Strained Terpenes as Targets:
Total Synthesis of the Dichrocephone Sesquiterpenes
and
Studies towards Xenicane Diterpenes

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Hiermit versichere ich, die vorliegende Dissertation selbständig und ohne unerlaubte Hilfe angefertigt zu haben. Beim Verfassen der Dissertation wurden keine anderen als die im Text aufgeführten Hilfsmittel verwendet. Ein Promotionsverfahren zu einem früheren Zeitpunkt an einer anderen Hochschule oder bei einem anderen Fachbereich wurde nicht beantragt.

Volker Martin Schmiedel, Berlin, den 13.03.2018

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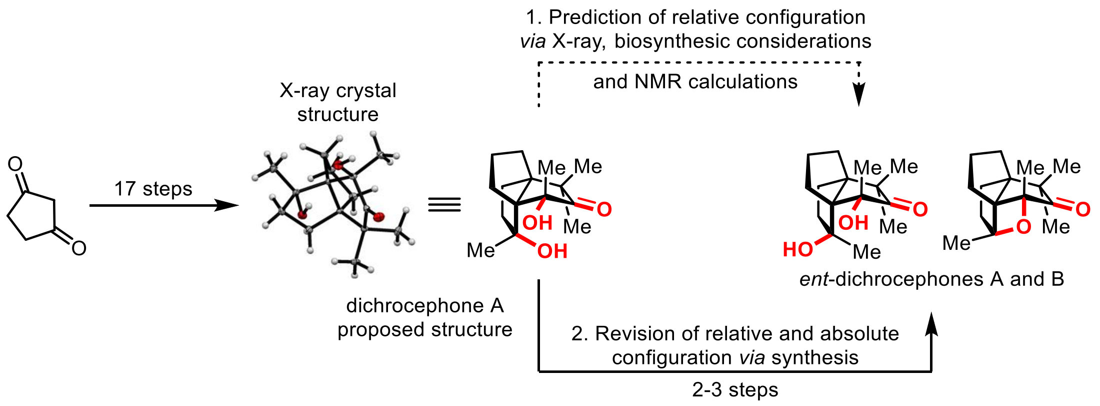
Abstract

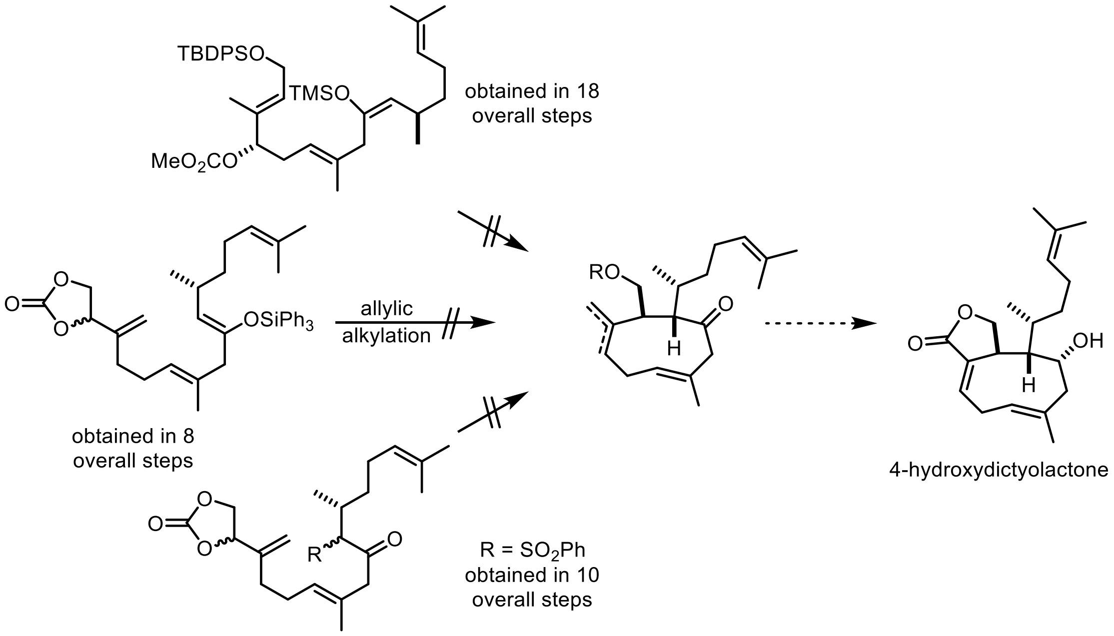
This thesis aimed at the total synthesis of three terpene natural products, which exhibit strain due to their unusual carbocyclic structures. The main project describes the first total synthesis and structure revision of dichrocephones A and B. Both sesquiterpenes were isolated in 2013 from *Dichrocephala benthamii*, a flowering plant found in the south of China. Their oxidation pattern and the inverted absolute configuration of their [3.3.3]propellane core proposed upon isolation, as well as the unique tetracyclic structure of dichrocephone B distinguish them from previously described compounds of the modhephane family.

A newly developed synthetic methodology for the enantioselective synthesis of the [3.3.3]propellane core was based on desymmetrization of prochiral triketones by a catalytic asymmetric Wittig reaction, vinyl cuprate addition and ring closing metathesis. Further key steps in the synthesis of the fully substituted cyclopentanone found in the natural products were the consecutive cyclopropanation and hydroxy-directed epoxidation of a pseudo-symmetric dienone. The obtained pentacyclic intermediate then underwent double reductive ring-opening to the proposed structure of dichrocephone A.



Mismatching spectroscopic data led to the conclusion that the structure of dichrocephone A was proposed falsely upon isolation. An interdisciplinary approach utilizing X-ray crystallography, biosynthetic considerations and NMR calculations led to the prediction of an epimer as the correct structure of the natural product. This prediction could be verified by synthetic modification of the proposed structure to both dichrocephones A and B. By comparison of the optical rotations with literature values, the absolute configurations were reassigned as well.

The second project was aimed at the synthesis of 4-hydroxydictyolactone, a xenicane diterpene isolated in 1993 from the brown alga *Dictyota ciliolata*. Several members of this natural product class show potent biological activities. An efficient synthetic approach to the (*E*)-cyclononene motif is still missing, which prevents further biological evaluation of these natural products due to the low yield of current synthetic approaches.

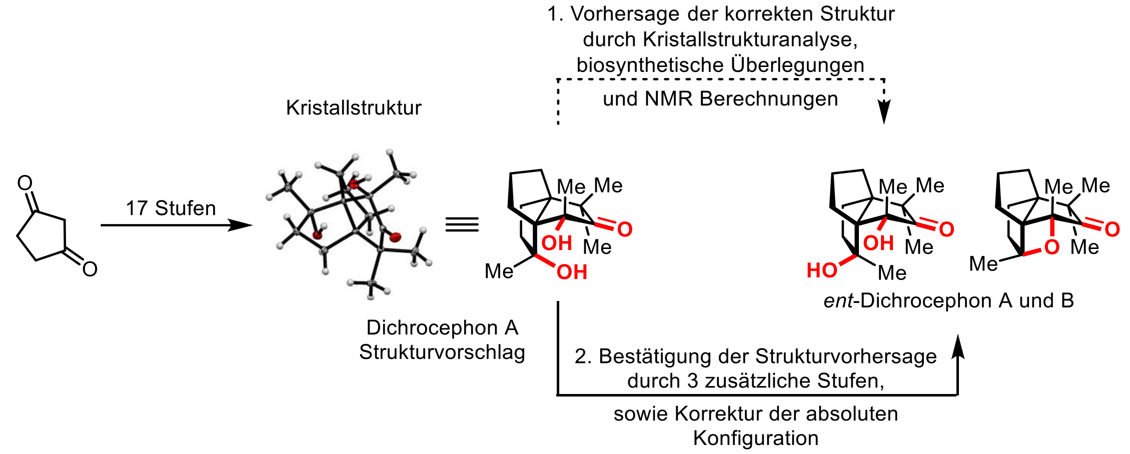


The approach described in this thesis was aimed at mimicking the proposed biosynthesis of the carbocyclic core, by ring formation from an acyclic precursor. Several substrates were employed in the envisaged allylic alkylation key step, which were obtained from terpene-pool starting materials. None of the substrates underwent formation of the nine-membered carbocycle. The failure of this strategy was attributed to the high strain energy, which needs to be overcome in the transition state of the cyclization.

Zusammenfassung

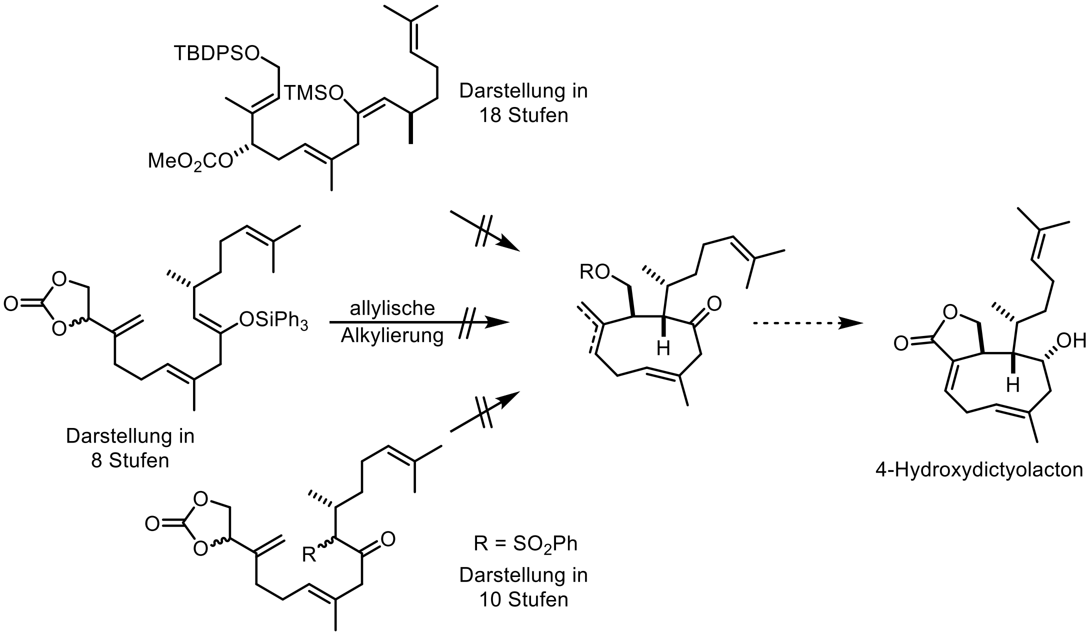
Die vorliegende Arbeit hatte die Totalsynthese drei gespannter Terpene zum Ziel. Der erste Teil beschreibt die Synthese und Strukturaufklärung der Sesquiterpene Dichrocephon A und Dichrocephon B, welche 2013 aus *Dichrocephala benthamii* im Süden Chinas isoliert wurden. Sie unterscheiden sich von anderen Vertretern der Modhephane durch ihr ungewöhnliches Oxidationsmuster, die invertierte absolute Konfiguration ihres Propellangerüsts und die tetracyclische Struktur von Dichrocephon B, welche noch in keinem anderen Naturstoff beobachtet wurde.

Die in dieser Arbeit beschriebene Methode zum enantioselektiven Aufbau des [3.3.3]Propellangerüsts basiert auf Desymmetrisierung durch eine katalytische, asymmetrische Wittig-Reaktion, nachfolgende Cuprat-Addition und abschließende Ringschlussmetathese. Die Synthese der ursprünglich vorgeschlagenen Struktur von Dichrocephon A konnte durch Cyclopropanierung und gerichtete Epoxidierung eines Dienons mit anschließender reduktiver Öffnung der beiden Dreiringe abgeschlossen werden.



Dieser Strukturvorschlag von Dichrocephon A stellte sich jedoch als nicht korrekt heraus. Durch einen interdisziplinären Ansatz, Kristallstrukturanalyse in Kombination mit biosynthetischen Überlegungen und NMR Berechnungen, konnte eine korrigierte Strukturvorhersage getroffen werden. Diese wurde durch drei zusätzliche synthetische Schritte bestätigt, was zusätzlich zur Korrektur der absoluten Konfiguration von Dichrocephon A und Dichrocephon B führte.

Der zweite Teil der Arbeit hatte die Synthese von 4-Hydroxydictyolacton zum Ziel, einem Xenican-Diterpen, welches 1993 aus der Alge *Dictyota ciliolata* isoliert werden konnte. Vertreter dieser Substanzklasse zeigen vielversprechende biologische Aktivitäten. Eine genauere Untersuchung ist jedoch bislang nicht möglich gewesen, da noch keine effiziente Methode zur Darstellung des zugrundeliegenden (*E*)-Cyclononen-Motivs beschrieben wurde.



Der synthetische Ansatz, den diese Arbeit verfolgte, orientiert sich an der vorgeschlagenen Biosynthese der Substanzklasse. Diverse Ringschlussvorläufer, welche den 9-gliedrigen Ring direkt aus einem linearen Molekül aufbauen sollten, konnten aus Terpenvorläufern dargestellt werden. Ein erfolgreicher Ringschluss war jedoch nicht möglich. Es wird angenommen, dass dies auf die hohe Ringspannung zurückzuführen ist, welche beim Aufbau dieses Motivs überwunden werden muss.

Parts of this thesis were already published in:

“Synthesis and Structure Revision of Dichrocephones A and B”
Volker M. Schmiedel, Young J. Hong, Dieter Lentz, Dean J. Tantillo, Mathias Christmann, *Angew. Chem. Int. Ed.* **2018***, 57*, 2419; *Angew. Chem.* **2018**, *130*, 2443.

“Asymmetric Synthesis of Carbocyclic Propellanes”
Lisa M. Schneider, Volker M. Schmiedel, Tommaso Pecchioli, Dieter Lentz, Christian Merten, Mathias Christmann, *Org. Lett.* **2017**, *19*, 2310.

1. Motivation and Background

1.1. Natural Product Synthesis

The development of chemical synthesis has made an impact on modern civilization that can hardly be exaggerated. Since the early 19th century, the chemical industry enabled the growth of human population to its current state, and allowed us to become older while maintaining higher standards of living. Organic synthesis has been responsible for advances in medicine, materials science and pest control among numerous other fields. Besides the production of chemicals on an industrial scale, the exploration of new synthetic routes to complex molecules on a laboratory level has been constantly pursued, and is not restricted to academic curiosity. To explain to outsiders why this scientific discipline retains its fascination after 200 years of development, some enthusiasts compare the development of a complex molecule synthesis to a game of chess[1] or the unfolding of classical Greek literature.[2] Others draw comparisons to mountaineering[3] or architecture[4] to reflect the continuous need for new techniques and methodologies, which drive the field ahead.

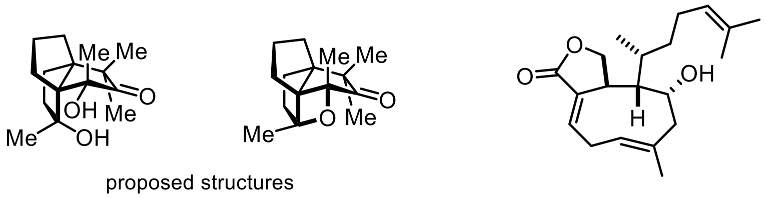
In search for challenging objectives chemists often turn towards nature, which offers a plethora of complex molecular scaffolds. Organisms employ a near endless variety of secondary metabolites, and often only a single species evolved to produce a specific compound. These comparably small molecules, referred to as natural products by chemists, often serve important ecological functions. They may protect the organism from predators, attract sexual partners or are necessary to survive under extreme environmental conditions. Humans have been utilizing some of these compounds for millennia: in religious rites,[5] as flavors and fragrances,[6] or to treat diseases.[7] Emerging with the ability to specifically alter the structure of organic molecules, natural products were used as leads in medicinal and pesticide chemistry. In these cases, the secondary metabolite serves as a starting point for optimization of its properties by chemical derivatization, due to promising biological activity upon *in-vitro* screenings after the initial isolation.[8] The success of this strategy is reflected in the fact that 25% of drugs approved since 1981 are unaltered or derivatized natural products.[9]

One inherent disadvantage for the application of secondary metabolites is their low yield of extraction from the producing organisms, which is often unable to fulfill the human demand for these compounds. The development of a synthetic route from readily available starting materials may provide larger amounts of the desired molecule.

The synthesis of natural products also serves other purposes: unprecedented structural features of isolated substances intrigue chemists by presenting new synthetic challenges. This leads to the development of new methodologies, when known chemical reactions are deemed too ineffective to accomplish the task. A methodology initially intended to access a single natural product[10] is then introduced to the synthetic community, further developed, and finally utilized as a tool for the synthesis of compounds that are not related to the original target molecule.[11]

Due to the small amounts of natural products isolated from nature, their unprecedented structural motifs and the inherent limitations of available analytical techniques, the total synthesis of a natural product often serves as final proof of its structure.[12] Where a false structure was proposed, the first synthesis leads to revision of the natural product, often supported by X-ray crystallography of crystalline intermediates or the final product.

The presented thesis displays a case in which unusual structural features of two terpene classes led to curiosity-driven attempts at their syntheses. The intricate polycyclic structures of dichrocephones A and B (**1** and **2**, Figure 1) prompted the question, how their tricyclic carbon core could be accessed in an enantioselective way, while allowing further functionalization into the densely functionalized natural products. The herein developed methodology enabled the synthesis of the proposed structure of dichrocephone A (**1**), which did not correlate to the natural isolate. By an interdisciplinary approach, employing X-ray crystallography, biosynthetic reasoning and NMR calculations, the correct structure could be predicted from this initial result. Synthetic modification of the proposed structure finally led to verification of these predictions and the first total synthesis of dichrocephones A and B.



proposed structures

dichrocephone A (**1**) dichrocephone B (**2**) 4-hydroxydictyolactone (**3**)

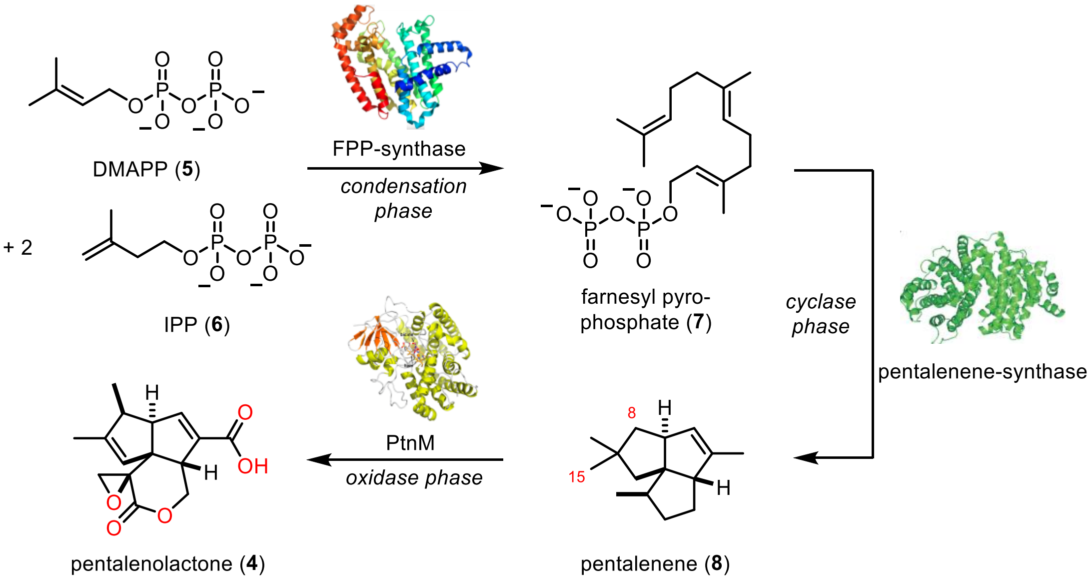
Figure 1: The target molecules approached in this thesis.

The second part of this thesis describes attempts to synthesize the xenican diterpene 4-hydroxydictyolactone (**3**, Figure 1). The employed retrosynthetic disconnection to this compound was aimed to mimic the pathway of its putative biosynthesis, by direct cyclization of an acyclic precursor. The motivation was to allow for biological screenings of larger amounts of the target molecule, a task which could not be accomplished by the previously described total synthesis.

All three molecules shown in Figure 1 are terpenes exhibiting strain due to the substitution pattern and spatial orientation of their carbocyclic structures. The two following chapters give a short introduction to the biosynthesis of terpene natural products, how strain is caused and how similarly strained structures have been synthesized in the recent past.

1.2. Biosynthesis of Terpene Natural Products

Terpenes are the structurally most diverse and fascinating class of natural products, with more than 50.000 isolated compounds to date.[13] These range from small, volatile monoterpenes such as menthol to larger, polycyclic compounds such as lanosterol, a triterpene that acts as the biosynthetic precursor for all steroids in higher animals.[14] The shared biosynthesis[15] of these molecules consists of specific phases, which are exemplified at pentalenolactone (**4**),[16] an antibiotic sesquiterpene isolated in 1957 (Scheme 1).



Scheme 1: The phases of terpene biosynthesis, exemplified at sesquiterpene pentalenolactone (**4**). Reprinted and adapted with permission from PICARD *et al.*[17] ((© 2018, Elsevier), DICKSCHAT[13] (© 2015, Royal Society of Chemistry) and DUAN *et al.*[18] (© 2016 American Chemical Society).

In the first phase, a transferase-catalyzed condensation of dimethylallyl pyrophosphate (**5**, DMAPP) with one or more units of 3-isopentenyl pyrophosphate (**6,** IPP) forms an acyclic terpene pyrophosphate, which determines the size of terpene that is later formed. The condensation reaction ultimately leading to pentalenolactone is catalyzed by farnesyl pyrophosphate synthase (FPPS), an enzyme encountered in a wide variety of biological organisms that produce sesquiterpenes,[19] and produces farnesyl pyrophosphate (**7**). In this thesis sesquiterpenes, formed by condensation of DMAPP (**5**) with two units of IPP (**6**), and diterpenes, which are formed with three equivalents of **6** are discussed.

In the next phase shown in Scheme 1, a type I cyclase enzyme folds the acyclic terpene pyrophosphate into a highly specific conformation. An allylic cation is generated by diphosphate abstraction, which cyclizes with one or more olefins in the chain that in turn are acting as the nucleophile. Other reactions in this cyclase phase consist of hydride shifts, methyl shifts and ring rearrangements, each of them transferring the positive charge to neighboring carbon atoms, which allows for an immense variety of cyclization possibilities. All intermediately build-up carbocations are stabilized by the enzyme, which steers the cyclization reaction into one specific uncharged hydrocarbon cyclization product. In the biosynthesis of **4**, the intermediate hydrocarbon is pentalenene (**8**), a tricyclic triquinane natural product, which has been identified 23 years after the initial isolation of **4** in the same source, *Streptomyces griseochomogenes*.[20] The large amount of possible cyclization pathways is reflected in over 120 hydrocarbon scaffolds of sesquiterpenes alone, which have been isolated from nature. With each additional IPP unit added in the condensation phase, the amount of possible cyclizations grows immensely.

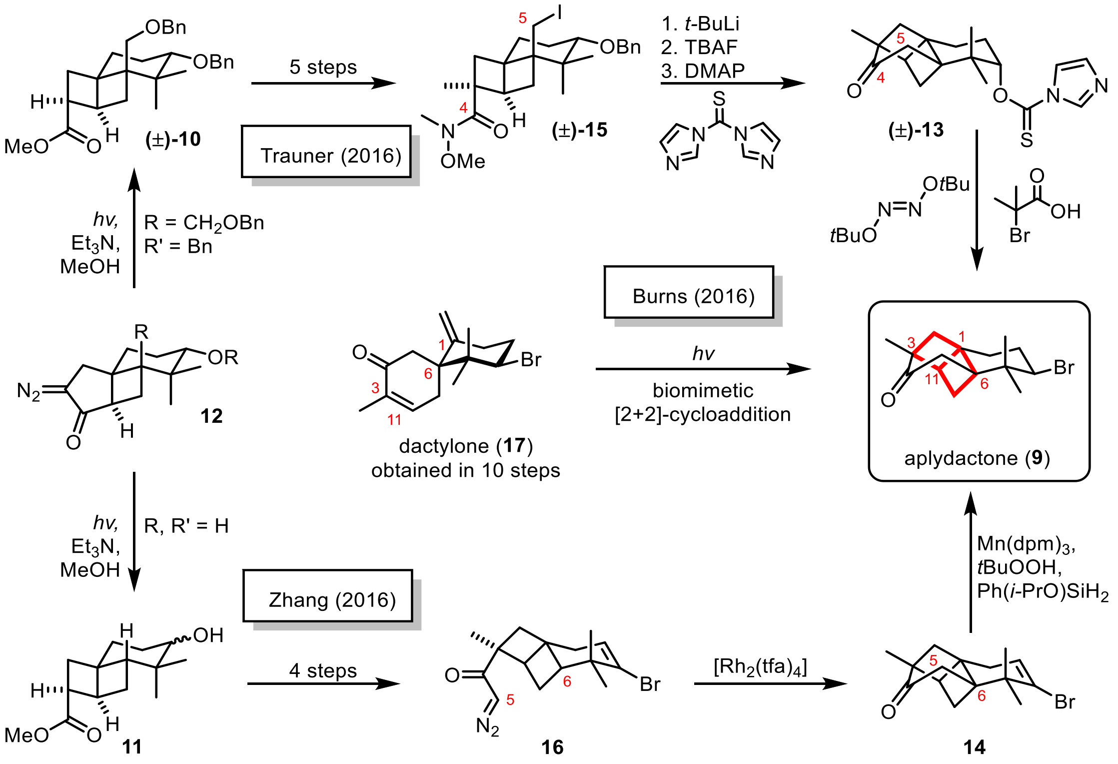
After cyclization, site specific oxidation of the (poly-)cyclic hydrocarbon occurs in the oxidase phase. Depicted in Scheme 1 is PtnM, a cytochrome P450 enzyme isolated from *Streptomyces arenae*, which was recently found to induce the last step of the biosynthesis of **4**.[18] It catalyzes the oxidative 1,2-alkyl shift of the C-15 methyl group in **8**, by C–H oxidation and generation of a carbocation at the neopentylic C-8 position. Detailed understanding of single steps in the oxidase phase of terpene biosynthesis is rarely described in literature, which reflects the complexity of the involved transformations. Nonetheless, this enzymatic introduction of functional groups into the carbon scaffold allows the biosynthesis of a large variety of secondary metabolites from the same cyclase product. The oxidation pattern of the final product is highly important for the bioactivity of the compound and thus the role of the molecule in the organism.

The large number of terpenes, which are produced by this shared biosynthesis, can adopt a wide variety of structural features, ranging from a plethora of unique ring systems and incorporation of different heteroatoms to the reaction with other secondary metabolites, leading to new natural product subclasses.[21]

1.3. Strained Terpenes – Occurrence and Synthesis

The described biosynthetic principle may build up one or more structural motifs that induce strain in the final terpene. The corresponding natural products are higher in energy than expected, which can be determined by comparison of their heats of combustion with calculated values of the unstrained molecules.[22] It often remains unclear why nature invests additional energy to synthesize these strained natural products from the acyclic starting materials. Due to the small yield of extraction, biological evaluation of most secondary metabolites is limited to their potential activity in humans, rather than their initial purpose in the producing organism. Total synthesis might contribute to these intriguing questions by providing larger amounts of strained terpenes for further studies. But obtaining these molecules by chemical synthesis bears an additional challenge: the higher energy observed for the natural product directly correlates to the activation enthalpy in the transition state of the reaction that builds up the strained motif. This has been shown for the synthesis of unsubstituted cycloalkanes, for which data was available for all ring sizes, and is universally valid for cyclization reactions.[23] A higher activation enthalpy for the cyclization step is therefore to be expected in the synthesis of highly strained molecules. This might also increase the probability for the starting material to undergo undesired side reactions. Nonetheless, these unusual structural features often inspire chemists to attempt their total syntheses, which has led to the development of new synthetic methodologies necessary to overcome the unprecedented challenges. Examples of creative approaches towards strained terpenes published over the course of this thesis are described in the following section, with a focus set on the steps that install the strained motifs.

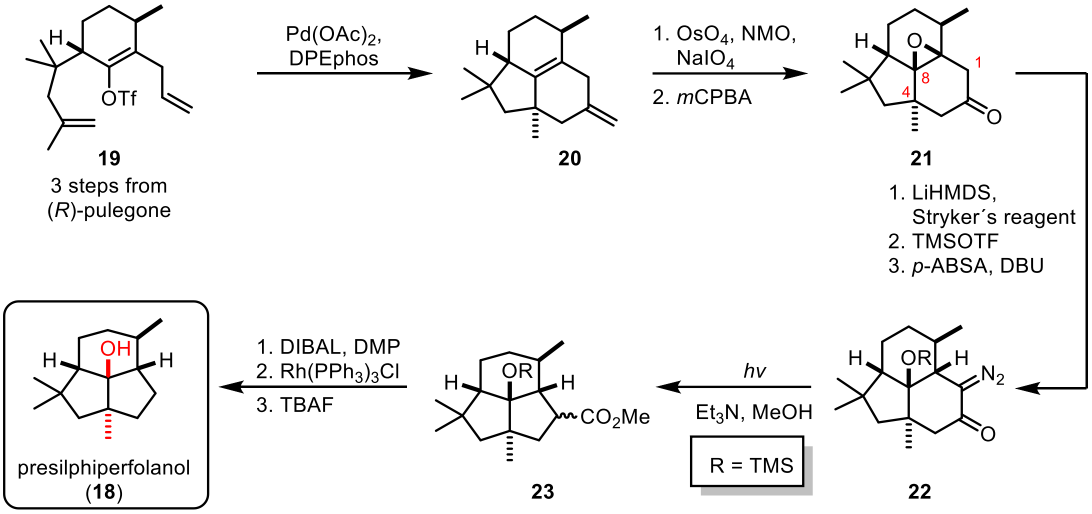
The most common structural motifs exhibiting strain are small carbocycles, with cyclopropane (29 kcal/mol) and cyclobutane (26 kcal/mol) being the most strained in a row of cycloalkane homologs.[22] Both compounds mostly show Baeyer strain,[22] which is caused by angles between C–C bonds deviating from the ideal tetrahedral geometry expected from these formally sp^3-hybridized carbon atoms. Additionally, the low conformational freedom in these systems leads to torsional strain, caused by the eclipsing of vicinal hydrogen atoms or larger substituents. These effects can be utilized in a variety of synthetic methodologies, which are based on facile opening of small cyclic molecules due to strain release.[24] A prominent example of a recently synthesized terpene, in which the strain of the compound is caused by small rings in the carbocyclic scaffold is aplydactone (**9**, Scheme 2). Upon isolation from the sea hare *Aplysia dactylomela* in 2001,[25] the structure of this tetracyclic compound was unambiguously confirmed by X-ray crystallography. Although no energy values for the natural product were given, the strain of the bicyclo[2.2.0]hexane system (ladderane) is apparent from the highly distorted C–C bond angles of 85° to 87° for the four adjacent carbon atoms C-1, C-3, C-6 and C-11. The first synthesis of **(±)-9** has been reported 15 years after its isolation by Trauner and coworkers,[26] and was shortly followed by two enantioselective syntheses, which have been performed by the groups of Burns[27] and Zhang.[28] Both Trauner and Zhang follow similar approaches, in that their groups employ a Wolff-rearrangement[29] to build up the strained ladderanes **(±)-10** and **11** by ring contraction from the less strained bicyclo[3.2.0]heptane systems **12** (Scheme 2, top and bottom).



Scheme 2: Strategies employed by Trauner, Burns and Zhang to obtain aplydactone (**9**). The strained ladderane system of the natural product is highlighted in red.

Both strategies differ mainly in their respective approaches to the cyclohexanone systems **(±)-13** and **14**. Whereas Trauner facilitates C-4/C-5 bond formation by intramolecular attack of an organolithium species to a Weinreb amide **(±)-15**,[30] Zhang forms the neighboring C-5/C-6 bond by a Rh-catalyzed intramolecular C–H bond insertion in **16**, a methodology that was developed in the same group. In contrast to these approaches, Burns employs a biomimetic strategy, directly following the synthesis of aplydactone (**9**) from its biosynthetic precursor dactylone (**17**). This natural product, which can also be found in *Aplysia dactylomela,* was obtained by BURNS in ten steps and underwent a photoinduced [2+2]-cycloaddition upon careful irradiation at 350 nm. This led to the formation of two carbocycles and three stereogenic centers in a single, reagent-free step (Scheme 2, center). The approach by BURNS shows impressively that the synthesis of such complex strained terpenes can be simplified by following the biosynthetic precedent, allowing fast retrosynthetic disconnections to simpler intermediates.

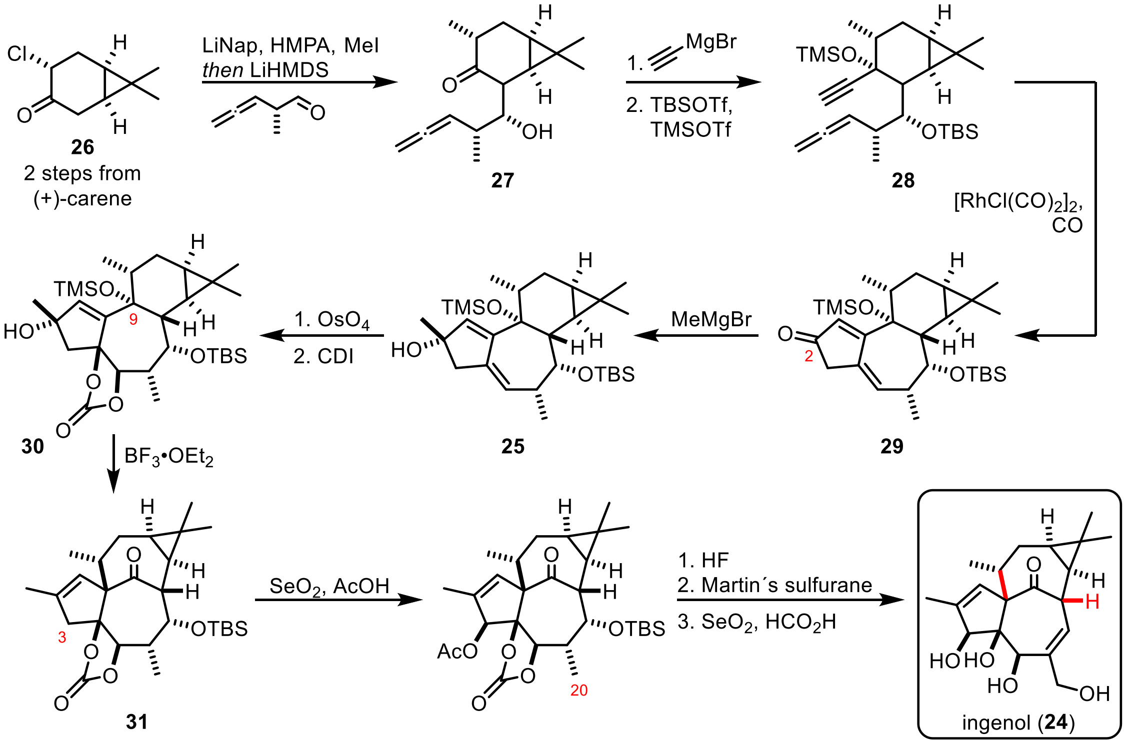
Strained terpenes can also be formed when no small cycloalkane is present in the molecule. In these cases unusual substitution patterns of the polycyclic system often cause the observed strain, as seen in presilphiperfolanol (**18**, Scheme 3), which has been isolated in 1981 from *Eriophyllum staechadifolium*.[31] This fused tricyclic sesquiterpene is built up of two cyclopentanes and one cyclohexane, which typically show no bond angle distortions. But the 1,2-*trans* fusion of the bicyclo[3.3.0]octane motif, which has been observed in only 35 natural products to date, adds approximately 13 kcal/mol of strain to **18**. This is caused by the unfavored spatial arrangement of the skeletal bonds, as shown by studies performed by WERTZ and coworkers.[32]



Scheme 3: Synthesis of presilphiperfolanol (**18**) by SNYDER. The strained 1,2-*trans*-fusion of the natural product is highlighted in red.

