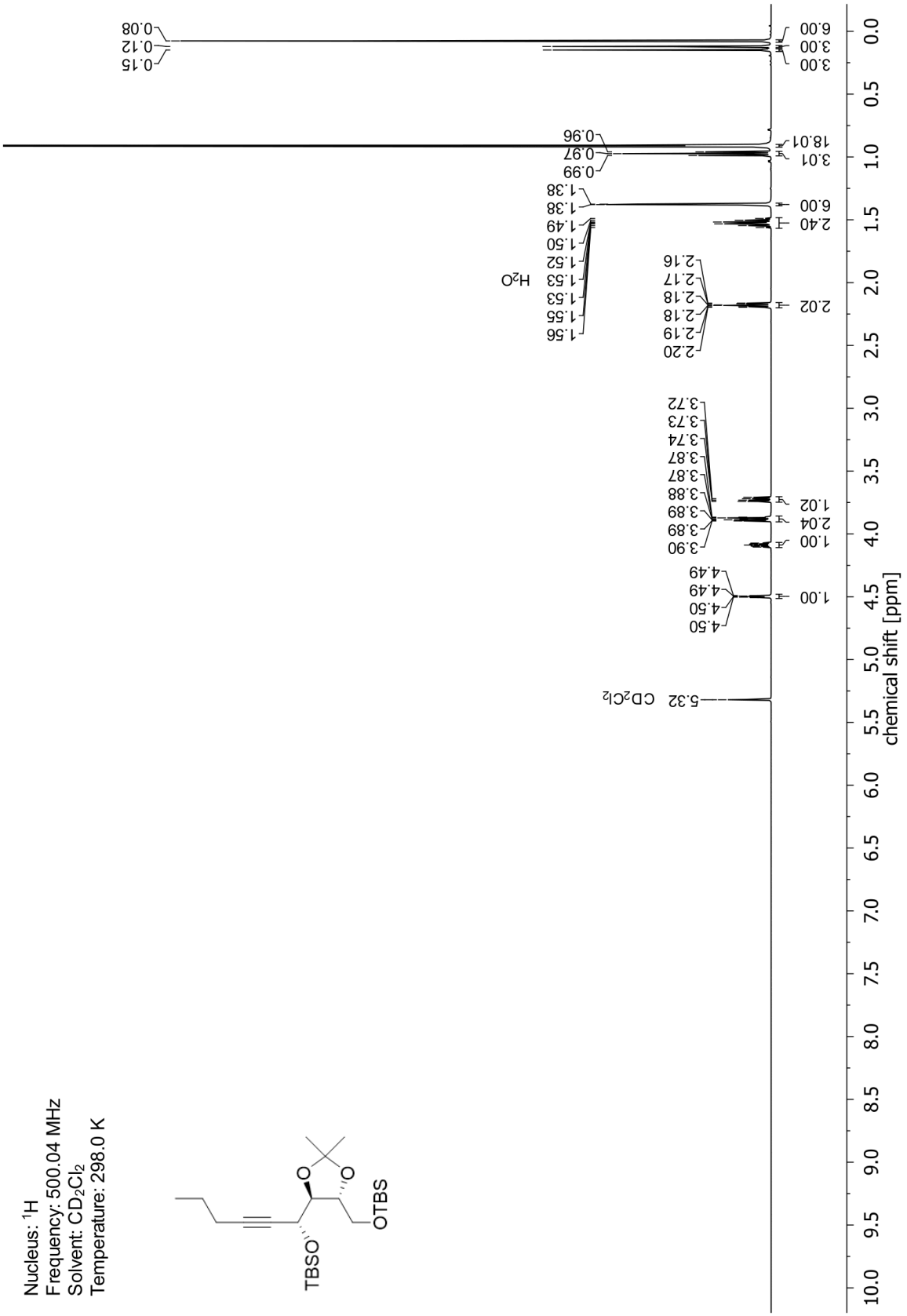

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
F3C
O
Ph
OMe
O
O
O
OTBS
CD2Cl2
27.5
27.0
26.2
22.3
21.1
18.8
13.8
132.9
130.3
129.0
127.8
126.4
124.7
123.1
121.5
110.5
90.1
85.2
85.0
84.8
84.7
78.5
77.9
73.8
66.6
63.9
56.1
166.1
-5.1
-5.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

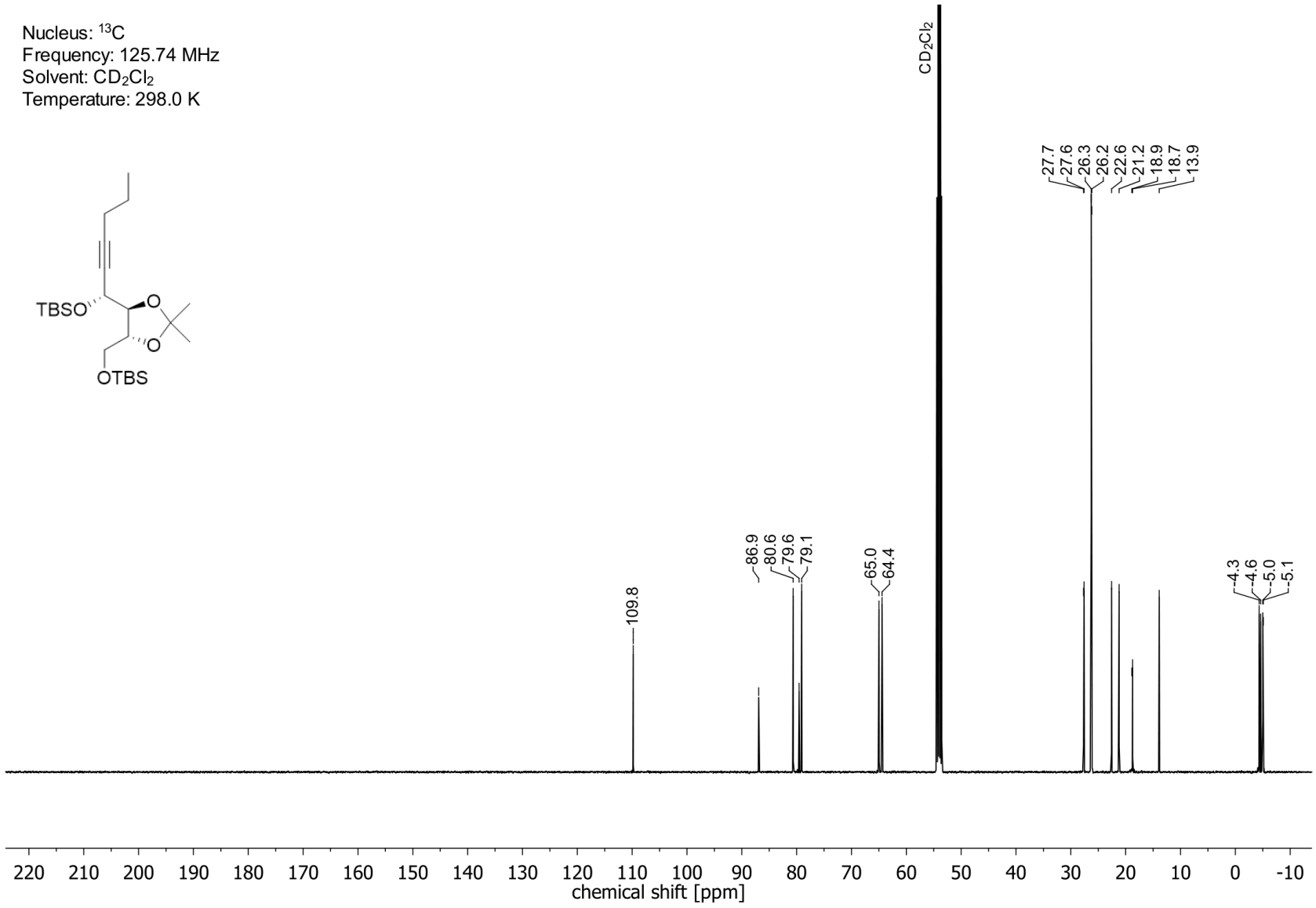
NMR-Spectra of Compound **360-(*R*)**:



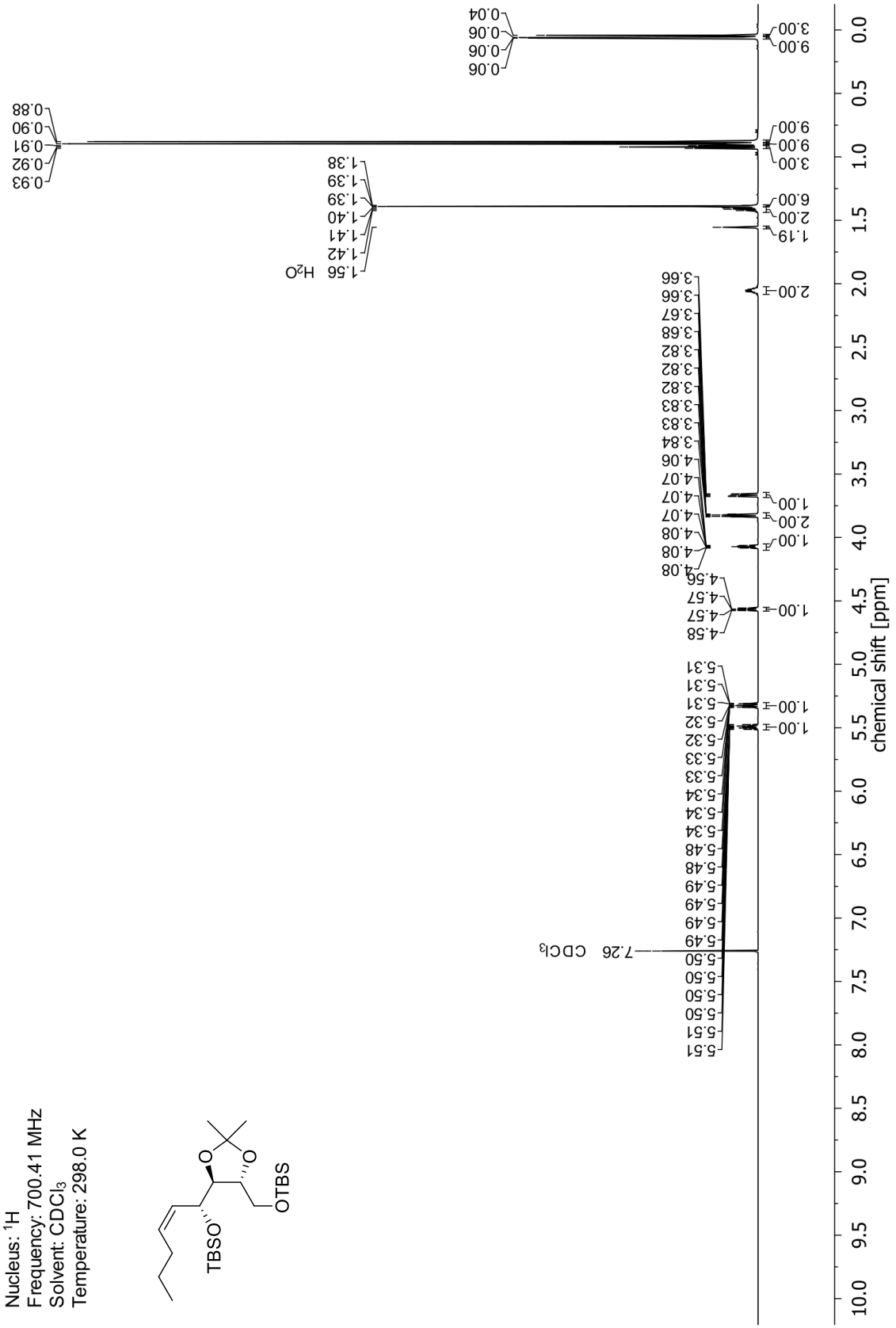

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
F3C
MeO
Ph
O
O
O
O
OTBS
CD2Cl2
27.5
27.2
26.2
22.3
21.1
18.8
13.8
132.5
130.3
129.0
128.1
126.4
124.7
123.1
121.4
166.0
110.5
90.1
85.5
85.4
85.2
85.1
78.3
78.1
73.4
66.7
64.1
56.1
-5.1
-5.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **328**:

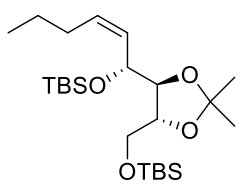



Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
O
O
OTBS
CD2Cl2
27.7
27.6
26.3
26.2
22.6
21.2
18.9
18.7
13.9
109.8
86.9
80.6
79.6
79.1
65.0
64.4
-4.3
-4.6
-5.0
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

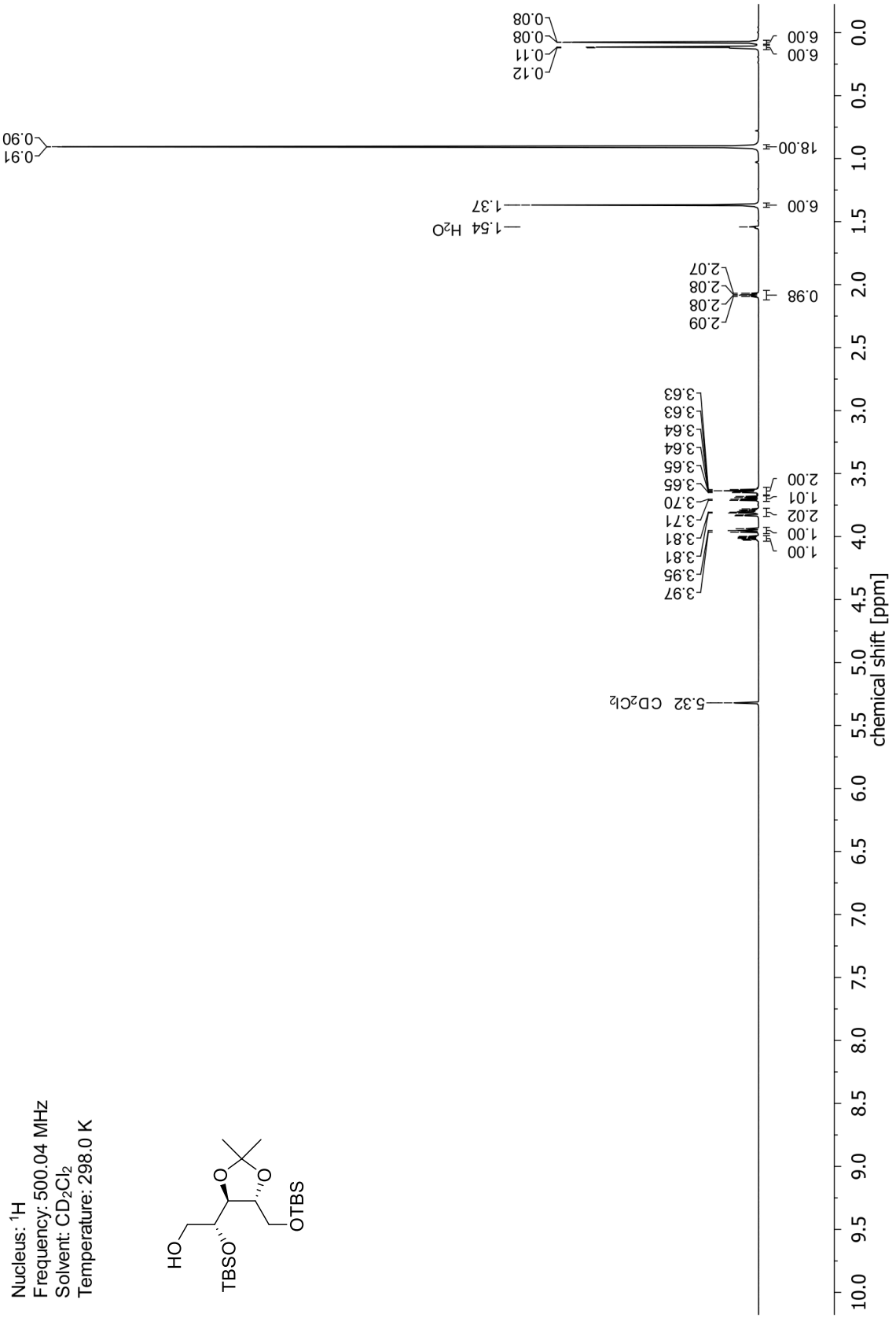
NMR-Spectra of Compound **329**:



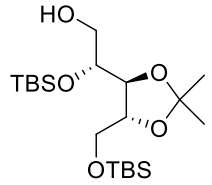
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CDCl_3$
Temperature: 298.0 K



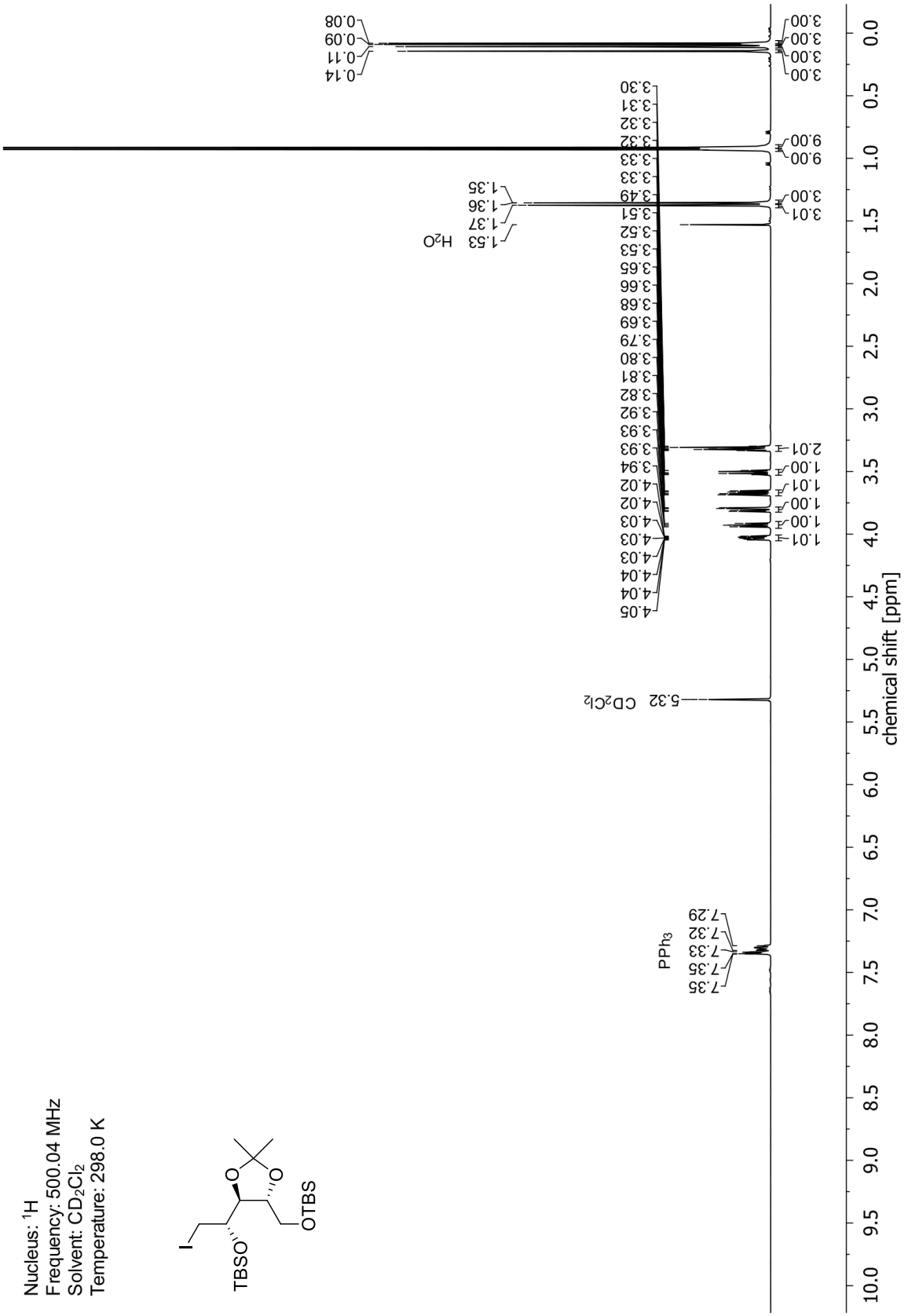
NMR-Spectra of Compound **330**:



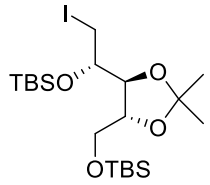
Nucleus: $^{13}C$
Frequency: 125.74 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



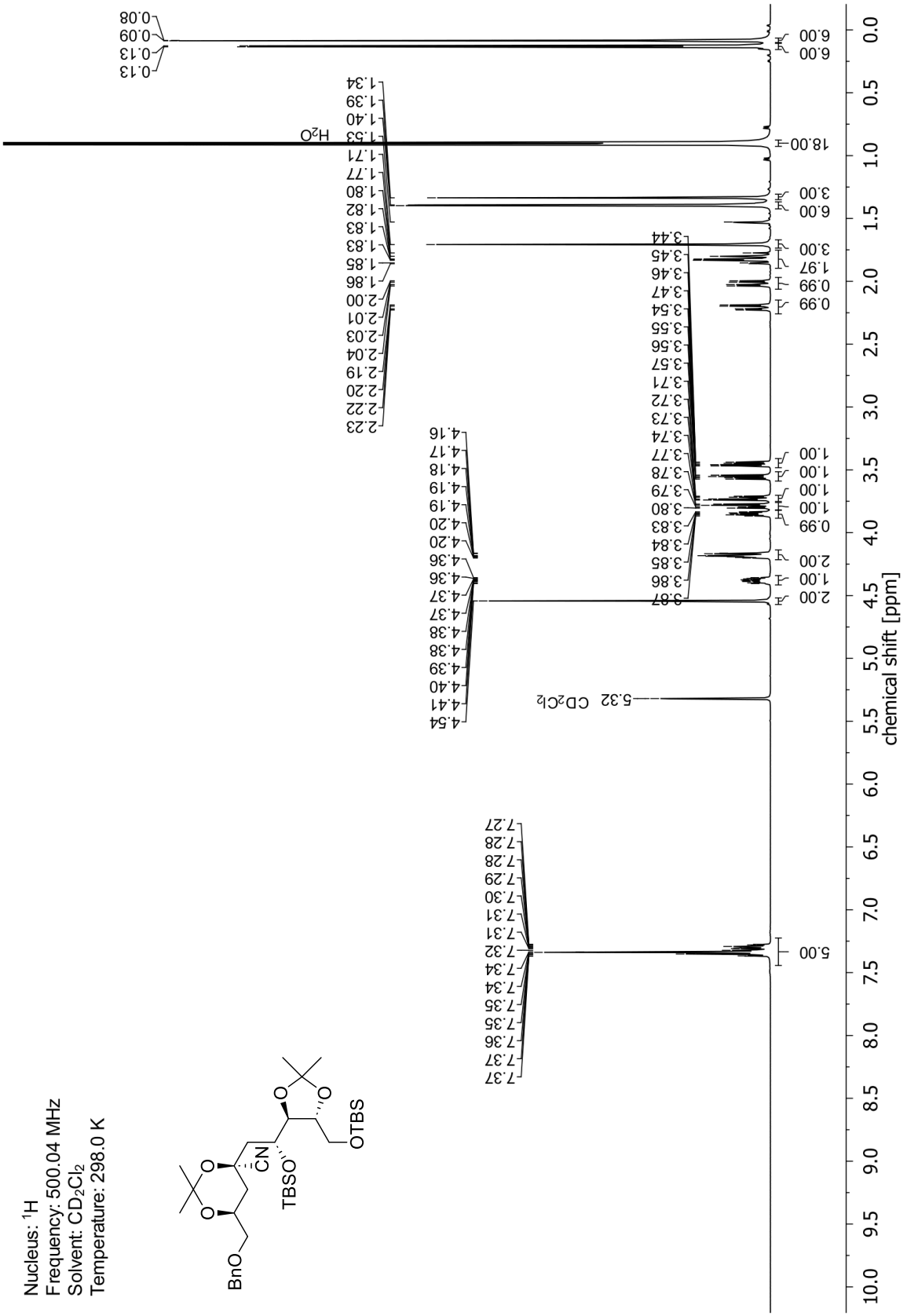
NMR-Spectra of Compound **165**:

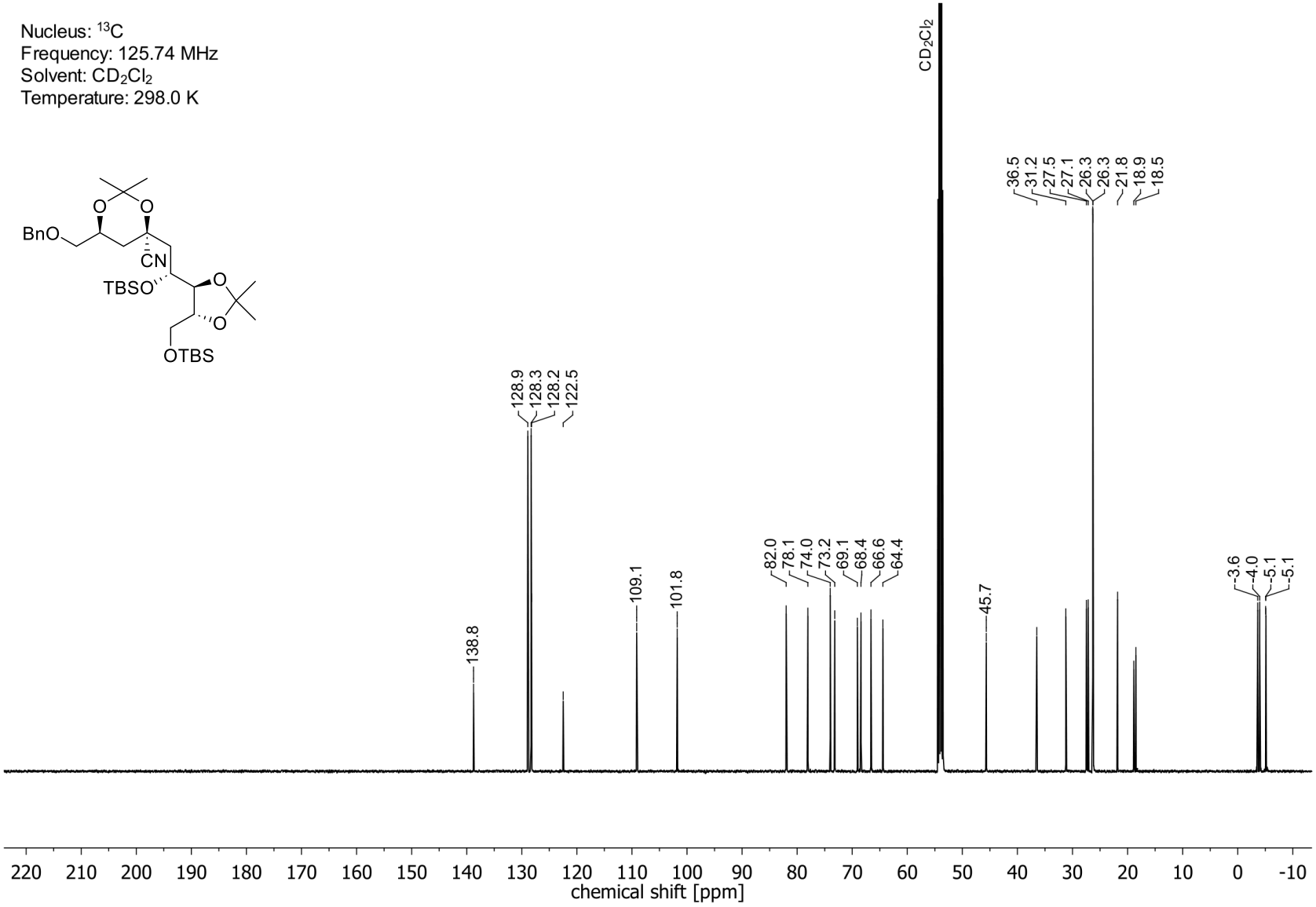


Nucleus: $^{13}C$
Frequency: 125.74 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

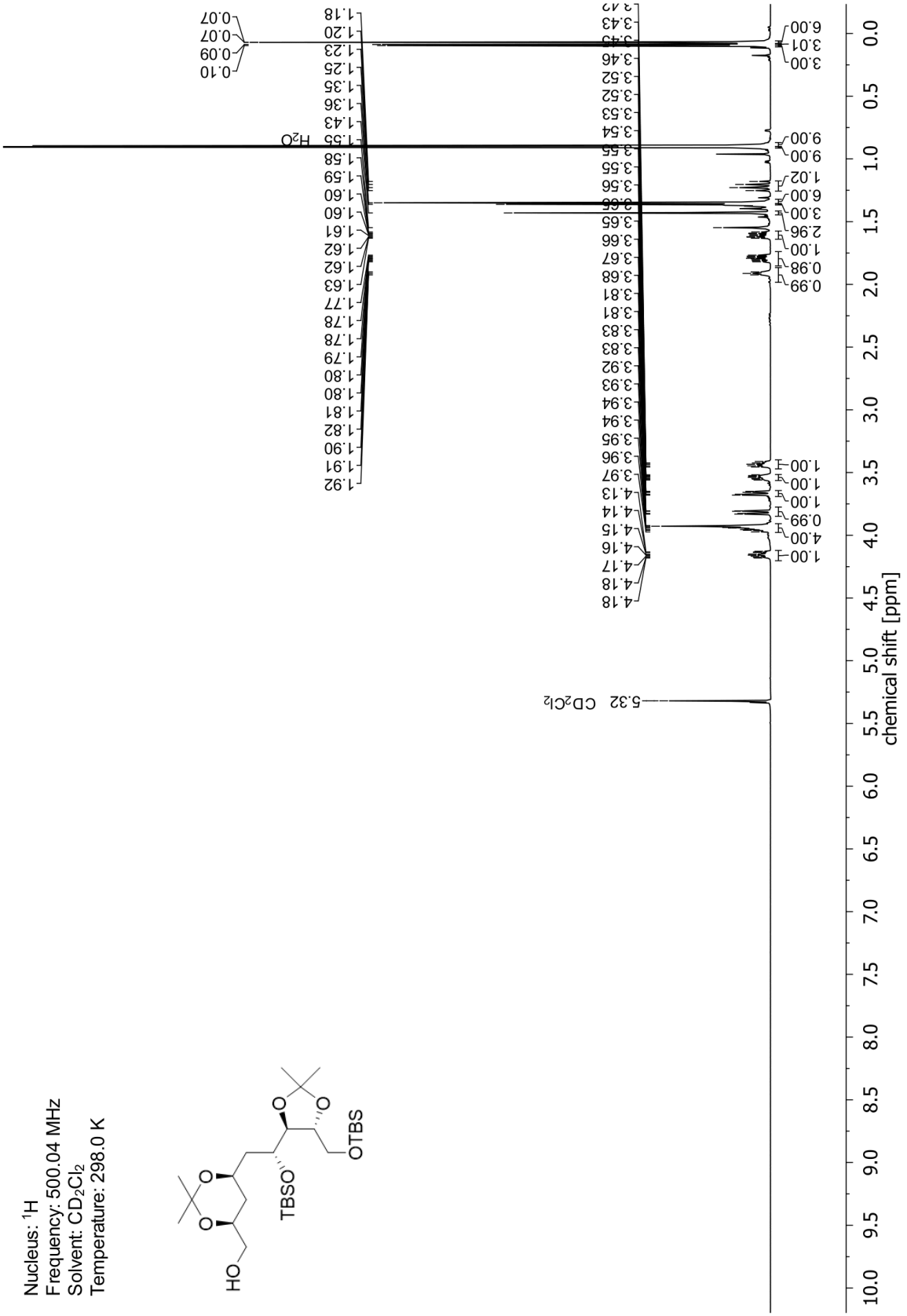


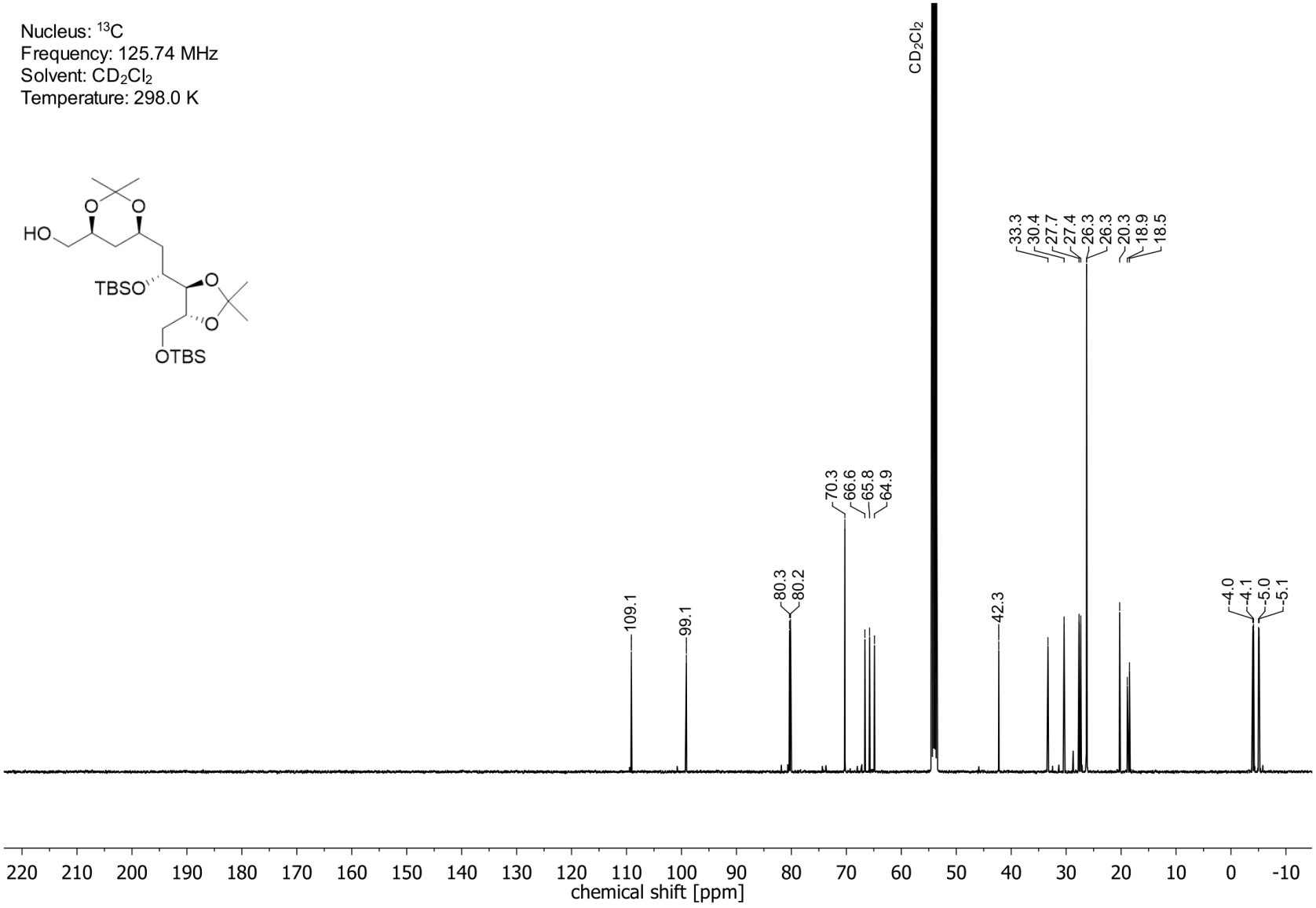
NMR-Spectra of Compound **331**:



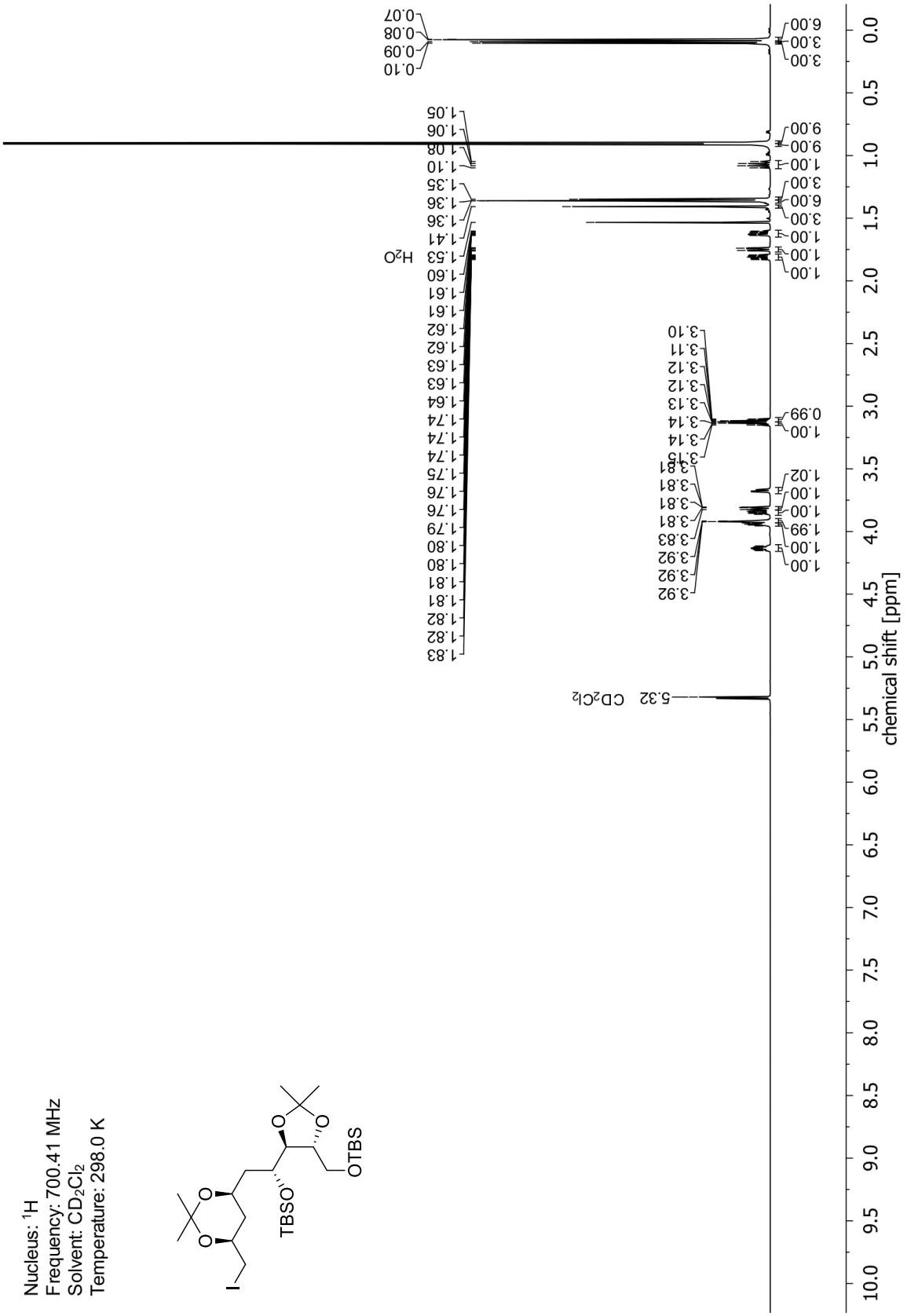

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CN
TBSO
OTBS
CD2Cl2
36.5
31.2
27.5
27.1
26.3
26.3
21.8
18.9
18.5
128.9
128.3
128.2
122.5
138.8
109.1
101.8
82.0
78.1
74.0
73.2
69.1
68.4
66.6
64.4
45.7
-3.6
-4.0
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

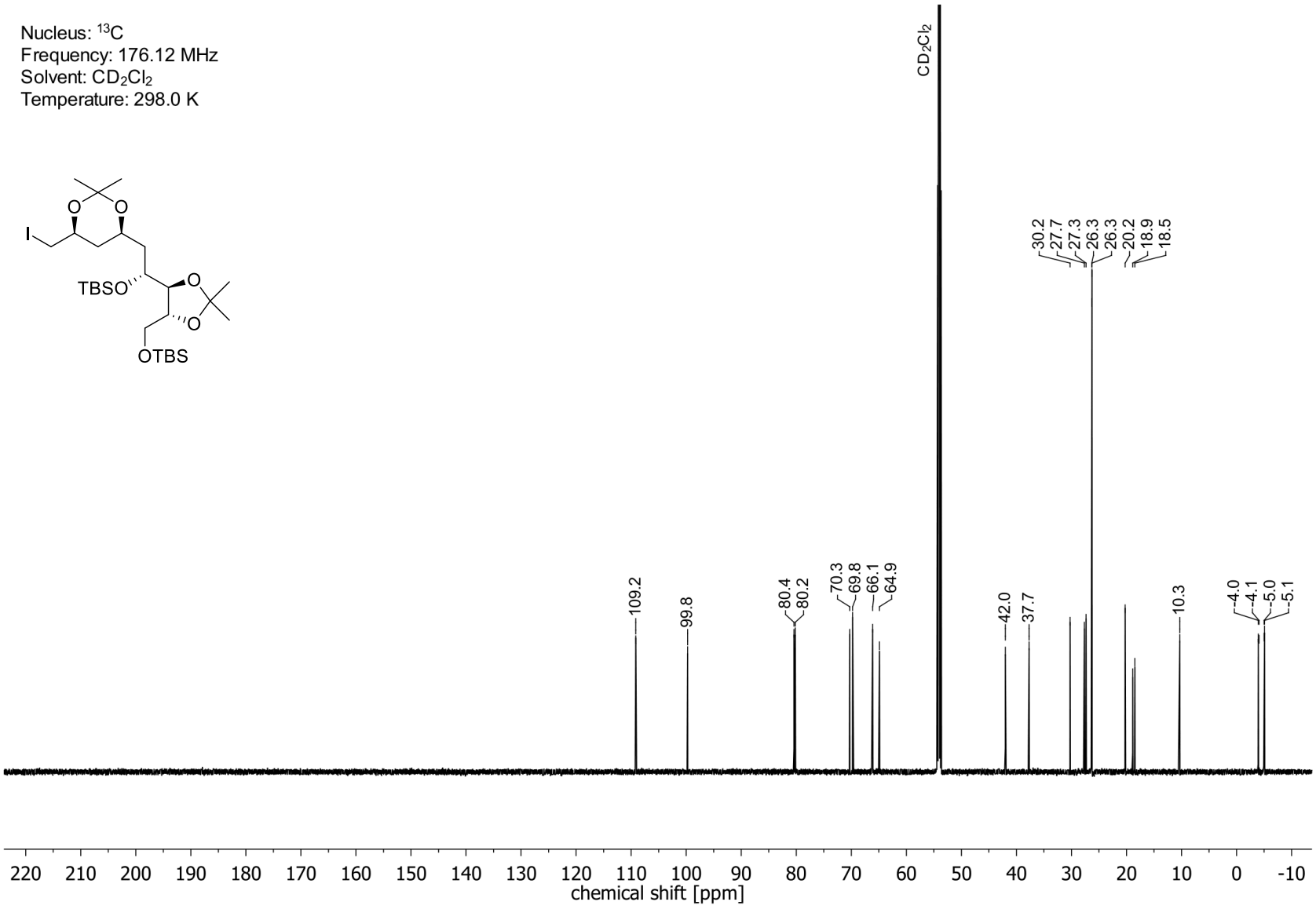
NMR-Spectra of Compound **163**:



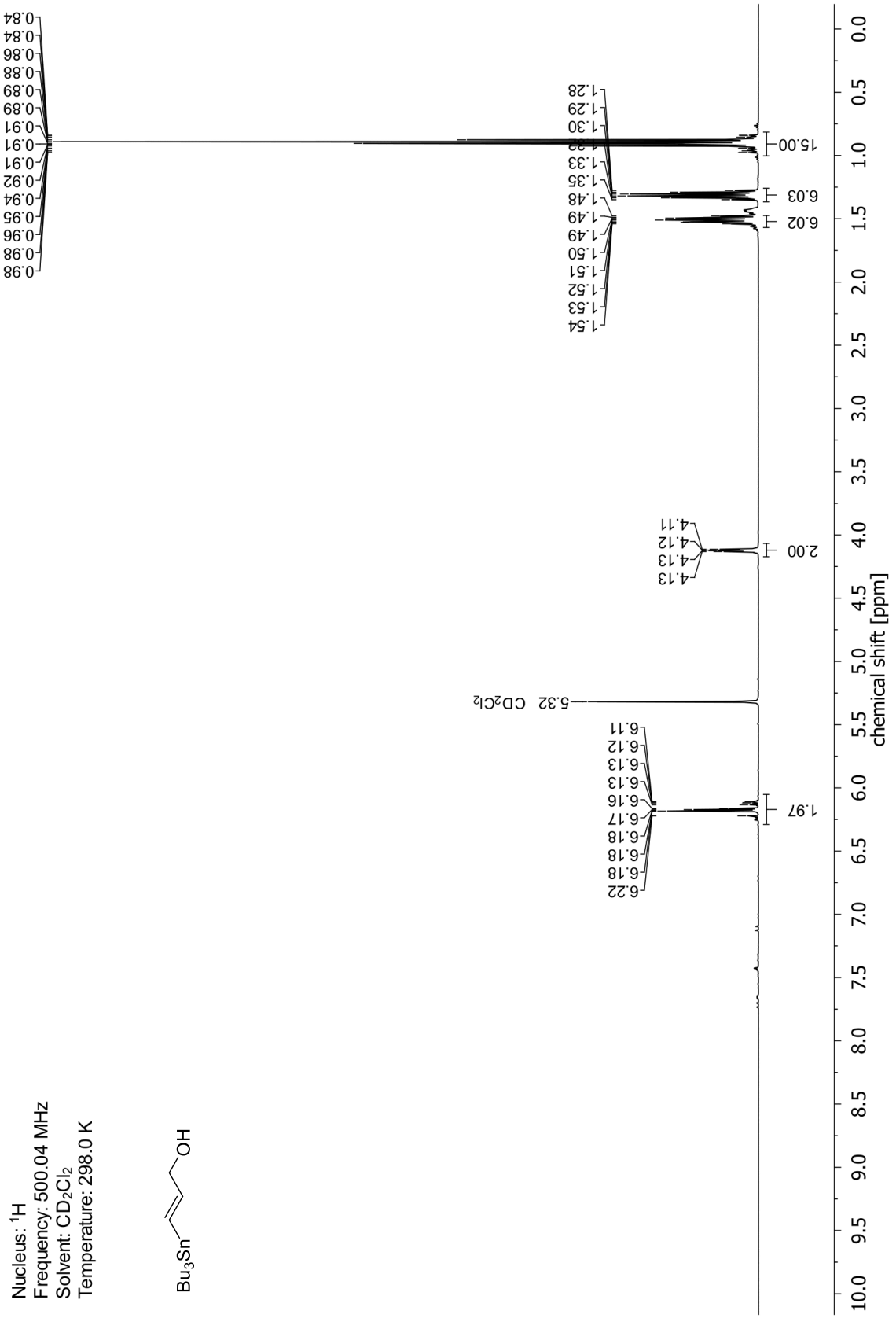

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
OTBS
CD2Cl2
33.3
30.4
27.7
27.4
26.3
26.3
20.3
18.9
18.5
70.3
66.6
65.8
64.9
109.1
99.1
80.3
80.2
42.3
-4.0
-4.1
-5.0
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **163**:

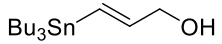



Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
I
TBSO
OTBS
CD2Cl2
30.2
27.7
27.3
26.3
26.3
20.2
18.9
18.5
109.2
99.8
80.4
80.2
70.3
69.8
66.1
64.9
42.0
37.7
10.3
-4.0
-4.1
-5.0
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

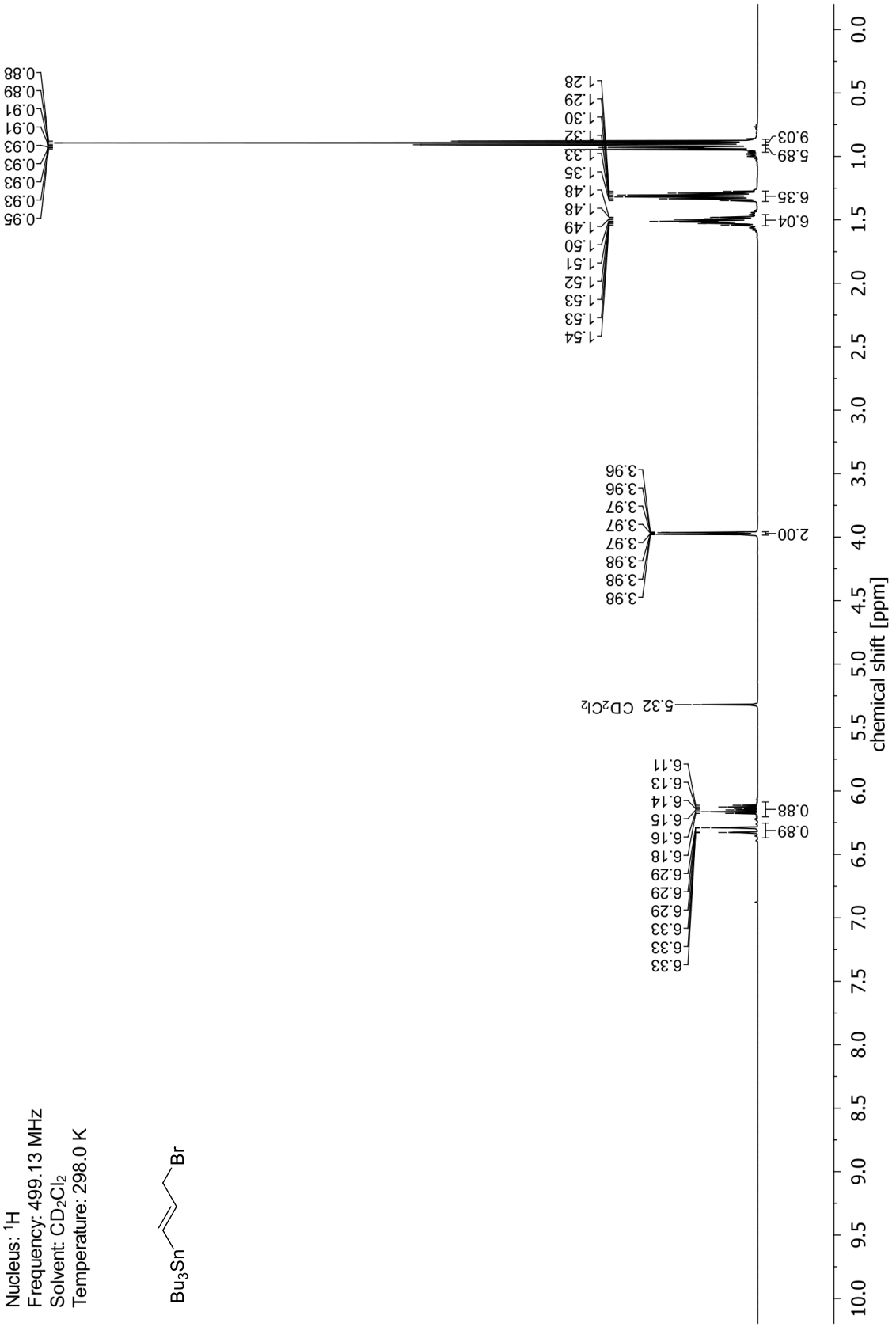
NMR-Spectra of Compound **338**:



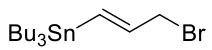
Nucleus: $^{13}C$
Frequency: 125.74 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



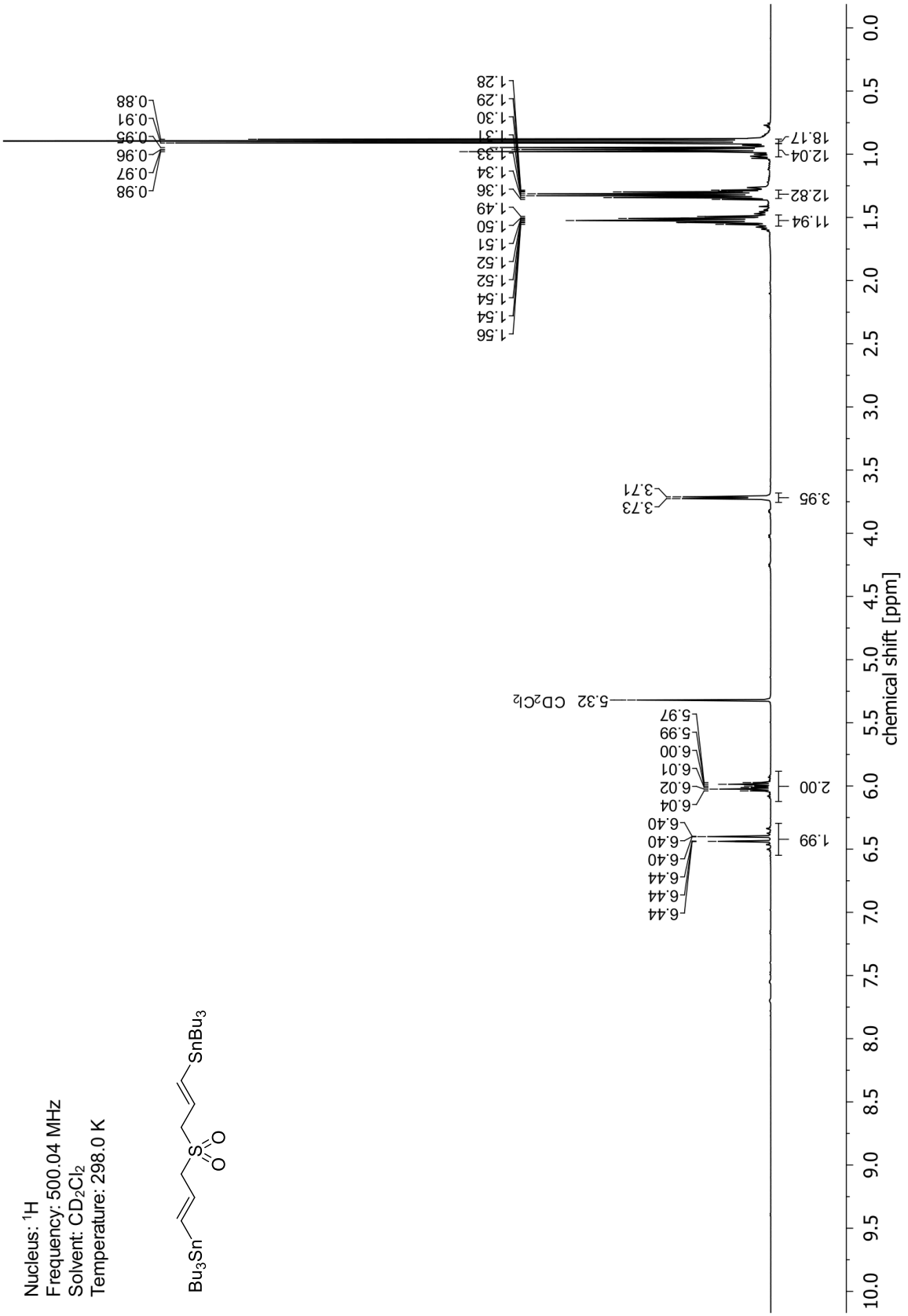
NMR-Spectra of Compound **339**:

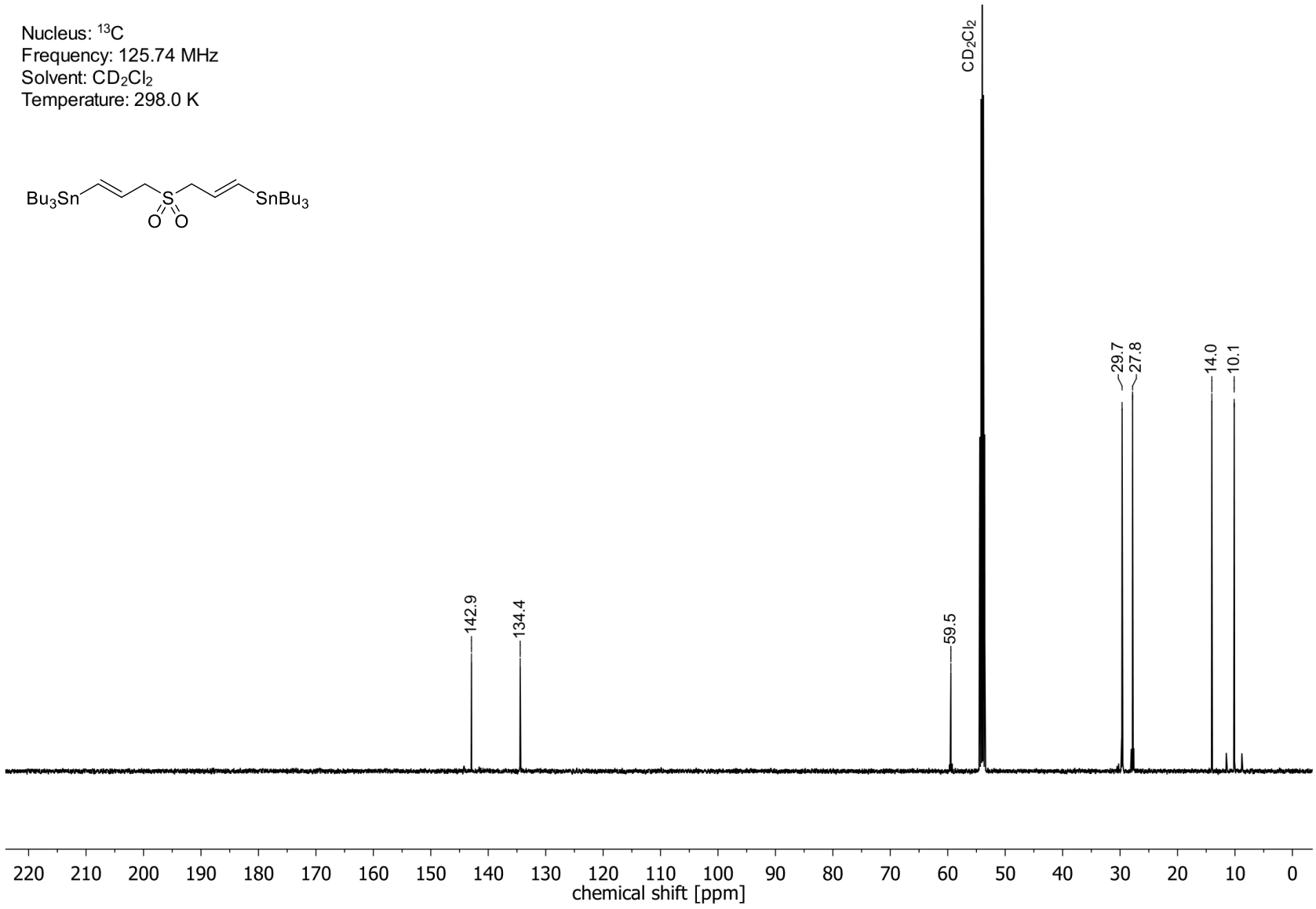


Nucleus: $^{13}C$
Frequency: 125.52 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

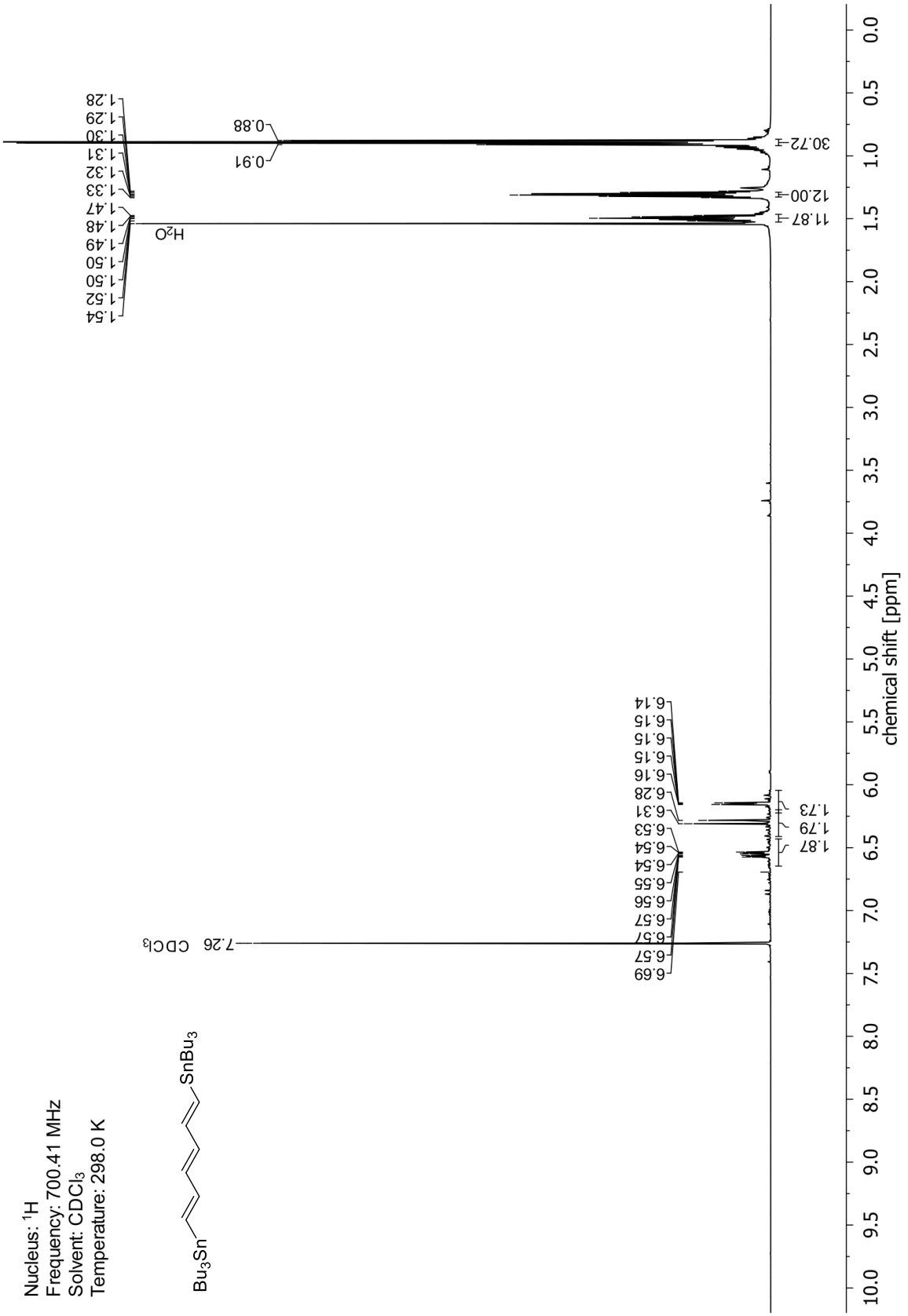


NMR-Spectra of Compound **228**:

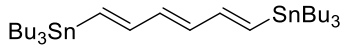



Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
Bu3Sn
SnBu3
O
O
CD2Cl2
142.9
134.4
59.5
29.7
27.8
14.0
10.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

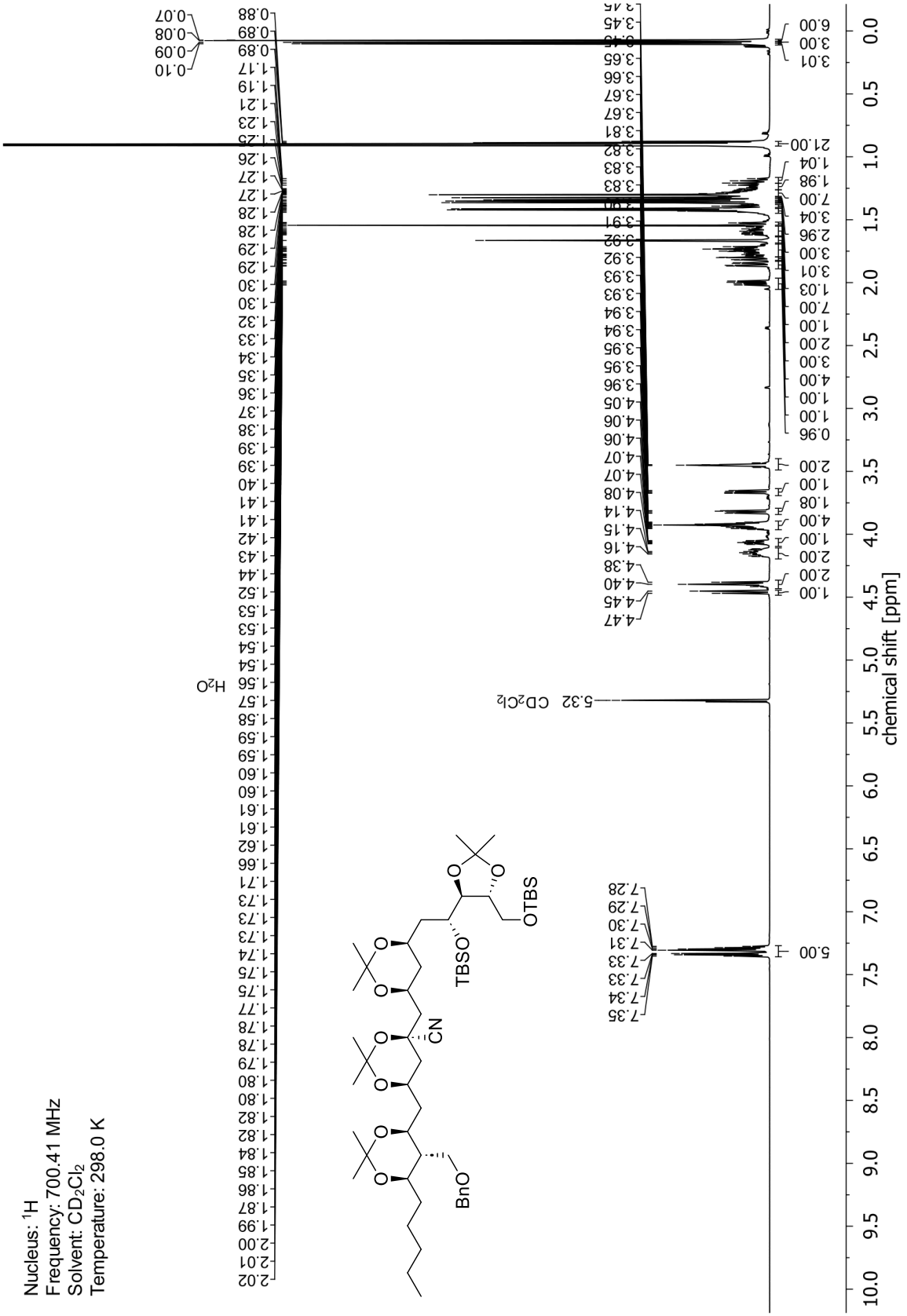
NMR-Spectra of Compound **148**:

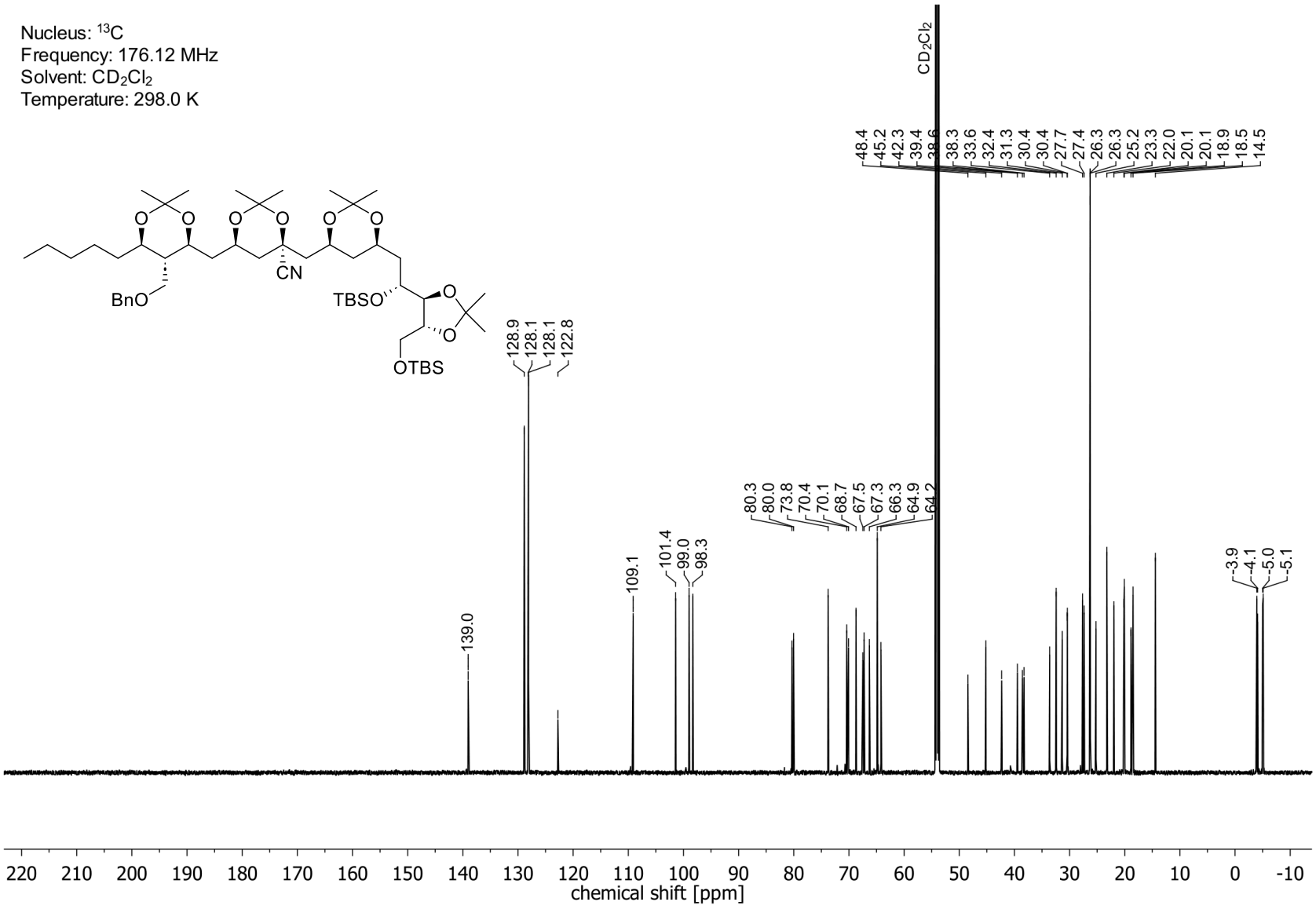


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CDCl_3$
Temperature: 298.0 K

