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COMMON INTERMEDIATE-BASED TOTAL SYNTHESIS: APPLICATION TO *LAURENCIA* ETHERS AND THE MANGINOID FAMILY

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ABSTRACT

Common Intermediate-Based Total Synthesis: Application to *Laurencia* Ethers and the Manginoid Family

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Natural products have always been a valuable source for scientists who try to identify molecules possessing unique bioactivities and functions. Due to the rapid evolution of synthetic methodologies and strategies over the past two centuries, the field of natural product total synthesis has advanced to an awe-inspiring level. Meanwhile, a number of new concepts to guide the development of next generation total synthesis have emerged. One of the most evoking terms is divergent synthesis, which is also known as common intermediate-based synthesis. It aims to efficiently assemble a collection of structurally distinct natural products, instead of one single molecule, via a well-designed common synthetic intermediate. Such process is of particular significance for research in the pharmaceutical industry, material science, and agricultural industry, where high level of molecular diversity is demanded. This dissertation describes our efforts to utilize a divergent approach in completing a range of natural products in the *Laurencia* ethers and the manginoid family.

Thus, Chapter 1 will provide a brief overview of divergent total synthesis and introduce the general challenges and opportunities in this area. Three previous successful works using this principle are discussed to showcase how the common intermediates of their choice necessitate innovation of new chemical tools. Moreover, these examples will also highlight how the development of novel strategies could lead to a versatile common intermediate and synthetic route with high degree of divergence.

Chapter 2 will detail our efforts to synthesize five members of the *Laurencia* ethers encompassing two distinct 8-menbered ring motifs from a common intermediate. In this work, we will describe a new variant of BDSB-induced ring expansion with an enyne substrate, which could fashion the 8-membered ring with the bromoallene appendage present in microcladallenes. Meanwhile, we will also demonstrate that the BDSB-induced ring expansions (with an alkene or enyne) could proceed in the presence of an additional ring attached to the tetrahydrofuran core. These results, along with the completion of our five targets, will showcase the power of common intermediate-based strategy in the synthesis of *Laurencia* natural products.

Finally, in Chapter 3, we will propose a divergent synthesis towards members of the manginoid family and a range of natural products containing a similar *trans*-hydrindane system. Then the first total synthesis of manginoid A via a number of highly chemo- and stereo-selective operations based on the designed common intermediate will be presented. The establishment of a concise and robust preparation of the plausible common intermediate lays the foundation for our global approach towards all other target molecules.

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Ac	acetyl
AIBN	2,2'-azobis(2-methylpropionitrile)
BDSB	bromodiethylsulfonium bromopentachloroantimate
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
$Br(coll)_2PF_6$	bis-collidine bromonium hexafluorophosphate
DDQ	2,3-dicyano-5,6-dichlorobenzoquinone
DIBAL-H	diisobutylaluminum hydride
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethylsulfoxide
DMVSCl	chlorodimethylvinylsilane
HMPA	hexamethylphosphoramide
KHMDS	potassium bis(trimethylsilyl)amide

LDA	lithium diisopropylamide
LiHMDS	lithium bis(trimethylsilyl)amide
mCPBA	*meta*-chloroperoxybenzoic acid
Ms	methanesulfonyl
NaHMDS	sodium bis(trimethylsilyl)amide
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMO	4-methylmorpholine *N*-oxide
PCC	pyridinium chlorochromate
PMB	*para*-methoxybenzyl
TBAF	tetrabutylammonium fluoride
TBCO	2,4,4,6-tetrabromo-2,5-cyclohexadien-1-one
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
TCCA	trichloroisocyanuric acid
Tf	trifluoromethanesulfonate

TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMG	tetramethylguanidine
THP	tetrahydropyran
TMS	trimethylsilane
Tris	2,4,6-triisopropylben-zenesulfonyl
Ts	tosyl
***p*-TsOH•H2O**	*p*-toluenesulfonic acid monohydrate
$VO(acac)_2$	vanadyl acetylacetonate

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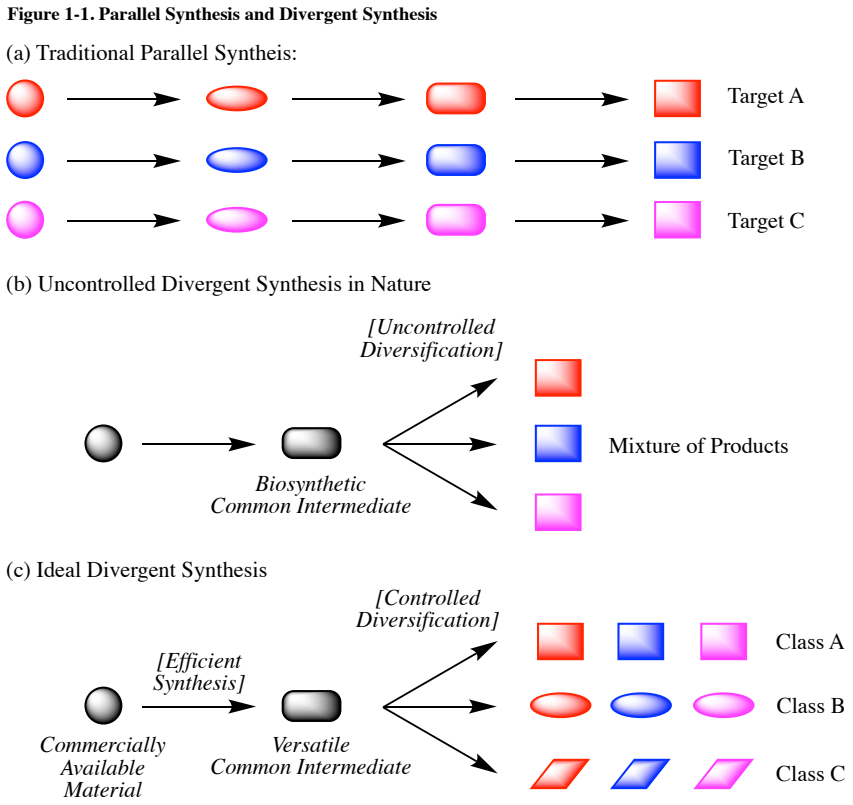
CHAPTER 1

AN OVERVIEW OF DIVERGENT SYNTHESIS

1.1 An Overview of Divergent Synthesis

Figure 1-1. Parallel Synthesis and Divergent Synthesis



Ever since the first synthesis of urea by Wöhler in 1828,[1] the area of natural product synthesis has advanced substantially over the past two centuries. Molecules ranging from commonly seen amino acids or glucose to highly complex taxol or palytoxin have been successfully synthesized by organic chemists in laboratory setting.[2] In 2013, Danishefsky and coworkers achieved the first synthesis of wild-type erythropoietin (EPO) with a molecular weight nearly 18000, which unquestionably marked a milestone for this field.[3] This enormous success was largely achieved by the profound innovation of synthetic strategies as well as the rapid evolution of bond-forming capacities. Today, natural product synthesis is still a rapidly growing area as it remains to be the inspiration and arena of emerging synthetic methods.[4]

To a certain extent nowadays organic chemists armed with modern synthetic technologies are capable of making nearly any given natural product, granted that sufficient time, money, and manpower are provided. In most cases, a "brute-force" approach can only lead to production of one compound at a time (Figure 1-1a), which is inefficient when a broader collection of compounds is required, despite of being recognized as a laboratory-level academic success. As natural products continues to serves as a source of bioactive entities and pharmaceuticals,[5] higher levels of synthetic efficiency will always be demanded in providing robust entry to the diversity given by Nature. Recently, concepts enabling synthetic efficiency such as atom economy,[6] protecting group free synthesis,[7] and green chemistry[8] have been studied and incorporated by organic chemists around the world. Prevalence of those terms suggests the recognition and motivation of the chemistry community to identify areas for development in previous works, bridge the gaps and eventually obtain not only higher efficiency but also higher ideality[9] in natural product synthesis.

Along with those trends, the concept of divergent synthesis also emerged. It was first defined by Boger in 1984 as a synthesis of at least two members within the same class of natural products via an identical intermediate, preferably an advanced intermediate.[10] Such strategy focuses on achieving molecular diversity via maximal overall efficiency from a single synthetic sequence, rather than pursuing each target through individual route. If successfully executed, this approach will be of strategic benefit particularly when the goal is to build up a large assembly of bioactive natural products and their analogues.

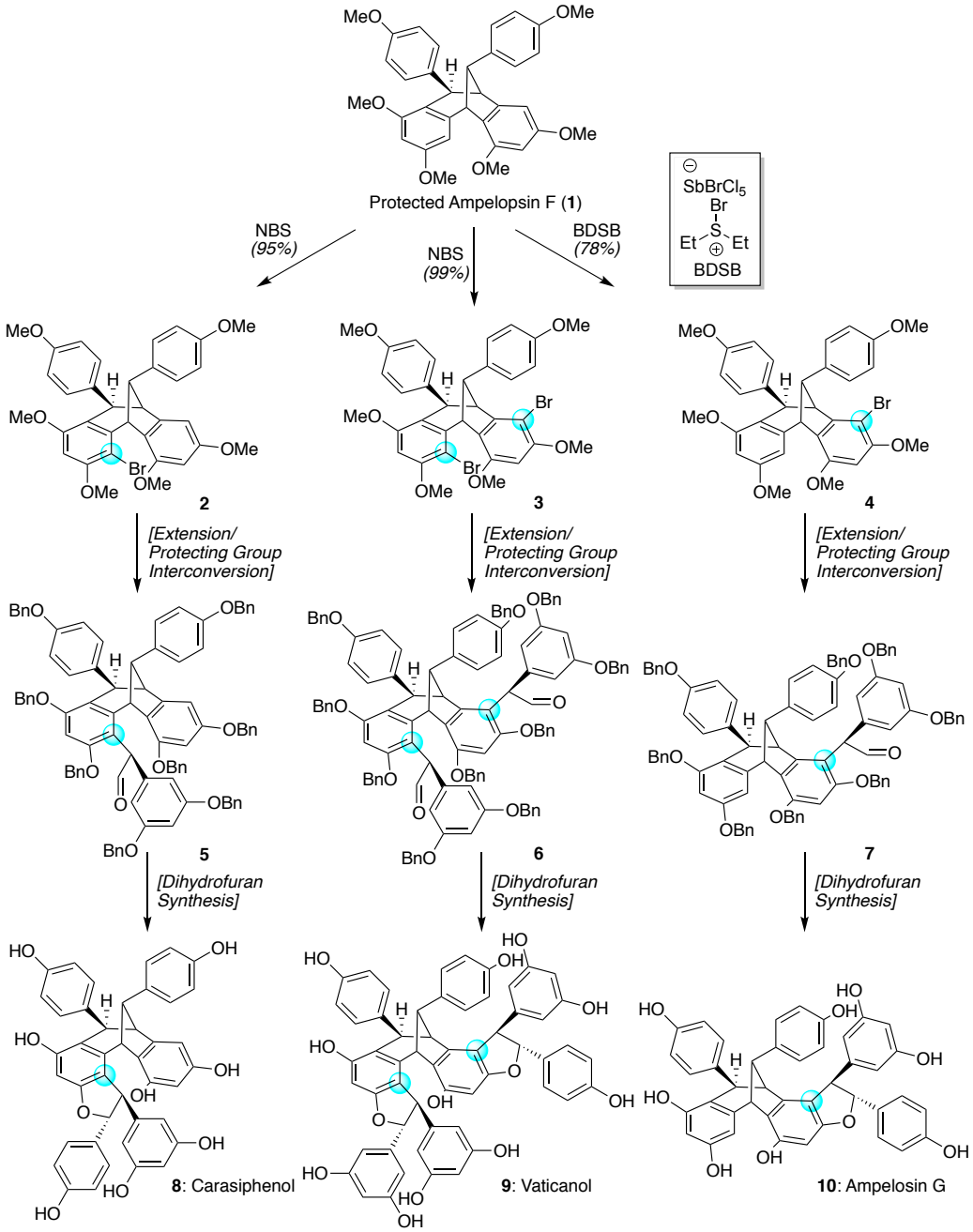
Indeed, divergent synthesis is widely deployed by Nature to fashion its tremendous collections of secondary metabolites sharing common core skeletons (Figure 1-1b).[11] In many cases, post-common intermediate functionalization were mediated by a series of enzymes, in an uncontrolled manner, therefore there is a greater tendency to produce mixtures of several distinct

compounds. Such an outcome is typically not preferred by organic chemists, but is of evolutionary advantage in nature, as it enables the producing species to obtain diverse biochemical reactivity in response to a specific environmental stress.[12] Indeed similar diversity generation has been observed for several natural product collections, such as phytoalexin-based polyphenols.[13] In general, divergent synthesis in lab seeks to diversify a common intermediate into the each individual products in a selective manner.

From a strategic perspective, there are three key components essential in an ideal divergent synthesis: 1) identification of a versatile common intermediate, 2) efficient preparation of that common intermediate on a reasonable scale, 3) rapid diversification of the common intermediate into multiple target molecules. Typically, selecting a suitable common intermediate based on the structural similarity of the desired products is the first step of the synthetic design. Such compound could either arise from the biomimetic pathway or be a complete artifact depending on the ease and efficiency of the subsequent elaborations. In either case, diversification and preparation of the common intermediate would be opportunistic in the innovation of novel reactions and creative synthetic strategies.

As part of the synthetic campaign towards an array of polyphenol oligomeric natural products (Scheme 1-1),[14] Snyder and coworkers achieved a divergent synthesis of carasiphenol B (**8**), vaticanol C (**9**), and ampelopsin G (**10**) via a biomimetic common intermediate **1**. The key to success was the use of a unique bromenium source, BDSB. This reagent could mediate the regioselective bromination of **1** efficiently to give **4** as the major product, while other common bromination conditions (i.e. NBS) only yielded **2** and **3**. With three brominated isomers in hand, the subsequent sequence was able to install the remaining dihydrofuran ring and completed the syntheses of the desired natural products.

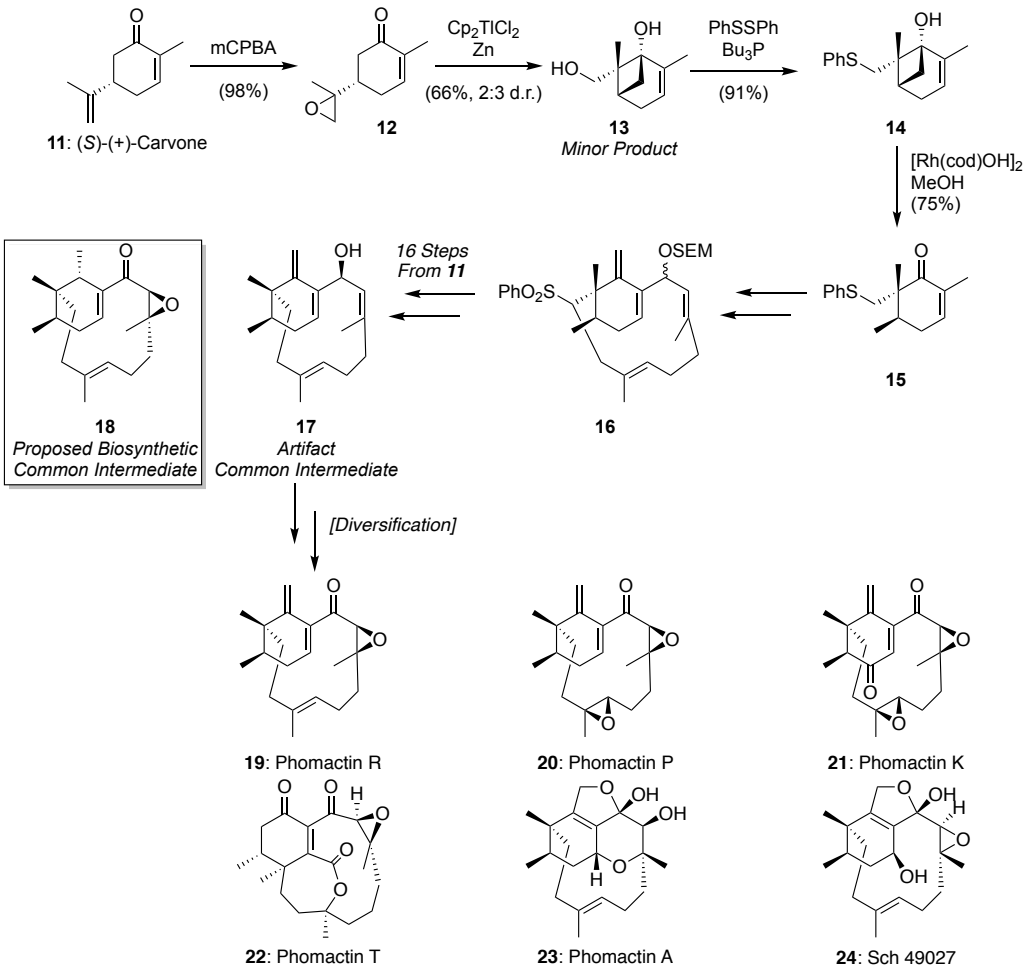
Scheme 1-1. Snyder's Divergent Syntheses of Resveratrol Oligomers Empowered by a Unique Regioselective Bromination



In the divergent syntheses of a number of phomactins (**19-24**) by Sarpong and coworkers (Scheme 1-2),[15] an artifact material **17** was chosen as the common intermediate, as the following diversification may be challenging if the proposed biosynthetic intermediate **18** was used. To fashion the highly intricate poly-substituted cyclohexane core of **17**, a unique approach starting

from (*S*)-(+)-carvone (**11**) was developed. This route highlighted a radical-based coupling with epoxide **12** to forge the strained ring system in **13**. This motif was next subjected to a fragmentation catalyzed by $[Rh(cod)OH]_2$ to provide **15,** which contains the substituted cyclohexene ring present in the target structure. Overall, this set of operations completed a 16-step enantioselective synthesis of the common intermediate **17**. This compound was next efficiently diversified into seven members of the phomactin family that ultimately enabled studies of their bioactivities.

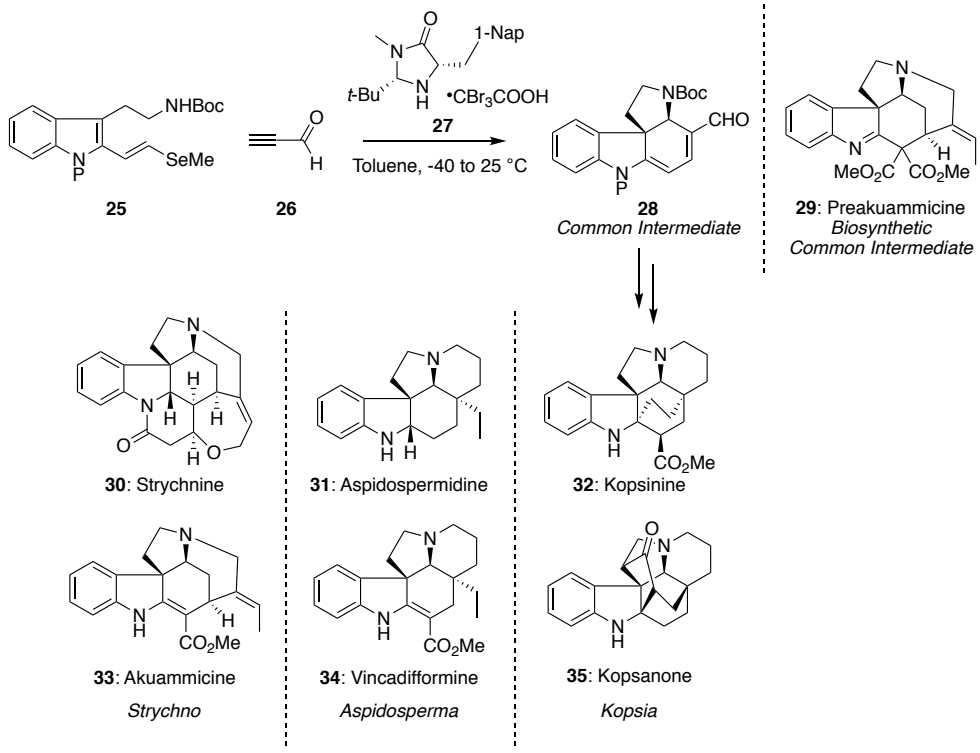
Scheme 1-2. Sarpong's Divergent Syntheses of an Array of Phomactins



Divergent synthesis can be used to assemble collections of indole alkaloids as well. In recent work, MacMillan and coworkers completed the syntheses of six natural products across three distinct families readily from an artifact common intermediate **28** (Scheme 1-3).[16] Access

to this compound was enabled by the development of a powerful cascade transformation mediated by organocatalyst **27**. As **28** was not considered to be of biosynthetic relevance, its ability to diverge into six targets demonstrates that well-designed common intermediates could be as versatile as their counterparts (i.e. **29** in this case) in the biosynthesis. Hence, with advanced synthetic methods and modern techniques, organic chemists can design and execute synthetic routes with high level of divergence that are comparable to that produced by Nature.

Scheme 1-3. MacMillan's Divergent Syntheses of Three Families of Indole Alkoloids



Overall, these three impressive pieces of work showcased the power of common intermediate-based divergent synthesis in fashioning a range of natural products from distinct classes.[17] Arguably, the success of divergent synthesis not only promotes innovation of synthetic methods and strategies, but also fuels bioactivity studies on the family level. As many families of valuable natural products are yet to be accessed, divergent synthesis could be applied as a developable approach to address this challenge, as well as providing a test ground for novel

chemical tools on versatile molecular architectures. With this, we present our efforts toward the divergent syntheses of *Laurencia* ethers and the manginoid family in the next two chapters.

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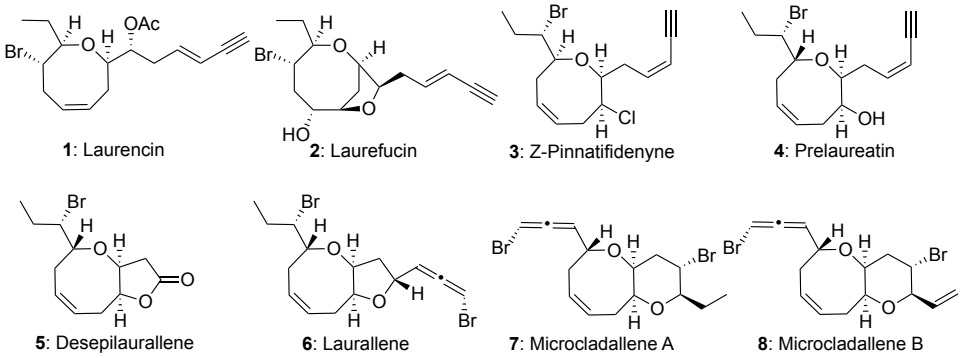
CHAPTER 2

A DIVERGENT SYNTHETIC APPROACH FOR THE LAURENCIA FAMILY OF NATURAL PRODUCTS

2.1 Introduction

2.1.1 Structures of Selected Members of the Laurencia Family of Natural Products

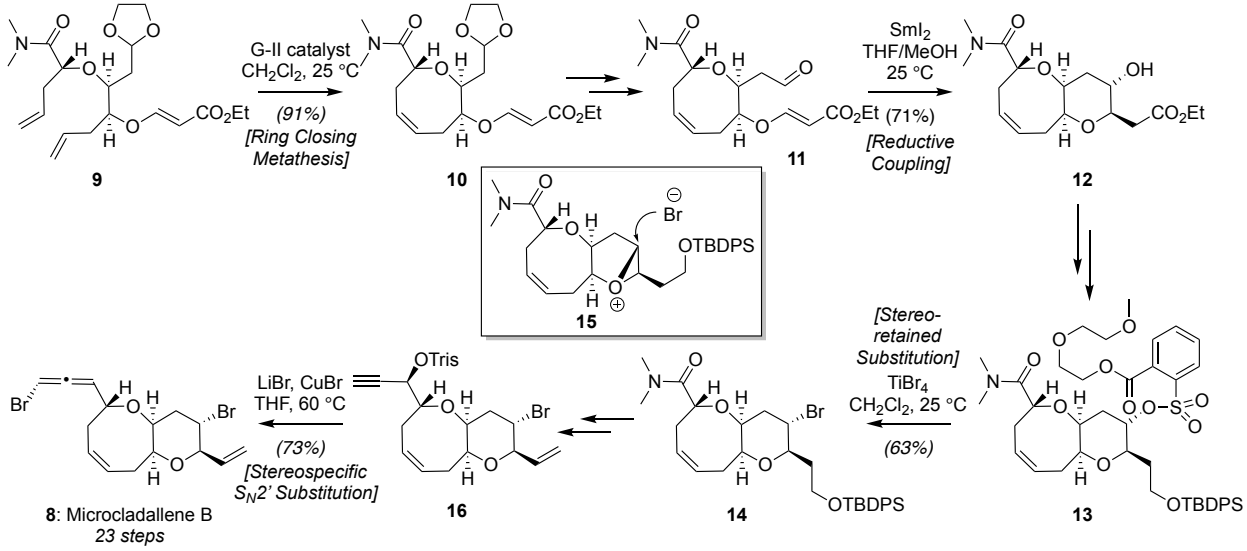
Figure 2-1. Structures of Selected Members of the *Laurencia* Family of Natural Products



The *Laurencia* family of C_{15}-acetogenins is Nature's largest collection of halogenated natural products. Ever since the first isolation of laurencin (**1**, Figure 2-1) in 1965, chemists have identified more than 150 halogenated ether compounds from red algae of the *Laurencia* genus.[1] Over a third of these natural products possess an 8-membered ring (oxocane ring), typically with *endo*- or *exo*-cyclic bromine atoms (as in **1**-**8**), dibromination (as in **6**-**8**), as well as additional appendage ring systems (as in **2** and **5**-**8**). Such compact 15-carbon framework with dense of stereogenic centers and functional groups has captivated the attention of organic chemists around the world. Tremendous synthetic efforts have been made in order to synthesize such natural products. Indeed, nearly 20 total syntheses have been reported to date, for laurencin (**1**) alone.[2] These endeavors have demonstrated the range of creative solutions that can be deployed to fashion such a strained oxocane ring with incorporation of the desired bromine in a stereoselective manner.

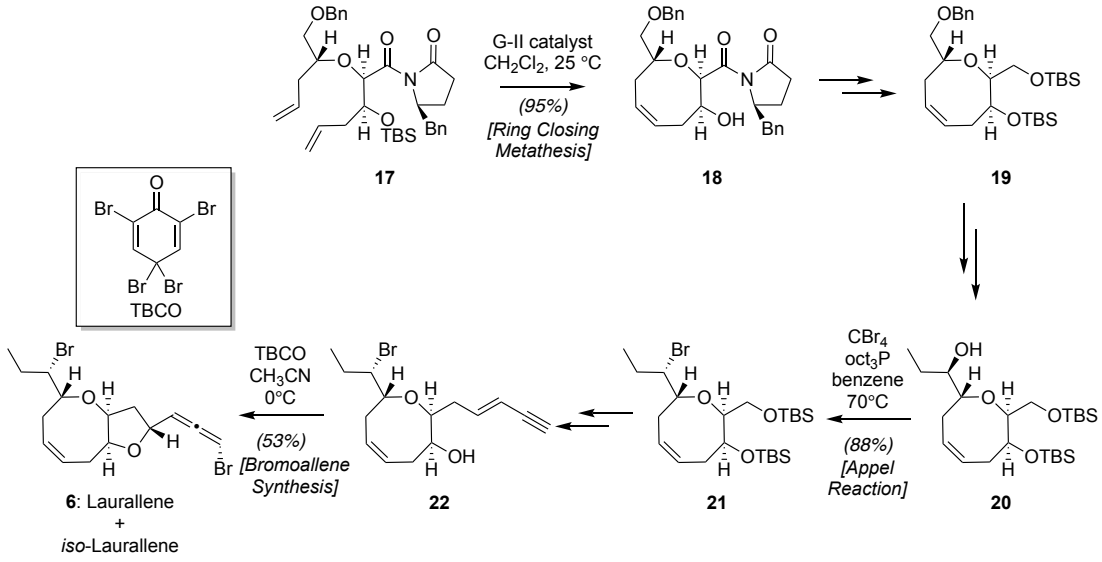
2.1.2 Selected Previous Total Syntheses of Microcladallene B (8) and Lauraallene (6)

Scheme 2-1. Kim's Total Synthesis of Microcladallene B (8)



For example, Kim and co-workers reported the first enantioselective synthesis of microcladallene B in 2007.[3] In this work (Scheme 2-1), the key operations to construct the bicyclic system were a ring closing metathesis to forge the 8-membered ring of **10** from enantiopure material **9**, and a subsequent SmI_2-induced reductive coupling to form tetrahydropyran ring of **12**. Next, the combination of $TiBr_4$ and a unique leaving group (as shown in **13**) promoted a stereo-retained substitution to install the bromine atom, presumably via oxonium intermediate **15**. In the end, the stereo-specific S_N2' substitution facilitated by a sterically hindered leaving group (OTris as shown in **16**) furnished the bromoallene motif in **8** and completed the target molecule in total 23 steps.

Scheme 2-2. Crimmins' Total Synthesis of Laurallene A (6)

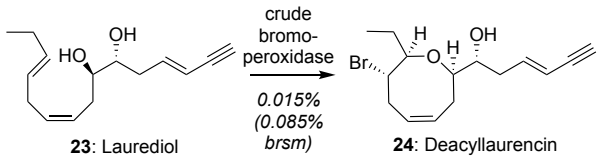


In Crimmins' enantioselective synthesis of laurallene (**6**),[4] a similar ring closing metathesis was deployed to forge the 8-membered ring, while the exocyclic bromine was introduced via an Appel reaction with complete stereochemical inversion (Scheme 2-2). After installing the *E*-enyne side chain to arrive at **22**, a TBCO-induced ring closure completed the tetrahydrofuran and yielded laurallene (**6**) and its diastereomer (not shown) as a 1:1 mixture in overall 20 steps.

Although these syntheses, together with numerous efforts toward the same targets or other members of the *Laurencia* family, featured an array of novel and unique tactics in making these natural products, few of them (mainly from the Kim and Paton groups)[5] were able to deliver several structurally distinct members using a single synthetic sequence. As additional compounds of the *Laurencia* collection were isolated, questions regarding their biogenesis have garnered increasing significance, as it might inspired more general synthetic approaches toward multiple members in the class.[6]

2.1.3 Proposed Biogenesis and Examples of Successful Biomimetic Syntheses

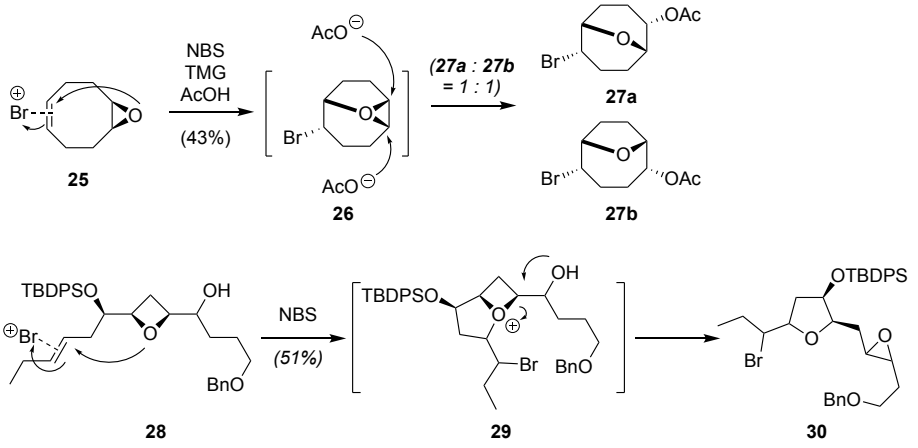
Scheme 2-3. Murai's Biomimetic Synthesis of Deacyllaurencin (24) from Laurediol (23)



23: Laurediol **24**: Deacyllaurencin

The first critical insight came from Murai's hypothesis on the biogenesis of deacyllaurencin (also known as deacetyllaurencin) via a bromonium-induced cyclization from the linear precursor laurediol (**23**, Scheme 2-3).[7] Indeed, upon exposure of **23** to the crude bromoperoxidase, formation of the desired target (**24**) was observed in 0.015% yield (0.085% based on recovered starting material). However, detailed mechanism of this process was not elucidated. Key, though, was that it provided the feasibility that such a bromine atom could be incorporated biosynthetically as an electrophile,[7c] not as a nucleophile. Indeed, nearly every laboratory synthesis has installed such bromines via alcohol substitution chemistry.[8][9]

Scheme 2-4. Selected Examples of Oxonium Formation from Epoxide and Oxetane



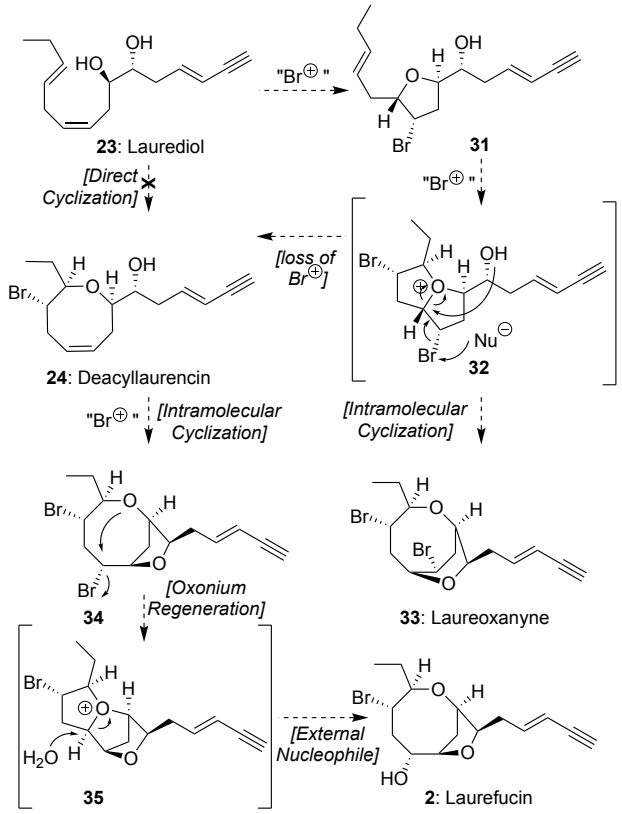
25 **26** **27a** **27b**

28 **29** **30**

Given a direct bromonium-induced 8-*endo*-trig cyclization was likely to be an entropically and enthalpically unfavorable event, we hereby proposed a biosynthetic alternative to achieve this core transformation. Our efforts have focused on the use of tetrahydrofuran-containing precursors

to form the 8-membered rings via ring expansion processes. Of note, our notion was largely inspired by an array of elegant endeavors that sought to construct complex ring systems via initial formation of a smaller, cyclic ether which can serve as the nucleophilic partner to attack a bromonium-activated alkene (Scheme 2-4).[10][11]

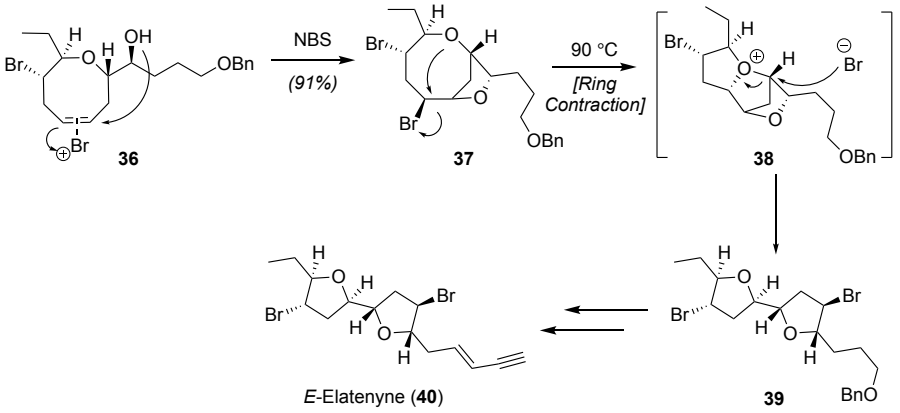
Scheme 2-5. Proposed Biosynthesis of Several Members of the Lauroxocane Class Based on a Series of 5-*endo*-trig Cyclizations and Ring Expansions



As shown in the Scheme 2-5, key tetrahydrofuran derivative **31** could arise from laurediol (**23**) through a bromonium-induced 5-*endo*-trig cyclization. Next, if the oxygen atom of the tetrahydrofuran ring of **31** were to engage a second bromonium-induced cyclization to afford oxonium intermediate **32**, arrow-pushing analysis suggests that subsequent elimination of the endocyclic bromine atom, potentially facilitated by an external nucleophile, could then complete the formal 8-*endo*-trig cyclization to generate deacyllaurencin (**24**). Significantly, that same

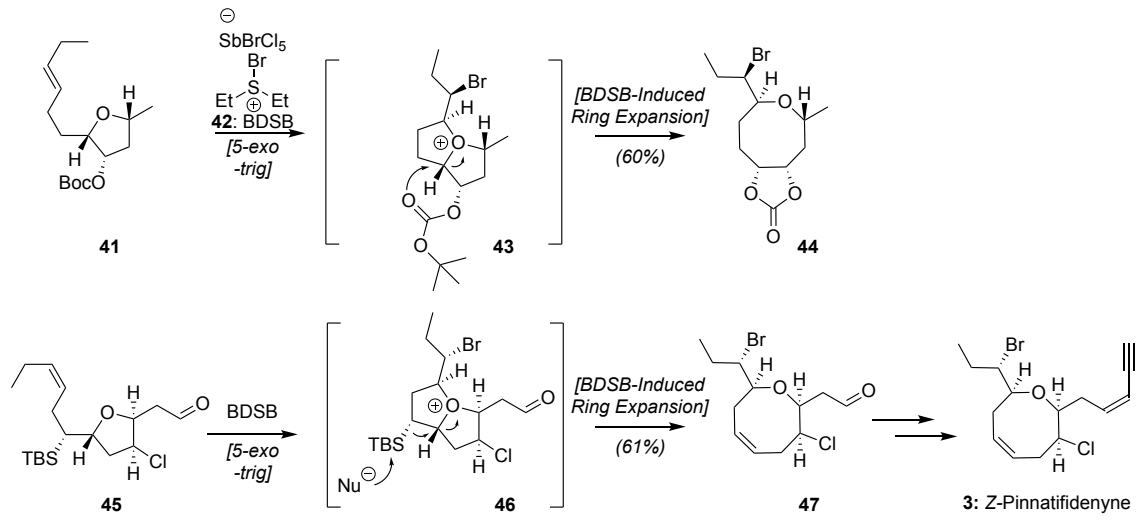
intermediate (**32**) could also afford reasonable biosynthetic pathways to laureoxanyne (**33**) and laurefucin (**2**) through a sequence of potential oxonium regeneration and rearrangement.

Scheme 2-6. Burton and Kim's Synthesis of *E*-Elatenyne (40) via a NBS-Induced Ring Contraction



Indeed, several strategies that used the opposite perspective on this idea (as shown in Scheme 2-6), which involved an initial ring contraction of oxocanes to generate a similar bicyclic oxonium intermediate (as shown in **38**), have enabled the total syntheses of several tetrahydrofuran containing natural products.[12-14]

Scheme 2-7. Selected Examples of BDSB-Induced Ring Expansions to Give 8-Membered Rings and a Successful Synthesis of *Z*-Pinnatifidenyne (3) Based on That Strategy



After extensive efforts, our group found that such potentially biomimetic tetrahydrofuran-based ring expansion could be reduced into practice to generate 8-membered ether ring with high levels of stereoselectivity, when the right bromenium source was utilized. As shown in Scheme 2-7, treatment of **41** with our reactive bromenium source BDSB (**42**, $Et_2SBr{\cdot}SbCl_5Br$)[15] activated the exocyclic alkene to incur a subsequent cyclization and ring expansion to give **44** with the mask diol in 60% yield as a single diastereomer.[16] In another example leading to the total synthesis of Z-pinnatifidenyne (**3**), a similar ring expansion event with fully functionalized substrate **45** yielded alkene-containing product **47** in 61% yield.[17]

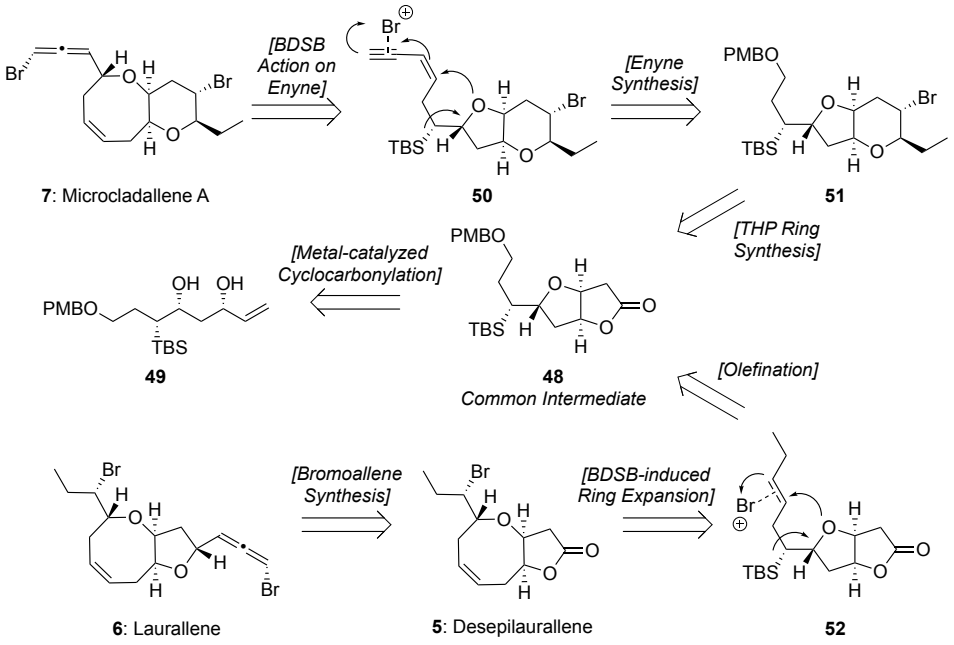
2.2 A Divergent Synthetic Approach for Laurencia Family of Natural Products

2.2.1 Overview of the Design

Here, we presented our efforts to extent this notion and further develop a general synthetic approach to a number of additional members in the *Laurencia* collection. These targets included prelaureatin (**4**),[2b, 4, 18−20] desepilaurallene (**5**),[21] laurallene (**6**) [4, 20b, 22−24] and microcladallenes A and B (**7** and **8**),[3,25] Our principal goal was to demonstrate that the bromonium-induced ring expansions could be effected in the presence of various allied ring systems, to empower syntheses of multiple structurally distinct *Laurencia* natural products. Two questions were of particular interest. First, how does the presence or absence of the ring attached to the tetrahydrofuran impact the viability of the ring expansion process? Since the additional ring could incur extra conformational restrain of the system, it might potentially impact the overall diastereoselectivity by destabilizing the transition state necessary for stereocontrol, as well as the efficiency of the process. Second, could a new variant of the bromonium-induced ring-expansion process be developed to simultaneously forge an 8-membered ring and a bromoallene motif as found in **7** and **8**? If so, could such an event proceed with reasonable stereocontrol since the enyne is more remote

from the 8-membered ring? Of note, despite extensive exploration using both alcohol and carboxylic acid nucleophiles to attack a bromonium activated enyne, particularly by the Tang group,[26] use of an internal ether oxygen for such purposes has not been reported.

Scheme 2-8. Proposed Divergent Approach Towards Several Members of the *Laurencia* Family of Natural Products via a Common Intermediate



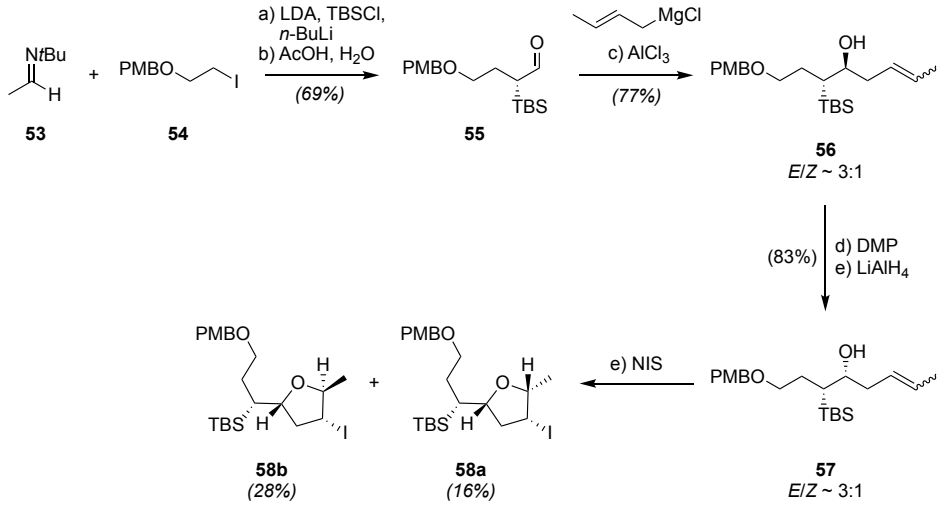
Key designs of our approach were outlined retrosynthetically in Scheme 2-8. We posited that bicyclic lactone **48** was an ideal common intermediate as it not only contained the tetrahydrofuran and the silyl group that were essential for the ring expansion, but also presented functional groups (i.e. PMB-protected alcohol, lactone) that could be readily diversified into various desired structural elements. Presumably **48** could be prepared via a metal-catalyzed cyclocarbonylation from diol **49**. In the case of microcladallene A (**7**), if the newly designed enyne-initiated ring expansion could successfully occur, it could be traced back to **51**, in which the brominated 6-membered ether ring could be ultimately forged from the lactone of **48**. As for the synthesis of laurallene (**6**), construction of the final tetrahydrofuran ring could be completed through a sequence similar to that in the Crimmins' synthesis (Scheme 2-2), presumably from

natural product desepilaurallene (**5**). This material potentially could be obtained via a BDSB-induced ring expansion with **52** in a format generally similar to that previously deployed as part of our *Z*-pinnatifidenyne (**3**, Scheme 2-7). How the lactone ring could influence the ring-expansion event was to be explored. From here, **52** was expected to be readily prepared also from common intermediate **48**.

2.2.2 Model Studies of BDSB-Induced Ring Expansions with Enyne Substrates

A critical element of the overall plan described above, one of equal significance from a biosynthetic perspective, was the ability in effecting the enyne-mediated ring expansion leading to 8-membered rings with appended bromoallene motif. Thus, to assess the feasibility and the stereoselectivity of such transformation, we elected to pursue model studies using simplified enyne substrates.

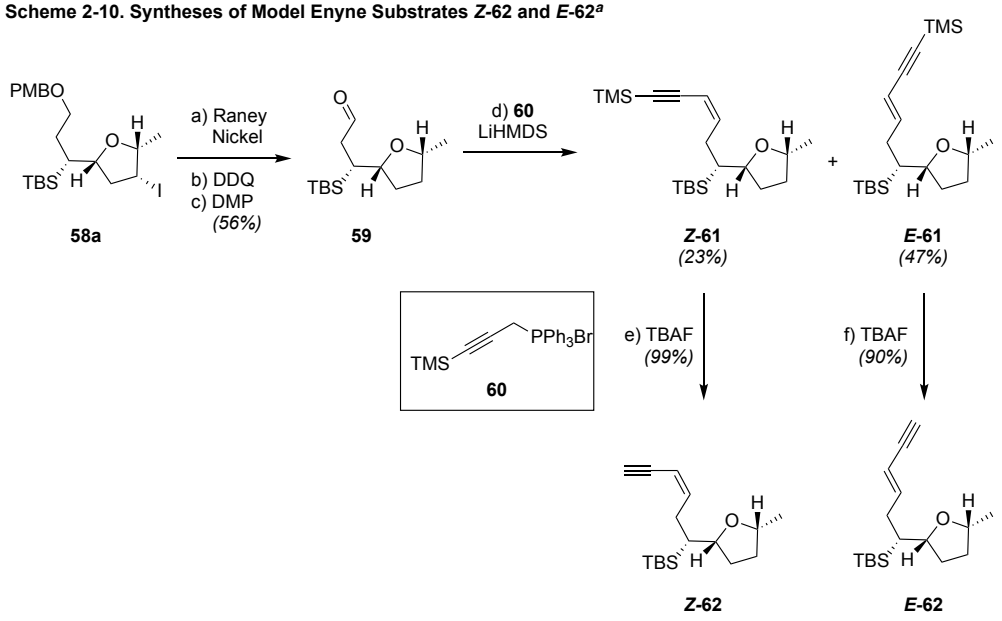
Scheme 2-9. Syntheses of Tetrahydrofuran Derivatives 58a and 58b[a]



[a] Reagents and conditions: (a) LDA (1.05 equiv), THF, 0 °C, 30 min; TBSCl (0.99 equiv), *n*-Bu_4I (0.02 equiv), 25 °C, 4 h; *n*-BuLi (1.05 equiv), 0 °C, 30 min; **54** (1.5 equiv), 25 °C, 12 h; (b) 1 M AcOH, CH_2Cl_2, 25 °C, 1 h, 69% over 2 steps; (c) 2-butenyl magnesium chloride (3.0 equiv), $AlCl_3$ (6.0 equiv) Et_2O, -78 to 0 °C, 30 min, 77%, *E*:*Z* ~ 3:1; (d) Dess-Martin periodinane (1.1 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 2 h, 96%; (e) $LiAlH_4$ (2.0 equiv), THF, 25 °C, 15 min, 86%, *E*:*Z* ~ 3:1; (f) NIS (1.0 equiv), CH_2Cl_2, 25 °C, 12 h, 16% **58a**, 28% **58b**.

As shown in Scheme 2-9, preparation of the model substrates commenced with the syntheses of tetrahydrofuran derivative **58a** and **58b**. After silylating and alkylating imine **53** with TBSCl and alkyl iodide **54** to arrive at aldehyde **55**,[27] allylation mediated by the combination of 2-butenyl magnesium chloride and aluminum chloride delivered crotylated product **56** as an inseparable mixture of 3:1 *E/Z* isomers.[28] Next, a 2-step redox operation smoothly inverted the stereochemistry of the alcohol to give **57**, setting the stage for the subsequent ring closuring. Upon treatment of **57** with NIS, the desired iodoetherification proceeded to give **58a** and **58b** in 16% and 28% yield respectively.

Scheme 2-10. Syntheses of Model Enyne Substrates *Z*-62 and *E*-62[a]

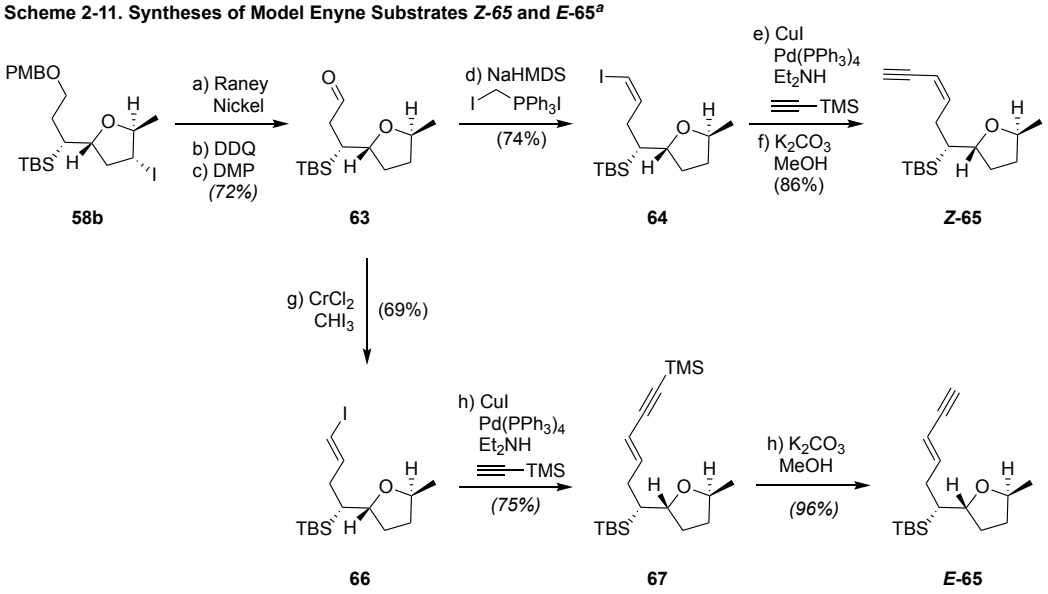


[a] Reagents and conditions: (a) Raney Nickel (excess), EtOH, 25 °C, 1 h, 77%; (b) DDQ (1.5 equiv), CH_2Cl_2, 25 °C, 1 h, 89%; (c) Dess-Martin periodinane (1.1 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 2 h, 81%; (d) LiHMDS (2.0 equiv), **60** (3.0 equiv), THF, 0 °C, 30 min, 23% ***Z*-61**, 47% ***E*-61**; (e) TBAF (1.1 equiv), THF, 0 °C, 30 min, 99%; (f) TBAF (1.0 equiv), THF, 0 °C, 30 min, 90%.

58a was then converted into aldehyde **59** via a 3-step sequence in 56% overall yield (Scheme 2-10). These operations involved a deiodination, PMB deprotection, and oxidation of the resultant alcohol. **59** was next subjected to a Wittig olefination modulated by the anion derived from **60** to afford a separable mixture of enyne ***E*-61** and ***Z*-61** in 2:1 ratio.[28] After subsequent

desilylation with these two compounds individually, desired model enyne substrates ***Z*-62** and ***E*-62** were achieved.

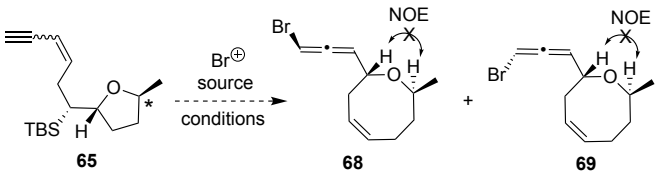
Scheme 2-11. Syntheses of Model Enyne Substrates *Z*-65 and *E*-65[a]



[a] Reagents and conditions: (a) Raney Nickel (excess), EtOH, 25 °C, 1 h, 97%; (b) DDQ (1.5 equiv), CH_2Cl_2, 25 °C, 1 h, 85%; (c) Dess-Martin periodinane (1.1 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 2 h, 87%; (d) (Iodomethyl)triphenylphosphonium iodide (1.3 equiv), NaHDMS (1.3 equiv), THF, 0 °C, 30 min, 74%; (e) CuI (0.10 equiv), $Pd(PPh_3)_4$ (0.10 equiv), TMS acetylene (3.0 equiv), THF/Et_2NH, 25 °C, 6 h, 90%; (f) K_2CO_3 (2.0 equiv), THF/MeOH, 0 °C, 6 h, 96%; (g) $CrCl_2$ (6.0 equiv), CHI_3 (1.1 equiv), THF, 0 °C, 3 h, 69%; (e) CuI (0.10 equiv), $Pd(PPh_3)_4$ (0.10 equiv), TMS acetylene (3.0 equiv), THF/Et_2NH, 25 °C, 6 h, 75%; (h) K_2CO_3 (2.0 equiv), THF/MeOH, 0 °C, 6 h, 96%;

Following the same procedure as above, **58b** was converted into aldehyde **63** in 72% overall yield. From here, alternative approaches to install the enyne side chain were deployed in order to achieve better stereocontrol (Scheme 2-11). Indeed, a sequence involving a Wittig olefination,[29] Sonogashira coupling,[30] and final TMS cleavage converted **63** to model enyne ***Z*-65** selectively via the *Z*-vinyliodine intermediate **64**. ***E*-65** was also obtained from **63** through a similar set of operations with the Wittig olefination replaced by a Takai olefination.[31]

Table 2-1. Screening of Conditions to Achieve Bromoallene-Containing 8-Membered Ring



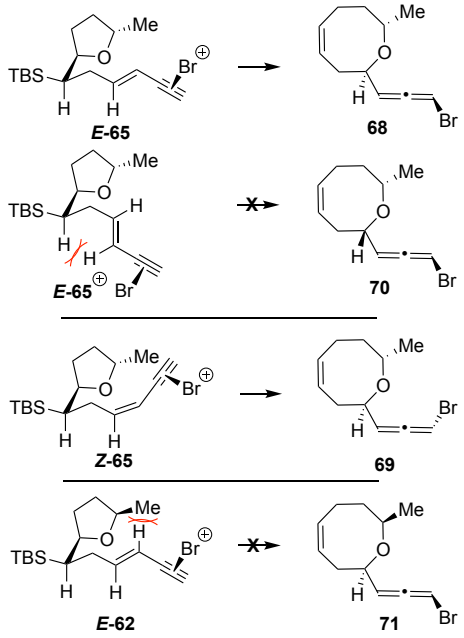
Entry	Substrate and Br^+ source	Solvent	Temp. (°C)	Yield (%)	**68**:**69**
1	*E*-**65**, NBS (1.0 equiv)	$MeNO_2$	23	0	-
2	*E*-**65**, NBS (1.0 equiv), DABCO	$MeNO_2$	23	0	-
3	*E*-**65**, $Br(Coll)_2PF_6$ (1.2 equiv)	$MeNO_2$	-25	32[a]	1.0 : 1.0
4	*E*-**65**, BDSB (0.8 equiv)	$MeNO_2$	-25	30[b]	2.7 : 1.0
5	*E*-**65**, BDSB (0.8 equiv)	$EtNO_2$	-78	60	1.9 : 1.0
6	*Z*-**65**, BDSB (0.8 equiv)	$EtNO_2$	-78	61	1.0 : 1.9
7	*E*-**62**, BDSB (0.8 equiv)	$EtNO_2$	-78	0[c]	-
8	*Z*-**62**, BDSB (0.8 equiv)	$EtNO_2$	-78	0[c]	-

[a] Conversion was ~40% with a yield b.r.s.m. being 80%, [b] large amount of side-products observed, [c]starting material decomposed.

With all model enyne substrates (***Z***/***E*-62** and ***Z***/***E*-65**) in hand, the stage was set to explore the key bromonium-induced ring expansion. As shown in Table 2-1, using the ***E*-65** for most of our condition screening, we first deployed the most conventional bromonium source, NBS, in polar aprotic solvent $MeNO_2$. However, no conversion was observed even with the presence of DABCO as a promoter (entry 1, 2).[26a] Encouragingly, upon switching NBS to $Br(coll)_2PF_6$,[32] ring-expanded products **68** and **69** were formed as a 1:1 mixture in modest yield with partial conversion (entry 3); such results suggested that using a more reactive bromenium source was critical for effective enyne activation. Indeed, when we deployed our bromenium source (BDSB) in $MeNO_2$ at -25 °C, full consumption of starting material was observed. Although the yield was modest due to significant formation of side products, some product control (2.7 : 1) was detected (entry 4). Pleasingly, if $EtNO_2$ was used as solvent which enabled the temperature to be lowered to −78 °C, the same reaction with BDSB afford **68** and **69** in overall ~60% yield as a 1.9:1 mixture of diastereomers (entry 5).[33] Moreover, using ***Z*-65** as the starting material under the same condition gave opposite stereoselectivity in similar yield, which suggested the specificity of this process relative to the enyne geometry. Treatment of ***Z***/***E*-62** with BDSB were also attempted but only led

to complete degradation. Of note, as we were unable to obtain suitable crystal sample of **68** or **69** for X-ray diffraction analysis, the structural assignments of their oxocane ring were largely based on NOE analysis; the bromoallene configuration was initially assigned based on transition state analysis and later confirmed by our total synthesis of the microcladallenes.

Scheme 2-12. Proposed Transition State Analysis to Account for Observed Ring Expansion Results with Enyne Substrates



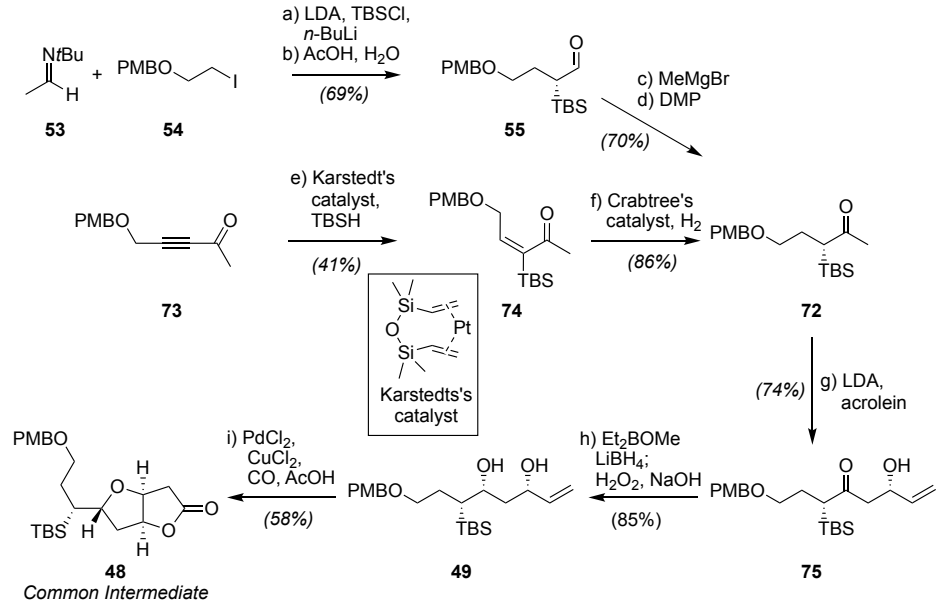
Our proposed transition state analysis to account for the results of the ring expansion mainly considered the substituents on the tetrahydrofuran ring coupled and the geometry of the enyne. As shown in Scheme 2-12, we presumed that the C−Si bond and the C−O bond likely adopt an antiperiplanar orientation so the electrons in the C−Si bond can hyperconjugate with the C−O antibonding orbital.[2b, 34] Such alignment, one was typical in the cases of β-silicon effect, would lower the overall energy of the system and increase the nucleophilicity of the oxygen atom. Next, the enyne side-chain within ***E*-65** could exist in two different possible orientations, and we believed that the first drawing is more favored on energetic grounds as the indicated interaction in the second would significantly destabilize the oxonium intermediate. These features would potentially

explain the exclusive formation of the *trans* oxocane ring of **68** instead of the *cis*-substituted ring of **70** in the ring expansion. Similar analysis of ***Z*-65**, with only the productive transition state shown here, can rationalize the observed formation of **69** as the major product. Critically, the bromenium addition is expected to occur preferentially from the indicated side in both cases, simply to minimize the steric interaction between the reagent and the tetrahydrofuran-containing ring; our tentative assignments of the bromoallene configuration within **68** and **69** were based on such suppositions. However, such steric interaction was not strong enough to completely prevent bromenium addition from occurring on the other side of the enyne. Therefore **69** was observed as the minor product with ***E*-65** and **68** as the minor product with ***Z*-65**. Finally, the configuration of the substituent on the tetrahydrofuran ring was also critical to the outcome of the process. Failure of our attempts to effect the ring expansion with ***E*/*Z*-62** to give **71** could be due to the indicated steric clash (shown here with ***E*-62**); as no productive transition state could be obtained, decomposition pathways would be resulted.

Overall, these initial results highlighted that under appropriate conditions, enyne motif could be activated by the bromenium source and engaged with a tetrahydrofuran oxygen atom to incur the subsequent ring expansion. Such process could yield oxocane ring with bromoallene appendage, a system that resembled the core structure of microcladallenes (**7** and **8**). In addition, although the enyne motif was remote from the tetrahydrofuran core, some product selectivity could be observed with the use of BDSB, in a manner dependent upon the initial geometry of the enyne. With these, the stage was now set for our target-based syntheses toward five *Laurencia* natural products. Our goals were to investigate the feasibility and stereoselectivity of a similar ring expansion with appended ring systems, and to probe the potential of such a process being part of the biogenies.

2.2.3 Racemic Synthesis of Key Common Intermediate 48

Scheme 2-13. Racemic Synthesis of Common Intermediate 48[a]



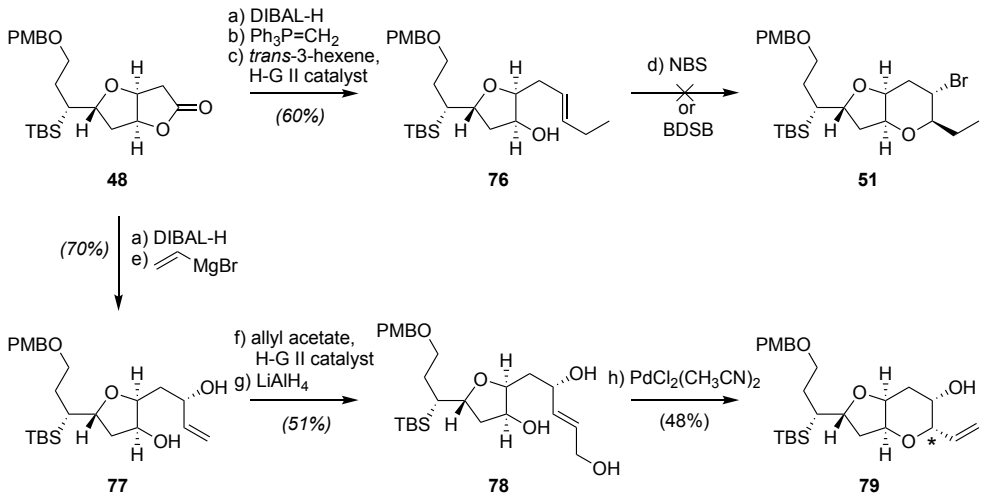
[a] Reagents and conditions: (a) LDA (1.05 equiv), THF, 0 °C, 30 min; TBSCl (0.99 equiv), *n*-Bu_4I (0.02 equiv), 25 °C, 4 h; *n*-BuLi (1.05 equiv), 0 °C, 30 min; **54** (1.5 equiv), 25 °C, 12 h; (b) 1 M AcOH, CH_2Cl_2, 25 °C, 1 h, 69% over 2 steps; (c) MeMgBr (2.2 equiv), THF, -78 °C, 30 min, 85%; (d) Dess-Martin periodinane (1.05 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 2 h, 82%; (e) Karstedt's catalyst (0.05 equiv), TBSH (1.5 equiv), CH_2Cl_2, 25 °C, 12 h, 41%; (f) Crabtree's catalyst (0.05 equiv), H_2 (balloon), CH_2Cl_2, 25 C, 12 h, 86%; (g) LDA (1.5 equiv), THF, -78 °C, 30 min; acrolein (1.6 equiv), -78 °C, 30 min, 74%, d.r. ~5:1; (h) Et_2BOMe (1.2 equiv), THF, -78 °C, 30 min; $LiBH_4$ (15.0 equiv), -78 to 25 °C, 4 h; NaOH (2.5 equiv), H_2O_2 (26 equiv), 0 °C, 1 h, 85%; (i) $PdCl_2$ (0.4 equiv), $CuCl_2$ (3.0 equiv), NaOAc (5.0 equiv), CO (balloon), AcOH, 25 °C, 12 h, 58%.

As shown in Scheme 2-13, our efforts toward microcladallenes (**7** and **8**) commenced with the synthesis of common intermediate **48**. The first set of operations was to prepare ketone **72**, a precursor which could be readily elaborated to **48** with a few additional transformations. In total, we established two different racemic routes to this compound. The first deployed a nucleophilic addition/ oxidation approach with aldehyde **55**,[27] formed by silylating and alkylating imine **53** with TBSCl and alkyl iodine **54**. The second used Karstedt's catalyst[35] to affect the addition of TBSH across the alkyne of **73**,[36] followed by alkene reduction as modulated by Crabtree's catalyst. While the latter route was shorter, the first one proved more suitable for scale-up and, as a result, was used for material supplies in our initial studies. Pressing forward, treatment of ketone **72** with LDA followed by addition of acrolein afforded the β-hydroxy ketone **75** as the major adduct in an

inseparable 5:1 mixture of diastereomers. A Narasaka−Prasad reduction (Et_2BOMe, $LiBH_4$) was next carried out to convert **75** into the desired 1,3-*cis*-diol product **49** in 85% yield.[37] This material contained a few inseparable isomers which could be easily removed in the subsequent step. Of note, several other nonchelating hydride sources (such as $LiAl(Ot\text{-}Bu)_3H$ and L-Selectride) were also examined in hopes that the reduction follows the Felkin−Ahn model of stereoselection; none delivered a higher yield of product. Finally, with all stereogenic centers and key functionality in place, the stage was set to initiate a metal-mediated cyclocarbonylation reaction to sew up the two ring systems in the form of bicyclic lactone **48**. Following some modest condition screening, we found that exposure of **49** to $PdCl_2$ and $CuCl_2$ in the presence of a CO atmosphere in AcOH smoothly effected its conversion to common intermediate **48** in 58% yield.[38]

2.2.4 Total Syntheses of Microcladallenes A and B (7 and 8)

Scheme 2-14. Initial Failures to Generate the Brominated Tetrahydropyran Ring of Microcladallenes[a]

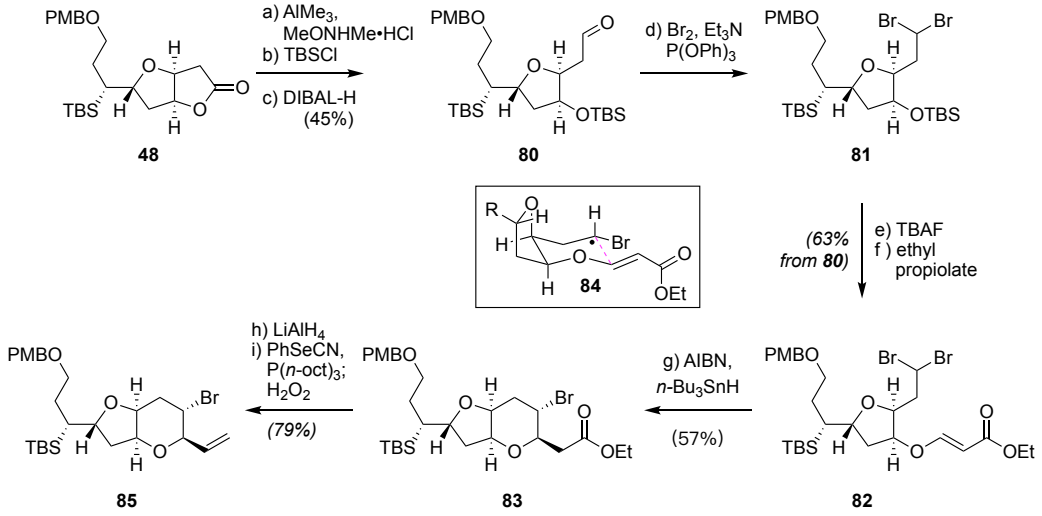


[a] Reagents and conditions: (a) DIBAL-H (1.1 equiv), CH_2Cl_2, -78 °C, 15 min, 79%; (b) *t*-BuOK (3.1 equiv), Ph_3PCH_3Br (3.0 equiv), THF, 0 °C, 6 h, 85%; (c) Hoveyda-Grubbs II catalyst (0.05 equiv), *trans*-3-hexene (8.0 equiv), CH_2Cl_2, 25 °C, 3 h, 90%; (d) NBS (1.2 equiv), CH_2Cl_2, 0 °C, 2 h; (e) vinylmagnesium bromide (10 equiv), toluene, 25 °C, 2 h, 88%; (f) H-G II cat. (0.1 equiv), allyl acetate, 25 °C, 4 h, 54%; (g) $LiAlH_4$ (1.0 equiv), THF, 25 °C, 94%; (h) $PdCl_2(CH_3CN)_2$ (0.05 equiv), THF, 0 °C, 3 h, 48%.

With the common intermediate **48** in hand, the next synthetic challenge was to convert its lactone into the key 6-membered bromoether of microcladallenes. As shown in Scheme 2-14, our

first attempt was to carry out a high-risk, biomimetic bromonium-induced 6-*endo*-trig cyclization from a alcohol/alkene-containing substrate. Although such cyclization might be the way that Nature fashioned the desired ring system, it would be difficult to realize without the assistance of enzymes. In contrast, 5-*exo*-trig cyclization generally was a more favorable process as documented both in several total syntheses as well as our own endeavors,[39a-k] unless an aromatic group was present as a substituent of the alkene.[39l-n] Still, we felt such a test was worthwhile since its success would afford a highly concise solution and the test substrate was expected to be easily accessed. Indeed, starting from **48**, DIBAL-H reduction to lactol with following Wittig olefination and cross metathesis[40] readily afforded test substrate **76** in 60% yield over 3 steps, poised for the projected cyclization. As originally feared, subsequent efforts to induce that 6-*endo*-trig bromoetherification with a variety of bromenium sources, shown here with NBS and BDSB, failed to deliver **51**. Instead, complex mixtures were observed. As such, an alternative approach to construct the tetrahydropyran ring empowered by an intramolecular Tsuji-Trost-type cyclization was pursued. As shown in the lower portion of Scheme 2-14, the requisite substrate **78** was readily synthesized through a four-step sequence which included a DIBAL-H reduction, Grignard addition, olefin metathesis and acetate cleavage.[41] Next, exposure of **78** to $PdCl_2(CH_3CN)_2$ smoothly effected the desired tetrahydropyran formation and give **79** in 48% yield,[42] but unfortunately the configuration of the newly generated stereogenic center (mark with a star) was incorrect based on our analysis from NOE experiments.

Scheme 2-15. Successful Synthesis of the Brominated Tetrahydropyran Core from Common Intermediate 48[a]

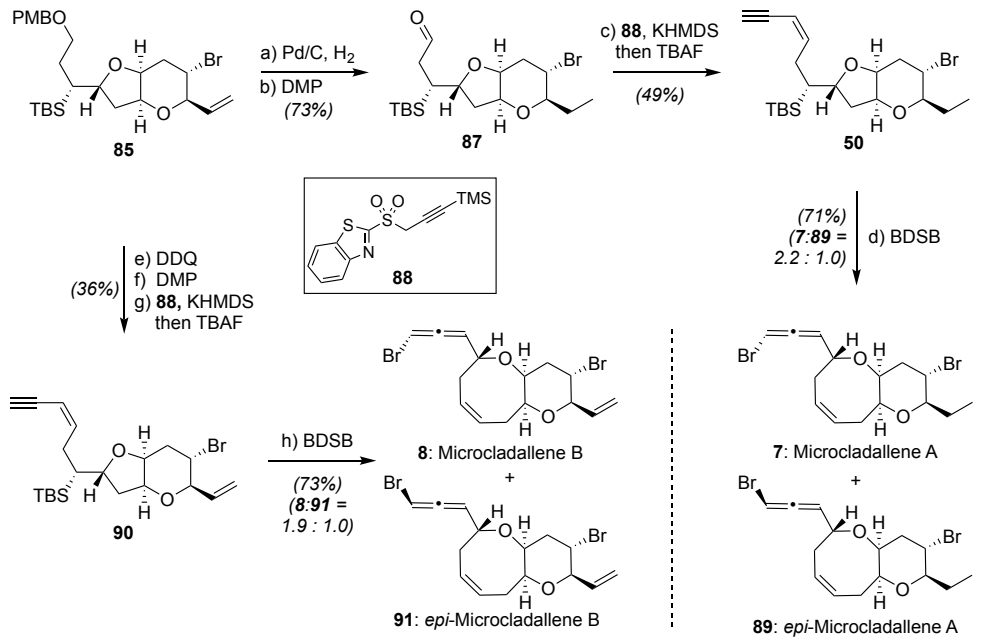


[a] Reagents and conditions: (a) $AlMe_3$ (2.5 equiv), MeONHMe•HCl (5.0 equiv), THF, 0 to 25 °C, 3 h; (b) TBSCl (2.0 equiv), imidazole (6.0 equiv), DMF, 25 °C, 12 h, 57% over 2 steps; (c) DIBAL-H (1.1 equiv), CH_2Cl_2, -78 °C, 15 min, 79%; (d) Br_2 (1.7 equiv), $P(OPh)_3$ (2.0 equiv), Et_3N (3.0 equiv), CH_2Cl_2, -78 to 25 °C, 12 h; (e) TBAF (6.2 equiv), THF, 0 to 25 °C, 2 h; (f) NMM (5.0 equiv), ethyl propiolate (5.0 equiv), CH_2Cl_2, 25 °C, 4 h, 63% over 3 steps; (g) *n*-Bu_3SnH (1.2 equiv), AIBN (0.5 equiv), benzene, 90 °C, 1 h, 57%; (h) $LiAlH_4$ (1.1 equiv), THF, -78 °C, 30 min, 82%; (i) $P(n\text{-}Oct)_3$ (10 equiv), PhSeCN (5.0 equiv), H_2O_2 (21 equiv), THF, 0 to 25 °C, 12 h, 96%.

In the end, we identified a more efficacious solution where a radical-based cyclization inspired by Lee,[43] could install the bromine atom and tetrahydropyran ring simultaneously. As indicated in Scheme 2-15, following an initial 3-steps ring opening sequence (Weinreb amide formation, alcohol protection, DIBAL-H reduction) to arrive at aldehyde **80**,[44] treatment with Br_2 and $P(OPh)_3$ in the presence of Et_3N, effected its debromination of the aldehyde group to give **81**.[45] Subsequent TBS deprotection and an oxa-Michael-type addition of the unveiled alcohol onto ethyl propiolate successfully afforded vinylogous ester **82** and set the stage for the key ring closure event. Upon its exposure to *n*-Bu_3SnH in the presence of AIBN in benzene at 80 °C, the desired radical-based cyclization occurred to yield **83** as a single diastereomer in 57% yield. Of note, the amount of *n*-Bu_3SnH was critical as it could also promote second radical debromination after the ring closure. We presumed that the observed stereoselectivity could be explained by the chairlike transition state (as shown in **84**), in which the bromine atom and ester side chain both adopted the equatorial position. Our stereoslection was consistent with that reported by Lee in their

system.[43] Next, the ester side chain was converted into the vinyl group of **85** in 79% yield through a sequence including a $LiAlH_4$-mediated reduction and a following dehydration.

Scheme 2-16. Total Syntheses of Microcladallenes A and B (7 and 8)[a]



[a] Reagents and conditions: (a) Pd/C (0.30 equiv), H_2 (balloon), EtOAc, 25 °C, 6 h; (b) Dess-Martin periodinane (1.1 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 1 h, 73% over 2 steps; (c) **88** (3.0 equiv), KHMDS (2.5 equiv), THF, -20 to 0 °C, 1 h; TBAF (3.0 equiv), 0 °C, 10 min, 49%; (d) BDSB (1.0 equiv), $EtNO_2$, -78 °C, 30 min, 49% **7**, 22% **89**; (e) DDQ (1.5 equiv), CH_2Cl_2/H_2O (10/1 v/v), 25 °C, 1 h; (f) Dess-Martin periodinane (1.1 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 1 h, 83% over 2 steps; (g) **88** (3.0 equiv), KHMDS (2.5 equiv), THF, -20 to 0 °C, 1 h; TBAF (3.0 equiv), 0 °C, 10 min, 43%; (h) BDSB (1.0 equiv), $EtNO_2$, -78 °C, 30 min, 48% **8**, 25% **91**.

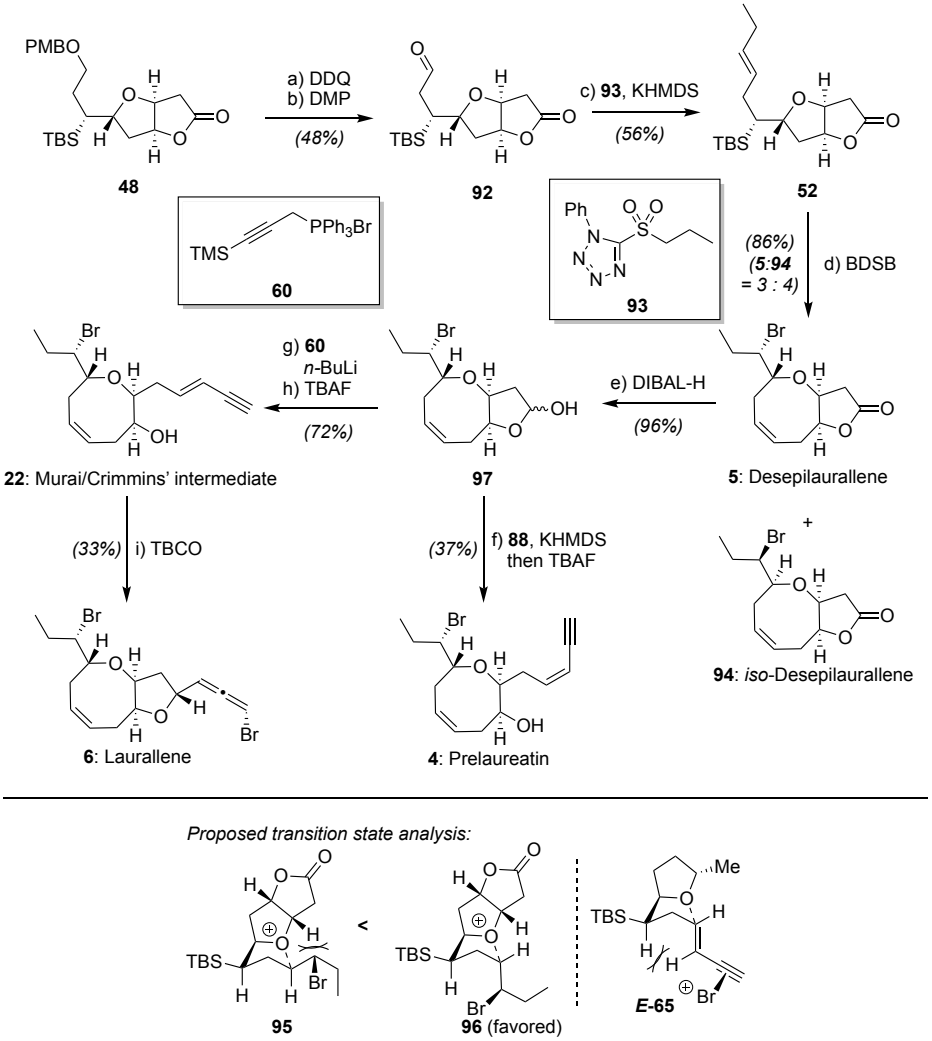
With the bromine atom and the ring system in place, the stage was now set to commence the final set of operations leading to the bromonium-induced ring expansion. As shown in Scheme 2-16, these operations started with a 3-step sequence to convert the PMB-alcohol into the requisite *Z*-enyne side chain. These transformations, including a concurrent PMB deprotection and alkene reduction, oxidation of the resultant alcohol to aldehyde, and Julia-Kociensky olefintion mediated by the anion derived from **88**,[46] successfully delivered enyne **50** in 36% overall yield, poised for the key ring expansion. Ultimately, upon treatment with 1.0 equiv of BDSB in $EtNO_2$ at -78 °C, a condition we previously developed, **50** successfully underwent the desired ring expansion to afford microladallene A (**7**) and its bromoallene epimer **89** in 49% and 22% yield respectively. A similar

set of operations could convert **85** into **90**, another substrate that contains a vinyl group. Surprisingly, this compound could also go through the ring expansion to give a 1.9 : 1 mixture of microcladallene B (**8**) and its epimer **91** in a combined 73% yield, indicating that the enyne could be chemoselectively activated in the presence of the external alkene. Of note, the stereoselectivity of the bromoallene observed in these two key ring expansion matched those in the earlier model studies. These results suggested that the additional tetrahydropyran ring had little or no effect in determining the stereochemical outcome of the core cyclization event. As such, if Nature utilized a similar ring expansion in her biosynthetic sequence (noting of course she would not use a silyl-containing substrate), the presence of 6-membered bromoether was not essential for high stereocontrol.[47] On the contrary, enzymatic control might be much more important in dictating product stereochemistry.

Overall, we accomplished 20-step racemic total syntheses of these two natural products, microcladallene A (**7**) and microcladallene B (**8**) respectively. Such level of efficiency is comparable to the only reported synthesis from Kim's group,[3] yet executed here via an entirely distinct strategy.

2.2.5 Total Syntheses of Desepilaurallene (5), Prelaureatin (4), Laurallene (6)

Scheme 2-17. Total Syntheses of Desepilaurallene (5), Prelaureatin (4), and Laurallene (6)[a]



[a] Reagents and conditions: (a) DDQ (1.5 equiv), CH_2Cl_2/H_2O (10:1 v/v), 25 °C, 1 h; (b) Dess-Martin periodinane (1.1 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 1 h, 48% over 2 steps; (c) **93** (3.0 equiv), KHMDS (2.7 equiv), DME, -78 °C, 30 min, 56%; (d) BDSB (0.8 equiv), toluene, -20 °C, 1 h, 86%, **5**:**94** = 3:4; (e) DIBAL-H (1.05 equiv), CH_2Cl_2, -78 °C, 15 min, 96%; (f) **51** (5.0 equiv), KHMDS (4.5 equiv), THF, -20 to 0 °C, 6 h; TBAF (5.0 equiv), THF, 0 °C, 10 min, 37%; (g) **58** (3.0 equiv), *n*-BuLi (2.7 equiv), THF, 0 °C, 2 h, 84%; (h) TBAF (1.1 equiv), THF, 0 °C, 10 min, 86%; (i) TBCO (1.3 equiv), CH_2Cl_2, 25 °C, 12 h, 33%.

With the racemic routes to microcladallenes completed, we next began to explore the versatility of our common intermediate **48** by looking into synthesizing a broader selection of natural products, namely despilaurallene (**5**), prelaureatin (**4**), and laurallene (**6**). Here, the BDSB-induced ring expansion would be carried out with an olefin/lactone containing substrate **52**. As shown in Scheme 2-17, advancing **48** to the key ring expansion precursor was achieved through a

3-step functional groups interconversion. Those operations included a DDQ-mediated PMB deprotection, oxidation of the resultant alcohol and a Julia−Kocienski olefination using the anion derived from sulfone **93**.[48] All these steps proceeded to give **52** in overall 27% yield over 3 steps. Next, exposure of **52** to 0.8 equiv of BDSB in toluene at -20 °C delivered a 3:4 mixture of despilaurallene (**5**) and its isomer **94** together in 86% yield. Of note, this material contained some impurities which could be removed in the following steps; as **5** and **94** could not be separated directly, their isolation and characterization required a reduction-oxidation sequence (see experimental section 2.6). We presumed that the observed selectivity in this ring expansion could be rationalized by the following transition state analysis. As shown in the lower portion of Scheme 2-17, there is potentially a minor destabilizing steric interaction as marked within **95** that made **96** energetically more favored and yielded **94** as the major product. However, the overall impact is modest as a near equal (3:4) mixture of products was formed. Furthermore, we postulated that the greater sp^3 character of the brominated carbon in **96** might explain the erosion of selectivity in terms of the oxocane ring formation, noting that only the *trans*-oxocane was formed in our earlier explored enyne-initiated ring expansion. As shown here with a drawing of oxonium intermediate ***E*-65** (also see Scheme 2-12), a strong 1,4-interaction induced by the sp^2-hybridization of the bromoallene carbon would disable its effective formation, thus no *cis*-oxocane product could be obtained. In contrast, due to the sp^3 character of the brominated carbon in **96**, such destabilizing effect was not prominent in **96,** therefore **94** was formed in large proportion. Optimization of this reaction was attempted but no satisfactory results were obtained. Increasing the amount of BDSB only led to inferior yield. More intriguingly, choice of solvent had significant impact on the outcome. Although the reaction proceeded in a variety of solvent (hexanes, $MeNO_2$, $EtNO_2$,

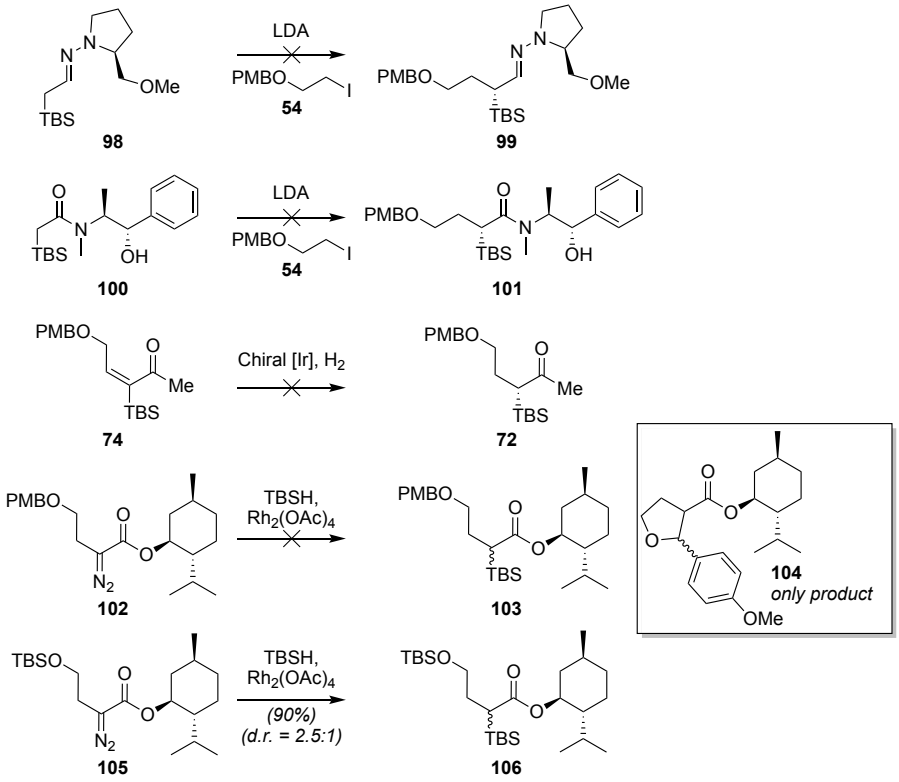
CH_2Cl_2), toluene gave the best selectivity of the desired product and collective yield, while CH_2Cl_2 gave the undesired isomer **94** exclusively.

Though despilaurallene (**5**) was obtained as the minor product, we viewed the overall throughput as acceptable with three bonds cleaved and three bonds forged in one single operation. From **5**, prelaureatin (**4**) could be synthesized in two further steps. These transformations involving a reduction of the lactone to the lactol, followed by a Julia−Kocienski olefination mediated by **88**[46] and *in situ* silyl cleavage, gave prelaureatin (**4**) in 37% overall yield. Similarly, **97** could be elaborated into **22** using Wittig reagent **60** to affect *E*-selectivity in its enyne formation.[28] Then a final TBCO-induced cyclization, as developed originally by Murai[7] and Crimmins,[4] completed the bromoallene motif to give target natural product laurallene (**6**) in 66% combined yield as a 1:1 mixture with another, unassigned diastereomer (not drawn). Of note, BDSB was tested in this key cyclization but it only led to material decomposition, presumably due to the presence of the more reactive olefin within the 8-membered ring .

In conclusion, these operations in the context of Scheme 2-17 completed three additional natural products despilaurallene (**5**), prelaureatin (**4**), laurallene (**6**) from our common intermediate **48** in 11, 13, and 15 steps respectively in their longest linear sequences. These endeavors showed the value of common intermediate-based synthesis in reaching complex, structural diversity[49] given that these targets process a core entirely different from that of the microcladallenes. They also further highlighted the power of the tetrahydrofuran-based ring expansion process, one that succeeds in the presence of an array of functional groups and appended ring systems.

2.2.6 Asymmetric Synthesis of Key Common Intermediate 48

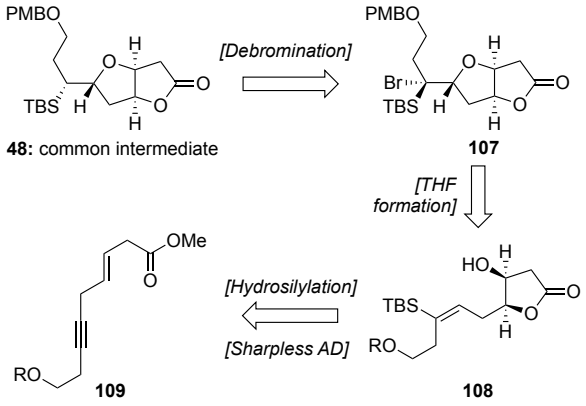
Scheme 2-18. Failed Efforts to Effect a Direct Asymmetric Synthesis of Ketone 72



With the racemic total syntheses of five *Laurencia* natural products completed, we next sought to develop an enantioselective synthesis of the common intermediate **48** to afford a formal, asymmetric solution to all targets. Our initial efforts focused on identifying the means to forge the lone silicon-based stereogenic center of **72** with enantiocontrol. To our best knowledge, a general strategy for enantioselective synthesis of α-silylated ketone had not been developed. Our first attempt was to utilize asymmetric alkylation mediated by chiral auxiliaries. However, such a process proved far from trivial to execute. For example, as indicated in Scheme 2-18, Enders' hydrazone derivative **98** failed to react with alkyl iodide **54**, despite the fact that other published examples with different nucleophiles have demonstrated successful alkylation.[50] Similarly, alkylation using Myer's psudoephdrine amide auxiliary (**100**)[51] or Evans' oxazolidinone auxiliary

(not shown) with attached TBS group failed as well. These result might be due to the low nucleophilicity of the substrate and the instability of the α-TBS group to basic conditions. Transition metal-catalyzed enantioselective hydrogenation was next pursued. Although Crabtree's catalyst was able to effect the reduction of enone **74** smoothly (see Scheme 2-13), none of any tested chiral iridium or rhodium-based catalysts could promote the desired transformation.[52] Only recovery or decomposition of the starting material was observed. Efforts to use a Rh-mediated Si-H insertion[53] from diazo ketone **102** or **105** were also unsatisfactory. Indeed, in the former case only **104** was formed via a much faster intramolecular carbene insertion into the benzylic C-H bond, while in the latter case the adduct **106** was formed as an 2.5 : 1 mixture of two diastereomers which could not be separated even after extensive trials. Due to all these failure, the idea of pursuing enantiomerically pure ketone **72** was abandoned.

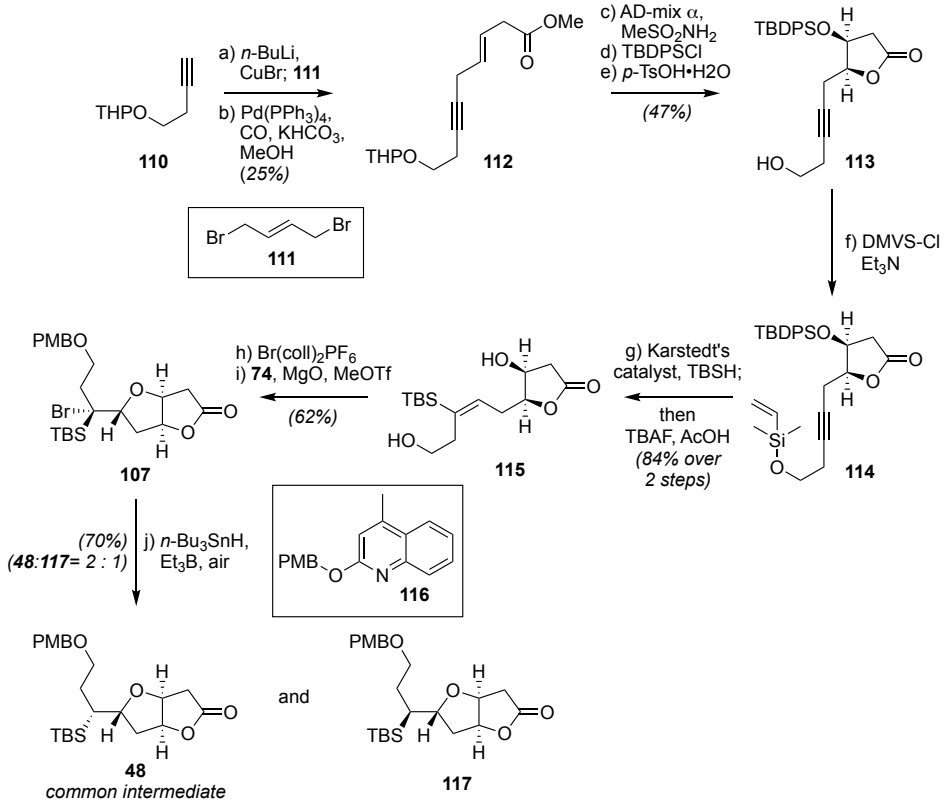
Scheme 2-19. Proposed Retrosynthetic Analysis to Achieve an Asymmetric Synthesis of Common Intermediate 48



Ultimately we developed a fully distinct enantioselective approach from the racemic route to synthesize common intermediate **48**. As shown retrosynthetically in Scheme 2-19, this route was in part inspired by our previous synthesis of *Z*-pinnatifidenyne[17] where a radical-based debromination was used to generate the requisite silicon-containing stereogenic center. Here the overall sequence would hinge on the ability to install the key diol with enantiocontrol via a

Sharpless asymmetric dihydroxylation followed by the regioselective hydrosilylation. These operations would then be followed by a bromoetherification and subsequent radical-based debromination, which need to proceed with retention of the configuration under substrate-control to give **48** as a single diastereomer.

Scheme 2-20. Asymmetric Synthesis of Common Intermediate 48[a]



[a] Reagents and conditions: (a) *n*-BuLi (1.05 equiv), THF, -78 °C, 10 min; CuBr (1.1 equiv), 0 °C, 1 h; **111** (2.5 equiv), 25 °C, 4 h, 33%; (b) $Pd(PPh_3)_4$ (0.05 equiv), $KHCO_3$ (1.1 equiv), CO (75 atm), MeOH, 25 °C, 24 h, 76%; (c) AD-mix-α, $MeSO_2NH_2$ (1.1 equiv), *t*-BuOH/H_2O (1:1 v/v), 0 °C, 36 h; (d) TBDPSCl (2.0 equiv), imidazole (4.0 equiv), CH_2Cl_2, 25 °C, 6 h; (e) *p*-TsOH•H_2O (0.1 equiv), MeOH, 25 °C, 3 h, 47% over 3 steps; (f) DMVSCl (1.2 equiv), Et_3N (1.5 equiv), CH_2Cl_2, 0 °C, 30 min, 88%; (g) Karstedt's catalyst (0.02 equiv), TBSH (1.5 equiv), THF, 40 °C, 2 h; AcOH (2.2 equiv), TBAF (2.2 equiv), 25 °C, 3 h, 95%; (h) $Br(coll)_2PF_6$ (1.2 equiv), $MeNO_2$, 0 °C, 30 min; (i) **116** (2.5 equiv), MgO (3.0 equiv), MeOTf (1.1 equiv), $PhCF_3$, 0 °C, 4 h, 62%; (j) *n*-Bu_3SnH (1.5 equiv), Et_3B (0.1 equiv), air, toluene, -78 °C, 30 min, 47% **48**, 23% **117**.