Presilphiperfolanol (**18**) has been synthesized for the first time in 2017 by SNYDER and coworkers.[33] Their strategy is based on a newly developed Heck-cyclization[34] cascade to access the tricyclic core of the natural product. Employing this methodology, triflate **19** is converted into the bicyclo[4.3.0]nonene system **20** in a single step. A subsequent stereoselective epoxidation yields **21**, implementing the oxygen functionality at C-8 in the desired *trans*-relation to the methyl group at C-4. After additional functionalization of C-1 to the corresponding α-diazoketone **22**, the bicyclo[4.3.0]nonane is converted to the strained bicyclo[3.3.0]octane **23** by a photo-induced Wolff-rearrangement, comparable to the syntheses of aplydactone by TRAUNER and ZHANG. Further C–C bond cleavage of this intermediate yields the natural product **18**.

Strain caused by orientation of the substituents can also be observed in larger carbocycles. The complex diterpene ingenol (**24**) was isolated in 1968 from *Euphorbia ingens*, and its structure could be unambiguously verified by X-ray crystallography.[35] The higher energy observed for this compound stems from the unique bicyclo[4.4.1]undecane system. The 7-membered rings in this bridged system are arranged in an *in,out*-configuration, which is approximately 10 kcal/mol higher in energy than the corresponding *out,out*-configuration, as shown by calculations performed on the pure hydrocarbon bicyclo[4.4.1]undecane.[36] The synthesis reported by BARAN and coworkers in 2013[37] follows an intriguing approach, in which the terpene biosynthesis is mimicked by a two-phase approach (Scheme 4).



Scheme 4: BARAN's total synthesis of ingenol (**24**), following a separated cyclase phase/oxidase phase approach. The strained *in,out*-substitution pattern of the natural product is highlighted in red.

Initial assembly of the complete carbon skeleton observed in **25** would correspond to the cyclase phase and was to be followed by further rearrangements and site-specific functionalizations, in analogy to the oxidase phase, to obtain the natural product **24**.

The synthesis commenced with ketone **26**, which is readily available from the chiral terpene pool in two steps and incorporates the cyclopropane of **24**. Consecutive alkylations of both α-positions of the carbonyl functionality gave allene **27**, which was further converted to the alkyne **28** in two additional steps. Synthesis of the tetracyclic system **29** was achieved by a Rh-catalyzed Pauson-Khand reaction. Addition of MeMgBr to the carbonyl functionality at C-2 produced **25**, corresponding to the carbon scaffold of the tigliane diterpenes, which marked the end of BARAN´S artificial cyclization phase.

Main goal of the subsequent oxidase phase was the envisaged 1,2-shift to obtain the *in,out*-bicyclo[4.4.1]undecane system of **24**. This could be achieved after dihydroxylation of **25** by desilylation of the TMS-silyl ether at C-9 of **30**. The allylic alcohol then underwent a vinylogous Pinacol-rearrangement to the desired bridged bicyclic system **31**, mimicking the putative biosynthesis of the ingenane diterpenes from the tigliane scaffold observed in **25**. Further Riley-oxidations at C-3 and C-20 completed the oxidation pattern of the natural product, which allowed the total synthesis of ingenol (**24**) in 14 overall steps. Prior syntheses of this compound have been reported by WINKLER in 2002,[38] KUWAJIMA in 2003[39] and NICKEL in 2004,[40] employing 37 to 45 synthetic steps. The more efficient biomimetic synthesis of the natural product developed by BARAN again underlines the usefulness of these transformations in total synthesis, comparable to the strategy of BURNS applied to aplydactone.

Motivation for theses syntheses had in case of aplydactone and presilphiperfolanol (**18**) come from the unusual structures themselves, or to showcase the application of a newly developed methodology. In the case of ingenol (**24**) the study was driven by the biological activity of the compound. The synthesis was developed to obtain larger amounts of ingenol-mebutate, which is tested as a medication against the pre-cancerous skin-condition actinic keratosis. Previously, both ingenol and ingenol-mebutate were obtained by isolation in 2-275 mg from 1 kg of dried plant material. The two-phase approach was then further developed to allow for the synthesis of tigliane natural product phorbol[41] and access a variety of ingenol derivatives, which were subsequently tested as potential protein kinase C activators.[42]

2. Total Synthesis of the Dichrocephone Sesquiterpenes

2.1. Introduction

2.1.1. Propellanes – Strain and Occurrence in Natural Products

An unusual motif of strain in natural products are propellanes: caged compounds in which three ring systems are annulated to a central C–C bond.[43] The term propellane stems from the shape of the molecule, with each carbocycle resembling a rotor blade when seen along the central bond. It was proposed by David Ginsburg, who published seminal work on the structure and synthesis of this motif.[44] Depending on the size of the rings, the bridgehead carbon atoms show a more or less inverted tetrahedral geometry, which is most strongly expressed in the smallest member, the [1.1.1]propellane **32** (Figure 2).

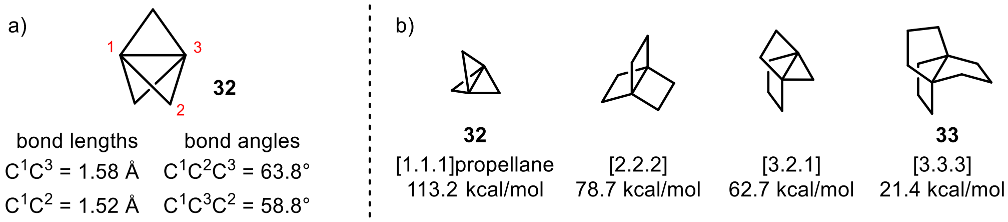
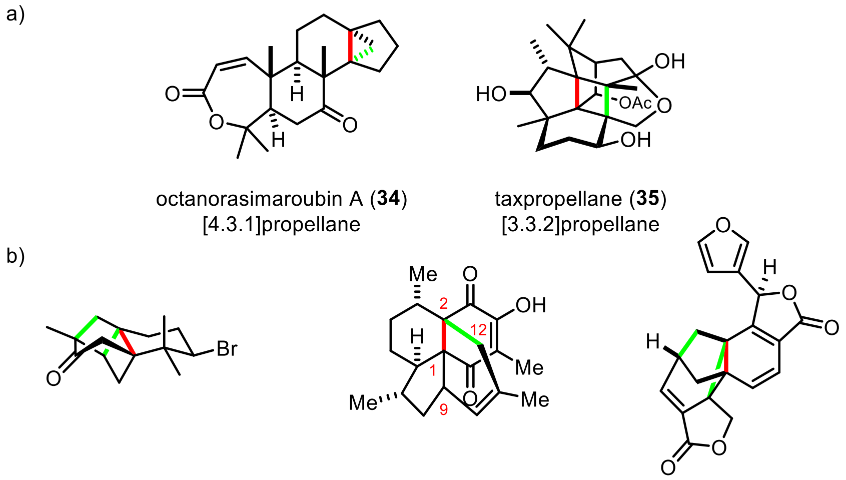


Figure 2: a) Bond lengths and angles in the smallest propellane **32** and b) calculated ring strain of selected carbocyclic propellanes.

The angles between the C–C bonds for **32** are highly distorted and range between 58.8° and 63.8°, much smaller than the typical tetrahedral angles of 109° at sp^3-hybridized carbon atoms. The C–C bond length between the bridgehead atoms is with 1.58 Å only slightly longer than that in regular hydrocarbons. Due to the unusual bond geometry at these bridgehead carbons the binding motif is still debated, with some studies describing small ring propellanes as completely distinct, and incomparable to other classes of hydrocarbons.[45] Extreme strain is observed in these compounds, e.g. 113.2 kcal/mol for the unfunctionalized [1.1.1]propellane (**32**). This makes **32** one of the most strained isolable compounds found to date. The strain can be utilized for facile nucleophilic ring opening reactions of the central bond, leading to bridgehead functionalized bicyclo[1.1.1]pentanes.[46] With larger ring sizes the binding motif becomes more similar to that of a typical tetrahedral sp^3-hybridized carbon atom, with 21.4 kcal/mol of ring strain observed for the unsubstituted [3.3.3]propellane **33**, which resembles the carbon core of the natural products discussed in this thesis. The calculated strain of **33** is thereby comparable to the small cycloalkanes, with values of 27.5 kcal/mol and 26.3 kcal/mol for cyclopropane and cyclobutane, respectively.

A wide variety of natural products with propellane motifs, in which at least one of the bridges contains a heteroatom, were isolated from natural sources.[47] The structurally simplest compounds stem from epoxidation of a tetrasubstituted double bond, but also alkaloids with amine bridges were reported. In contrast, natural products with purely carbocyclic propellanes as substructures rarely occur. Only a few natural product families are known, in which more than one compound shows this propellane structure (Figure 3a). Some steroids implement a cyclopropane in the CD-ring system, which results in a [4.3.1]propellane unit, as seen in octanorasimaroubin A (**34**). These are the most common carbocyclic propellane natural products.[48] Lately, some taxane derivatives like taxpropellane (**35**) have been isolated,[49] in which the propellane structure stems from a formal [2+2]cycloaddition. No synthesis of these compounds has been reported so far.



octanorasimaroubin A (**34**)
[4.3.1]propellane

taxpropellane (**35**)
[3.3.2]propellane

aplydactone (**9**)
[4.4.2]propellane

colombiasin A (**37**)
[4.4.4]propellane

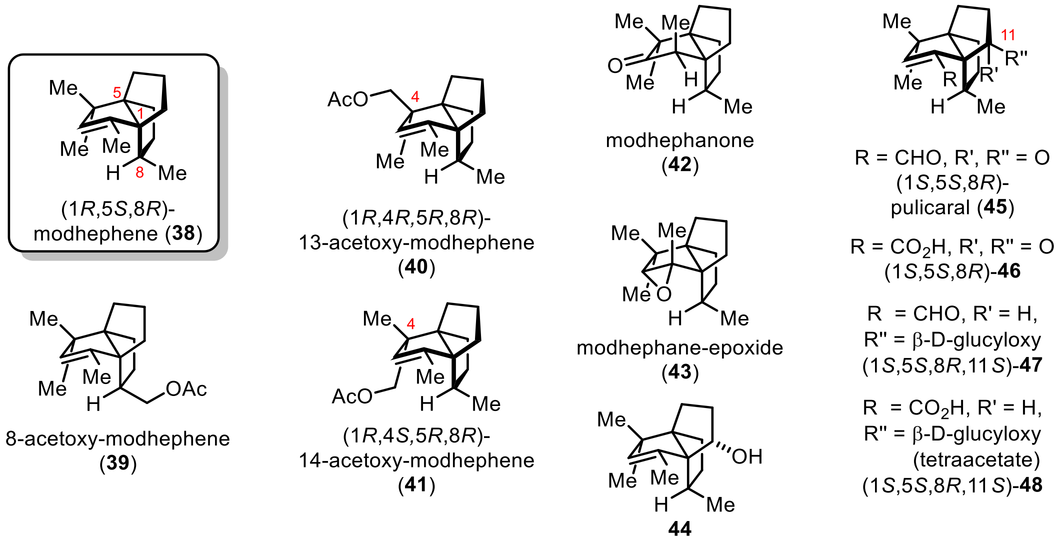
salvileucalin B (**36**)
[4.3.1]propellane

Figure 3: a) Two terpene families containing a carbocyclic propellane and b) Synthesized terpenes, in which only a single compound from the family constitutes a propellane motif. The central C–C bond is highlighted in red. Bonds formed in the oxidase phase to build up the propellane are highlighted in green.

Additionally, a few natural products in which the propellane is a unique cyclization product derived from known polycyclic scaffolds are known (Figure 3b). Besides the aforementioned aplydactone (**9**, see Chapter 1.3), only two other terpenes containing carbocyclic propellanes have succumbed to total synthesis (excluding the modhephanes, see Chapter 2.1.4). Salvileucalin B (**36**) was isolated in 2008 from *Salvia leucantha*.[50] Its [4.3.1]propellane unit is biosynthetically build up by a Diels-Alder reaction from Salvileucalin A, a rearranged neoclerodane diterpene, which has been isolated from the same source. **36** has been synthesized by REISMAN and coworkers, who utilized a copper-catalyzed arene-cyclopropanation to build up the propellane unit.[51]

Colombiasin A (**37**) was isolated in 2001 from *Pseudopterogorgia elisabethae*.[52] It is biosynthetically directly derived from the diterpene elisabethin A,[53] by C-2/C-12 bond formation *via* an oxidation/allylic alkylation. Upon its isolation, **37** drew immediate attention of the synthetic community, which resulted in three total syntheses until 2005. The groups of NICOLAOU,[54] RYCHNOVSKY[55] and HARROWVEN[56] all employed the same strategy to obtain the [4.4.4]propellane structure, an intramolecular Diels-Alder reaction that simultaneously formed the C-2/C-12 and C-1/C-9 bonds. All of the terpenes shown in Figure 3 are assumed to undergo formation of the propellane unit in the oxidase phase of their respective biosyntheses.

The only known terpene class in which the carbocyclic propellane unit is built up in its cyclase phase are the modhephanes (Figure 4). Including the two natural products discussed in the next chapter, 13 members of this terpene family have been isolated to date.



(1*R*,5*S*,8*R*)-modhephene (**38**)

(1*R*,4*R*,5*R*,8*R*)-13-acetoxy-modhephene (**40**)

modhephanone (**42**)

R = CHO, R', R'' = O (1*S*,5*S*,8*R*)-pulicaral (**45**)

R = CO_2H, R', R'' = O (1*S*,5*S*,8*R*)-**46**

R = CHO, R' = H, R'' = β-D-glucyloxy (1*S*,5*S*,8*R*,11*S*)-**47**

R = CO_2H, R' = H, R'' = β-D-glucyloxy (tetraacetate) (1*S*,5*S*,8*R*,11*S*)-**48**

8-acetoxy-modhephene (**39**)

(1*R*,4*S*,5*R*,8*R*)-14-acetoxy-modhephene (**41**)

modhephane-epoxide (**43**)

44

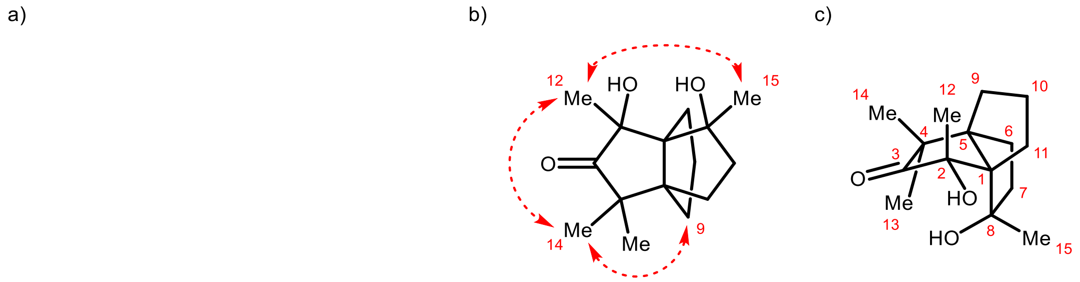
Figure 4: 11 of the 13 isolated modhephanes. Stereodescriptors are given in the name, in case the absolute configuration of the compound is known.

They are named after the first propellane isolated from nature, modhephene (**38**),[57] which is considered as the cyclase-phase-product of this natural product class. All other compounds are derived by oxidation and further functionalization. The modhephanes share the [3.3.3]propellane substructure, in which three 5-membered carbocycles build up the central scaffold. They mainly differ in the oxidation pattern of their core and glycosylation to different carbohydrates at C-11, which was observed in two members,

47 and **48**, isolated from *Pulicaria paludosa.* All known modhephanes were isolated from *Asteraceae*,[58] a widespread family of flowering plants.

2.1.2. Isolation of Dichrocephones A and B

In 2013 the group of DING and ZOU reported the isolation of two additional modhephanes from *Dichrocephala benthamii*, an *Asteraceae* found in the Xishuangbanna region in the south of China (Figure 5a).[59] The extraction of 20 kg of dried plant material led to the isolation of 5 mg of a previously undescribed natural product **1**, which was named dichrocephone A in relation to its isolation source. By a combination of HMBC NMR spectroscopy and mass spectrometric fragmentation studies, the structure shown in Figure 5b could be derived, which shows the connectivity of carbon atoms and the [3.3.3]propellane unit present in all modhephanes. Further ROESY studies of the compound led to the relative configuration depicted in Figure 5c, with key interactions being observed between C-9/C-14 and the C-12/C-14 and C-12/C-15 methyl groups, respectively.



dichrocephone A (**1**)

Figure 5: a) *Dichrocephala benthamii*, an *Asteraceae* found in southern China; b) HMBC derived 2D-structure of dichrocephone A, with key ROESY interactions (red) and c) thereby derived relative configuration of the natural product.

Unusual for this natural product class was the high oxidation state of the [3.3.3]propellane core, in which the former C-2/C-3 olefin of modhephene (**38**) had been oxidized to the corresponding α-hydroxy ketone. Additionally, the tertiary carbon atom at C-8 now shows a hydroxy functionality. This makes dichrocephone A the highest oxidized member of the modhephane family isolated to date. Further complexity stems from the substitution pattern of the cyclopentanone, being fully substituted at C-1, C-2, C-4 and C-5. This sterically crowded motif had not been observed in any natural product up to the isolation of dichrocephone A. However, recently two isolation studies have described additional secondary metabolites, in which cycloadditions in their respective biosyntheses build up comparable structural motifs, leading also to propellane substructures.[60]

To derive the absolute configuration of naturally isolated **1**, the experimentally obtained ECD spectrum of the natural product was compared to calculated spectra of both enantiomers of **1**, generated by time-dependent density functional theory calculations of the structure shown in Figure 65. Although the comparison shows discrepancies in case of both absorption maxima of up to 40 nm, the experimentally derived ECD spectrum fits better with the calculated spectrum of (1*S*,2*R*,5*S*,8*R*)-**1** (red). This assignment was therefore adopted as the absolute configuration of the natural product.

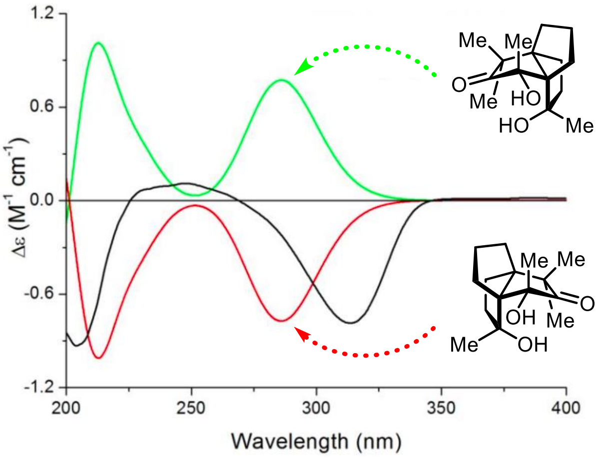
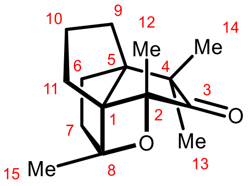


Figure 6: Comparison of the experimental ECD spectrum (black) with the calculated spectra for both enantiomers of **1**. Reprinted and adapted with permission from Tian *et al.*[59] (© 2013, Royal Society of Chemistry).

Ding and Zhou were able to obtain 9 mg of an additional natural product from the same extraction. Electrospray ionization mass spectrometry indicated that this second isolate is a dehydration product of **1**. Further similarities in the NMR spectra of both natural products led to the conclusion that dehydration of the 1,3-diol forms an additional oxetane, which is fused to both functionalized carbocycles.



dichrocephone B (**2**)

Figure 7: Structure of dichrocephone B (**2**), the second natural product obtained from *Dichrocephala benthamii*.

This leads to the tetracyclic structure **2** shown in Figure 7, which was named dichrocephone B. Its absolute configuration was derived from the configuration of dichrocephone A as (1*S*,2*R*,5*S*,8*R*).

Both compounds were tested for their biological activities against a variety of cancer cell lines. It was determined that dichrocephone B (**2**) is the more biologically active compound, with IC_{50} values against HeLa, KB and A549 cell lines of 5.9-6.9 µM. Dichrocephone A (**1**) showed IC_{50} values of 23.5-29.5 µM against the same cell lines.

Interestingly, the absolute configuration of **1** and **2** was described as the mirror image of all previously fully described members of the modhephane family (Figure 8).[58c, 61] These absolute configurations were either derived from enantioselective syntheses of the corresponding natural products or the known absolute configuration of a biosynthetic precursors isolated from the same plant.

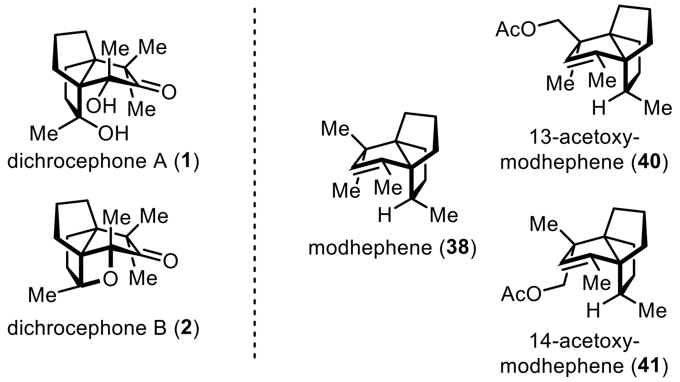
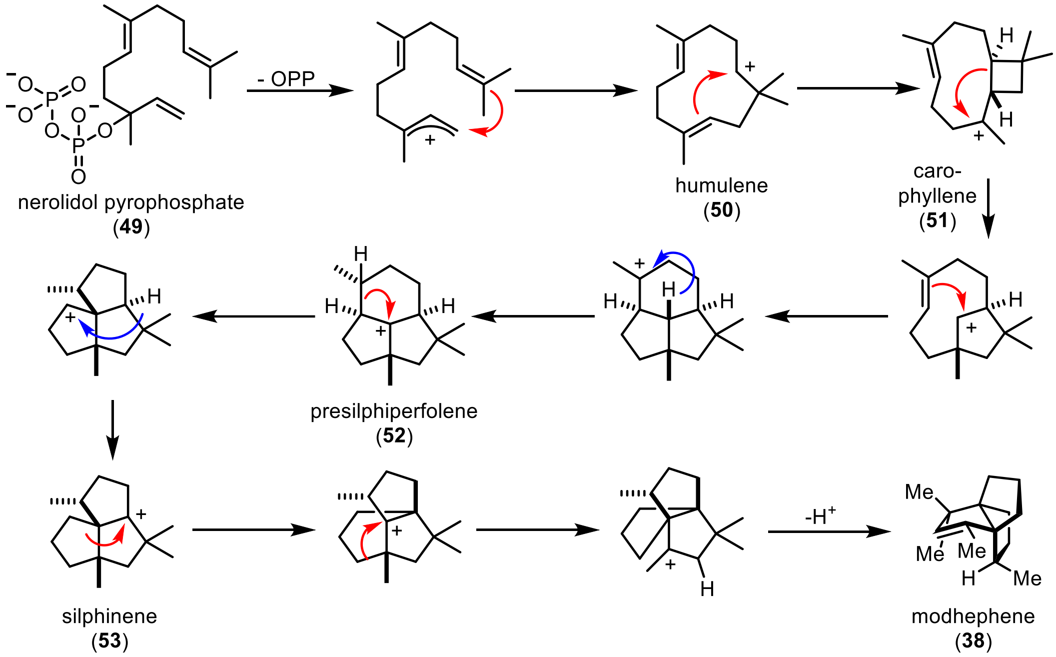


Figure 8: Inverted absolute configurations of the dichrocephones compared to other fully characterized modhephanes.

2.1.3. Biosynthesis of Modhephane Sesquiterpenes

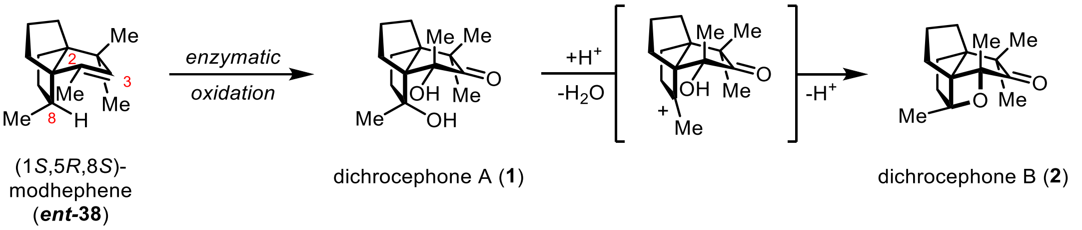
An isolation of two or more natural products that possess enantiomeric carbon cores from the same species occurs only rarely.[62] It is mostly observed for monoterpenes, in which often two or less C–C bond formations from the acyclic pyrophosphate build up the carbon core of the respective natural products. When more complex cyclic systems are build up, additional cationic intermediates need to be stabilized by the terpene cyclases (see chapter 1.2), and the simultaneous evolution of a second enzyme that catalyzes the reaction to the enantiomer becomes less likely. Therefore, reports of enantiomeric sesquiterpene scaffolds are mostly associated with carbon scaffolds derived from further cyclization of germacrene D, a monocyclic sesquiterpene that is found in both enantiomeric forms in the same species.[63]

The first isolation of modhephanes with inverted absolute configuration was therefore most intriguing. The biosynthesis of (1*R*,5*S*,8*R*)-modhephene (**38**) has been described in a computational study by TANTILLO and coworkers, who employed DFT calculations to search for transition states and energetic minima along the reaction pathway (Scheme 5).[64] It starts from nerolidol pyrophosphate (**49**) and does not involve the germacrene scaffold. During the cyclase phase eleven C–C bonds are formed or cleaved, delivering the modhephane core in ten consecutive cationic intermediates. Several cyclization steps of this proposed biosynthesis are noteworthy, as the uncharged counterparts to the observed intermediates are the carbon core of other sesquiterpene families: humulene (**50**), carophyllene (**51**), presilphiperfolene (**52**) and silphinene (**53**).



Scheme 5: Proposed biosynthesis of modhephene (**38**) according to TANTILLO and coworkers, based on a computational study. New C–C bonds are annotated in red, 1,3-hydride shifts are annotated in blue.

In the beginning of this project, it was assumed that the biosynthesis of the dichrocephones proceeds *via* the previously not identified enantiomer (1*S*,5*R*,8*S*)-modhephene (***ent*-38**), which would be produced exclusively by *Dichrocephala benthamii* (Scheme 6).

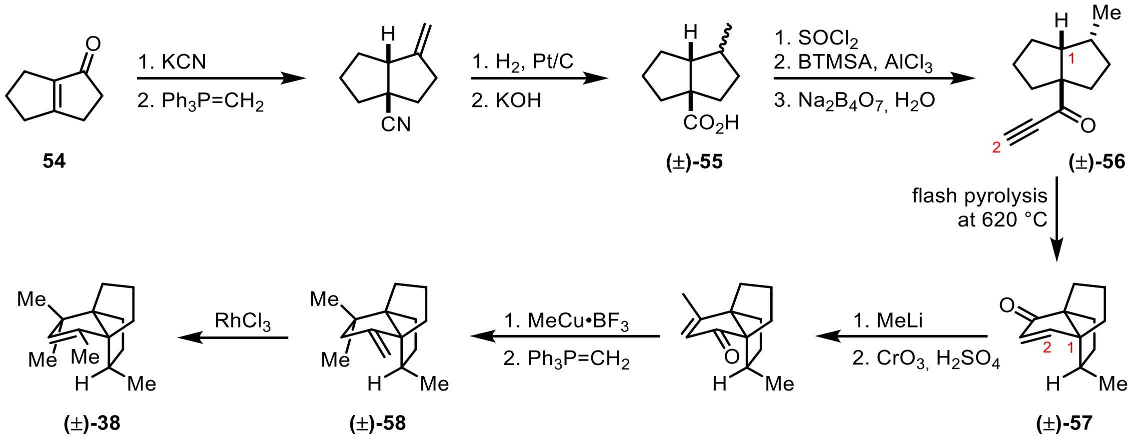


Scheme 6: Putative oxidase phase in the biosynthesis of the dichrocephones.

The conversion of ***ent*-38** into both natural products would then occur in the oxidase phase by enzymatic conversion of the C-2/C-3 olefin to the corresponding α-hydroxy ketone and selective oxidation of the tertiary C–H bond at C-8 to give the corresponding alcohol, as found in **1**. Dichrocephone B could subsequently be formed by acid-catalyzed etherification of the 1,3-diol unit to build up the oxetane motif.

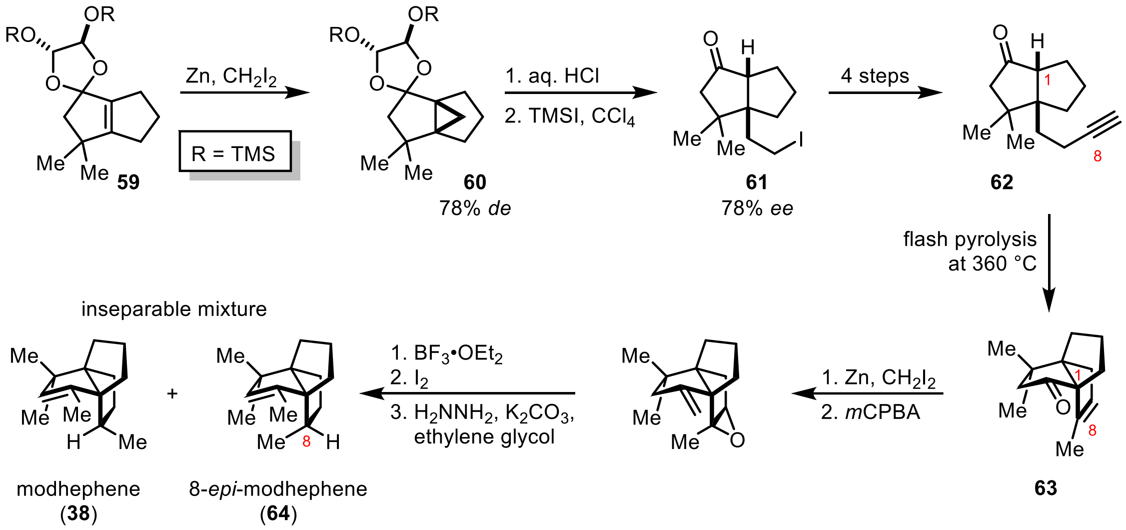
2.1.4. Total Syntheses of Modhephane Sesquiterpenes

Due to its unprecedented polycyclic structure, the isolation of modhephene (**38**) in 1979 led to immense interest of the synthetic community, culminating in 19 formal or total syntheses of the natural product.[61a, 65] In line with the topic of this thesis, the studies that led to a complete structure elucidation of **38** and the synthesis reported for oxygenated derivatives will be discussed, to show previous approaches towards the [3.3.3]propellane core. The first synthesis of **(±)-38** was published in 1980 by Dreiding and coworkers and confirmed the connectivity and relative configuration of the hydrocarbon scaffold[65a] (Scheme 7). The structure was until then based on X-ray crystallography of a synthetic derivative of the natural product. Starting point of the synthesis of **(±)-38** was the bicyclic enone **54**, which was functionalized to carboxylic acid **(±)-55** in four steps. By alkynylation of the corresponding acid chloride, cyclization precursor **(±)-56** was obtained as a single diastereomer. **(±)-56** underwent 5-*endo*-dig cyclization under flash pyrolysis conditions at 620 °C, to build up the C-1/C-2 bond of the natural product, which completed the synthesis of the propellane core **(±)-57**. A series of nucleophilic additions, an oxidative rearrangement and a Wittig reaction enabled regioselective introduction of the missing carbon atoms, leading to exocyclic olefin **(±)-58**, which could be isomerized under Rh-catalysis to yield **(±)-38** in 13 steps overall.



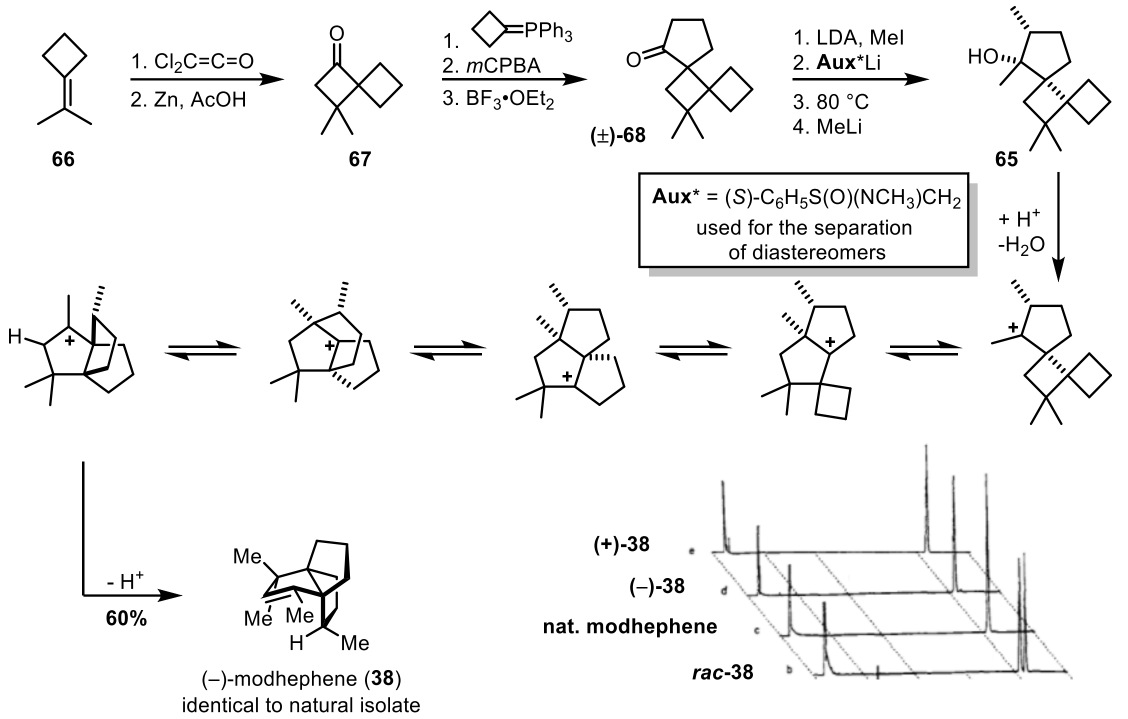
Scheme 7: First synthesis of (±)-modhephene by Dreiding.

The first asymmetric synthesis of modhephene was equally based on a flash pyrolysis to form the propellane core, and reported by Mash and coworkers in 1988 (Scheme 8).[65d] By employing a chiral auxiliary in acetal **59**, the synthesis of cyclopropyl propellane **60** was achieved with 78% diastereomeric excess, resulting in the corresponding enantiomeric excess of **61** after acetal cleavage and cyclopropane opening. Nucleophilic substitution enabled the synthesis of alkyne **62**, which underwent C-1/C-8 bond formation formation under flash pyrolysis conditions to give [3.3.3]propellane **63**, in analogy to the synthesis of DREIDING. The last stereocenter at C-8 could not be introduced selectively, which inevitably led to an inseparable mixture of modhephene **38** and 8-*epi*-modhephene **64.** This prevented the attempt to confirm the absolute configuration of the natural isolate by comparison of its optical rotation with the synthetic material.