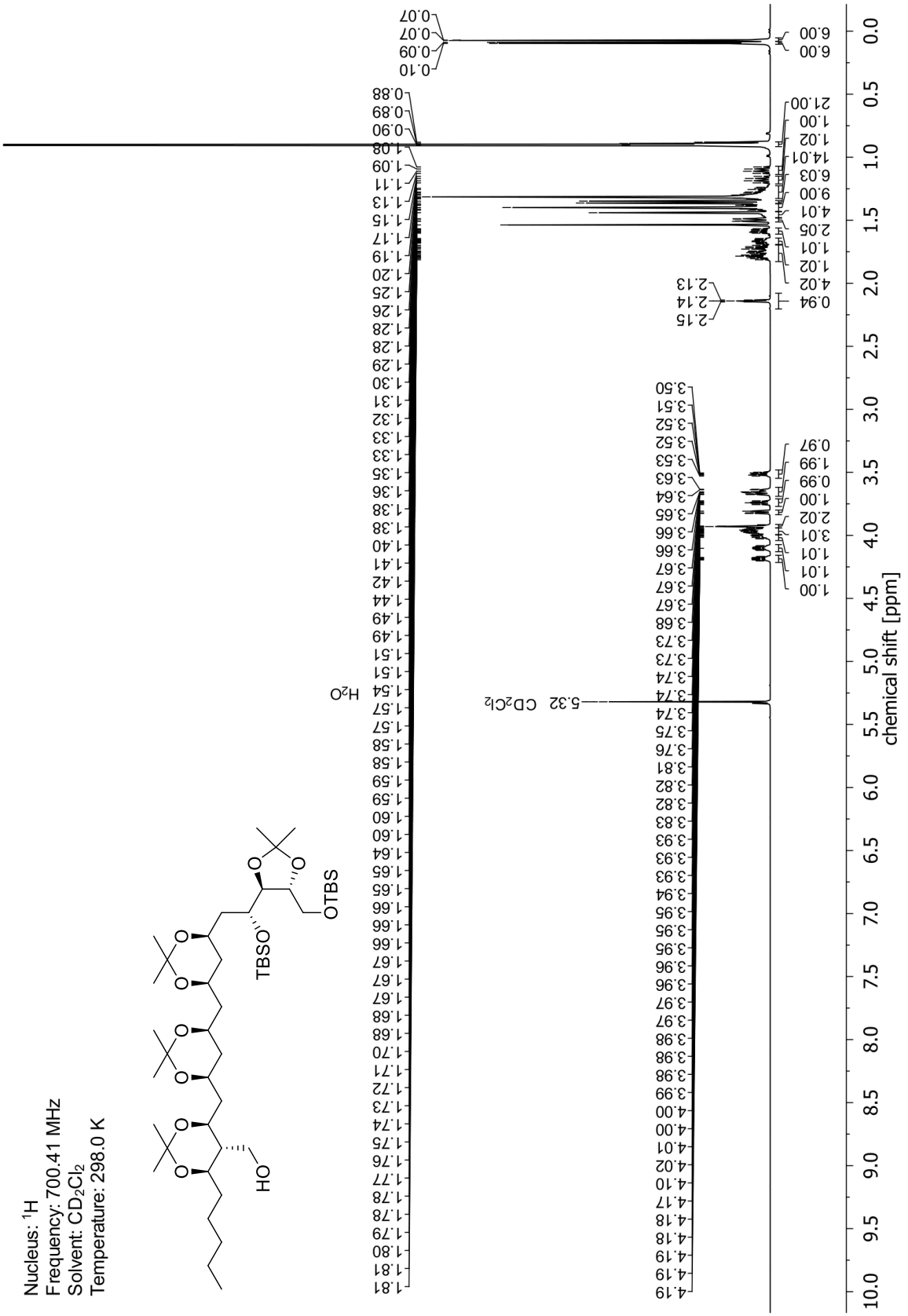


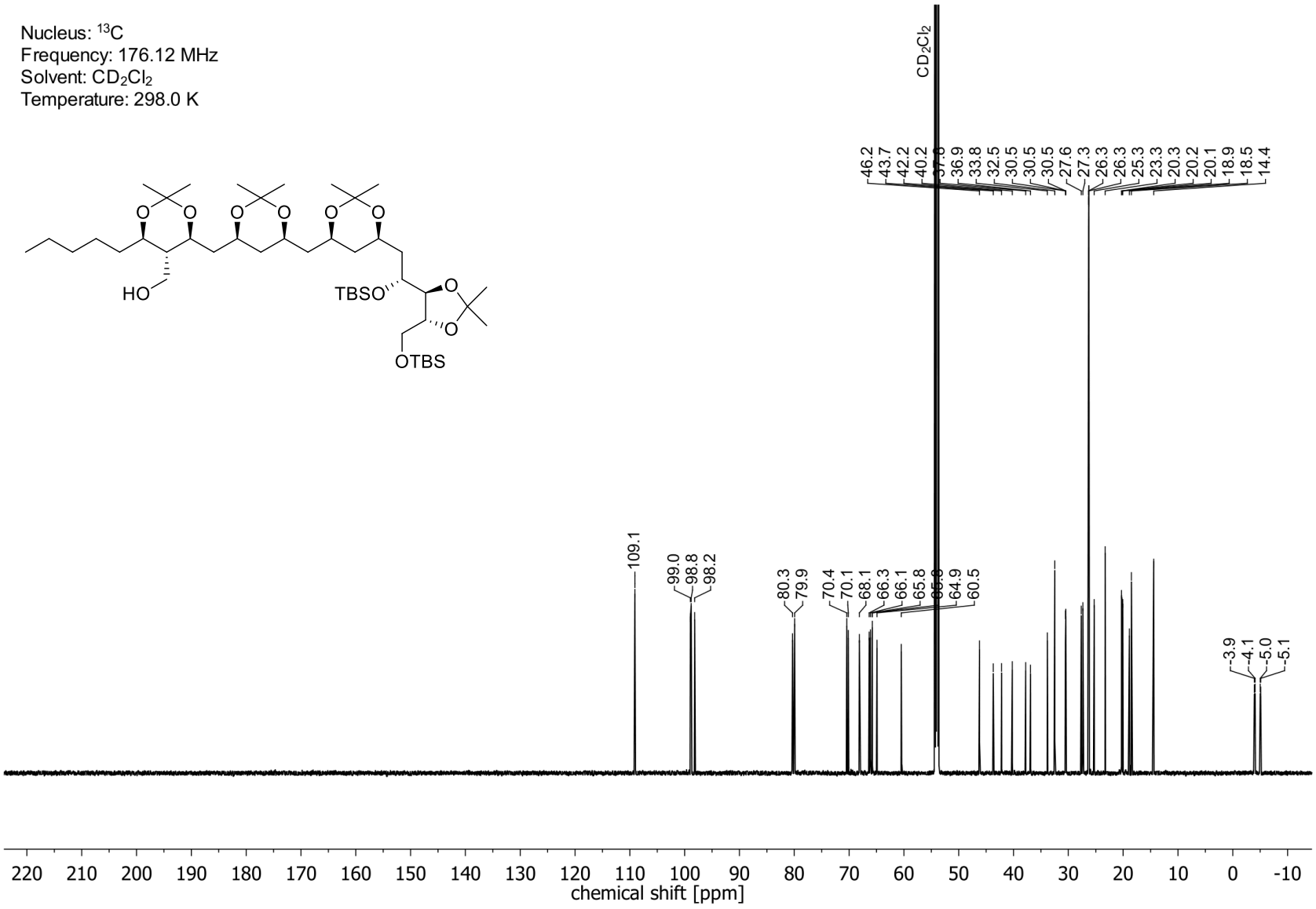
NMR-Spectra of Compound **333**:



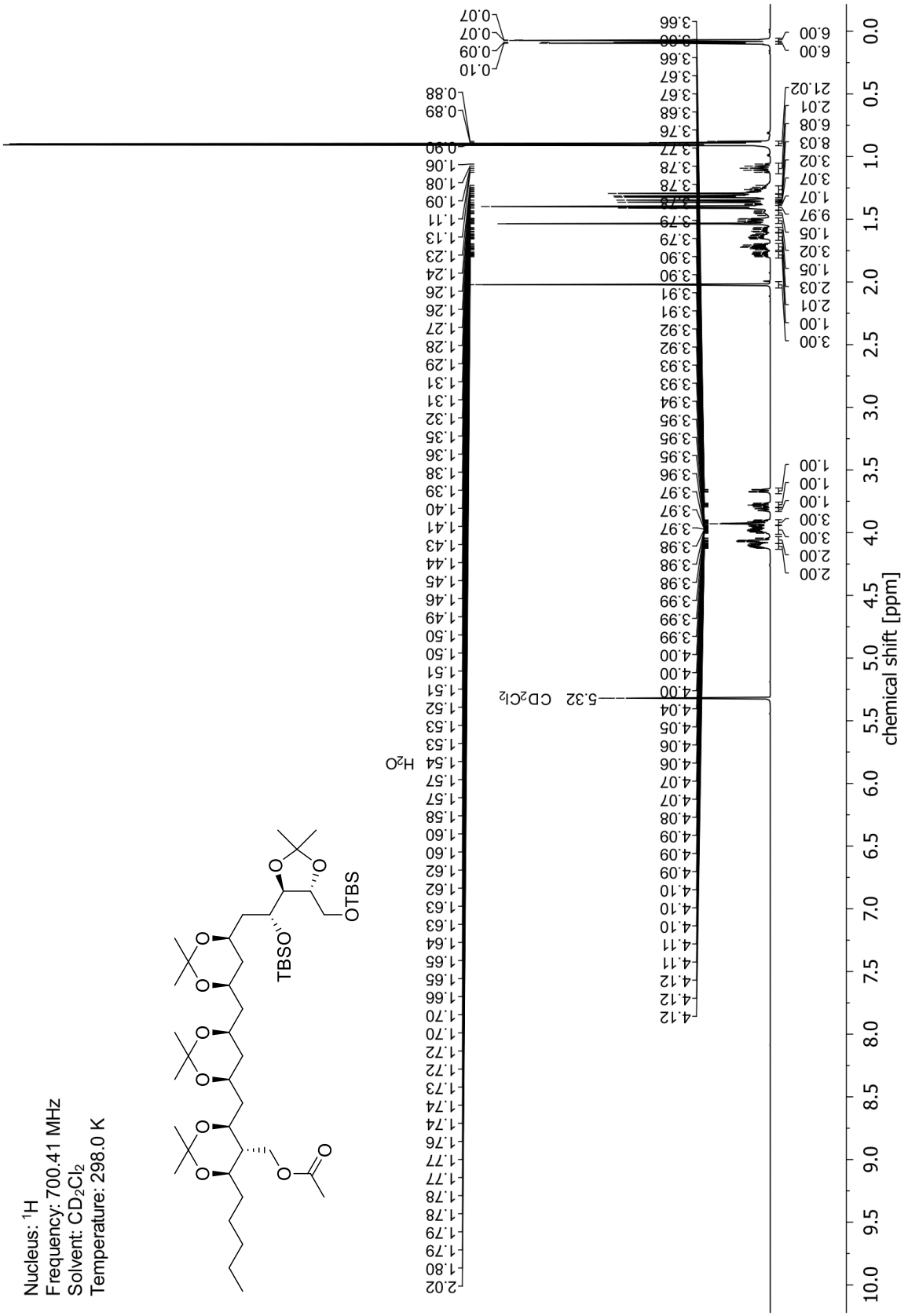

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
CD2Cl2
48.4
45.2
42.3
39.4
38.6
38.3
33.6
32.4
31.3
30.4
30.4
27.7
27.4
26.3
26.3
25.2
23.3
22.0
20.1
20.1
18.9
18.5
14.5
BnO
CN
TBSO
OTBS
128.9
128.1
128.1
122.8
139.0
109.1
101.4
99.0
98.3
80.3
80.0
73.8
70.4
70.1
68.7
67.5
67.3
66.3
64.9
64.2
-3.9
-4.1
-5.0
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

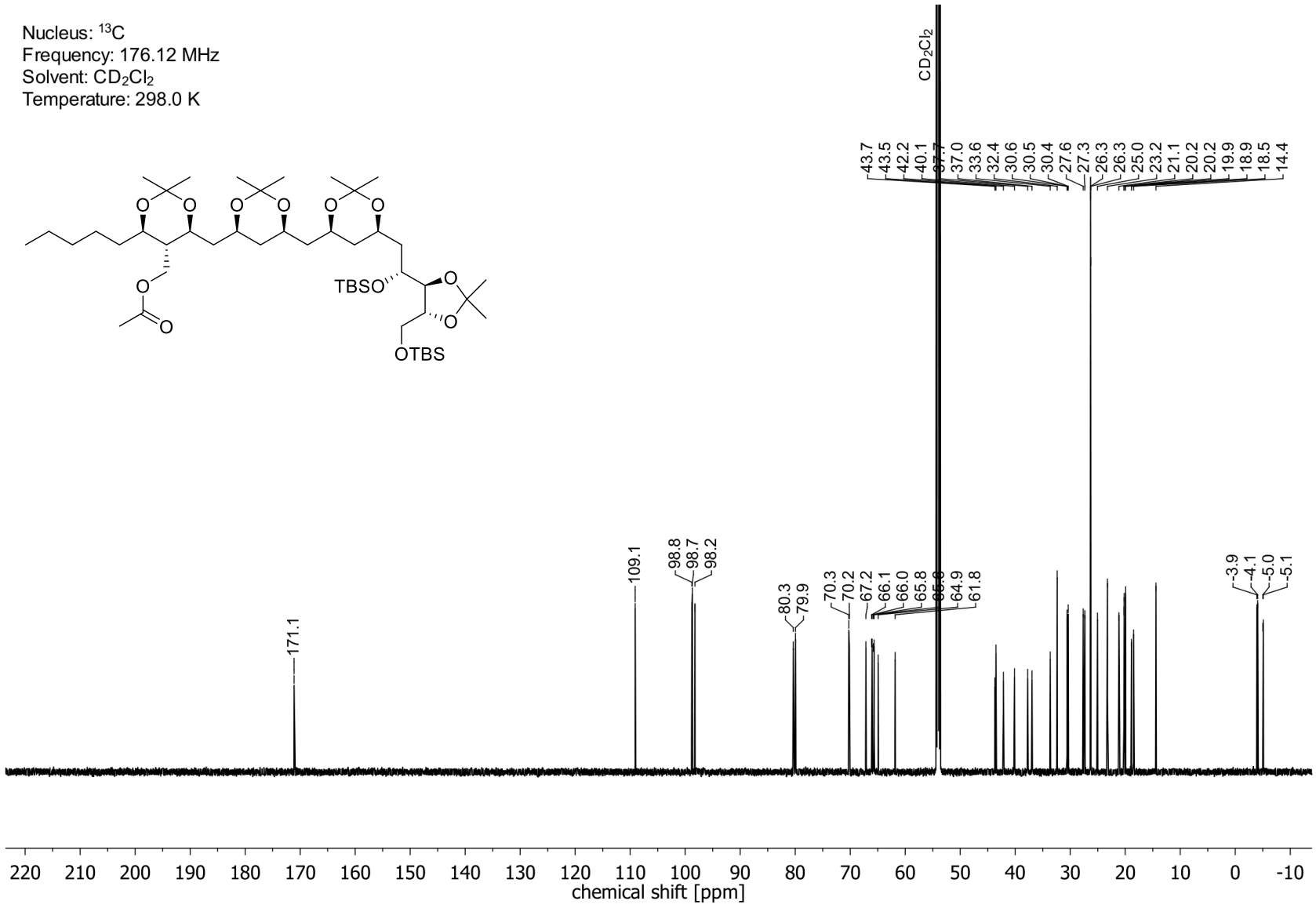
NMR-Spectra of Compound **162**:



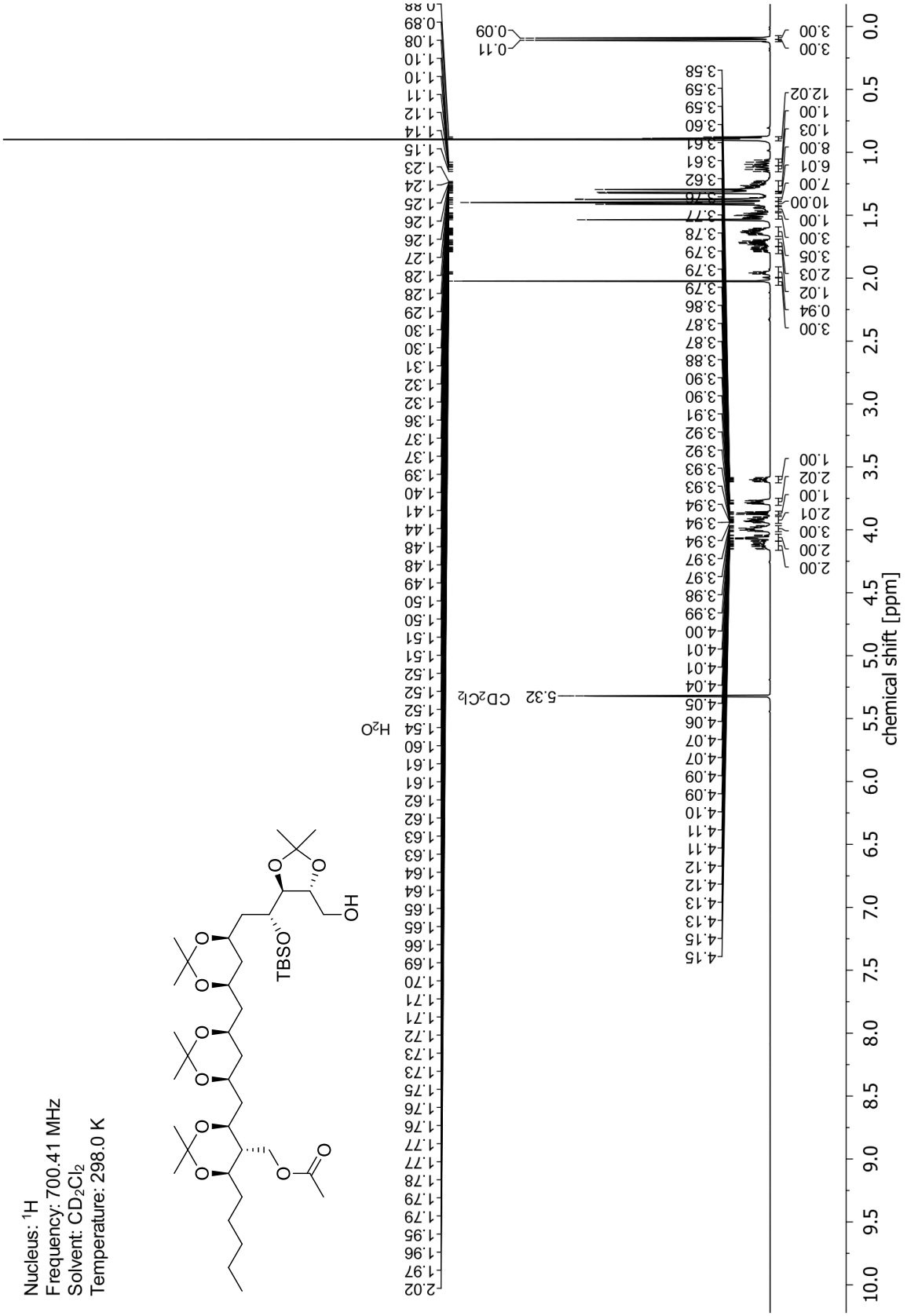

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
OTBS
CD2Cl2
46.2
43.7
42.2
40.2
37.8
36.9
33.8
32.5
30.5
30.5
30.5
27.6
27.3
26.3
26.3
25.3
23.3
20.3
20.2
20.1
18.9
18.5
14.4
109.1
99.0
98.8
98.2
80.3
79.9
70.4
70.1
68.1
66.3
66.1
65.8
65.6
64.9
60.5
-3.9
-4.1
-5.0
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

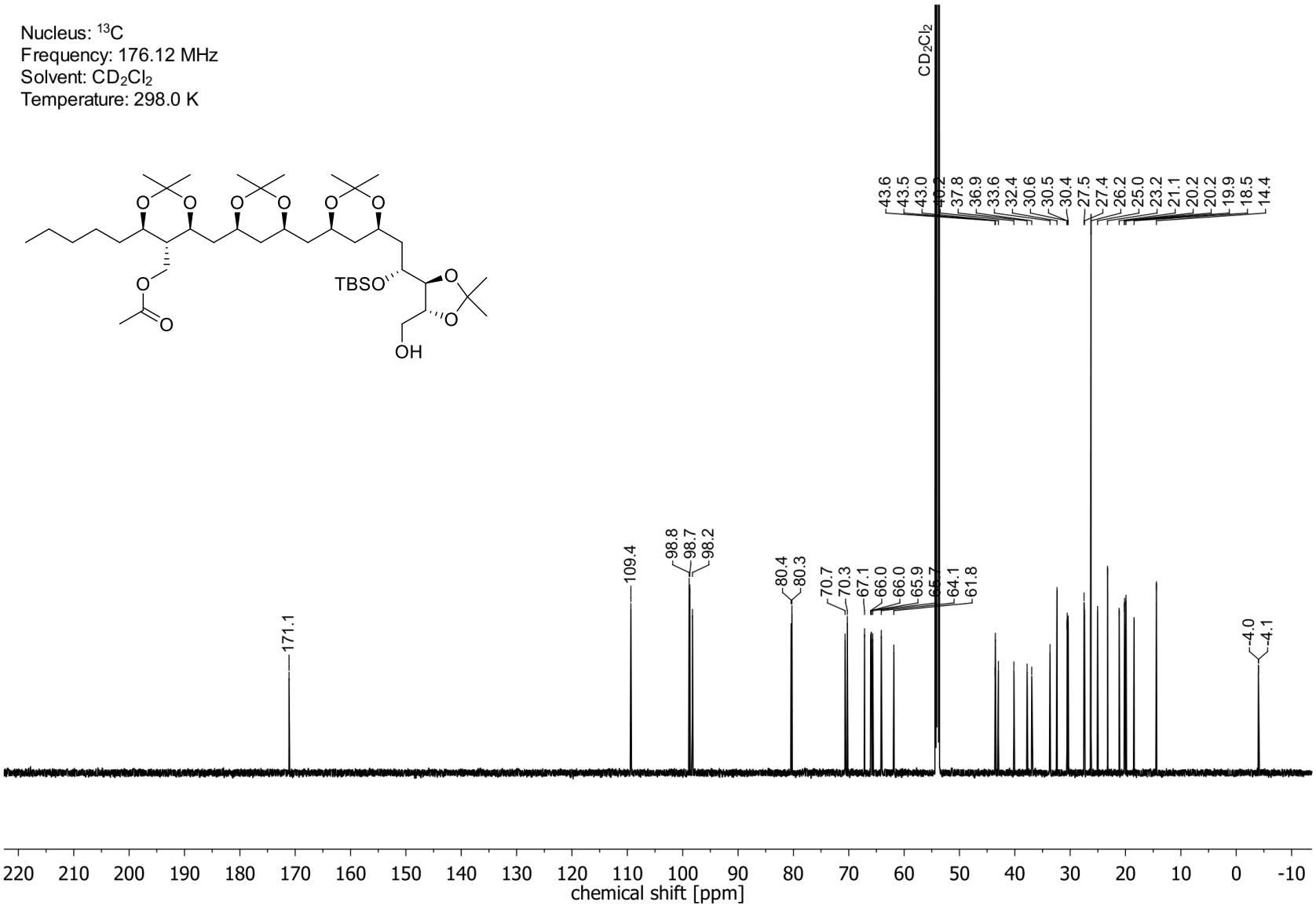
NMR-Spectra of Compound **291**:



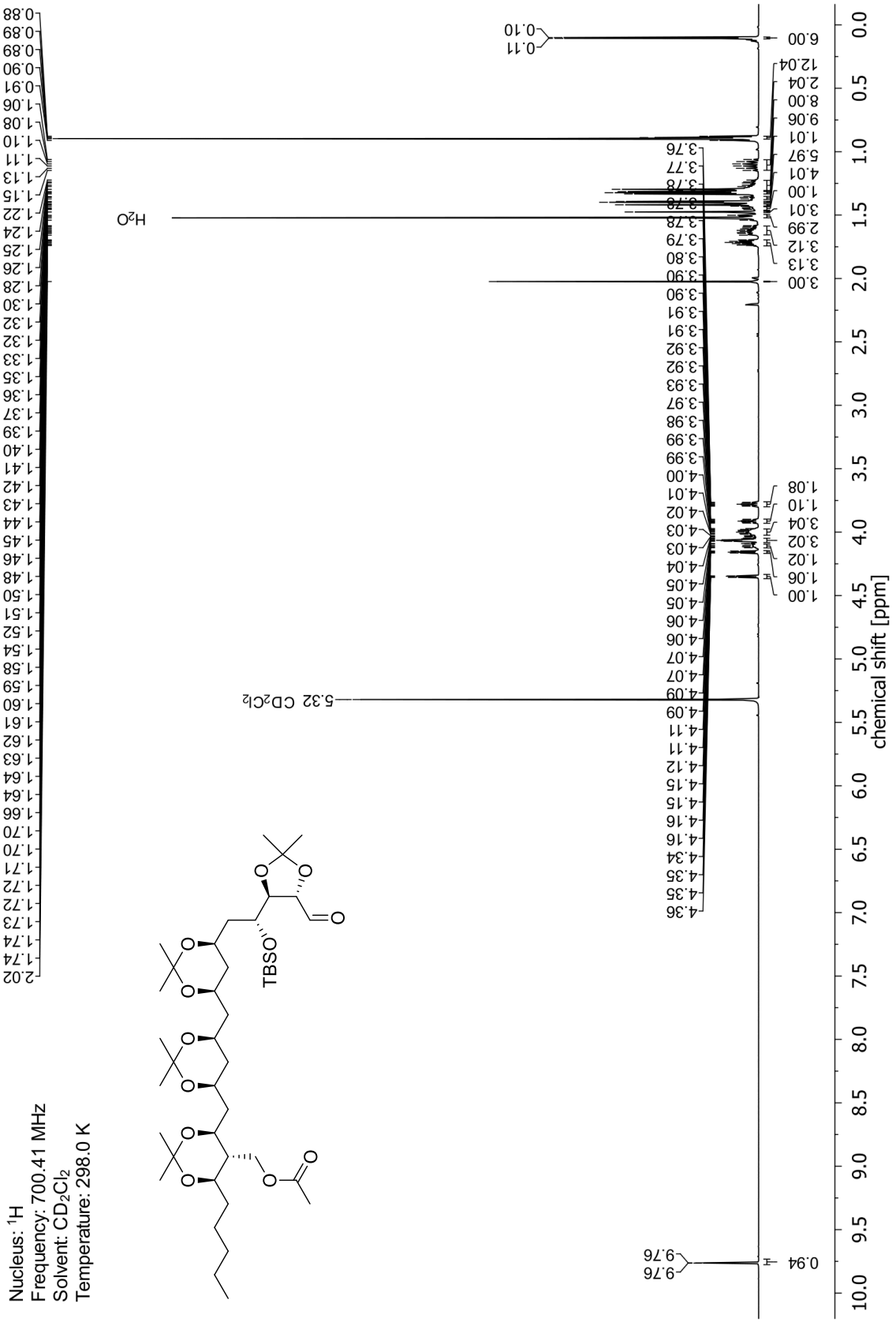

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OTBS
CD2Cl2
43.7
43.5
42.2
40.1
37.0
33.6
32.4
30.6
30.5
30.4
27.6
27.3
26.3
26.3
25.0
23.2
21.1
20.2
20.2
19.9
18.9
18.5
14.4
171.1
109.1
98.8
98.7
98.2
80.3
79.9
70.3
70.2
67.2
66.1
66.0
65.8
64.9
61.8
-3.9
-4.1
-5.0
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

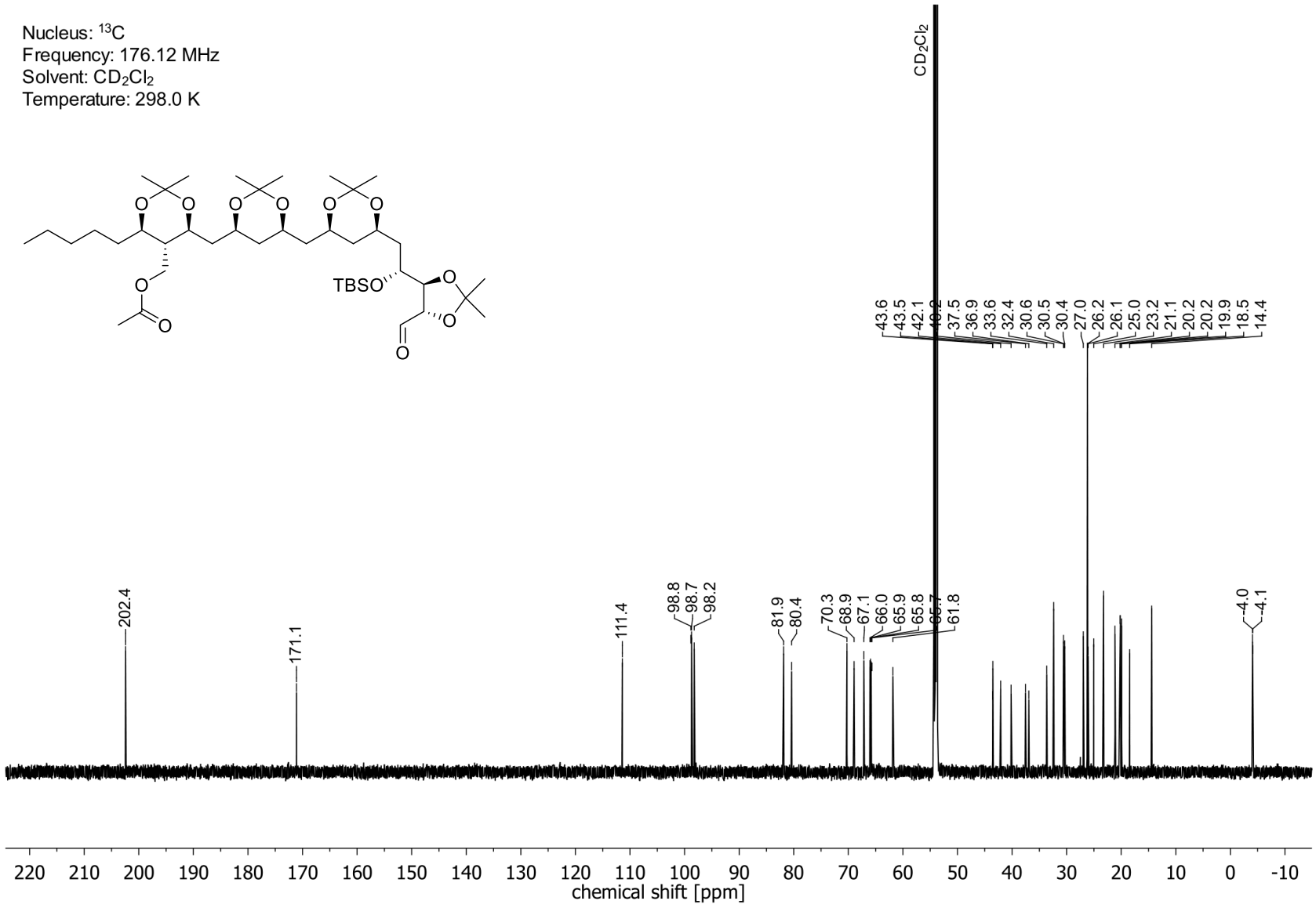
NMR-Spectra of Compound **293**:



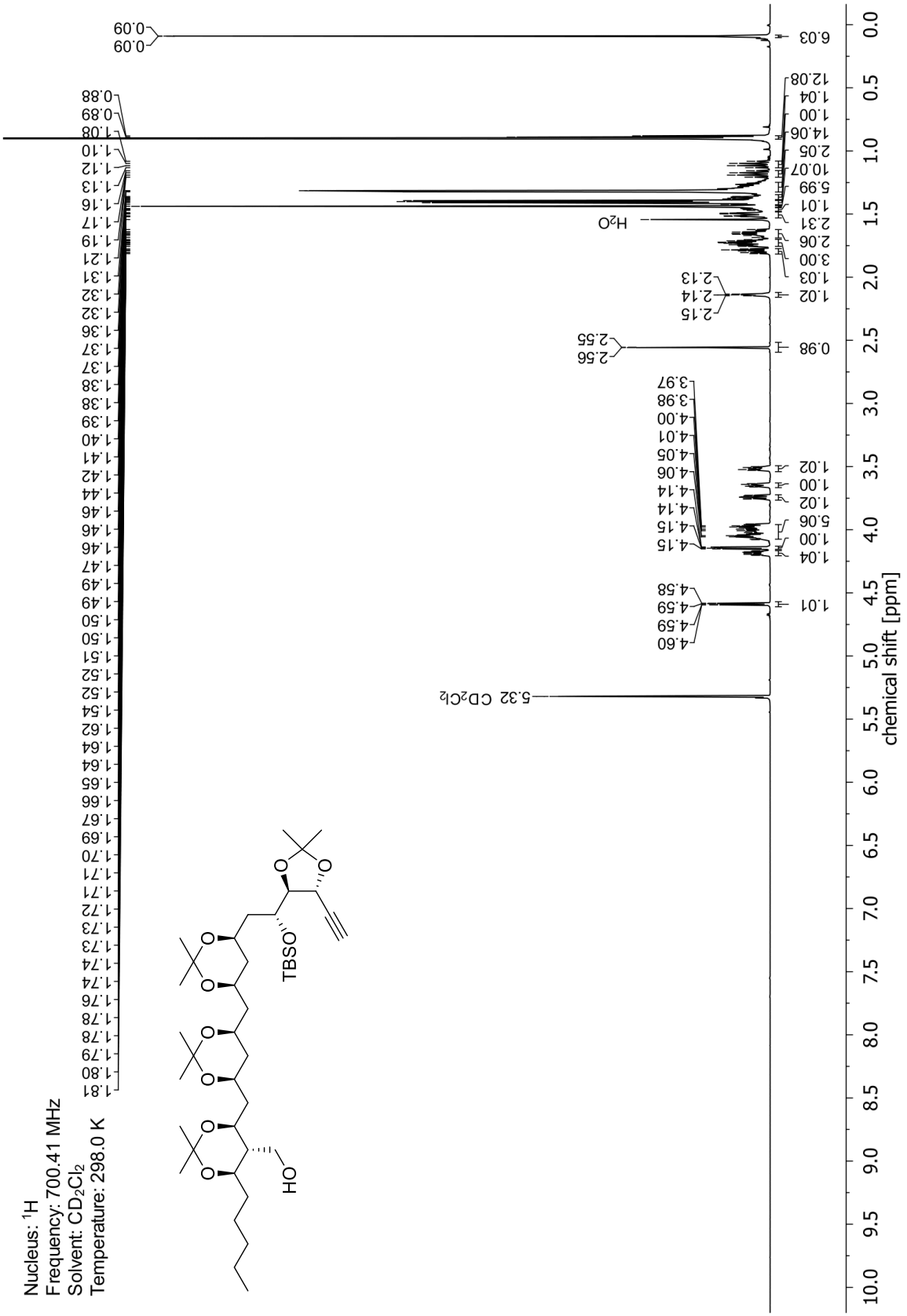

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
CD2Cl2
43.6
43.5
43.0
37.8
36.9
33.6
32.4
30.6
30.5
30.4
27.5
27.4
26.2
25.0
23.2
21.1
20.2
20.2
19.9
18.5
14.4
171.1
109.4
98.8
98.7
98.2
80.4
80.3
70.7
70.3
67.1
66.0
66.0
65.9
64.1
61.8
-4.0
-4.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

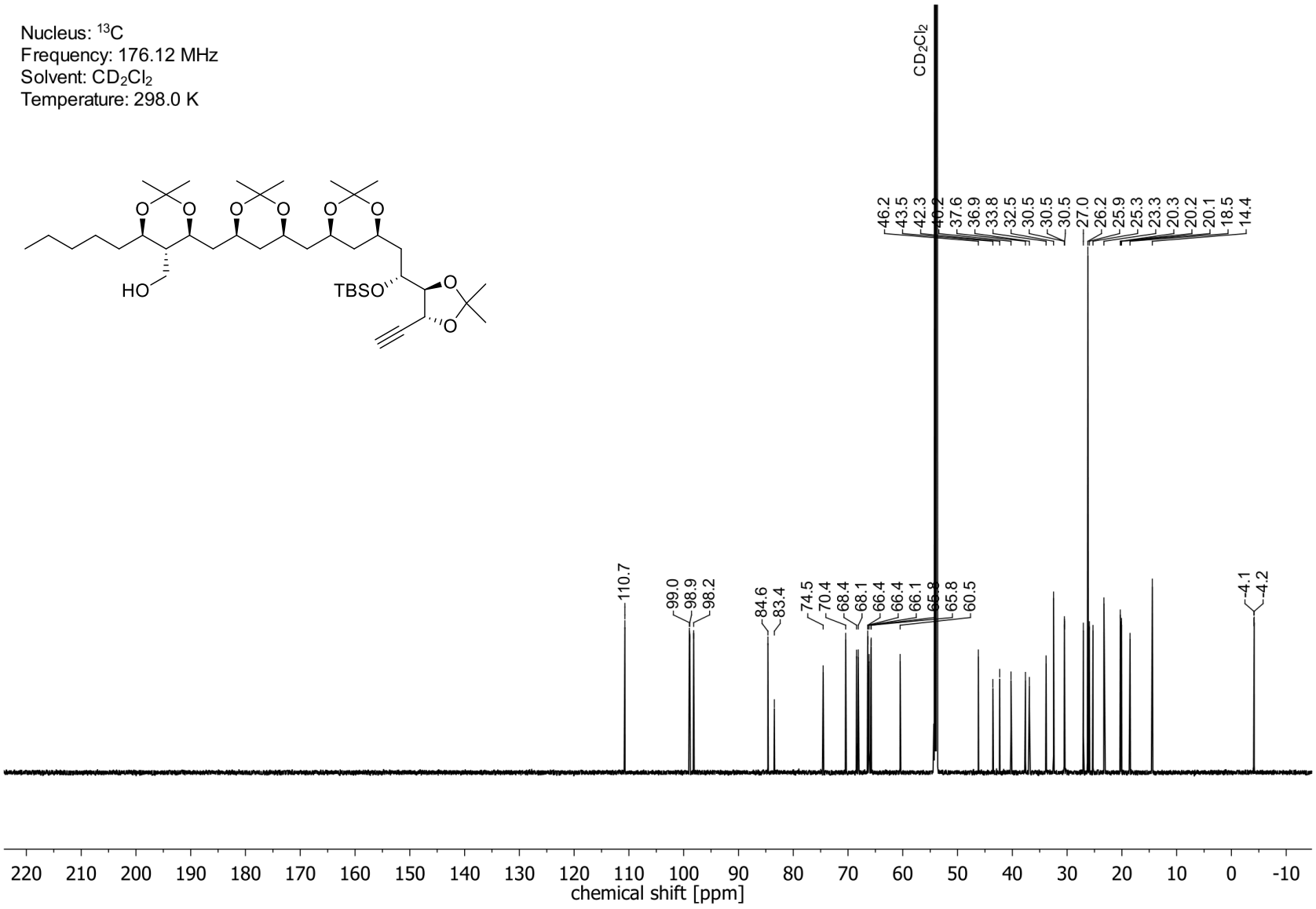
NMR-Spectra of Compound **334**:



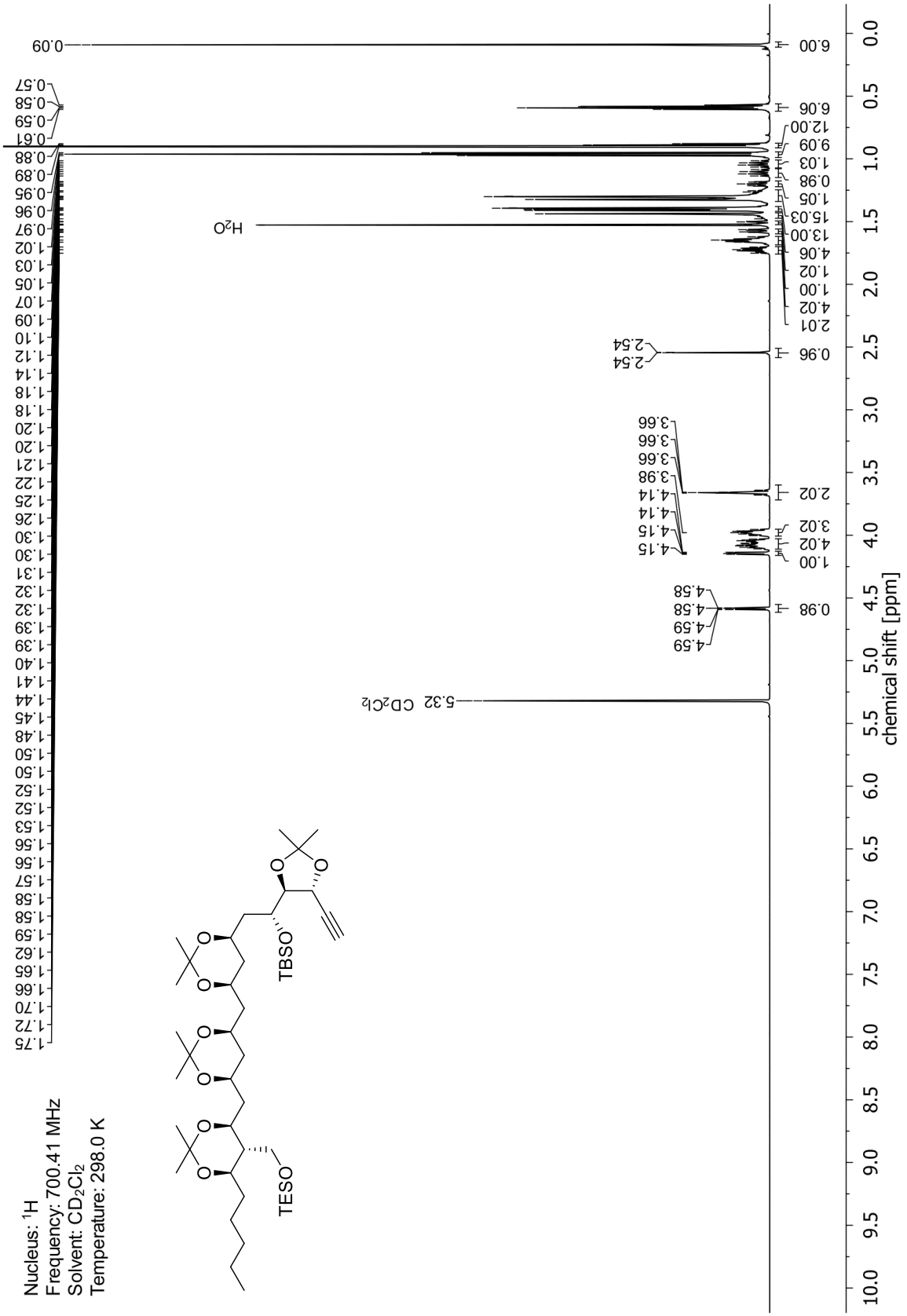

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
CD2Cl2
43.6
43.5
42.1
37.5
36.9
33.6
32.4
30.6
30.5
30.4
27.0
26.2
26.1
25.0
23.2
21.1
20.2
20.2
19.9
18.5
14.4
202.4
171.1
111.4
98.8
98.7
98.2
81.9
80.4
70.3
68.9
67.1
66.0
65.9
65.8
61.8
-4.0
-4.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

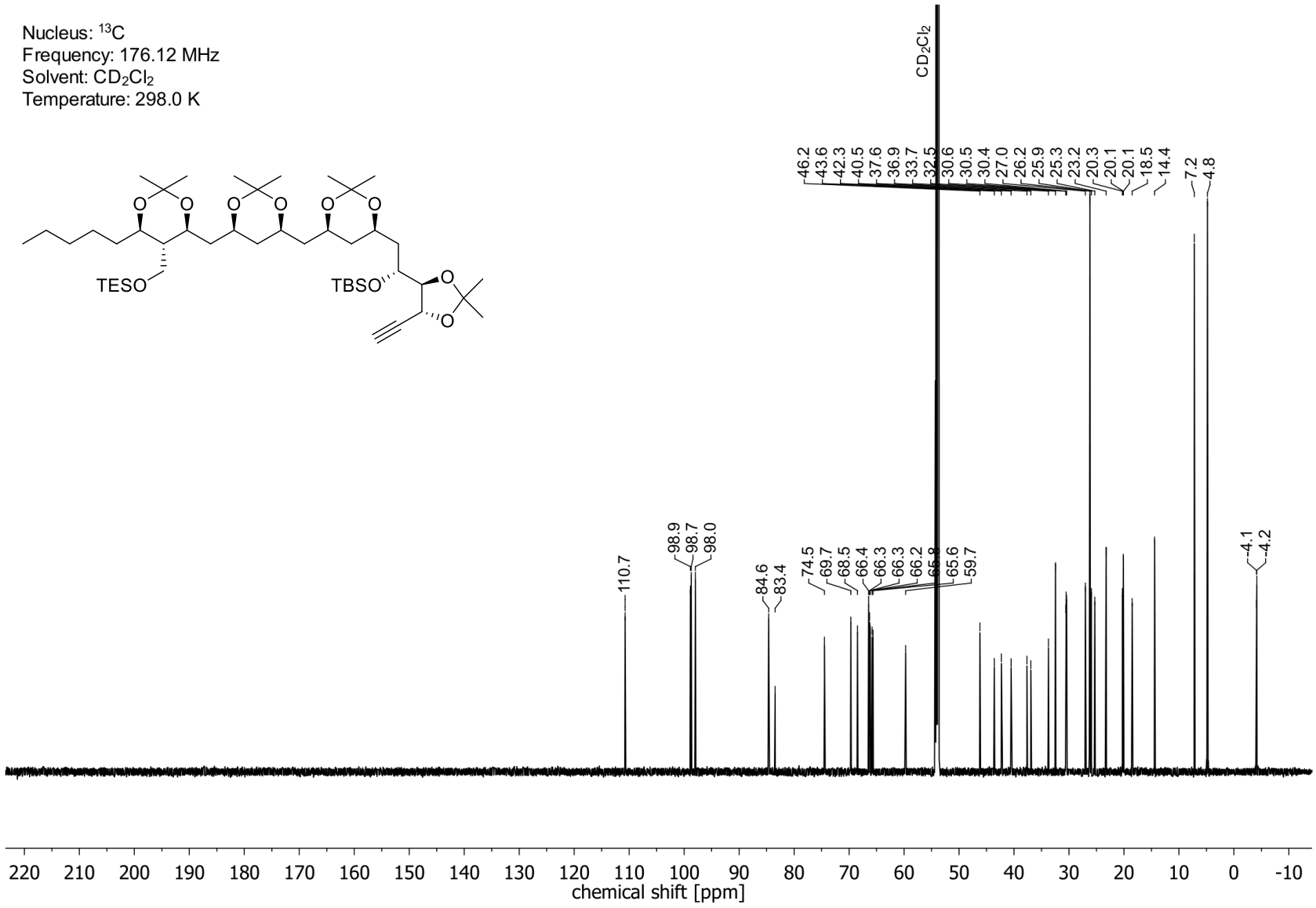
NMR-Spectra of Compound **336**:



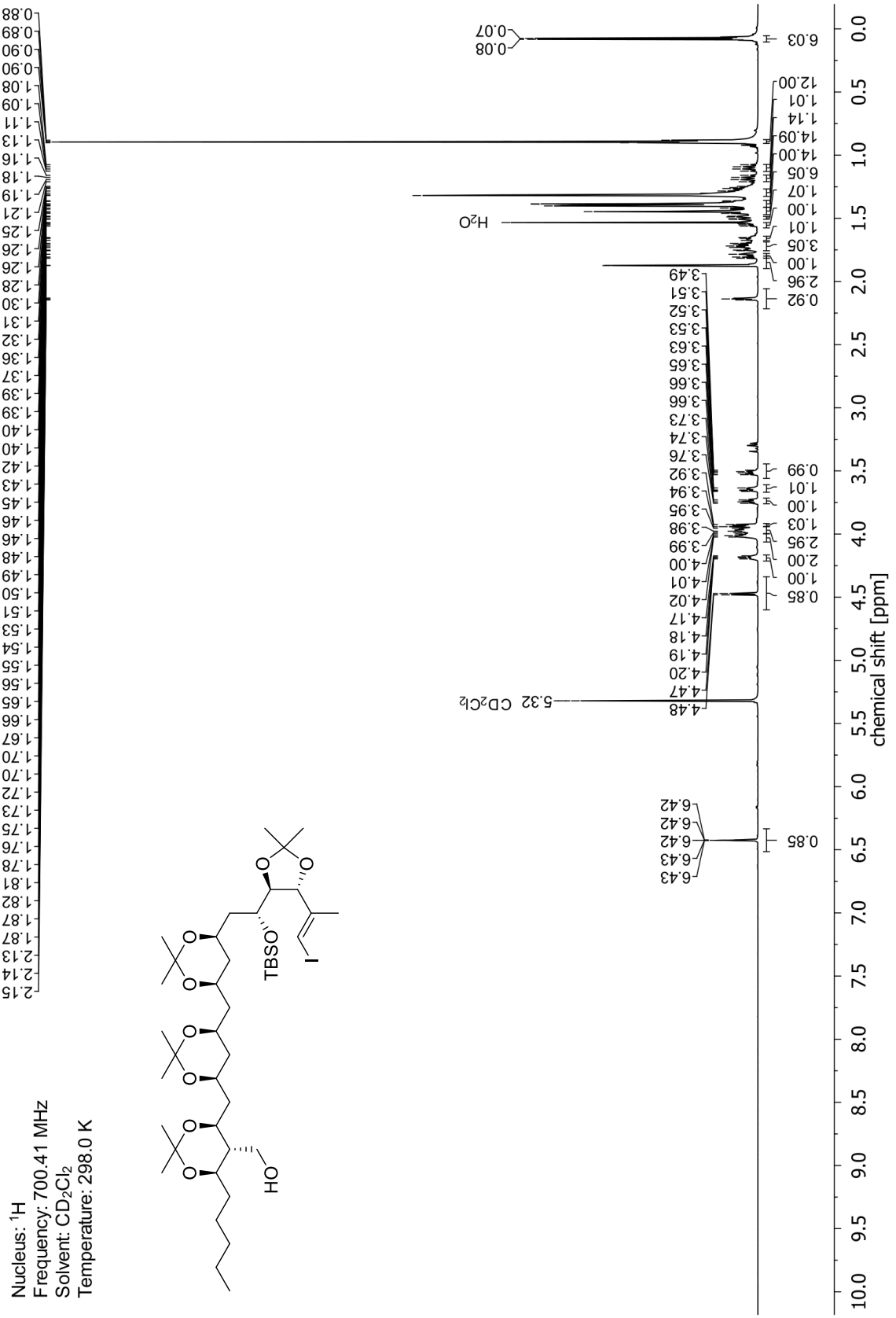

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
CD2Cl2
46.2
43.5
42.3
40.2
37.6
36.9
33.8
32.5
30.5
30.5
30.5
27.0
26.2
25.9
25.3
23.3
20.3
20.2
20.1
18.5
14.4
110.7
99.0
98.9
98.2
84.6
83.4
74.5
70.4
68.4
68.1
66.4
66.4
66.1
65.8
60.5
-4.1
-4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

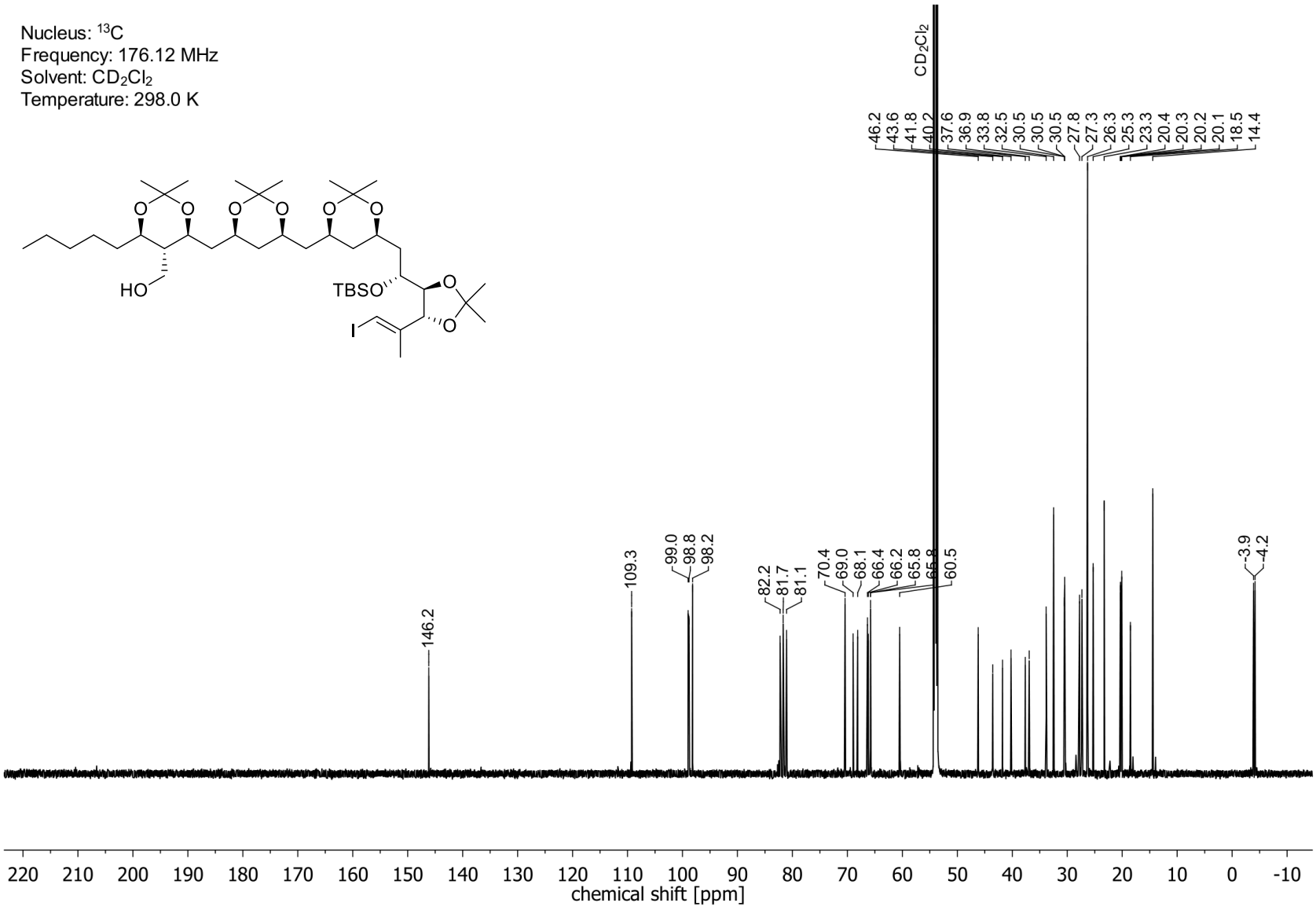
NMR-Spectra of Compound **295**:



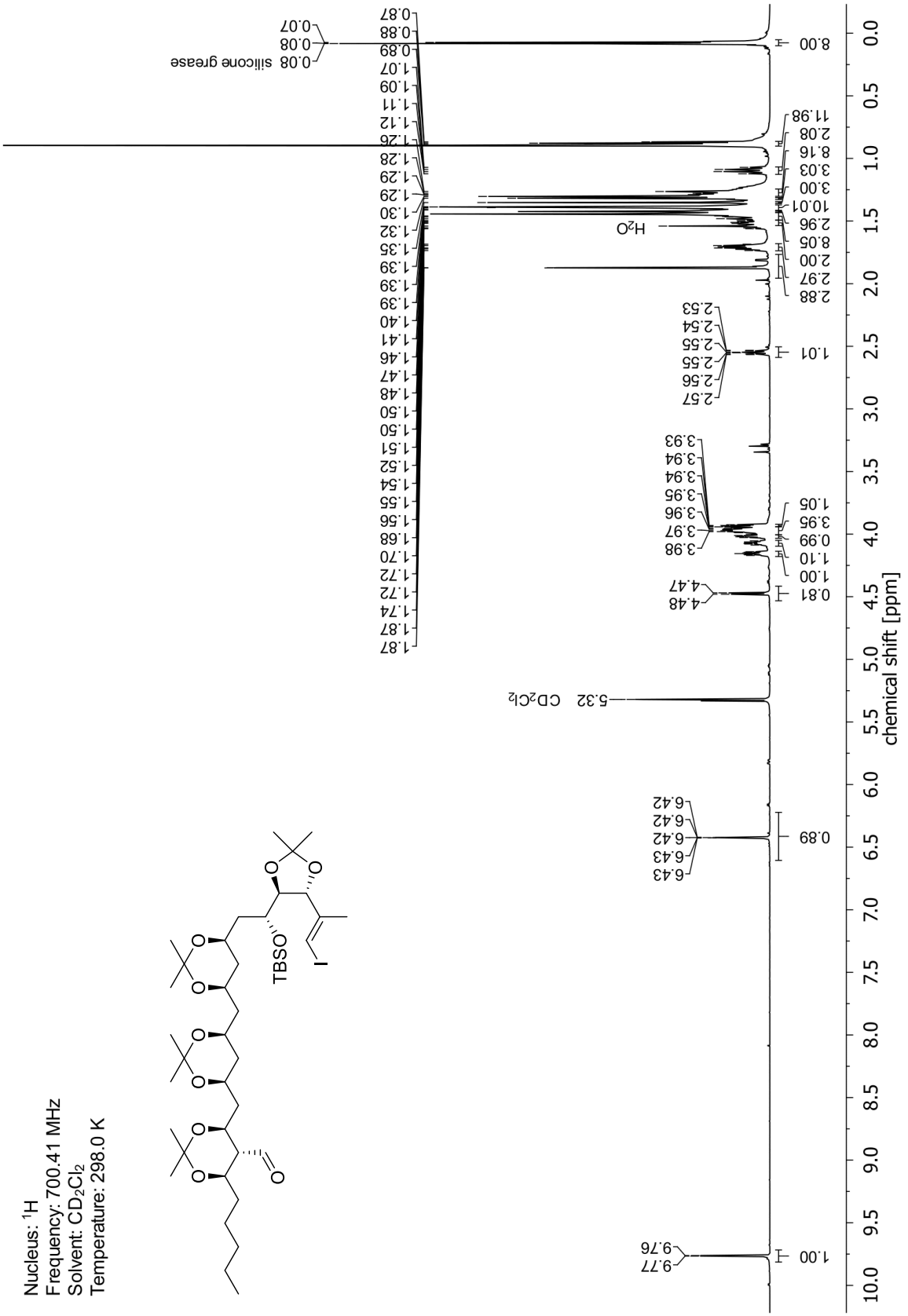

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TESO
TBSO
CD2Cl2
46.2
43.6
42.3
40.5
37.6
36.9
33.7
32.5
30.6
30.5
30.4
27.0
26.2
25.9
25.3
23.2
20.3
20.1
20.1
18.5
14.4
7.2
4.8
110.7
98.9
98.7
98.0
84.6
83.4
74.5
69.7
68.5
66.4
66.3
66.3
66.2
65.8
65.6
59.7
-4.1
-4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

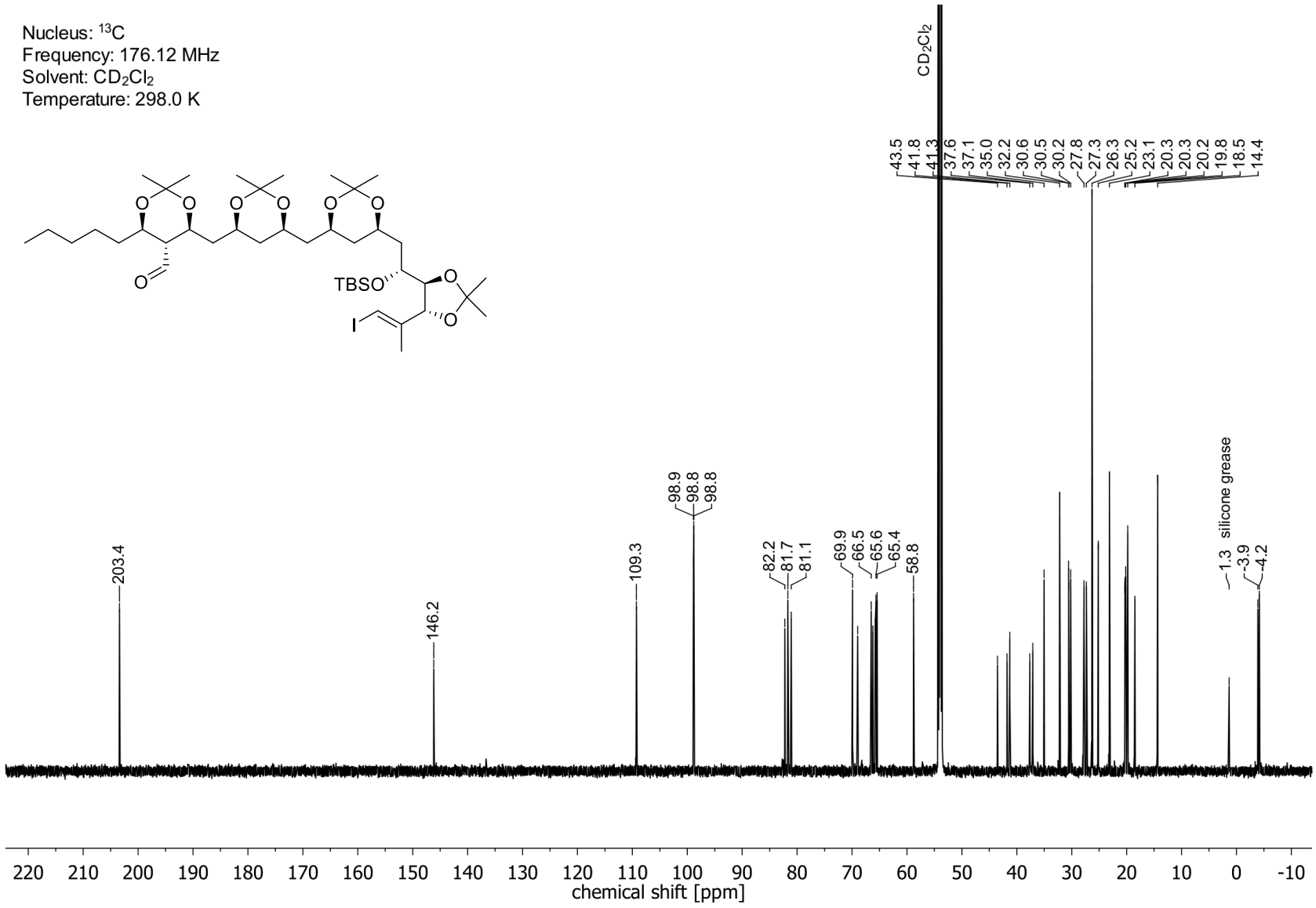
NMR-Spectra of Compound **296**:



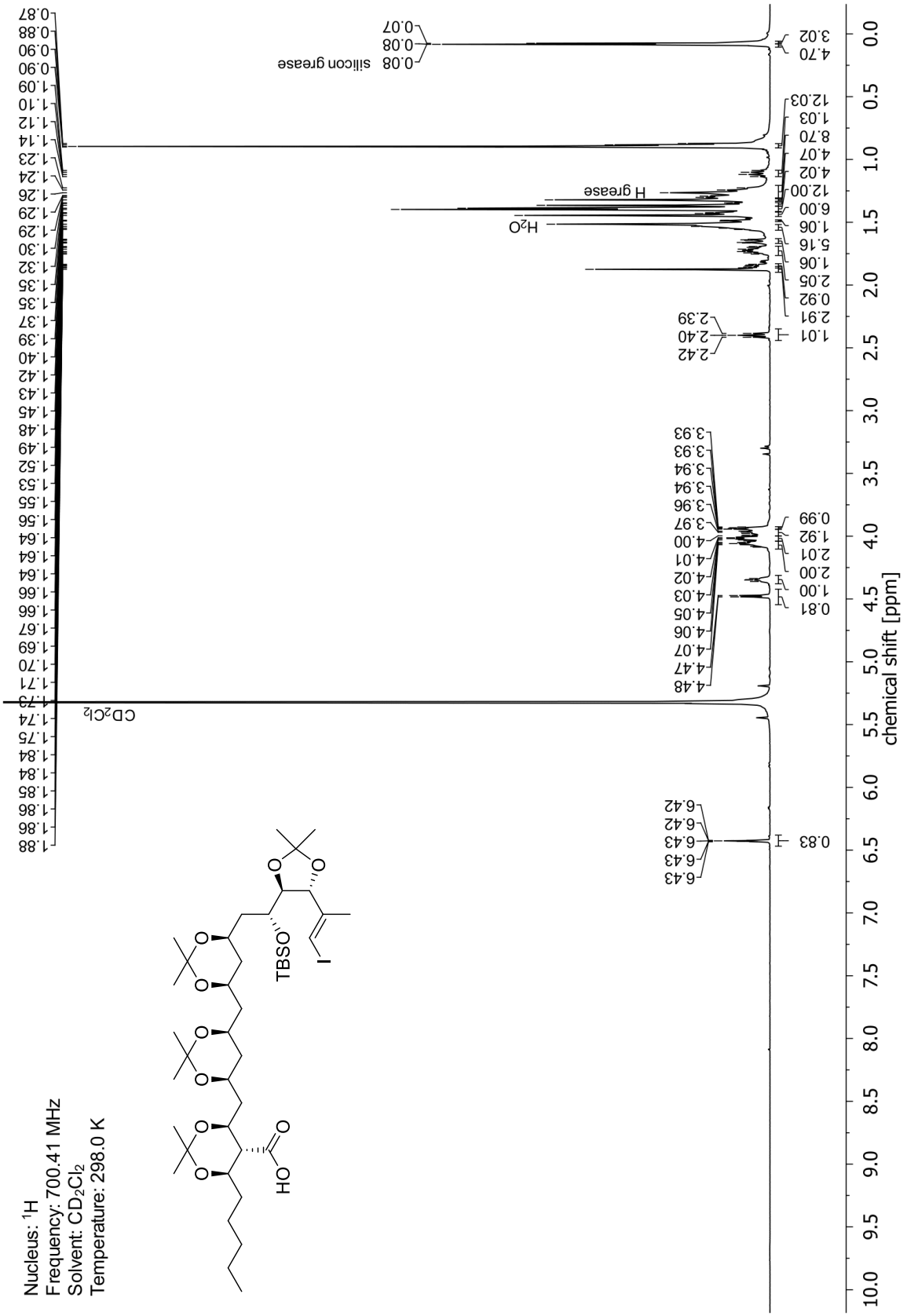

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
I
CD2Cl2
46.2
43.6
41.8
40.2
37.6
36.9
33.8
32.5
30.5
30.5
30.5
27.8
27.3
26.3
25.3
23.3
20.4
20.3
20.2
20.1
18.5
14.4
146.2
109.3
99.0
98.8
98.2
82.2
81.7
81.1
70.4
69.0
68.1
66.4
66.2
65.8
65.8
60.5
-3.9
-4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

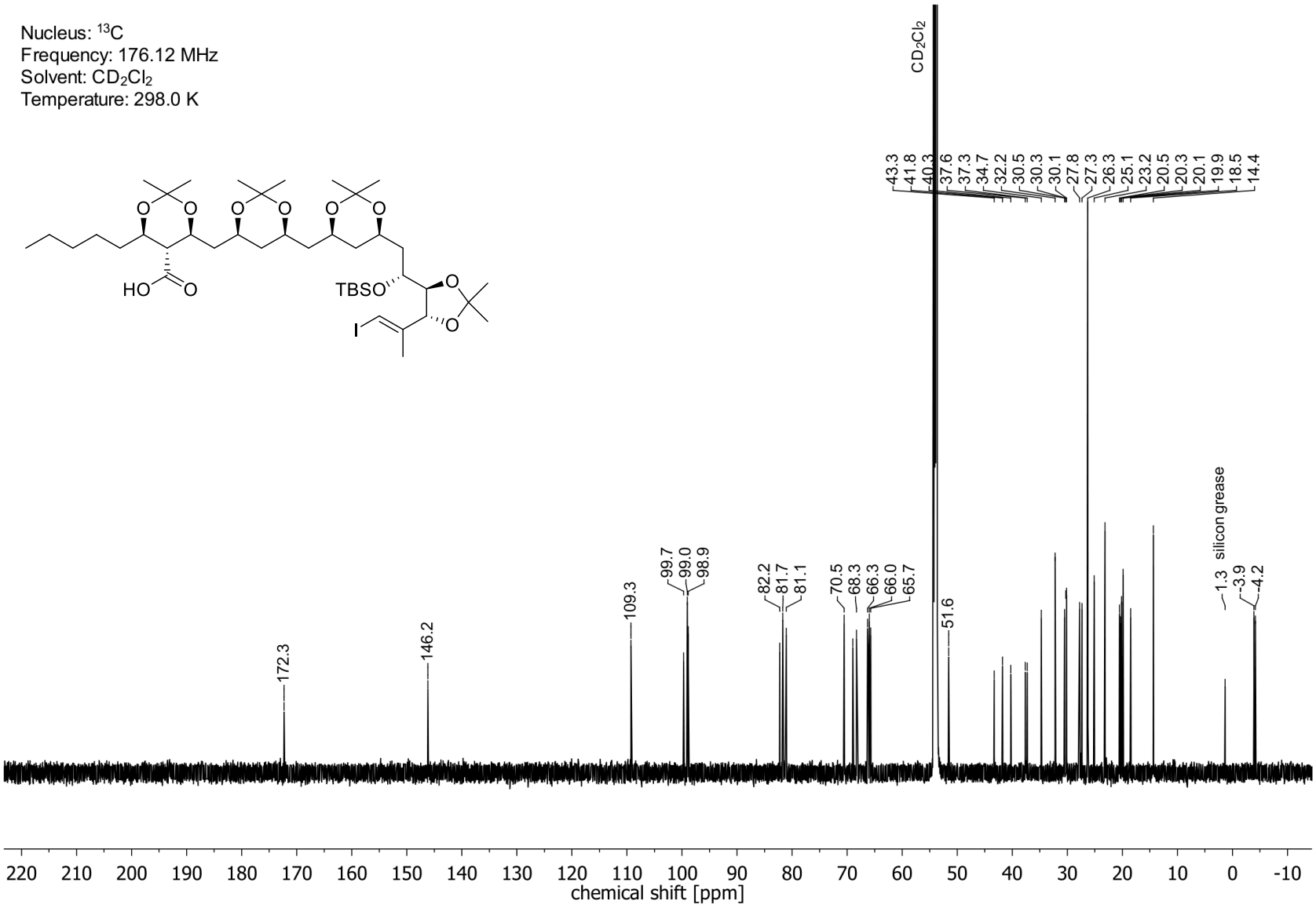
NMR-Spectra of Compound **337**:



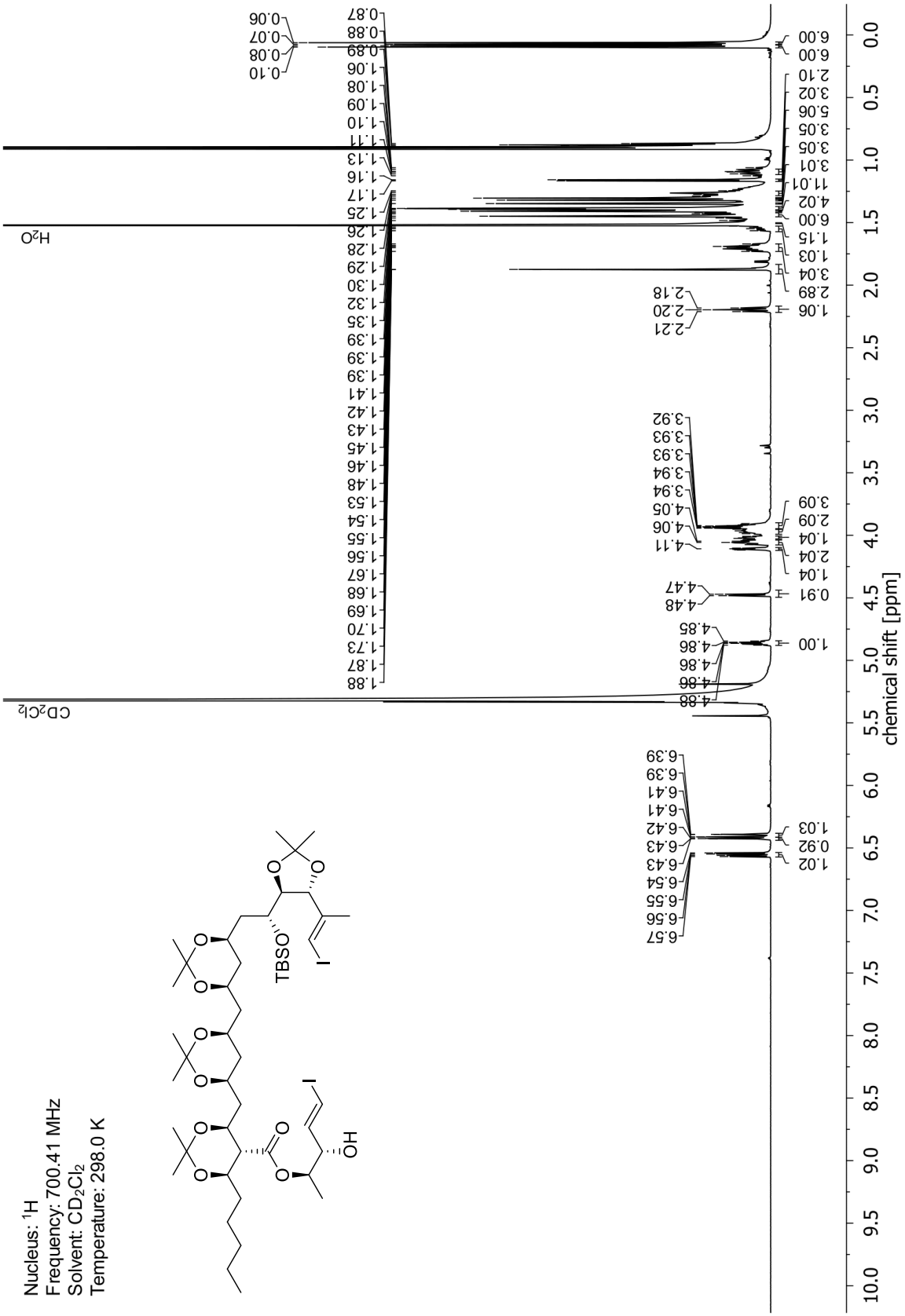

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
I
CD2Cl2
43.5
41.8
41.3
37.6
37.1
35.0
32.2
30.6
30.5
30.2
27.8
27.3
26.3
25.2
23.1
20.3
20.3
20.2
19.8
18.5
14.4
203.4
146.2
109.3
98.9
98.8
98.8
82.2
81.7
81.1
69.9
66.5
65.6
65.4
58.8
1.3 silicone grease
-3.9
-4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

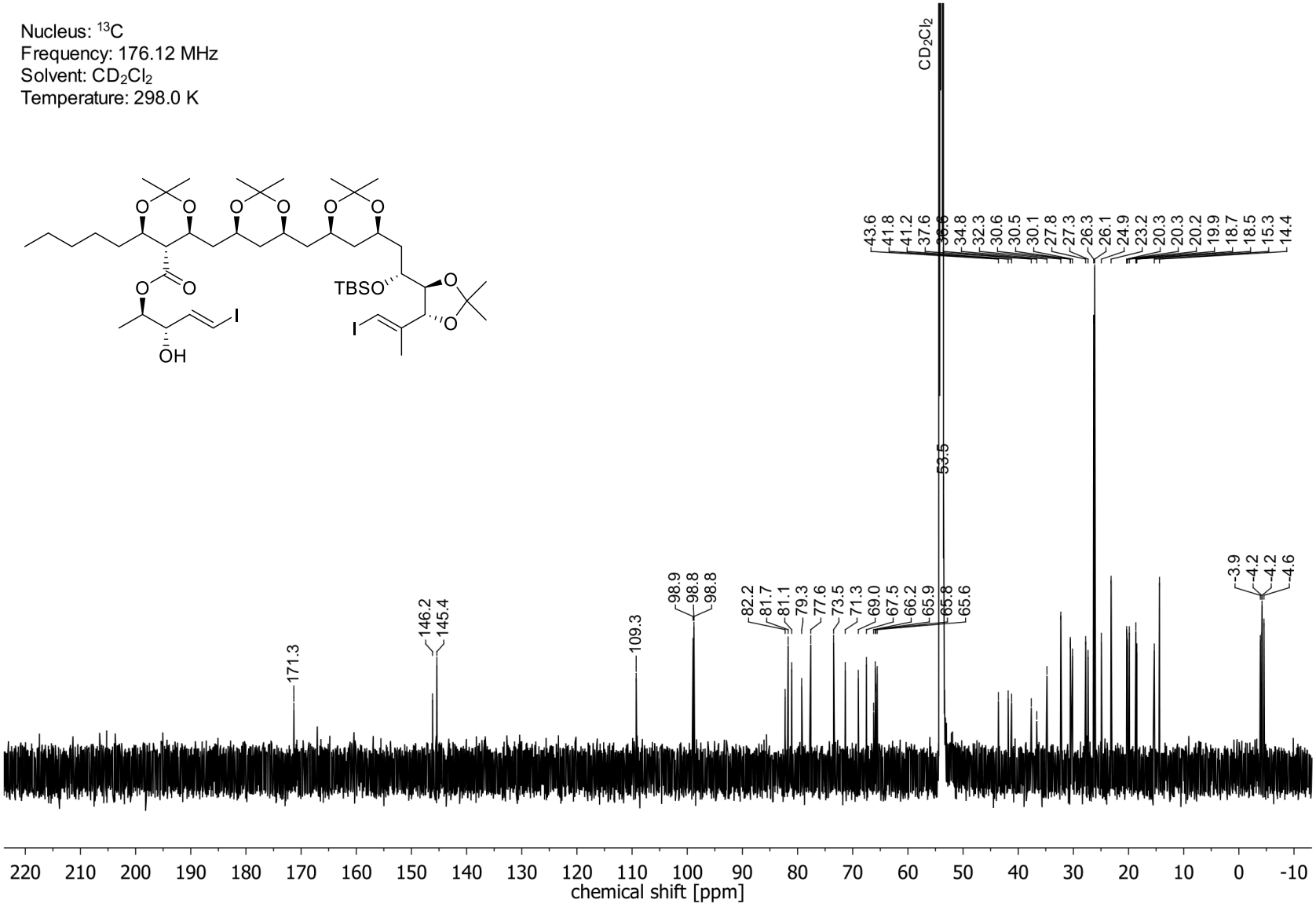
NMR-Spectra of Compound **152**:



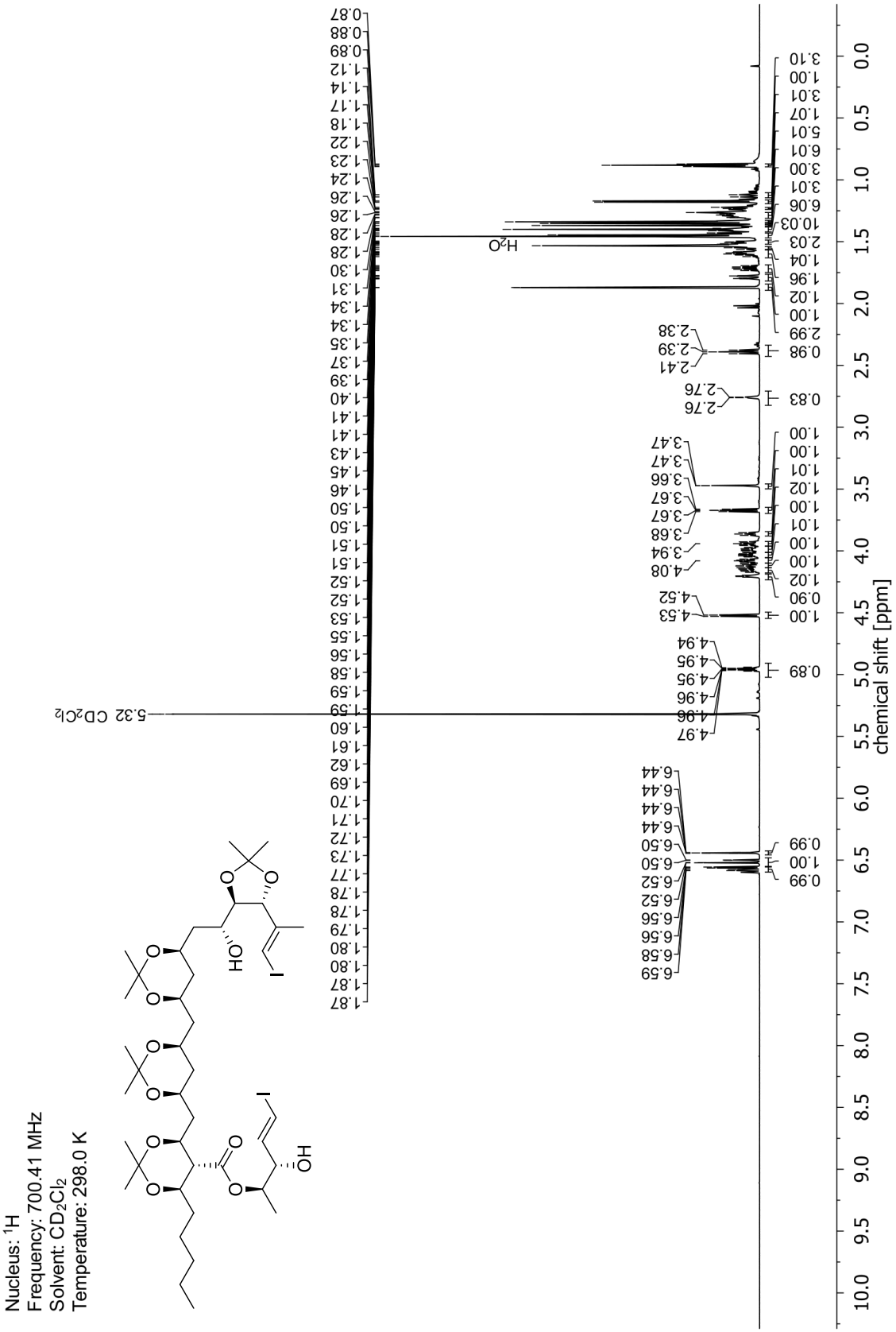

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
O
TBSO
O
O
O
O
O
O
O
O
O
I
CD2Cl2
43.3
41.8
40.3
37.6
37.3
34.7
32.2
30.5
30.3
30.1
27.8
27.3
26.3
25.1
23.2
20.5
20.3
20.1
19.9
18.5
14.4
172.3
146.2
109.3
99.7
99.0
98.9
82.2
81.7
81.1
70.5
68.3
66.3
66.0
65.7
51.6
1.3
silicon grease
-3.9
-4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

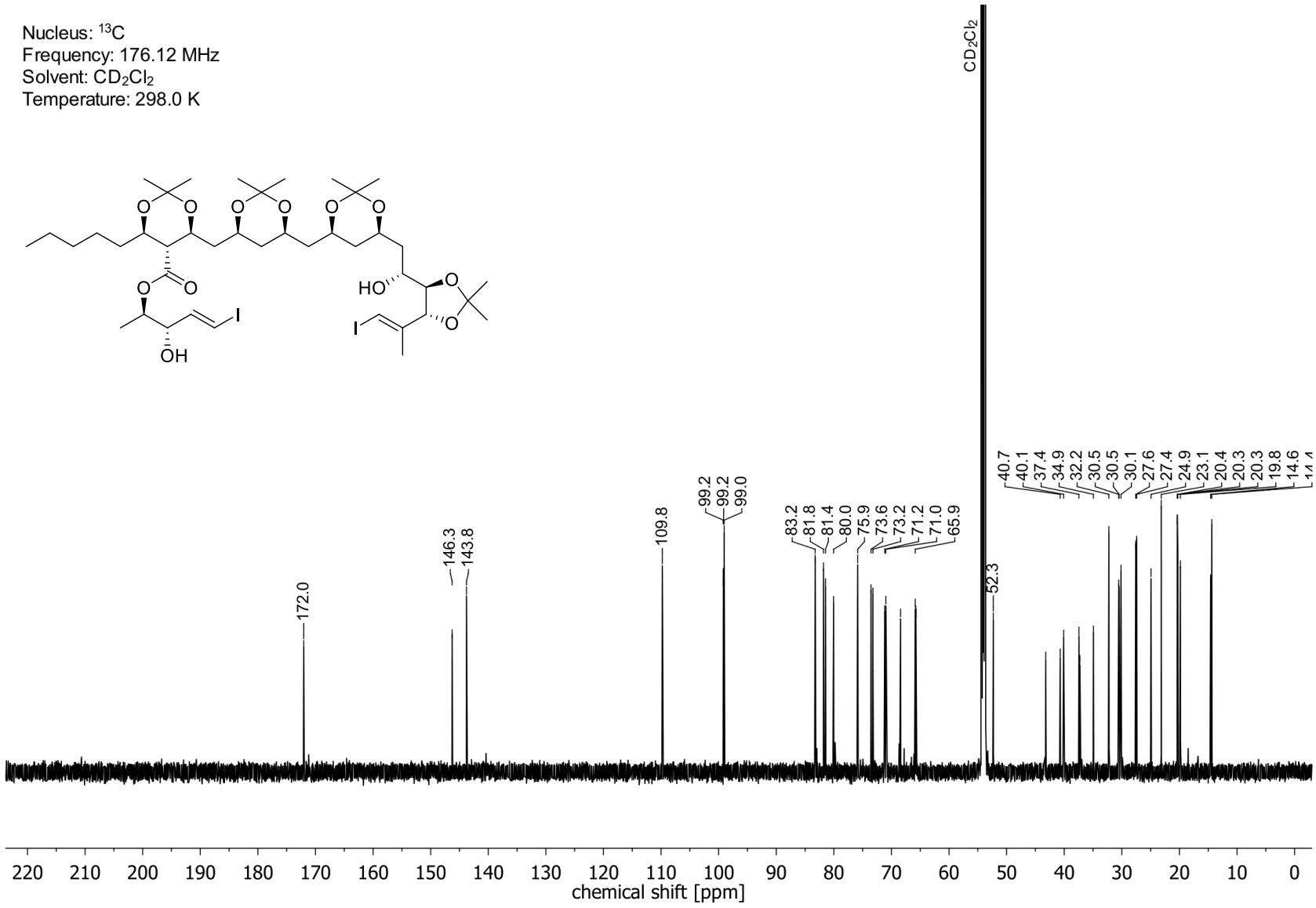
NMR-Spectra of Compound **150**:



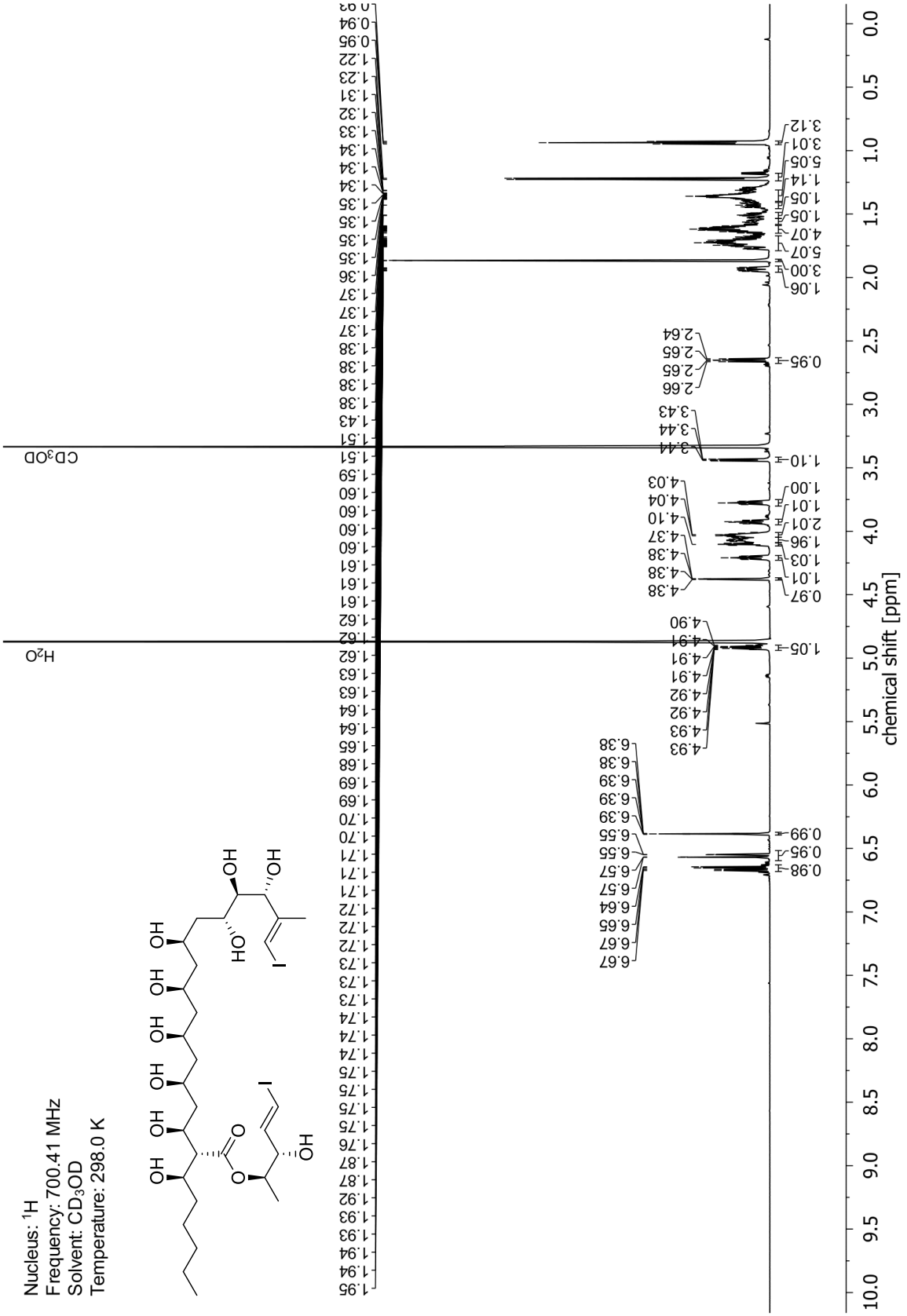

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
I
I
CD2Cl2
43.6
41.8
41.2
37.6
36.8
34.8
32.3
30.6
30.5
30.1
27.8
27.3
26.3
26.1
24.9
23.2
20.3
20.3
20.2
19.9
18.7
18.5
15.3
14.4
53.5
171.3
146.2
145.4
109.3
98.9
98.8
98.8
82.2
81.7
81.1
79.3
77.6
73.5
71.3
69.0
67.5
66.2
65.9
65.8
65.6
-3.9
-4.2
-4.2
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

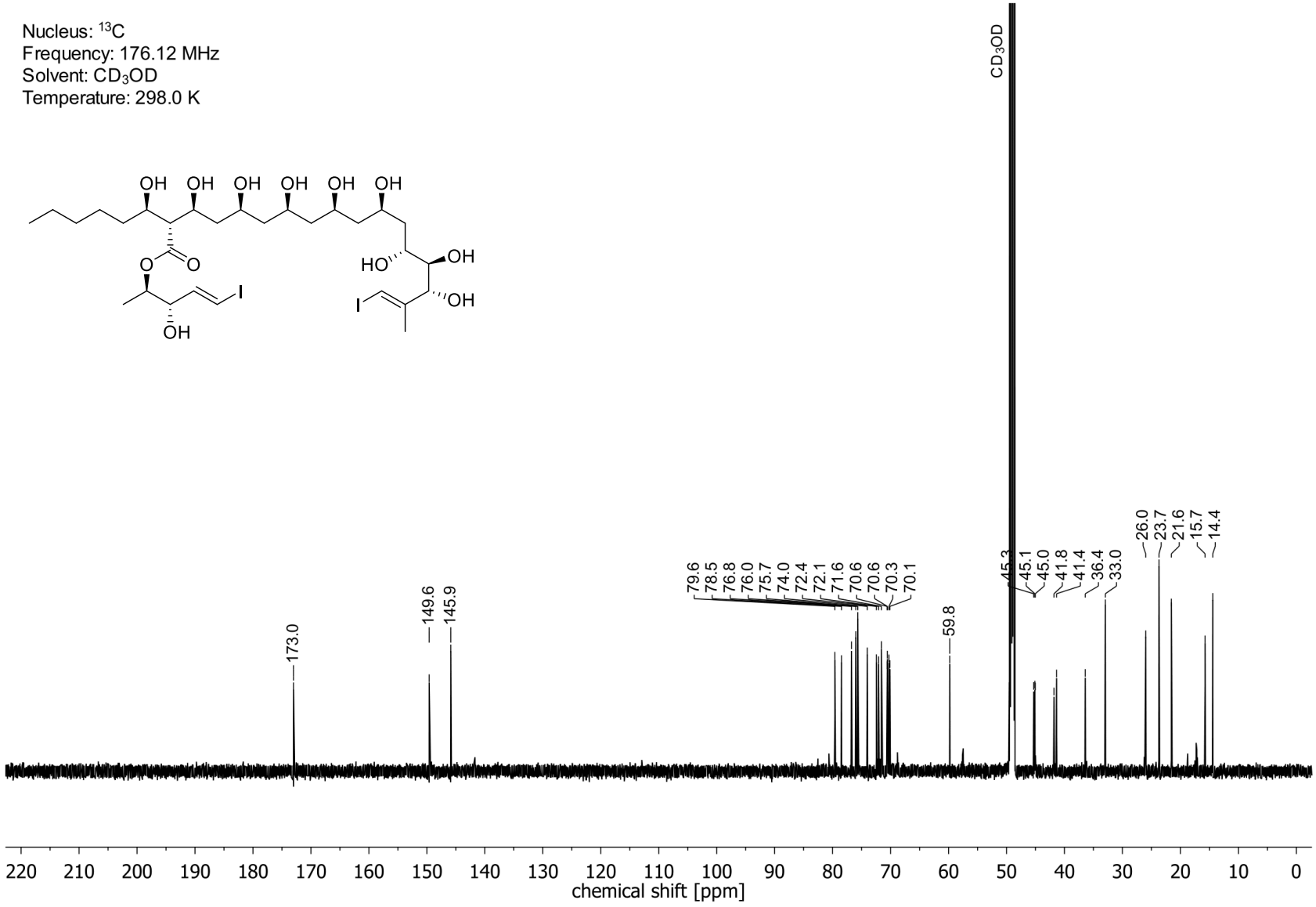
NMR-Spectra of Compound **308**:



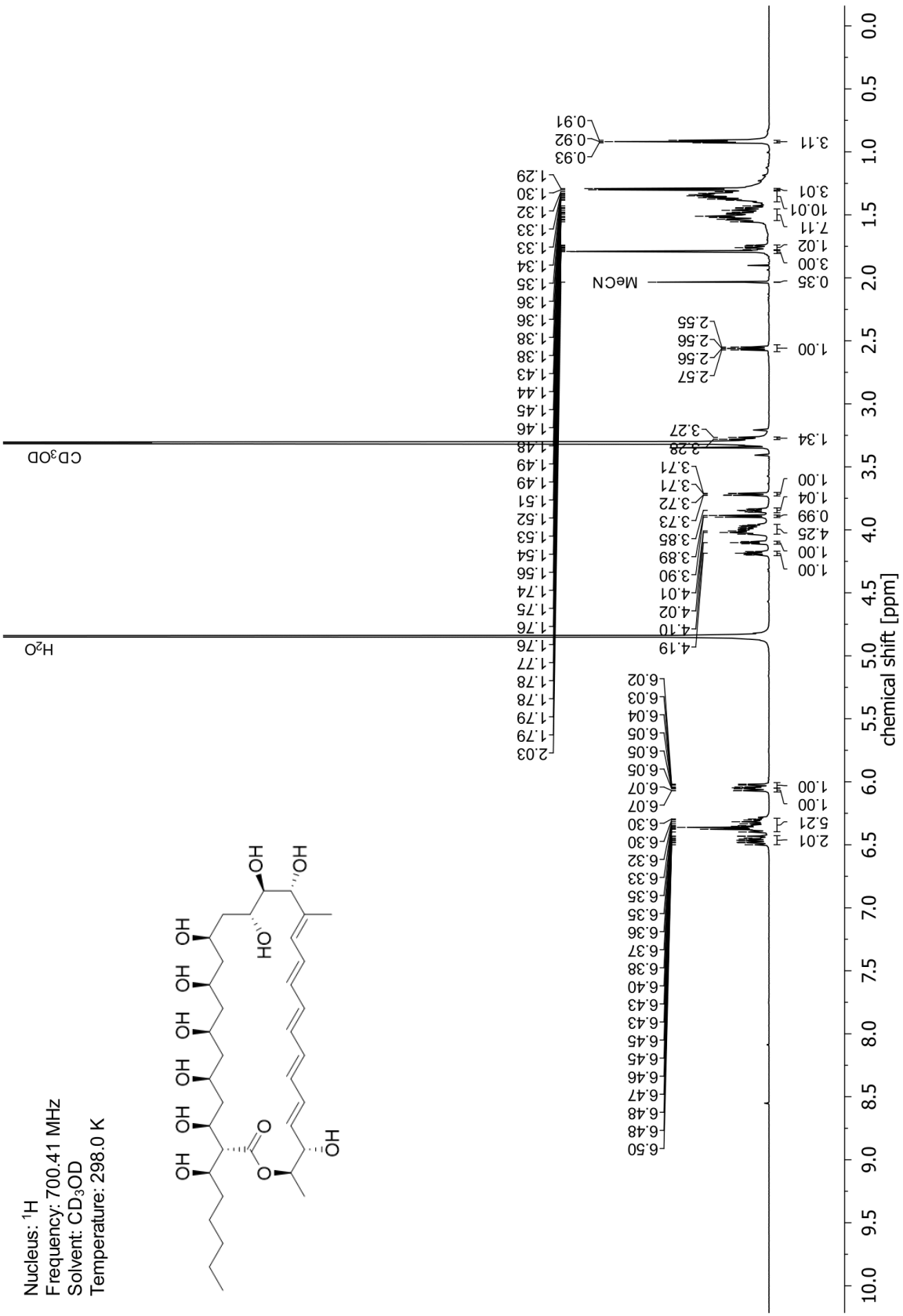

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
CD2Cl2
172.0
146.3
143.8
109.8
99.2
99.2
99.0
83.2
81.8
81.4
80.0
75.9
73.6
73.2
71.2
71.0
65.9
52.3
40.7
40.1
37.4
34.9
32.2
30.5
30.5
30.1
27.6
27.4
24.9
23.1
20.4
20.3
20.3
19.8
14.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

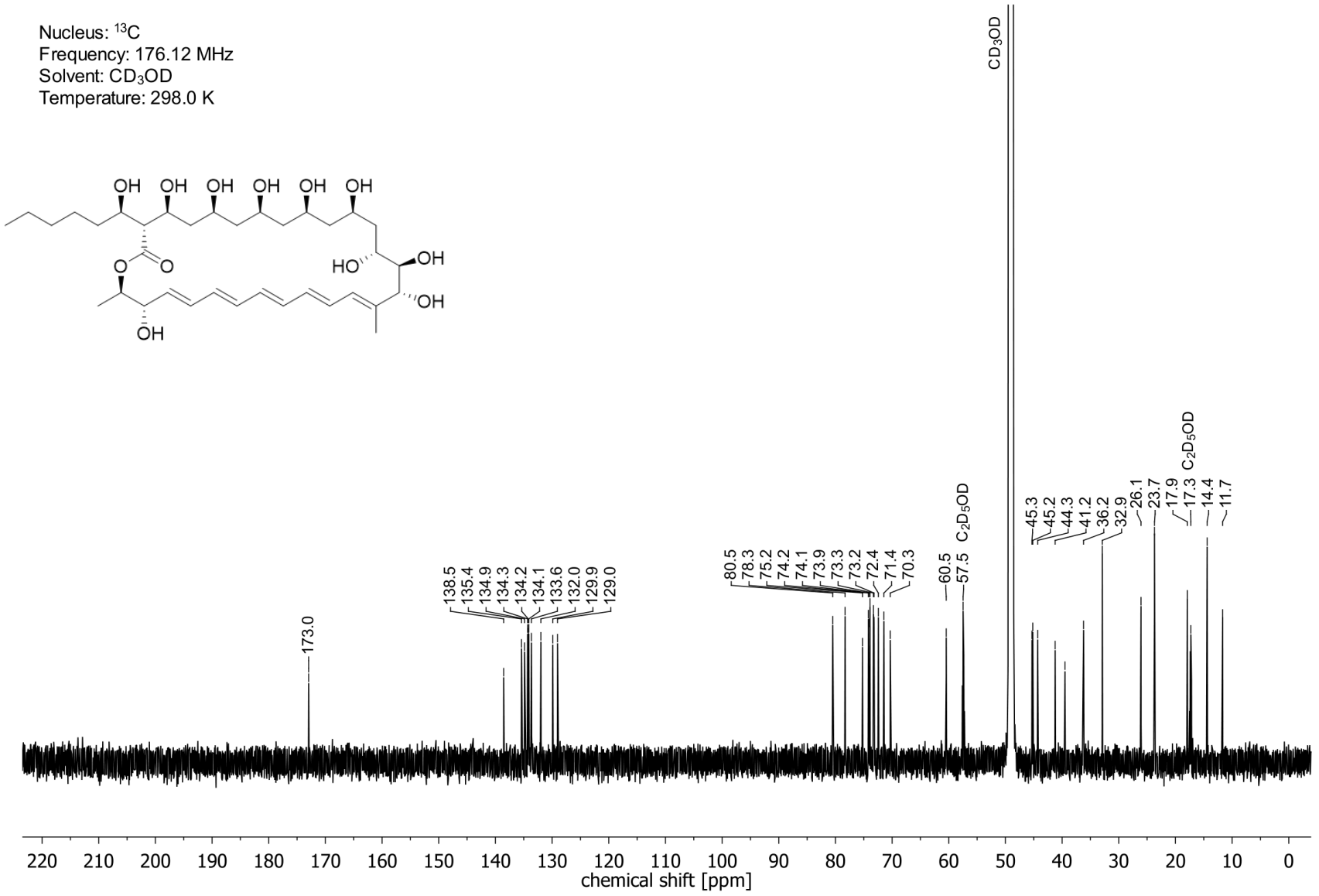
NMR-Spectra of Compound **147**:



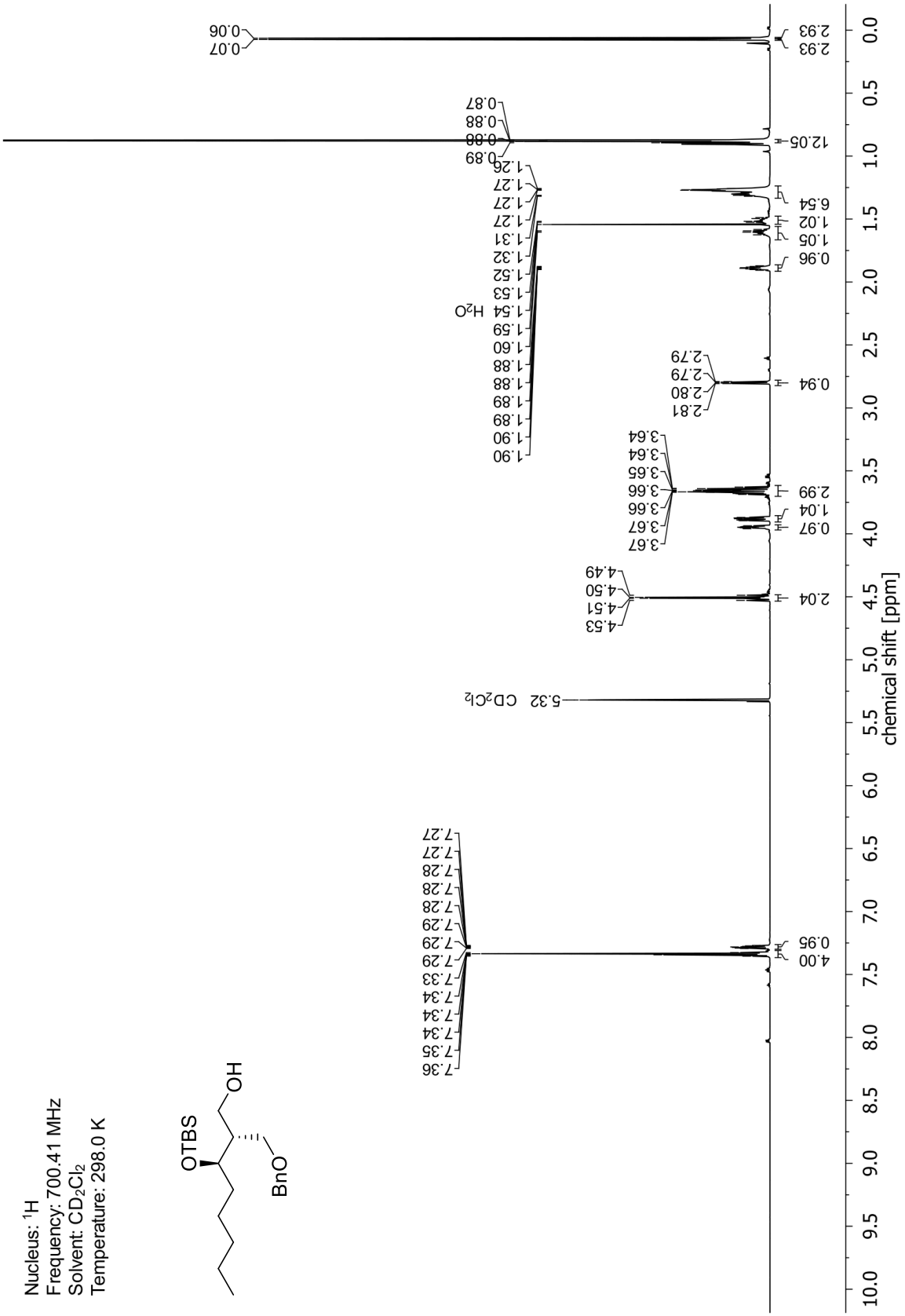

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD3OD
Temperature: 298.0 K
OH OH OH OH OH OH
O O
HO OH
OH
I
I
OH
CD3OD
173.0
149.6
145.9
79.6
78.5
76.8
76.0
75.7
74.0
72.4
72.1
71.6
70.6
70.6
70.3
70.1
59.8
45.3
45.1
45.0
41.8
41.4
36.4
33.0
26.0
23.7
21.6
15.7
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

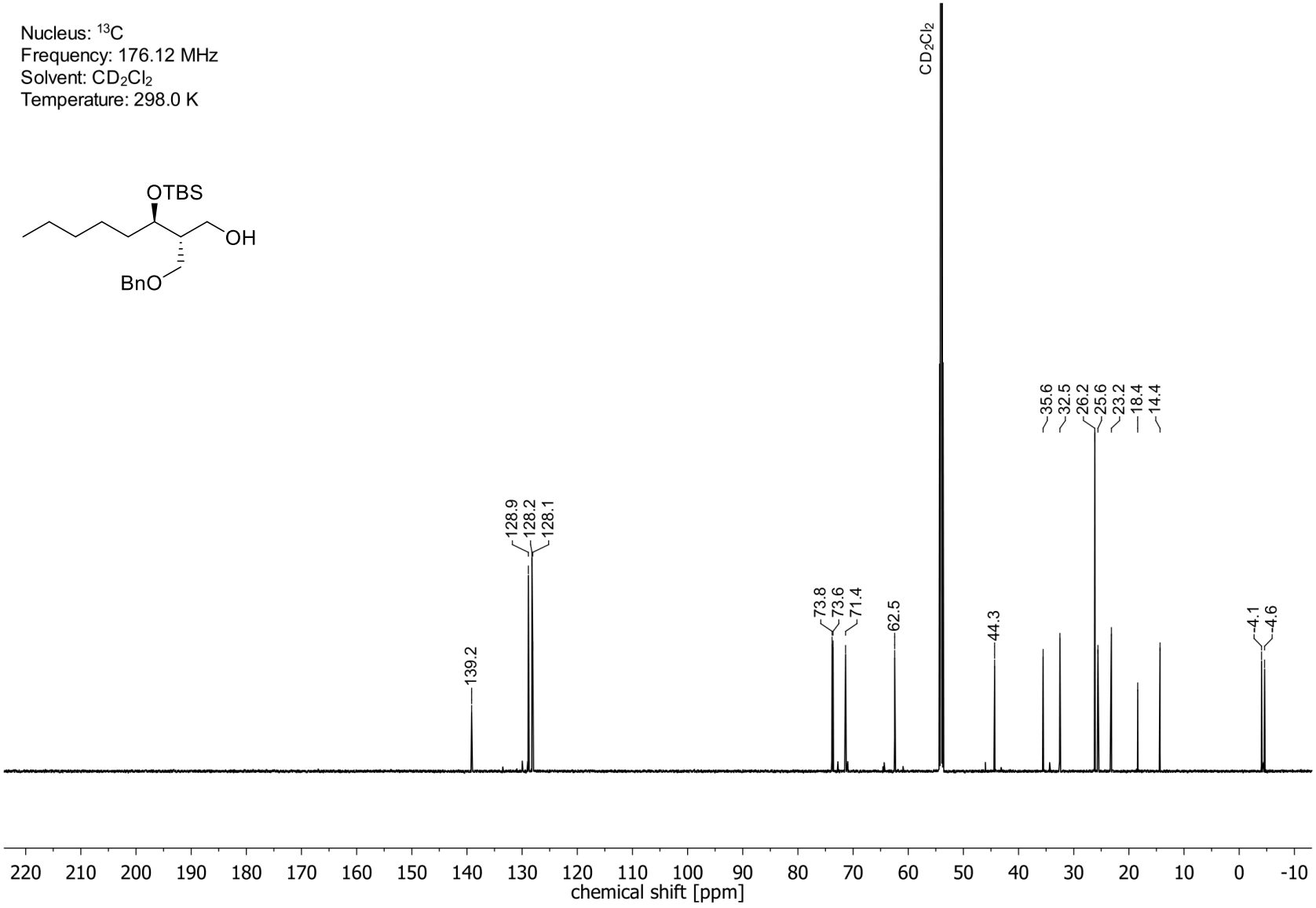
NMR-Spectra of Pentamycin (**10**):



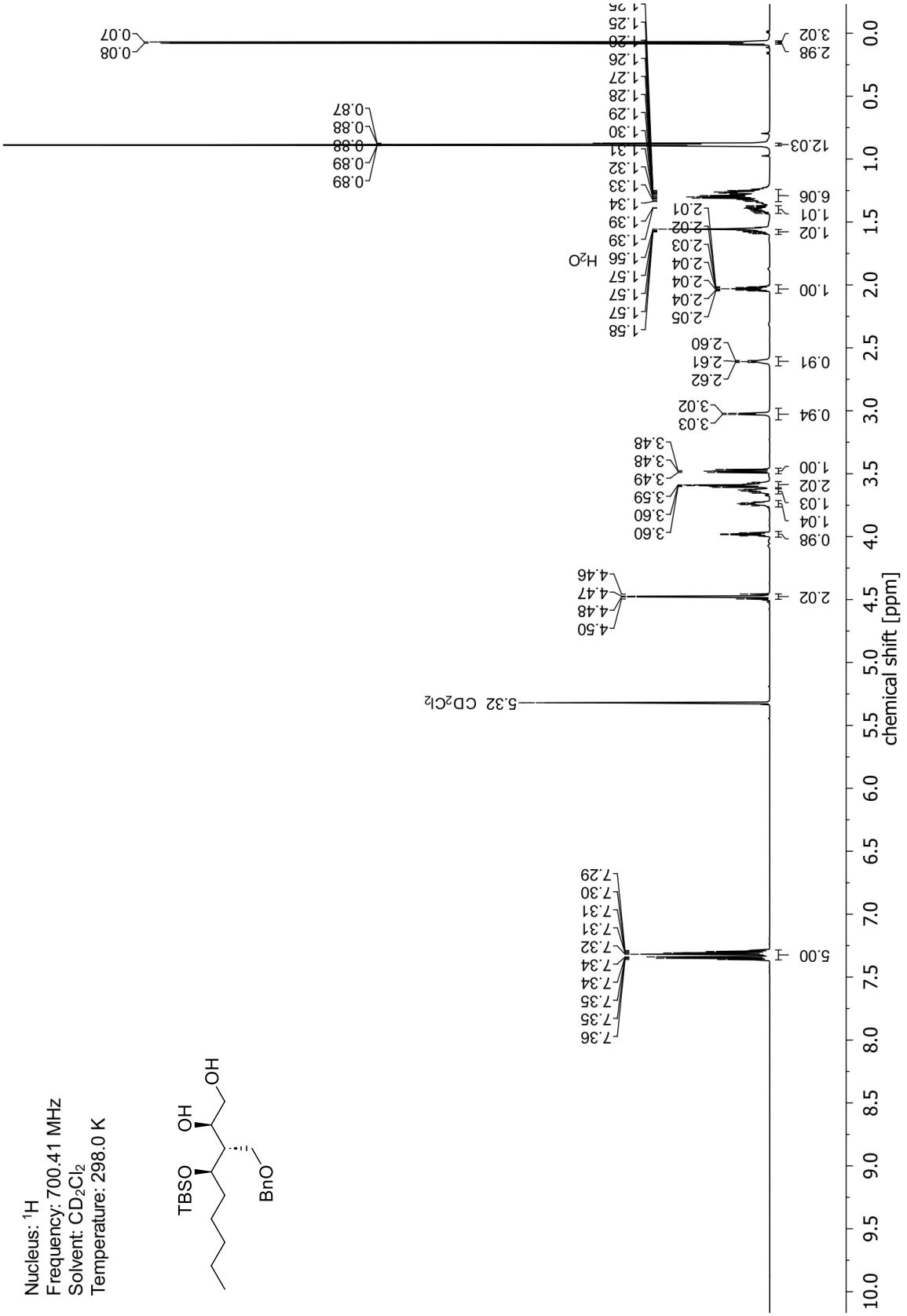

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD3OD
Temperature: 298.0 K
OH OH OH OH OH OH
O O
HO
OH
OH
OH
CD3OD
C2D5OD
C2D5OD
173.0
138.5
135.4
134.9
134.3
134.2
134.1
133.6
132.0
129.9
129.0
80.5
78.3
75.2
74.2
74.1
73.9
73.3
73.2
72.4
71.4
70.3
60.5
57.5
45.3
45.2
44.3
41.2
36.2
32.9
26.1
23.7
17.9
17.3
14.4
11.7
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

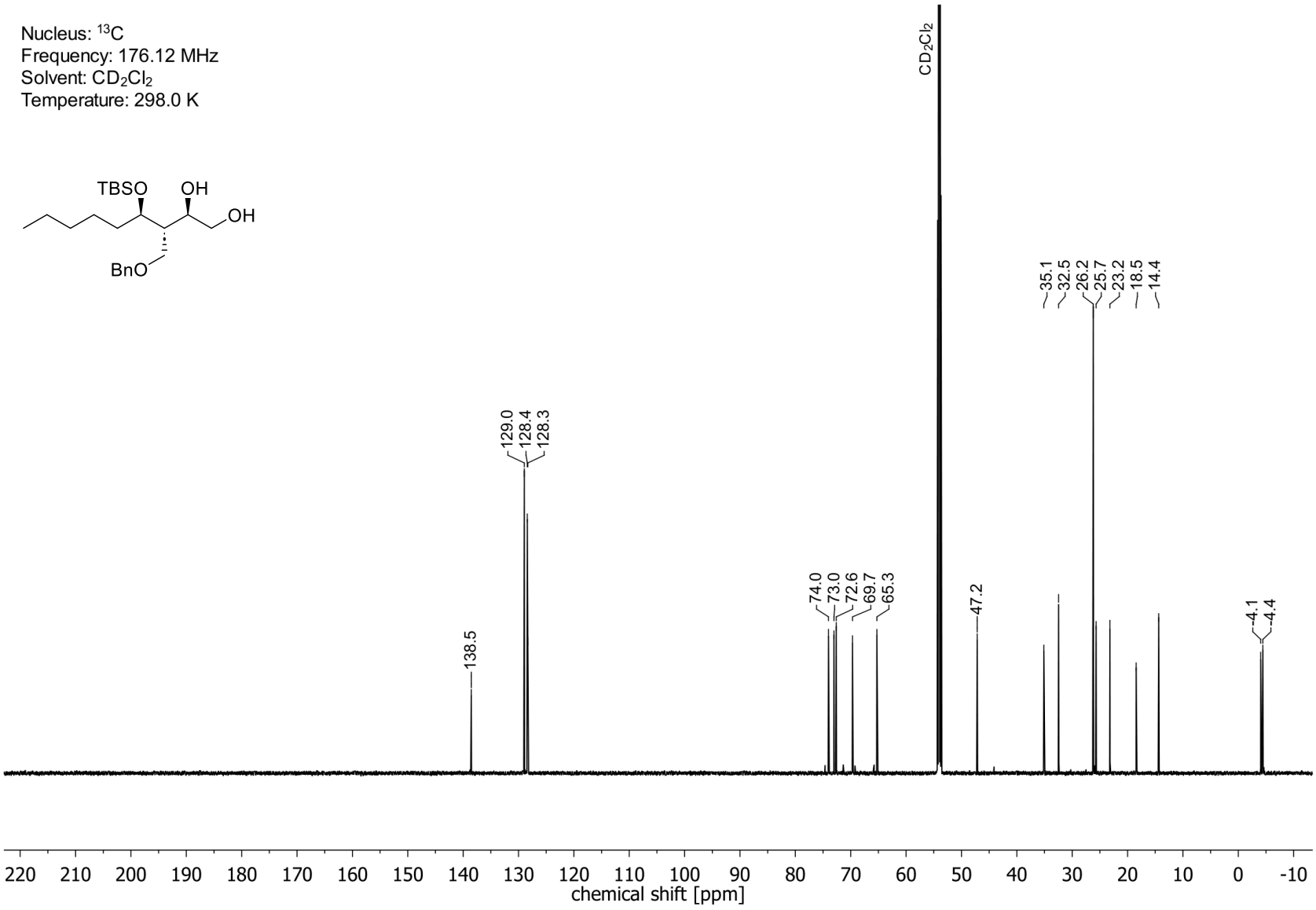
NMR-Spectra of Compound **240**:

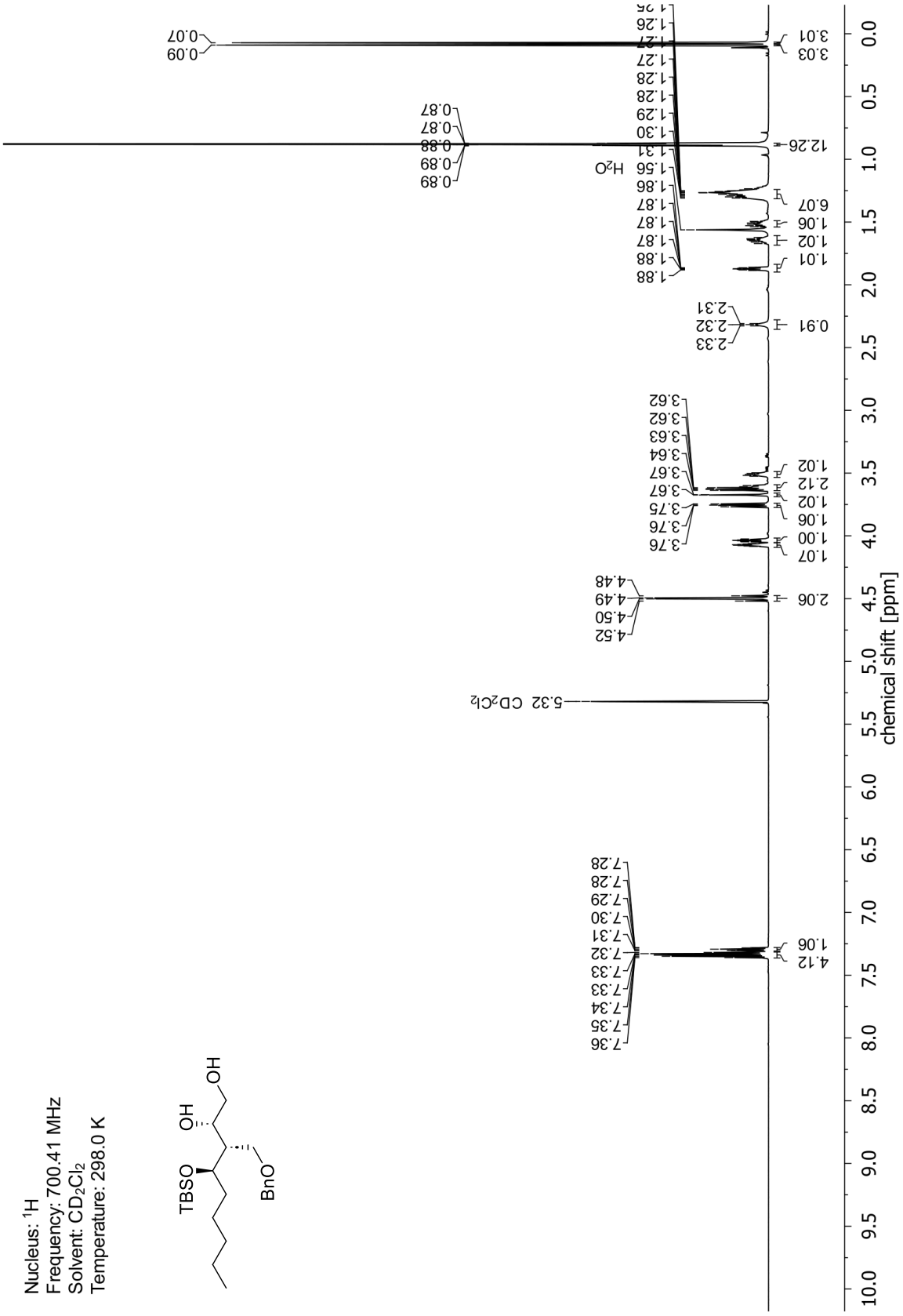


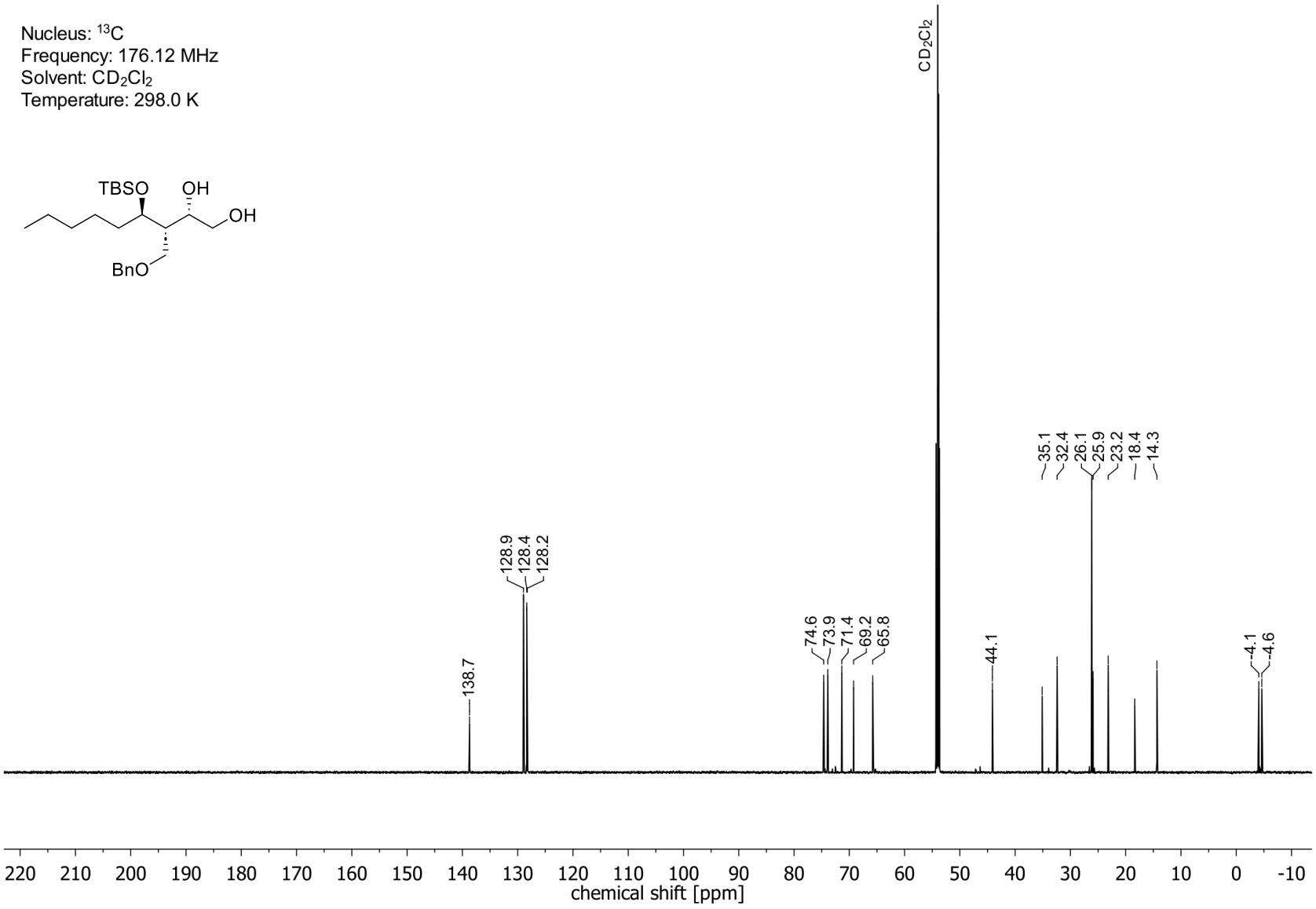

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
OTBS
OH
BnO
CD2Cl2
35.6
32.5
26.2
25.6
23.2
18.4
14.4
128.9
128.2
128.1
73.8
73.6
71.4
62.5
44.3
139.2
-4.1
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **243**:

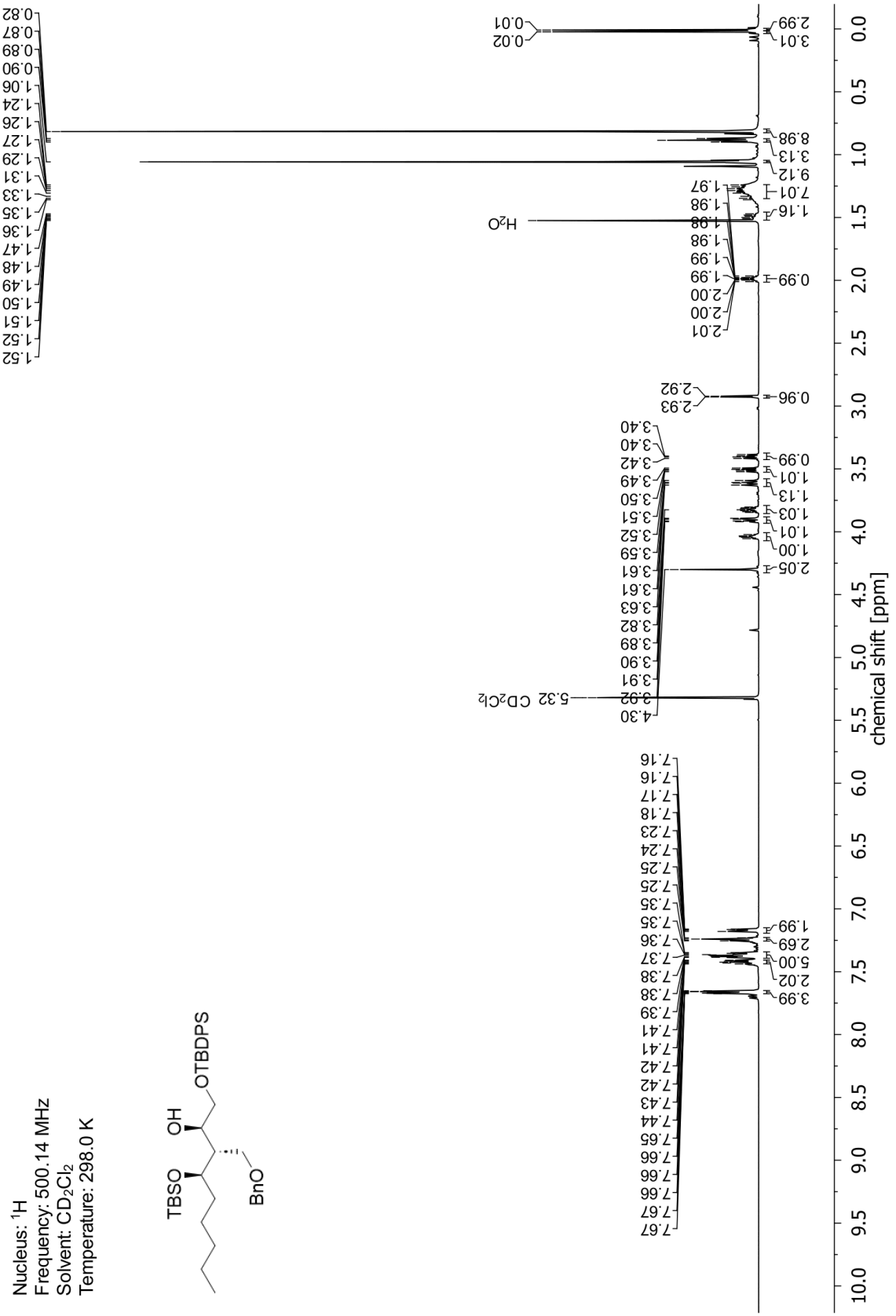


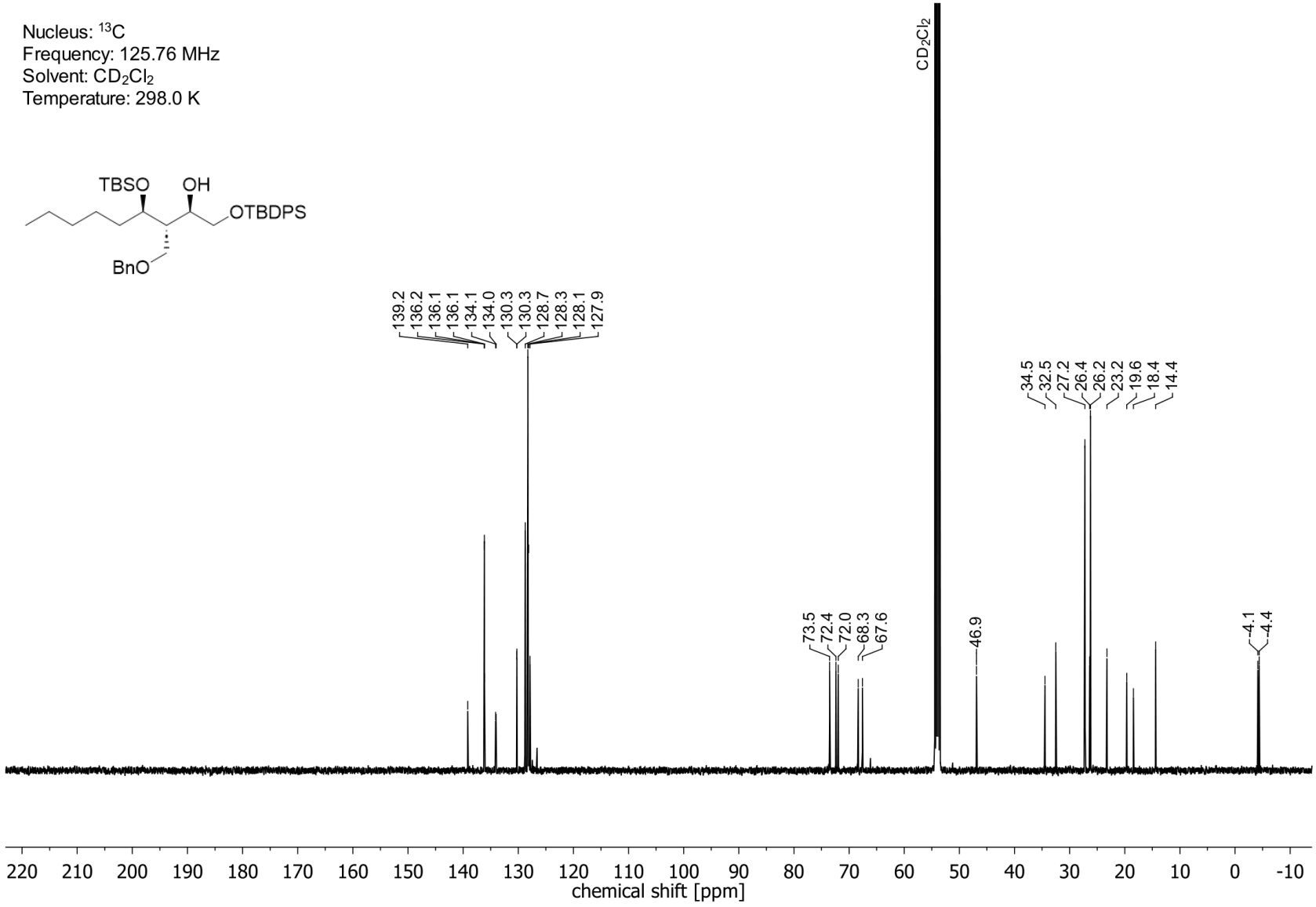

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
OH
BnO
CD2Cl2
35.1
32.5
26.2
25.7
23.2
18.5
14.4
129.0
128.4
128.3
74.0
73.0
72.6
69.7
65.3
47.2
138.5
-4.1
-4.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]


Nucleus: 1H
Frequency: 700.41 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
OH
BnO
chemical shift [ppm]
5.32 CD2Cl2
H2O

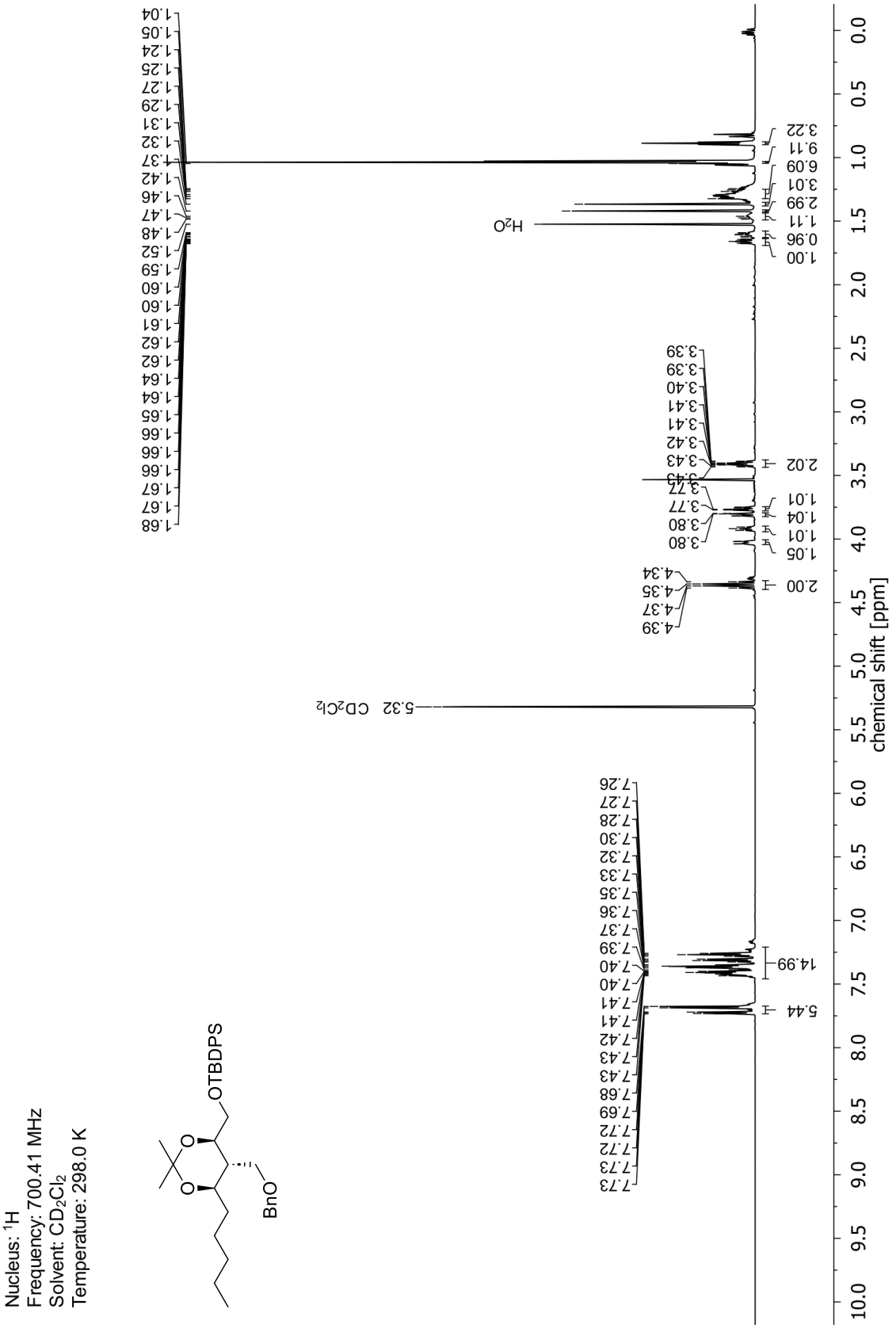

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
OH
BnO
CD2Cl2
35.1
32.4
26.1
25.9
23.2
18.4
14.3
128.9
128.4
128.2
74.6
73.9
71.4
69.2
65.8
138.7
44.1
-4.1
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

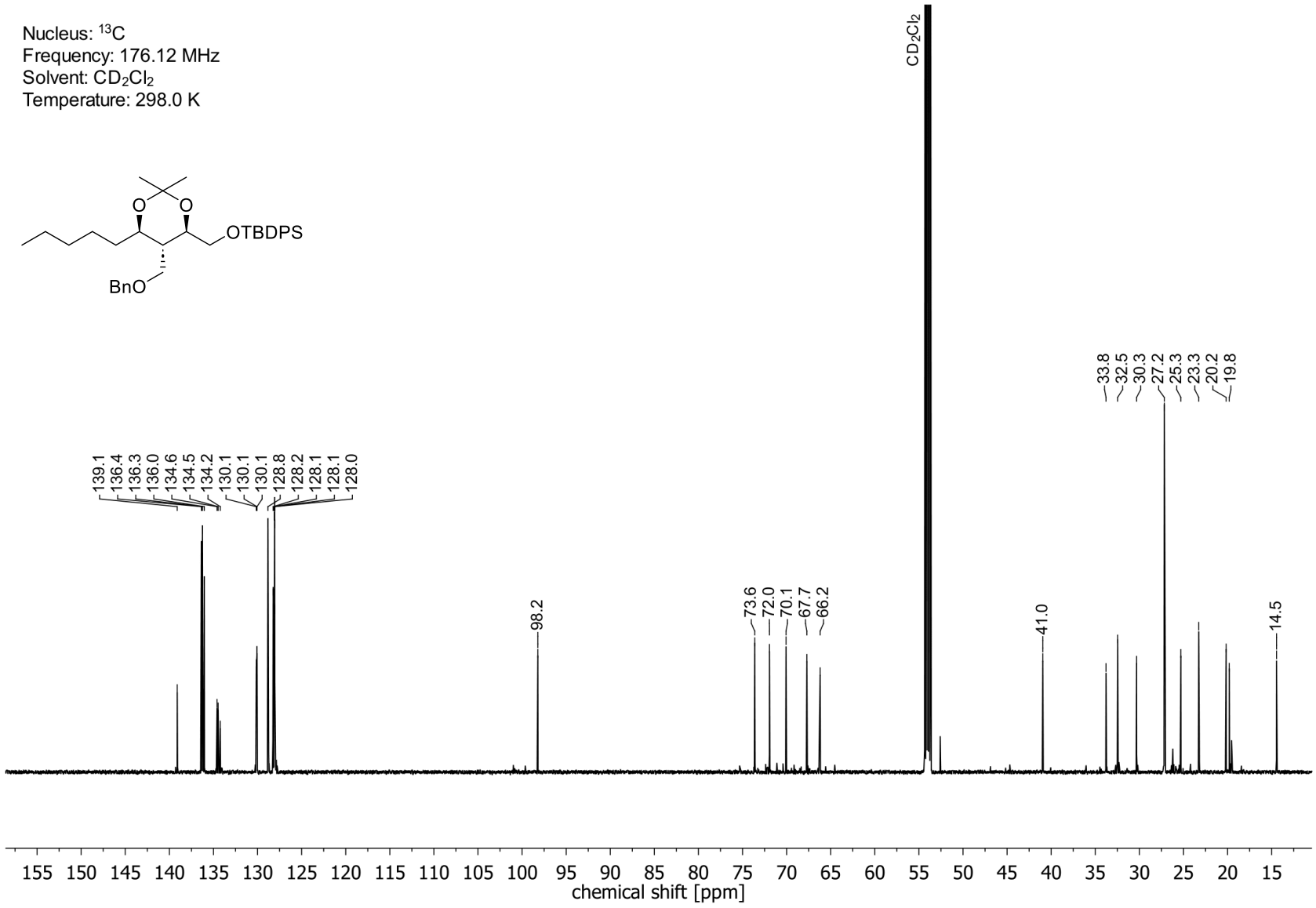
NMR-Spectra of Compound **244**:



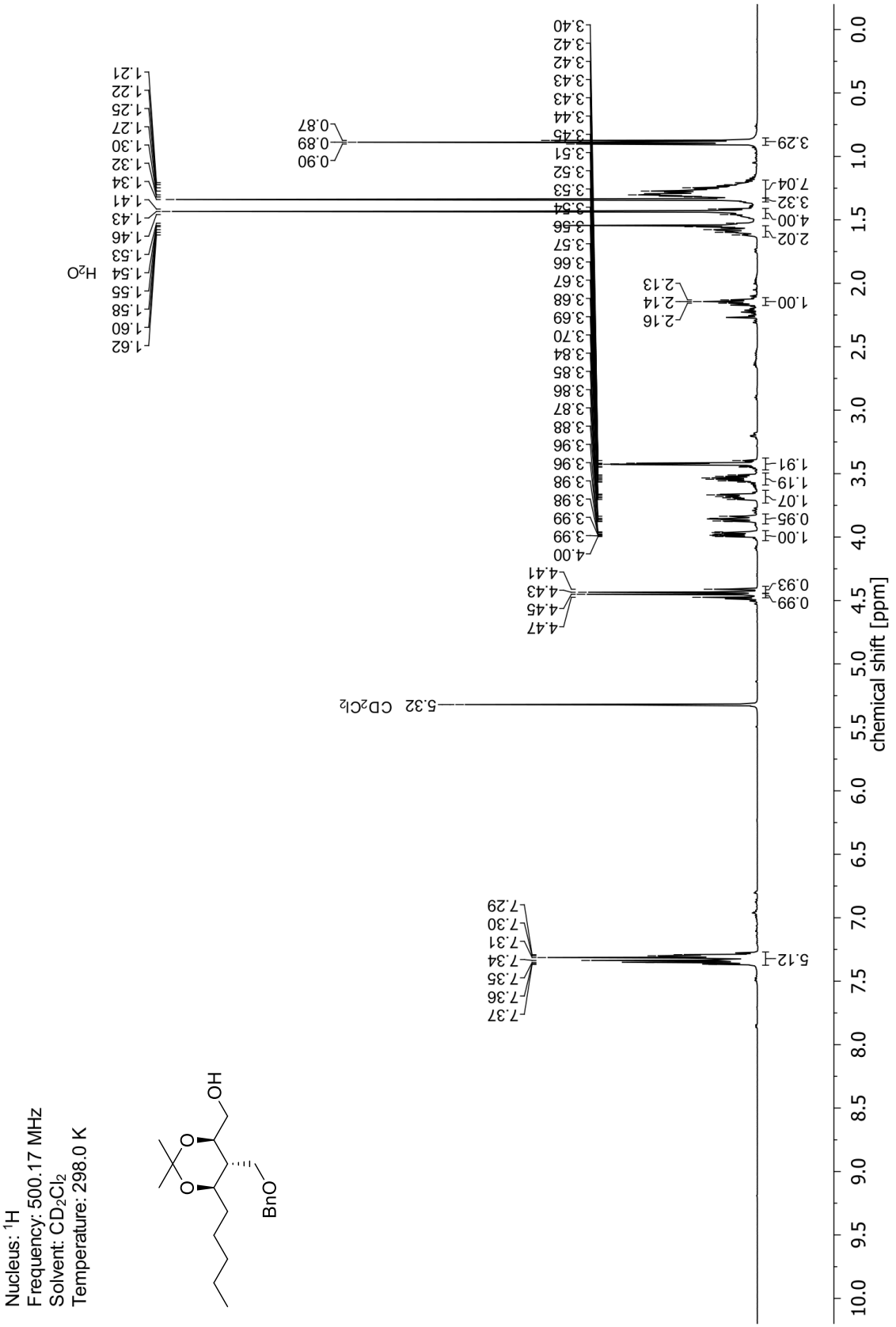

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
OTBDPS
BnO
CD2Cl2
139.2
136.2
136.1
136.1
134.1
134.0
130.3
130.3
128.7
128.3
128.1
127.9
73.5
72.4
72.0
68.3
67.6
46.9
34.5
32.5
27.2
26.4
26.2
23.2
19.6
18.4
14.4
-4.1
-4.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

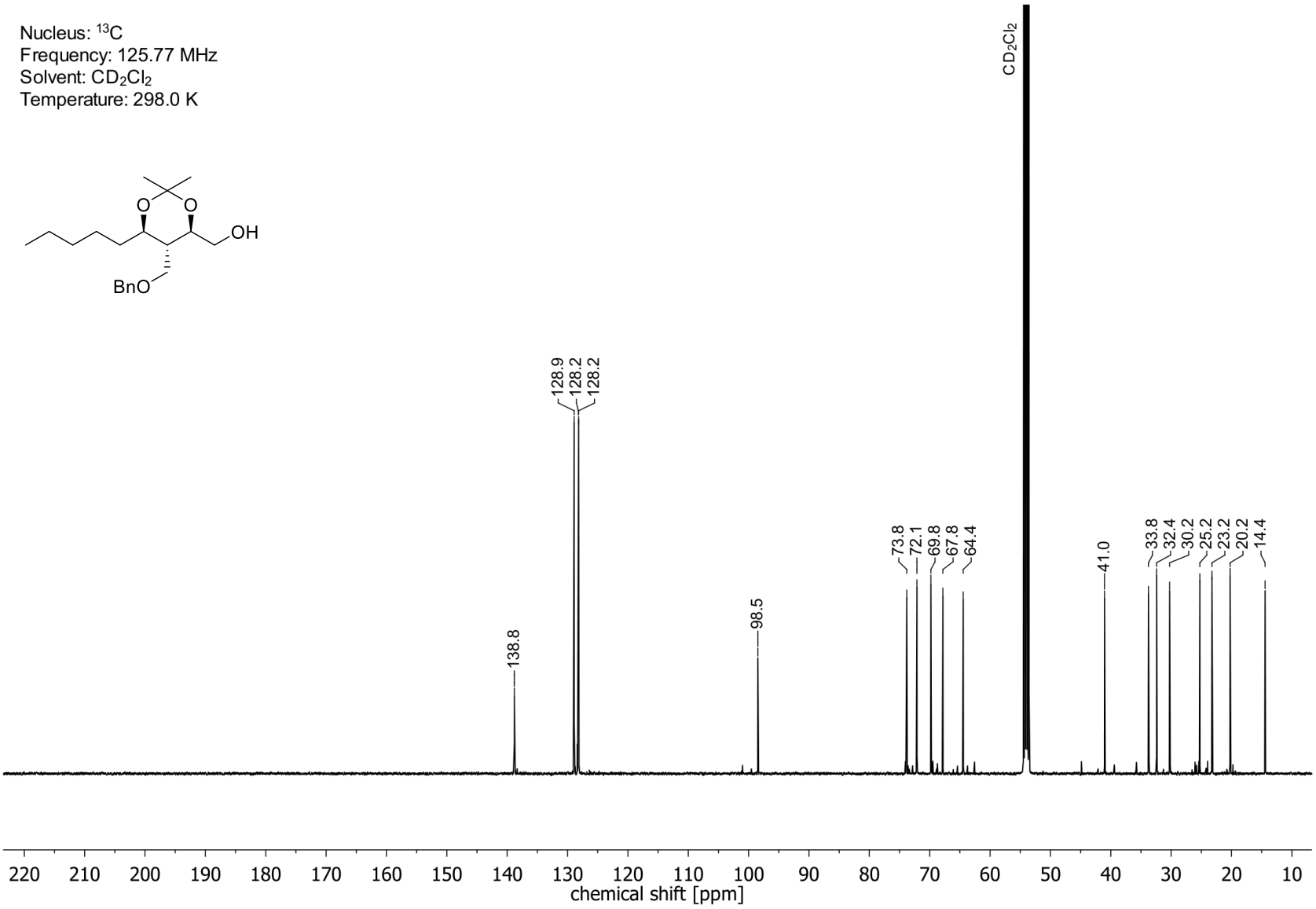
NMR-Spectra of Compound **245**:



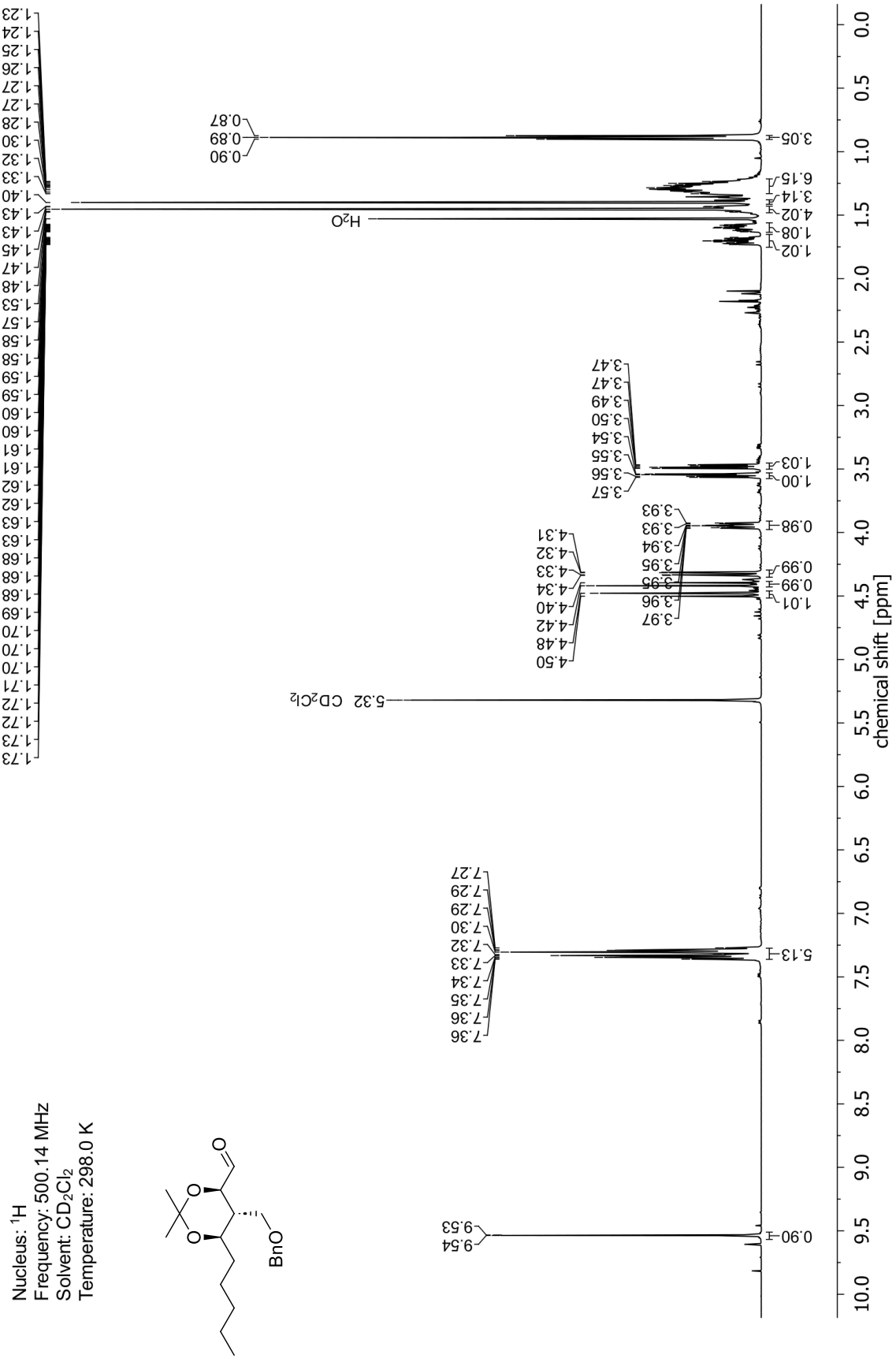

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OTBDPS
BnO
CD2Cl2
33.8
32.5
30.3
27.2
25.3
23.3
20.2
19.8
139.1
136.4
136.3
136.0
134.6
134.5
134.2
130.1
130.1
130.1
128.8
128.2
128.1
128.1
128.0
98.2
73.6
72.0
70.1
67.7
66.2
41.0
14.5
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
chemical shift [ppm]

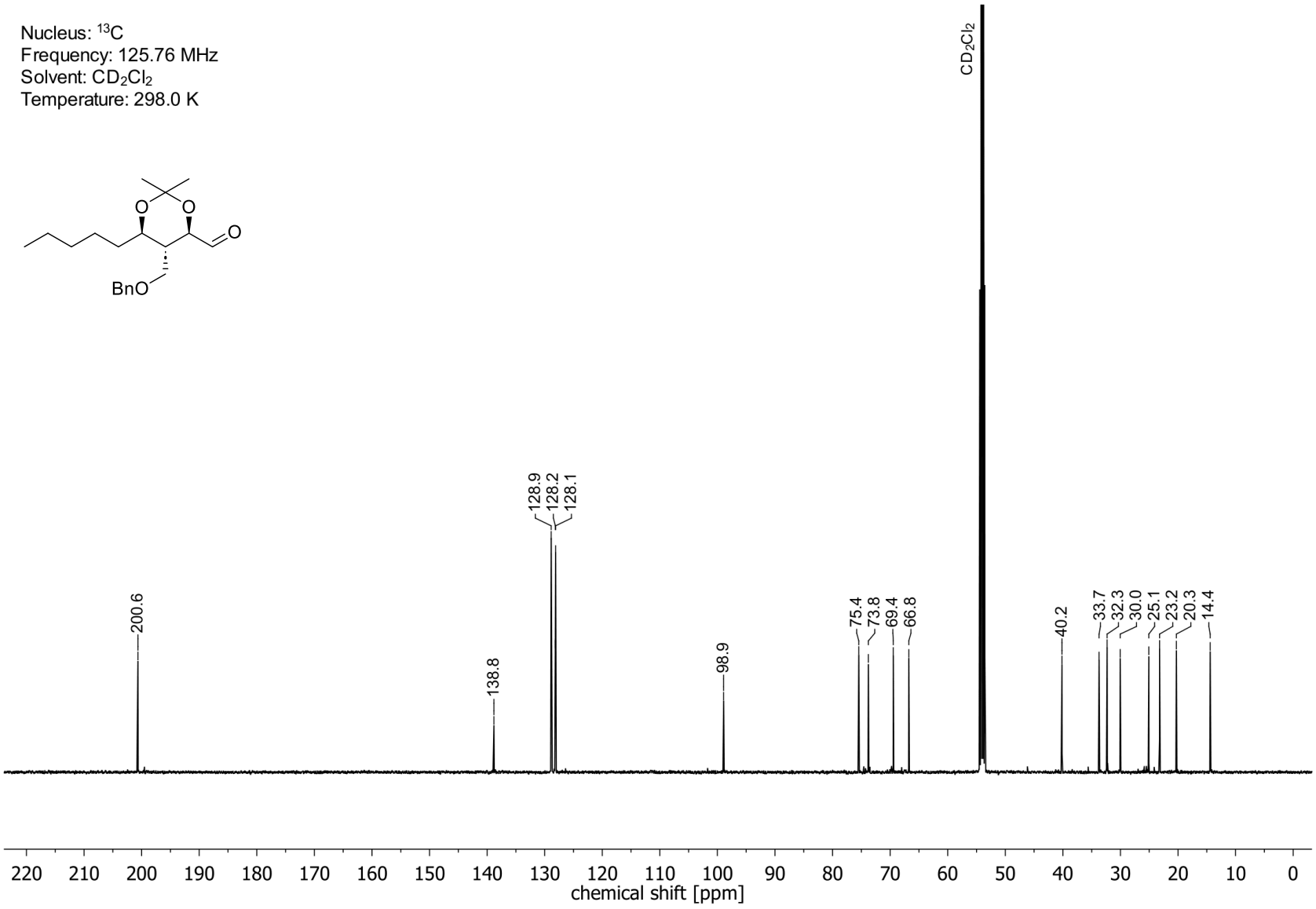
NMR-Spectra of Compound **246**:



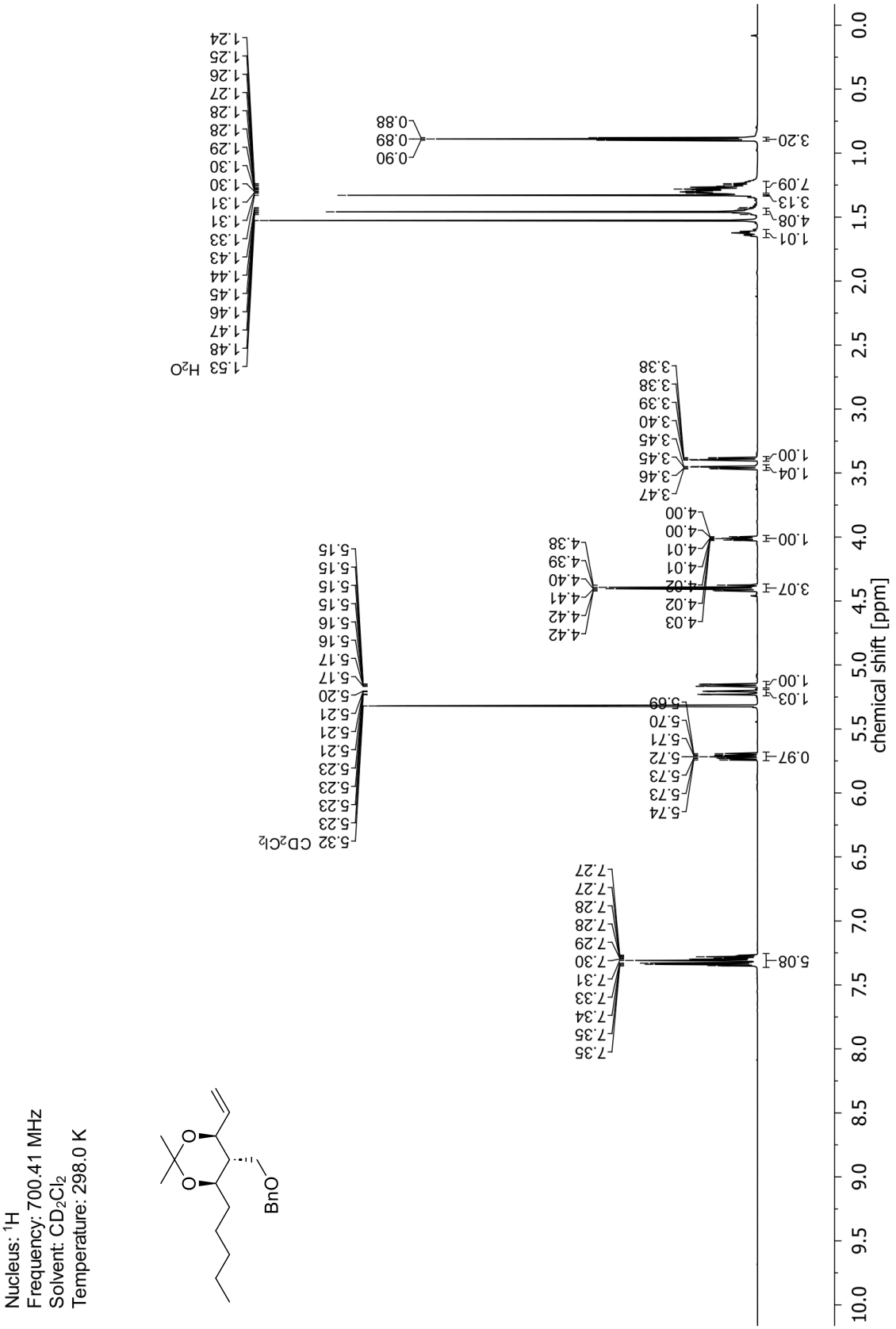

Nucleus: 13C
Frequency: 125.77 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OH
BnO
CD2Cl2
128.9
128.2
128.2
138.8
98.5
73.8
72.1
69.8
67.8
64.4
41.0
33.8
32.4
30.2
25.2
23.2
20.2
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
chemical shift [ppm]

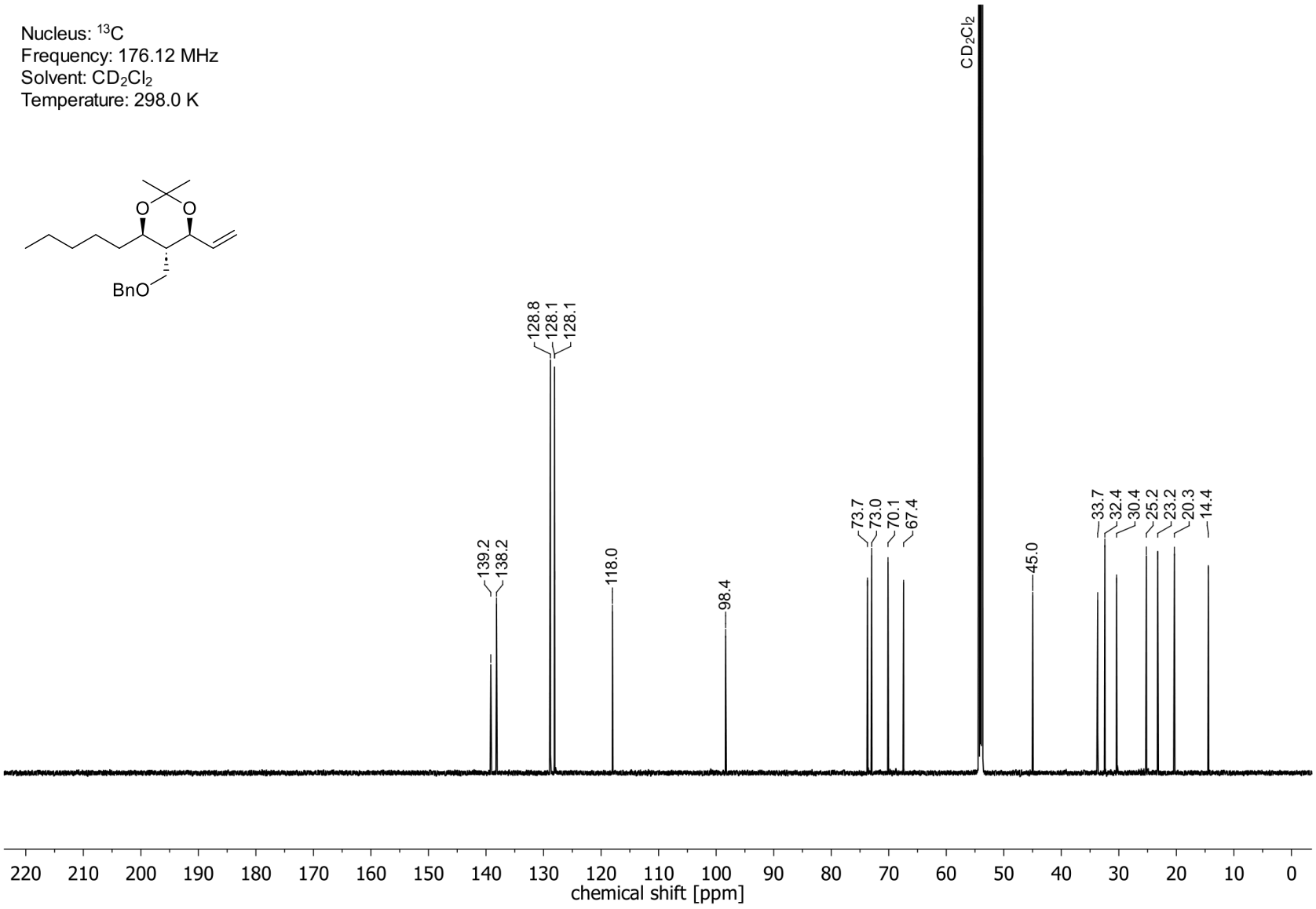
NMR-Spectra of Compound **247**:



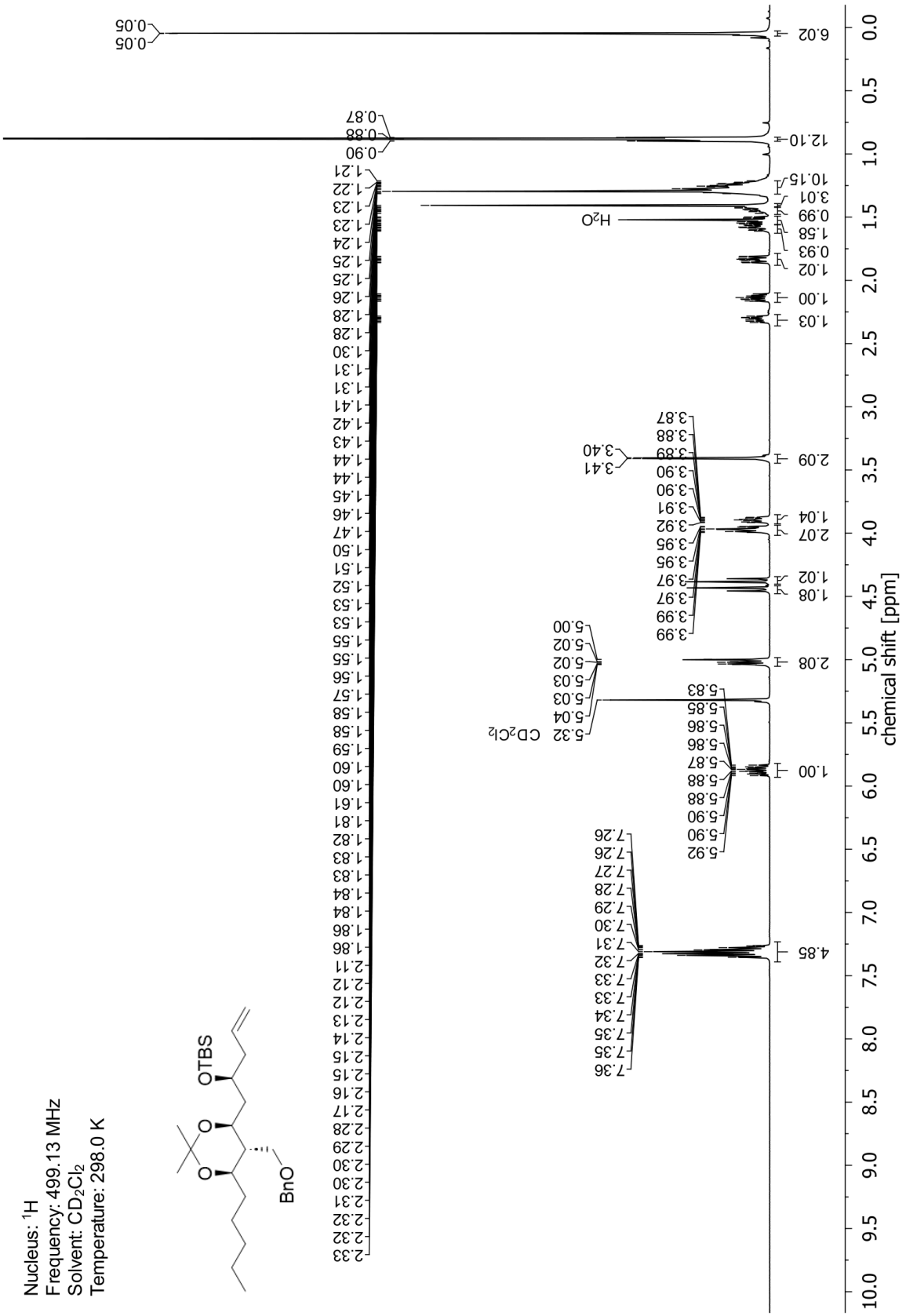

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
O
BnO
CD2Cl2
200.6
138.8
128.9
128.2
128.1
98.9
75.4
73.8
69.4
66.8
40.2
33.7
32.3
30.0
25.1
23.2
20.3
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

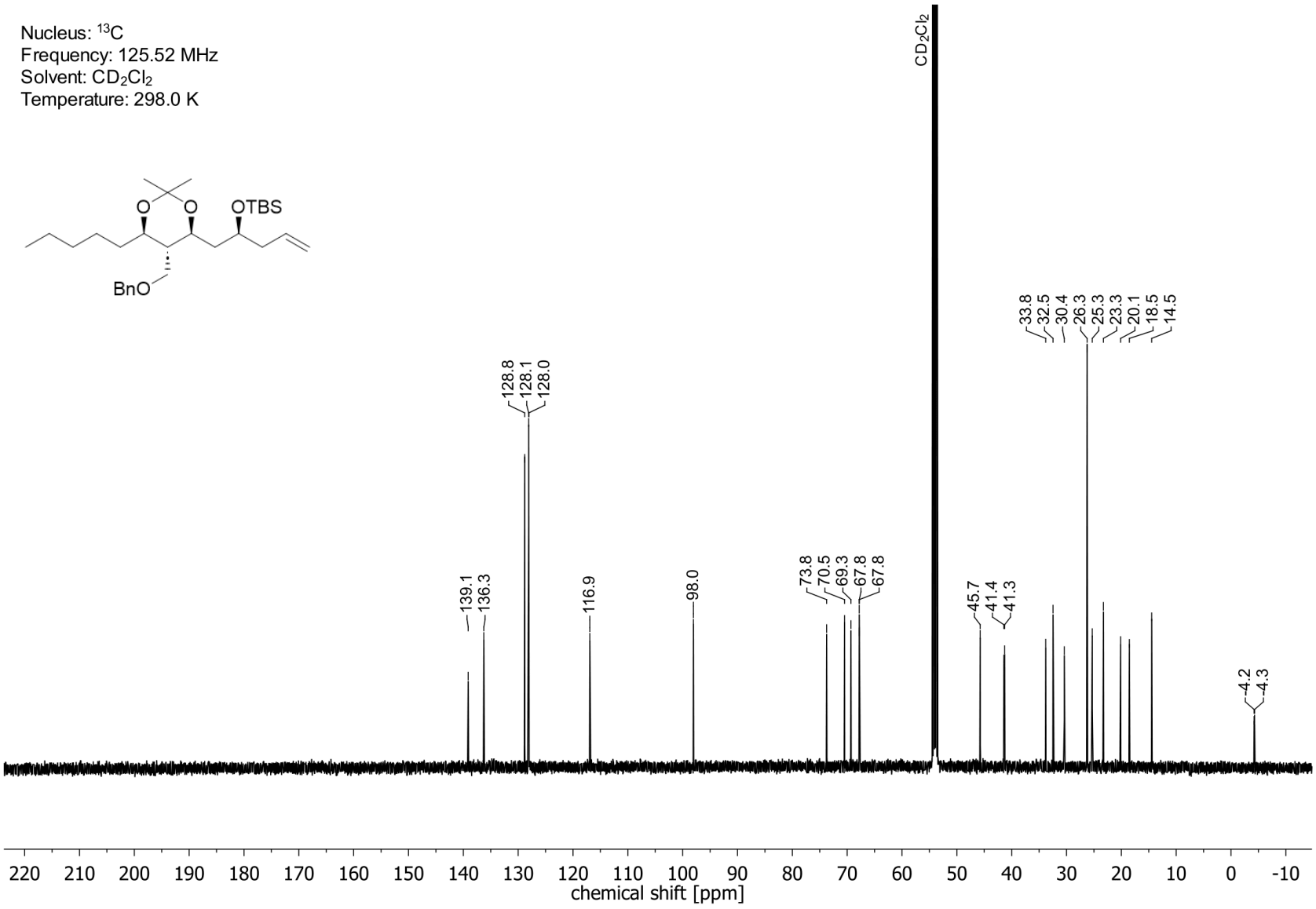
NMR-Spectra of Compound **248**:



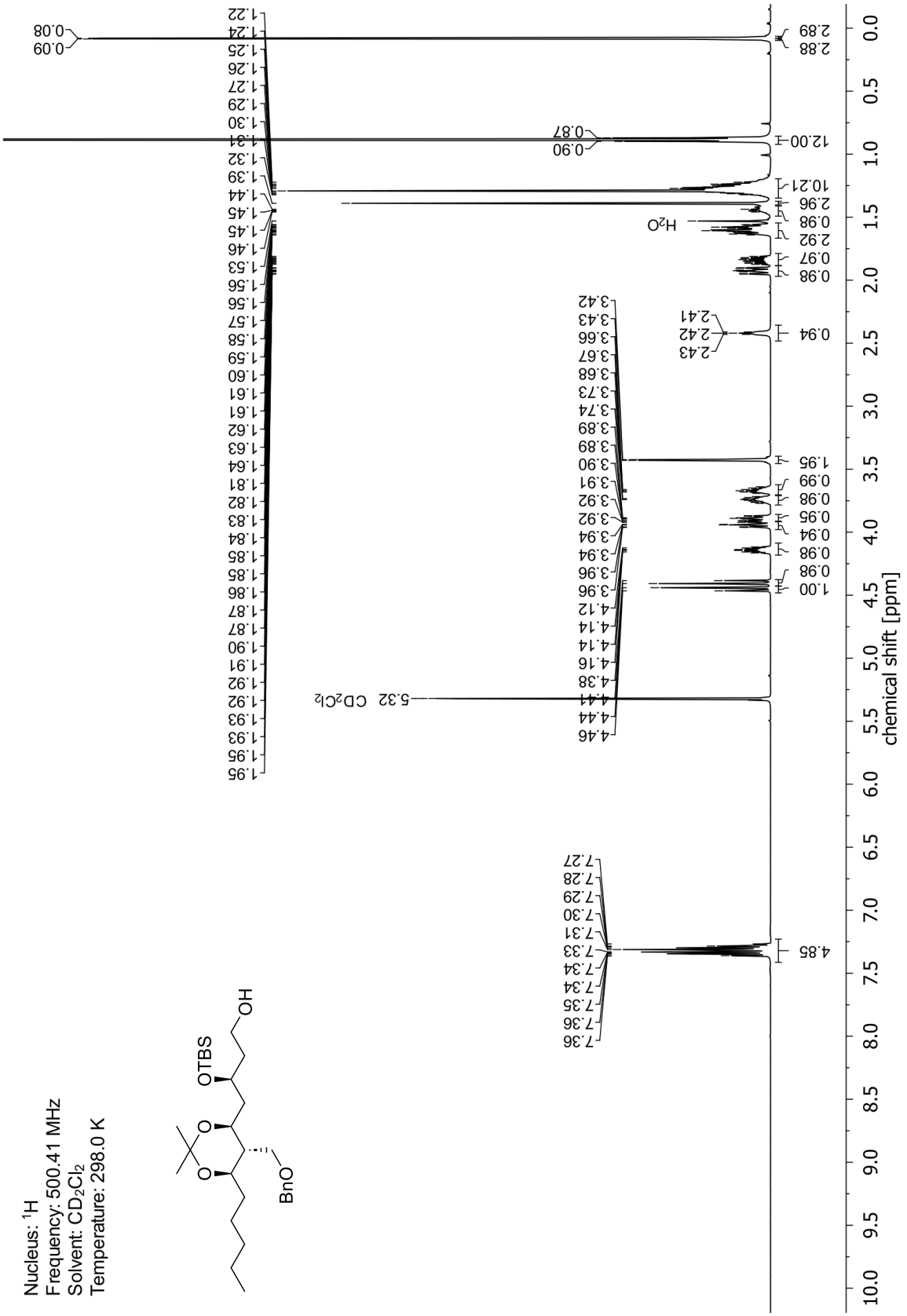

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CD2Cl2
128.8
128.1
128.1
139.2
138.2
118.0
98.4
73.7
73.0
70.1
67.4
45.0
33.7
32.4
30.4
25.2
23.2
20.3
14.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

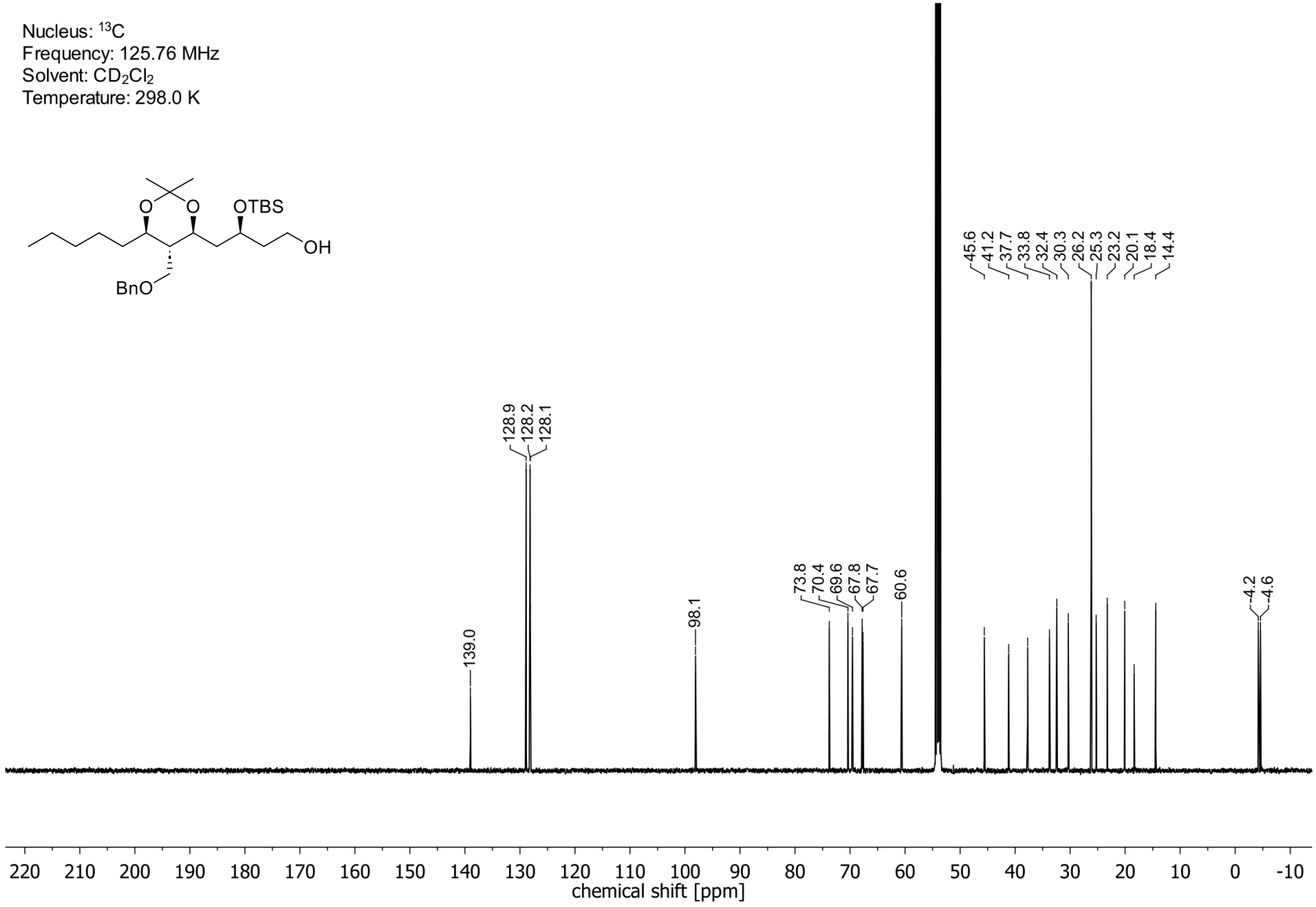
NMR-Spectra of Compound **251**:



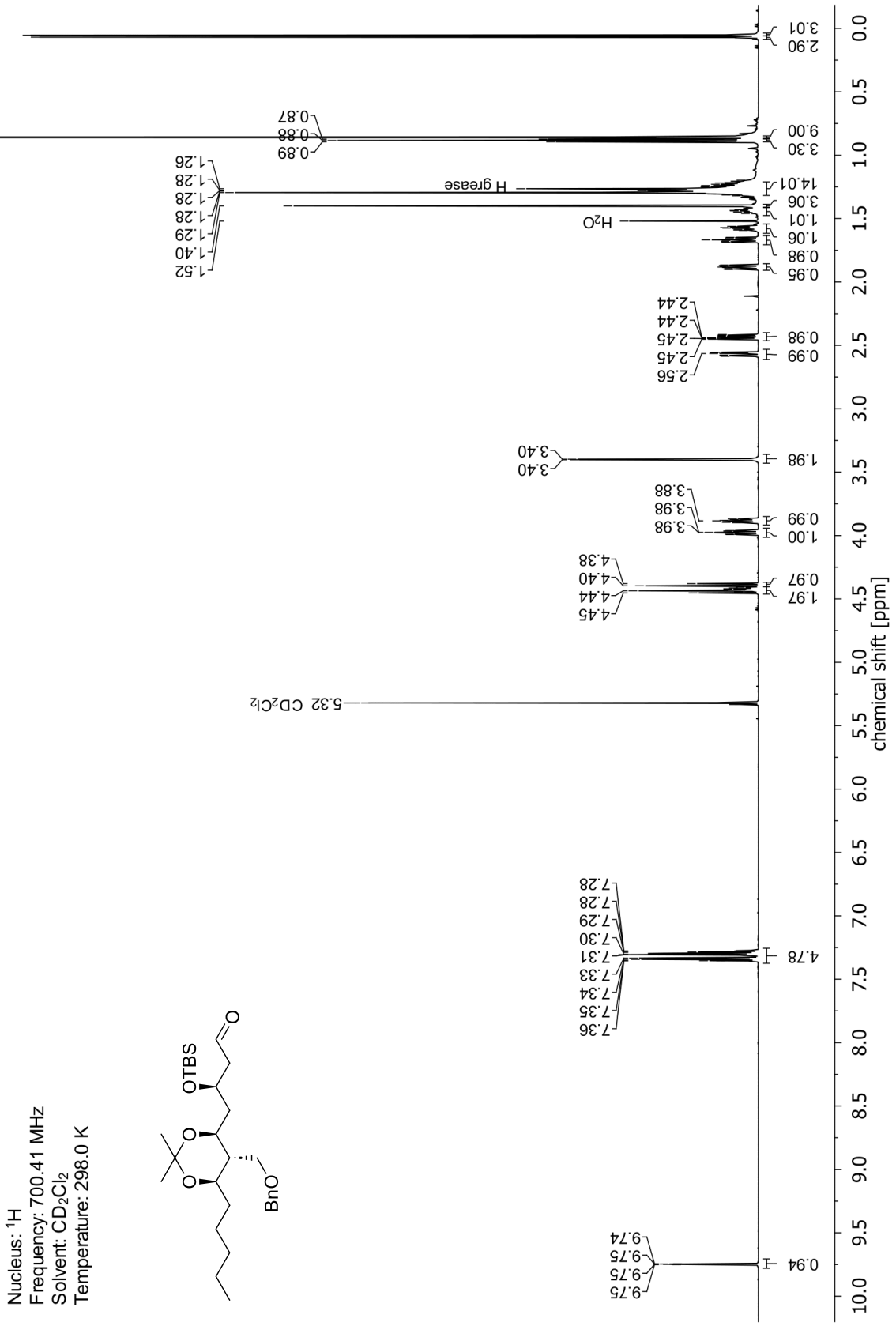

Nucleus: 13C
Frequency: 125.52 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OTBS
BnO
CD2Cl2
33.8
32.5
30.4
26.3
25.3
23.3
20.1
18.5
14.5
128.8
128.1
128.0
139.1
136.3
116.9
98.0
73.8
70.5
69.3
67.8
67.8
45.7
41.4
41.3
4.2
4.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

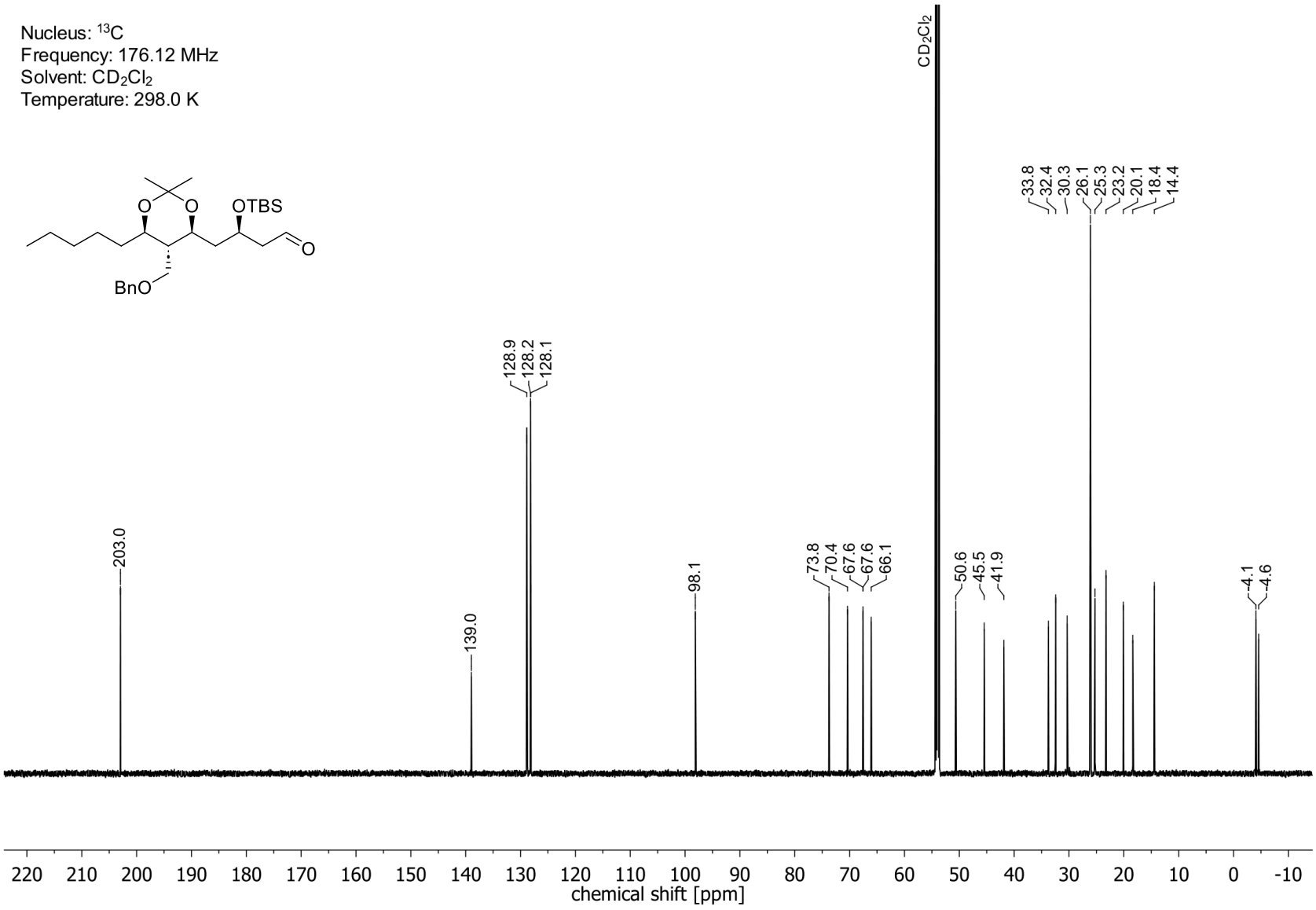
NMR-Spectra of Compound **253**:



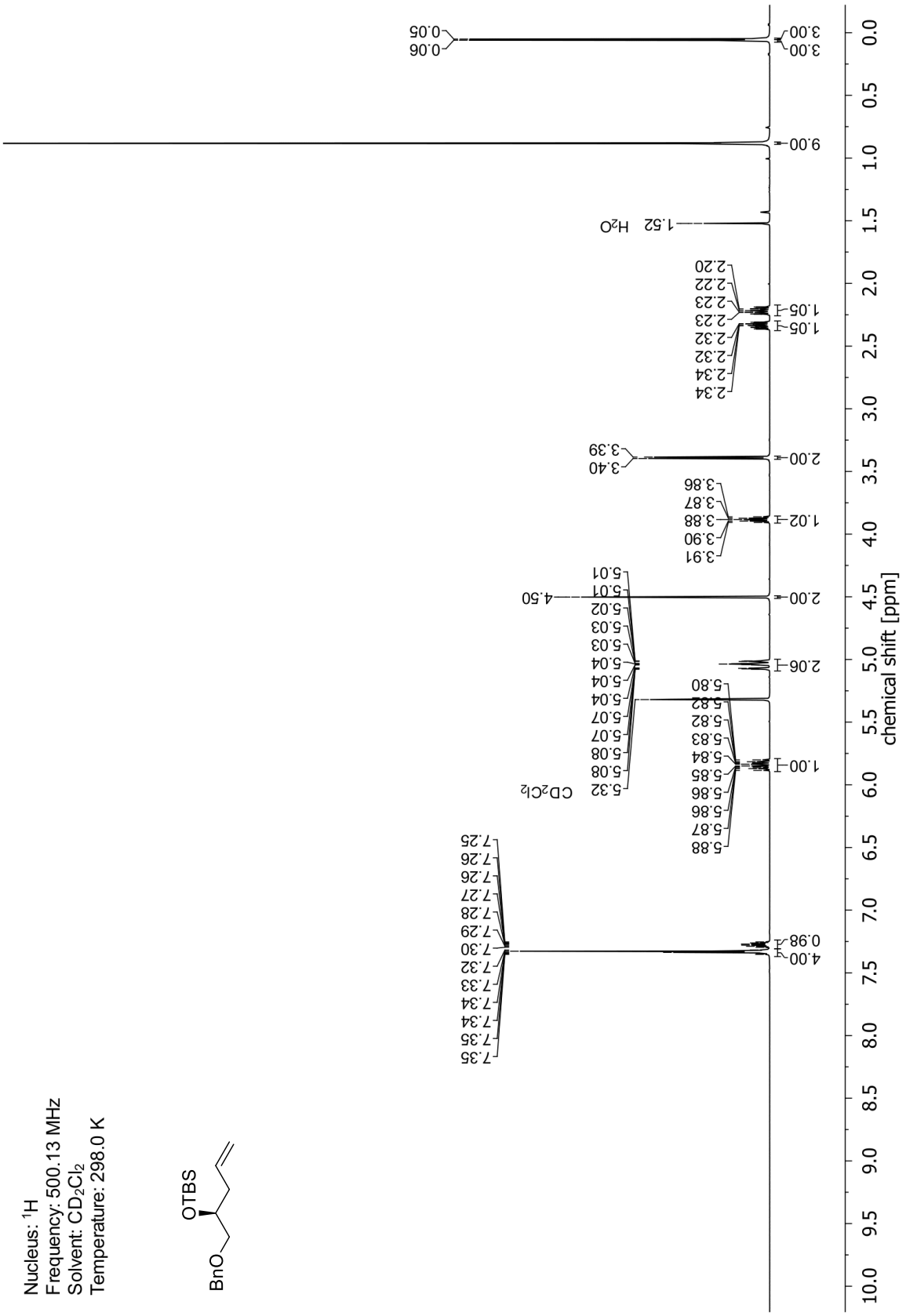

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OTBS
OH
BnO
45.6
41.2
37.7
33.8
32.4
30.3
26.2
25.3
23.2
20.1
18.4
14.4
128.9
128.2
128.1
139.0
98.1
73.8
70.4
69.6
67.8
67.7
60.6
-4.2
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **252**:

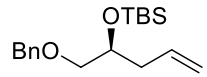



Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
O
O
OTBS
O
BnO
CD2Cl2
33.8
32.4
30.3
26.1
25.3
23.2
20.1
18.4
14.4
128.9
128.2
128.1
203.0
139.0
98.1
73.8
70.4
67.6
67.6
66.1
50.6
45.5
41.9
-4.1
-4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

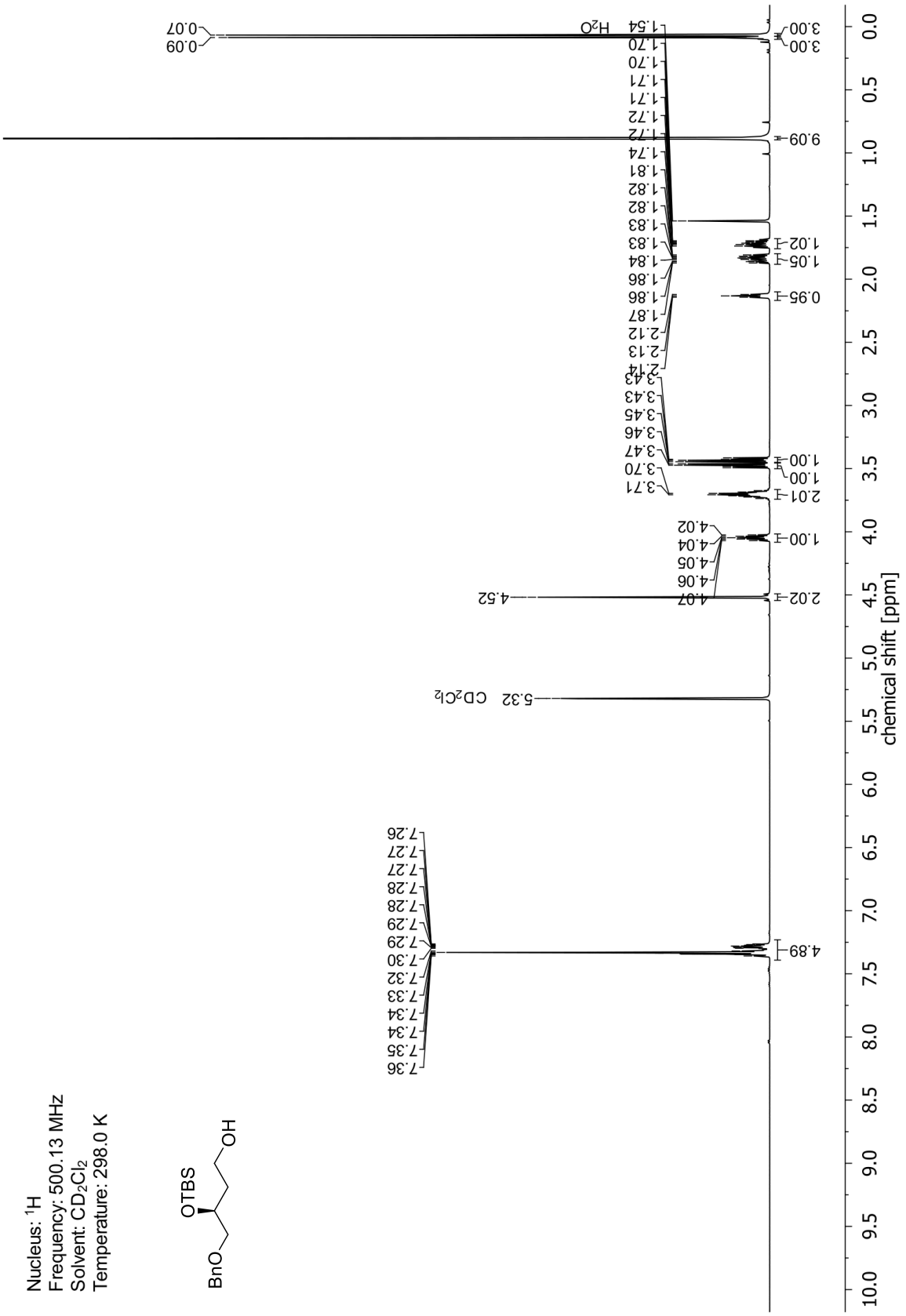
NMR-Spectra of Compound **257**:



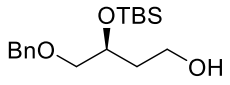
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



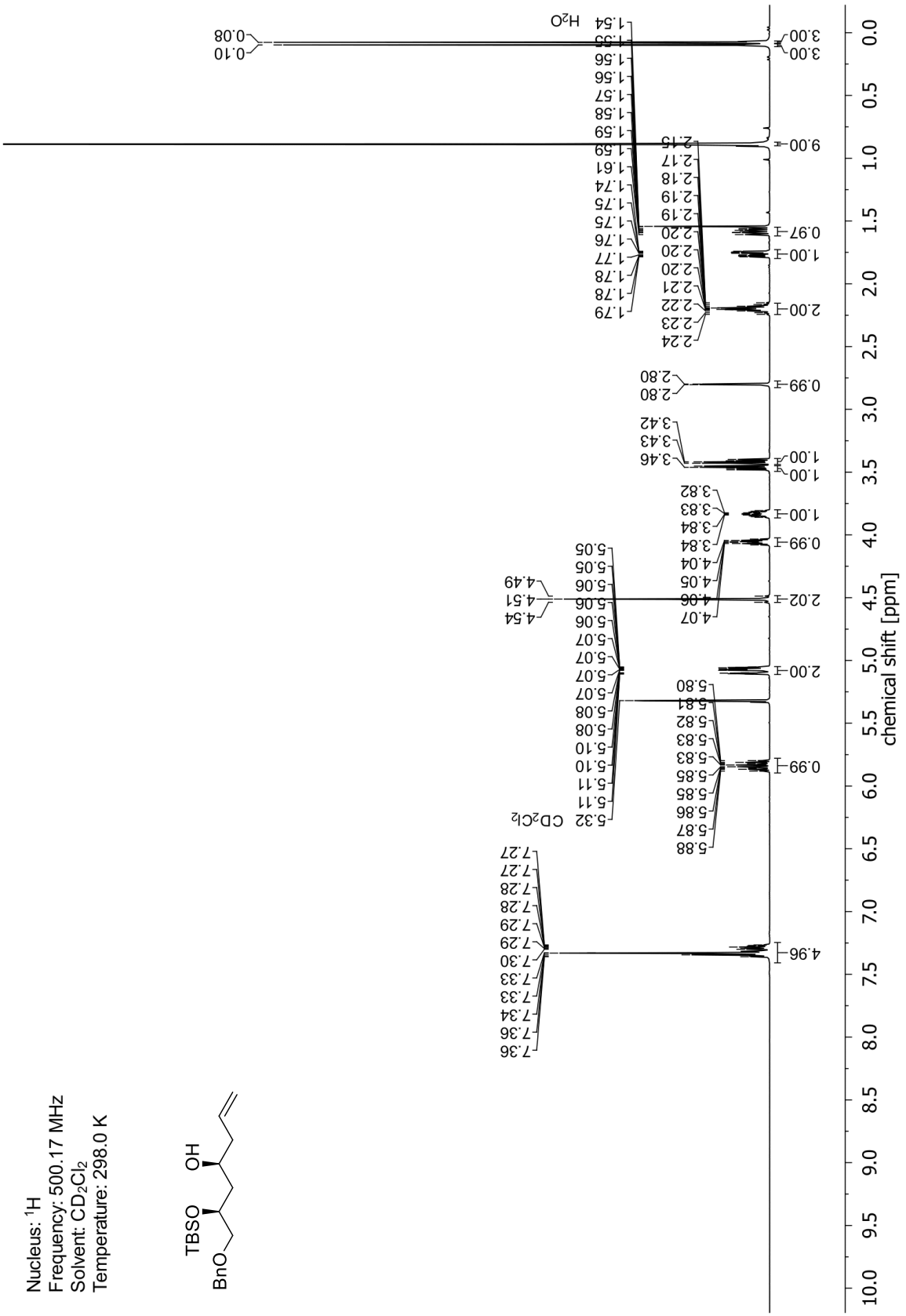
NMR-Spectra of Compound **258**:

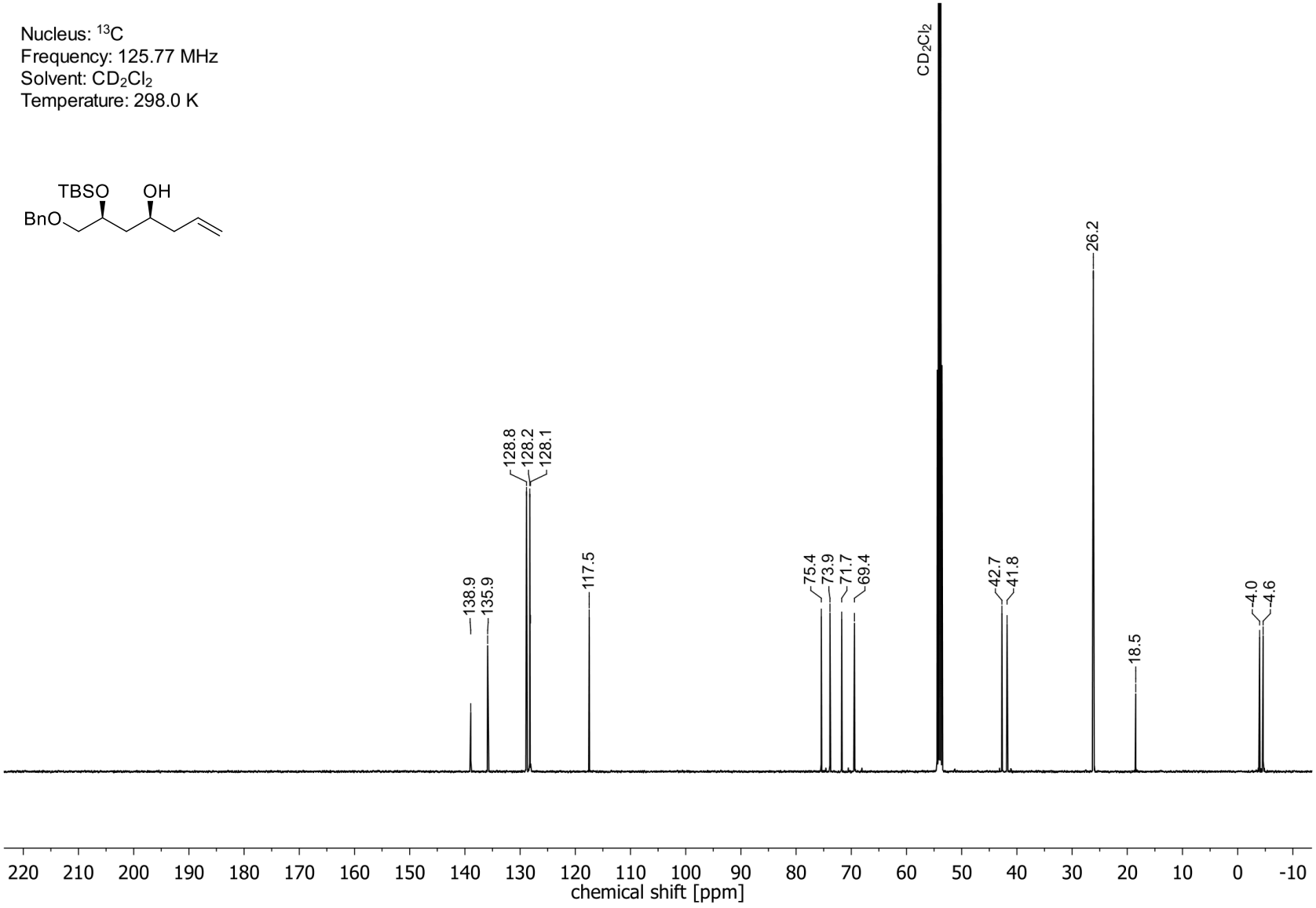


Nucleus: $^{13}C$
Frequency: 125.76 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

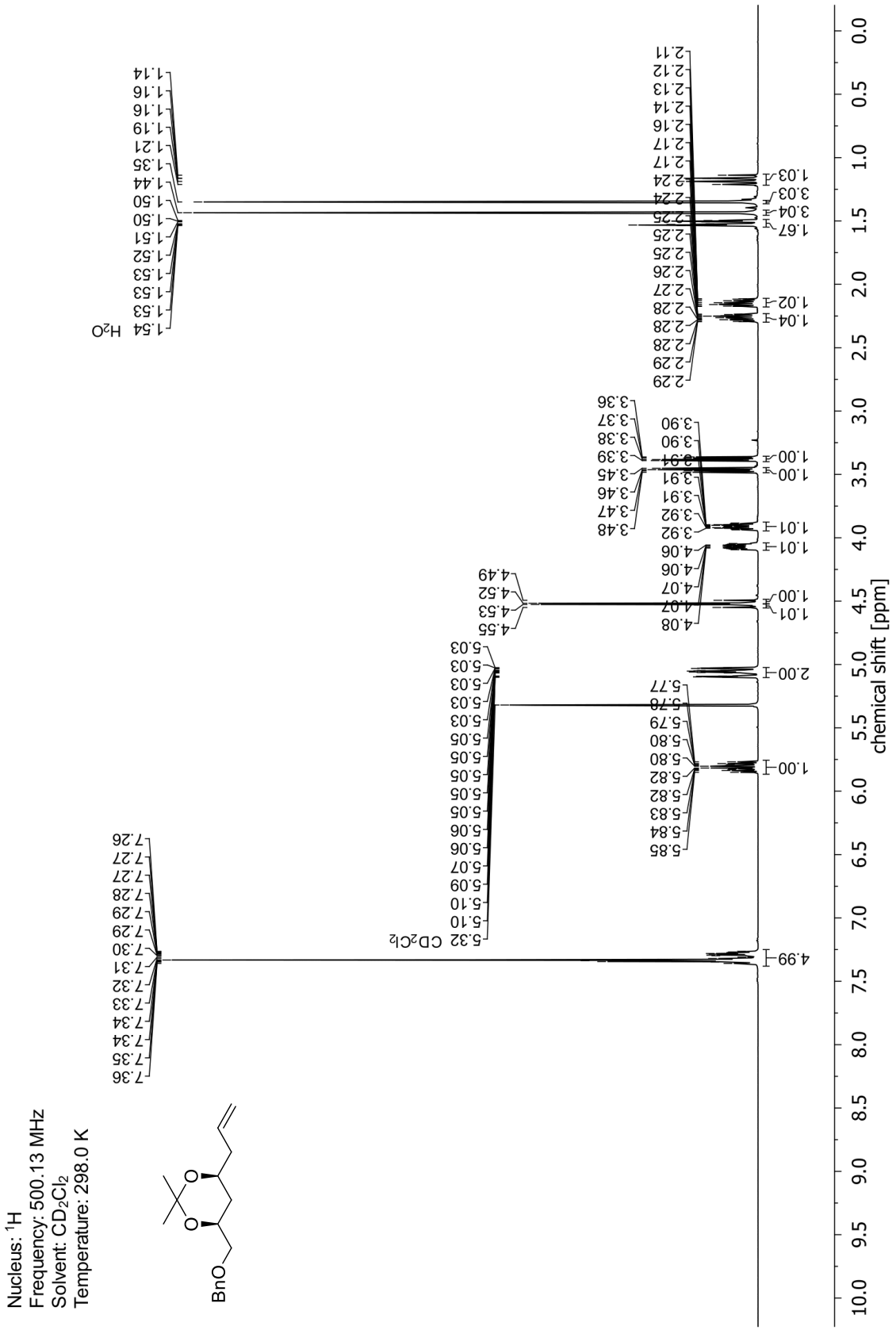


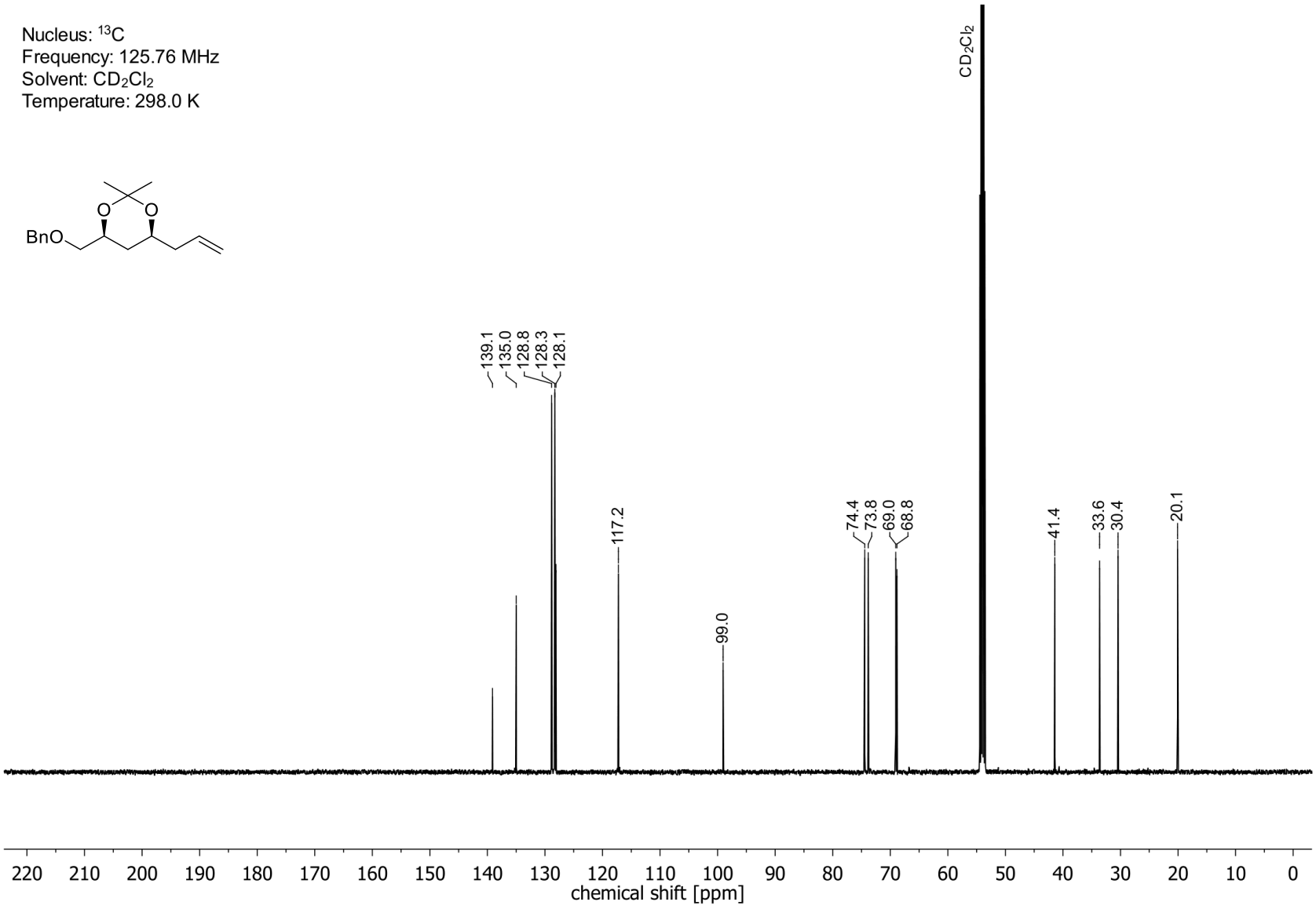
NMR-Spectra of Compound **259**:



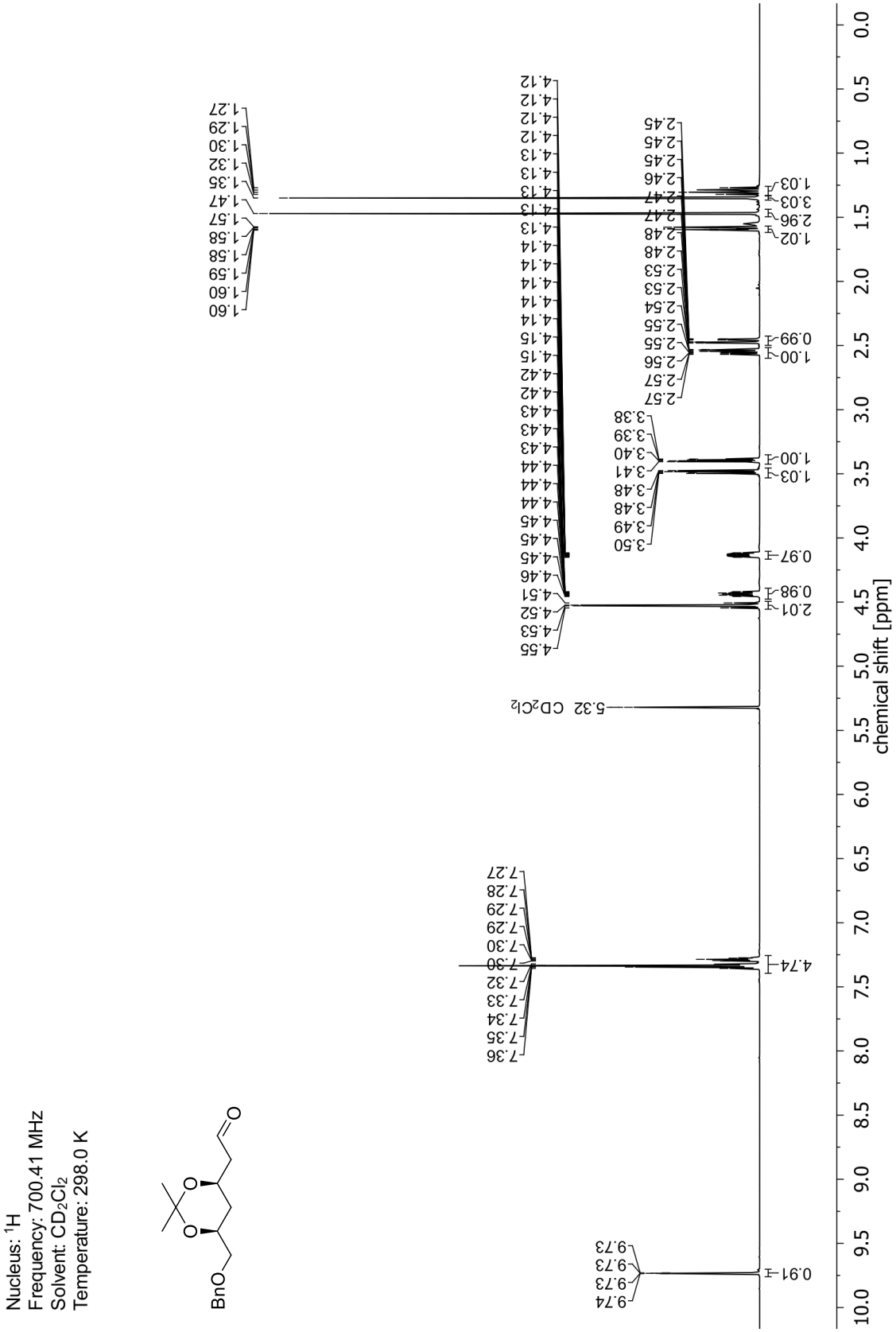

Nucleus: 13C
Frequency: 125.77 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
OH
BnO
CD2Cl2
26.2
128.8
128.2
128.1
138.9
135.9
117.5
75.4
73.9
71.7
69.4
42.7
41.8
18.5
4.0
4.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **260**:

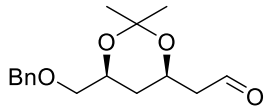



Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
CD2Cl2
139.1
135.0
128.8
128.3
128.1
117.2
99.0
74.4
73.8
69.0
68.8
41.4
33.6
30.4
20.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

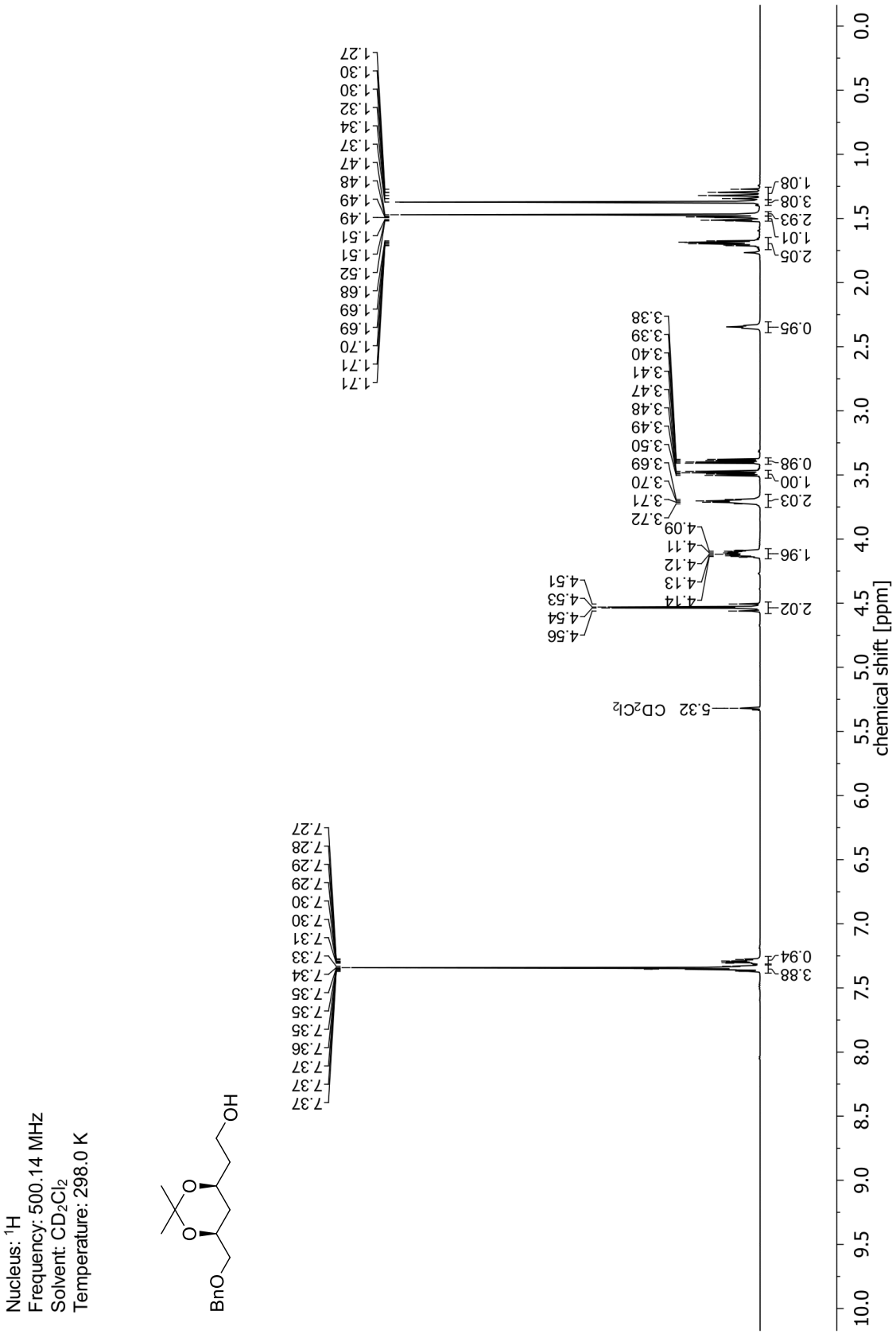
NMR-Spectra of Compound **157**:



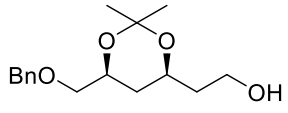
Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



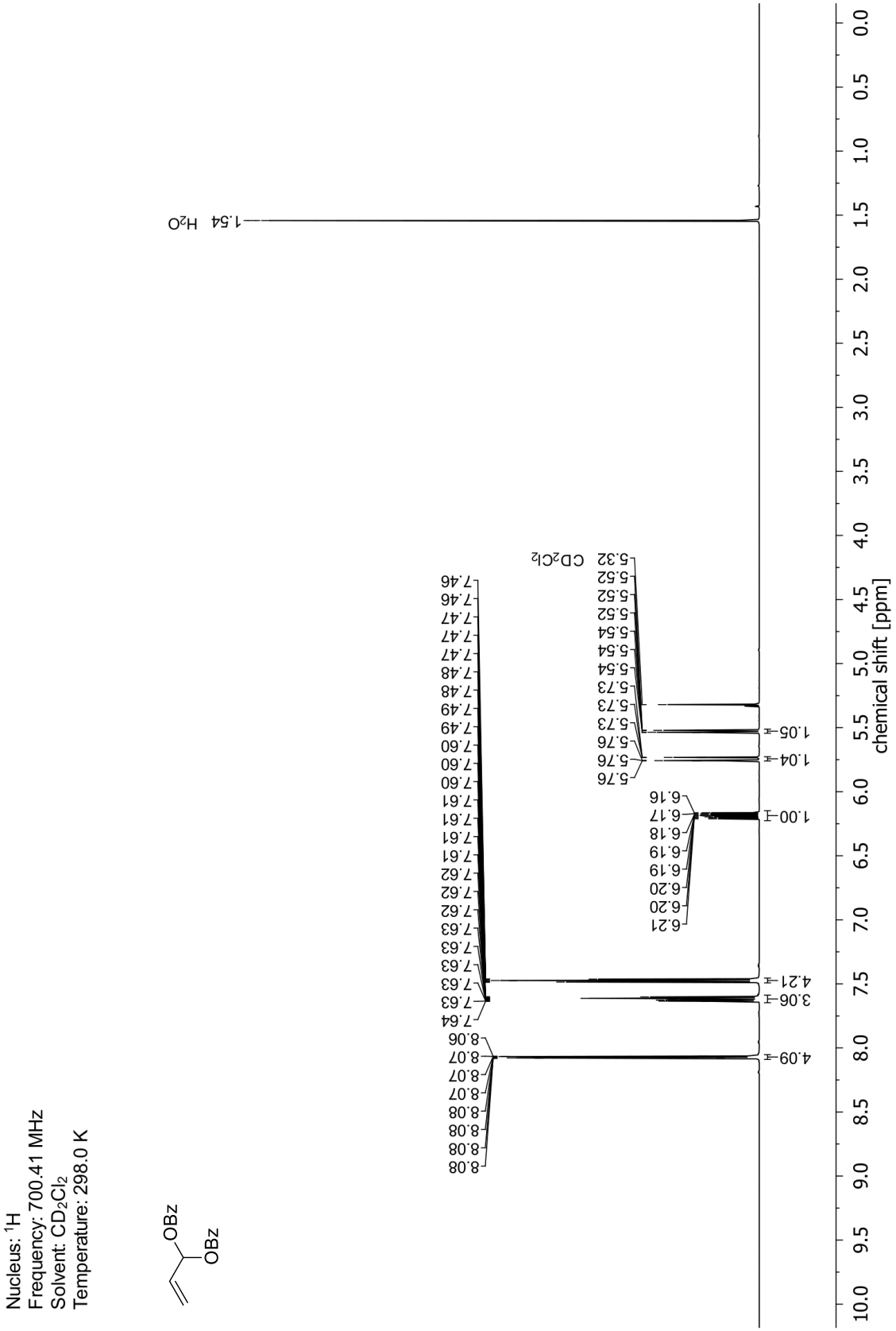
NMR-Spectra of Compound **158**:



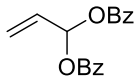
Nucleus: $^{13}C$
Frequency: 125.76 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K



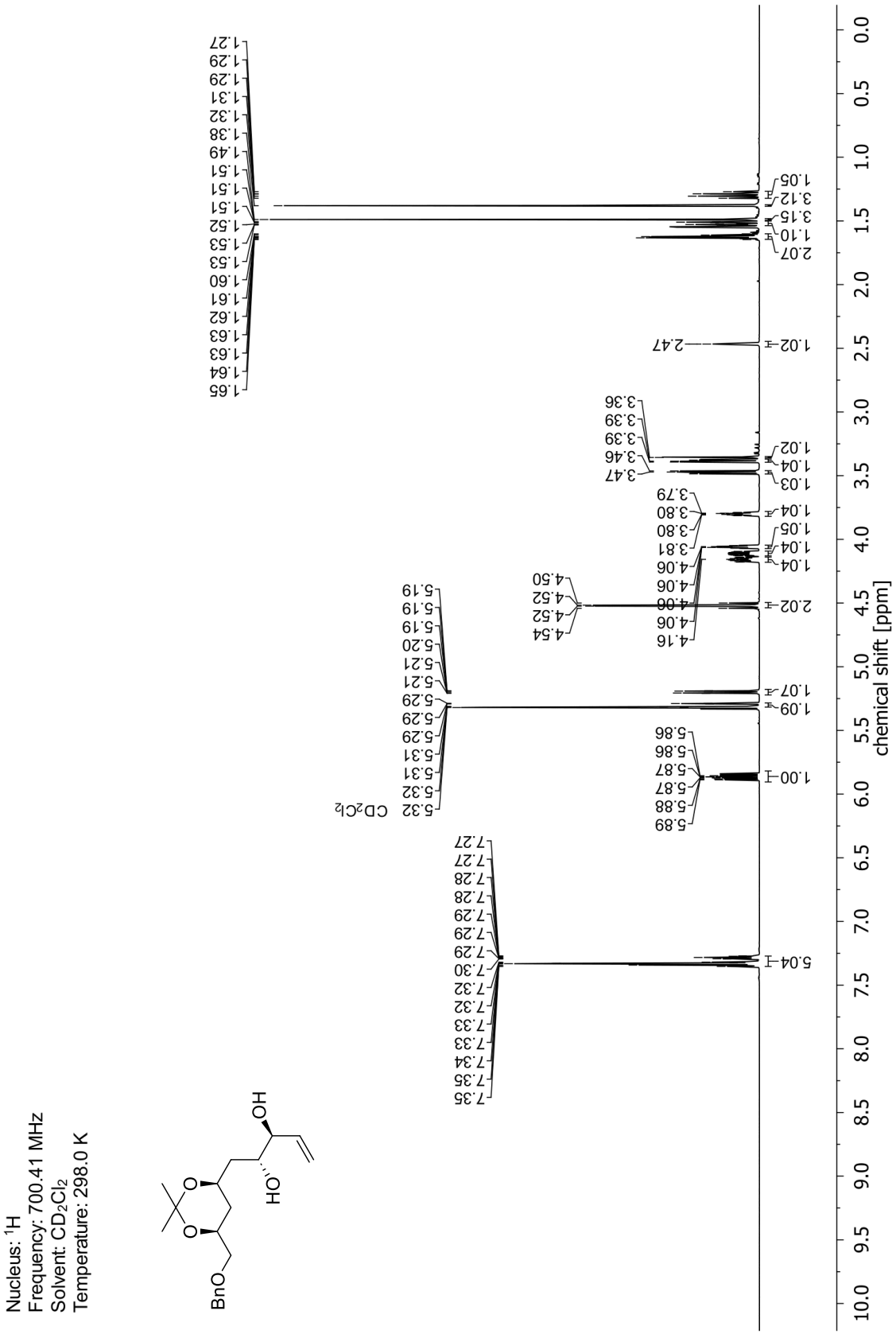
NMR-Spectra of Compound **180**:

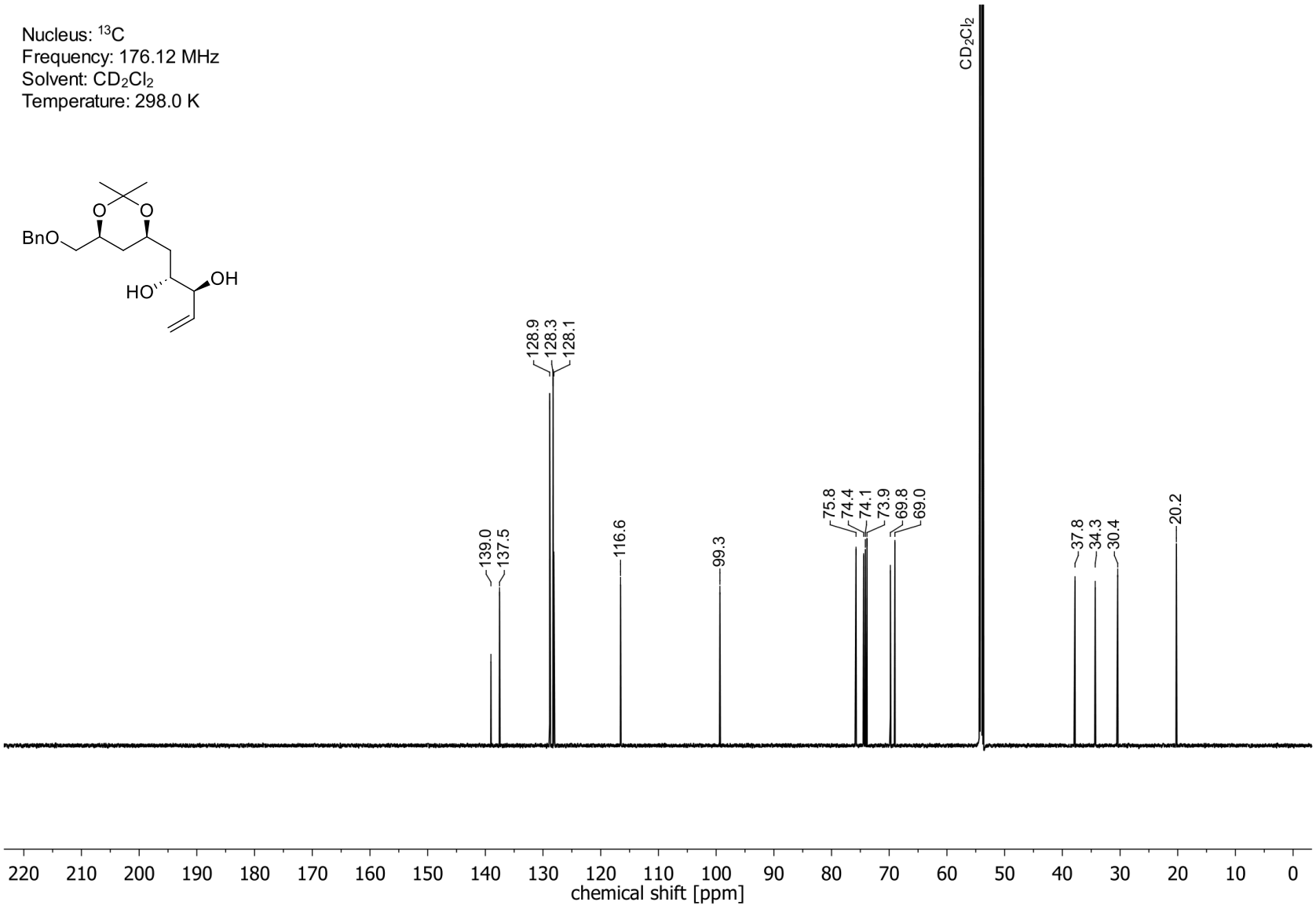


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

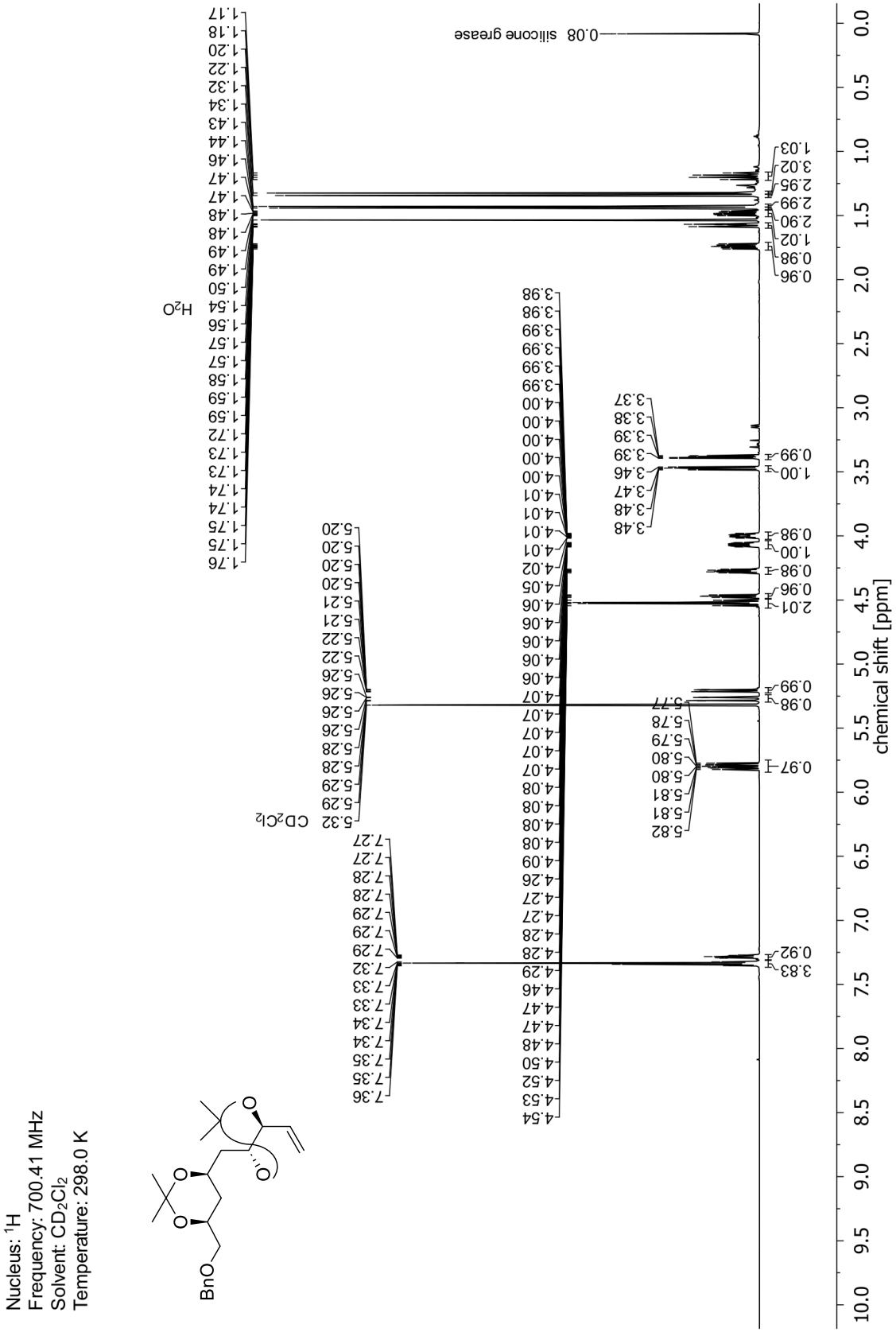


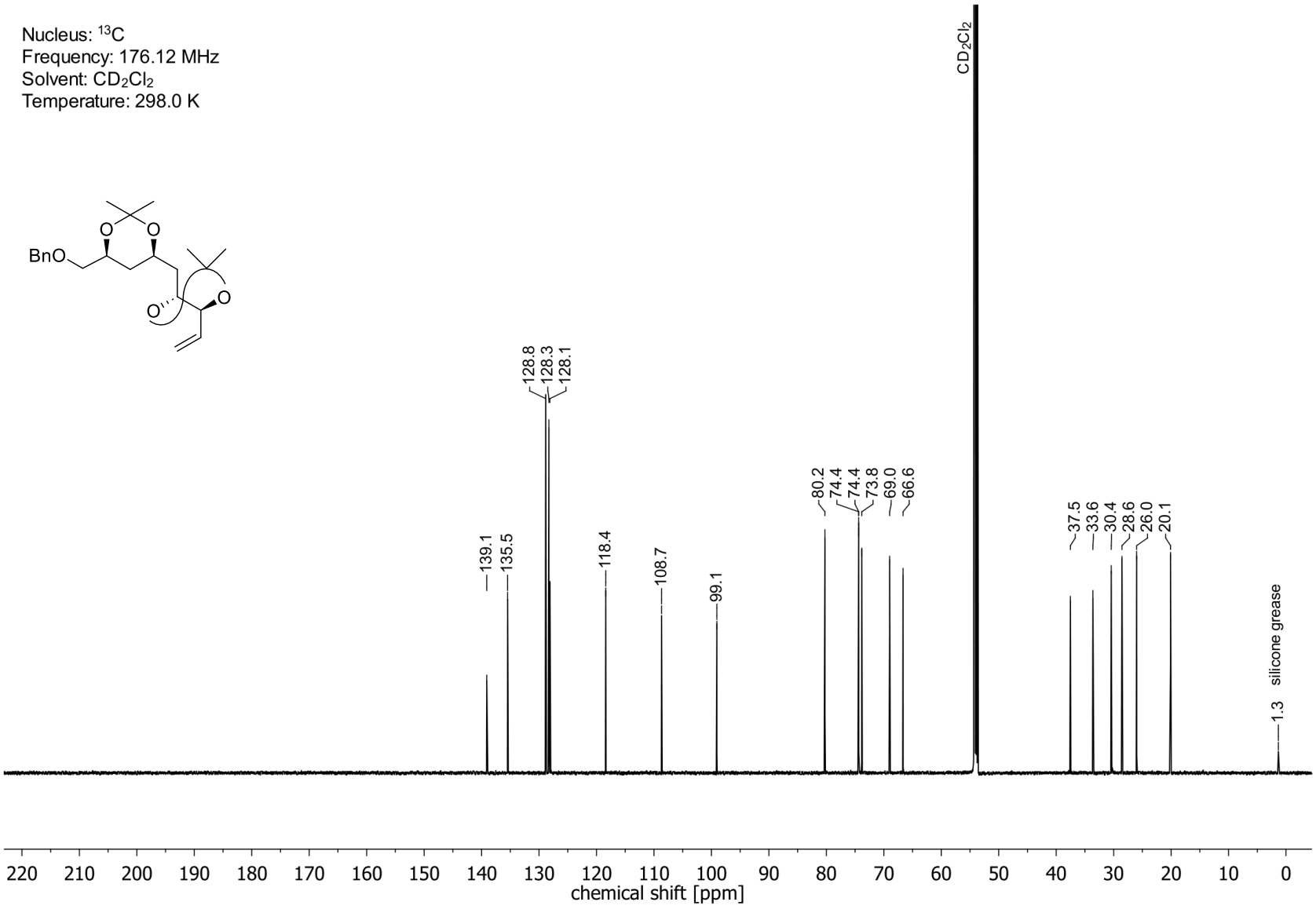
NMR-Spectra of Compound **159**:



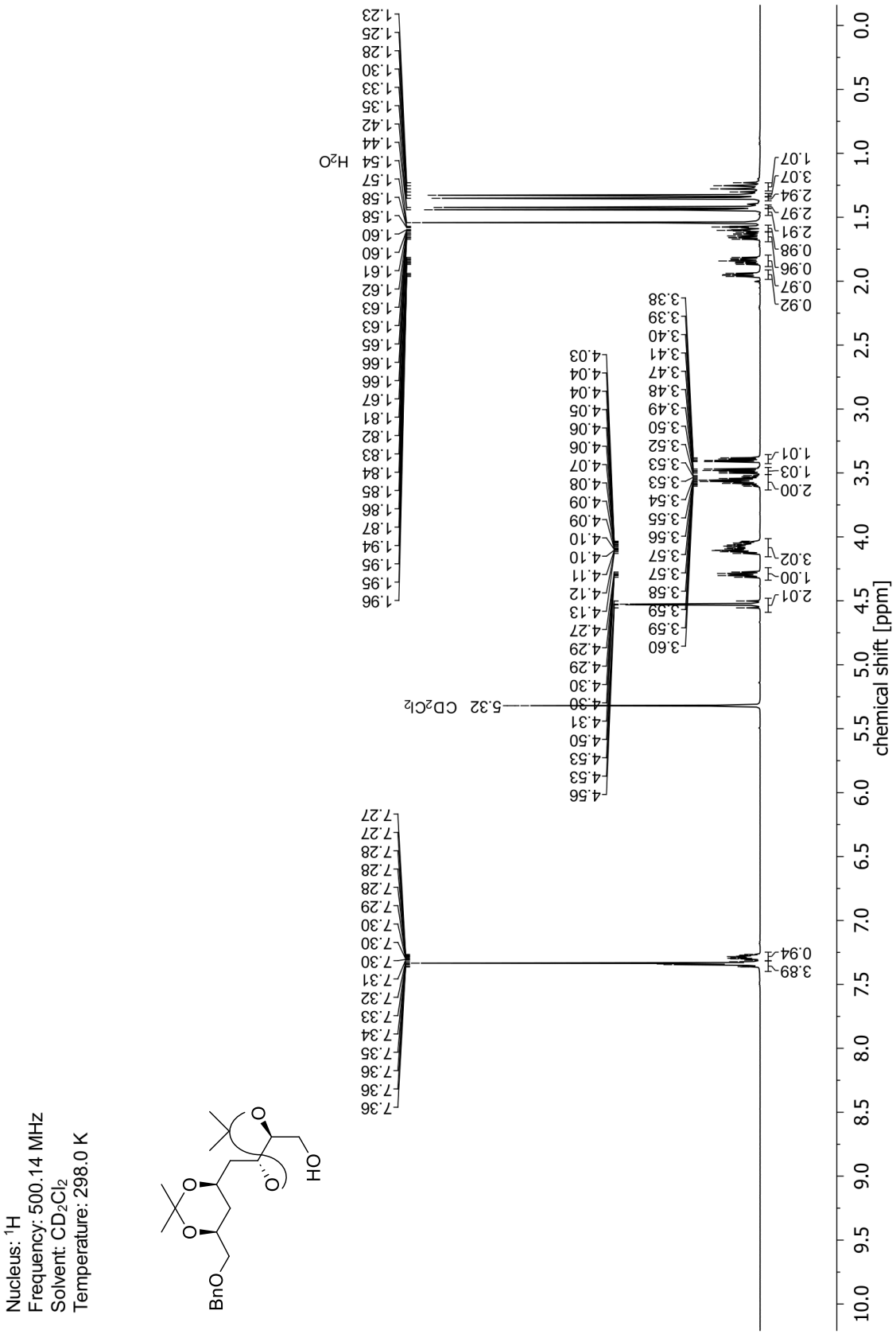

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
HO
OH
CD2Cl2
128.9
128.3
128.1
139.0
137.5
116.6
99.3
75.8
74.4
74.1
73.9
69.8
69.0
37.8
34.3
30.4
20.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

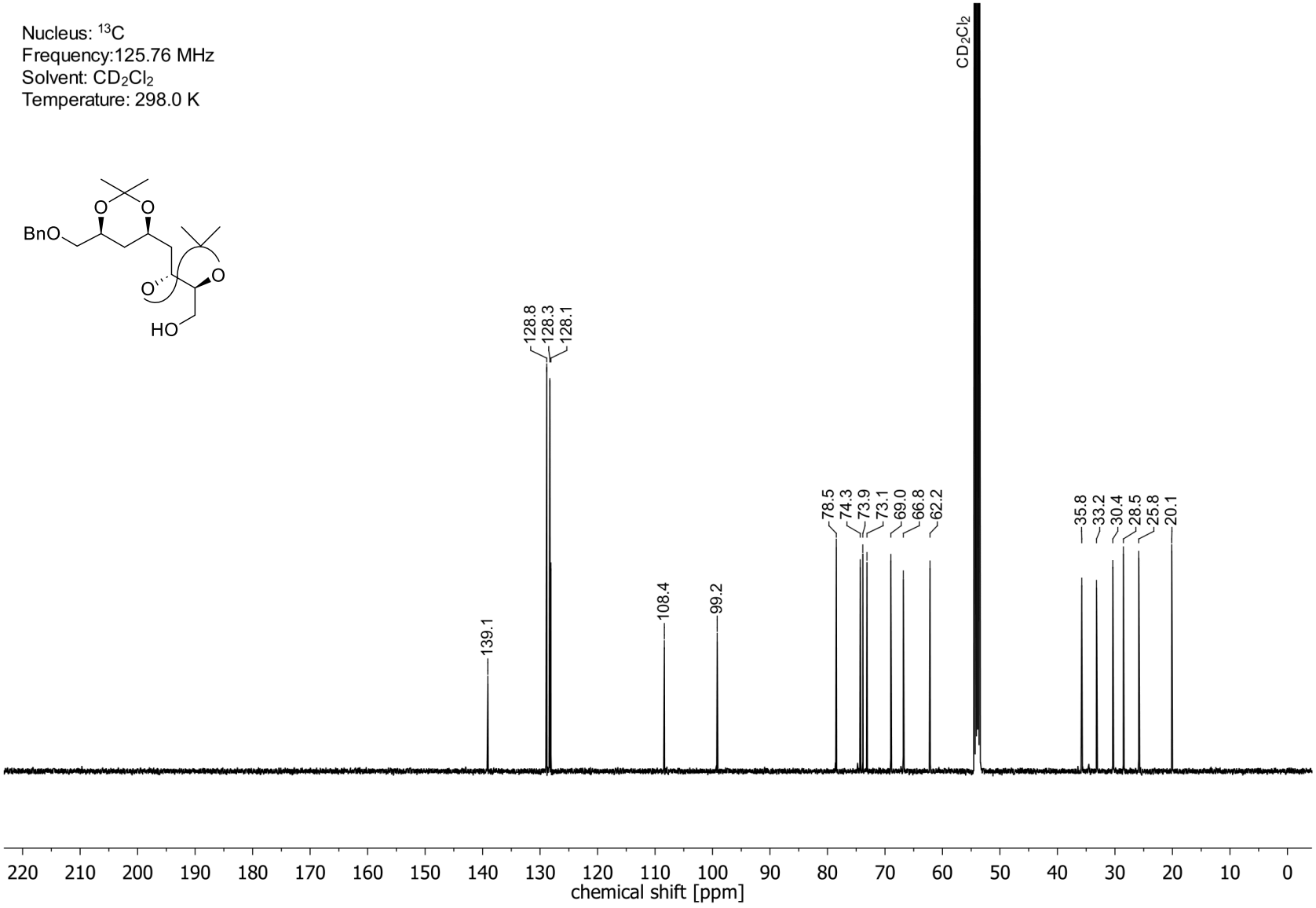
NMR-Spectra of Compound **263**:



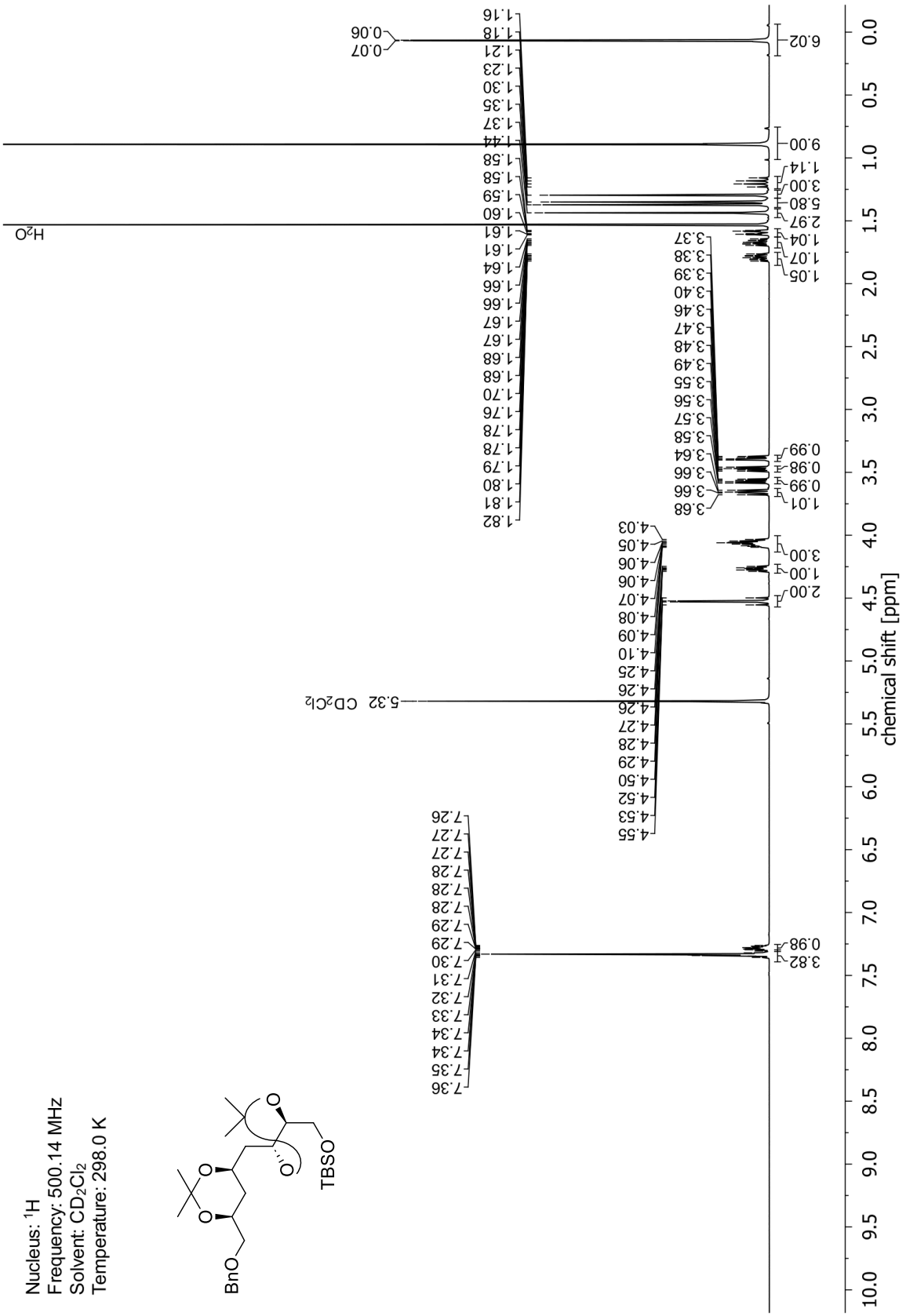

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
O
CD2Cl2
128.8
128.3
128.1
139.1
135.5
118.4
108.7
99.1
80.2
74.4
74.4
73.8
69.0
66.6
37.5
33.6
30.4
28.6
26.0
20.1
1.3
silicone grease
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
chemical shift [ppm]

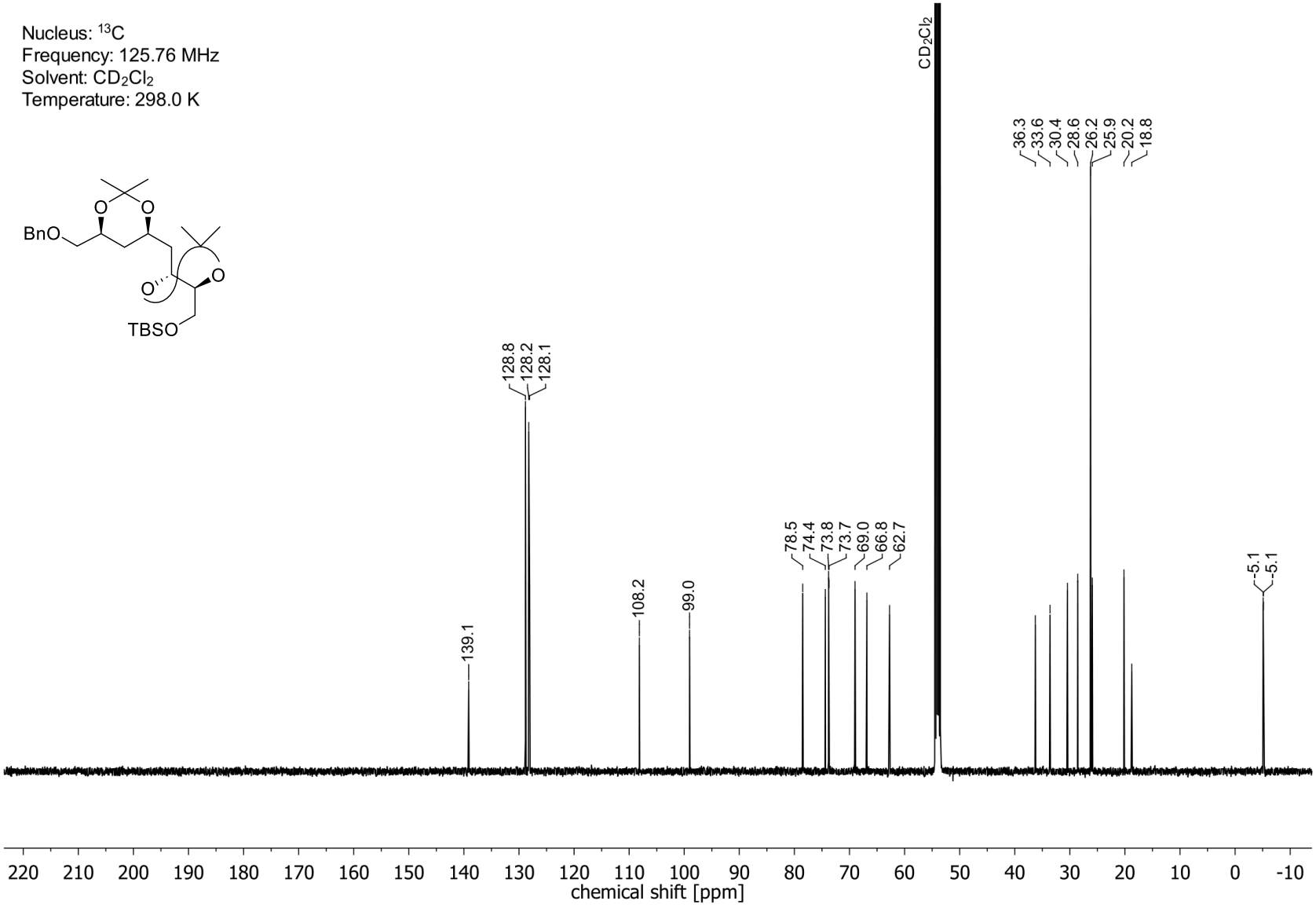
NMR-Spectra of Compound **264**:



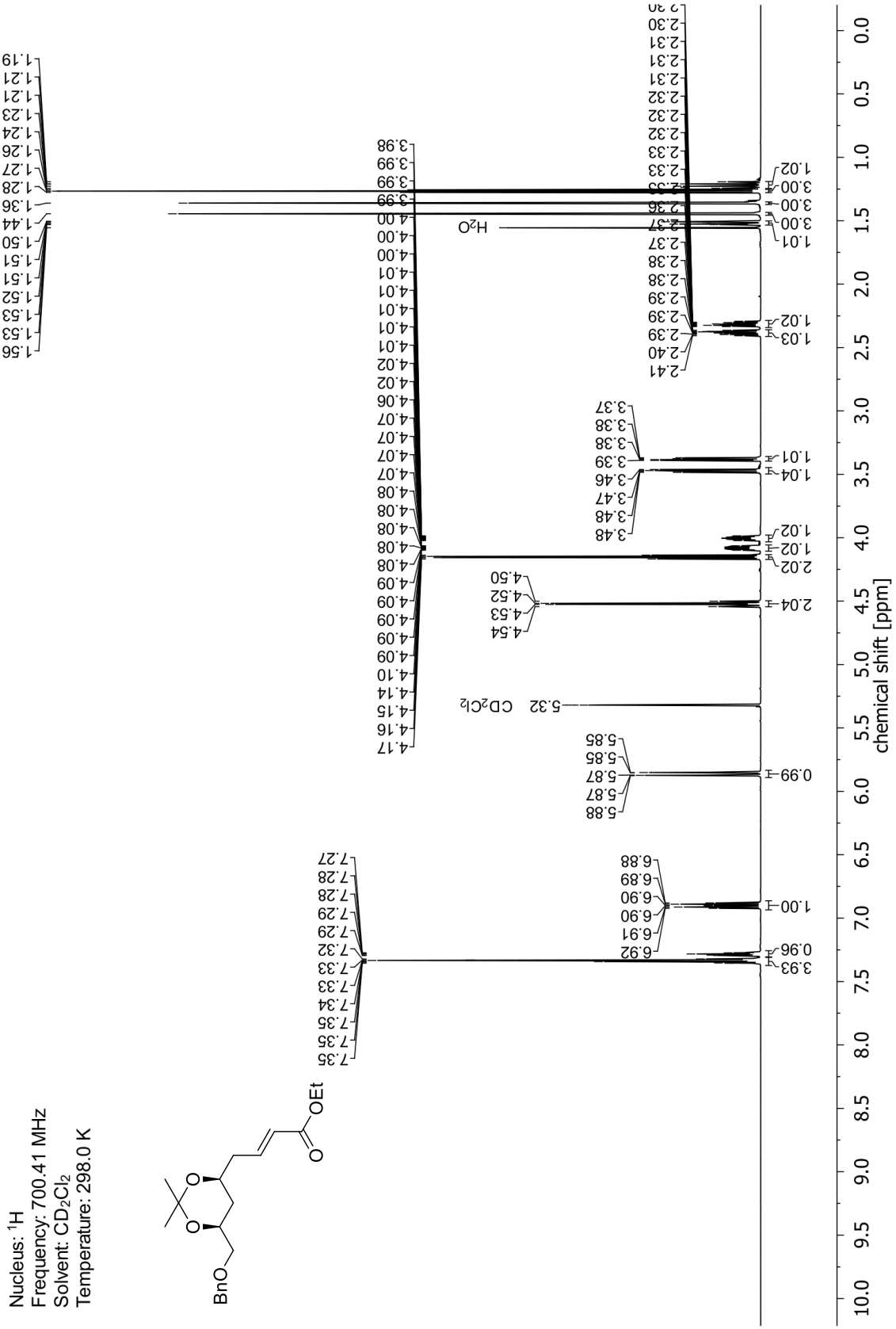

Nucleus: 13C
Frequency:125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
O
HO
CD2Cl2
128.8
128.3
128.1
139.1
108.4
99.2
78.5
74.3
73.9
73.1
69.0
66.8
62.2
35.8
33.2
30.4
28.5
25.8
20.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

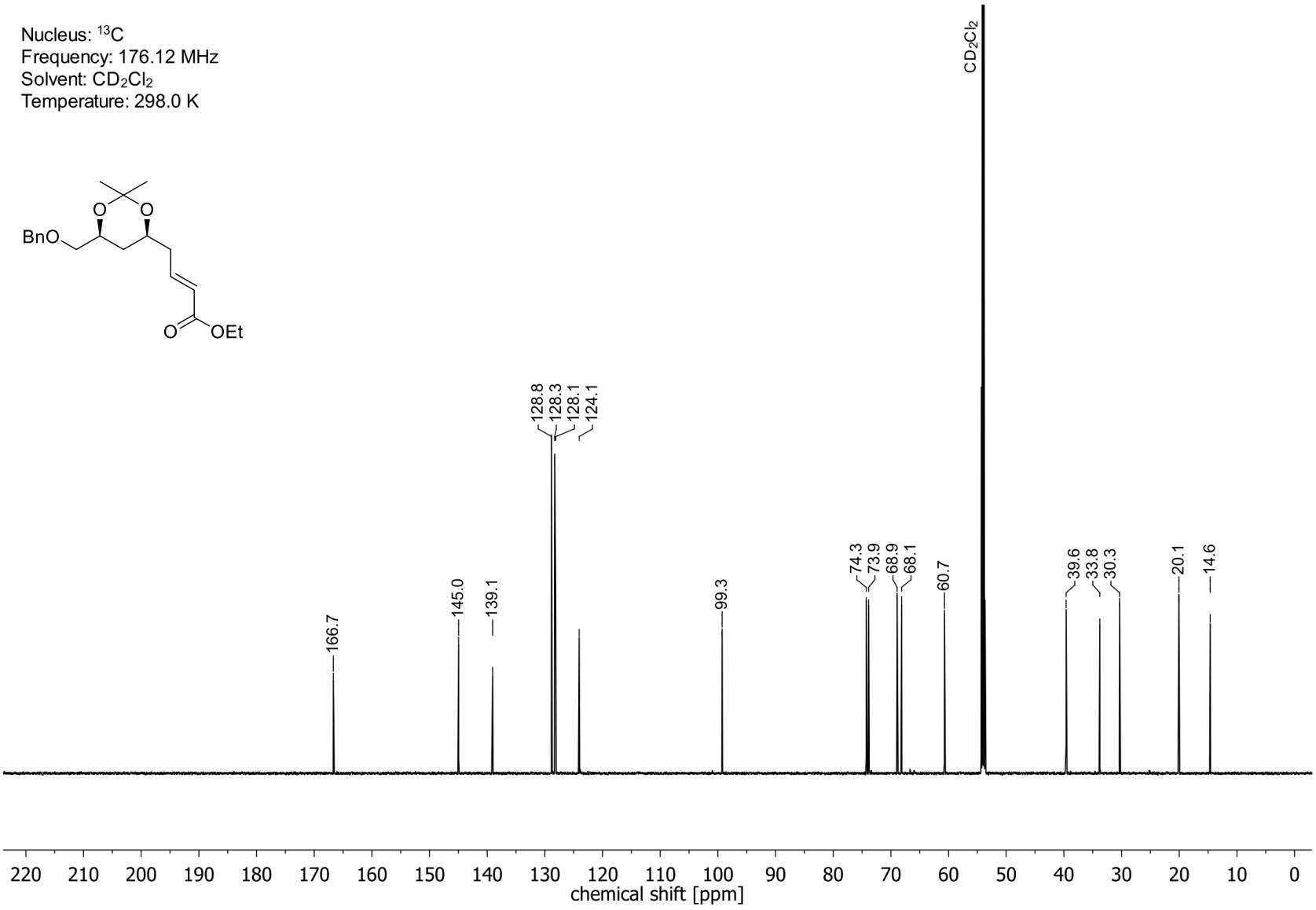
NMR-Spectra of Compound **255**:

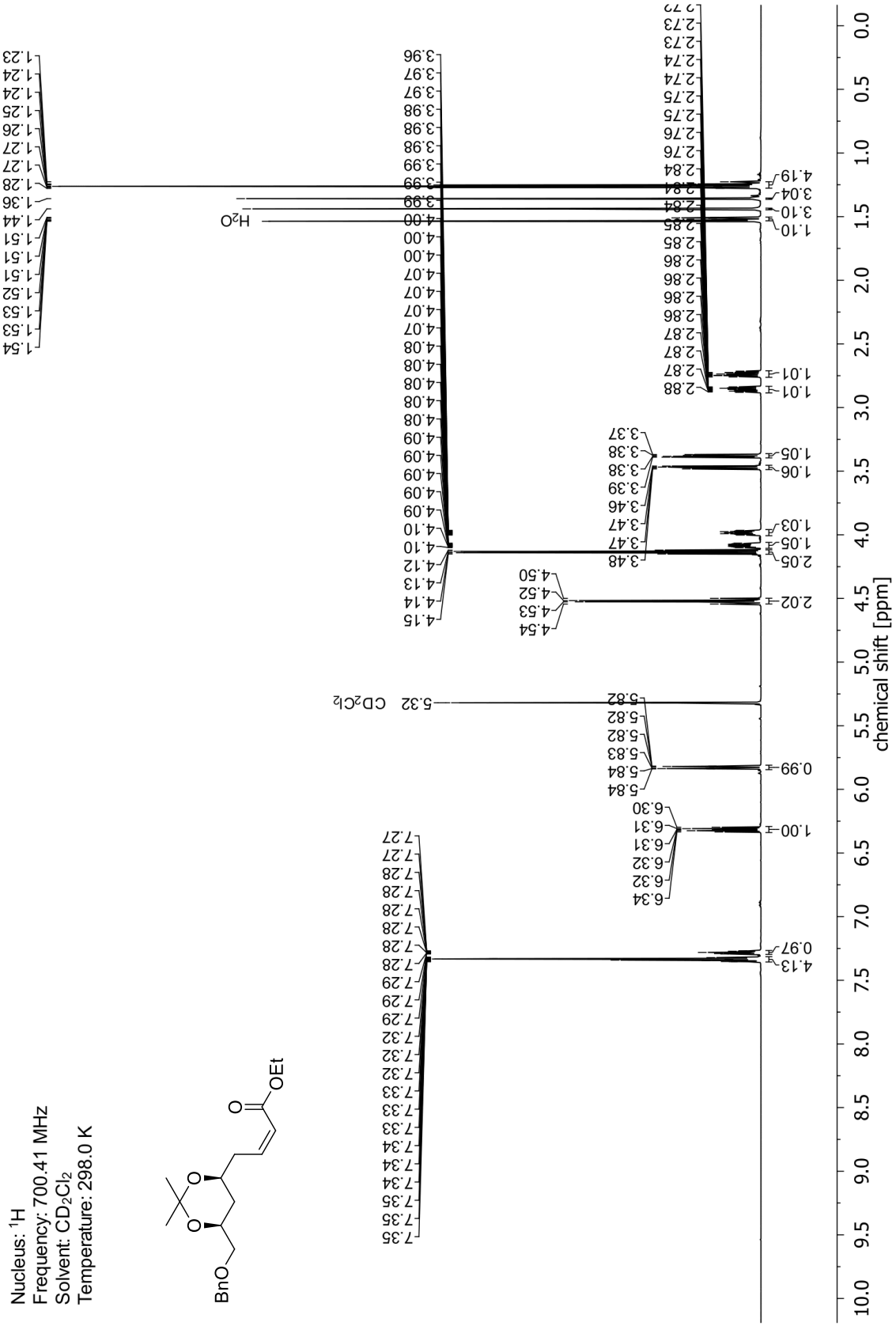


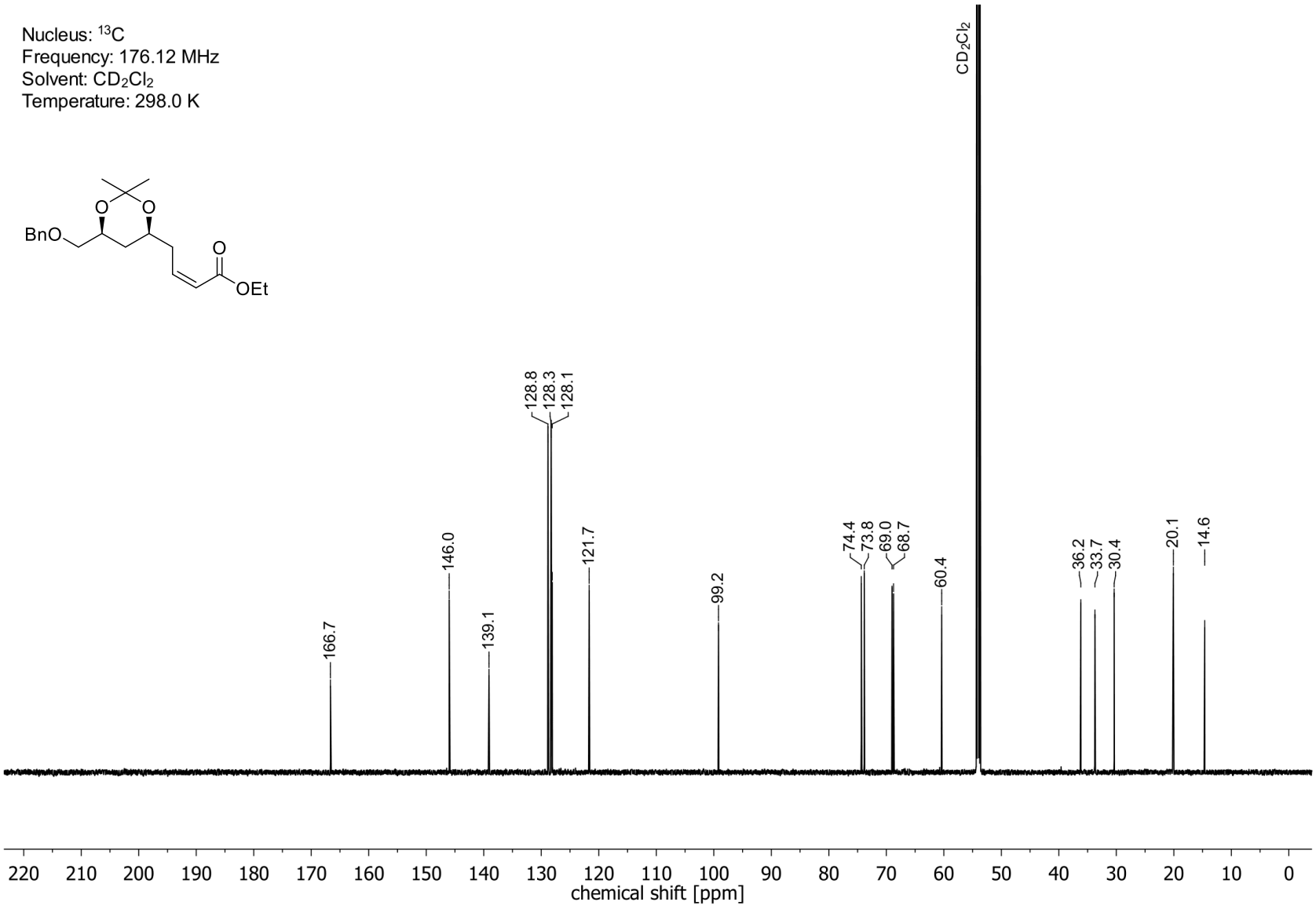

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
O
TBSO
CD2Cl2
36.3
33.6
30.4
28.6
26.2
25.9
20.2
18.8
128.8
128.2
128.1
139.1
108.2
99.0
78.5
74.4
73.8
73.7
69.0
66.8
62.7
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **265**:

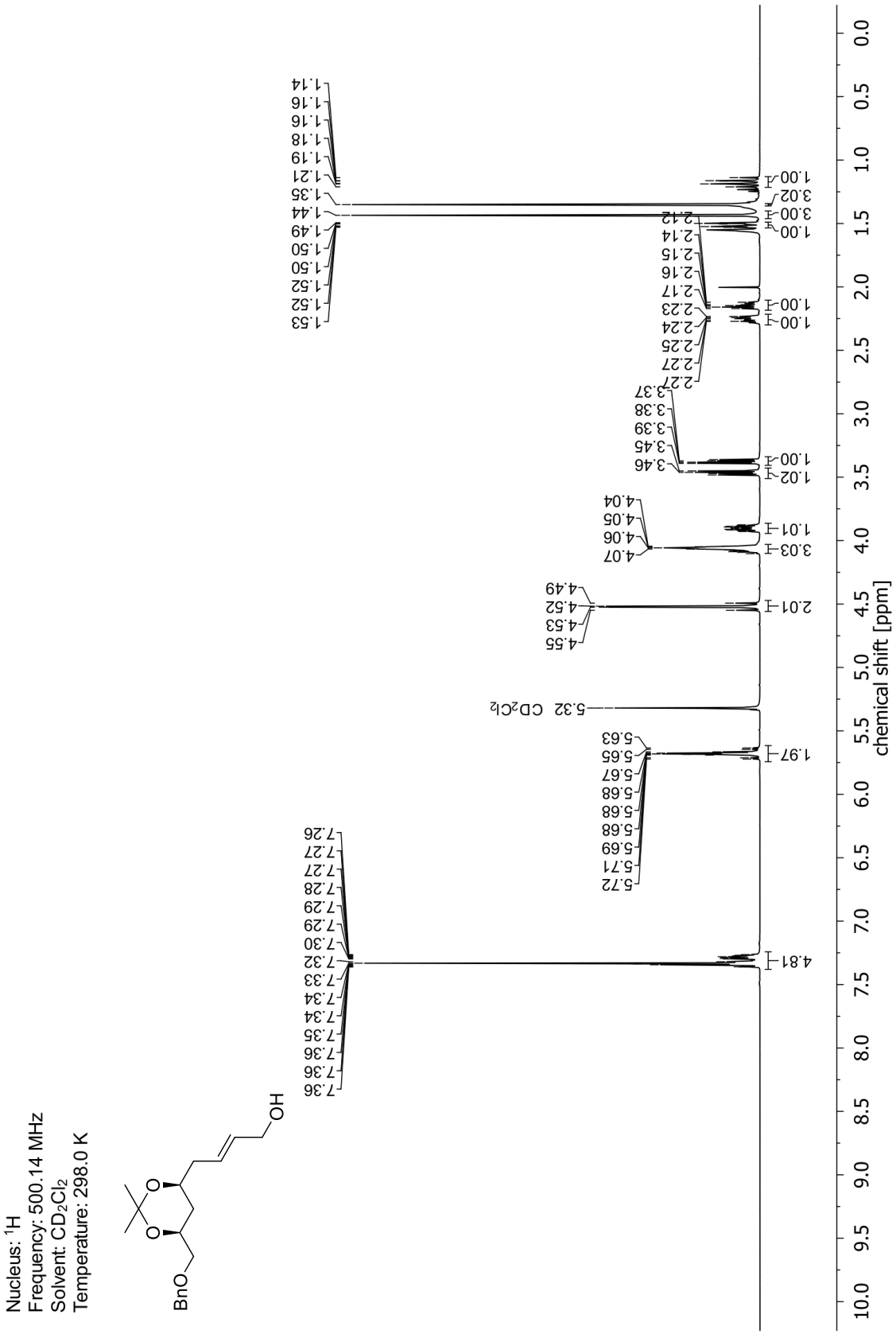


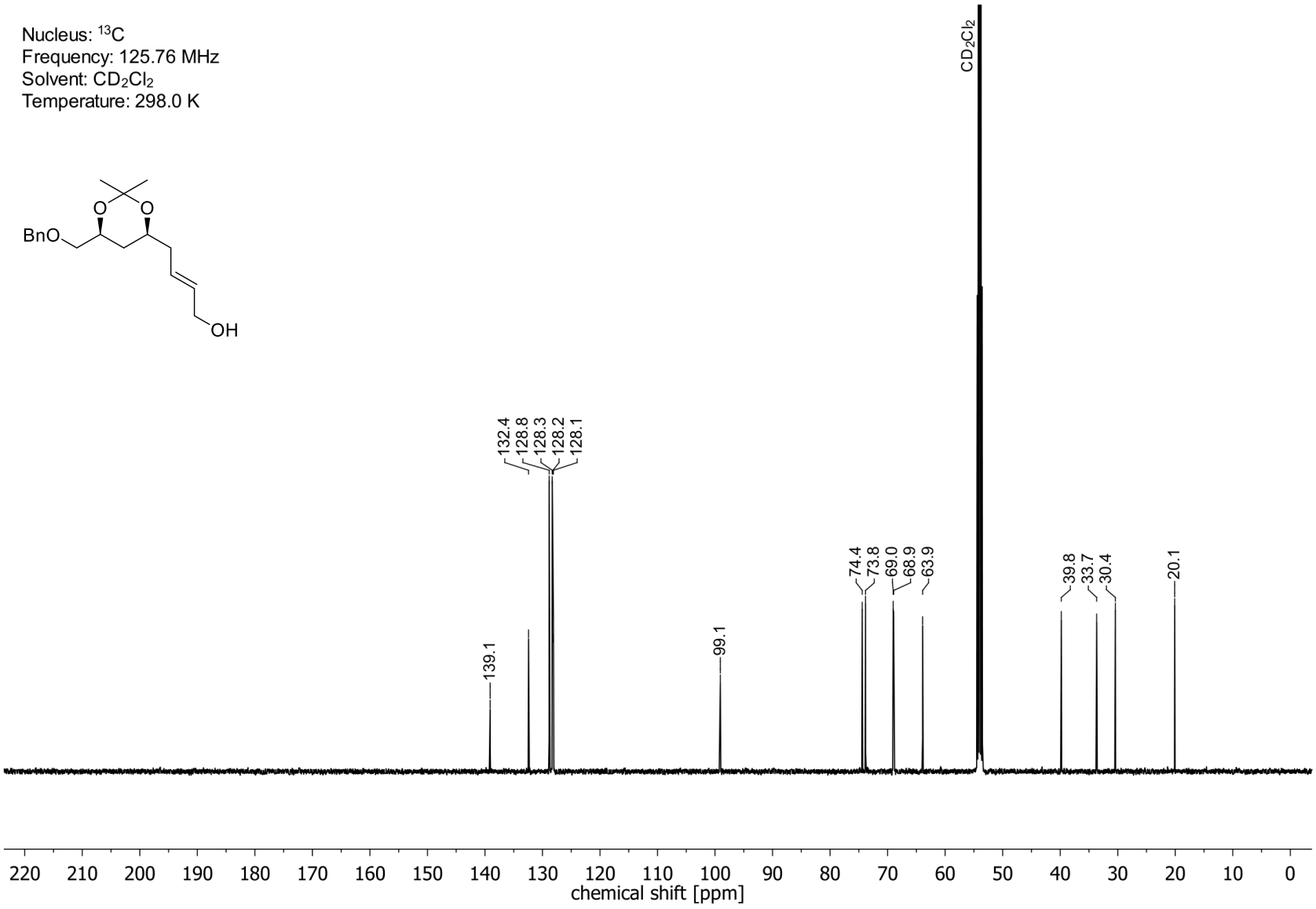

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
OEt
CD2Cl2
166.7
145.0
139.1
128.8
128.3
128.1
124.1
99.3
74.3
73.9
68.9
68.1
60.7
39.6
33.8
30.3
20.1
14.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]


Nucleus: 1H
Frequency: 700.41 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
OEt
O
H2O
CD2Cl2
chemical shift [ppm]

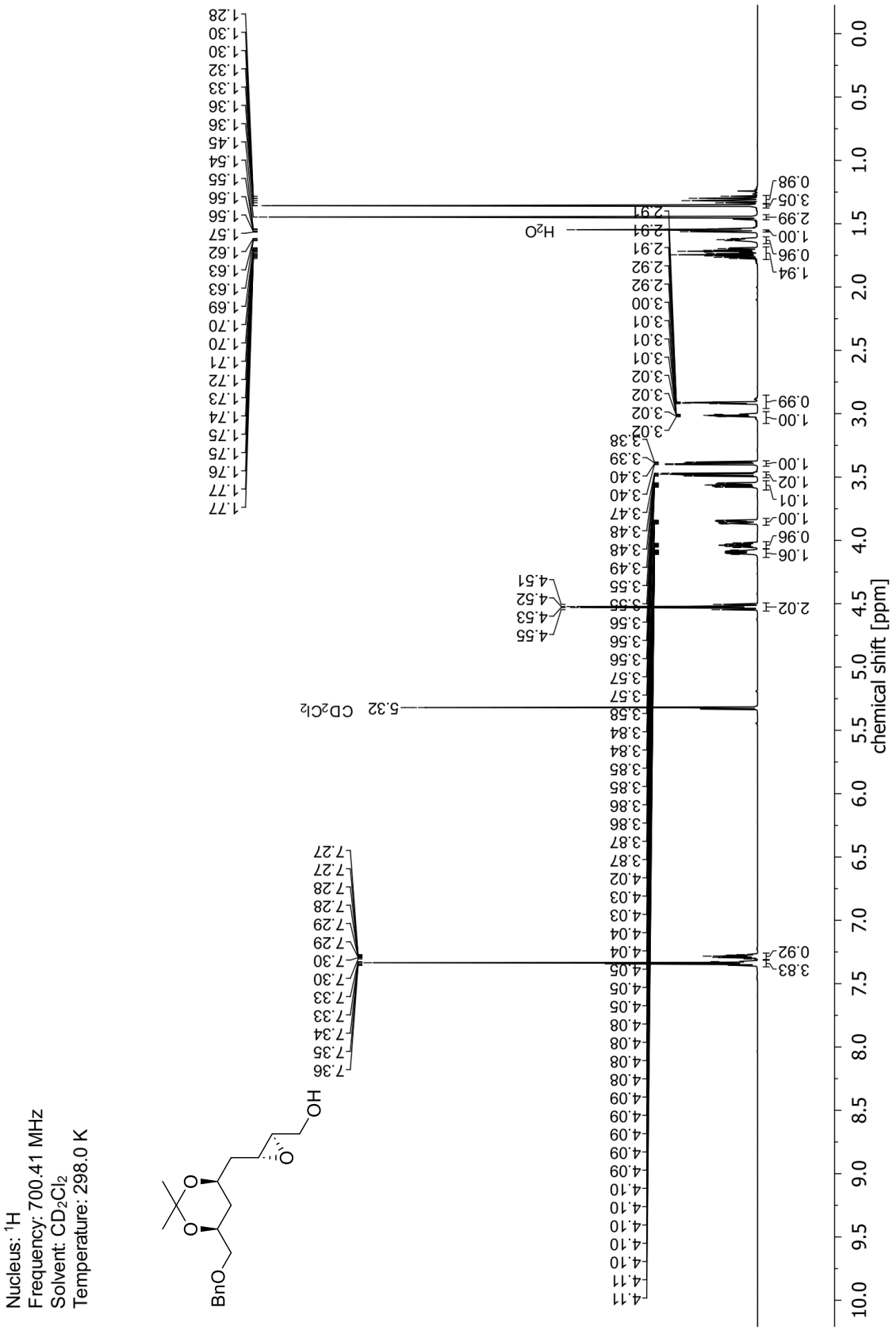

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
OEt
CD2Cl2
128.8
128.3
128.1
166.7
146.0
139.1
121.7
99.2
74.4
73.8
69.0
68.7
60.4
36.2
33.7
30.4
20.1
14.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

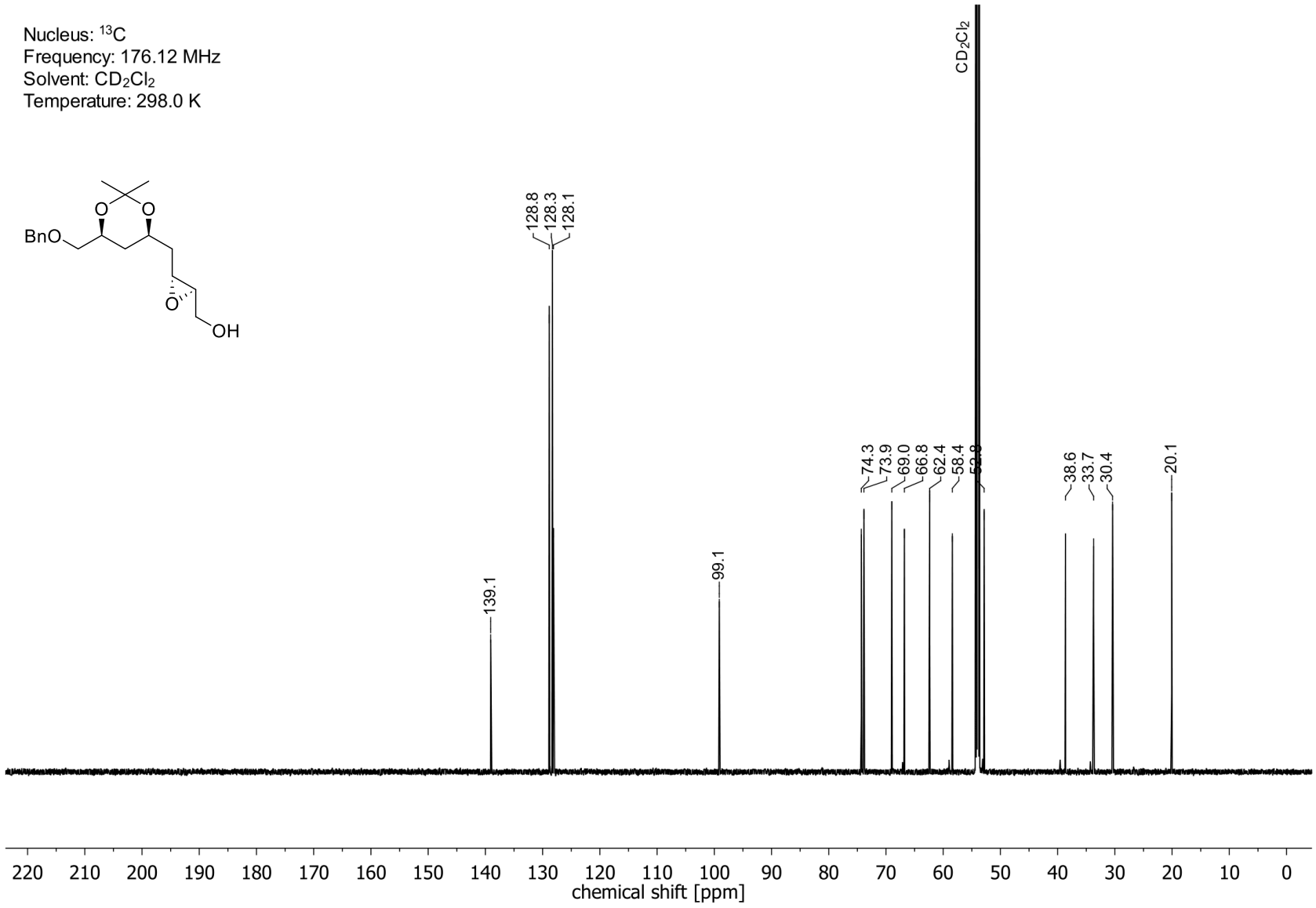
NMR-Spectra of Compound **266**:



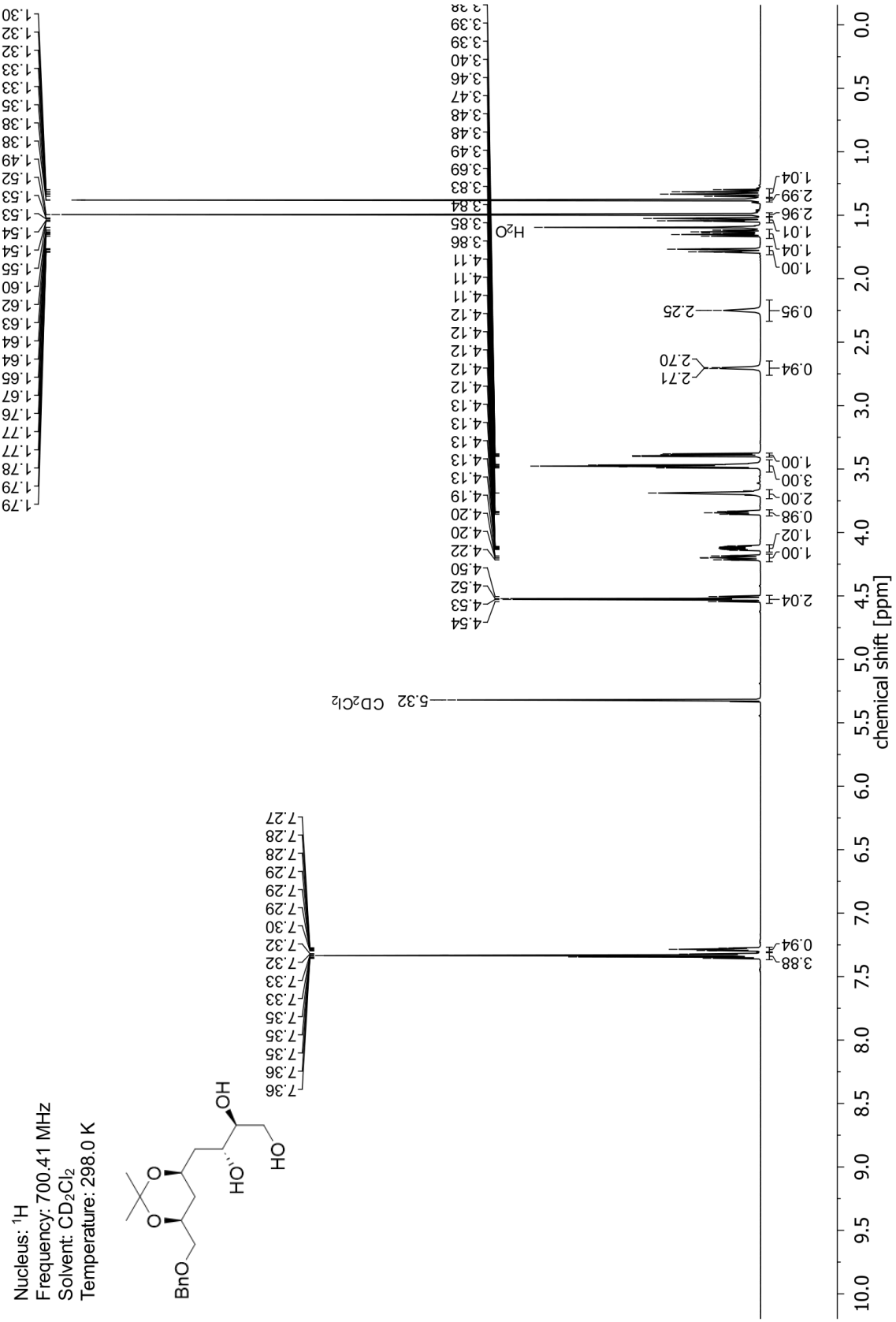

Nucleus: 13C
Frequency: 125.76 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
OH
CD2Cl2
132.4
128.8
128.3
128.2
128.1
139.1
99.1
74.4
73.8
69.0
68.9
63.9
39.8
33.7
30.4
20.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

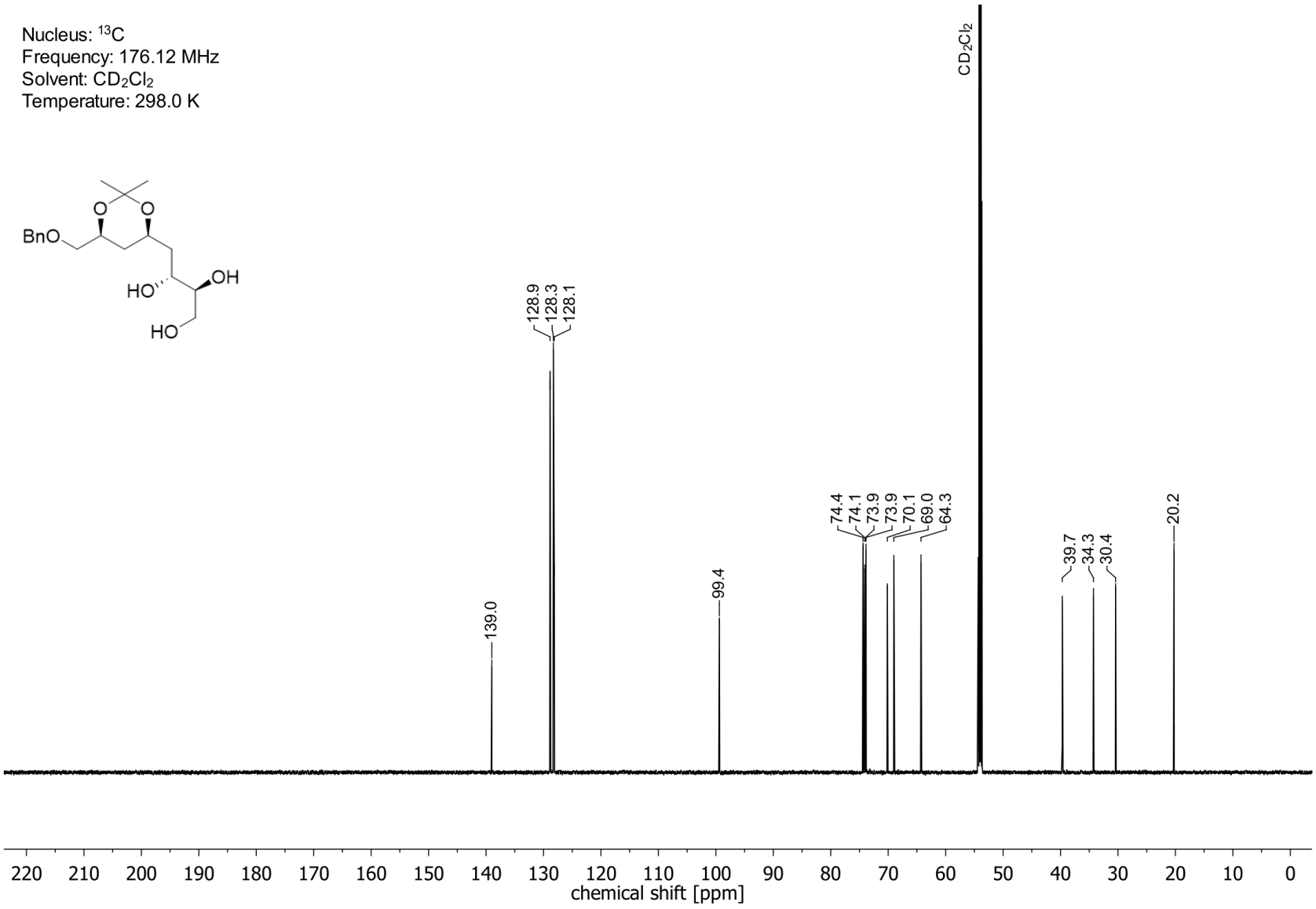
NMR-Spectra of Compound **160**:



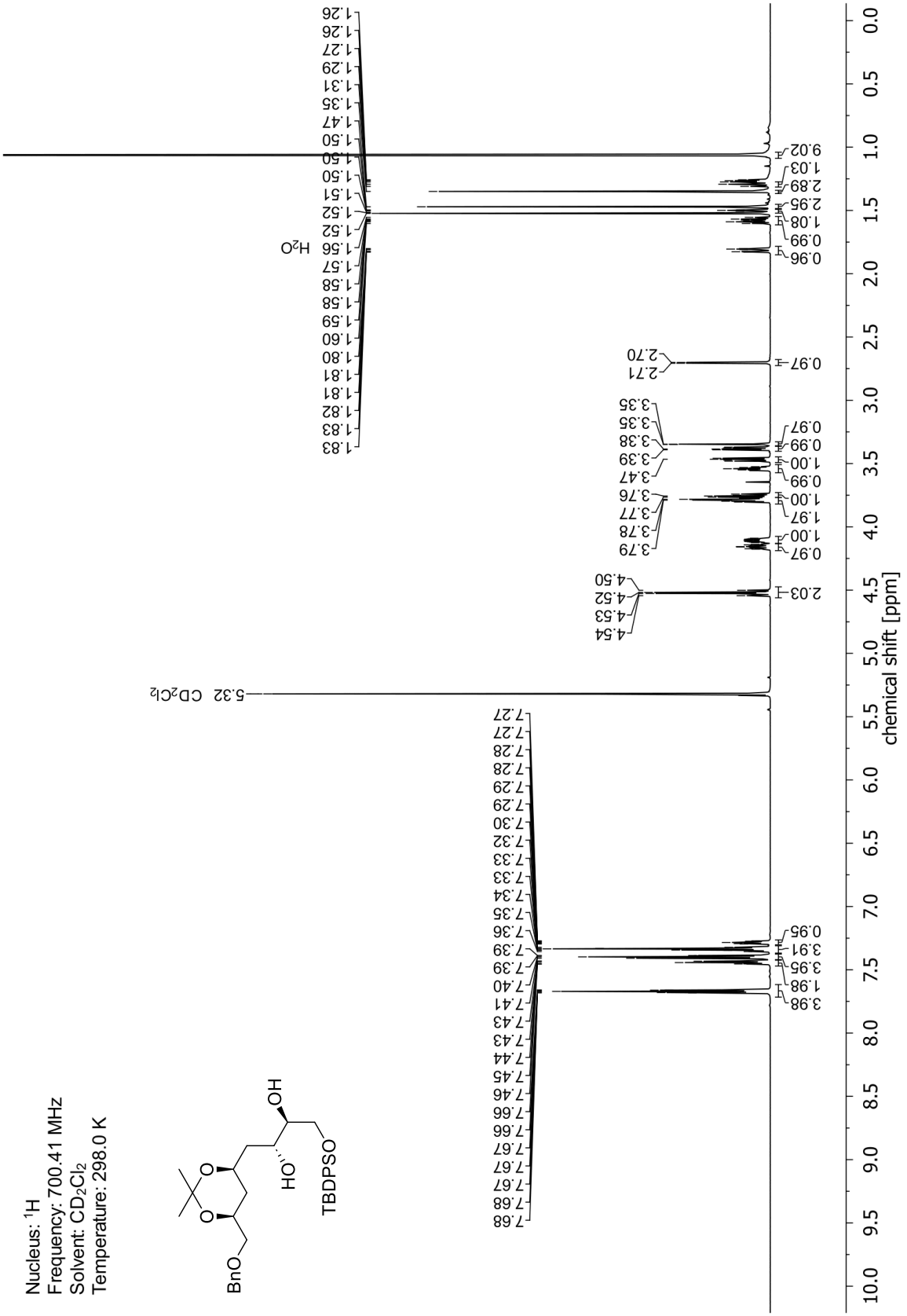

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
OH
CD2Cl2
128.8
128.3
128.1
139.1
99.1
74.3
73.9
69.0
66.8
62.4
58.4
38.6
33.7
30.4
20.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

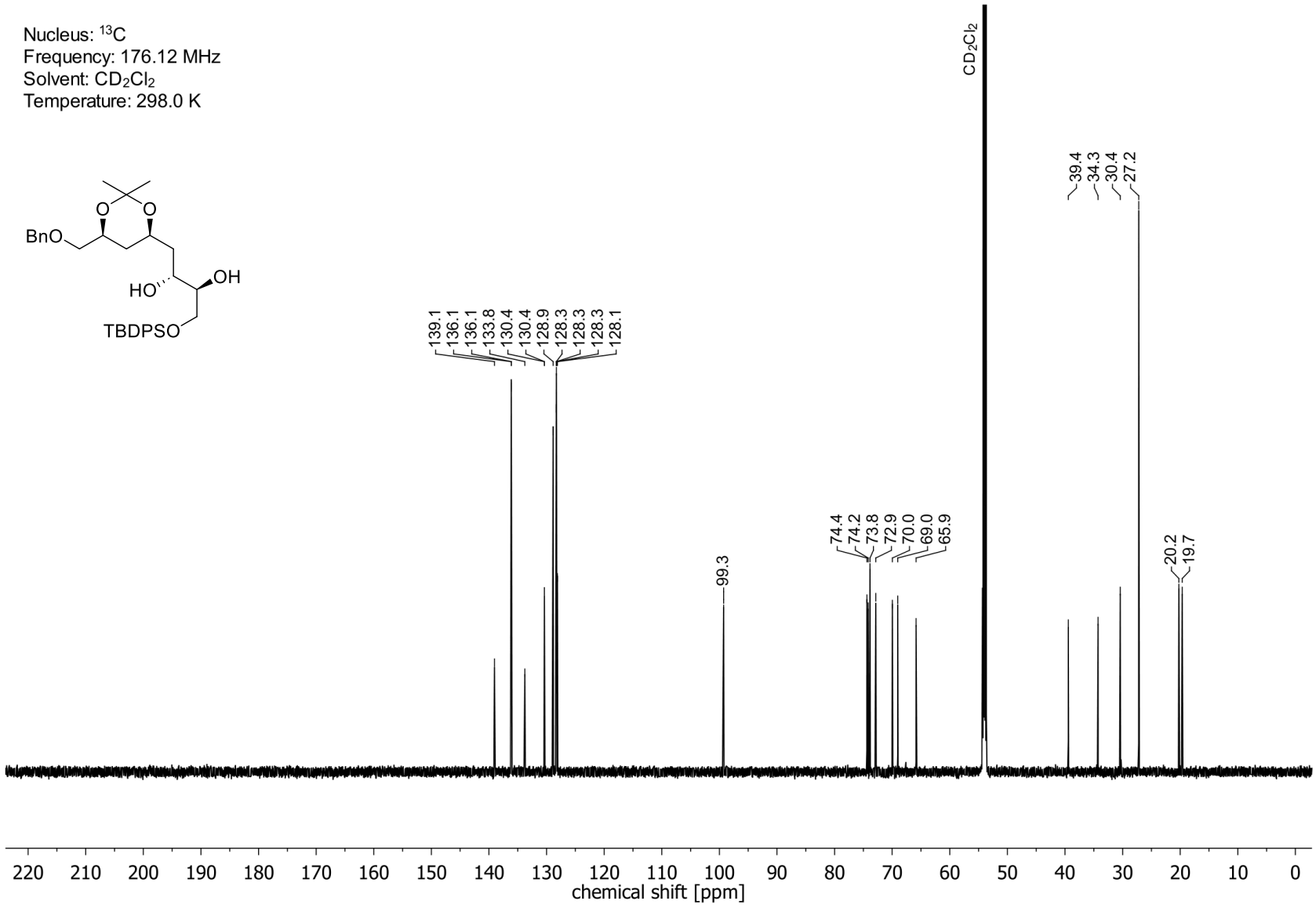
NMR-Spectra of Compound **161**:



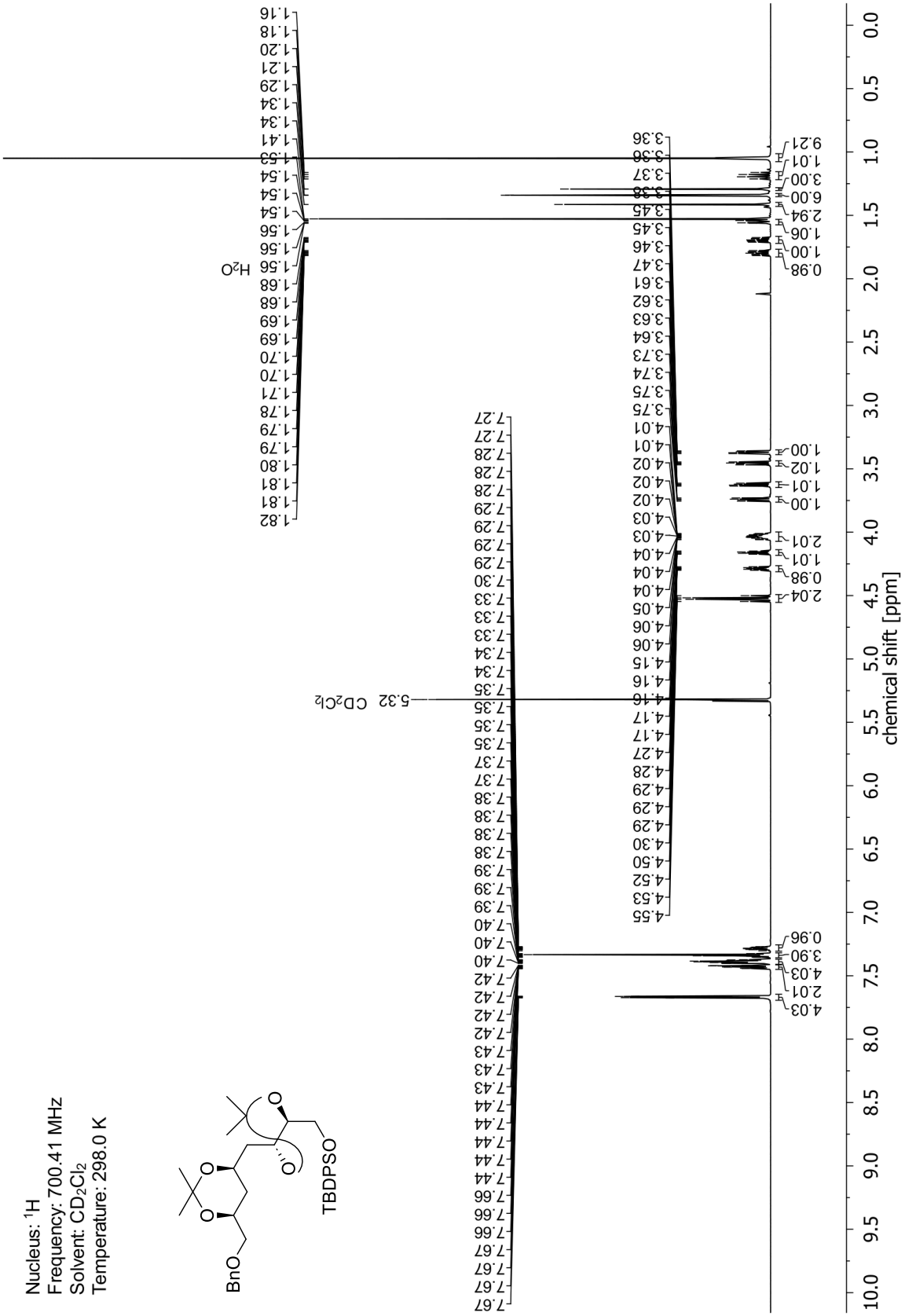

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
HO
OH
HO
CD2Cl2
128.9
128.3
128.1
139.0
99.4
74.4
74.1
73.9
73.9
70.1
69.0
64.3
39.7
34.3
30.4
20.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

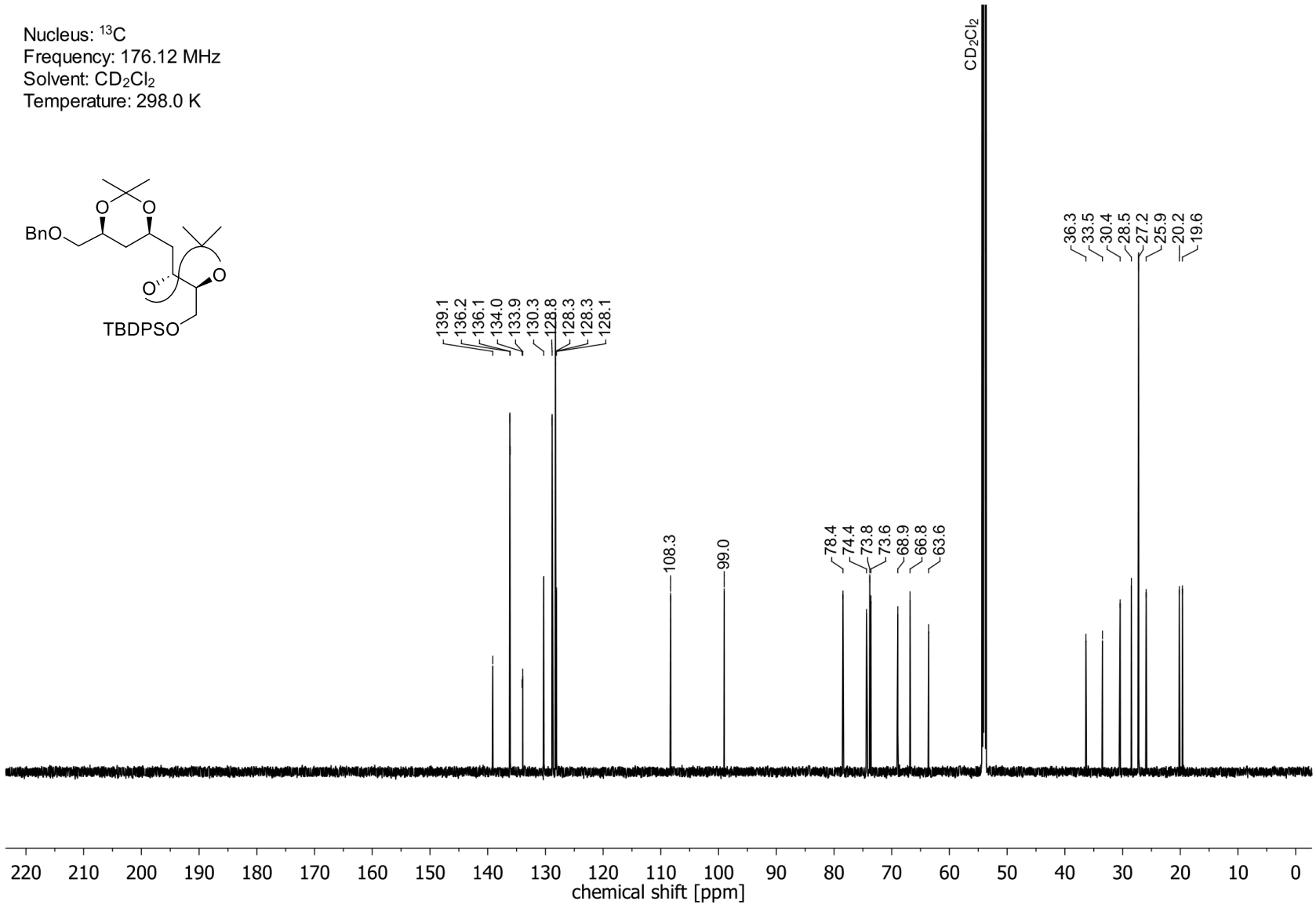
NMR-Spectra of Compound **269**:



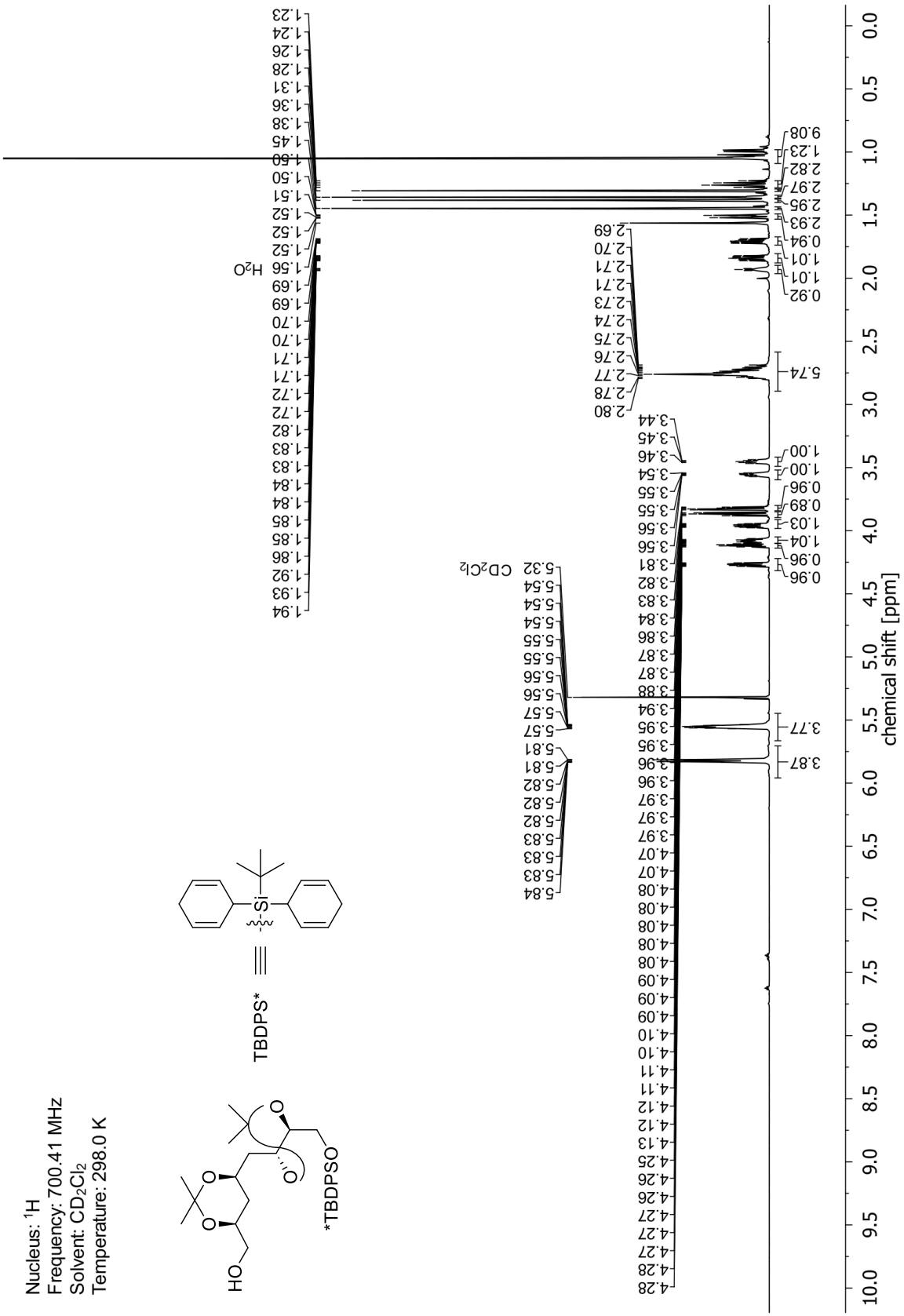

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
HO
OH
TBDPSO
139.1
136.1
136.1
133.8
130.4
130.4
128.9
128.3
128.3
128.3
128.1
99.3
74.4
74.2
73.8
72.9
70.0
69.0
65.9
CD2Cl2
39.4
34.3
30.4
27.2
20.2
19.7
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

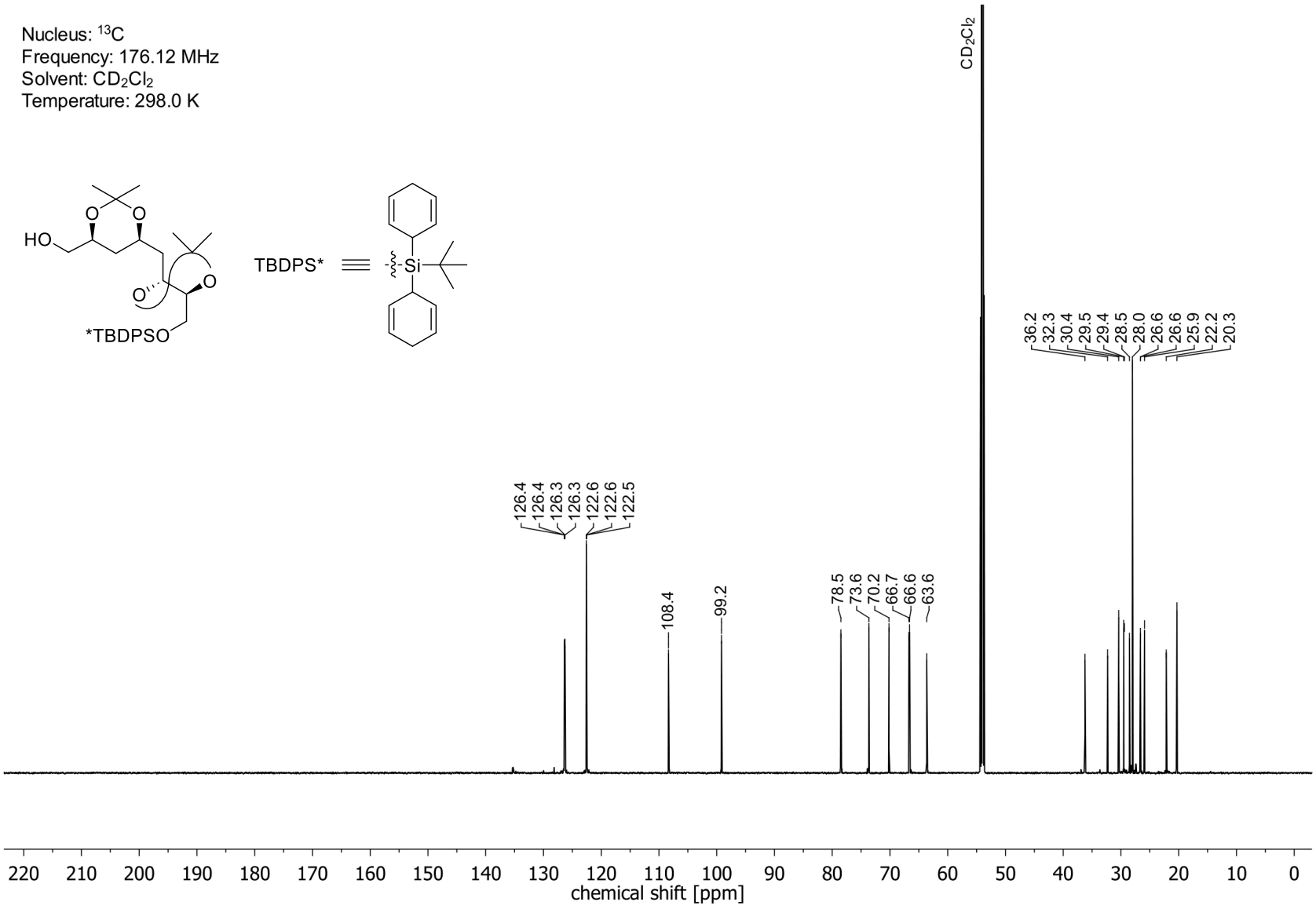
NMR-Spectra of Compound **256**:



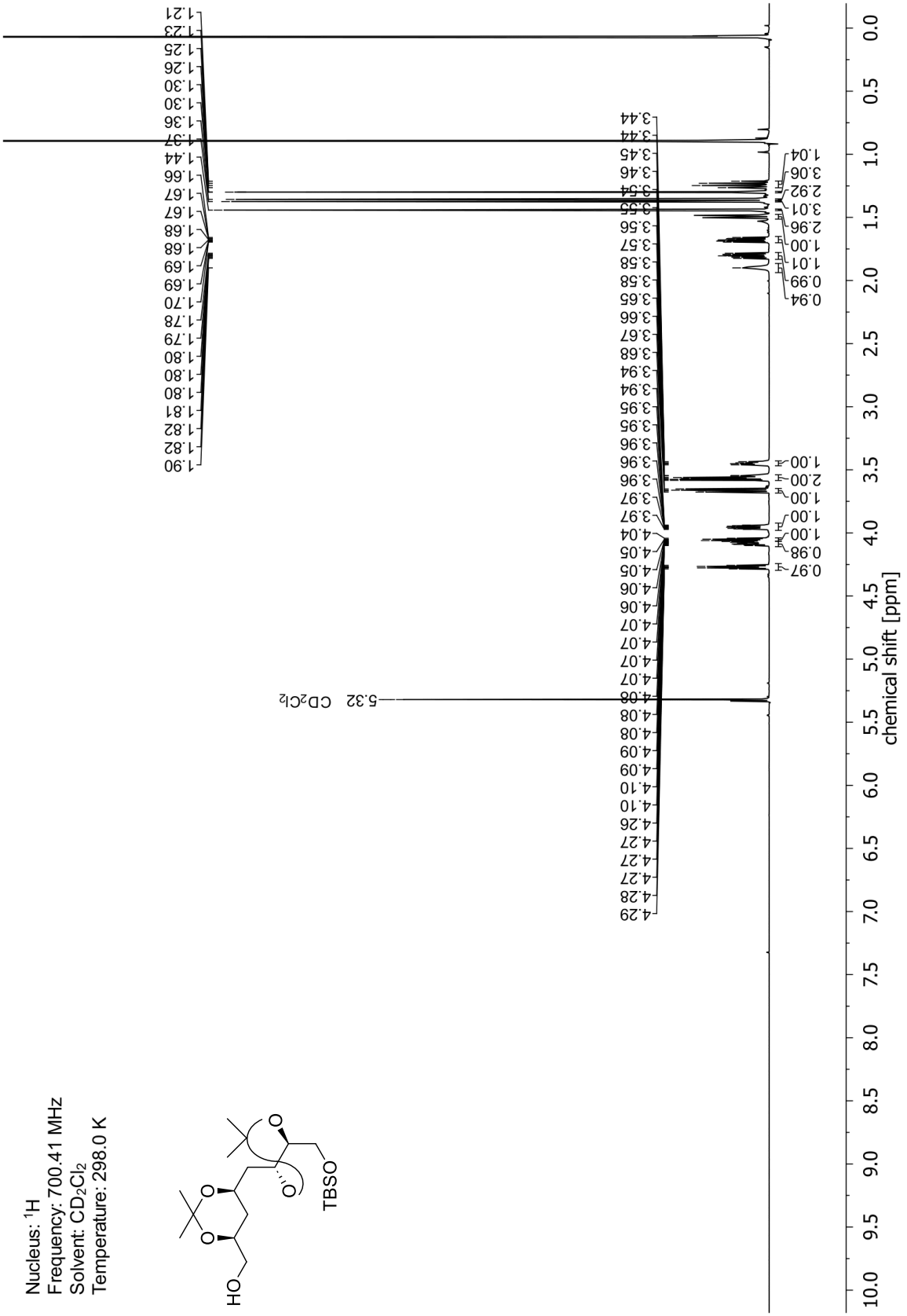

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
O
O
O
O
TBDPSO
CD2Cl2
139.1
136.2
136.1
134.0
133.9
130.3
128.8
128.3
128.3
128.1
108.3
99.0
78.4
74.4
73.8
73.6
68.9
66.8
63.6
36.3
33.5
30.4
28.5
27.2
25.9
20.2
19.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

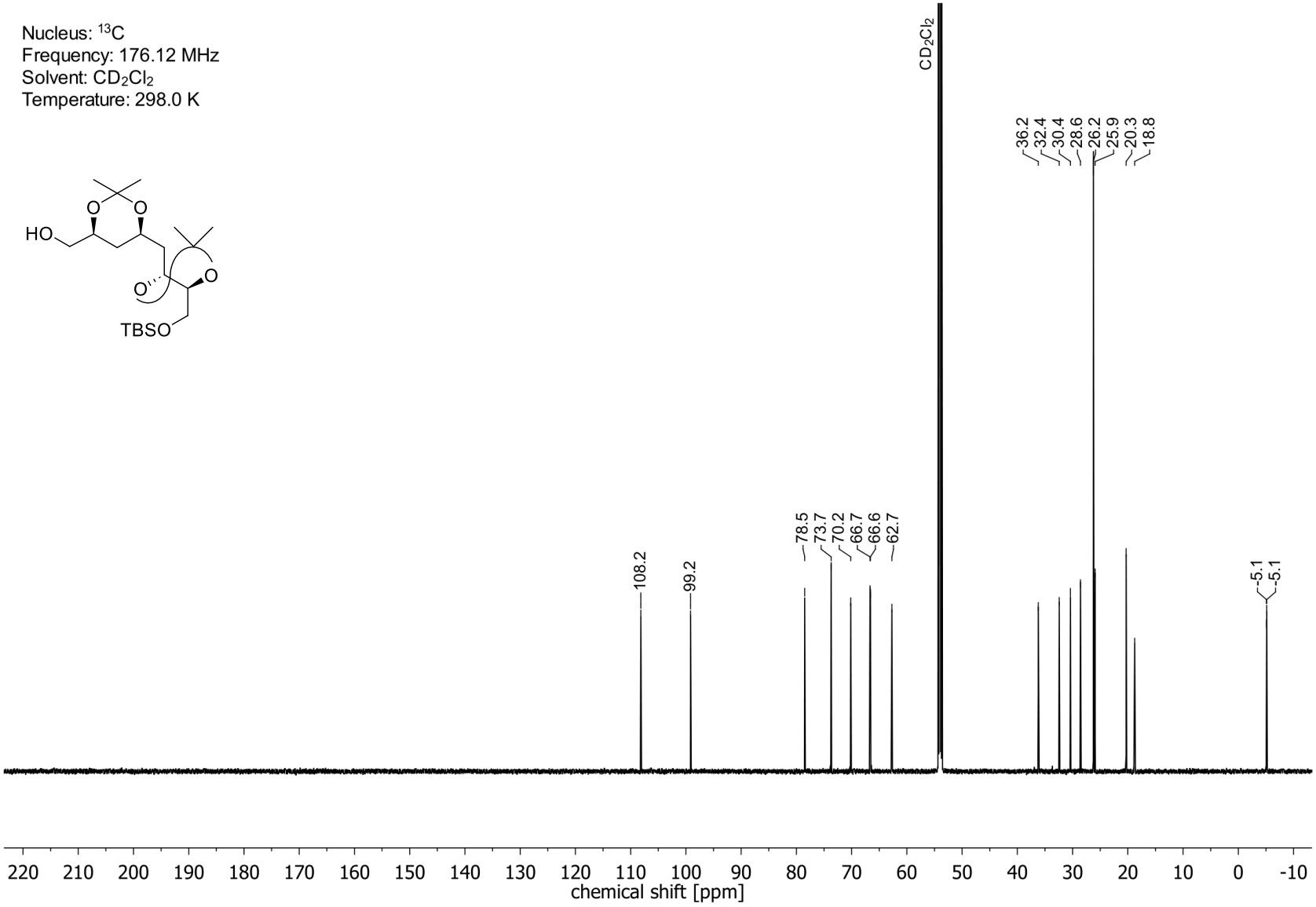
NMR-Spectra of Compound **270**:



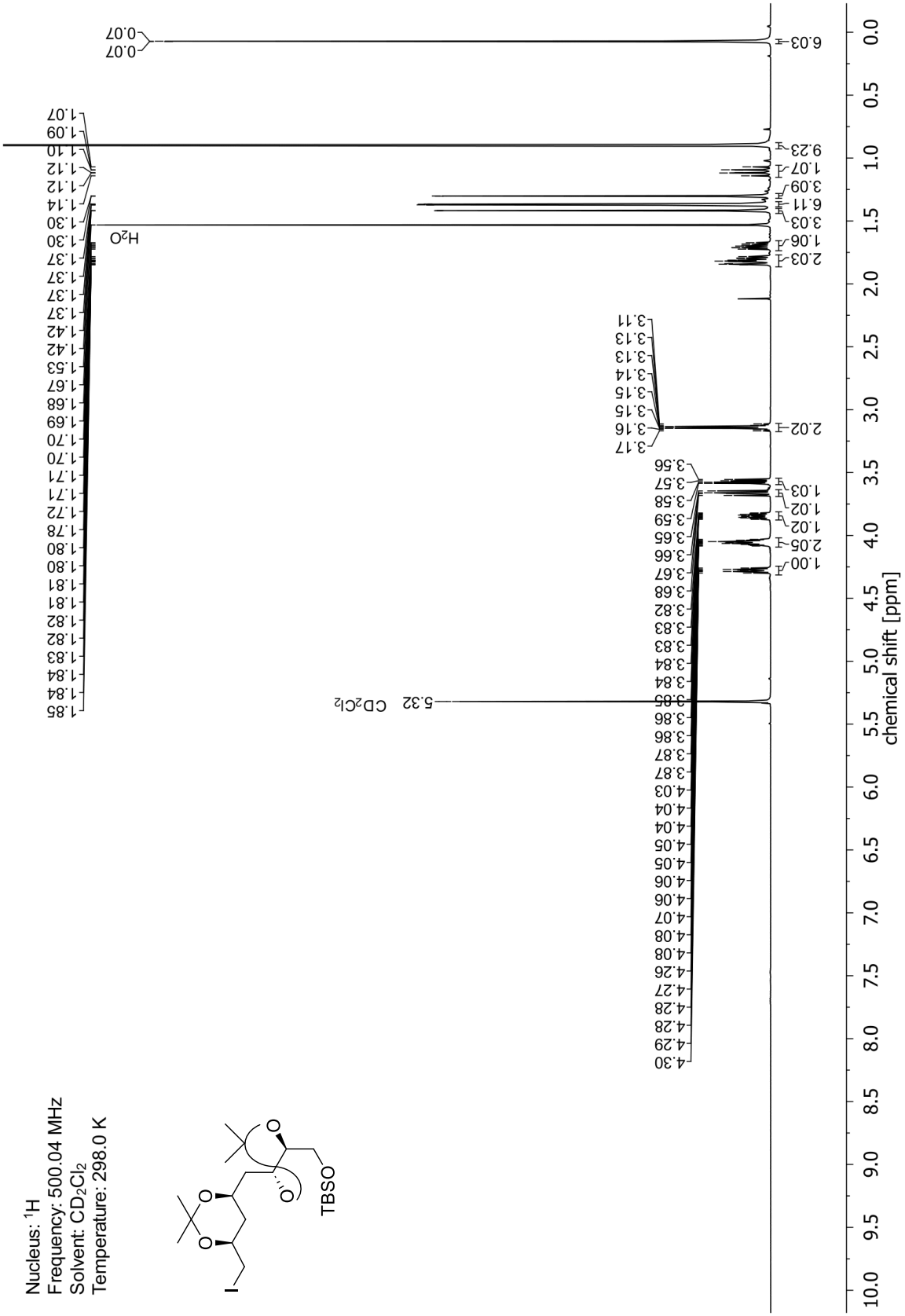

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
O
O
O
O
*TBDPSO
TBDPS*
Si
CD2Cl2
36.2
32.3
30.4
29.5
29.4
28.5
28.0
26.6
26.6
25.9
22.2
20.3
126.4
126.4
126.3
126.3
122.6
122.6
122.5
108.4
99.2
78.5
73.6
70.2
66.7
66.6
63.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

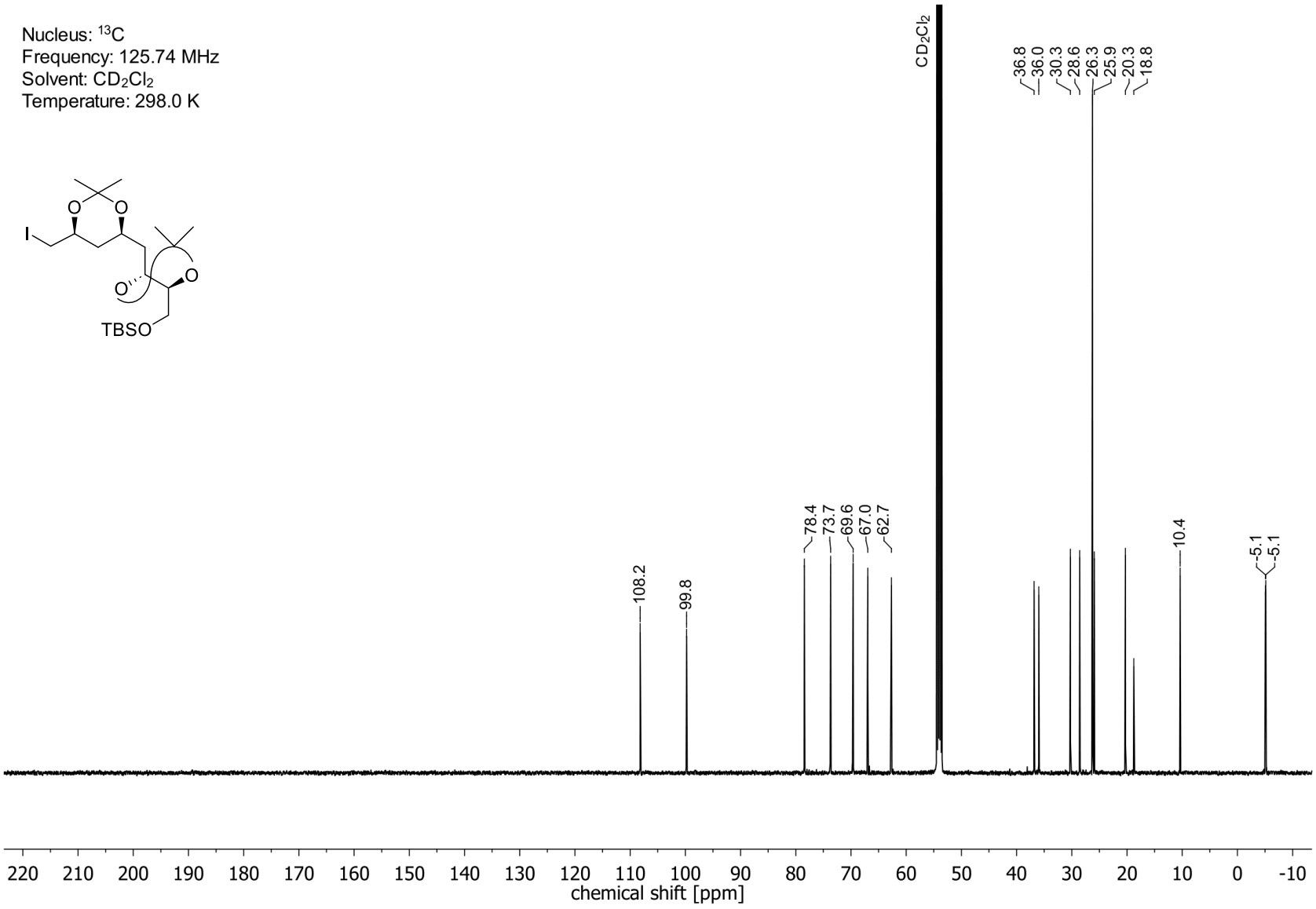
NMR-Spectra of Compound **271**:



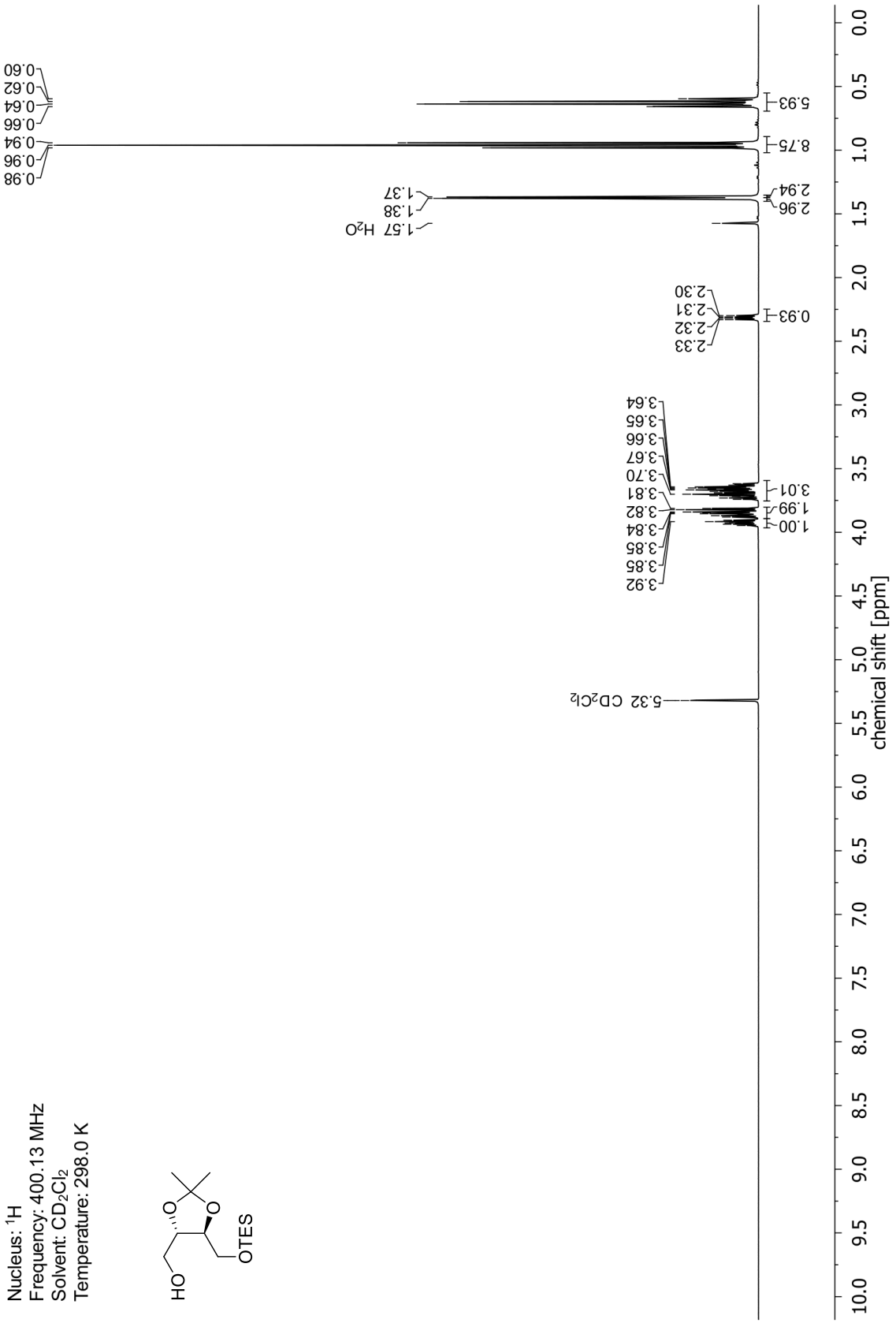

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
O
O
O
O
TBSO
CD2Cl2
36.2
32.4
30.4
28.6
26.2
25.9
20.3
18.8
108.2
99.2
78.5
73.7
70.2
66.7
66.6
62.7
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

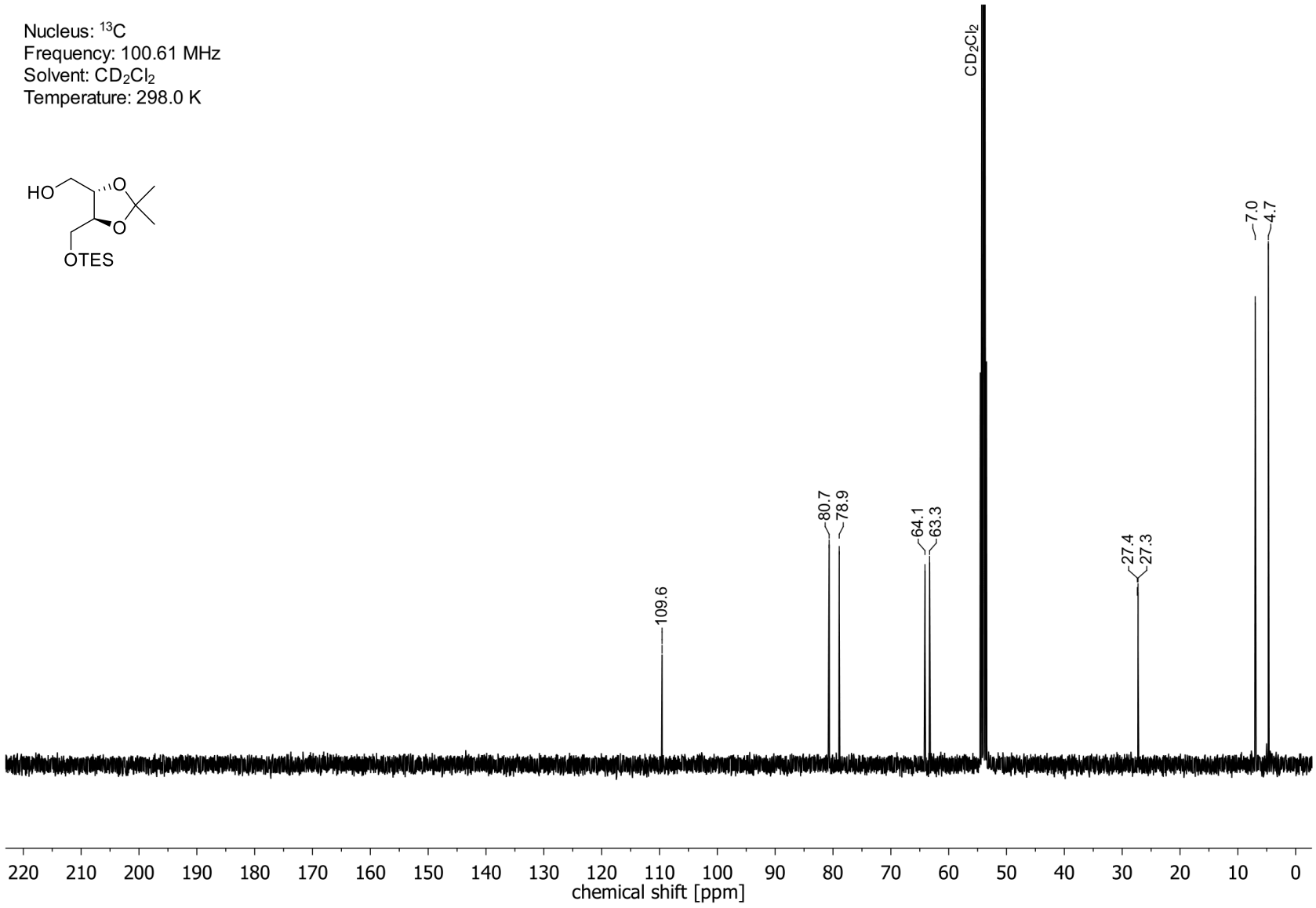
NMR-Spectra of Compound **156**:



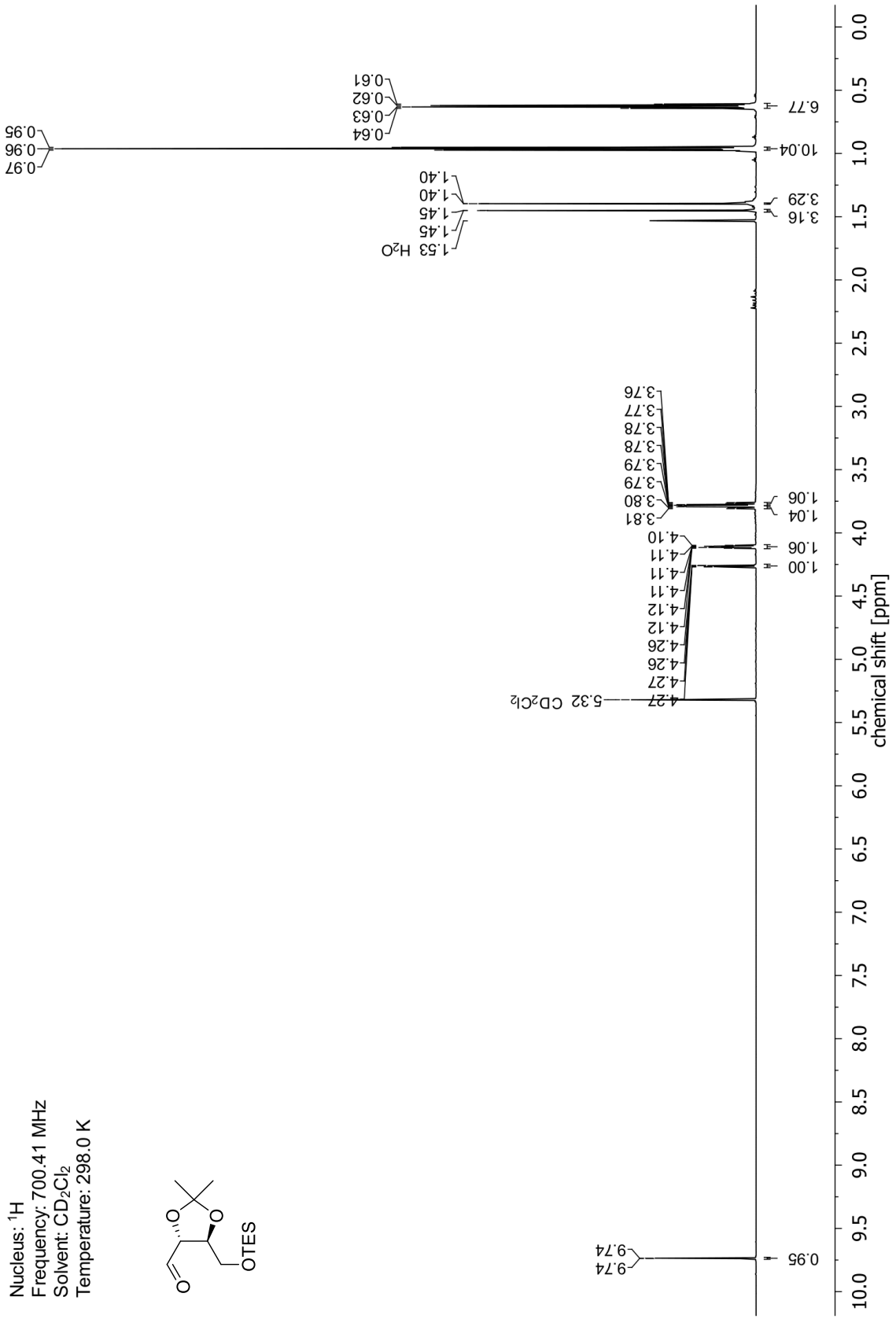

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
I
O
O
O
O
TBSO
CD2Cl2
36.8
36.0
30.3
28.6
26.3
25.9
20.3
18.8
108.2
99.8
78.4
73.7
69.6
67.0
62.7
10.4
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **275**:

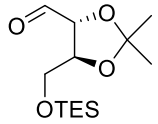



Nucleus: 13C
Frequency: 100.61 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
O
O
OTES
CD2Cl2
109.6
80.7
78.9
64.1
63.3
27.4
27.3
7.0
4.7
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

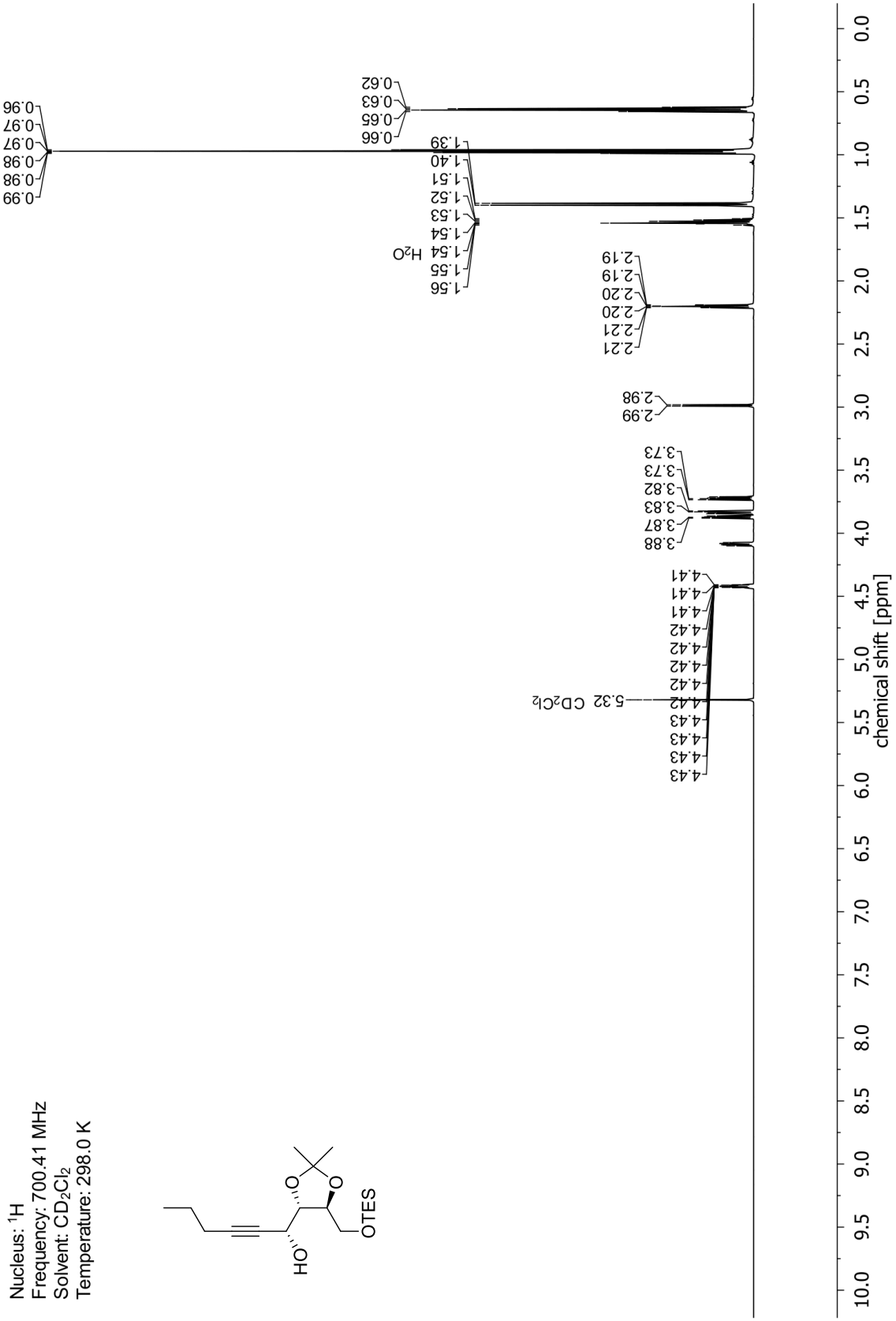
NMR-Spectra of Compound **276**:

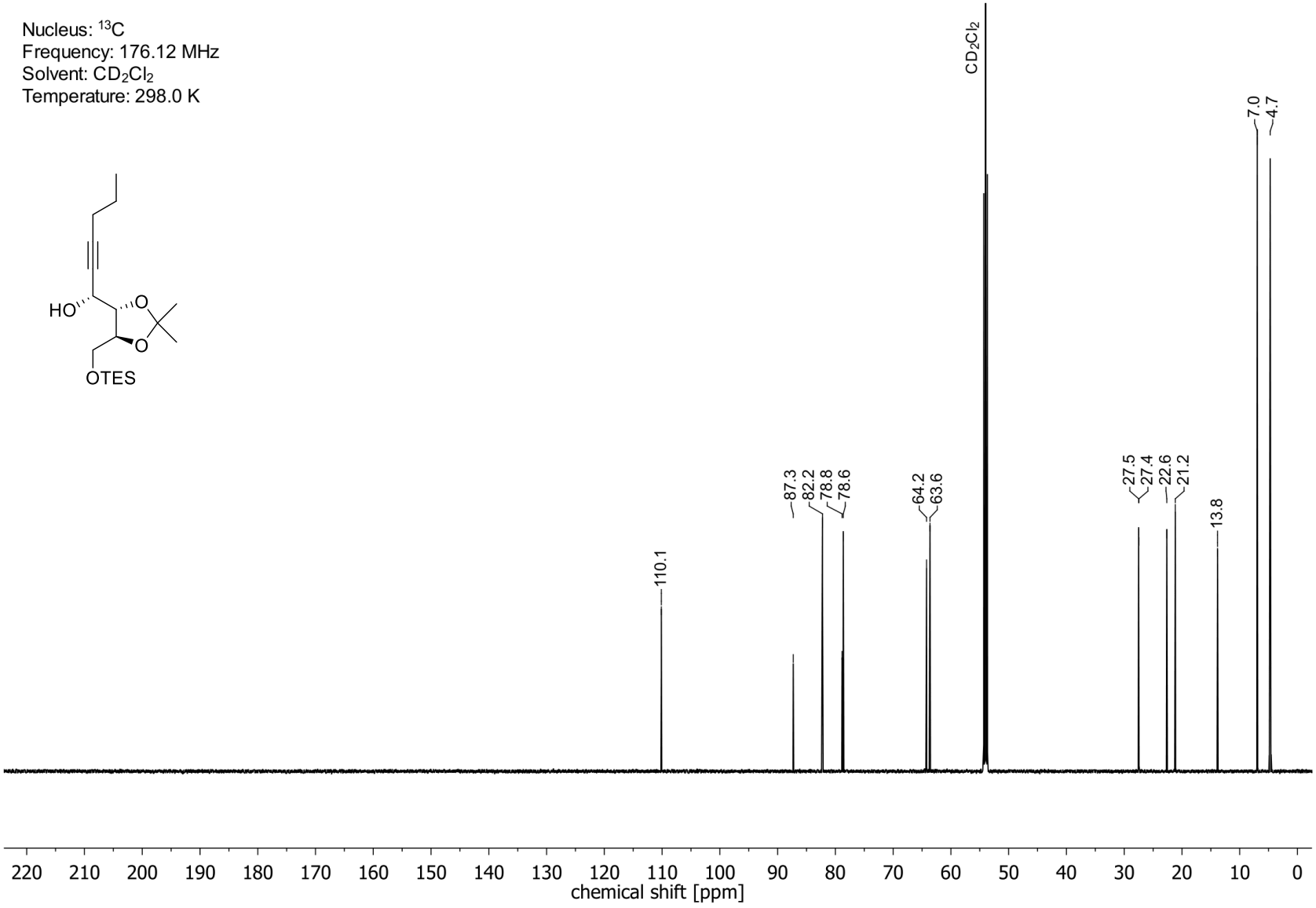


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

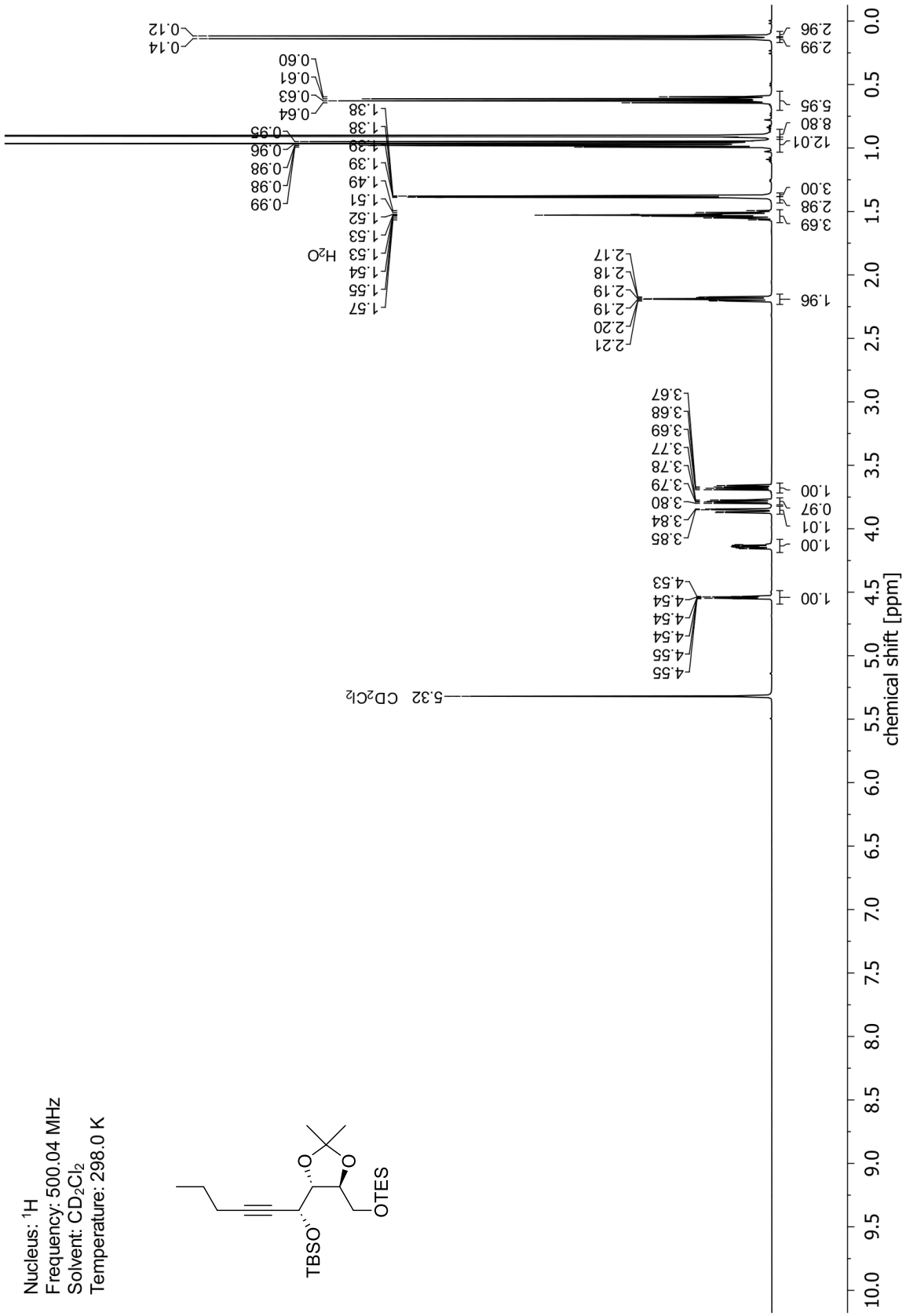


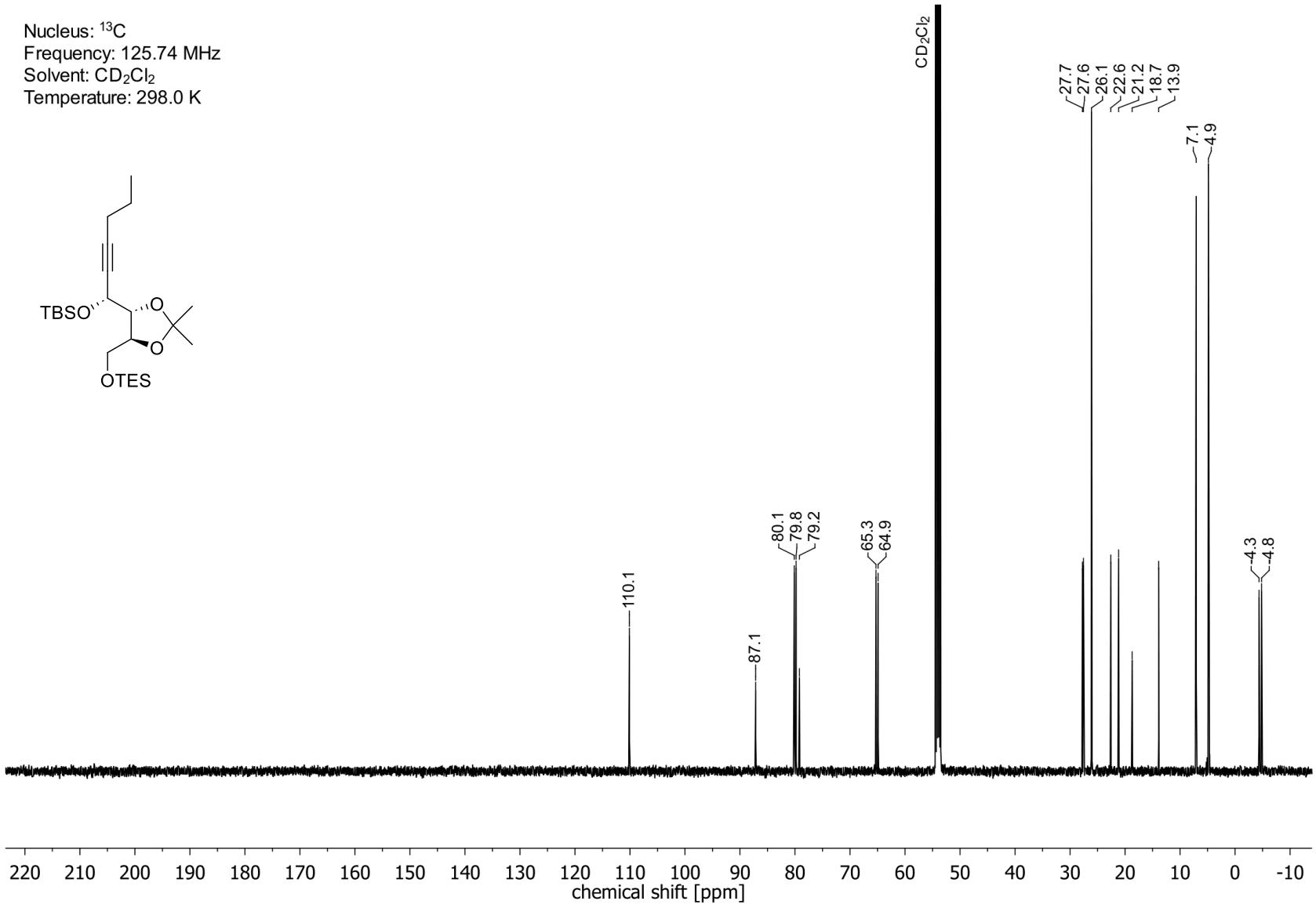
NMR-Spectra of Compound **278**:



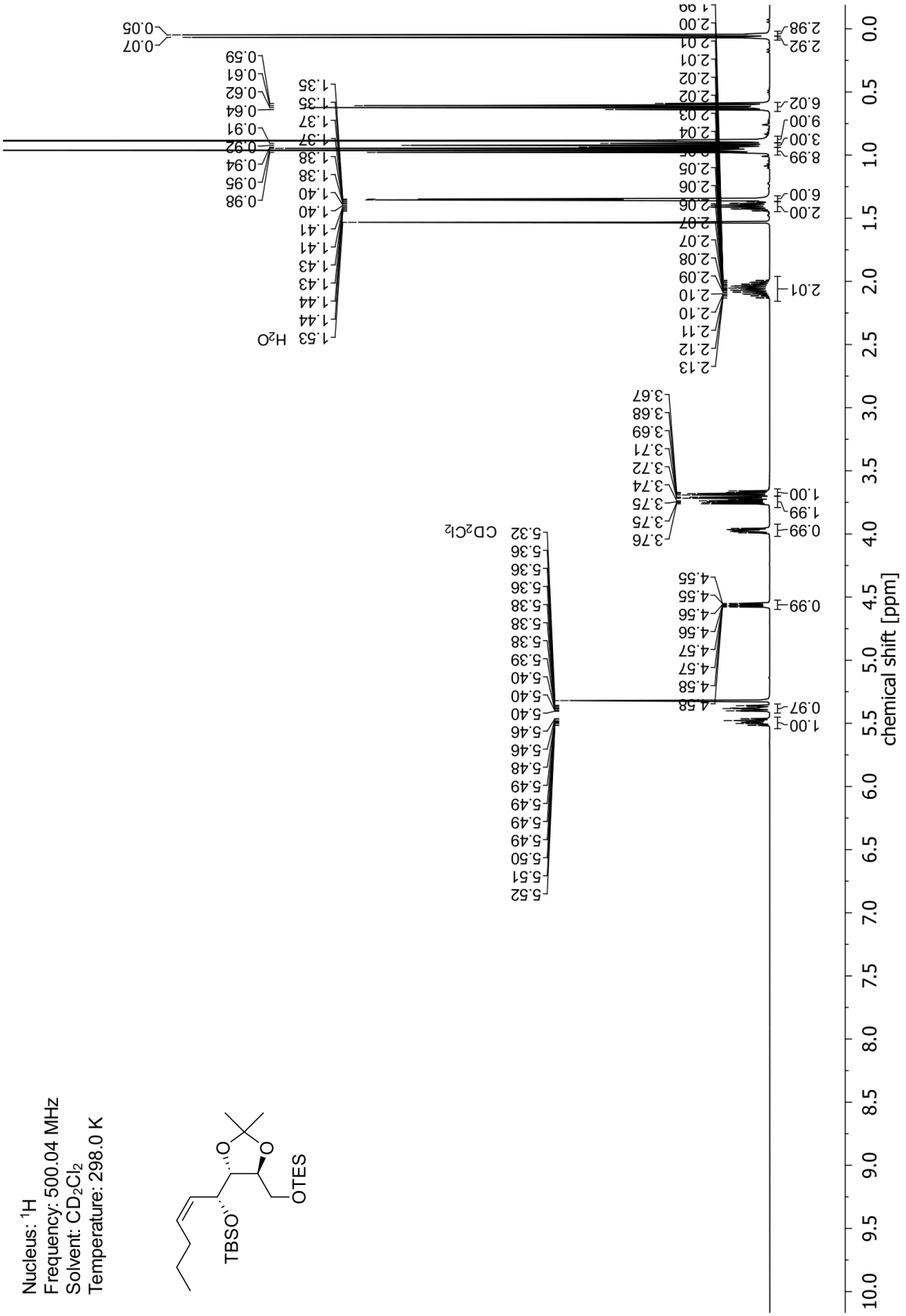

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
O
O
OTES
CD2Cl2
7.0
4.7
110.1
87.3
82.2
78.8
78.6
64.2
63.6
27.5
27.4
22.6
21.2
13.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

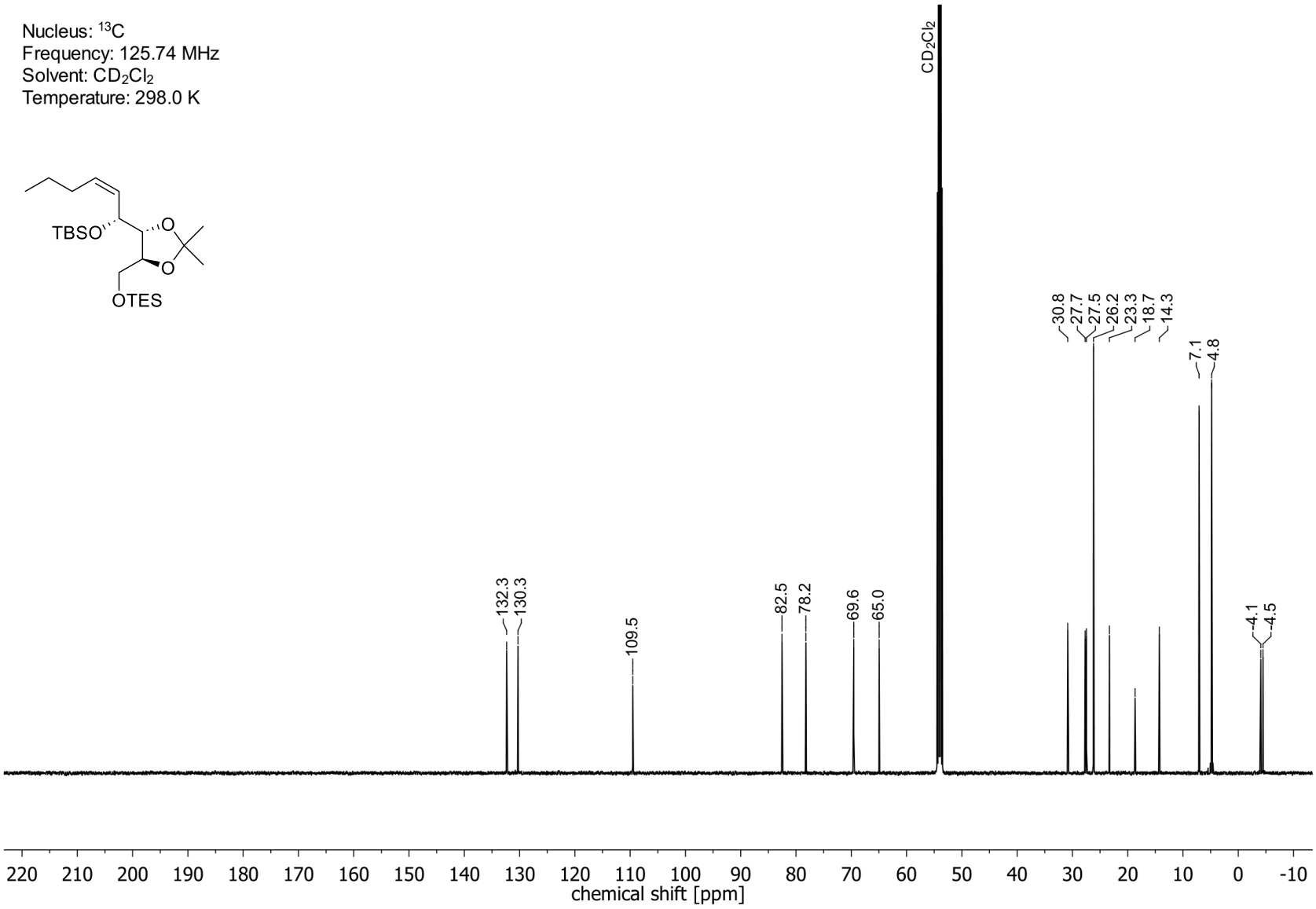
NMR-Spectra of Compound **279**:



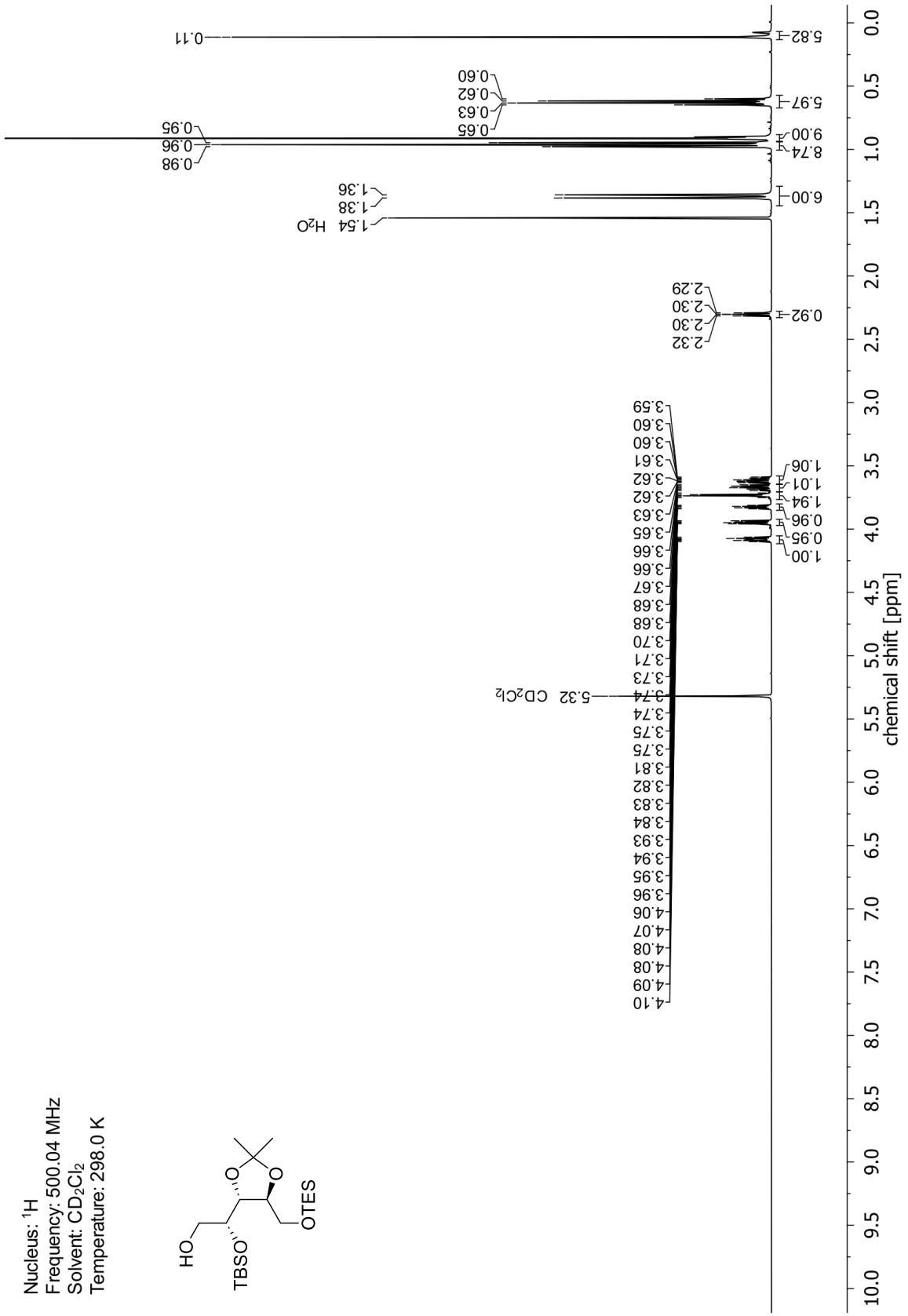

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
O
O
OTES
CD2Cl2
27.7
27.6
26.1
22.6
21.2
18.7
13.9
7.1
4.9
110.1
87.1
80.1
79.8
79.2
65.3
64.9
4.3
4.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

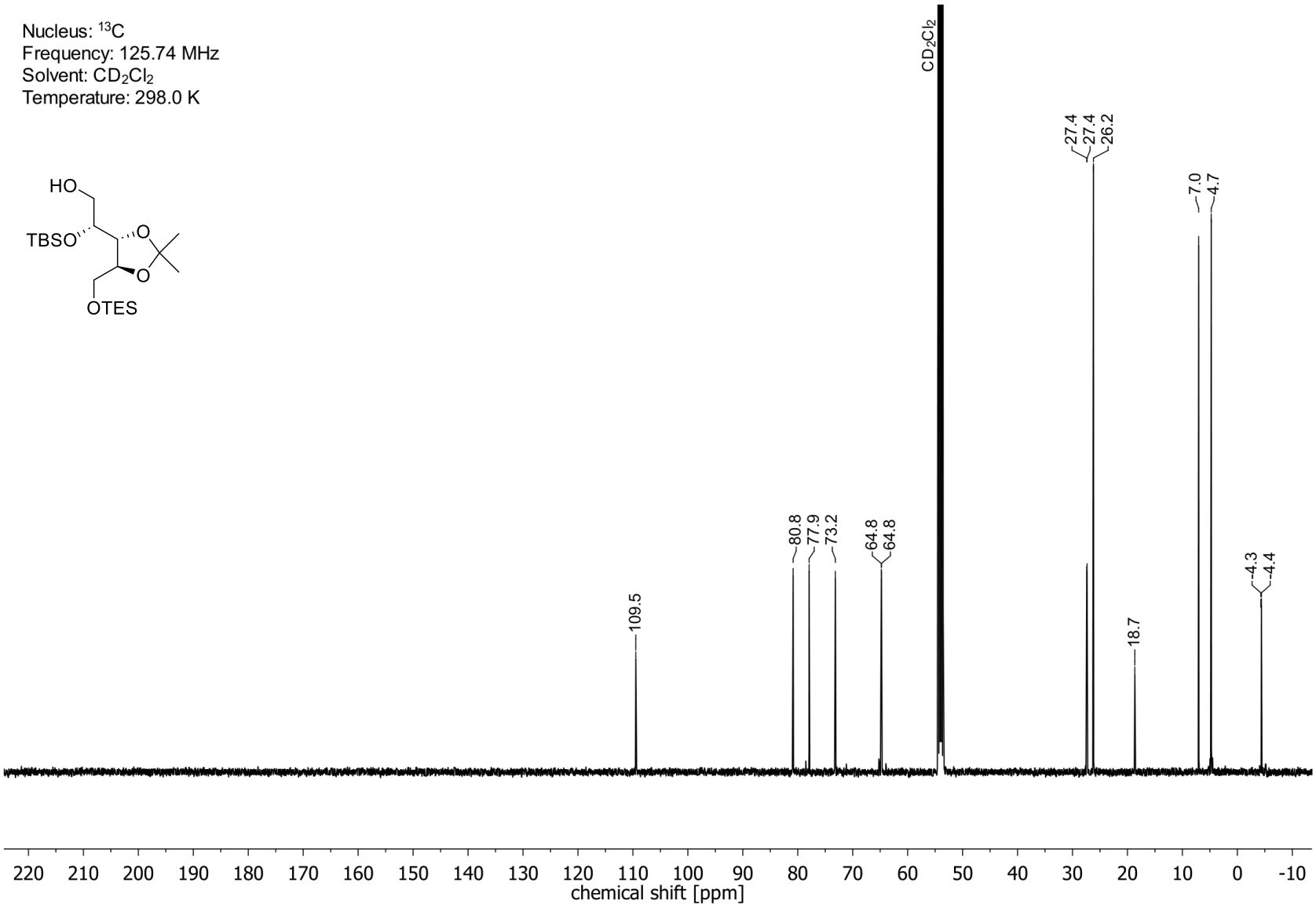
NMR-Spectra of Compound **280**:



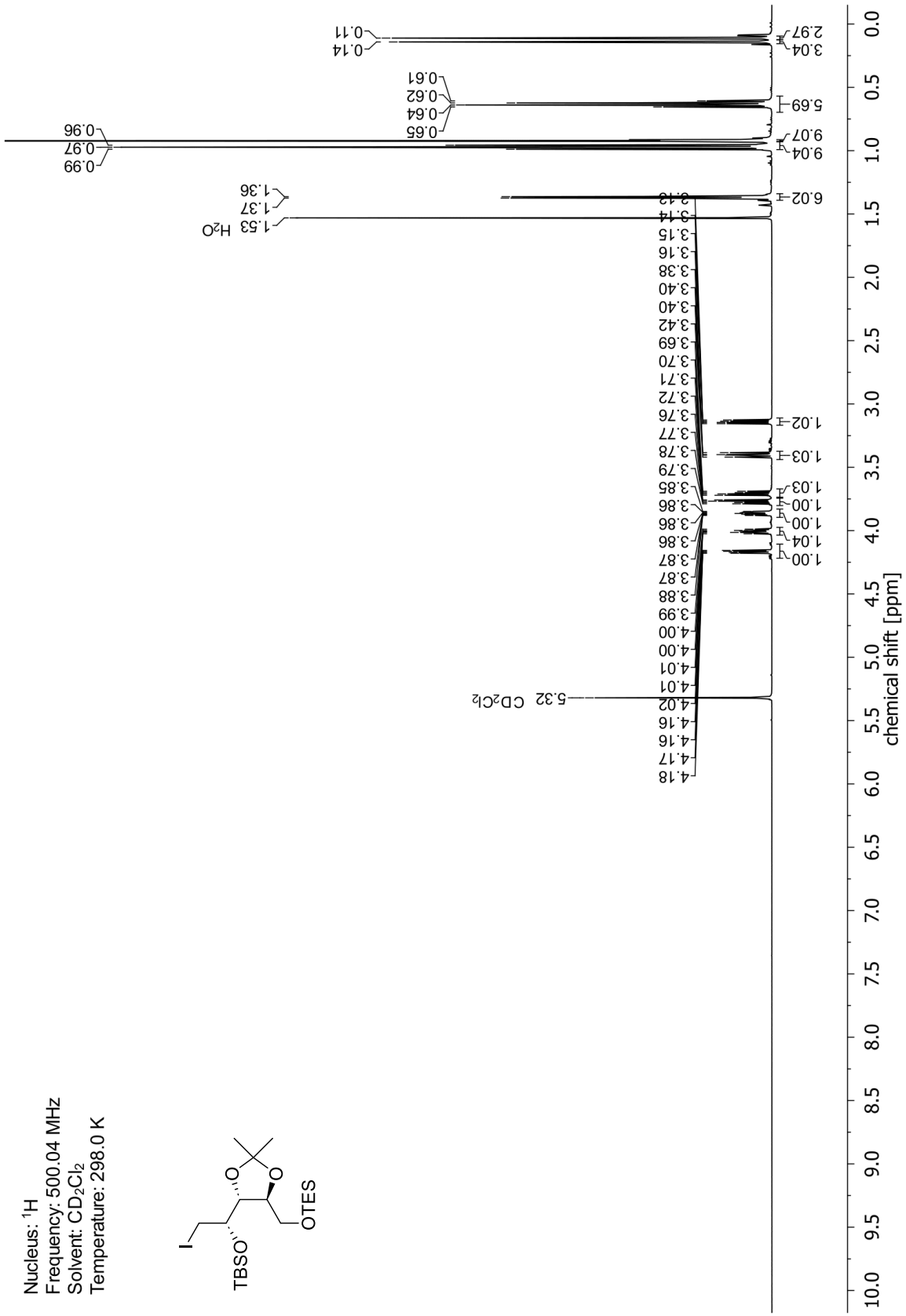

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TBSO
O
O
OTES
CD2Cl2
30.8
27.7
27.5
26.2
23.3
18.7
14.3
7.1
4.8
132.3
130.3
109.5
82.5
78.2
69.6
65.0
4.1
-4.5
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

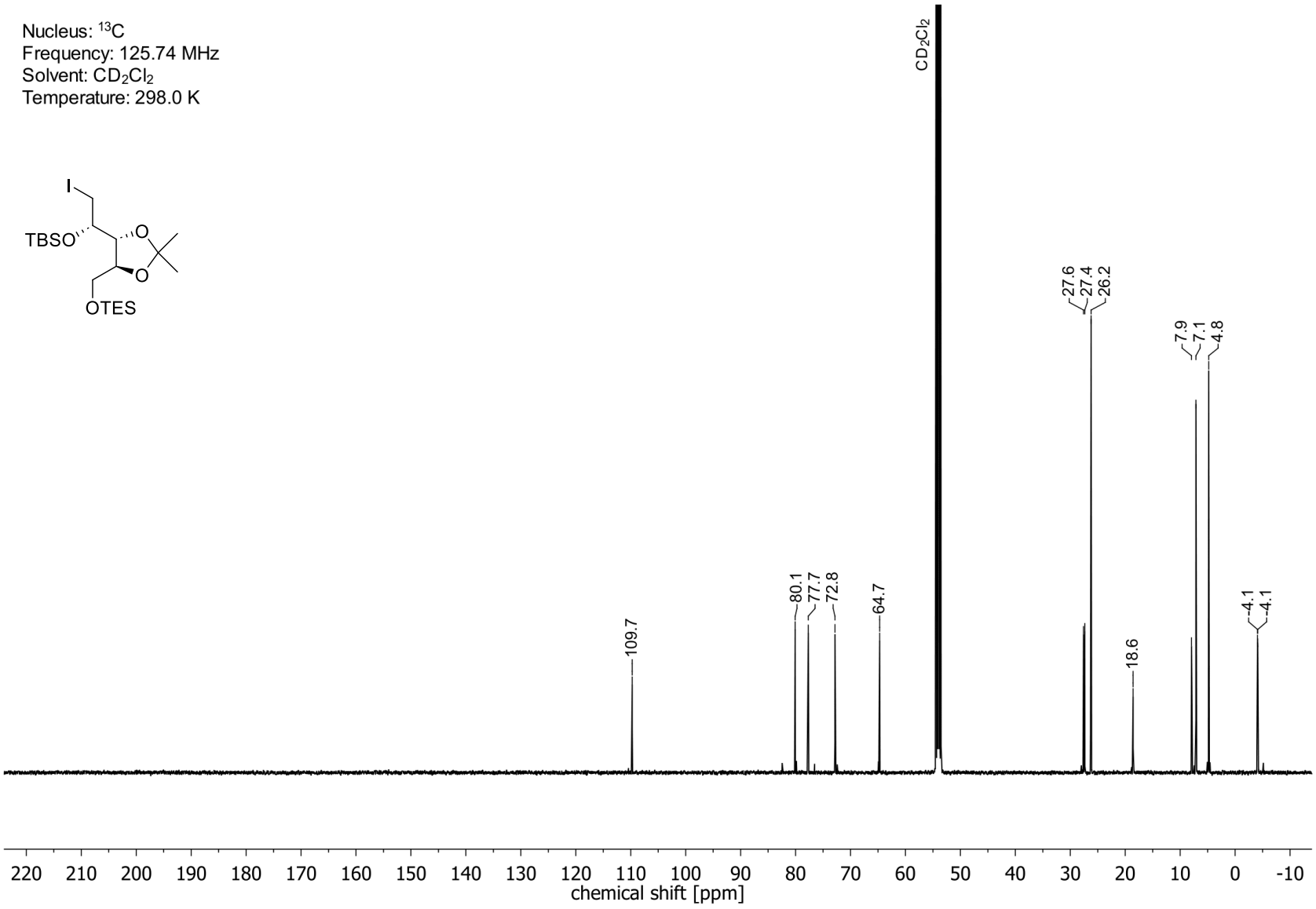
NMR-Spectra of Compound **281**:



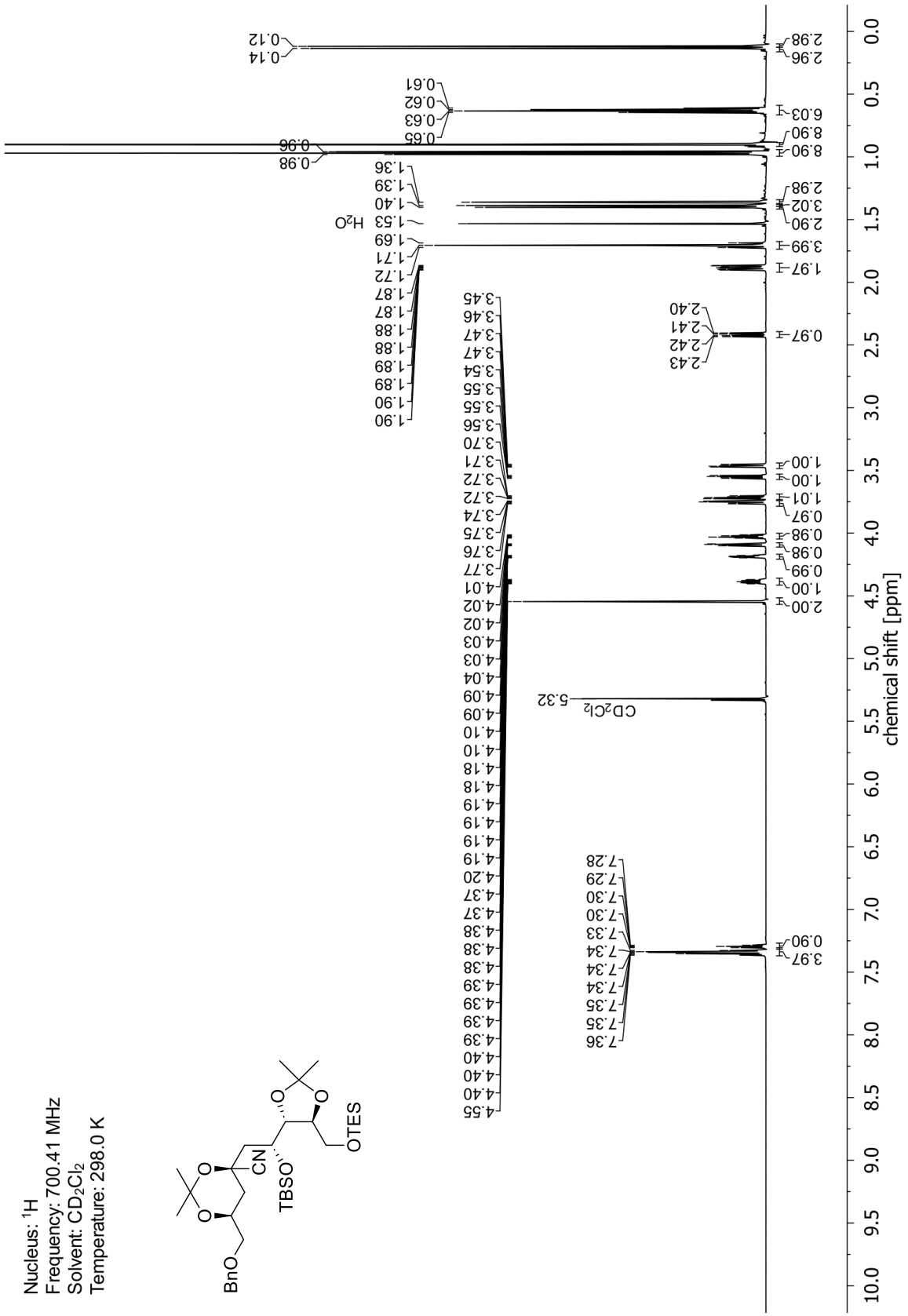

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
O
O
OTES
CD2Cl2
27.4
27.4
26.2
7.0
4.7
80.8
77.9
73.2
64.8
64.8
109.5
18.7
-4.3
-4.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

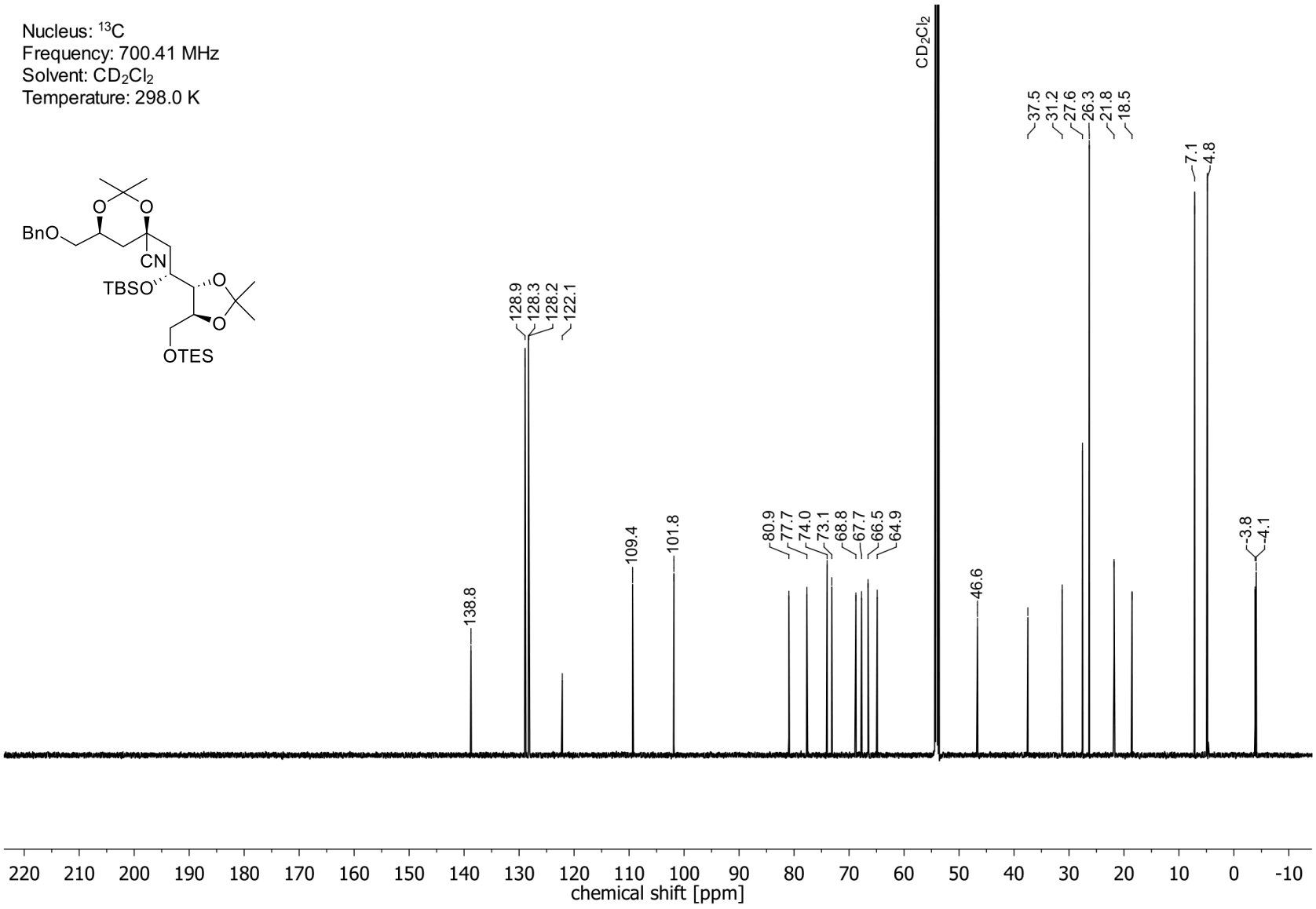
NMR-Spectra of Compound **282**:



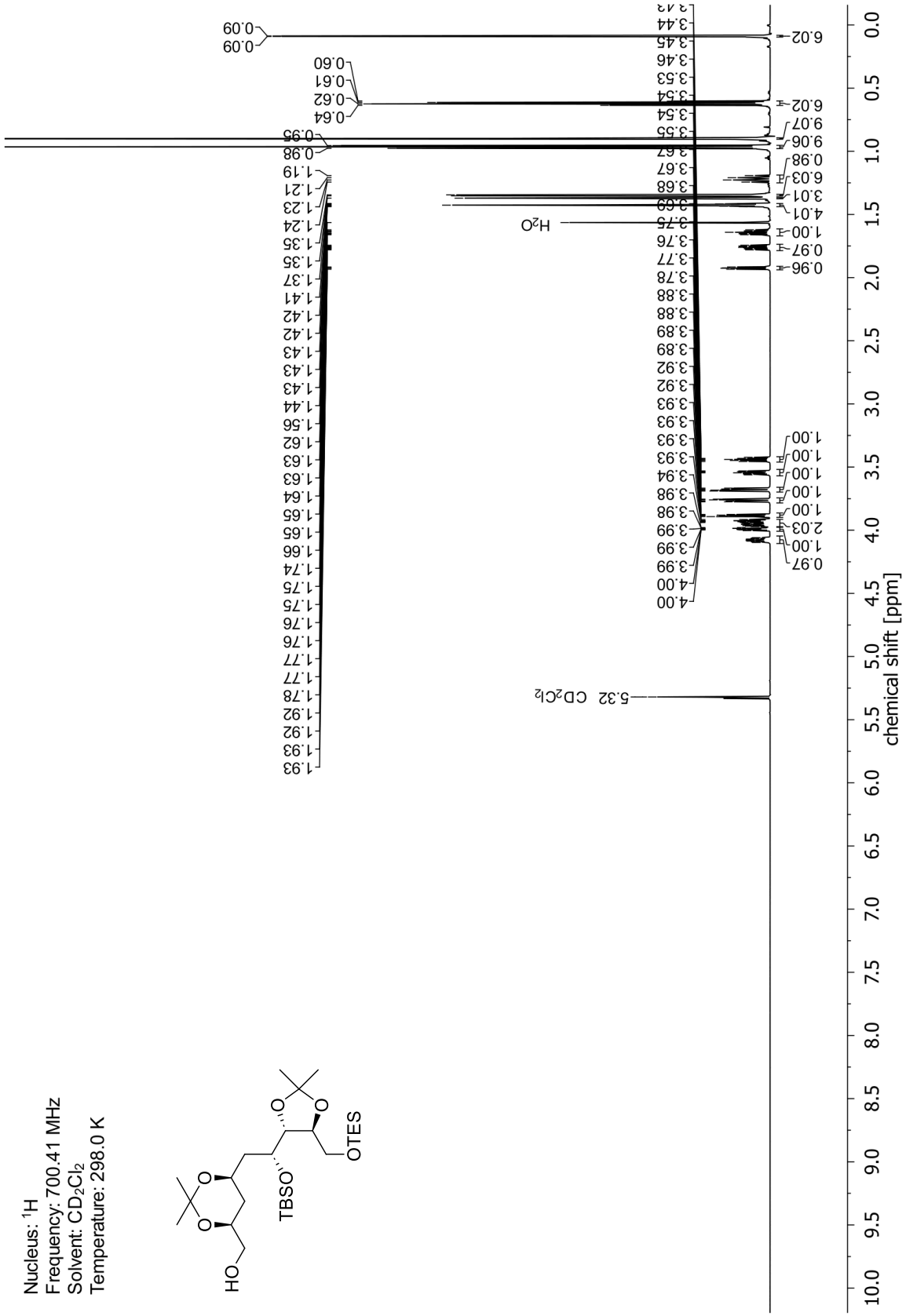

Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
I
TBSO
O
O
OTES
CD2Cl2
27.6
27.4
26.2
7.9
7.1
4.8
80.1
77.7
72.8
64.7
109.7
18.6
-4.1
-4.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

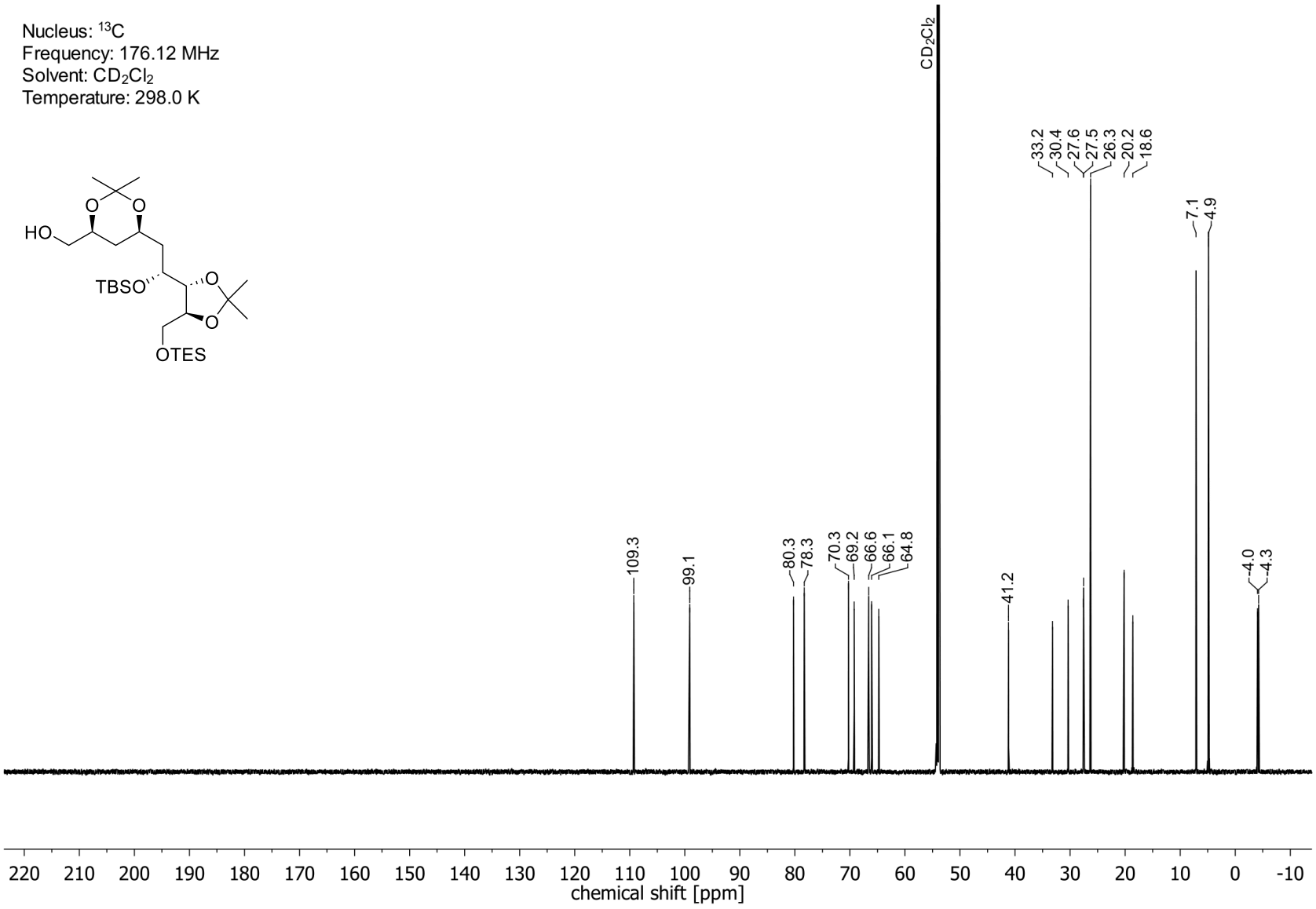
NMR-Spectra of Compound **283**:



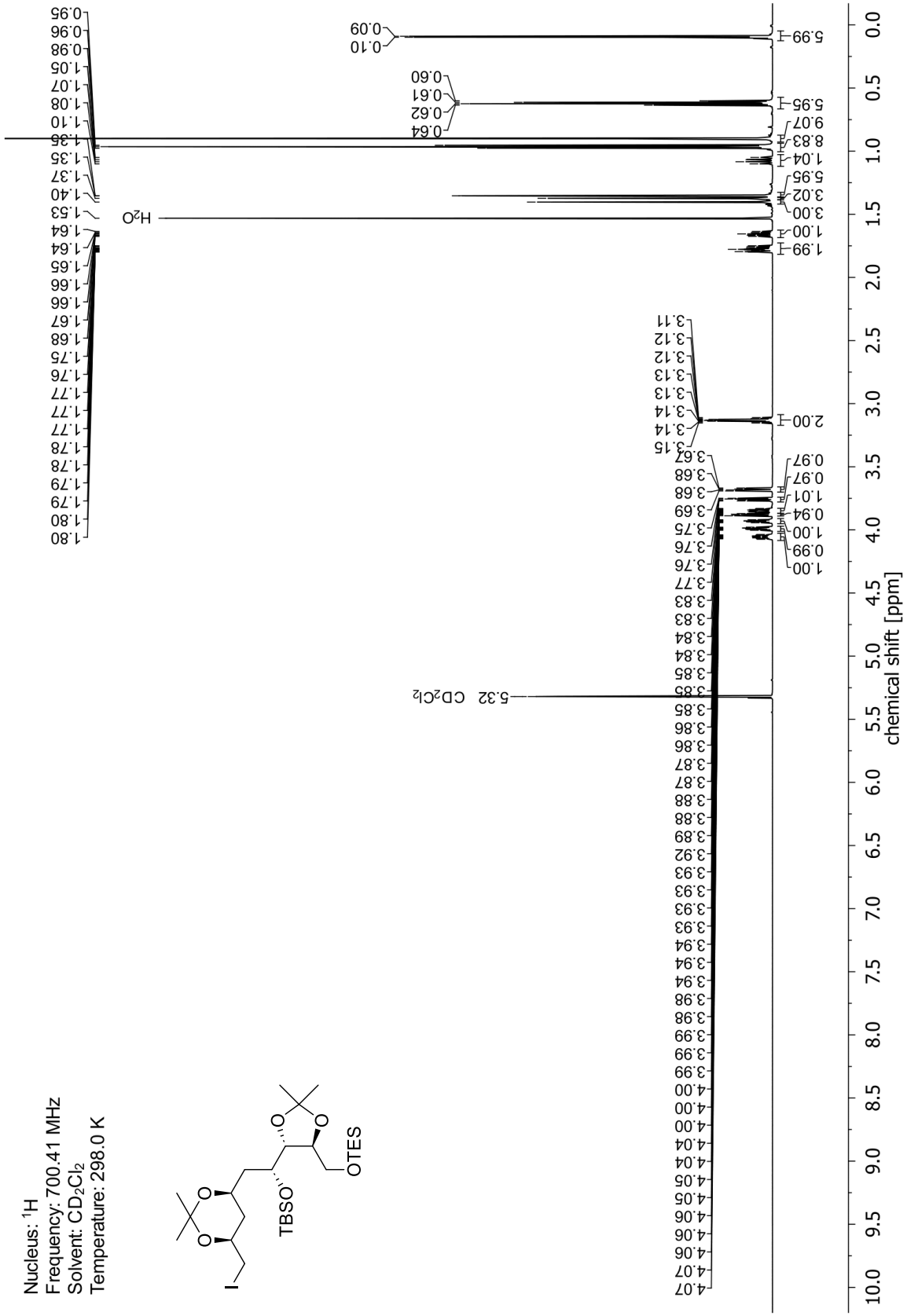

Nucleus: 13C
Frequency: 700.41 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CN
TBSO
OTES
CD2Cl2
37.5
31.2
27.6
26.3
21.8
18.5
7.1
4.8
128.9
128.3
128.2
122.1
109.4
101.8
80.9
77.7
74.0
73.1
68.8
67.7
66.5
64.9
138.8
46.6
-3.8
-4.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

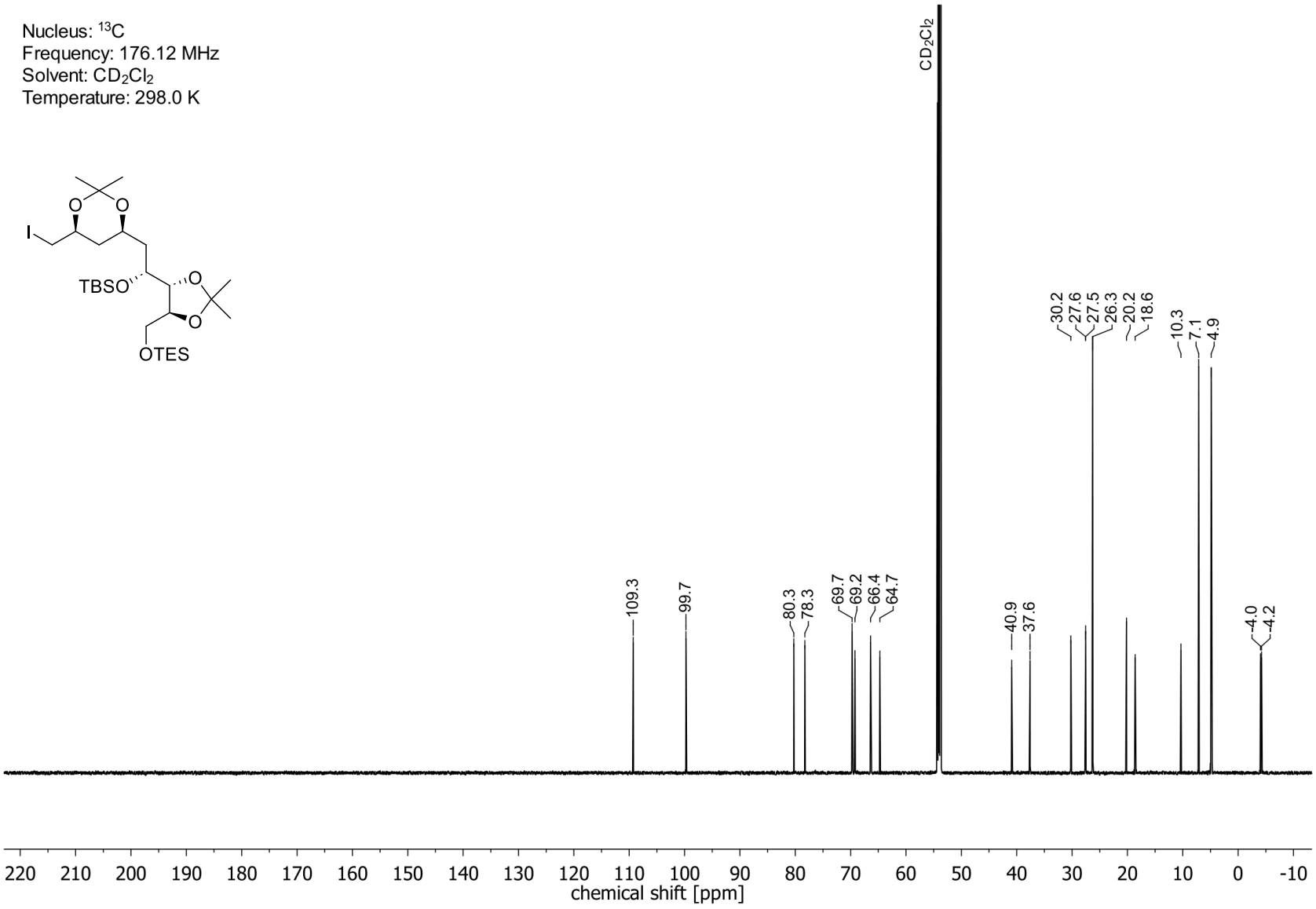
NMR-Spectra of Compound **284**:



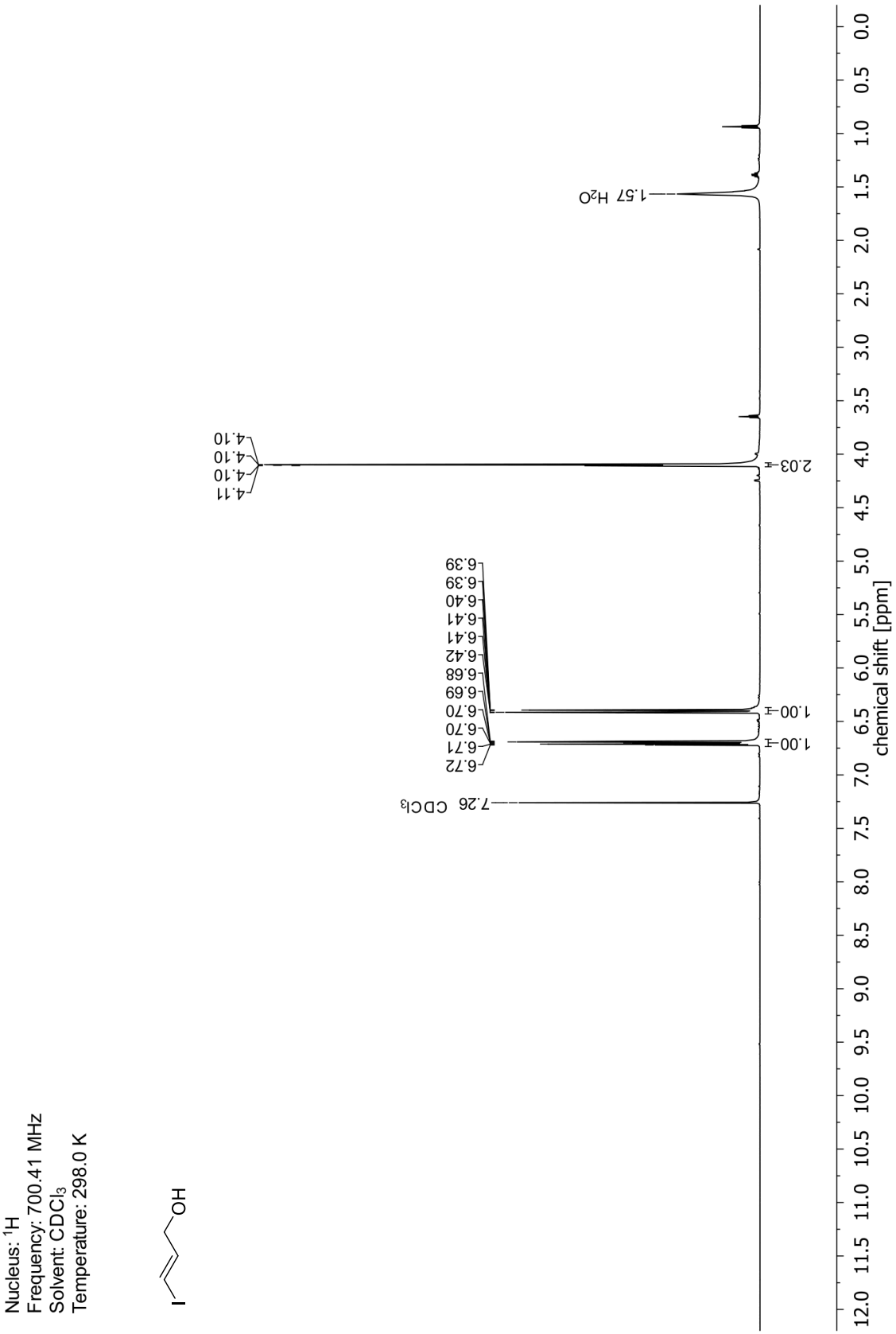

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
OTES
CD2Cl2
33.2
30.4
27.6
27.5
26.3
20.2
18.6
7.1
4.9
109.3
99.1
80.3
78.3
70.3
69.2
66.6
66.1
64.8
41.2
4.0
4.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **285**:

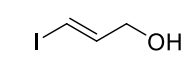



Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
I
TBSO
O
O
O
O
OTES
CD2Cl2
109.3
99.7
80.3
78.3
69.7
69.2
66.4
64.7
40.9
37.6
30.2
27.6
27.5
26.3
20.2
18.6
10.3
7.1
4.9
4.0
4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

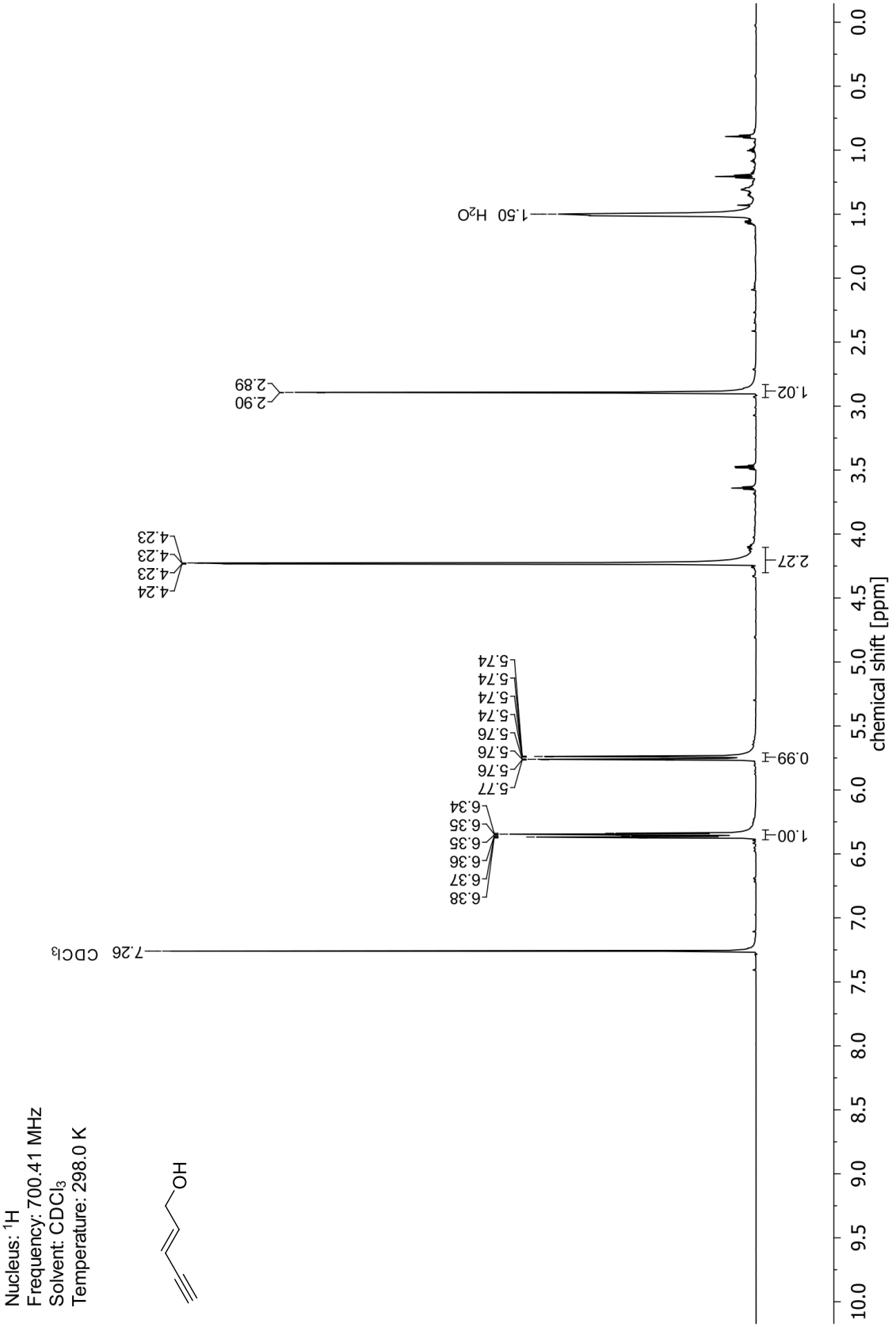
NMR-Spectra of Compound **230**:

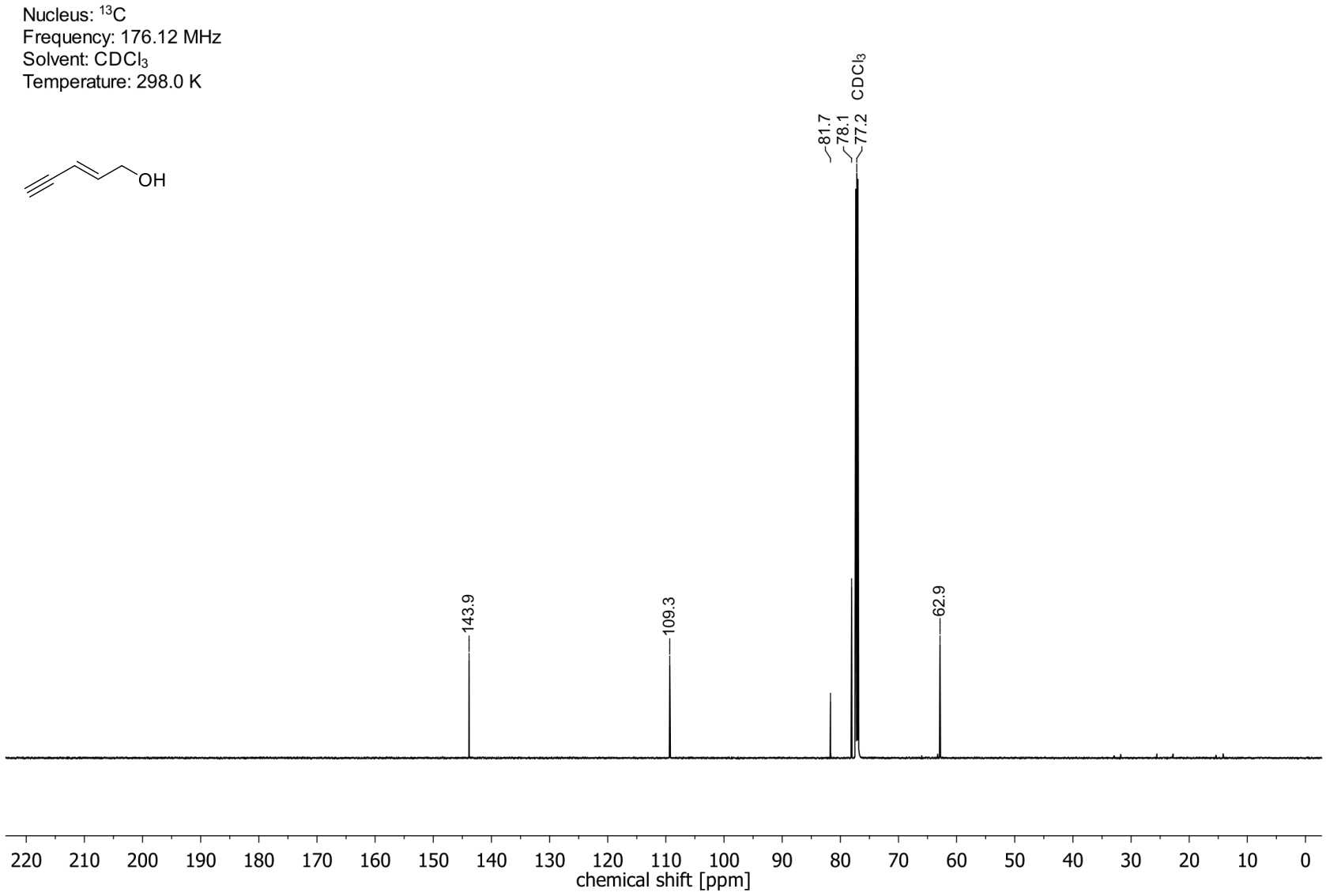


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CDCl_3$
Temperature: 298.0 K

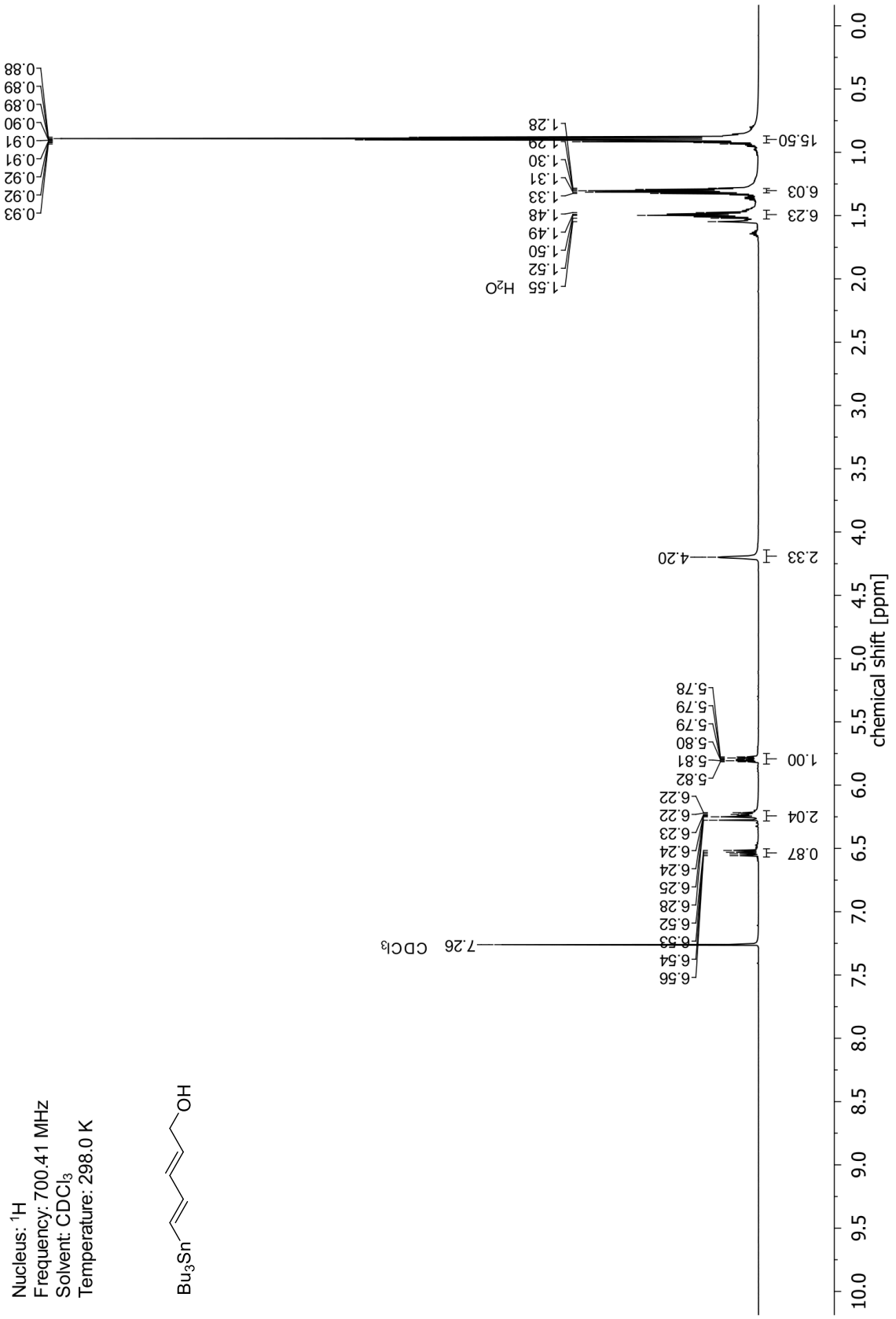


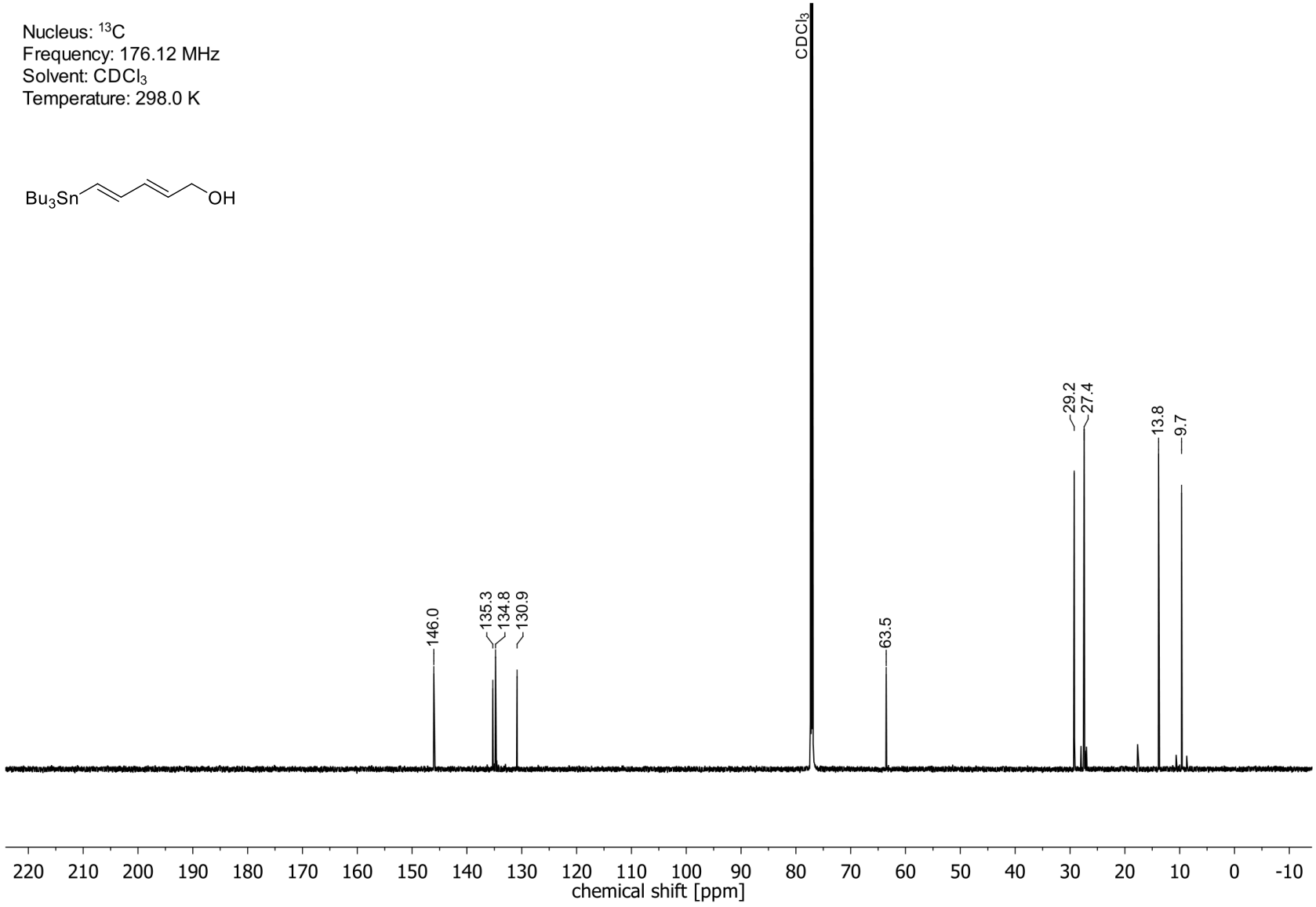
NMR-Spectra of Compound **231**:



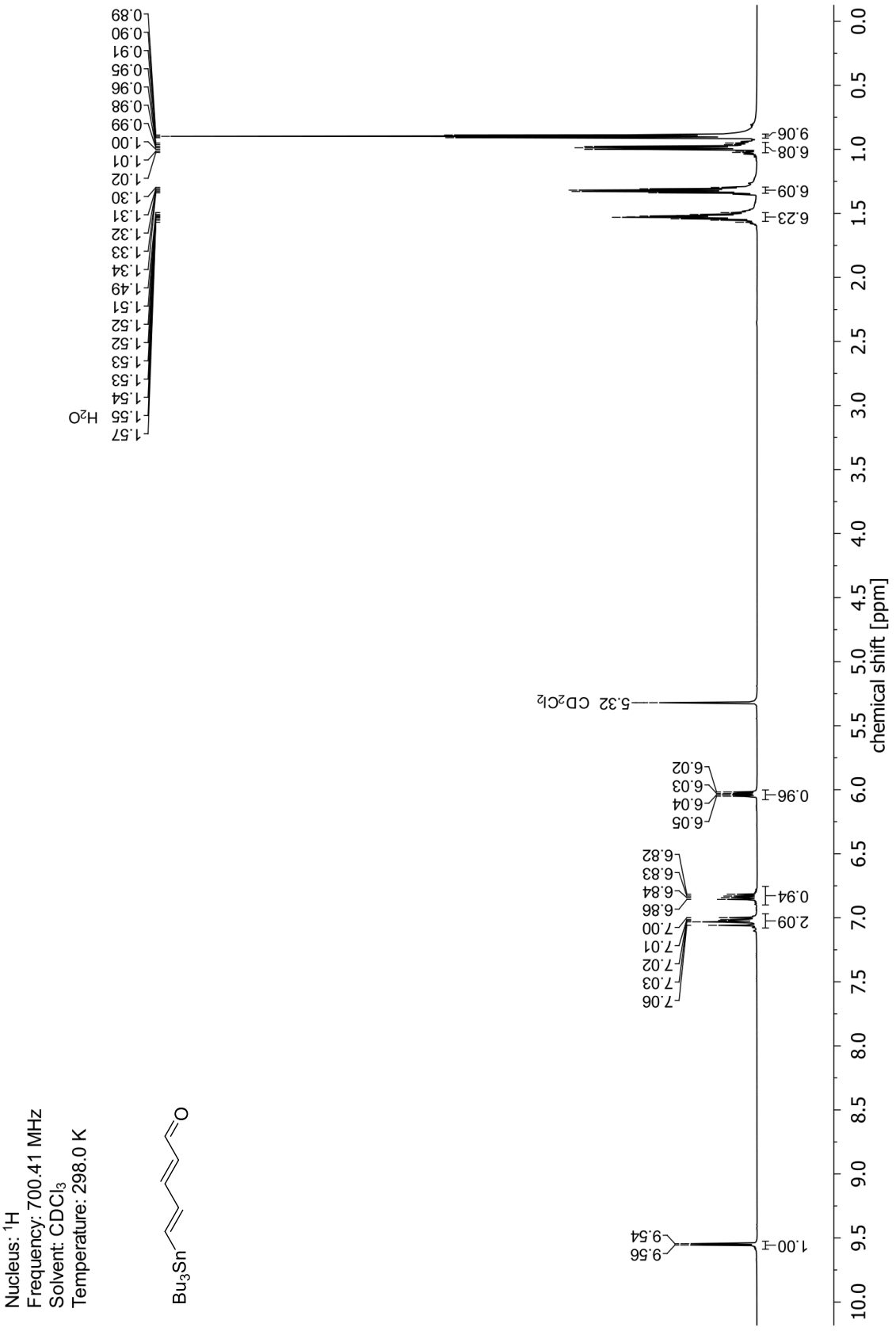

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CDCl3
Temperature: 298.0 K
OH
81.7
78.1
77.2
CDCl3
143.9
109.3
62.9
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
chemical shift [ppm]