Pleasingly, that overall plan could be reduced to practice. Starting from commercial THP-protected propargyl alcohol (**110**, Scheme 2-20), an initial allylation[54] followed by a Pd-catalyzed carboxymethylation[55] smoothly gave ester **112** in 25% overall yield. Of note, the allylation was the throughput limiting step of the whole sequence at 33% yield. Next, **112** was converted to **113**

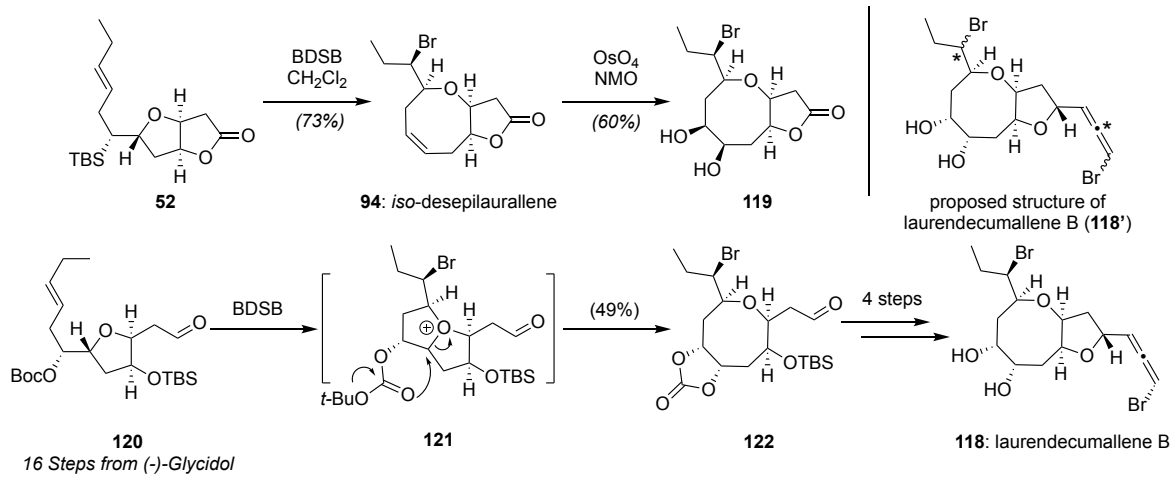
in 47% overall yield and in 90% *ee* through a well-established Sharpless asymmetric dihydroxylations[56] followed by conventional protecting group manipulations.[57] At this stage, our synthetic goal was to forge the vinyl TBS functionality. Following silylation of the unveiled alcohol with dimethylvinylsilyl chloride (DMVS-Cl) and Et_3N to arrive at **114**, exposure to Karstedt's catalyst and TBSH, a procedure developed by Tomooka,[58] facilitated the hydrosilyaltion across the alkyne with excellent regiocontrol. After an *in situ* TBAF-mediated desilylation, **115** was obtained in 84% overall yield. Critical to the final operation was the use of AcOH to neutralize trace amount of NaOH typically existing in the TBAF solution, to avoid elimination of the β-hydroxyl group on the lactone ring. With these operations completed, the remaining tasks were to forge the tetrahydrofuran ring of **48** along with its silicon-containing stereogenic center. The first set of transformations along this lines, a $Br(coll)_2PF_6$-induced bromoetherification followed by subsequent PMB protection of the primary alcohol with **116**,[59] proceeded smoothly to generate **107** in 62% yield over 2 steps. Of note, the use of other halenium source only gave inferior results in terms of either yield or stereoselectivity; the neutral condition in the second step was the key for successful protection as the bromide intermediate is not stable to acid and strong base. Finally, treatment of **107** with *n*-Bu_3SnH and Et_3B at -78 °C in the presence of air gave a 2:1 separable mixture of **48** and its epimer **117** in 70% overall yield, noting that other attempts with both radical and nonradical conditions failed (*n*-Bu_3SnH/AIBN, TTMS/AIBN, and Raney Nickel).

Overall, these operations completed a 10-step asymmetric synthesis of key lactone **48**, thereby establishing formal asymmetric syntheses of all five targets presented in this work.

2.3 Conclusion and a Follow-up Study: Total Synthesis of Laurendecumallene B (118)

The unique structures of the *Laurencia* family of natural products have inspired tremendous development of creative synthetic tactics and strategies over the past 50 years. Our work here presented a common intermediate-based divergent synthesis of five natural products in this class, empowered by two different types of BDSB-induced ring expansions. Those compounds encompassing two distinct 8-membered rings could arise from a single common intermediate. Of critical importance, we demonstrated that for the first time such ring-expansion process could be initiated effectively with an activated enyne, and that could proceed with good levels of stereocontrol with the presence of an additional lactone or 6-membered bromoether ring attached to the core tetrahydrofuran system. With these results and our previously successful syntheses of an array of related ring systems through similar approaches, we postulated that the core bromonium-induced ring-expansion process could have biosynthetic relevance, with Nature's utilization of tetrahydrofuran rings as a prelude for her preparation of 8-membered, polycyclic materials. Along with this key reaction, we have also demonstrated a number of chemoselective processes on advanced frameworks, which potentially could inspire syntheses of other materials in the *Laurencia* family. A recent example was our total synthesis of laurendecumallene B (**118**) experimentally carried out by Cooper Taylor, a graduate student in Snyder group.

Scheme 2-21. Total Synthesis of Laurendecumallene B (118)



Laurendecumallene B (**118**) was an additional member of the *Laurencia* family natural products which was isolated in 2007 by Wang and co-workers.[60] Although it possessed the standard 15-carbon skeleton of the class, its proposed structure presented a rare *cis*-oxocane ring system and two unassigned stereogenic centers (marked here with stars, Scheme 2-21). As noted earlier in section 2.4.5, we found that the use of CH_2Cl_2 as solvent in the ring expansion with **52** exclusively yielded *iso*-desepilaurallene (**94**), which also contains the *cis*-oxocane ring (Scheme 2-17). Initially, we envisioned to use this material to complete the total synthesis of **118**, relying on using an Upjohn dihydroxylation to forge its *cis*-diol motif. If success could be achieved, it would give our previously established approach higher degree of divergence. However, such test of dihydroxylation with **94** only yielded **119** with the stereochemistry of the newly generated diol opposite to desired. Thus, we pursued a distinct ring expansion approach to complete the synthesis of **118** and elucidate its absolute configuration. After extensive synthetic efforts, we identified that the BDSB-induced ring expansion with aldehyde **120**, formed through a 16-step sequence from (-)-glycidol, could afford protected diol **122** with desired stereoselectivity. This compound could be further elaborated into of laurendecumallene B (**118**) in four additional steps. Of note, attempts to use protected/free alcohol variants of aldehyde **120** in the ring expansion only led to

decomposition of the starting materials. Overall, these operations enabled a 21-step enantioselective total synthesis of laurendecumallene B (**118**) and completed its structural assignment; the only other synthetic study towards this target was reported by Fujii and Ohno, which was not able to obtain the natural product definitively after a 28-step sequence.[61]

2.4 Experimental Section

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, dimethylformamide (DMF), diethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous materials, unless otherwise stated. Steps refer to operations conducted in a single reaction flask; filtration, extraction, or other form of purification denotes the end of an individual step. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F254) using UV light as visualizing agent, and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. SiliCycle silica gel (60, academic grade, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker 500 MHz instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, app = apparent. IR spectra were recorded on a Perkin-Elmer 1000 series FT-IR spectrometer. High-resolution mass spectra (HRMS)

were recorded on Agilent 6244 Tof-MS using ESI (Electrospray Ionization) or APCI (Atmospheric Pressure Chemical Ionization) at the University of Chicago Mass Spectroscopy Core Facility. Chiral high-performance liquid chromatography (HPLC) analysis was performed using a Shimadzu Prominence analytical chromatograph with commercial ChiralPak columns (AD-H).

Aldehyde 55. To a solution of *i*-Pr_2NH (4.70 mL, 3.37 g, 33.3 mmol, 1.1 equiv) in THF (48.0 mL) at 0 °C was slowly added *n*-BuLi (12.7 mL, 2.5 M in hexanes, 31.8 mmol, 1.05 equiv) and then the reaction mixture was stirred at 0 °C for 10 min. Next, acetaldehyde *N*-*t*-butylimine **53** (3.00 g, 30.3 mmol, 1.0 equiv) was added to the freshly prepared solution of LDA and the resultant solution was stirred for an additional 30 min at 0 °C before TBSCl (4.50 g, 29.9 mmol, 0.99 equiv) and *n*-Bu_4NI (0.223 g, 0.606 mmol, 0.02 equiv) were added sequentially. The resultant reaction mixture was then allowed to warm to 25 °C and stirred for an additional 4 h at 25 °C. The resultant dark red solution was cooled 0 °C, and a second aliquot of *n*-BuLi (12.7 mL, 2.5 M in hexanes, 31.8 mmol, 1.05 equiv) was added slowly. After stirring at 0 °C for 30 min, the PMB-protected iodide **54** (13.3 g, 45.5 mmol, 1.5 equiv) was added and the resultant mixture was stirred at 25 °C for 12 h. Upon completion, the reaction contents were quenched by the addition of brine (100 mL), diluted with CH_2Cl_2 (50 mL), and poured into a separatory funnel. The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were then dried (Na_2SO_4), filtered, and concentrated to provide the desired intermediate. Pressing forward without any further purification, the crude product was dissolved in CH_2Cl_2 (50.0 mL), AcOH (50.0 mL, 1.0 M in H_2O) was added, and the resultant biphasic mixture was stirred vigorously at 25 °C for 1 h. Upon completion, the mixture was poured directly into a separatory funnel. The two phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were then dried (Na_2SO_4), filtered, and concentrated.

Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 20:1→10:1→5:1) afforded the desired aldehyde **55** (6.40 g, 69% yield) as a yellow oil. **55**: R_f = 0.20 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 2999, 2955, 2858, 1697, 1613, 1514, 1249, 1099, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.67 (d, *J* = 3.4 Hz, 1 H), 7.22 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 4.42–4.35 (m, 2 H), 3.80 (s, 3 H), 3.46–3.27 (m, 1 H), 2.55 (ddd, *J* = 11.6, 3.5, 2.0 Hz, 1 H), 2.34 (ddt, *J* = 14.2, 11.7, 6.0 Hz, 1 H), 1.73 (dtd, *J* = 13.7, 6.7, 2.2 Hz, 1 H), 0.94 (s, 9 H), 0.08 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 159.2, 130.5, 129.2, 113.8, 72.6, 69.9, 55.3, 44.9, 26.9, 25.5, 17.8, –6.4, –6.5; HRMS (ESI) calcd for $C_{18}H_{30}O_3SiNa$ $[M+Na]^+$ 345.1856, found 345.1855.

Alcohols 57. To a stirring solution of 2-butenyl magnesium chloride (11.7 mL, 0.5 M in THF, 5.85 mmol, 3.0 equiv) was added a solution of $AlCl_3$ (1.56 g, 11.7 mmol, 6.0 equiv) in Et_2O (5.9 mL) dropwise at –78 °C, and the resultant mixture was stirred for 15 min at –78 °C. A solution of aldehyde **55** (0.600 g, 1.95 mmol, 1.0 equiv) in THF (5.0 mL) was added, and the reaction contents were then warmed to 0 °C and stirred for 15 min at that temperature. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (30 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (30 mL). The two phases were separated and the aqueous layer was washed with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) afforded an inseparable mixture of alcohols **56** (*E*:*Z* = ~ 3:1, 0.570 g, 77% yield) as a colorless oil. Next, the so-obtained alcohols **56** (*E*:*Z* = ~ 3:1, 0.570 g, 1.51 mmol, 1.0 equiv) were dissolved in CH_2Cl_2 (37.0 mL). Solid $NaHCO_3$ (0.633 g, 7.54 mmol, 5.0 equiv) and Dess–Martin periodinane (0.707 g, 1.66 mmol, 1.1 equiv) were then added sequentially at 25 °C. After stirring at 25 °C for 2 h, the reaction contents were concentrated

directly. Purification of the resultant crude residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) gave an inseparable mixture of ketones (*E*:*Z* = ~ 3:1, 0.549 g, 96% yield) as a colorless oil. Pressing forward, the so-obtained ketones (*E:Z* = ~ 3:1, 0.549 g, 1.46 mmol, 1.0 equiv) were dissolved in THF (29.0 mL) at 25 °C and the reaction solution was then cooled to 0 °C. A solution of $LiAlH_4$ (2.92 mL, 1.0 M in THF, 2.92 mmol, 2.0 equiv) was carefully introduced and the resulting mixture was stirred at 0 °C for 15 min. Upon completion, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle's salt (60 mL) and then were stirred vigorously at 25 °C for 30 min. The contents were then transferred into a separatory funnel and diluted with EtOAc (60 mL). The resultant two layers were separated and the aqueous layer was extracted with EtOAc (3 × 60 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) yielded an inseparable mixture of alcohols **57** (*E:Z* = ~ 3:1, 0.465 g, 86% yield). **57**: R_f = 0.25 (silica gel, hexanes:EtOAc, 5:1). [Note: At this point, the stereoisomers were still inseparable despite exhaustive separation efforts; therefore, the mixture was carried forward.]

Iodine 58a and **iodine 58b**. To a solution of alcohols **57** (*E:Z* = ~ 3:1, 0.602 g, 1.59 mmol, 1.0 equiv) in CH_2Cl_2 (32.0 mL) at 25 °C was sequentially added $NaHCO_3$ (0.668 g, 7.95 mmol, 5.0 equiv) and NIS (1.79 g, 7.95 mmol, 5.0 equiv). The resultant reaction contents were stirred for 12 h at 25 °C. Upon completion, the reaction mixture was concentrated directly, and the resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 30:1→20:1→10:1) to afford iodine **58a** (0.149 g, 16% yield) and iodine **58b** (0.261 g, 28% yield) as a colorless oil. **58a**: R_f = 0.25 (silica gel, hexanes:EtOAc, 10:1); **58b**: R_f = 0.40 (silica gel, hexanes:EtOAc, 10:1).

Aldehyde 59. A suspension of Raney® Nickel (reagent grade, 10 mL of an aqueous slurry, excess) was added to a round-bottom flask under an Ar atmosphere, and rinsed with EtOH (3 × 6 mL), removing the solvent each time with a Pasteur pipette. To the so-obtained Raney® Nickel was added EtOH (6 mL) to prepare the desired suspension. Next, to a solution of iodine **58a** (0.149 g, 0.295 mmol, 1.0 equiv) in EtOH (6.0 mL) at 25 °C was slowly added the above Raney® Nickel suspension and the resultant mixture was stirred vigorously at 25 °C for 1 h. Upon completion, the reaction mixture was filtered through Celite, rinsing with EtOAc (20 mL), and the filtrate was concentrated directly. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 20:1) to give deiodinated alcohol (86.2 mg, 77% yield) as a colorless oil. To a solution of this alcohol (86.2 mg, 0.227 mmol, 1.0 equiv) in CH_2Cl_2/H_2O (10:1 v/v, 4.4 mL) at 25 °C was added DDQ (77.3 mg, 0.341 mmol, 1.5 equiv). After stirring for 1 h at 25 °C, the reaction contents were quenched by the addition of saturated aqueous Na_2CO_3 (10 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were washed with saturated aqueous Na_2CO_3 (30 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) afforded the desired alcohol (52.2 mg, 89% yield) as a pale oil. Next, to the solution of the so-obtained alcohol (52.2 mg, 0.202 mmol, 1.0 equiv) in CH_2Cl_2 (4.0 mL) at 25 °C was added $NaHCO_3$ (84.9 mg, 1.02 mmol, 5.0 equiv) and Dess–Martin periodinane (94.7 mg, 0.222 mmol, 1.1 equiv) sequentially. The reaction was stirred for 1 h at 25 °C and concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes: EtOAc, 20:1) afforded aldehyde **59** (42.3 mg, 81% yield) as a colorless oil. **59**: R_f = 0.20 (silica gel, hexanes:EtOAc, 20:1); IR (film) ν_{max} 2957, 2930, 2858, 2717, 1722, 1471, 1387, 1251, 1087, 835

cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.64 (d, *J* = 4.7 Hz, 1 H), 4.11 (td, *J* = 7.7, 3.8 Hz, 1 H), 3.82 (dt, *J* = 8.4, 6.1 Hz, 1 H), 2.38 (ddd, *J* = 16.0, 11.1, 4.7 Hz, 1 H), 2.21 (dd, *J* = 16.3, 3.1 Hz, 1 H), 2.13 (dt, *J* = 11.1, 3.5 Hz, 1 H), 1.99–1.87 (m, 1 H), 1.83–1.73 (m, 1 H), 1.63–1.53 (m, 1 H), 1.41–1.31 (m, 1 H), 1.15 (d, *J* = 6.0 Hz, 3 H), 0.93 (s, 9 H), –0.01 (s, 3 H), –0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 79.8, 74.9, 40.2, 33.8, 27.6, 27.0, 22.7, 19.9, 17.3, –6.3, –6.4; HRMS (ESI+APCI): no molecular ion peak was observed.

Enyne *Z*-61 and enyne *E*-61. To a solution of Wittig Salt **60** (0.178 g, 0.393 mmol, 3.0 equiv, prepared according to the literature procedure reported by Diederich and co-workers[28] with all the spectroscopic data matching that reported in Ref. 28) in THF (2.0 mL) was added LiHMDS (0.262 mL, 1.0 M in THF, 0.262 mmol, 2.0 equiv) dropwise at 0 °C. The resultant dark solution was stirred at 0 °C for 30 min before a solution of **59** (33.6 mg, 0.131 mmol, 1.0 equiv) in THF (2.0 mL) was added in a single portion at 0 °C. The reaction solution was then warmed to 25 °C and stirred for an additional 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (10 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. Purification of the crude residue by flash column chromatography (silica gel, hexanes:EtOAc, 20:1) gave a mixture of ***Z/E*-61**, which was separated by preparative thin layer chromatography (silica gel, hexanes:CH_2Cl_2, 1:1) to provide enyne ***Z*-61** (10.6 mg, 23% yield) and enyne ***E*-61** (21.5 mg, 47% yield), both as colorless oils. ***Z*-61**: R_f = 0.35 (silica gel, hexanes:CH_2Cl_2, 1:1); ***E*-61**: R_f = 0.40 (silica gel, hexanes:CH_2Cl_2, 1:1).

Enyne *Z*-62. To a solution of enyne ***Z*-61** (16.8 mg, 47.9 μmol, 1.0 equiv) in THF (1.0 mL) was added TBAF (52.7 μL, 1.0 M in THF, 52.7 μmol, 1.1 equiv) at 0 °C. After stirring at 0 °C for

30 min, the reaction contents were quenched by the slow addition of saturated aqueous NH_4Cl (5 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 50:1) to yield ***Z*-62** (13.4 mg, 99% yield) as a colorless oil. ***Z*-62**: R_f = 0.25 (silica gel, hexanes:CH_2Cl_2, 3:1); IR (film) ν_{max} 3313, 2957, 2928, 2856, 1464, 1388, 1363, 1250, 1088, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.17 (dt, *J* = 10.8, 7.2 Hz, 1 H), 5.35 (dd, *J* = 10.8, 2.1 Hz, 1 H), 4.06 (td, *J* = 7.8, 4.1 Hz, 1 H), 3.82 (dt, *J* = 8.2, 6.1 Hz, 1 H), 3.08 (d, *J* = 2.6 Hz, 1 H), 2.69–2.41 (m, 2 H), 1.94 (ddt, *J* = 11.7, 9.0, 5.6 Hz, 1 H), 1.86–1.74 (m, 1 H), 1.70–1.57 (m, 1 H), 1.54–1.37 (m, 2 H), 1.21 (d, *J* = 6.1 Hz, 3 H), 0.91 (s, 9 H), 0.01 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 106.3, 81.4, 81.0, 80.9, 74.3, 33.7, 28.6, 28.0, 27.2, 27.0, 20.6, 17.3, –5.7, –5.9; HRMS (ESI) calcd for $C_{17}H_{30}OSiNa$ $[M+Na]^+$ 301.1958, found 301.1953.

Enyne *E*-62. To a solution of enyne ***E*-61** (17.6 mg, 51.2 μmol, 1.0 equiv) in THF (1.0 mL) was added TBAF (56.3 μL, 1.0 M in THF, 56.3 μmol, 1.1 equiv) at 0 °C. After stirring at 0 °C for 30 min, the reaction contents were quenched by the slow addition of saturated aqueous NH_4Cl (5 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 50:1) to yield ***E*-62** (12.7 mg, 90% yield) as a colorless oil. ***E*-62**: R_f = 0.25 (silica gel, hexanes:CH_2Cl_2, 3:1); IR (film) ν_{max} 3315, 2957, 2928, 2857, 1470, 1388, 1362, 1250, 1089, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.52–6.13 (m, 1 H), 5.39 (dq, *J* = 15.9, 1.8 Hz, 1 H), 4.07–3.95 (m, 1 H), 3.82 (dt, *J* = 8.2, 6.1 Hz, 1 H), 2.76

(d, J = 2.3 Hz, 1 H), 2.37–2.15 (m, 2 H), 2.04–1.90 (m, 1 H), 1.86–1.74 (m, 1 H), 1.60–1.52 (m, 1 H), 1.41–1.35 (m, 2 H), 1.23 (d, J = 6.0 Hz, 3 H), 0.89 (s, 9 H), –0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 107.7, 82.7, 80.8, 75.4, 74.4, 33.7, 30.5, 28.9, 27.8, 27.2, 20.7, 17.3, –5.6, –5.8; HRMS (ESI+APCI) calcd for $C_{17}H_{31}OSi$ $[M+H]^+$ 279.2139, found 279.2148.

Aldehyde 63.[62] A suspension of Raney® Nickel (reagent grade, 10 mL of an aqueous slurry, excess) was added to a round-bottom flask under an Ar atmosphere, and rinsed with EtOH (3 × 6 mL), removing the solvent each time with a Pasteur pipette. To the so-obtained Raney® Nickel was added EtOH (6 mL) to prepare the desired suspension. Next, to a solution of iodine **S9** (0.230 g, 0.456 mmol, 1.0 equiv) in EtOH (2.0 ml) was slowly added the above Raney® Nickel suspension and the resultant mixture was stirred vigorously at 25 °C for 1 h. Upon completion, the reaction contents were filtered through a pad of Celite, washed with EtOAc (50 mL), and concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 20:1) afforded deiodinated alcohol (0.167 g, 97% yield) as a colorless oil. To a solution of this alcohol (0.172 g, 0.454 mmol, 1.0 equiv) in CH_2Cl_2/H_2O (10/1 v/v, 4.4 mL) at 25 °C was added DDQ (0.155 g, 0.683 mmol, 1.5 equiv). After stirring for 1 h at 25 °C, the reaction contents were quenched by the addition of saturated aqueous Na_2CO_3 (15 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with saturated aqueous Na_2CO_3 (15 mL), dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) afforded alcohol (0.100 g, 85% yield) as a colorless oil. Next, to the solution of the so-obtained alcohol (0.100 g, 0.386 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) at 25 °C was sequentially added $NaHCO_3$ (0.163 g, 1.94 mmol, 5.0 equiv) and Dess–Martin periodinane (0.180 g, 0.426

mmol, 1.1 equiv). The resultant mixture was then stirred at 25 °C for 1 h and concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 20:1) afforded the desired aldehyde **63** (86.4 mg, 87% yield) as a colorless oil. **63**: R_f = 0.20 (silica gel, hexanes:EtOAc, 20:1); IR (film) ν_{max} 2959, 2930, 2858, 2718, 1718, 1465, 1364, 1251, 1071, 826, 771 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.53 (d, *J* = 5.5 Hz, 1 H), 4.28 (ddd, *J* = 10.1, 5.8, 4.3 Hz, 1 H), 3.74 (dp, *J* = 8.7, 6.0 Hz, 1 H), 2.45–2.10 (m, 3 H), 2.01 (dddd, *J* = 12.4, 7.6, 5.3, 2.0 Hz, 1 H), 1.79 (dtd, *J* = 12.2, 6.5, 5.6, 2.1 Hz, 1 H), 1.65–1.53 (m, 1 H), 1.48 (tdd, *J* = 11.3, 8.8, 7.0 Hz, 1 H), 1.14 (d, *J* = 6.1 Hz, 3 H), 0.93 (s, 9 H), –0.01 (s, 3 H), –0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 79.6, 74.0, 40.0, 34.8, 28.6, 27.1, 23.9, 21.3, 17.3, –6.3, –6.4; HRMS (ESI+APCI) calcd for $C_{14}H_{29}O_2Si$ $[M+H]^+$ 257.1931, found 257.1923.

Enyne *Z*-65. (Iodomethyl)triphenylphosphonium iodide (95% purity, 0.164 g, 0.294 mmol, 1.3 equiv) was dissolved in a mixture of THF (8.2 mL) and HMPA (0.15 mL) at 25 °C and the resultant solution was then cooled to 0 °C. Next, NaHMDS (0.294 mL, 1.0 M in THF, 0.294 mmol, 1.3 equiv) was then added dropwise and the resultant yellow solution was stirred at 0 °C for 30 min before cooling to –78 °C. A solution of aldehyde **63** (58.0 mg, 0.226 mmol, 1.0 equiv) in THF (2.0 mL) was then added in a single portion, and the resultant mixture was stirred for an additional 30 min at –78 °C. Upon completion, the reaction was quenched by the addition of saturated aqueous NH_4Cl (10 mL), warmed to 25 °C, poured into a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 50:1) afforded iodine **64** (63.6 mg, 74% yield) as a yellow oil. Next, to the solution of the so-obtained iodine **64** (63.6 mg, 0.168 mmol, 1.0 equiv) in THF/Et_2NH (1:1 v/v, 2.0 mL) at 25 °C

was sequentially added CuI (3.2 mg, 16.8 μmol, 0.10 equiv), $Pd(PPh_3)_4$ (20.0 mg, 16.8 μmol, 0.10 equiv) and TMS acetylene (72.0 μL, 50.0 mg, 0.504 mmol, 3.0 equiv). The reaction contents were then stirred at 25 °C for 6 h. Upon completion, the reaction contents were concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 50:1) furnished the TMS-protected enyne (53.0 mg, 90% yield) as a brown oil. Pressing forward, solid K_2CO_3 (35.1 mg, 0.254 mmol, 2.0 equiv) was added to a solution of so-obtained enyne (43.0 mg, 0.123 mmol, 1.0 equiv) in THF/MeOH (1:1 v/v 1.2 mL) at 0 °C. After stirring at 0 °C for 6 h, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue ws purified by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 3:1) to yield *Z trans* enyne ***Z*-65** (33.0 mg, 96% yield) as a colorless oil. ***Z*-65**: R_f= 0.15 (silica gel, hexanes:CH_2Cl_2, 3:1); IR (film) ν_{max} 3313, 3027, 2959, 2928, 2857, 1470, 1250, 1075, 835, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.14 (dt, *J* = 11.0, 7.2 Hz, 1 H), 5.35 (dt, *J* = 10.8, 2.0 Hz, 1 H), 4.24 (dt, *J* = 10.2, 5.4 Hz, 1 H), 4.01 (dt, *J* = 8.7, 6.0 Hz, 1 H), 3.07 (d, *J* = 2.4 Hz, 1 H), 2.53–2.34 (m, 2 H), 2.13–1.98 (m, 1 H), 1.92–1.78 (m, 1 H), 1.70 (dtd, *J* = 12.4, 10.3, 7.6 Hz, 1 H), 1.54–1.42 (m, 2 H), 1.17 (d, *J* = 6.1 Hz, 3 H), 0.91 (s, 9 H), 0.00 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9, 105.9, 81.3, 81.0, 80.4, 74.4, 34.8, 29.8 (2C), 28.7, 27.3, 21.6, 17.3, –5.8 (2C); HRMS (APCI) calcd for $C_{17}H_{31}OSi$ $[M+H]^+$ 279.2139, found 279.2120.

Enyne *E*-65. $CrCl_2$ (0.401 g, 3.28 mmol, 6.0 equiv) was added to THF (4.0 mL) at 25 °C and the resultant suspension was stirred vigorously for 30 min. The suspension was then cooled to 0 °C and CHI_3 (0.235 g, 0.601 mmol, 1.1 equiv) was added. The resultant brown-yellow mixture

was stirred at 0 °C for 30 min before a solution of aldehyde **63** (0.140 g, 0.546 mmol, 1.0 equiv) in THF (2.0 mL) was added. After stirring the resultant mixture at 0 °C for an additional 3 h, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (20 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (20 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 5:1) afforded iodine **66** (0.147 g, 69% yield) as a yellow oil. Next, to the solution of the so-obtained **66** (0.147 g, 0.381 mmol, 1.0 equiv) in THF/Et_2NH (1:1 v/v, 5.0 mL) at 25 °C was sequentially added CuI (7.3 mg, 38.1 μmol, 0.10 equiv), $Pd(PPh_3)_4$ (44.0 mg, 38.1 μmol, 0.10 equiv) and TMS acetylene (0.162 mL, 0.112 g, 1.14 mmol, 3.0 equiv). The reaction contents were then stirred at 25 °C for 6 h. Upon completion, the reaction contents were concentrated directly. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 50:1) to furnish the TMS-protected enyne (0.100 g, 75% yield) as a brown oil. Pressing forward, solid K_2CO_3 (79.1 mg, 0.572 mmol, 2.0 equiv) was added to a solution of the so-obtained enyne (0.100 g, 0.286 mmol, 1.0 equiv) in THF/MeOH (1:1 v/v, 3.0 mL) at 0 °C. After stirring the resultant mixture at 0 °C for 6 h, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with CH_2Cl_2 (10 mL), and transferred into a separatory funnel. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 3:1) afforded enyne ***E*-65** (76.5 mg, 96% yield) as a colorless oil. ***E*-65**: R_f = 0.15 (silica gel, hexanes:CH_2Cl_2, 3:1); IR (film) ν_{max} 3312, 2957, 2929, 2857, 1470, 1251, 1079, 825, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.35 (dt, J = 15.9, 7.2 Hz, 1 H), 5.66–5.27 (m, 1 H), 4.20

(dt, J = 10.4, 5.4 Hz, 1 H), 4.03 (dt, J = 8.5, 6.0 Hz, 1 H), 2.75 (d, J = 2.3 Hz, 1 H), 2.32–2.19 (m, 2 H), 2.03 (dddd, J = 13.7, 7.8, 5.6, 2.2 Hz, 1 H), 1.86 (dddd, J = 12.5, 7.8, 5.9, 2.4 Hz, 1 H), 1.75–1.54 (m, 1 H), 1.53–1.38 (m, 2 H), 1.18 (d, J = 6.0 Hz, 3 H), 0.90 (s, 9 H), –0.02 (s, 3 H), –0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 107.4, 82.7, 80.2, 75.3, 74.5, 34.7, 30.4, 30.2, 28.6, 27.2, 21.6, 17.3, –5.6, –5.8; HRMS (APCI) calcd for $C_{17}H_{31}OSi$ $[M+H]^+$ 279.2139, found 279.2149.

Bromoallene 68 and **bromoallene 69**. Enyne ***Z*-65** (14.0 mg, 50.3 μmol, 1.0 equiv) was dissolved in $EtNO_2$ (2.5 mL) and the resultant solution was cooled to –78 °C. Next, solid BDSB[15b] (22.1 mg, 40.2 μmol, 0.80 equiv) was added at –78 °C in a single portion and the reaction was stirred at –78 °C for additional 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with CH_2Cl_2 (10 ml), warmed to 25 °C, and transferred into a separatory funnel. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by preparative thin layer chromatography (silica gel, hexanes:Et_2O, 20:1) afforded bromoallene **68** (2.4 mg, 20% yield) and bromoallene **69** (4.5 mg, 37%), both as colorless liquids. **68**: R_f = 0.70 (silica gel, hexanes:Et_2O, 20:1); IR (film) ν_{max} 3055, 3021, 2966, 2928, 1458, 1375, 1328, 1191, 1120, 1090, 707, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.09 (dd, J = 5.8, 2.4 Hz, 1 H), 5.91 (dt, J = 10.5, 7.9 Hz, 1 H), 5.77–5.69 (m, 1 H), 5.57 (dd, J = 5.8, 4.4 Hz, 1 H), 4.46–4.40 (m, 1 H), 3.79–3.70 (m, 1 H), 2.48 (dt, J = 13.9, 9.5 Hz, 1 H), 2.32–2.04 (m, 3 H), 1.75–1.45 (m, 2 H), 1.13 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.2, 133.3, 126.5, 101.7, 74.0, 73.0, 69.9, 37.8, 31.0, 25.1, 23.8. HRMS (ESI) calcd for $C_{22}H_{31}Br_2O_2$ $[2M+H]^+$ 485.0685, found 485.0677. **69**: R_f = 0.65 (silica gel, hexanes:Et_2O, 20:1); IR (film) ν_{max} 3056, 3021, 2966, 2928, 2856, 1727, 1686, 1653, 1457, 1375, 1193, 1079, 725,659

cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.10 (dd, *J* = 5.7, 2.7 Hz, 1 H), 5.92 (dt, *J* = 10.4, 7.8 Hz, 1 H), 5.82–5.64 (m, 1 H), 5.58 (t, *J* = 5.2 Hz, 1 H), 4.61–4.31 (m, 1 H), 3.85–3.76 (m, 1 H), 2.46 (dt, *J* = 13.9, 9.2 Hz, 1 H), 2.32–2.20 (m, 2 H), 2.20–2.03 (m, 1 H), 1.70–1.45 (m, 2 H), 1.13 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.4, 133.2, 126.6, 101.2, 74.1, 72.9, 69.8, 37.8, 30.8, 25.1, 23.8; HRMS (APCI) calcd for $C_{11}H_{16}BrO$ $[M+H]^+$ 243.0379, found 243.0354.

Bromoallene 68 and bromoallene 69. Enyne ***E*-65** (31.0 mg, 0.115 mmol, 1.0 equiv) was dissolved in $EtNO_2$ (5.7 mL) and the resultant solution was cooled to –78 °C. Next, solid BDSB[15b] (50.5 mg, 92.0 μmol, 0.80 equiv) was added at –78 °C in a single portion and the reaction was stirred at –78 °C for additional 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with CH_2Cl_2 (10 ml), warmed to 25 °C, and transferred into a separatory funnel. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by preparative thin layer chromatography (silica gel, hexanes:Et_2O, 20:1) afforded bromoallene **68** (10.9 mg, 40% yield) and bromoallene **69** (5.8 mg, 21%), both as colorless liquids.

Ketone 72. To a solution of aldehyde **55** (2.46 g, 7.63 mmol, 1.0 equiv) in THF (76.0 mL) at –78 °C was added MeMgBr (5.60 mL, 3.0 M in Et_2O, 16.8 mmol, 2.2 equiv). After stirring the resultant mixture at –78 °C for 30 min, the reaction contents were quenched by the slow addition of saturated aqueous NH_4Cl (50 mL), warmed to 25 °C, poured into a separatory funnel, and diluted with CH_2Cl_2 (100 mL). The two phases were then separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 5:1) afforded the desired secondary alcohol (2.18 g, 85% yield) as a

colorless liquid. Pressing forward, to a solution of the secondary alcohol (2.18 g, 6.72 mmol, 1.0 equiv) in CH_2Cl_2 (70.0 mL) at 25 °C was added solid $NaHCO_3$ (2.82 g, 33.6 mmol, 5.0 equiv) and Dess–Martin periodinane (3.01 g, 7.10 mmol, 1.05 equiv). The resultant mixture was stirred at 25 °C for 2 h. Upon completion, the reaction contents were concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) afforded the desired methyl ketone **72** (1.78 g, 82% yield) as a colorless oil. **72**: R_f = 0.20 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 2955, 2931, 2857, 1689, 1613, 1513, 1465, 1362, 1249, 1171, 1101, 824 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.5 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 4.44–4.22 (m, 2 H), 3.80 (s, 3 H), 3.39–3.26 (m, 2 H), 2.64 (dd, *J* = 11.9, 2.1 Hz, 1 H), 2.28 (ddt, *J* = 14.0, 11.7, 5.8 Hz, 1 H), 2.05 (s, 3 H), 1.73 (dtd, *J* = 13.9, 6.7, 2.0 Hz, 1 H), 0.93 (s, 9 H), 0.05 (s, 3 H), 0.00 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.5, 159.1, 130.6, 129.2, 113.7, 72.4, 70.0, 55.2, 42.4, 32.1, 28.4, 26.8, 17.9, –6.1, –7.1; HRMS (ESI+APCI) calcd for $C_{19}H_{33}O_3Si$ $[M+H]^+$ 337.2193, found 337.2177.

Enone 74 and **enone *iso*-74**. Ynone **73** (0.280 g, 1.28 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (10.0 mL) and then TBSH (0.320 mL, 0.224 g, 1.93 mmol, 1.5 equiv) and Karstedt's catalyst[31] (0.640 mL, 0.10 M in xylenes, 64.0 μmol, 0.05 equiv) were added sequentially at 25 °C. The resultant yellow solution was then stirred at 25 °C for 12 h. Upon completion, the reaction contents were concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 30:1→20:1) afforded a separable mixture of enone **74** (0.176 g, 41% yield) and its regioisomer ***iso-74*** (0.111 g, 26% yield), both as colorless liquids. **35**: R_f = 0.40 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3020, 3000, 2955, 2856, 1684, 1613, 1514, 1464, 1361, 1249, 1084, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 5.92 (s, 1 H), 4.41 (s, 2 H), 4.05 (s, 2 H), 3.80 (s, 3 H), 2.19 (s, 3 H),

0.91 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.6, 159.3, 148.4, 139.1, 129.9, 129.5, 113.8, 72.5, 68.5, 55.3, 31.9, 26.6, 17.6, –5.6; HRMS (ESI) calcd for $C_{19}H_{31}O_3Si$ $[M+H]^+$ 335.2037, found 335.2023. ***iso*-74**: R_f= 0.50 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3025, 2999, 2954, 2856, 1682, 1613, 1514, 1390, 1249, 1182, 1089, 836 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 6.3 Hz, 2 H), 6.85 (d, *J* = 6.3 Hz, 2 H), 6.37 (s, 1 H), 4.55 (s, 2 H), 4.40 (s, 2 H), 3.80 (s, 3 H), 2.22 (s, 3 H), 0.88 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 159.2, 159.1, 135.25, 130.3, 129.6, 113.6, 72.8, 72.0, 55.2, 31.2, 27.2, 17.2, –4.4; HRMS (ESI+APCI) calcd for $C_{19}H_{31}O_3Si$ $[M+H]^+$ 335.2037, found 335.2023.

Ketone 72. To a solution of **74** (0.138 g, 0.413 mmol, 1.0 equiv) in CH_2Cl_2 (4.0 mL) at 25 °C was added Crabtree's catalyst (17.0 mg, 20.7 μmol, 0.05 equiv). The resultant organic solution was purged by direct bubbling with a balloon of H_2 gas at 25 °C for 30 min. The reaction contents was then placed under a H_2 atmosphere and stirred at 25 °C for 12 h. Upon completion, the reaction contents were concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) afforded methyl ketone **72** (0.119 g, 86% yield) as a colorless liquid.

Diol 49. To a solution of *i*-Pr_2NH (0.794 mL, 0.569 g, 5.63 mmol, 1.6 equiv) in THF (30.0 mL) at 0 °C was slowly added *n*-BuLi (2.11 mL, 2.5 M in hexanes, 5.28 mmol, 1.5 equiv). The resultant solution was then stirred at 0 °C for 10 min. Next, a solution of methyl ketone **72** (1.18 g, 3.52 mmol, 1.0 equiv) in THF (10.0 mL) was added to the freshly prepared LDA solution at –78 °C and the resultant solution was stirred at –78 °C for an additional 30 min. Acrolein (0.376 mL, 0.316 g, 5.63 mmol, 1.6 equiv) was then added and the resultant mixture was allowed to stir at –78 °C for 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (50 mL) and poured into a separatory funnel. The two phases were

separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to afford the desired β-hydroxy ketone **75** (1.02 g, 74% yield) as a colorless liquid and as a mixture of two inseparable diastereomers (d.r. ~5:1). Next, to a solution of **75** (1.02 g, 2.60 mmol, 1.0 equiv) in THF/MeOH (4:1, 26.0 mL) at –78 °C was added Et_2BOMe (3.12 mL, 1.0 M in THF, 3.12 mmol, 1.2 equiv). The resultant reaction mixture was then stirred for 30 min at –78 °C, at which point $LiBH_4$ (0.850 g, 39.0 mmol, 15.0 equiv) was added in a single portion. The resultant heterogeneous mixture was then warmed slowly to 25 °C over the course of 4 h [Caution: large amounts of gas were generated during this period]. Upon completion, the reaction contents were quenched at 0 °C by the slow addition of solid NaOH (0.260 g, 6.50 mmol, 2.5 equiv) and H_2O_2 (7.07 mL, 30% w/w in water, 68.6 mmol, 26.4 equiv). The resultant mixture was stirred at 0 °C for an additional 1 h, diluted with H_2O (30 mL) and EtOAc (30 mL), and poured into a separatory funnel. The two phases were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with 1 M aqueous NaOH (100 mL), dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1→1:1) to afford the desired diol **49** (0.870 g, 85% yield) as a viscous, colorless oil containing ~15% of an inseparable isomer which could be removed during the purification procedure in the subsequent synthetic step. **49**: R_f = 0.20 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 3364 (br), 2953, 2930, 2856, 1612, 1514, 1465, 1249, 1083, 824 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 5.85 (ddd, *J* = 17.2, 10.5, 5.8 Hz, 1 H), 5.26 (d, *J* = 17.1 Hz, 1 H), 5.07 (d, *J* = 10.4 Hz, 1 H), 4.62–4.27 (m, 3 H), 4.12–4.03 (m, 1 H), 3.80 (s, 3 H), 3.63 (m, 1 H), 3.35 (m, 1 H), 1.84 (m, 1 H), 1.74–1.62 (m, 2 H), 1.46–1.39 (m, 1 H),

1.28 (m, 1 H), 0.88 (s, 9 H), –0.03 (s, 3 H), –0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 141.0, 129.5, 129.2, 113.93, 113.89, 73.6, 73.4, 73.0, 71.1, 55.3, 41.0, 30.8, 27.3, 27.0, 25.8, 17.4, –6.0, –6.5; HRMS (ESI+APCI): no molecular ion peak was observed.

Lactone 48. $CuCl_2$ (0.466 g, 3.51 mmol, 3.0 equiv), NaOAc (0.479 g, 5.84 mmol, 5.0 equiv) and diol **49** (0.460 g, 1.17 mmol, 1.0 equiv) were dissolved in glacial AcOH (12.0 mL), and the resulting solution was purged by direct bubbling with a balloon containing CO gas for 30 min at 25 °C. Next, $PdCl_2$ (0.083 g, 0.468 mmol, 0.4 equiv) was added and the reaction flask was outfitted with a CO balloon and stirred at 25 °C for 12 h. Upon completion, the reaction contents were filtered through a pad of Celite, washed with EtOAc (50 mL), and concentrated directly. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to afford the desired lactone **48** (0.283 g, 58% yield) as a light yellow oil. **48**: R_f = 0.25 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 2953, 2931, 2856, 1790, 1612, 1513, 1465, 1248, 1179, 1066, 826 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.08 (t, *J* = 4.7 Hz, 1 H), 4.70 (t, *J* = 5.3 Hz, 1 H), 4.42 (s, 2 H), 4.29 (m, 1 H), 3.80 (s, 3 H), 3.53 (m, 1 H), 3.36 (m, 1 H), 2.72 (dd, *J* = 18.7, 6.5 Hz, 1 H), 2.60 (d, *J* = 18.8 Hz, 1 H), 2.21 (dd, *J* = 13.9, 4.6 Hz, 1 H), 1.87–1.50 (m, 3 H), 1.30 (m, 1 H), 0.89 (s, 9 H), –0.04 (s, 3 H), –0.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 159.2, 130.6, 129.2, 113.7, 85.2, 80.3, 76.75, 72.5, 71.1, 55.3, 36.8, 36.1, 27.2, 26.5, 23.5, 17.3, –5.8, –6.1; HRMS (ESI) calcd for $C_{46}H_{72}O_{10}Si_2Na$ $[2M+Na]^+$ 863.4556, found 863.4551.

Alkene 76. To a solution of lactone **48** (0.230 g, 0.547 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) at –78 °C was slowly added DIBAL-H (0.602 mL, 1.0 M in hexanes, 0.602 mmol, 1.1 equiv). After stirring the resultant solution for 15 min at –78 °C, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle's salt (5 mL), warmed to 25 °C, stirred vigorously

for 30 min, and transferred to a separatory funnel. The two layers were separated and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 3:1→2:1) furnished the desired lactol (0.203 g, 79% yield) as a colorless liquid. To a solution of methyltriphenylphosphonium bromide (65.9 mg, 0.185 mmol, 3.0 equiv) in THF (1.0 mL) at 0 °C was added *t*-BuOK (0.19 mL, 1.0 M in THF, 0.190 mmol, 3.1 equiv). The resultant yellow mixture was then stirred at 0 °C for 30 min and then a solution of the so-obtained lactol (26.1 mg, 61.8 μmol, 1.0 equiv) in THF (1.0 mL) was added. The resultant reaction solution was stirred at 0 °C for 6 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (4 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (hexanes:EtOAc, 5:1) afforded the desired terminal alkene (22.0 mg, 85% yield) as a colorless liquid. Next, to the solution of the so-obtained terminal alkene (22.0 mg, 52.3 μmol, 1.0 equiv) in CH_2Cl_2 (0.5 mL) at 25 °C was sequentially added *trans*-3-hexene (52.0 μL, 35.2 mg, 0.418 mmol, 8.0 equiv) and the second generation Hoveyda–Grubbs Catalyst™ (1.6 mg, 2.62 μmol, 0.05 equiv). The resultant reaction mixture was stirred at 25 °C for 3 h. Upon completion, the reaction contents were concentrated directly. The resultant residue was purified by flash column chromatography (hexanes:EtOAc, 5:1) to yield the desired alkene **76** (21.1 mg, 90% yield) as a colorless liquid. **76**: R_f = 0.50 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 3438, 2956, 2929, 2855, 1613, 1513, 1464, 1390, 1250, 1092, 826, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 5.62 (dt, *J* = 15.4, 6.3 Hz, 1 H), 5.41 (ddd, *J* = 15.4, 7.6, 6.1 Hz, 1 H),

4.67–4.36 (m, 3 H), 4.31–4.24 (m, 1 H), 3.80 (m , 4 H), 3.62 (td, *J* = 9.5, 6.1 Hz, 1 H), 3.39 (td, *J* = 9.5, 6.2 Hz, 1 H), 2.38–2.21 (m, 2 H), 2.02 (t, *J* = 7.4 Hz, 2 H), 1.88 (ddt, *J* = 14.6, 10.4, 5.0 Hz, 2 H), 1.68 (ddd, *J* = 13.3, 9.5, 6.2 Hz, 2 H), 1.33 (dt, *J* = 7.2, 4.6 Hz, 1 H), 0.98 (t, *J* = 7.5 Hz, 3 H), 0.89 (s, 9 H), –0.04 (s, 3 H), –0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 134.7, 130.8, 129.2, 124.9, 113.7, 81.8, 79.4, 73.7, 72.5, 71.7, 55.3, 38.6, 32.9, 27.2, 26.2, 25.6, 25.0, 17.4, 13.7, –5.9, –6.1; HRMS (ESI) calcd for $C_{26}H_{45}O_4Si$ $[M+H]^+$ 449.3082, found 449.3093.

Diol 77. To a solution of lactone **48** (0.230 g, 0.547 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) at –78 °C was slowly added DIBAL-H (0.602 mL, 1.0 M in hexanes, 0.602 mmol, 1.1 equiv). After stirring the resultant solution for 15 min at –78 °C, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle's salt (5 mL), warmed to 25 °C, stirred vigorously for 30 min, and transferred to a separatory funnel. The two layers were separated and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 3:1→2:1) furnished the desired lactol (0.203 g, 79% yield) as a colorless liquid. Pressing forward, to a solution of the so-obtained lactol (0.203 g, 0.481 mmol, 1.0 equiv) in toluene (4.8 mL) at 25 °C was added vinylmagnesium bromide (4.81 mL, 1.0 M in THF, 4.81 mmol, 10.0 equiv). The resultant dark solution was stirred for 2 h at 25 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (10 mL) and transferred into a separatory funnel. The two layers were separated and the aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 2:1→1:1) to afford the desired diol **77** (0.191 g, 88% yield) as a colorless oil. **77**: R_f = 0.15 (silica gel, hexanes:EtOAc, 2:1); IR (film) ν_{max} 3403, 2953, 2929, 2856, 1612, 1513,

1464, 1362, 1249, 1173, 1087, 922, 826, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2 H), 6.86 (d, *J* = 8.5 Hz, 2 H), 5.91 (ddd, *J* = 16.3, 10.4, 5.6 Hz, 1 H), 5.28 (d, *J* = 17.2 Hz, 1 H), 5.12 (dd, *J* = 10.4, 1.4 Hz, 1 H), 4.64–4.39 (m, 3 H), 4.33 (t, *J* = 3.8 Hz, 1 H), 4.25 (t, *J* = 7.3 Hz, 1 H), 3.96 (td, *J* = 7.2, 3.3 Hz, 1 H), 3.80 (s, 3 H), 3.61 (td, *J* = 9.1, 6.6 Hz, 1 H), 3.38 (td, *J* = 9.1, 6.5 Hz, 1 H), 2.68 (br s, 1 H), 2.41 (br s, 1 H), 2.01–1.76 (m, 4 H), 1.76–1.59 (m, 2 H), 1.31 (dd, *J* = 6.9, 4.6 Hz, 1 H), 0.90 (s, 9 H), –0.04 (s, 3 H), –0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 140.9, 130.9, 129.2, 114.5, 113.7, 80.9, 79.37, 73.9, 72.5, 71.7, 70.7, 55.3, 38.1, 36.2, 27.2, 26.2, 24.6, 17.4, –5.9, –6.1; HRMS (ESI+APCI): No molecular ion peak was observed.

Alkene 79. To diol **77** (57.2 mg, 0.126 mmol, 1.0 equiv) was added allyl acetate (1.0 mL) and the second generation Hoveyda–Grubbs Catalyst™ (7.9 mg, 12.6 μmol, 0.10 equiv) at 25 °C. The resultant brown mixture was then stirred at 25 °C for 4 h. Upon completion, the reaction mixture was purified directly by flash column chromatography (silica gel, hexanes:EtOAc, 3:1→2:1) to afford the desired allyl acetate (36.0 mg, 54% yield) as a colorless liquid. Next, to a solution of the so-obtained allyl acetate (36.0 mg, 68.9 μmol, 1.0 equiv) in THF (1.0 mL) at 0 °C was added $LiAlH_4$ (69.0 μL, 1.0 M in THF, 0.690 μmol, 1.0 equiv). After stirring the resultant solution at 0 °C for 30 min, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle's salt (5 mL), warmed to 25 °C, stirred vigorously for 30 min, and transferred to a separatory funnel. The two layers were separated and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (hexanes:EtOAc, 2:1→0:1) furnished the desired triol **78** (31.1 mg, 94% yield) as a colorless liquid. Pressing forward, the so-obtained triol **78** (31.1 mg, 65.0 μmol, 1.0 equiv) was dissolved in THF (1.0 mL) and cooled to 0 °C. $Pd(CH_3CN)_2Cl_2$ (0.84 mg, 3.23 μmol, 0.05 equiv) was then added and the resultant solution

was stirred at 0 °C for 3 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (3 mL) and transferred to a separatory funnel. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to afford the desired alkene **79** (14.7 mg, 48% yield) as a colorless liquid. **79**: R_f = 0.25 (silica gel, hexanes:EtOAc, 2:1); IR (film) ν_{max} 3423, 2927, 2855, 1613, 1513, 1464, 1248, 1075, 1037, 826, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.9 Hz, 2 H), 6.86 (d, *J* = 8.5 Hz, 2 H), 6.09 (ddd, *J* = 17.1, 10.8, 6.2 Hz, 1 H), 5.54–5.20 (m, 2 H), 4.51 (dt, *J* = 10.5, 5.3 Hz, 1 H), 4.42 (q, *J* = 11.6 Hz, 2 H), 4.31 (t, *J* = 6.0 Hz, 1 H), 4.27 (s, 1 H), 4.10 (dd, *J* = 10.7, 5.0 Hz, 1 H), 3.97 (d, *J* = 3.2 Hz, 1 H), 3.80 (s, 3 H), 3.60 (td, *J* = 9.6, 5.8 Hz, 1 H), 3.38 (td, *J* = 9.6, 5.8 Hz, 1 H), 2.11–2.00 (m, 1 H), 1.91 (dd, *J* = 13.1, 5.8 Hz, 1 H), 1.83–1.76 (m, 1 H), 1.75–1.59 (m, 3 H), 1.34–1.29 (m, 1 H), 0.90 (s, 9 H), –0.04 (s, 3 H), –0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 131.3, 130.8, 129.3, 120.4, 113.7, 80.5, 76.5, 76.3, 72.5, 71.9, 71.6, 64.4, 55.3, 36.8, 31.5, 27.2, 26.2, 24.9, 17.3, –5.9, –6.1; HRMS (APCI) calcd for $C_{26}H_{43}O_5Si$ $[M+H]^+$ 463.2874, found 463.2856.

Aldehyde 80. To a solution of *N*,*O*-dimethylhydroxylamine•HCl (0.339 g, 3.47 mmol, 5.0 equiv) in THF (6.0 mL) was added $AlMe_3$ (0.870 mL, 2.0 M in hexanes, 1.74 mmol, 2.5 equiv) at 0 °C and the resultant solution was stirred at that temperature for 30 min. Next, a solution of lactone **48** (0.291 g, 0.693 mmol, 1.0 equiv) in THF (4.0 mL) was added at 0 °C and the reaction mixture was then warmed to 25 °C and stirred at 25 °C for 3 h. Upon completion, the reaction contents were quenched by slow addition of saturated aqueous Rochelle's salt (20 mL), stirred vigorously at 25 °C for 30 min, poured into a separatory funnel, and diluted with EtOAc (30 mL). The two phases were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The

combined organic layers were dried (Na_2SO_4), filtered, and concentrated to provide the desired crude Weinreb amide as a colorless oil which was used in the next step without further purification. Thus, pressing forward, TBSCl (0.210 g, 1.39 mmol, 2.0 equiv) and imidazole (0.282 g, 4.16 mmol, 6.0 equiv) were dissolved in DMF (5.0 mL) at 25 °C and the resultant mixture was stirred at 25 °C for 30 min before a solution of the crude Weinreb amide (0.693 mmol assumed) in DMF (5.0 mL) was added. The reaction solution was then stirred at 25 °C for an additional 12 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (30 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (30 mL). The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 15:1→10:1→5:1) afforded recovered lactone **48** (31.2 mg) along with the desired TBS-protected Weinreb amide (0.235 g, 57% yield, 64% yield based on recovered starting material) as a colorless oil. Next, The so-obtained TBS-protected Weinreb amide (0.235 g, 0.395 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (4.0 mL) and cooled to –78 °C. DIBAL-H (0.440 mL, 1.0 M in hexanes, 0.435 mmol, 1.1 equiv) was then added slowly. After stirring at –78 °C for 15 min, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle's salt (15 mL). The resultant biphasic solution was warmed to 25 °C and stirred vigorously at that temperature for 30 min. The contents were then poured into a separatory funnel, the two phases were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 20:1→15:1) furnished the desired aldehyde **80** (0.167 g, 79% yield) as a colorless oil. **80**: R_f = 0.55 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 2954, 2929, 2856, 1725, 1613, 1513, 1464, 1249,

1076, 833, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (d, *J* = 1.8 Hz, 1 H), 7.25 (d, *J* = 8.4 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 4.54–4.38 (m, 3 H), 4.35 (br s, 1 H), 4.22 (br s, 1 H), 3.79 (s, 3 H), 3.59 (td, *J* = 9.4, 6.2 Hz, 1 H), 3.36 (td, *J* = 9.5, 6.2 Hz, 1 H), 2.65–2.63 (m, 2 H), 1.94–1.57 (m, 4 H), 1.35 (m, 1 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.01 (s, 3 H), –0.05 (s, 3 H), –0.06 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5, 159.1 130.8, 129.3, 113.7, 79.6, 77.5, 74.0, 72.5, 71.6, 55.2, 44.5, 38.8, 27.2, 26.2, 25.7, 24.1, 18.0, 17.3, –4.6, –5.1, –6.0, –6.1; HRMS (APCI) calcd for $C_{29}H_{50}O_4Si_2Na$ $[M+Na-H_2O]^+$ 541.3140, found 541.3136.

Dibromide 82. To a solution of Br_2 (62.3 μL, 0.193 g, 1.21 mmol, 1.7 equiv) in CH_2Cl_2 (7.0 mL) at –78 °C was added $P(OPh)_3$ (0.439 g, 1.42 mmol, 2.0 equiv). The resultant solution was stirred at –78 °C for 10 min before Et_3N (0.295 mL, 0.214 g, 2.12 mmol, 3.0 equiv) and a solution of **80** (0.380 g, 0.710 mmol, 1.0 equiv) in CH_2Cl_2 (7.0 mL) were added sequentially. The resultant mixture was allowed to warm to 25 °C slowly with stirring over the course of 12 h. Upon completion, the reaction contents were concentrated directly, and the resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 30:1→20:1) to afford TBS-protected dibromide **81** (0.556 g, >100% yield) as a brown oil containing inseparable impurities (~20%). Moving forward, the so-obtained **81** (0.556 g, 0.710 mmol assumed, 1.0 equiv) was dissolved in THF (8 mL), and TBAF (5.08 mL, 1.0 M in THF, 5.08 mmol, 7.2 equiv) was added at 0 °C. The reaction contents were then warmed to 25 °C and stirred for an additional 2 h. Upon completion, the reaction mixture was quenched with saturated aqueous NH_4Cl (30 mL) and poured into a separatory funnel. The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) afforded alcohol (0.330 g, 71% yield) as a colorless oil containing a

small amount of inseparable impurities (~5%) that are ultimately removed following the next step. Next, the so-obtained alcohol (0.330 g, 0.585 mmol assumed, 1.0 equiv) was dissolved in CH_2Cl_2 (10.0 mL), and NMM (0.322 mL, 0.296 g, 2.93 mmol, 5.0 equiv) and ethyl propiolate (0.303 mL, 0.287 g, 2.93 mmol, 5.0 equiv) were added sequentially at 25 °C. The reaction contents were stirred at 25 °C for 4 h. Upon completion, the reaction mixture was concentrated directly and the resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 20:1→10:1) to afford dibromide **82** (0.330 g, 63% yield over 3 steps from **80**) as a brown oil. **82**: R_f = 0.50 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 2954, 2930, 2856, 1710, 1644, 1623, 1513, 1248, 1240, 1038, 829 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 12.5 Hz, 1 H), 7.25 (d, *J* = 8.4 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.73 (dd, *J* = 10.4, 3.4 Hz, 1 H), 5.27 (d, *J* = 12.5 Hz, 1 H), 4.55 (t, *J* = 4.3 Hz, 1 H), 4.48–4.40 (m, 2 H), 4.35 (dt, *J* = 10.7, 5.3 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 3 H), 3.80 (s, 3 H), 3.56 (td, *J* = 9.3, 5.6 Hz, 1 H), 3.38 (td, *J* = 9.2, 6.0 Hz, 1 H), 2.73 (ddd, *J* = 14.6, 9.5, 3.4 Hz, 1 H), 2.47 (ddd, *J* = 14.6, 10.3, 3.1 Hz, 1 H), 2.11–2.01 (m, 1 H), 1.95–1.84 (m, 1 H), 1.77–1.70 (m, 1 H), 1.66–1.60 (m, 1 H), 1.30–1.27 (m, 4 H), 0.89 (s, 9 H), –0.04 (s, 3 H), –0.07 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 160.3, 159.1, 130.7, 129.2, 113.8, 98.6, 82.8, 80.0, 78.5, 72.6, 71.3, 60.0, 55.3, 45.7, 42.8, 36.1, 27.2, 26.5, 24.5, 17.4, 14.3, –5.8, –6.0; HRMS (ESI+APCI): no molecular ion peak was observed.

Bromide 83. To a solution of dibromide **82** (0.183 g, 0.276 mmol, 1.0 equiv) in benzene (5.0 mL) at 90 °C was slowly added a premixed solution of AIBN (22.6 mg, 0.138 mmol, 0.5 equiv) and *n*-Bu_3SnH (89.0 μL, 96.3 mg, 0.331 mmol, 1.2 equiv) in benzene (5.0 mL) over the course of 30 min via a syringe pump. After the addition was complete, the reaction mixture was stirred at 90 °C for an additional 30 min. Upon completion, the reaction contents were cooled to 25 °C and concentrated directly. The resultant crude residue was purified by flash column

chromatography (silica gel, hexanes:Et_2O, 10:1→5:1) to afford bromide **83** (92.1 mg, 57% yield) as a colorless oil. **83**: R_f = 0.55 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 2953, 2930, 2855, 1739, 1613, 1513, 1465, 1303, 1248, 1095, 1036, 826 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 4.66–4.30 (m, 3 H), 4.19–4.07 (m, 3 H), 3.98–3.91 (m, 1 H), 3.85 (td, *J* = 10.2, 9.5, 2.8 Hz, 1 H), 3.80 (s, 3 H), 3.76 (br s, 1 H), 3.56 (td, *J* = 10.2, 9.7, 5.6 Hz, 1 H), 3.36 (td, *J* = 9.8, 5.6 Hz, 1 H), 3.01 (dd, *J* = 15.9, 2.9 Hz, 1 H), 2.59 (ddd, *J* = 14.2, 4.5, 2.5 Hz, 1 H), 2.45 (dd, *J* = 15.9, 8.7 Hz, 1 H), 2.08 (ddd, *J* = 15.0, 11.7, 3.5 Hz, 1 H), 1.90 (dd, *J* = 13.2, 5.7 Hz, 1 H), 1.79–1.55 (m, 3 H), 1.29–1.24 (m, 4 H), 0.89 (s, 9 H), –0.06 (s, 3 H), –0.07 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 159.1, 130.7, 129.3, 113.7, 81.1, 78.4, 77.6, 76.8, 72.4, 71.4, 60.5, 55.3, 47.1, 39.3, 38.7, 37.1, 27.2, 26.1, 25.0, 17.3, 14.2, –5.9, –6.1; HRMS (ESI+APCI): no molecular ion peak was observed.

Alkene 85. $LiAlH_4$ (0.169 mL, 1.0 M in THF, 0.169 mmol, 1.1 equiv) was added to a solution of bromide **83** (90.2 mg, 0.154 mmol, 1.0 equiv) in THF (3.0 mL) at –78 °C, and the resultant mixture was stirred at –78 °C for 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous Rochelle's salt (6 mL), warmed to 25 °C, and stirred vigorously at 25 °C for 30 min. The reaction contents were then poured into a separatory funnel. The two phases were separated, and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 3:1) afforded the desired alcohol (68.9 mg, 82% yield) as a colorless oil. Next**,** *o*-nitrophenylselenocyanide (0.145 g, 0.637 mmol, 5.0 equiv) and P(*n*-Oct)$_3$ (0.478 g, 1.27 mmol, 10 equiv) were added to a solution of the so-obtained alcohol (68.9 mg, 0.127 mmol, 1.0 equiv) in THF (6.0 mL) at 0 °C. The ice bath was then removed, and the reaction contents were stirred at 25 °C for 3 h. An aqueous solution of

H_2O_2 (0.270 mL, 30% w/w in water, 2.62 mmol, 21 equiv) was carefully added, and the resultant mixture was stirred for an additional 12 h at 25 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (10 mL), poured into a separatory funnel, and CH_2Cl_2 (15 mL) was added to dilute the mixture. The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 1:1, followed by hexanes:EtOAc, 30:1) yielded the desired alkene **85** (64.2 mg, 96% yield) as a yellow oil. **85**: R_f = 0.15 (silica gel, hexanes:EtOAc, 20:1); IR (film) ν_{max} 2952, 2929, 2855, 1612, 1586, 1513, 1464, 1361, 1280, 1172, 1073, 1037, 925, 826 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 5.93 (ddd, *J* = 17.1, 10.5, 6.3 Hz, 1 H), 5.38 (dt, *J* = 17.2, 1.4 Hz, 1 H), 5.31–5.21 (m, 1 H), 4.56 (dt, *J* = 10.7, 5.5 Hz, 1 H), 4.47–4.35 (m, 2 H), 4.16 (br s, 1 H), 3.88 (ddd, *J* = 11.6, 9.8, 4.4 Hz, 1 H), 3.83–3.77 (m, 5 H), 3.62–3.54 (m, 1 H), 3.37 (td, *J* = 9.5, 9.0, 5.7 Hz, 1 H), 2.62 (ddd, *J* = 14.3, 4.5, 2.5 Hz, 1 H), 2.09 (ddd, *J* = 14.8, 11.7, 3.6 Hz, 1 H), 1.98 (dd, *J* = 13.2, 5.7 Hz, 1 H), 1.83–1.56 (m, 3 H), 1.36–1.28 (m, 1 H), 0.89 (s, 9 H), –0.05 (s, 3 H), –0.05 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 135.9, 130.7, 129.3, 118.6, 113.7, 81.1, 80.5, 78.0, 77.5, 72.5, 71.4, 55.3, 47.7, 38.6, 37.2, 27.2, 26.1, 25.0, 17.3, –5.9, –6.1; HRMS (APCI) calcd for $C_{26}H_{41}BrO_4SiNa$ $[M+Na]^+$ 547.1850, found 547.1841.

Aldehyde 87. Pd/C (20.7 mg, w/w 10%, 19.5 μmol, 0.30 equiv) was carefully added to a solution of alkene **85** (34.2 mg, 65.0 μmol, 1.0 equiv) in EtOAc (1.0 mL) at 25 °C. The suspension was then purged by direct bubbling with a balloon of H_2 gas for 30 min at 25 °C. The reaction contents were then placed under a H_2 atmosphere and stirred for 6 h at 25 °C. Upon completion, the reaction contents were filtered through a short pad of Celite and washed with EtOAc (10 mL).

The filtrate was concentrated directly to afford the desired crude alcohol as pale semi-viscous oil/solid, which was used in the next step without purification. Thus, pressing forward, the so-obtained alcohol (65.0 μmol assumed) was dissolved in CH_2Cl_2 (2.0 mL) at 25 °C and solid $NaHCO_3$ (27.4 mg, 0.326 mmol, 5.0 equiv) and Dess–Martin periodinane (30.5 mg, 72.1 μmol, 1.1 equiv) were added sequentially. The resultant mixture was stirred at 25 °C for 1 h. Upon completion, the reaction contents were concentrated directly and the resultant residue was purified by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 1:1→1:2) to afford the desired aldehyde **87** (19.1 mg, 73% yield over 2 steps) as a colorless liquid. **87**: R_f = 0.20 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 2955, 2928, 2856, 2720, 1715, 1465, 1363, 1252, 1100, 1059, 826 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.53 (d, *J* = 5.5 Hz, 1 H), 4.69–4.52 (m, 1 H), 4.08 (t, *J* = 3.0 Hz, 1 H), 3.92 (ddd, *J* = 11.9, 9.9, 4.6 Hz, 1 H), 3.51 (d, *J* = 3.7 Hz, 1 H), 3.29 (ddd, *J* = 9.9, 7.0, 2.8 Hz, 1 H), 2.54 (ddd, *J* = 14.3, 4.7, 2.5 Hz, 1 H), 2.32–2.15 (m, 2 H), 2.10–2.00 (m, 1 H), 1.93 (ddt, *J* = 15.0, 7.5, 3.8 Hz, 1 H), 1.83 (dd, *J* = 12.9, 5.4 Hz, 1 H), 1.71–1.58 (m, 3 H), 0.95 (s, 9 H), 0.92 (t, *J* = 7.4 Hz, 3 H), 0.00 (s, 3 H), –0.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6, 80.3, 77.9, 47.5, 40.0, 38.6, 36.6, 35.8, 27.1, 26.2, 24.7, 24.0, 17.3, 8.5, –6.4 (2 C); HRMS (ESI+APCI): no molecular ion peak was observed.

Enyne 50. To a solution of Julia–Kocienski reagent **88** (37.7 mg, 0.122 mmol, 3.0 equiv; prepared according to the literature procedure reported by Zajc and co-workers[46b] with all spectroscopic data matching that reported in Ref. 46b) in THF (2.0 mL) at –20 °C was added KHMDS (0.101 mL, 1.0 M in THF, 0.101 mmol, 2.5 equiv). The resultant dark colored solution was stirred at –20 °C for 30 min, and then a solution of aldehyde **87** (16.3 mg, 40.5 μmol, 1.0 equiv) in THF (2.0 mL) was added at –20 °C in a single portion. The reaction contents were then allowed to warm to 0 °C and stirred for an additional 1 h at 0 °C. Upon completion, TBAF (0.122

mL, 1.0 M in THF, 0.122 mmol, 3.0 equiv) was added at 0 °C, and the reaction was stirred for an additional 10 min at 0 °C. Saturated aqueous NH_4Cl (10 mL) was carefully added to quench the reaction, and the mixture was poured into a separatory funnel, diluting with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 3:1→1:1) afforded the desired enyne **50** (8.7 mg, 49% yield) as a brown oil. **50**: R_f = 0.25 (silica gel, hexanes:CH_2Cl_2, 1:1); IR (film) ν_{max} 3311, 2956, 2927, 2856, 1728, 1464, 1437, 1252, 1100, 1062, 825 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.12 (dt, *J* = 11.0, 7.1 Hz, 1 H), 5.34 (dd, *J* = 10.8, 1.9 Hz, 1 H), 4.57 (dt, *J* = 10.5, 5.3 Hz, 1 H), 4.09 (d, *J* = 3.1 Hz, 1 H), 3.96 (ddd, *J* = 11.9, 9.9, 4.6 Hz, 1 H), 3.84–3.80 (m, 1 H), 3.30 (ddd, *J* = 9.9, 7.0, 2.8 Hz, 1 H), 3.07 (d, *J* = 2.4 Hz, 1 H), 2.61 (ddd, *J* = 14.2, 4.5, 2.7 Hz, 1 H), 2.52–2.37 (m, 2 H), 2.09 (ddd, *J* = 15.4, 11.8, 3.6 Hz, 1 H), 1.92 (ddd, *J* = 18.5, 9.1, 4.3 Hz, 2 H), 1.82 (ddd, *J* = 13.1, 10.6, 3.7 Hz, 1 H), 1.64–1.53 (m, 2 H), 0.94–0.90 (s, 12 H), –0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 105.9, 81.5, 80.9, 80.8, 80.3, 78.2, 77.5, 47.9, 38.9, 36.9, 28.9, 27.2, 27.1, 26.2, 17.3, 8.6, –5.9 (2 C); HRMS (ESI+APCI) calcd for $C_{21}H_{36}BrO_2Si$ $[M+H]^+$ 427.1662, found 427.1651.

Microcladallene A (7) and ***epi*-Microcladallene A (89)**. Enyne **50** (13.4 mg, 31.4 μmol, 1.0 equiv) was dissolved in $EtNO_2$ (1.0 mL), the reaction contents were cooled to –78 °C, and then solid BDSB[15b] (17.3 mg, 31.4 μmol, 1.0 equiv) was added in a single portion. The reaction contents were then stirred at –78 °C for 1 h. Upon completion, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), warmed to 25 °C, poured into a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then dried (Na_2SO_4),

filtered, and concentrated. Purification of the resultant crude residue by preparative thin-layer chromatography (silica gel, hexanes:Et_2O, 10:1) afforded microcladallene A (**7**, 5.9 mg, 49% yield) and *epi*-microcladallene A (**89**, 2.7 mg, 22% yield), both as white foams. Microcladallene A (**7**): R_f = 0.65 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3054, 3027, 2925, 2851, 1729, 1455, 1378, 1193, 1082, 1064, 813, 749, 661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.11 (dd, *J* = 5.7, 3.1 Hz, 1 H), 5.93 (ddd, *J* = 10.7, 7.6, 7.6 Hz, 1 H), 5.79 (ddd, *J* = 11.6, 10.8, 6.0 Hz, 1 H), 5.44 (dd, *J* = 5.0, 5.0 Hz, 1 H), 4.87–4.68 (m, 1 H), 4.04 (ddd, *J* = 12.4, 10.0, 4.4 Hz, 1 H), 3.83 (br s, 1 H), 3.59 (dd, *J* = 10.8, 5.5 Hz, 1 H), 3.28 (ddd, *J* = 9.3, 9.3, 2.4 Hz, 1 H), 2.69 (dd, *J* = 13.6, 6.7 Hz, 1 H), 2.53 (ddd, *J* = 12.7, 9.9, 9.9 Hz, 1 H), 2.40 (ddd, *J* = 13.4, 3.9, 3.9 Hz, 1 H), 2.28 (ddd, *J* = 14.5, 8.4, 4.3 Hz, 2 H), 2.14–1.97 (m, 2 H), 1.55–1.48 (m, 1 H), 0.99 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 129.1, 129.0, 99.9, 83.4, 80.9, 74.6, 74.5, 70.2, 49.4, 43.7, 31.4, 30.1, 26.4, 9.7; HRMS (ESI) calcd for $C_{15}H_{19}Br_2O$ $[M+H–H_2O]^+$ 372.9797, found 372.9769. *epi*-Microcladallene A (**89**): R_f = 0.70 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3051, 2955, 2924, 2852, 1724, 1456, 1437, 1083, 1064, 971, 810, 662 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.09 (dd, *J* = 5.9, 2.8 Hz, 1 H), 5.95–5.84 (m, 1 H), 5.82–5.69 (m, 1 H), 5.43 (dd, *J* = 5.0, 5.0 Hz, 1 H), 4.87–4.78 (m, 1 H), 4.05 (ddd, *J* = 12.4, 10.0, 4.5 Hz, 1 H), 3.80 (s, 1 H), 3.58 (dd, *J* = 10.1, 5.0 Hz, 1 H), 3.28 (ddd, *J* = 9.4, 9.4, 2.6 Hz, 1 H), 2.67 (dd, *J* = 13.3, 6.9 Hz, 1 H), 2.53 (ddd, *J* = 12.8, 9.7, 9.7 Hz, 1 H), 2.49–2.41 (m, 1 H), 2.31–2.25 (m, 2 H), 2.07–2.02 (m, 2 H), 1.59–1.50 (m, 1 H), 0.98 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.6, 129.4, 128.6, 100.2, 83.5, 80.9, 75.0, 74.3, 70.2, 49.4, 43.6, 31.7, 30.2, 26.4, 9.7; HRMS (ESI) calcd for $C_{15}H_{20}Br_2O_2Na$ $[M+Na]^+$ 412.9722, found 412.9732.

Table 2-2. Comparative ^{1}H NMR Data for Microcladallene A (7)

Natural (Suzuki)[25b] (400 MHz, $CDCl_3$)	Synthetic (Kim)[3b] (500 MHz, $CDCl_3$)	Synthetic (this work) (500 MHz, $CDCl_3$)
6.11 (dd, *J* = 5.3, 2.9 Hz, 1 H)	6.11 (dd, *J* = 5.7, 3.1 Hz, 1 H)	6.11 (dd, *J* = 5.7, 3.1 Hz, 1 H)
5.93 (ddd, *J* = 10.3, 8.3, 7.8 Hz, 1 H)	5.93 (ddd, *J* = 7.8, 7.8, 7.8 Hz, 1 H)	5.93 (ddd, *J* = 10.7, 7.6, 7.6 Hz, 1 H)
5.79 (dddd, *J* = 10.3, 9.7, 7.3, 1.7 Hz, 1 H)	5.79 (ddd, *J* = 9.6, 9.6, 9.6 Hz, 1 H),	5.79 (ddd, *J* = 11.6, 10.8, 6.0 Hz, 1 H)
5.44 (dd, *J* = 5.3, 4.9, Hz, 1 H)	5.44 (dd, *J* = 4.7, 4.7 Hz, 1 H)	5.44 (dd, *J* = 5.0, 5.0 Hz, 1 H)
4.79 (ddd, *J* = 7.8, 4.9, 2.9 Hz, 1 H)	4.81–4.77 (m, 1 H)	4.87–4.68 (m, 1 H)
4.04 (ddd, *J* = 12.2, 10.3, 4.9, 1.0 Hz, 1 H)	4.04 (ddd, *J* = 14.3, 4.4, 2.6 Hz, 1 H)	4.04 (ddd, *J* = 12.4, 10.0, 4.4 Hz, 1 H)
3.83 (br s, 1 H)	3.83 (br s, 1 H)	3.83 (br s, 1 H)
3.59 (ddd, *J* = 10.3, 4.9, 1.0 Hz, 1 H)	3.59 (dd, *J* = 10.3, 4.9 Hz, 1 H)	3.59 (dd, *J* = 10.8, 5.5 Hz, 1 H)
3.29 (ddd, *J* = 10.3, 9.3, 2.4 Hz, 1 H)	3.29 (ddd, *J* = 11.2, 11.2, 2.2 Hz, 1 H)	3.28 (ddd, *J* = 9.3, 9.3, 2.4 Hz, 1 H)

Table 2-2 continued

2.70 (m, 1 H)	2.70 (ddd, *J* = 13.2, 5.3, 5.3 Hz, 1 H)	2.69 (dd, *J* = 13.6, 6.7 Hz, 1 H)
2.54 (ddd, *J* = 12.7, 10.3, 9.7 Hz, 1 H)	2.54 (ddd, *J* = 10.0, 10.0, 10.0 Hz, 1 H)	2.53 (ddd, *J* = 12.7, 9.9, 9.9 Hz, 1 H)
2.40 (ddd, *J* = 13.2, 4.4, 3.9 Hz, 1 H)	2.40 (ddd, *J* = 13.4, 4.0, 4.0 Hz, 1 H)	2.40 (ddd, *J* = 13.4, 3.9, 3.9 Hz, 1 H),
2.28 (m, 1 H)	2.31–2.24 (m, 2 H)	2.28 (ddd, *J* = 14.5, 8.4, 4.3 Hz, 2 H)
2.27 (ddd, *J* = 12.7, 7.3, 4.9 Hz, 1 H)		
2.07 (ddd, *J* = 13.2, 12.2, 2.9 Hz, 1 H)	2.10–2.00 (m, 2 H)	2.14–1.97 (m, 2 H)
2.05 (ddq, *J* = 14.6, 7.3, 2.4 Hz, 1 H)		
1.55 (ddq, *J* = 14.6, 9.3, 7.3 Hz, 1 H)	1.60–1.49 (m, 1 H)	1.55–1.48 (m, 1 H)
0.99 (t, *J* = 7.3 Hz, 3 H)	0.99 (dd, *J* = 7.4, 7.4 Hz, 3 H)	0.99 (t, *J* = 7.4 Hz, 3 H)

Table 2-3. Comparative ^{13}C NMR Data for Microcladallene A (7)

Natural (Suzuki)[25b] (100 MHz, $CDCl_3$)	Synthetic (Kim)[3b] (125 MHz, $CDCl_3$)	Synthetic (this work) (125 MHz, $CDCl_3$)
203.1	203.1	203.1
129.1	129.1	129.1
129.0	129.0	129.0
99.9	99.9	99.9
83.4	83.4	83.4
80.6	80.9	80.9
74.6	74.6	74.6
74.5	74.5	74.5
70.2	70.1	70.2
49.3	49.4	49.4
43.7	43.7	43.7
31.4	31.3	31.4
31.1	30.1	30.1
26.4	26.4	26.4

Table 2-3 continued

11.0	9.7	9.7

Table 2-4. Comparative ^{1}H NMR Data for *epi*-Microcladallene A (89)

Synthetic (Kim) (500 MHz, $CDCl_3$)[3b]	Synthetic (this work) (500 MHz, $CDCl_3$)
6.09 (dd, J = 5.8, 2.7 Hz, 1 H)	6.09 (dd, J = 5.9, 2.8 Hz, 1 H)
5.89 (ddd, J = 8.0, 8.0, 8.0 Hz, 1 H)	5.95–5.84 (m, 1 H)
5.76 (ddd, J = 10.3, 10.3, 10.3 Hz, 1 H)	5.82–5.69 (m, 1 H)
5.42 (dd, J = 4.9, 4.9 Hz, 1 H)	5.43 (dd, J = 5.0, 5.0 Hz, 1 H)
4.84–4.80 (m, 1 H)	4.87–4.78 (m, 1 H),
4.05 (ddd, J = 12.4, 10.1, 4.4 Hz, 1 H)	4.05 (ddd, J = 12.4, 10.0, 4.5 Hz, 1 H)
3.80 (brs, 1 H)	3.80 (s, 1 H)
3.58 (ddd, J = 9.9, 4.7, 0.9 Hz, 1 H)	3.58 (dd, J = 10.1, 5.0 Hz, 1 H)
3.28 (ddd, J = 10.1, 10.1, 2.4 Hz, 1 H)	3.28 (ddd, J = 9.4, 9.4, 2.6 Hz, 1 H)
2.70–2.64 (m, 1 H)	2.67 (dd, J = 13.3, 6.9 Hz, 1 H)
2.53 (ddd, J = 12.6, 9.9, 9.9 Hz, 1 H)	2.53 (ddd, J = 12.8, 9.7, 9.7 Hz, 1 H)
2.44 (ddd, J = 13.4, 3.0, 3.0 Hz, 1 H)	2.49–2.41 (m, 1 H)

Table 2-4 continued

2.32–2.24 (m, 2 H)	2.31–2.25 (m, 2 H)
2.09–2.00 (m, 2 H)	2.07–2.02 (m, 2 H)
1.58–1.51 (m, 1 H)	1.59–1.50 (m, 1 H)
0.98 (dd, J = 7.4, 7.4 Hz, 3 H)	0.98 (t, J = 7.4 Hz, 3 H)

Table 2-5. Comparative ^{13}C NMR Data for *epi*-Microcladallene A (89)

Synthetic (Kim) (125 MHz, $CDCl_3$)[3b]	Synthetic (this work) (125 MHz, $CDCl_3$)
202.6	202.6
129.4	129.4
128.6	128.6
100.1	100.2
83.5	83.5
80.9	80.9
74.9	75.0
74.3	74.3
70.2	70.2

Table 2-5 continued

49.3	49.4
43.6	43.6
31.7	31.7
30.2	30.2
26.3	26.4
9.8	9.7

Enyne 90. To a solution of alkene **85** (63.9 mg, 0.122 mmol, 1.0 equiv) in CH_2Cl_2/H_2O (10:1 v/v, 2.2 mL) at 25 °C was added DDQ (41.4 mg, 0.183 mmol, 1.5 equiv) and the resultant solution was stirred for 1 h at 25 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous Na_2CO_3 (6 mL) and poured into a separatory funnel. The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with saturated aqueous Na_2CO_3 (20 mL), dried (Na_2SO_4), filtered, and concentrated to give the desired crude alcohol. Pressing forward without any further purification, the so-obtained alcohol (0.122 mmol assumed) was dissolved in CH_2Cl_2 (3.0 mL) and $NaHCO_3$ (51.2 mg, 0.610 mmol, 5.0 equiv) and Dess–Martin periodinane (56.7 mg, 0.134 mmol, 1.1 equiv) were added sequentially at 25 °C. The reaction contents were then stirred for 1 h at 25 °C. Upon completion, the reaction mixture was concentrated directly and the resultant residue was purified by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 1:1, followed by hexanes:Et_2O, 10:1) to furnish the aldehyde (39.2 mg, 83% yield over 2 steps from **85**) as a

colorless oil. To a solution of Julia–Kocienski reagent **88** (46.4 mg, 0.150 mmol, 3.0 equiv; prepared according to the literature procedure reported by Zajc and co-workers[46b] with all the spectroscopic data matching that reported in Ref. 46b) in THF (2.0 mL) at –20 °C was added KHMDS (0.124 mL, 1.0 M in THF, 0.124 mmol, 2.5 equiv). The resultant dark colored solution was stirred at –20 °C for 30 min, and then a solution of the so obtained aldehyde (20.2 mg, 50.1 μmol, 1.0 equiv) in THF (2.0 mL) was added at –20 °C in a single portion. The reaction contents were then allowed to warm up to 0 °C and stirred for an additional 1 h at 0 °C. Upon completion, TBAF (0.150 mL, 1.0 M in THF, 0.150 mmol, 3.0 equiv) was added at 0 °C, and the reaction was stirred for an additional 10 min at 0 °C. Saturated aqueous NH_4Cl (10 mL) was added carefully to quench the reaction, and the mixture was poured into a separatory funnel, diluting with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 3:1→1:1) afforded the desired enyne **90** (9.3 mg, 43% yield) as a brown oil. **90**: R_f = 0.25 (silica gel, hexanes:CH_2Cl_2, 1:1); IR (film) ν_{max} 3310, 2954, 2927, 2856, 1725, 1470, 1437, 1362, 1252, 1113, 1073, 927, 825, 641 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.17–6.05 (m, 1 H), 5.94 (ddd, *J* = 17.1, 10.6, 6.3 Hz, 1 H), 5.41–5.34 (m, 2 H), 5.28 (d, *J* = 10.5 Hz, 1 H), 4.65–4.56 (m, 1 H), 4.18 (s, 1 H), 3.98–3.74 (m, 3 H), 3.08 (s, 1 H), 2.71–2.63 (m, 1 H), 2.54–2.32 (m, 2 H), 2.17–2.08 (m, 1 H), 1.98 (dd, *J* = 13.2, 5.7 Hz, 1 H), 1.86 (td, *J* = 13.6, 12.1, 4.0 Hz, 1 H), 1.67–1.46 (m, 1 H), 0.92 (s, 9 H), 0.00 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 136.0, 118.6, 106.0, 81.5, 80.9, 80.7, 80.5, 78.1, 77.1, 47.8, 38.6, 36.9, 28.9, 27.2, 27.1, 17.3, –5.9 (2 C); HRMS (ESI+APCI): no molecular ion peak was observed.

Microcladallene B (8) and ***epi*-Microcladallene B (91)**. Enyne **90** (14.1 mg, 33.1 μmol, 1.0 equiv) was dissolved in $EtNO_2$ (1.0 mL), the reaction contents were cooled to –78 °C, and then solid BDSB[15b] (18.2 mg, 33.1 μmol, 1.0 equiv) was added in a single portion. The reaction contents were then stirred at –78 °C for 1 h. Upon completion, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), warmed to 25 °C, poured into a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant crude residue by preparative thin-layer chromatography (silica gel, hexanes:Et_2O, 10:1) afforded microcladallene B (**8**, 6.2 mg, 48% yield) and *epi*-microcladallene B (**91**, 3.3 mg, 25% yield), both as white foams. Microcladallene B (**8**): R_f = 0.65 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3053, 3027, 2924, 2850, 1726, 1455, 1436, 1409, 1285, 1064, 931, 752, 661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.12 (dd, *J* = 5.8, 3.1 Hz, 1 H), 6.02–5.86 (m, 2 H), 5.80 (ddd, *J* = 10.5, 9.9, 5.9 Hz, 1 H), 5.56–5.40 (m, 2 H), 5.31 (d, *J* = 10.5 Hz, 1 H), 4.81-4.79 (m, 1 H), 4.05 (ddd, *J* = 12.4, 10.1, 4.3 Hz, 1 H), 3.90–3.81 (m, 2 H), 3.69 (dd, *J* = 10.2, 4.9 Hz, 1 H), 2.68 (q, *J* = 7.3, 4.9 Hz, 1 H), 2.57 (ddd, *J* = 12.8, 9.8, 9.8 Hz, 1 H), 2.45 (ddd, *J* = 13.4, 3.8, 3.8 Hz, 1 H), 2.33-2.27 (m, 2 H), 2.10 (ddd, *J* = 12.9, 12.9, 3.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 135.4, 129.2, 129.0, 119.3, 99.7, 83.2, 80.6, 74.6, 74.6, 69.8, 48.0, 43.3, 31.3, 30.2; HRMS (ESI) calcd for $C_{15}H_{16}Br_2O$ $[M+H-H_2O]^+$ 370.9641, found 370.9615. *epi*-Microcladallene B (**91**): R_f = 0.70 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3056, 3027, 2956, 2924, 2853, 1727, 1462, 1286, 1123, 1066, 792, 656 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.10 (dd, *J* = 5.8, 2.7 Hz, 1 H), 6.03–5.85 (m, 2 H), 5.78 (ddd, *J* = 10.0, 9.5, 6.0 Hz, 1 H), 5.45–5.41 (m, 2 H), 5.31 (d, *J* = 11.4 Hz, 1 H), 4.83 (br s, 1 H), 4.06 (ddd, *J* = 12.4, 10.1, 4.3 Hz, 1 H), 3.92–3.78 (m, 2 H), 3.70–3.63 (m, 1 H), 2.66 (dt, *J* = 11.4, 5.7 Hz, 1 H), 2.56 (dt, *J* =

12.8, 9.6 Hz, 1 H), 2.49 (dt, *J* = 13.4, 3.8 Hz, 1 H), 2.36–2.26 (m, 2 H), 2.08 (td, *J* = 12.9, 3.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 135.4, 129.3, 128.7, 119.3, 100.0, 83.2, 80.6, 74.9, 74.3, 69.9, 48.0, 43.3, 31.7, 30.2; HRMS (ESI+APCI) calcd for $C_{15}H_{19}Br_2O_2$ $[M+H]^+$ 388.9746, found 388.9719.

Table 2-6. **Comparative ^{1}H NMR Data for Microcladallene B (8)**

Synthetic (Kim) (500 MHz, $CDCl_3$)[3b]	Synthetic (this work) (500 MHz, $CDCl_3$)
6.12 (dd, *J* = 5.7, 3.1 Hz, 1 H)	6.12 (dd, *J* = 5.8, 3.1 Hz, 1 H)
5.99–5.91 (m, 2 H)	6.02–5.86 (m, 2 H)
5.80 (dddd, *J* = 10.7, 8.4, 6.9, 1.3 Hz, 1 H)	5.80 (ddd, *J* = 10.5, 9.9, 5.9 Hz, 1 H)
5.46–5.41 (m, 2 H)	5.56–5.40 (m, 2 H)
5.30 (d, *J* = 10.6 Hz, 1 H)	5.31 (d, *J* = 10.5 Hz, 1 H)
4.81–4.77 (m, 1 H)	4.81-4.79 (m, 1 H)
4.04 (ddd, *J* = 12.4, 10.2, 4.3 Hz, 1 H)	4.05 (ddd, *J* = 12.4, 10.1, 4.3 Hz, 1 H)
3.89–3.86 (m, 2 H)	3.90–3.81 (m, 2 H)
3.68 (ddd, *J* = 10.1, 4.8, 1.1 Hz, 1 H)	3.69 (dd, *J* = 10.2, 4.9 Hz, 1 H)
2.71–2.66 (m, 1 H)	2.68 (q, *J* = 7.3, 4.9 Hz, 1 H)
2.57 (ddd, *J* = 12.5, 10.1, 10.1 Hz, 1 H)	2.57 (ddd, *J* = 12.8, 9.8, 9.8 Hz, 1 H)
2.45 (ddd, *J* = 13.5, 3.6, 3.6 Hz, 1 H)	2.45 (ddd, *J* = 13.4, 3.8, 3.8 Hz, 1 H)

Table 2-6 continued

2.33–2.26 (m, 2 H)	2.33-2.27 (m, 2 H)
2.10 (ddd, *J* = 12.7, 12.7, 3.3 Hz, 1 H)	2.10 (ddd, *J* = 12.9, 12.9, 3.3 Hz, 1 H)

Table 2-7. Comparative ^{13}C NMR Data for Microcladallene B (8)

Synthetic (Kim) (125 MHz, $CDCl_3$)[3b]	Synthetic (this work) (125 MHz, $CDCl_3$)
203.1	203.2
135.4	135.4
129.96	129.2
129.10	129.0
119.3	119.3
99.7	99.7
83.1	83.2
80.6	80.6
74.57	74.6
74.54	74.6
69.8	69.8

Table 2-7 continued

48.0	48.0
43.3	43.3
31.3	31.3
30.2	30.2

Table 2-8. Comparative ^{1}H NMR Data for *epi*-Microcladallene B (91)

Synthetic (Kim) (500 MHz, $CDCl_3$)[3b]	Synthetic (this work) (500 MHz, $CDCl_3$)
6.10 (dd, *J* = 5.9, 2.7 Hz, 1 H)	6.10 (dd, *J* = 5.8, 2.7 Hz, 1 H)
5.96 (ddd, *J* = 17.2, 10.5, 6.6 Hz, 1 H)	6.03–5.85 (m, 2 H)
5.90 (ddd, *J* = 10.9, 8.8, 8.8 Hz, 1 H)	
5.81–5.75 (m, 1 H)	5.78 (ddd, *J* = 10.0, 9.5, 6.0 Hz, 1 H)
5.45–5.41 (m, 2 H)	5.45–5.41 (m, 2 H)
5.30 (ddd, *J* = 10.5, 1.3, 0.9 Hz, 1 H)	5.31 (d, *J* = 11.4 Hz, 1 H)
4.84–4.81 (m, 1 H)	4.83 (br s, 1 H)
4.06 (ddd, *J* = 12.4, 10.2, 4.4, Hz, 1 H)	4.06 (ddd, *J* = 12.4, 10.1, 4.3 Hz, 1 H)
3.87 (dd, *J* = 10.2, 6.7 Hz, 1 H)	3.92–3.78 (m, 2 H)

Table 2-8 continued

3.84–3.83 (m, 1 H)	
3.67 (ddd, *J* = 9.8, 4.7, 1.2 Hz, 1 H)	3.70-3.63 (m, 1 H)
2.68–2.63 (m, 1 H)	2.69-2.63 (m, 1 H)
2.57 (ddd, *J* = 12.8, 7.7, 7.7 Hz 1 H)	2.56 (ddd, *J* = 12.8, 9.6, 9.6 Hz, 1 H)
2.49 (ddd, *J* = 13.5, 4.2, 3.5 Hz 1 H)	2.49 (ddd, *J* = 13.4, 3.8, 3.8 Hz, 1 H)
2.33–2.27 (m, 2 H)	2.36–2.26 (m, 2 H)
2.08 (ddd, *J* = 13.3, 12.6, 3.3 Hz 1 H)	2.08 (ddd, *J* = 12.9, 12.9, 3.3 Hz, 1 H)

Table 2-9. Comparative ^{13}C NMR data for *epi*-Microcladallene B (91)

Synthetic (Kim) (125 MHz, $CDCl_3$)[3b]	Synthetic (this work) (125 MHz, $CDCl_3$)
202.6	202.7
135.4	135.4
129.3	129.3
128.7	128.7
119.3	119.3
100.0	100.0

Table 2-9 continued

83.2	83.2
80.6	80.6
74.9	74.9
74.3	74.3
69.8	69.9
48.0	48.0
43.2	43.3
31.7	31.7
30.2	30.2

Alkene 52. To a solution of lactone **48** (0.463 g, 1.10 mmol, 1.0 equiv) in CH_2Cl_2/H_2O (10:1 v/v, 11.0 mL) at 25 °C was added DDQ (0.375 g, 1.65 mmol, 1.5 equiv) and the resultant solution was stirred for 1 h at 25 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous Na_2CO_3 (20 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (30 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with saturated aqueous Na_2CO_3 (50 mL), dried (Na_2SO_4), filtered, and concentrated to give the desired crude alcohol. Pressing forward without any further purification, the so-obtained alcohol (1.10 mmol assumed) was dissolved in CH_2Cl_2 (10.0 mL) and $NaHCO_3$ (0.462 g, 5.50 mmol, 5.0 equiv) and Dess–Martin

periodinane (0.515 g, 1.21 mmol, 1.1 equiv) were added sequentially at 25 °C. The reaction contents were then stirred for 1 h at 25 °C. Upon completion, the reaction mixture was concentrated directly and the resultant residue was purified by flash column chromatography (silica gel, CH_2Cl_2:Et_2O, 20:1) to furnish aldehyde **92** (0.157 g, 48% yield over 2 steps from **48**) as a colorless oil. Given that aldehyde **92** was not stable to storage, it was used immediately in the next step. Thus, to a solution of Julia–Kocienski reagent **93** (0.400 g, 1.58 mmol, 3.0 equiv, prepared according to the literature procedure reported by Zajc and co-workers[48b] with all the spectroscopic data matching that reported in Ref. 48b) in DME (4.0 mL) at –78 °C was slowly added KHMDS (1.42 mL, 1.0 M in THF, 1.42 mmol, 2.7 equiv). The resultant mixture was stirred at –78 °C for 30 min, and then a solution of aldehyde **92** (0.157 g, 0.527 mmol, 1.0 equiv) in DME (2.0 mL) was added in one portion at –78 °C. The resultant mixture was stirred for another 30 min at –78 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (10 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 1:2, followed by hexanes:EtOAc, 6:1) to afford alkene **52** (95.4 mg, 56% yield) as a brown liquid. **52**: R_f = 0.20 (silica gel, hexanes:EtOAc, 6:1); IR (film) ν_{max} 2958, 2930, 2856, 1786, 1464, 1251, 1178, 1159, 1062, 968, 825, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.51–5.28 (m, 2 H), 5.09 (t, *J* = 4.7 Hz, 1 H), 4.74 (t, *J* = 5.5 Hz, 1 H), 4.26 (dt, *J* = 10.7, 5.1 Hz, 1 H), 2.73 (dd, *J* = 18.7, 6.5 Hz, 1 H), 2.61 (d, *J* = 18.8 Hz, 1 H), 2.29 (dd, *J* = 14.0, 4.7 Hz, 1 H), 2.22–2.05 (m, 2 H), 2.04–1.92 (m, 2 H), 1.77 (ddd, *J* = 13.9, 11.0, 4.9 Hz, 1 H), 1.33–1.24 (m, 1 H), 0.95 (t, *J* = 7.4 Hz, 3 H), 0.89 (s, 9 H), –0.01 (s, 3 H), –0.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 132.3, 130.0, 85.2, 80.3, 76.7, 37.3, 36.8, 30.3, 28.3,

27.3, 25.5, 17.3, 13.8, –5.3, –5.5; HRMS (ESI) calcd for $C_{18}H_{32}O_3SiNa$ $[M+Na]^+$ 347.2013, found 347.2016.

Desepilaurallene (5) and ***iso*-desepilaurallene (94)**. Alkene **52** (49.9 mg, 0.154 mmol, 1.0 equiv) was dissolved in toluene (3.0 mL), the reaction contents were cooled to –20 °C, and then solid BDSB[15b] (67.6 mg, 0.123 mmol, 0.8 equiv) was added in a single portion. The reaction contents were then stirred at –20 °C for 1 h. Upon completion, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), warmed to 25 °C, and poured into a separatory funnel. The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were then dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant crude residue by preparative thin-layer chromatography (silica gel, hexanes:EtOAc, 5:1→4:1) afforded an inseparable mixture of desepilaurallene and *iso*-desepilaurallene (**5** and **94**, 38.2 mg, 86% yield, ~3:4, favoring *iso*-desepilaurallene) as white solid. The additional operations denoted below were effected to achieve separation of these two compounds. **5** and **94**: R_f = 0.25 (silica gel, hexanes:EtOAc, 3:1).

Lactol 97 and ***iso*-97**. The mixture of desepilaurallene and iso-desepilaurallene (**5** and **94**, ~3:4, 42.0 mg, 0.146 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (3.0 mL) and cooled to –78 °C. DIBAL-H (0.153 mL, 1.0 M in hexanes, 0.153 mmol, 1.05 equiv) was then added slowly. After stirring at –78 °C for 15 min, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle's salt (6 mL). The resultant biphasic solution was warmed to 25 °C and stirred vigorously at 25 °C for 30 min. The reaction contents were then poured into a separatory funnel, the two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, CH_2Cl_2:Et_2O, 30:1, followed by

hexanes:EtOAc, 3:1→2:1) afforded lactol **97** (17.1 mg, 41% yield, 96% yield based on the amount of **5**) and the lactol ***iso*-97** derived from **94** (22.8 mg, 54% yield, 95% yield based on the amount of **94**), both as white solids. This reaction was performed on a similar scale several times. ***Iso*-97**: R_f= 0.25 (silica gel, CH_2Cl_2:Et_2O, 10:1). **97**: R_f= 0.30 (silica gel, CH_2Cl_2:Et_2O, 10:1).

Desepilaurallene (5). To a solution of 8-membered lactol **97** (17.0 mg, 58.4 μmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 25 °C was added PCC (25.3 mg, 0.117 mmol, 2.0 equiv). The resultant solution was then stirred at 25 °C for 12 h. Upon completion, the reaction contents were filtered directly through a pad of Celite and rinsed with EtOAc (5 mL). After concentrating the filtrate, the resultant residue was purified by flash column chromatography (silica gel, hexanes:Et_2O, 2:1→1:1) to afford desepilaurallene (**5**, 14.5 mg, 85% yield) as a white foam for characterization purposes. **5**: R_f= 0.25 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 3031, 2923, 2850, 1766, 1455, 1285, 1206, 1154, 1033, 994, 896, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.93–5.83 (m, 1 H), 5.81–5.68 (m, 1 H), 4.49 (dd, *J* = 11.7, 4.3 Hz, 1 H), 4.42 (t, *J* = 3.4 Hz, 1 H), 4.16 (dt, *J* = 9.8, 5.0 Hz, 1 H), 4.08 (td, *J* = 8.7, 3.2 Hz, 1 H), 2.83–2.65 (m, 4 H), 2.60–2.45 (m, 2 H), 1.91 (dtt, *J* = 14.8, 7.3, 3.7 Hz, 1 H), 1.73 (dt, *J* = 15.1, 7.6 Hz, 1 H), 1.08 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 129.0, 126.5, 84.2, 79.7, 70.0, 57.8, 37.4, 30.5, 28.1, 28.0, 11.3; HRMS (ESI+APCI) calcd for $C_{12}H_{18}BrO_3$ $[M+H]^+$ 289.0439, found 289.0421.