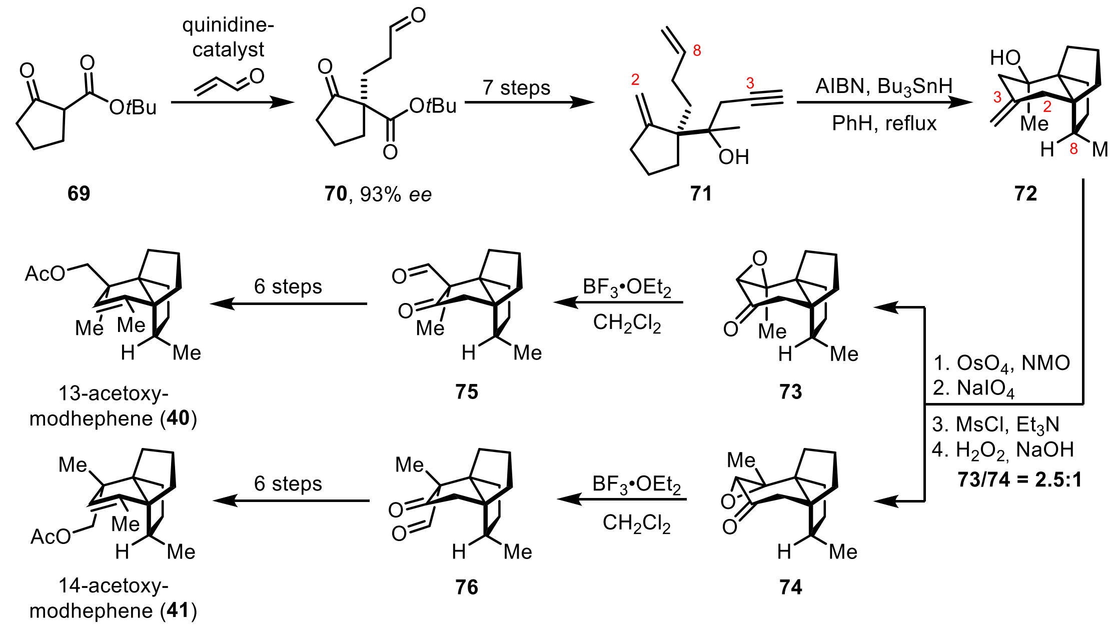
Scheme 8: First asymmetric synthesis of modhephene by MASH, based on desymmetrization using a chiral acetal auxiliary.

The absolute configuration of modhephene could finally be determined in a series of detailed synthetic studies by FITJER and coworkers in 1988 and 1991 (Scheme 9).[61a, 66] Both enantiomers of **38** were obtained separately by utilizing a cationic rearrangement cascade of enantiopure **65**, which was obtained in nine steps from olefin **66**. Initial [2+2]-cycloaddition of dichloro ketene delivered the spirocyclic ketone **67** in two steps, which was converted to the tricyclic compound **(±)-68** *via* a Wittig reaction, epoxidation and subsequent Wagner-Meerwein rearrangement. Separation of the enantiomers was possible by addition of a chiral auxiliary to the carbonyl functionality of α-methylated **(±)-68**, which was cleaved after chromatographic separation of the diastereomers. Further conversion to the enantiomerically pure cyclization precursor **65** was achieved by addition of methyl lithium. The fascinating cationic cascade was initiated by treating **65** with TsOH, which led to rearrangement of all three carbocycles to **38** in 60% yield. The absolute configuration of the natural product was then derived from chiral gas chromatography of both synthetic enantiomers and the natural isolate, leading to the absolute configuration of naturally occurring modhephene (**38**) as depicted in Scheme 9.



Scheme 9: A rearrangement cascade employed by FITJER for the enantiospecific synthesis of (–)-modhephene and comparison with the natural isolate by chiral gas chromatography. Reprinted and adapted with permission from FITJER.[61a] (© 1991 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim)

The only total synthesis of functionalized modhephanes prior to this thesis was performed by MOON and coworkers on 13- and 14-acetoxy modhephenes (**40** and **41**, Scheme 10).[61b] It commenced with an asymmetric Michael addition of β-carbonyl ester **69** to acrolein, facilitated by a quinidine catalyst, which delivered the stereogenic center in **70** with 93% enantiomeric excess. Further functionalizations of this monocyclic compound, comprised of Wittig reactions and nucleophilic additions, delivered dienyne **71** in seven steps. This compound served as a starting material for the radical cyclization cascade, which simultaneously formed the C-1/C-8 and C-2/C-3 bonds of the natural products. The obtained [4.3.3]propellane **72** was converted to epoxyketones **73** and **74** in a four-step sequence consisting of dihydroxylation and diol cleavage of the exocyclic olefin, followed by elimination of the tertiary alcohol and Weitz-Scheffer epoxidation. **73** and **74** were obtained as a separable 2.5:1-mixture. Both epoxides underwent Lewis-acid induced ring contraction to the desired [3.3.3]propellane structures **75** and **76**. Parallel synthetic strategies were employed to obtain both natural products **40** and **41** in a series of redox transformations and alkylations.



Scheme 10: Total synthesis of the acetoxy modhephenes **40** and **41** by Moon and coworkers.

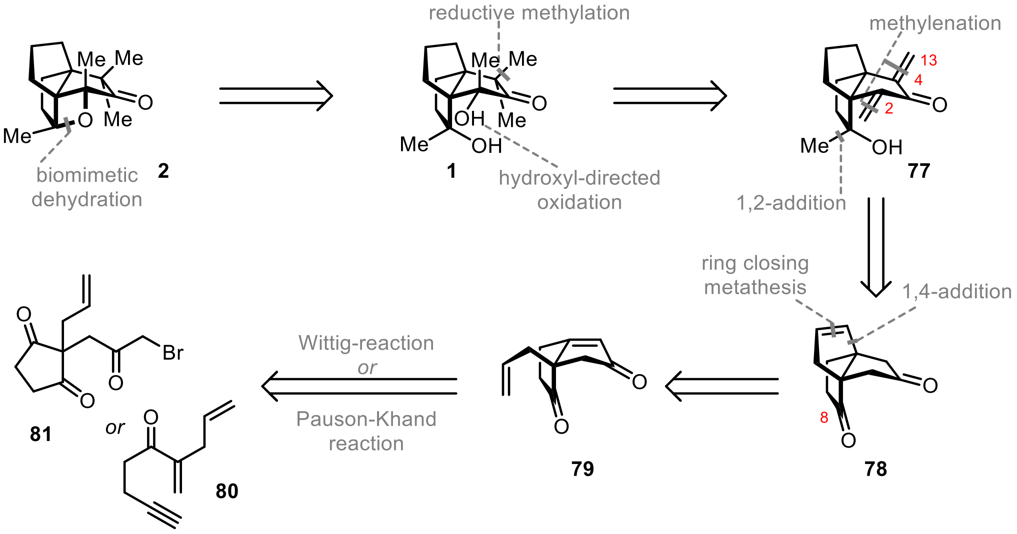
As outlined above, the previously reported syntheses of modhephanes led to a variety of creative approaches, which were necessary to obtain the unprecedented ring system of this natural product class. A majority of the 19 synthetic strategies were based on ring rearrangements under harsh reaction conditions. This often allowed fast synthetic access to the hydrocarbon backbone, but was not deemed useful to obtain the dichrocephones, due to the low functional group tolerance of these reactions. One should also note that only the strategy employed by Moon and coworkers to obtain **40** and **41** allows for the catalytic asymmetric conversion of an achiral starting material into the natural products. All strategies towards modhephene (**38**) were either aimed towards a racemic mixture of the natural product or used auxiliaries for chiral induction. Methodologies to obtain natural products containing a carbocyclic propellane in an enantioselective fashion were rarely reported.[27, 51, 54a]

2.2. Results

2.2.1. Retrosynthetic Analysis of Dichrocephones A and B

The fascinating structure of dichrocephones A and B (**1** and **2**), created by their oxidation pattern and the unique tetracyclic core of **2**, in combination with the puzzling biosynthetic origin of the enantiomeric carbon core were the main motivation for the total synthesis of both natural products described in this thesis. Dichrocephones A and B offer a variety of synthetic challenges, which have not been addressed by previous studies: the high oxidation state of the carbon scaffold, with oxygen functionalities at two of the three carbocycles was believed incompatible to previously described cyclization strategies. These usually harsh rearrangement conditions would likely result in low functional group tolerance. Both **1** and **2** contain four adjacent stereogenic centers at C-1/C-2/C-5 and C-8 (complete numeration see Figure 7, Chapter 2.1.2). The three adjacent quaternary carbon-atoms are partly embedded in this stereotetrade and build up a fully substituted cyclopentanone ring. This structural motif had been unprecedented upon isolation of **1** and **2**, and only recently six members of a natural product family isolated from *Aspergillus flavipes* have shown a comparably functionalized cyclopentanone structure.[60, 67] Additionally, the fully substituted oxetane motif present in **2** is found in only two other natural products.[68] No synthetic studies were reported for any of these compounds. It was believed to induce additional strain, due to fusion of the small heterocycle to the already strained propellane core. The synthesis of the fused system of **2** was therefore considered highly challenging.

In analogy to the previously described syntheses of aplydactone (Scheme 2) and ingenol (Scheme 4), the synthesis of the most strained ring system was intended by a biomimetic reaction. Thereby, dichrocephone B (**2**) would be formed by an acid catalyzed dehydration from the structurally less complex dichrocephone A (**1**, Scheme 11).

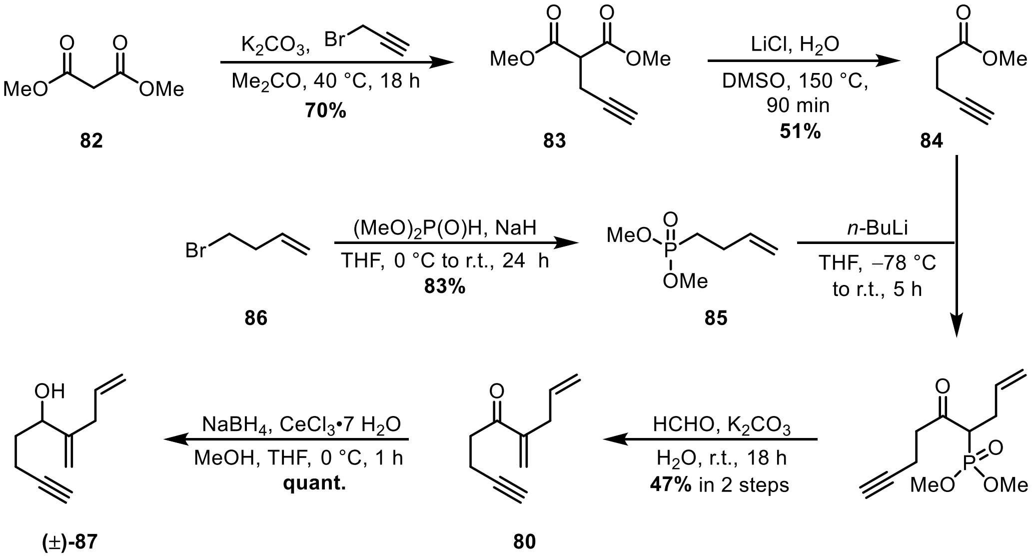


Scheme 11: Retrosynthetic analysis of dichrocephones A and B.

Introduction of the substitution pattern of **1** was planned by oxidation at C-2 and reductive methylation of the C-4/C-13 olefin of enone **77**, in order to obtain the geminal dimethyl group at C-4, respectively. Regio- and stereoselectivity of this pseudo-desymmetrization could either be steered by steric influence of the substituted C-8 in the reductive methylation step, or by the directing capabilities of the hydroxy group for either of the two reactions. To introduce the two methylene groups in **77**, Eschenmoser methylenation of ketone **78** at C-2 and C-4 was envisaged.[69] The tertiary alcohol at C-8 could be introduced by 1,2-addition of a methyl nucleophile to the neopentylic carbonyl functionality of propellane **78**. The synthesis of the strained propellane core was planned by ring closing metathesis of a 1,6-diene,[70] a strategy that has been previously employed for the synthesis of several strained carbocyclic systems.[71] To obtain this diene, a stereoselective 1,4-addition of a vinyl nucleophile to bicyclic enone **79** was envisaged. **79** in turn can be considered as a truncated derivative of the Hajos-Parrish ketone,[72] which was to be obtained by either Pauson-Khand reaction from **80** or an intramolecular Wittig-reaction from **81**.

2.2.2. First Approach towards the Bicyclic Enones: Pauson-Khand Reaction

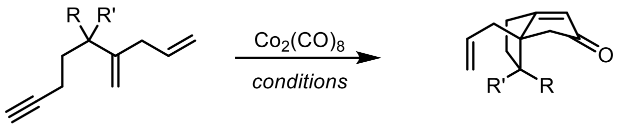
The first strategy towards the enone **79** was based on a Pauson-Khand reaction,[73] which would allow its synthesis from acyclic enyne **80**. Enantioselective versions of this type of reaction are literature known,[74] and mostly employ chiral transition metal catalysis and gaseous carbon monoxide. To test the feasibility of this approach without employing the toxic gas, a synthesis of the racemic mixture of bicyclic enone **(±)-79** using stoichiometric amounts of the stable $Co_2(CO)_8$-complex was envisaged. Access to the cyclization precursor **80** was realized in a four-step sequence, starting from dimethyl malonate (**82**, Scheme 12).[75]



Scheme 12: Synthesis of cyclization precursors **80** and **(±)-87** from dimethyl malonate (**82**).

Monoalkylation under basic conditions using propargyl bromide gave alkyne **83**, followed by decarboxylation to the monoester **84** under Krapcho conditions.[76] The addition of deprotonated phosphonic acid ester **85**, which is available in a single step from 1-bromobut-3-ene (**86**),[77] to **84** and subsequent Horner-Wadsworth-Emmons reaction with paraformaldehyde[78] gave enone **80** in 47% yield over two steps. The complete sequence was achieved on gram scale using distillation to purify the products.

The obtained cyclization precursor **80** was converted to the bicycle **(±)-79** by Pauson-Khand reaction with stoichiometric amounts of $Co_2(CO)_8$ (Table 1).[79] In all cases, complete selectivity of the reaction to the desired bicyclo[3.3.0]octene system was observed. Therefore, the initially formed Co-alkyne complex preferably reacts with the electron deficient enone system, instead of the electronically favored terminal olefin. Initial experiments were focused on conversion of the starting material in refluxing toluene, which gave **(±)-79** in 6% yield (entry 1). These unsatisfying results were thought to be caused by slow coordination of the Co-alkyne complex to the electron deficient double bond, leading to prior decomposition of the intermediate. Therefore, several additives known to open the coordination sphere of the intermediately formed cobalt complex by release of CO were employed (entries 2–4).[80]



80 (R, R' = O)
(±)-87 (R = H, R' = OH)

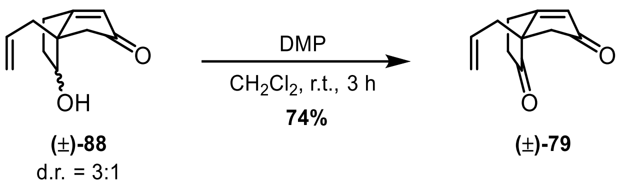
(±)-79 (R, R' = O)
(±)-88 (R = H, R' = OH)

Table 1: Pauson-Khand reaction of cyclization precursors **80** and **(±)-87**.

	Starting material	Additive	Conditions	Product	Yield, d.r.[a]
1	**80**	none	PhMe, reflux, 7 h	**(±)-79**	6%, n.d.
2		$NMO \cdot H_2O$	CH_2Cl_2, 0 °C, 2 h		12%, n.d.
3		NMO[b]	CH_2Cl_2, 0 °C, 2 h		No conversion
4		BuSMe	DCE, 70 °C, 18 h		18%, n.d.
5	**(±)-87**	none	PhMe, reflux, 18 h	**(±)-88**	24%, 1:1[c]
6		$NMO \cdot H_2O$	CH_2Cl_2, 0 °C, 18 h		50%, 3:1[c]
7		NMO[b]	CH_2Cl_2, 0 °C, 18 h		26%, 5:2[c]
8		BuSMe	DCE, 70 °C, 18 h		35%, 1:1[c]

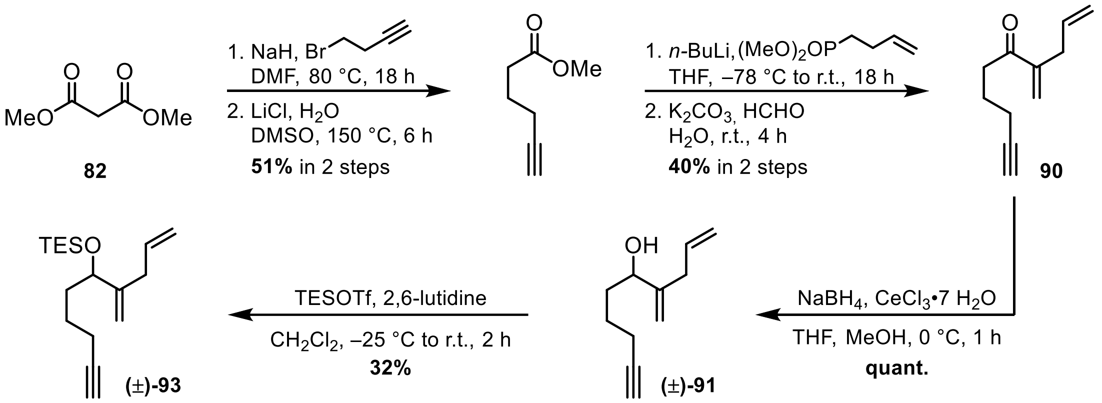
[a] Determined by ^1H NMR, relative configuration not assigned; [b] Dried under heat in vacuo; [c] Products not separable by column chromatography.

Despite higher reactivity of **80** under these conditions, product yields did not exceed 18% (entry 4). To raise the electron density at the olefin functionality, **80** was reduced under Luche conditions[81] to the corresponding allylic alcohol **(±)-87** in quantitative yield (Scheme 12). This compound was then treated under conditions analogous to those employed for **80** (entries 5–8). The bicyclic alcohol **(±)-88** could be isolated in significantly higher yields of up to 50% (entry 6) as a mixture of diastereomers, which were not separable by column chromatography. Reoxidation of **(±)-88** using Dess-Martin periodinane[82] completed the synthesis of **(±)-79** (Scheme 13), which was obtained in seven steps and 6.3% yield starting from malonic dimethyl ester (**82**).



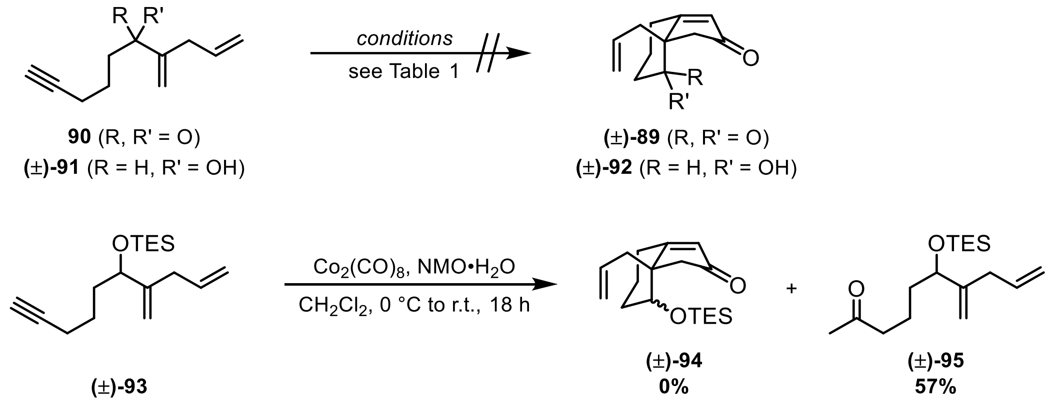
Scheme 13: Synthesis of bicyclic enone **(±)-79** by oxidation of bicyclic alcohol **(±)-88**.

In cooperation with LISA SCHNEIDER and TOMMASO PECCHIOLI, a general methodology to synthesize carbocyclic propellanes *via* bicyclic enones like **79** was established.[83] To allow for the synthesis of a higher homolog **89**, with a reversed ring system compared to the Hajos-Parris-ketone,[72, 84] the initial alkylation step was performed using 4-bromobut-1-yne. Following the sequence described in Scheme 12 to access the cyclization precursors, the desired enone **90** was obtained in 20% yield over four steps (Scheme 14), along with the allylic alcohol **(±)-91** after subsequent Luche-reduction.



Scheme 14: Synthesis of the cyclization precursors **90**, **(±)-91** and **(±)-93**.

Neither **90** nor **(±)-91** could be successfully transferred to the corresponding bicyclic enones **(±)-89** or **(±)-92** under Pauson-Khand conditions (Scheme 15). Whereas initial formation of the Co-alkyne complex was observed by thin layer chromatography, no further conversion under the previously tested conditions for the bicyclo[3.3.0]octenes **(±)-88** and **(±)-79** could be obtained. Harsher reaction conditions led to decomposition of the starting materials. ADRIO and coworkers could show that a free hydroxy group may hinder successful cyclization under Pauson-Khand conditions, which can be avoided by a variety of protecting groups.[80b] In case of the silyl ether derivative **(±)-93**, which was obtained in one additional step from **(±)-91**, conversion of the starting material was observed. However, rather than the desired cyclization to **94**, a hydration of the alkyne gave the corresponding methyl ketone **(±)-95** in 57% yield. Upon the unsatisfying results described in Scheme 15, the synthesis of **(±)-89** by a Pauson-Khand strategy was no longer pursued.



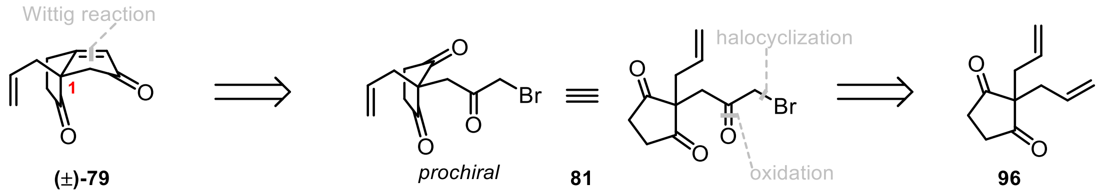
Scheme 15: Attempted Pauson-Khand cyclizations of **90**, **(±)-91** and **(±)-93**.

These disappointing outcome may likely be caused by the higher conformational freedom of the acyclic Co-alkyne complex compared to **(±)-87**, rendering the intramolecular reaction comparably slow, which leads to prior decomposition of the intermediate. This is also reflected in literature where the highest yield for Pauson-Khand bicyclization incorporating a 6-membered carbocycle are reported for compounds, in which an existing ring systems prealignes the reactive centers.[85]

Due to comparably low yields in the formation of bicyclic enone **(±)-79**, caused by the cyclization step and the need for additional redox transformations, the Pauson-Khand strategy was abandoned.

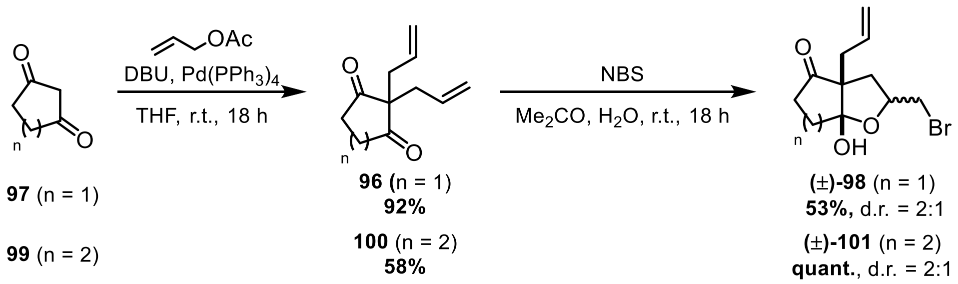
2.2.3. Second Approach towards the Bicyclic Enones: Wittig Reaction

The revised synthetic strategy employed an intramolecular Wittig reaction to obtain **79** by annulation from a monocyclic triketone **81** (Scheme 16). Access to a truncated derivative of **81** was already accomplished in a study by WERNER and coworkers,[86] in a sequence consisting of halocyclization and oxidative lactol opening from a corresponding methyl cyclopentanedione derivative. Notably, triketone **81** is prochiral and already incorporates a quaternary all-carbon atom, which after cyclization constitutes the first stereocenter of the natural products at C-1. Desymmetrization of prochiral quaternary carbon atoms is a well-established synthetic strategy, successfully employed in the asymmetric synthesis of numerous natural products.[87] This retrosynthetic analysis would therefore possibly enable an asymmetric synthesis of the natural products.



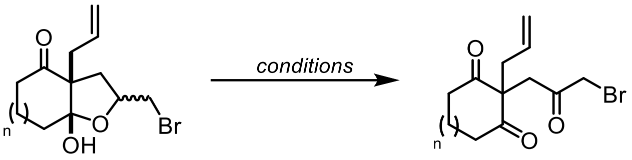
Scheme 16: Revised synthetic strategy to enone **(±)-79** by intramolecular Wittig reaction of **81**.

In contrast to the reported synthesis of the truncated derivative of **79**,[86] the allyl motif necessary for the planned ring closing metathesis retrosynthetically leads to diallylated cyclopentanedione **96**. This molecule was accessible in a single step from commercially available 1,3-cyclopentanedione (**97**) by double Tsuji-Trost allylation,[88] employing DBU as the base (Scheme 17). Further bromocyclization led to lactol **(±)-98**, which could not be obtained in pure form, probably due to competing difunctionalization of the second allyl moiety. The sequence was again applied to a higher homolog, by employing 1,3-cyclohexanedione (**99**) as the starting material. Whereas diallylation to **100** proceeded only in 58% yield, the following bromocyclization gave **(±)-101** in quantitative yield as a 2:1 mixture of diastereomers.



Scheme 17: Synthesis of lactols **(±)-98** and **(±)-101.**

Due to higher purity of **(±)-101**, conditions for the oxidative lactol opening were screened with this compound (Table 2). Whereas the originally reported conditions[86] led to decomposition of the starting material (entry 1), the desired product **102** could be obtained in 25% yield by lowering the reaction temperature to 0 °C (entry 2). It was assumed that the strong acidic conditions led to decomposition of the second allyl rest. Therefore a variety of conditions employing chromium-based oxidants under neutral or basic conditions were employed (entries 3–6).[89] Unfortunately, no conversion could observed. Chromium-free oxidative conditions, developed for oxidative lactol openings missing the halo substituent,[90] either led to decomposition or no conversion (entries 7–8). Homolog **(±)-98** was therefore oxidized using the conditions of entry 2, which delivered triketone **81** in 35% yield (entry 9).



(±)-98 (n = 0)
(±)-101 (n = 1)

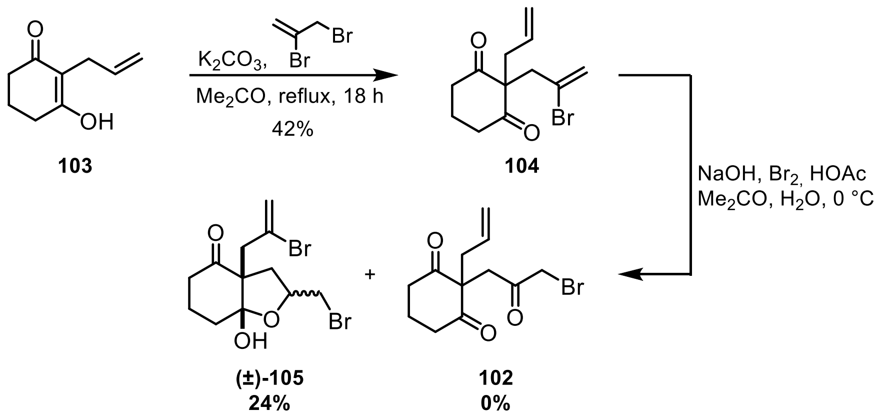
81 (n = 0)
102 (n = 1)

Table 2: Oxidative lactol opening of **(±)-98** and **(±)-101**..

	n	Oxidant	Conditions	Product, Yield
1	1	CrO_3	H_2SO_4, Me_2CO, H_2O, r.t.	Decomposition
2		CrO_3	H_2SO_4, Me_2CO, H_2O, 0 °C	**102**, 25%[a]
3		CrO_3	Me_2CO, H_2O, 0 °C	No conversion
4		PDC	CH_2Cl_2, r.t.	No conversion
5		PCC	NaOAc, CH_2Cl_2, r.t.	Low conversion[b]
6		PCC	NaOAc, CH_2Cl_2, reflux	Low conversion[b]
7		DMDO	CH_2Cl_2, Me_2CO, 0 °C	Decomposition
8		TPAP, NMO	4Å MS, CH_2Cl_2, r.t.	No conversion
9	0	CrO_3	H_2SO_4, Me_2CO, H_2O, 0 °C	**81**, 35%[a]

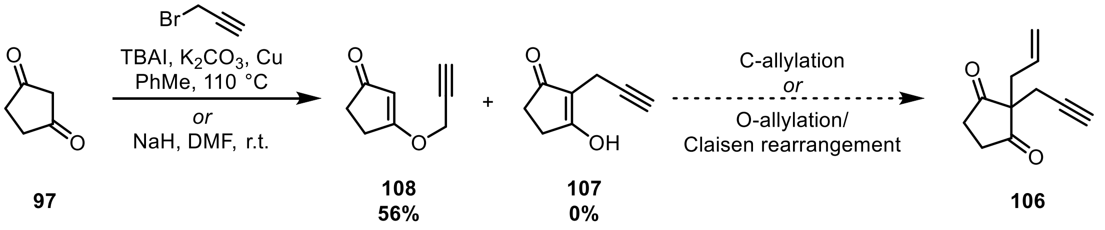
[a] Isolated yield; [b] Determined by ^1H NMR.

Since oxidative conditions led to low yields of the desired triketones **81** and **102**, an alternative approach was envisioned in which the oxidation state of the α-bromo carbonyl motif was to be incorporated by a suitable alkylating reagent. In a first attempt, by following a method developed by WEINREB and coworkers,[91] a direct halocyclization of vinyl bromide **104** to triketone **102** was examined, which was obtained in two steps from enol **103** (Scheme 18).[92] The conditions led to preferred halocyclization with the unfunctionalized allyl rest to give **(±)-105**.



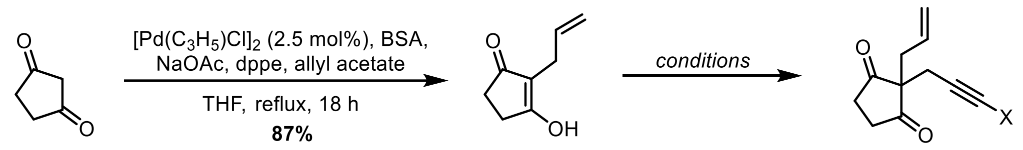
Scheme 18: Attempted direct synthesis of triketone **102** by halocyclization.

The next strategy aimed at introduction of the α-bromo ketone from alkyne **106.** Initial attempts at propargylation of 1,3-cyclopentanedione (**97**) failed to give the desired product **107** under a variety of conditions.[93] In each case the O-alkylated enol ether **108** was obtained as the only product (Scheme 19). Interestingly, propargylation of 1,3-cyclohexanedione (**99**) under these conditions proceeds with high yields to the desired C-alkylation product.[83]



Scheme 19: Failed strategy to obtain alkyne **106** by a consecutive alkynylation/allylation approach.

The problem shown in Scheme 19 was overcome by reversing the reaction sequence. Initial Tsuji-Trost allylation of **97**[94] was followed by propargylation of enol **109**. As shown in Table 3, a variety of basic conditions could be employed to obtain the desired C-alkylation, using propargyl bromide as the alkylating reagent (entries 1–7).[95] The best results were obtained with KO*t*-Bu in DMSO, which gave alkyne **106** in 61% yield.[96] The reaction could be performed in decagram scale without the need to purify the starting material **109** after the allylation (entries 8–9). A direct synthesis of **110** from **109** with 1,3-dibromo propyne could be realized, but was disregarded for further optimization due to its low yield (entry 10) and additional need for reagent preparation.[97]

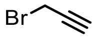
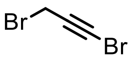


97

109

106 (X = H)
110 (X = Br)

Table 3: Propargylation of enol **109**.

	Alkylating agent (equiv.)		Conditions	Product	Yield[a]
1		(1.0).	NaOH, H_2O, 60 °C	**106**	16%
2		(2.0)	NaH, THF, r.t.		6%
3		(2.6)	K_2CO_3, TBAHS, MeCN, r.t.		57%
4		(2.0)	$NaHCO_3$, H_2O, 80 °C		10%
5		(1.6)	K_2CO_3, Me_2CO, 60 °C		26%
6		(1.2)	K_2CO_3, MeCN, reflux		20%
7		(1.2)	KO*t*-Bu, DMSO, r.t.		60%
8		(1.2)	KO*t*-Bu, DMSO, 0 °C to r.t.		61%[b]
9		(1.2)	KO*t*-Bu, DMSO, 0 °C to r.t.		53%[b,c]
10		(2.0)	K_2CO_3, TBAHS, MeCN, r.t.	**110**	33%

[a] Reactions performed in 0.5 mmol scale, unless otherwise noted; [b] Reaction performed on 50 mmol scale; [c] Combined yield starting from **97** with a single purification.

To convert **106** into **110**, chemoselective bromination was performed using NBS and $AgNO_3$ as a Lewis acid additive to activate the alkyne (Table 4).[98] **110** was obtained in 79% yield when using stoichiometric amounts of the silver salt (entry 1). When employing catalytic amounts, a competing halocyclization with the allyl functionality was observed, which led to lower yields of the desired product (entry 3). To obtain larger quantities of **110** for the following multi-step synthesis, a scale-up of the reaction was deemed necessary, preferably using catalytic amounts of a transition metal additive. After several unsuccessful experiments employing a variety of Ag- and Cu-salts,[99] it was found that silver(I)-nitrate was essential for successful conversion. By changing the bromonium source to the corresponding 4-nitrophthalimide, the reaction could be run with 5 mol% $AgNO_3$, which led to formation of **110** in 91% isolated yield (entry 7). Conversion to the product proceeded cleaner compared to the reactions in entries 1–3, so that the reaction could be run at room temperature, although additional 0.15 equivalents of the bromonium source needed to be employed, due to impurities caused by unoptimized reagent synthesis.

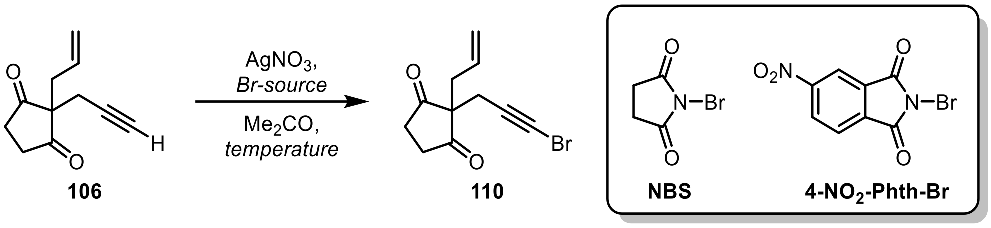
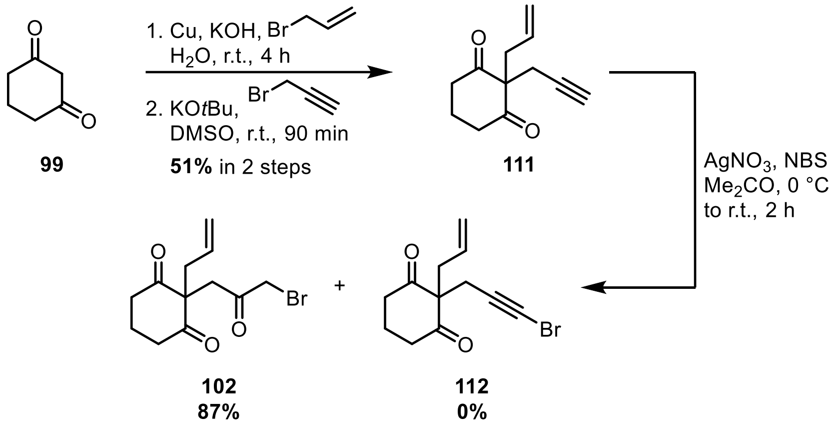


Table 4: Bromination of alkyne **106**.