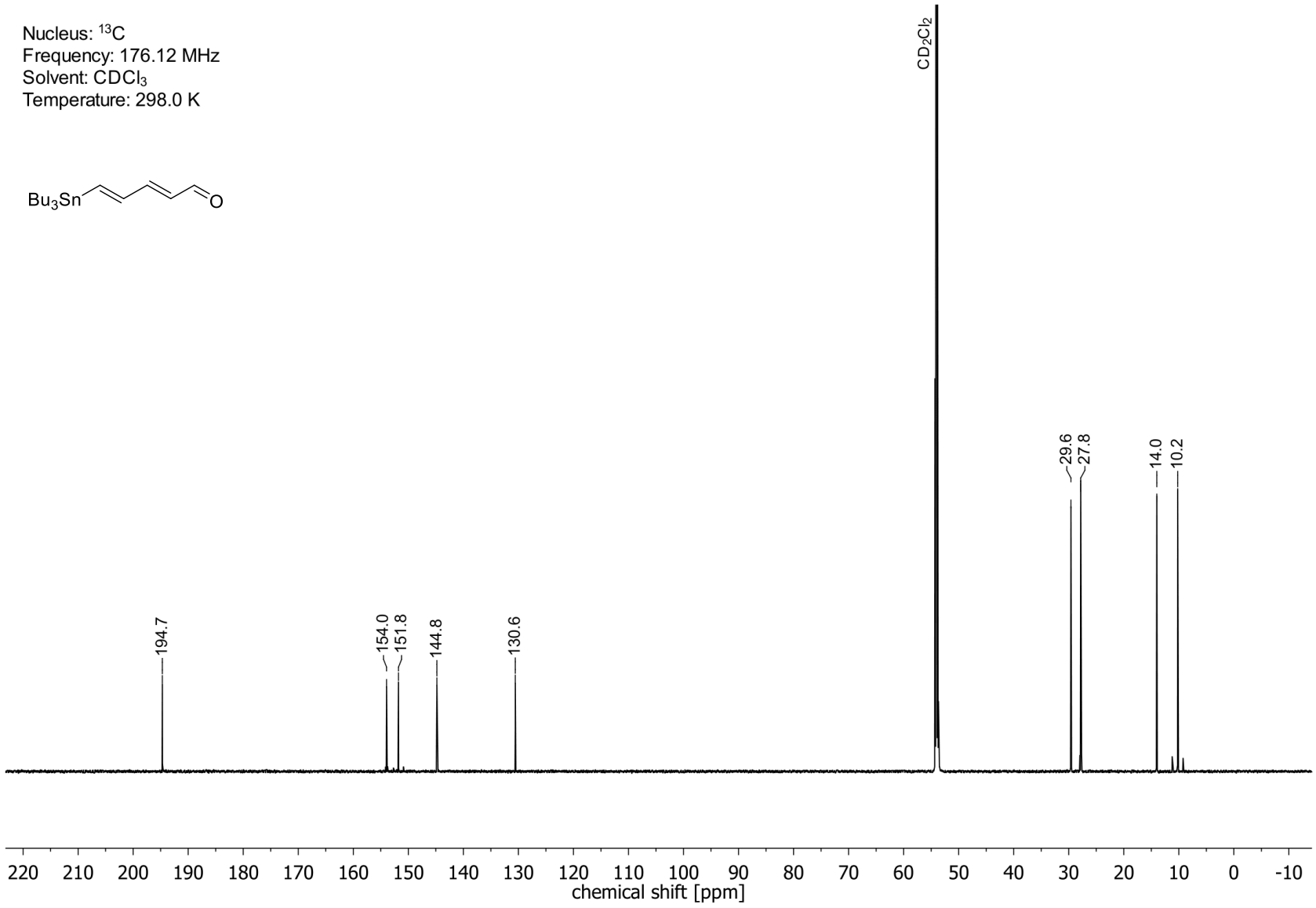
NMR-Spectra of Compound **232**:



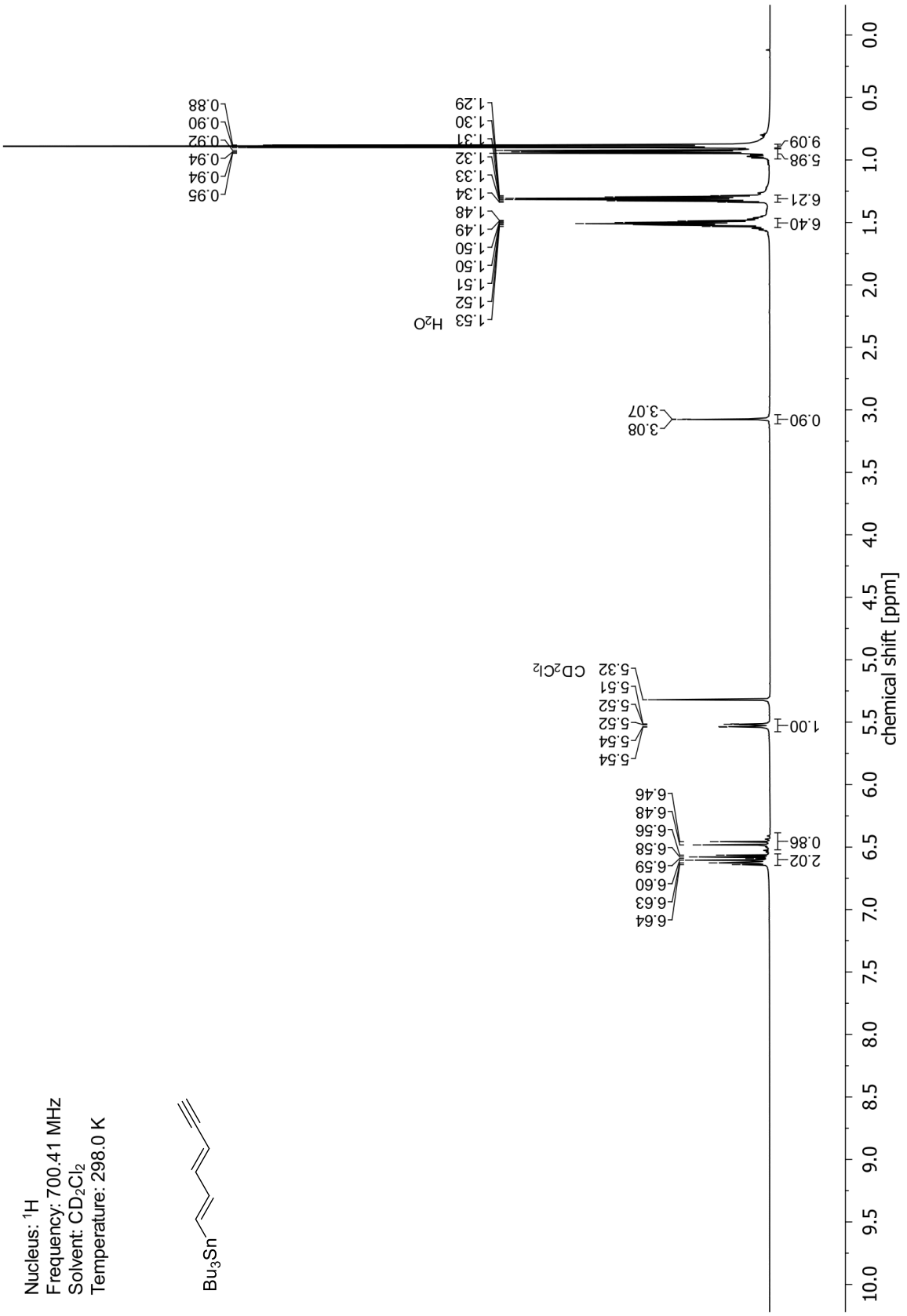

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CDCl3
Temperature: 298.0 K
Bu3Sn
OH
CDCl3
146.0
135.3
134.8
130.9
63.5
29.2
27.4
13.8
9.7
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **233**:

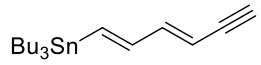



Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CDCl3
Temperature: 298.0 K
Bu3Sn
O
CD2Cl2
194.7
154.0
151.8
144.8
130.6
29.6
27.8
14.0
10.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

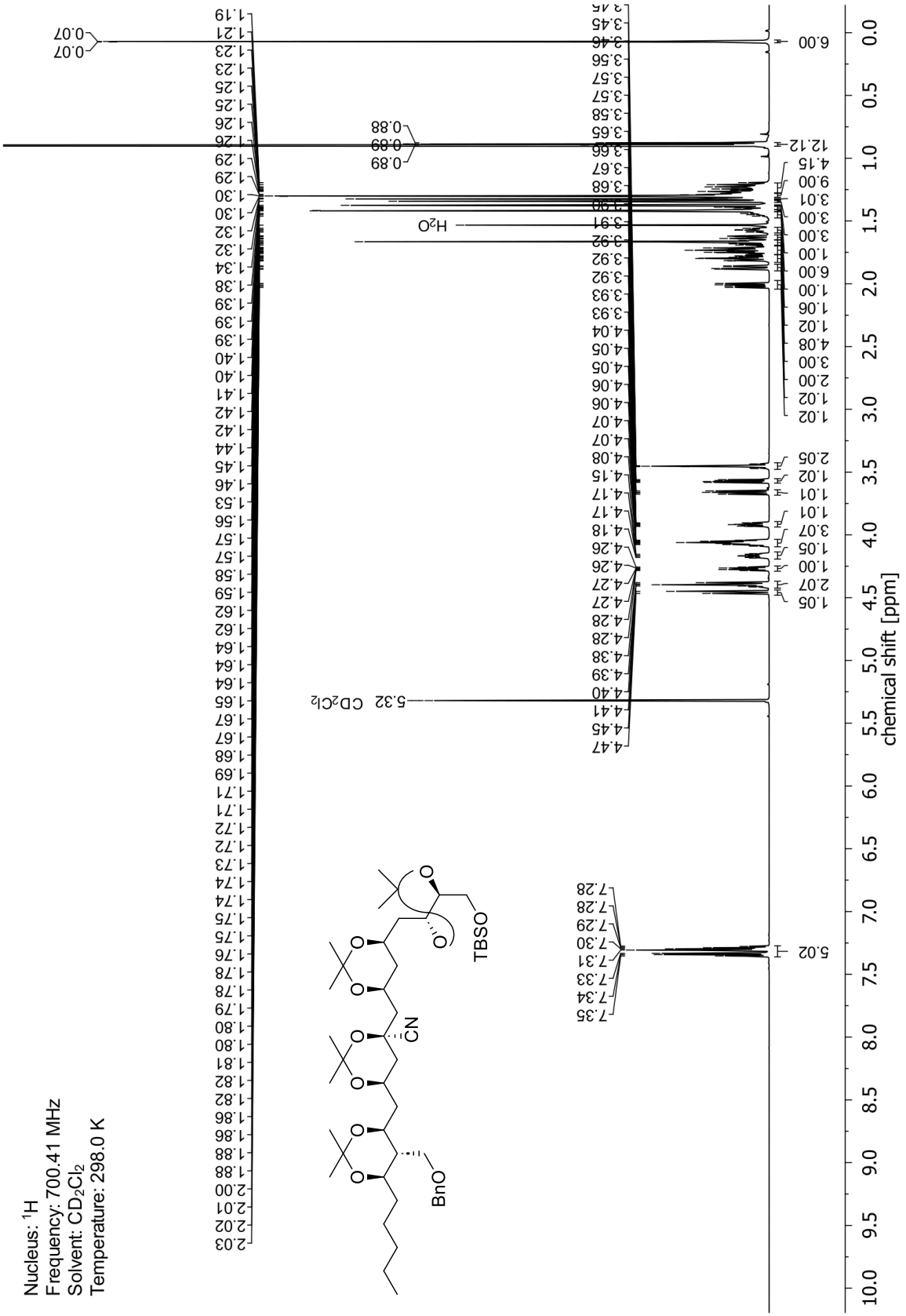
NMR-Spectra of Compound **235**:

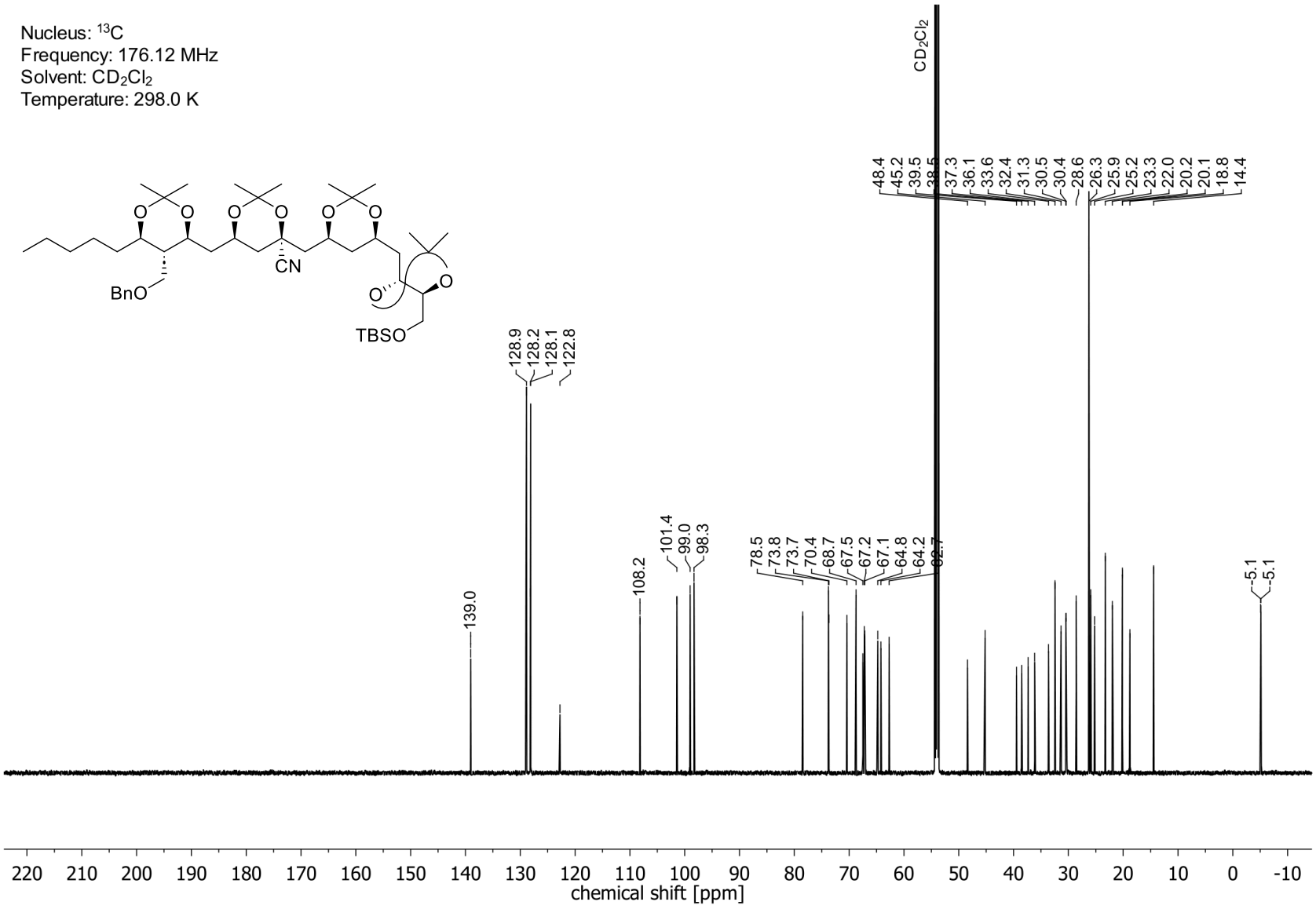


Nucleus: $^{13}C$
Frequency: 176.12 MHz
Solvent: $CD_2Cl_2$
Temperature: 298.0 K

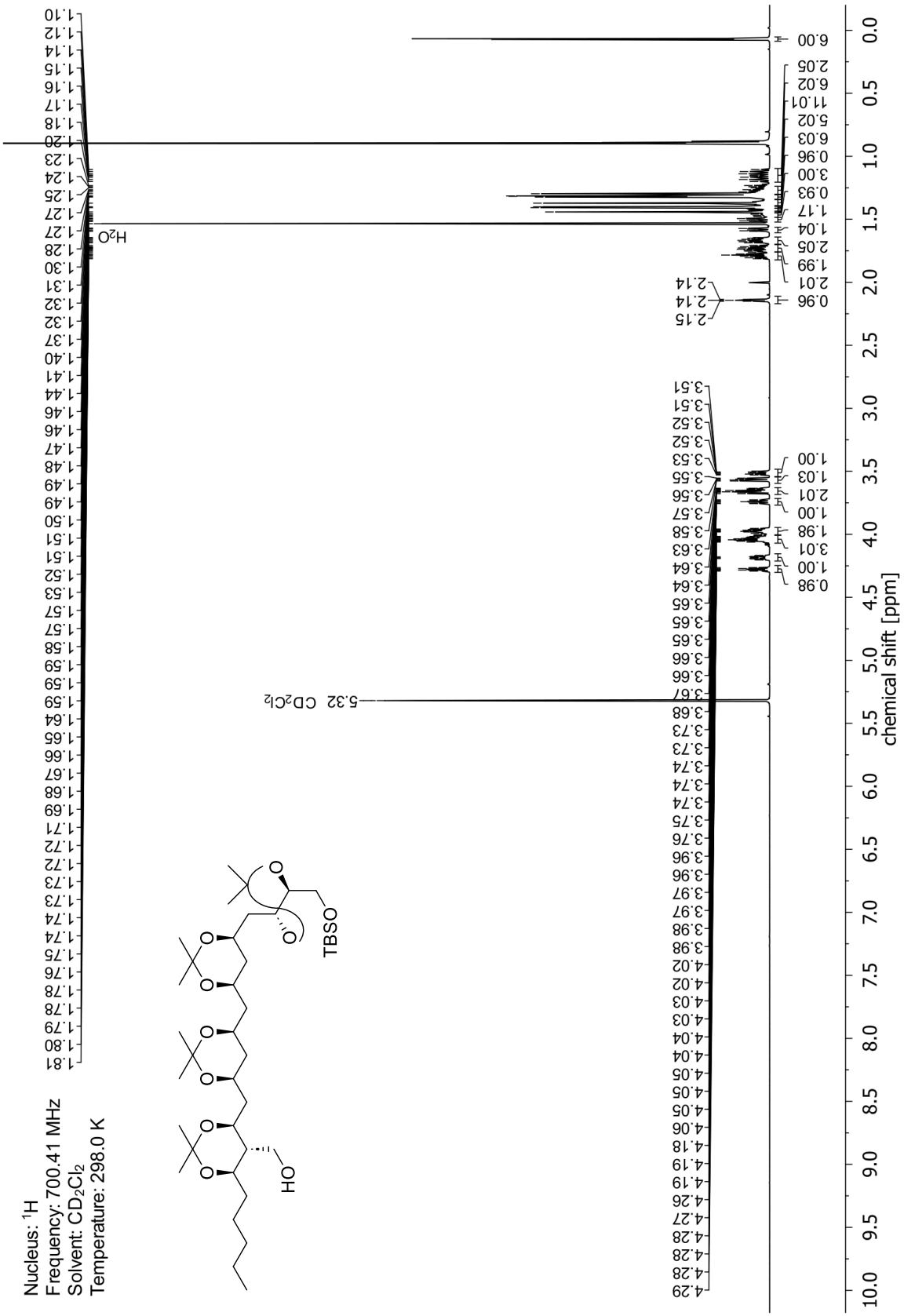


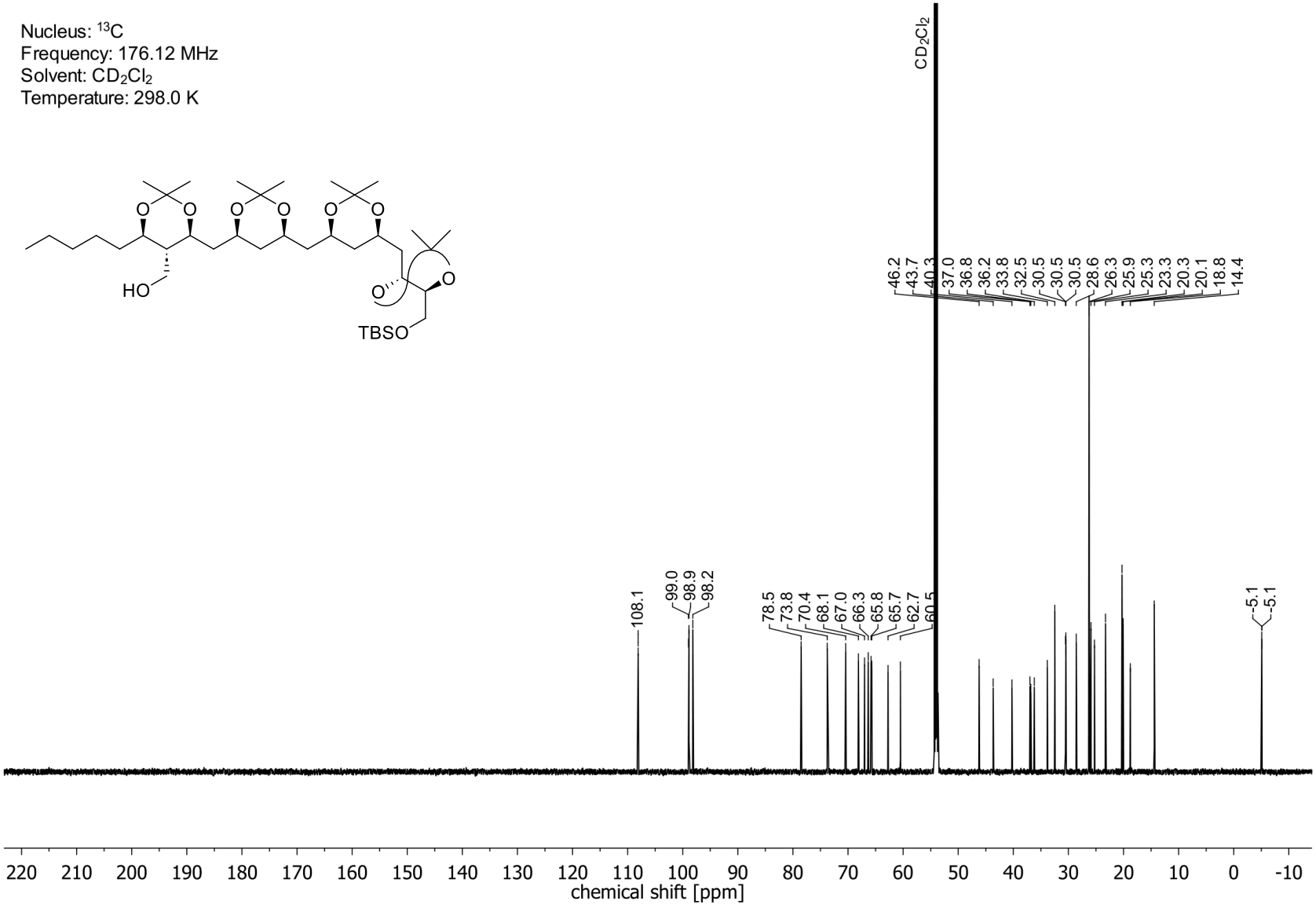
NMR-Spectra of Compound **272**:



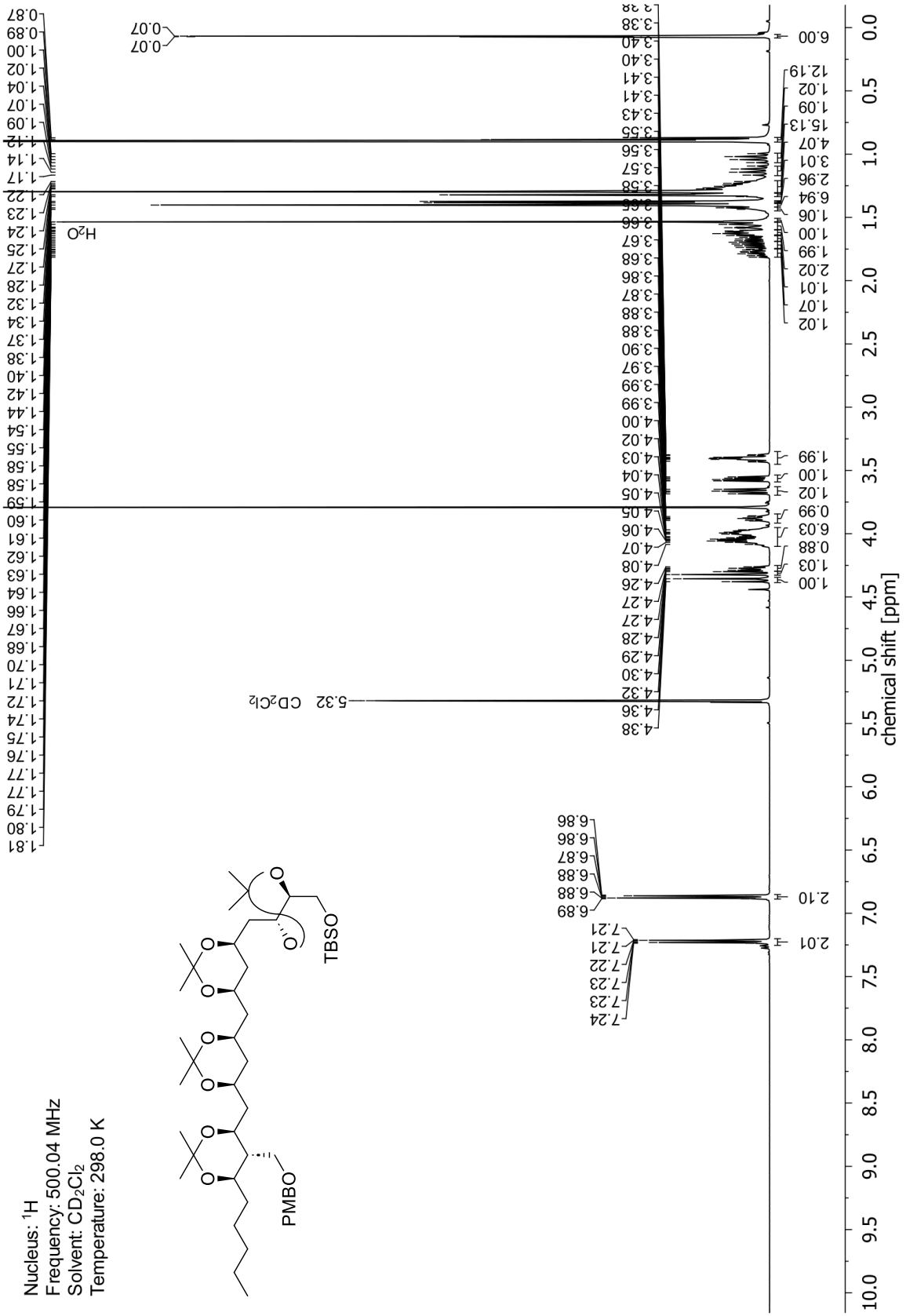

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CN
TBSO
CD2Cl2
48.4
45.2
39.5
38.5
37.3
36.1
33.6
32.4
31.3
30.5
30.4
28.6
26.3
25.9
25.2
23.3
22.0
20.2
20.1
18.8
14.4
139.0
128.9
128.2
128.1
122.8
108.2
101.4
99.0
98.3
78.5
73.8
73.7
70.4
68.7
67.5
67.2
67.1
64.8
64.2
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

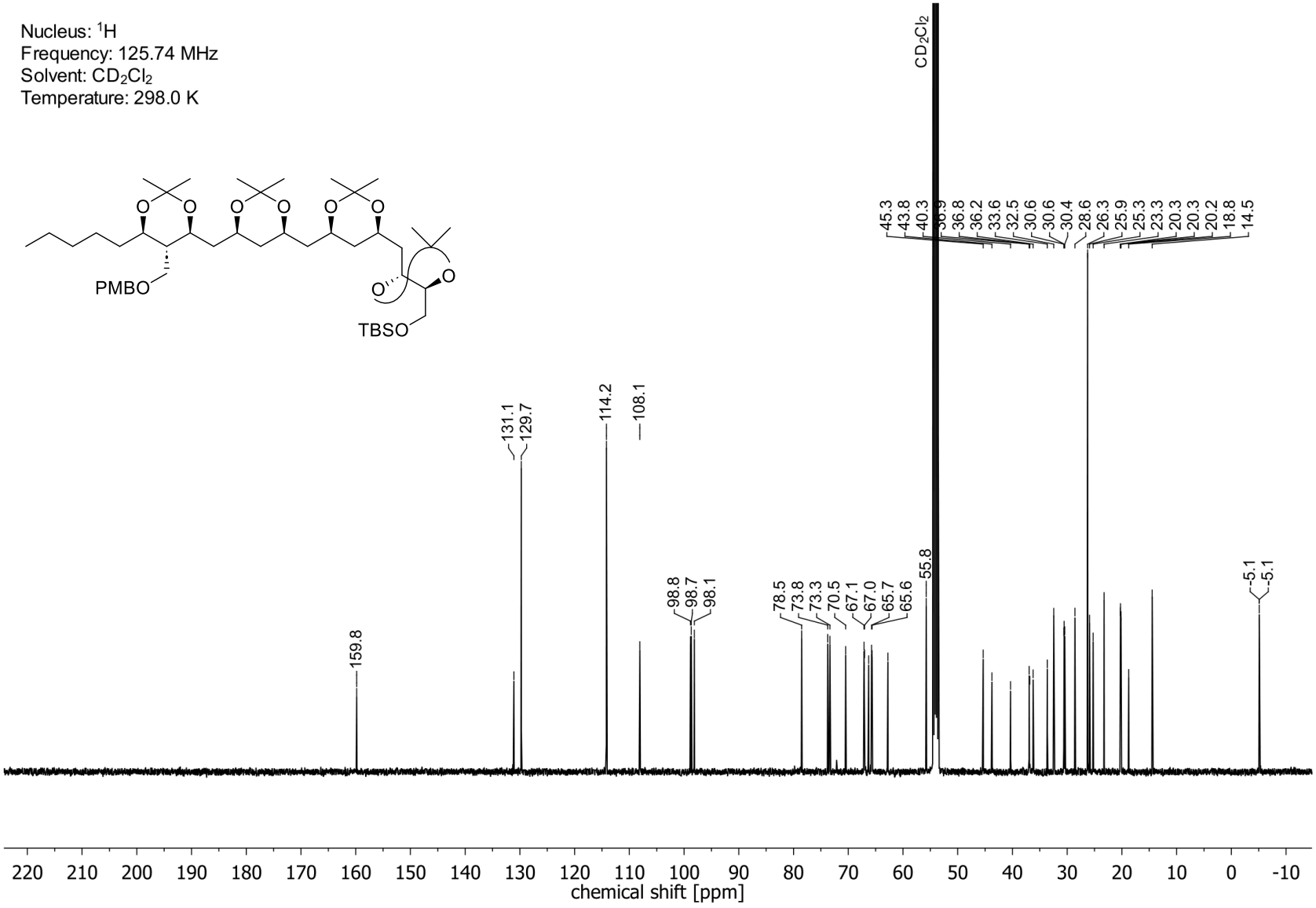
NMR-Spectra of Compound **155**:



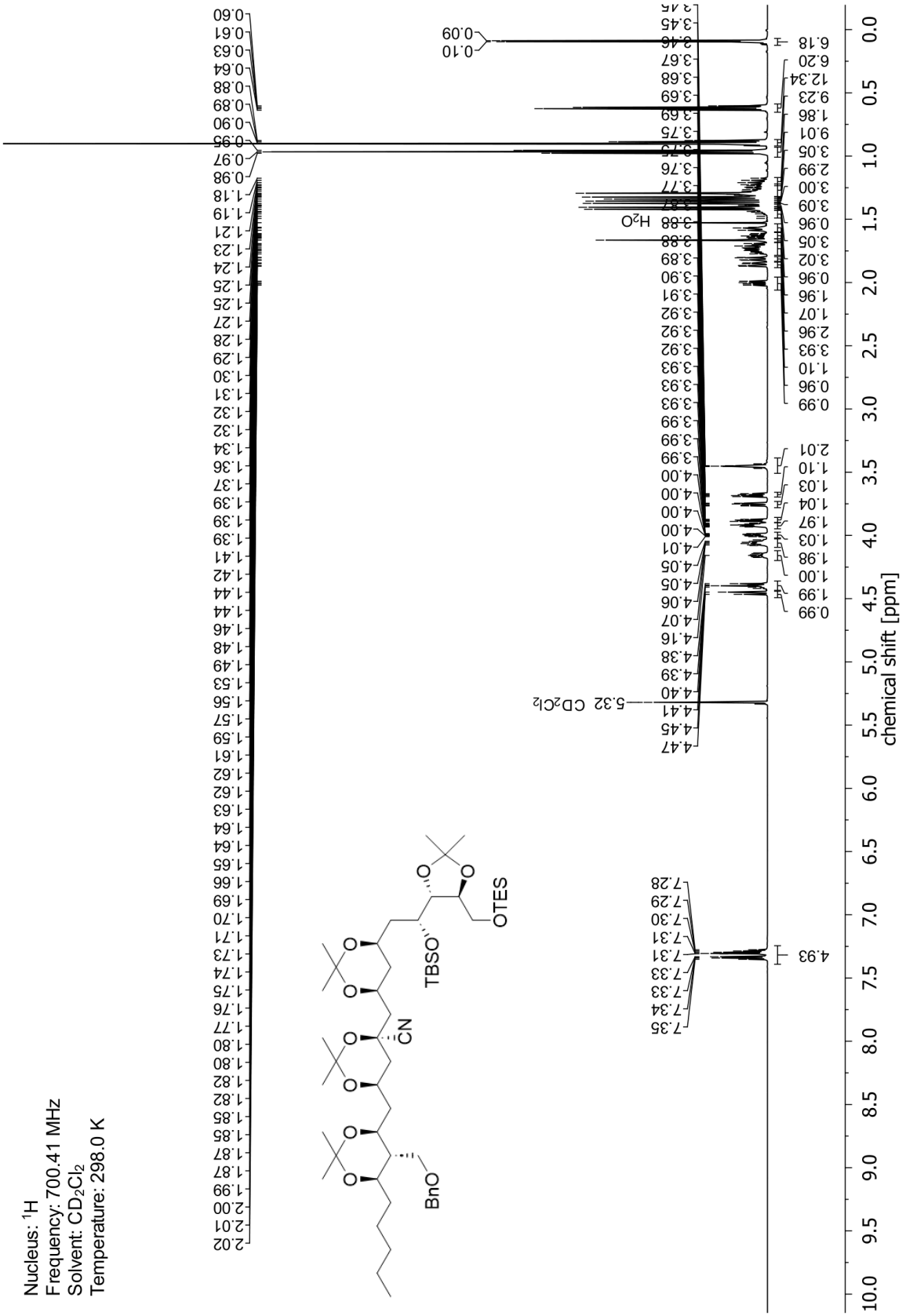

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
CD2Cl2
46.2
43.7
40.3
37.0
36.8
36.2
33.8
32.5
30.5
30.5
30.5
28.6
26.3
25.9
25.3
23.3
20.3
20.1
18.8
14.4
108.1
99.0
98.9
98.2
78.5
73.8
70.4
68.1
67.0
66.3
65.8
65.7
62.7
60.5
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

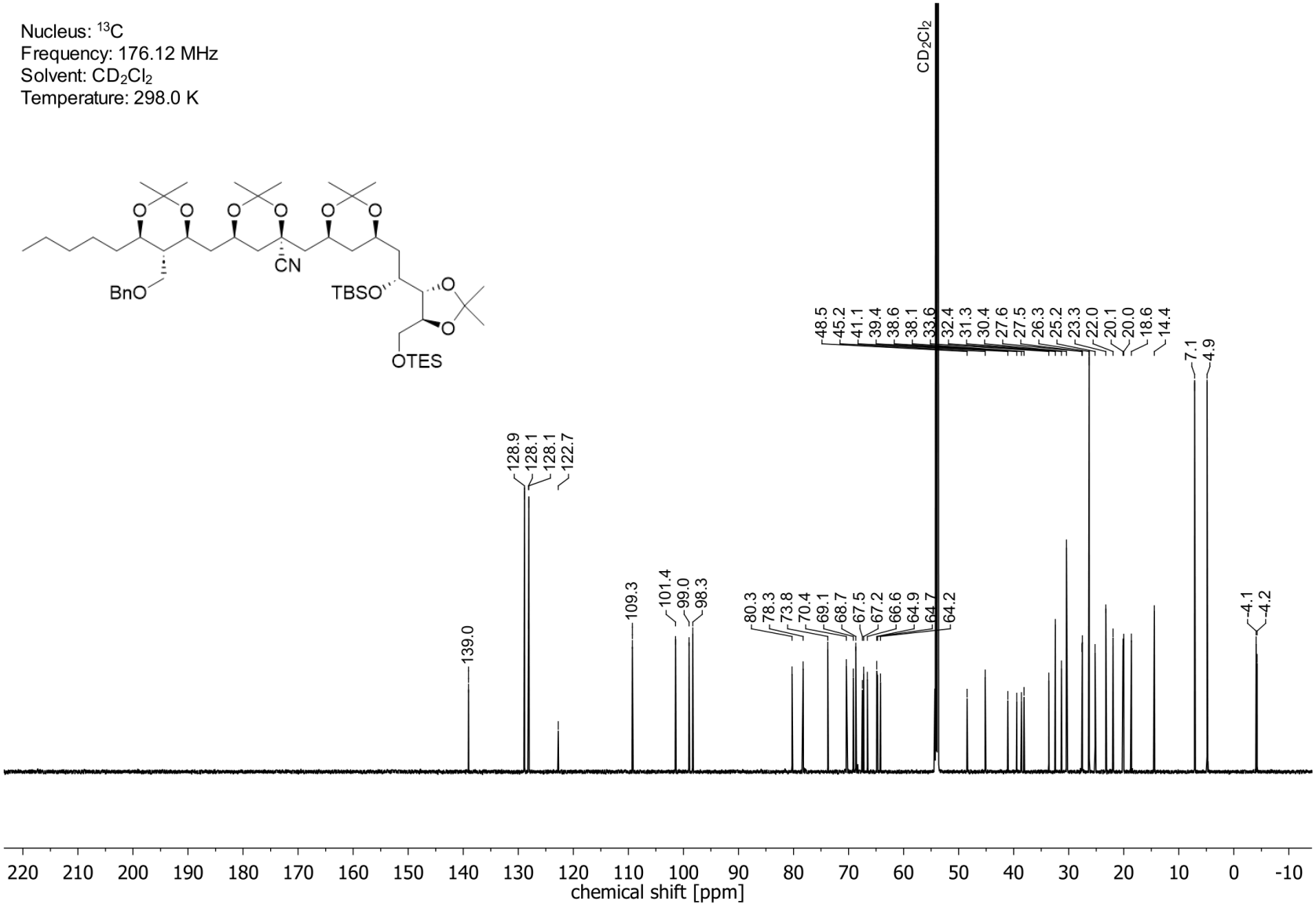
NMR-Spectra of Compound **273**:



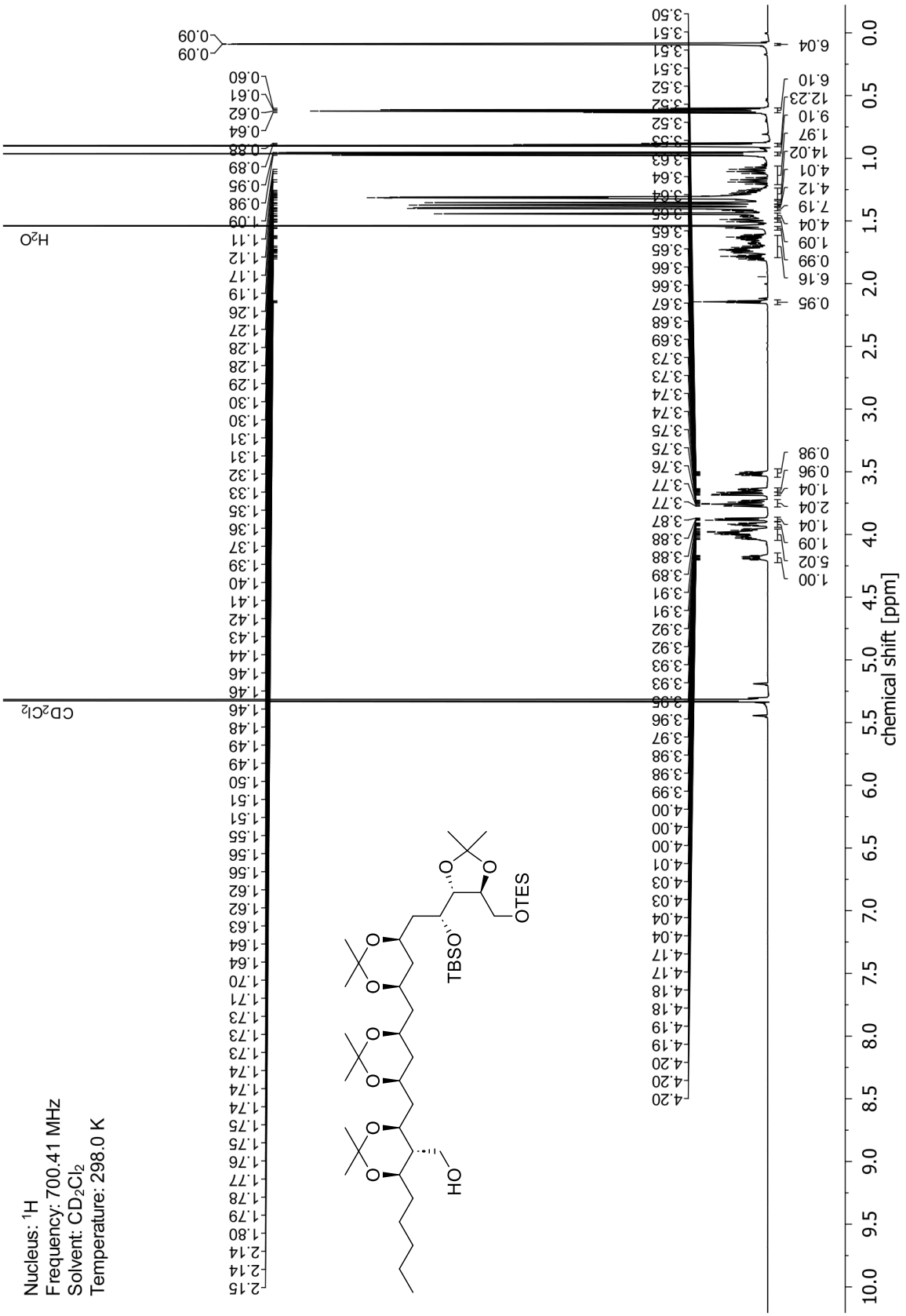

Nucleus: 1H
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
PMBO
TBSO
CD2Cl2
45.3
43.8
40.3
36.8
36.2
33.6
32.5
30.6
30.6
30.4
28.6
26.3
25.9
25.3
23.3
20.3
20.3
20.2
18.8
14.5
131.1
129.7
114.2
108.1
98.8
98.7
98.1
78.5
73.8
73.3
70.5
67.1
67.0
65.7
65.6
55.8
159.8
-5.1
-5.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

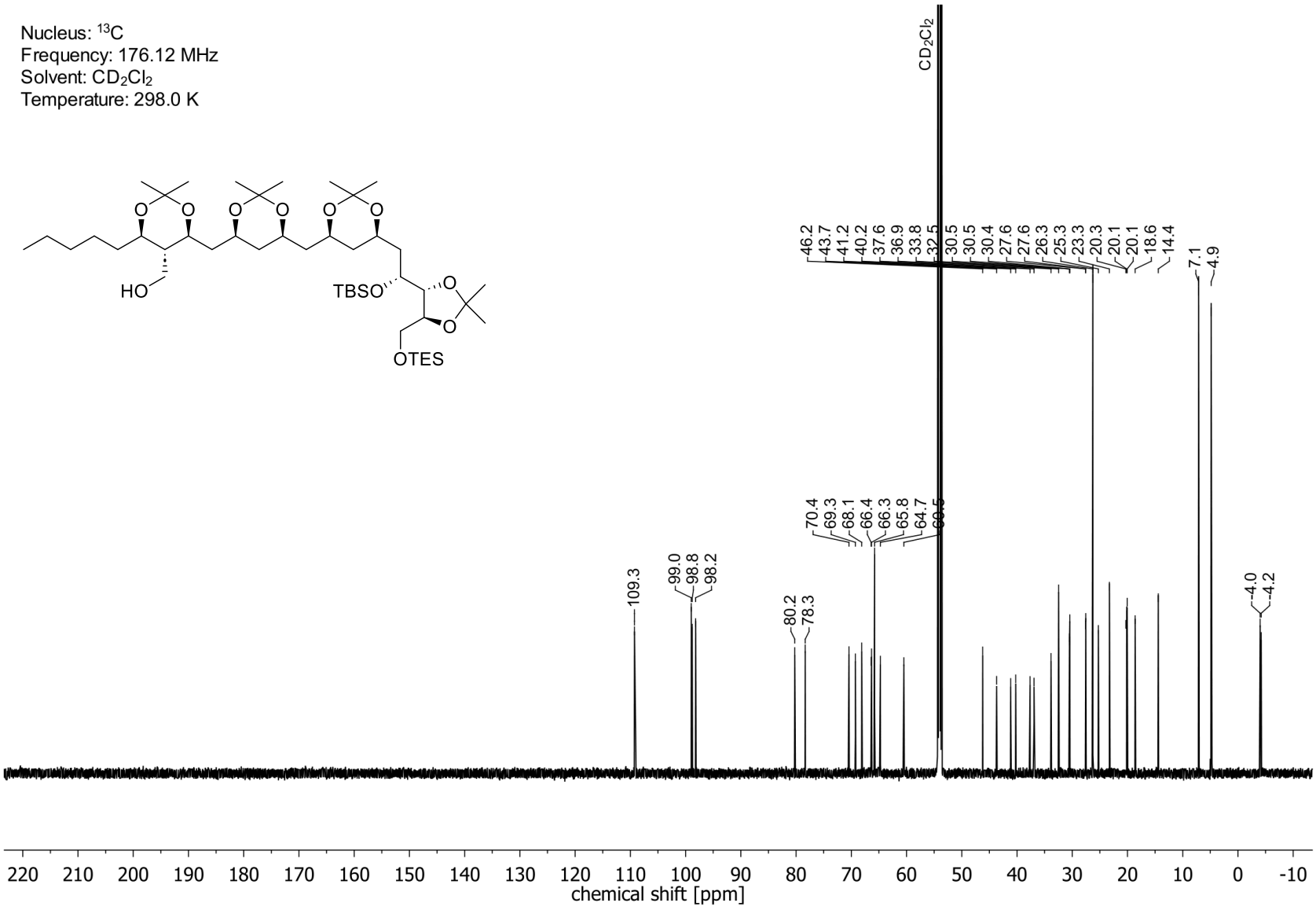
NMR-Spectra of Compound **286**:



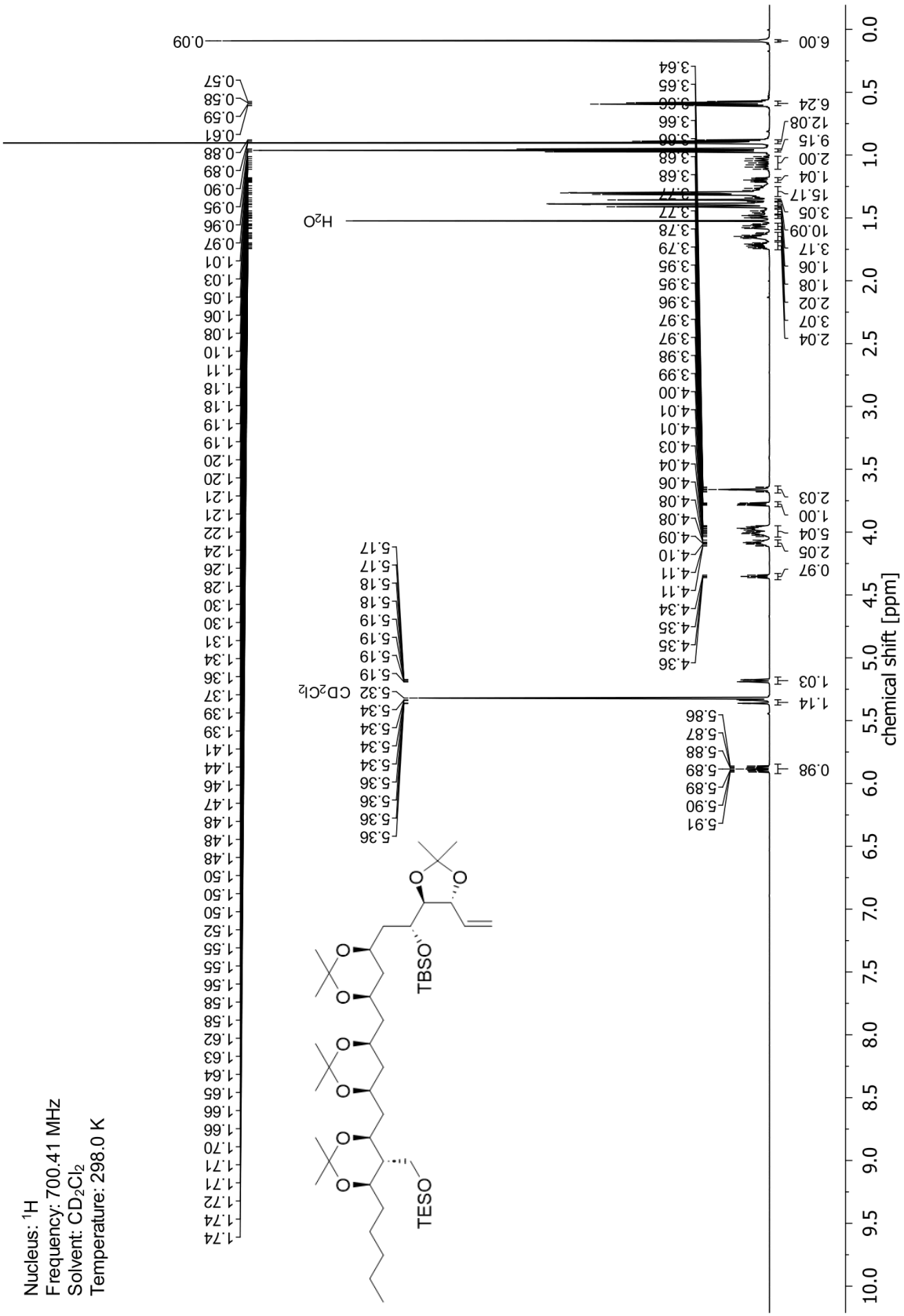

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
BnO
CN
TBSO
OTES
CD2Cl2
48.5
45.2
41.1
39.4
38.6
38.1
33.6
32.4
31.3
30.4
27.6
27.5
26.3
25.2
23.3
22.0
20.1
20.0
18.6
14.4
7.1
4.9
128.9
128.1
128.1
122.7
139.0
109.3
101.4
99.0
98.3
80.3
78.3
73.8
70.4
69.1
68.7
67.5
67.2
66.6
64.9
64.7
64.2
-4.1
-4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

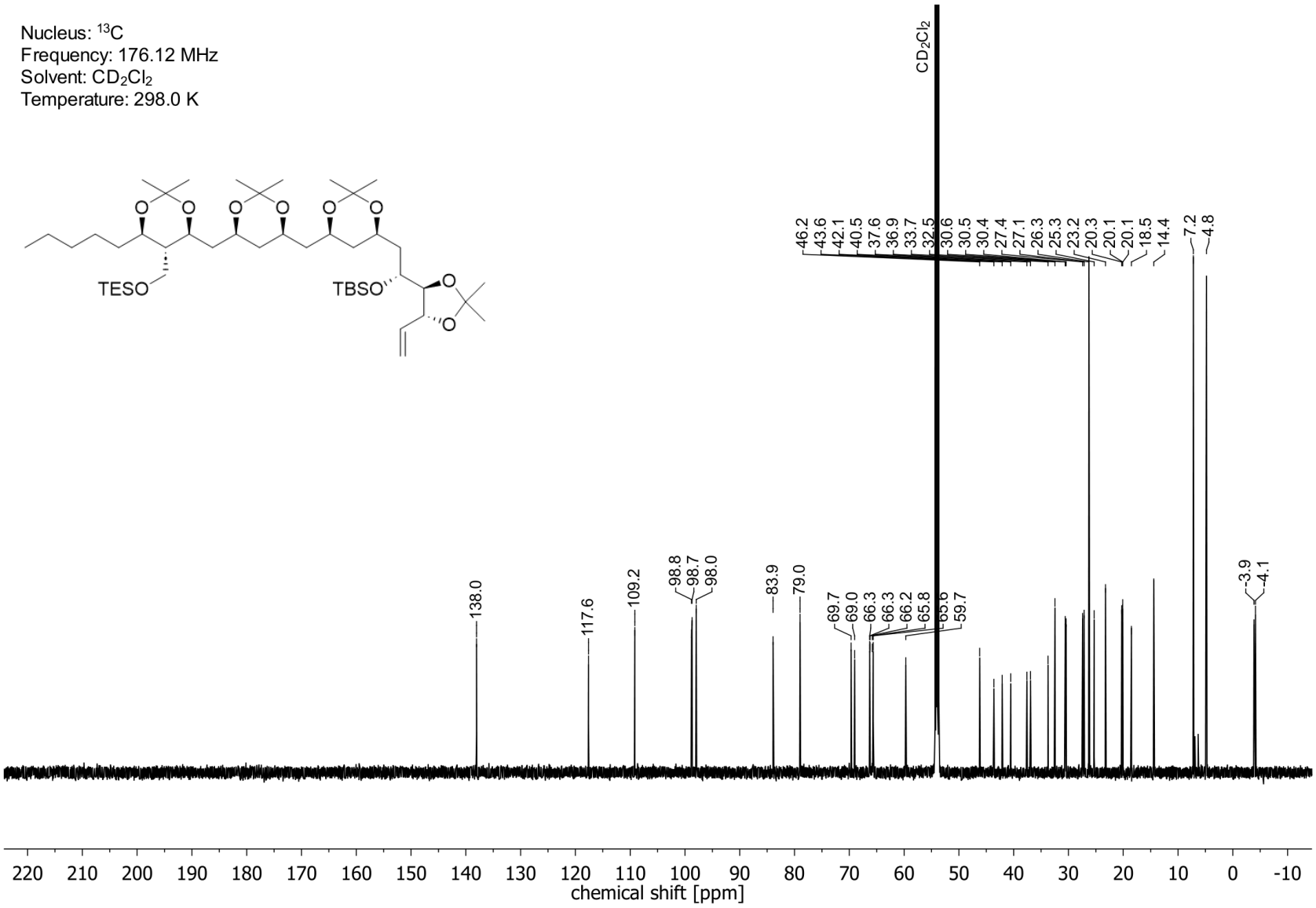
NMR-Spectra of Compound **287**:



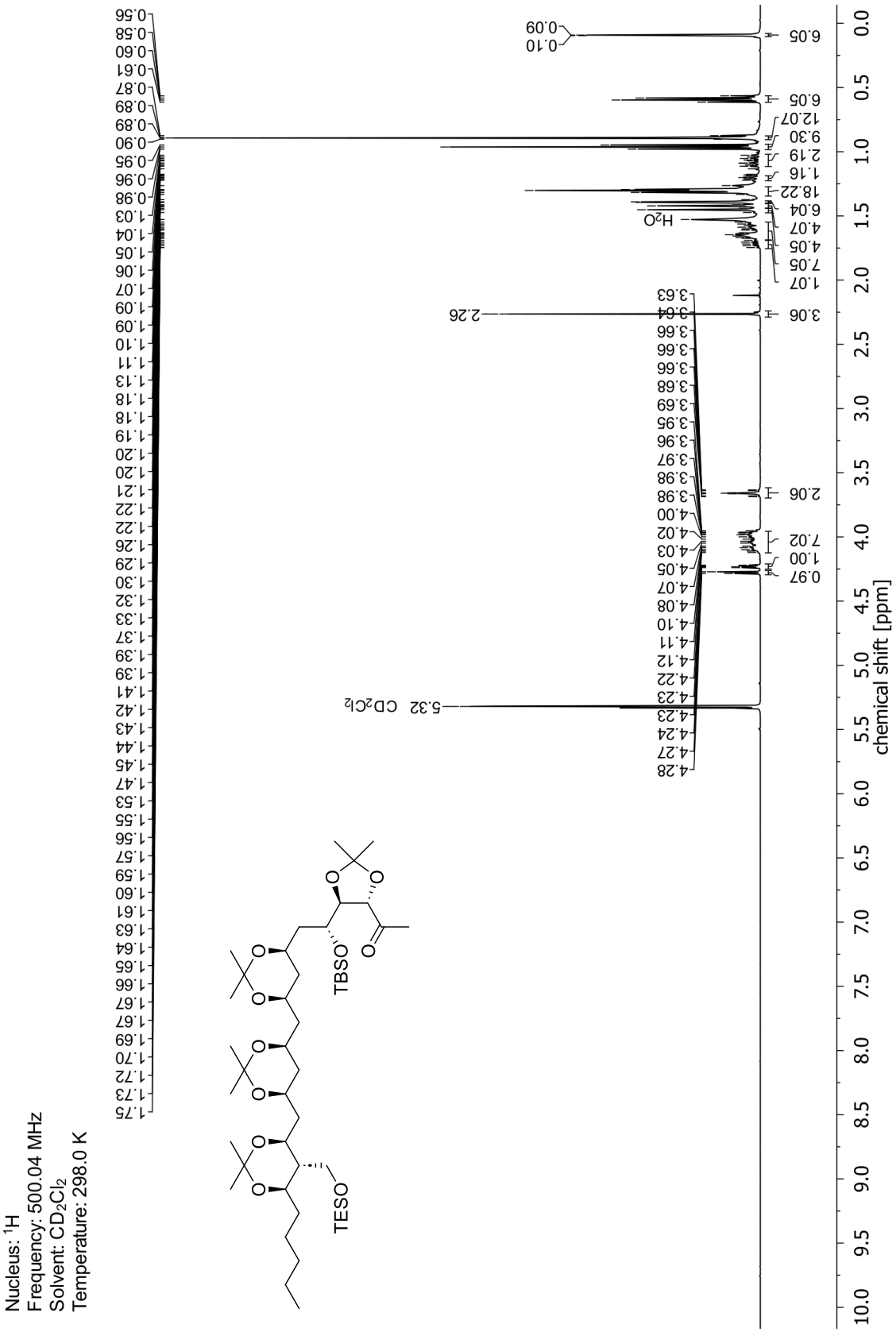

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
HO
TBSO
OTES
CD2Cl2
46.2
43.7
41.2
40.2
37.6
36.9
33.8
32.5
30.5
30.5
30.4
27.6
27.6
26.3
25.3
23.3
20.3
20.1
20.1
18.6
14.4
7.1
4.9
70.4
69.3
68.1
66.4
66.3
65.8
64.7
109.3
99.0
98.8
98.2
80.2
78.3
4.0
4.2
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

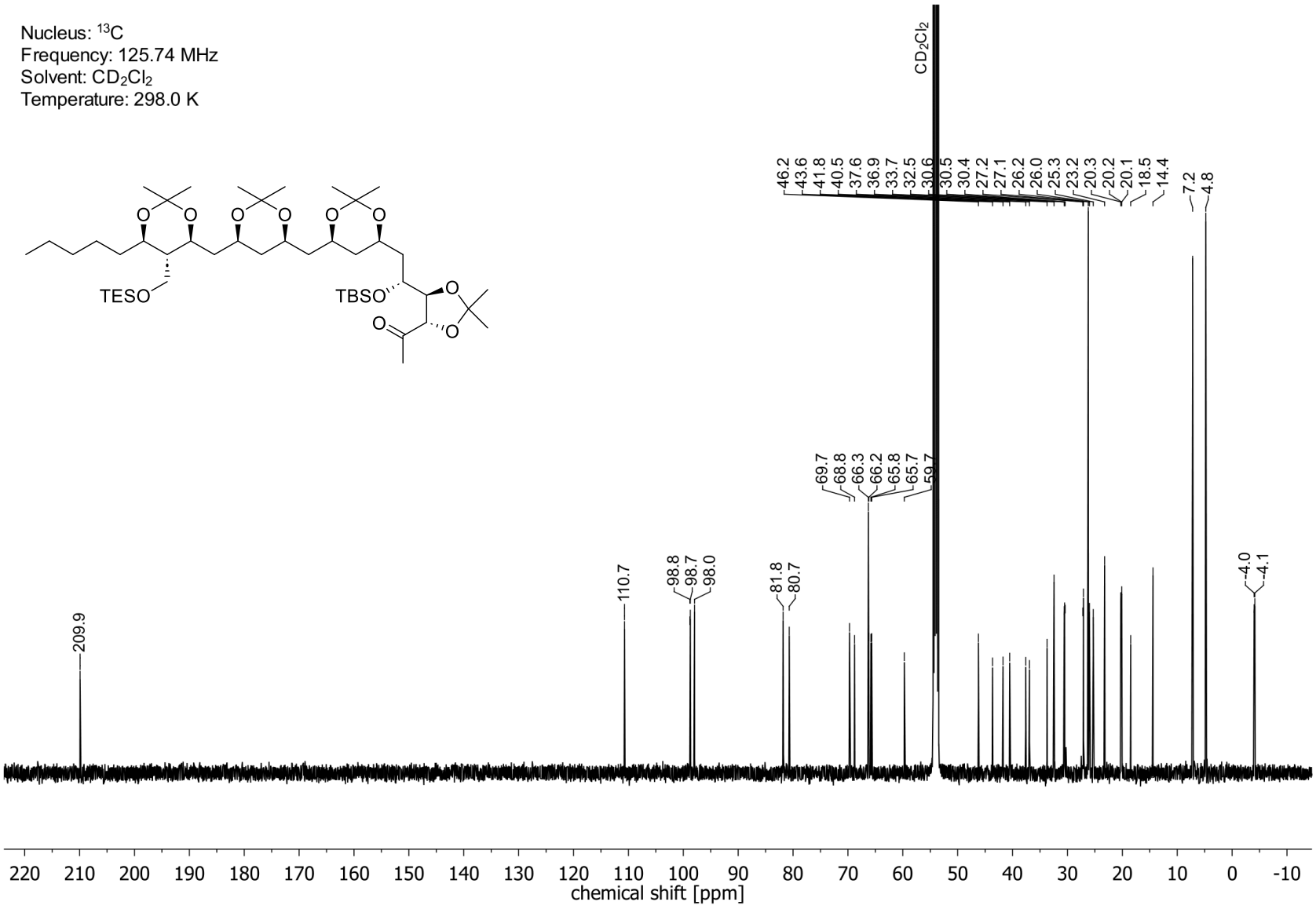
NMR-Spectra of Compound **299**:



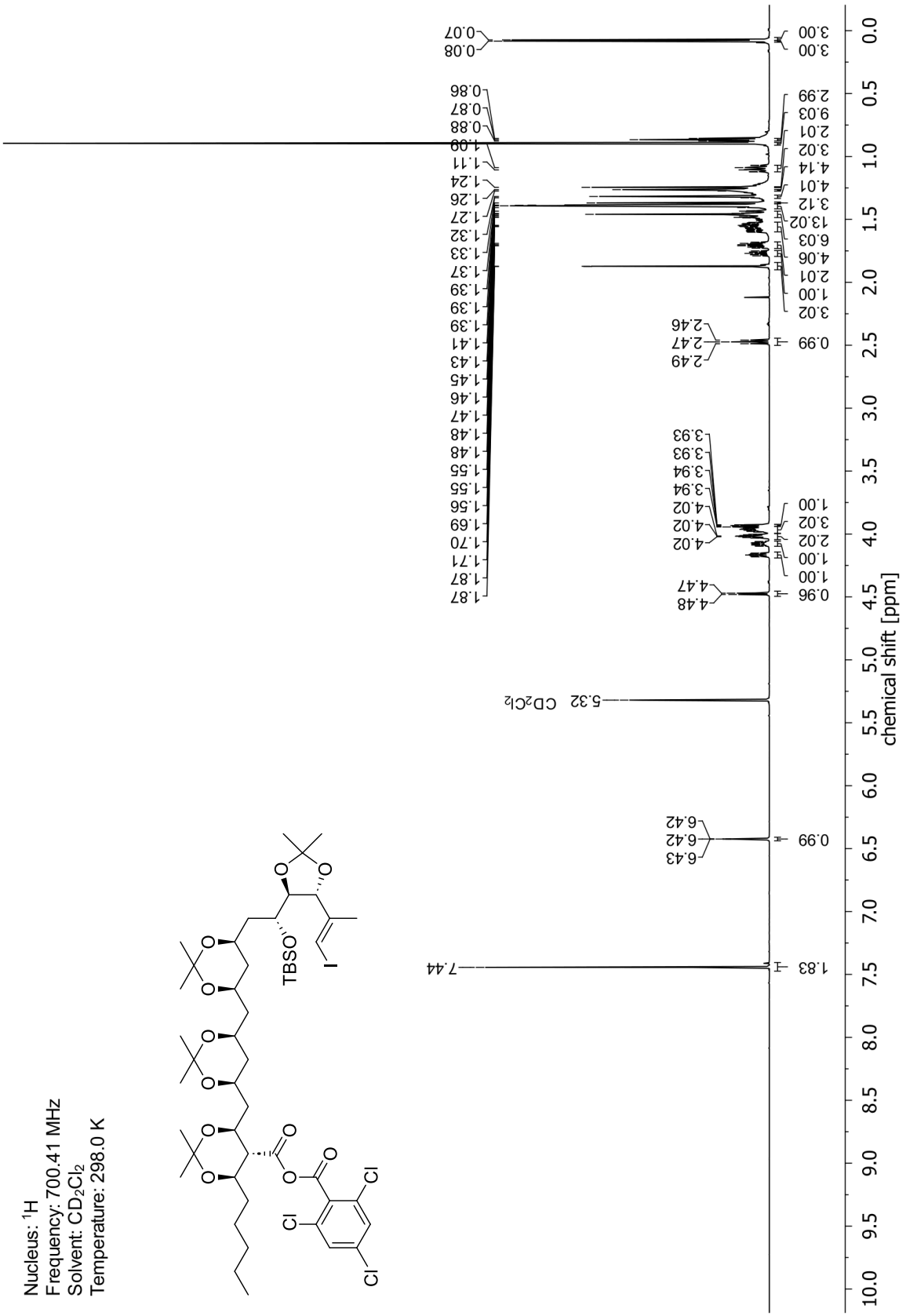

Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TESO
TBSO
CD2Cl2
46.2
43.6
42.1
40.5
37.6
36.9
33.7
32.5
30.6
30.5
30.4
27.4
27.1
26.3
25.3
23.2
20.3
20.1
20.1
18.5
14.4
7.2
4.8
138.0
117.6
109.2
98.8
98.7
98.0
83.9
79.0
69.7
69.0
66.3
66.3
66.2
65.8
65.6
59.7
-3.9
-4.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

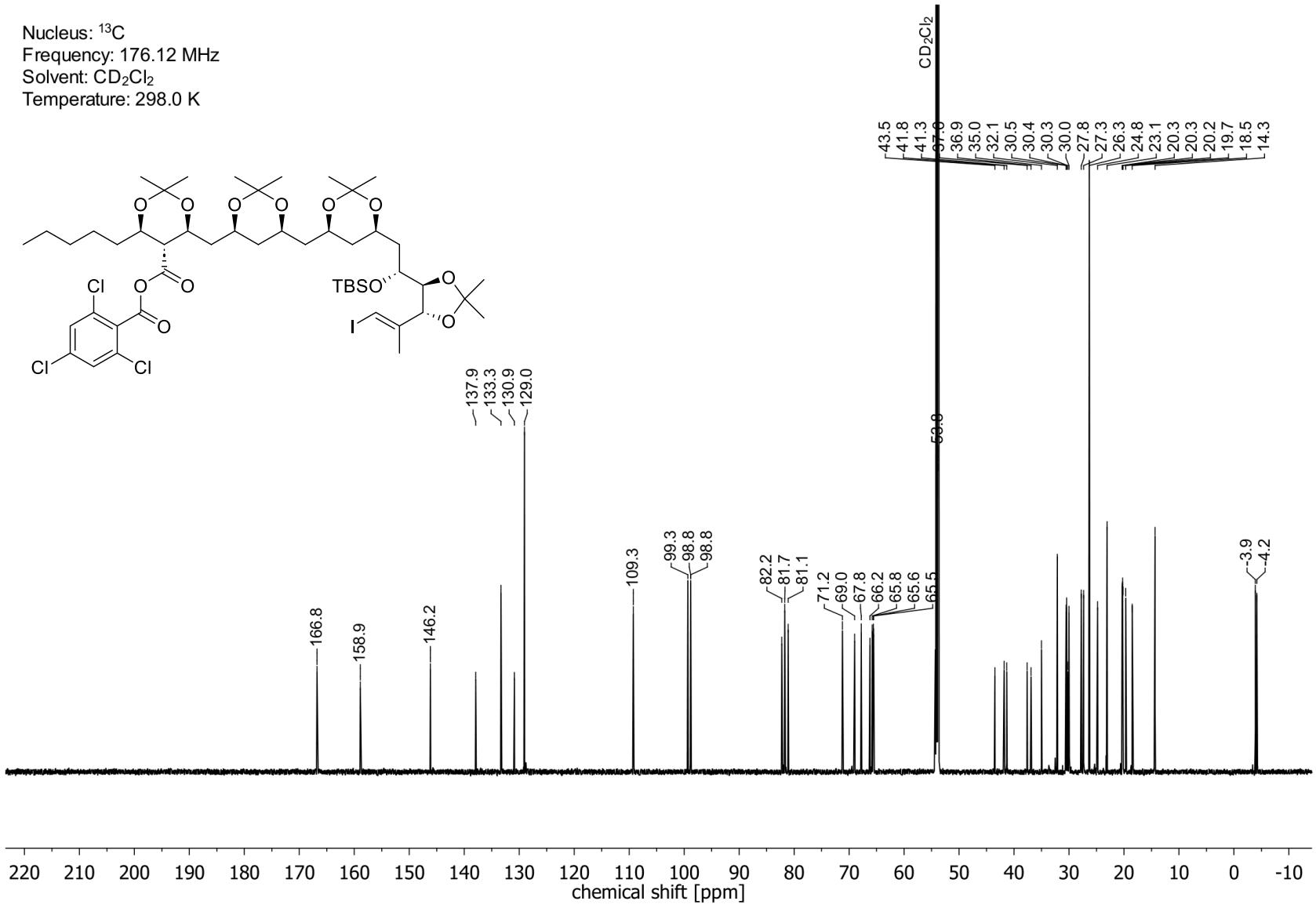
NMR-Spectra of Compound **300**:




Nucleus: 13C
Frequency: 125.74 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
TESO
TBSO
CD2Cl2
46.2
43.6
41.8
40.5
37.6
36.9
33.7
32.5
30.6
30.5
30.4
27.2
27.1
26.2
26.0
25.3
23.2
20.3
20.2
20.1
18.5
14.4
7.2
4.8
69.7
68.8
66.3
66.2
65.8
65.7
59.7
209.9
110.7
98.8
98.7
98.0
81.8
80.7
-4.0
-4.1
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

NMR-Spectra of Compound **307**:




Nucleus: 13C
Frequency: 176.12 MHz
Solvent: CD2Cl2
Temperature: 298.0 K
CD2Cl2
50.0
43.5
41.8
41.3
37.0
36.9
35.0
32.1
30.5
30.4
30.3
30.0
27.8
27.3
26.3
24.8
23.1
20.3
20.3
20.2
19.7
18.5
14.3
137.9
133.3
130.9
129.0
109.3
99.3
98.8
98.8
82.2
81.7
81.1
71.2
69.0
67.8
66.2
65.8
65.6
65.5
166.8
158.9
146.2
-3.9
-4.2
TBSO
Cl
Cl
Cl
I
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

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