Table 2-10. Comparative ^1H NMR Data for Desepilaurallene (5)

Natural (Ji) (500 MHz, $CDCl_3$)[21]	Synthetic (this work) (500 MHz, $CDCl_3$)
5.87 (dddd, *J* =11.1, 7.0, 7.0, 1.5 Hz, 1 H)	5.93–5.83 (m, 1 H)
5.76 (ddd, *J* =11.1, 7.3, 7.3 Hz, 1 H)	5.81–5.68 (m, 1 H)

Table 2-10 continued

4.50 (ddd, *J* =11.8, 4.1, 3.8 Hz, 1 H)	4.49 (dd, *J* = 11.7, 4.3 Hz, 1 H)
4.43 (ddd, *J* =6.3, 3.8, 2.3 Hz, 1 H)	4.42 (dd, *J* = 3.4, 3.4 Hz, 1 H)
4.17 (ddd, *J* =8.6, 5.8, 4.4 Hz, 1 H)	4.16 (ddd, *J* = 9.8, 5.0, 5.0 Hz, 1 H)
4.08 (td, *J* =8.6, 3.0 Hz, 1 H)	4.08 (td, *J* = 8.7, 3.2 Hz, 1 H)
2.77 (m, 2 H)	2.83–2.65 (m, 4 H)
2.75 (dd, *J* =17.4, 6.3 Hz, 2 H)	
2.54 (m, 2 H)	2.60–2.45 (m, 2 H)
1.91 (dqd, *J* =14.9, 7.2, 3.0 Hz, 1 H)	1.91 (dtt, *J* = 14.8, 7.3, 3.7 Hz, 1 H)
1.73 (dq, *J* =14.9, 7.2 Hz, 1 H)	1.73 (dt, *J* = 15.1, 7.6 Hz, 1 H)
1.08 (t, *J* =7.2 Hz, 1 H)	1.08 (t, *J* = 7.2 Hz, 3 H)

Table 2-11. Comparative ^{13}C NMR Data for Desepilaurallene (5)

Natural (Ji) (125 MHz, $CDCl_3$)[21]	Synthetic (this work) (125 MHz, $CDCl_3$)
174.7	174.6
129.0	129.0
126.5	126.5

Table 2-11 continued

84.3	84.2
79.7	79.7
70.0	70.0
57.8	57.8
37.4	37.4
30.5	30.5
28.1	28.1
28.0	28.0
11.3	11.3

***iso*-desepilaurallene 54**. To a solution of 8-membered lactol ***iso*-97** (25.0 mg, 85.9 μmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 25 °C was added PCC (37.2 mg, 0.172 mmol, 2.0 equiv). The resultant solution was then stirred at 25 °C for 12 h. Upon completion, the reaction contents were filtered directly through a pad of Celite and rinsed with EtOAc (5 mL). After concentrating the filtrate, the resultant residue was purified by flash column chromatography (silica gel, hexanes:Et_2O, 2:1→1:1) to give a pure sample of *iso*-desepilaurallene (**94**, 17.1 mg, 69% yield) as a white foam for characterization purposes. **94**: R_f = 0.25 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 3024, 2968, 2933, 2852, 1781, 1454, 1405, 1290, 1202, 1154, 1035, 928, 762, 710 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.04–5.84 (m, 1 H), 5.80–5.67 (m, 1 H), 4.45 (dt, *J* = 11.9, 4.2 Hz, 1

H), 4.12 (t, J = 4.8 Hz, 1 H), 3.96–3.86 (m, 1 H), 3.48 (dd, J = 10.1, 5.0 Hz, 1 H), 2.90–2.64 (m, 3 H), 2.51 (dt, J = 11.7, 6.3 Hz, 2 H), 2.36 (dd, J = 14.0, 8.5 Hz, 1 H), 1.93–1.82 (m, 2 H), 1.05 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.4, 130.9, 126.5, 88.7, 85.1, 80.0, 61.5, 37.8, 32.3, 27.6, 26.3, 12.2; HRMS (ESI+APCI) calcd for $C_{12}H_{18}BrO_3$ $[M+H]^+$ 289.0439, found 289.0425.

Prelaureatin (4). To a solution of Julia–Kocienski reagent **88** (58.8 mg, 0.190 mmol, 5.0 equiv; prepared according to the literature procedure reported by Zajc and co-workers[46b] with all the spectroscopic data matching that reported in Ref. 46b) in THF (2.0 mL) at –20 °C was added KHMDS (0.171 mL, 1.0 M in THF, 0.171 mmol, 4.5 equiv) dropwise. The resultant dark colored solution was stirred at –20 °C for 30 min, and then a solution of lactol **97** (11.1 mg, 38.6 μmol, 1.0 equiv) in THF (1.0 mL) was added at –20 °C. The reaction contents were then allowed to warm up to 0 °C and stirred for an additional 10 min at 0 °C. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:Et_2O, 10:1→5:1) provided a sample of prelaureatin (**4**) containing a small amount of impurities (~5%). This material was further purified by preparative thin layer chromatography (silica gel, hexanes:EtOAc, 5:1) to furnish the desired prelaureatin **(4)** (4.4 mg, 37% yield) as a colorless oil. **4**: R_f = 0.30 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 3461 (br), 3291, 3024, 2970, 2927, 2853, 1732, 1651, 1621, 1557, 1455, 1393, 1280, 1204, 1065, 907, 801, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.09 (dt, J = 10.8, 7.7 Hz, 1 H), 5.93–5.70 (m, 2 H), 5.64–5.52 (m, 1 H), 4.09 (ddd, J = 10.1, 7.8, 3.0 Hz, 1 H), 3.98 (dd, J = 8.8, 5.3 Hz, 1 H), 3.83–3.63 (m, 2 H), 3.16

(d, J = 2.6 Hz, 1 H), 2.70 (dt, J = 13.7, 8.2 Hz, 1 H), 2.65–2.48 (m, 3 H), 2.39 (ddd, J = 14.5, 12.1, 8.9 Hz, 1 H), 2.27–2.16 (m, 2 H), 1.81 (ddq, J = 14.6, 9.8, 7.2 Hz, 1 H), 1.11 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 130.6, 128.0, 110.9, 82.4, 80.3, 79.6, 74.0, 71.9, 60.2, 34.7, 32.9, 30.1, 29.8, 12.1; HRMS (ESI+APCI) calcd for $[M+Na]^+$ 335.0617, found 335.0593.

Table 2-12. Comparative ^{1}H NMR Data for Prelaureatin (4)

Natural (Murai)[18] (400 MHz, $CDCl_3$)	Synthetic (Crimmins)[4] (400 MHz, $CDCl_3$)	Synthetic (this work) (500 MHz, $CDCl_3$)
6.09 (dt, J = 11, 8 Hz, 1 H)	6.07 (ddt, J = 10.8, 8.0, 0.8 Hz, 1 H)	6.09 (dt, J = 10.8, 7.7 Hz, 1 H)
5.81 (m, 2 H)	5.87–5.72 (m, 2 H)	5.93–5.70 (m, 2 H)
5.58 (dq, J = 11, 1 Hz, 1 H)	5.56 (dq, J = 10.8, 1.2 Hz, 1 H)	5.64–5.52 (m, 1 H)
4.09 (ddd, J = 9.3, 7.8, 3.9 Hz, 1 H)	4.07 (ddd, J = 9.6, 7.6, 2.8 Hz, 1 H)	4.09 (ddd, J = 10.1, 7.8, 3.0 Hz, 1 H)
3.98 (dd, J = 7.8, 5.4 Hz, 1 H)	3.96 (dd, J = 8.8, 5.2 Hz, 1 H)	3.98 (dd, J = 8.8, 5.3 Hz, 1 H)
3.75 (br d, J = 5.4 Hz, 1 H)	3.74 (ddd, J = 10.8, 6.8, 1.6 Hz, 1 H)	3.83–3.63 (m, 2 H)
3.70 (ddd, J = 10.7, 7.8, 2.0 Hz, 1 H)	3.69 (ddd, J = 12.0, 8.0, 2.0 Hz, 1 H)	
3.16 (d, J = 1 Hz, 1 H)	3.14 (dd, J = 2.4, 0.8 Hz, 1 H)	3.16 (d, J = 2.6 Hz, 1 H)
2.74–2.48 (m, 4 H)	2.72–2.47 (m, 4 H)	2.70 (dt, J = 13.7, 8.2 Hz, 1 H)

Table 2-12 continued

		2.65–2.48 (m, 3 H)
2.40 (ddd, *J* = 14.2, 12.2, 8.8 Hz, 1 H)	2.37 (ddd, *J* = 14.2, 12.0, 8.4 Hz, 1 H)	2.39 (ddd, *J* = 14.5, 12.1, 8.9 Hz, 1 H)
2.23 (m, 2 H)	2.27–2.16 (m, 2 H)	2.27–2.16 (m, 2 H)
1.81 (ddq, *J* = 16.6, 9.3, 7.3 Hz, 1 H)	1.79 (ddq, *J* = 22.3, 9.5, 7.4 Hz, 1 H)	1.81 (ddq, *J* = 14.6, 9.8, 7.2 Hz, 1 H)
1.11 (t, *J* = 7.3 Hz, 3 H)	1.08 (t, *J* = 7.2 Hz, 3 H)	1.11 (t, *J* = 7.2 Hz, 3 H)

Table 2-13. Comparative ^{13}C NMR data for Prelaureatin (4)

Synthetic (Crimmins) (400 MHz, $CDCl_3$)[4]	Synthetic (this work) (500 MHz, $CDCl_3$)
141.1	141.1
130.5	130.6
127.9	128.0
110.9	110.9
82.4	82.4
80.3	80.3
79.5	79.6

Table 2-13 continued

73.9	74.0
71.9	71.9
60.2	60.2
34.7	34.7
32.9	32.9
30.1	30.1
29.8	29.8
12.1	12.1

(*E*)-Prelaureatin (22). To a solution of Wittig salt **60** (46.8 mg, 0.105 mmol, 3.0 equiv, prepared according to the literature procedure reported by Diederich and co-workers[28] with all the spectroscopic data matching that reported in Ref. 28) in THF (1.0 mL) at 0 °C was added *n*-BuLi (59.0 μL, 1.6 M in hexanes, 94.4 μmol, 2.7 equiv) dropwise. The resultant dark suspension was stirred at 0 °C for 30 min, before a solution of freshly prepared lactol **97** (10.0 mg, 34.3 μmol, 1.0 equiv) in THF (1.0 mL) was added at 0 °C. The resultant reaction mixture was stirred at 0 °C for 2 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue

by flash column chromatography (silica gel, hexanes:Et_2O, 10:1→5:1) afforded TMS-protected enyne (11.2 mg, 85% yield) as a brown liquid. Pressing forward, the so-prepared enyne (11.2 mg, 29.2 μmol, 1.0 equiv) was dissolved in THF (1.0 mL) and cooled to 0 °C. TBAF (32.1 μL, 1.0 M in THF, 32.1 μmol, 1.1 equiv) was then added at 0 °C, and the reaction was stirred for an additional 10 min at 0 °C. Upon completion, saturated aqueous NH_4Cl (5 mL) was carefully added to quench the reaction, and the mixture was poured into a separatory funnel, diluting with CH_2Cl_2 (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:Et_2O, 10:1→5:1) yielded (*E*)-prelaureatin **(22**, 7.7 mg, 84% yield) as a colorless oil. **22**: R_f = 0.18 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 3445 (br), 3294, 3024, 2930, 2852, 1715, 1645, 1633, 1455, 1394, 1280, 1063, 960, 908 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (dt, *J* = 15.6, 7.6 Hz, 1 H), 5.90–5.73 (m, 2 H), 5.56 (dd, *J* = 15.9, 1.8 Hz, 1 H), 4.20–3.94 (m, 2 H), 3.75–3.70 (m, 1 H), 3.68 (q, *J* = 6.5 Hz, 1 H), 2.83 (d, *J* = 2.4 Hz, 1 H), 2.52–2.42 (m, 4 H), 2.38–2.30 (m, 1 H), 2.22 (dd, *J* = 14.1, 6.8 Hz, 1 H), 2.10 (ddd, *J* = 14.6, 7.3, 3.3 Hz, 1 H), 1.78 (ddt, *J* = 14.3, 9.6, 7.2 Hz, 1 H), 1.09 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 130.4, 127.9, 111.8, 82.0, 79.3, 76.6, 74.0, 71.6, 61.2, 37.8, 32.9, 30.2, 29.2, 12.2; HRMS (APCI) calcd for $C_{15}H_{22}BrO_2$ $[M+H]^+$ 313.0798, found 313.0800.

Table 2-14. Comparative ^1H NMR Data for (*E*)-Prelaureatin (22)

Synthetic (Crimmins) (400 MHz, $CDCl_3$)[4]	Synthetic (this work) (500 MHz, $CDCl_3$)
6.21 (dt, *J* =16.0, 7.6 Hz, 1 H)	6.24 (dt, *J* = 15.6, 7.6 Hz, 1 H)

Table 2-14 continued

5.86–5.71 (m, 2 H)	5.90–5.73 (m, 2 H)
5.58 (dq, *J* =15.8, 1.2 Hz, 1 H)	5.56 (dd, *J* = 15.9, 1.8 Hz, 1 H)
4.04–3.98 (m, 2 H)	4.20–3.94 (m, 2 H)
3.71 (ddd, *J* =11.6, 6.4, 1.2 Hz, 1 H)	3.75–3.70 (m, 1 H)
3.66 (ddd, *J* =7.9, 6.4, 6.4 Hz, 1 H)	3.68 (q, *J* = 6.5 Hz, 1 H)
2.81 (d, *J* =2.4 Hz, 1 H)	2.83 (d, *J* = 2.4 Hz, 1 H)
2.53–2.41 (m, 4 H)	2.52–2.42 (m, 4 H)
2.30 (dddd, *J* =13.8, 7.0, 5.2, 1.6 Hz, 1 H)	2.38–2.30 (m, 1 H)
2.22–2.16 (m, 2 H)	2.22 (dd, *J* = 14.1, 6.8 Hz, 1 H)
2.07 (ddq, *J* =14.7, 7.4, 3.6 Hz, 1 H)	2.10 (ddd, *J* = 14.6, 7.3, 3.3 Hz, 1 H)
1.76 (ddq, *J* =22.0, 9.6, 7.2 Hz, 1 H)	1.78 (ddt, *J* = 14.3, 9.6, 7.2 Hz, 1 H)
1.07 (t, *J* =7.2 Hz, 3 H)	1.09 (t, *J* = 7.3 Hz, 3 H)

Table 2-15. Comparative ^{13}C NMR Data for (*E*)-Prelaureatin (22)

Synthetic (Crimmins) (400 MHz, $CDCl_3$)[4]	Synthetic (this work) (125 MHz, $CDCl_3$)
142.0	142.0

Table 2-15 continued

130.4	130.4
127.9	127.9
111.7	111.8
82.0	82.0
79.2	79.3
76.6	76.6
73.9	74.0
71.5	71.6
61.1	61.2
37.8	37.8
32.9	32.9
30.1	30.2
29.2	29.2
12.2	12.2

Laurallene (6). To a solution of (*E*)-prelaureatin (**22**, 6.0 mg, 19.5 μmol, 1.0 equiv) in CH_2Cl_2 (0.60 mL) at 25 °C was added TBCO (90% purity, 11.4 mg, 25.0 μmol, 1.3 equiv), and the resultant reaction mixture was stirred for 12 h at 25 °C. Upon completion, the reaction contents

were quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL), poured into a separatory funnel, and diluted with CH_2Cl_2 (5 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:CH_2Cl_2, 2:1→1:1) afforded an inseparable mixture of a major by-product tentatively assigned as a diastereomer of laurallene along with laurallene (**6**, 4.7 mg combined, 63% yield, ~1:1 ratio) as a colorless oil. **6** and its diastereomer: R_f= 0.45 (silica gel, hexanes:CH_2Cl_2, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.10–6.06 (m, 1 H), 5.86–5.73 (m, 3 H), 5.48–5.42 (m, 1 H), 4.90–4.81 (m, 1 H), 4.29–4.21 (m, 1 H), 4.16–4.06 (m, 2 H), 2.77–2.67 (m, 1 H), 2.67–2.48 (m, 2 H), 2.38–2.28 (m, 1 H), 2.21–1.97 (m, 3 H), 1.83–1.74 (m, 1 H), 1.13–1.06 (m, 3 H); Laurallene **(6)**: ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 129.5, 127.4, 102.7, 82.9, 79.8, 74.3, 73.5 73.4, 57.9, 39.4, 30.54, 29.4, 28.1, 11.2; Diastereomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 129.5, 127.35, 102.2, 82.8, 79.9, 74.0, 73.8, 73.6, 57.88, 39.1, 30.52, 29.5, 28.1, 11.2.

Ester 112. To a solution of **110** (2.00 mL, 2.03 g, 13.2 mmol, 1.0 equiv) in THF (26.0 mL) at –78 °C was added *n*-BuLi (5.54 mL, 2.5 M in hexanes, 13.86 mmol, 1.05 equiv). After stirring the resultant solution for 10 min at –78 °C, the reaction contents were warmed to 0 °C and then CuBr (2.05 g, 14.3 mmol, 1.1 equiv) was added. The resultant green suspension was stirred vigorously at 0 °C for 1 h and then **111** (6.94 g, 32.4 mmol, 2.5 equiv) in added in a single portion. The resultant mixture was then warmed to 25 °C and stirred for an additional 4 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (50 mL), diluted with CH_2Cl_2 (50 ml), and transferred into a separatory funnel. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column

chromatography (silica gel, hexanes:Et_2O, 30:1→ 20:1→10:1) to afford the bromide minterediate (1.24 g, 33% yield) as a colorless liquid. [Note: because this material was not stable, it was subjected to the next step immediately]. Pressing forward, the so-obtained bromide (1.24 g, 4.32 mmol, 1.0 equiv) was dissolved in MeOH (8.0 ml) at 25 °C, transferred into a Parr bomb, and then $KHCO_3$ (0.475 g, 4.75 mmol, 1.1 equiv) and $Pd(PPh_3)_4$ (0.250 mg, 0.216 mmol, 0.05 equiv) were added sequentially. After the bomb was quickly assembled, it was purged three times with CO (20 atm) and the pressure of CO was finally brought to 75 atm. The resultant reaction mixture was then stirred at 25 °C for 24 h. Upon completion, the CO pressure was released and the reaction contents were transferred into a round-bottomed flask and concentrated directly. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) to afford ester **112** (0.873 g, 76% yield) as a colorless oil. **112**: R_f= 0.15 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 2947, 2873, 1741, 1436, 1353, 1258, 1201, 1070, 1034, 970 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.86–5.73 (m, 1 H), 5.58–5.51 (m, 1 H), 4.70–4.57 (m, 1 H), 3.87 (ddd, *J* = 11.3, 8.2, 3.2 Hz, 1 H), 3.80 (dt, *J* = 9.6, 7.1 Hz, 1 H), 3.68 (s, 3 H), 3.58–3.45 (m, 2 H), 3.06 (dd, *J* = 7.1, 1.4 Hz, 2 H), 2.95–2.82 (m, 2 H), 2.54–2.46 (m, 2 H), 1.87–1.77 (m, 1 H), 1.77–1.64 (m, 1 H), 1.62–1.47 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 129.1, 123.2, 98.7, 79.2, 77.8, 66.1, 62.2, 51.8, 37.5, 30.6, 25.4, 22.0, 20.2, 19.4; HRMS (ESI+APCI): No molecular ion peak was observed.

Alcohol 113. To a solution of ester **112** (0.873 g, 3.28 mmol, 1.0 equiv) in *t*-BuOH/H_2O (1:1 v/v, 32.0 mL) at 0 °C was sequentially added methanesulfonamide (0.343 g, 3.61 mmol, 1.1 equiv) and AD-mix-α (4.92 g). The resultant yellow suspension was then stirred at 0 °C for 36 h. Upon completion, the reaction contents were quenched by the addition of brine (50 mL), diluted with EtOAc (50 mL), and transferred into a separatory funnel. The two phases were separated and

the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic layers were then dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 1:1) to yield the desired lactone (0.820 g, 94% yield) as a cloudy liquid containing ~10% of an inseparable side-product which could be removed during the purification procedure in the subsequent synthetic step. Thus, pressing forward, to a solution of the so-prepared lactone (0.820 g, 3.08 mmol assumed, 1.0 equiv) in CH_2Cl_2 (31.0 mL) at 25 °C was sequentially added TBDPSCl (1.60 mL, 1.69 g, 6.16 mmol, 2.0 equiv) and imidazole (0.838 g, 12.3 mmol, 4.0 equiv). The resultant reaction mixture was stirred at 25 °C for 6 h. Upon completion, the reaction contents were concentrated directly. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) afforded the desired alcohol (1.20 g, 77% yield) as a colorless oil containing ~5% of an inseparable side-product which could be removed during the purification procedure in the subsequent synthetic step. Pressing forward, to a solution of so-obtained alcohol (1.20 g, 2.37 mmol assumed, 1.0 equiv) in MeOH (24.0 mL) at 25 °C was added *p*-TsOH•H_2O (45.0 mg, 0.237 mmol, 0.10 equiv). The resultant reaction solution was stirred at 25 °C for 3 h. Next, Et_3N (66.0 μL, 47.9 mg, 0.474 mmol, 0.20 equiv) was added, and the reaction contents were concentrated directly. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 3:1→2:1) to afford alcohol **113** (0.650 g, 47% yield over 3 steps from **112**) as a colorless oil. **113**: R_f = 0.30 (silica gel, hexanes:EtOAc, 1:1); IR (film) ν_{max} 3437 (br), 3071, 3049, 2999, 2931, 2858, 1781, 1472, 1428, 1202, 1153, 1112, 1037, 980, 703, 622 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 19.4, 7.9 Hz, 4 H), 7.50–7.37 (m, *J* = 28.1, 7.2 Hz, 6 H), 4.58 (brs, 1 H), 4.46–4.30 (m, 1 H), 3.68 (brs, 2 H), 2.81 (brs, 2 H), 2.55–2.32 (m, 4 H), 1.09 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 135.8, 135.7, 132.9, 132.2, 130.3, 130.2, 128.0, 82.3, 79.4, 69.9, 61.1, 38.5, 26.8, 23.2, 19.5, 19.3; HRMS (ESI) calcd

for $C_{50}H_{61}O_8Si_2$ $[2M+H]^+$ 845.3899, found 845.3894; $[\alpha]_D^{20}$ = –11.6° (c = 1.6, acetone). The enantiopurity was determined using chiral HPLC (AD-H column, 4.6 × 25 mm, hexanes/i-PrOH, 9:1, 1 mL/min, UV detector at 215 nm) tR,minor = 12.55 min, tR,major = 10.97 min, ee = 90%.

Alcohol 115. To a solution of alcohol **113** (0.650 g, 1.54 mmol, 1.0 equiv) in CH_2Cl_2 (15.0 mL) at 0 °C was sequentially added Et_3N (0.320 mL, 0.233 g, 2.31 mmol, 1.5 equiv) and chloro(dimethyl)vinylsilane (0.255 mL, 0.223 g, 1.85 mmol, 1.2 equiv). The resultant reaction solution was stirred at 0 °C for 30 min. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (30 mL), diluted with CH_2Cl_2 (30 ml), and transferred into a separatory funnel. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude material was purified by flash column chromatography (silica gel, hexanes:EtOEt, 10:1) to yield DMVS-protected alcohol **114** (0.685 g, 88% yield) as a colorless liquid, which was used immediately for the next step. Pressing forward, to the solution of the so-obtained **114** (0.685 g, 1.35 mmol, 1.0 equiv) in THF (14.0 mL) at 25 °C was sequentially added TBSH (0.336 mL, 0.235 g, 2.02 mmol, 1.5 equiv) and Karstedt's catalyst[58] (0.270 mL, 0.10 M in xylenes, 27.0 μmol, 0.02 equiv). The resultant colorless solution was stirred then warmed to 40 °C and stirred at that temperature for 2 h. Upon completion, the reaction mixture was cooled to 0 °C and a mixture of TBAF (3.00 mL, 1.0 M in THF, 3.00 mmol, 2.2 equiv) and AcOH (0.171 mL, 0.180 g, 3.00 mmol, 2.2 equiv) was added. The resultant reaction solution was then warmed to 25 °C and stirred at the same temperature for an additional 3 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (20 mL), diluted with EtOAc (20 mL), and transferred into a separatory funnel. The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried (Na_2SO_4),

filtered, and concentrated. The crude material was purified by flash column chromatography (silica gel, EtOAc) to afford alcohol **115** (0.384 g, 95% yield) as a colorless liquid. **115**: R_f = 0.50 (silica gel, EtOAc); IR (film) ν_{max} 3400 (br), 2953, 2928, 2856, 1766, 1612, 1471, 1408, 1360, 1249, 1161, 1038, 824, 769 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (dd, *J* = 9.0, 5.2 Hz, 1 H), 4.49–4.43 (m, 1 H), 4.41 (dd, *J* = 5.4, 3.1 Hz, 1 H), 4.31 (brs, 1 H), 3.75–3.67 (m, 1 H), 3.65–3.55 (m, 1 H), 2.87 (dt, *J* = 17.1, 8.6 Hz, 1 H), 2.71–2.60 (m, 2 H), 2.52 (d, *J* = 17.5 Hz, 1 H), 2.40–2.32 (m, 1 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 139.1, 137.3, 84.2, 68.4, 61.6, 39.1, 33.2, 28.1, 26.9, 17.3, –5.2, –5.7; HRMS (APCI) calcd for $C_{15}H_{28}O_4SiNa$ $[M+Na]^+$ 323.1649, found 323.1651; $[\alpha]_D^{20}$ = – 4.4° (c = 1.4, acetone).

Lactone 107. To a solution of **115** (0.274 g, 0.913 mmol, 1.0 equiv) in $MeNO_2$ (18.0 mL) at 0 °C was added $Br(coll)_2PF_6$ (0.511 g, 1.10 mmol, 1.2 equiv; prepared according to the literature procedure reported by Rousseau and co-workers[32] with all spectroscopic data matching that reported in Ref. 32). The resultant reaction solution was stirred at 0 °C for 30 min. Upon completion, the reaction contents were diluted with CH_2Cl_2 (30 mL) and quenched by the addition of saturated aqueous $KHSO_4$ (18 mL). The resultant biphasic solution was stirred vigorously at 25 °C for 30 min and then the reaction contents were transferred into a separatory funnel. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the resultant residue by flash column chromatography (silica gel, hexanes:EtOAc, 1:1) afforded bicyclic lactone (0.315 g, 92% yield) as a yellow solid containing ~5% of an inseparable side-product which could be removed during the purification procedure in the subsequent synthetic step. Pressing forward, to a solution of the so-obtained bicyclic lactone (0.315 g, 0.833 mmol assumed, 1.0 equiv) in $PhCF_3$ (5.6 mL) at 0 °C was sequentially added PMB reagent **116** (0.581 g, 2.08

mmol, 2.5 equiv; prepared according to the literature procedure reported by Dudley and co-workers[59] with all spectroscopic data matching that reported in Ref. 59), MgO (0.100 g, 2.50 mmol, 3.0 equiv) and MeOTf (0.100 mL, 0.150 g, 0.914 mmol, 1.1 equiv). The resultant yellow reaction solution was then warmed to 25 °C and stirred for 4 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (10 mL), diluted with CH_2Cl_2 (10 mL), and transferred into a separatory funnel. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to afford lactone 107 (0.282 g, 62% yield over 2 steps from **73**) as a colorless liquid. **107**: R_f= 0.25 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 2959, 2932, 2858, 1788, 1612, 1513, 1466, 1249, 1179, 1066, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2 H), 6.88 (d, *J* = 6.9 Hz, 2 H), 5.04 (s, 1 H), 4.79 (s, 1 H), 4.44 (s, 2 H), 4.40–4.25 (m, 1 H), 3.81 (s, 3 H), 3.79–3.65 (m, 2 H), 2.83–2.59 (m, 2 H), 2.53–2.31 (m, 3 H), 2.28–2.18 (m, 1 H), 0.98 (s, 9 H), 0.21 (s, 3 H), 0.18 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 159.3, 130.5, 129.4, 113.8, 84.6, 83.8, 78.5, 72.7, 69.2, 64.9, 55.3, 38.6, 37.4, 37.1, 28.5, 19.4, –3.9, –4.2; HRMS (ESI+APCI): No molecular ion peak was observed; $[\alpha]_D^{20}$ = – 2.9° (c = 1.1, acetone).

Lactone 48. To the solution of lactone **66** (0.242 g, 0.486 mmol, 1.0 equiv) in toluene (5.0 mL) at –78 °C was sequentially added *n*-Bu_3SnH (0.197 mL, 0.213 g, 0.729 mmol, 1.5 equiv) and Et_3B (49.0 μL, 1.0 M in THF, 49.0 μmol, 0.10 equiv). The reaction solution was then purged by direct bubbling with a balloon containing air for 5 min and the reaction mixture was left to stir at –78 °C for 30 min. Upon completion, the reaction contents were concentrated directly. The resultant residue was purified by flash column chromatography (silica gel, CH_2Cl_2:Et_2O, 40:1→20:1) to afford lactone **48** (96.1 mg, 47% yield) and **117** (48.0 mg, 23% yield) as a colorless

oil. **48**: R_f = 0.20 (silica gel, CH_2Cl_2:Et_2O, 40:1); all spectroscopic data were in full agreement with the racemic compound reported above; $[\alpha]_D^{20}$ = +24.5° (c = 1.1, acetone). The enantiopurity was determined using chiral HPLC (AD-H column, 4.6 × 25 mm, hexanes/i-PrOH, 9:1, 1 mL/min, UV detector at 254 nm) tR,minor = 17.82 min, tR,major = 15.17 min, ee = 88%. **117**: R_f = 0.25 (silica gel, CH_2Cl_2:Et_2O, 40:1); IR (film) ν_{max} 2953, 2931, 2855, 1790, 1612, 1513, 1465, 1361, 1248, 1176, 1061, 839 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28–7.23 (m, 2 H), 6.88 (d, *J* = 8.2 Hz, 2 H), 5.08 (t, *J* = 5.2 Hz, 1 H), 4.73 (t, *J* = 6.1 Hz, 1 H), 4.42 (s, 2 H), 4.28–4.18 (m, 1 H), 3.81 (s, 3 H), 3.55–3.30 (m, 1 H), 2.73 (dd, *J* = 19.0, 6.8 Hz, 1 H), 2.58 (d, *J* = 18.6 Hz, 1 H), 2.26–2.14 (m, 1 H), 1.86–1.74 (m, 2 H), 1.73–1.62 (m, 1 H), 0.97–0.91 (m, 1 H), 0.89 (s, 9 H), 0.01 (s, 3 H), –0.02 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 159.2, 130.6, 129.2, 113.8, 84.9, 79.6, 76.9, 72.6, 71.1, 55.3, 37.7, 36.6, 27.2, 26.5, 23.6, 17.5, –5.4, –5.7; HRMS (ESI) calcd for $C_{46}H_{72}O_{10}Si_2Na$ $[2M+Na]^+$ 863.4556, found 863.4526; $[\alpha]_D^{20}$ = +9.3° (c = 1.0, acetone).

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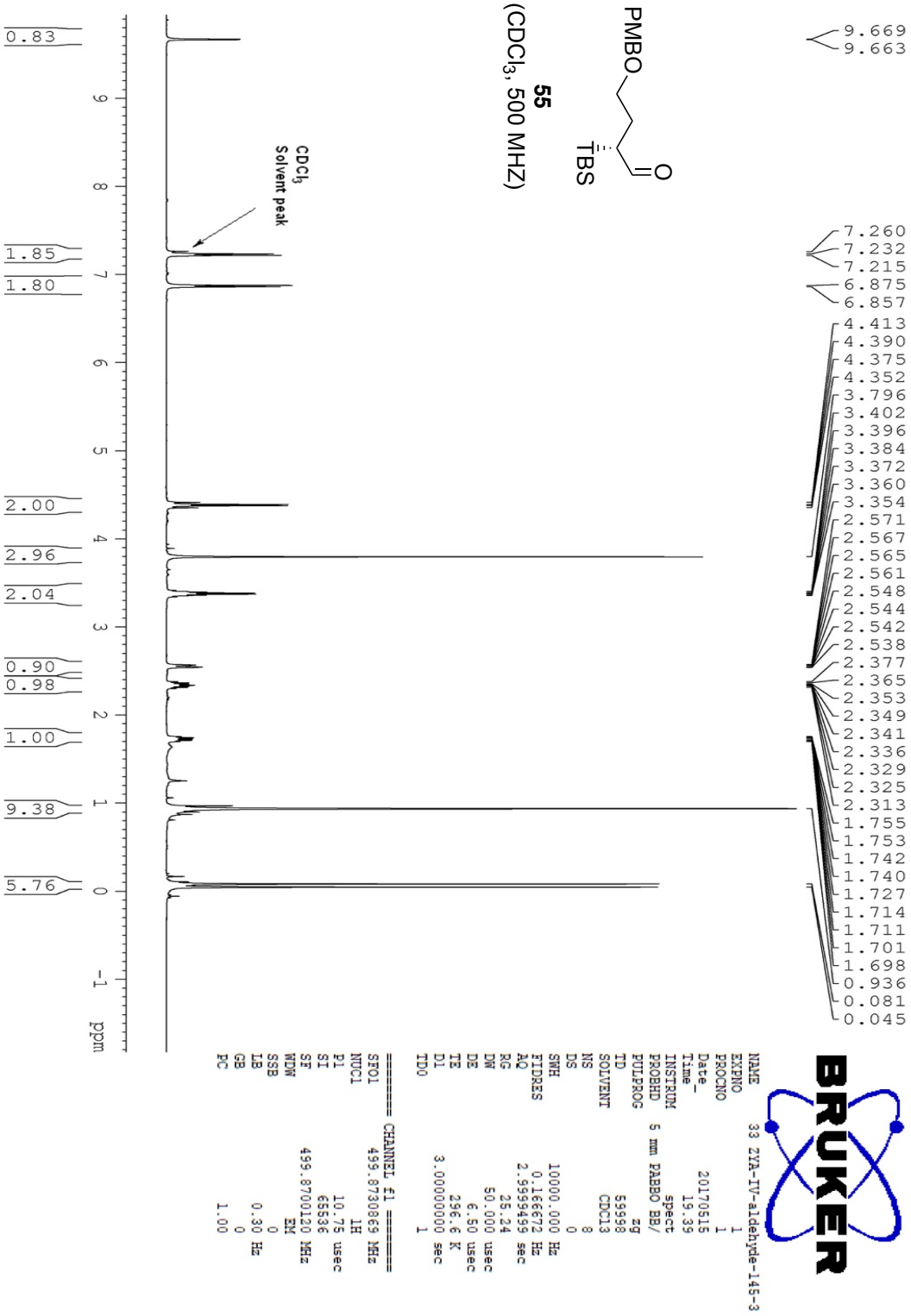
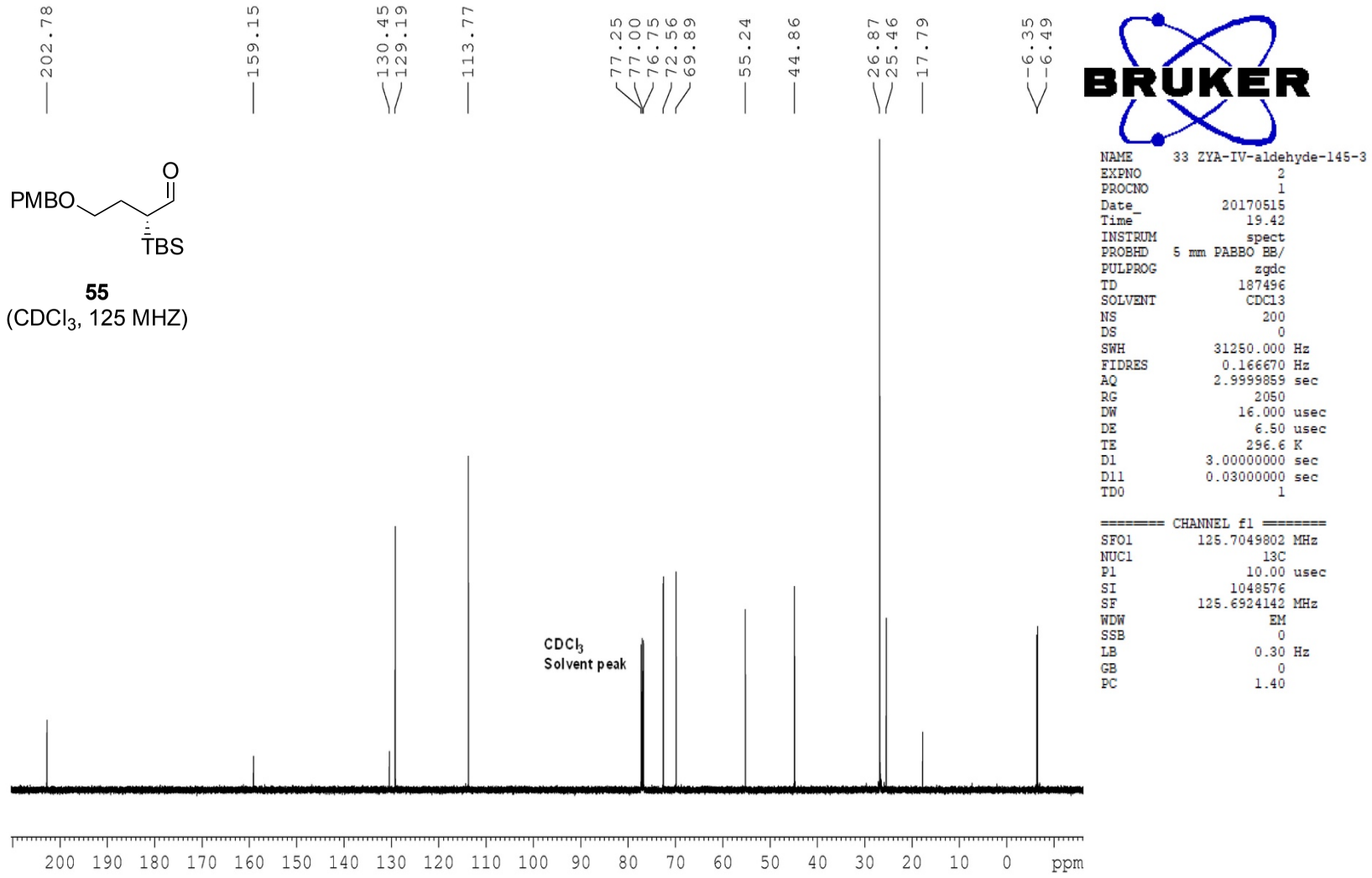
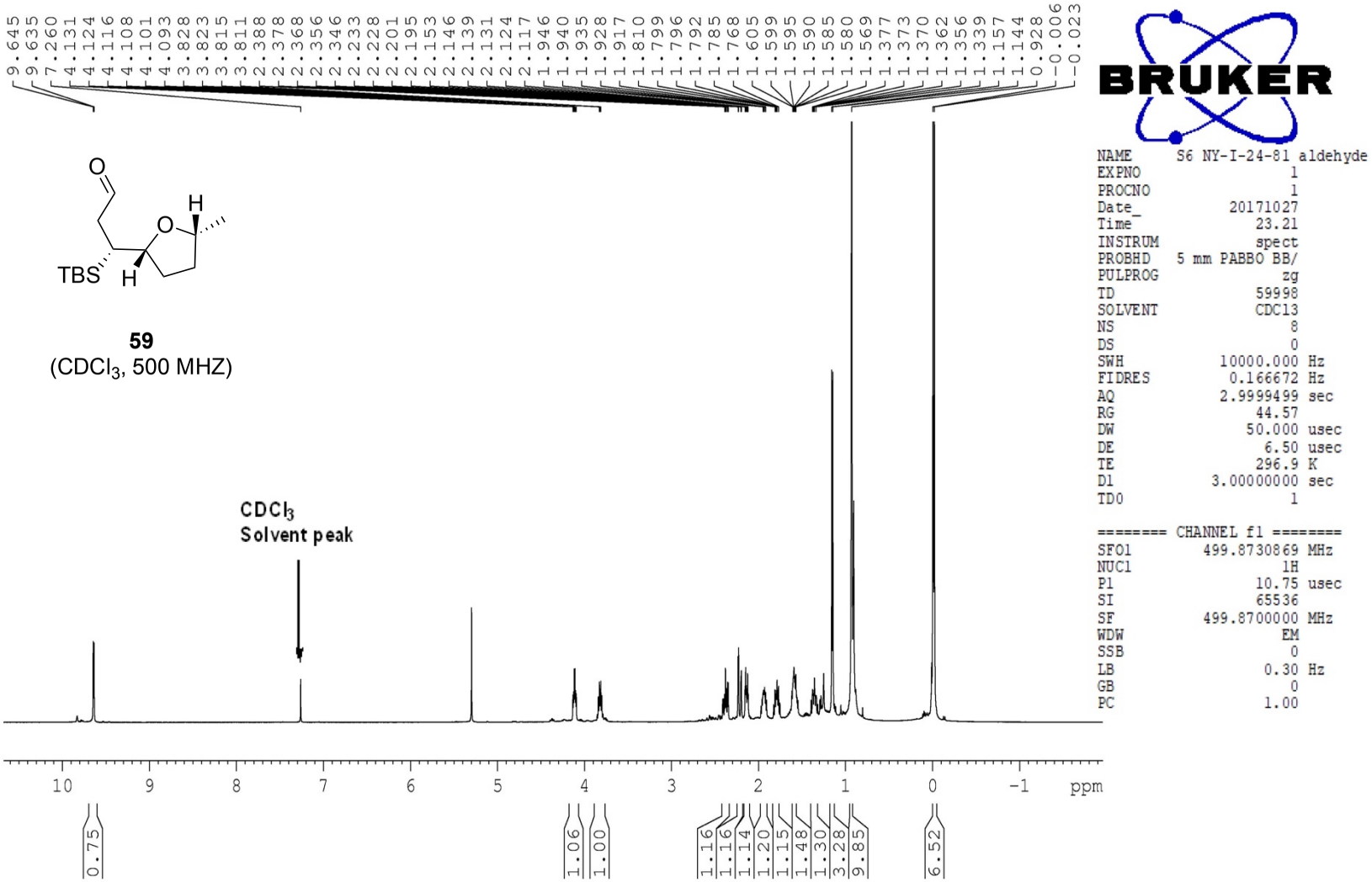
2.6 NMR Spectra of Selected Intermediates and HPLC Information





BRUKER

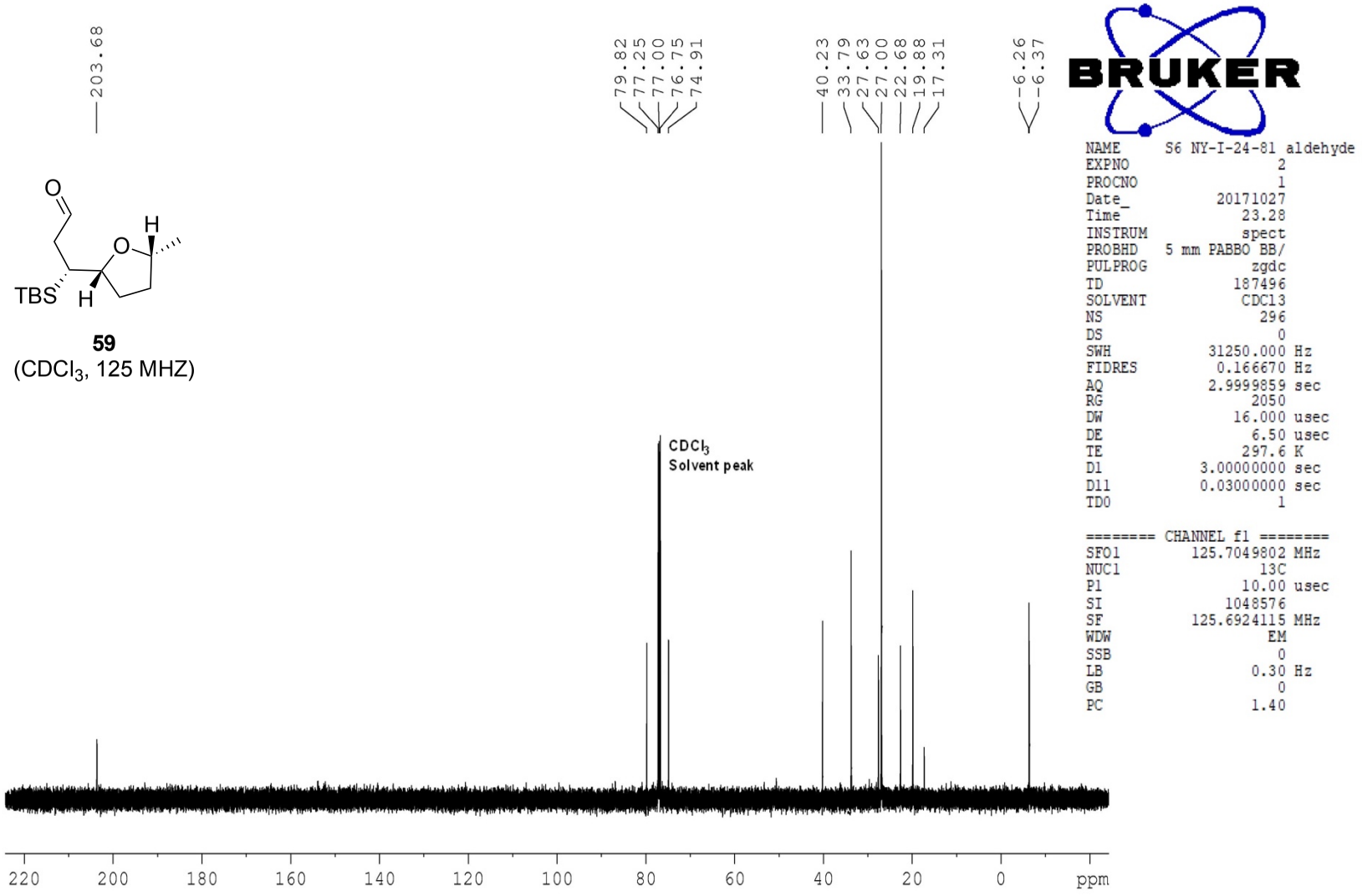
NAME	33 ZYA-IV-aldehyde-145-3
EXPNO	2
PROCNO	1
Date_	20170515
Time	19.42
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	200
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.6 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924142 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



59
($CDCl_3$, 500 MHZ)

BRUKER

NAME	S6 NY-I-24-81 aldehyde
EXPNO	1
PROCNO	1
Date_	20171027
Time	23.21
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	44.57
DW	50.000 usec
DE	6.50 usec
TE	296.9 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



59
($CDCl_3$, 125 MHZ)

```
NAME        S6 NY-I-24-81 aldehyde
EXPNO                    2
PROCNO                   1
Date_             20171027
Time                23.28
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG              zgdc
TD                 187496
SOLVENT             CDCl3
NS                    296
DS                      0
SWH             31250.000 Hz
FIDRES          0.166670 Hz
AQ              2.9999859 sec
RG                   2050
DW                 16.000 usec
DE                  6.50 usec
TE                 297.6 K
D1              3.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1          125.7049802 MHz
NUC1                   13C
P1                  10.00 usec
SI                1048576
SF            125.6924115 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.40
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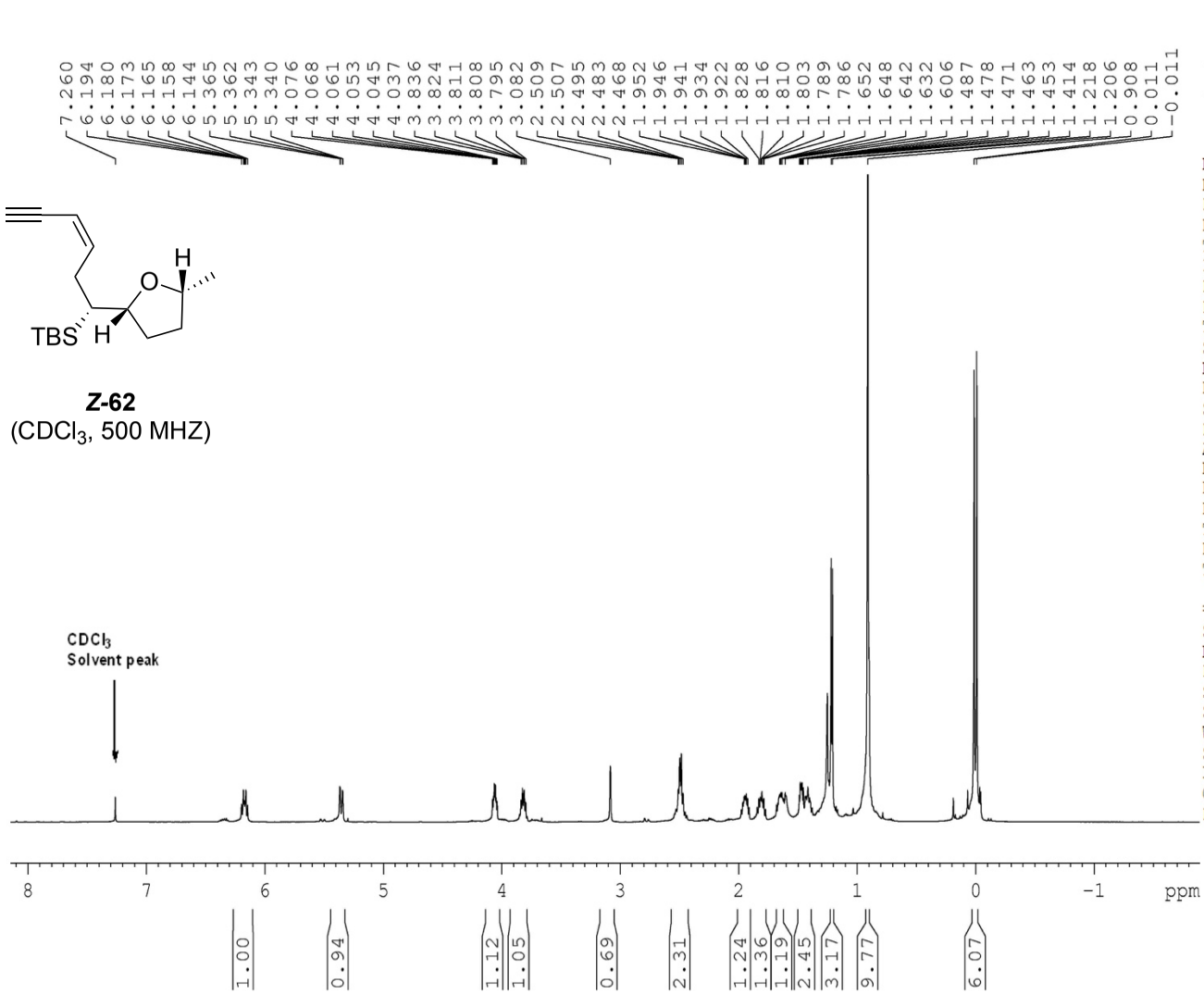
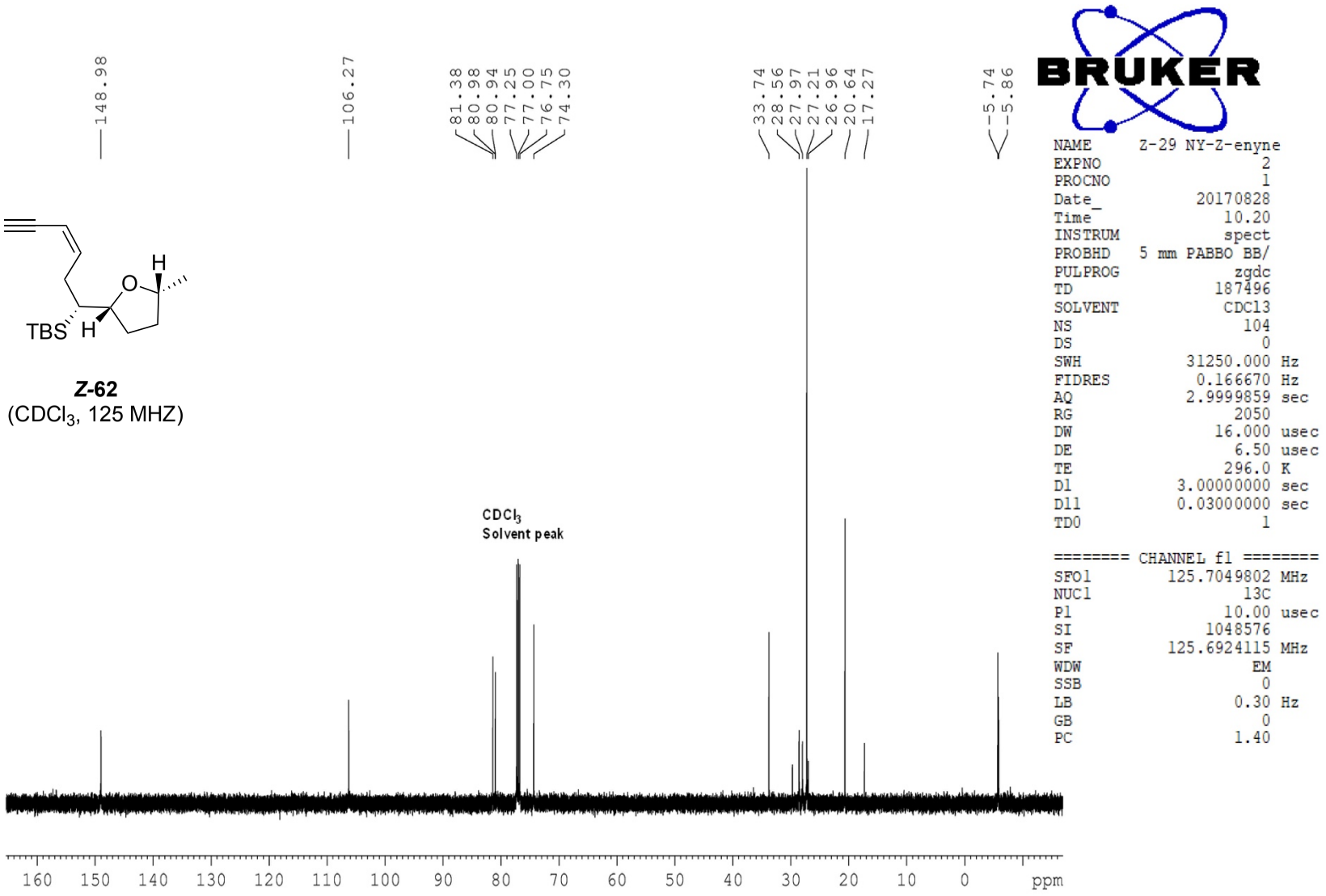


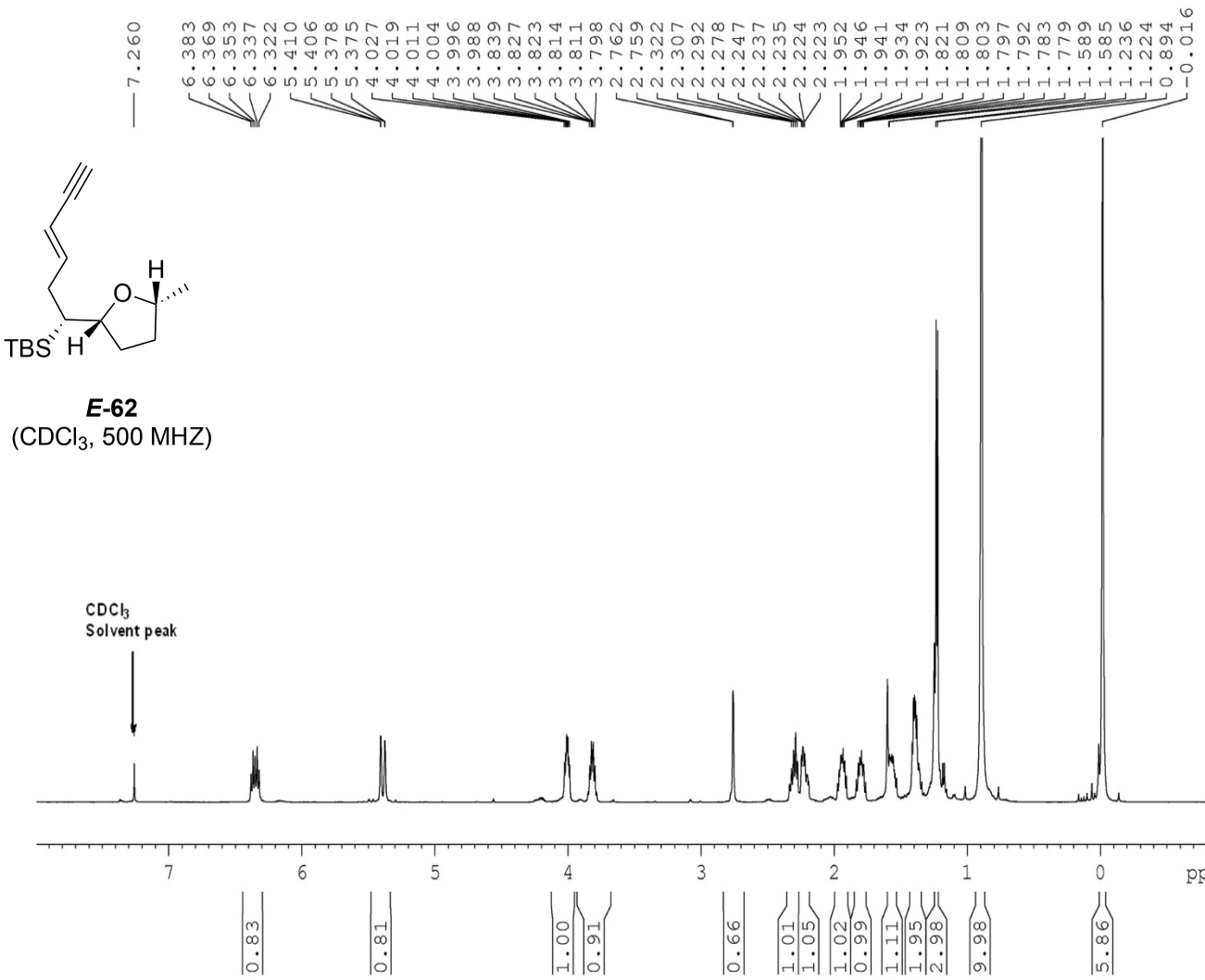
***Z*-62**
($CDCl_3$, 500 MHZ)

```
NAME        Z-29 NY-Z-enyne
EXPNO                     1
PROCNO                    1
Date_              20170828
Time                  10.01
INSTRUM               spect
PROBHD    5 mm PABBO BB/
PULPROG                  zg
TD                    59998
SOLVENT               CDCl3
NS                        8
DS                        0
SWH           10000.000 Hz
FIDRES         0.166672 Hz
AQ             2.9999499 sec
RG                    29.95
DW                50.000 usec
DE                 6.50 usec
TE                 295.8 K
D1            3.00000000 sec
TD0                       1

======== CHANNEL f1 ========
SFO1         499.8730869 MHz
NUC1                    1H
P1                 10.75 usec
SI                    65536
SF           499.8700000 MHz
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```



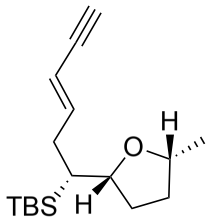
***Z*-62**
($CDCl_3$, 125 MHZ)



***E*-62**
($CDCl_3$, 500 MHZ)

BRUKER

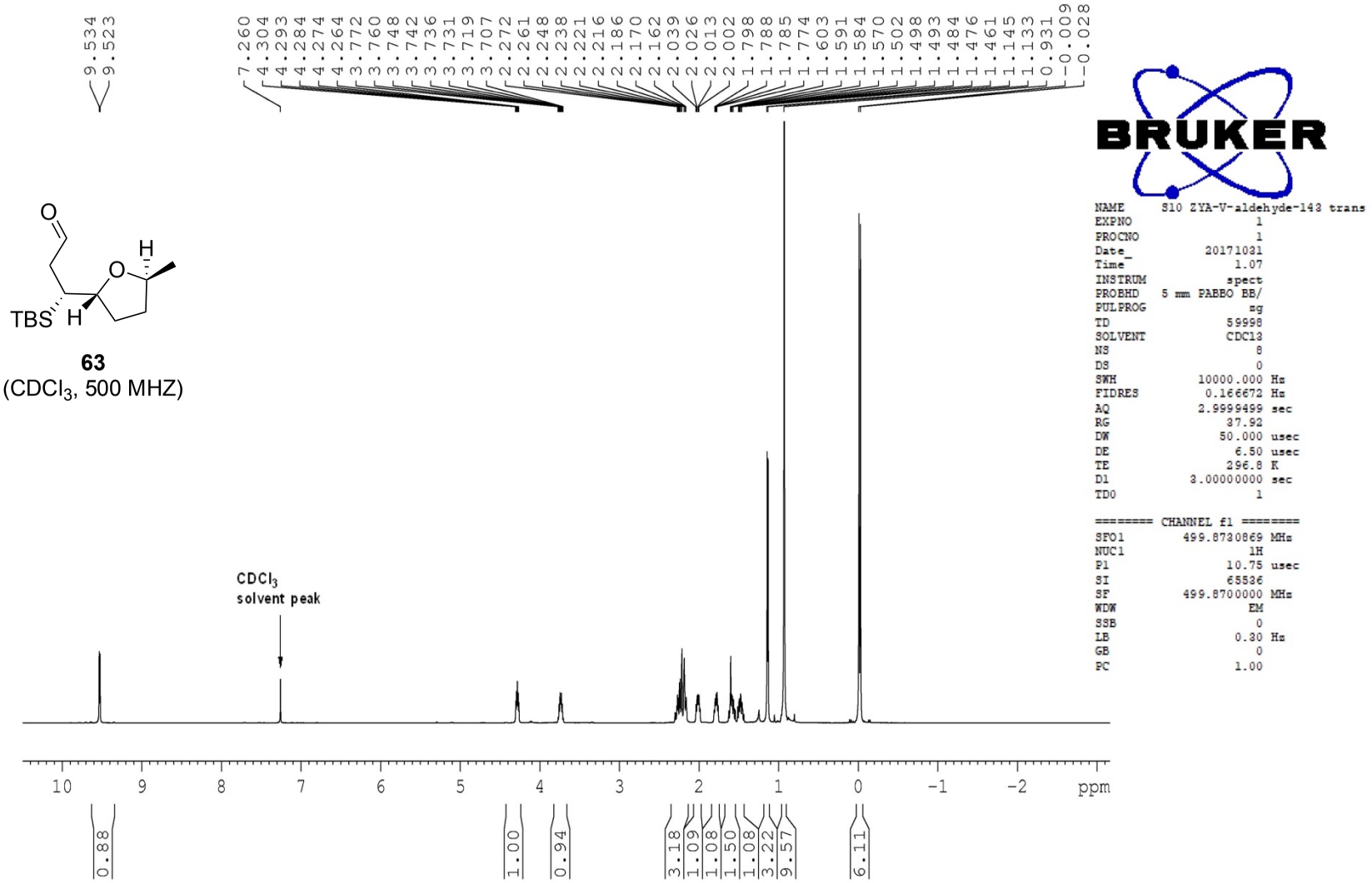
NAME	E-29 NY-E-enyne
EXPNO	1
PROCNO	1
Date_	20170824
Time	11.41
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	30.11
DW	50.000 usec
DE	10.00 usec
TE	294.2 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	500.1330885 MHz
NUC1	1H
P1	8.00 usec
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



***E*-62**
($CDCl_3$, 125 MHZ)

BRUKER

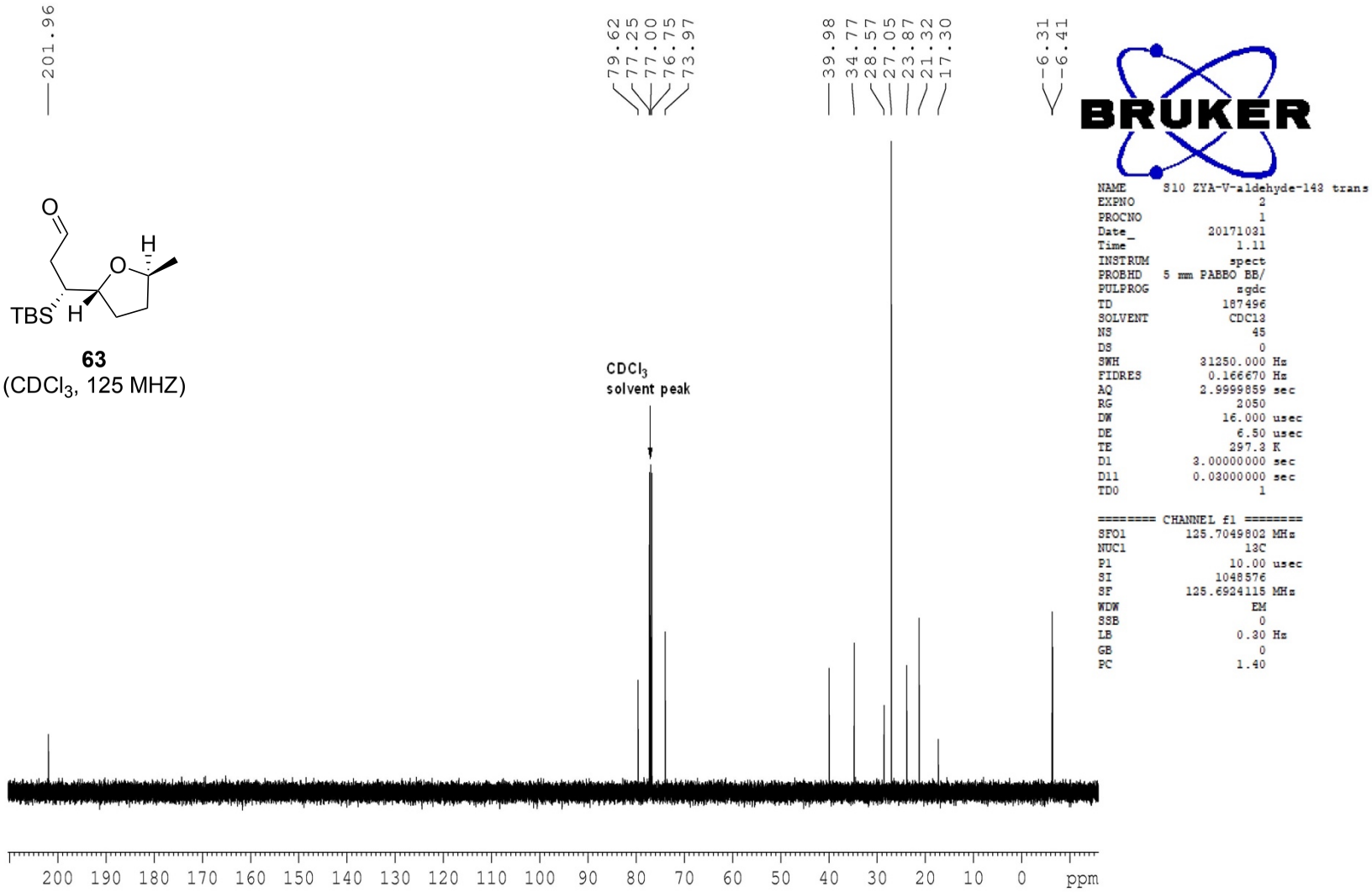
NAME	E-29 NY-E-enyne
EXPNO	2
PROCNO	1
Date_	20170824
Time	12.48
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zgdc
TD	178568
SOLVENT	CDCl3
NS	125
DS	0
SWH	29761.904 Hz
FIDRES	0.166670 Hz
AQ	2.9999924 sec
RG	196.79
DW	16.800 usec
DE	10.00 usec
TE	294.2 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7703643 MHz
NUC1	13C
P1	14.00 usec
SI	131072
SF	125.7577920 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40



63
($CDCl_3$, 500 MHZ)

BRUKER

NAME	S10 ZYA-V-aldehyde-143 trans
EXPNO	1
PROCNO	1
Date_	20171031
Time	1.07
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	37.92
DW	50.000 usec
DE	6.50 usec
TE	296.8 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00


201.96
79.62
77.25
77.00
76.75
73.97
39.98
34.77
28.57
27.05
23.87
21.32
17.30
6.31
-6.41
O
H
O
TBS
H
63
(CDCl3, 125 MHZ)
CDCl3
solvent peak
BRUKER
NAME 310 ZYA-V-aldehyde-143 trans
EXPNO 2
PROCNO 1
Date_ 20171031
Time 1.11
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgdc
TD 187496
SOLVENT CDCl3
NS 45
DS 0
SWH 31250.000 Hz
FIDRES 0.166670 Hz
AQ 2.9999859 sec
RG 2050
DW 16.000 usec
DE 6.50 usec
TE 297.3 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7049802 MHz
NUC1 13C
P1 10.00 usec
SI 1048576
SF 125.6924115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
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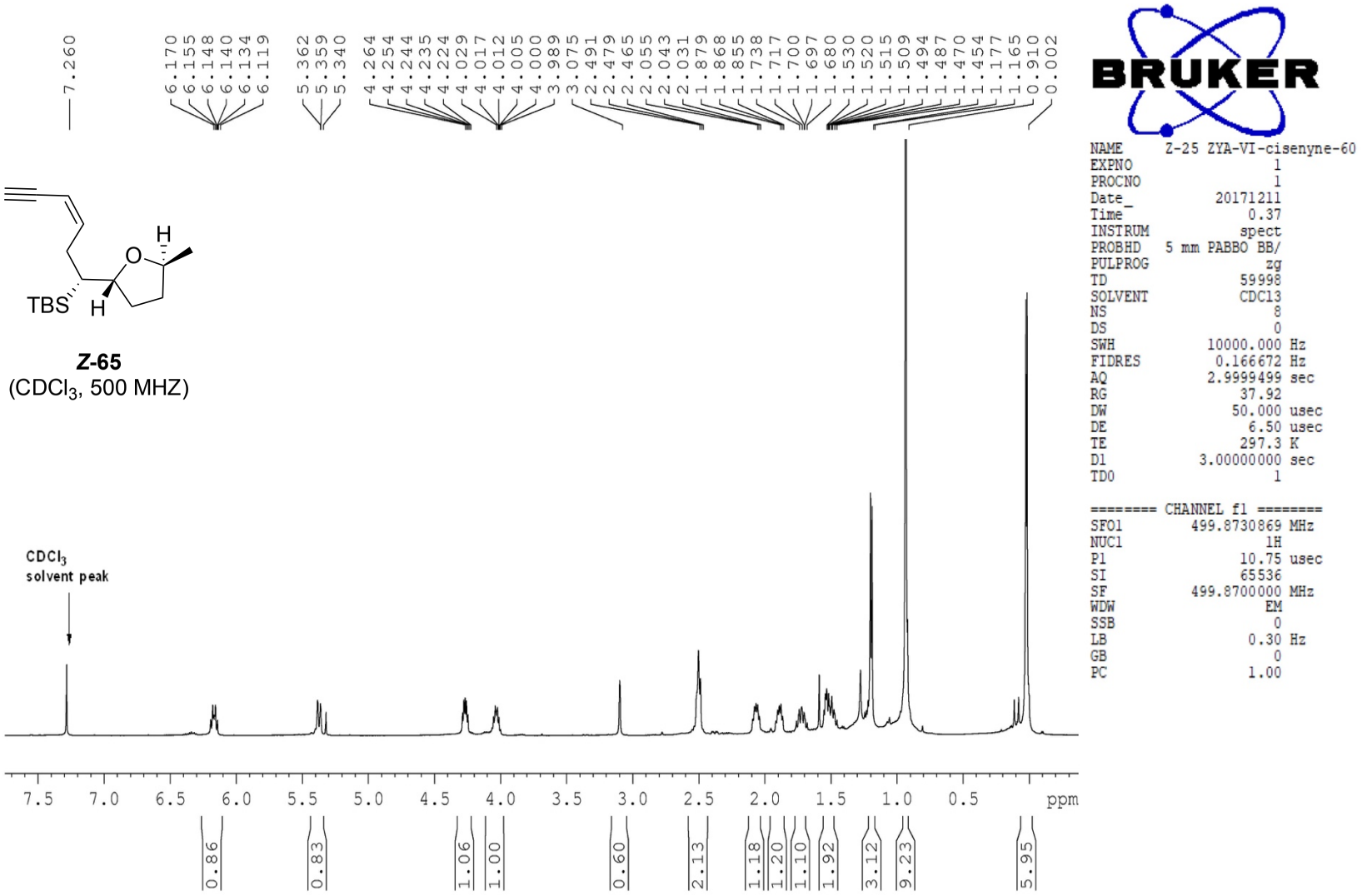
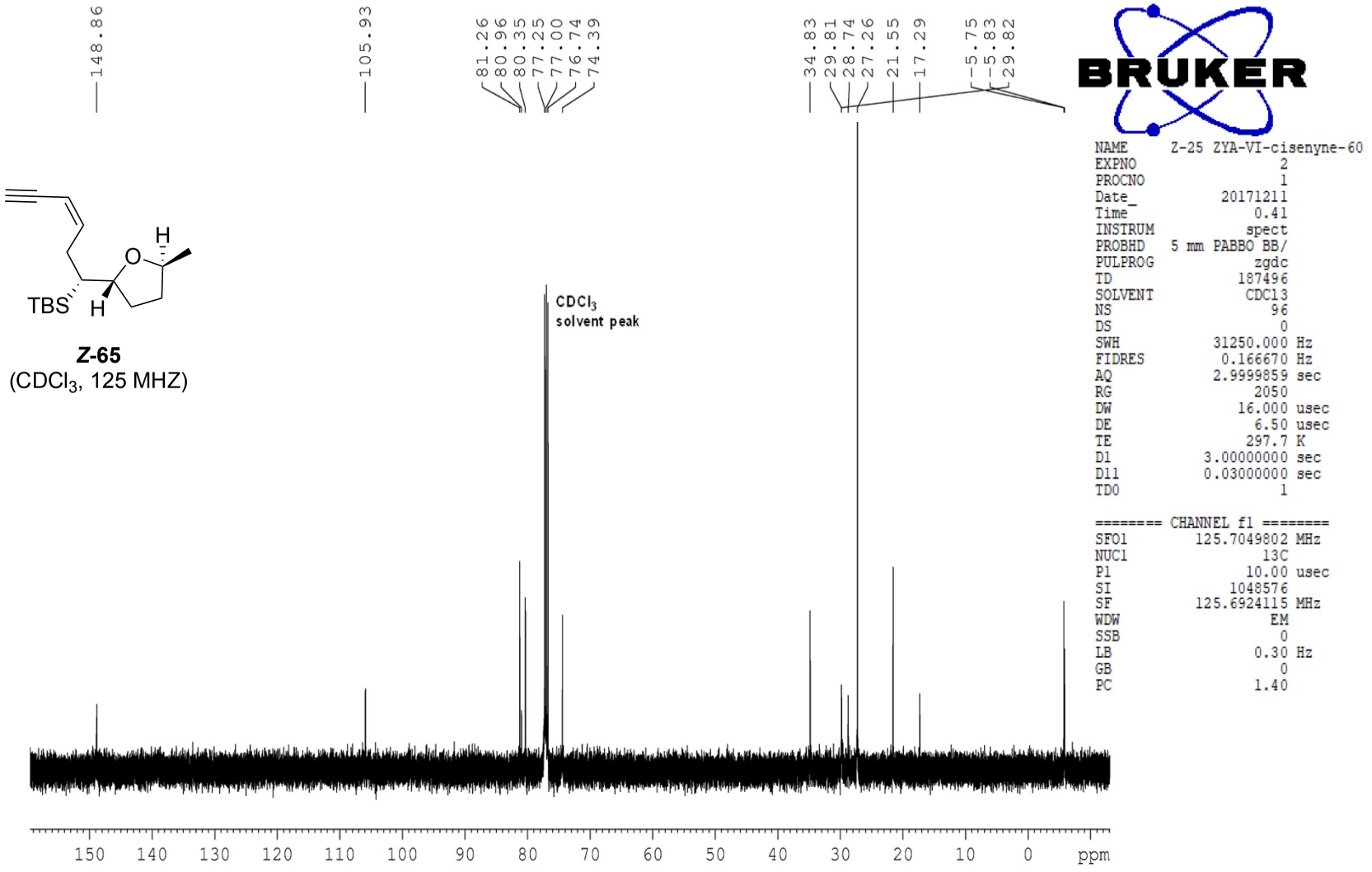


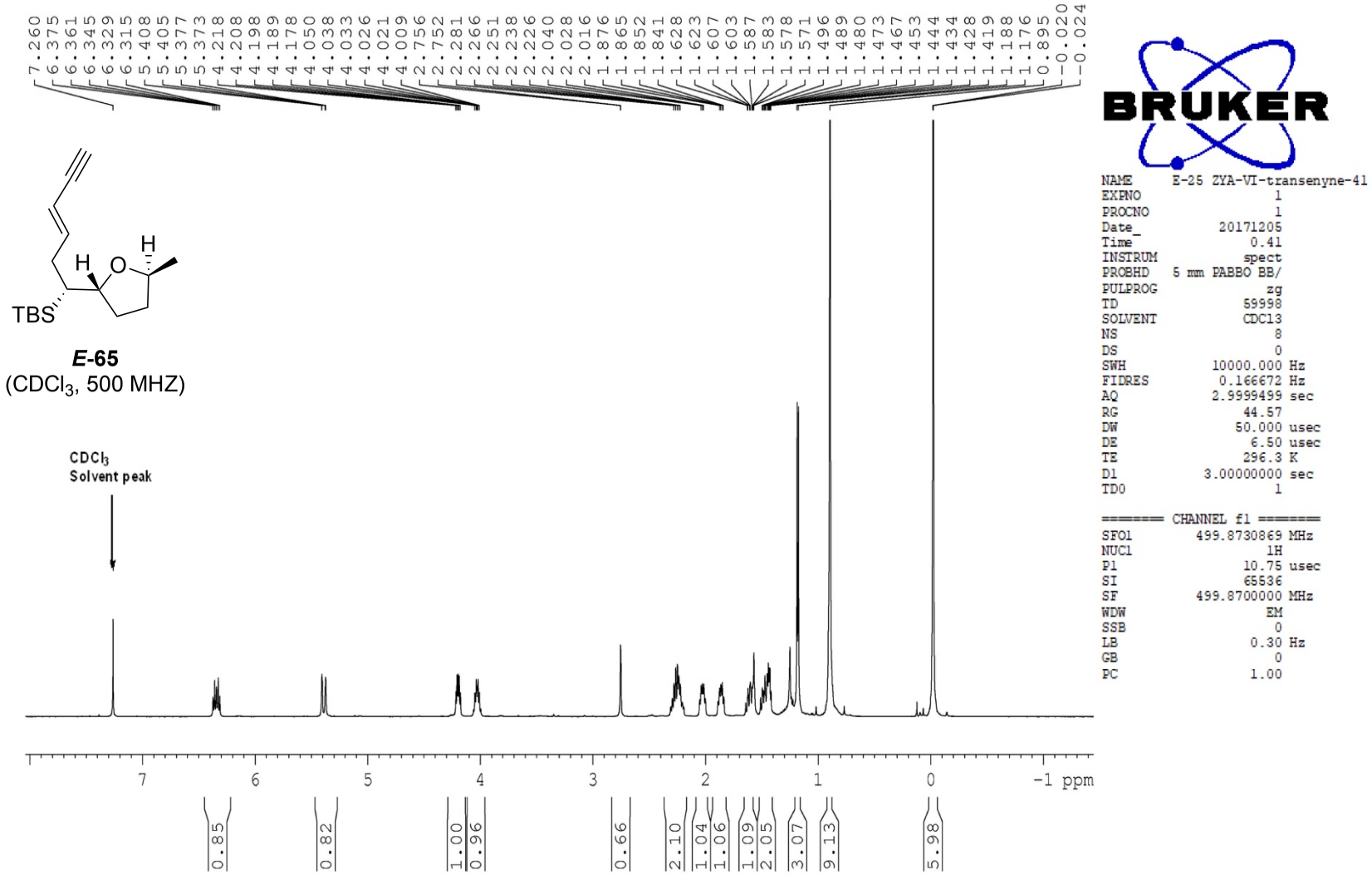
***Z*-65**
($CDCl_3$, 500 MHZ)

```
NAME        Z-25 ZYA-VI-cisenyne-60
EXPNO                             1
PROCNO                            1
Date_                      20171211
Time                           0.37
INSTRUM                       spect
PROBHD    5 mm PABBO BB/
PULPROG                          zg
TD                            59998
SOLVENT                       CDCl3
NS                                8
DS                                0
SWH                   10000.000 Hz
FIDRES                    0.166672 Hz
AQ                        2.9999499 sec
RG                            37.92
DW                           50.000 usec
DE                            6.50 usec
TE                           297.3 K
D1                    3.00000000 sec
TD0                               1

======== CHANNEL f1 ========
SFO1                499.8730869 MHz
NUC1                          1H
P1                          10.75 usec
SI                            65536
SF                  499.8700000 MHz
WDW                           EM
SSB                               0
LB                            0.30 Hz
GB                                0
PC                             1.00
```



***Z*-65**
($CDCl_3$, 125 MHZ)

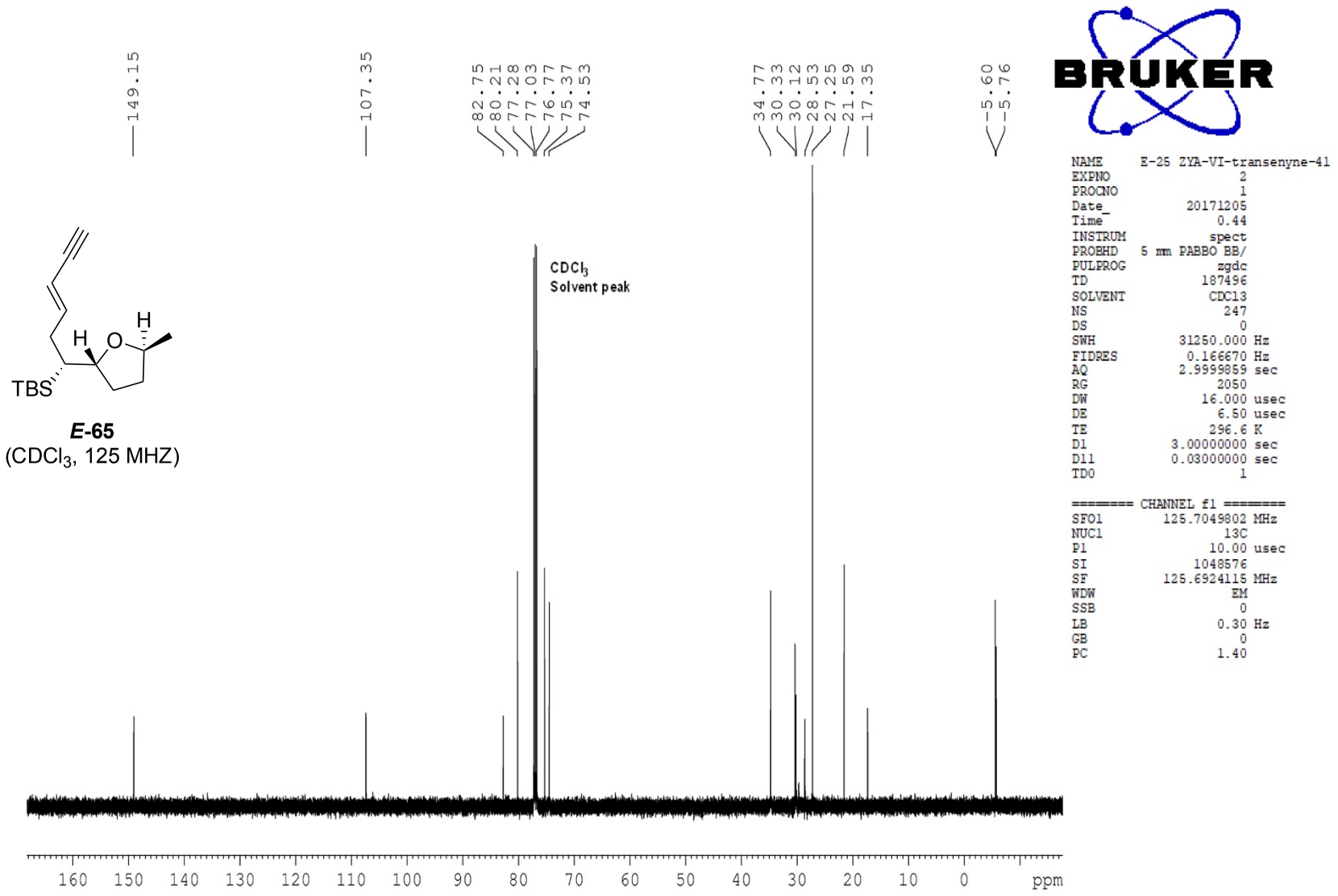


***E*-65**

($CDCl_3$, 500 MHZ)

BRUKER

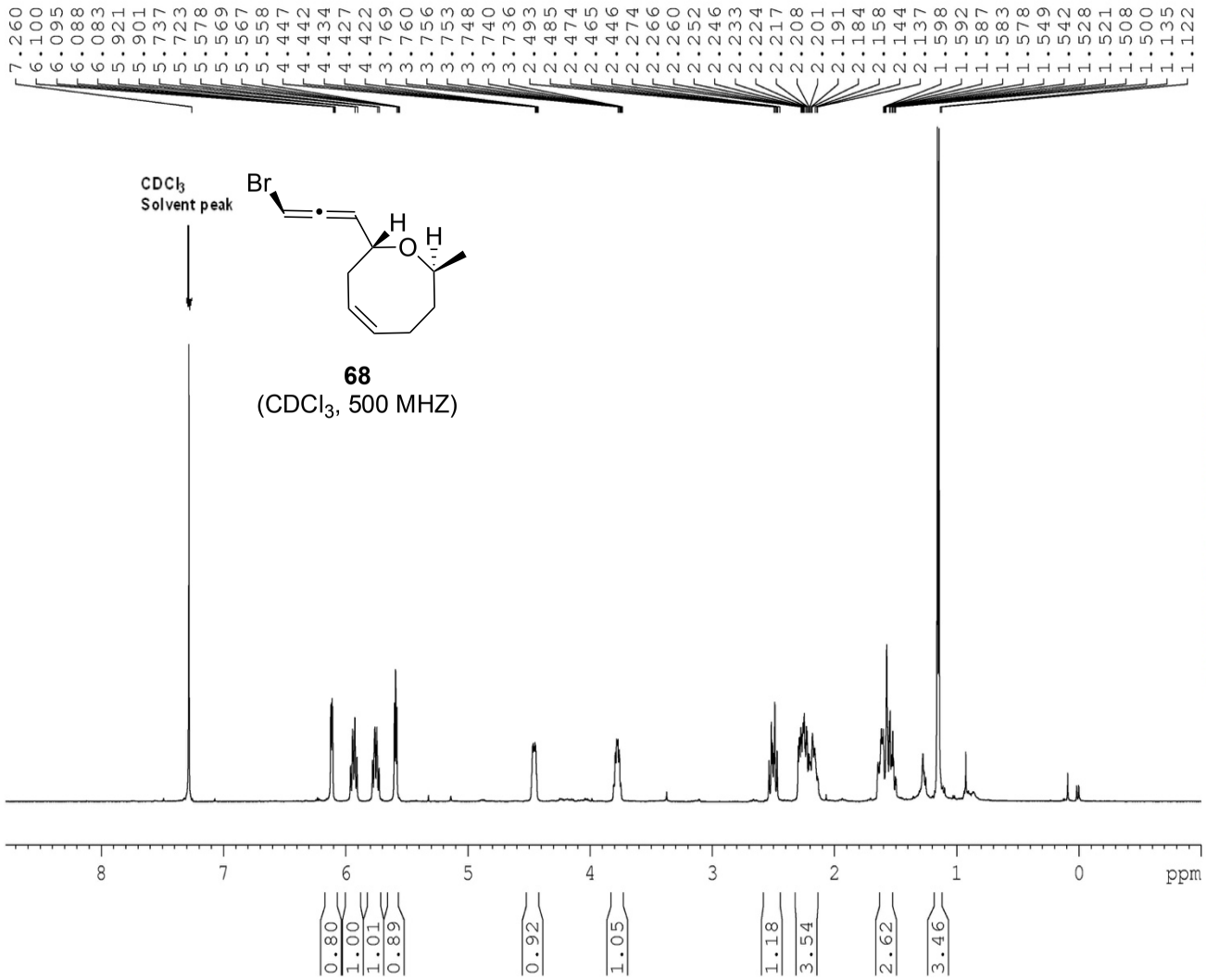
NAME	E-25 ZYA-VI-transenyne-41
EXPNO	1
PROCNO	1
Date_	20171205
Time	0.41
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	44.57
DW	50.000 usec
DE	6.50 usec
TE	296.3 K
D1	3.00000000 sec
TD0	1
=======	CHANNEL f1 =======
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



***E*-65**
($CDCl_3$, 125 MHZ)

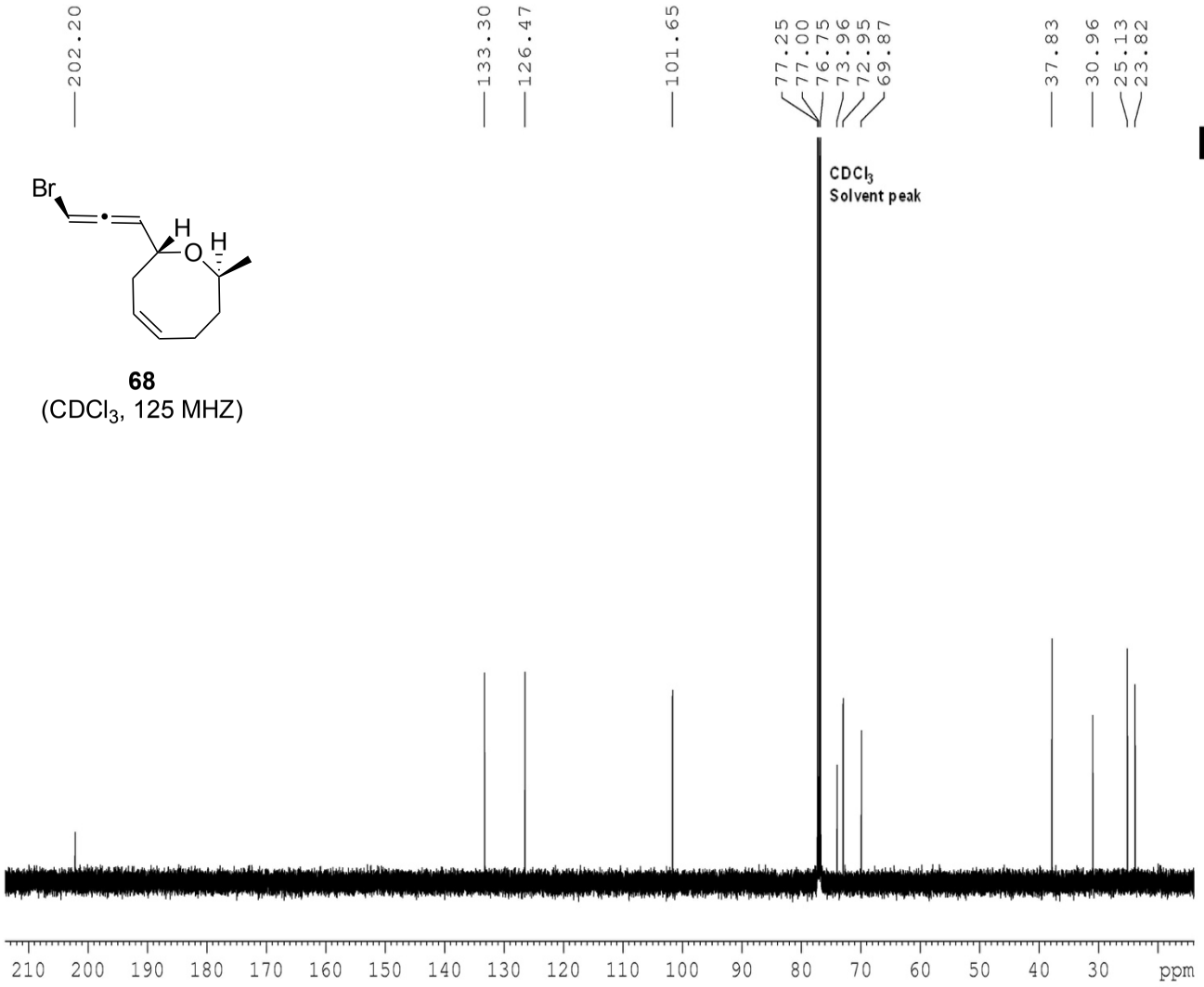
```
NAME      E-25 ZYA-VI-transenyne-41
EXPNO                 2
PROCNO                1
Date_          20171205
Time               0.44
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG            zgdc
TD                187496
SOLVENT            CDCl3
NS                   247
DS                     0
SWH           31250.000 Hz
FIDRES        0.166670 Hz
AQ            2.9999859 sec
RG                  2050
DW              16.000 usec
DE               6.50 usec
TE                296.6 K
D1           3.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        125.7049802 MHz
NUC1                  13C
P1                10.00 usec
SI                1048576
SF          125.6924115 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.40
```



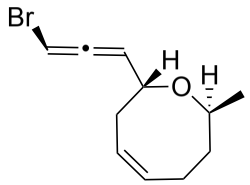
BRUKER

NAME	26 ZYA-VI-bromoallene-33-major
EXPNO	1
PROCNO	1
Date_	20171130
Time	0.40
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	70.49
DW	50.000 usec
DE	6.50 usec
TE	297.2 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

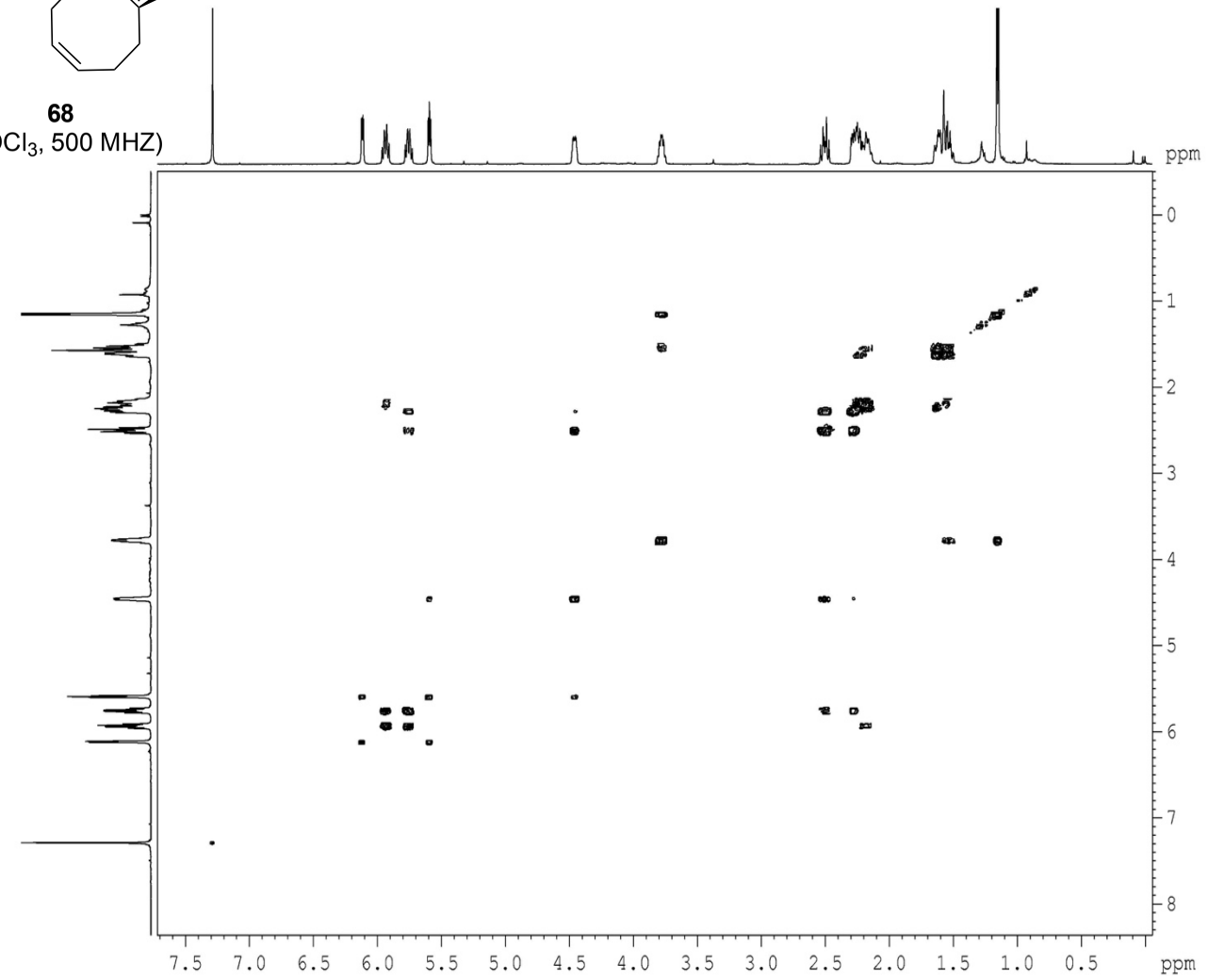


BRUKER

NAME	26 ZYA-VI-bromoallene-33-major
EXPNO	2
PROCNO	1
Date_	20171130
Time	0.47
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	364
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	297.8 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
=======	CHANNEL f1 =======
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

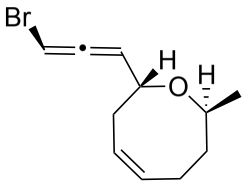


68
($CDCl_3$, 500 MHZ)