	$AgNO_3$ equiv.	Br-source (equiv.)	Temperature	Yield
1	1.0	NBS (1.05)	0 °C	79%[a]
2	1.0	NBS (1.05)	0 °C to r.t.	49%[b]
3	0.5	NBS (1.05)	0 °C	32%
4	1.0	4-NO_2-Phth-Br (1.05)	0 °C	85%
5	1.0	4-NO_2-Phth-Br (1.2)	r.t.	95%
6	0.5	4-NO_2-Phth-Br (1.2)	r.t.	94%
7	0.05	4-NO_2-Phth-Br (1.2)	r.t.	91%[a]

[a] Reactions performed at 22 mmol scale; [b] Triketone **81** was obtained in 4% yield.

Surprisingly, when the corresponding cyclohexanedione **111** was employed in the bromination step,[100] the bromination conditions described in entry 1 did not lead to the expected bromoalkyne **112** (Scheme 20). Instead, the corresponding bromoketone **102** was obtained in very good yields.



Scheme 20: Unexpected hydration of alkyne **111** under the bromination conditions.

It was assumed that the stereoelectronic differences influenced by the ring sizes of the 1,3-diketones allow direct hydration of this compound (see Scheme 21). The water molecule necessary for the hydration step probably comes from the solvent, which was not dried prior to the reaction.

Trying to enable the analogous hydration of bromoalkyne **110**, the conditions employed in Scheme 20 did not lead to the corresponding triketone **81**. Rather, decomposition of the bromoalkyne was observed after prolonged reaction time at room temperature, with only marginal amounts of **81** isolated from the reaction (Table 4, entry 2). To facilitate hydration of **81**, a variety of transition metal catalyzed reactions were tested (Table 5). Most methodologies employed were originally developed to convert haloalkynes in conjugation to an aromatic system into the corresponding haloketones. These reaction conditions either led to no conversion or decomposition of the starting material (entries 1–6).[101]

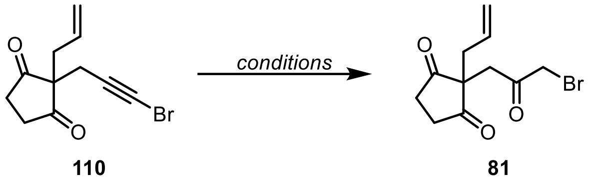


Table 5: Transition metal catalyzed hydration of bromoalkyne **110**.

	Catalyst (mol%)	Conditions	Yield
1	$FeCl_2{\cdot}4H_2O$ (5)	MsOH, DCE, 60 °C	No conversion
2	$Cu(OAc)_2{\cdot}H_2O$ (10)	TFA, H_2O, 70 °C	No conversion
3	AgF (5)	TFA, H_2O, 40 °C	No conversion
4	$AgBF_4$ (20)	AcOH, H_2O, 110 °C	Decomposition
5	$PdCl_2(MeCN)_2$ (5)	MeCN, H_2O, r.t.[b]	No conversion
6	*t*Bu_3PAuCl (5)	DCM, H_2O, r.t.	No conversion
7	PPh_3AuNTf_2 (4)	DCE, H_2O (10 equiv.), r.t.	59%
8	PPh_3AuNTf_2 (2x2)[a]	DCE, H_2O (10 equiv), r.t.	74%
9	PPh_3AuNTf_2 (2x2)[a]	DCE,[c] H_2O (3 equiv.), r.t.	88%[d]

[a] Catalyst was added in 2 charges in a 12 h interval; [b] The reaction was performed using sonication; [c] 1,2-DCE was dried over 4Å MS; [d] Reaction was performed on 24 mmol scale.

The only catalyst employed in this study able to facilitate the hydration reaction was the Gagosz-catalyst, Ph_3AuNTf_2.[102] By employing the reaction conditions developed by HE and coworkers, triketone **81** was initially isolated in 59% yield (entry 7).[103] Visible desolvation of the catalyst after prolonged reaction times was observed. When adding the catalyst in two charges of 2 mol%, 74% yield of the desired triketone **81** could be obtained, without full conversion of the starting material. By lowering the amount of excess water in the reaction, full conversion could be achieved. Thereby, employing pre-dried solvent with 4 mol% of the Gagosz-catalyst in two charges led to 88% yield of

81 on gram scale (entry 9). **81** was obtained as a crystalline solid, which after diffusion crystallization gave single crystals suitable for X-ray crystal structure analysis (Figure 9).

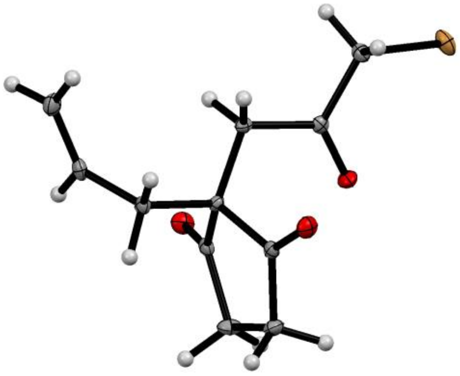
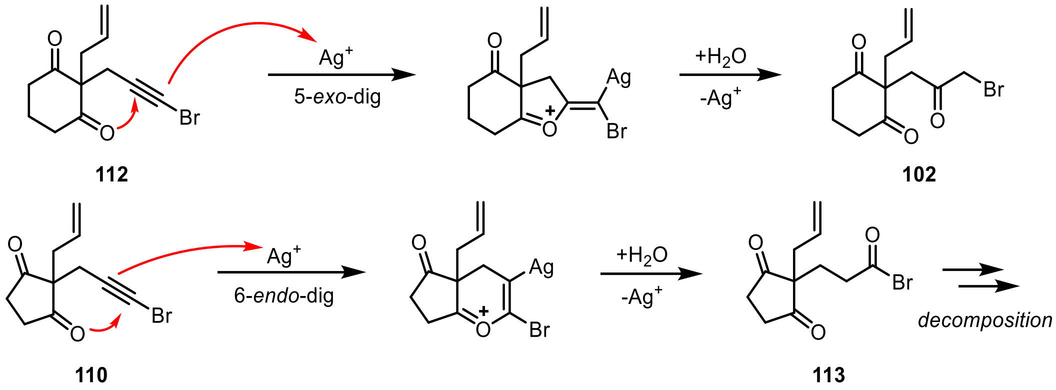


Figure 9: X-ray crystal structure of triketone **81**. Ellipsoids drawn at 50% probability.

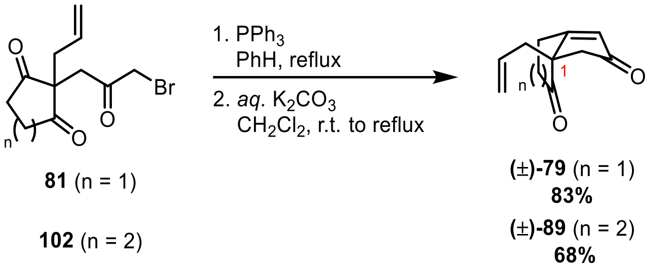
The different reactivities of alkynes **110** and **112** towards hydration are presumably caused by the differing angles of the alkyne with the proximal carbonyl functionality. A study by UTIMOTO and coworkers on Pd-catalyzed hydrations of cyclic ketones functionalized in α-position with propargyl rests, showed that cyclohexanone derivatives undergo reaction to the corresponding 1,4-diketones *via* a transition state that is build up by a 5-*exo*-dig cyclization with the proximal carbonyl functionality.[101a] Analogous cyclopentanones underwent hydration following a 6-*endo*-dig cyclization to the 1,5-diketones. Transferring these observations to **110** and **112** (Scheme 21), cyclohexanedione **112** would undergo a silver catalyzed 5-*exo*-dig cyclization, giving the observed bromo ketone **102** after hydrolysis.



Scheme 21: Different reactivity upon carbonyl assisted hydration of **110** and **112.**

On the other hand, cyclopentanedione **110** would follow 6-*endo*-dig cyclization mode to the corresponding acyl bromide **113**, which could easily decompose with a nucleophile, as for instance water remaining in the reaction mixture. For this reason, activation of the alkyne of **110** with the external Au-catalyst was necessary, which leads to a non-carbonyl assisted mechanism to obtain **81** in high yield.

The bromo ketones **81** and **102** could be successfully converted into the corresponding bicyclic enones **(±)-79** and **(±)-89** by an intramolecular Wittig reaction (Scheme 22). The reaction was performed in a two-step procedure,[104] where initial transformation of the starting material to the corresponding phosphonium salts is followed by a change of solvent to dichloromethane, in which deprotonation and ring closure were performed. In case of **81** the reaction could be scaled up to 21 mmol in consistently high yield for further studies towards the racemic mixtures of dichrocephones A and B.



Scheme 22: Wittig reaction of triketones **81** and **102** to the corresponding bicyclic enones.

The Wittig reaction shown above leads to desymmetrization of the C_2-symmetric triketones **81** and **102** by building up the first quaternary stereogenic center at C-1. To allow the asymmetric synthesis of the natural products, it was planned to perform this step in an enantioselective way. In 2014, WERNER and coworkers reported conditions for the first asymmetric catalytic Wittig reaction on a comparable substrate,[86] which were used as a starting point for the asymmetric synthesis of the natural products.

In contrast to the reactions shown in Scheme 22, which led to the racemates of **79** and **89**, the reaction described by WERNER and coworkers utilizes a chiral phosphine. This leads to one enantiomer of the respective enones as the preferred reaction product. The mechanism of the reaction is described in Figure 10, using **81** as the starting material. Initially, the chiral catalyst **114** substitutes the bromide at C-6, analogous to the mechanism of standard Wittig-reactions, to yield **115**. The bromide anion then facilitates epoxide opening of butylene oxide **116** to alcoholate **117**, which acts as the base in the subsequent step. Formation of ylide **118** is then followed by intramolecular [2+2]-cycloaddition. Due to its chiral environment, the ylide preferably reacts with one of the enantiotopic carbonyl functionalities at the 5-membered ring. Cycloreversion of oxaphosphetane **119**, analogous to the standard Wittig reaction, gives enone **79** in enantioenriched form. Regeneration of the catalyst occurs by reduction of the intermediately obtained phosphine oxide **120** with phenyl silane.[105]

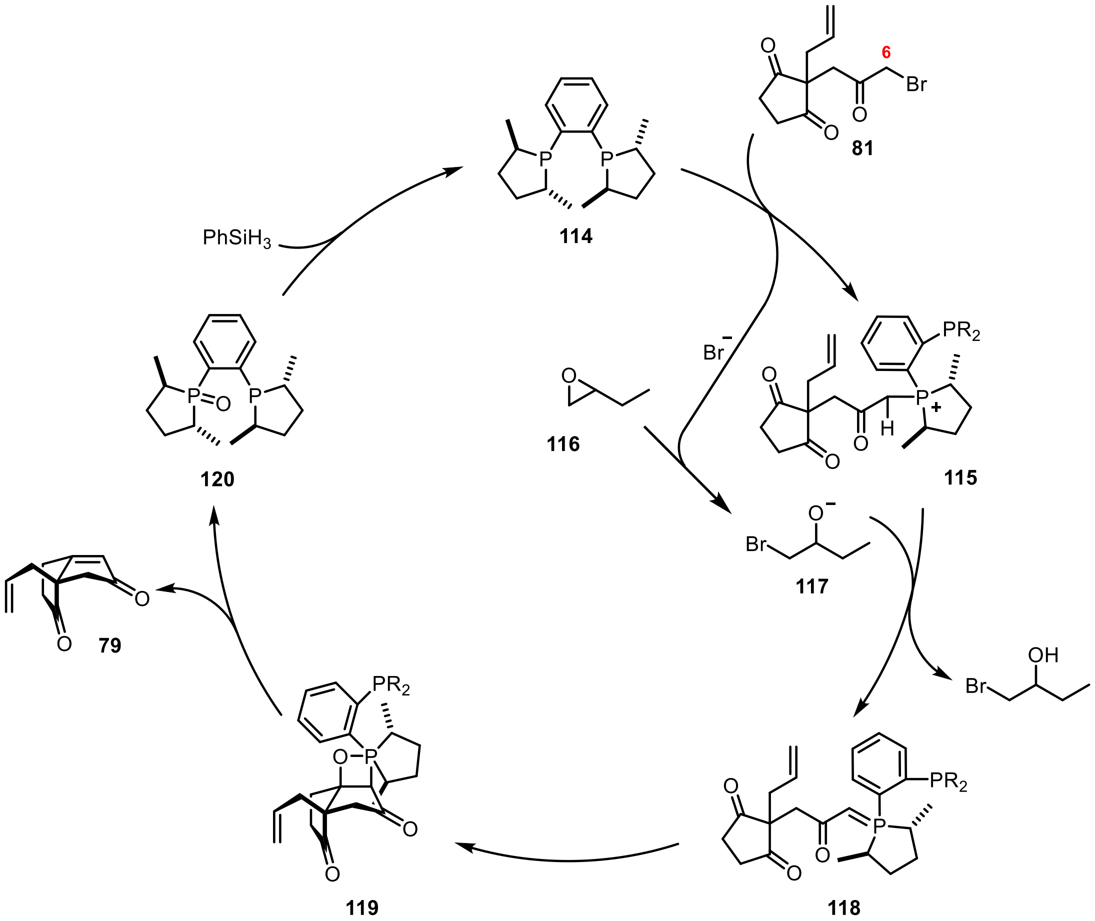


Figure 10: Proposed mechanism of the catalytic asymmetric Wittig reaction developed by WERNER and coworkers.

The reaction conditions developed by WERNER were applied to **81**, which led to isolation of **79** in 35% yield (Table 6, entry 1). The product was surprisingly obtained in 95% enantiomeric excess, a value that was never observed in the studies by WERNER. The reason for this high enantioselectivity might be the increased steric influence of the allyl rest, compared to a methyl group in the only literature example. Motivated by this promising initial result, further optimizations were performed to raise the yield of **79**. Additional catalyst led to a marginally better outcome (entry 2), but strongly diminished yields were observed when lowering catalyst loadings (entry 3). Whereas additional base had virtually no influence on the reaction (not shown), the yields could be raised by employing additional reducing agent, which allowed the isolation of up to 60% of the desired enone **79** (entries 5–7). This observation led to the assumption that regeneration of the catalyst from the corresponding phosphine oxide **120** might be the rate determining step. A recent study by KEGLEVICH described phenyl silane as the most reactive silane for phosphine oxide reductions.[106] For this reason, no other reducing agents were employed. The alternative conditions reported by WERNER, which use a combination of

$HSi(OMe)_3$ and Na_2CO_3 as reducing agent and base, led to poor yields of the product and were therefore dismissed for further optimization studies (entry 4).

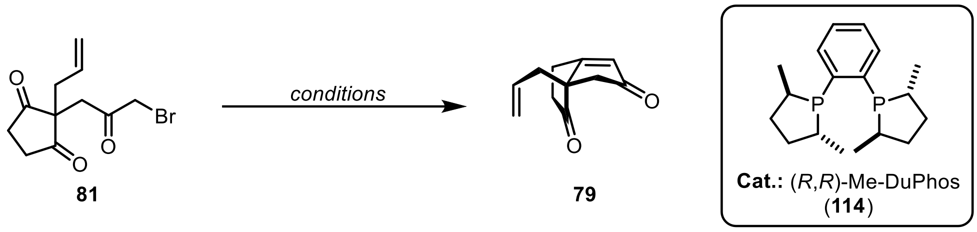
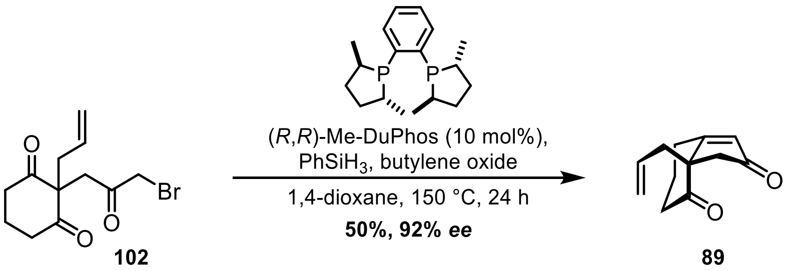


Table 6: Enantioselective catalytic Wittig reaction of triketone **81**.

	Cat. mol%	$PhSiH_3$ equiv.	Conditions[a]	Time	Yield, *ee*
1	10	1.5	butylene oxide, dioxane	18 h	35%, 95%
2	20	1.5	butylene oxide, dioxane	18 h	37%, 94%
3	5	1.5	butylene oxide, dioxane	18 h	21%, n.d.
4	10	3[b]	Na_2CO_3, PhMe, 110 °C	20 h	14%, n.d.
5	10	2	butylene oxide, dioxane	18 h	44%, 96%
6	10	4.5	butylene oxide, dioxane	18 h	55%, 96%
7	10	4.5	butylene oxide, dioxane	24 h	60%, 96%[c]

[a] Reactions performed at 150 °C in a sealed vial, unless otherwise noted; [b] Using $HSi(OMe)_3$ as the reducing agent; [c] Performed on 5 mmol scale.

Transferring the reaction conditions to the cyclohexanedione derivative **102** allowed isolation of the corresponding enone **89** in 50% yield, with an enantiomeric excess of 92% (Scheme 23). This compound was not accessible by the Pauson-Khand approach described earlier (Scheme 15). The absolute configuration of the main enantiomers was unknown at this point, but assumed to be (*S*)-configured, due to the results of WERNER.[86]



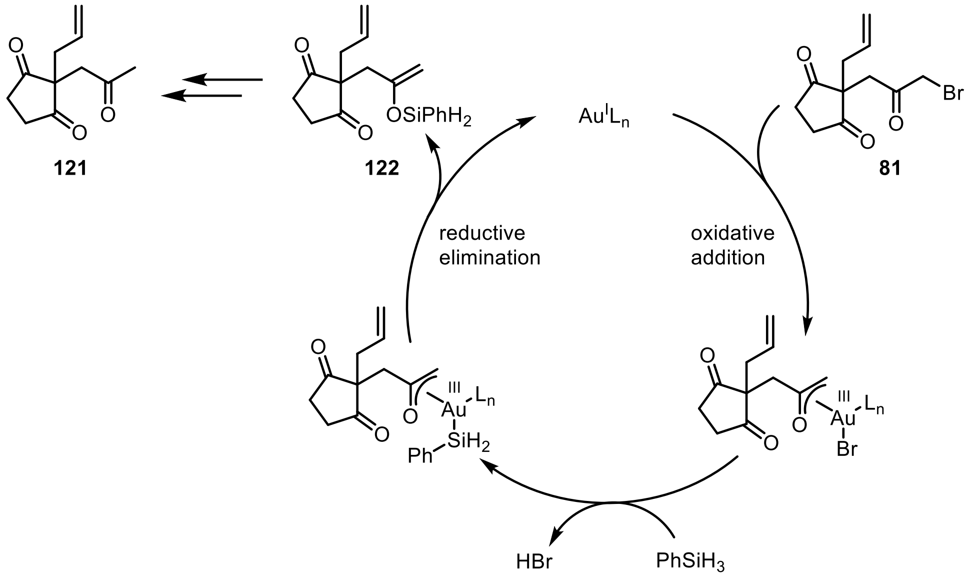
(*R*,*R*)-Me-DuPhos (10 mol%), $PhSiH_3$, butylene oxide

1,4-dioxane, 150 °C, 24 h

50%, 92% *ee*

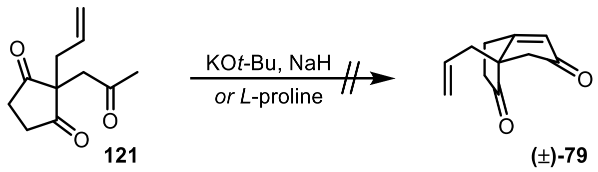
Scheme 23: Catalytic asymmetric Wittig reaction of triketone **102** under optimized reaction conditions.

Whereas the cyclization of **102** was easily reproducible every time the reaction was performed, the analogous reaction of 5-membered **81** could fail for no apparent reason. In these cases, debrominated starting material **121** (Scheme 24) was isolated in up to quantitative yields. After an intense screening of conditions, it was found that the purity of starting material **81** had substantial influence on the ratio of desired enone **79** and side product **121**. This catalytic debromination of the starting material stems from residual amounts of the gold(I)-catalyst, employed earlier for the hydration reaction of **110**. Analogous reactions have been described in literature with a variety of transition metals,[107] and the reaction presumably proceeds by oxidative addition of gold(I) into the α-bromo carbonyl functionality, which is isoelectronic to allylic bromides.



Scheme 24: Possible mechanism for the reductive dehalogenation of **81** to **121** under Wittig reaction conditions, with residual gold-contaminations present in the reaction mixture.

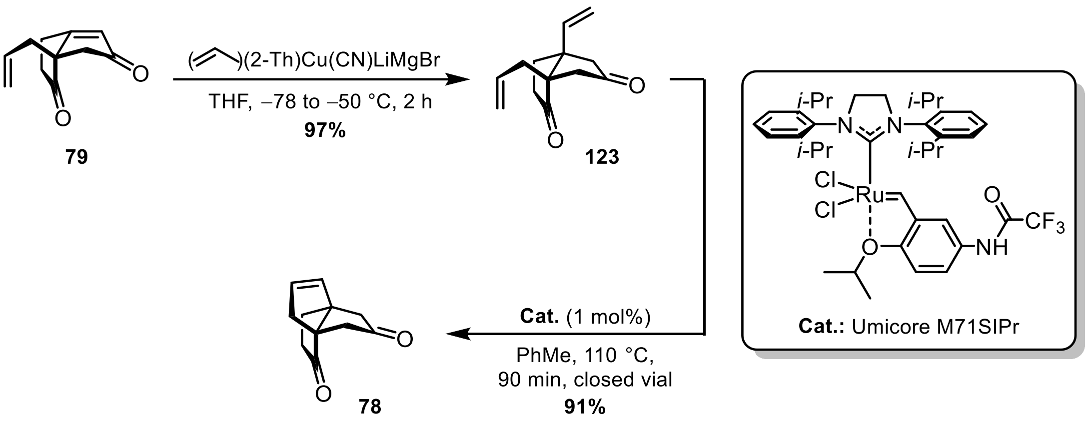
Ligand exchange of the bromide with phenyl silane and reductive elimination produces silyl enol ether **122**, which finally undergoes hydrolysis to the defunctionalized triketone **121** upon aqueous work-up. Even multiple purifications of bromo ketone **81** by column chromatography were unable to eliminate all catalyst residues, leading to dehalogenation under the reaction conditions in less than one hour. The undesired side reaction could be avoided by additional bulb-to-bulb distillation of starting material **81** after a single column chromatography. **81** was then obtained in sufficient purity with marginal loss of yield, which allowed reproducibility of the results shown in Table 6. Any attempts to use the debromination product **121** in cyclization reactions to bicyclic enone **79** by an intramolecular aldol condensation remained unsuccessful. Alkaline conditions yielded decomposition of the starting material, whereas organocatalysis led to no conversion (Scheme 25).[84] This outcome can be rationalized by an additional set of Baldwin rules[108] developed for the cyclization of enolates,[109] stating 5-(enol-*endo*)-*exo*-trig cyclizations are not possible due to conformational restrictions.



Scheme 25: Failed attempts to access enone **(±)-79** by intramolecular Aldol condensation.

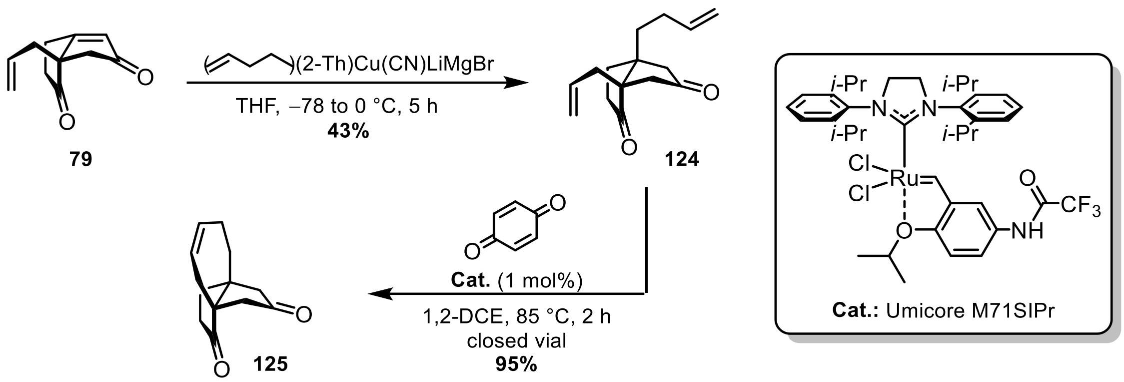
2.2.4. Synthesis of the Propellane Structures

The alkenyl rest necessary for ring closing metathesis was introduced by 1,4-addition of a mixed cuprate to enone **79**, according to a procedure developed by LIPSHUTZ and coworkers.[110] Employing 3 equivalents of the cuprate derived from vinyl magnesium bromide delivered diene **123** in near quantitative yield (Scheme 26). The *cis*-diene **123** was obtained diastereomerically pure, due to the preferred attack of nucleophiles to the convex side of the bicyclic systems. **123** was then subjected to ring closing metathesis, using Umicore M71SIPr as the catalyst. The strained [3.3.3]propellane **78** was obtained in near quantitative yields when heating a toluene solution of starting material in presence of 1 mol% of the catalyst.



Scheme 26: Synthesis of [3.3.3]propellane **78** by 1,4-addition of a vinyl cuprate to enone **79** and subsequent ring closing metathesis.

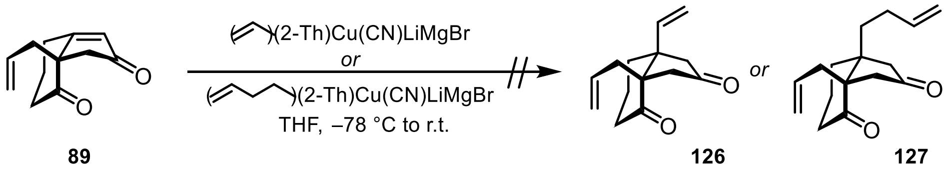
The reaction conditions described in Scheme 26 were successfully transferred to the synthesis of a higher homologue, by employing 3-butenylmagnesium bromide as the metal organyl (Scheme 27). Since the reaction proceeded more sluggishly compared to the vinyl addition to **79**, 10 equivalents of the nucleophile were necessary to achieve full conversion. The corresponding diene **124** was obtained in 43% yield.



Scheme 27: Synthesis of the [5.3.3]propellane **125** by 1,4-addition of a butenyl cuprate and subsequent ring closing metathesis.

To suppress double bond isomerization prior to the ring closing metathesis, which LISA SCHNEIDER could observe for similar substrates as **124**, slightly altered reaction conditions were employed for the synthesis of the [5.3.3]propellane **125**. The reaction was performed in the presence of benzoquinone, which was reported to suppress this isomerization.[111] Thereby, **125** was obtained in 95% yield in isomerically pure form.

Unfortunately, the high yields of 1,4-addition obtained when employing enone **79** could not be observed when **89** was used as the starting material, since neither **126** or **127** could be isolated (Scheme 28). Rather, the starting material decomposed under the reaction conditions, which could not be influenced by altering reaction conditions or equivalents of the reagents.



Scheme 28: Attempted addition of mixed cuprates to **89**.

This difference in reactivity of various bicyclic enones towards mixed cuprates was also observed in reactions performed by LISA SCHNEIDER and TOMMASO PECCHIOLI.[83] There is currently no explanation for this behavior of the substrate. Thereby, the two propellanes **78** and **125** were accessible by the developed reaction sequence consisting of an asymmetric Wittig-reaction, followed by cuprate addition and ring closing metathesis. From this point on, studies on propellane **78** were aimed towards the synthesis of dichrocephones A and B.

2.2.5. Determination of the Absolute Configuration

Since assumptions on the enantioinduction of the asymmetric Wittig reaction shown in Table 6 and Scheme 23 were solely based on the results of WERNER and coworkers,[86] further studies were necessary to assure which absolute configuration of the propellanes **78** and **125** was obtained in the reaction sequence. Since none of the compounds were crystalline solids, determination of the absolute configuration by X-ray crystallography was deemed unfeasible. Due to the highly rigid structures of **78** and **125**, calculations of the conformers present in solution was deemed comparably simple. Therefore, VCD-spectroscopy was chosen as the method to determine their absolute configuration.[112] As **78** and **125** were obtained from the same enantioselective cyclization reaction, a positive control of the results would be possible by examination of both compounds. Quantum chemical calculations of the conformers and the measurements were performed in collaboration with CHRISTIAN MERTEN at Ruhr-Universität Bochum. These calculations led to the conclusion that the [3.3.3]propellane **78** is highly rigid and exists in solution mainly as a single conformer. On the other hand, the 7-membered ring of the [5.3.3]propellane **125** allows higher flexibility and it adopts two conformers that contribute nearly equally to the population present in solution (Figure 11).

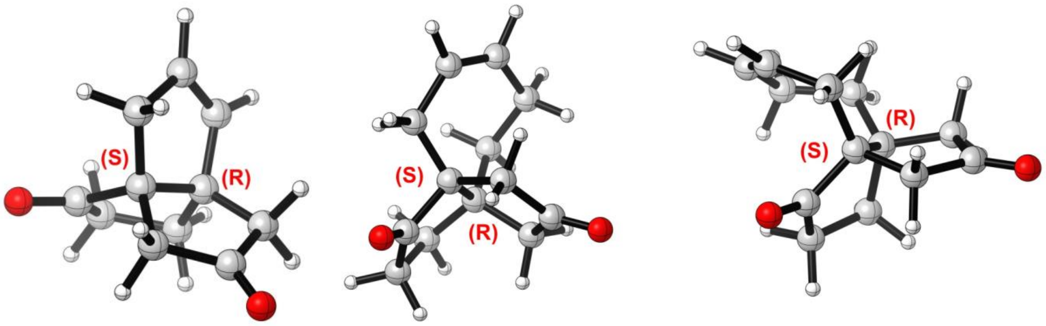


Figure 11: Main contributing conformers of [3.3.3]propellane **78** (left), and [5.3.3]propellane **125** (middle and right). Reprinted with permission from *Schneider* et al.[83] (© 2017 American Chemical Society).

Derived from these conformers, the respective IR and VCD spectra of **78** and **125** were calculated and compared to their experimentally determined IR and VCD spectra (Figure 12). Although two regions in the experimentally obtained spectra had to be removed, due to total absorbance by the carbonyl group and the solvent, the data clearly points towards the (*1S,5R)*-configuration of **78** and **125** shown in Figure 11. These findings corroborate the observations made by WERNER and coworkers during initial development of the reaction conditions.

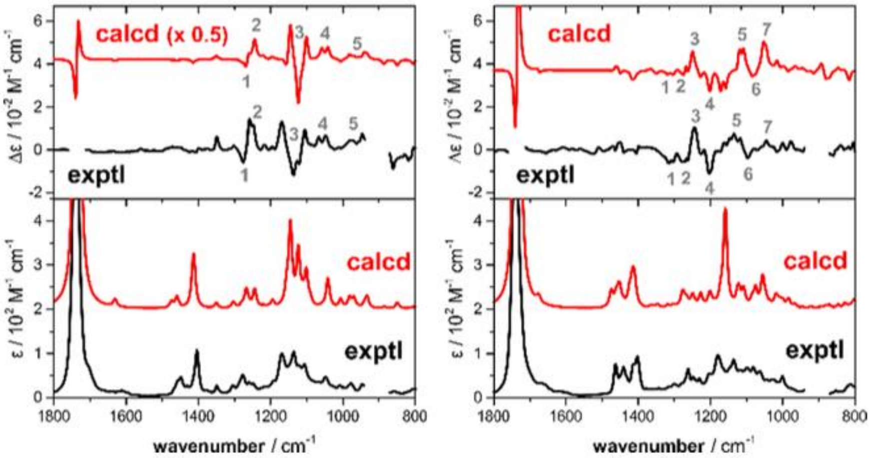
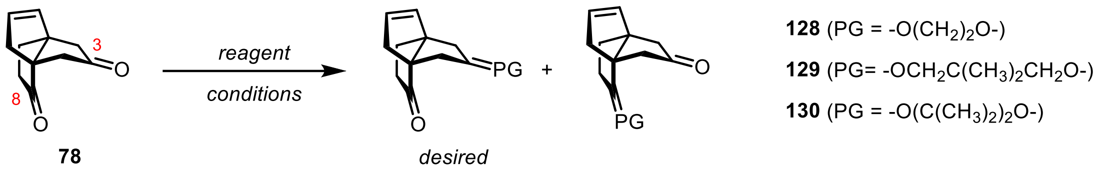


Figure 12: Comparison of calculated and experimental VCD and IR spectra of propellanes **78** (left) and **125** (right). Reprinted with permission from *Schneider* et al.[83] (© 2017 American Chemical Society).

2.2.6. Functionalization of the Propellane Structure

Synthesis of the [3.3.3]propellane core **78** and determination of its absolute configuration was followed by stereoselective functionalization of the three carbocycles to the motifs present in the dichrocephones. Initial studies were aimed at introduction of a sterically demanding protecting group at C-3, to allow for regio- and diastereoselective addition of a methyl nucleophile to the C-8 carbonyl functionality from the less hindered side of the unsaturated ring.

A first strategy envisaged acetal functionalization of C-3. As seen in Table 7, this approach suffered from low regioselectivity. Standard reaction conditions, using 2,2-dimethyl-1,3-dioxolane as the reagent, gave an inseparable mixture of regioisomeric acetals **128** (entry 1). At lower reaction temperatures conversion of the starting material was not sufficient (entry 2). When using sterically more demanding diols, the ratio of regioisomers could be shifted towards the desired product, but suffered from low conversion.



128 (PG = -O$(CH_2)_2$O-)
129 (PG= -O$CH_2C(CH_3)_2CH_2$O-)
130 (PG = -O$(C(CH_3)_2)_2$O-)

Table 7: Attempted acetal functionalization of [3.3.3]propellane **78.**

	Reagent	Conditions	Product	Yield, C-3:C-8
1	2,2-dimethyl-1,3-dioxolane	TsOH, *neat*, r.t.	**128**	45%,[a] 10:8
2	Bis-TMS-ethylenglycol	TMSOTf, CH_2Cl_2, –78 °C	**128**	Low conversion
3	neopentylglycol	TsOH, DME, r.t.	**129**	No conversion
4	neopentylglycol	TsOH, DME, 45 °C	**129**	50%,[a] 4:1
5	pinacol	TsOH·H_2O, $CHCl_3$, reflux	**130**	32%,[a] >20:1

[a] Starting material could be isolated after 24 h reaction time.

The regioisomeric mixtures can be explained by product distribution under thermodynamic control, when performing the acetalisation of **78**. Whereas functionalization to the sterically unhindered 1,3-dioxolane led to 1:1 mixtures of the possible regioisomers (entry 1), more hindered diols like pinacol gave preferred functionalization of the sterically more accessible C-3 to give **130** as a single regioisomer (entries 4–5). Nonetheless, due to the low yield this strategy was no longer pursued.