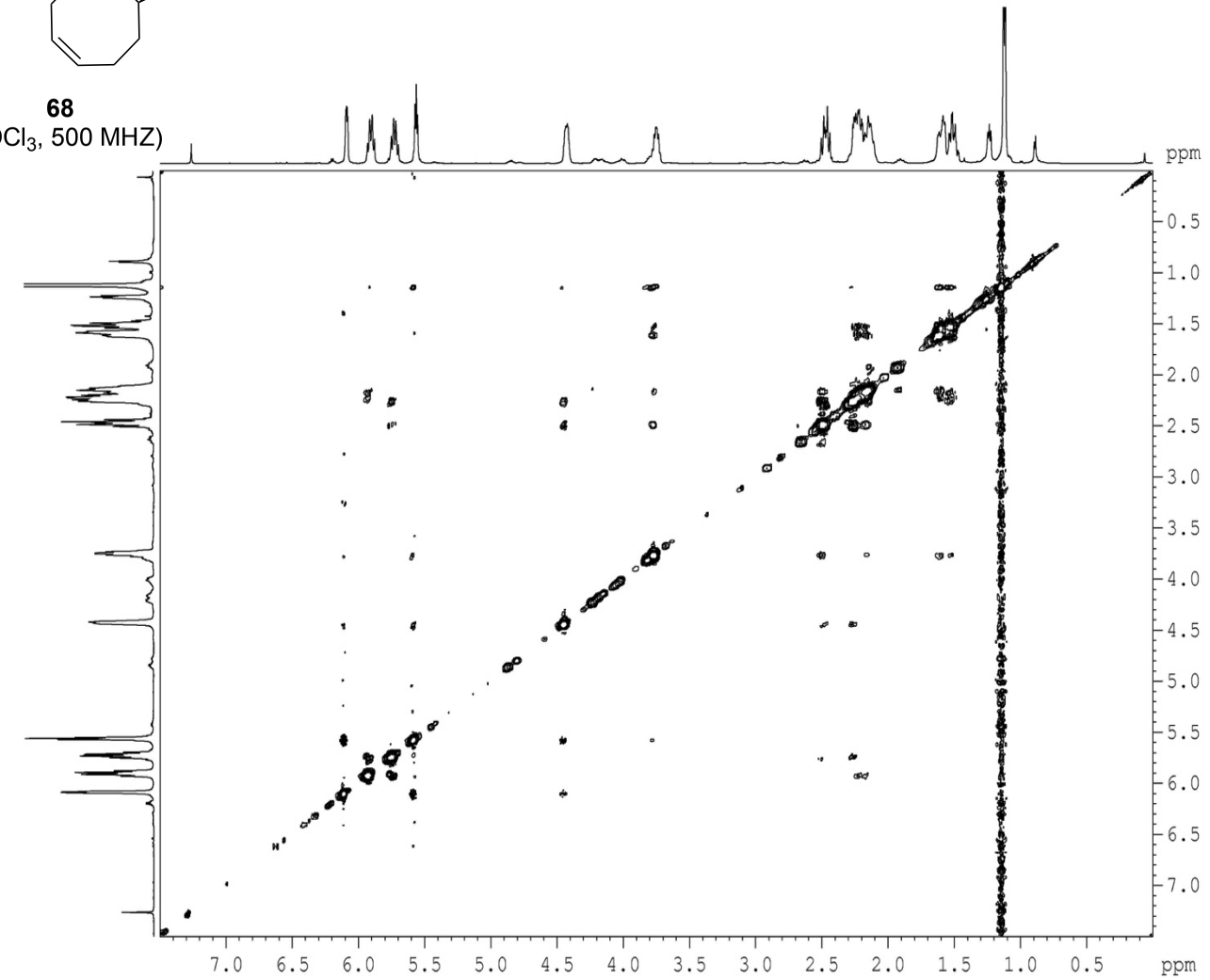


BRUKER

NAME	26 ZYA-VI-bromoallene-33-major
EXPNO	3
PROCNO	1
Date_	20180131
Time	1.31
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	cosygpmfqf
TD	2048
SOLVENT	CDCl3
NS	1
DS	8
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2048500 sec
RG	64.36
DW	100.000 usec
DE	10.00 usec
TE	294.3 K
D0	0.00000300 sec
D1	2.00000000 sec
D13	0.00000400 sec
D16	0.00020000 sec
IN0	0.00020000 sec
======= CHANNEL f1 =======	
SFO1	500.1320005 MHz
NUC1	1H
P1	8.00 usec
ND0	1
TD	128
SFO1	500.132 MHz
FIDRES	39.062500 Hz
SW	9.997 ppm
FnMODE	QF
SI	1024
SF	500.1300000 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.40
SI	1024
MC2	QF
SF	500.1300000 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0



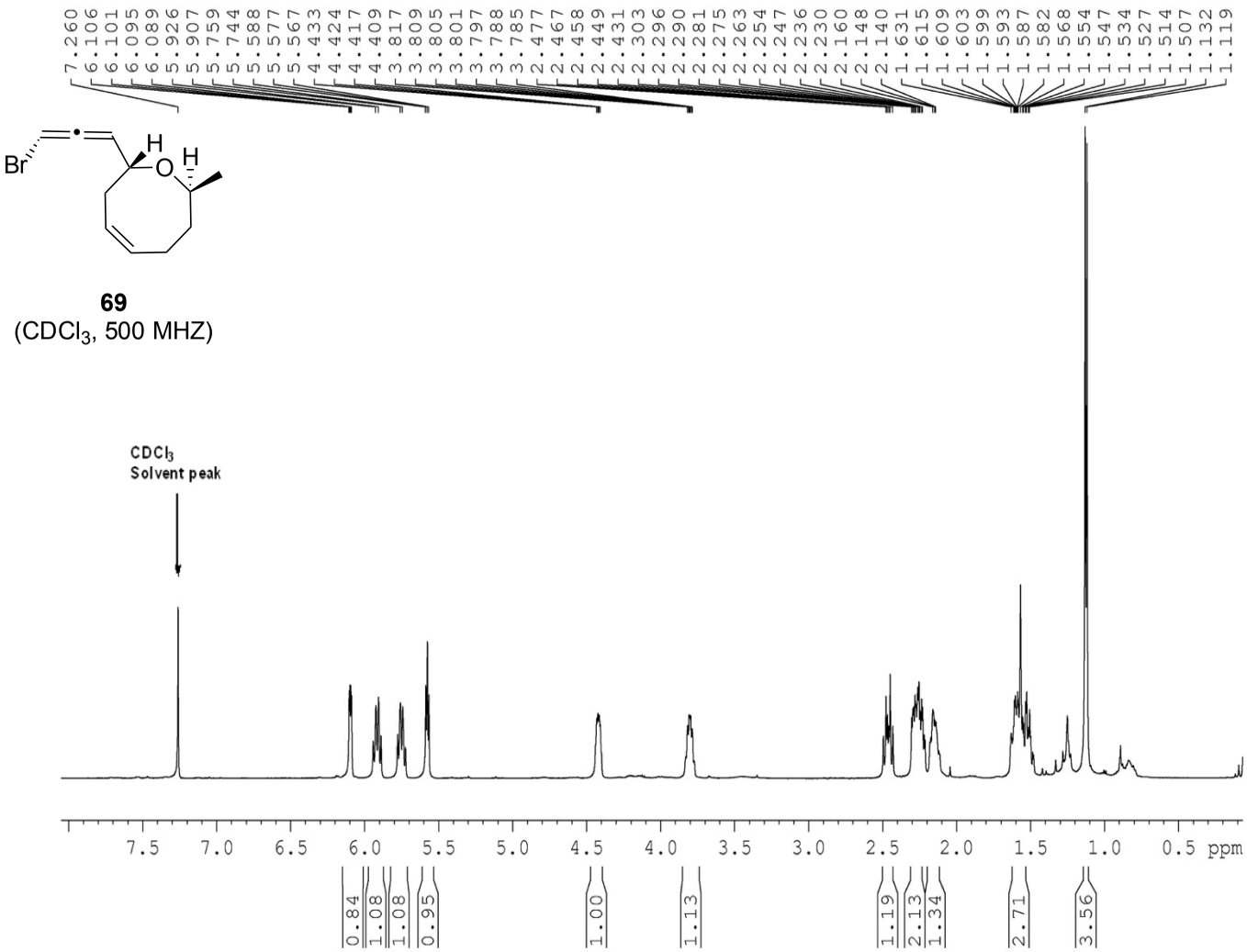
68
($CDCl_3$, 500 MHZ)



BRUKER

```
NAME        26 ZYA-VI-bromoallene-33-major
EXPNO                   4
PROCNO                  1
Date_            20160107
Time                18.49
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG      noesygpphpp
TD                   2048
SOLVENT             CDCl3
NS                      2
DS                      4
SWH           3748.126 Hz
FIDRES        1.830140 Hz
AQ            0.2732532 sec
RG                 77.07
DW               133.400 usec
DE                 6.50 usec
TE                296.9 K
D0            0.00011939 sec
D1            2.00000000 sec
D8            0.69999999 sec
D11           0.03000000 sec
D12           0.00002000 sec
D16           0.00020000 sec
IN0           0.00026680 sec

======== CHANNEL f1 ========
SFO1         499.8718745 MHz
NUC1                   1H
P1                 11.00 usec
P2                 22.00 usec
P17              2500.00 usec
ND0                     1
TD                    256
SFO1          499.8719 MHz
FIDRES       14.641117 Hz
SW                 7.498 ppm
FnMODE       States-TPPI
SI                   1024
SF           499.8700000 MHz
WDW                 QSINE
SSB                     2
LB                   0.00 Hz
GB                      0
PC                   1.00
SI                   1024
MC2          States-TPPI
SF           499.8700000 MHz
WDW                 QSINE
SSB                     2
LB                   0.00 Hz
GB                      0
```

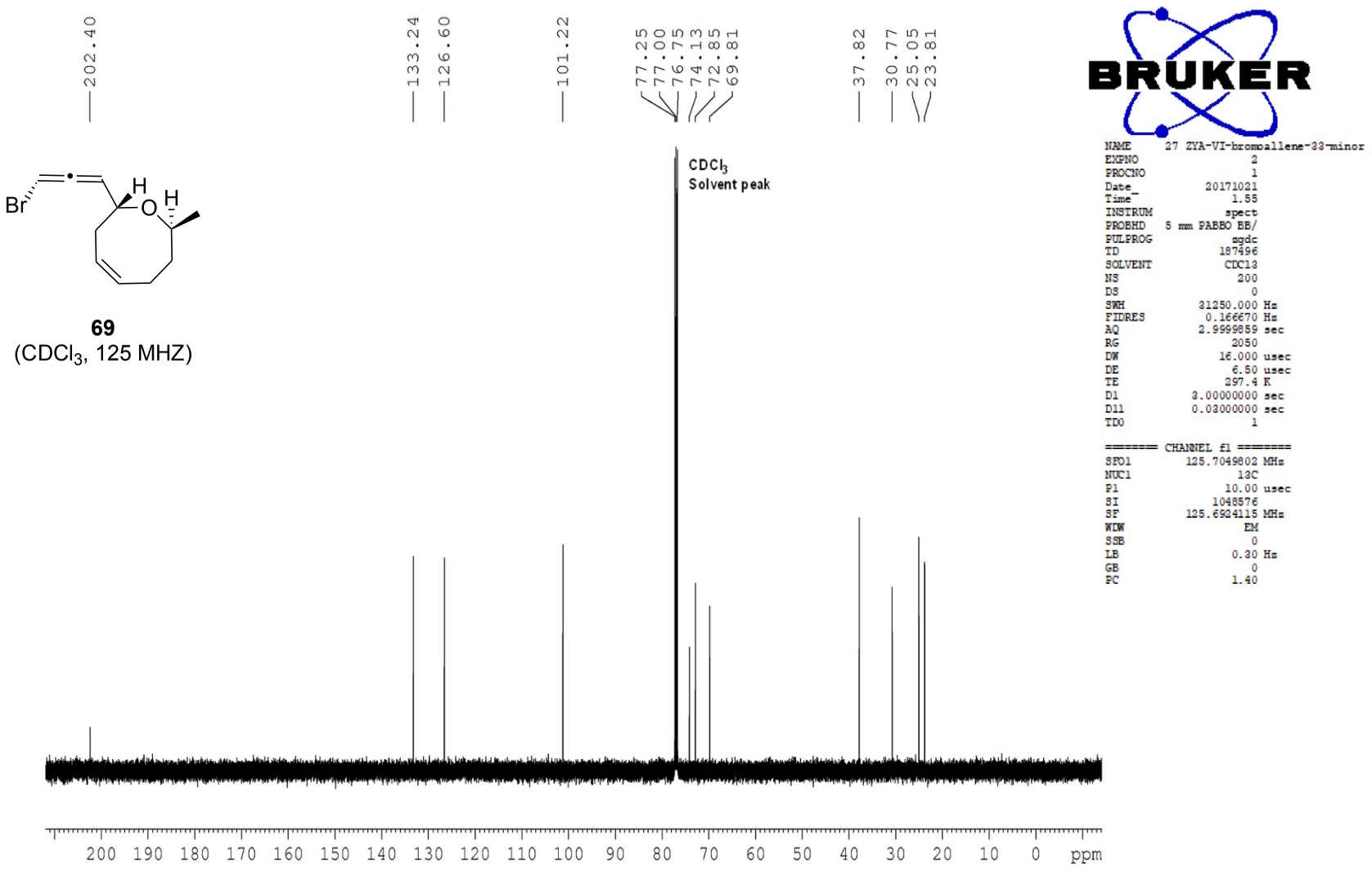


69
($CDCl_3$, 500 MHZ)

BRUKER

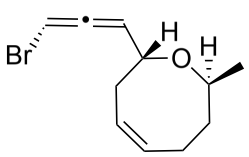
```
NAME        27 ZYA-VI-bromoallene-33-minor
EXPNO                    1
PROCNO                   1
Date_             20171021
Time                 1.47
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG                 zg
TD                   59998
SOLVENT              CDCl3
NS                       8
DS                       0
SWH              10000.000 Hz
FIDRES               0.166672 Hz
AQ                2.9999499 sec
RG                   70.49
DW                  50.000 usec
DE                   6.50 usec
TE                  296.7 K
D1               3.00000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1            499.8730869 MHz
NUC1                    1H
P1                   10.75 usec
SI                   65536
SF              499.8700000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```



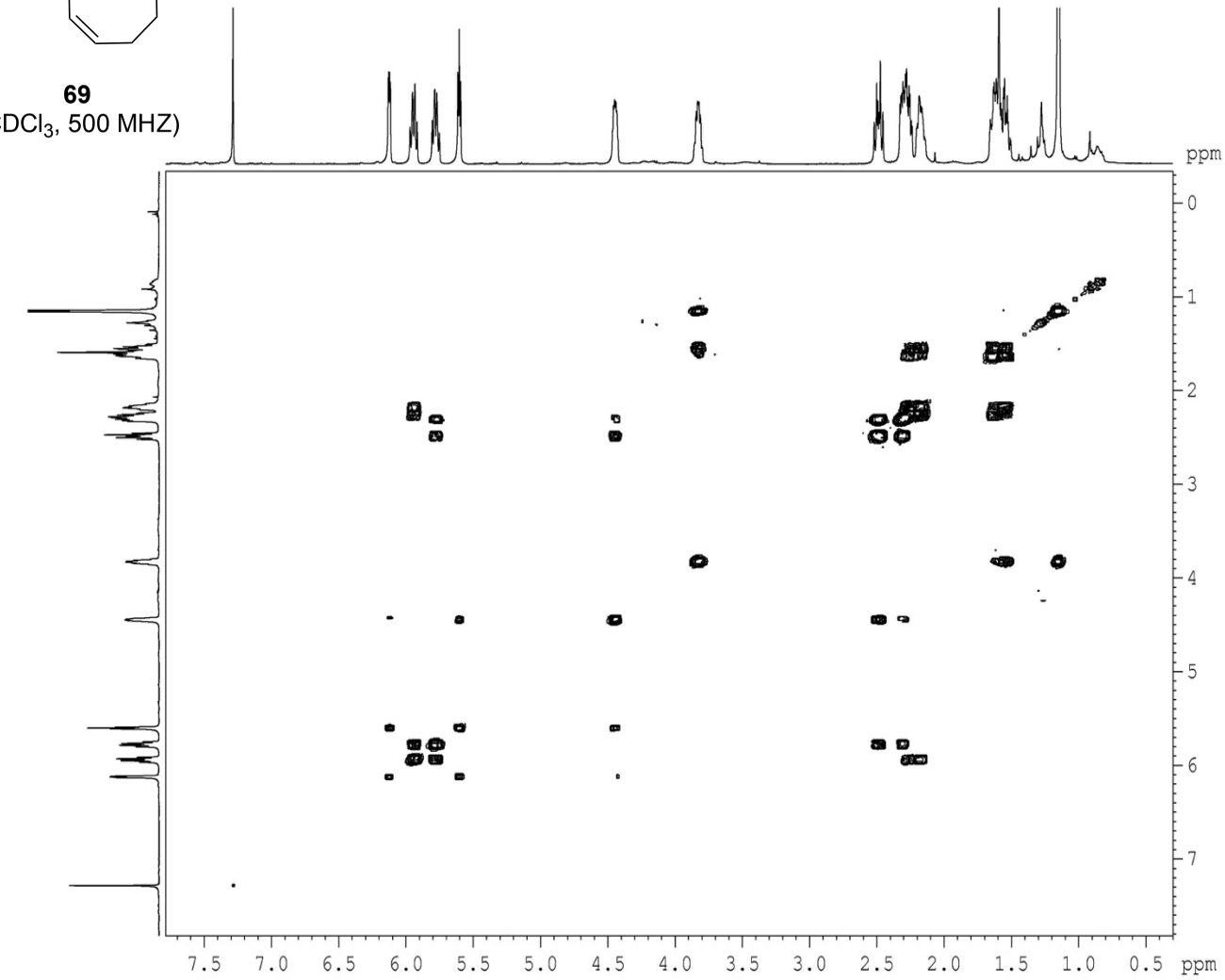
69
($CDCl_3$, 125 MHZ)

NAME	27 ZYA-VI-bromoallene-33-minor
EXPNO	2
PROCNO	1
Date_	20171021
Time	1.55
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	200
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	297.4 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
=======	CHANNEL f1 =======
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



69

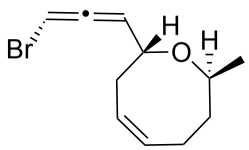
($CDCl_3$, 500 MHZ)



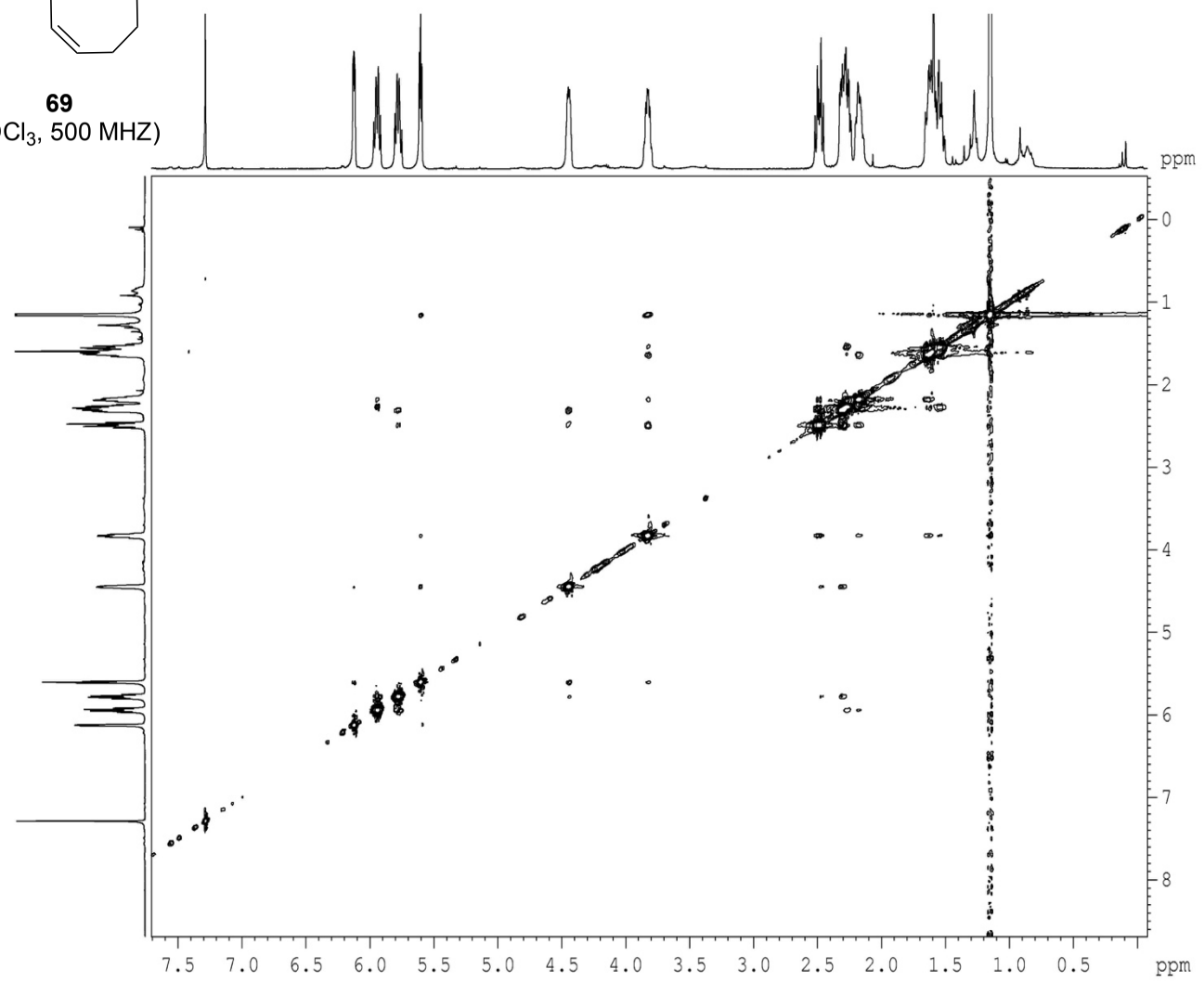
BRUKER

```
NAME        27 ZYA-VI-bromoallene-33-minor
EXPNO                    3
PROCNO                   1
Date_             20171021
Time                 15.20
INSTRUM              spect
PROBHD    5 mm PATXI 1H/
PULPROG       cosygpmfqf
TD                    2048
SOLVENT             CDCl3
NS                       1
DS                       8
SWH               5000.000 Hz
FIDRES            2.441406 Hz
AQ                0.2048500 sec
RG                   64.36
DW                 100.000 usec
DE                  10.00 usec
TE                  293.4 K
D0                0.00000300 sec
D1                2.00000000 sec
D13               0.00000400 sec
D16               0.00020000 sec
IN0               0.00020000 sec

======== CHANNEL f1 ========
SFO1             500.1320005 MHz
NUC1                      1H
P1                     8.00 usec
ND0                      1
TD                     128
SFO1              500.132 MHz
FIDRES           39.062500 Hz
SW                 9.997 ppm
FnMODE                   QF
SI                     1024
SF               500.1300000 MHz
WDW                    SINE
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.40
SI                     1024
MC2                      QF
SF               500.1300000 MHz
WDW                    SINE
SSB                      0
LB                    0.00 Hz
GB                       0
```

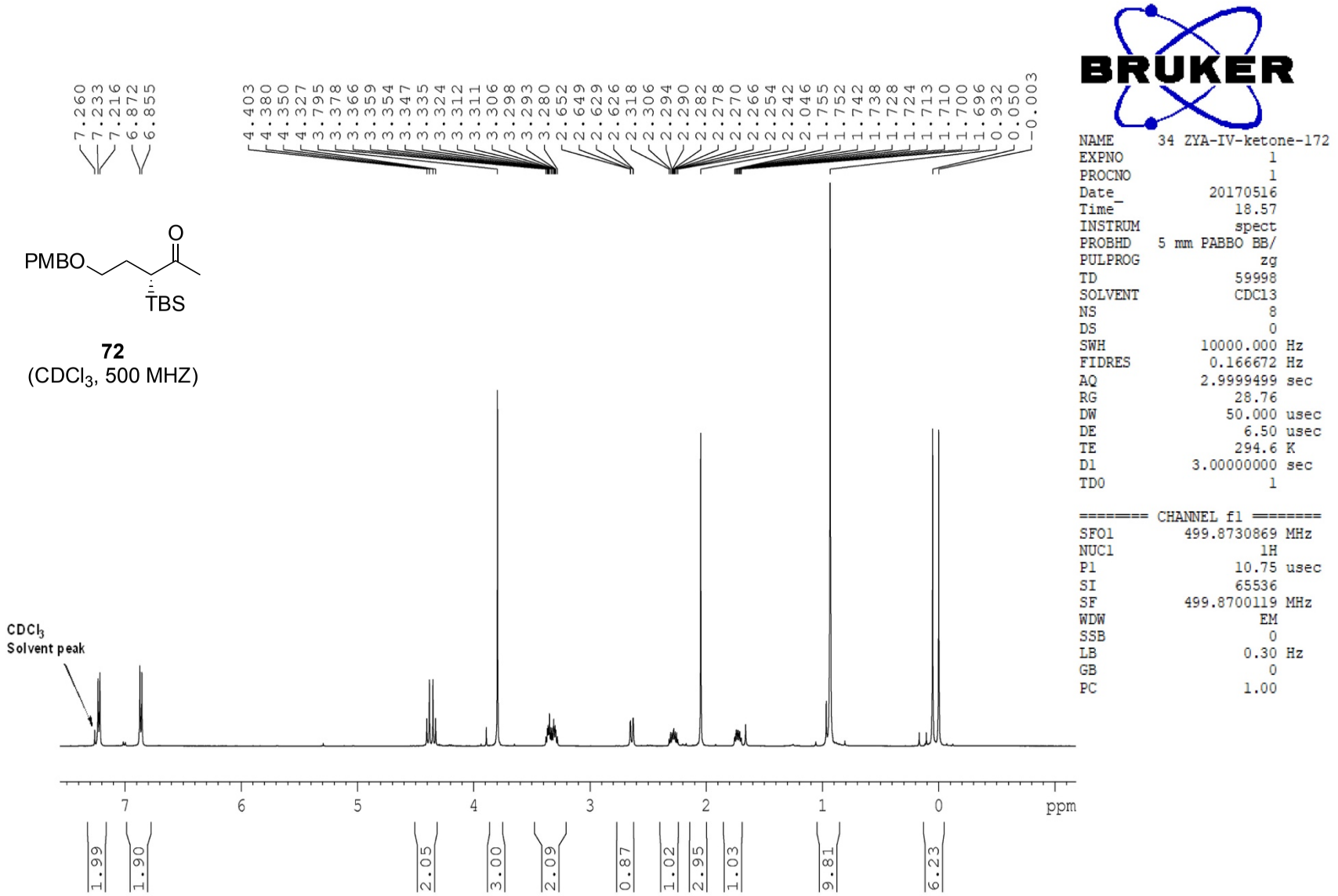


69
($CDCl_3$, 500 MHZ)



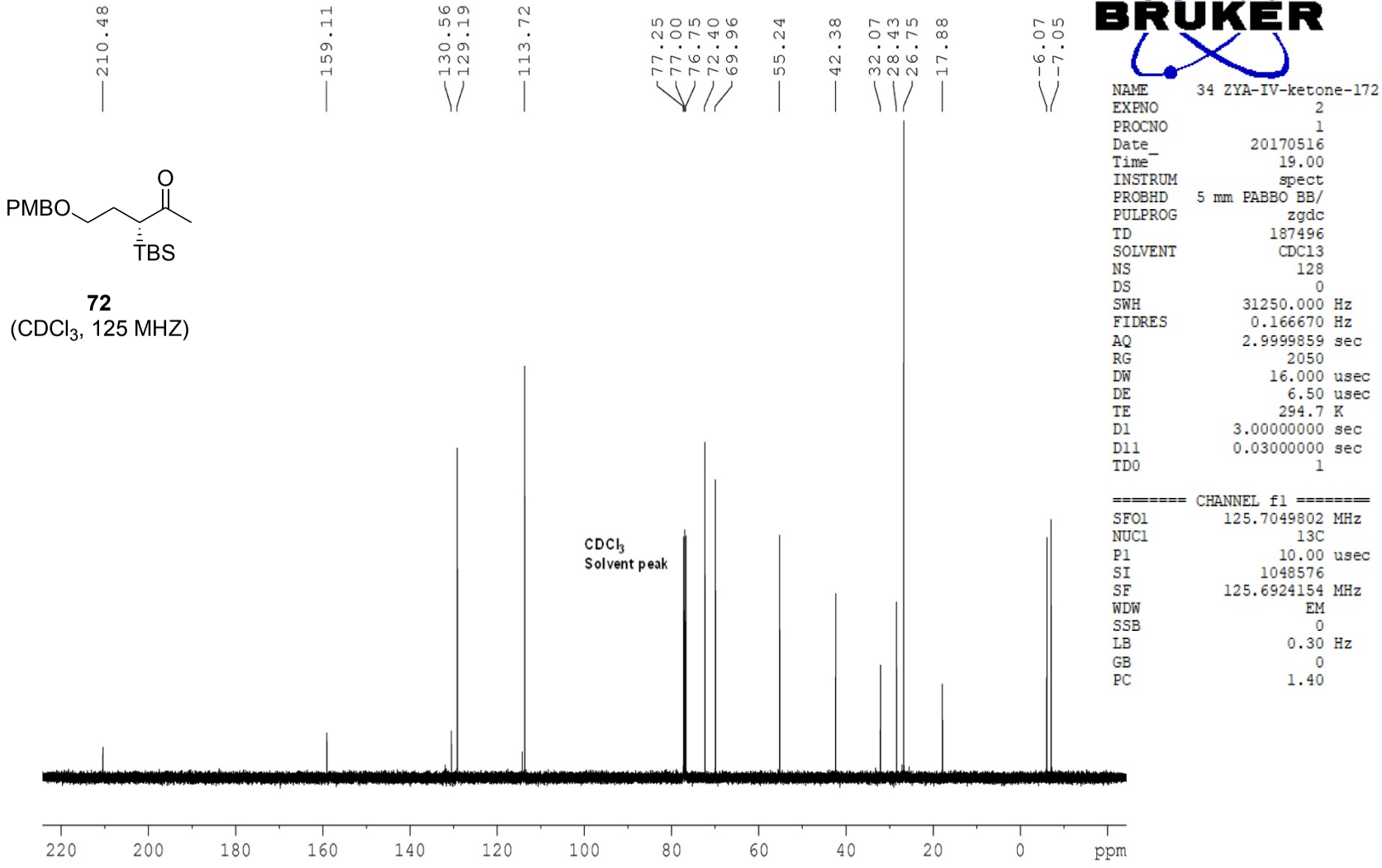
BRUKER

NAME	27 ZYA-VI-bromoallene-33-minor
EXPNO	4
PROCNO	1
Date_	20171021
Time	23.59
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	noesygpphpp
TD	2048
SOLVENT	CDCl3
NS	4
DS	16
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2048500 sec
RG	196.79
DW	100.000 usec
DE	10.00 usec
TE	293.3 K
D0	0.00008981 sec
D1	2.00000000 sec
D8	0.80000001 sec
D11	0.03000000 sec
D12	0.00002000 sec
D16	0.00020000 sec
IN0	0.00020000 sec
======== CHANNEL f1 ========	
SFO1	500.1320005 MHz
NUC1	1H
P1	8.00 usec
P2	16.00 usec
P17	2500.00 usec
ND0	1
TD	256
SFO1	500.132 MHz
FIDRES	19.531250 Hz
SW	9.997 ppm
FnMODE	States-TPPI
SI	1024
SF	500.1300000 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.00
SI	1024
MC2	States-TPPI
SF	500.1300000 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0



BRUKER

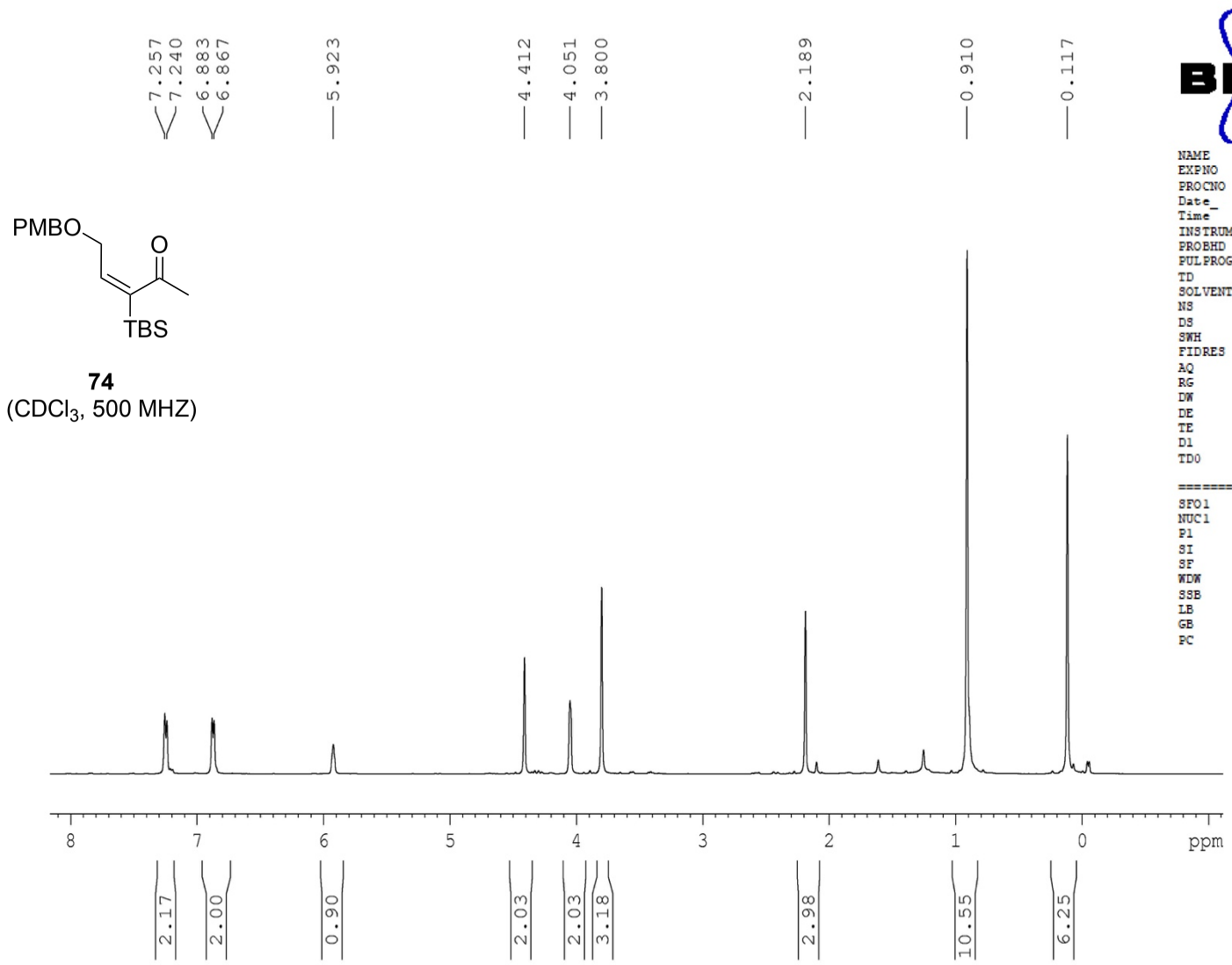
NAME	34 ZYA-IV-ketone-172
EXPNO	1
PROCNO	1
Date_	20170516
Time	18.57
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	28.76
DW	50.000 usec
DE	6.50 usec
TE	294.6 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700119 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



72
($CDCl_3$, 125 MHZ)

BRUKER

NAME	34 ZYA-IV-ketone-172
EXPNO	2
PROCNO	1
Date_	20170516
Time	19.00
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	128
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	294.7 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924154 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

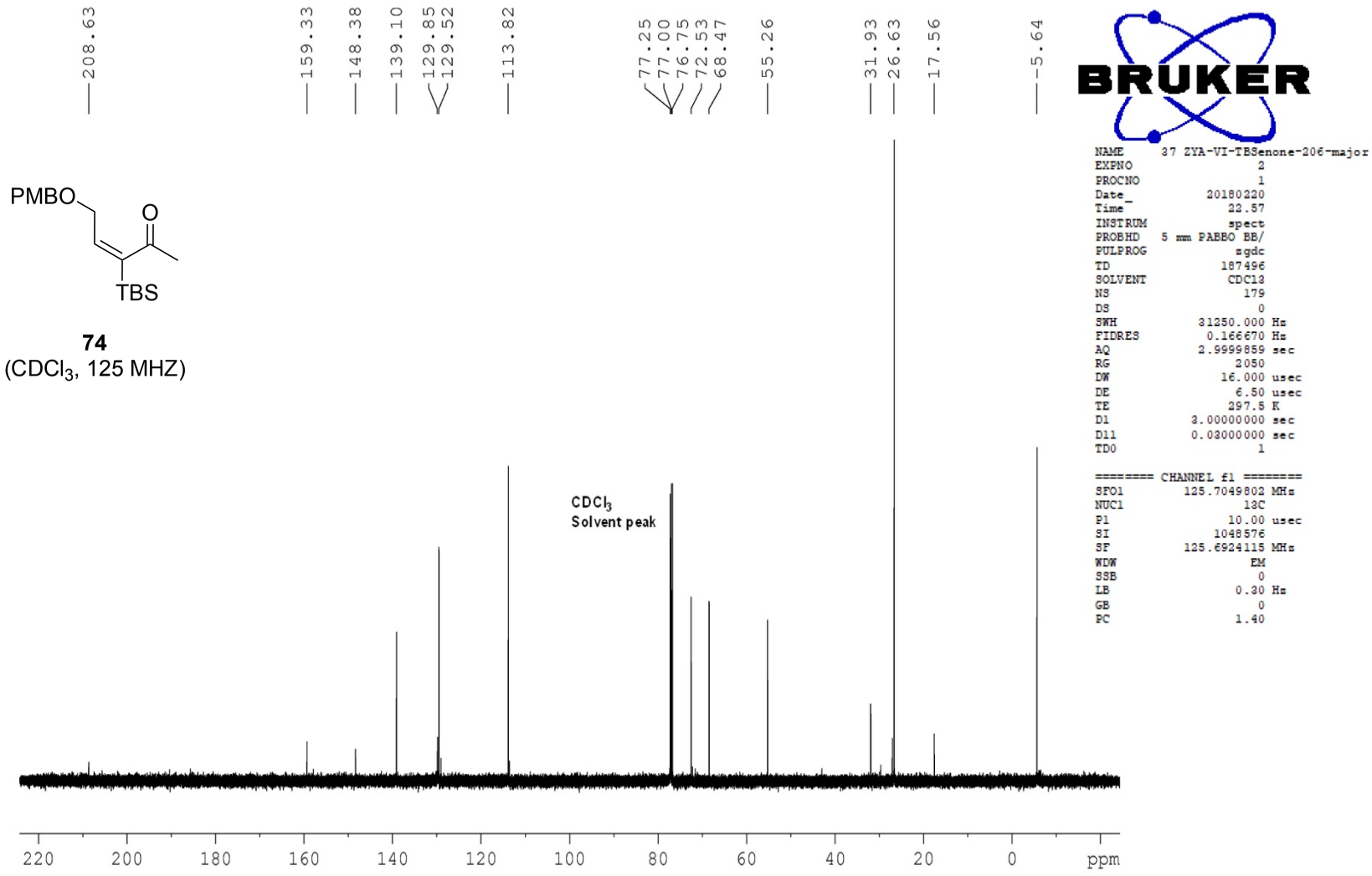


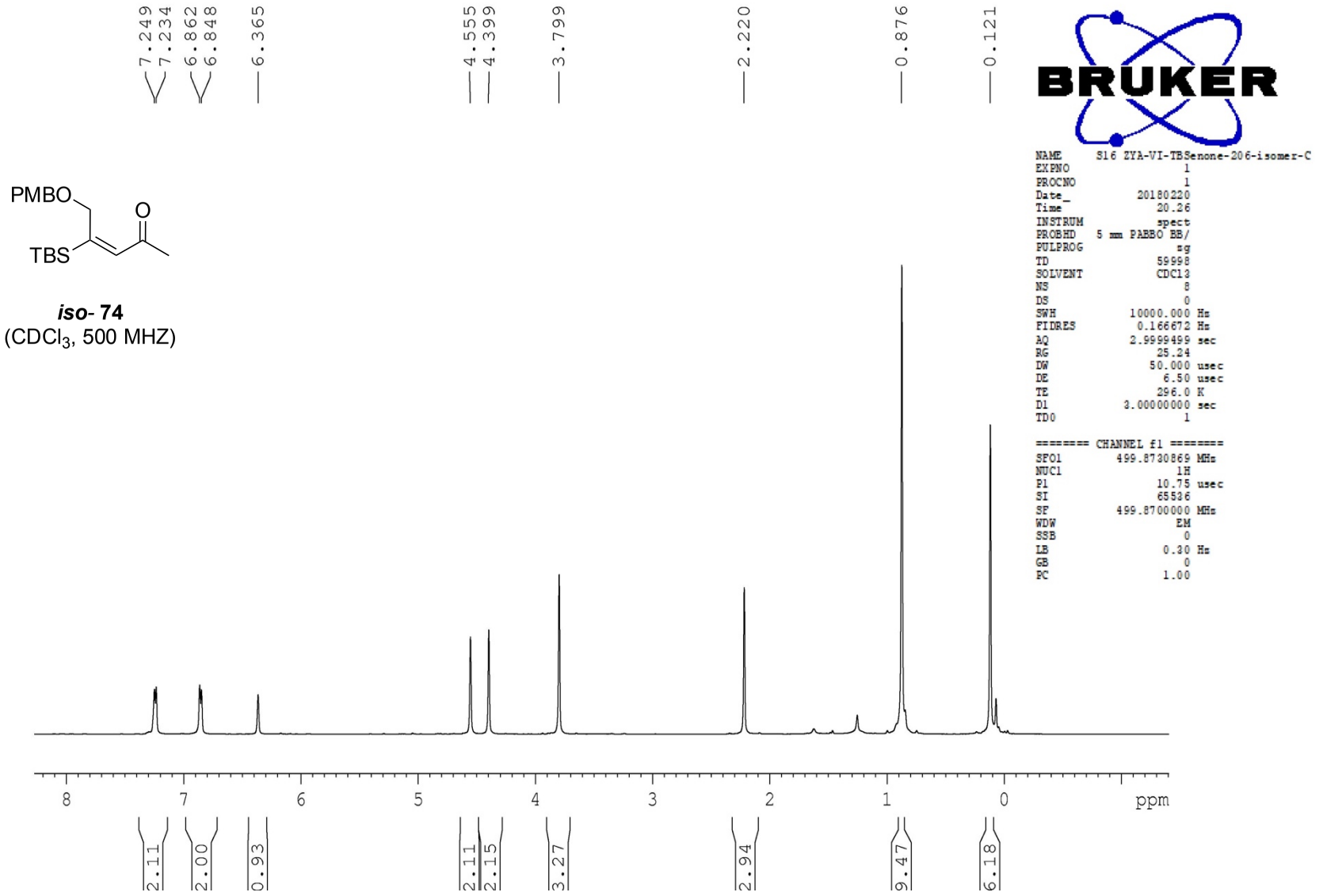
74

($CDCl_3$, 500 MHZ)

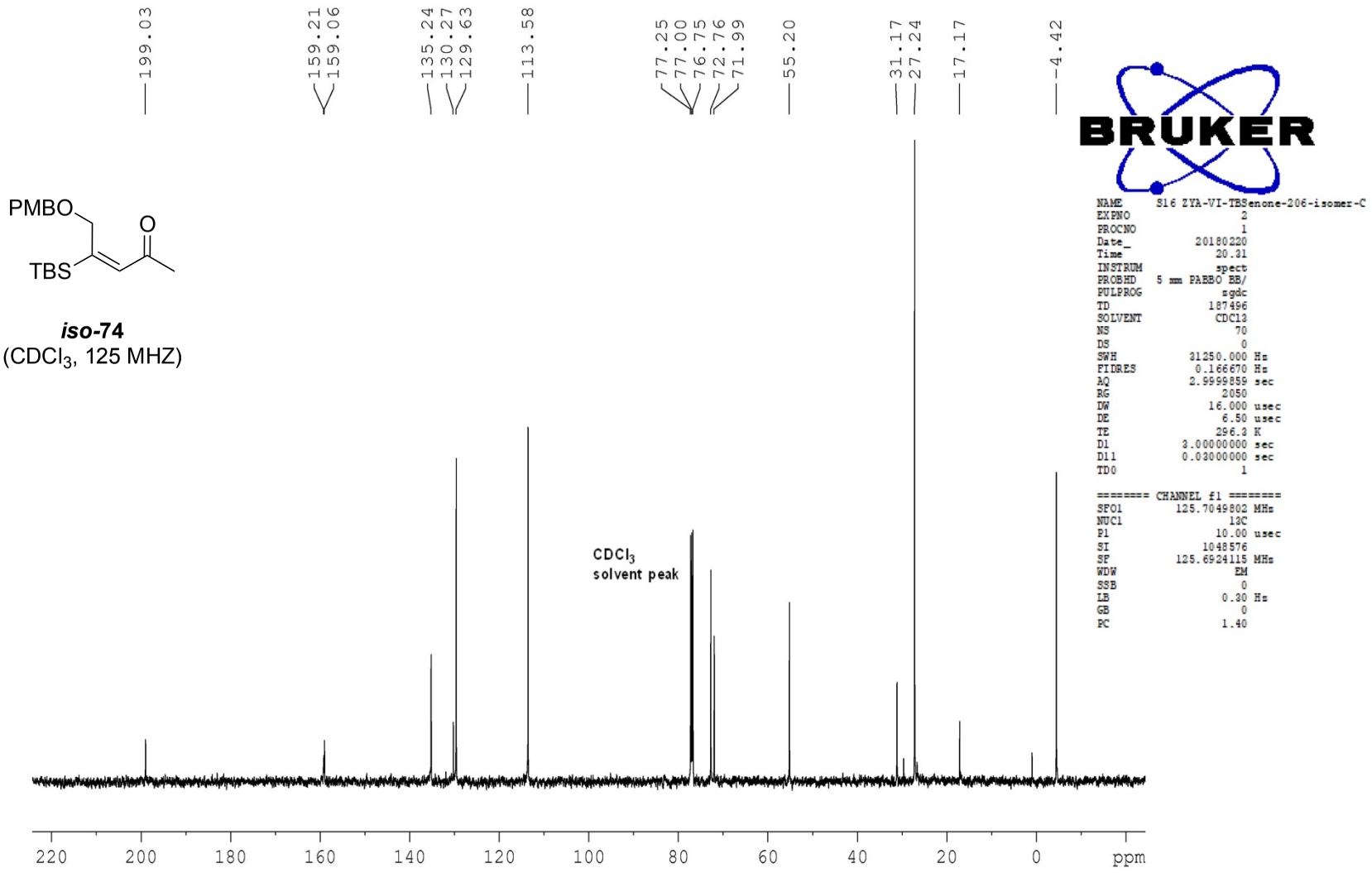
```
NAME      37 ZYA-VI-TBSenone-206-major
EXPNO                 1
PROCNO                1
Date_          20180220
Time              22.48
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG             zg
TD                59998
SOLVENT           CDCl3
NS                    8
DS                    0
SWH           10000.000 Hz
FIDRES         0.166672 Hz
AQ             2.9999499 sec
RG                29.95
DW               50.000 usec
DE                6.50 usec
TE                296.7 K
D1            3.00000000 sec
TD0                   1

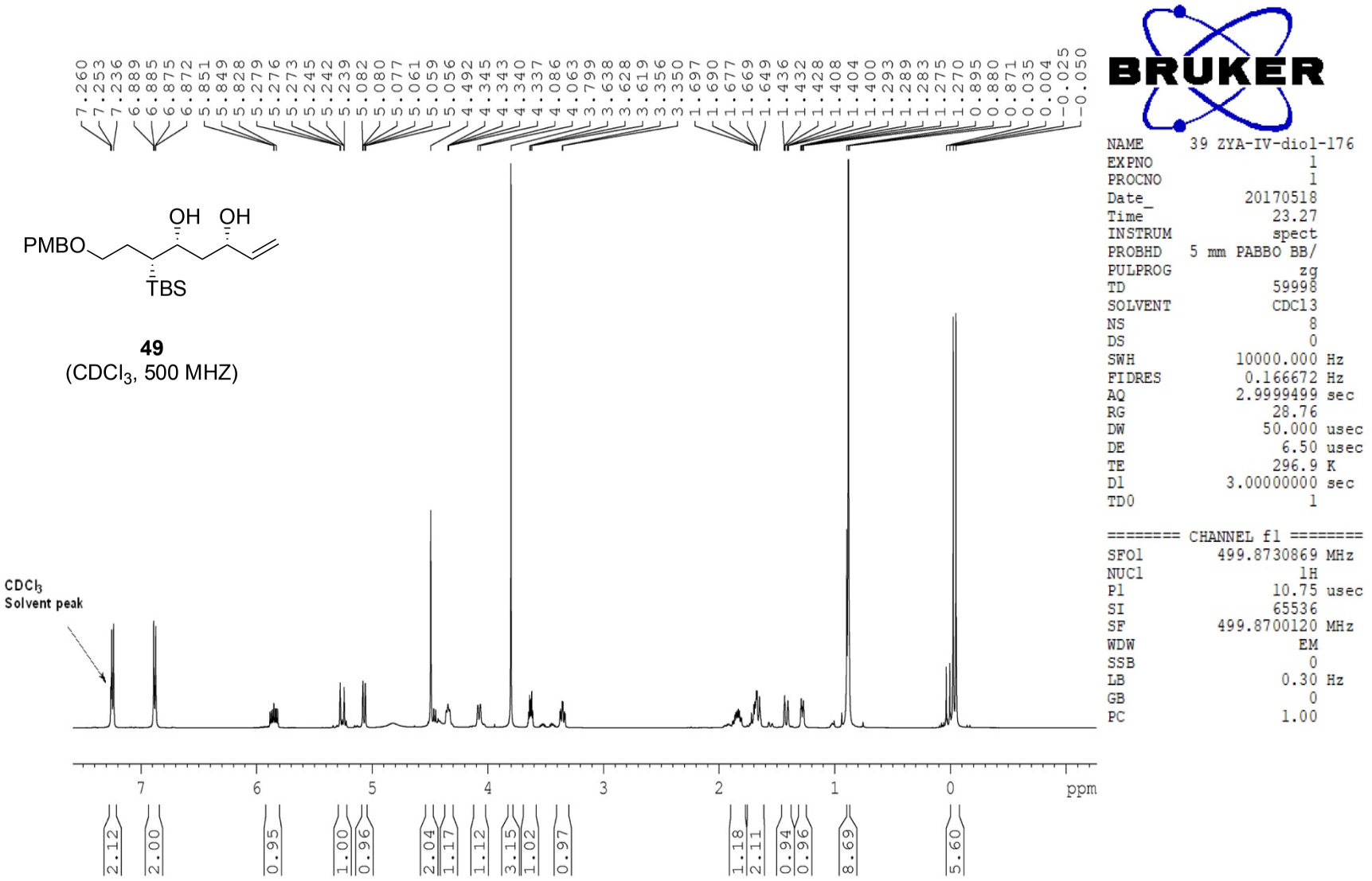
======== CHANNEL f1 ========
SFO1        499.8730869 MHz
NUC1                  1H
P1                10.75 usec
SI                65536
SF          499.8700000 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```


208.63
159.33
148.38
139.10
129.85
129.52
113.82
77.25
77.00
76.75
72.53
68.47
55.26
31.93
26.63
17.56
5.64
PMBO
O
TBS
74
(CDCl3, 125 MHZ)
CDCl3
Solvent peak
220
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME 37 ZYA-VI-TBSenone-206-major
EXPNO 2
PROCNO 1
Date_ 20180220
Time 22.57
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgdc
TD 187496
SOLVENT CDCl3
NS 179
DS 0
SWH 31250.000 Hz
FIDRES 0.166670 Hz
AQ 2.9999859 sec
RG 2050
DW 16.000 usec
DE 6.50 usec
TE 297.5 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7049802 MHz
NUC1 13C
P1 10.00 usec
SI 1048576
SF 125.6924115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40



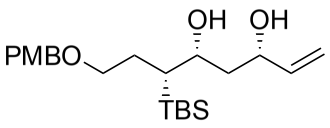
***iso*- 74**
($CDCl_3$, 500 MHZ)


199.03
159.21
159.06
135.24
130.27
129.63
113.58
77.25
77.00
76.75
72.76
71.99
55.20
31.17
27.24
17.17
4.42
PMBO
O
TBS
iso-74
(CDCl3, 125 MHZ)
CDCl3
solvent peak
BRUKER
NAME S16 ZYA-VI-TBSenone-206-isomer-C
EXPNO 2
PROCNO 1
Date_ 20180220
Time 20.31
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgdc
TD 187496
SOLVENT CDCl3
NS 70
DS 0
SWH 31250.000 Hz
FIDRES 0.166670 Hz
AQ 2.9999859 sec
RG 2050
DW 16.000 usec
DE 6.50 usec
TE 296.3 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7049802 MHz
NUC1 13C
P1 10.00 usec
SI 1048576
SF 125.6924115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
220
200
180
160
140
120
100
80
60
40
20
0
ppm



BRUKER

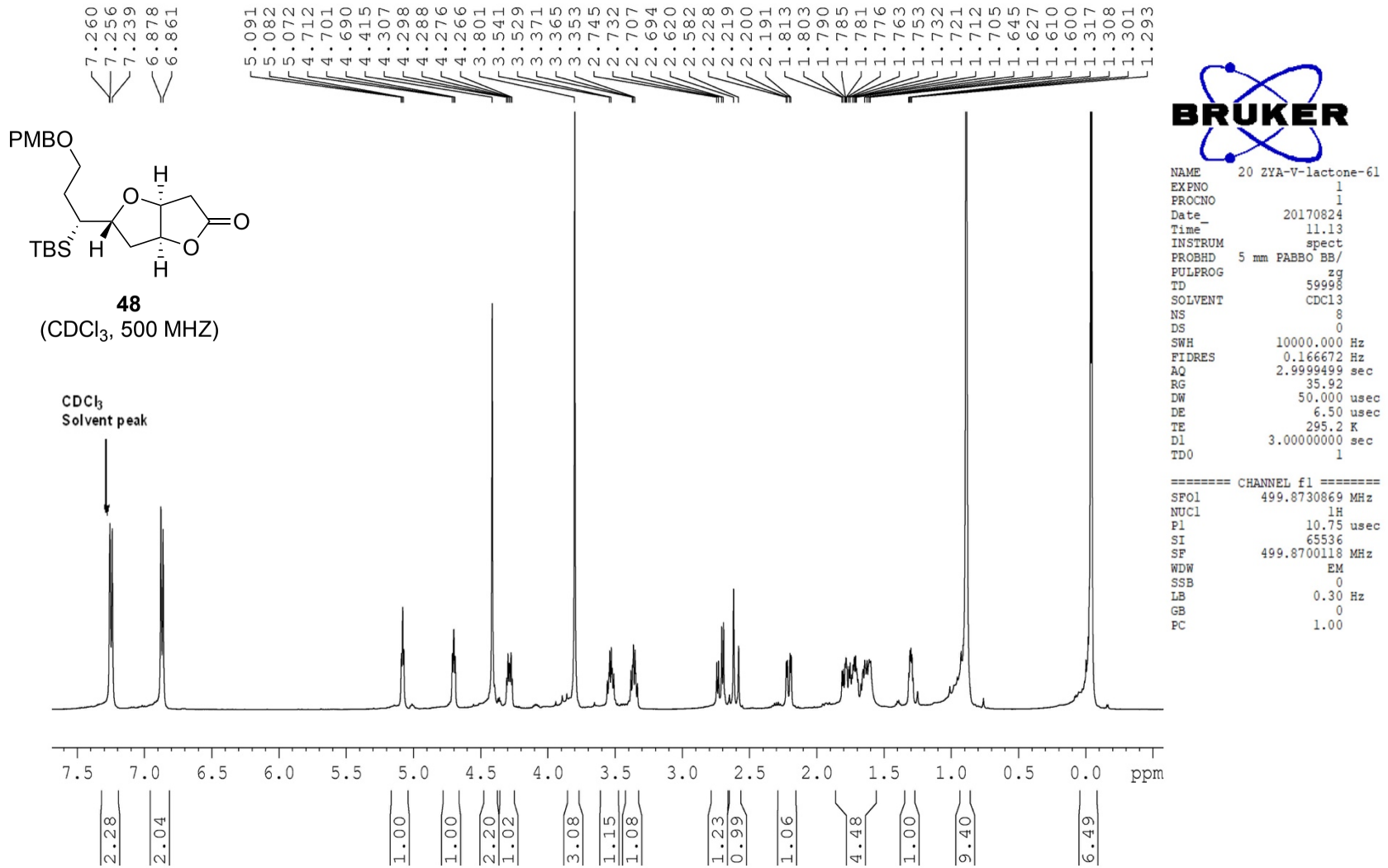
NAME	39 ZYA-IV-diol-176
EXPNO	1
PROCNO	1
Date_	20170518
Time	23.27
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	28.76
DW	50.000 usec
DE	6.50 usec
TE	296.9 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700120 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



49
($CDCl_3$, 125 MHZ)

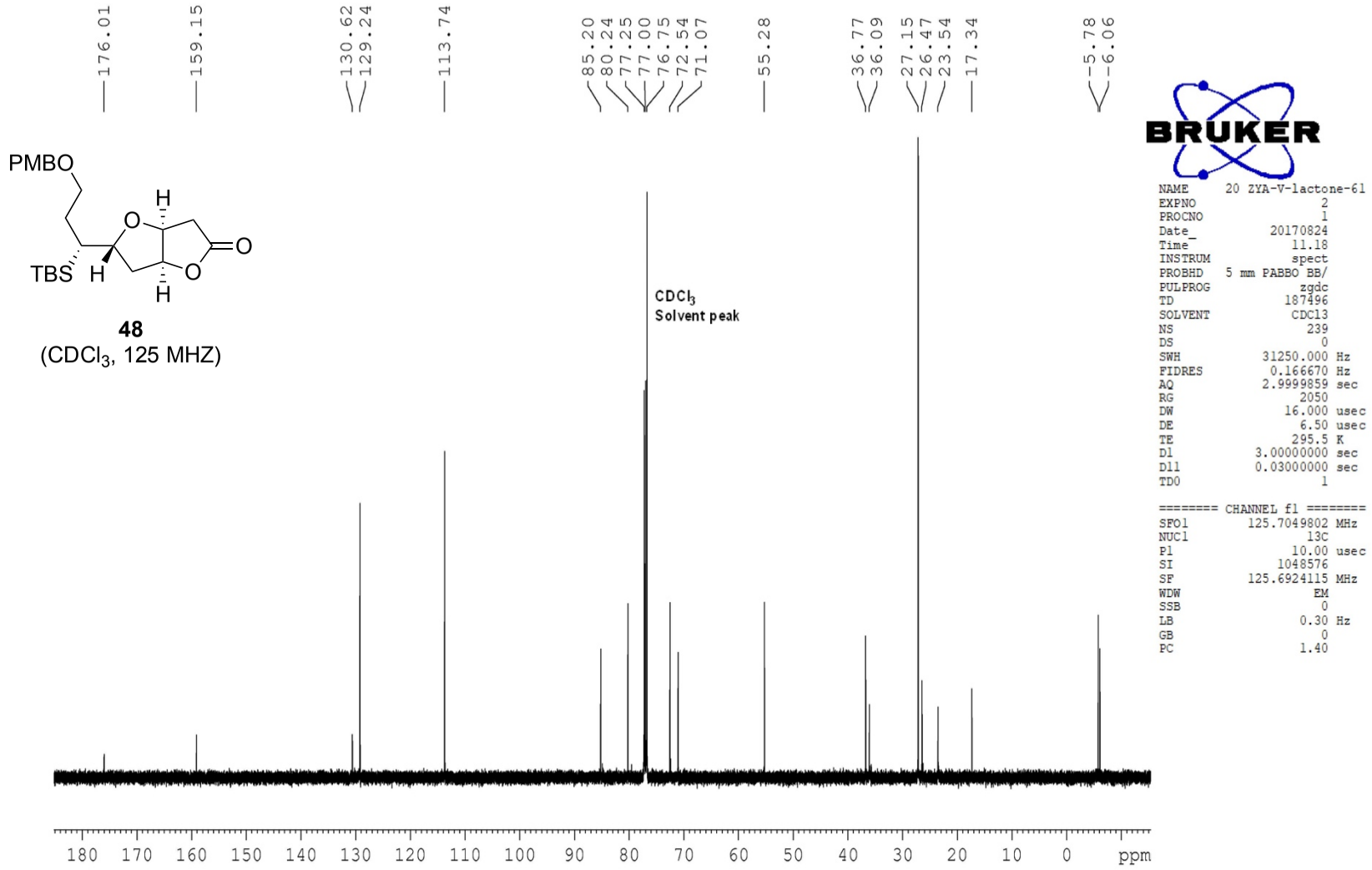
BRUKER

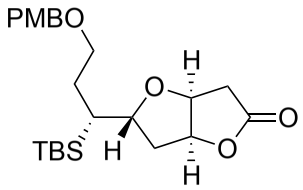
NAME	39 ZYA-IV-diol-176
EXPNO	2
PROCNO	1
Date_	20170518
Time	23.36
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	185
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	297.6 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924146 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

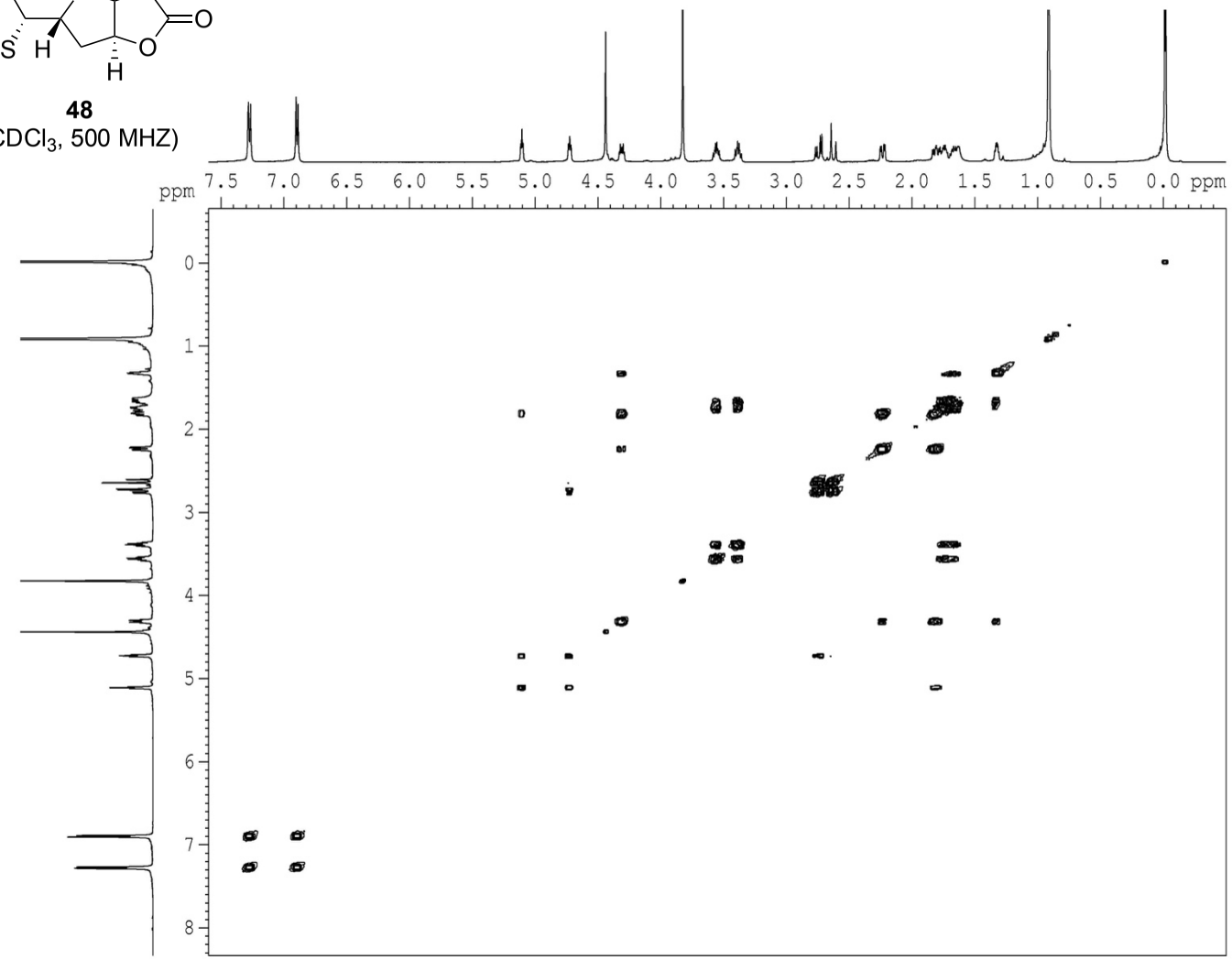
NAME	20 ZYA-V-lactone-61
EXPNO	1
PROCNO	1
Date_	20170824
Time	11.13
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	35.92
DW	50.000 usec
DE	6.50 usec
TE	295.2 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700118 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00


176.01
159.15
130.62
129.24
113.74
85.20
80.24
77.25
77.00
76.75
72.54
71.07
55.28
36.77
36.09
27.15
26.47
23.54
17.34
5.78
6.06
PMBO
TBS
H
O
O
O
H
H
48
(CDCl3, 125 MHZ)
CDCl3
Solvent peak
BRUKER
NAME 20 ZYA-V-lactone-61
EXPNO 2
PROCNO 1
Date_ 20170824
Time 11.18
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgdc
TD 187496
SOLVENT CDCl3
NS 239
DS 0
SWH 31250.000 Hz
FIDRES 0.166670 Hz
AQ 2.9999859 sec
RG 2050
DW 16.000 usec
DE 6.50 usec
TE 295.5 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7049802 MHz
NUC1 13C
P1 10.00 usec
SI 1048576
SF 125.6924115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



48

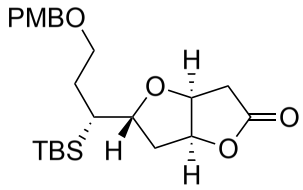
($CDCl_3$, 500 MHZ)



BRUKER

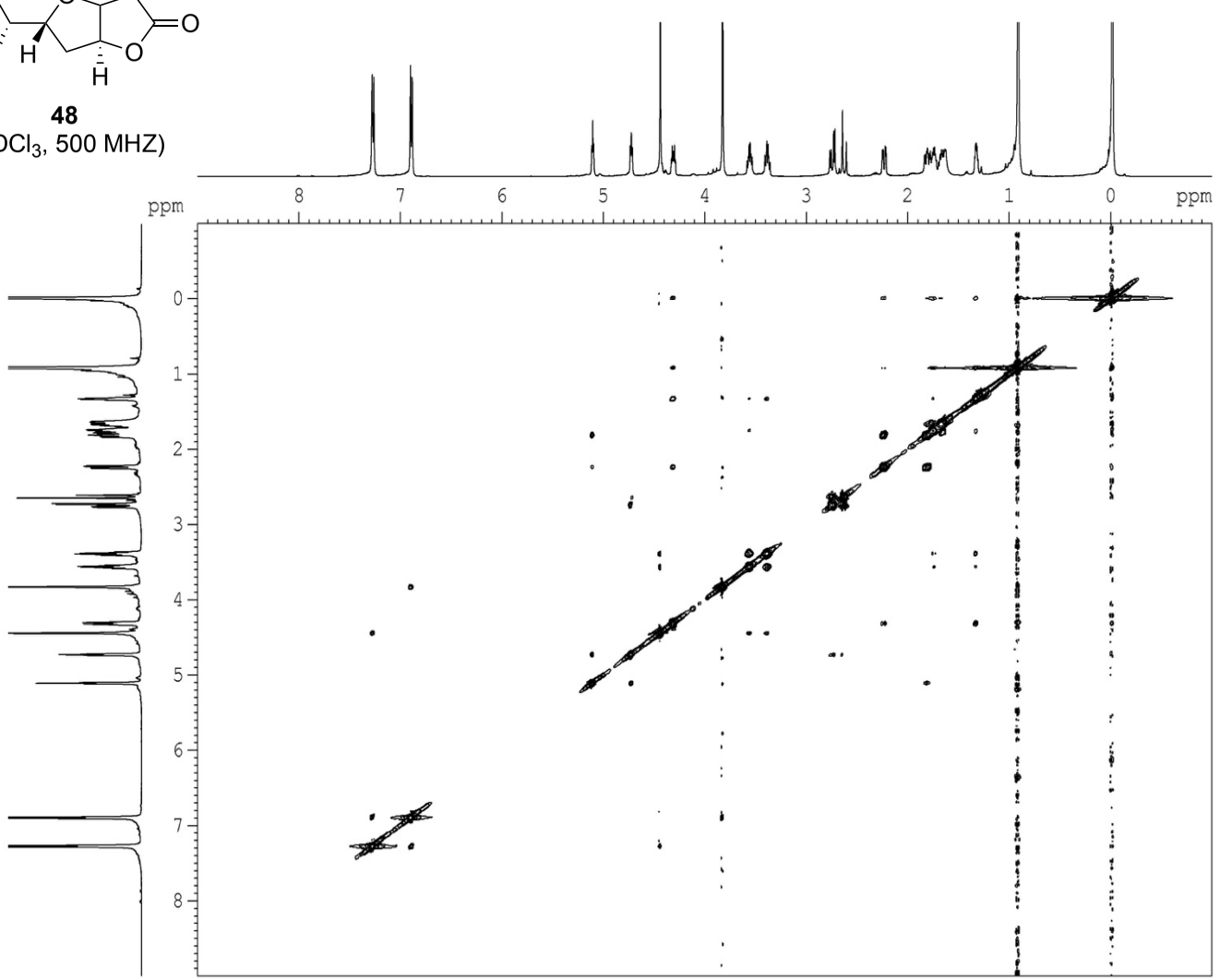
```
NAME        20 ZYA-V-lactone-61
EXPNO                        3
PROCNO                       1
Date_                 20170927
Time                      0.40
INSTRUM                  spect
PROBHD    5 mm PATXI 1H/
PULPROG          cosygpmfqf
TD                        2048
SOLVENT                 CDCl3
NS                           1
DS                           8
SWH                5000.000 Hz
FIDRES                2.441406 Hz
AQ                 0.2048500 sec
RG                        64.36
DW                   100.000 usec
DE                    10.00 usec
TE                    293.5 K
D0                 0.00000300 sec
D1                 2.00000000 sec
D13                0.00000400 sec
D16                0.00020000 sec
IN0                0.00020000 sec

======== CHANNEL f1 ========
SFO1            500.1320005 MHz
NUC1                      1H
P1                     8.00 usec
ND0                          1
TD                         128
SFO1                500.132 MHz
FIDRES              39.062500 Hz
SW                     9.997 ppm
FnMODE                    QF
SI                        1024
SF              500.1300000 MHz
WDW                     SINE
SSB                          0
LB                     0.00 Hz
GB                           0
PC                        1.40
SI                        1024
MC2                       QF
SF              500.1300000 MHz
WDW                     SINE
SSB                          0
LB                     0.00 Hz
GB                           0
```



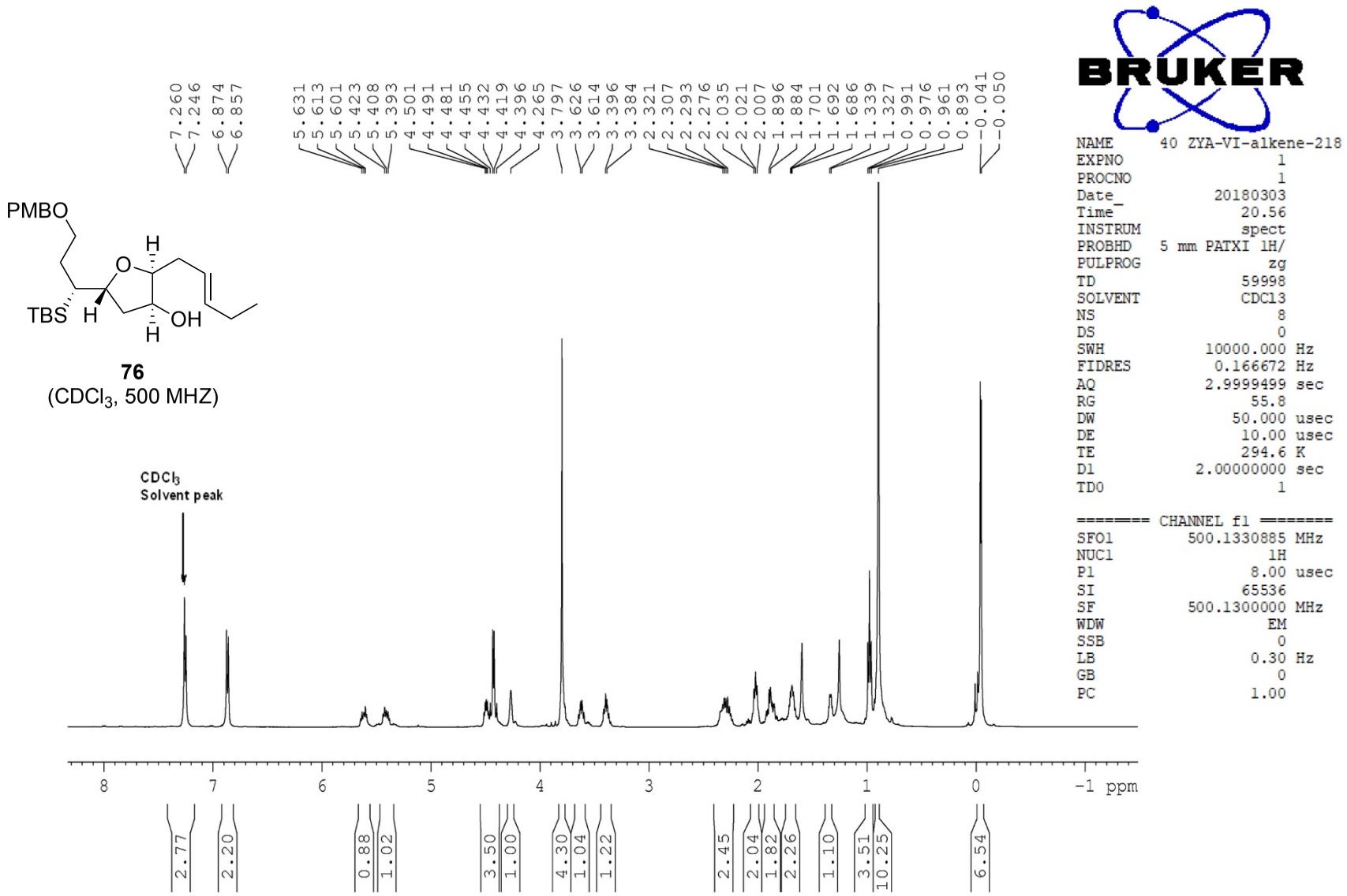
48

($CDCl_3$, 500 MHZ)




```
NAME        20 ZYA-V-lactone-61
EXPNO                        4
PROCNO                       1
Date_                 20170927
Time                      0.48
INSTRUM                  spect
PROBHD     5 mm PATXI 1H/
PULPROG       noesygpphpp
TD                        2048
SOLVENT                 CDCl3
NS                           4
DS                          16
SWH                 5000.000 Hz
FIDRES              2.441406 Hz
AQ                  0.2048500 sec
RG                      11.29
DW                    100.000 usec
DE                     10.00 usec
TE                     293.7 K
D0                  0.00008981 sec
D1                  2.00000000 sec
D8                  0.80000001 sec
D11                 0.03000000 sec
D12                 0.00002000 sec
D16                 0.00020000 sec
IN0                 0.00020000 sec

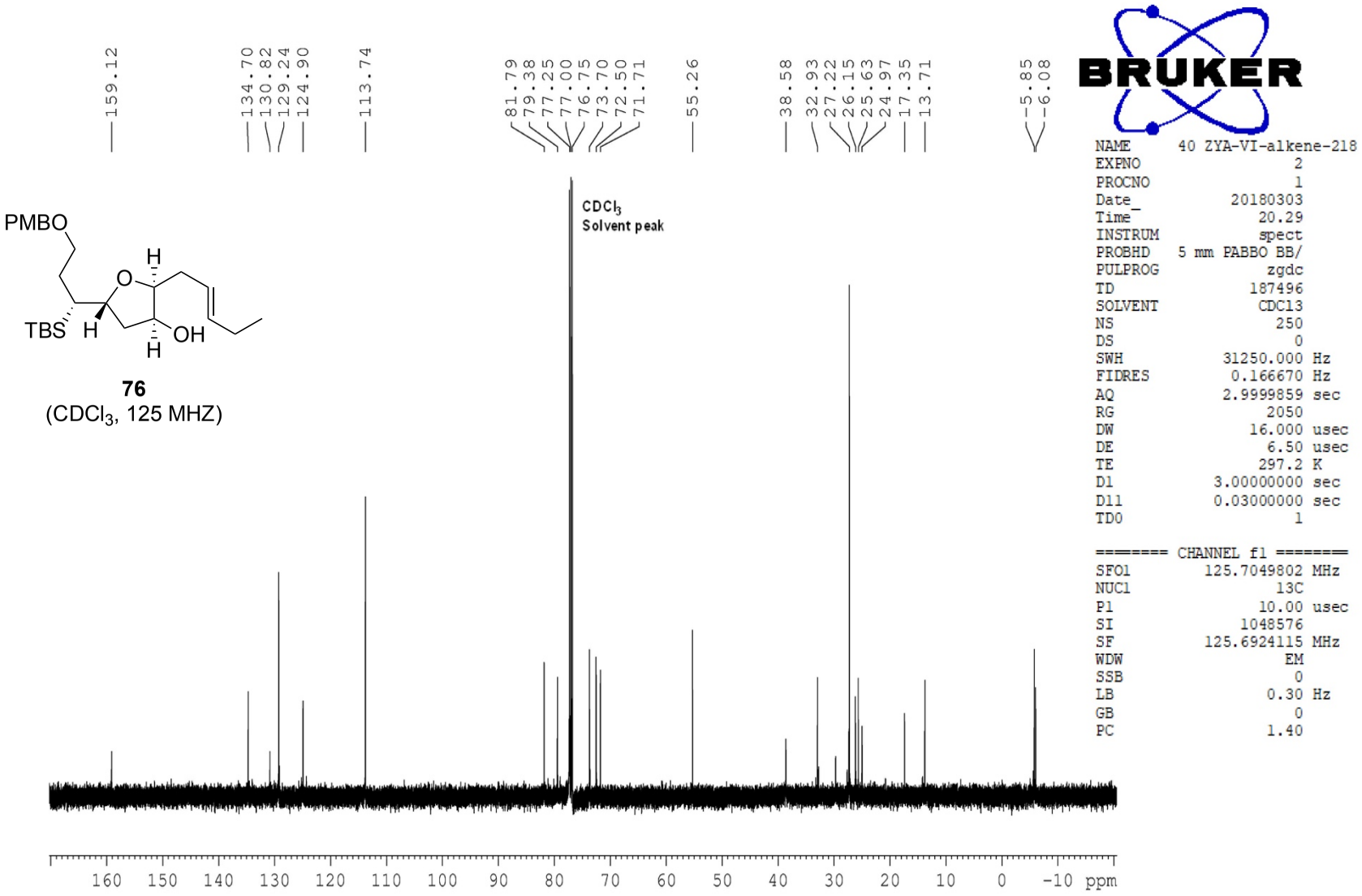
======== CHANNEL f1 ========
SFO1             500.1320005 MHz
NUC1                       1H
P1                       8.00 usec
P2                      16.00 usec
P17                   2500.00 usec
ND0                         1
TD                        256
SFO1                  500.132 MHz
FIDRES               19.531250 Hz
SW                        9.997 ppm
FnMODE            States-TPPI
SI                        1024
SF                500.1300000 MHz
WDW                     QSINE
SSB                         2
LB                       0.00 Hz
GB                          0
PC                       1.00
SI                        1024
MC2               States-TPPI
SF                500.1300000 MHz
WDW                     QSINE
SSB                         2
LB                       0.00 Hz
GB                          0
```



76
($CDCl_3$, 500 MHZ)

BRUKER

NAME	40 ZYA-VI-alkene-218
EXPNO	1
PROCNO	1
Date_	20180303
Time	20.56
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	55.8
DW	50.000 usec
DE	10.00 usec
TE	294.6 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	500.1330885 MHz
NUC1	1H
P1	8.00 usec
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

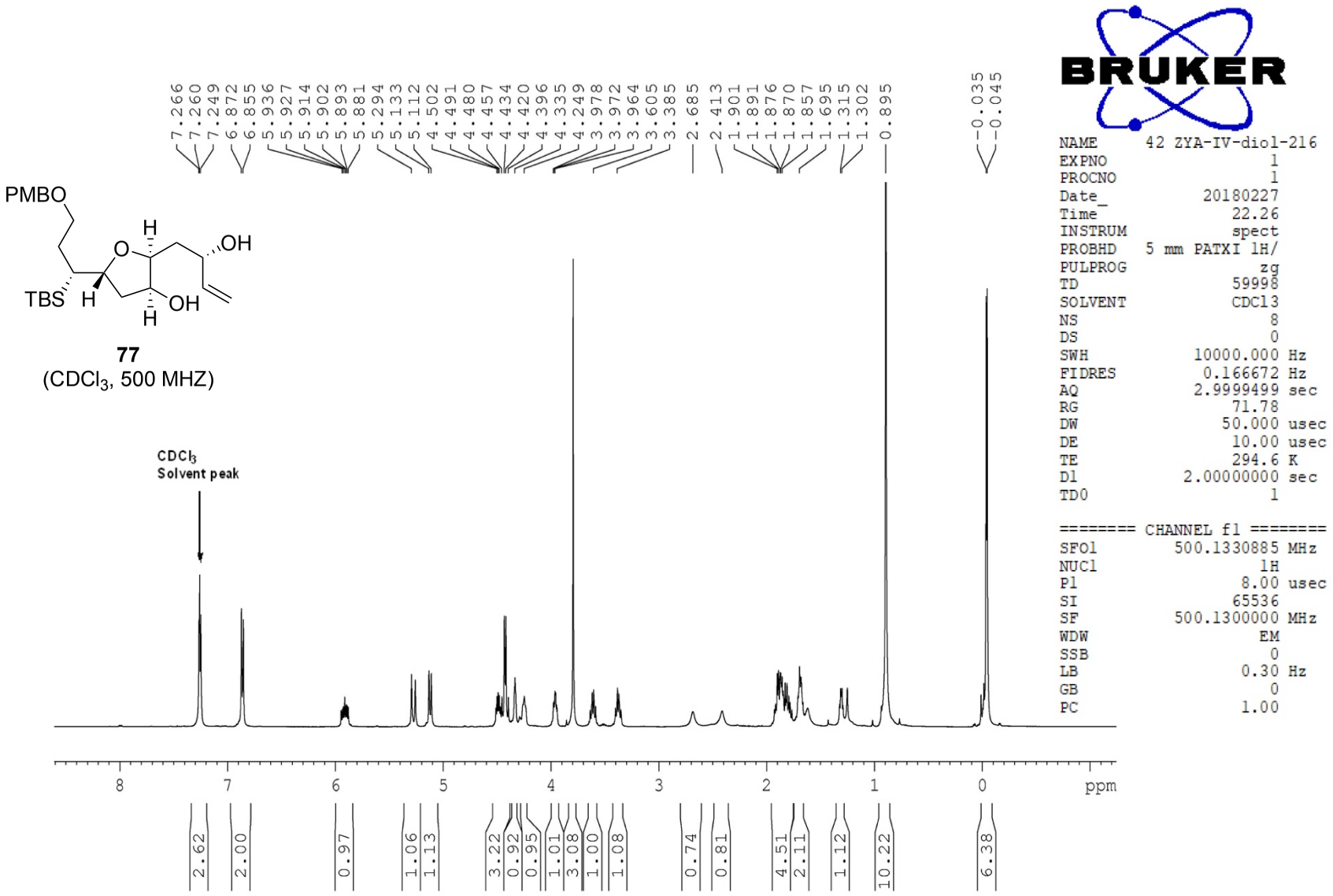


76

($CDCl_3$, 125 MHZ)

```
NAME          40 ZYA-VI-alkene-218
EXPNO                            2
PROCNO                           1
Date_                     20180303
Time                         20.29
INSTRUM                      spect
PROBHD       5 mm PABBO BB/
PULPROG                       zgdc
TD                          187496
SOLVENT                      CDCl3
NS                             250
DS                               0
SWH                   31250.000 Hz
FIDRES                 0.166670 Hz
AQ                     2.9999859 sec
RG                          2050
DW                        16.000 usec
DE                         6.50 usec
TE                        297.2 K
D1                    3.00000000 sec
D11                   0.03000000 sec
TD0                              1

======== CHANNEL f1 ========
SFO1                125.7049802 MHz
NUC1                         13C
P1                        10.00 usec
SI                        1048576
SF                  125.6924115 MHz
WDW                            EM
SSB                              0
LB                         0.30 Hz
GB                               0
PC                            1.40
```

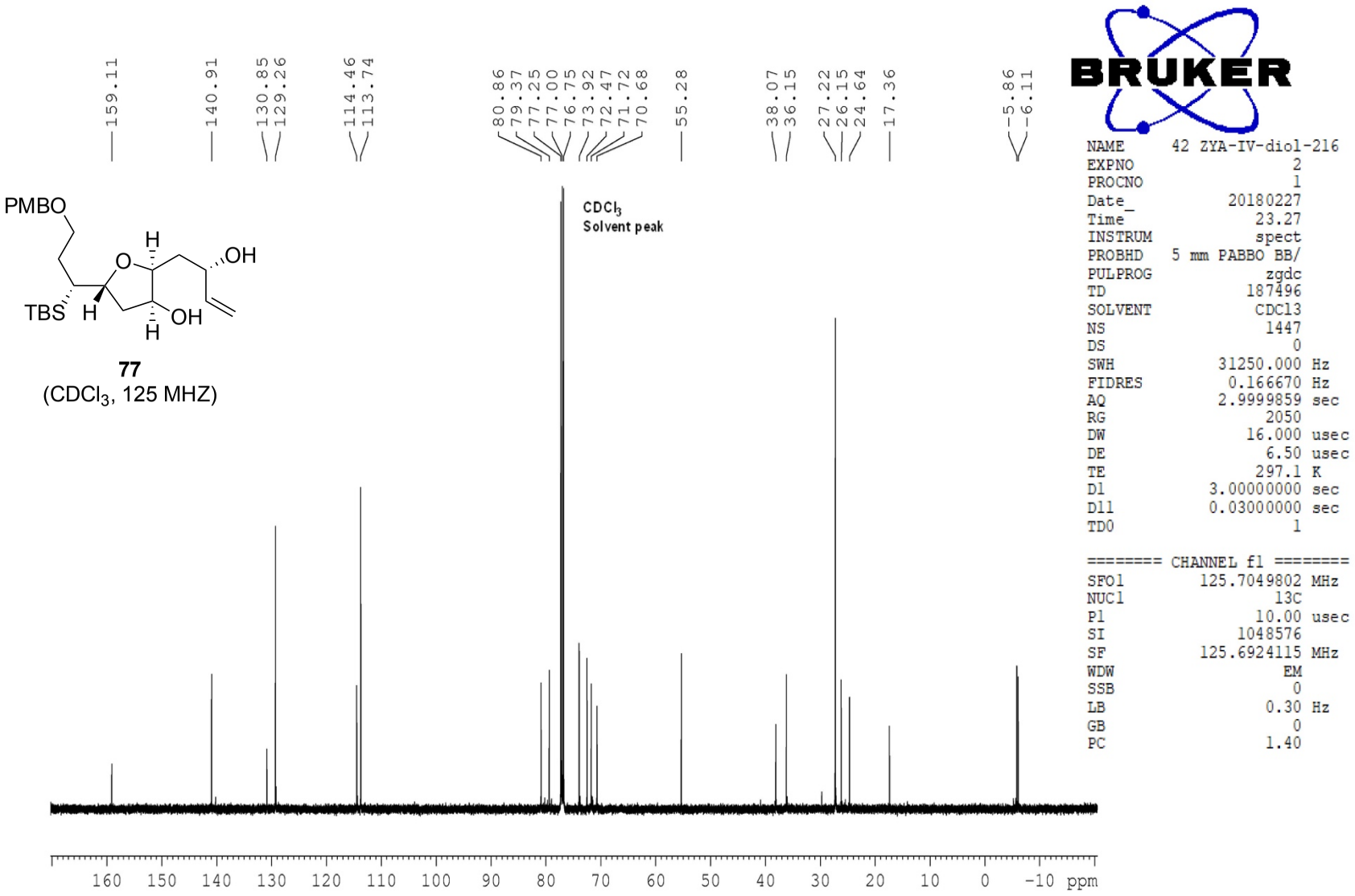


77

($CDCl_3$, 500 MHZ)

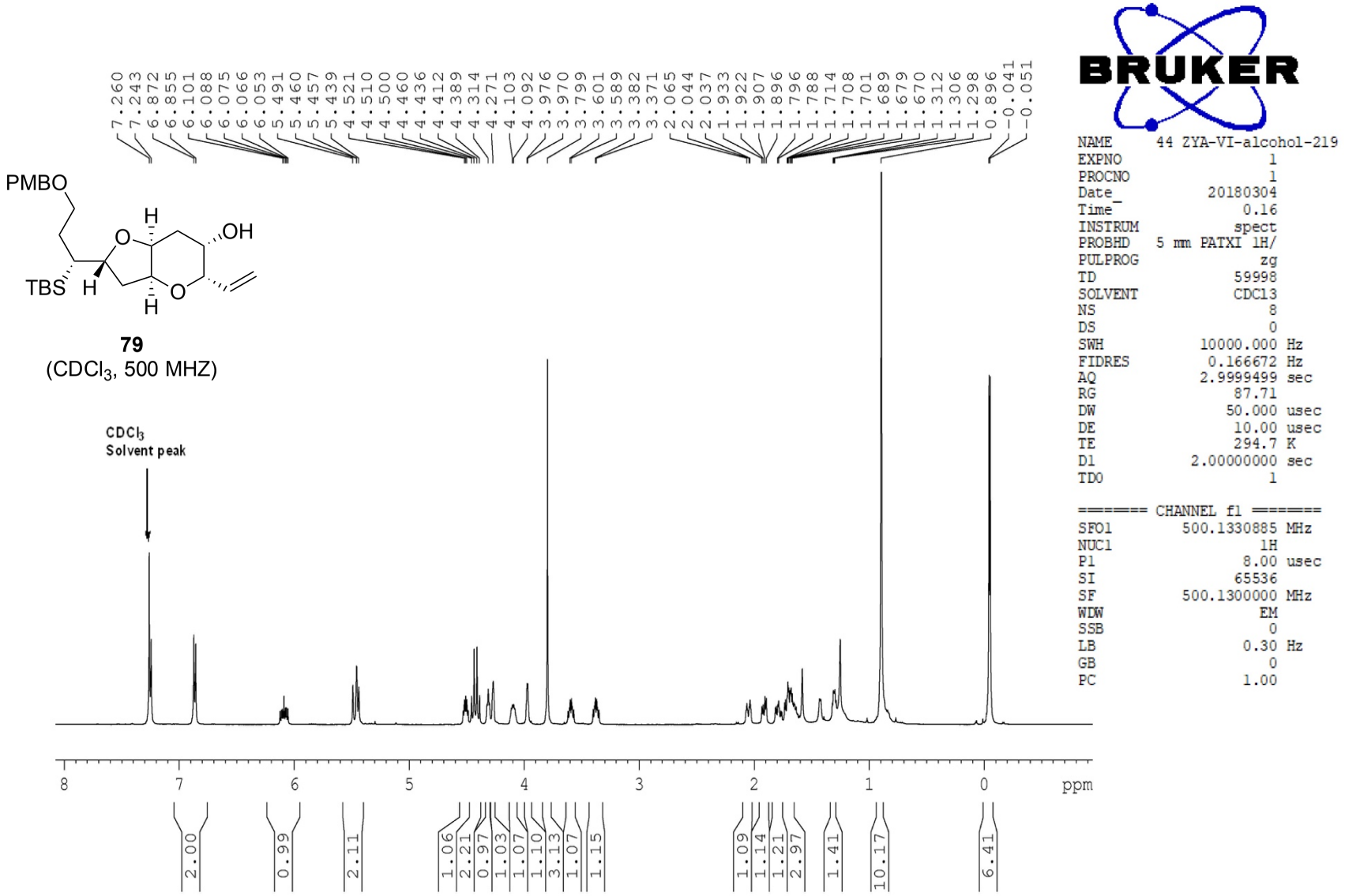
```
NAME        42 ZYA-IV-diol-216
EXPNO                        1
PROCNO                       1
Date_                 20180227
Time                     22.26
INSTRUM                  spect
PROBHD    5 mm PATXI 1H/
PULPROG                     zg
TD                       59998
SOLVENT                  CDCl3
NS                           8
DS                           0
SWH                10000.000 Hz
FIDRES              0.166672 Hz
AQ                  2.9999499 sec
RG                       71.78
DW                     50.000 usec
DE                     10.00 usec
TE                     294.6 K
D1                 2.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1            500.1330885 MHz
NUC1                        1H
P1                     8.00 usec
SI                       65536
SF              500.1300000 MHz
WDW                         EM
SSB                          0
LB                     0.30 Hz
GB                           0
PC                        1.00
```



BRUKER

NAME	42 ZYA-IV-diol-216
EXPNO	2
PROCNO	1
Date_	20180227
Time	23.27
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	1447
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	297.1 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

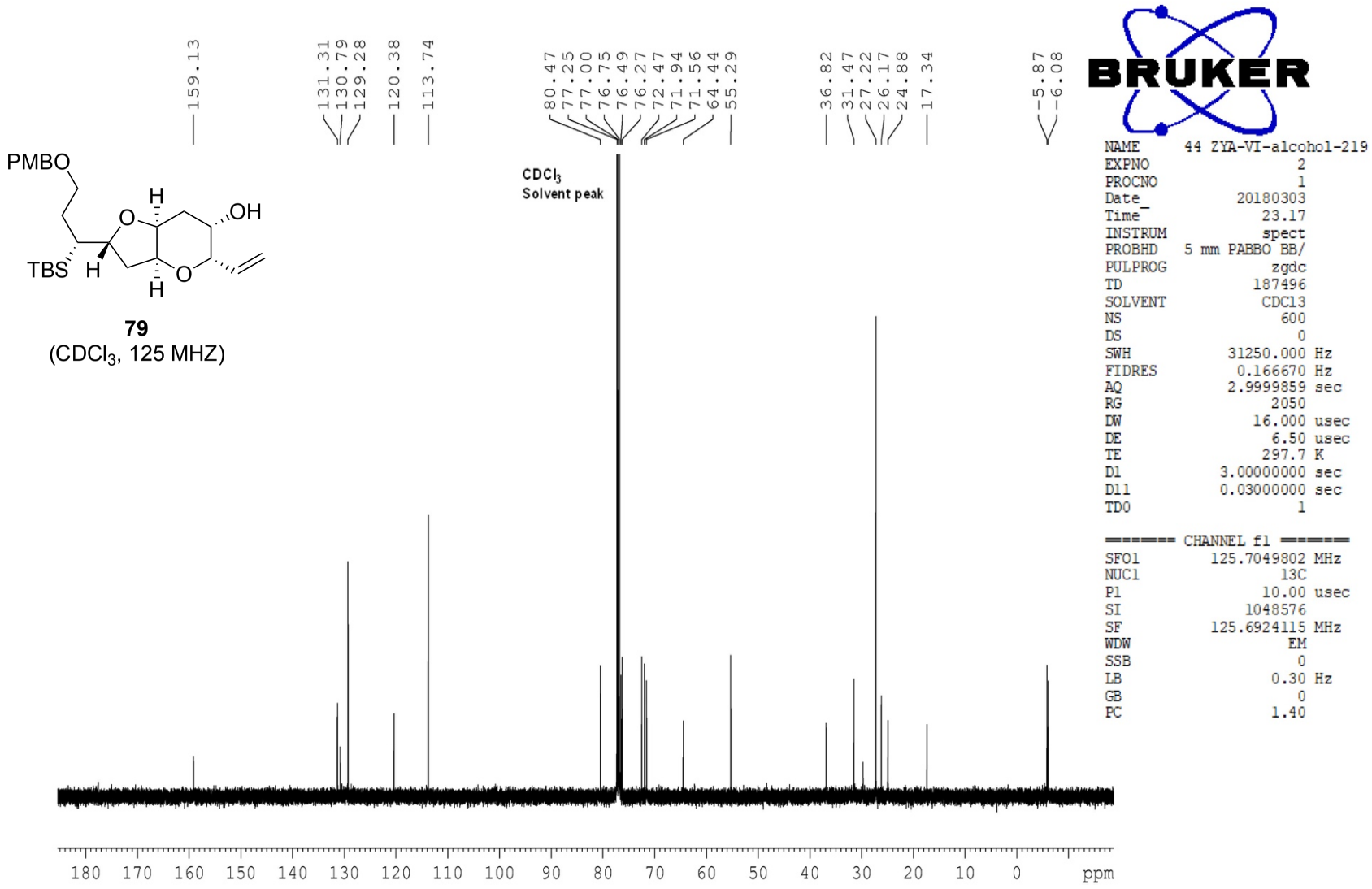


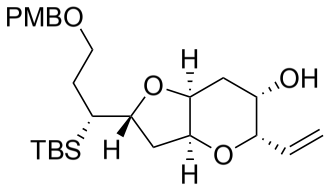
79

($CDCl_3$, 500 MHZ)

BRUKER

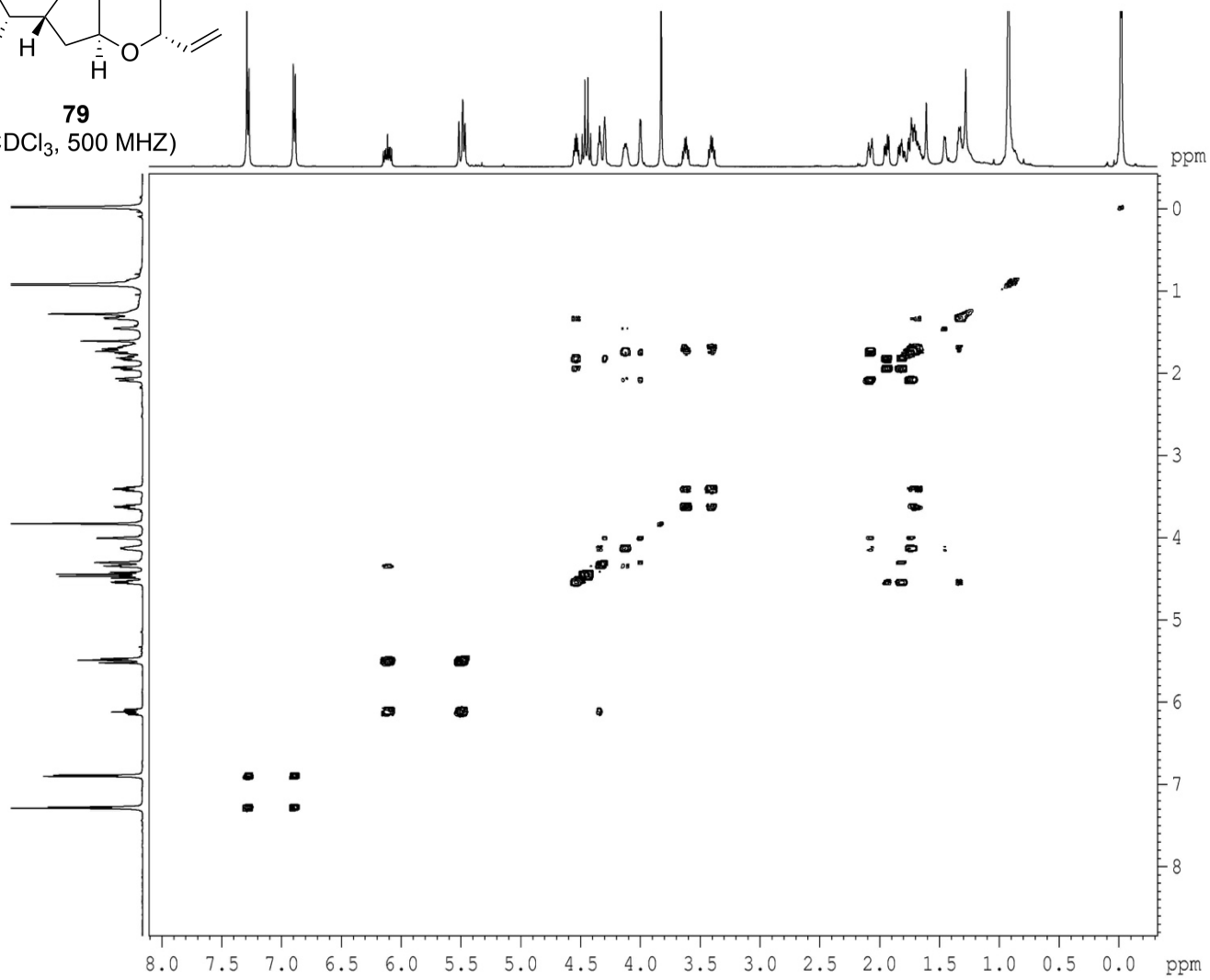
NAME	44 ZYA-VI-alcohol-219
EXPNO	1
PROCNO	1
Date_	20180304
Time	0.16
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	87.71
DW	50.000 usec
DE	10.00 usec
TE	294.7 K
D1	2.00000000 sec
TD0	1
======= CHANNEL f1 =======	
SFO1	500.1330885 MHz
NUC1	1H
P1	8.00 usec
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00


159.13
131.31
130.79
129.28
120.38
113.74
80.47
77.25
77.00
76.75
76.49
76.27
72.47
71.94
71.56
64.44
55.29
36.82
31.47
27.22
26.17
24.88
17.34
-5.87
-6.08
CDCl3
Solvent peak
PMBO
TBS
OH
H
O
H
H
O
79
(CDCl3, 125 MHZ)
BRUKER
NAME 44 ZYA-VI-alcohol-219
EXPNO 2
PROCNO 1
Date_ 20180303
Time 23.17
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgdc
TD 187496
SOLVENT CDCl3
NS 600
DS 0
SWH 31250.000 Hz
FIDRES 0.166670 Hz
AQ 2.9999859 sec
RG 2050
DW 16.000 usec
DE 6.50 usec
TE 297.7 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1
======= CHANNEL f1 ======
SFO1 125.7049802 MHz
NUC1 13C
P1 10.00 usec
SI 1048576
SF 125.6924115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



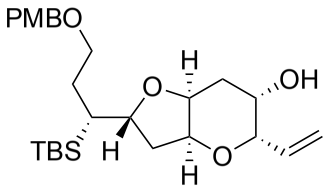
79

($CDCl_3$, 500 MHZ)



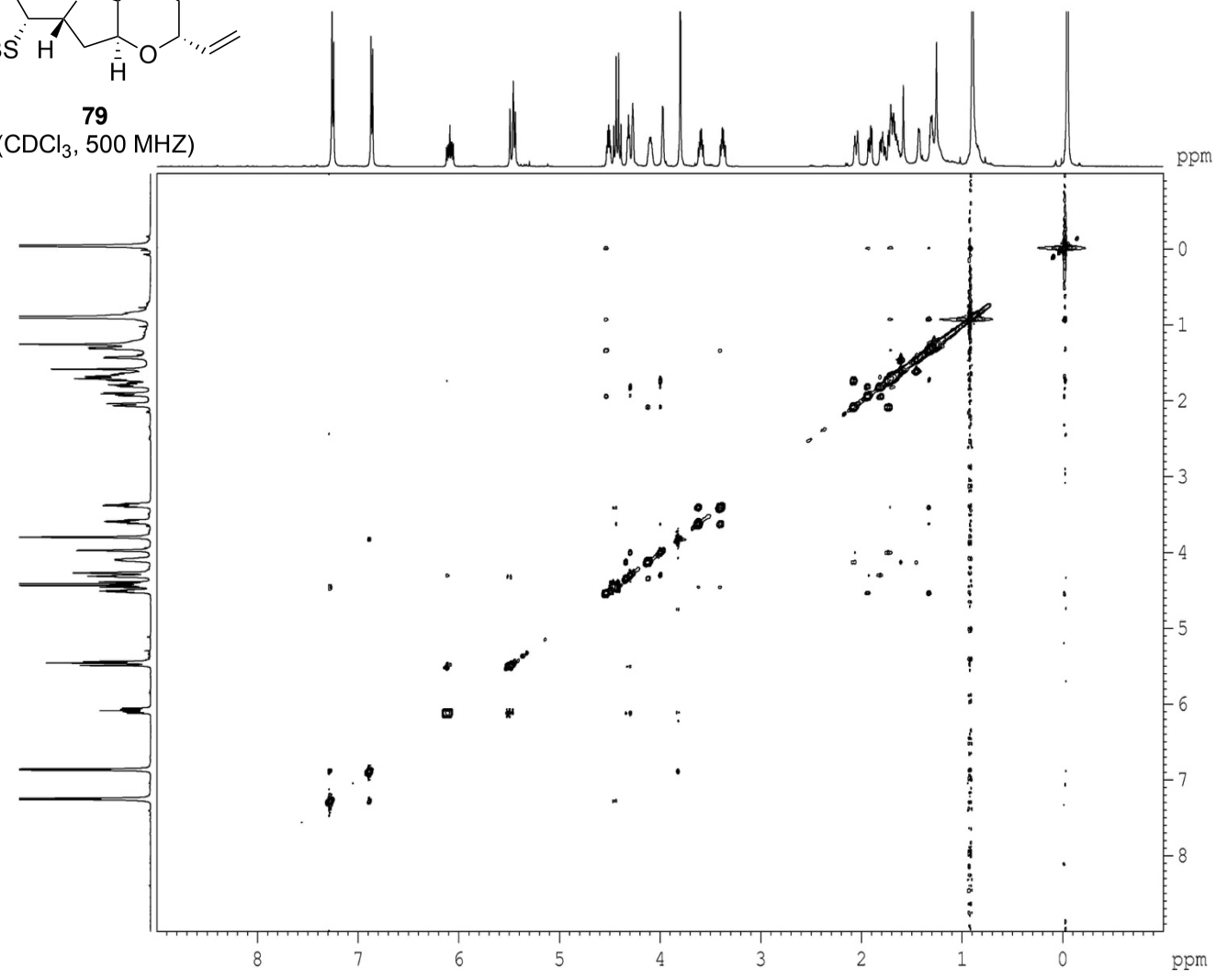
BRUKER

NAME	44 ZYA-VI-alcohol-219
EXPNO	3
PROCNO	1
Date_	20180304
Time	0.18
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	cosygpmfqf
TD	2048
SOLVENT	CDCl3
NS	1
DS	8
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2048500 sec
RG	64.36
DW	100.000 usec
DE	10.00 usec
TE	294.7 K
D0	0.00000300 sec
D1	2.00000000 sec
D13	0.00000400 sec
D16	0.00020000 sec
IN0	0.00020000 sec
======= CHANNEL f1 =======	
SFO1	500.1320005 MHz
NUC1	1H
P1	8.00 usec
ND0	1
TD	128
SFO1	500.132 MHz
FIDRES	39.062500 Hz
SW	9.997 ppm
FnMODE	QF
SI	1024
SF	500.1300000 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.40
SI	1024
MC2	QF
SF	500.1300000 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0



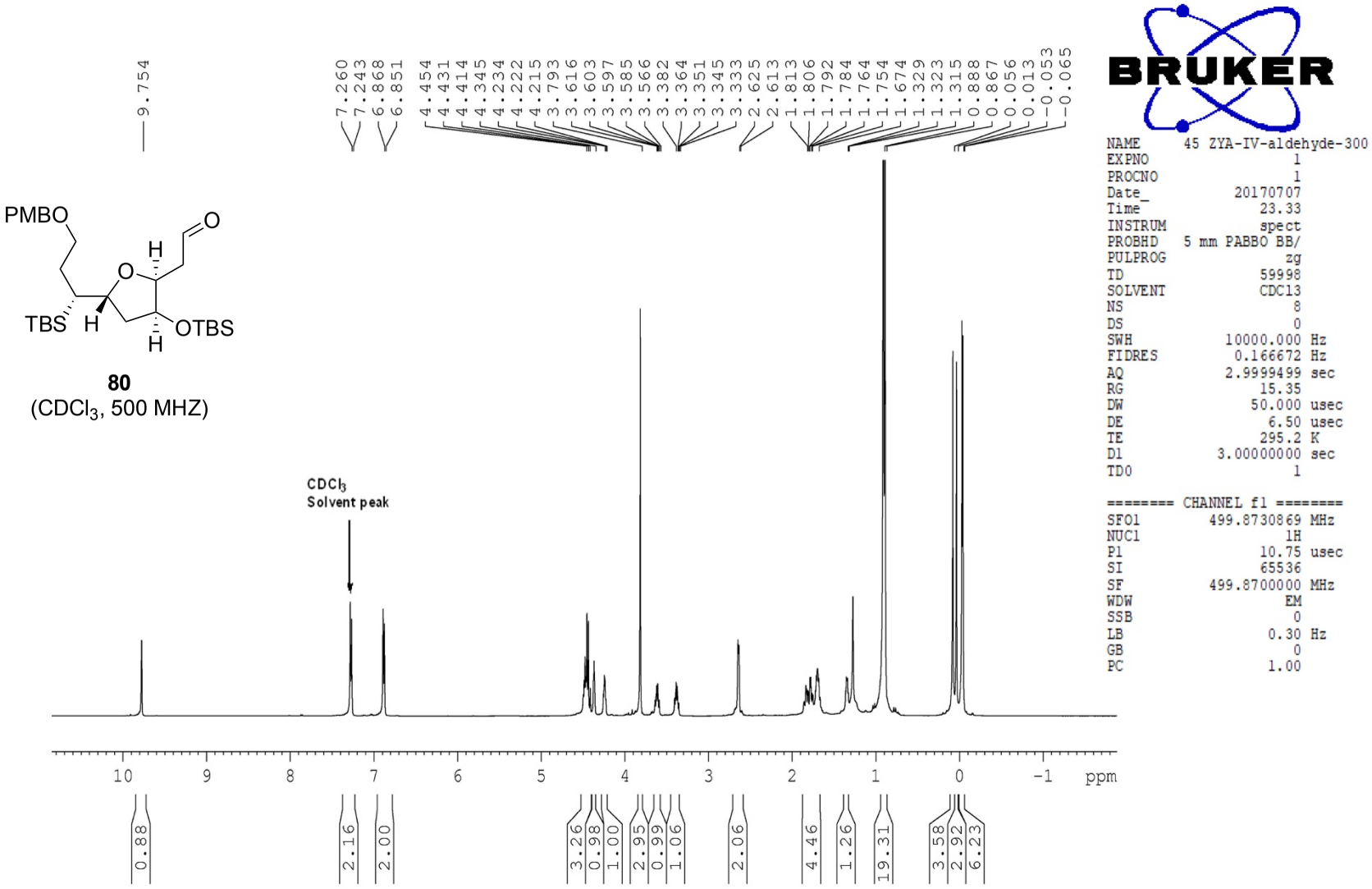
79

($CDCl_3$, 500 MHZ)



BRUKER

NAME	44 ZYA-VI-alcohol-219
EXPNO	4
PROCNO	1
Date_	20180304
Time	0.27
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	noesygpphpp
TD	2048
SOLVENT	CDCl3
NS	4
DS	16
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2048500 sec
RG	11.29
DW	100.000 usec
DE	10.00 usec
TE	294.6 K
D0	0.00008981 sec
D1	2.00000000 sec
D8	0.80000001 sec
D11	0.03000000 sec
D12	0.00002000 sec
D16	0.00020000 sec
IN0	0.00020000 sec
======= CHANNEL f1 =======	
SFO1	500.1320005 MHz
NUC1	1H
P1	8.00 usec
P2	16.00 usec
P17	2500.00 usec
ND0	1
TD	256
SFO1	500.132 MHz
FIDRES	19.531250 Hz
SW	9.997 ppm
FnMODE	States-TPPI
SI	1024
SF	500.1300000 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.00
SI	1024
MC2	States-TPPI
SF	500.1300000 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

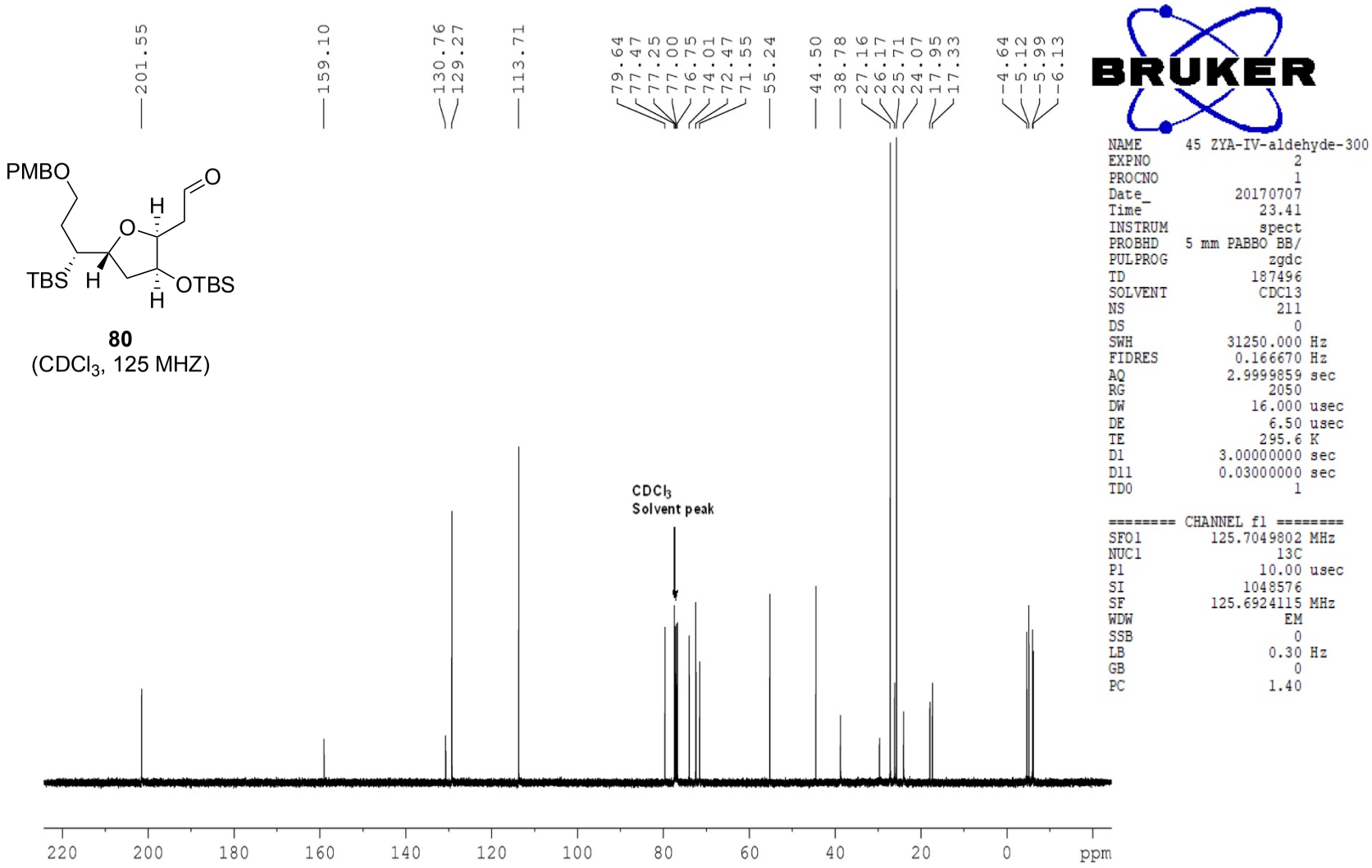


80

($CDCl_3$, 500 MHZ)

```
NAME        45 ZYA-IV-aldehyde-300
EXPNO                            1
PROCNO                           1
Date_                     20170707
Time                         23.33
INSTRUM                      spect
PROBHD    5 mm PABBO BB/
PULPROG                         zg
TD                           59998
SOLVENT                      CDCl3
NS                               8
DS                               0
SWH                  10000.000 Hz
FIDRES                0.166672 Hz
AQ                    2.9999499 sec
RG                           15.35
DW                        50.000 usec
DE                         6.50 usec
TE                        295.2 K
D1                   3.00000000 sec
TD0                              1

======== CHANNEL f1 ========
SFO1               499.8730869 MHz
NUC1                         1H
P1                        10.75 usec
SI                           65536
SF                 499.8700000 MHz
WDW                          EM
SSB                           0
LB                         0.30 Hz
GB                            0
PC                         1.00
```

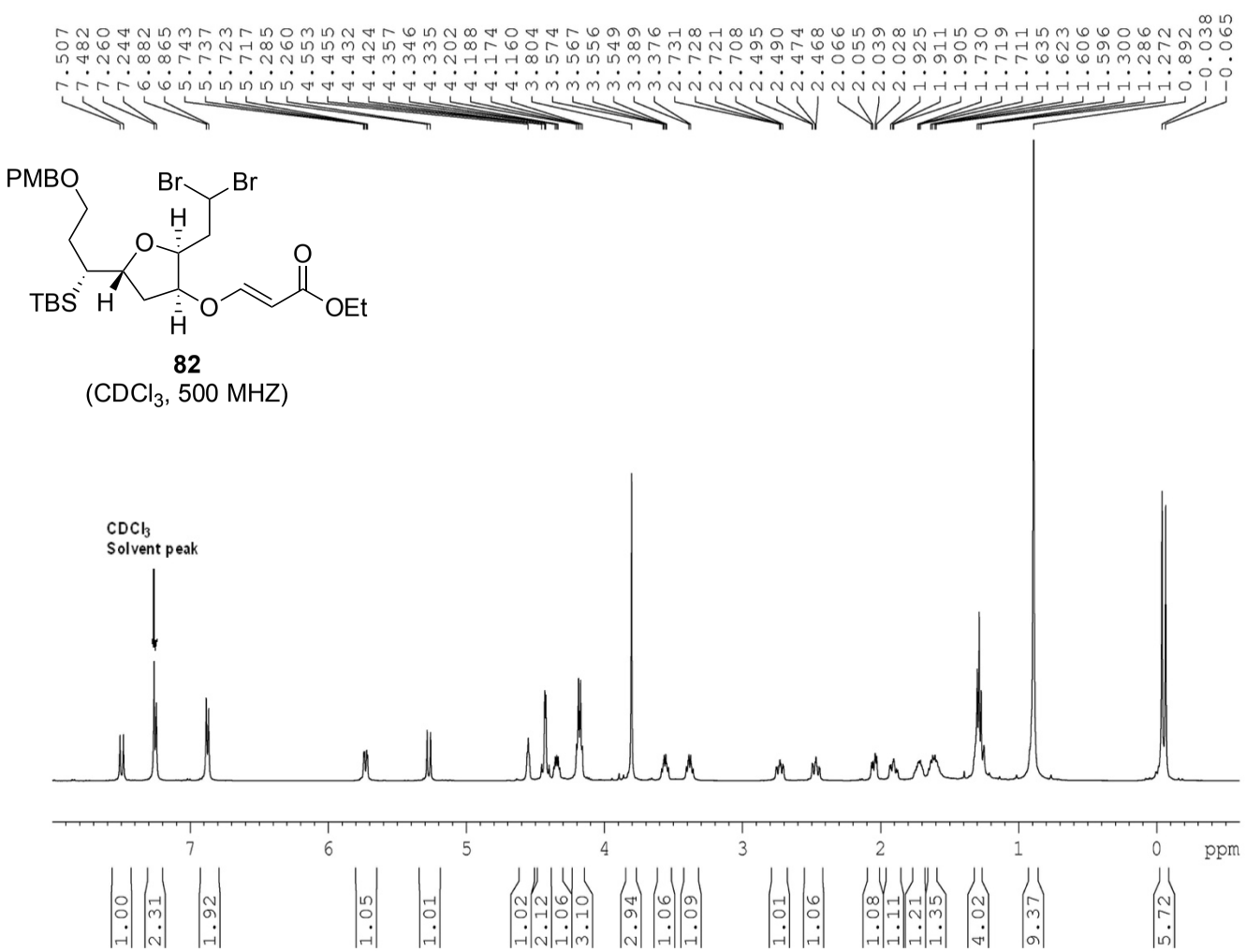


80

($CDCl_3$, 125 MHZ)

BRUKER

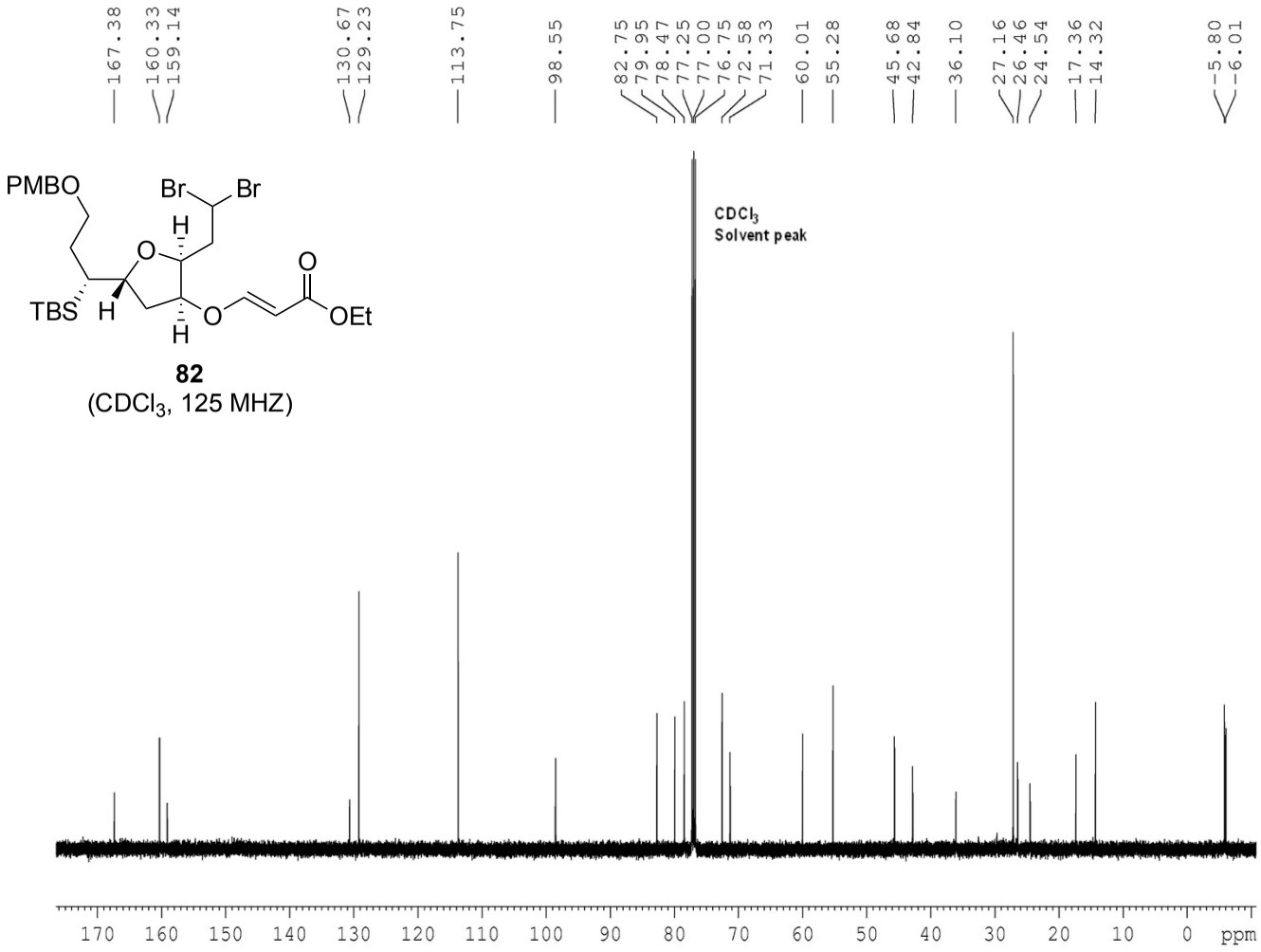
NAME	45 ZYA-IV-aldehyde-300
EXPNO	2
PROCNO	1
Date_	20170707
Time	23.41
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	211
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	295.6 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

```
NAME        47 ZYA-V-dibromide-26
EXPNO                           1
PROCNO                          1
Date_                    20170727
Time                         0.38
INSTRUM                     spect
PROBHD   5 mm PABBO BB/
PULPROG                        zg
TD                          59998
SOLVENT                     CDCl3
NS                              8
DS                              0
SWH                   10000.000 Hz
FIDRES                 0.166672 Hz
AQ                     2.9999499 sec
RG                         44.57
DW                        50.000 usec
DE                          6.50 usec
TE                         295.2 K
D1                    3.00000000 sec
TD0                             1

======= CHANNEL f1 =======
SFO1                499.8730869 MHz
NUC1                        1H
P1                        10.75 usec
SI                          65536
SF                  499.8700000 MHz
WDW                            EM
SSB                             0
LB                         0.30 Hz
GB                              0
PC                          1.00
```

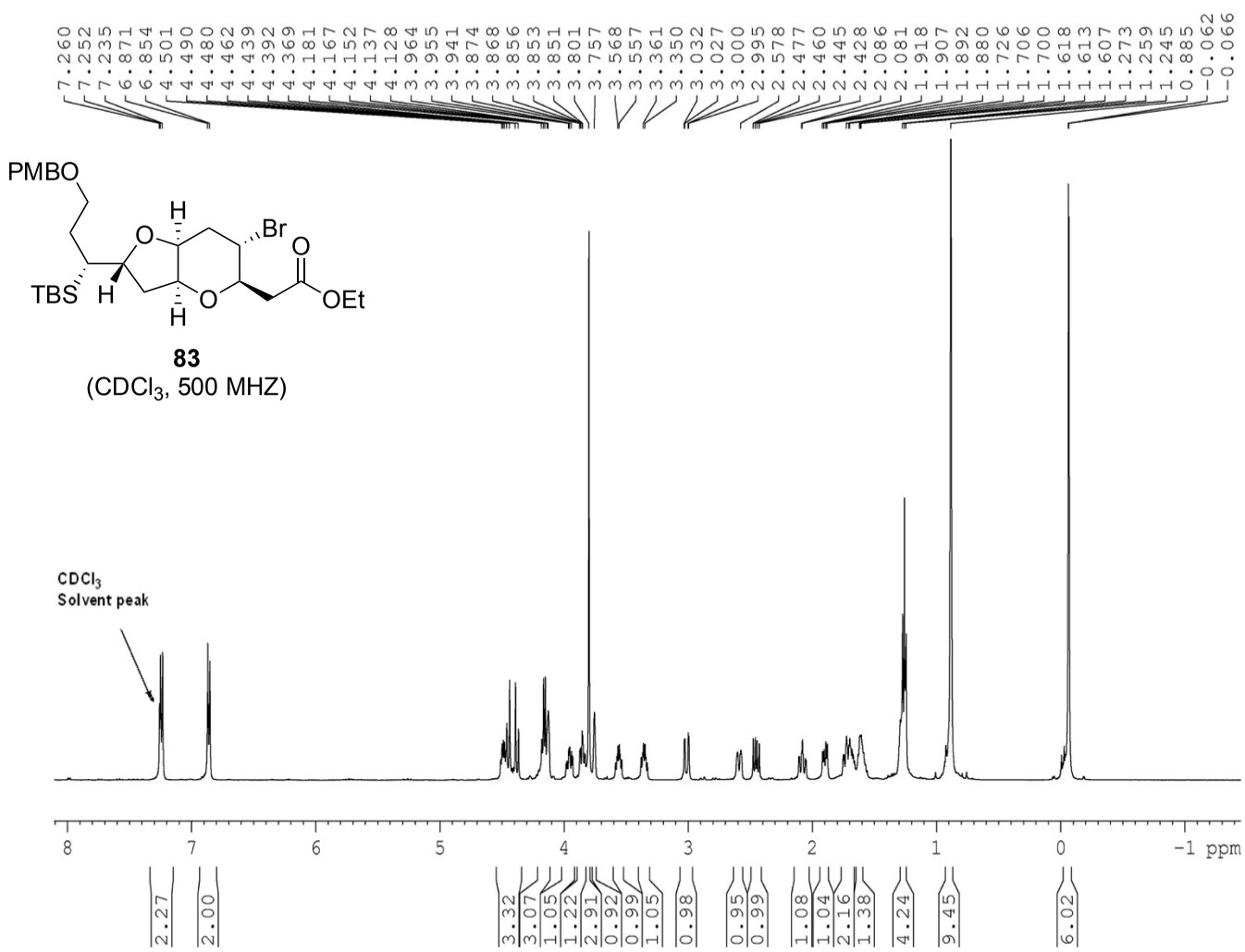


82

($CDCl_3$, 125 MHZ)

BRUKER

NAME	47 ZYA-V-dibromide-26
EXPNO	2
PROCNO	1
Date_	20170727
Time	0.41
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	323
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	295.2 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======= CHANNEL f1 =======	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

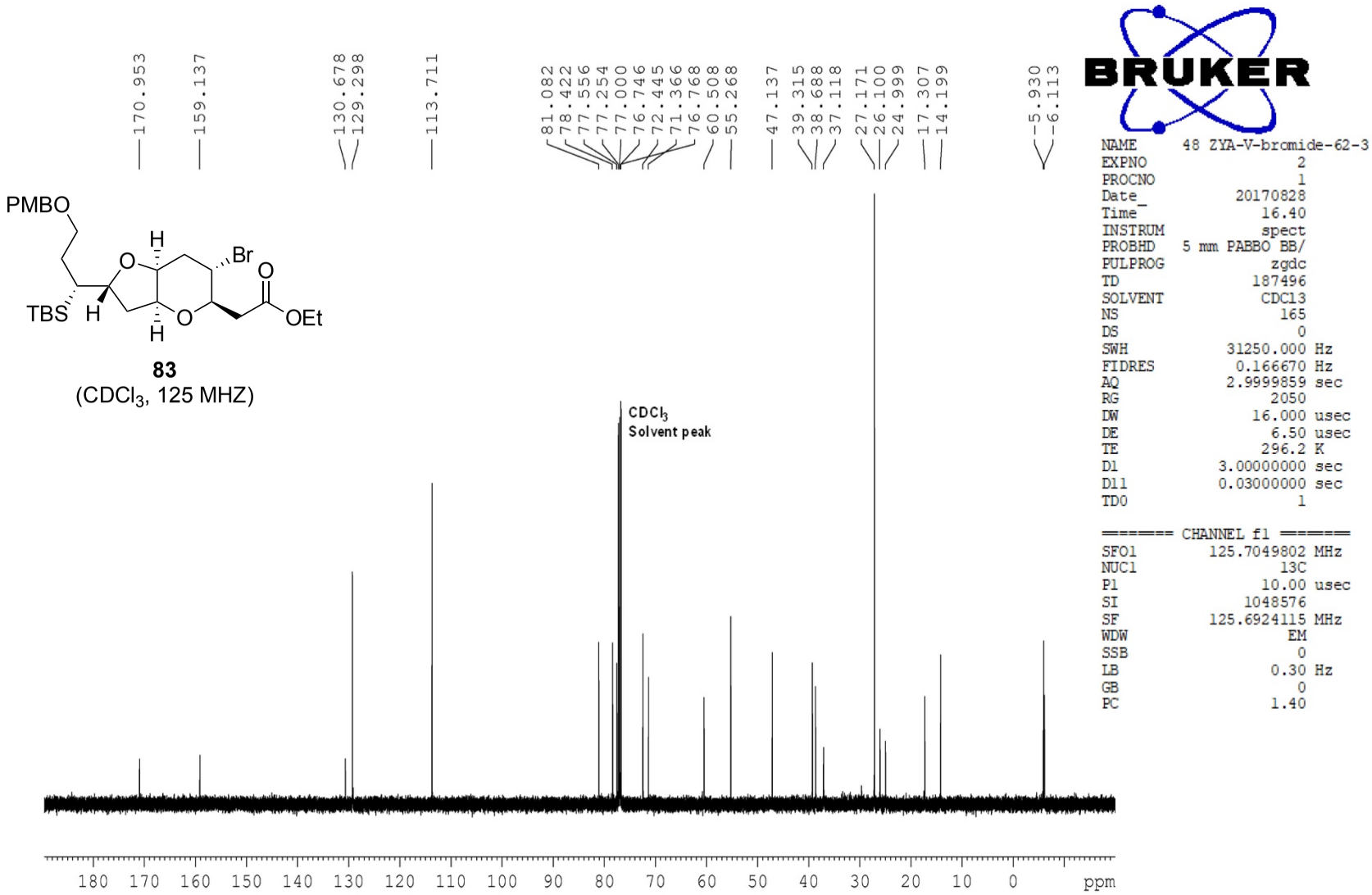


83

($CDCl_3$, 500 MHZ)

BRUKER

NAME	48 ZYA-V-bromide-62-3
EXPNO	1
PROCNO	1
Date_	20170828
Time	16.31
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	35.92
DW	50.000 usec
DE	6.50 usec
TE	295.6 K
D1	3.00000000 sec
TD0	1
======= CHANNEL f1 =======	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



83

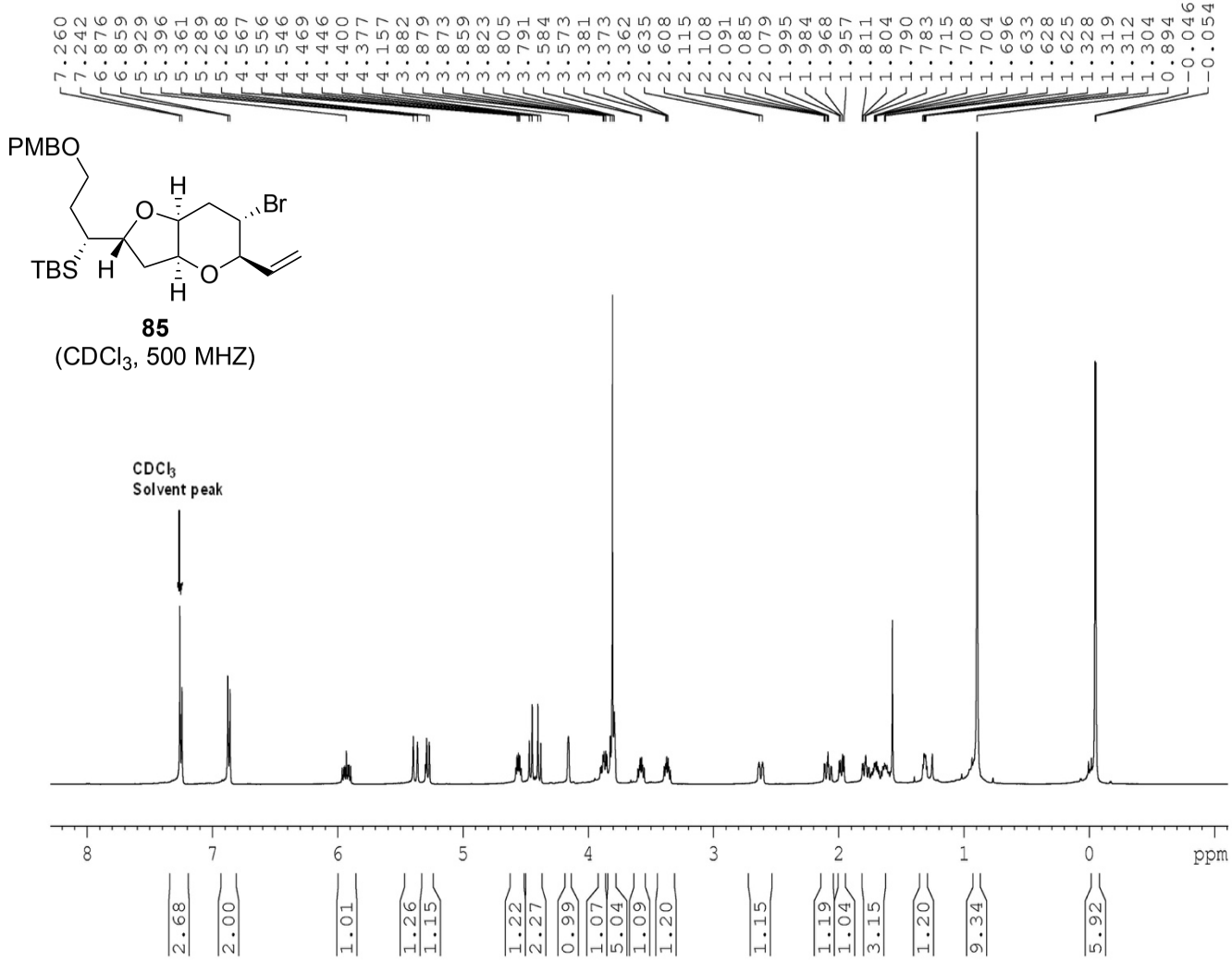
($CDCl_3$, 125 MHZ)

BRUKER

NAME	48 ZYA-V-bromide-62-3
EXPNO	2
PROCNO	1
Date_	20170828
Time	16.40
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	165
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.2 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1

======= CHANNEL f1 ======

SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

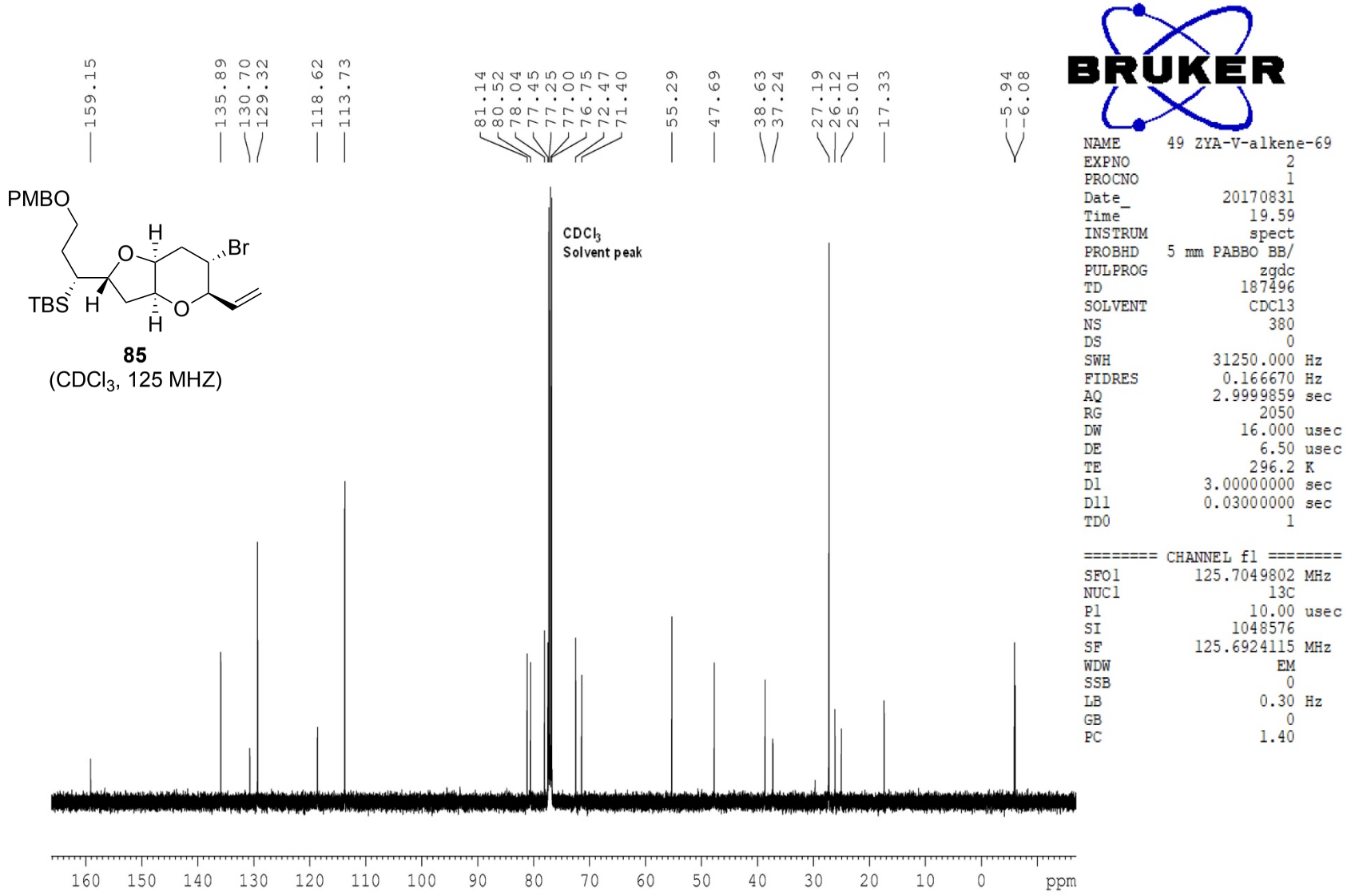


85

($CDCl_3$, 500 MHZ)

BRUKER

NAME	49 ZYA-V-alkene-69
EXPNO	1
PROCNO	1
Date_	20170831
Time	19.54
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	51.11
DW	50.000 usec
DE	6.50 usec
TE	295.7 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

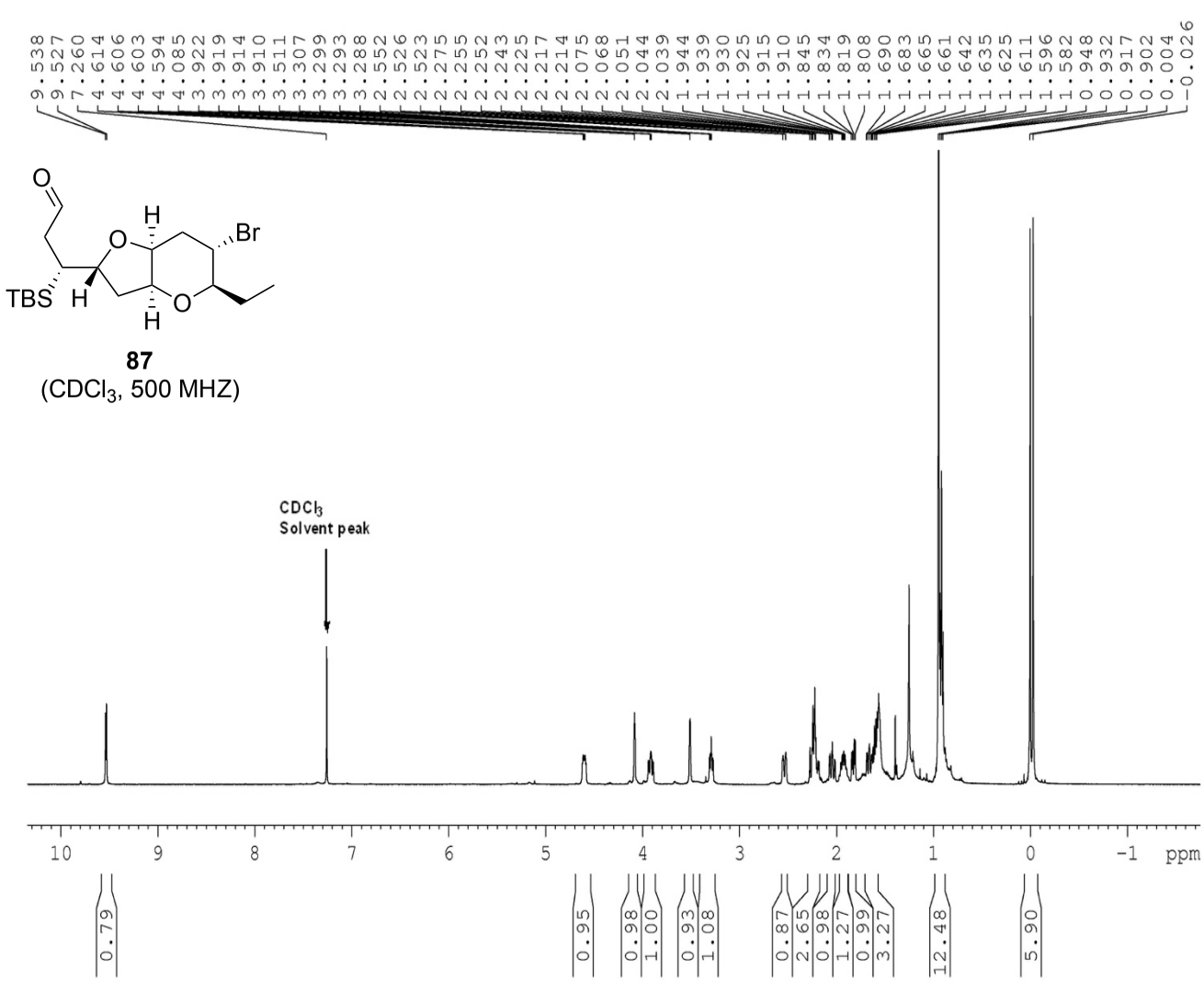


85

($CDCl_3$, 125 MHZ)

BRUKER

NAME	49 ZYA-V-alkene-69
EXPNO	2
PROCNO	1
Date_	20170831
Time	19.59
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	380
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.2 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

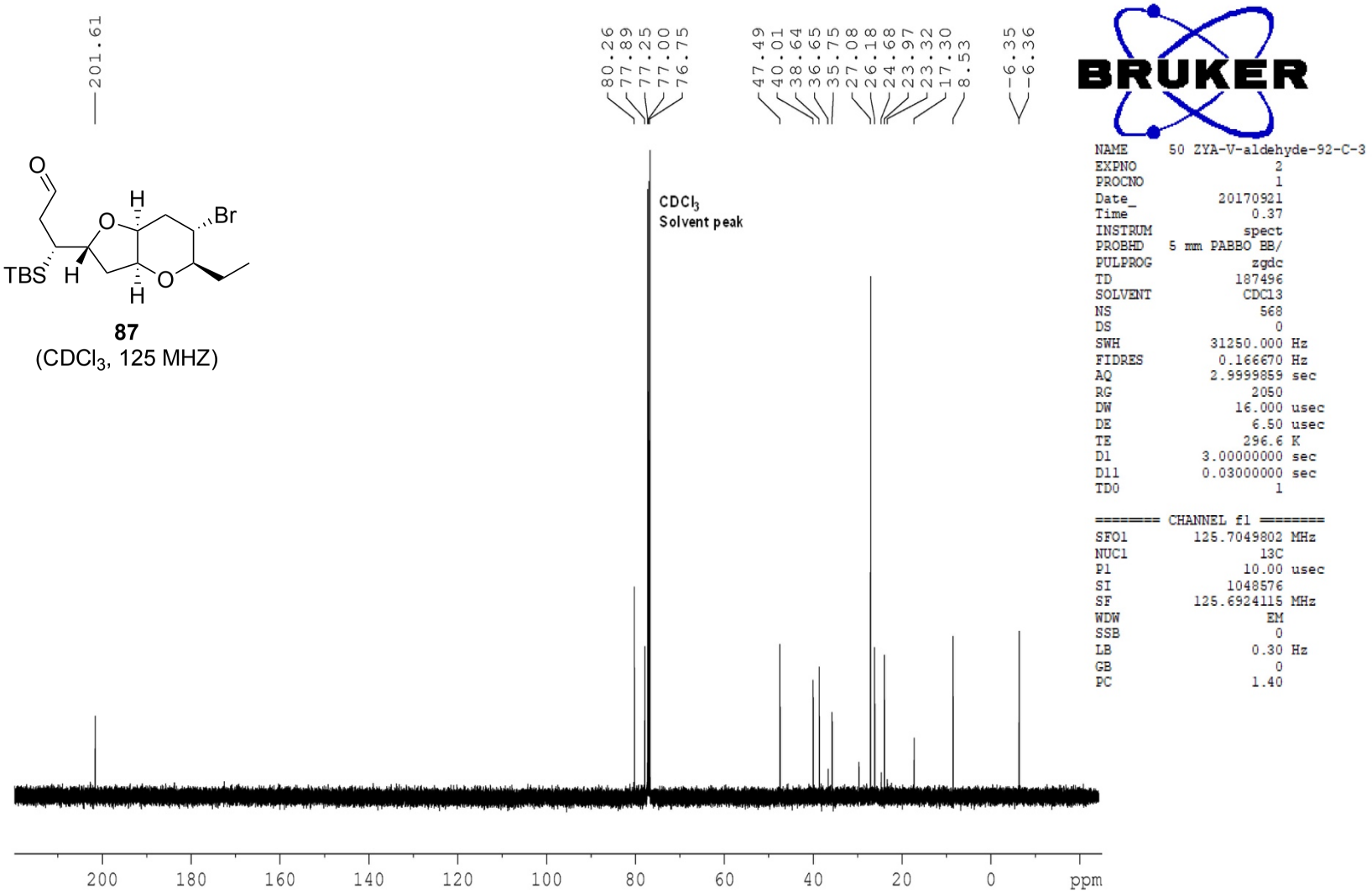


87

($CDCl_3$, 500 MHZ)

BRUKER

NAME	50 ZYA-V-aldehyde-92-C-3
EXPNO	1
PROCNO	1
Date_	20170921
Time	0.33
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	62.78
DW	50.000 usec
DE	6.50 usec
TE	296.8 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

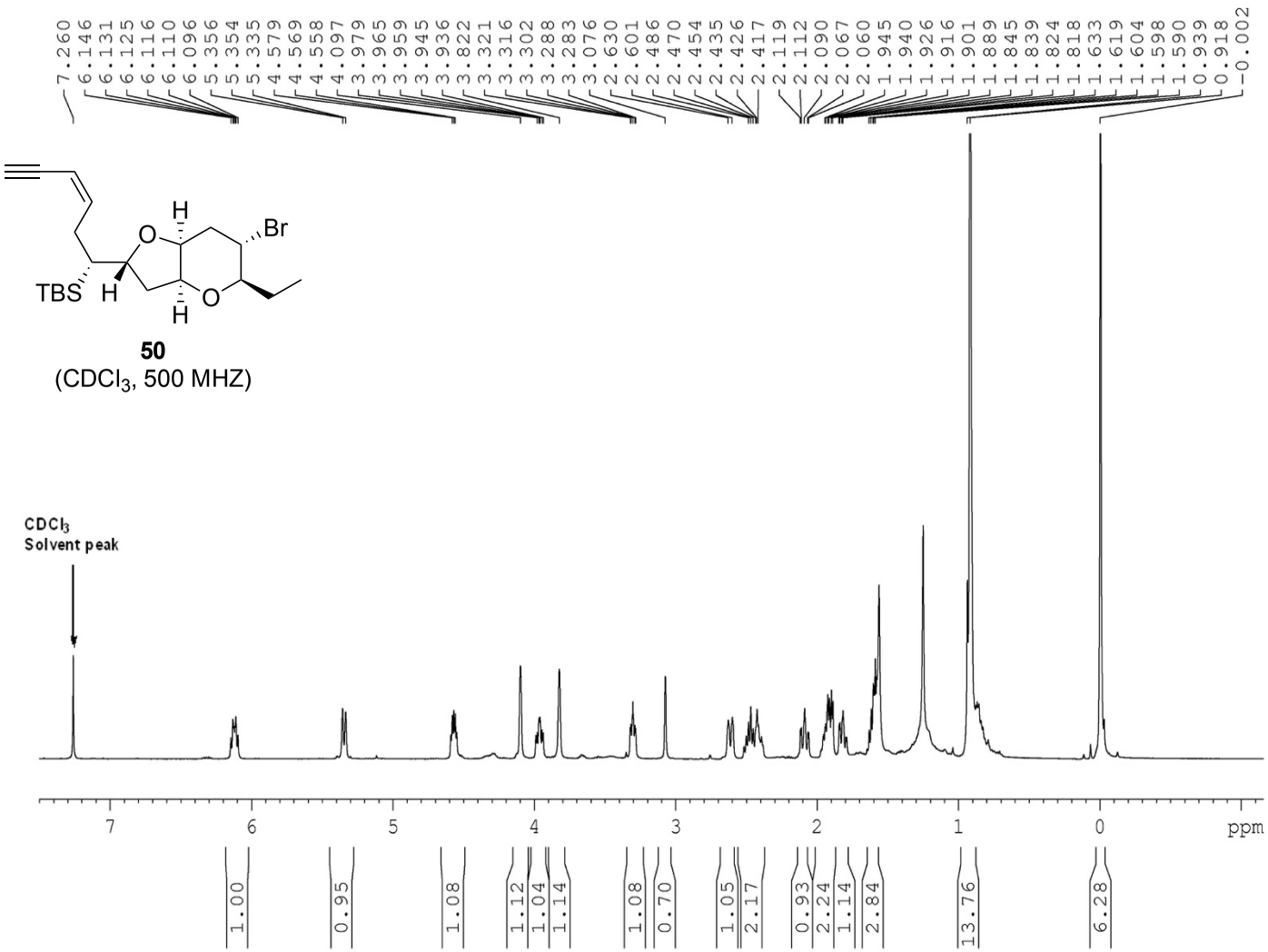


87

($CDCl_3$, 125 MHZ)

```
NAME        50 ZYA-V-aldehyde-92-C-3
EXPNO                              2
PROCNO                             1
Date_                       20170921
Time                            0.37
INSTRUM                        spect
PROBHD    5 mm PABBO BB/
PULPROG                         zgdc
TD                            187496
SOLVENT                       CDCl3
NS                              568
DS                                0
SWH                     31250.000 Hz
FIDRES                    0.166670 Hz
AQ                        2.9999859 sec
RG                             2050
DW                          16.000 usec
DE                           6.50 usec
TE                          296.6 K
D1                     3.00000000 sec
D11                    0.03000000 sec
TD0                               1

======== CHANNEL f1 ========
SFO1                  125.7049802 MHz
NUC1                          13C
P1                          10.00 usec
SI                          1048576
SF                    125.6924115 MHz
WDW                            EM
SSB                               0
LB                           0.30 Hz
GB                                0
PC                            1.40
```

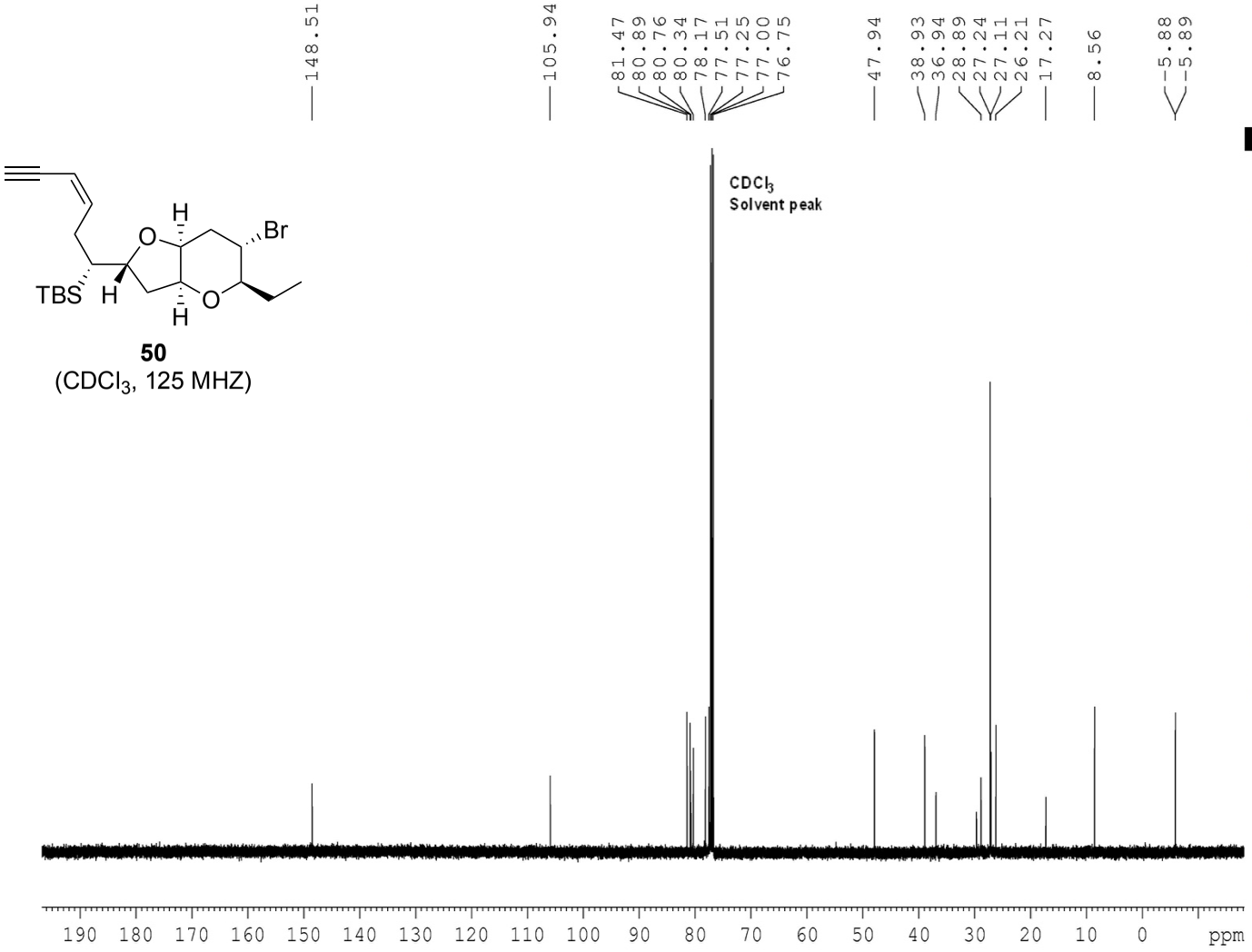


50

($CDCl_3$, 500 MHZ)

BRUKER

NAME	23 ZYA-V-enyne-93
EXPNO	1
PROCNO	1
Date_	20170923
Time	17.06
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	16
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	56.75
DW	50.000 usec
DE	6.50 usec
TE	295.5 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

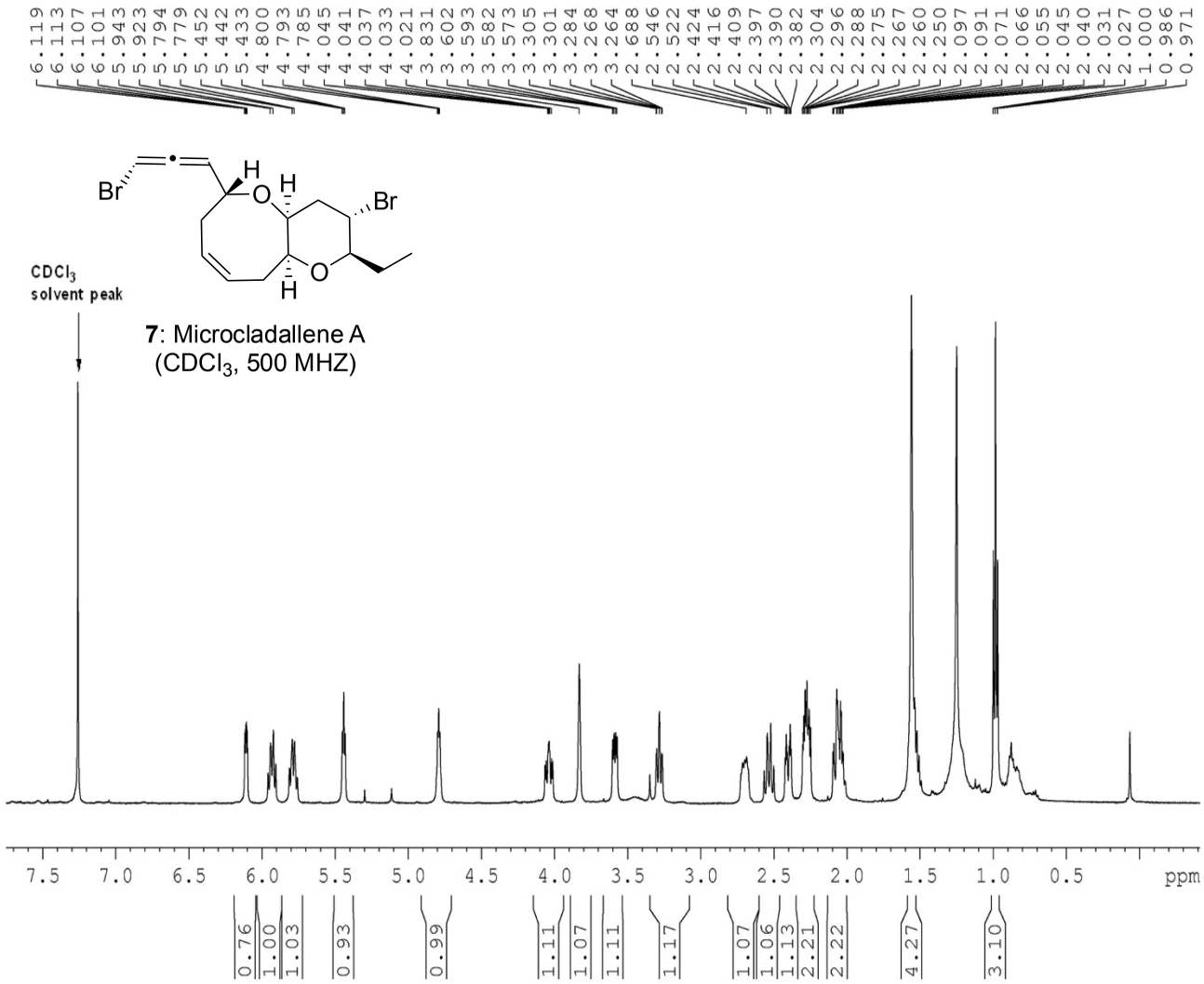


50

($CDCl_3$, 125 MHZ)

BRUKER

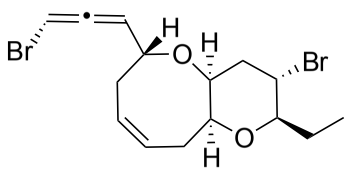
NAME	23 ZYA-V-enyne-93
EXPNO	2
PROCNO	1
Date_	20170923
Time	23.09
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	723
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.8 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924131 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



7: Microcladallene A
($CDCl_3$, 500 MHZ)

BRUKER

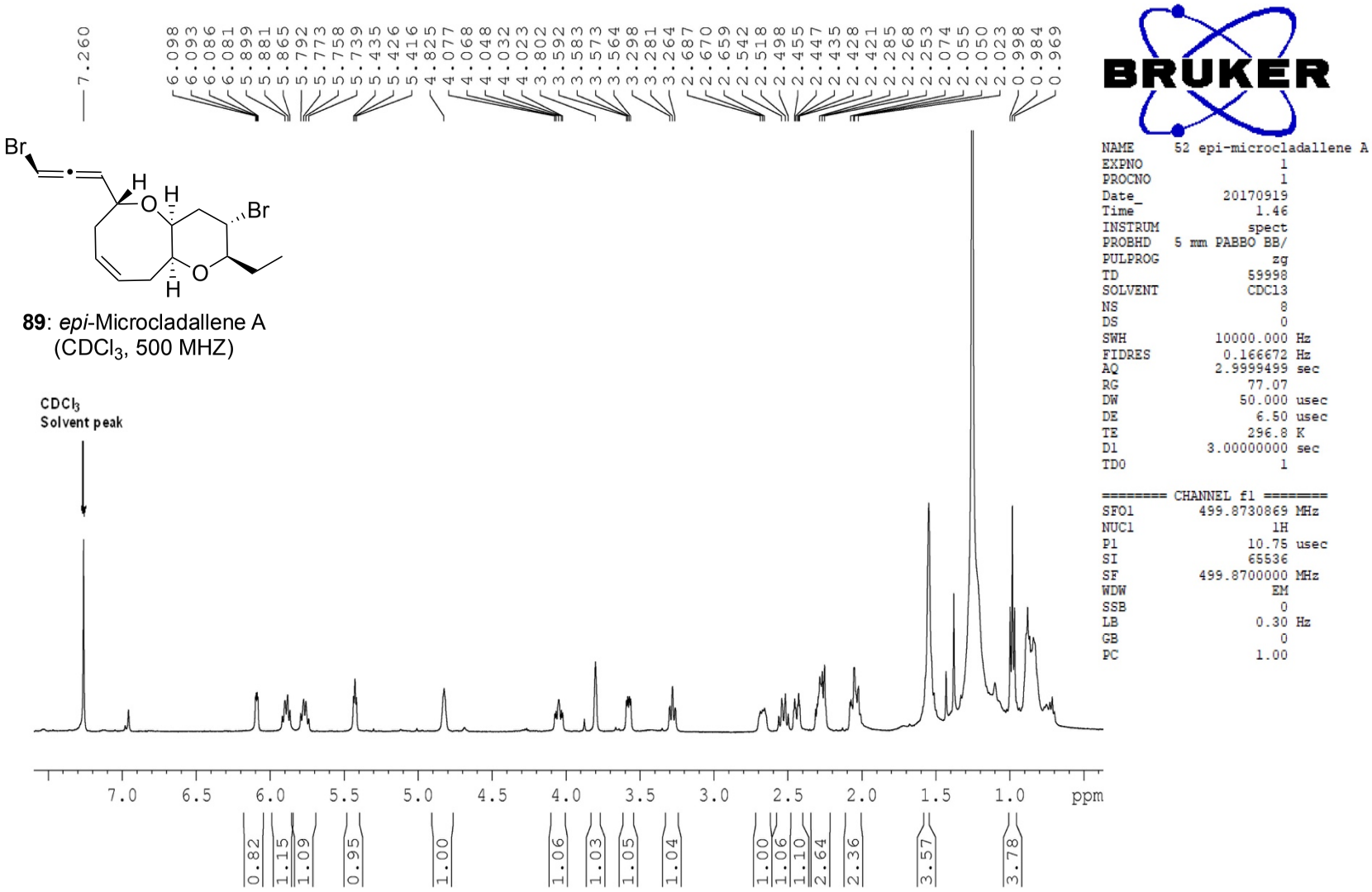
NAME	7 microcladallene A
EXPNO	1
PROCNO	1
Date_	20170830
Time	2.13
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	70.49
DW	50.000 usec
DE	6.50 usec
TE	295.5 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



7: Microcladallene A
($CDCl_3$, 125 MHZ)


```
NAME        7 microcladallene A
EXPNO                         2
PROCNO                        1
Date_                  20170830
Time                       2.17
INSTRUM                   spect
PROBHD   5 mm PABBO BB/
PULPROG                    zgdc
TD                       187496
SOLVENT                   CDCl3
NS                         4000
DS                            0
SWH                  31250.000 Hz
FIDRES               0.166670 Hz
AQ                   2.9999859 sec
RG                         2050
DW                     16.000 usec
DE                      6.50 usec
TE                      295.8 K
D1                   3.00000000 sec
D11                  0.03000000 sec
TD0                           1

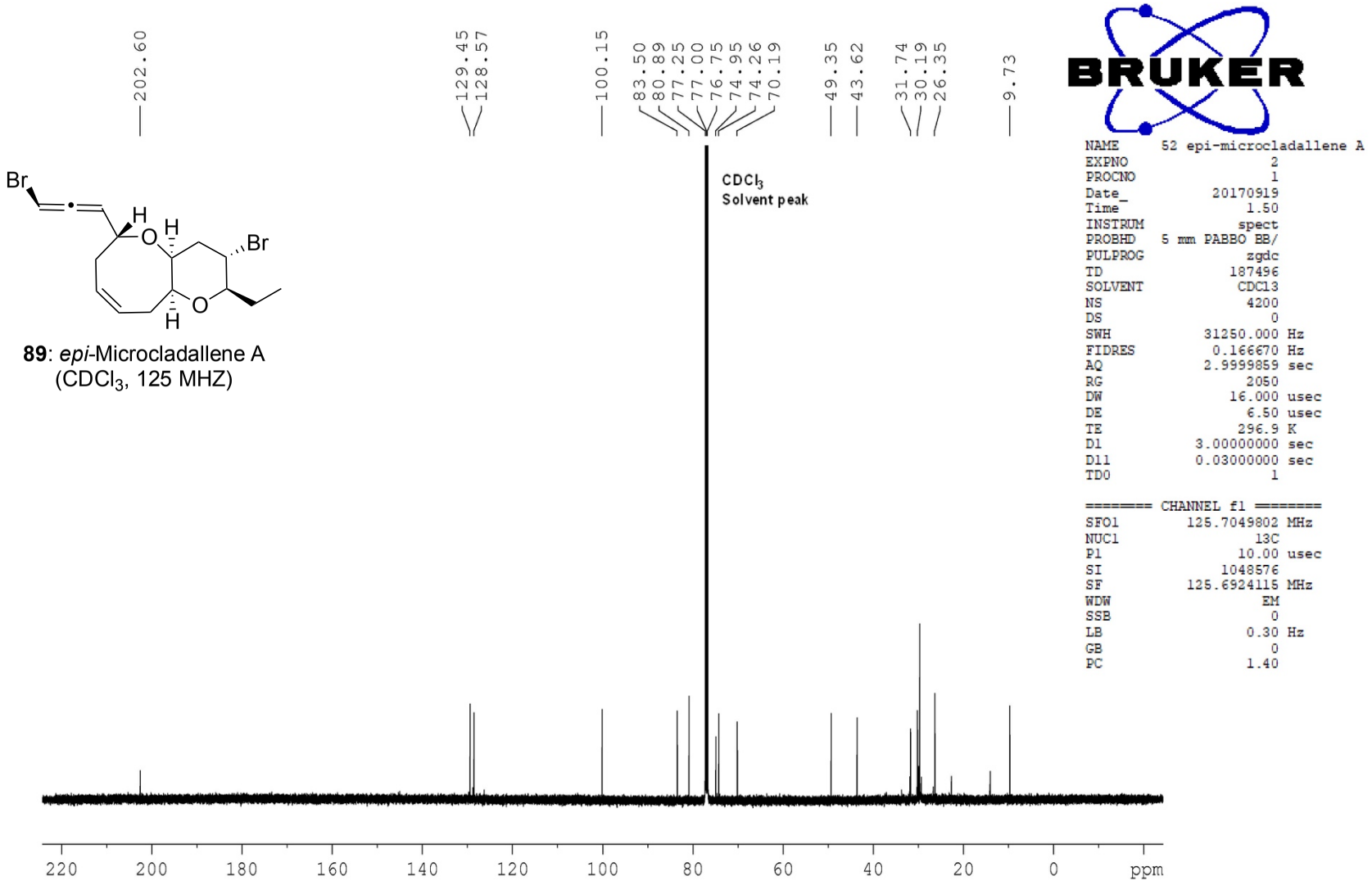
======== CHANNEL f1 ========
SFO1               125.7049802 MHz
NUC1                        13C
P1                     10.00 usec
SI                       1048576
SF                 125.6924115 MHz
WDW                          EM
SSB                           0
LB                      0.30 Hz
GB                            0
PC                         1.40
```



89: *epi*-Microcladallene A
($CDCl_3$, 500 MHZ)

BRUKER

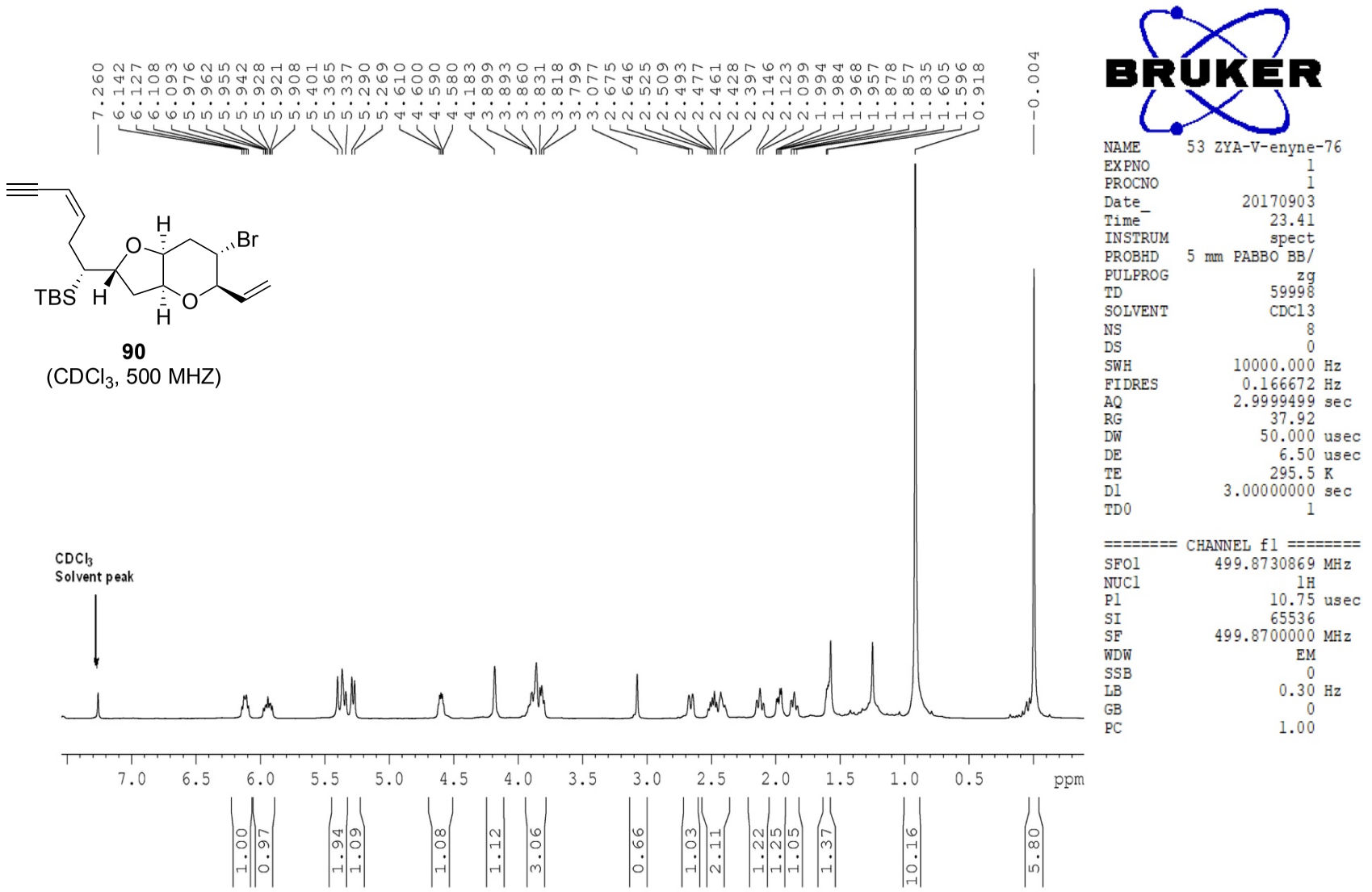
NAME	52 epi-microcladallene A
EXPNO	1
PROCNO	1
Date_	20170919
Time	1.46
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	77.07
DW	50.000 usec
DE	6.50 usec
TE	296.8 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



89: *epi*-Microcladallene A
($CDCl_3$, 125 MHZ)

```
NAME      52 epi-microcladallene A
EXPNO                2
PROCNO               1
Date_         20170919
Time              1.50
INSTRUM          spect
PROBHD   5 mm PABBO BB/
PULPROG           zgdc
TD               187496
SOLVENT           CDCl3
NS                4200
DS                   0
SWH          31250.000 Hz
FIDRES        0.166670 Hz
AQ            2.9999859 sec
RG                2050
DW              16.000 usec
DE               6.50 usec
TE              296.9 K
D1           3.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1       125.7049802 MHz
NUC1              13C
P1              10.00 usec
SI             1048576
SF         125.6924115 MHz
WDW               EM
SSB                  0
LB              0.30 Hz
GB                   0
PC               1.40
```

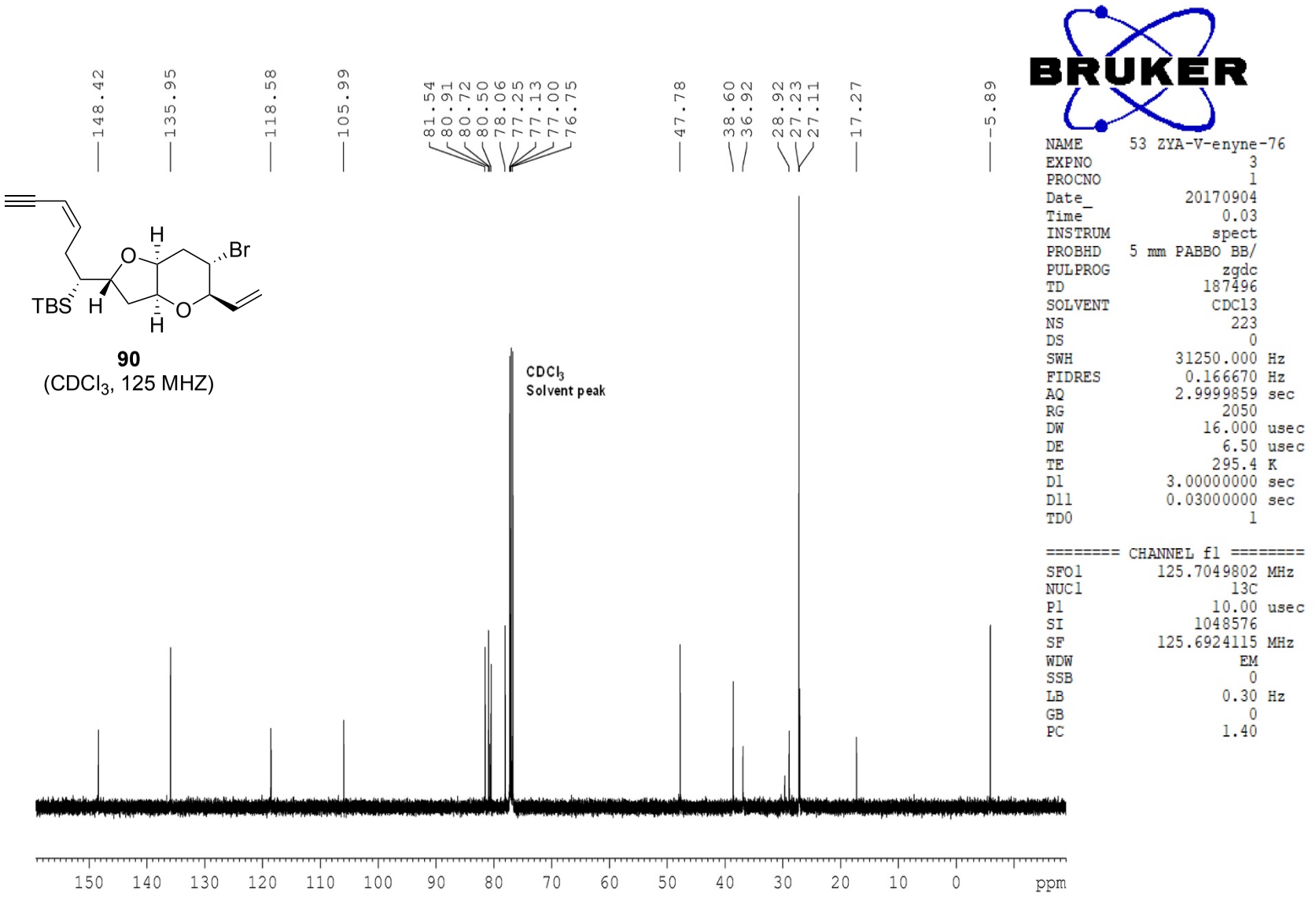


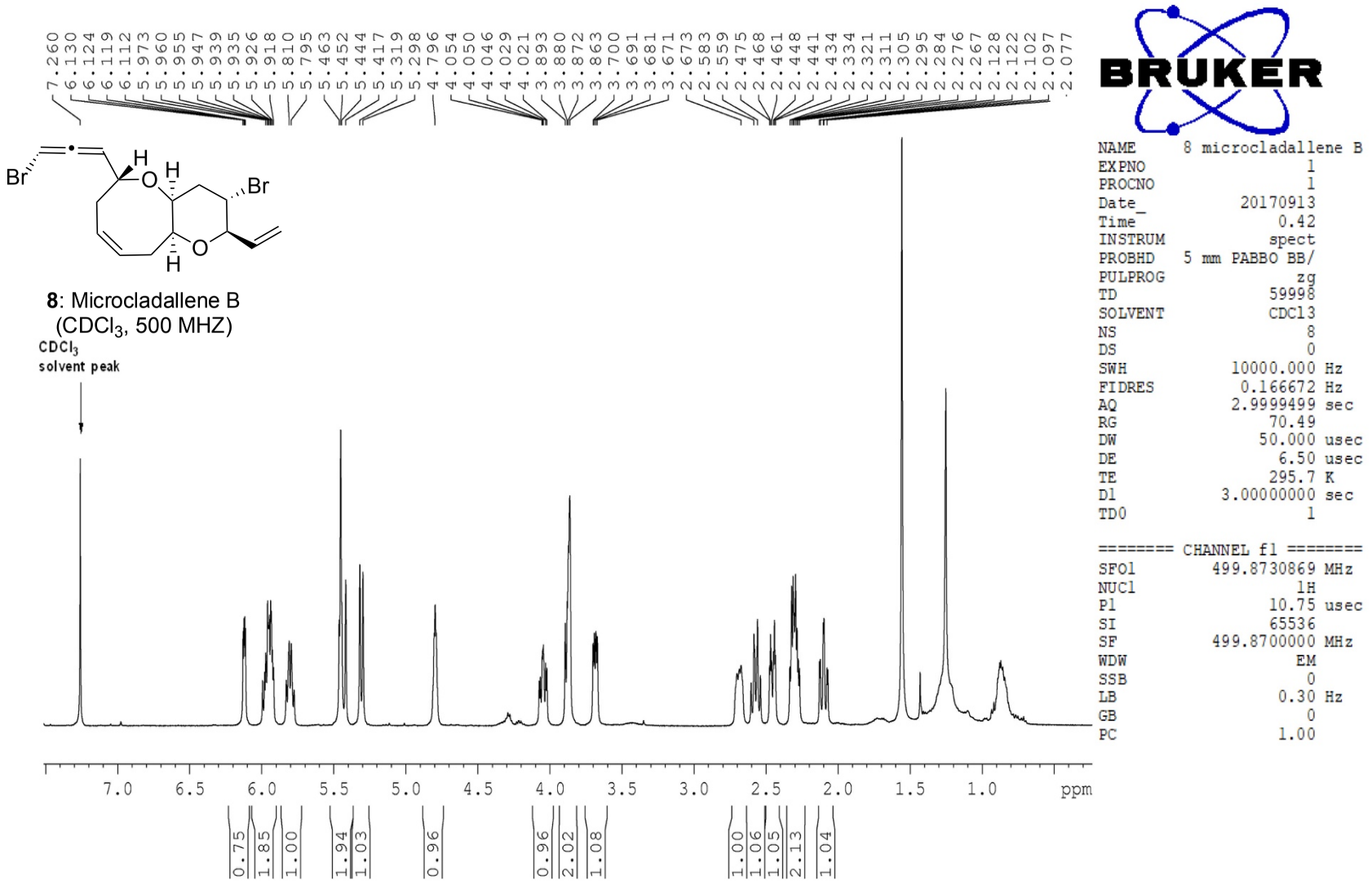
90

($CDCl_3$, 500 MHZ)

```
NAME        53 ZYA-V-enyne-76
EXPNO                       1
PROCNO                      1
Date_                20170903
Time                    23.41
INSTRUM                 spect
PROBHD   5 mm PABBO BB/
PULPROG                    zg
TD                      59998
SOLVENT                 CDCl3
NS                          8
DS                          0
SWH                10000.000 Hz
FIDRES             0.166672 Hz
AQ                 2.9999499 sec
RG                      37.92
DW                     50.000 usec
DE                      6.50 usec
TE                     295.5 K
D1                 3.00000000 sec
TD0                         1

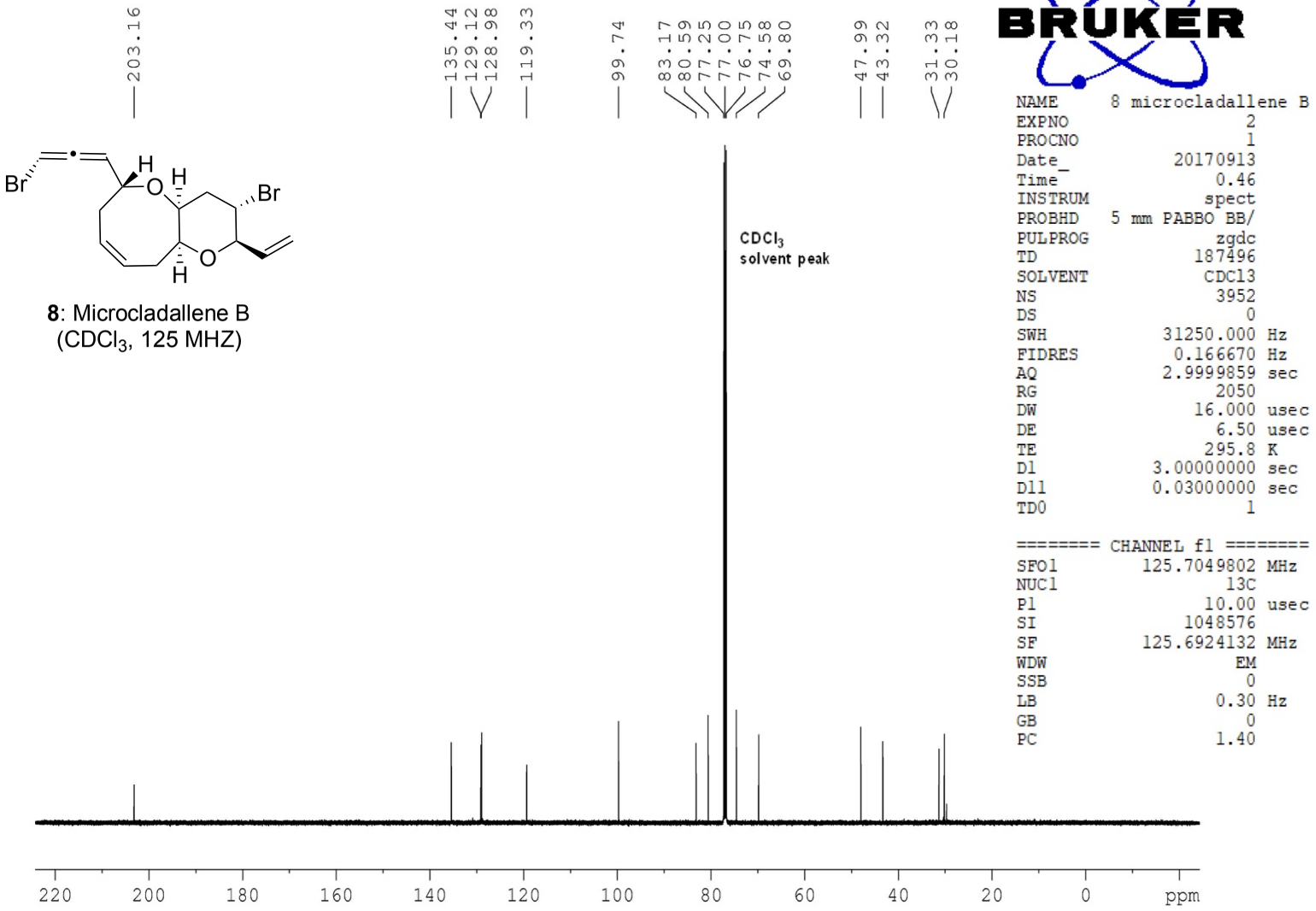
======== CHANNEL f1 ========
SFO1            499.8730869 MHz
NUC1                      1H
P1                     10.75 usec
SI                     65536
SF              499.8700000 MHz
WDW                        EM
SSB                         0
LB                      0.30 Hz
GB                          0
PC                      1.00
```


148.42
135.95
118.58
105.99
81.54
80.91
80.72
80.50
78.06
77.25
77.13
77.00
76.75
47.78
38.60
36.92
28.92
27.23
27.11
17.27
5.89
BRUKER
NAME 53 ZYA-V-enyne-76
EXPNO 3
PROCNO 1
Date_ 20170904
Time 0.03
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgdc
TD 187496
SOLVENT CDCl3
NS 223
DS 0
SWH 31250.000 Hz
FIDRES 0.166670 Hz
AQ 2.9999859 sec
RG 2050
DW 16.000 usec
DE 6.50 usec
TE 295.4 K
D1 3.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 125.7049802 MHz
NUC1 13C
P1 10.00 usec
SI 1048576
SF 125.6924115 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
H
O
Br
TBS
H
H
O
90
(CDCl3, 125 MHZ)
CDCl3
Solvent peak
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



BRUKER

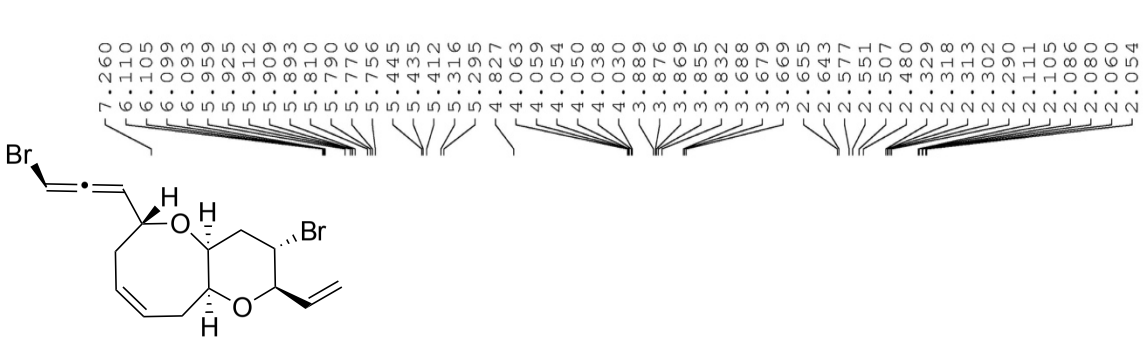
NAME	8 microcladallene B
EXPNO	1
PROCNO	1
Date_	20170913
Time	0.42
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	70.49
DW	50.000 usec
DE	6.50 usec
TE	295.7 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



8: Microcladallene B
($CDCl_3$, 125 MHZ)

```
NAME        8 microcladallene B
EXPNO                         2
PROCNO                        1
Date_                  20170913
Time                       0.46
INSTRUM                   spect
PROBHD    5 mm PABBO BB/
PULPROG                    zgdc
TD                       187496
SOLVENT                   CDCl3
NS                         3952
DS                            0
SWH                 31250.000 Hz
FIDRES               0.166670 Hz
AQ                   2.9999859 sec
RG                        2050
DW                      16.000 usec
DE                       6.50 usec
TE                      295.8 K
D1                  3.00000000 sec
D11                 0.03000000 sec
TD0                           1

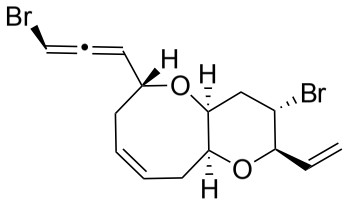
======== CHANNEL f1 ========
SFO1               125.7049802 MHz
NUC1                       13C
P1                       10.00 usec
SI                      1048576
SF                 125.6924132 MHz
WDW                        EM
SSB                           0
LB                       0.30 Hz
GB                            0
PC                        1.40
```



91: *epi*-Microcladallene B
($CDCl_3$, 500 MHZ)


```
NAME      54 epi-microcladallene B
EXPNO                1
PROCNO               1
Date_         20180211
Time             20.56
INSTRUM          spect
PROBHD   5 mm PATXI 1H/
PULPROG             zg
TD               59998
SOLVENT          CDCl3
NS                   8
DS                   0
SWH          10000.000 Hz
FIDRES        0.166672 Hz
AQ            2.9999499 sec
RG               126.24
DW               50.000 usec
DE               10.00 usec
TE               294.3 K
D1           2.00000000 sec
TD0                  1

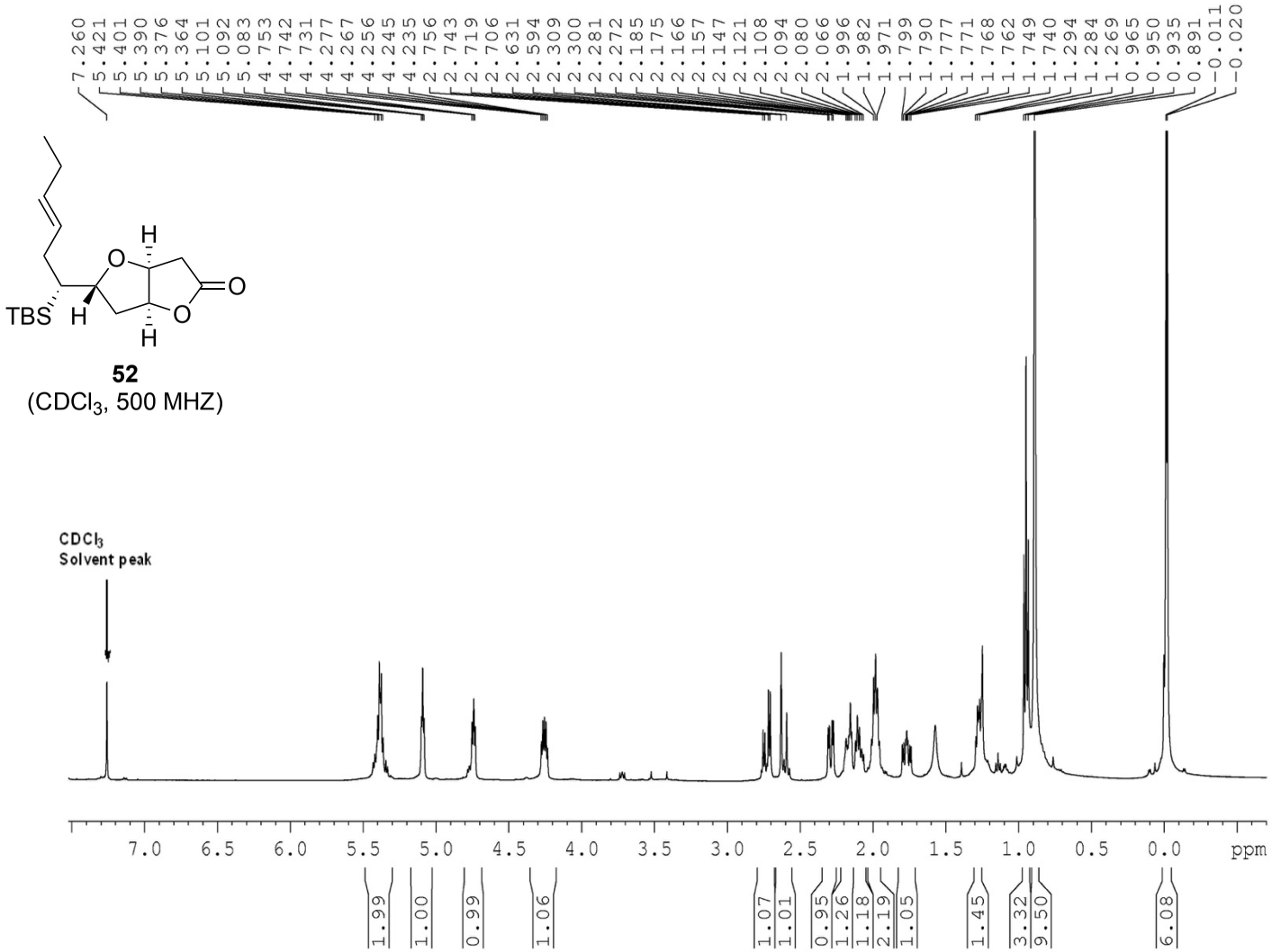
======== CHANNEL f1 ========
SFO1       500.1330885 MHz
NUC1               1H
P1                8.00 usec
SI               65536
SF         500.1300000 MHz
WDW                EM
SSB                0
LB              0.30 Hz
GB                 0
PC              1.00
```



91: *epi*-Microcladallene B
($CDCl_3$, 125 MHZ)

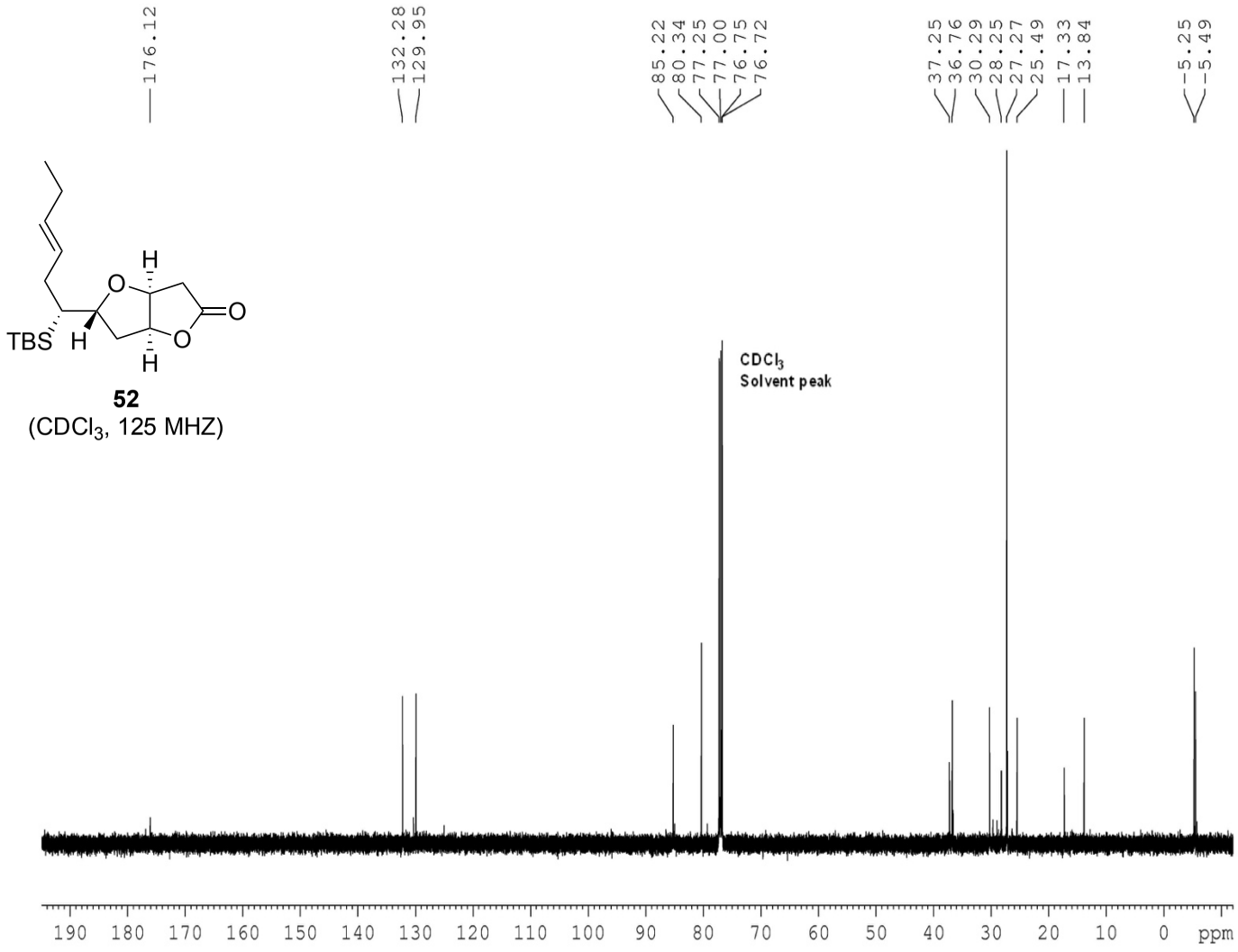
BRUKER

NAME	54 epi-microcladallene B
EXPNO	2
PROCNO	1
Date_	20180207
Time	1.11
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	361
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.7 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	4.00 Hz
GB	0
PC	1.40



BRUKER

NAME	21 ZYA-V-alkene-65
EXPNO	1
PROCNO	1
Date_	20170826
Time	23.09
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	44.57
DW	50.000 usec
DE	6.50 usec
TE	295.7 K
D1	3.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

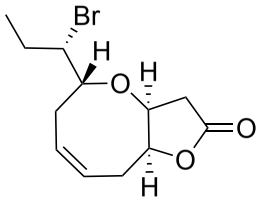


52

($CDCl_3$, 125 MHZ)

BRUKER

NAME	21 ZYA-V-alkene-65
EXPNO	2
PROCNO	1
Date_	20170826
Time	23.13
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	187
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

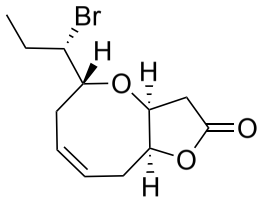


5: Desepilaurallene
($CDCl_3$, 500 MHZ)

BRUKER

```
NAME        5 ZYA-V-lactone-78 trans
EXPNO                             1
PROCNO                            1
Date_                      20170909
Time                          20.11
INSTRUM                       spect
PROBHD   5 mm PABBO BB/
PULPROG                          zg
TD                            59998
SOLVENT                       CDCl3
NS                                8
DS                                0
SWH                   10000.000 Hz
FIDRES                    0.166672 Hz
AQ                        2.9999499 sec
RG                            51.11
DW                           50.000 usec
DE                             6.50 usec
TE                            296.8 K
D1                    3.00000000 sec
TD0                               1

======== CHANNEL f1 ========
SFO1                499.8730869 MHz
NUC1                          1H
P1                         10.75 usec
SI                            65536
SF                  499.8700000 MHz
WDW                           EM
SSB                            0
LB                          0.30 Hz
GB                             0
PC                          1.00
```