Selective functionalization of **78** could be achieved by selective reduction of the C-3 carbonyl functionality (Table 8). For this purpose, **78** was subjected to a variety of reducing agents at low temperatures.

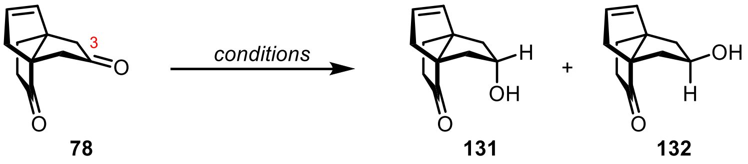


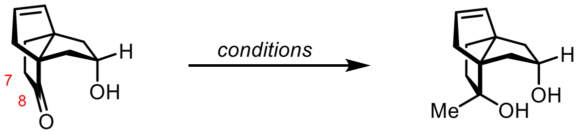
Table 8: Selective reduction of the C-3 carbonyl functionality of **78**.

	Reducing agent	Conditions	Yield
1	$NaBH_4$	THF, –78 °C, 30 min	84%[a]
2[b]	L-Selectride	THF, –78 °C, 30 min	32% **131** + 56% **132**
3[b]	K-Selectride	THF, –78 °C, 2 h	52% **131** + 28% **132**
4	K-Selectride	THF, –98 °C,[c] 4 h	77% **131**

[a] Complex mixture of regio- and stereoisomers obtained; [b] Products were separable by column chromatography; [c] MeOH/N_2-cooling bath.

Whereas employing $NaBH_4$ led to an inconsequential mixture of the possible regio- and stereoisomers (entry 1), the use of L-selectride at –78 °C allowed complete conversion of the starting material to a separable 5:3-mixture of the two alcohols **131** and **132** (entry 2). Higher selectivity towards diastereomer **131** was achieved when using K-selectride (entry 3) and could be obtained isomerically pure in 77% yield, when performing the reaction at –98 °C (entry 4). Structure determination of both synthesized alcohols **131** and **132** was attempted by GOESY spectroscopy. However, none of the obtained spectra showed a significant coupling of the proton at C-3 to the adjacent carbocycles. Since it was assumed that the configuration at C-3 did not play a role in stereoselectivity of the following synthesis of the C-8 tertiary alcohol, the conditions shown in entry 4 were used in further studies due to the high yield and purity of the obtained product. In retrospect, the configuration of both structure could be assigned by the crystal structure of diol **133** (Figure 13).

The C-8 methyl group was introduced by the addition of methyl nucleophiles to ketone **131** (Table 9). Initial experiments were performed at room temperature, to allow for higher stereoselectivities of the reaction, but failed due to unexpectedly low reactivity of the starting material towards the employed reaction conditions (entries 1–3). The addition of Ti-salts, aimed to increase reactivity, equally led to no conversion of the starting material (entries 2–3).[113]



131 **133**

Table 9: Addition of methyl nucleophiles to ketone **131**.

	Nucleophile (equiv.)	Conditions	Yield[a]
1	MeMgBr (6)	THF, r.t.	No conversion
2	MeLi (15), ClTi(O*i*Pr)$_3$	Et$_2$O, r.t.	No conversion
3	MeTi(O*i*Pr)$_3$ (10)	Et$_2$O, r.t.	No conversion
4	MeLi (70)	Et$_2$O, r.t.	28%
5	MeLi (70)	Et$_2$O, reflux	45%
6	MeMgCl (70)	THF, 40 °C	47%
7	MeMgCl (70)	THF, reflux	64%
8	MeMgCl (6)	THF, reflux	62%[b]
9	MeLi (6), CeCl$_3$ (6)	THF, r.t. to 40 °C	46%

[a] All reactions led to recovery of starting material, independent of the reaction time; [b] 92% yield, based on recovered starting material.

By using a large excess of the nucleophile, the desired diol **133** could be obtained in 28% yield (entry 4). The yields could be raised with higher reaction temperatures. Whereas 45% of the desired diol was obtained in refluxing diethyl ether (entry 5), the yield was further raised to 62% by switching to refluxing THF (entries 6–8). All reactions described in entries 4–9 led to isolation of diol **133** as a single diastereomer, independent of the reaction conditions and the employed nucleophile. As seen in Table 9, every performed reaction led to partial recovery of starting material **131**. Most likely, the quaternary stereogenic center at C-1 causes high steric shielding of the carbonyl group at C-8. In combination with the approach of the nucleophile along the Bürgi-Dunitz angle nearly parallel to the rigid unsaturated carbocycle,[114] the reaction will proceed comparably slow. Therefore, the employed Grignard-reagent can alternatively act as a base, which leads to deprotonation of the sterically more accessible C-7 and formation of the corresponding enolate. This enolate is build up irreversibly under the reaction conditions, and is converted to the starting material upon aqueous work-up. Comparable reactivity was observed in the addition of nucleophiles to steroids at C-17, the carbonyl functionality being shielded by the adjacent all-carbon quaternary center. In these cases, cerium-based nucleophiles were successfully employed to obtain full conversion, since the lower basicity of these compounds leads to a preferred 1,2-addition.[115] As seen in entry 9, this methodology could not be transferred to the problem at hand. The addition of pre-dried $CeCl_3$ to the reaction mixture led to isolation of only 46% of the desired product **133**.

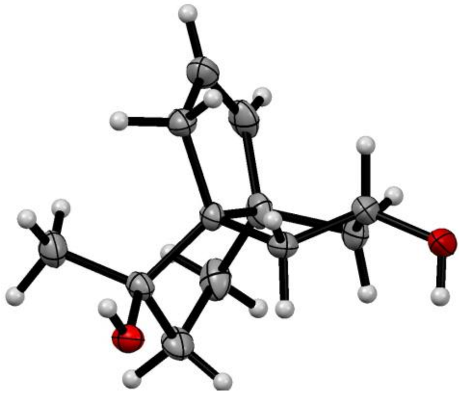
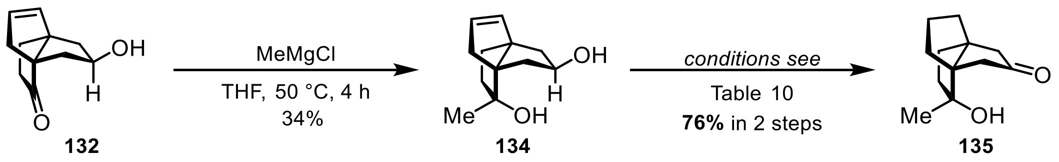


Figure 13: X-ray crystal structure of diol **133**. Ellipsoids drawn at 50% probability.

Single crystals of diol **133** were subjected to X-ray crystal structure analysis (Figure 13). The crystal structure unambiguously proved the stereoselectivity of the reactions described above.

When alcohol **132**, which is obtained as the main product in the reduction of **78** with L-selectride (Table 8, entry 2), was used in the addition reaction of MeMgBr, an isomerically pure diol **134** was obtained (Scheme 29). This diol could be converted into ketone **135** after hydrogenation and oxidation of the C-3 alcohol as described in the next chapter. Therefore, the addition of methyl nucleophiles occurs independently of the configuration at C-3 selectively from the side of the unsaturated bridge.



Scheme 29: Analogous sequence of addition, hydration and oxidation of alcohol **132**, leading to ketone **135**.

Stereoselective introduction of the tertiary alcohol at C-8 was followed by further conversion of the two other carbocycles to the motifs present in the natural products. Hydrogenation of olefin **133** was realized employing palladium on charcoal under atmospheric hydrogen pressure. The saturated compound **136** was obtained in near quantitative yields after 18 h, and could be used in the following oxidation without additional purification. The conversion of the secondary alcohol at C-3 in **136** to the corresponding ketone **135** required additional optimization, due to unexpected reactivity of the tertiary alcohol at C-8. Initially employed Swern- and Parekh-Doering oxidations[116] led to low conversion of the starting material (Table 10, entries 1–2). When using Dess-Martin periodinane,[82] a mixture of products was obtained, in which elimination at C-8 competed with the desired oxidation of the secondary alcohol (entries 3–4).

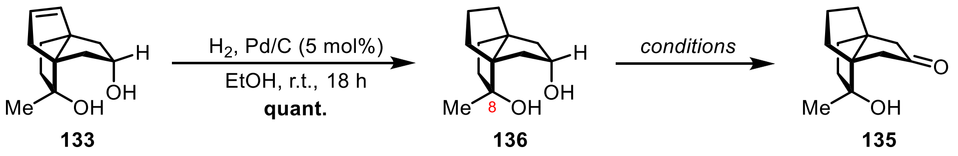


Table 10: Hydrogenation of olefin **133** and chemoselective oxidation of alcohol **136**.

	Oxidant	Conditions	Yield
1	$(COCl)_2$, DMSO, Et_3N	CH_2Cl_2, –78 to 0 °C	Low conversion
2	$pySO_3$, DMSO, Et_3N	CH_2Cl_2, r.t.	Low conversion
3	DMP (4 equiv.)	CH_2Cl_2, 0 °C to r.t.	36%[a]
4	DMP (2 equiv.)	CH_2Cl_2, 0 °C to r.t.	48%[a]
5	PDC	CH_2Cl_2, 0 °C	74%
6	PCC	3Å MS, CH_2Cl_2, r.t.	55%
7	PCC	3Å MS, AcOH, CH_2Cl_2, r.t.	82%

[a] Elimination of the alcohol at C-8 was observed in ^{1}H NMR of the crude product.

This was probably caused by acetic acid produced by decomposition of the reagent, since better yields of the desired ketone were obtained, when less reagent was employed. The best yields of **135** were obtained by employing chromium(VI)-based oxidants as the Cornforth-[117] and Corey-reagent[118] (entries 5–6). In this case activation of the oxidant with acetic acid was necessary to obtain the product in 82% yield, whereas no elimination could be observed (entry 7).

Synthesis of the pseudo-symmetric dienone **77** was achieved by double methenylation of ketone **135** (Table 11). Standard reaction conditions using Eschenmoser salt[69] led to slow conversion of the starting material, which was not completed after 2 days of reaction time (entry 1). RIOFSKI and coworkers described a methodology to obtain α-methylenation of sterically congested ketones, by simultaneous release of trifluoroacetate from the starting material as the thermodynamic driving force.[119] By employing a two-step approach (entry 2), **135** was first converted to the trifluoromethyl 1,3-diketone by Claisen-condensation with a trifluoromethyl ester. Further reaction of this intermediate with formaldehyde under alkaline conditions then led to the undesired enone **137** in 59% yield, due to simultaneous trifluoroacetylation of the tertiary alcohol under the reaction conditions. Low yields of saponification to **77** rendered this route undesirable.

The best yield of dienone **77** was obtained when using a method developed by DESOLMS,[120] who utilized tetramethyldiamino methane and acetic anhydride to obtain the corresponding Mannich reagent *in situ.* The methylenation was performed at elevated reaction temperatures, which led to isolation of **77** in 73% yield.

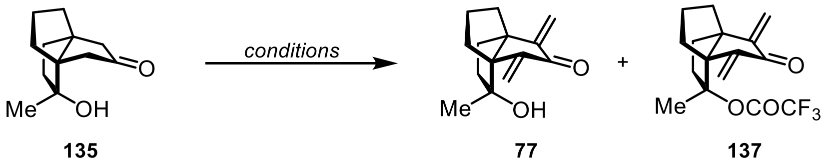


Table 11: Methenylation of ketone **135**.

	Carbon source	Conditions	Time	Yield
1	Me_2NCH_2I, Et_3N	CH_2Cl_2, 40 °C, 2 d	2 d	Low conversion
2[a]	KHMDS, $CF_3CO_2CH_2CF_3$,	THF, 0 °C to r.t.	60 min	59% **137**
	then K_2CO_3, HCHO	PhH, reflux	18 h	in 2 steps
3	Ac_2O, $(Me_2N)_2CH_2$	DMF, 95 °C	90 min	73% **77**
4	Ac_2O, $(Me_2N)_2CH_2$	*m*-CPBA, DMF, 95 °C	90 min	71% **77**
5	Ac_2O, $(Me_2N)_2CH_2$	DMF, 95 °C	5 h	42% **77**

[a] Subsequent saponification with aq. KOH delivered **77** in 60% yield.

Judging by thin layer chromatography, the reaction seemed to run cleanly to the desired product. Nonetheless, the yield could not be optimized over 73%, and no starting material could be recovered (entry 3). Employing reagents known to accelerate the final elimination step like *m*-CPBA did not lead to better yields of **77** (entry 4). Longer reaction times even led to lower isolated yields of the desired compound (entry 5). It was assumed that previously described reactivity of *cis*-enones to undergo dimerization by hetero Diels-Alder reaction might cause decomposition at prolonged reaction times.[121]

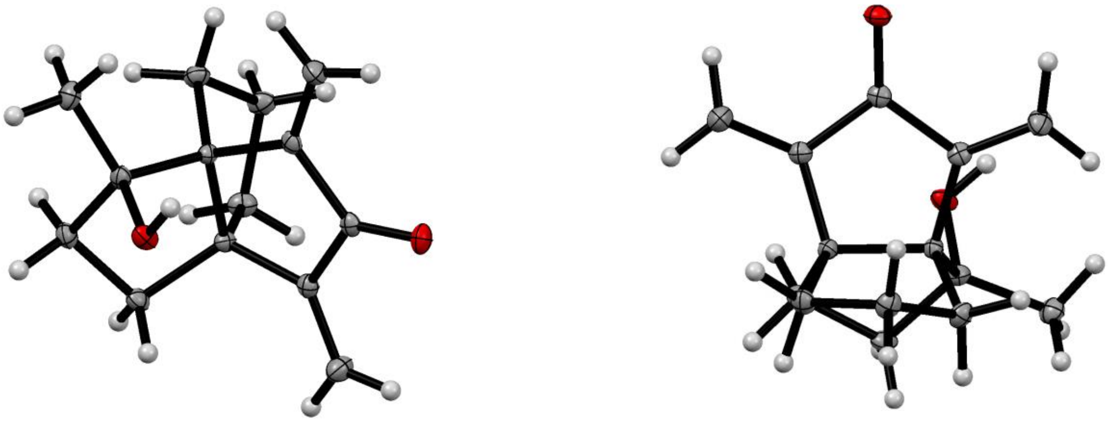
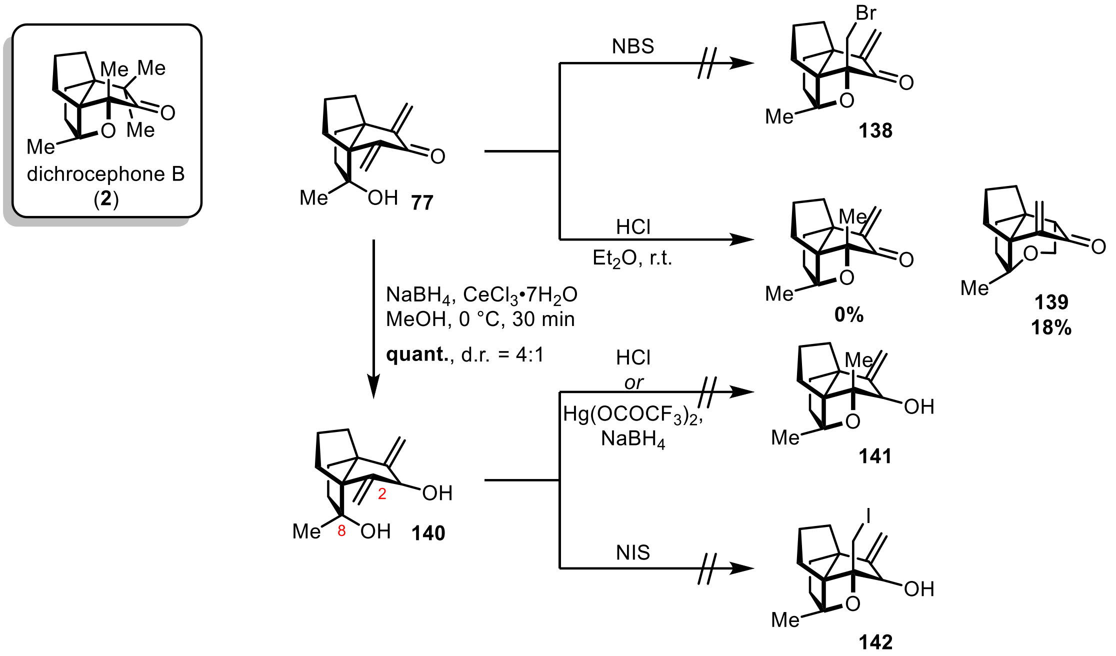


Figure 14: X-ray crystal structure of dienone **77** (left), with focus on the pseudo-symmetry of the dienone (right). Ellipsoids drawn at 50% probability.

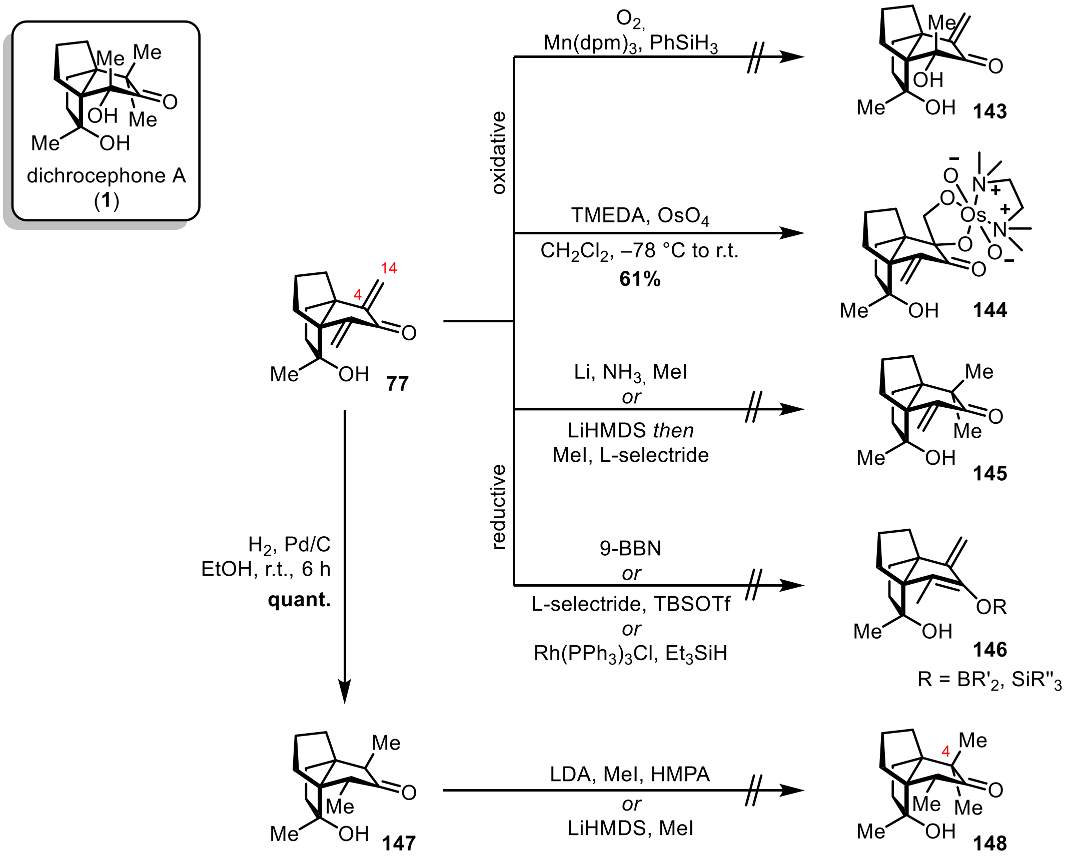
Dienone **77** was obtained as a solid, which gave single crystals suitable for X-ray crystal structure analysis after vapor diffusion crystallization from pentane/diethyl ether (Figure 14).

Selective conversion of the dienone **77** into the natural products proved highly challenging. A short description of the failed strategies is shown in the following schemes. Functionalization of **77** was initially aimed at introduction of the oxetane motif found in dichrocephone B (**2**) by either acid catalyzed ring closure or halocyclization with subsequent reductive dehalogenation (Scheme 30). The dienone system of **77** did not facilitate this kind of reactions, which resulted either in decomposition in case of the employed halocyclizations to **138**, or undesired 6-*endo*-trig cyclization with C-14 to the corresponding pyran **139**. Dienone **77** was therefore converted to the diallylic alcohol **140**, which was obtained as a 4:1 mixture of epimers at C-3. It was assumed that deconjugation of the double bonds would allow selective etherification of the C-8 hydroxy group with the tertiary carbon at C-2, as seen in the corresponding Markovnikov products **141** or **142**. All employed conditions led to complex reaction mixtures, probably due to the two hydroxy groups in close proximity to both olefins.



Scheme 30: Attempted functionalizations of dienone **77** and allylic alcohol **140** to the corresponding oxetanes.

Attempts to use redox transformations to desymmetrize the dienone system of **77** are summarized in Scheme 31. Employing a method developed by Magnus *et al.*,[122] which was employed to facilitate α-oxidation of **77** to the corresponding α-hydroxy ketones **143** led to a complex product mixture. Directed dihydroxylation using a OsO_4-TMEDA complex[123] surprisingly led to selective oxidation of the C-4/C-14 enone system farther away of the directing group, which could be clearly observed in the HMBC spectrum of osmium complex **144**. All attempts of reductive 1,4-functionalization to either **145** or **146** failed, since no regioselectivity of the reactions could be achieved. Hydrogenation of dienone **77** to the corresponding saturated ketone **147** gave a mixture of all possible diastereomers in quantitative yield. All attempts to obtain the geminal C-4 dimethyl group in **148** by deprotonation of **147** with a sterically hindered base and methylation gave a complex product mixture, with O-methylation of the tertiary alcohol as the predominant product observable in ^{1}H NMR of the crude mixture.



Scheme 31: Failed attempts at selective redox functionalizations of **77**.

In the end, the selective functionalization of dienone **77** was achieved by monocyclopropanation of the dienone (Table 12). Whereas a hydroxy-directed Simmons-Smith reaction[124] led to decomposition of the starting material (entry 1), Corey-Chaykovsky[125] reaction conditions led to clean cyclopropanation of the double bonds. In a first experiment, **77** was treated with two equivalents of deprotonated trimethylsulfoxonium iodide at room temperature (entry 2). Instead of the desired monofunctionalization at the sterically less hindered C-4, the bisspirocyclic compound **149** was obtained in near quantitative yield. The reaction was repeated using one equivalent of the cyclopropanation reagent, which led to an inseparable mixture of mono- and double functionalization (entry 2). To enable a selective reaction, the DMSO-solution of the reagent was diluted at room temperature with THF, effectively lowering the freezing point, which allowed to lower the reaction temperature to 0 °C. Addition of **77** at this temperature enabled monofunctionalization to **150** in 63% yield, and the corresponding regioisomer **151** in 30% yield, which were separable by column chromatography.

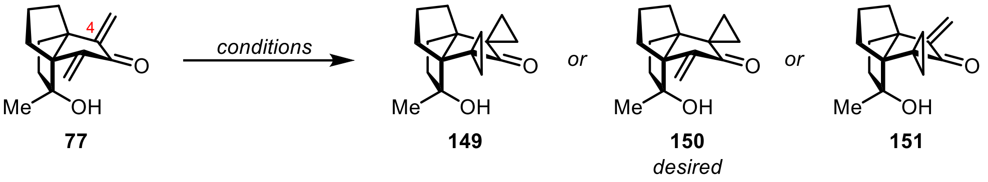


Table 12: Cyclopropanation of dienone **77**.

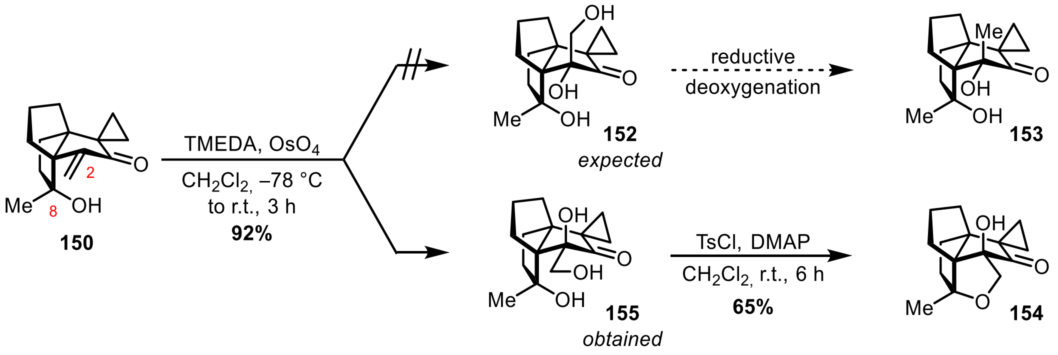
	Reagents	Conditions	Yield
1	Et_2Zn, CH_2I_2 (1.1 equiv.)	CH_2Cl_2, –78 °C to r.t.	Decomposition
2	NaH, Me_3SOI (2.1 equiv.)	DMSO, r.t.	94% **149**
3[a]	NaH, Me_3SOI (1.1 equiv.)	DMSO, r.t.	86% **149/150/151**
4[b]	NaH, Me_3SOI (1.05 equiv.)	DMSO, THF, 0 °C[c]	63% **150** + 30% **151**

[a] Inseparable mixture with remaining starting material; [b] Products separable by column chromatography; [b] Reagent prepared at r.t., reaction performed at 0 °C.

With this, the synthesis of the carbocyclic scaffold of both natural products was completed. Further redox transformations of tetracyclic ketone **150** were aimed to introduce the tertiary alcohol at C-2 and hydrogenolytic C-13/C-14 bond cleavage of the cyclopropane, to obtain the C-4 dimethyl group present in the natural products.

2.2.7. Synthesis of the Reported Structure of Dichrocephone A

The stereoselective introduction of the hydroxy group at C-2 of enone **150** was planned by an oxidation directed by the tertiary alcohol at C-8. By applying the previously employed hydroxy-directed dihydroxylation to **150**, a corresponding triol was obtained in excellent yield (Scheme 32). Following the mechanistical proposal[123] of the reaction, it was assumed that **152** was obtained as the main product. nOe studies of the compound again led to no further conclusion of the spatial arrangement of substituents.

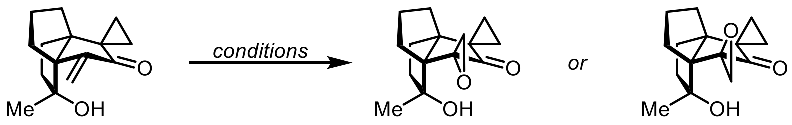


Scheme 32: Attempted stereoselective C-2 oxidation by directed dihydroxylation/deoxygenation of **150**.

In an attempt at reductive deoxygenation to 153**,** by converting the C-12 alcohol to the corresponding tosylate, ring closure to furan **154** was observed in 65% yield. Therefore, the initial dihydroxylation of **150** was not directed by the tertiary alcohol, but rather led to the approach of the oxidant from the sterically less hindered side of the enone to build up **155**. In face of this result, the stereoselectivity of the previously described dihydroxylation to osmate ester **144** (Scheme 31) might also be caused by minimized steric interaction, leading to its corresponding C-4 diastereomer.

An alternate strategy envisaged introduction of the last oxygen functionality by directed epoxidation of **150** to **156** (Table 13). Catalytic epoxidations employing titanium or vanadium catalysts led to low conversion of the starting material (entries 1–2). GLOTTER and coworkers studied the epoxidation of electron deficient enones, using these catalytic systems.[126] According to this study, a perpendicular alignment of the directing group and the plane of the enone are ideal for nucleophilic attack of the metal-coordinated peroxide to the β-carbon of the enone. Most likely, the rigid ring system of **150** leaves minimal conformational freedom for such an alignment. The crystal structure of dienone **77** shows an angle of roughly 45° between the two functional groups (Figure 14), and a similar angle was assumed for enone **150**.

Initial success was observed under Prilezhaev-conditions (entries 3–4).[127] A large excess of *m*-CPBA led to an inseparable 4:1 mixture of epimeric epoxides **156** and **157** in 72% yield, as observed by ^{1}H NMR spectroscopy. Stereoselectivity and yield could be improved under Weitz-Scheffer conditions using Triton B, which was shown to coordinate to tertiary alcohols.[128] Under these conditions, a 10:1 mixture of **156** and **157** was obtained in 82% yield (entry 5).



150 **156** *desired* **157**

Table 13: Stereoselective epoxidation of enone **150**.

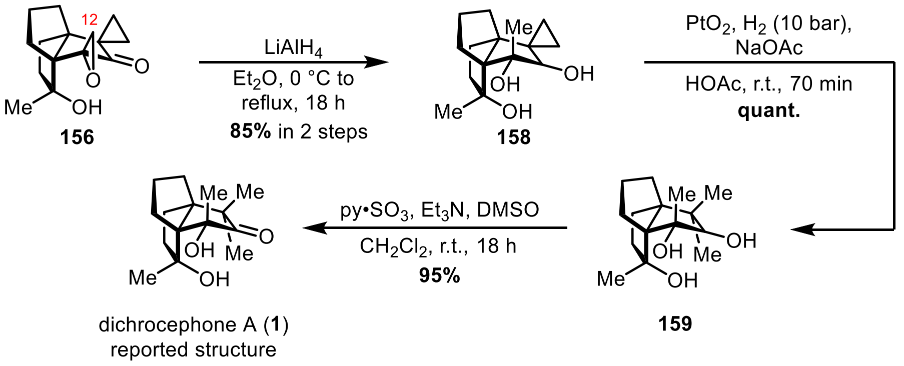
	Oxidant	Conditions	Yield[a]
1	VO(acac)$_2$, *t*BuOOH	CH$_2$Cl$_2$, 40 °C	Low conversion
2	Ti(O*i*Pr)$_4$, *t*BuOOH	3Å MS, CH$_2$Cl$_2$, 0 °C	Low conversion
3	*m*-CPBA (2 equiv.)	CH$_2$Cl$_2$, 0 °C	Low conversion
4	*m*-CPBA (10 equiv.)	CH$_2$Cl$_2$, 0 °C	72%, d.r. = 4:1[b]
5	Triton B, H$_2$O$_2$	THF, H$_2$O, 0 °C	86%, d.r. = 10:1[b]
6	TFAA, H$_2$O$_2$	Na$_2$HPO$_4$, CH$_2$Cl$_2$, –40 to 0 °C	Quant., d.r.>20:1[b]

[a] Yield of crude product, since decomposition of the product was observed upon attempted chromatography; [b] Determined by ^{1}H NMR.

Lowering the reaction temperature did not improve selectivity. Ideal conditions were found by using *in-situ* prepared trifluoro peracetic acid as the oxidant. Thereby, the reaction of enone **150** at –40 °C allowed selective conversion to epoxide **156** in near quantitative yields (entry 6). It was later confirmed by X-ray crystallography of **1** that the reactions in entries 4–6 delivered the desired stereoisomer **156** as the main product (Figure 15). Since column chromatography led to decomposition of **156**, the crude product was used directly in the next step.

The synthesis of the reported structure of dichrocephone A (**1**) was completed by three consecutive redox transformations (Scheme 33). The epoxide **156** was selectively opened at C-12 with an excess of $LiAlH_4$ in refluxing diethyl ether, leading to isolation of tertiary alcohol **158** in 85% yield over 2 steps. The simultaneous reduction of the carbonyl functionality observed under the conditions was intended. It was assumed that the following hydrogenolysis of the C-13/C-14 bond would not proceed regioselectively, if the carbonyl functionality remained in the starting material. Similar behavior was observed by SCHULTZ and coworkers,[129] who described preferred oxidative addition of metal catalysts into the α–β-bond of α-cyclopropyl ketones under hydrogenolysis conditions, which would not lead to the desired geminal dimethyl substitution of the natural products.

The cyclopropane hydrogenolysis was performed under H_2-atmosphere using Adams´ catalyst.[130] Due to elimination of the tertiary alcohols at longer reaction times and low reactivity under atmospheric pressure, ring opening was performed under 10 bar of hydrogen pressure with 6 equivalents of Adams' catalyst, with additional sodium acetate acting as a pH buffer. This led to the formation of **159** in quantitative yield after 70 minutes. Oxidation of the secondary alcohol in **159** under Parekh-Doering conditions allowed conversion to the corresponding ketone **1** in excellent yields.[116a]



Scheme 33: Synthesis of the reported structure of dichrocephone A (**1**) by double reductive ring opening of **156** and Parikh-Doering oxidation of **159**.

The racemate of **1** was obtained as a solid, and crystals suitable for X-ray crystal structure analysis were obtained after vapor diffusion crystallization. This verified that the obtained structure **1** corresponds to the one reported by DING and ZOU for dichrocephone A (Figure 5c, Chapter 2.1.2),[59] and confirms the regio- and stereoselectivities of the reaction sequence from dienone **77**.

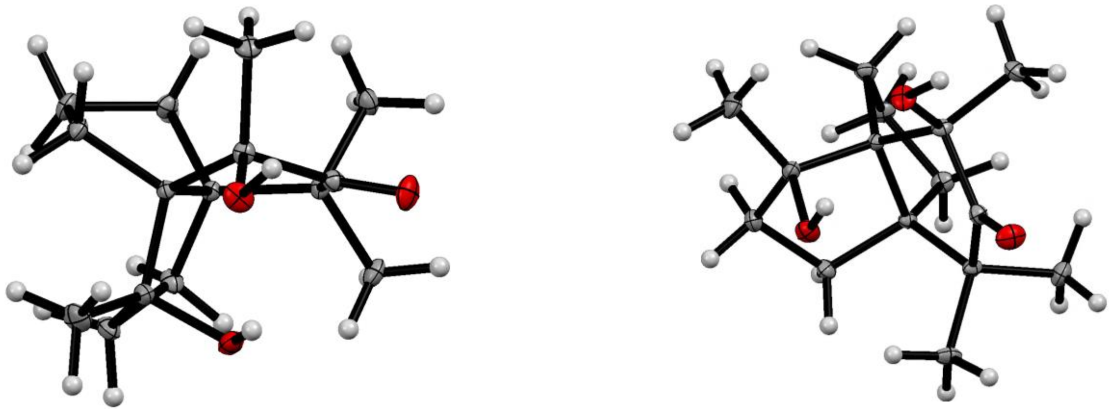


Figure 15: X-ray crystal structure of the reported structure of dichrocephone A (**1**) seen along the central C–C bond (left), and with focus on the stereotetrade (right). Ellipsoids drawn at 50% probability.

Unfortunately, the ^{13}C NMR spectra of **1** deviated from the reported data, with signal shifts of up to 5.6 ppm (full comparison of ^{1}H and ^{13}C NMR data in Table 16, experimental part). Figure 16 shows the comparison of ^{13}C NMR spectra for synthetically obtained **1** with the spectra obtained for the natural isolate (a full ^{13}C NMR spectrum showing the carbonyl signal was not included in the publication by DING and ZHOU).

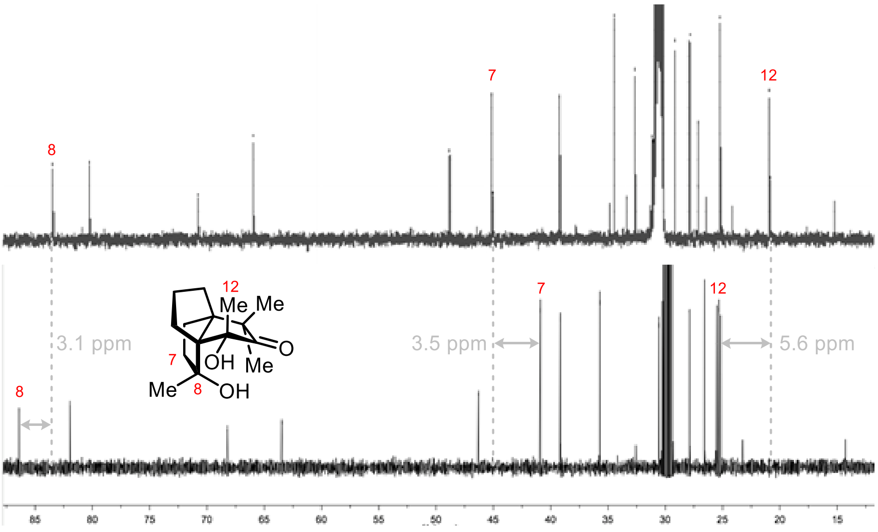


Figure 16: Part of the ^{13}C NMR spectra of isolated dichrocephone A (top) and synthetic diol **1** (bottom).The three highest shift deviations are annotated in grey. Reprinted and adapted with permission from TIAN *et al*.[59] (© 2013, Royal Society of Chemistry).

In combination with the unambiguous proof of structure by X-ray crystallography, it was concluded that naturally occurring dichrocephone A does not possess the initially proposed structure shown in Scheme 33. A seen in Figure 16 and Table 16 (in experimental part), the highest deviations of ^{13}C NMR signals of **1** and the natural isolate were found in proximity to the stereotetrade, with up to 5.6 ppm for the C-12 methyl group.

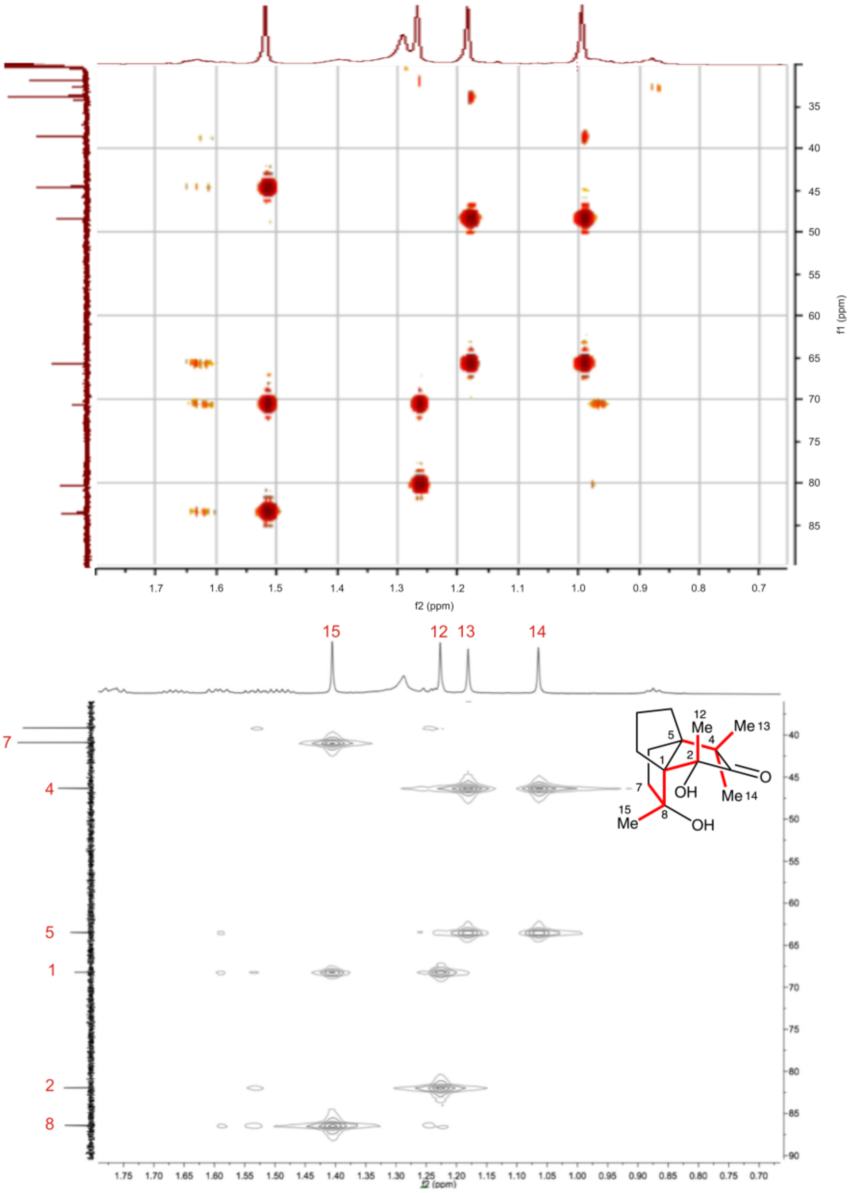


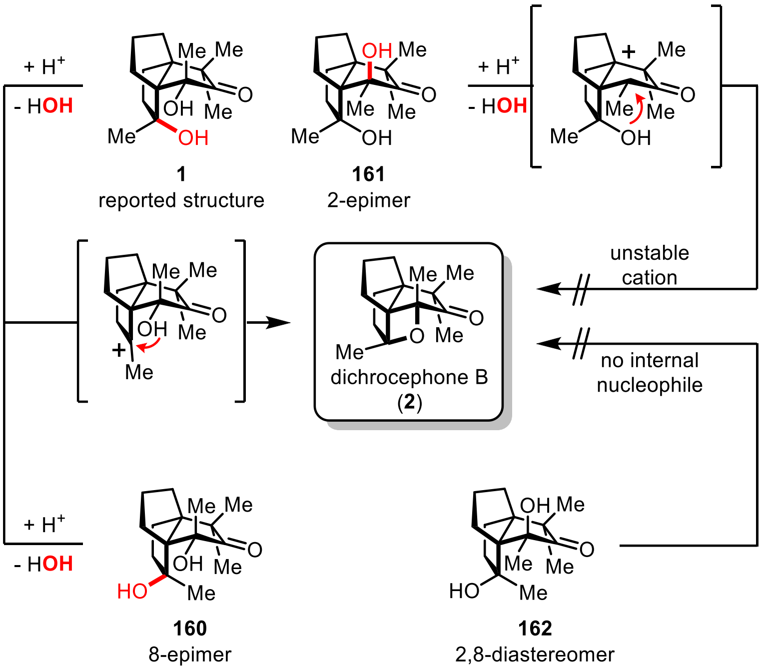
Figure 17: Part of the HMBC spectrum of isolated dichrocephone A (top) and the same part of the HMBC spectrum of synthetic diol **1** (bottom) focusing on coupling in the stereotetrade and the quaternary carbon atoms (highlighted in red). Reprinted and adapted with permission from Tian *et al*.[59] (© 2013, Royal Society of Chemistry).

Nonetheless, a comparison of the two dimensional NMR spectra of **1** with the one reported for dichrocephone A showed high structural similarity in this part of the spectra, concerning the connection of the carbon atoms. In Figure 17 the part of the HMBC spectra of synthetic **1** and isolated dichrocephone A is shown, from which coupling of the

4 methyl groups with the quaternary carbon atoms at C-1/C-5 and the tertiary alcohols at C-2/C-8 is clearly indicated for both compounds. Based on the overall similarity of ^1H and ^{13}C NMR spectra of both compounds, as well as the ^2J- and ^3J-coupling derived from 2D spectra, it was assumed that dichrocephone A is a diastereomer of the synthesized compound **1**. Unfortunately, nOe studies of **1** did not lead to additional information about the structural relationship of **1** and the natural product. A C-12/C-15 coupling was observed, which was also the case for the natural isolate. Therefore, nOe spectroscopy again proved to be unfit for determination of the triquinane structure, which was already observed for alcohols **131**/**132** and triol **158**.

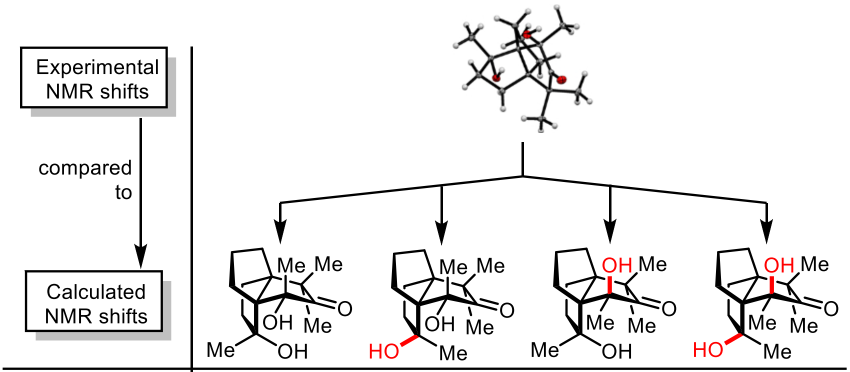
2.2.8. Structure Revision of Dichrocephone A

To predict the correct structure of the natural product, the biosynthetic connection of dichrocephones A and B was taken into consideration (Scheme 34). As reported in the initial publication, dichrocephone B is presumably a dehydration product of dichrocephone A. In *Dichrocephala benthamii* this reaction likely takes place under acidic conditions, leading to heterolytic cleavage of either the C-2 or C-8 alcohol to the corresponding carbocation. The positive charge is then quenched by attack of the remaining hydroxy functionality, which builds up the oxetane motif found in dichrocephone B. In the corroborated structure of dichrocephone A (**1**) the carbocation would most likely be build up at C-8 and quenched by the C-2 alcohol. As shown in Scheme 34, only one other diastereomer of **1** is able to undergo etherification to form **2**: Facilitated by an external acid, the inverted C-8 hydroxy group of **160** can be cleaved to the same carbocation as **1**, and was therefore equally considered as a biosynthetic precursor to **2**. The C-2 epimer **161** would need to undergo preferred cleavage of the alcohol in α-position to the carbonyl functionality, which would lead to a destabilized carbocation, due to the negative inductive effect of the ketone.[131] On the other hand, both hydroxy groups in diastereomer **162** point towards the unfunctionalized carbocycle and are therefore unable to perform an intramolecular reaction.



Scheme 34: Biosynthetic considerations for correct structure prediction of dichrocephone A.

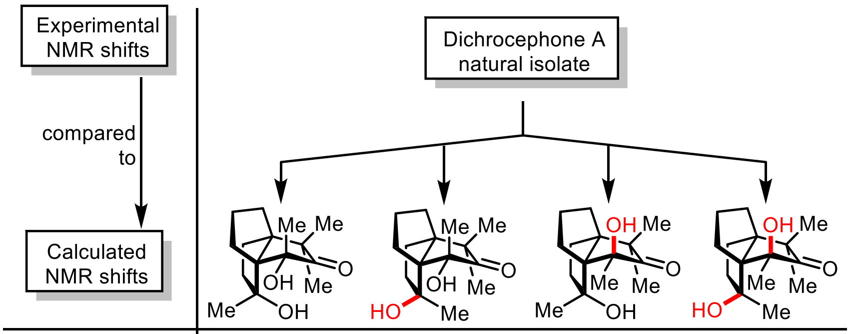
To confirm the biosynthetic considerations shown in Scheme 34 by calculation of NMR spectra, a cooperation with Dean Tantillo and Young Hong at the University of California, Davis was initiated. Structure optimization of **1** and **160–162** was used to obtain a weighed distribution of all conformers present in solution. This allowed to calculate the ^{1}H and ^{13}C NMR spectra for all four diastereomers in acetone-d_6, and compare them to the experimentally obtained data. To test the quality of these calculations, the calculated spectra were initially compared to the shifts obtained for **1**, since its structure was unambiguously confirmed by X-ray crystal structure analysis. The lowest mean absolute deviation (MAD) of ^{13}C chemical shifts from the experimental data was indeed obtained for the calculated spectrum of **1** (Figure 18). Nonetheless, the structure could not be verified this way, due to low deviation to the MADs obtained for **161** and **162**. Therefore, the DP4 method was used to verify the structure of **1** with higher certainty.[132] It improves results by compensating for large shift deviations of a few signals, and provides its result as a probability for structure assignment. Thereby, the structure of **1** previously verified by X-ray crystallography could be additionally corroborated by NMR calculations with 96.8% probability, and 100% probability when taking ^{1}H NMR shifts into consideration.



^{13}C MAD [ppm]	**2.13**	2.67	2.40	2.42
^{13}C DP4	**96.8%**	0.0%	0.0%	3.2%
^{1}H & ^{13}C DP4	**100%**	0.0%	0.0%	0.0%

Figure 18: Comparison of calculated NMR shifts for **1**, **160**, **161** and **162** with spectra obtained for synthetic **1**, leading to structure verification by DP4 method.

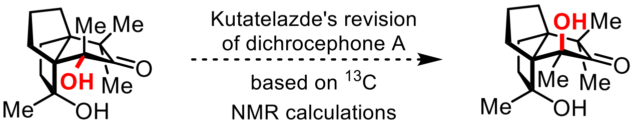
After successful proof-of-principle, the chemical shifts reported from the isolation of dichrocephone A by DING and ZHOU were compared to the calculated spectra. As seen in Figure 19, comparing MAD values on their own again did not allow a reliable structure prediction, with **160** and **162** differing by only 0.01 ppm. By combined DP4 analysis of ^{1}H and ^{13}C NMR data, **160** was predicted with 99.8% probability. These results support the biosynthetic consideration of Scheme 34, pointing towards **160** as the correct structure of dichrocephone A.



^{13}C MAD [ppm]	3.01	**1.79**	2.55	1.80
^{13}C DP4	0.3%	**75.6%**	11.2%	11.5%
^{1}H & ^{13}C DP4	0.0%	**99.8%**	0.2%	0.0%

Figure 19: Analogous comparison of calculated NMR data to spectra obtained after isolation of dichrocephone A lead to prediction of **160** as the correct structure of the natural isolate.

Interestingly, a study by KUTATELAZDE and coworkers was published after initial results were obtained by YOUNG HONG.[133] This publication reevaluated several triquinane natural products by comparison of their calculated and reported NMR spectra. Contrary to our conclusions derived from Scheme 34 and Figure 19, deviations in the data of Kutatelazde led them to assume the C-2 epimer **161** as the correct structure of dichrocephone A (Figure 20). This contradictory results obtained by NMR calculations indicate the complexity of triquinane structure elucidation. As part of Kutatelazde´s study, the structure proposal for tetracyclic dichrocephone B (**2**) by Ding and Zhou could be confirmed.

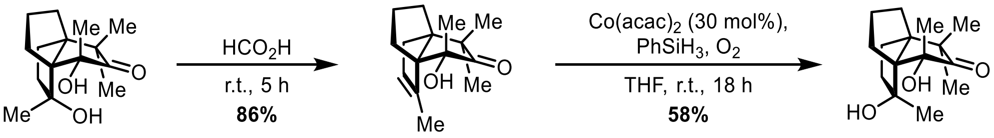


1 **161**

Figure 20: Structure revision of dichrocephone A by Kutatelazde and coworkers.

2.2.9. Completion of Dichrocephones A and B

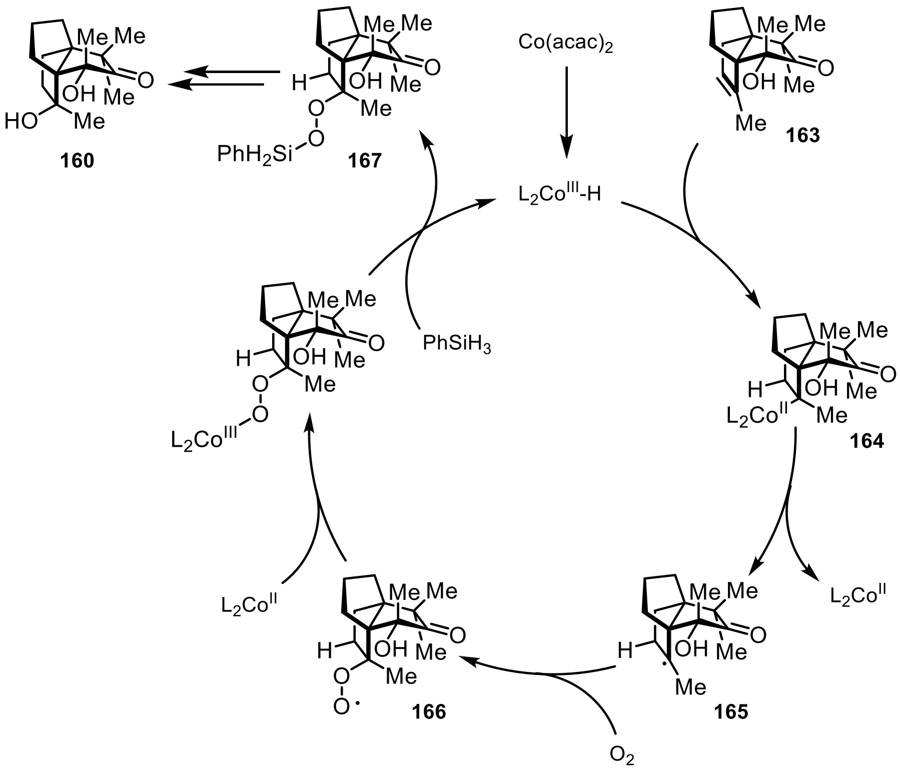
To test our hypothesis of structure revision for dichrocephone A, diol **1** was epimerized at C-8 by an elimination/hydration approach. Mildly acidic conditions were employed to prevent immediate cyclization to the oxetane or undesired elimination of the C-2 alcohol. Therefore, **1** was taken up in formic acid, which led to selective elimination of the tertiary alcohol at C-8 (Scheme 35). After aqueous work-up, endocyclic olefin **163** was obtained in 86% yield as a single regioisomer. To complete the epimerization, the olefin was subjected to Mukaiyama hydration conditions,[134] which gave the desired diol **160** as a single diastereomer in 58% yield.



1 **163** **160**

Scheme 35: Synthesis of the 8-epimer **160** by elimination and Mukaiyama hydration.

The stereoselectivity of the reaction can be explained by the shielding of the olefin from one side by the highly substituted cyclopentanone (Scheme 36). After addition of the cobalt hydride complex to starting material **163**, **164** is produced. Homolytic Co–C bond cleavage then leads to a sp^2-hybridized carbon radical **165,** which undergoes attack of molecular oxygen from the side of the unsubstituted carbocycle to give **166**. Further reaction of **166** with the cobalt complex and phenyl silane yields back the cobalt hydride complex and a silane peroxide **167**, which after reduction gives diol **160**.[135]



Scheme 36: Mechanism of the Mukaiyama hydration of **163**.

As predicted, naturally isolated dichrocephone A and the obtained diol **160** were identical in terms of their ^{1}H and ^{13}C NMR spectra (Table 17), leading to revision of the relative configuration of dichrocephone A to **160** (full comparison of ^{1}H and ^{13}C NMR in Table 17, experimental part). Unfortunately, a comparison of the reported optical rotation value with that of synthetic **160** led to the conclusion that the enantiomer of naturally occurring dichrocephone A was obtained (Figure 23). Since the absolute configuration of the synthetic material was corroborated by VCD spectroscopy of both [3.3.3]propellane **78** and [5.3.3]propellane **125**, it was concluded that the wrongly assigned relative configuration at C-8 of naturally occurring dichrocephone A led to a mistake in determination of the absolute configuration by ECD spectroscopy upon isolation. This assumption is further supported by the absolute configuration of all previously isolated modhephanes, which are the mirror image of the described structure of dichrocephone A and B (Figure 8, Chapter 2.1.2). Therefore, this thesis led to the synthesis of *ent*-dichrocephone A by correction of the relative configuration at C-8, as well as correction of the absolute configuration of dichrocephone A.

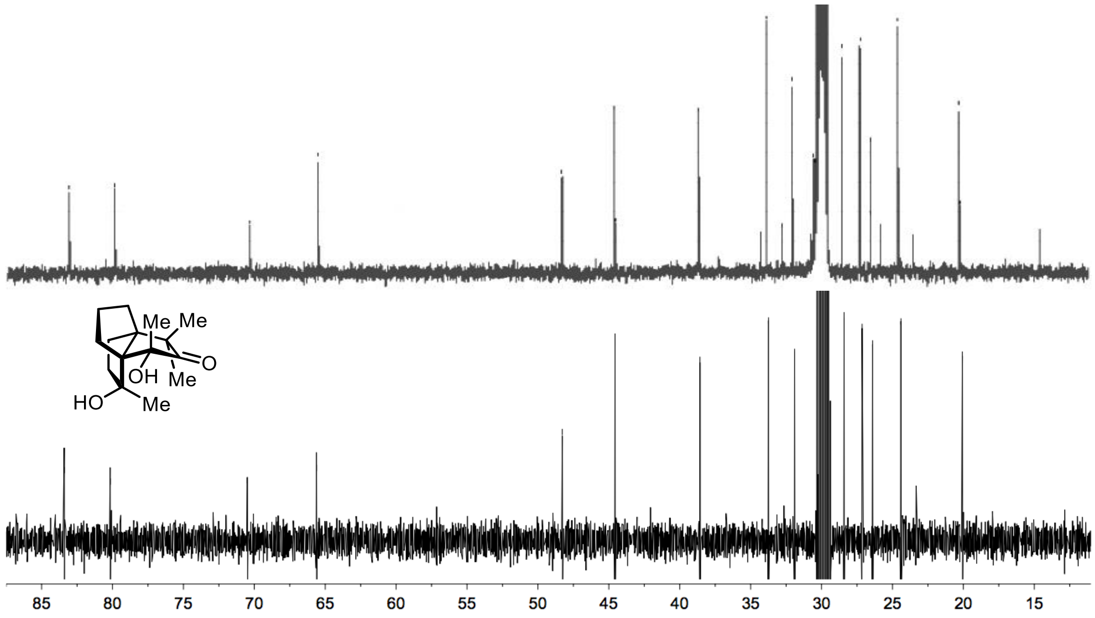


Figure 21: Part of the ^{13}C NMR spectrum of isolated dichrocephone A (top) and synthetic **160** (bottom). Reprinted with permission from TIAN *et al*.[59] (© 2013, Royal Society of Chemistry).

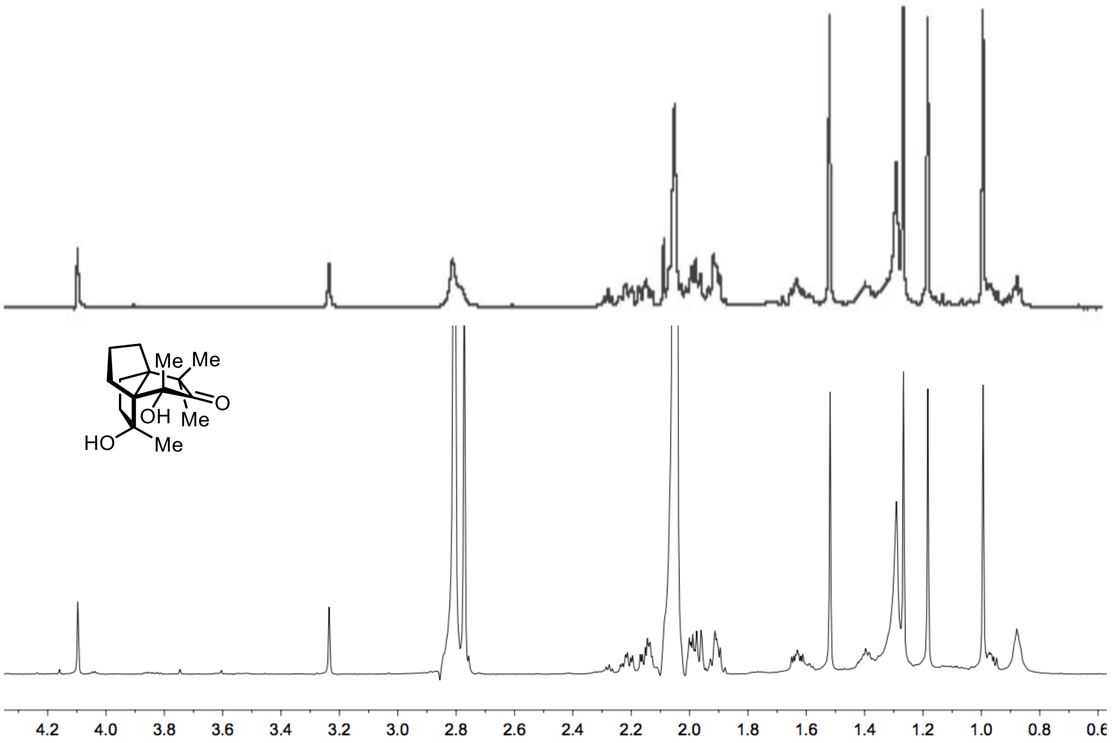
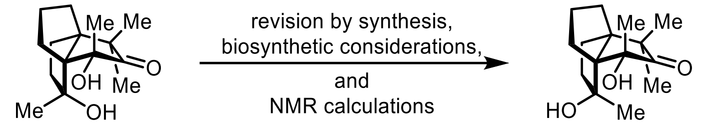


Figure 22: ^{1}H NMR spectra of isolated dichrocephone A (top) and synthetic **160** (bottom). Reprinted with permission from TIAN *et al*.[59] (© 2013, Royal Society of Chemistry).



reported structure of dichrocephone A

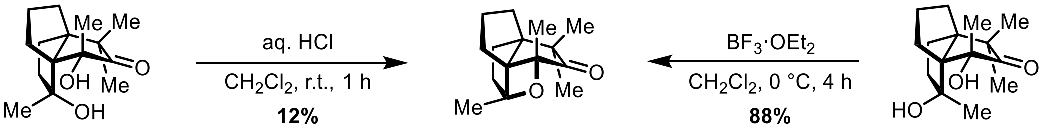
corrected structure of *ent*-dichrocephone A

$[\alpha]_D$ +59.1 (c = 0.22)

Lit. –63.3 (c = 0.18)

Figure 23: Comparison of optical rotation values and structure revision of dichrocephone A.

To obtain tetracyclic *ent*-dichrocephone B (**2**), the biomimetic dehydration of the 1,3-diol unit was approached next. As shown in Scheme 34, both diols **1** and **160** should be amenable for etherification of the C-2/C-8 diol, and therefore be potential synthetic precursors for this second natural product. This assumption was verified by subjecting both compounds to strongly acidic conditions (Scheme 37), which allowed construction of the oxetane motif. Whereas the addition of 1M HCl to **1** led to isolation of cyclized compound **2** in 12% yield, the reaction of dichrocephone A (**160**) with $BF_3{\cdot}OEt_2$ enabled the synthesis of the same compound in 88% yield.



1

2

ent-dichrocephone A (**160**)

Scheme 37: Acid catalyzed dehydration of **1** and **160** to dichrocephone B (**2**).

Presumably, both reactions proceed *via* the cationic transition state shown in Scheme 34. The low yield of dehydration of **1** might be explained with a S_N1-like transition state, in which the hydroxy group needs to be completely removed from the molecule, to allow for the attack of the nucleophile on the carbocation, which may also lead to undesired side reactions. In **160**, activation of the tertiary alcohol at C-8 by a Lewis acid may lead to back side attack of the nucleophile without the need for a fully formed carbocation, comparable to a S_N2 reaction. Due to the little amount of starting material left, no further optimization of the dehydrations of **1** and **160** were performed. Comparison of the NMR spectra of the isolated and synthesized **2** verified the structure of dichrocephone B (Figure 24, Figure 25 and Table 18 in experimental part).

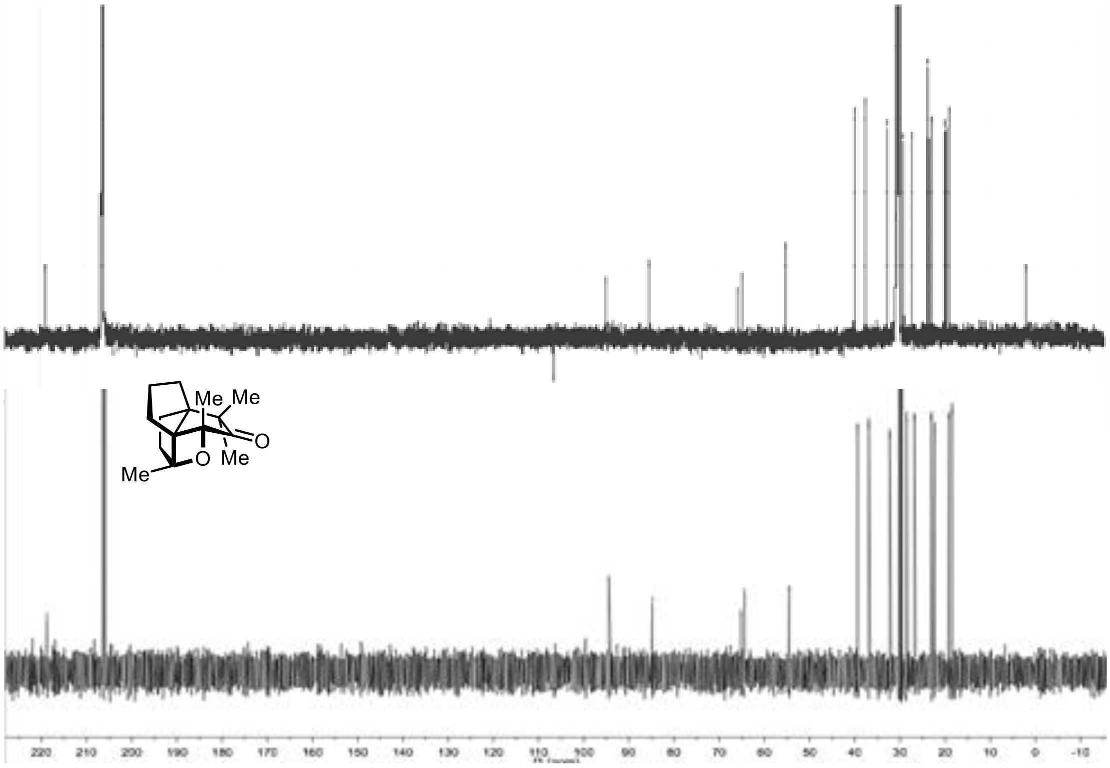


Figure 24: ^{13}C NMR spectra of isolated dichrocephone B (top) and synthetic **2** (bottom). Reprinted with permission from TIAN *et al*.[59] (© 2013, Royal Society of Chemistry).

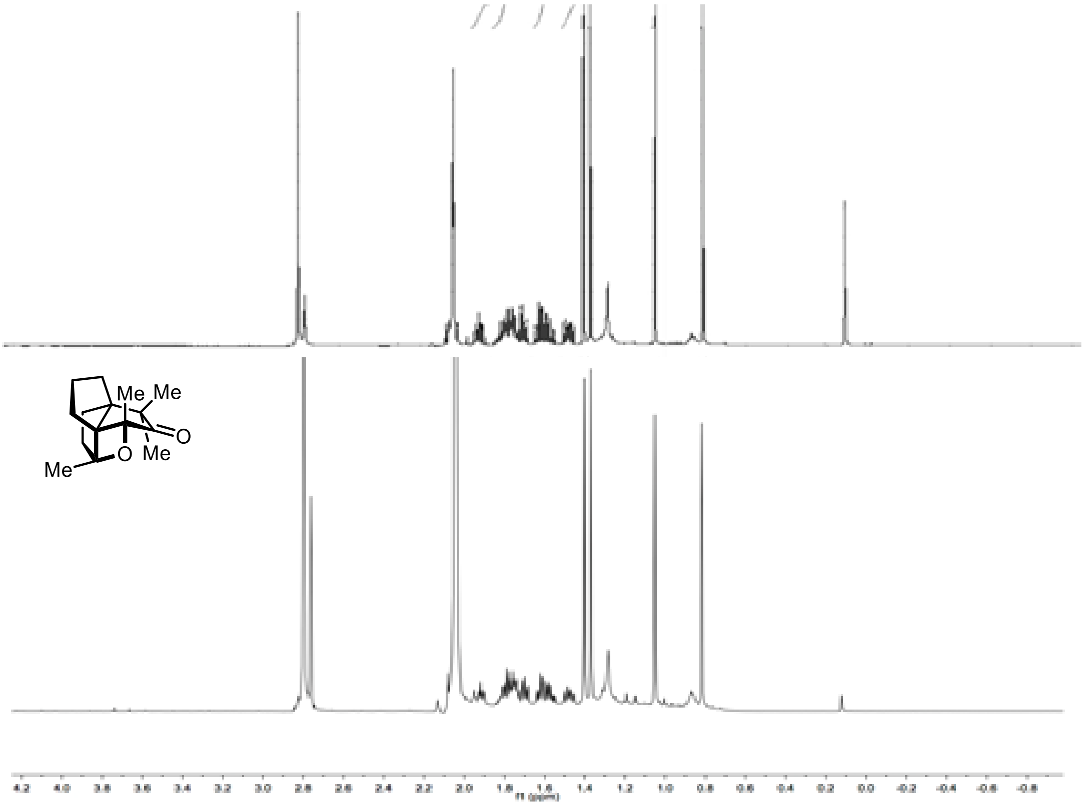
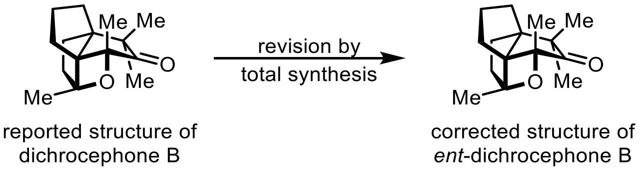


Figure 25: ^{1}H NMR spectra of isolated dichrocephone B (top) and synthetic **2** (bottom). Reprinted with permission from TIAN *et al*.[59] (© 2013, Royal Society of Chemistry).

Analogous to the correction of absolute configuration of dichrocephone A, the optical rotation value of synthetic **2** did not match the reported value for the natural product. Therefore, the absolute configuration of dichrocephone B needed to be reassigned as well (Figure 26).



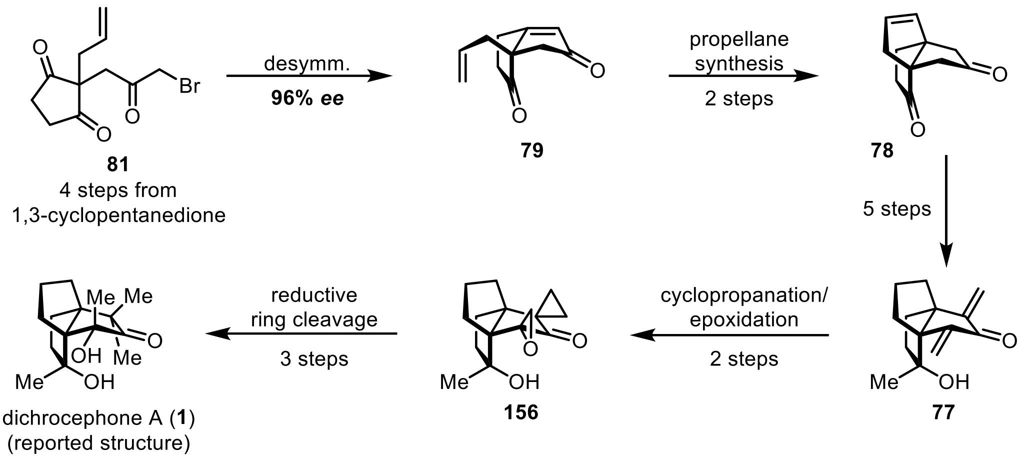
$[\alpha]_D$ +7.1 (c = 0.11)
Lit. –8.0 (c = 0.19)

Figure 26: Structure revision of dichrocephone B.