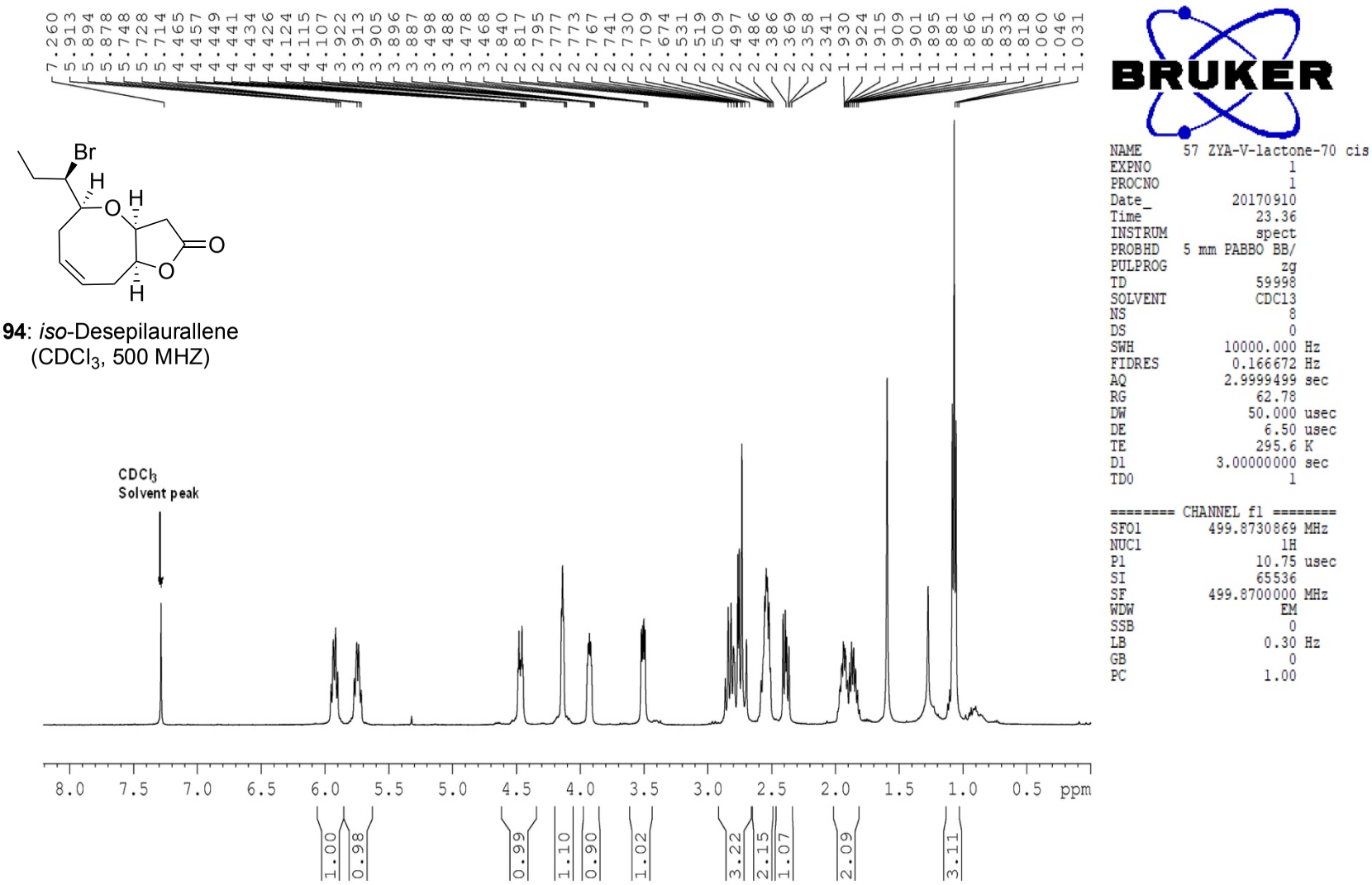


5: Desepilaurallene
($CDCl_3$, 125 MHZ)

BRUKER

```
NAME        5 ZYA-V-lactone-78 trans
EXPNO                          2
PROCNO                         1
Date_                   20170909
Time                       20.14
INSTRUM                    spect
PROBHD     5 mm PABBO BB/
PULPROG                     zgdc
TD                        187496
SOLVENT                    CDCl3
NS                           225
DS                             0
SWH                   31250.000 Hz
FIDRES                 0.166670 Hz
AQ                     2.9999859 sec
RG                          2050
DW                        16.000 usec
DE                         6.50 usec
TE                        296.8 K
D1                    3.00000000 sec
D11                   0.03000000 sec
TD0                            1

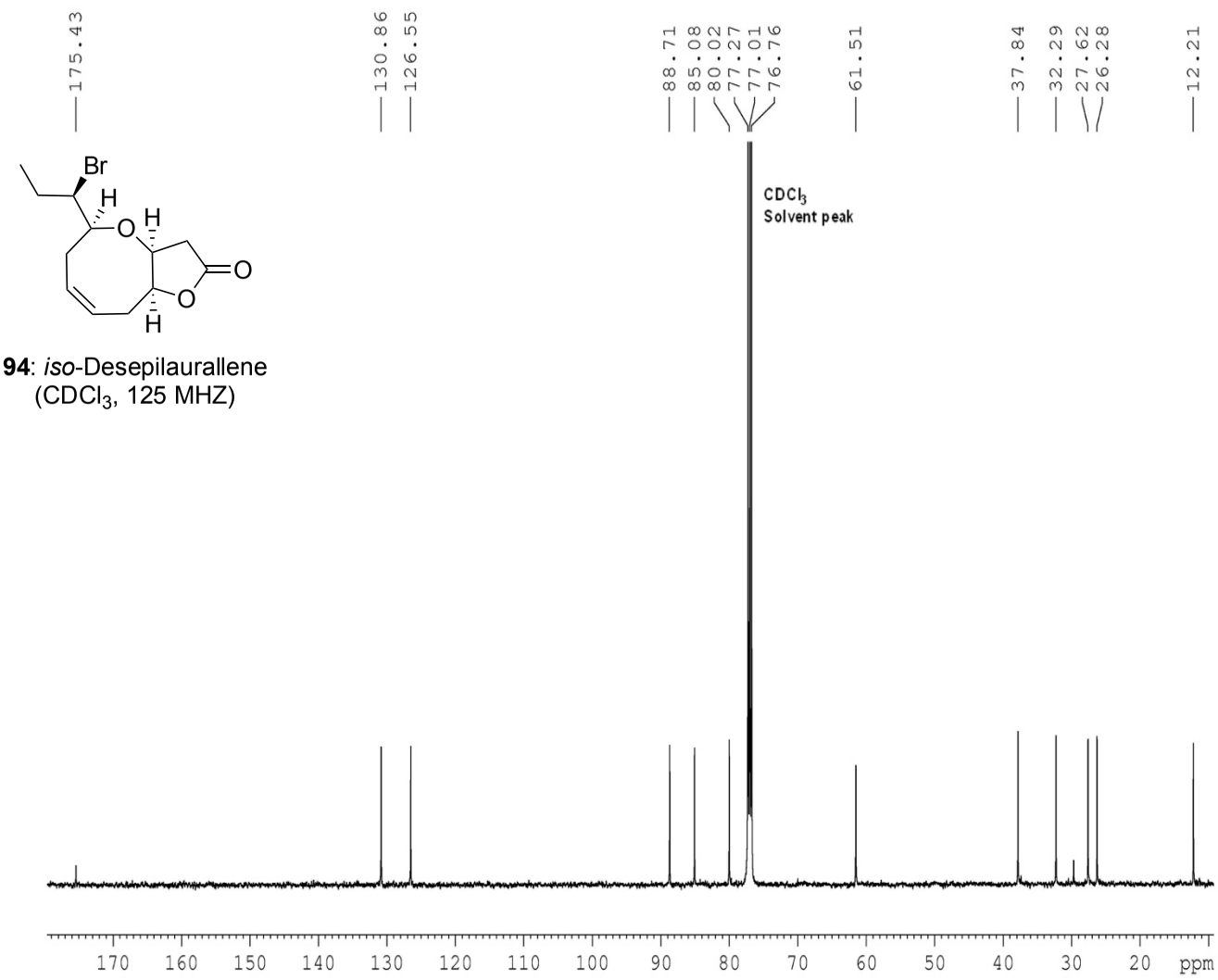
======== CHANNEL f1 ========
SFO1                125.7049802 MHz
NUC1                        13C
P1                        10.00 usec
SI                       1048576
SF                  125.6924160 MHz
WDW                           EM
SSB                            0
LB                         4.00 Hz
GB                             0
PC                          1.40
```



94: *iso*-Desepilaurallene
($CDCl_3$, 500 MHZ)

```
NAME      57 ZYA-V-lactone-70 cis
EXPNO                  1
PROCNO                 1
Date_           20170910
Time              23.36
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG              zg
TD                59998
SOLVENT           CDCl3
NS                    8
DS                    0
SWH           10000.000 Hz
FIDRES         0.166672 Hz
AQ             2.9999499 sec
RG                62.78
DW               50.000 usec
DE                6.50 usec
TE               295.6 K
D1            3.00000000 sec
TD0                   1

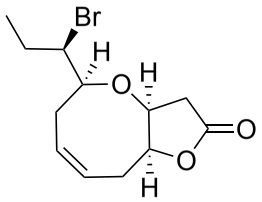
======== CHANNEL f1 ========
SFO1         499.8730869 MHz
NUC1                 1H
P1                10.75 usec
SI                65536
SF           499.8700000 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



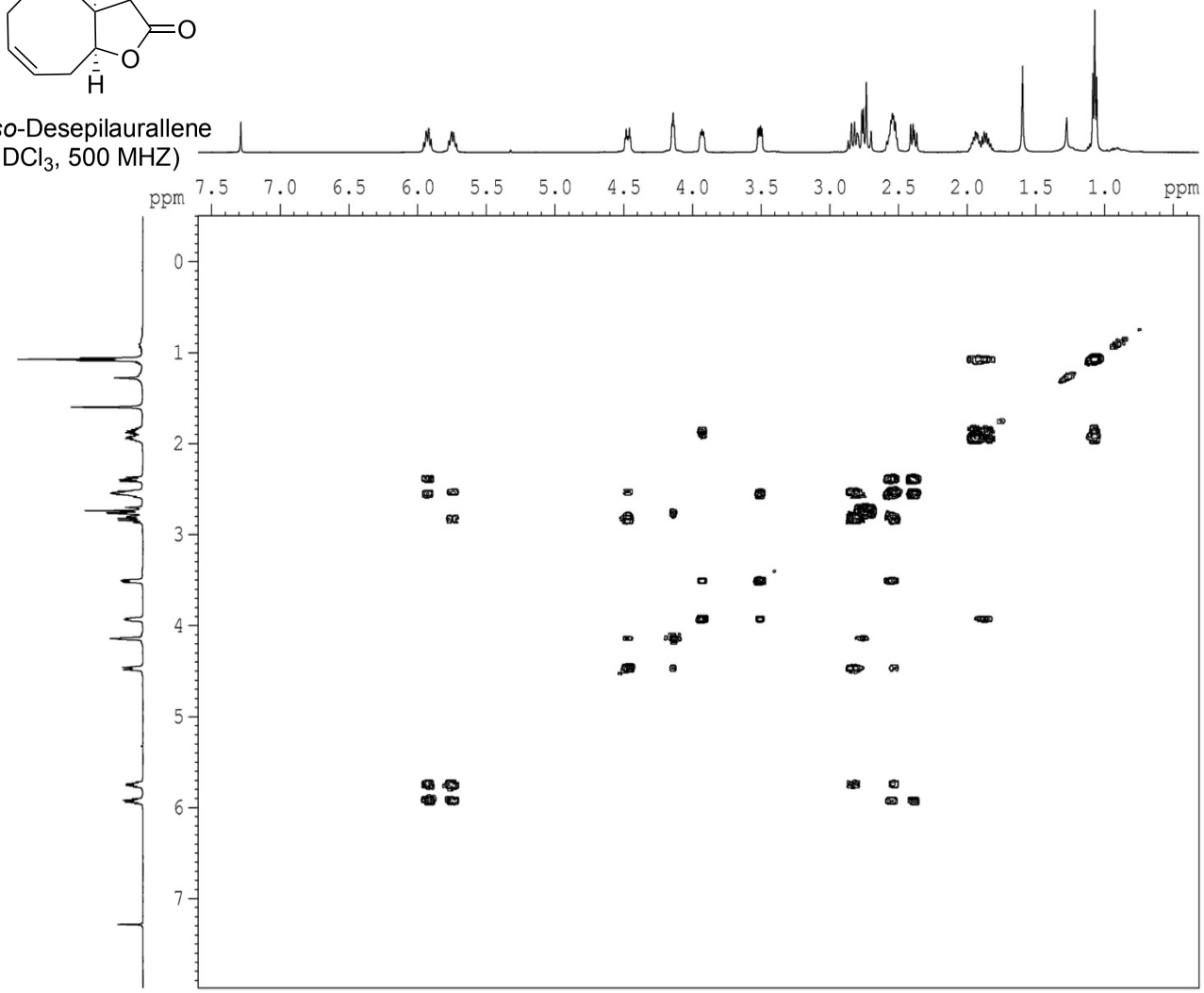
94: *iso*-Desepilaurallene
($CDCl_3$, 125 MHZ)

BRUKER

NAME	57 ZYA-V-lactone-70 cis
EXPNO	2
PROCNO	1
Date_	20170910
Time	23.45
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	1340
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.4 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	4.00 Hz
GB	0
PC	1.40



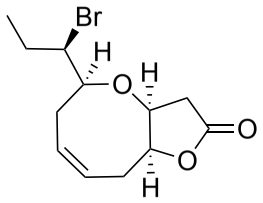
94: *iso*-Desepilaurallene
($CDCl_3$, 500 MHZ)



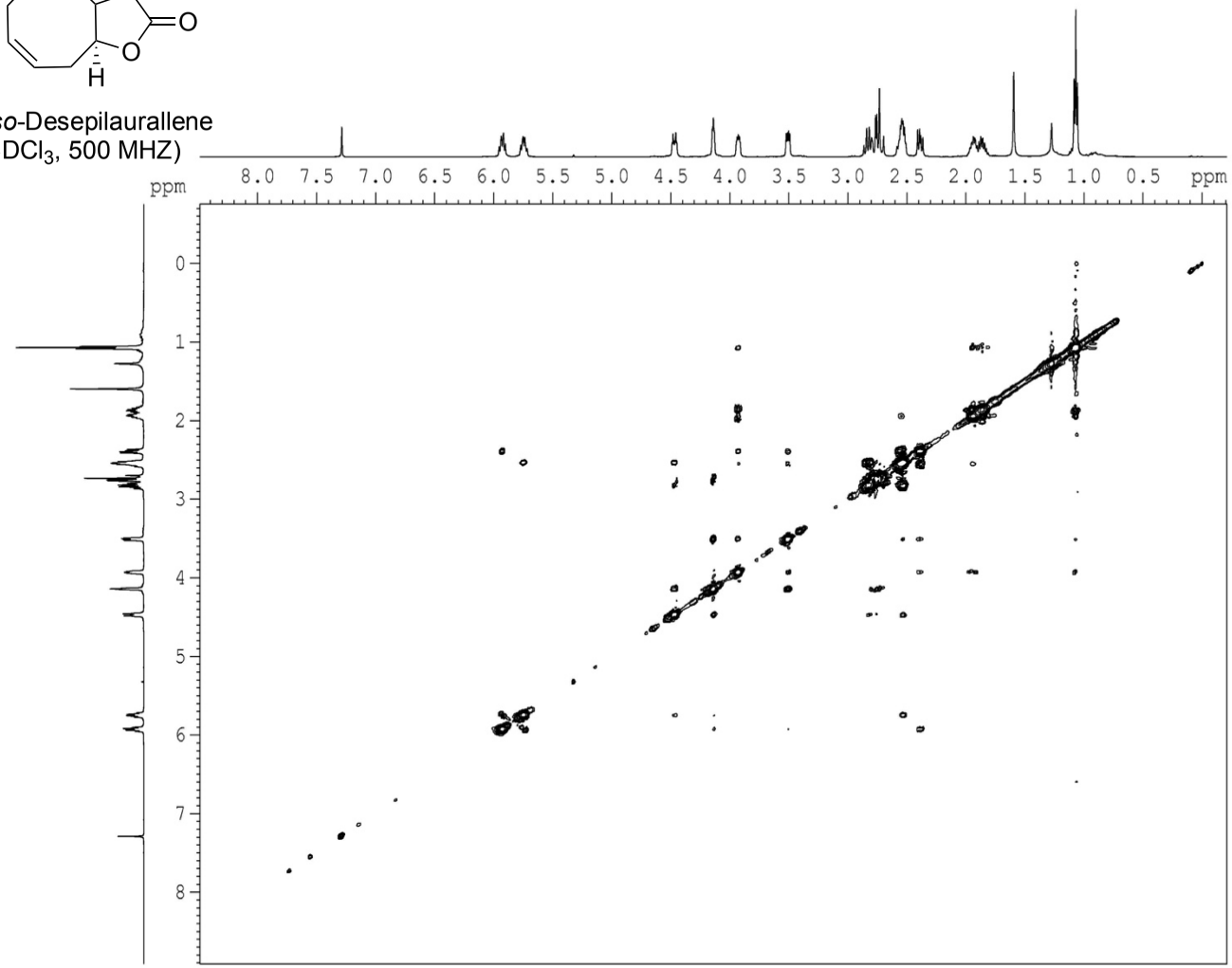
BRUKER

```
NAME        57 ZYA-V-lactone-70 cis
EXPNO                         3
PROCNO                        1
Date_                  20170930
Time                      23.19
INSTRUM                   spect
PROBHD    5 mm PATXI 1H/
PULPROG            cosygpmfqf
TD                         2048
SOLVENT                  CDCl3
NS                            1
DS                            8
SWH                5000.000 Hz
FIDRES             2.441406 Hz
AQ                 0.2048500 sec
RG                        64.36
DW                  100.000 usec
DE                   10.00 usec
TE                    295.2 K
D0                 0.00000300 sec
D1                 2.00000000 sec
D13                0.00000400 sec
D16                0.00020000 sec
IN0                0.00020000 sec

======== CHANNEL f1 ========
SFO1            500.1320005 MHz
NUC1                      1H
P1                     8.00 usec
ND0                       1
TD                      128
SFO1                500.132 MHz
FIDRES             39.062500 Hz
SW                     9.997 ppm
FnMODE                   QF
SI                      1024
SF              500.1300000 MHz
WDW                     SINE
SSB                        0
LB                      0.00 Hz
GB                         0
PC                      1.40
SI                      1024
MC2                      QF
SF              500.1300000 MHz
WDW                     SINE
SSB                        0
LB                      0.00 Hz
GB                         0
```



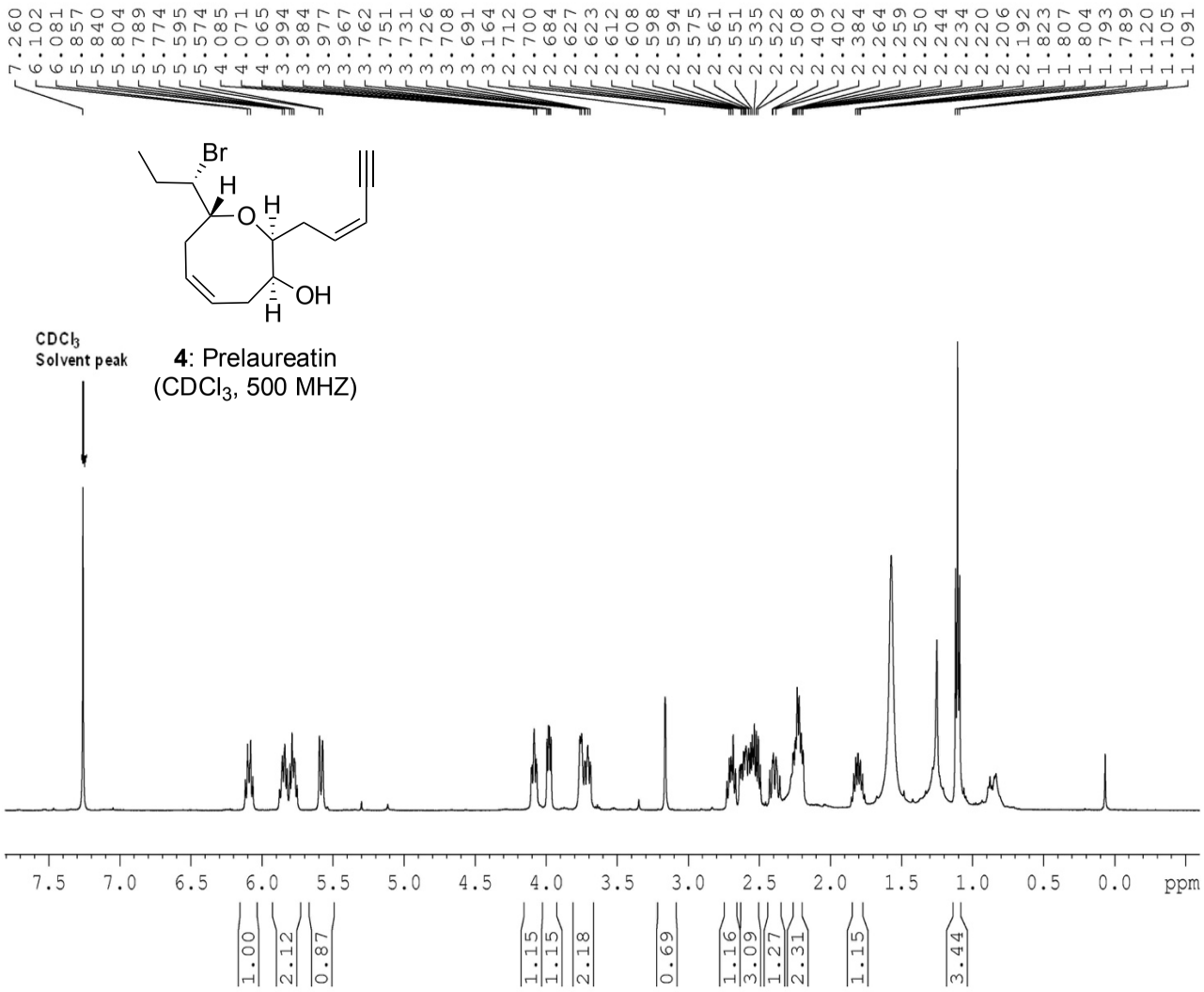
94: *iso*-Desepilaurallene
($CDCl_3$, 500 MHZ)



BRUKER

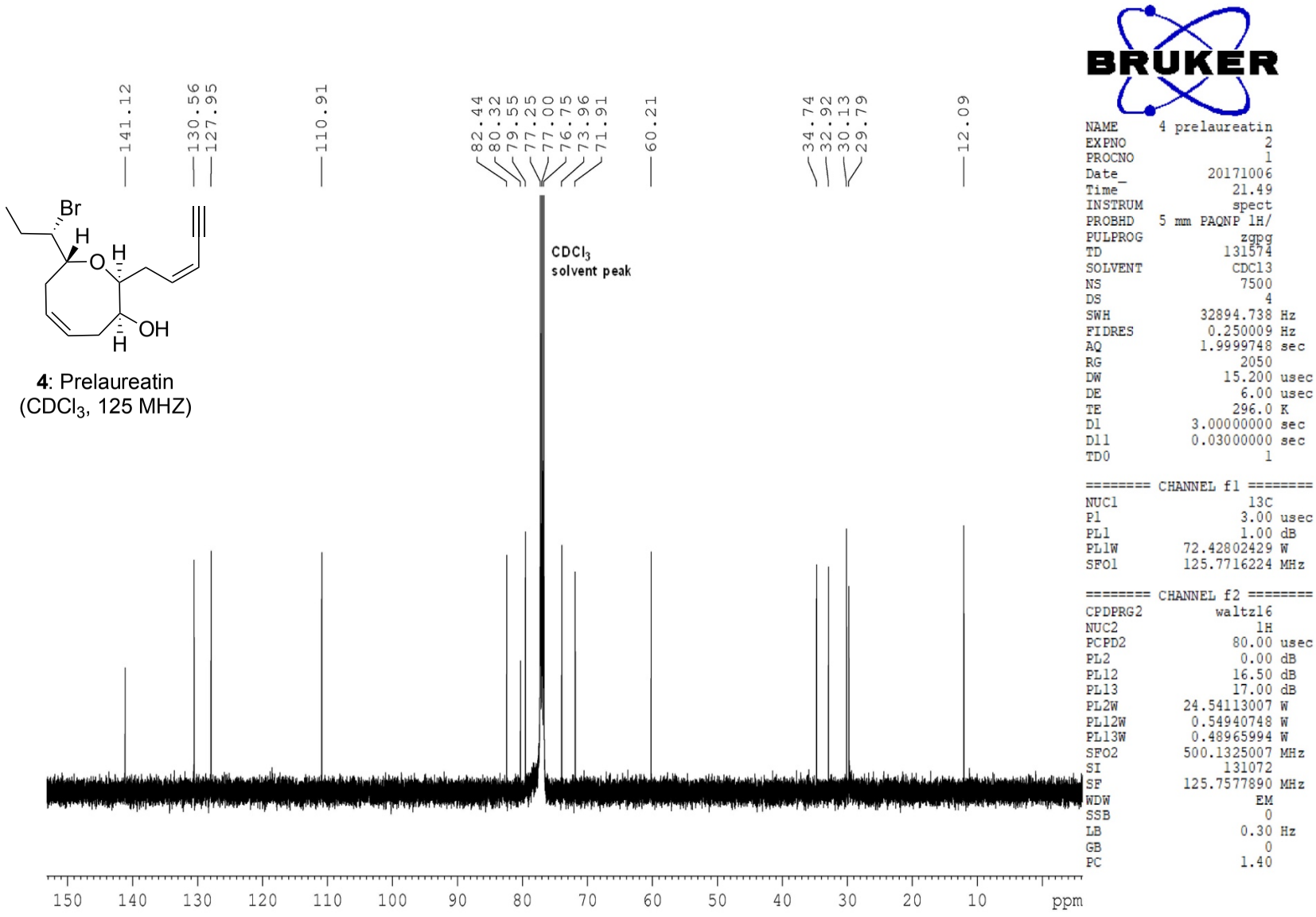
```
NAME      57 ZYA-V-lactone-70 cis
EXPNO                4
PROCNO               1
Date_         20170930
Time             23.27
INSTRUM          spect
PROBHD   5 mm PATXI 1H/
PULPROG     noesygpphpp
TD                2048
SOLVENT           CDCl3
NS                   4
DS                  16
SWH           5000.000 Hz
FIDRES        2.441406 Hz
AQ           0.2048500 sec
RG               11.29
DW             100.000 usec
DE              10.00 usec
TE              295.2 K
D0           0.00008981 sec
D1           2.00000000 sec
D8           0.80000001 sec
D11          0.03000000 sec
D12          0.00002000 sec
D16          0.00020000 sec
IN0          0.00020000 sec

======== CHANNEL f1 ========
SFO1        500.1320005 MHz
NUC1               1H
P1               8.00 usec
P2              16.00 usec
P17           2500.00 usec
ND0                  1
TD                 256
SFO1           500.132 MHz
FIDRES       19.531250 Hz
SW               9.997 ppm
FnMODE      States-TPPI
SI                1024
SF          500.1300000 MHz
WDW               QSINE
SSB                  2
LB               0.00 Hz
GB                   0
PC               1.00
SI                1024
MC2         States-TPPI
SF          500.1300000 MHz
WDW               QSINE
SSB                  2
LB               0.00 Hz
GB                   0
```



BRUKER

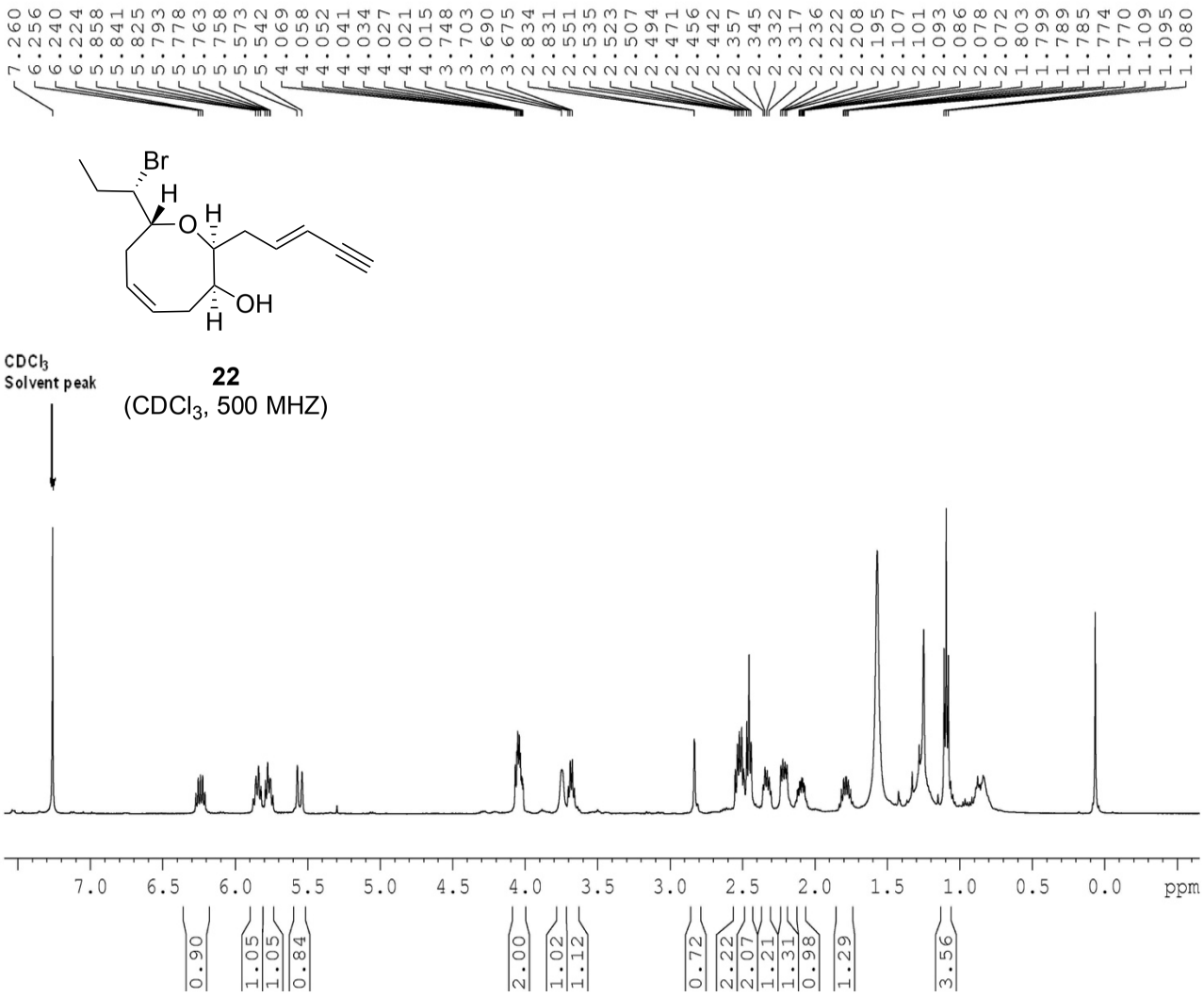
NAME	4 prelaureatin
EXPNO	1
PROCNO	1
Date_	20171007
Time	17.28
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	32
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	196.79
DW	50.000 usec
DE	10.00 usec
TE	293.6 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	500.1330885 MHz
NUC1	1H
P1	8.00 usec
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



4: Prelaureatin
($CDCl_3$, 125 MHZ)

BRUKER

NAME	4 prelaureatin
EXPNO	2
PROCNO	1
Date_	20171006
Time	21.49
INSTRUM	spect
PROBHD	5 mm PAQNP 1H/
PULPROG	zgpg
TD	131574
SOLVENT	CDCl3
NS	7500
DS	4
SWH	32894.738 Hz
FIDRES	0.250009 Hz
AQ	1.9999748 sec
RG	2050
DW	15.200 usec
DE	6.00 usec
TE	296.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	3.00 usec
PL1	1.00 dB
PL1W	72.42802429 W
SFO1	125.7716224 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	0.00 dB
PL12	16.50 dB
PL13	17.00 dB
PL2W	24.54113007 W
PL12W	0.54940748 W
PL13W	0.48965994 W
SFO2	500.1325007 MHz
SI	131072
SF	125.7577890 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

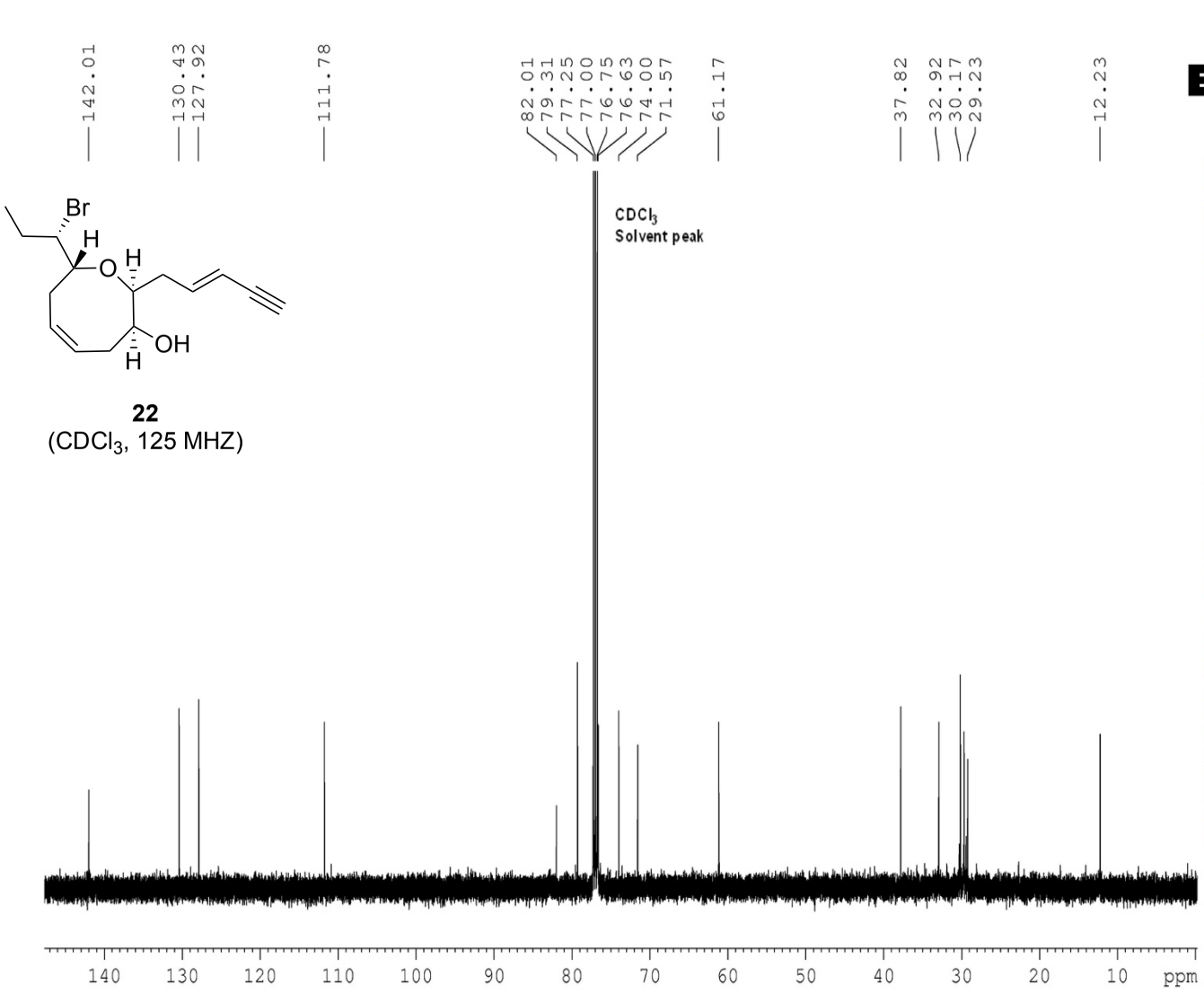


22

($CDCl_3$, 500 MHZ)

BRUKER

NAME	62 ZYA-V-enyne-86
EXPNO	1
PROCNO	1
Date_	20171007
Time	17.37
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	32
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	196.79
DW	50.000 usec
DE	10.00 usec
TE	293.7 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	500.1330885 MHz
NUC1	1H
P1	8.00 usec
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

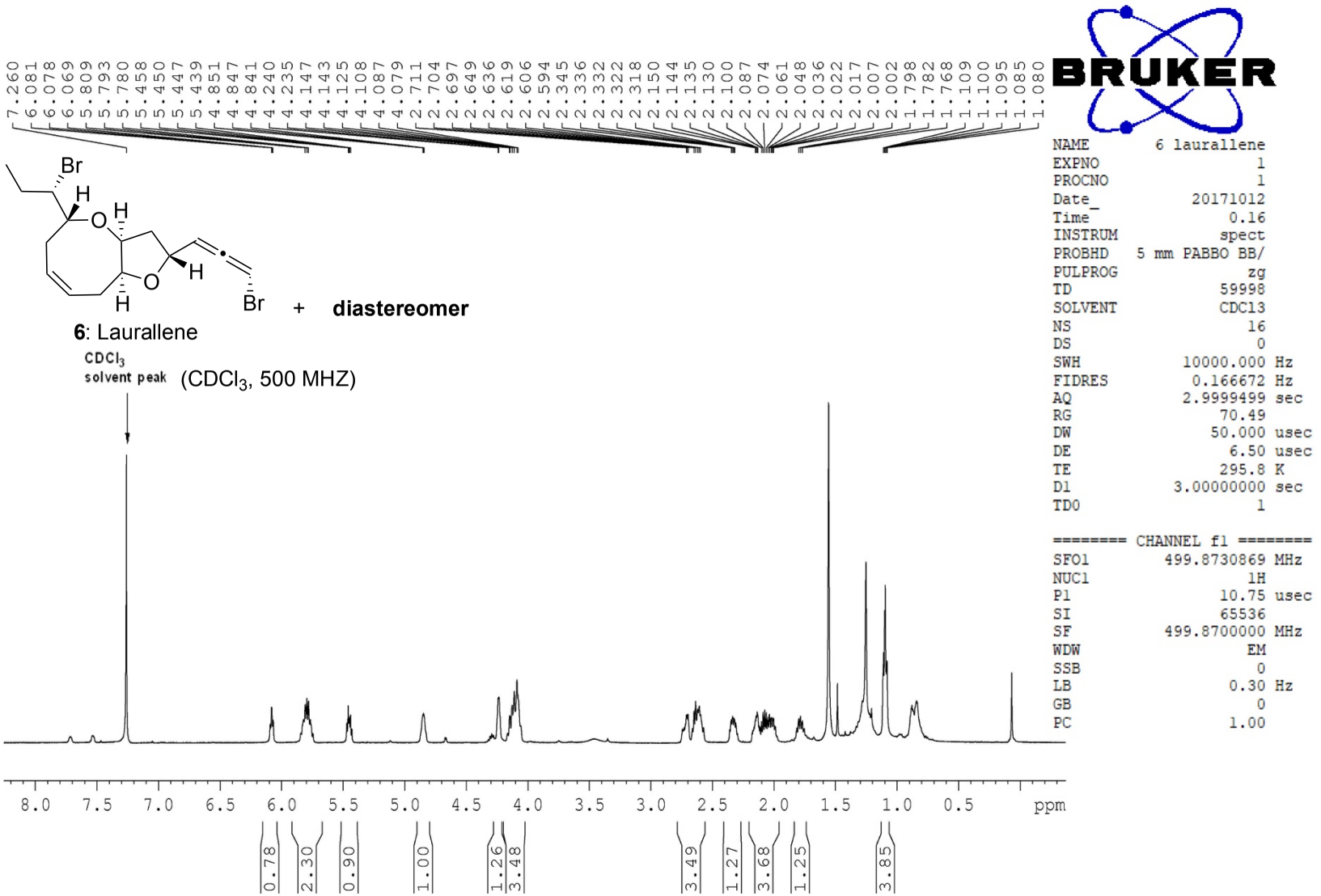


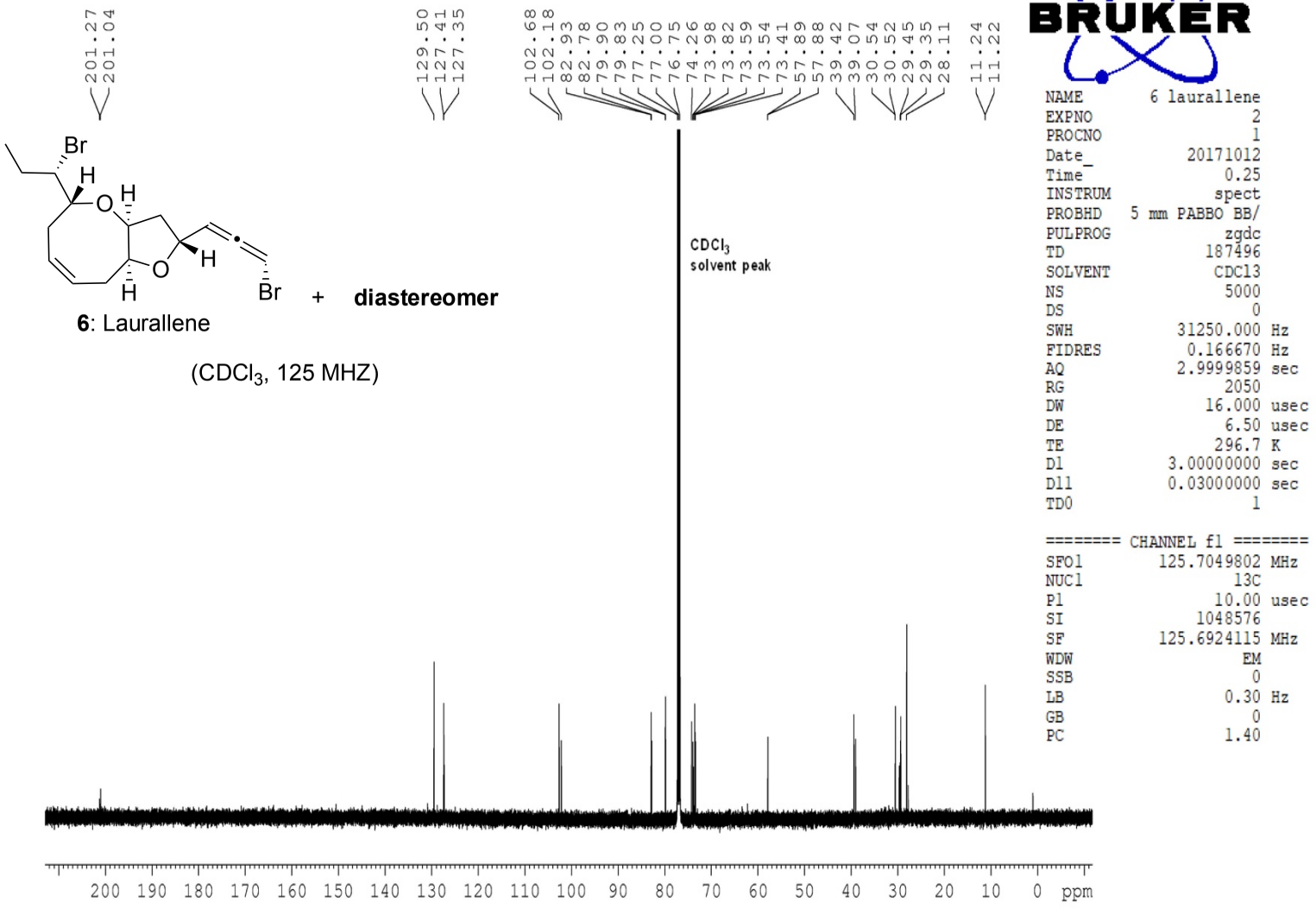
22
($CDCl_3$, 125 MHZ)

BRUKER

```
NAME        62 ZYA-V-enyne-86
EXPNO                    2
PROCNO                   1
Date_             20170914
Time                 14.40
INSTRUM              spect
PROBHD    5 mm PABBO BB/
PULPROG                zgdc
TD                   187496
SOLVENT              CDCl3
NS                     334
DS                       0
SWH              31250.000 Hz
FIDRES            0.166670 Hz
AQ                2.9999859 sec
RG                    2050
DW                  16.000 usec
DE                   6.50 usec
TE                  295.7 K
D1                3.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1            125.7049802 MHz
NUC1                    13C
P1                    10.00 usec
SI                  1048576
SF              125.6924148 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.40
```


7.260 6.081 6.078 6.069 5.809 5.793 5.780 5.458 5.450 5.447 5.439 4.851 4.847 4.841 4.240 4.235 4.147 4.143 4.125 4.108 4.087 4.079 2.711 2.704 2.697 2.649 2.636 2.619 2.606 2.594 2.345 2.336 2.332 2.322 2.318 2.150 2.144 2.135 2.130 2.100 2.087 2.074 2.061 2.048 2.036 2.022 2.017 2.007 2.002 1.798 1.782 1.768 1.109 1.100 1.095 1.085 1.080
BRUKER
Br
H
O
H
O
H
H
Br
+ diastereomer
6: Laurallene
CDCl3
solvent peak
(CDCl3, 500 MHZ)
NAME 6 laurallene
EXPNO 1
PROCNO 1
Date_ 20171012
Time 0.16
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 59998
SOLVENT CDCl3
NS 16
DS 0
SWH 10000.000 Hz
FIDRES 0.166672 Hz
AQ 2.9999499 sec
RG 70.49
DW 50.000 usec
DE 6.50 usec
TE 295.8 K
D1 3.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 499.8730869 MHz
NUC1 1H
P1 10.75 usec
SI 65536
SF 499.8700000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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 ppm
0.78 2.30 0.90 1.00 1.26 3.48 3.49 1.27 3.68 1.25 3.85

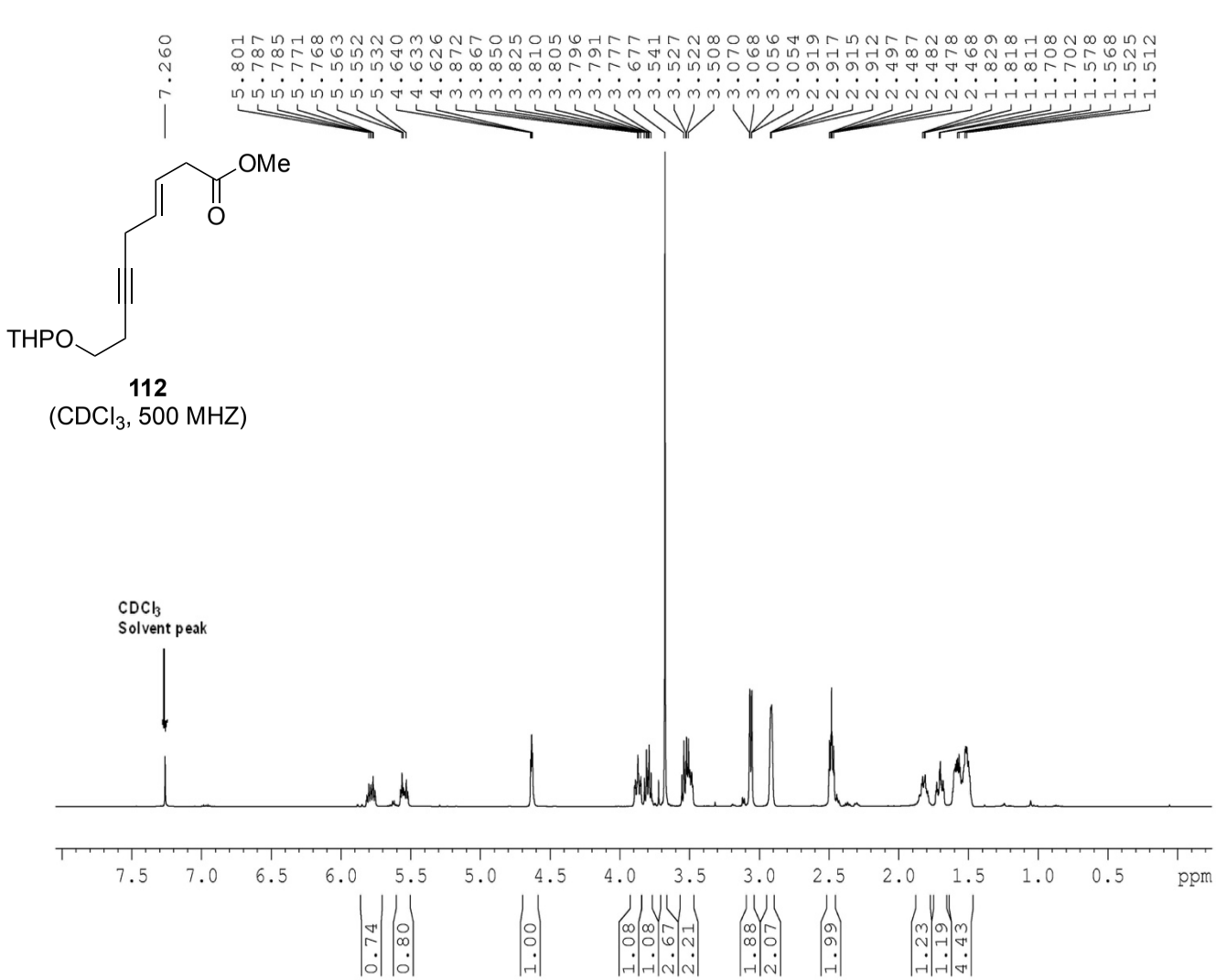


6: Laurallene

($CDCl_3$, 125 MHZ)

BRUKER

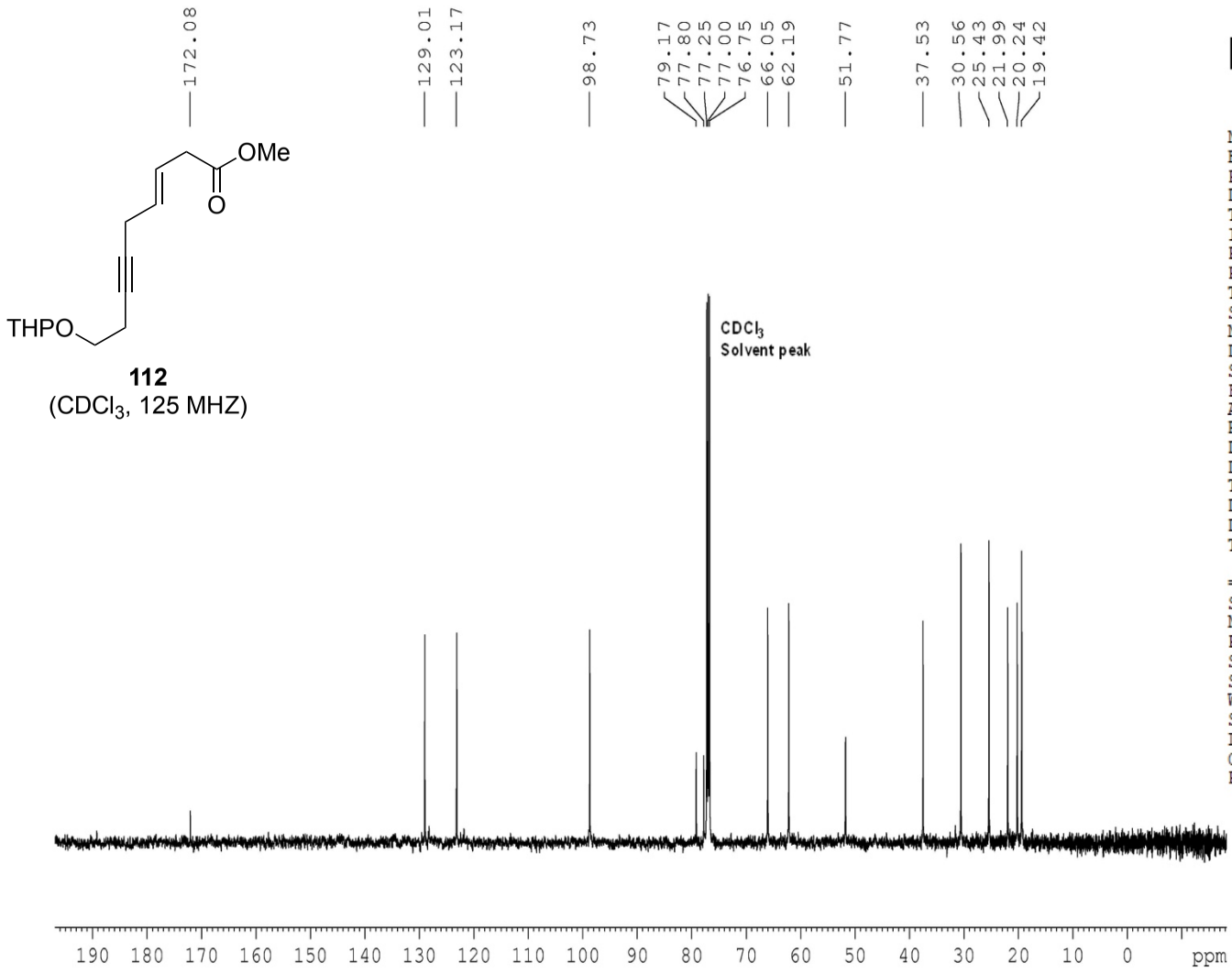
NAME	6 laurallene
EXPNO	2
PROCNO	1
Date_	20171012
Time	0.25
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	5000
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.7 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



112
($CDCl_3$, 500 MHZ)

BRUKER

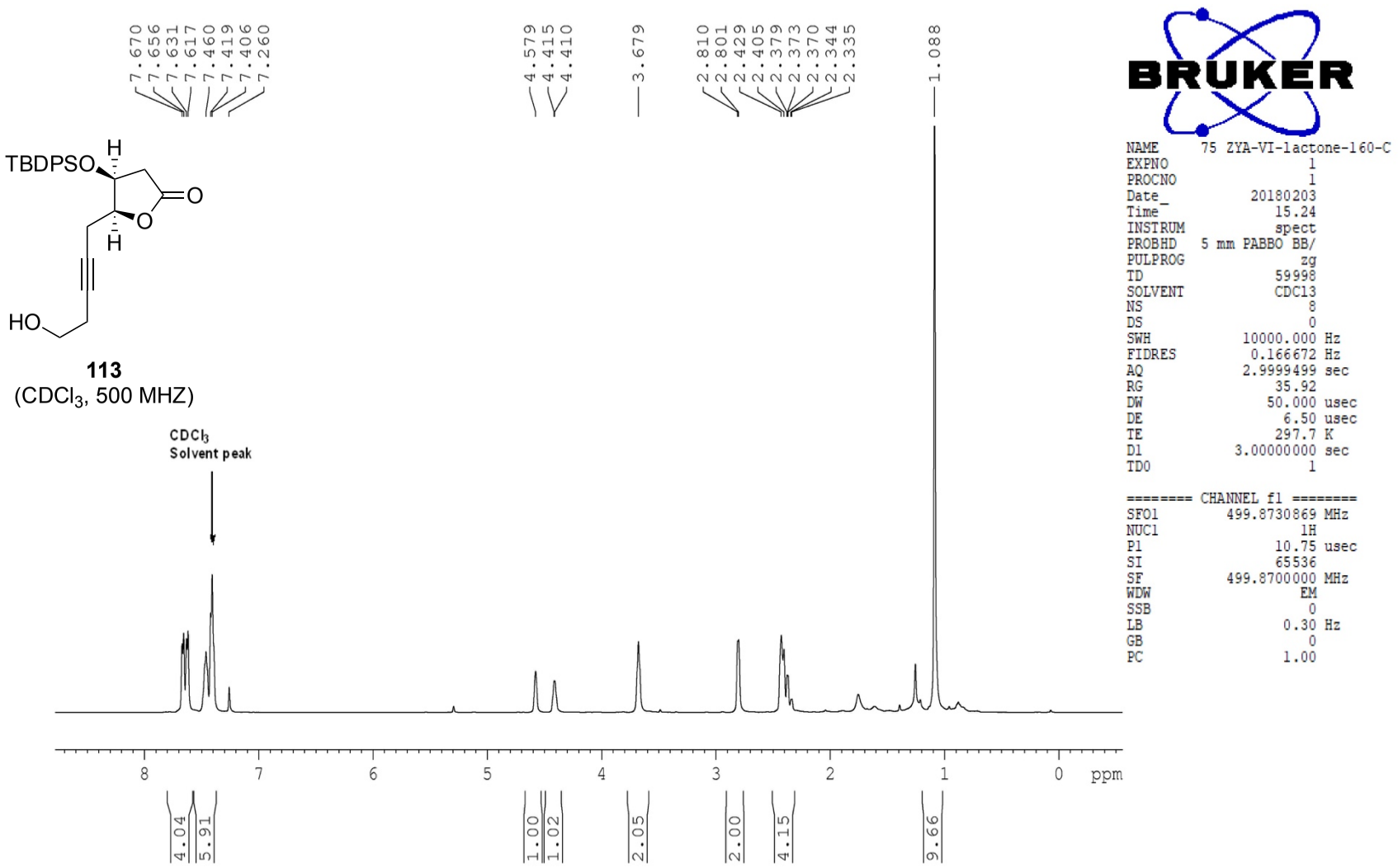
NAME	74 ZYA-VI-ester-201-C
EXPNO	1
PROCNO	1
Date_	20180211
Time	21.24
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	52.86
DW	50.000 usec
DE	10.00 usec
TE	294.4 K
D1	2.00000000 sec
TD0	1
======= CHANNEL f1 =======	
SFO1	500.1330885 MHz
NUC1	1H
P1	8.00 usec
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



112
($CDCl_3$, 125 MHZ)

```
NAME        74 ZYA-VI-ester-201-C
EXPNO                       2
PROCNO                      1
Date_                20180211
Time                    21.27
INSTRUM                 spect
PROBHD   5 mm PATXI 1H/
PULPROG                 zgdc
TD                    178568
SOLVENT                 CDCl3
NS                        506
DS                          0
SWH                29761.904 Hz
FIDRES             0.166670 Hz
AQ                 2.9999924 sec
RG                    196.79
DW                    16.800 usec
DE                    10.00 usec
TE                    294.7 K
D1                 3.00000000 sec
D11                0.03000000 sec
TD0                         1

======= CHANNEL f1 =======
SFO1              125.7703643 MHz
NUC1                      13C
P1                    14.00 usec
SI                      131072
SF                125.7577890 MHz
WDW                       EM
SSB                         0
LB                     4.00 Hz
GB                          0
PC                     1.40
```



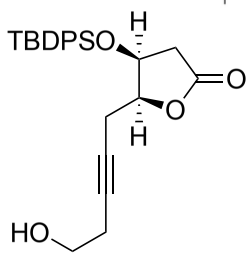
113

($CDCl_3$, 500 MHZ)

BRUKER

```
NAME        75 ZYA-VI-lactone-160-C
EXPNO                             1
PROCNO                            1
Date_                      20180203
Time                          15.24
INSTRUM                       spect
PROBHD   5 mm PABBO BB/
PULPROG                          zg
TD                            59998
SOLVENT                       CDC13
NS                                8
DS                                0
SWH                   10000.000 Hz
FIDRES                 0.166672 Hz
AQ                     2.9999499 sec
RG                            35.92
DW                       50.000 usec
DE                        6.50 usec
TE                          297.7 K
D1                    3.00000000 sec
TD0                               1

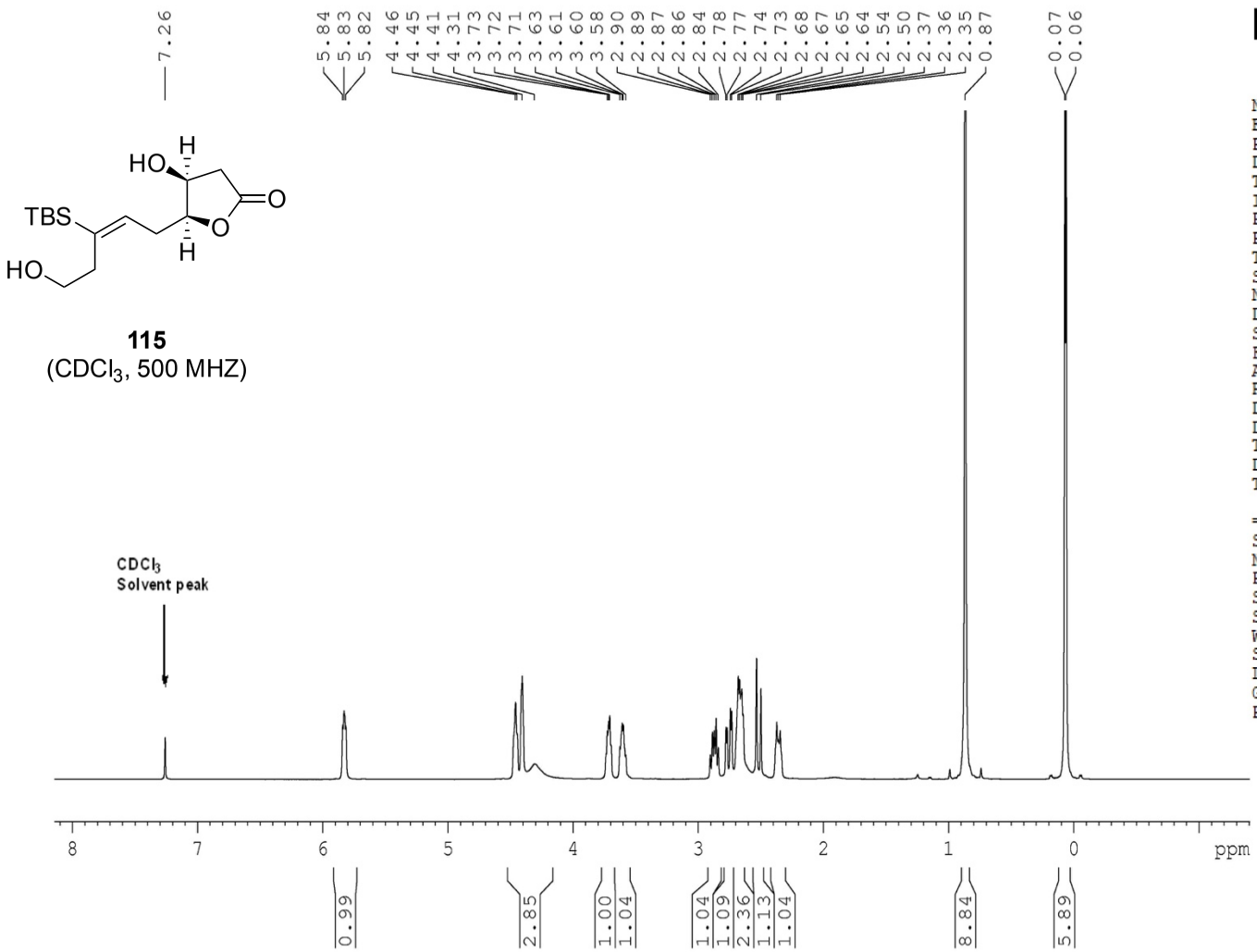
======== CHANNEL f1 ========
SFO1                499.8730869 MHz
NUC1                           1H
P1                       10.75 usec
SI                            65536
SF                  499.8700000 MHz
WDW                           EM
SSB                            0
LB                        0.30 Hz
GB                             0
PC                         1.00
```



113
($CDCl_3$, 125 MHZ)


```
NAME      75 ZYA-VI-lactone-160-C
EXPNO                           2
PROCNO                          1
Date_                    20180203
Time                        15.26
INSTRUM                     spect
PROBHD   5 mm PABBO BB/
PULPROG                      zgdc
TD                         187496
SOLVENT                     CDCl3
NS                            159
DS                              0
SWH                    31250.000 Hz
FIDRES                 0.166670 Hz
AQ                     2.9999859 sec
RG                          2050
DW                       16.000 usec
DE                        6.50 usec
TE                        297.7 K
D1                   3.00000000 sec
D11                  0.03000000 sec
TD0                             1

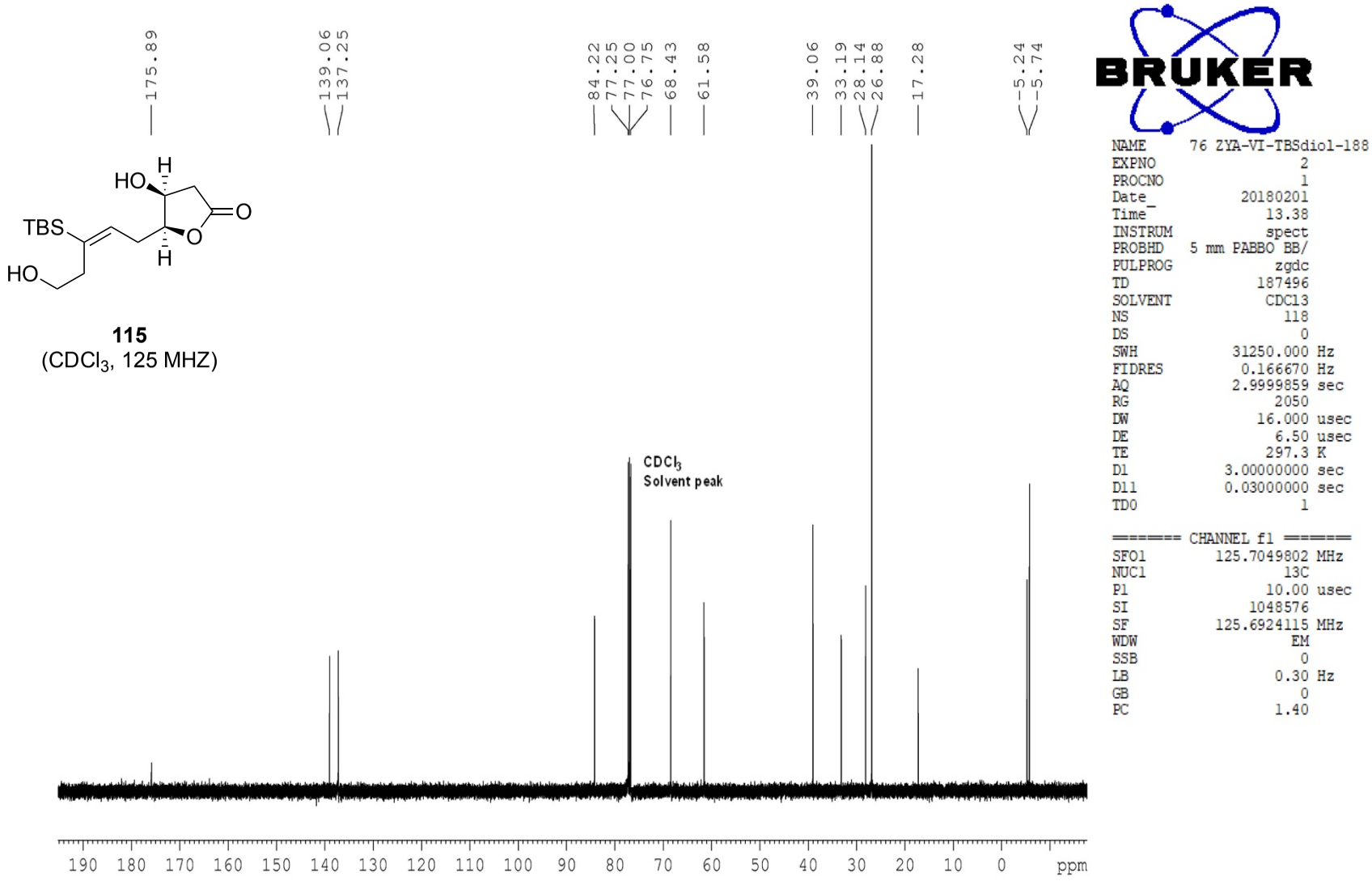
======== CHANNEL f1 ========
SFO1                125.7049802 MHz
NUC1                        13C
P1                       10.00 usec
SI                       1048576
SF                  125.6924115 MHz
WDW                          EM
SSB                             0
LB                        0.30 Hz
GB                              0
PC                        1.40
```



115
($CDCl_3$, 500 MHZ)

BRUKER

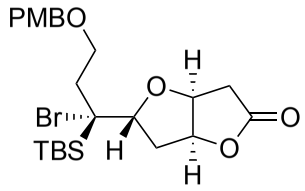
NAME	76 ZYA-VI-TBSdiol-188
EXPNO	1
PROCNO	1
Date_	20180201
Time	13.33
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	28.76
DW	50.000 usec
DE	6.50 usec
TE	296.8 K
D1	3.00000000 sec
TD0	1
======= CHANNEL f1 =======	
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



115
($CDCl_3$, 125 MHZ)

BRUKER

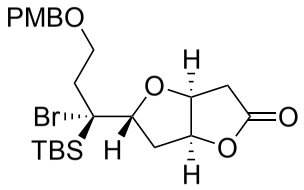
NAME	76 ZYA-VI-TBSdiol-188
EXPNO	2
PROCNO	1
Date_	20180201
Time	13.38
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	118
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	297.3 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======= CHANNEL f1 =======	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



107
($CDCl_3$, 500 MHZ)


```
NAME      69 ZYA-VI-PMB-179-C
EXPNO                   1
PROCNO                  1
Date_            20180130
Time                23.41
INSTRUM             spect
PROBHD    5 mm PABBO BB/
PULPROG                 zg
TD                  59998
SOLVENT             CDCl3
NS                      8
DS                      0
SWH           10000.000 Hz
FIDRES         0.166672 Hz
AQ             2.9999499 sec
RG                  56.75
DW                 50.000 usec
DE                  6.50 usec
TE                 297.5 K
D1            3.00000000 sec
TD0                     1