This correction of absolute configurations of both compounds also led to the conclusion that the earlier described biosynthesis of dichrocephones A and B by enzymatic oxidation of unprecedented *ent*-modhephene is incorrect (Scheme 5 and Scheme 6 in Chapter 2.1.3). Rather, dichrocephones A and B follow the previously described cyclase phase of nerolidol pyrophosphate to (–)-modhephene, as all other members of the natural product family, followed by oxidations and cyclization to the oxetane specific to *Dichrocephala benthamii*.

2.3. Conclusion

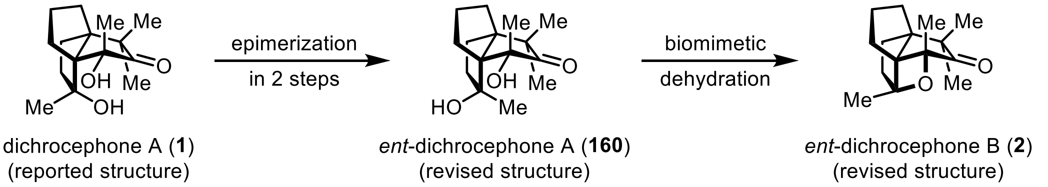
Dichrocephones A and B are two sesquiterpenes of the modhephane family, recently isolated from *Dichrocephala benthamii* in southern china. They are the highest oxidized molecules of this compound class, and show several unique structural features, such as fully substituted oxetane and cyclopentanone motifs, as well as four adjacent stereogenic centers and three adjacent quaternary all-carbon atoms, resulting in a sterically highly congested core structure. In preliminary studies, both compounds showed micromolar activities against HeLa, KB and A549 cell lines. As part of this thesis, both structures were synthesized, starting from commercially available 1,3-cyclopentanedione (**97,** Scheme 38). The synthesis features several highly stereoselective conversions, aimed to build up the [3.3.3]propellane structure and subsequently introduce the unique oxidation and substitution pattern of the natural products. Noteworthy is the catalytic asymmetric Wittig reaction, which allowed desymmetrization of **81** with excellent enantioselectivity. Subsequently, the synthesis of [3.3.3]propellane **78** was achieved by diastereoselective 1,4-addition and ring closing metathesis. The stereoselective introduction of the demanding cyclopentanone substitution pattern was enabled by cyclopropanation/epoxidation of dienone **77**, followed by two reductive ring opening reactions to yield the reported structure of dichrocephone A **1**.



Scheme 38: Stereoselective synthesis of the reported structure of dichrocephone A (**1**).

Comparison of the spectral data of **1**, whose structure could be unambiguously confirmed by X-ray crystal structure analysis, and the natural isolate led to structural revision of dichrocephone A based on biosynthetic considerations and DFT-based calculations of NMR spectra. The correct structure was then synthesized by selective elimination of the C-8 hydroxy functionality and subsequent Mukaiyama hydration, which led to an epimerization at this position.

The assumed biosynthetic connection of the two natural products could be supported by facile dehydration of **160**, yielding the second natural product dichrocephone B **2** (Scheme 39). By comparison of the optical rotation of **160** and **2** with the literature values, the absolute configuration of both natural products was revised as well.

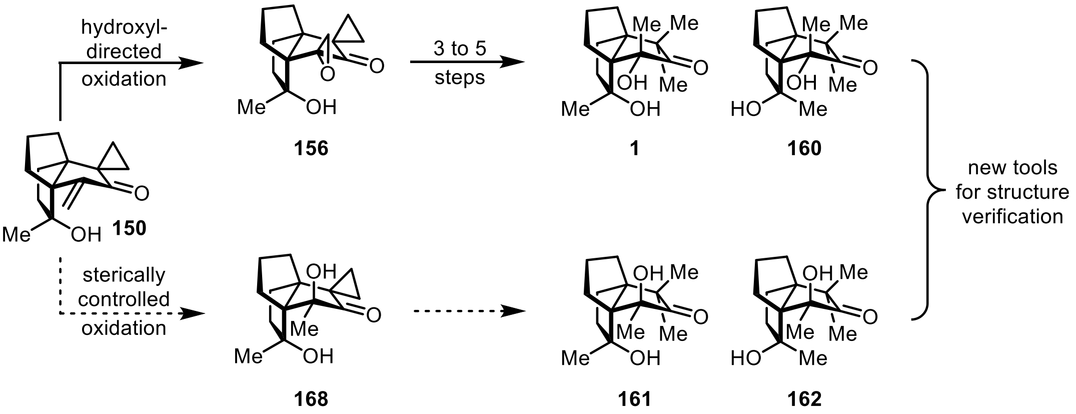


Scheme 39: Completion of dichrocephone A (**160**) and B (**2**) and revision of both structures.

Additional to the total synthesis of both dichrocephones A and B, this thesis showcases the need for interdisciplinary approaches in the structure elucidation of small molecules. Computational chemistry was used to assign the absolute configuration of **78** and helped predict the revised structure of dichrocephone A, with the support of the biosynthetic considerations, which could be confirmed by further synthetic studies.

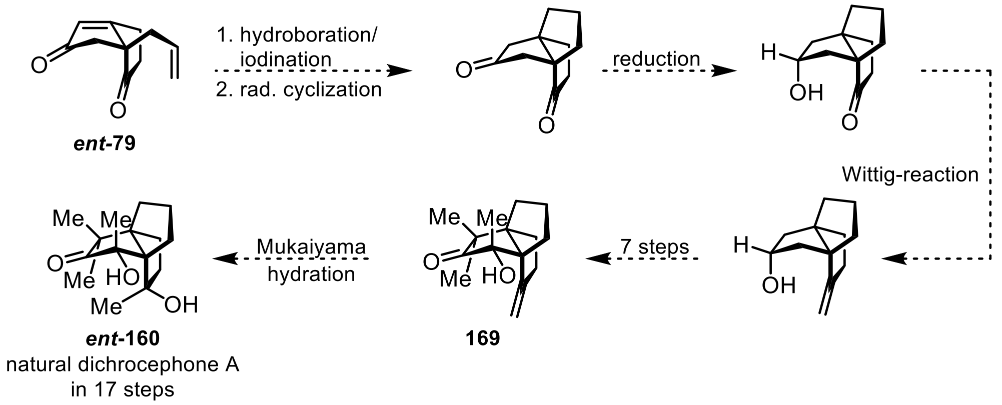
2.4. Outlook

Only three unnatural diastereomers of dichrocephone A are possible, which were shown in Scheme 34. These rigid ring systems also enable reliable calculation of the conformers in solution, as demonstrated by the computational NMR comparison performed by YOUNG HONG. Since the synthesis developed in this thesis introduces the stereogenic center at C-2 on a late stage, α-oxidation of enone **150** under steric control, followed by a reaction sequence analogous to the natural product would allow the synthesis of the two missing isomers **161** and **162**. Further analytical studies on all isomers would allow the development of new tools for structure verification on comparable triquinane natural products, which are considered challenging in NMR-based stereochemical assignement.[133] Initial studies on the synthesis of **168**, and differentiation of **1** and **160** by ion mobility mass spectrometry were already performed during the preparation of this thesis. This state-of-the-art analytical technique allows separation isobaric ions by their size and shape.



Scheme 40: Synthesis of all four stereoisomers of dichrocephone A for further analytical studies.

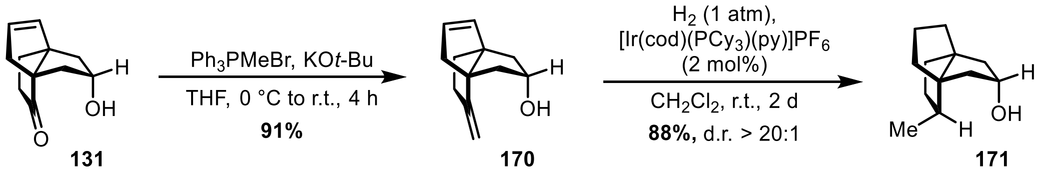
Due to the upon isolation incorrectly assigned relative configuration of dichrocephone A, the complete synthetic sequence contains additional steps, as an epimerization at C-8 was necessary to obtain dichrocephone A. A second generation of the synthesis could be shortened by two steps by aiming directly for the correct structure of dichrocephone A, including relative and absolute configuration of the stereogenic centers. These changes, shown in Scheme 41, include one C–C bond formation less, by utilizing a radical cyclization to access the propellane core as developed by KERR and coworkers.[80c] The correct configuration of the C-8 alcohol would in this strategy be obtained at a late stage by Mukaiyama hydration of terminal olefin **169**. The steric shielding of the fully substituted cyclopentanone would provide stereoselectivity of this final step.



Scheme 41: Next generation synthesis of the correct structure of dichrocephone A.

Additionally, the yield of several reactions might improve, since absence of the labile tertiary alcohol at C-8 would lead to minimized loss of yields by undesired side reactions. One disadvantage of this strategy might be low stereocontrol in the introduction of the C-2 hydroxy group in **169** due to the missing directing group.

The feasibility of a Wittig olefination at the sterically hindered neopentylic carbonyl functionality of **131** could already be shown in additional studies aimed at stereoselective introduction of the C-8 methyl group, as found in modhephene and other members of the natural product family (Scheme 42). Wittig reaction of secondary alcohol **131** with deprotonated methyl triphenylphosphonium bromide gave exocyclic olefin **170** in near quantitative yield. Simultaneous hydrogenation of both present olefins utilizing Crabtree´s catalyst enabled the synthesis of the corresponding saturated compound **171** as a single diastereomer.



Scheme 42: Stereoselective introduction of the C-8 methyl group, present in other modhephanes.

Selective introduction of this methyl group was problematic in several of the previously reported syntheses of modhephene.[65b, d, f, g, i, k] Developing a sequence to functionalize the tetrasubstituted ring in analogous fashion to that to the dichrocephones, would allow the synthesis of a range of other modhephanes with complete stereocontrol (Figure 4, see Chapter 2.1.2).

3. Synthetic Studies towards Xenicane Diterpenes

3.1. Introduction

3.1.1. *(E)*-Cycloalkenes – Strain and Occurrence in Natural Products

The second topic of this thesis was based on a natural product class that develops ring strain in its medium-sized carbocycle. As previously discussed in Chapter 1.3, small cycloalkanes are up to 29 kcal/mol higher in energy than expected, mainly due to the strain caused by their distorted bond angles. Whereas cyclopentane and cyclohexane are nearly strain free, medium-sized carbocycles with 8 to 11 skeletal atoms are again higher in energy than expected. This is mostly due to eclipsing of vicinal or transannular substituents,[136] which is caused by the conformers these cycles will form.[137] The highest value is observed for cyclononane, with 12.6 kcal/mol of additional energy, whereas in cycloalkanes with more than eleven carbon atoms this effect again becomes negligible. Additionally, cycles with more than 8 skeletal atoms can exist with (*E*)-configured olefins as part of their ring system. The smallest compound isolated showing this motif is (*E*)-cyclooctene (**172**), which is 9.2 kcal/mol higher in energy than the (*Z*)-isomer. This is caused by a twisted distortion of the p-orbitals of the two sp^2-hybridized carbon atoms, which in this small ring system are no longer able to overlap in a fully parallel fashion (Figure 27).[138]

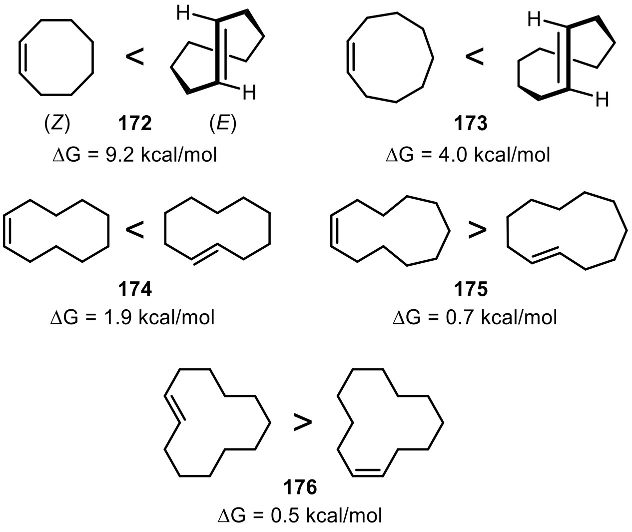


Figure 27: Comparison of strain in (*E*)- and (*Z*)-cycloalkenes.

For the next two homologs **173** and **174**, the (*E*)-configured isomers are also higher in energy, but the effect is less pronounced due to additional conformational freedom stemming from the additional skeletal atoms. The effect is reversed when macrocyclic cycloalkenes are considered, where starting from cycloundecene **175** the (*E*)-configured isomers are more stable. The energy differences between these compounds and their less strained isomers were assessed by comparing the free energies of hydrogenation, or the equilibrium state of acid catalyzed (*E*/*Z*)-isomerization in the gas phase.

A side-effect of this strain is planar chirality, caused by the enantiomorphic conformers in which these molecules exist. BLOOMQUIST and coworkers predicted this behavior in 1952 upon the first synthesis of **172**.[139] It was confirmed by COPE and coworkers, who accomplished the resolution of a racemic mixture of **172** by ligand exchange in a chiral Pt-complex, resulting in two separable, diastereomeric Pt-species.[140] The activation barrier for racemization of **172** is 35.6 kcal/mol and optically active **172** shows a racemization half-life of 122 h at 132 °C (Figure 28).[141] Compared to this, the additional carbon atom in (*E*)-cyclononene **173** allows higher conformational freedom, which is reflected in a lower activation barrier of 20 kcal/mol, and a $t_{1/2}$ = 4 min at 0 °C for racemization.[142] Additional functionalization of the ring can alter this behavior. A study by L. J. WILLIAMS and coworkers showed that a corresponding (*E,Z*)-cyclononadienone has a racemization half-life of 23 h at room temperature, reflecting the additional strain due to functionalization.[143] This effect can also be observed in a modified form in the NMR spectra of the natural product dealed with in this part of the thesis (Figure 31).

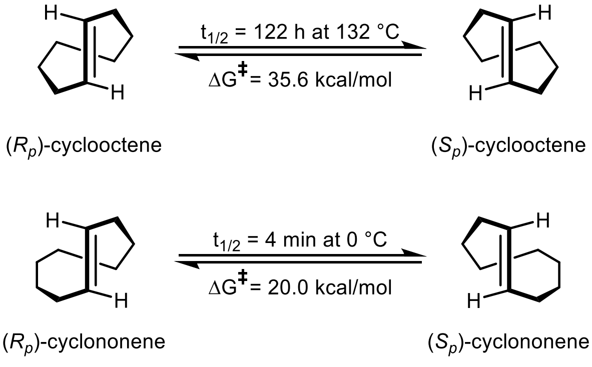


Figure 28: Enantiomorphic conformers and racemization of (*E*)-cyclooctene and (*E*)-cyclononene.

Medium-sized heterocycles containing (*E*)-olefins could also be shown to express planar chirality.[144] The synthesis and properties of these systems has been intensely studied by TAMOOKA and coworkers.[145]

In addition to the previously described activation enthalpy that needs to be overcome in the synthesis of strained molecules from unstrained starting material, a second effect comes into play when considering medium-sized cycles: competing oligomerization of the two functional groups intended to undergo ring closure is highly increased in medium sized cycloalkanes. Every additional skeletal atom leads to a 7.6 fold decrease of the cyclization rate, without considering the strain of the build-up carbocycle.[23] This is caused by the additional degrees of freedom of the longer alkyl chain, leading to a entropically disfavored transition state.

Whereas no natural product containing an (*E*)-cyclooctene motif has been isolated, natural products containing an (*E*)-cyclononene motif have been described. The most prominent compound is carophyllene (**51**, see Scheme 5, Chapter 2.1.3), a bicyclic sesquiterpene, which shows an annulated cyclobutane in addition to the unsaturated 9-membered ring. Several strategies employed to synthesize strained nine-membered carbocycles[146] and natural products containing this motif[147] have recently been highlighted by Magauer and coworkers. Mainly two reaction pathways were chosen in the past: direct cyclization of acyclic precursors or ring opening reactions, to obtain the strained medium-sized rings from a less strained bicyclic system.

3.1.2. Isolation and Synthesis of 4-Hydroxydictyolactone

A natural product that incorporates the previously described motifs of strain is 4-hydroxydictyolactone (**3**), a member of the xenicane diterpenes that has been isolated in 1993 by Pietra and coworkers from the brown alga *Dictyota ciliolata* south of Dakar.[148]

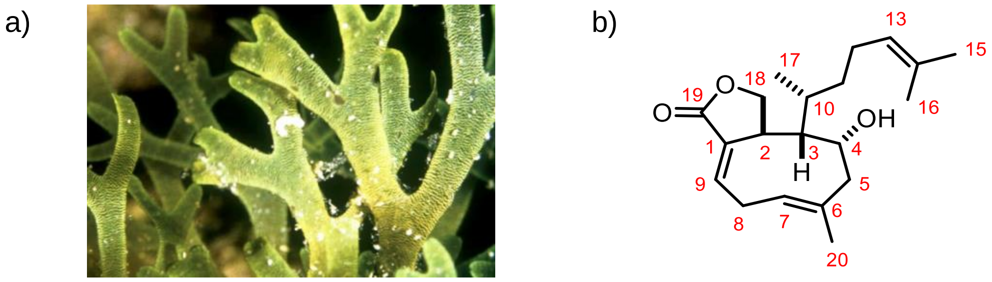
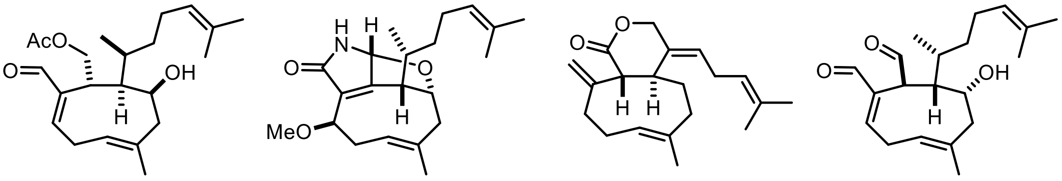


Figure 29: a) Brown alga *Dictyota ciliolata* and b) structure of 4-hydroxydictyolactone (**3**) with numeration of the carbon scaffold. Reprinted with permission of Romeo.[149]

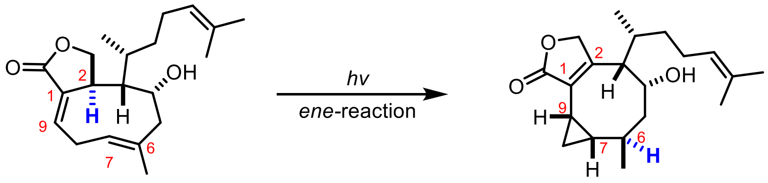
The enantiomer of **3** had been synthesized prior to the isolation by Tokoroyama and coworkers from furukinolal (**177**) in their studies to establish the structure of this natural product (Figure 30).[150] Interestingly, the xenicanes are therefore one of the rare cases, in which both mirror images of a diterpene scaffold have been isolated from nature, pointing towards a comparably simple cyclization phase in the biosynthesis of these natural products. Members of this compound family have shown a variety of biological activities, ranging from anti-bacterial activities, anti-fungal activities,[151] and ichiotoxicity[152] to inhibition of HIV-1 transcriptase, and are therefore considered highly interesting targets in the search for new lead structures in medicinal chemistry (Figure 30).[153] The main structural motif is the (*E,Z*)-cyclononadiene carbocycle, which leads to high ring strain for the reasons described above. This motif has been associated with the biological activity of the compound. The (*E)*-configured olefin at C-6/C-7 was described for all members of this natural product class. Further, 4-hydroxydictyolactone (**3**) comprises a γ-lactone fused to the carbocycle, which neighbors four contiguous stereogenic centers, one of them located in the acyclic part of the molecule.



furukinolal (**177**) joalin (**178**) deoxyxeniolide B (**179**) 4-hydroxy-dictyodial (**180**)

Figure 30: Examples of bioactive xenicane-diterpenes.

The strain in the ring system of the compound class was observed in two ways. Along with **3**, the structurally related natural product 4-hydroxycrenulide (**181**) was isolated, which constitutes a less strained bicyclo[6.1.0]nonene system (Scheme 43).[148a] Due to the natural habitat of *Dictyota ciliolata* in shallow waters, a photoinduced formation of **181** from **3** was assumed as the biosynthetic pathway in the formation of the natural product. This connection of both natural products could be synthetically corroborated after photoirradiation of **3**, which led to quantitative formation of **181** in 7 hours**.** Notably, under photochemical conditions this formal ene-reaction would need to undergo an antarafacial 1,5-hydrogen shift to conserve orbital symmetry, which would lead to the C-6 epimer of 4-hydroxycrenulide (**181**).



3 **181**

Scheme 43: Biosynthesis of 4-hydroxycrenulide (**181**) by photoinduced *ene*-reaction of 4-hydroxydictyolactone (**3**).

It was therefore proposed that the conversion of **3** to **181** either follows a free radical mechanism, or a photocatalyzed (*E,Z*)-isomerization of the C-6/C-7 olefin takes place prior to the ene-reaction. Both reactions were associated with strain relief of the unusual carbocyclic motif.

Additionally, NMR spectroscopy of **3** shows two distinctive sets of signals, which are not caused by impurities of the natural isolate (Figure 31). Rather, the strained carbocyclic system exists in an equilibrium of two semistable conformers. These are observed in an 95:5 ratio at room temperature,[154] in analogy to the planar chirality observed in unsubstituted (*E*)-cyclononene **173** (Figure 28).

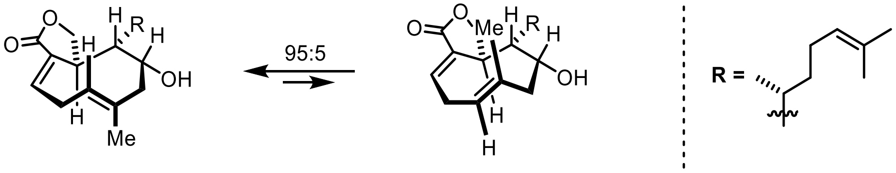
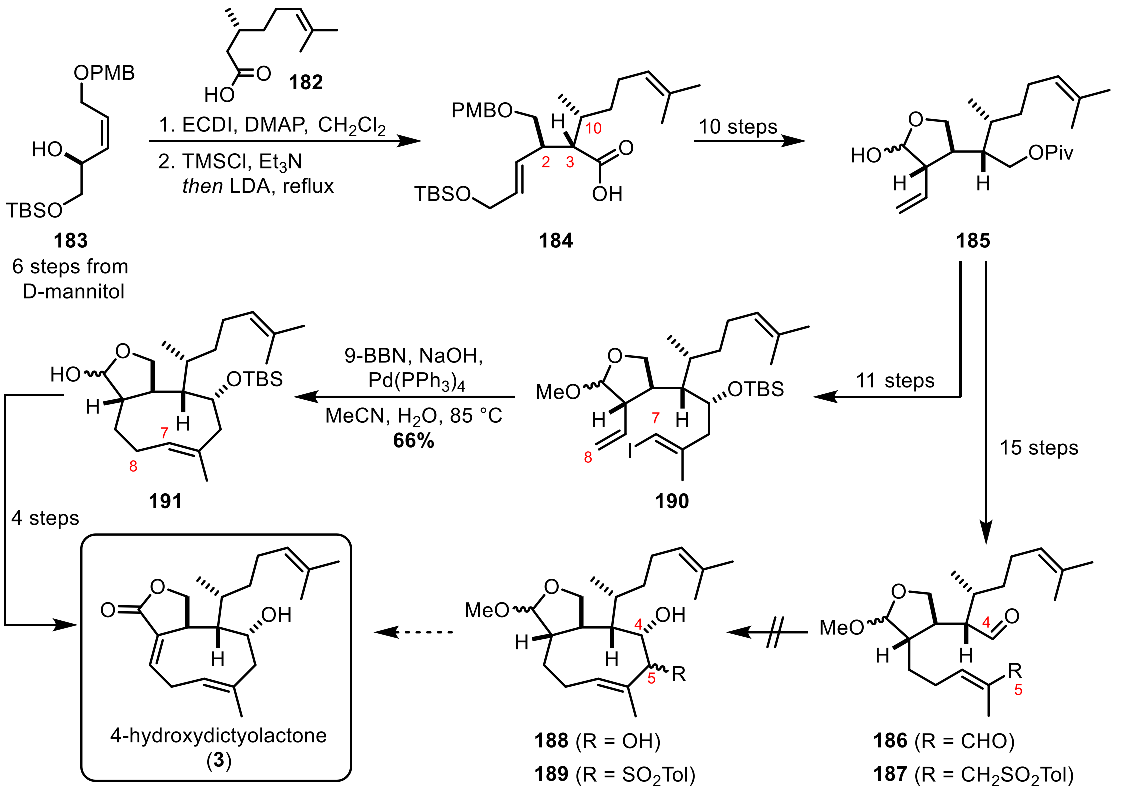


Figure 31: Equilibrium of conformers of the carbocycle of 4-hydroxydictyolactone observed by NMR spectroscopy.

This clearly indicated strain was also the main challenge to overcome in the only reported synthesis of **3**, which was performed by D. R. WILLIAMS and coworkers in 2009 (Scheme 44).[155] Their overall strategy for the synthesis of the natural product was an initial stereoselective synthesis of the northern fragment of the compound, followed by several attempts to close the (*E*)-cyclononene motif of the natural product. The synthesis of **3** commenced with D-mannitol and (*R*)-citronellic acid (**182**), two chiral pool starting materials that incorporate the correct stereoinformation for C-2 and C-10 of the final product. D-mannitol-derived **183** underwent ester formation with **182**. Subsequent Claisen-rearrangement[156] allowed stereoselective construction of the C-2/C-3/C-10 stereotriade in the early stage of the synthesis to give carboxylic acid **184**. Further functionalization of **184** led to the synthesis of terminal olefin **185**, which served as the point of divergence for the following ring closing attempts. The initial strategy envisaged C-4/C-5 bond formation. Therefore, **185** was converted to dialdehyde **186** and sulfone **187** by formation of the C-8/C-9 bond employing an intermolecular B-alkyl Suzuki-coupling with a suitable vinyl iodide (not shown). Attempts at cyclization of both **186** and **187** to **188** or **189** failed, which was associated with the strain of the desired products. The challenging cyclization could be achieved by reversal of the previously attempted strategy, aiming at a B-alkyl Suzuki-coupling to close the carbocycle at C-7/C-8. Therefore, **185** was functionalized to vinyl iodide **190**, which underwent coupling to give lactol **191** in 66% yield. Additional oxidations were necessary to obtain the lactone motif and implement the C-1/C-9 olefin by selenium oxide elimination, followed by a final desilylation to obtain the natural product. 30 synthetic steps were necessary to obtain 4-hydroxydictyolactone (**3**), which highlights the problems associated with the unusual ring size.

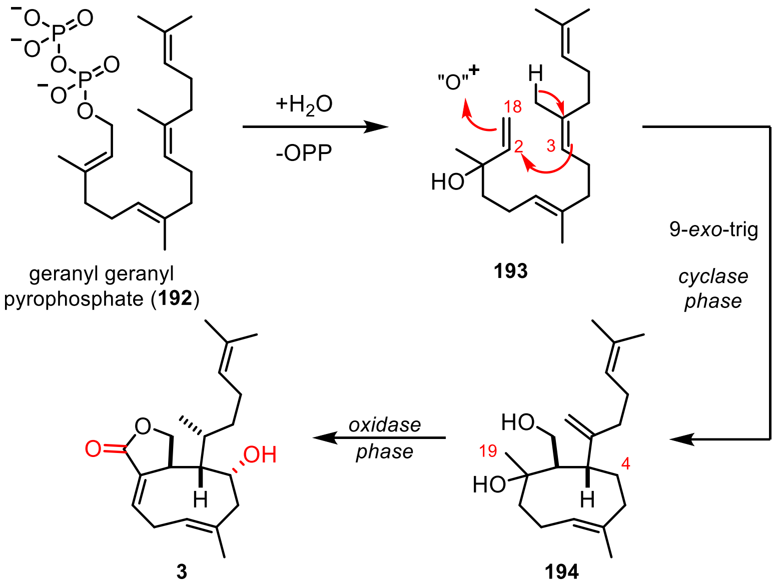


Scheme 44: Total synthesis of 4-hydroxydictyolactone (**3**) by WILLIAMS and coworkers.

Previous work in the CHRISTMANN group by DANIEL KÖNNING was aimed at a short synthesis to the northern fragment of **3**, to allow a more efficient entry to the natural product class compared to the work by WILLIAMS. The developed reaction sequence was based on a TEMPO-catalyzed oxidation/isomerization of (*Z*)-butene diol[157] and a subsequent addition of (*R*)-citronellal to the obtained Michael-acceptor.[158]

3.1.3. Biosynthesis of Xenicane Diterpenes

In analogy to the biosyntheses described earlier (Chapters 1.2 and 2.1.3), the formation of **3** follows a cyclase and oxidase phase. In a study by SCHMITZ and VAN DER HELM,[159] a biosynthetic pathway to this unusual carbocycle was described starting from geranylgeranyl pyrophosphate (**192**, GGPP), which is converted to geranyl linalool **193** in a single step (Scheme 45). In contrast to the earlier described biosyntheses, **193** then undergoes direct oxidative cyclization, a cyclization mode in which no allylic cation is involved. This is initiated by nucleophilic attack of the C-2/C-18 olefin on an electrophilic oxygen species, to form the nine-membered ring **194** by C-2/C-3 bond formation. This proposed cyclase phase therefore consists of two steps, a comparably simple biosynthetic pathway, which might also be the reason why both enantiomers of this carbon scaffolds were isolated from nature. The cyclized compound **194** then undergoes specific oxidations and cyclization in various positions of the carbon skeleton, to build up the diverse natural products of the substance class. In the case of 4-hydroxydictyolactone (**3**), these oxidations introduce the hydroxy functionality at C-4 and the carboxylic acid oxidation state at C-19, whereas the C-1/C-9 olefin is obtained by elimination of the initially formed tertiary alcohol.



Scheme 45: Biosynthesis of the xenicanes from GGPP (**192**) as described by van der Helm, followed by oxidation to 4-hydroxydictyolactone (**3**). Numbering of carbon atoms is based on the xenicane scaffold.

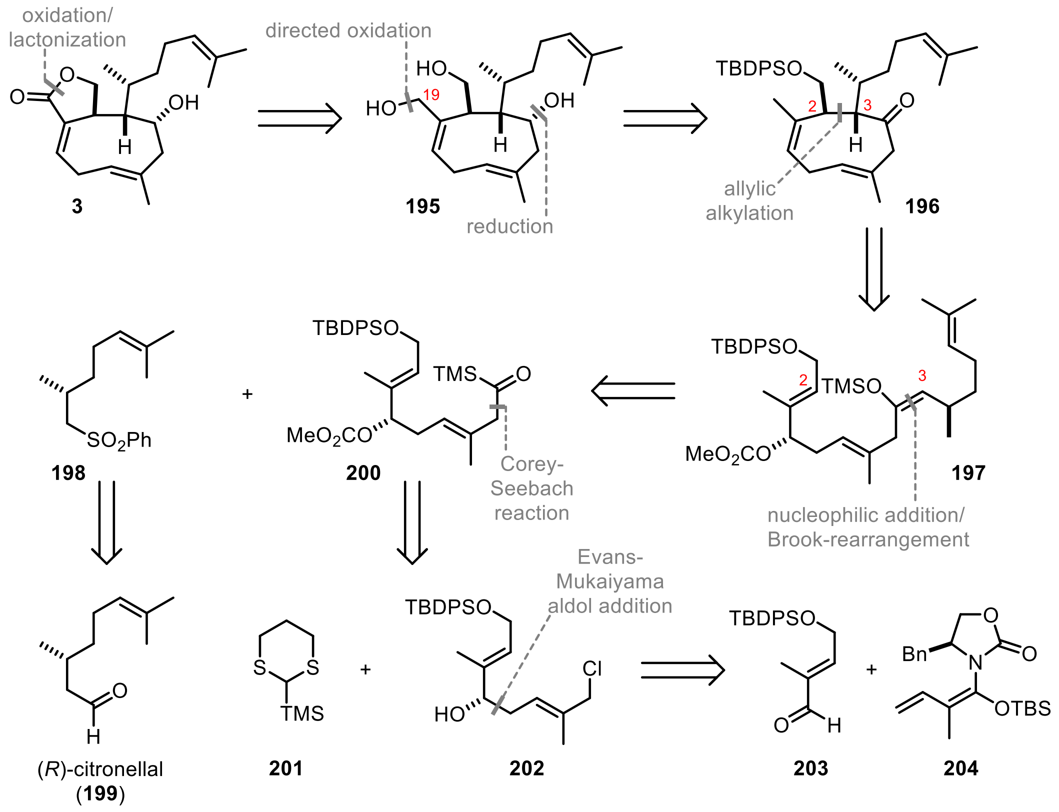
An alternative proposal for the biosynthesis of this compound class is based on initial formation of an 11-membered ring by C-10/C-18 bond formation, which then further undergoes transannular cyclization to a [7.2.0]bicyclic system by formation of a cyclobutane.[160] The initially formed C-10/C-18 bond is then oxidatively cleaved to yield the 9-membered monocyclic system, followed by site-specific C–H oxidations to yield the respective natural products.

3.2. Results

3.2.1. Retrosynthetic Analysis of 4-Hydroxydictyolactone

The aim of this project was a shortened synthetic access to 4-hydroxydictyolactone (**3**), to allow for further biological screening of the compound. It was hoped to achieve this goal by utilizing a minimal number of C–C bond formations to access the carbocyclic scaffold. The retrosynthesis is shown in Scheme 46, which aimed to obtain the natural product from triol **195** by chemoselective oxidation of the allylic alcohol, followed by lactonization with the primary alcohol at C-19. To install the allylic alcohol in **195**, an oxidation of the corresponding methyl group was planned by a method developed by

Takahashi and coworkers, which utilizes the coordination of a strong base to the primary alcohol at C-18.[161] This allows deprotonation of the proximal allylic position, which can then be reacted with molecular oxygen to give the allylic alcohol after reductive work-up. Due to the considerable problems associated with ring strain that were observed in the total synthesis by Williams and coworkers, this project aimed to mimic the biosynthesis of the carbocyclic core described by van der Helm to facilitate ring closure. It was assumed that the C-2/C-3 bond formation in the biosynthesis could be mimicked by utilizing a selectively functionalized diterpene-like cyclization precursor. For this reason, an allylic alkylation of silyl enol ether **197** was envisaged to obtain (*E*)-cyclononene **196**. Utilizing a silyl enol ether as the nucleophile would allow regioselective bond formation under neutral conditions, preventing isomerization of the β,γ-olefin to the corresponding enone. This methodology has been reviewed by Braun and coworkers.[162] Similar cyclizations to (*E*)-cycloalkene natural products from acyclic starting materials were previously reported by Corey and coworkers for the syntheses of araneosene[163] and antheliolide A.[164]

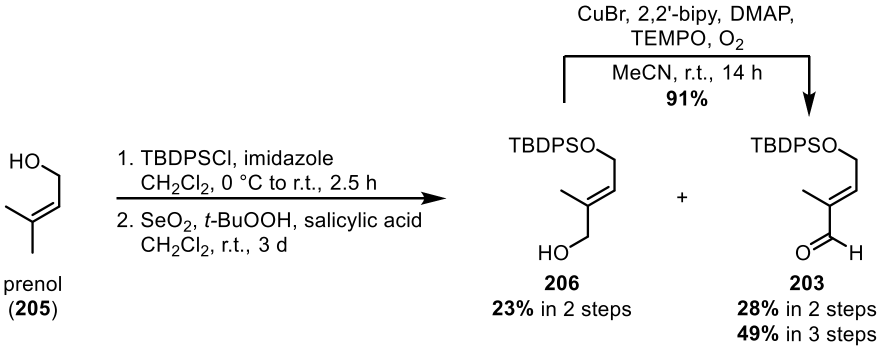


Scheme 46: First generation retrosynthesis of 4-hydroxydictyolactone (**3**).