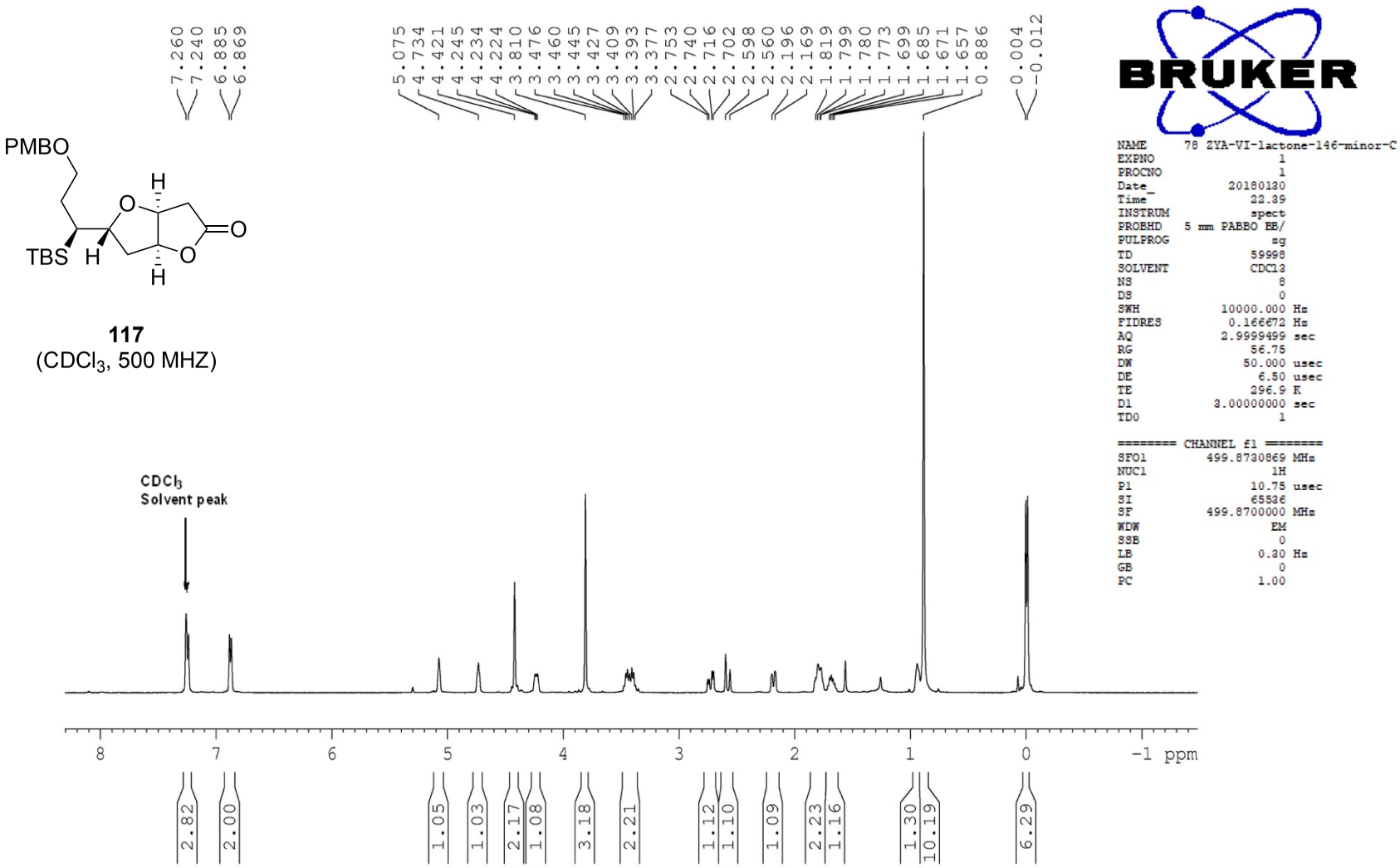
======== CHANNEL f1 ========
SFO1         499.8730869 MHz
NUC1                   1H
P1                 10.75 usec
SI                 65536
SF           499.8700000 MHz
WDW                    EM
SSB                     0
LB                  0.30 Hz
GB                      0
PC                  1.00
```

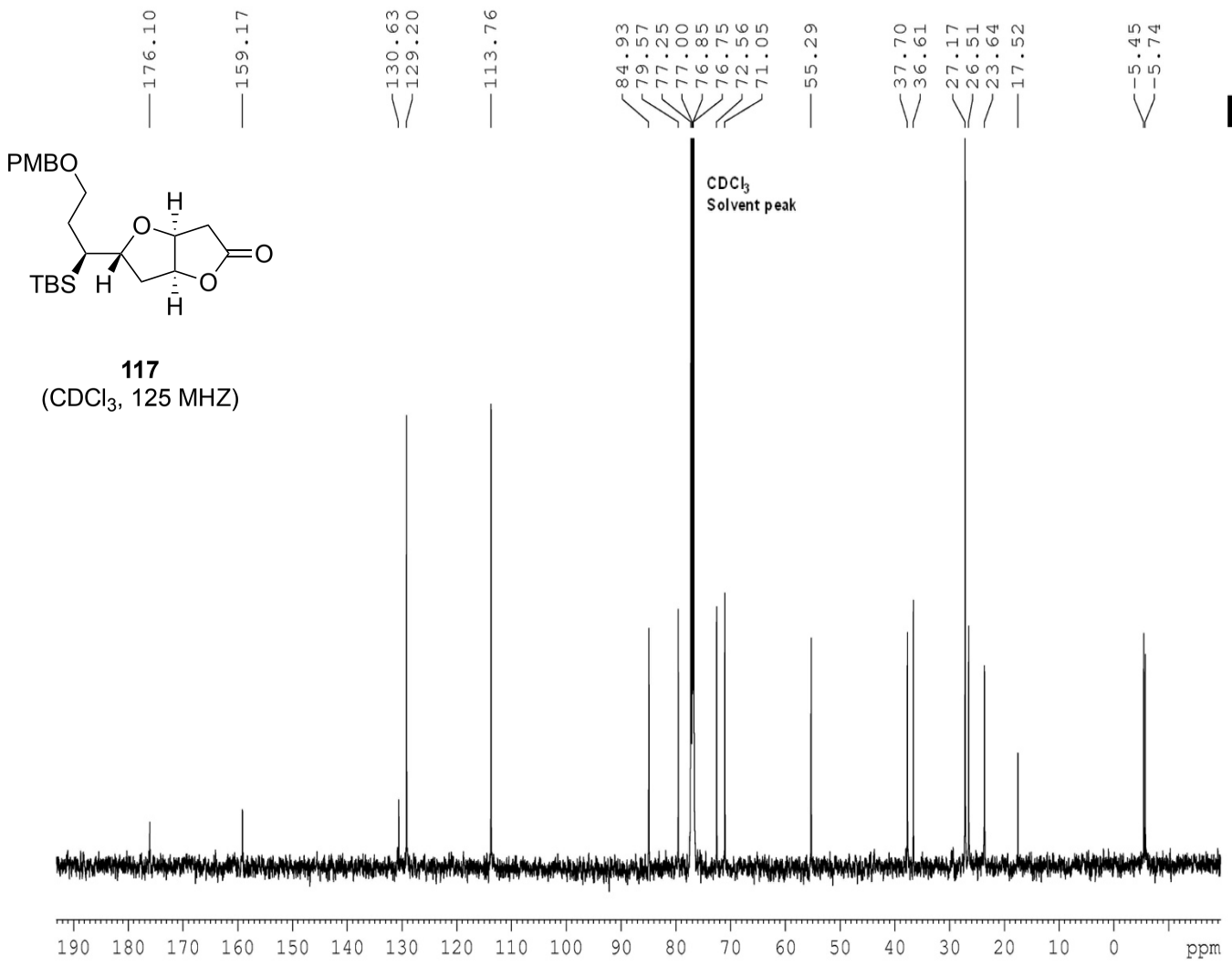


107
($CDCl_3$, 125 MHZ)

BRUKER

NAME	69 ZYA-VI-PMB-179-C
EXPNO	2
PROCNO	1
Date_	20180130
Time	23.48
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	769
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40


PMBO
H
O
TBS
H
O
O
H
117
(CDCl3, 500 MHZ)
7.260
7.240
6.885
6.869
5.075
4.734
4.421
4.245
4.234
4.224
3.810
3.476
3.460
3.445
3.427
3.409
3.393
3.377
2.753
2.740
2.716
2.702
2.598
2.560
2.196
2.169
1.819
1.799
1.780
1.773
1.699
1.685
1.671
1.657
0.886
0.004
-0.012
CDCl3
Solvent peak
8
7
6
5
4
3
2
1
0
-1 ppm
2.82
2.00
1.05
1.03
2.17
1.08
3.18
2.21
1.12
1.10
1.09
2.23
1.16
1.30
10.19
6.29
BRUKER
NAME 78 ZYA-VI-lactone-146-minor-C
EXPNO 1
PROCNO 1
Date_ 20180130
Time 22.39
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg
TD 59998
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.166672 Hz
AQ 2.9999499 sec
RG 56.75
DW 50.000 usec
DE 6.50 usec
TE 296.9 K
D1 3.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 499.8730869 MHz
NUC1 1H
P1 10.75 usec
SI 65536
SF 499.8700000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



117
($CDCl_3$, 125 MHZ)

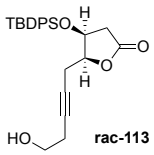
BRUKER

NAME	78 ZYA-VI-lactone-146-minor-C
EXPNO	2
PROCNO	1
Date_	20180130
Time	22.55
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	sgdc
TD	187496
SOLVENT	CDCl3
NS	404
DS	0
SWH	31250.000 Hz
FIDRES	0.166670 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	297.4 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	4.00 Hz
GB	0
PC	1.40

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-161-rac-purified.lcd

Acquired by	: Admin
Sample Name	: ZYA-VI-lactone-161-rac-purified
Sample ID	: ZYA-VI-lactone-161-rac-purified
Tray#	: 1
Vail #	: -1
Injection Volume	: 20 uL
Data File Name	: ZYA-VI-lactone-161-rac-purified.lcd
Method File Name	: AD-H 90-10.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 2/23/2018 5:46:00 PM
Data Processed	: 2/24/2018 4:28:44 PM

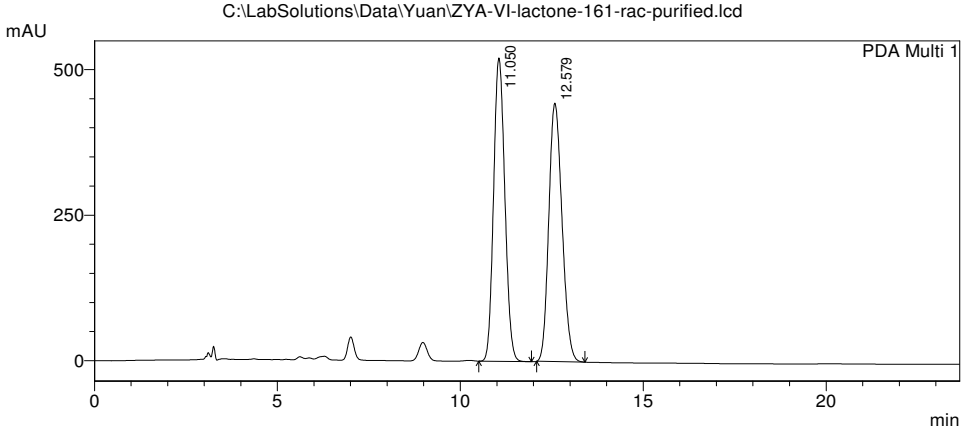


rac-113

<Chromatogram>

AD-H column, 4.6 × 25 mm, hexanes/i-PrOH, 9:1, 1 mL/min, UV detector at 215 nm

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-161-rac-purified.lcd



1 PDA Multi 1/215nm 4nm

PeakTable

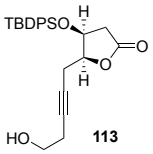
PDA Ch1 215nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.050	11163149	520931	50.021	53.998
2	12.579	11153678	443790	49.979	46.002
Total		22316827	964721	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-160-pured-3.lcd

Acquired by	: Admin
Sample Name	: ZYA-VI-lactone-160-pured-3.lcd
Sample ID	: ZYA-VI-lactone-160-pured-3
Tray#	: 1
Vail #	: -1
Injection Volume	: 20 uL
Data File Name	: ZYA-VI-lactone-160-pured-3.lcd
Method File Name	: AD-H 90-10.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 2/24/2018 11:34:38 PM
Data Processed	: 3/5/2018 2:35:36 AM

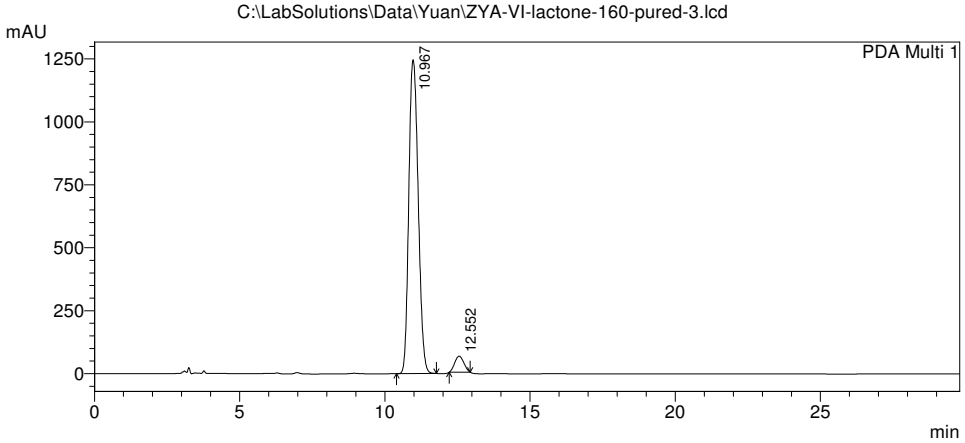


113

<Chromatogram>

AD-H column, 4.6 × 25 mm, hexanes/i-PrOH, 9:1, 1 mL/min, UV detector at 215 nm

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-160-pured-3.lcd



1 PDA Multi 1/215nm 4nm

PeakTable

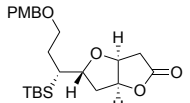
PDA Ch1 215nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.967	28049452	1247128	95.245	95.125
2	12.552	1400258	63919	4.755	4.875
Total		29449710	1311047	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-212-rac-PTLC-4.lcd

Acquired by	: Admin
Sample Name	: ZYA-VI-lactone-212-rac-PTLC-4
Sample ID	: ZYA-VI-lactone-212-rac-PTLC-4
Tray#	: 1
Vail #	: -1
Injection Volume	: 20 uL
Data File Name	: ZYA-VI-lactone-212-rac-PTLC-4.lcd
Method File Name	: AD-H 90-10.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 3/5/2018 8:18:24 PM
Data Processed	: 3/5/2018 8:44:49 PM

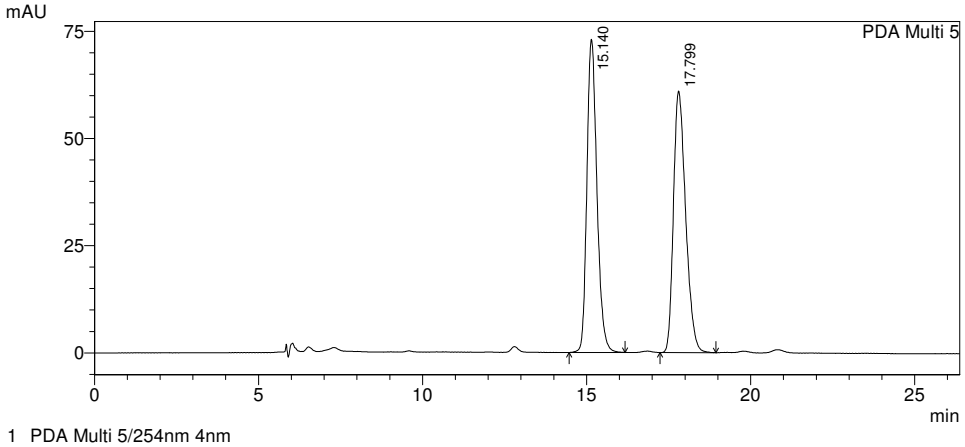


rac-48

<Chromatogram>

AD-H column, 4.6 × 25 mm, hexanes/i-PrOH, 9:1, 1 mL/min, UV detector at 254 nm

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-212-rac-PTLC-4.lcd



1 PDA Multi 5/254nm 4nm

PeakTable

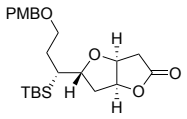
PDA Ch5 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.140	1555021	73041	49.642	54.478
2	17.799	1577469	61034	50.358	45.522
Total		3132490	134075	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-200-PLC-8.lcd

Acquired by	: Admin
Sample Name	: ZYA-VI-lactone-200-PLC-8
Sample ID	: ZYA-VI-lactone-200-PLC-8
Tray#	: 1
Vail #	: -1
Injection Volume	: 20 uL
Data File Name	: ZYA-VI-lactone-200-PLC-8.lcd
Method File Name	: AD-H 90-10.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 3/5/2018 2:47:37 PM
Data Processed	: 9/27/2018 5:54:56 PM

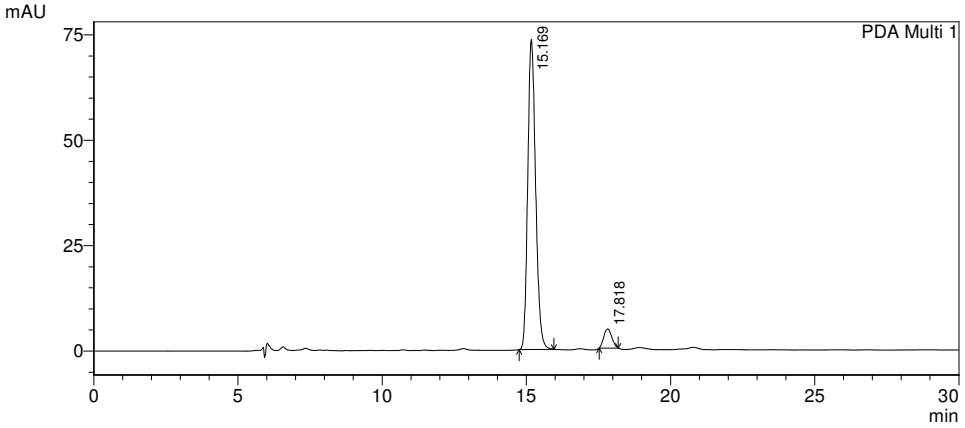


48

<Chromatogram>

AD-H column, 4.6 × 25 mm, hexanes/i-PrOH, 9:1, 1 mL/min, UV detector at 254 nm

C:\LabSolutions\Data\Yuan\ZYA-VI-lactone-200-PLC-8.lcd



1 PDA Multi 1/254nm 1nm

PeakTable

PDA Ch1 254nm 1nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.169	1392385	73487	93.999	94.163
2	17.818	88895	4556	6.001	5.837
Total		1481280	78042	100.000	100.000

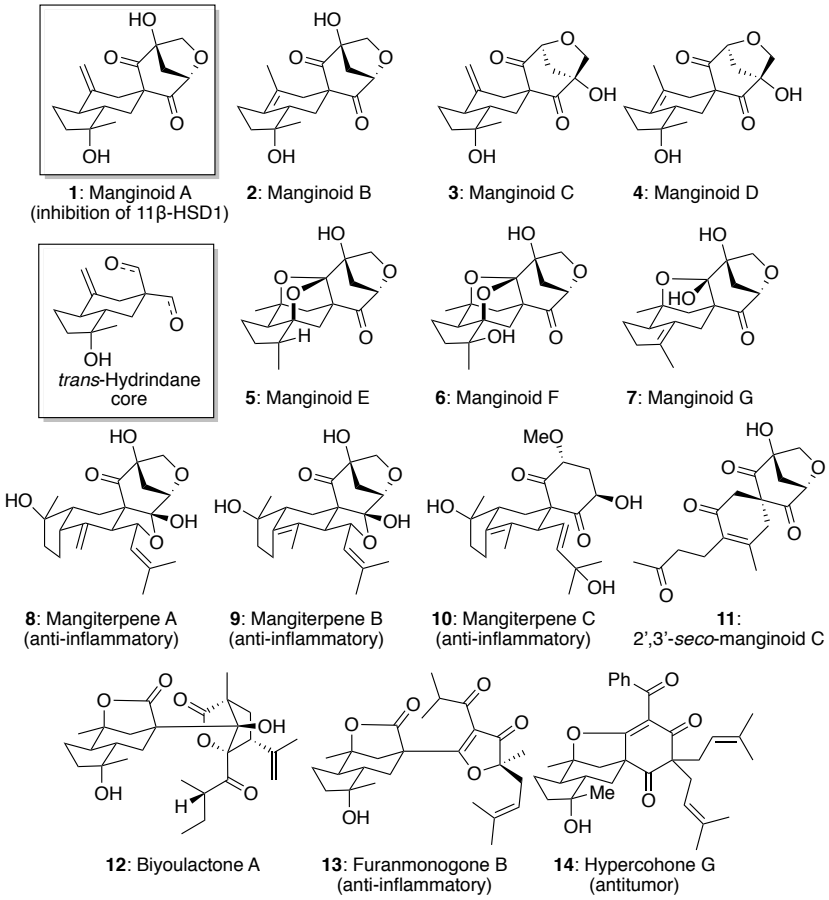
CHAPTER 3

DEVELOPING A DIVERGENT SYTHESIS TOWARDS NATURAL PRODUCTS CONTAINING A TRANS-HYDRINDANE: TOTAL SYNTHESIS OF MANGINOID

3.1 Introduction

3.1.1 Structures of Manginoids and Related Natural Products

Figure 3-1. Structures of Manginoids and Related Natural Products Containing the *trans*-Hydrindane Cores

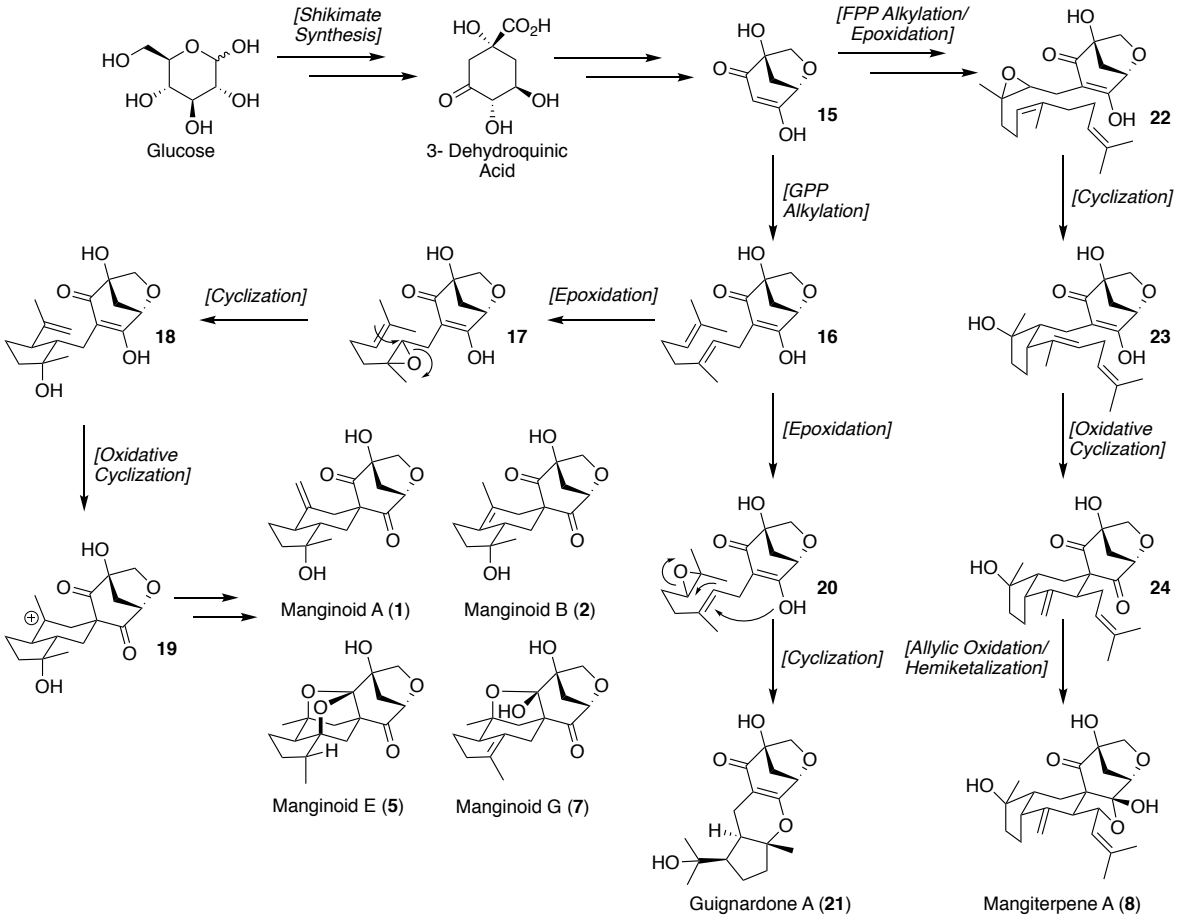


Manginoids are a family of monoterpene-shikimate-conjugated meroterpenoid natural products that were isolated from the fermentation of *Guignardia mangiferae* in 2017 by Zhang, Zhu and coworkers.[1] As a representative member of the family (Figure 3-1), manginoid A (**1**) displays potent inhibition (IC_{50} = 0.84 ± 0.07 μM) of 11*β*-hydroxysteroid dehydrogenase type 1 (11*β*-HSD1), an enzyme that catalyzes intracellular conversion of inactive cortisone to active glucocorticoid (GC) hormone cortisol. Recent studies indicated that over activation of GC hormone might play an important role in a variety of metabolic syndromes such as obesity,

osteoporosis, insulin resistance and diabetes. Thus, inhibition of 11β-HSD1 could potentially be a novel therapy in the treatment of such diseases by lowing GC hormone concentration.[2] From the perspective of chemical structures, manginoids A-D (**1**-**4**) are four alkene and/or epimeric isomers, all possessing an unique 6-oxaspiro[bicyclo[3.2.1]octane3,5′-indene] ring system. They represent the first examples of a spiro meroterpenoid containing a bridge spirocyclohexanedione motif while maginoids E and F (**5**, **6**) are the first meroterpenoids bearing a 2,4- dioxatricyclo[3.3.1.$0^{3,7}$]nonane system. More recently, four additional bioactive sesquiterpene/monoterpene-shikimate-conjugated meroterpenoid, namely mangiterpene A-C (**8**-**10**) and *2',3'-seco*-manginoid (**11**) were also isolated by the Zhang, Zhu and coworkers in 2019.[3] Possessing remarkably complex polycyclic system (**8, 9**) and potent anti-inflammatory activity (**10**), these compounds undoubtedly enrich the structural and biological diversity of terpene-shikimate-conjugated spirocyclic meroterpenoids. Despite their unique core motif, manginoids also share general structural features with an array of bioactive PPAP-type natural products,[4] most notably of which is the highly oxidized *trans*-hydrindane system as shown in Figure 1. To the best of our knowledge, no synthetic study towards either such challenging polysubstituted *trans*-hydrindane, or any structurally related natural product, has been reported.

3.1.2 Proposed Biogenesis of Manginoids and Related Natural Products

Scheme 3-1. Proposed Biogenesis of Manginoids and Related Natural Products

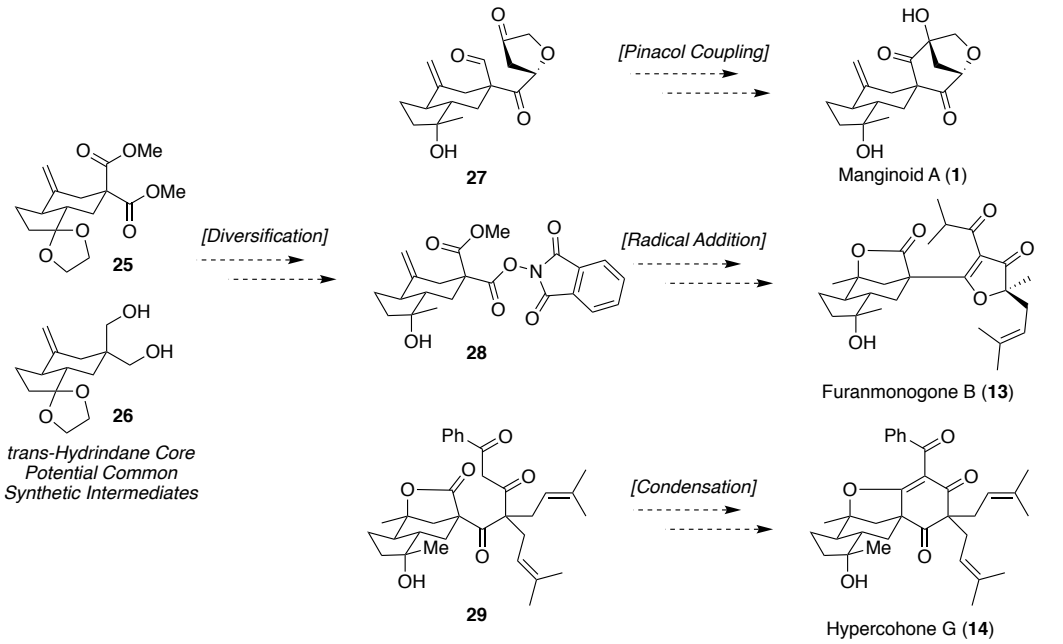


Manginoids **1**-**7** were isolated alongside with several members of the guignardone natural product family[5] from the same fermentation. As they shared common structural features, a unified mechanism to account for their collective biosynthesis was proposed. As shown in scheme 3-1, the tentative key intermediate for both families was diketone **15** (shown here with its enol form), a potential metabolite of the shikimate pathway. After its coupling with geranylgeranyl pyrophosphate to arrive at **16**, epoxidation with either olefin would yield two distinct skeletons respectively. While epoxide **20** could undergo a polyene cyclization type reaction to afford members of the guignardone family (shown here with **21**), epoxide **17** may go through a Prins-

type cyclization to give intermediate **18**. Next, a potential oxidative coupling between the α-carbon of the diketone and the isopropenyl side chain would forge the six-membered ring and yield cationic species **19**, which could further undergo an E1 elimination or intramolecular cyclization to deliver various members of the manginoid class. These biosynthetic pathways were further confirmed by the isolation of mangiterpene A (**8**),[3] which can also reasonably derived from **15** via a similar sequence leading to maginoids.

3.2 Proposed Divergent Approach Towards Manginoids and Related Natural Products

Scheme 3-2. Proposed Divergent Approach Towards Several Natural Products Containing a *trans*-Hydrindane Core via a Common Intermediate



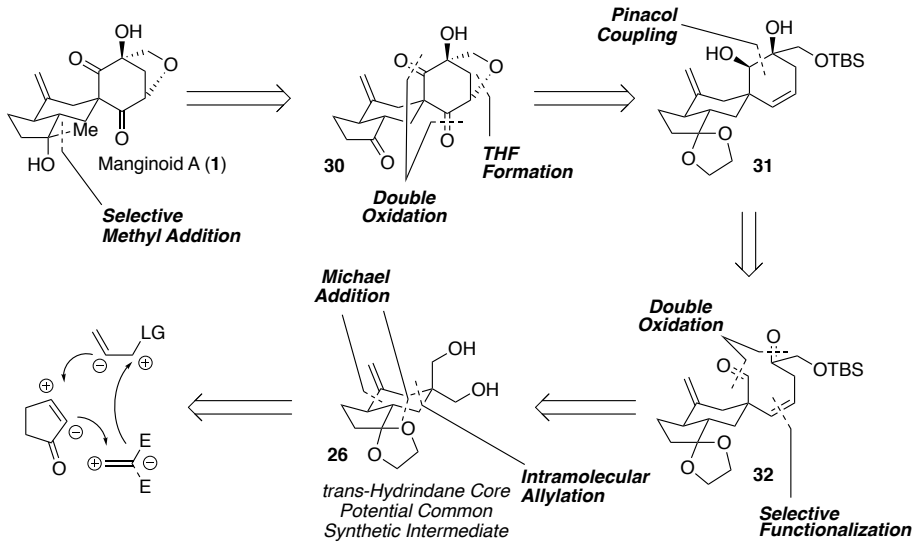
Although some of the proposed enzymatic transformations would be challenging to realize in a laboratory setting, the biosynthetic pathways, in principle, outlined a collective synthetic approach towards the manginoid class of natural products through the use of diketone **15** as a key intermediate (Scheme 3-2). In our design, we aimed to identify a solution with an even higher degree of divergence that could lead to not only the manginoid members, but also several structurally distinct natural products such as furanmonogone B (**13**) and hypercohone G (**14**). For

that purpose, **25** or **26** could potentially be an effective common intermediate as they not only process the *trans*-hydrindane core that resembles the target molecules, but also contain two versatile handles (gem-diester or diol) for future diversification. We envisioned that we could access all desired natural products from **25** or **26** with appropriate ordering of chemical bonds formations and functional groups interconversions. With this idea in mind, we chose the total synthesis of manginoid A (**1**) as an opportunity to showcase the feasibility of our notion and explore several fundamental synthetic questions of this global approach.

3.3 Total Synthesis of Manginoid A (1)

3.3.1 Retrosynthetic Analysis of Manginoid A (1)

Scheme 3-3. Retrosynthetic Analysis of Manginoid A (1)

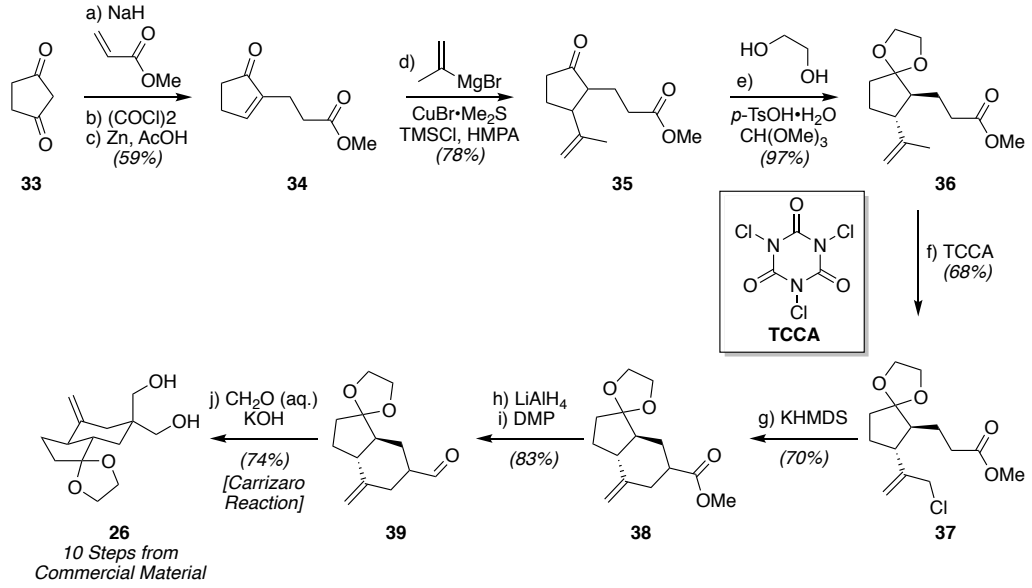


Key elements of our overall approach to synthesize manginoid A (**1**) from the potential common intermediate **26** are shown in Scheme 3-3. Our synthetic design for manginoid A was predicated on introducing the methyl group via a regio- and stereoselective Grignard addition in the final step. We surmised that the steric hindrance exerted by the adjacent spiro quaternary carbon and the oxa-bridged ring could prevent the methyl addition from occurring at the 1,3-

diketone, thus providing the desired chemoselectivity. Such quaternary center-induced stereoelectonic effects have previously facilitated several successful total syntheses in our group.[6] After reducing the oxidation state and cleaving the oxa-bridged ring to arrive at **31**, the presence of the 1,2-diol functionality suggested its potential construction via a SET-mediated reductive coupling (also known as pinacol coupling) from 1,6-diketone **32**.[7] However, this transformation would be challenging for several reasons. First, **32** might be quite unstable as its combination of three sensitive functional groups (aldehyde, β,γ-unsaturated ketone, and α-silyoxy ketone) might incur undesired decomposition. Second, for the ring closure to productively occur, the SET process needed to initiate at the hindered aldehyde instead of the α-silyoxy ketone, as the latter event could induce the α-deoxygenation and other unfavored reaction pathways thereafter. Although potentially problematic, it would still be advantageous to explore whether the SET reagent could preferentially engage the hindered aldehyde over the more accessible ketone. Last but not least, even if the cyclization were possible, the facial selectivity would be challenging to predict given no similar reductive coupling in such systems with densely packed stereogenic centers has been reported. Assuming the designed pinacol coupling was viable, a selective functionalization of the equatorial alcohol would trace **32** back to diol **26**. As both alcohols of **26** were expected to have similar reactivity, a reliable differentiation operation needed to be developed in order to achieve the desired selectivity. Finally, to readily fashion the *trans*-hydrindane system starting from commercial material, we projected a sequence of Michael additions and intramolecular allylation could rise to the occasion.

3.3.2 Synthesis of Key Diol 26

Scheme 3-4. First Generation Synthesis of Key Diol 26[a]

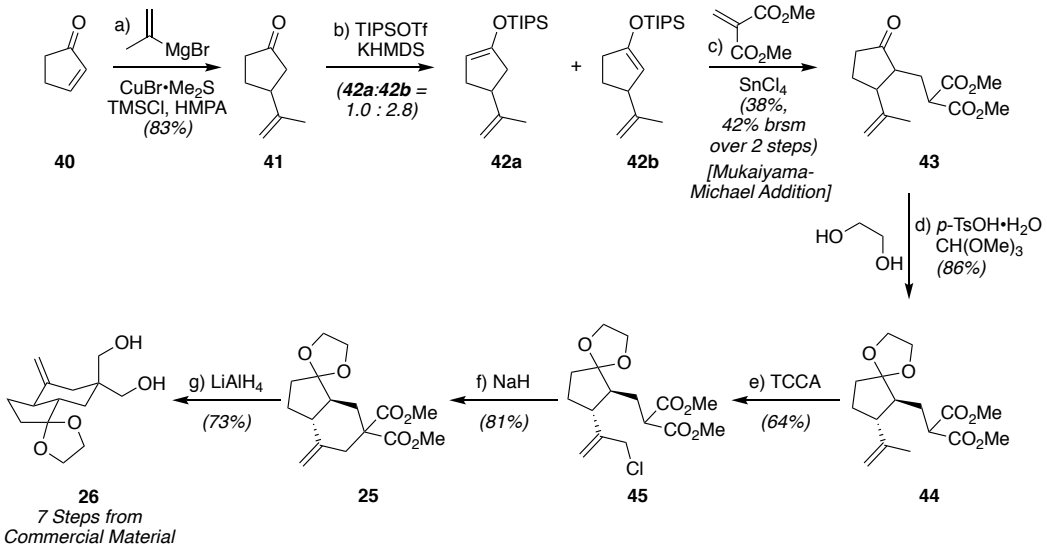


[a] Reagents and conditions: (a) NaH (1.2 equiv), methyl acrylate (2.8 equiv), DMF, 0 to 80 °C, 12 h; (b) $(COCl)_2$ (1.5 equiv), CH_2Cl_2, 0 to 25 °C, 15 min, 77% over 2 steps; (c) Zn (6.0 equiv), NH_4Cl (3.0 equiv), MeOH, 60 °C, 30 min, 76%; (d) isopropenylmagnesium bromide (1.6 equiv), $CuBr•Me_2S$ (0.20 equiv), TMSCl (3.0 equiv), HMPA (2.0 equiv), THF, -78 °C, 30 min, 78%; (e) ethylene glycol (5.0 equiv), $CH(OMe)_3$ (5.0 equiv), *p*-$TsOH•H_2O$ (0.10 equiv), toluene, 90 °C, 12 h, 97%; (f) TCCA, EtOAc, -78 °C, 45 min, 68%; (g) KHMDS (1.2 equiv), THF, -78 °C, 1 h, 70%; (h) $LiAlH_4$ (1.0 equiv), THF, 0 °C, 15 min; (i) Dess-Martin periodinane (1.0 equiv), CH_2Cl_2, 25 °C, 83% over 2 steps; (j) CH_2O (20 equiv), KOH (10 equiv), MeOH/ H_2O, 45 °C, 1 h, 74%.

Our target-based efforts commenced with the preparation of the key diol intermediated **26** (Scheme 3-4). In total we developed two different routes to this compound. The first started with the synthesis of cyclopentenone **34** from commercially available cyclopentadione **33** via a 3-step sequence. Those transformation, a Michael addition,[8] chlorination and Zn-mediated reduction,[8] proceeded in 59% overall yield. Next, **34** was subjected to a another Michael addition effected by isopropenylmagnesium bromide to give ketone **35** as a pair of inseparable diastereomers in 78% yield. This addition could potentially be rendered enantioselective by utilizing a chiral copper complex as catalyst. Indeed, asymmetric Michael additions with similar substrates and nucleophile have been reported and applied in several total syntheses.[9] Pressing forward, treatment of **35** with ethylene glycol, trimethyl orthoformate and *p*-$TsOH•H_2O$ in toluene at 90 °C protected the ketone as the acetal group and epimerized the α-carbon to convert both diastereomers of **35** into **36** in

excellent yield. With the *trans* fusion of the hydrindane ring established, the next task was to identify the means to construct the six-membered ring and set up the key bicyclic system. Thus, an allylic chlorindation/intramolecular allylation approach was developed. By treating **36** with TCCA in EtOAc at -78 °C, allylic chlorination occurred smoothly to deliver **37** in 68% yield,[10] albeit containing few inseparable side products which could be removed in the following steps. Next, exposure of **37** to KHMDS in THF at -78 °C enabled its smooth cyclization to afford **38** in 70% yield.[11] Several other chlorination reagents (i.e. SO_2Cl_2, NaClO)[12] and strong bases (i.e. such as Li/NaHMDS, LDA) were also examined in this sequence but none delivered a higher yield of product. The stage was now set for the installation of the last single-carbon unit. Our initial endeavors were to perform a direct α-acylation. However, all attempts to deprotonate the α-carbon of the ester group were unsuccessful (confirmed by deuteration experiments). An alternative strategy empowered by the Cannizzaro reaction was thereby investigated. Here, following a 2-step redox manipulation to arrive at aldehyde **39**, subsequent treatment with formaldehyde and KOH in MeOH/H_2O afforded the diol motif[13] and completed the target intermediate in 61% yield over 3 steps. Overall, these operations achieved a 10-step synthesis of the key diol **26** in 12.9% yield, starting from commercially available material.

Scheme 3-5. Second Generation Synthesis of Key Diol 26[a]



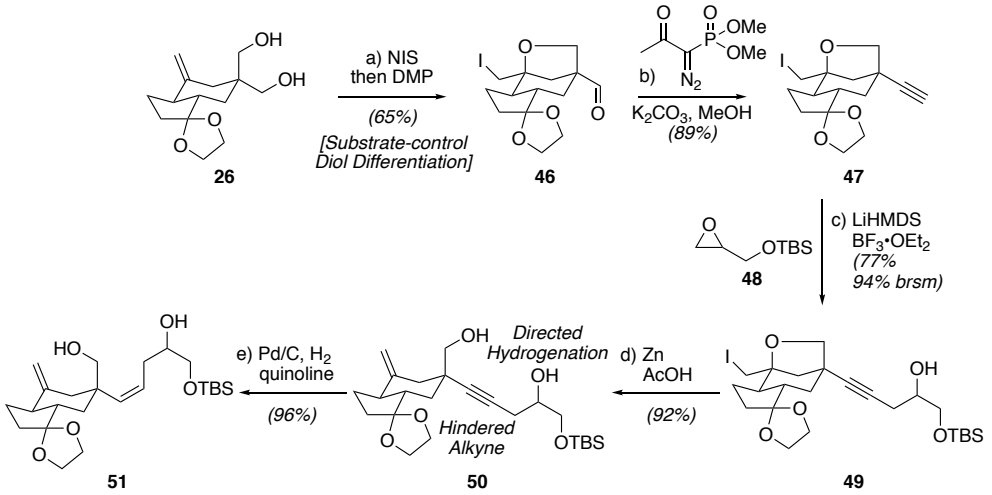
[a] Reagents and conditions: (a) isopropenylmagnesium bromide (1.6 equiv), $CuBr•Me_2S$ (0.20 equiv), TMSCl (3.0 equiv), HMPA (2.0 equiv), THF, -78 °C, 30 min, 83%; (b) KHMDS (1.4 equiv), TIPSOTf (1.2 equiv), THF, -78 to 25 °C, 2 h; (c) methylene dimethyl malonate (1.5 equiv), $SnCl_4$ (0.20 equiv), CH_2Cl_2, -78 to 25 °C 1.5 h, 38%, 42% brsm over 2 steps; (d) ethylene glycol (5.0 equiv), $CH(OMe)_3$ (5.0 equiv), *p*-TsOH•H_2O (0.10 equiv), toluene, 90 °C, 12 h, 86%; (e) TCCA, EtOAc, -78 °C, 45 min, 64%; (f) NaH (3.0 equiv), DMF, 0 to 25 °C, 3 h, 81%; (g) $LiAlH_4$ (2.0 equiv), THF, 0 °C, 15 min, 73%.

To shorten the synthetic sequence and improve efficiency, a second synthesis of **26** was developed (Scheme 3-5). This route started with the syntheses of sily enol ethers **42a** and **42b** from ketone **41**, which could be readily prepared in either a racemic or an enantioselective manner from commercial cyclopentenone **40** in one step.[10a, b] Then, exposure of the crude mixture of **42a** and **42b** to methylene dimethyl malonate in the presence of $SnCl_4$ effected a Mukaiyama-Michael addition to give diester **43** in 38% yield over 2 steps.[14] $BF_3•Et_2O$ and $TiCl_4$ were also tested as the Lewis acid catalyst in this transformation but neither gave better results. In the case of $BF_3•Et_2O$, low conversion was observed while $TiCl_4$ led to significant decomposition of the desired product. Next, similar to our first route, a 3-step sequence of ketone protection, allylic chlorination and intramolecular cyclization successfully converted **43** into **25** in 45% yield over 3 steps. In the end, a diester reduction effected by $LiAlH_4$ unveiled the diol motif and furnished **26**.[15] Overall, the second route completed **26** in just 7 steps with 11.3% yield, which was comparable to

that of the first route, yet greatly enhanced the throughput of material due to reduced number of steps.

3.3.3 Exploration of the Key Pinacol Coupling to Synthesize cis-Diol 31

Scheme 3-6. Synthesis of 1,6-Diol 51[a]

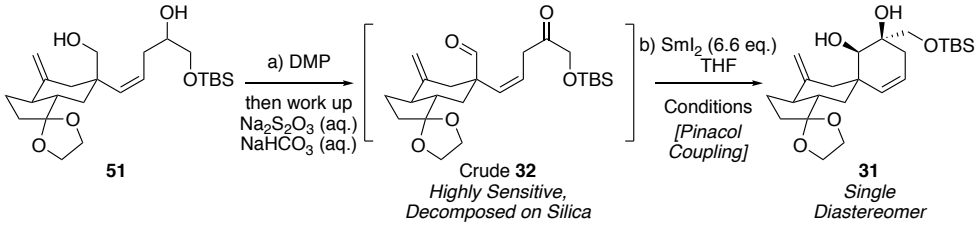


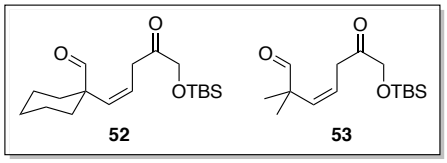
[a] Reagents and conditions: (a) NIS (1.1 equiv), CH_2Cl_2, 25 °C, 1 h; then Dess-Martin periodinane (1.2 equiv), CH_2Cl_2, 25 °C, 1 h, 65%; (b) Ohira-Bestmann reagent (1.5 equiv), K_2CO_2, MeOH, 25 °C, 2 h, 89%; (c) LiHMDS (1.3 equiv), BF_3•Et_2O (1.3 equiv), TBS glycidyl ether **48** (3.0 equiv), THF, -78 to 25 °C, 3 h, 77%, 94% brsm; (d) Zn (30 equiv), AcOH (10 equiv), MeOH/Et_2O, 40 °C, 1 h, 92%; (e) H_2 (balloon), Pd/C (0.05 equiv), quinoline (0.35 equiv), EtOAc, 25 °C, 7 h, 96%.

With the key intermediate **26** in hand, our next synthetic goals were to differentiate the two alcohols and convert the equatorial aicohol into a *cis*-1,2-disubstituted alkene side chain. Since the two alcohols are in similar steric environment, reagent-controled selective functionalization would be of particular challenge. Here, as shown in Scheme 3-6, we took advantage of the proximity between the axial alcohol and the olefin to implement a substrate-controled differentiation strategy.[16] Upon its exposure to NIS in CH_2Cl_2, **26** underwent a facial-specific iodoetherification to mask the axial alcohol. After an *in situ* oxidation mediated by Dess-Martin periodinane, aldehyde **46** was formed as an exclusive product in 65% yield. Critically, no cyclization of the equatorial alcohol was observed due to the structural restraints of the *trans*-hydrindane system. Next, a Seyferth-Gilbert homologation[17] followed by the nucleophilic addition of the resultant

alkyne **47** onto the protected glycidol **48** delivered **49** in 69% yield over 2 steps.[18] The desired product was obtained as an inconsequential mixture of two diastereomers in terms of the secondary alcohol-based stereogenic centers, as they would be eventually converge in the coming oxidation. The following synthetic objectives were to regenerate the primary alcohol and partially reduce the alkyne to its *cis*-alkene. Exposure of **49** to Zn powder in the presence of AcOH in MeOH/Et_2O smoothly effected the reductive ring opening to afford **50**.[19] Then subsequent partial hydrogenation mediated by Pd/C poisoned by quinoline established the desired *cis*-alkene and delivered 1,6-diol **51** in 88% yield over 2 steps. Of note, Lindlar catalyst was not able to promoted this reduction due to its low activity. In addition, the order of ring opening/alkyne hydrogenation was critical. Without the primary alcohol, the sterically hinder alkyne could not be effectively reduced without severe material degradation.[20] This result suggested that the hydroxyl group might participate in the hydrogenation as a directing group, delivering the catalyst directly to the alkyne.

Scheme 3-7. Optimization of the Key Pinacol Coupling and Synthesis of Diol 31[a]





Failed Model Substrates

Conditions:

Entry	Additive	T. (°C)	Yield (from XX)
1.	-	r.t.	~10%
2.	LiCl/LiBr	r.t.	~10%
3.	HMPA	r.t.	Decomp.
4.	MeOH/t-BuOH	r.t.	Decomp.
5.	-	-78	34%

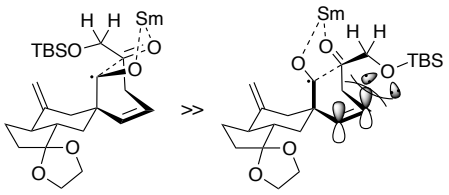
[a] Reagents and conditions: (a) DMP (3.5 equiv), CH_2Cl_2, 25 °C, 2 h; then workup with $Na_2S_2O_3$ (aq.), $NaHCO_3$ (aq.); (b) SmI_2 (6.6 equiv), THF, -78 °C, 1 h, 34% over 2 steps.

From here, the task now was to build up the 1,6-dicarbonyl functionality leading to the key pinacol coupling as shown in Scheme 3-7. With our will to execute a direct double oxidation of **51**, a variety of conditions were screened. However, significant decomposition of material was observed in most cases due to the presence of several labile functional groups within the desired product. Moreover, **32** was highly sensitive to silica gel resulting in purification through flash column chromatography leading to constant poor mass recovery, further impeding the material supply. Ultimately, we found that by using Dess-Martin periodinane in CH_2Cl_2 followed by a work up with aqueous saturated $NaHCO_3$ and $Na_2S_2O_3$ solution, the crude diketone **32** could be prepared with good yielding and purity. This material could be directly used in the next key pinacol coupling without additional purification. Of note, in our model studies, double oxidation of the corresponding diols to dicarbonyls **52** and **53** were attempted but both failed, as these compounds decomposed under every oxidation condition probed, including the one that ultimately enabled our successful synthesis of **32**. This result again highlighted the sensitive nature of this type of dicarbonyl substrate and that the *trans*-hydrindane skeleton, for some unknown reasons, was critical to the stability of **32**.

With diketone **32** in hand, our next goal was to execute the key pinacol coupling. As shown in Scheme 3-7, we were pleased to find that our initial treatment of crude **32** with SmI_2 in THF at room temperature gave the desired diol **31** as a single diastereomer in a messy mixture of unidentified side products.[21] Although the yield was only ~10%, this result was still encouraging as it demonstrated that not only such reductive cyclization was viable, but it also proceeded with excellent and favorable stereo control. Next, additives effects of lithium salts (LiCl, LiBr),[22] alcohol (MeOH, *t*-BuOH)[23] and HMPA[24] were investigated but no satisfactory results were obtained. In the cases of lithium there were no reactions profiles changed, while the other two

additives both led to complete material decomposition. Eventually, we found that the reaction temperature had a crucial impact on this cyclization event. Simply by lowering the reaction temperature to -78 °C, the yield was improved to 34% (over 2 steps).

Scheme 3-8. Proposed Tansition State Analysis to Accout for Observed Pinacol Coupling Results



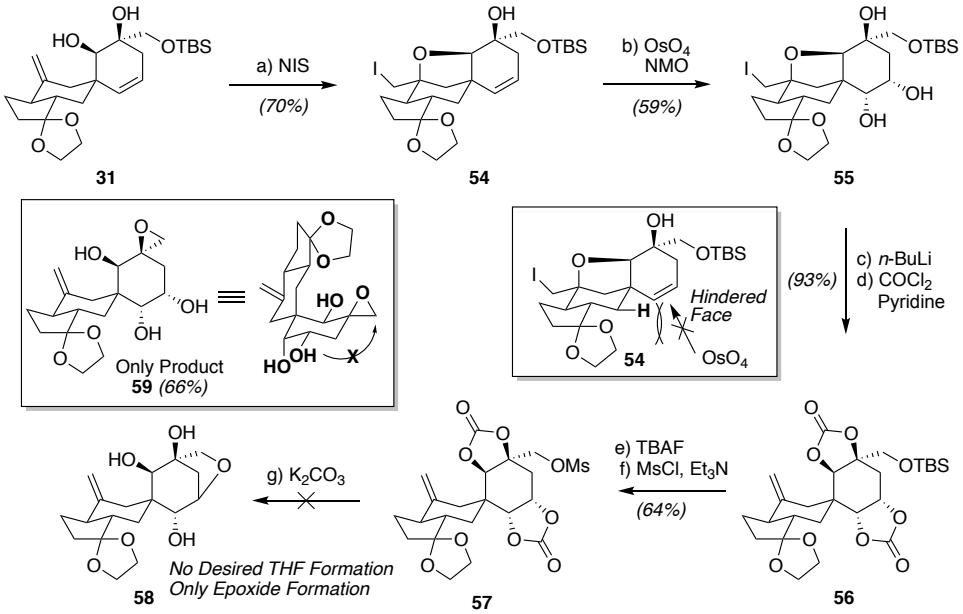
54
Favored

55
Unfavored

As noted earlier in the retrosynthetic analysis, we believed it is imperative for the successful coupling that the initiation of the SET process occurred at the aldehyde, for if it did so at the ketone, undesired side reactions would result. Decomposition caused by the addition of MeOH or *t*-BuOH[25] supported our hypothesis as alcoholic additives were widely used as promotors for SmI_2-induced α-deoxygenation. We presumed that the low temperature could promote a more selective binding of SmI_2 to the sterically hindered aldehyde and therefore improved the yield. To explained the observed stereochemical outcomes of the coupling, a transition state analysis was proposed. As shown in Scheme 3-8, we believed that transition state **54**, one that led to the desired product **31**, was more favored on energetic ground due to the indicated steric and electronic repulsion in **55**. At this stage, because the ring closure could be performed on the hundreds of milligrams scale and produced the key diol **31** in a reliable manner, no further optimization was attempted.

3.3.4 Initial Failures to Generate the oxa-Bridged Ring of Manginoid A (1)

Scheme 3-9. Synthetic Studies to Forge the Key Oxa-Bridged Ring via Dihydroxylation[a]

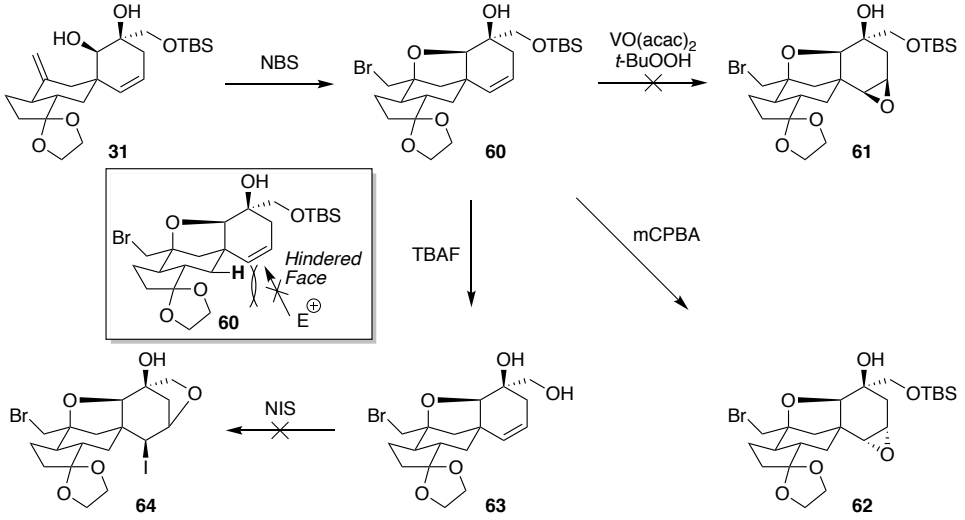


[a] Reagents and conditions: (a) NIS (1.5 equiv), CH_2Cl_2, 25 °C, 30 min, 70%; (b) OsO_4 (0.10 equiv), NMO (3.0 equiv), Acetone/H_2O, 25 °C, 6 h, 59%; (c) n-BuLi (6.0 equiv), THF, -78 °C, 15 min; (d) $COCl_2$ (3.0 equiv), pyridine (6.0 equiv), CH_2Cl_2, 25 °C, 2 h, 93% over 2 steps; (e) TBAF (1.1 equiv), THF, 25 °C, 10 min, 64%; (f) MsCl (1.2 equiv), Et_3N (3.0 equiv), 25 °C, 30 min, 89%; (g) K_2CO_3 (5.0 equiv), MeOH, 50 °C, 12 h, 66% **59**.

With both the *trans*-hydrindane and spirocycle in place, the stage was set to explore the means to forge the oxa-bridged ring as well as the 1,3-diketone motif. The projected approach was to first install the requisite oxygen atoms on the 1,2-disubstituted alkene via an epoxidation or dihydroxylation, then make use of the TBS-protected hydroxyl group in the following ring closure event. Through this sequence, once the oxa-bridged was installed, two secondary alcohols would also be in place for the double oxidation that could potentially yield the 1,3-diketone. A key premise for the success of this strategy was the protection of the more reactive external olefin, as it would also undergo any reactions we tried to perform on the desired alkene. Here, we deployed the haloetherification strategy again to regenerate the THF ring and mask the problematic olefin.[26] As shown in Scheme 3-9, upon treatment of **31** with NIS in CH_2Cl_2, **54** was formed in 70% yield. Of note, NBS could also promote the same cyclization and give the corresponding brominated

product in a similar yield. With the external olefin masked, the dihydroxylation approach was then investigated. Exposure of **54** to OsO_4 and NMO smoothly installed the diol with desired facial selectivity to afford **55** in 59% yield. Critically, this result indicated that the back face of the alkene was more accessible as the front was probably blocked by the equatorial hydrogen as shown in the boxed structure of **54** in Scheme 3-9. After the ring opening mediated by *n*-BuLi[27] and protection of the resultant tetraol to arrive at carbonate **56**, subsequent desilylation/mesylation gave **57** in 53% yield over 4 steps. Of note, the previously used condition with Zn/AcOH could not initiate the ring opening of the **54**. Our next plan was to execute a global deprotection of both carbonate groups with the hope that an intramolecular cyclization would simultaneously occur to forge the oxa-bridged ring. Unfortunately, after stirring with K_2CO_3 in MeOH, only epoxide **59** was isolated and no desired product was observed even under elevated temperature. This result suggested that the epoxide formation was a more rapid process than the desired cyclization. Additionally, due to the rigidity of the skeleton as shown in Scheme **3-**9, nucleophilic attack of the alcohol onto the epoxide could not be achieved.

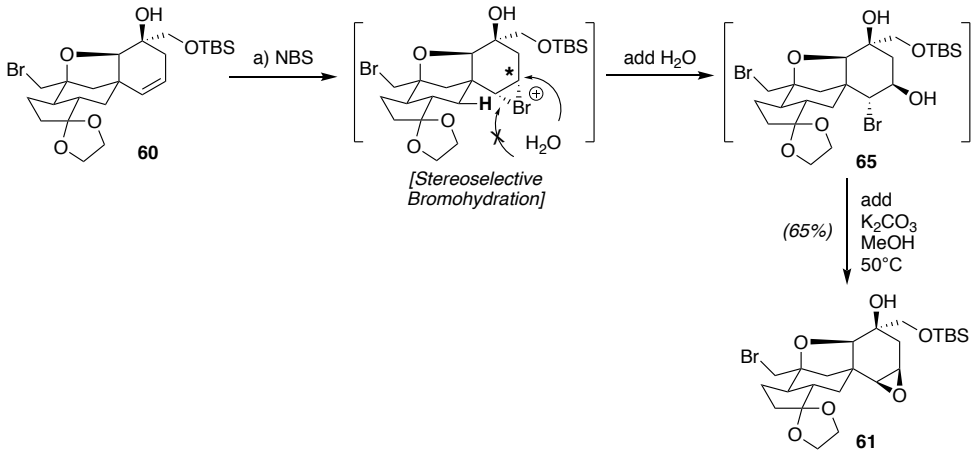
Scheme 3-10. Synthetic Studies to Forge the Key Oxa-Bridged Ring via Epoxidation or Haloetherification



We then turned our attention to the epoxidation approach. In this case, the epoxide needed to occur from the front face. If not, then the subsequent ring closure by the alcohol would be forbidden. However, as the back face was more accessible, common epoxidation condition would presumably only yield the undesired product. Indeed, treatment of bromoether **60** with mCPBA gave epoxide **62** as a single diastereomer (Scheme 3-10). Of note, iodoether **54** decomposed in the presence of mCPBA due to the the labile iodine atom. Thus, metal-catalyzed epoxidation was probed with our hope to utilize the tertiary alcohol as a directing group to override the intrinsic facial selectivity. However, none of these conditions, shown here with $VO(acac)_2$/*t*-BuOOH, were able to promote the desired epoxidation. Intramolecular NIS-induced iodoetherification of **63** was also tested but no desired product was obtained. Failure of these reactions again highlighted the difficulty of activating the alkene from the front face.

3.3.5 Elaboration of cis-Diol 31 to Manginoid A (1)

Scheme 3-11. Synthesis of Epoxide 61 via Stereoselective Bromohydration[a]

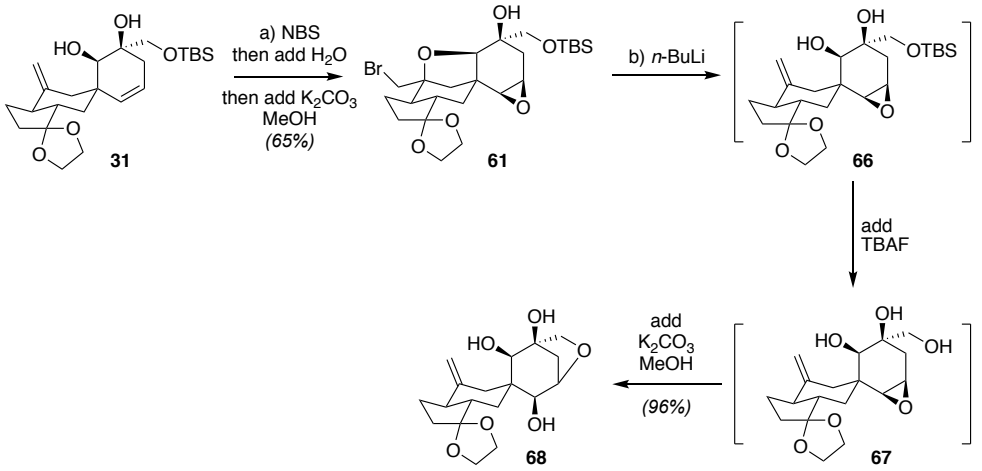


[a] Reagents and conditions: (a) NBS (2.1 equiv), THF, 25 °C, 15 min; then add H_2O, THF, 25 °C, 4 h; then add MeOH, K_2CO_3 (5.0 equiv), 50 °C, 4 h, 65%.

After all of these setbacks, we again carefully scrutinized the molecular model of **60**. We found that though the indicated hydrogen heavily shielded the front face, one sp^2 carbon (marked with the star, Scheme 3-11) in fact was not sterically hindered. Small nucleophile such as water

might be able to attack this carbon selectively from the front of the alkene if it was activated by a bromenium coming from behind. If such stereo- and regioselective bromohydration could be achieved, a following intramolecular ring closure could deliver the epoxide with the desired geometry. Pleasingly, this design could be reduced to practice, as shown in Scheme 3-11. Upon treatment with NBS and water in THF, bromohydrin **65** was formed as a single diastereomer. Subsequent ring closure was smoothly carried out by stirring with K_2CO_3 in MeOH which eventually yielded epoxide **61**.[28] Moreover, this sequence of bromoetherification, bromohydration, and epoxidation could be conveniently conducted in one pot to give **61** in 65% overall yield.

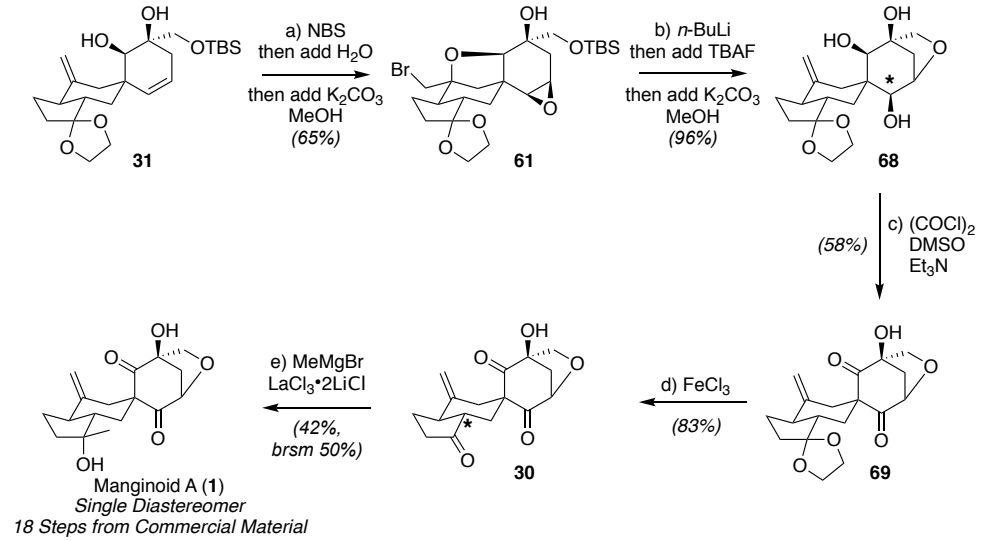
Scheme 3-12. Synthesis of Triol 68[a]



[a] Reagents and conditions: (a) NBS (2.1 equiv), THF, 25 °C, 15 min; then add H_2O, THF, 25 °C, 4 h; then add MeOH, K_2CO_3 (5.0 equiv), 50 °C, 4 h, 65%; (b) *n*-BuLi (4.0 equiv), THF, -78 °C, 10 min; then add MeOH (8.0 equiv), TBAF (5.0 equiv), THF, 25 °C, 2 h; then add MeOH, K_2CO_3 (10 equiv), 50 °C, 4 h, 96%.

From here, construction of the oxa-bridged ring was straightforward. As shown in Scheme 3-12, after ring opening and sily ether cleavage to arrive at **67**, K_2CO_3 effected its cyclization to afford **68** in 96% overall yield. Critically, all three of these operations could also be done in one pot.

Scheme 3-13. Total Synthesis of Manginoid A (1)[a]



[a]Reagents and conditions: (a) NBS (2.1 equiv), THF, 25 °C, 15 min; then add H_2O, THF, 25 °C, 4 h; then add MeOH, K_2CO_3 (5.0 equiv), 50 °C, 4 h, 65%; (b) *n*-BuLi (4.0 equiv), THF, -78 °C, 10 min; then add MeOH (8.0 equiv), TBAF (5.0 equiv), THF, 25 °C, 2 h; then add MeOH, K_2CO_3 (10 equiv), 50 °C, 4 h, 96%; (c) DMSO (20 equiv), $(COCl)_2$ (10 equiv), Et_3N (30 equiv), CH_2Cl_2, -78 to 25°C, 4 h, 58%; (d) $FeCl_3$ (0.20 equiv), acetone, 25 °C, 12 h, 83%; (e) MeMgBr (2.1 equiv), $LaCl_3$•2LiCl (2.1 equiv), THF, -78 to 25°C, 2 h, 42%, brsm 50%.

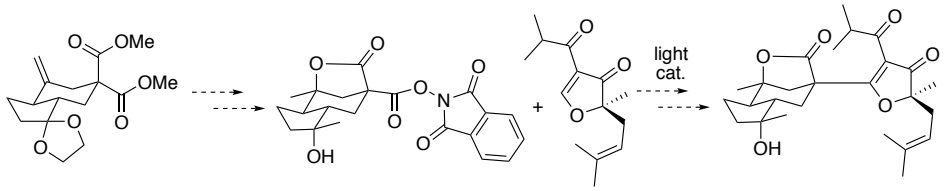
With the tetracyclic system and requisite atoms in place, the stage was now set to commence the final set of functional group manipulations leading to manginoid A (**1**). As shown in Scheme 3-13, those operations started with a Swern oxidation which converted both secondary alcohols into ketones to give **69** in 58% yield, along with an unknown major side product. Of note, Dess-Martin periodinane was also tested in this event. In that case, oxidation of the first alcohol (marked here with a star in **68**) could be rapidly accomplished while that of the second turned out to be extremely sluggish due to the steric encumbrance of that position. Next, exposure of **69** to the mild condition of $FeCl_3$ in acetone unveiled the ketone and deliver triketone **30** in 83% yield without racemization of the indicated α-carbon, an event that could be observed upon heating with $TsOH•H_2O$. In the end, the Grignard addition rose to the occasion to install the final methyl group and complete manginoid A (**1**). Excitingly, following some modest condition optimization, we observed that the combination of MeMgBr (2.1 equiv) and $LaCl_3$•2LiCl (2.1 equiv)[29] in THF at -78°C provided manginoid A (**1**) as a single diastereomer (in terms of the methyl addition) in 42%

yield (50% brsm), along with 16% recovered **30** and a messy mixture of further addition products. This result confirmed our original hypothesis that the cyclopentanone was more reactive than the 1,3-dione due to the steric demanding of the latter. However, such steric effect was not strong enough to completely preclude any methyl additions, as over addition products were always observed before the full consumption of **30**. Pleasingly, all spectral and data of our final product perfectly matched that of the natural sample as reported by Zhu, Zhang and coworkers.

3.4 Conclusion and Outlook

In conclusion, we have accomplished the first total synthesis of manginoid A (**1**) in 19 steps utilizing a series of highly chemo- and stereo-selective transformations. Significantly, as we established an efficient synthesis of the diester **25**, a plausible common intermediate, this work lays the foundation for a family-oriented approach towards a range of natural products containing the *trans*-hydrindane system. We also anticipate our final Grignard addition could be a general solution to fashion the common tertiary alcohol motif presented in these compounds.

Scheme 3-14. Proposed Synthesis of Furanmonogone B (13)



25
Key Common Intermediate

70

71

13: Furanmonogone B

Indeed, efforts to elaborate diester **25** into furanmonogone B (**13**) are currently underway. In this case, we envision the employment of a radical-based coupling to merge the functionalized fragments **70** and **71** to forge the full carbon framework of the target molecule. In collaboration with Dr. Samantha Maki, a postdoctoral researcher in the Snyder lab, we are currently conducting synthetic studies toward the two fragments as well as model studies of the key coupling reaction.

3.5 Experimental Section

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, dimethylformamide (DMF), diethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous materials, unless otherwise stated. Steps refer to operations conducted in a single reaction flask; filtration, extraction, or other form of purification denotes the end of an individual step. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent, and an ethanolic solution of phosphomolybdic acid and cerium sulfate, *p*-anisaldehyde, and heat as developing agents. SiliCycle silica gel (60, academic grade, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker 500 MHz instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, app = apparent. IR spectra were recorded on a Perkin-Elmer 1000 series FT-IR spectrometer. Highresolution mass spectra (HRMS) were recorded on Agilent 6244 Tof-MS using ESI (Electrospray Ionization) or APCI (Atmospheric Pressure Chemical Ionization) at the University of Chicago Mass Spectroscopy Core Facility.

Enone 34. To a solution of 1,3-cyclopentanedion (8.00 g, 81.6 mmol, 1.0 equiv) in DMF (100 mL) at 0 °C was slowly added NaH (60% dispersion in mineral oil, 3.92 g, 97.9 mmol, 1.2 equiv) and then the reaction mixture was stirred at 0 °C for 10 min. Next, methyl acrylate (24.4 mL, 28.1 g, 226.4 mmol, 2.8 equiv) was added and the solution was then stirred for 12 h at 80 °C. Upon completion, the reaction contents were cooled to 0 °C, quenched by careful addition of 3 M aqueous HCl (50 mL), diluted with CH_2Cl_2 and transferred into a separatory funnel. The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (5 × 100 mL). The combined organic extracts were then dried (Na_2SO_4), filtered, and concentrated at 60 °C under reduced pressure (to remove DMF) to provide the crude desired adduct. Pressing forward without further purification, this crude adduct (assumed 81.6 mmol) was dissolved in CH_2Cl_2 (300 mL) and oxalyl chloride (10.5 mL, 15.5 g, 122.4 mmol, 1.5 equiv) was slowly added at 0 °C. After stirring at 25 °C for 15 min, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to give chlorinated product (12.62 g, 77% yield over 2 steps) as a yellow liquid. Next, to a solution of this chlorinated material (14.03 g, 69.3 mmol, 1.0 equiv) in MeOH (200 mL) at 25 °C was added Zn powder (27.02 g, 415.7 mmol, 6.0 equiv) and NH_4Cl (11.12 g, 207.9 mmol, 3.0 equiv). The reaction mixture was then vigorously stirred at 60 °C for 30 min. Upon completion, the reaction mixture was filtered through Celite, rinsing with EtOAc (200 ml), and the filtrated was concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, CH_2Cl_2:Et_2O, 20:1→15:1→10:1) to give enone **34** (8.85 g, 76% yield) as a yellow liquid. **34**: R_f = 0.20 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 2953, 2924, 1738, 1700, 1438, 1370, 1298, 1249, 1200, 1164, 1065, 1003, 922, 870, 791 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (td, *J* = 2.7, 1.3 Hz, 1. H), 3.66 (s, 3. H), 2.60–2.54 (m, 2 H), 2.52 (d, *J* = 3.0 Hz, 4 H), 2.41–

2.36 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.4, 173.2, 158.3, 144.5, 51.6, 34.5, 31.9, 26.5, 20.4; HRMS (ESI+APCI) calcd for $C_9H_{13}O_3$ [M+H]+ 169.0856, found 169.0859.

1,3-Dioxolane 36. To a solution of **34** (4.90 g, 29.1 mmol, 1.0 equiv) in THF (100 ml) at 25 °C was added CuBr•Me_2S (1.19 g, 5.82 mmol, 0.20 equiv) and HMPA (10.1 mL, 10.43 g, 58.2 mmol, 2.0 equiv). The reaction mixture was then cooled to -78 °C and TMSCl (11.1 mL, 9.48 g, 87.3 mmol, 3.0 equiv), isopropenylmagnesium bromide (93.0 mL, 0.5 M in THF, 46.6 mmol, 1.6 equiv) were added sequentially. After stirring at -78 °C for 30 min, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (100 mL), transferred to a separatory funnel, and diluted with EtOAc (150 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (2 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 15:1→10:1→6:1) to give the desired adduct **35** (5.75 g, 78% yield) as a yellow liquid and as a mixture of two inseparable epimers. Pressing forward, to a solution of the so-obtained **35** (5.75 g, 27.3 mmol, 1.0 equiv) in toluene (100 mL) at 25 °C was added ethylene glycol (7.6 mL, 8.47 g, 136.5 mmol, 5.0 equiv), triethyl orthoformate (22.7 mL, 20.2 g, 136.5 mmol, 5.0 equiv) and *p*-TsOH•H_2O (0.519 g, 2.73 mmol, 0.10 equiv). After stirring at 90 °C for 12 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 15:1→10:1) to give 1,3-dioxolane **36** (6.47 g, 97% yield) as a yellow liquid. **36**: R_f = 0.20 (silica gel, hexanes:EtOAc, 10:1); IR (film) ν_{max} 3073, 2951, 2882, 1739, 1644, 1437, 1377, 1304, 1173, 1037, 995, 947, 890, 806 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.78 (d, *J* = 2.2 Hz, 1 H), 4.74 (p, *J* = 1.5 Hz, 1 H), 3.98–3.90 (m, 3 H), 3.89–3.83 (m, 1 H), 3.64 (s, 3 H), 2.38 (ddd, *J* = 9.0, 7.0, 1.8 Hz, 2 H), 2.35–2.25 (m, 1 H), 1.95 (ddd, *J* = 11.1, 8.0, 5.4 Hz, 1 H), 1.84–1.71 (m, 4 H), 1.69 (t, *J* = 1.1 Hz, 3 H), 1.67–1.59 (m,

1 H), 1.57–1.47 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 146.6, 117.7, 111.3, 64.3, 64.0, 51.4, 51.3, 47.3, 35.6, 32.1, 27.3, 23.0, 18.6; HRMS (ESI) calcd for $C_{14}H_{23}O_4$ [M+H]+ 255.1591, found 255.1594.

Ester 38. To a solution of **36** (3.63 g, 14.3 mmol, 1.0 equiv) in EtOAc (100 mL) at -78 °C was added trichloroisocyanuric acid (3.48 g, 15.0 mmol, 1.05 equiv). After stirring at -78 °C for 45 min, the reaction contents were quenched by the addition of saturated aqueous $Na_2S_2O_3$ (100 mL), warmed to 25 °C and then transferred to a separatory funnel. The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to give chlorinated product **37** (2.79 g, 68% yield) as a colorless liquid containing inseparable impuritys (~5-10%). Pressing forward, to a solution of the so-obtained **37** (2.79 g, 9.68 mmol, 1.0 equiv) in THF (100 mL) at -78 °C was added KHMDS (11.6 mL, 1.0 M in THF, 11.6 mmol, 1.2 equiv) 0.519 g, 2.73 mmol, 0.10 equiv). After stirring at -78 °C for 1 h, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (50 mL), transferred to a separatory funnel, diluted with EtOAc (50 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to give ester **38** (1.71 g, 70%) as a colorless liquid containing a small amount of inseparable impurities (~5-10%) that are ultimately removed in the following steps. **38**: R_f = 0.40 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 3077, 2951, 2876, 1736, 1654, 1435, 1283, 1195, 1161, 1032, 946, 893 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.76 (q, *J* = 1.8 Hz, 1H), 4.63 (q, *J* = 1.8 Hz, 1 H), 4.01–3.84 (m, 4 H), 3.68 (s, 3 H), 2.55 (ddd, *J* = 13.4, 4.1, 1.6 Hz, 1 H), 2.40 (tt, *J* = 12.4, 3.8 Hz,

1 H), 2.21–2.13 (m, 1 H), 2.12–2.01 (m, 2 H), 1.98 (ddd, *J* = 13.5, 10.9, 2.5 Hz, 1 H), 1.89 (dd, *J* = 14.0, 8.7 Hz, 1 H), 1.81 (dddd, *J* = 11.7, 8.6, 5.8, 2.4 Hz, 1 H), 1.68–1.55 (m, 2 H), 1.44 (td, *J* = 12.6, 3.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 148.5, 116.6, 105.6, 65.1, 64.8, 53.2, 51.7, 46.5, 44.3, 37.7, 36.3, 27.5, 23.9; HRMS (ESI) calcd for $C_{14}H_{21}O_4$ [M+H]+ 253.1434, found 253.1441.

Diol 26. To a solution of **38** (1.40 g, 5.55 mmol, 1.0 equiv) in THF (50.0 mL) at 0 °C was slowly added $LiAlH_4$ (5.60 mL, 1.0 M in THF, 5.60 mmol, 1.0 equiv). After stirring at 0 °C for 15 min, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle salt (50 mL) at 0 °C, transferred to a separatory funnel, diluted with EtOAc (50 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give the crude alcohol **S4**. Pressing forward without further purification, the so-obtained crude **S4** (assumed 5.55 mmol) was dissolved in CH_2Cl_2 (50 mL) and then Dess-Martin periodinane (2.35 g, 5.55 mmol, 1.0 equiv) was added at 25 °C. After stirring at 25 °C for 30 min, the reaction contents were concentrated directly and the resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to give aldehyde **39** (1.03 g, 83% over 2 steps) as a colorless liquid containing a small amount of inseparable impurities (~5-10%) that are ultimately removed in the next step. Next, to the solution of **39** (1.03 g, 4.64 mmol, 1.0 equiv) in MeOH (50.0 mL) at 25 °C was added aqueous formaldehyde solution (9.20 mL, 37 wt.% in water, 3.71 g, 116.0 mmol, 20 equiv) and KOH (2.60 g, 46.4 mmol, 10 equiv). After stirring at 45 °C for 1 h, the reaction contents were quenched by the addition of brine (50 mL), transferred to a separatory funnel, diluted with CH_2Cl_2 (100 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The

resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 1:1→0:1, followed by CH_2Cl_2:MeOH, 20:1) to give diol **26** (0.876 g, 74%) as a white solid. **26**: R_f = 0.15 (silica gel, pure EtOAc); IR (film) ν_{max} 3113, 2979, 2888, 2852, 1650, 1451, 1302, 1281, 1190, 1120, 1029, 949, 821, 541 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.72 (s, 1 H), 4.66 (q, *J* = 1.8 Hz, 1 H), 4.00–3.91 (m, 2 H), 3.91–3.81 (m, 2 H), 3.67–3.49 (m, 4 H), 2.25–2.16 (m, 2 H), 2.06 (td, *J* = 12.2, 5.7 Hz, 1 H), 1.99 (ddd, *J* = 13.7, 10.9, 2.5 Hz, 1 H), 1.91 (dt, *J* = 14.1, 8.8 Hz, 1 H), 1.85–1.77 (m, 2 H), 1.64 (td, *J* = 11.5, 8.7 Hz, 1 H), 1.55 (td, *J* = 12.9, 3.6 Hz, 1 H), 1.34–1.20 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.3, 116.9, 106.3, 73.0, 66.2, 65.0, 64.8, 49.1, 47.5, 41.8, 39.5, 36.4, 27.3, 23.7; HRMS (ESI) calcd for $C_{14}H_{22}O_4Na$ [M+Na]+ 277.1410, found 277.1414.

Dioxolane 44. To a solution of cyclopentenone **40** (3.06 mL, 3.00 g, 36.6 mmol, 1.0 equiv) in THF (100 ml) at 25 °C was added CuBr•Me_2S (0.752 g, 3.66 mmol, 0.10 equiv) and HMPA (12.7 mL, 13.12 g, 73.2 mmol, 2.0 equiv). The reaction mixture was then cooled to -78 °C and TMSCl (13.9 mL, 11.92 g, 109.8 mmol, 3.0 equiv), isopropenylmagnesium bromide (109.8 mL, 0.5 M in THF, 54.9 mmol, 1.5 equiv) were added sequentially. After stirring at -78 °C for 30 min, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (100 mL), transferred to a separatory funnel, and diluted with EtOAc (150 mL). The two layers were separated and the aqueous layer was extracted with EtOAc (2 × 150 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 15:1→10:1→6:1) to give ketone **41** (3.77 g, 83% yield) as a yellow liquidTo a solution of **41** (2.70 g, 21.7 mmol, 1.0 equiv) in THF (100 mL) at -78 °C was added KHMDS (30.4 mL, 1 M in THF, 30.4 mmol, 1.4 equiv). After stirring at -78 °C for 1 h, TIPSOTf (7.00 mL, 8.00 g, 26.1 mmol, 1.2 equiv) was add and the

reaction was stirred at -78 °C for another 1 h. The reaction contents were then warmed to 25 °C over the course of 1 h, quenched by the addition of saturated aqueous $NaHCO_3$ (50 mL) transferred to a separatory funnel, and diluted with CH_2Cl_2 (100 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give the crude silyl enol ether **42a** and **42b** as a mixture of two regioisomer (2.8 : 1.0). Pressing forward without further purification, the crude mixture of **42a** and **42b** (assumed 21.7 mmol) was dissolved in CH_2Cl_2 (100 mL) and methylene dimethyl malonate (4.69 g, 32.6 mmol, 1.5 equiv) was added at 25 °C. Then the reaction mixture was cooled to -78 °C and $SnCl_4$ (4.30 mL, 1 M in CH_2Cl_2, 4.30 mmol, 0.20 equiv) was added slowly. After stirring at -78 °C for 30 min, the reaction contents were warmed to 25 °C over the course of 1 h, then quenched by the addition of saturated aqueous $NaHCO_3$ (100 mL), transferred to a separatory funnel, diluted with CH_2Cl_2 (50 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 1:0→10:1→5:1) to give recovered ketone **41** (0.263 g) and **diester 43** (2.21 g, 38% yield, 42% brsm over 2 steps) as a colorless liquid and as a mixture of two diastereomers, containing inseparable impurities. Next, to a solution of **43** (2.21 g, 8.24 mmol, 1.0 equiv) in toluene (50 mL) at 25 °C was added ethylene glycol (2.30 mL, 2.56 g, 41.2 mmol, 5.0 equiv), trimethyl orthroformate (6.87 mL, 6.12 g, 41.2 mmol, 5.0 equiv) and *p*-TsOH•H_2O (0.157 g, 0.824 mmol, 0.10 equiv). After stirring at 90 °C for 12 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1→3:1) to give dioxolane **44** (2.22 g, 86% yield) as a colorless liquid containing inseparable impurities (~5%) that are ultimately removed in the following steps. **44**: R_f

= 0.30 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 2954, 2888, 2853, 1753, 1735, 1644, 1436, 1377, 1239, 1151, 1098, 1031, 947, 892, 845 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.80 (dt, *J* = 1.8, 0.8 Hz, 1 H), 4.77 (dq, *J* = 2.9, 1.5 Hz, 1 H), 4.00–3.92 (m, 3 H), 3.88–3.83 (m, 1 H), 3.73 (d, *J* = 5.0 Hz, 3 H), 3.71 (s, 3 H), 3.67 (dd, *J* = 9.0, 5.8 Hz, 1 H), 2.33 (td, *J* = 10.3, 6.4 Hz, 1 H), 2.09–1.87 (m, 3 H), 1.86–1.65 (m, 3 H), 1.69 (t, *J* = 1.1 Hz, 3 H), 1.56–1.46 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 169.9, 146.0, 117.4, 111.7, 64.2, 64.0, 52.4, 52.3, 51.4, 49.3, 45.3, 35.4, 27.1, 26.9, 18.4; HRMS (ESI+APCI) calcd for $C_{16}H_{24}O_6Na$ [M+Na]+ 335.1465, found 335.1467.

Diester 25. To a solution of **44** (2.22 g, 7.11 mmol, 1.0 equiv) in EtOAc (70.0 mL) at -78 °C was added trichloroisocyanuric acid (1.82 g, 7.82 mmol, 1.1 equiv). After stirring at -78 °C for 45 min, the reaction contents were quenched by the addition of saturated aqueous $Na_2S_2O_3$ (100 mL), warmed to 25 °C and then transferred to a separatory funnel. The two layers were separated and the aqueous layer was extracted with EtOAc (3 × 70 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to give chlorinated product **45** (1.58 g, 64% yield) as a colorless liquid containg inseparable impurities (~5-10%). Pressing forward, to a solution of the so-obtained **45** (1.58 g, 4.56 mmol, 1.0 equiv) in DMF (90.0 mL) at 0 °C was added NaH (60% dispersion in mineral oil, 0.547 g, 13.7 mmol, 3.0 equiv). After stirring at 25 °C for 3 h, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (50 mL), transferred to a separatory funnel, diluted with CH_2Cl_2 (50 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated at 60°C (to remove the DMF). The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc,

10:1→5:1→3:1) to give diester **25** (1.14 g, 81%) as a colorless liquid containing a small amount of inseparable impurities (~5-10%) that are ultimately removed in the following steps. **25**: R_f = 0.40 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 3080, 2954, 2881, 1735, 1656, 1435, 1306, 1244, 1167, 1118, 1035, 981, 948, 892, 818, 638 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.82 (q, *J* = 1.8 Hz, 1 H), 4.67 (d, *J* = 1.7 Hz, 1 H), 3.99–3.91 (m, 2 H), 3.90–3.84 (m, 2 H), 3.71 (s, 3 H), 3.70 (s, 3 H), 2.98 (dd, *J* = 13.8, 2.1 Hz, 1 H), 2.43 (dtd, *J* = 12.3, 3.2, 1.8 Hz, 2 H), 2.15–2.02 (m, 1 H), 1.98–1.68 (m, 4 H), 1.65–1.51 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 170.9, 146.0, 116.6, 107.4, 65.1, 64.7, 57.1, 52.8, 52.5, 50.4, 46.3, 40.3, 36.2, 30.1, 23.6; HRMS (ESI) calcd for $C_{16}H_{22}O_6Na$ [M+Na]+ 333.1309, found 333.1318.

Diol 26. To a solution of **25** (1.14 g, 3.67 mmol, 1.0 equiv) in THF (50.0 mL) at 0 °C was slowly added $LiAlH_4$ (7.30 mL, 1.0 M in THF, 7.30 mmol, 2.0 equiv). After stirring at 0 °C for 15 min, the reaction contents were quenched by the slow addition of saturated aqueous Rochelle salt (50 mL) at 0 °C, transferred to a separatory funnel, diluted with CH_2Cl_2 (100 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 1:1 followed by CH_2Cl_2:MeOH, 20:1) to give diol **26** (0.684 g, 73%) as a white solid. **26**: R_f = 0.15 (silica gel, pure EtOAc); all spectroscopic data were in full agreement with the sample reported above.

Aldehyde 46. To a solution of diol **26** (0.684 g, 2.69 mmol, 1.0 equiv) in CH_2Cl_2 (55.0 mL) at 25 °C was added NIS (0.666 g, 2.96 mmol, 1.1 equiv). After stirring at 25 °C for 1 h, Dess-Martin periodinane (1.37 g, 3.23 mmol, 1.2 equiv) was then added and the reaction mixture was stirred for another 1 h. Upon completion, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc,

10:1→5:1→3:1) to give aldehyde **46** (0.659 g, 65% yield) as a brown liquid. **46**: R_f = 0.30 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 2937, 2872, 2720, 1723, 1457, 1307, 1281, 1174, 1122, 1037, 1002, 909, 824, 712, 626 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.60 (s, 1 H), 4.15 (dd, *J* = 8.5, 2.0 Hz, 1 H), 4.01–3.84 (m, 5 H), 3.37 (d, *J* = 10.5 Hz, 1 H), 3.28 (d, *J* = 10.5 Hz, 1 H), 2.30 (dd, *J* = 11.2, 2.1 Hz, 1 H), 2.06–2.00 (m, 1 H), 1.98–1.83 (m, 4 H), 1.71 (d, *J* = 11.2 Hz, 1 H), 1.69–1.58 (m, 2 H), 1.42 (qd, *J* = 11.3, 8.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.5, 115.2, 83.9, 73.7, 65.3, 65.0, 57.6, 49.1, 47.1, 45.5, 36.1, 26.8, 20.9, 9.5; HRMS (ESI+APCI): no molecular ion peak was observed.

Alkyne 47. To a solution of **46** (0.930 g, 2.46 mmol, 1.0 equiv) in MeOH (25.0 ml) at 25 °C was added Ohira-Bestmann reagent (0.709 g, 3.69 mmol, 1.5 equiv, prepared according to the literature procedure reported by Pietruszka and co-worker[17] with all the spectroscopic data matching that reported in Ref. 17) and K_2CO_3 (0.849 g, 6.15 mmol, 2.5 equiv). After stirring at 25 °C for 2 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to give alkyne **47** (0.820 g, 89% yield) as a white solide. **47**: R_f = 0.50 (silica gel, hexanes:EtOAc, 5:1); IR (film) ν_{max} 3289, 2938, 2876, 2113, 1457, 1312, 1278, 1071, 1035, 968, 904, 824 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.06–3.78 (m, 6 H), 3.30 (d, *J* = 10.4 Hz, 1 H), 3.22 (d, *J* = 10.4 Hz, 1 H), 2.28–2.17 (m, 2 H), 2.00 (ddd, *J* = 14.3, 10.9, 2.2 Hz, 1 H), 1.95–1.80 (m, 5 H), 1.80–1.69 (m, 1 H), 1.67–1.58 (m, 1 H), 1.43–1.31 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.4, 85.1, 83.1, 78.5, 70.2, 65.3, 65.0, 49.8, 48.5, 47.4, 39.6, 36.1, 34.1, 20.9, 9.8; HRMS (ESI) calcd for $C_{30}H_{38}I_2O_6Na$ [2M+Na]+ 771.0650, found 771.0642.

1,6-Diol 51. To a solution of **46** (0.820 g, 2.19 mmol, 1.0 equiv) in THF (30.0 mL) at -78 °C was added LiHMDS (2.85 mL, 1 M in THF, 2.85 mmol, 1.3 equiv). After stirring at -78 °C.

for 30 min, BF_3•Et_2O (0.352 mL, 0.404 g, 2.85 mmol, 1.3 equiv) was added and the reaction mixture was stirred -78 °C for another 30 min. Then a solution of TBS glycidyl ether **48** (1.24 g, 6.57 mmol, 3.0 equiv) in THF (10.0 mL) was added at -78 °C and the reaction mixture was warmed to 25 °C over the course of 1 h. After stirring at 25 °C for another 1 h, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (40 mL) transferred to a separatory funnel, and diluted with CH_2Cl_2 (100 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1→3:1) to give recovered **46** (0.215 g, ~70% purity) and alcohol **49** (0.925 g, 77% yield, 94% brsm). Next, to a solution of the so-obtained **49** (0.925 g, 1.69 mmol, 1.0 equiv) in MeOH/Et_2O (v/v 1:1, 20 mL) at 25 °C was added Zn powder (3.32 g, 50.7 mmol, 30 equiv) and AcOH (0.971 mL, 1.02 g, 16.9 mmol, 10 equiv). After stirring at 40 °C for 1 h, the reaction mixture was filtered through Celite, rinsing with EtOAc (150 mL). The filtrated was then transferred to a separatory funnel, neutralized by the addition of saturated aqueous $NaHCO_3$ (50 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to give alkyne **50** (0.685 g, 92% yield). Pressing forward, to a solution of the so-obtained **50** (0.685 g, 1.57 mmol, 1.0 equiv) in EtOAc (30.0 mL) was added quinoline (65.1 μL, 71.0 mg, 0.550 mmol, 0.35 equiv) and Pd/C (83.6 mg, w/w 10%, 0.079 mmol, 0.05 equiv). The suspension was then purged by direct bubbling with a balloon of H_2 gas for 1 h at 25 °C and then placed under a H_2 atmosphere and stirred for 6 h at 25 °C. Upon completion, the reaction contents were filtered through a short pad of Celite and washed with EtOAc (60 mL). The filtrated was then transferred

to a separatory funnel, neutralized by the addition of 1 M aqueous HCl (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to give **1,6-diol 51** (0.658 g, 96% yield).

1,2-Diol 31. To a solution of **51** (0.334 g, 0.761 mmol, 1.0 equiv) in CH_2Cl_2 (20.0 mL) at 25 °C was added Dess-Martin periodinane (1.13 g, 2.66 mmol, 3.5 equiv). After stirring at 25 °C for 2 h, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL) and saturated aqueous $Na_2S_2O_3$ (20 mL), and stirred vigorously for 30 min. Then the mixture was transferred to a separatory funnel, and diluted with CH_2Cl_2 (20 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give the crude dicarbonyl **32**. Pressing forward without further purification, the crude **32** (assumed 0.761 mmol) was dissolved in THF (15.0 mL) and SmI_2 (50.0 mL, 0.1 M in THF, 5.00 mmol, 6.6 equiv) was slowly added at -78 °C. After stirring at -78 °C for 1 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, CH_2Cl_2:EtOAc, 10:1→5:1→3:1) to give 1,2-diol **31** (0.115 g, 34% yield over 2 steps) as a yellow liquid. **31**: R_f = 0.20 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max} 3465, 2953, 2928, 2856, 1732, 1470, 1389, 1306, 1253, 1114, 1036, 948, 883, 837, 779, 719, 669 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.51 (ddd, *J* = 10.1, 5.6, 2.3 Hz, 1 H), 5.29–5.20 (m, 1 H), 4.71 (q, *J* = 1.6 Hz, 1 H), 4.67 (t, *J* = 1.9 Hz, 1 H), 4.00–3.89 (m, 2 H), 3.89–3.81 (m, 2 H), 3.67–3.62 (m, 2 H), 3.57–3.43 (m, 1 H), 2.25 (ddt, *J* = 28.9, 12.6, 2.6 Hz, 2 H), 2.11–1.78 (m, 7 H), 1.62 (qd, *J* = 11.2, 8.4 Hz, 2 H), 1.21 (d, *J* = 12.4 Hz, 1 H), 0.91 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 135.1, 122.0, 117.1,

106.8, 74.4, 71.6, 66.6, 65.1, 64.9, 49.6, 47.0, 45.1, 43.4, 36.4, 33.1, 30.3, 25.9, 23.9, 18.4, -5.3, -5.4; HRMS (ESI) calcd for $C_{24}H_{40}O_5SiNa$ [M+Na]+ 459.2537, found 459.2544.

Dicarbonate 56. To a solution of **31** (0.107 g, 0.245 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) at 25 °C was added NIS (83.1 mg, 0.368 mmol, 1.5 equiv). After stirring at 25 °C for 30 min, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to give iodine **54** (95.8 mg, 70% yield) as a yellow liquid. Next, to a solution of **54** (78.7 mg, 0.140 mmol, 1.0 equiv) in Aceton/H_2O (3:1 v/v, 2.0 mL) at 25 °C was added NMO (60.9 mg, 0.520 mmol, 3.0 equiv) and aqueous OsO_4 solution (90.0 μL, 4.0 wt.% in water, 3.6 mg, 0.014 mmol, 0.10 equiv). After stirring at 25 °C for 6 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, CH_2Cl_2:EtOAc, 1:1) to give triol **55** (49.0 mg, 59% yield) as a white wax. Next to a solution of **55** (49.0 mg, 0.082 mmol, 1.0 equiv) in THF (1.0 mL) at -78 °C was add *n*-BuLi (0.310 mL, 1.6 M in hexanes, 0.496 mmol, 6.0 equiv). After stirring at -78 °C for 15 min, the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (5.0 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated to give the crude tetraol. Pressing forward without further purification, to a solution of the so-obtained tetraol (assumed 0.082 mmol) in CH_2Cl_2 (3 mL) at 25 °C was added pyridine (39.8 μL, 38.9 mg, 0.492 mmol, 6.0 equiv) and phosgene (0.176 mL, 15% wt in toluene, 24.3 mg, 0.246 mmol, 3.0 equiv). After stirring for 2 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 3:1) to give dicarbonate **56** (39.7 mg, 93% yield over 2 steps) as a white solid. **56**: R_f = 0.30 (silica gel, hexanes:EtOAc, 3:1); IR (film) ν_{max}

2954, 2858, 1808, 1654, 1464, 1348, 1307, 1254, 1206, 1170, 1120, 1071, 839, 780, 765 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.05 (q, *J* = 8.5 Hz, 1 H), 4.83 (d, *J* = 1.9 Hz, 1 H), 4.78 (s, 1 H), 4.75–4.70 (m, 1 H), 4.59 (d, *J* = 8.7 Hz, 1 H), 4.01–3.92 (m, 2 H), 3.91–3.83 (m, 2 H), 3.79 (d, *J* = 11.0 Hz, 1 H), 3.54 (d, *J* = 11.0 Hz, 1 H), 2.68 (dd, *J* = 15.4, 8.1 Hz, 1 H), 2.43 (d, *J* = 14.0 Hz, 1 H), 2.11 (dt, *J* = 18.3, 12.4 Hz, 2 H), 2.05–1.95 (m, 3 H), 1.95–1.80 (m, 3 H), 1.71–1.55 (m, 2 H), 0.89 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 152.4, 145.0, 116.2, 109.5, 82.3, 78.1, 75.8, 71.6, 67.4, 65.2, 64.9, 48.1, 46.3, 42.2, 36.9, 36.2, 29.7, 29.4, 25.6, 23.7, 18.2, -5.4, -5.6; HRMS (ESI) calcd for $C_{26}H_{39}O_9Si$ [M+H]+ 523.2358, found 523.2362.

Epoxide 59. To a solution of **56** (39.7 mg, 0.076 mmol, 1.0 equiv) in THF (1.0 mL) at 25 °C was added TBAF (83.5 μL, 1.0 M in THF, 0.084 mmol, 1.1 equiv). After stirring at 25 °C for 10 min, the reaction contents were directly purified by flash column chromatography (silica gel, hexanes:EtOAc, 1:1→0:1) to give free alcohol (20.8 mg, 64% yield) as a colorless liquid. Next, to a solution of the so-obtained alcohol (20.8 mg, 0.051 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 25 °C was added Et_3N (21.3 μL, 15.5 mg, 0.153 mmol, 3.0 equiv) and MsCl (4.7 μL, 7.0 mg, 0.061 mmol, 1.2 equiv). After stirring at 25 °C for 30 min, the reaction contents were directly purified by flash column chromatography (silica gel, hexanes:EtOAc, 1:1) to give mesylate product (22.0 mg, 89% yield) as a white powder. Pressing forward, to a solution of this mesylate (22.0 mg, 0.045 mmol, 1.0 equiv) in MeOH (1.0 mL) was added K_2CO_3 (31.1 mg, 0.225 mmol, 5.0 equiv). After stirring at 50 °C for 12 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, pure EtOAc, followed by CH_2Cl_2:MeOH, 20:1) to give epoxide **59** (10.1 mg, 66% yield) as a white powder. **59**: R_f = 0.15 (silica gel, pure EtOAc); IR (film) ν_{max} 3432, 2925, 2853, 1735, 1675, 1648, 1559, 1438, 1398, 1307, 1202, 1119, 1087, 1040, 950, 922, 807, 726, 660 cm^{-1}; ^1H NMR (500 MHz, CD_3OD)

δ 4.68 (q, *J* = 1.9 Hz, 1 H), 4.66 (q, *J* = 2.0 Hz, 1 H), 4.13 (q, *J* = 3.5 Hz, 1 H), 3.99–3.87 (m, 4 H), 3.62 (d, *J* = 3.6 Hz, 1 H), 3.24 (s, 1 H), 2.89 (s, 2 H), 2.76–2.68 (m, 1 H), 2.54 (dd, *J* = 13.9, 3.5 Hz, 1 H), 2.44–2.32 (m, 1 H), 2.08–1.99 (m, 1 H), 2.00–1.86 (m, 3 H), 1.85–1.76 (m, 2 H), 1.66–1.54 (m, 2 H), 1.41–1.34 (m, 1 H); ^{13}C NMR (125 MHz, CD_3OD) δ 151.9, 119.5, 107.8, 75.2, 74.5, 72.9, 66.9, 66.7, 59.8, 56.0, 39.2, 38.1, 35.3, 30.1, 25.9, 20.2; HRMS (ESI) calcd for $C_{18}H_{27}O_6$ [M+H]+ 339.1802, found 339.1807.

Epoxide 61. To a solution of **31** (0.115 g, 0.263 mmol, 1.0 equiv) in THF (5.0 mL) at 25 °C was added NBS (98.2 mg, 0.552 mmol, 2.1 equiv). After stirring at 25 °C for 15 min, H_2O (0.50 mL) was added and the reaction was stirred for 4 h at 25 °C. Next, MeOH (15.0 mL) and K_2CO_3 (0.195 g, 1.32 mmol, 5.0 equiv) were added sequentially. After stirring at 50 °C for 4 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to give epoxide **61** (95.0 mg, 65% yield) as a colorless liquid. **61**: R_f = 0.50 (silica gel, hexanes:EtOAc, 2:1); IR (film) ν_{max} 3463, 2954, 2926, 2855, 1735, 1463, 1311, 1256, 1115, 1079, 1036, 947, 855, 838, 778, 670, 561 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.04–3.79 (m, 4 H), 3.71–3.36 (m, 5 H), 3.26 (d, *J* = 3.5 Hz, 1 H), 3.13 (t, *J* = 3.8 Hz, 1 H), 2.61–2.39 (m, 2 H), 2.31 (dd, *J* = 10.8, 2.3 Hz, 1 H), 2.23 (d, *J* = 16.2 Hz, 1 H), 2.05 – 1.96 (m, 2 H), 1.91 (td, *J* = 12.4, 5.6 Hz, 1 H), 1.87–1.73 (m, 2 H), 1.63–1.45 (m, 2 H), 1.42–1.33 (m, 1 H), 0.89 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.5, 87.6, 82.9, 71.7, 68.6, 65.2, 65.0, 56.9, 52.0, 50.2, 47.5, 46.4, 42.9, 37.1, 36.8, 36.5, 28.5, 25.8, 20.9, 18.2, -5.4, -5.5; HRMS (ESI+APCI): no molecular ion peak was observed.

Triol 68. To a solution of **61** (88.0 mg, 0.166 mmol, 1.0 equiv) in THF (3.0 mL) at -78 °C was added *n*-BuLi (0.420 mL, 1.6 M in hexanes, 0.672 mmol, 4.0 equiv). After stirring at -78 °C for 10 min, MeOH (54.0 μL, 42.8 mg, 1.33 mmol, 8.0 equiv) was added and the reaction contents

were warmed to 25 °C. Next, TBAF (0.830 mL, 1.0 M in THF, 0.830 mmol, 5.0 equiv) was added and the reaction mixture was stirred for 2 h. Next, MeOH (9.0 mL) and K_2CO_3 (0.229 g, 1.66 mmol, 10 equiv) were added sequentially. After stirring at 50 °C for 4 h, the reaction contents were concentrated directly. The resultant crude residue was purified by flash column chromatography (silica gel, EtOAc:MeOH, 60:1→40:1→20:1) to give triol **68** (53.7 mg, 96% yield) as a white solid. **68**: R_f = 0.20 (silica gel, EtOAc:MeOH, 20:1); IR (film) ν_{max} 3401, 2924, 2853, 1730, 1654, 1459, 1404, 1313, 1225, 1123, 1041, 919, 895, 852, 735, 647, 580 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.76 (s, 1 H), 4.73 (s, 1 H), 4.39 (t, *J* = 5.4 Hz, 1 H), 4.04 – 3.84 (m, 4 H), 3.76 (d, *J* = 8.4 Hz, 1 H), 3.73 – 3.67 (m, 2 H), 3.46 (d, *J* = 4.5 Hz, 1 H), 3.17 – 3.07 (br, 1 H), 2.63 (dd, *J* = 14.6, 2.5 Hz, 1 H), 2.46 (d, *J* = 11.4 Hz, 1 H), 2.29 (dt, *J* = 13.1, 2.9 Hz, 1 H), 2.11 (dt, *J* = 12.3, 7.2 Hz, 1 H), 2.02 – 1.74 (m, 5 H), 1.69 – 1.58 (m, 2 H), 1.43 (d, *J* = 6.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 117.0, 107.8, 80.1, 78.2, 75.8, 73.9, 71.4, 65.0, 64.7, 48.3, 47.1, 46.3, 44.4, 36.3, 31.4, 29.2, 23.9; HRMS (ESI) calcd for $C_{18}H_{27}O_6$ [M+H]+ 339.1802, found 339.1804.

1,3-Diketone 69. To a solution of DMSO (0.140 mL, 0.154 g, 1.96 mmol, 20 equiv) in CH_2Cl_2 (10.0 mL) at -78 °C was add oxayl chloride (84.0 µL, 0.124 g, 0.980 mmol, 10 equiv). After stirring at -78 °C for 10 min, a solution of **68** (33.0 mg, 0.098 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL) was slowly added at -78 °C. After stirring at -78 °C for 2 h, Et_3N (0.410 mL, 0.297 g, 2.94 mmol, 30 equiv) was added and the reaction mixture was warmed to 25 °C over the course of 2 h. Then the reaction contents were quenched by the addition of saturated aqueous NH_4Cl (30 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (20 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→3:1) to give 1,3-diketone **69** (18.9

mg, 58% yield) as a white powder. **69**: R_f = 0.45 (silica gel, hexanes: EtOAc, 1:1); IR (film) ν_{max} 3436, 2926, 2881, 2854, 1737, 1702, 1452, 1307, 1216, 1148, 1114, 1079, 1057, 1031, 940, 889, 736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.75 (d, *J* = 1.8 Hz, 1 H), 4.67 (t, *J* = 1.8 Hz, 1 H), 4.61 (d, *J* = 6.3 Hz, 1 H), 4.00–3.79 (m, 6 H), 2.71 (dd, *J* = 13.1, 6.4 Hz, 1 H), 2.57–2.42 (m, 3 H), 2.23 (t, *J* = 13.0 Hz, 1 H), 2.18–2.09 (m, 1 H), 1.98 (dd, *J* = 13.3, 2.4 Hz, 2 H), 1.92 (dt, *J* = 13.7, 8.5 Hz, 1 H), 1.84 (dddd, *J* = 11.7, 8.8, 5.8, 2.5 Hz, 1 H), 1.75 (td, *J* = 11.3, 8.3 Hz, 1 H), 1.64 (ddd, *J* = 13.5, 4.1, 1.9 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.9, 205.0, 145.3, 116.7, 107.8, 81.7, 81.0, 71.4, 65.1, 64.7, 60.7, 48.7, 45.8, 44.4, 36.0, 35.6, 29.6, 23.5; HRMS (ESI) calcd for $C_{18}H_{23}O_6$ [M+H]+ 335.1489, found 335.1475.

Manginoid A (1). To a solution of **69** (18.9 mg, 0.057 mmol, 1.0 equiv) in acetone (1.0 mL) at 25 °C was added $FeCl_3$ (1.8 mg, 0.011 mmol, 0.20 equiv). After stirring at 25 °C for 12 h, the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (5.0 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 3:1) to give triketone **30** (13.8 mg, 83% yield) as a colorless liquid. Next, to a solution of the so-obtained **30** (9.0 mg, 0.031 mmol, 1.0 equiv) in THF (1.0 mL) at – 78 °C was added $LaCl_3$•2LiCl (0.11 mL, 0.6 M in THF, 0.066 mmol, 2.1 equiv). After stirring at -78 °C for 30 min, MeMgBr (0.20 mL, ~0.33 M in THF/dibutyl ether, 0.066 mmol, 2.1 equiv) was added. After stirring at -78 °C for another 30 min, the reaction mixture was then warmed to 25 °C over the course of 1 h. Then the reaction contents were quenched by the addition of saturated aqueous $NaHCO_3$ (5.0 mL), transferred to a separatory funnel, and diluted with CH_2Cl_2 (10 mL). The two layers were separated and the aqueous layer was extracted with CH_2Cl_2

(3 × 10 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The resultant crude residue was purified by flash column chromatography (silica gel, CH_2Cl_2:EtOAc, 5:1→3:1) to give recovered **30** (1.4 mg) and manginoid A (**1**) (4.0 mg, 42% yield, 50% brsm) as a colorless liquid. **1**: R_f = 0.30 (silica gel, CH_2Cl_2:EtOAc, 3:1); IR (film) ν_{max} 3457, 2957, 2925, 2854, 1737, 1702, 1651, 1454, 1377, 1351, 1258, 1147, 1058, 1034, 974, 893, 737, 650 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.76 (p, *J* = 1.3 Hz, 1 H), 4.66 (d, *J* = 1.6 Hz, 1 H), 4.63 (d, *J* = 6.4 Hz, 1 H), 3.97 – 3.90 (m, 2 H), 2.73 (dd, *J* = 13.1, 6.4 Hz, 1 H), 2.58 (dd, *J* = 14.2, 2.0 Hz, 1 H), 2.49–2.42 (m, 1 H), 2.38–2.27 (m, 1 H), 2.18 (t, *J* = 13.0 Hz, 1 H), 2.11–1.97 (m, 2 H), 1.96–1.89 (m, 1 H), 1.88–1.76 (m, 2 H), 1.72–1.60 (m, 2 H), 1.28 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 205.1, 146.1, 107.4, 81.7, 81.1, 78.9, 71.4, 61.2, 51.4, 46.2, 44.6, 40.2, 35.8, 29.6, 26.8, 23.9; HRMS (ESI) calcd for $C_{17}H_{23}O_5$ [M+H]+ 307.1540, found 307.1535.

Table 3-1. Comparative ^1H NMR Data for Manginoid A (1)

Natural (Zhang) (400 MHz, $CDCl_3$)[1]	Synthetic (this work) (500 MHz, $CDCl_3$)
4.75 (brs, 1 H)	4.76 (p, *J* = 1.3 Hz, 1 H)
4.64 (brs, 1 H)	4.66 (d, *J* = 1.6 Hz, 1 H)
4.61 (d, *J* = 6.3 Hz, 1 H)	4.63 (d, *J* = 6.4 Hz, 1 H)
3.93 (d, *J* = 8.6 Hz, 1 H)	3.97–3.90 (m, 2 H)
3.91 (d, *J* = 8.6 Hz, 1 H)	
2.72 (dd, *J* = 13.0, 6.3 Hz, 1 H)	2.73 (dd, *J* = 13.1, 6.4 Hz, 1 H)
2.56 (d, *J* = 14.2 Hz, 1 H)	2.58 (dd, *J* = 14.2, 2.0 Hz, 1 H)

Table 3-1 continued

2.43 (d, J = 14.2 Hz, 1 H)	2.49–2.42 (m, 1 H)
2.30 (m, 1 H)	2.38–2.27 (m, 1 H)
2.16 (t, J =13.0 Hz, 1 H)	2.18 (t, J = 13.0 Hz, 1 H)
2.01 (m, 1 H)	2.11–1.97 (m, 2 H)
2.00 (d, J = 13.0 Hz, 1 H)	
1.90 (m, 1 H)	1.96–1.89 (m, 1 H)
1.85 (m, 1 H)	1.88–1.76 (m, 2 H)
1.81 (m, 1 H)	
1.64 (m, 1 H)	1.72–1.60 (m, 2 H)
1.61 (m, 1 H)	
1.27 (s, 3 H)	1.28 (s, 3 H)

Table 3-2. Comparative ^{13}C NMR Data for Manginoid A (1)

Natural (Zhang) (100 MHz, $CDCl_3$)[1]	Synthetic (this work) (125 MHz, $CDCl_3$)
209.2	209.3
205.2	205.1

Table 3-2 continued

146.0	146.1
107.4	107.4
81.7	81.7
81.1	81.1
78.9	78.9
71.3	71.4
61.1	61.2
51.4	51.4
46.1	46.2
44.6	44.6
40.0	40.2
35.7	35.8
29.5	29.6
26.7	26.8
23.9	23.9

3.6 References

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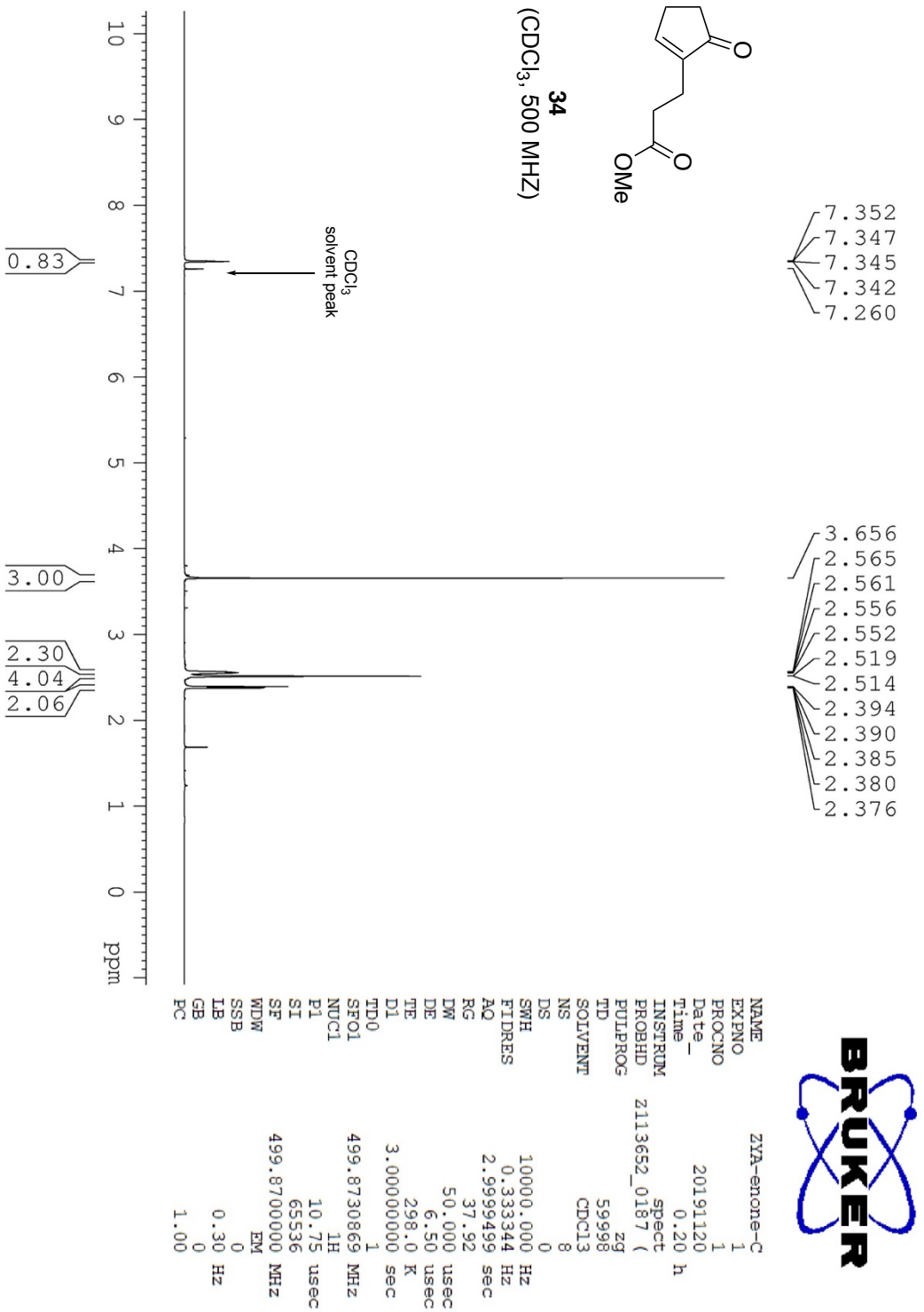
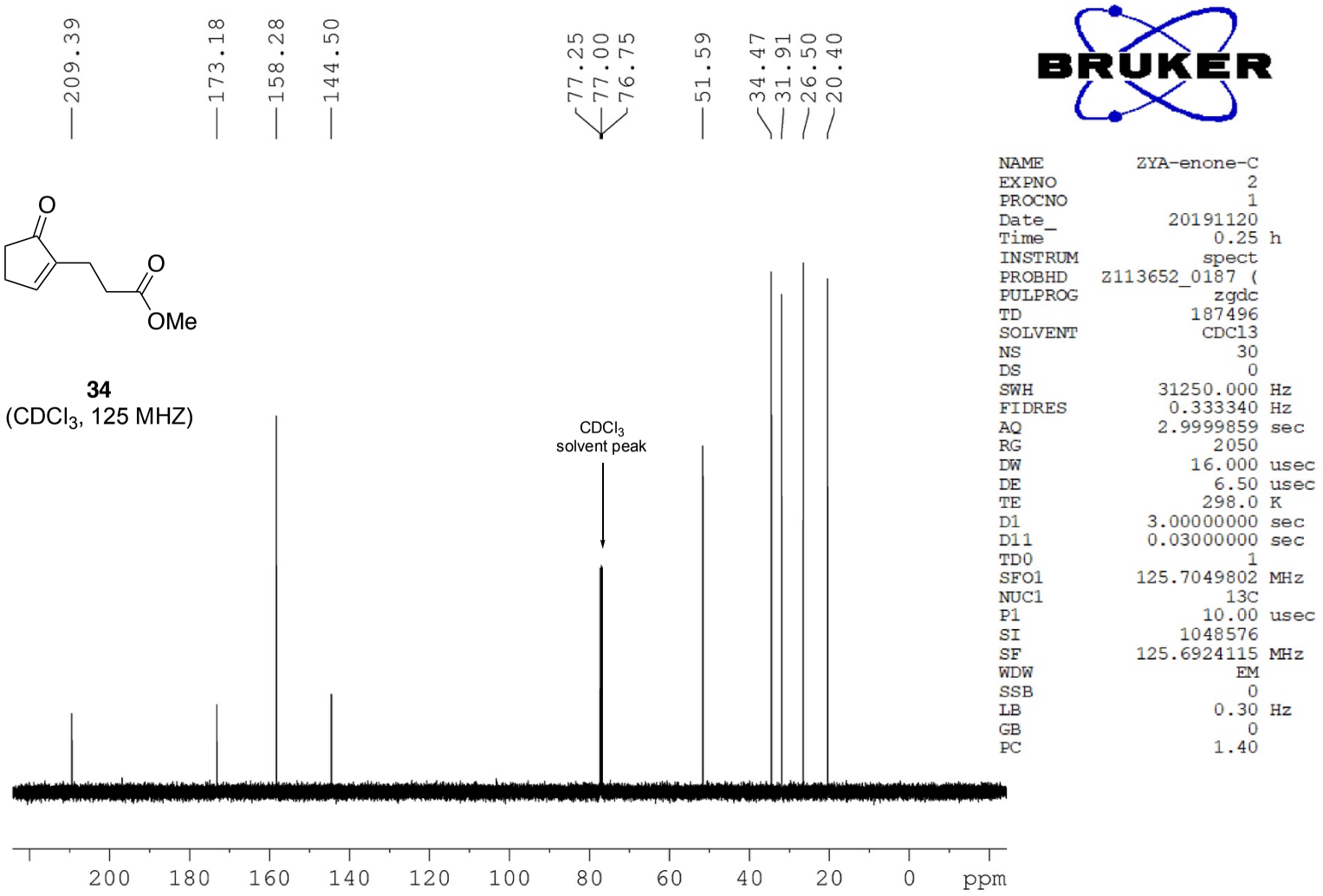
3.7 NMR Spectra of Selected Intermediates





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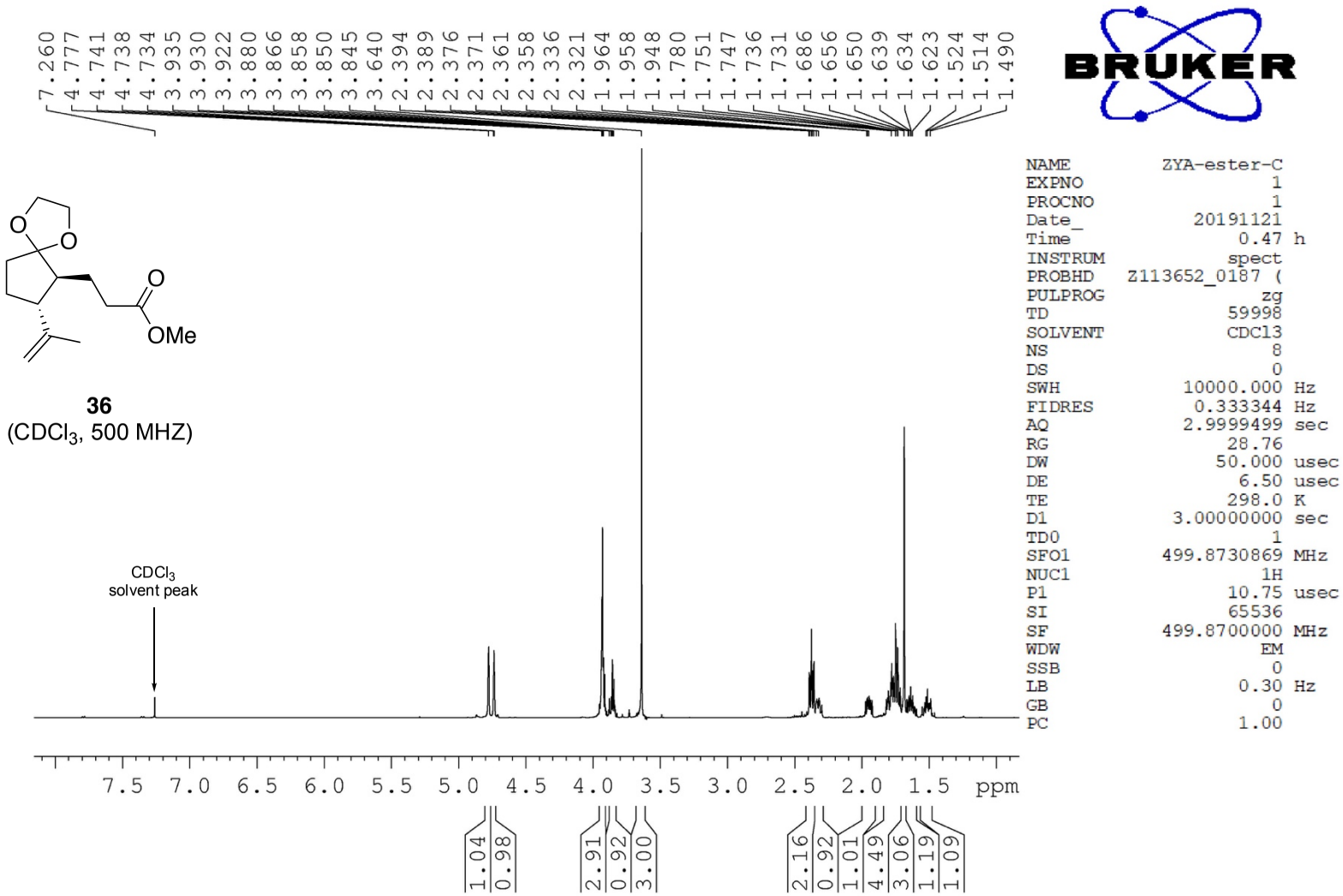
NAME	ZYA-enone-C
EXPNO	2
PROCNO	1
Date_	20191120
Time	0.25 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	30
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



36
($CDCl_3$, 500 MHZ)

BRUKER

NAME	ZYA-ester-C
EXPNO	1
PROCNO	1
Date_	20191121
Time	0.47 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	28.76
DW	50.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
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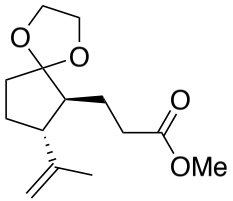
GB	0
PC	1.00



36
($CDCl_3$, 125 MHZ)

BRUKER

NAME	ZYA-ester-C
EXPNO	2
PROCNO	1
Date_	20191121
Time	0.51 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	18
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
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SF	125.6924115 MHz
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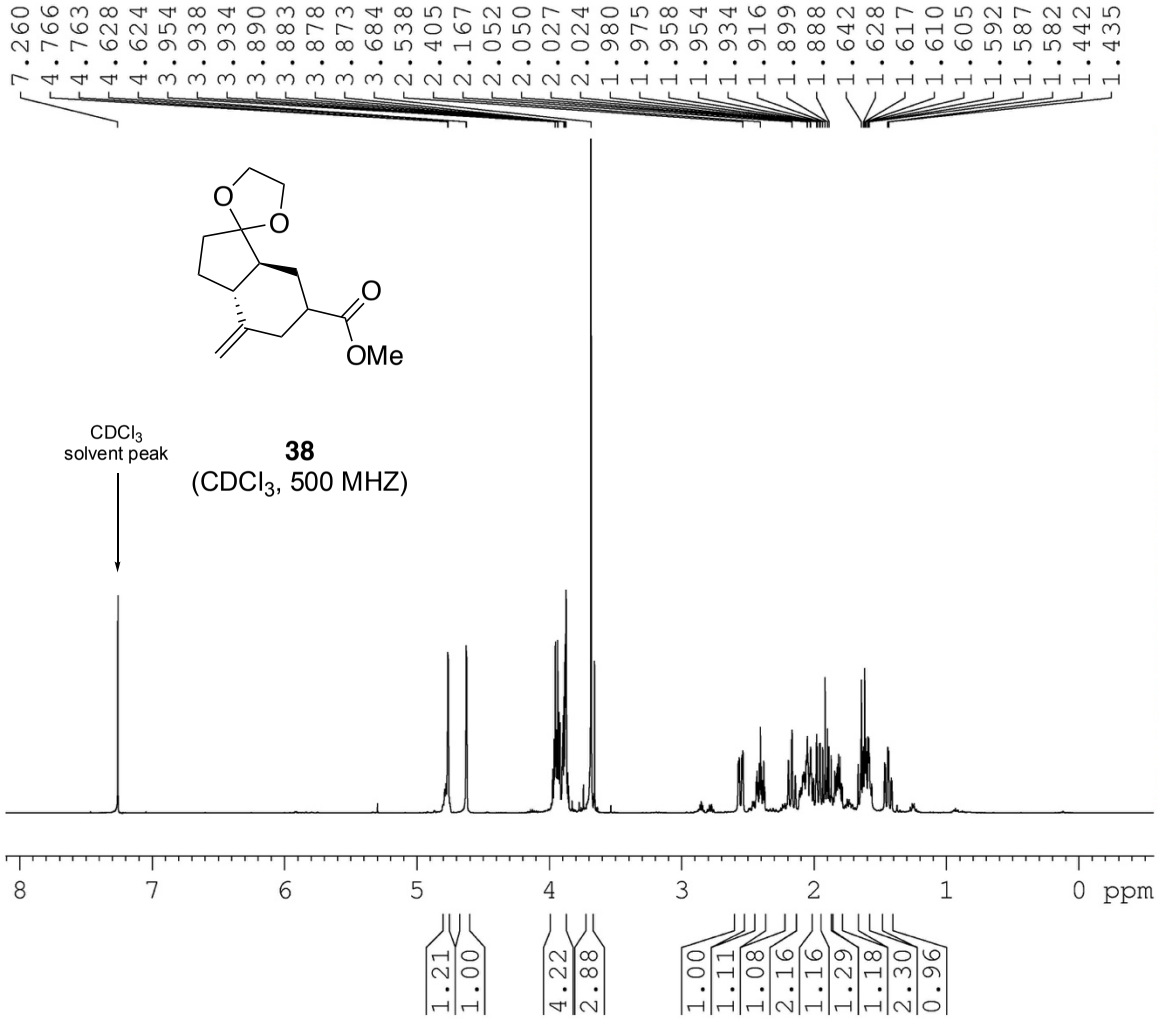
PC	1.40



BRUKER

NAME	AM-I-alkeneester-C
EXPNO	1
PROCNO	1
Date_	20191108
Time	21.58 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	56.75
DW	50.000 usec
DE	6.50 usec
TE	295.5 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
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SF	499.8700000 MHz
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SSB	0
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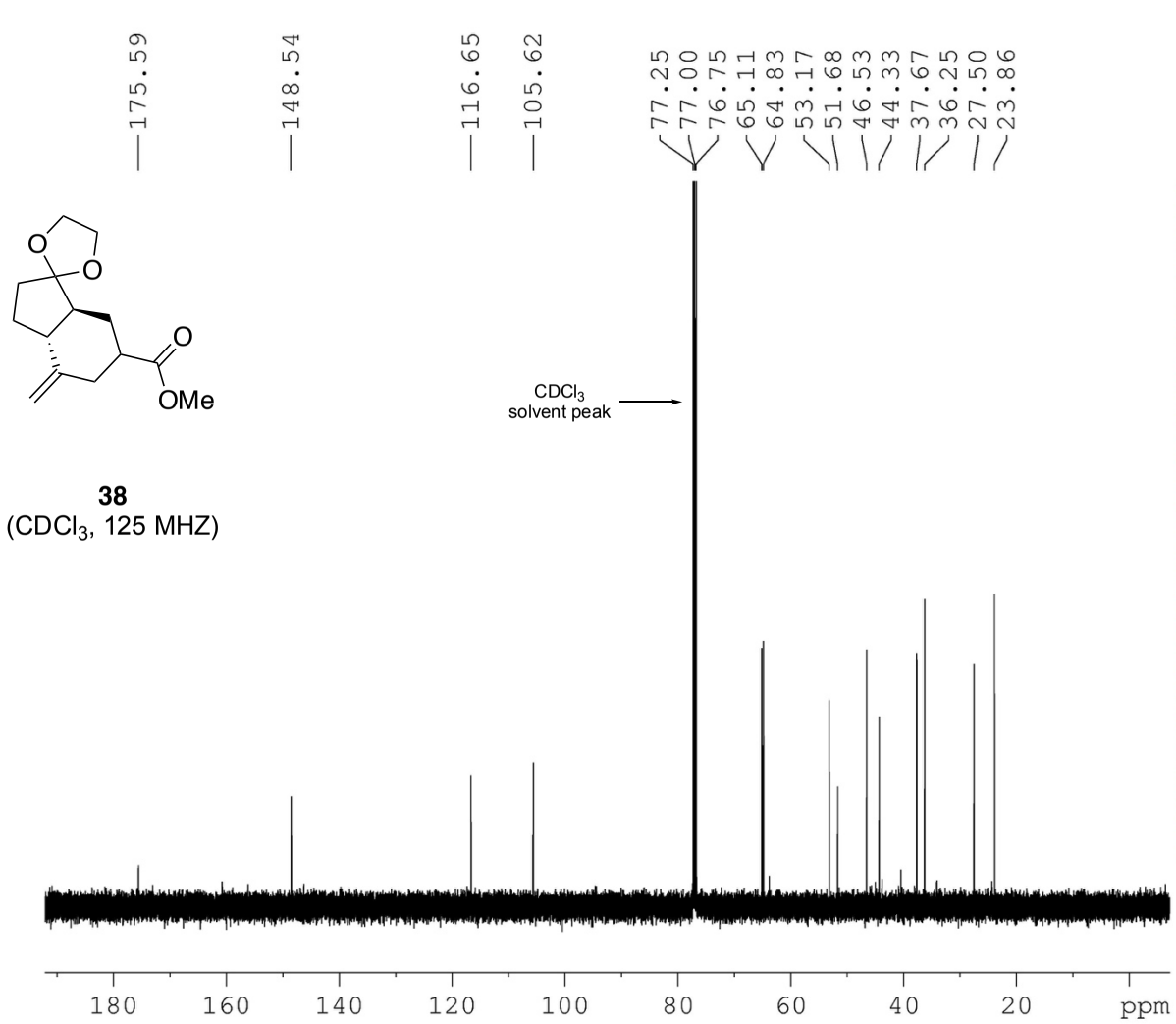
GB	0
PC	1.00



38
($CDCl_3$, 125 MHZ)

BRUKER

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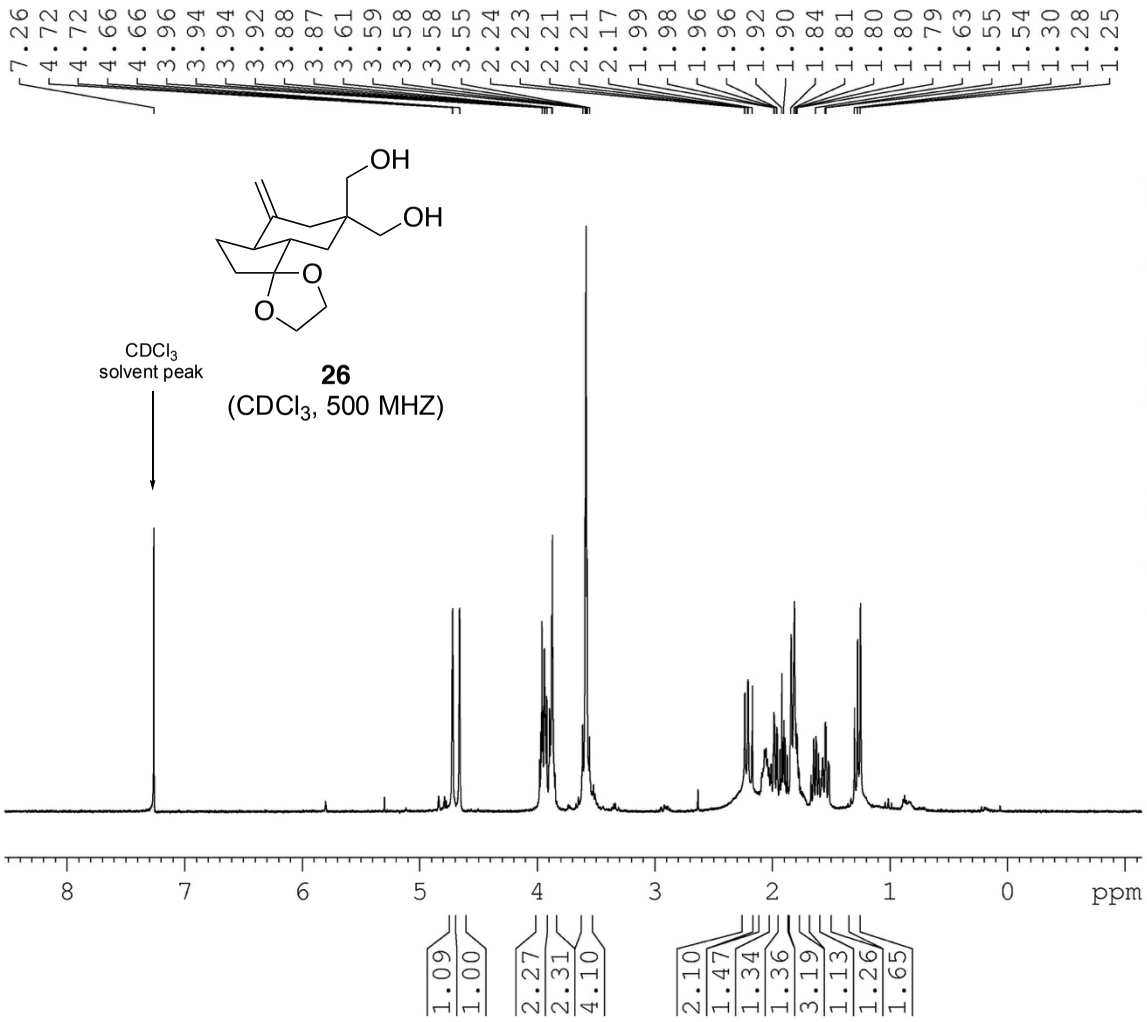
PROCNO	1
Date_	20191108
Time	22.17 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	154
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	295.9 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

NAME	AM-I-diol-C
EXPNO	1
PROCNO	1
Date_	20191108
Time	20.30 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	0.98
DW	50.000 usec
DE	6.50 usec
TE	295.3 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
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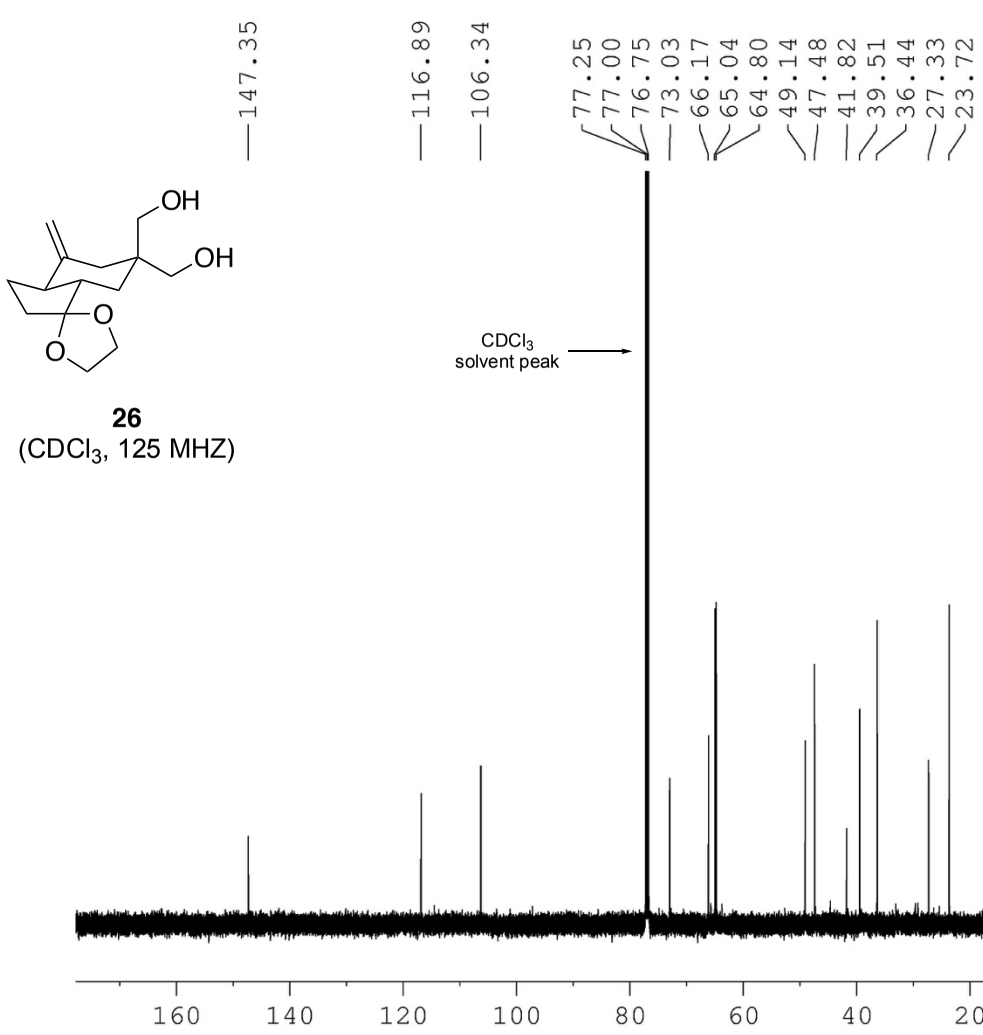

26
($CDCl_3$, 125 MHZ)

BRUKER

NAME	AM-I-diol-C	
EXPNO	2	
PROCNO	1	
Date_	20191108	
Time	21.14	h
INSTRUM	spect	
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PULPROG	zgdc	
TD	187496	
SOLVENT	CDCl3	
NS	415	
DS	0	
SWH	31250.000	Hz
FIDRES	0.333340	Hz
AQ	2.9999859	sec
RG	2050	
DW	16.000	usec
DE	6.50	usec
TE	296.1	K
D1	3.00000000	sec
D11	0.03000000	sec
TD0	1	
SFO1	125.7049802	MHz
NUC1	13C	
P1	10.00	usec
SI	1048576	
SF	125.6924115	MHz
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SSB	0	
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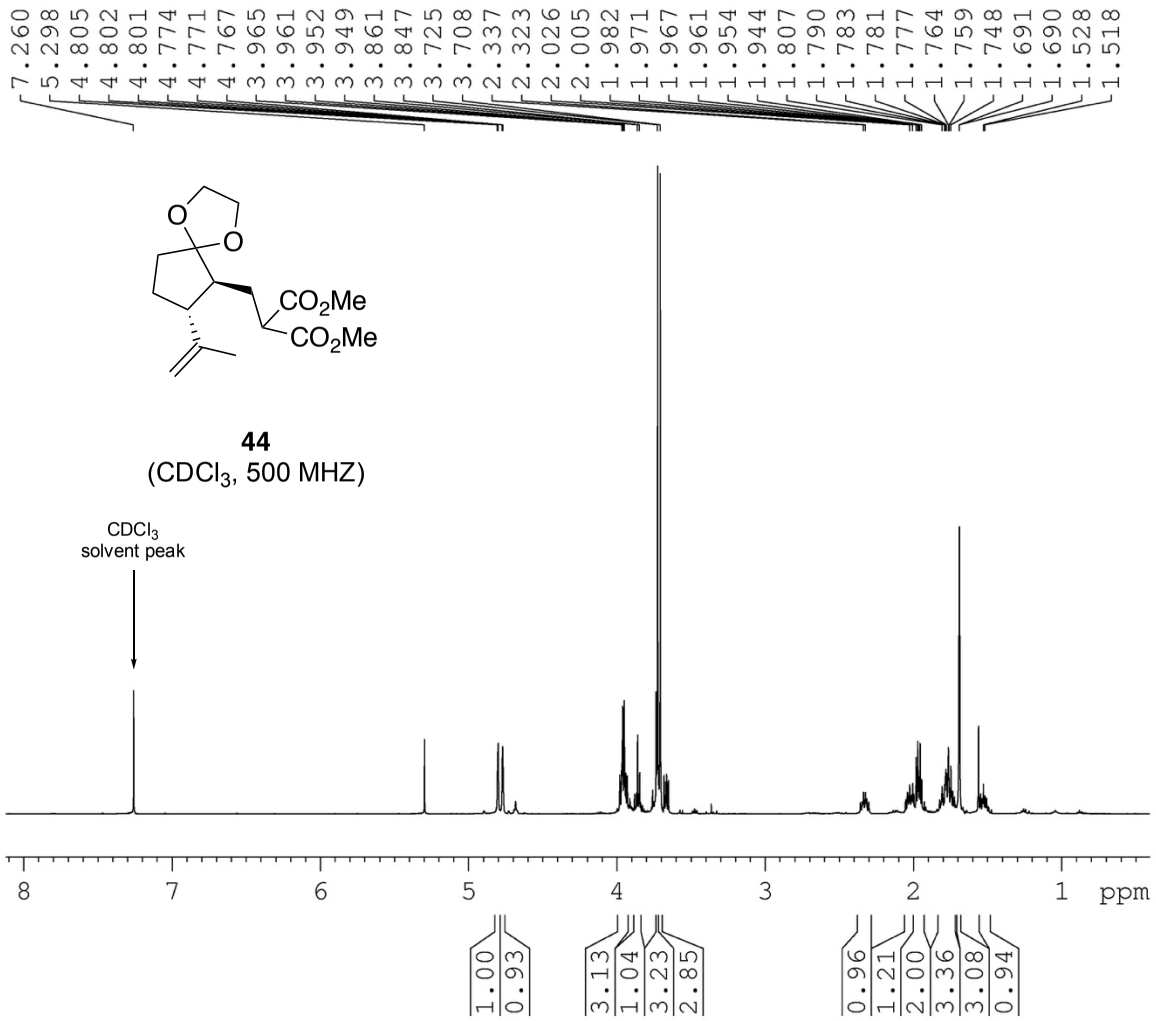
GB	0	
PC	1.40	



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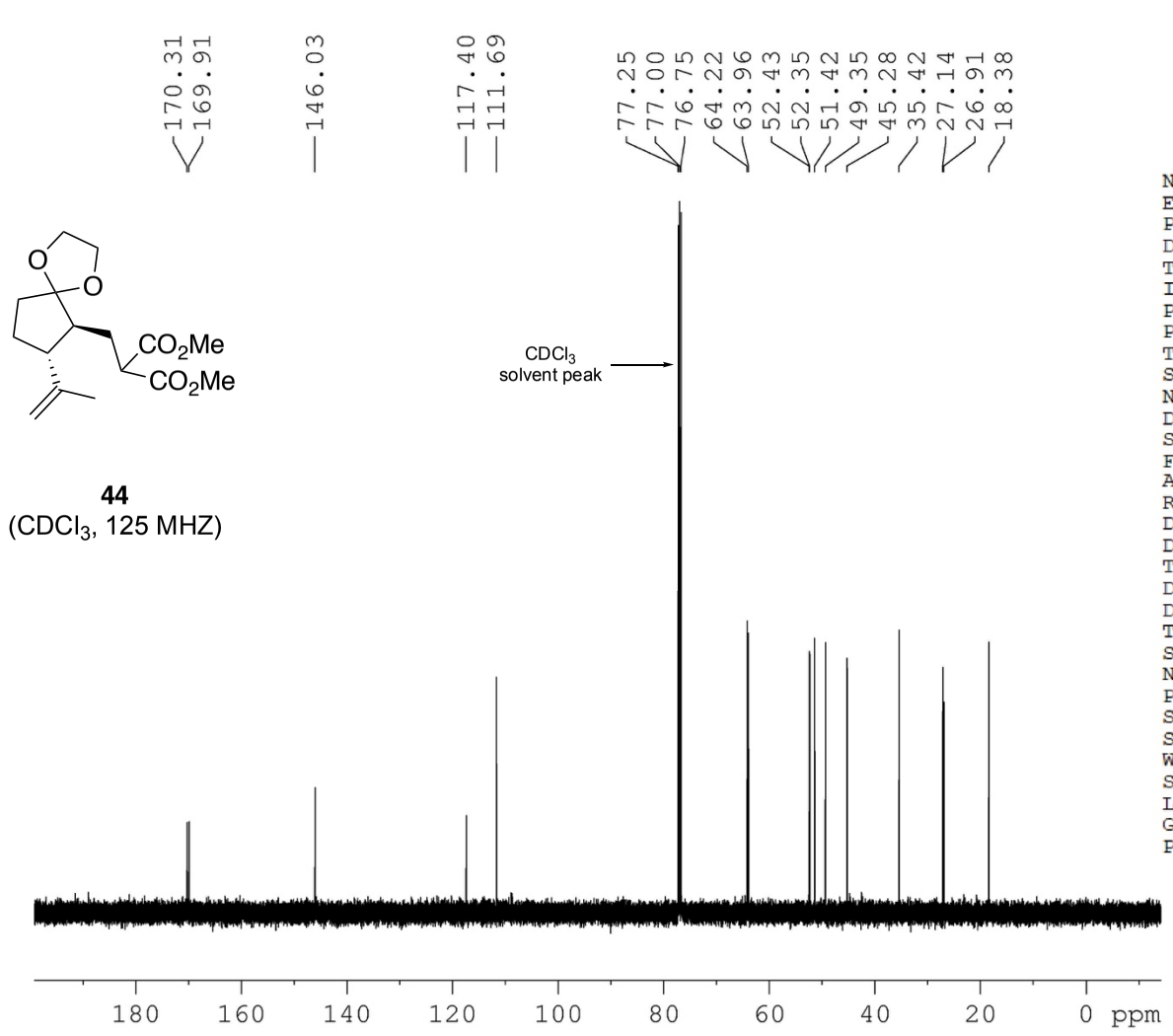
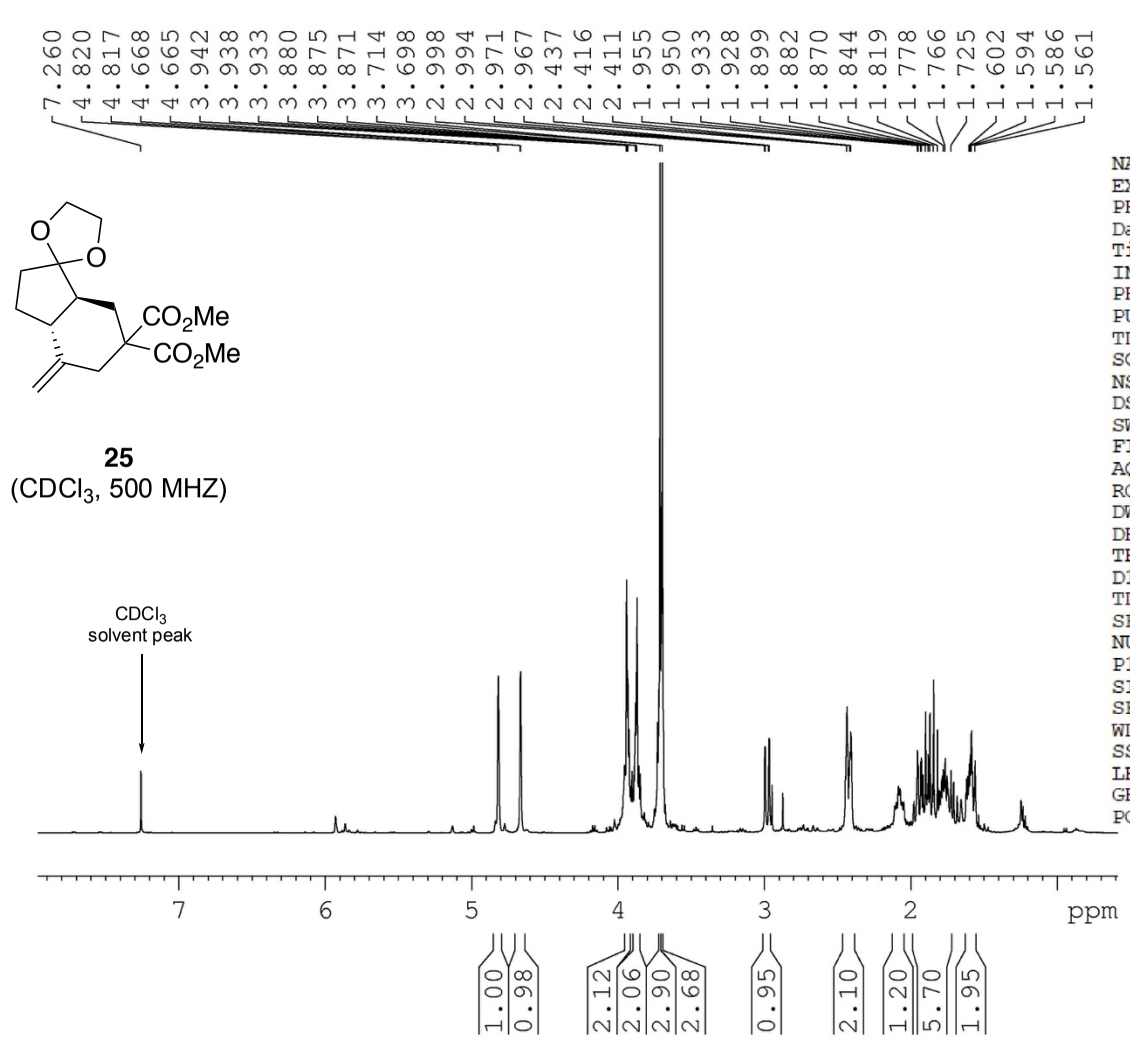
PROCNO	1
Date_	20191121
Time	0.58 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	56.75
DW	50.000 use
DE	6.50 use
TE	298.0 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 use
SI	65536
SF	499.8700124 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



44
($CDCl_3$, 125 MHZ)

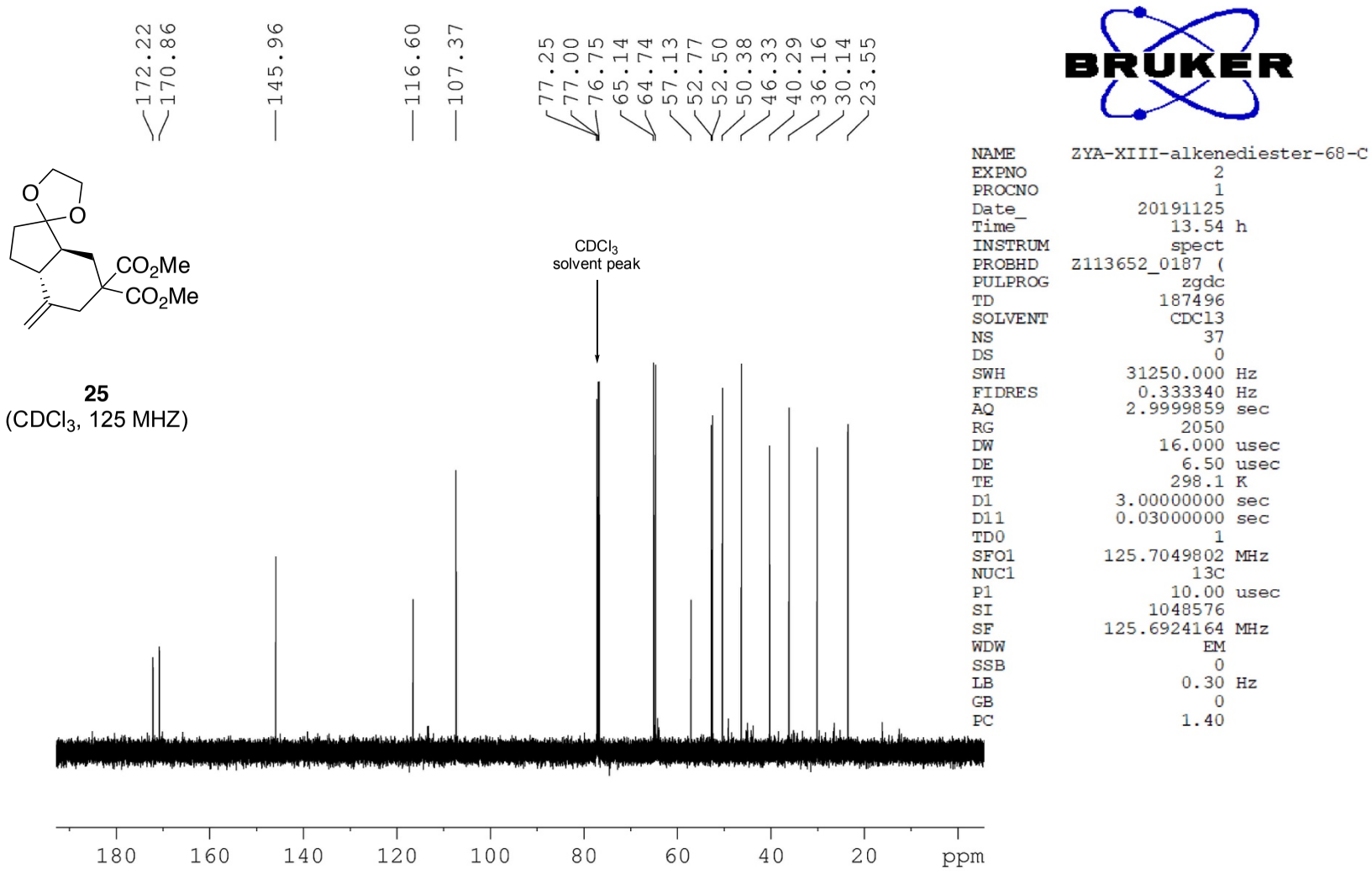
BRUKER

NAME	ZYA-XIII-diester-62-C
EXPNO	2
PROCNO	1
Date_	20191121
Time	1.16 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	162
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924148 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



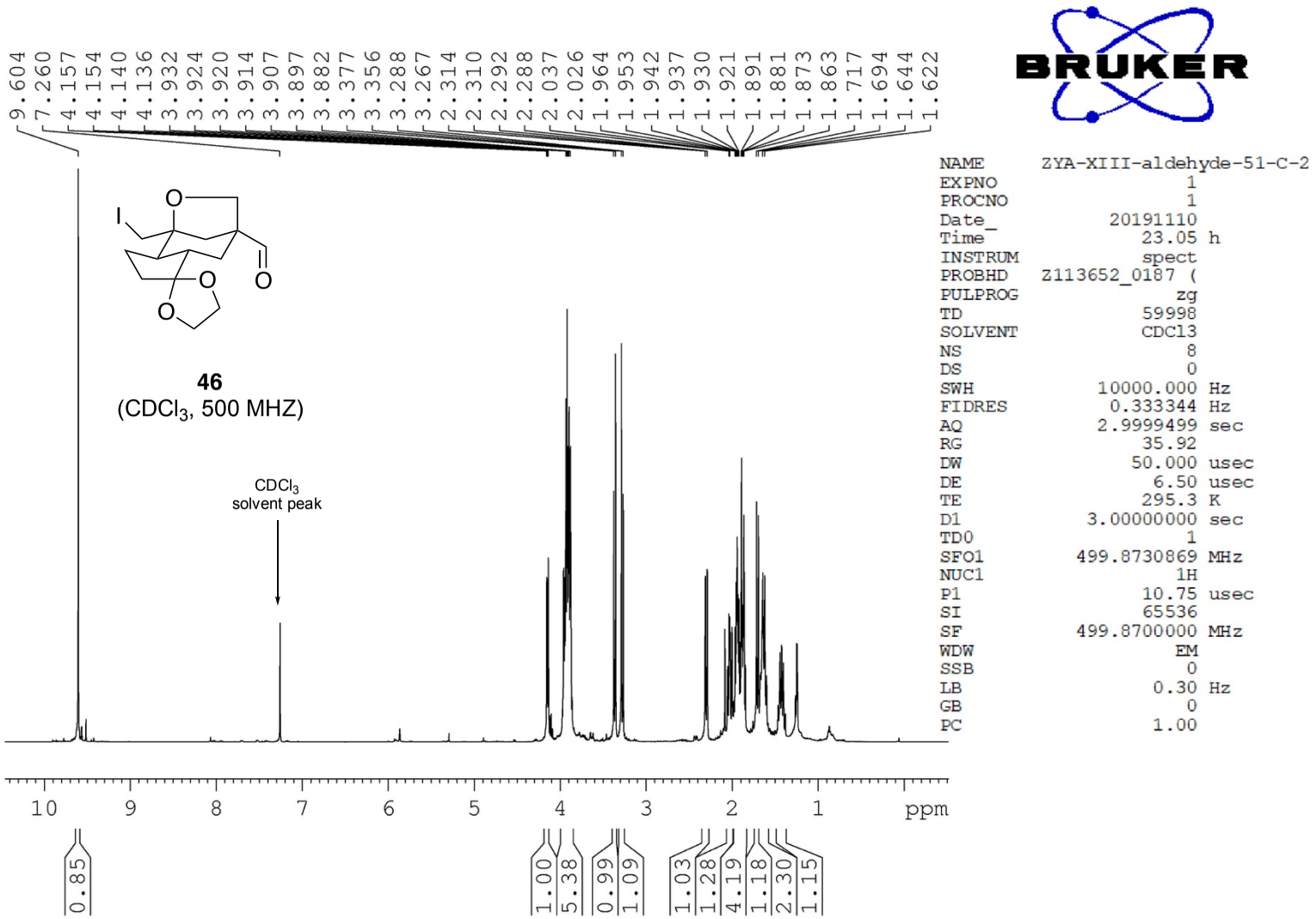
25
($CDCl_3$, 500 MHZ)

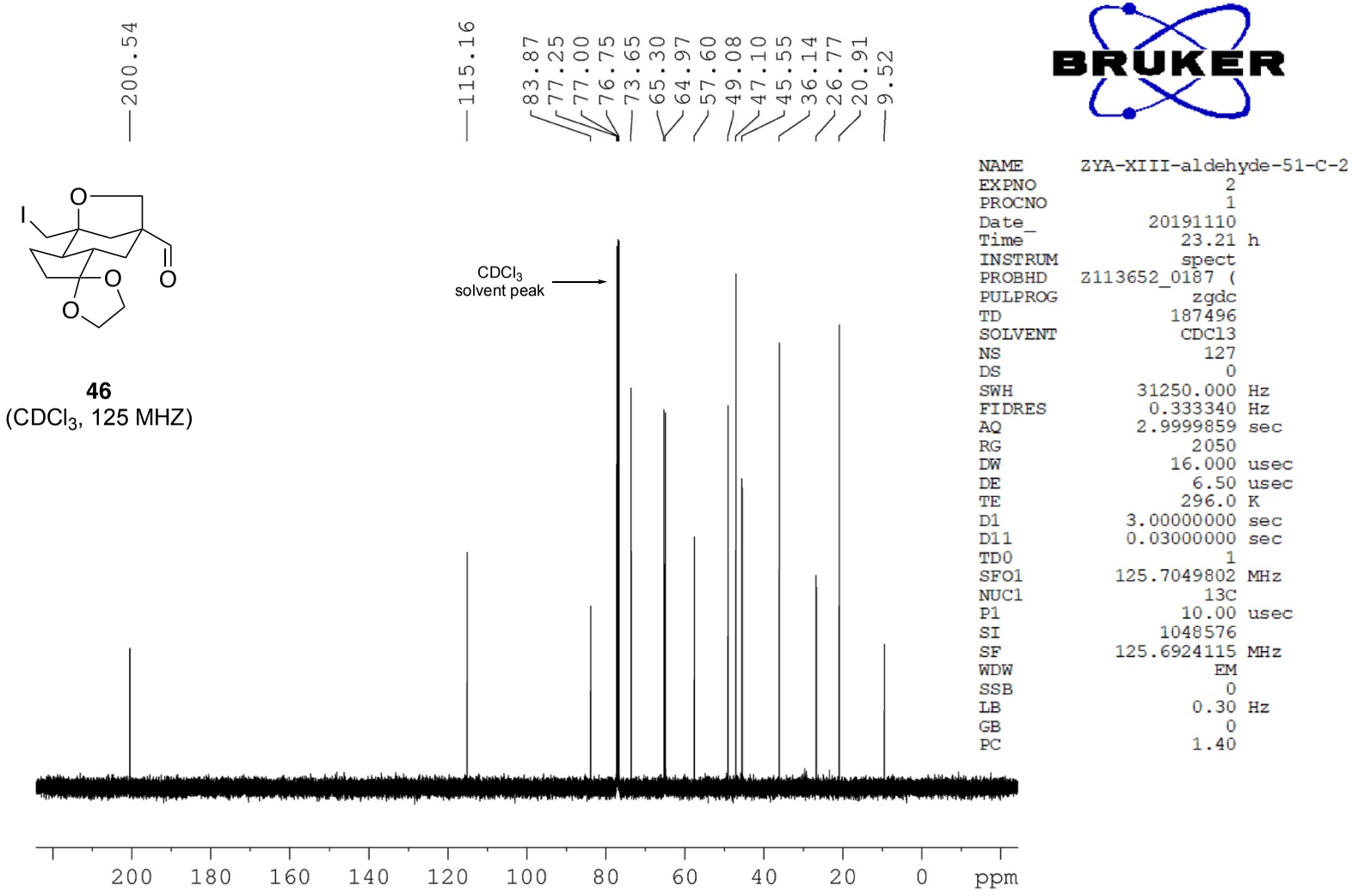
NAME	ZYA-XIII-alkenediester-68-C
EXPNO	1
PROCNO	1
Date_	20191125
Time	13.48 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	29.95
DW	50.000 usec
DE	6.50 usec
TE	298.1 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700123 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



25
($CDCl_3$, 125 MHZ)

NAME	ZYA-XIII-alkenediester-68-C
EXPNO	2
PROCNO	1
Date_	20191125
Time	13.54 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	37
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.1 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924164 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40

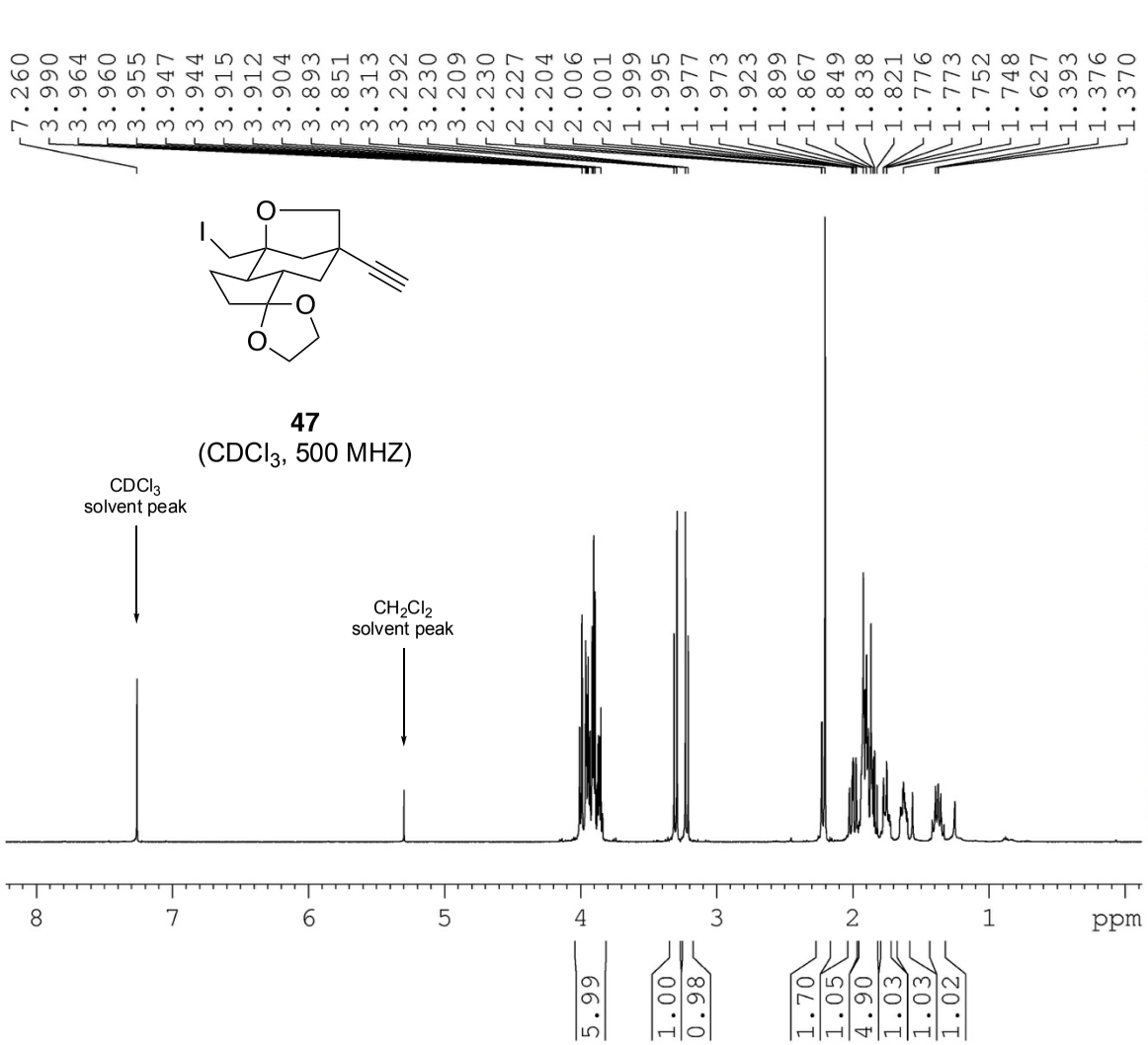

9.604
7.260
4.157
4.154
4.140
4.136
3.932
3.924
3.920
3.914
3.907
3.897
3.882
3.377
3.356
3.288
3.267
2.314
2.310
2.292
2.288
2.037
2.026
1.964
1.953
1.942
1.937
1.930
1.921
1.891
1.881
1.873
1.863
1.717
1.694
1.644
1.622
46
(CDCl3, 500 MHZ)
CDCl3
solvent peak
NAME ZYA-XIII-aldehyde-51-C-2
EXPNO 1
PROCNO 1
Date_ 20191110
Time 23.05 h
INSTRUM spect
PROBHD Z113652_0187 (
PULPROG zg
TD 59998
SOLVENT CDCl3
NS 8
DS 0
SWH 10000.000 Hz
FIDRES 0.333344 Hz
AQ 2.9999499 sec
RG 35.92
DW 50.000 usec
DE 6.50 usec
TE 295.3 K
D1 3.00000000 sec
TD0 1
SFO1 499.8730869 MHz
NUC1 1H
P1 10.75 usec
SI 65536
SF 499.8700000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
ppm
0.85
1.00
5.38
0.99
1.09
1.03
1.28
4.19
1.18
2.30
1.15



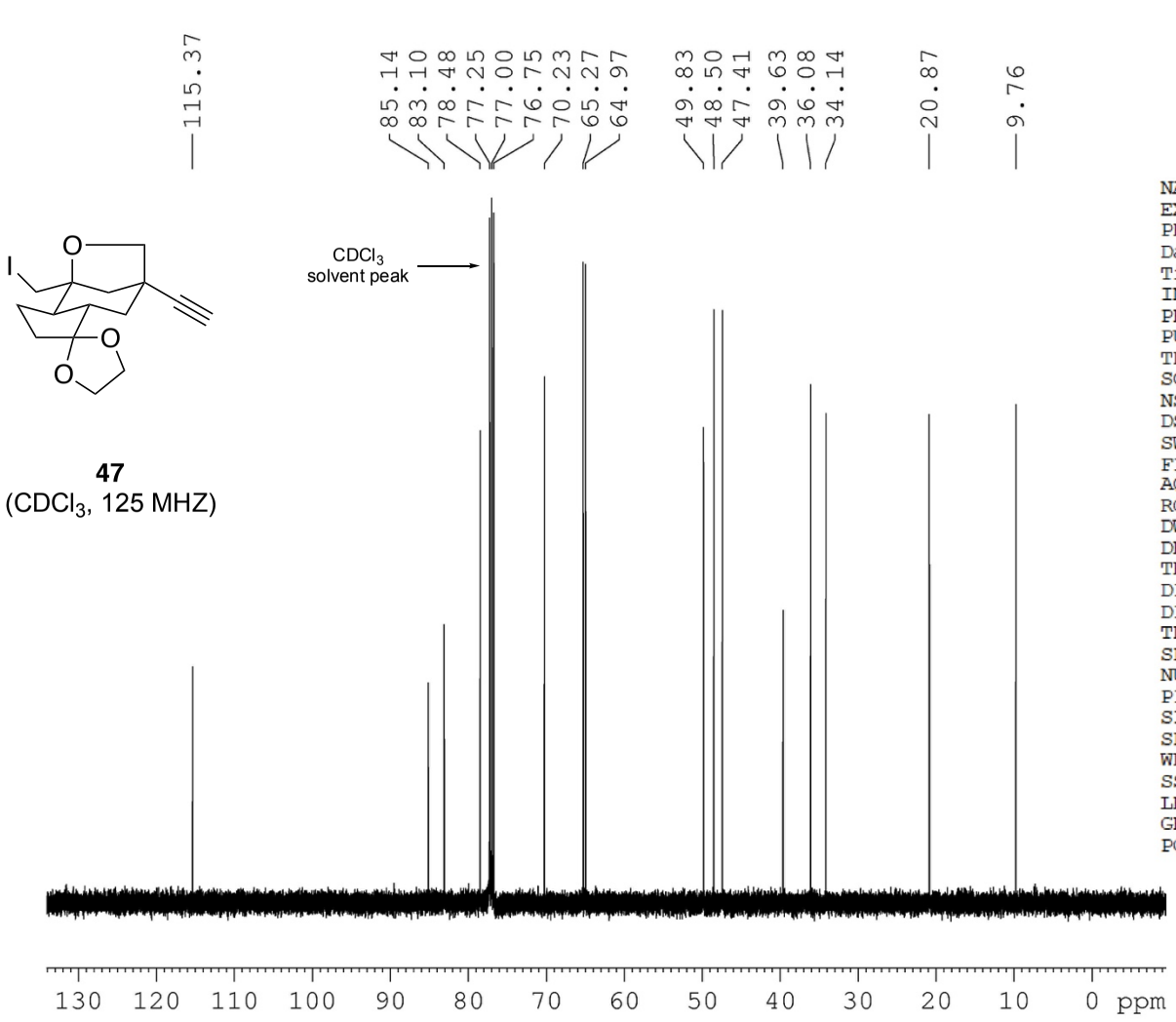
46
($CDCl_3$, 125 MHZ)

BRUKER

NAME	ZYA-XIII-aldehyde-51-C-2
EXPNO	2
PROCNO	1
Date_	20191110
Time	23.21 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	127
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



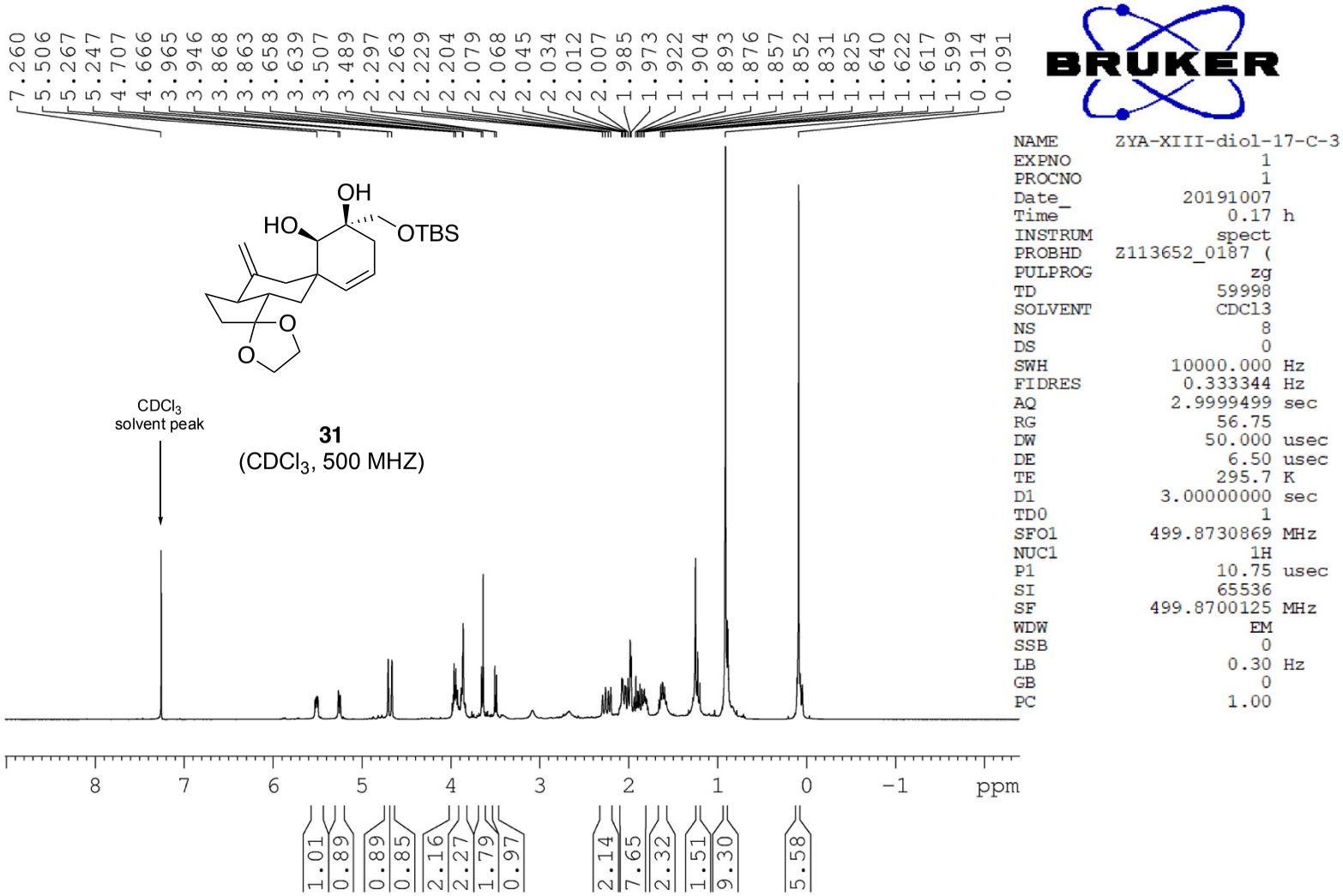
NAME	AM-I-alkyne-C
EXPNO	1
PROCNO	1
Date_	20191116
Time	23.58 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	56.75
DW	50.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



47
($CDCl_3$, 125 MHZ)

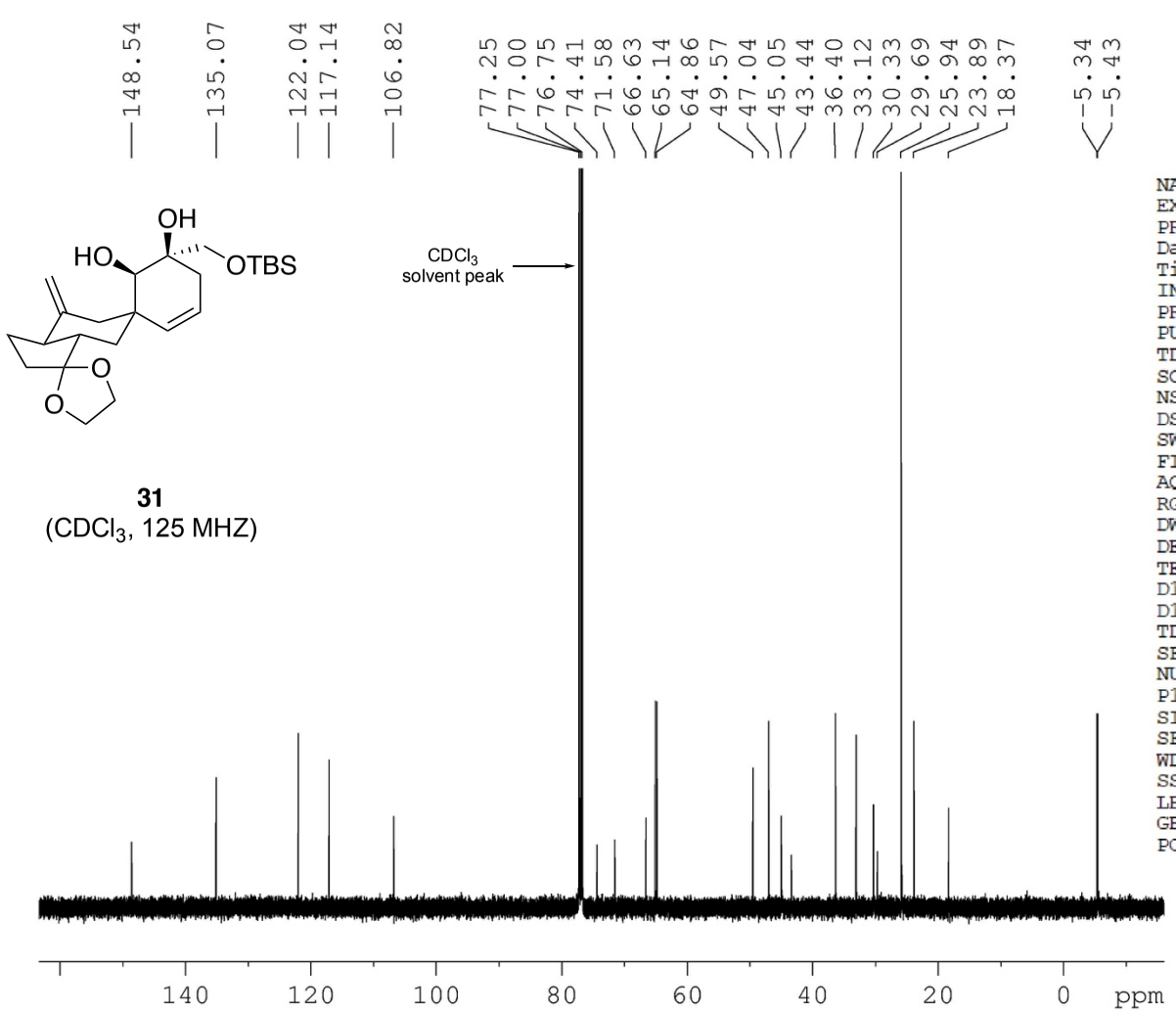
BRUKER

NAME	AM-I-alkyne-C
EXPNO	2
PROCNO	1
Date_	20191117
Time	0.16 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	139
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924115 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

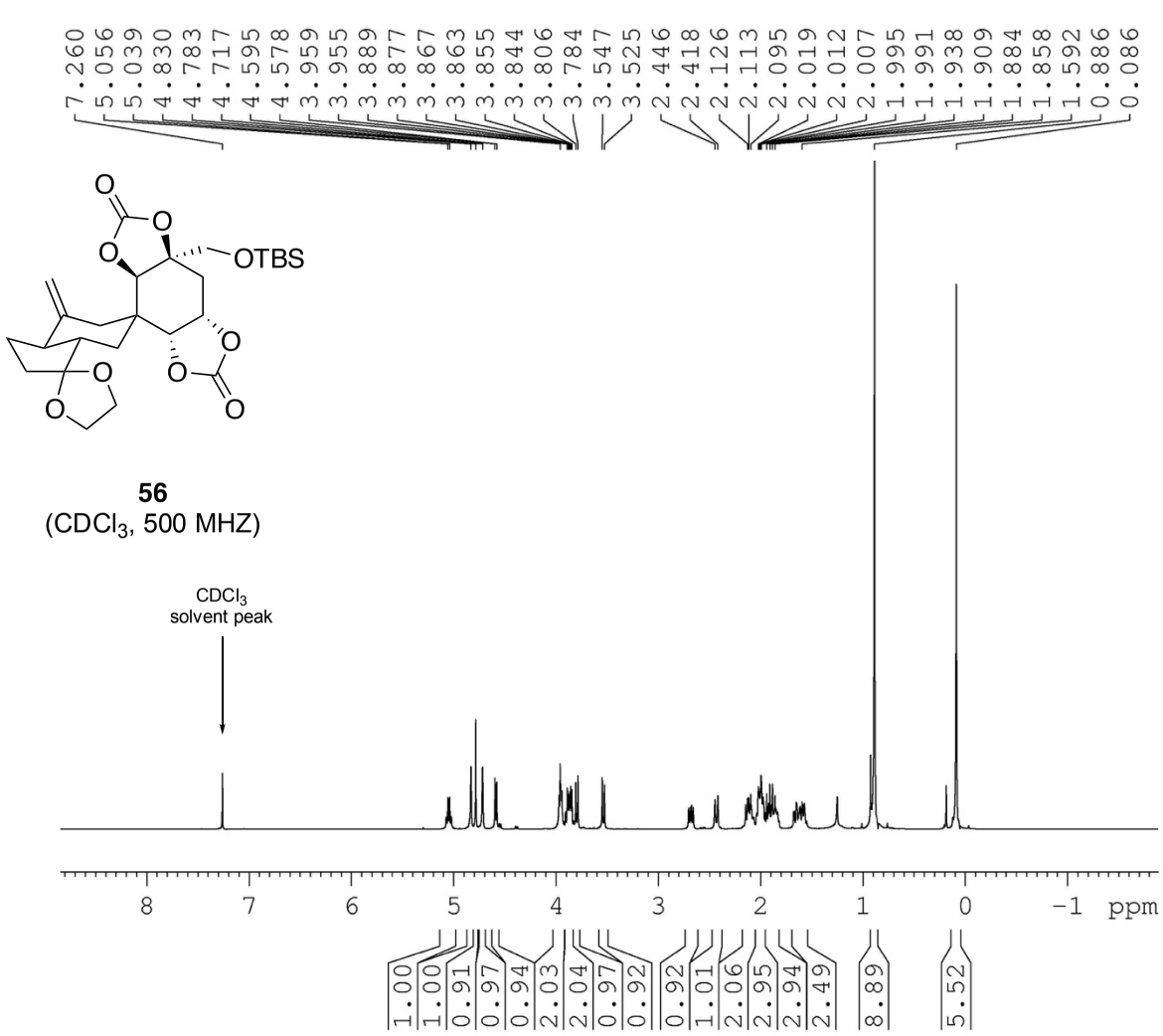
NAME	ZYA-XIII-diol-17-C-3
EXPNO	1
PROCNO	1
Date_	20191007
Time	0.17 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	56.75
DW	50.000 usec
DE	6.50 usec
TE	295.7 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700125 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



31
($CDCl_3$, 125 MHZ)

BRUKER

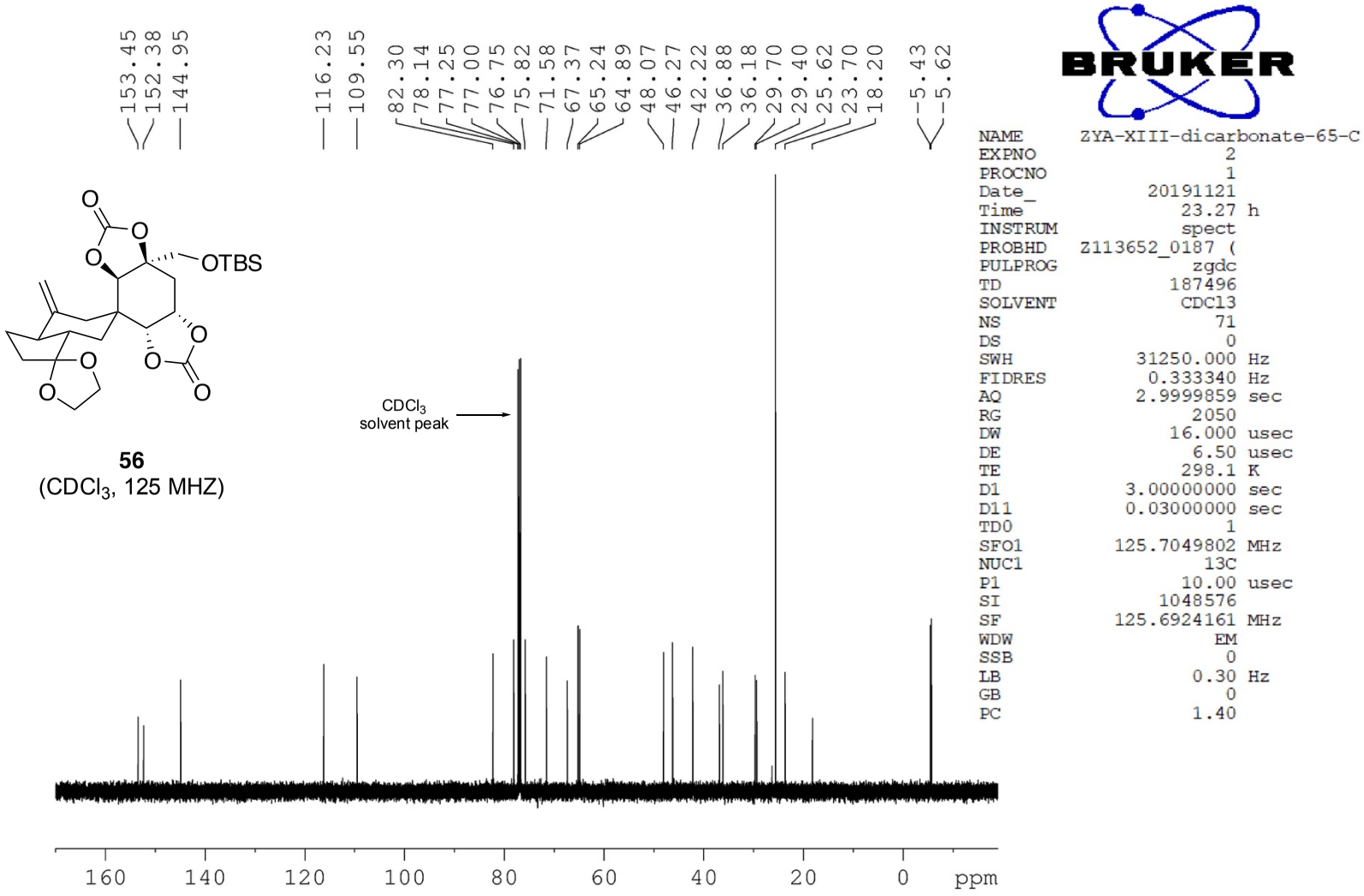
NAME	ZYA-XIII-diol-17-C-3
EXPNO	2
PROCNO	1
Date_	20191007
Time	1.13 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	521
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.0 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924134 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



56
($CDCl_3$, 500 MHZ)

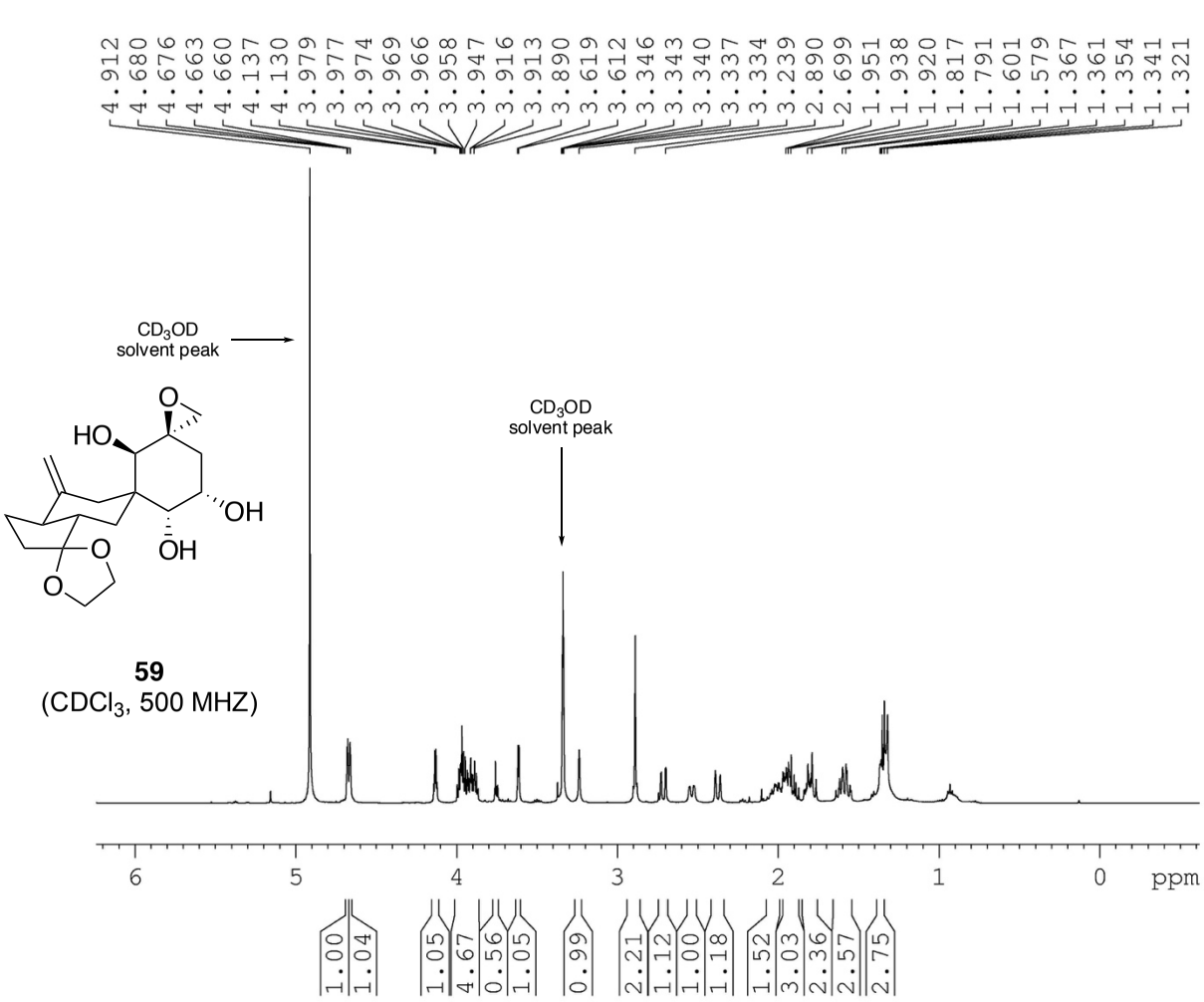
BRUKER

NAME	ZYA-XIII-dicarbonate-65-C
EXPNO	1
PROCNO	1
Date_	20191121
Time	23.18 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	37.92
DW	50.000 usec
DE	6.50 usec
TE	298.2 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700123 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



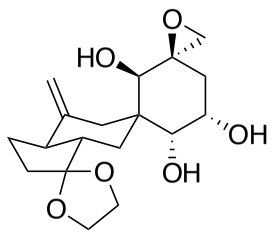
56
($CDCl_3$, 125 MHZ)

NAME	ZYA-XIII-dicarbonate-65-C
EXPNO	2
PROCNO	1
Date_	20191121
Time	23.27 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	71
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.1 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924161 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

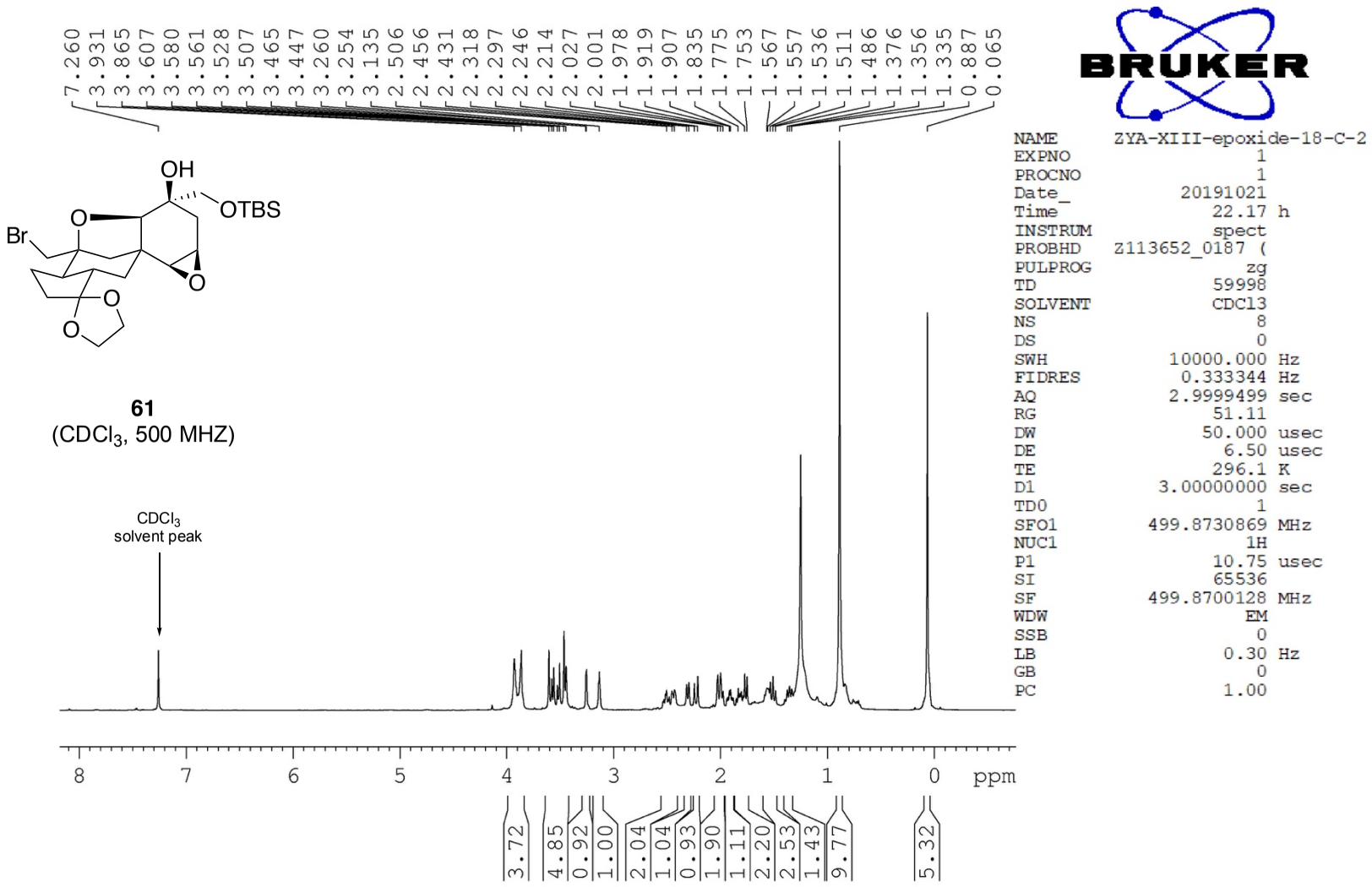
NAME	ZYA-XIII-epoxidetriol-76-C
EXPNO	1
PROCNO	1
Date_	20191205
Time	22.14 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CD3OD_SPE
NS	16
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	56.75
DW	50.000 usec
DE	6.50 usec
TE	295.2 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8699947 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



59
($CDCl_3$, 125 MHZ)

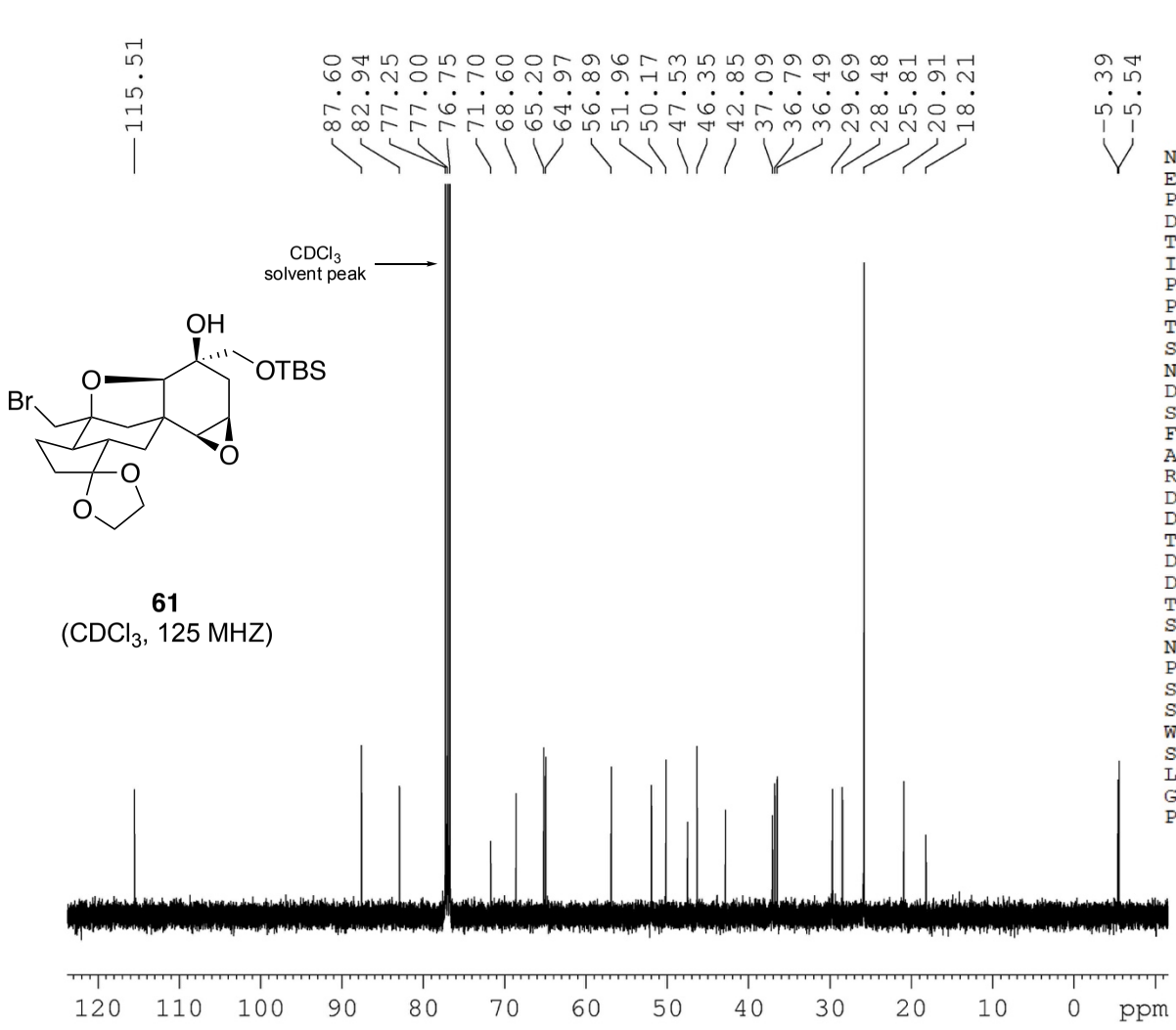
BRUKER

NAME	ZYA-XIII-epoxidetriol-76-C
EXPNO	2
PROCNO	1
Date_	20191205
Time	23.34 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CD3OD_SPE
NS	768
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	295.8 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6921271 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

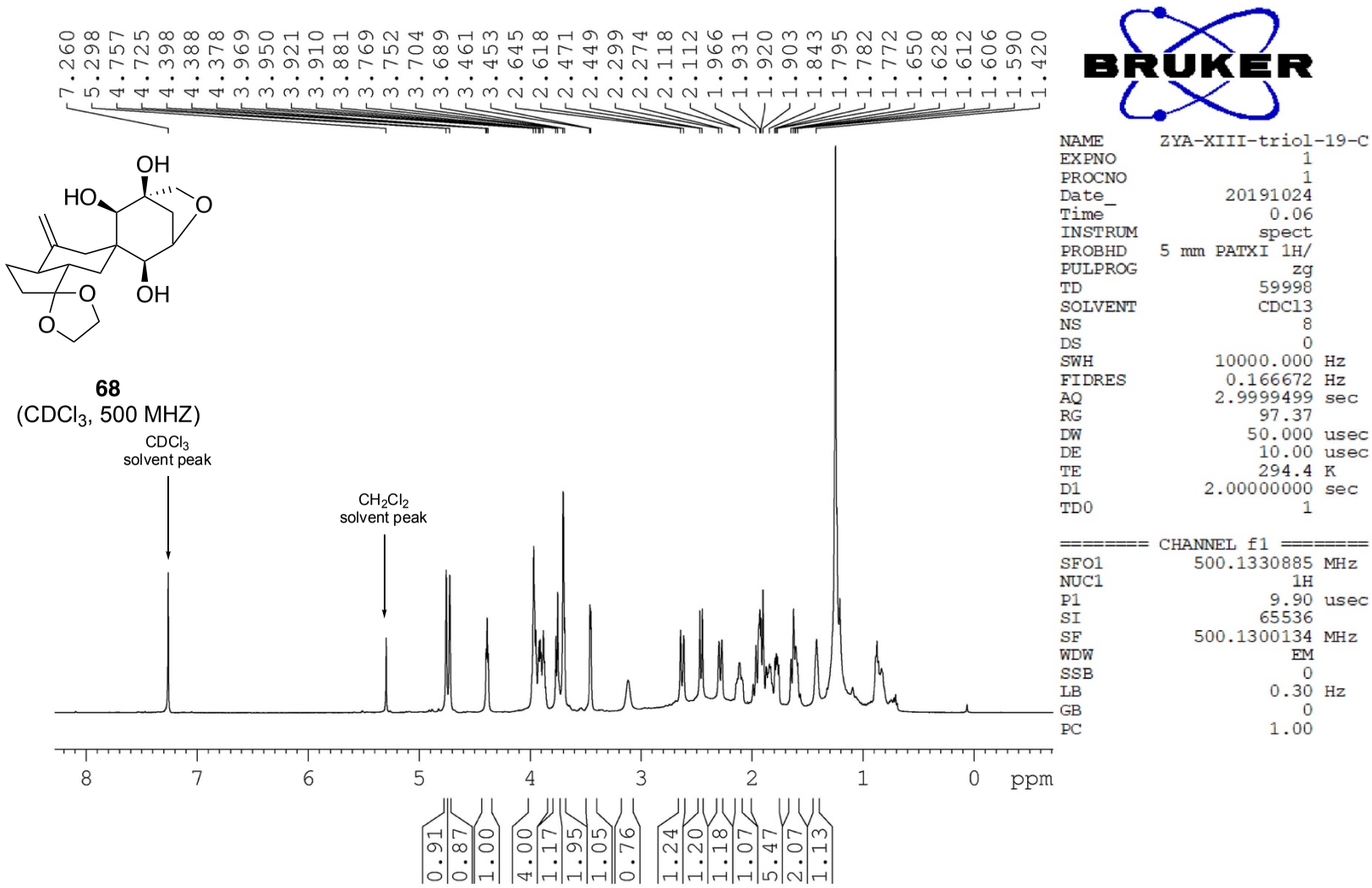
NAME	ZYA-XIII-epoxide-18-C-2
EXPNO	1
PROCNO	1
Date_	20191021
Time	22.17 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	51.11
DW	50.000 usec
DE	6.50 usec
TE	296.1 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700128 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



61
($CDCl_3$, 125 MHZ)

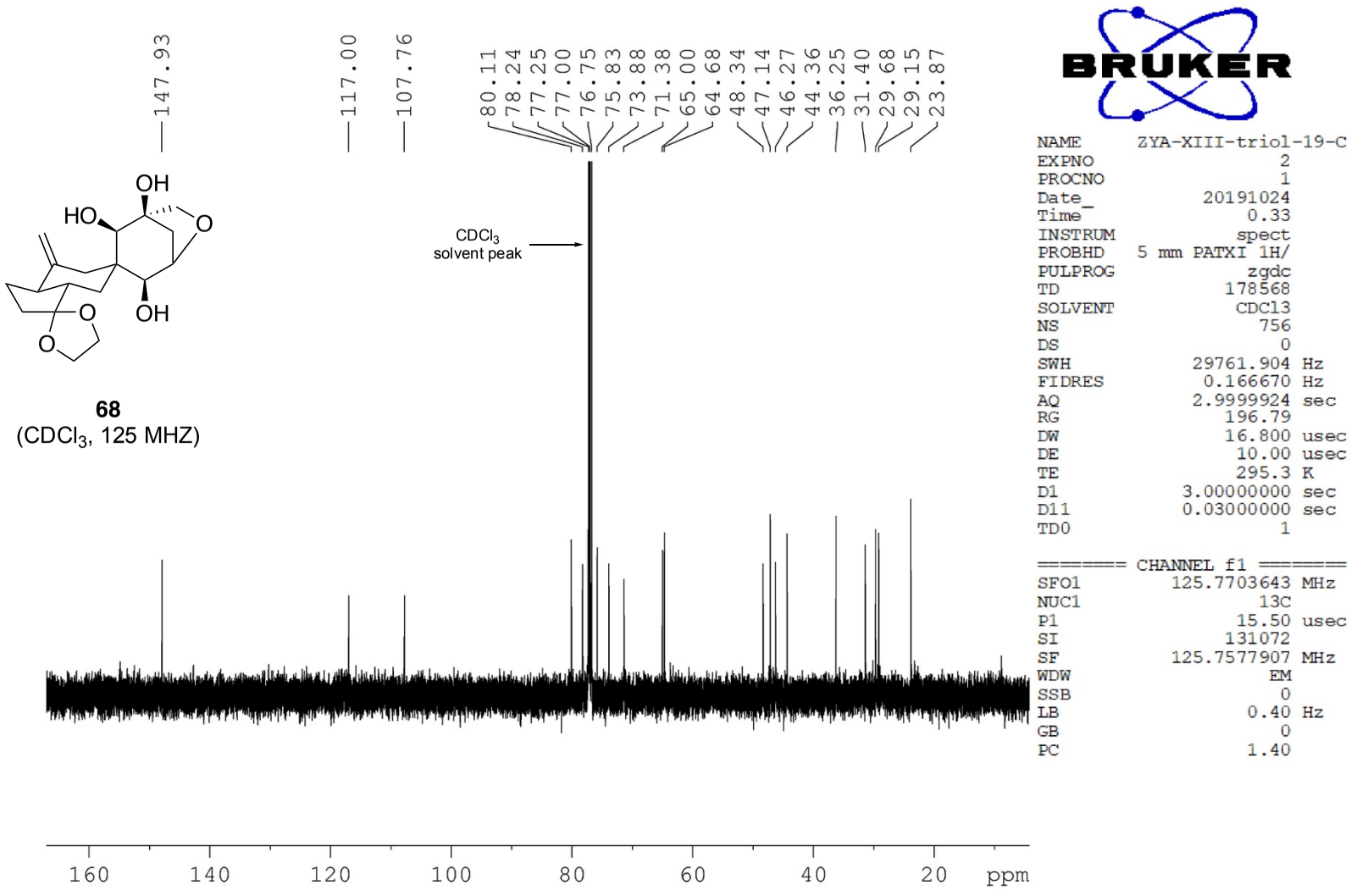
BRUKER

NAME	ZYA-XIII-epoxide-18-C-2
EXPNO	2
PROCNO	1
Date_	20191021
Time	23.04 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	307
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	296.4 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924134 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

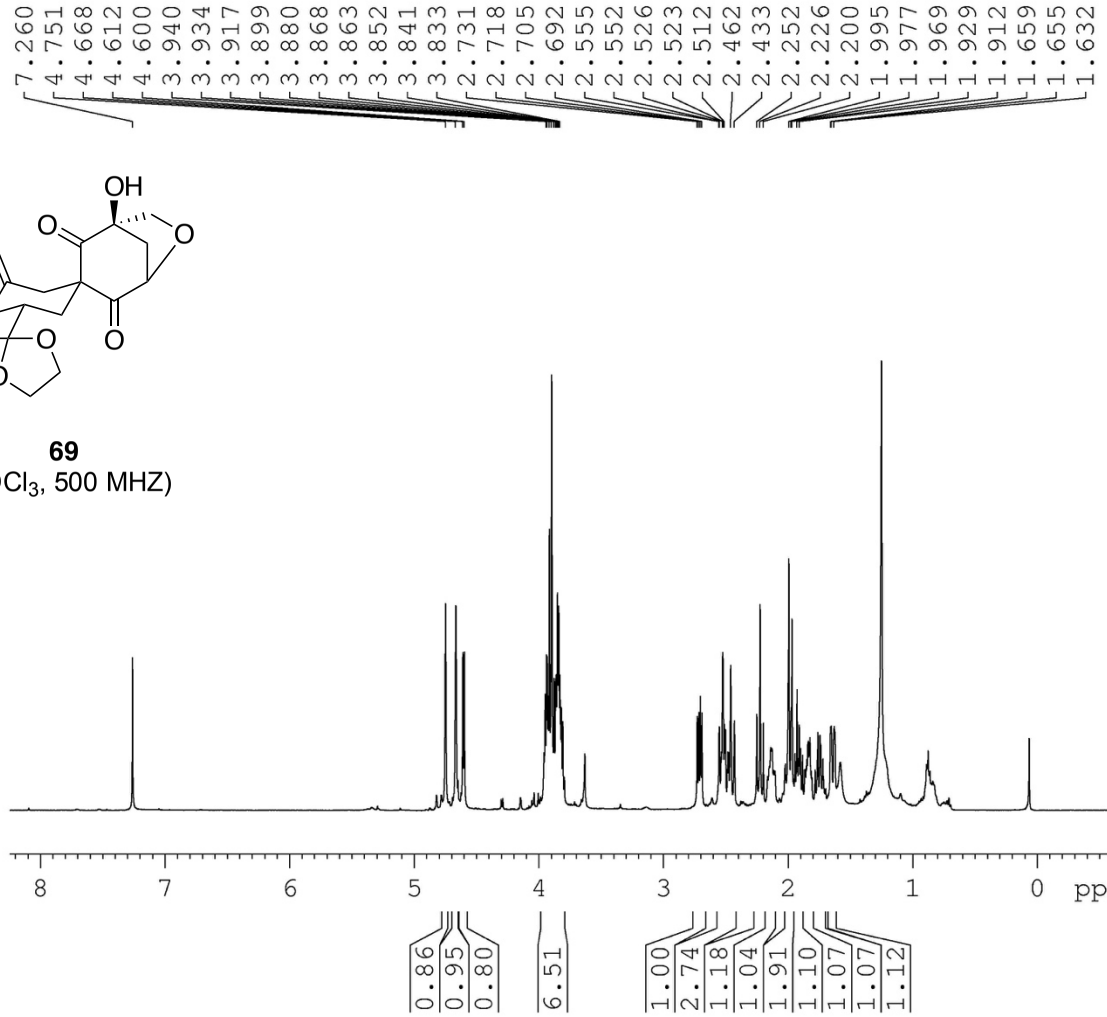
NAME	ZYA-XIII-triol-19-C
EXPNO	1
PROCNO	1
Date_	20191024
Time	0.06
INSTRUM	spect
PROBHD	5 mm PATXI 1H/
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.166672 Hz
AQ	2.9999499 sec
RG	97.37
DW	50.000 usec
DE	10.00 usec
TE	294.4 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	500.1330885 MHz
NUC1	1H
P1	9.90 usec
SI	65536
SF	500.1300134 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



68
($CDCl_3$, 125 MHZ)

BRUKER

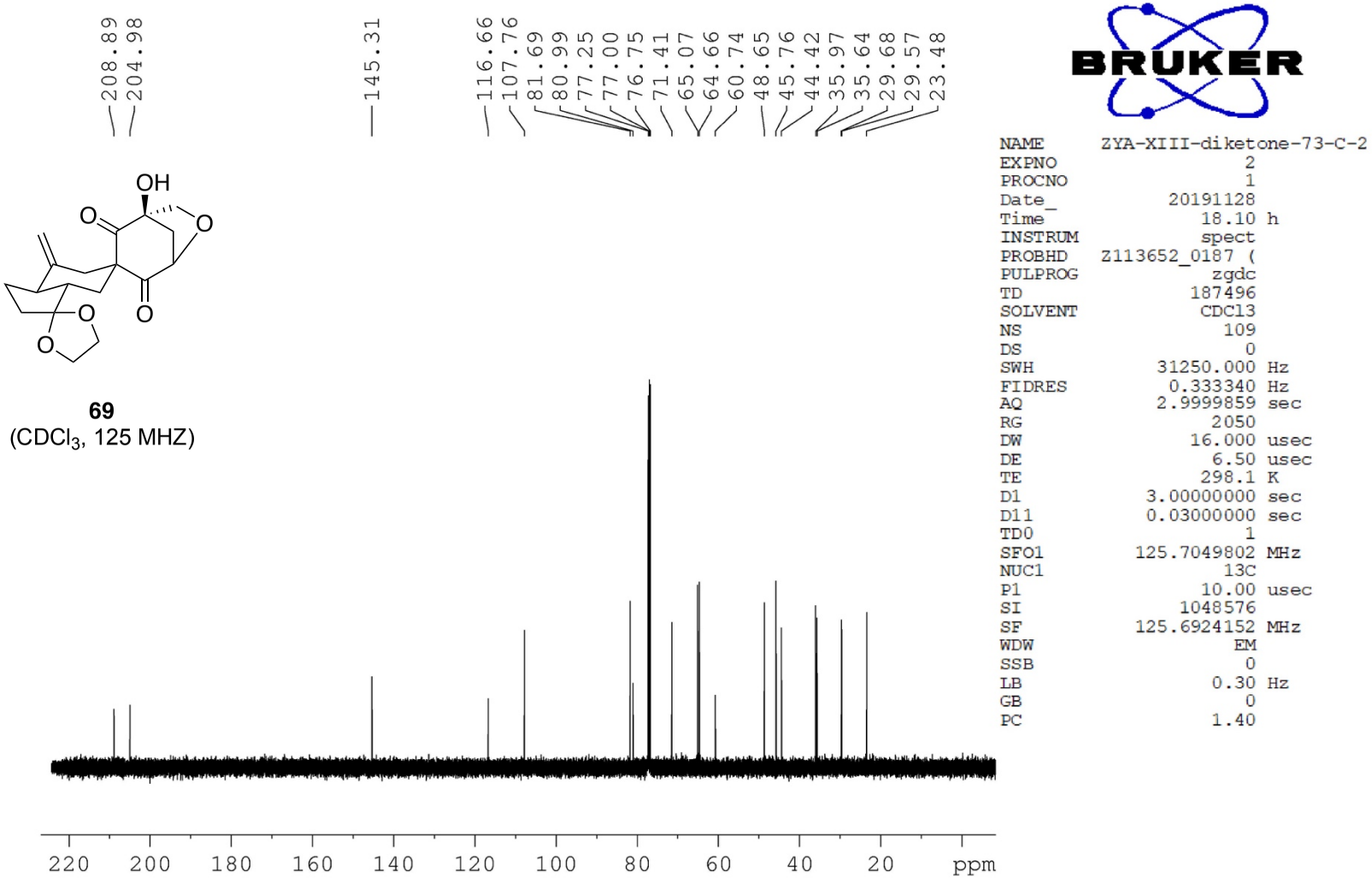
NAME	ZYA-XIII-triol-19-C	
EXPNO	2	
PROCNO	1	
Date_	20191024	
Time	0.33	
INSTRUM	spect	
PROBHD	5 mm PATXI 1H/	
PULPROG	zgdc	
TD	178568	
SOLVENT	CDCl3	
NS	756	
DS	0	
SWH	29761.904	Hz
FIDRES	0.166670	Hz
AQ	2.9999924	sec
RG	196.79	
DW	16.800	usec
DE	10.00	usec
TE	295.3	K
D1	3.00000000	sec
D11	0.03000000	sec
TD0	1	
======= CHANNEL f1 =======		
SFO1	125.7703643	MHz
NUC1	13C	
P1	15.50	usec
SI	131072	
SF	125.7577907	MHz
WDW	EM	
SSB	0	
LB	0.40	Hz
GB	0	
PC	1.40	



69
($CDCl_3$, 500 MHZ)

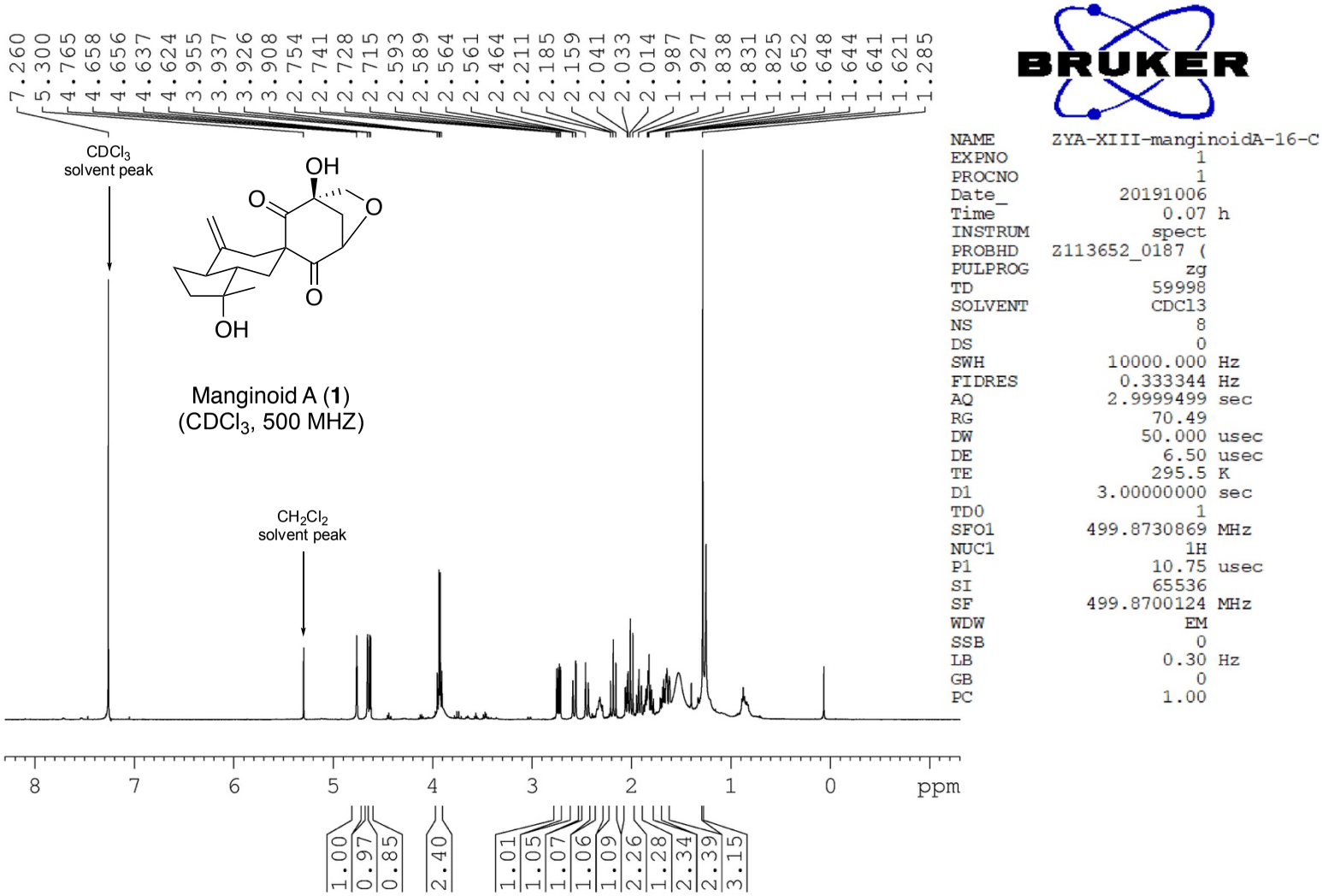
BRUKER

NAME	ZYA-XIII-diketone-73-C-2
EXPNO	1
PROCNO	1
Date_	20191128
Time	17.45 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	44.57
DW	50.000 usec
DE	6.50 usec
TE	298.2 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700123 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



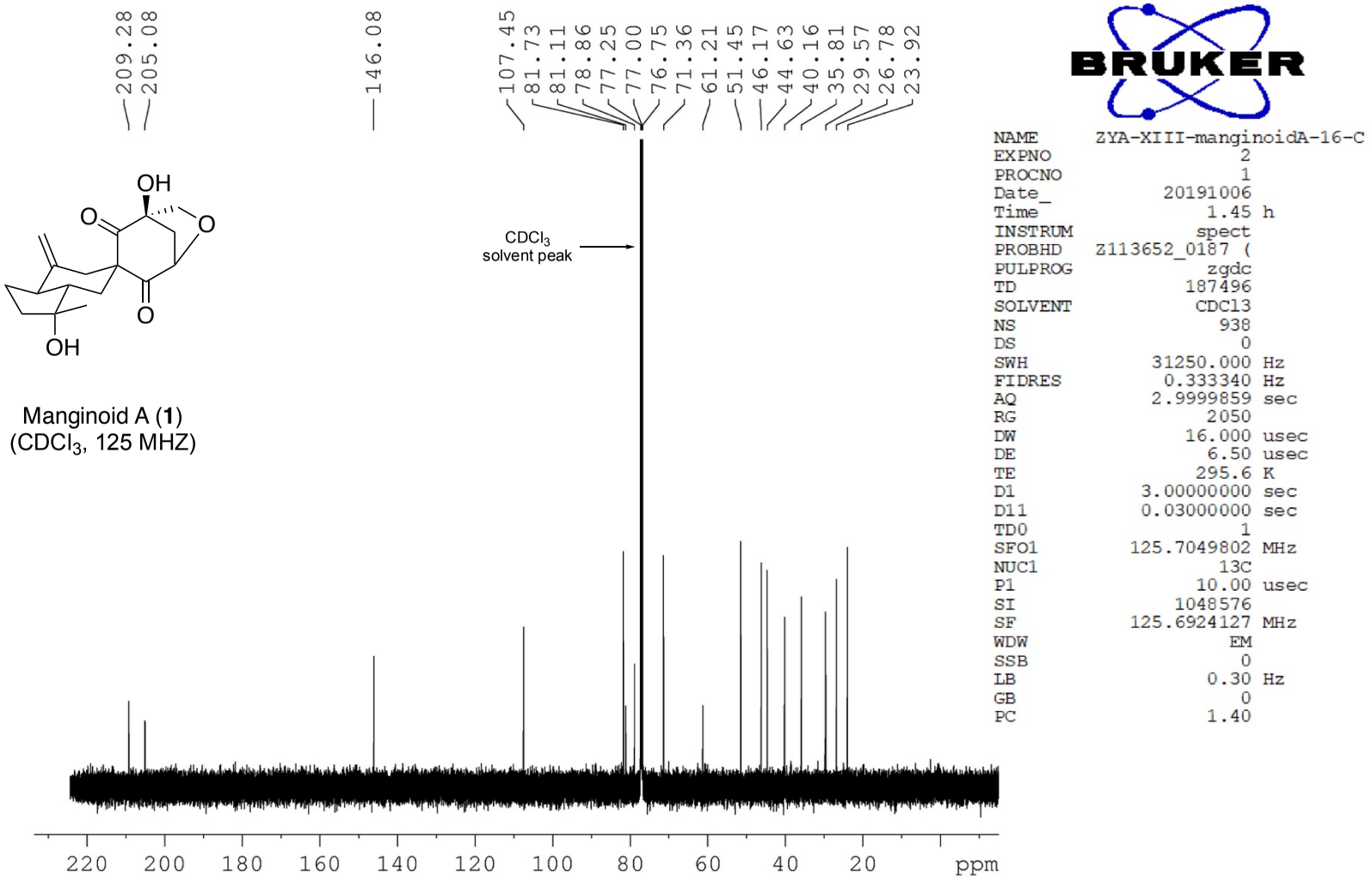
69
($CDCl_3$, 125 MHZ)

NAME	ZYA-XIII-diketone-73-C-2
EXPNO	2
PROCNO	1
Date_	20191128
Time	18.10 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	109
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	298.1 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924152 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40



BRUKER

NAME	ZYA-XIII-manginoidA-16-C
EXPNO	1
PROCNO	1
Date_	20191006
Time	0.07 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zg
TD	59998
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.333344 Hz
AQ	2.9999499 sec
RG	70.49
DW	50.000 usec
DE	6.50 usec
TE	295.5 K
D1	3.00000000 sec
TD0	1
SFO1	499.8730869 MHz
NUC1	1H
P1	10.75 usec
SI	65536
SF	499.8700124 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



Manginoid A (**1**)
($CDCl_3$, 125 MHZ)

BRUKER

NAME	ZYA-XIII-manginoidA-16-C
EXPNO	2
PROCNO	1
Date_	20191006
Time	1.45 h
INSTRUM	spect
PROBHD	Z113652_0187 (
PULPROG	zgdc
TD	187496
SOLVENT	CDCl3
NS	938
DS	0
SWH	31250.000 Hz
FIDRES	0.333340 Hz
AQ	2.9999859 sec
RG	2050
DW	16.000 usec
DE	6.50 usec
TE	295.6 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
SFO1	125.7049802 MHz
NUC1	13C
P1	10.00 usec
SI	1048576
SF	125.6924127 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.40