Recent studies on this reaction with silyl enol ethers were performed by Stoltz[165] and Hartwig,[166] which allow stereoselective allylic alkylations by generation of the chiral transition-metal allyl complexes. To build up the silyl enol ether motif in **197** regioselectively, a strategy consisting of a nucleophilic addition and Brook-rearrangement was envisaged that would simultaneously build up the corresponding C–C bond.[167] Sulfone **198** would be accessible from citronellal (**199**), a commercially available monoterpene, which incorporates the methyl group at C-10 of the xenicanes with correct stereoinformation. The synthesis of acylsilane **200** was planned by a Corey-Seebach homologation with **201**[168] to form the C-8/C-9 bond and a vinylogous Evans-Mukaiyama aldol addition to generate the C-4/C-5 bond in **202** from aldehyde **203** and Mukaiyama reagent **204**.

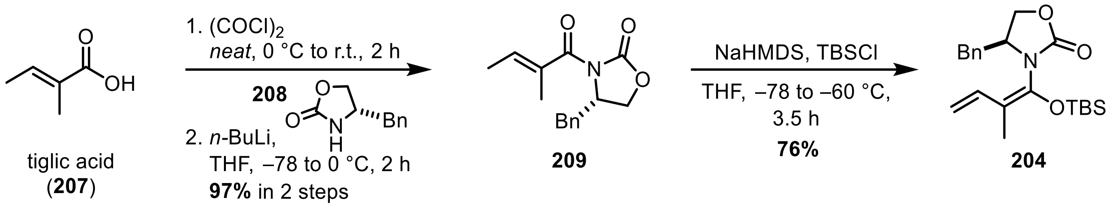
3.2.2. First Generation Approach to the Xenicane System

The first synthetic approach to the cyclization precursor **197** commenced with prenol (**205**), a commercially available C_5-building block (Scheme 47). Silylation of the hydroxygroup with TBDPSCl proceeded in near quantitative yield.[169] Subsequent Riley oxidation[170] was performed with 15 mol% of selenium dioxide and *t*-BuOOH as the terminal oxidant,[171] which gave a separable mixture of aldehyde **203** and the corresponding allylic alcohol **206** in 28% and 23% yield, respectively. TEMPO catalyzed oxidation[172] converted the allylic alcohol to the aldehyde in 91% yield. **203** was obtained in 49% yield in 3 overall steps.



Scheme 47: Synthesis of C_5-building block **203** from prenol (**205**).

The synthesis of the second fragment **204** for the Evans-Mukaiyama aldol addition started from tiglic acid (**207**). After facile conversion of **207** to the corresponding acid chloride, a subsequent reaction with the phenylalanine-derived Evans-auxiliary[173] **208** produced oxazolidinone **209** in near quantitative yield. Deprotonation in γ-position of **209** using NaHMDS and reaction of the intermediately formed dienolate with TBSCl led to formation of the corresponding *N,O*-silyl ketene acetal **204** in 76% yield.[174]



Scheme 48: Synthesis of Mukaiyama reagent **204** starting from tiglic acid (**207**).

With both C_5-building blocks in hand, optimization of the first C–C bond formation was investigated. Different Lewis acids were screened to promote the nucleophilic addition of **204** to the carbonyl functionality of **203** (Table 14). Using triphenyl borane, only low conversion to the desired product was observed, independent of previously described solvent mixtures (entries 1–2).[175] The starting materials could be reisolated after 24 h. On the other hand, addition of $BF_3 \cdot OEt_2$ led to decomposition of the Mukaiyama reagent **204**, with no observable product formation (entry 3). When employing $B(C_6F_5)_3$, the 1,4-addition product **210** could be isolated as a mixture of C-2 epimers in 38% yield (entry 4). Changing the Lewis acid to $TiCl_4$ finally enabled isolation of the desired 1,2-addition product **211** in 34% yield as a single stereoisomer (entry 5). This yield could be raised to 49% when adding water to the reaction mixture, which was previously reported by KOBAYASHI to accelerate the addition (entry 6).[176]

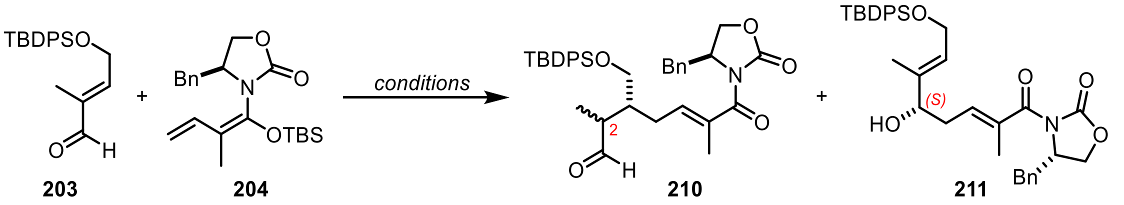


Table 14: Vinylogous Evans-Mukaiyama aldol addition of **204** to **203**.

	Lewis acid	Conditions	Yield, d.r.[a]
1	BPh_3	CH_2Cl_2, Et_2O, –78 °C to r.t.	8% **211**
2	BPh_3	CH_2Cl_2, –78 °C to r.t.	No conversion
3	$BF_3 \cdot OEt_2$	CH_2Cl_2, Et_2O, –78 °C	Decomposition of **204**
4	$B(C_6F_5)_3$	CH_2Cl_2, Et_2O, –78 °C to r.t.	38% **210**, d.r. = 1:1
5	$TiCl_4$	CH_2Cl_2, –78 °C to r.t.	34% **211**, d.r. > 20:1
6[b]	$TiCl_4$	H_2O, CH_2Cl_2, –78 °C to r.t.	49% **211**, d.r. > 20:1

[a] Diastereomeric ratios determined by ^1H NMR spectroscopy; [b] Performed on 5 mmol scale.

The use of $TiCl_4$ as the Lewis acid led to complete selectivity towards the (*S*)-configured allylic alcohol **211**. The mechanism of the vinylogous Evans-Mukaiyama aldol addition is depicted in Figure 32,[177] which explains the observed stereoselectivity towards one exclusive product. It proceeds *via* approach of the electrophile to the Mukaiyama reagent

204 from below the plane, due to higher steric repulsion with the chiral auxiliary when attacking from the top face. To further minimize interaction between the methyl substituent at C-2 of **204** and the bulky alkenyl rest of the aldehyde **203**, the carbonyl group is approached from the *Si*-face in an open transition state. This leads to the desired (*S*)-configured 1,2-adduct **211**, when utilizing $TiCl_4$ as the Lewis-acid.

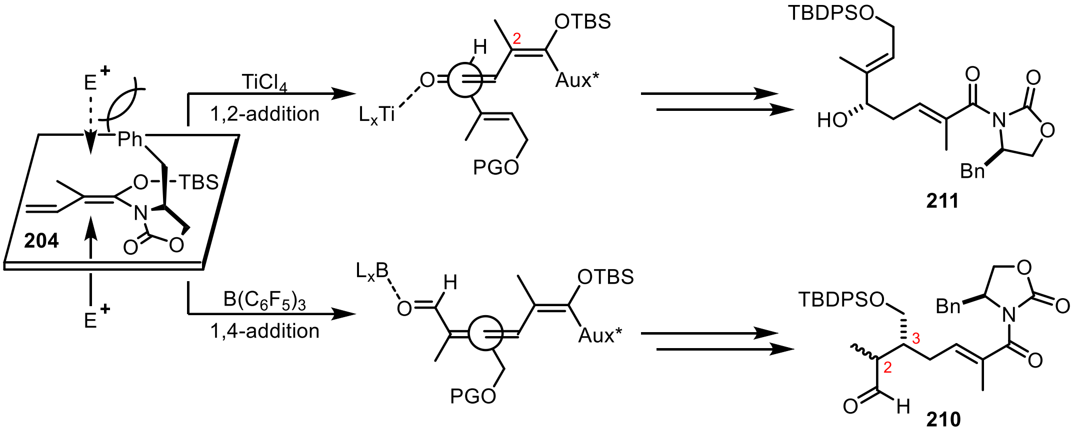
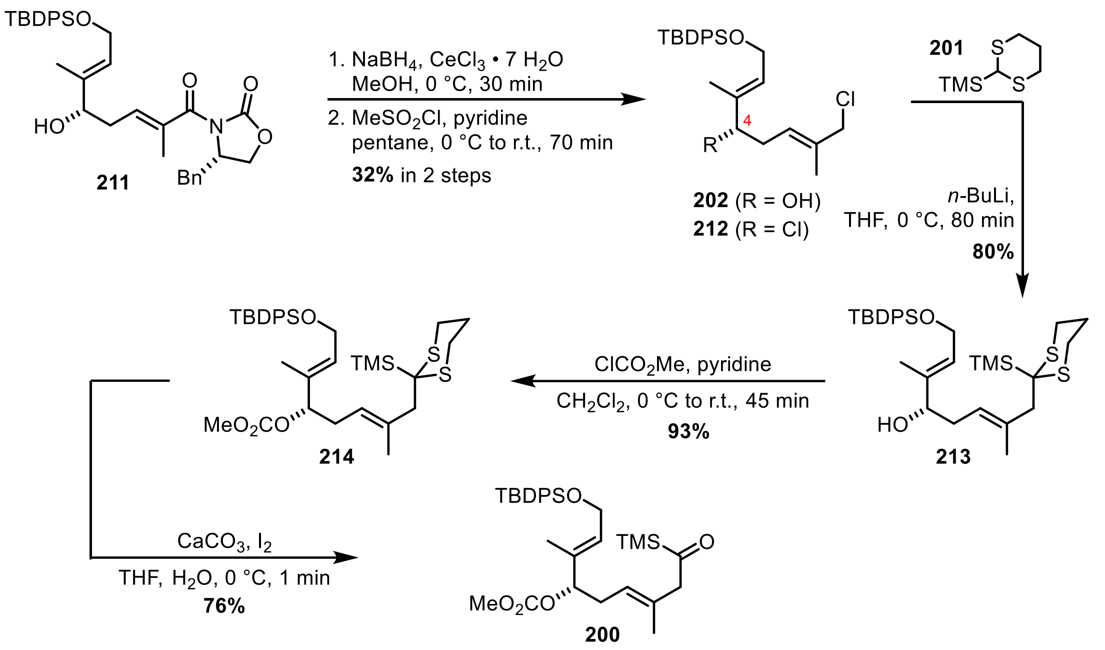


Figure 32: Explanation for the stereoselectivity of the vinylogous Evans-Mukaiyama aldol addition, and assumed mechanism of the observed 1,4-addition to **210**.

When using $B(C_6F_5)_3$ as the additive (Table 14, entry 4), the reaction delivered a 1:1 mixture of two epimeric aldehydes **210**. This reaction is unprecedented for Evans-auxiliary derived *N,O*-silyl ketene acetals, but was already reported for the corresponding pyrrole derivatives.[178] It was assumed that this bulkier Lewis acid does not allow the previously observed formation of the 1,2-adduct when coordinating to the carbonyl functionality. Rather, a vinylogous Mukaiyama-Michael addition[179] takes place, which shows complete selectivity over the new stereogenic center at C-3 due to the depicted approach of **204** to **203**. The observed mixture of epimers stems from unselective quench of the enolate at C-2 in the aqueous work-up.

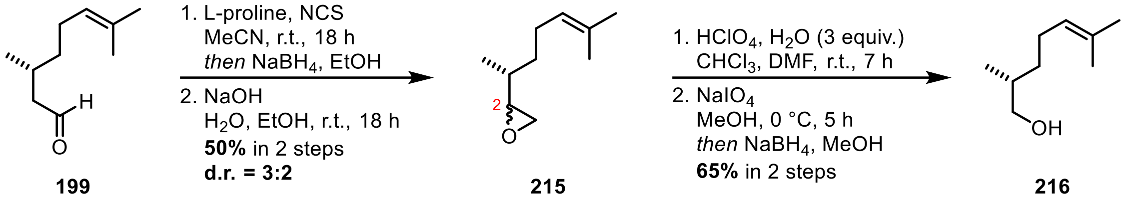
After the optimization of the first C–C bond formation, the auxiliary was cleaved under Luche conditions[81, 180] to give the corresponding allylic alcohol (Scheme 49). Subsequent substitution of the sterically less hindered hydroxy functionality delivered chloride **202** in 32% yield in two steps.[181] Longer reaction times led to diminished yields by undesired substitution of the secondary alcohol at C-4 to the corresponding dichloride **212.**



Scheme 49: Functionalization of allylic alcohol **211** to the acyl silane **200**.

Homologation of **202** to **213** was then achieved by Corey-Seebach reaction[168] with TMS-functionalized 1,3-dithiane **201** in 80% yield.[182] At this point, the remaining allylic alcohol was converted to the corresponding methyl carbonate **214**. The product tended to decompose upon prolonged reaction times, caused by elimination to the corresponding conjugated triene under the alkaline conditions. This undesired reactivity could also be observed in later attempts at ring closure (Table 15). When running the reaction for 45 min, **214** was obtained in 93% yield. Conversion of the dithiane to the corresponding acyl silane **200** proceeded in 76% yield and completed the synthesis of the C_{11}-fragment in 8 steps in the longest linear sequence.

The synthesis of the second fragment necessary for the pivotal coupling reaction to the functionalized diterpene commenced with (*R*)-citronellal (**199**), and was achieved by C–C bond fragmentation in 4 steps (Scheme 50). A one-pot sequence consisting of proline catalyzed α-chlorination,[183] followed by reduction of the aldehyde to the corresponding alcohol and subsequent epoxide formation under alkaline conditions delivered **215** as an inconsequential 3:2 mixture of C-2 epimers in 50% yield. Epoxide opening to the corresponding vicinal diol using perchloric acid was achieved in a solvent mixture of DMF and $CHCl_3$.[184] Subsequent diol cleavage using sodium periodate followed by reduction with sodium borohydride delivered truncated alcohol **216** in 65% yield over 2 steps.[185]



Scheme 50: Synthesis of the truncated alcohol **216** starting from (*R*)-citronellal (**199**).

Interestingly, when the epoxide opening of **215** was initially performed in an aqueous solution of perchloric acid, the only isolated product was cyclohexane diol **217** (Figure 33). The reaction to **217** most likely proceeds *via* activation of the epoxide under the harsh acidic conditions, followed by opening of the three-membered ring at the sterically less hindered position with the nucleophilic olefin to form the C-1/C-6 bond. The intermediately formed tertiary carbocation would then be quenched by the excess of water in the solvent mixture. Notably, a single diastereomer was obtained as the product, although the starting material was an inseparable 3:2-mixture of epimers. It was assumed that the chair like transition state depicted in Figure 33 can only lead to ring closure of this specific stereoisomer, due to preferred equatorial position of the substituents.

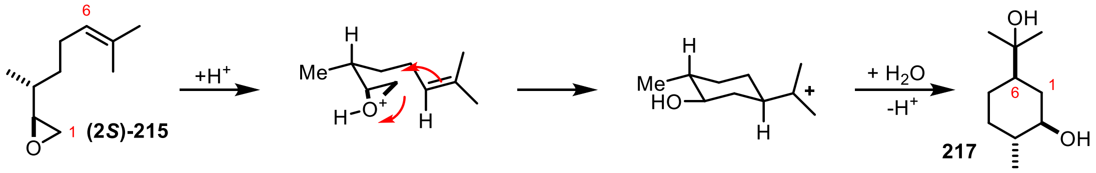
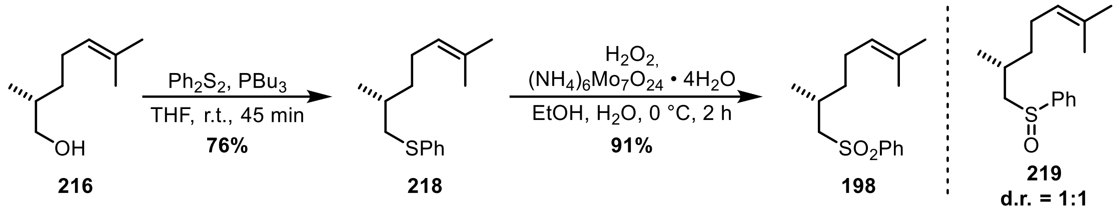


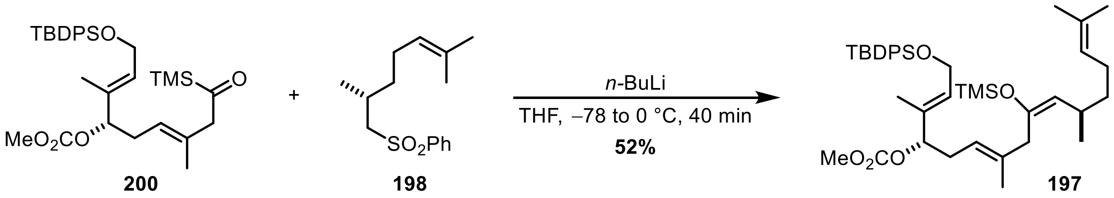
Figure 33: Proposed mechanism for the diastereospecific formation of **217** in an aqueous $HClO_4$-solution.

Substitution of the alcohol **216** with phenyl disulfide allowed formation of thioether **218** in 76% yield (Scheme 51). Subsequent oxidation using ammonium molybdate and hydrogen peroxide initially delivered the desired sulfone **198**, alongside an inseparable mixture of sulfoxides **219** in 42% yield. By extending the reaction time to 2 h, the isolation of the intermediate was suppressed, and **198** could be obtained in 91% yield.



Scheme 51: Substitution of alcohol **216** and oxidation to sulfone **198.**

The coupling reaction of the C_{11}-fragment **200** and the C_9-fragment **198** was achieved by a methodology developed by REICH and coworkers.[167] The reaction was initiated by deprotonation of **198** with *n*-BuLi at –78 °C, followed by addition to acylsilane **200** (Scheme 52). Formation of the desired silyl enol ether **197** by Brook-rearrangement[186] was achieved by raising the reaction temperature to 0 °C, which could be observed by thin layer chromatography. The cyclization precursor **197** was obtained in 52% yield and the silyl enol ether proved stable upon purification by column chromatography.



Scheme 52: Synthesis of silyl enol ether **197** by coupling of sulfone **198** and acylsilane **200**.

The product was obtained as a single (*E*)-isomer in agreement with the literature-known examples of the reaction.[167] The observed selectivity can be explained by the highly ordered transition state of the reaction, which starts by generation of the nucleophile from sulfone **198** by deprotonation with *n*-BuLi (Figure 34). Nucleophilic addition proceeds *via* a chair-like transition state, with the larger substituents preferably arranged in the equatorial positions. This leads to C–C bond formation with high selectivity towards the *erythro* product. Subsequent 1,2-Brook rearrangement of the silyl group to the former carbonyl oxygen and anti-periplanar elimination of the sulfone leads to formation of (*E*)-silyl enol ether **197** as the reaction product.

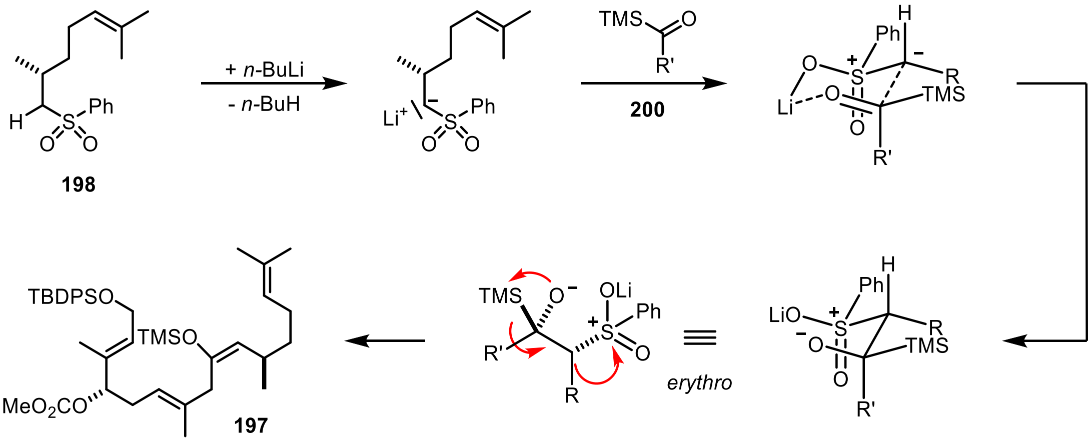


Figure 34: Mechanism of addition and Brook-rearrangement forming silyl enol ether **197**.

With **197** in hand, studies on the key step commenced (Table 15). Initial attempts to achieve ring closure to product **196** by activation of the allylic carbonate with an *in-situ* prepared palladium catalyst led to either no conversion or decomposition (entries 1–2).[163] It was initially assumed that the trimethylsilyl enol ether would act as the nucleophile without further activation, as observed in the total synthesis of araneosene by COREY. As seen in entry 1, the starting material proved to be stable under these reaction conditions and could be reisolated. By adding a fluoride source, the silyl enol ether was converted to the corresponding enolate to raise the reactivity of the functional group. This method was previously employed by STOLTZ and coworkers for asymmetric allylic alkylations of a variety of silyl enol ethers.[165] Whereas a combination of [18]-crown-6 and pre-dried potassium fluoride was not able to effect desilylation (entry 3), the addition of tetrabutylammonium difluorotriphenylsilicate (TBAT) led to full conversion of the starting material in a matter of minutes, as observed by thin layer chromatography (entry 4). TBAT was chosen over other fluoride sources such as TBAF due to its lower hygroscopy, since it was assumed that residual water would irreversibly quench the enolate anion. Unfortunately, only a complex mixture of products was obtained after prolonged reaction time. A catalytic system based on iridium complexes was also employed, which was introduced by HARTWIG and coworkers for an analogous allylation of silyl enol ethers.[166] Reactivity in respect to the fluoride sources was observed comparable to the previous employed conditions, but no desired product could be obtained (entries 5–6). Since the allylic carbonate was not activated by the transition metal catalysts, stoichiometric amounts of scandium triflate were added to the reaction, which led to formation of a complex product mixture, irrespective of the additional fluoride source added to the reaction (entries 7–8).

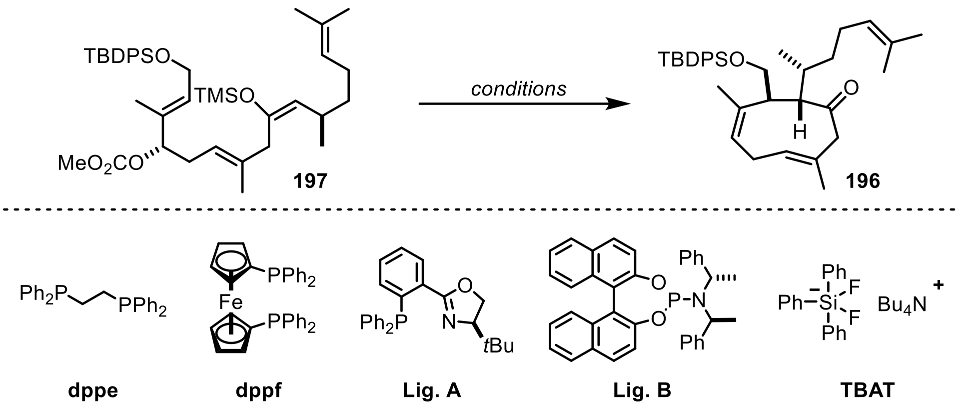
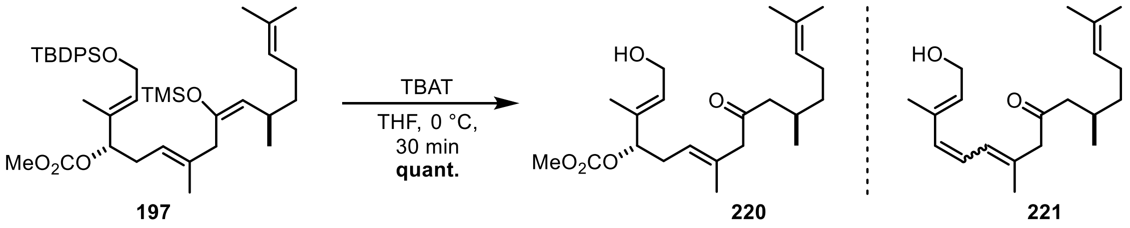


Table 15: Attempted cyclization of silyl enol ether **197** to (*E*)-cyclononene **196**.

	Catalyst	Additives[a]	Conditions	Result
1[b]	$Pd_2(dba)_3$, dppf	-	THF, 80 °C	No conversion
2[b]	$Pd_2(dba)_3$, dppe	-	THF, 80 °C	Complex mixture
3[b]	$Pd_2(dba)_3$, **Lig. A**	KF, [18]-crown-6	THF, 50 °C	No conversion
4[b]	$Pd_2(dba)_3$, **Lig. A**	TBAT	THF, r.t. to 80 °C	Complex mixture
5[c]	$[Ir(cod)Cl]_2$, **Lig. B**	KF, [18]-crown-6	THF, 50 °C	No conversion
6[c]	$[Ir(cod)Cl]_2$, **Lig. B**	TBAT	THF, 50 °C	Complex mixture
7	-	$Sc(OTf)_3$	MeCN, r.t. to 80 °C	Complex mixture
8	-	$Sc(OTf)_3$, TBAT	MeCN, r.t. to 80 °C	Complex mixture

[a] 1 equiv. of each additive was added; [b] 5 mol% Pd-catalyst, 7 mol% ligand A; [c] 2 mol% Ir-catalyst, 4 mol% ligand B.

Unfortunately, none of the attempts to obtain carbocycle **196** led to product formation. In general, unselective conversion to a complex product mixture was observed, which could not be separated by column chromatography. The main product obtained under the cyclization conditions could be identified by a control experiment. Reaction of the starting material with TBAT led to desilylation of the primary alcohol and the enol ether, producing ketone **220** in quantitative yield (Scheme 53). It was also possible to identify conjugated triene **221** as a further reaction product, which was obtained in considerable yield. This compound was also detected in the ESI-MS spectra of the crude product of attempted cyclizations.



Scheme 53: Selective conversion of cyclization precursor **197** to the main product of cyclization attempts **220**, and structure of the minor product **221**.

The reaction of **197** to both **220** and **221** can be explained by the desired activation of both functional groups without undergoing cyclization, as explained in Figure 35. First, the silyl enol ether is cleaved to the corresponding enolate by the fluoride source. **220** is build up by additional desilylation of the allylic silyl ether at C-18. To obtain **221,** the transition metal catalyst needs to coordinate to the carbonate and, by oxidative insertion and exclusion of CO_2 and methanolate, builds up the Pd-allyl complex. It was assumed that the enolate would undergo cyclization following a 9-*endo*-trig mode leading to C-2/C-3 bond formation, which builds up the ring system of the xenicanes. Unfortunately, no catalytic turnover of the palladium complex is observed, probably due to the high ring strain of the medium sized carbocycle. The low reactivity towards cyclization can also be explained by the tendency of 1,3-substituted acyclic Pd-allyl complexes to form the thermodynamically preferred (*E*,*E*)-isomer by rotation around the C-8/C-9 bond.[187]

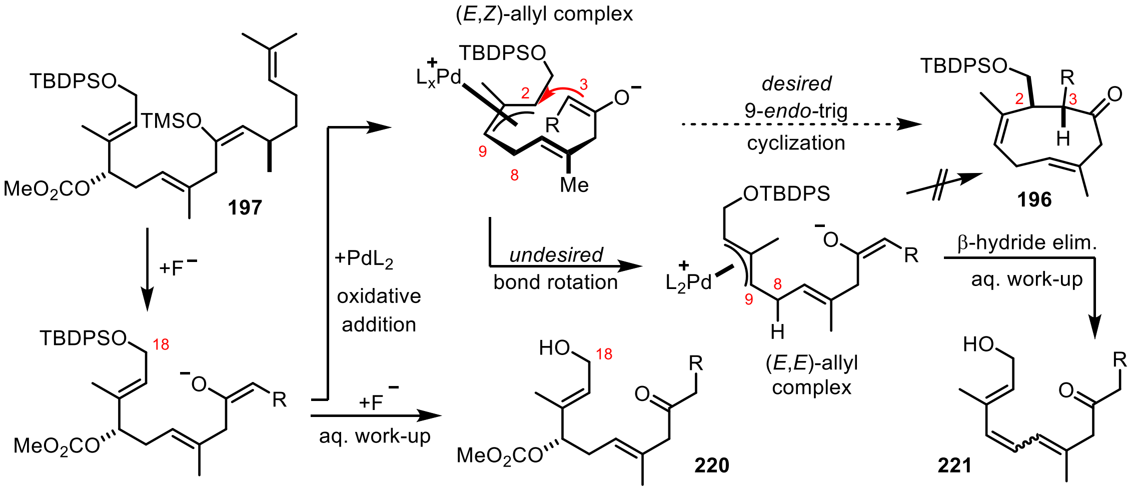
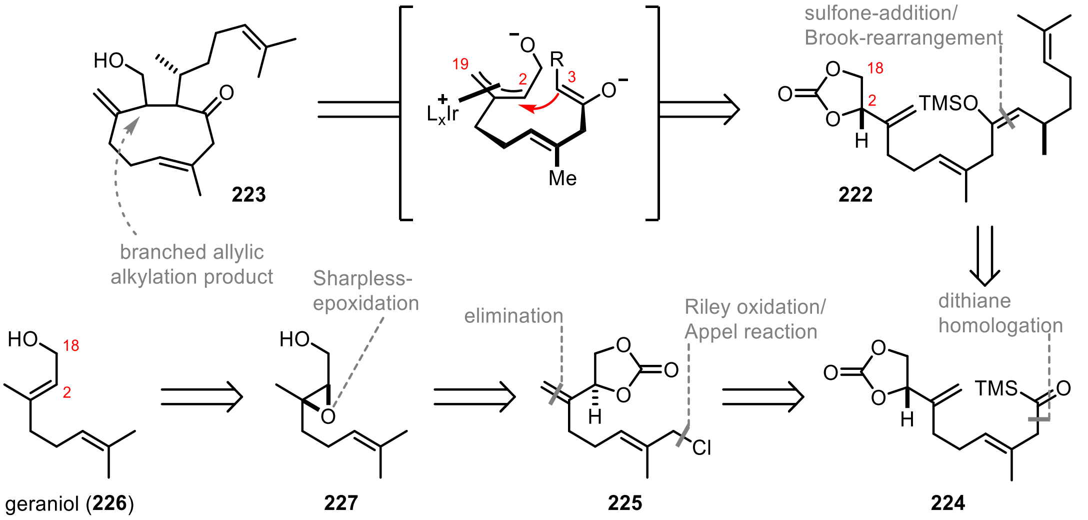


Figure 35: Unproductive mechanism of the ring closure to **196**. Carbon numeration based on xenicane scaffold.

With this, the nucleophile and electrophile are unable to undergo cyclization due to the increased distance between C-2 and C-3. The Pd-allyl complex decomposes in a β-hydride elimination and the carbonyl functionality is formed upon aqueous work-up to give triene **220**. Due to the unsuccessful cyclization attempts, this strategy towards the ring system of the xenicane diterpenes was abandoned.

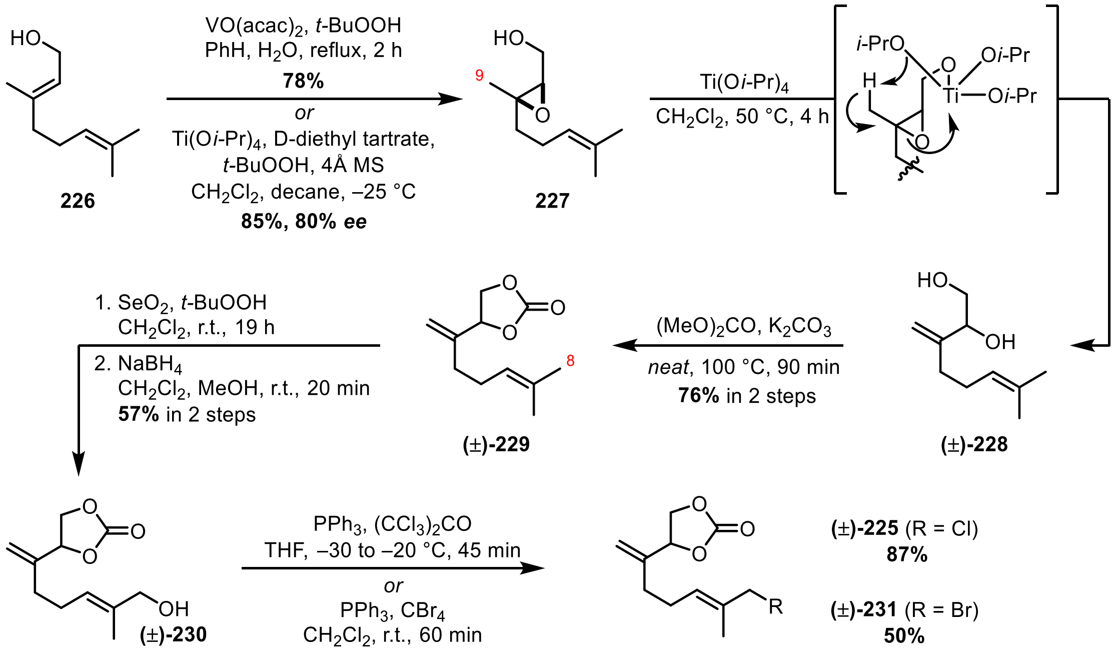
3.2.3. Second Generation Approach to the Xenicane System

The unsuccessful cyclization and undesired reactivity of **197** described in Figure 35 and Scheme 53 led to a revised cyclization precursor **222** (Scheme 54), which reflected these observations: 1) To facilitate cyclization, the pivotal transition-metal allyl complex should be devised, so that an exocyclic olefin is built up after cyclization to **223**. This allows for free rotation around its central carbon atom in the transition state and lowers the amount of sp^2-hybdridized atoms in the ring, thereby minimizing the strain that needs to be overcome. This changes the cyclization mode from a previously attempted 9-*endo*-trig cyclization to a 9-*exo*-trig cyclization. 2) Installing the leaving group at C-2 of **222** would suppress the elimination of the carbonate, since no thermodynamically favored conjugated triene can be build up. 3) Due to the low stability of the silyl-group under the previously employed cyclization conditions, the protecting group strategy was revised. To allow for orthogonal reactivity of the present oxygen functionalities, the vicinal hydroxy functionalities at C-2 and C-18 should be converted to a carbonate. 4) Pd-catalyzed allylic alkylation reactions usually lead to reaction of the allyl motif at the least sterically hindered carbon atom. Contrary to this, Ir-catalyzed reactions have been shown to deliver the branched products of allylic alkylations as the preferred outcome.[188]



Scheme 54: Retrosynthetic analysis to new cyclization precursor **222** and the envisioned Ir-catalyzed cyclization to **223**. Carbon numeration based on the xenicane scaffold.

Therefore, a key step based on an Ir-catalyzed allylic alkylation was envisaged for ring closure of the second cyclization precursor **222**, which would undergo C-2/C-3 cyclization to **223**, instead of the undesired C-3/C-19 regioisomer. Retrosynthetically, it was envisaged to obtain **222** in an analogous sequence used to synthesize **197** by addition of sulfone **198** to acylsilane **224**.[167] The previously described Corey-Seebach homologation would be used to obtain **224**. The corresponding allylic chloride **225** could be derived from geraniol (**226**), a commercially available monoterpene. To introduce both the vicinal diol at C-2/C-18 and the neighboring terminal olefin, the allylic alcohol at C-18 would be utilized as a directing group for Sharpless epoxidation to **227** and subsequent Ti-promoted regioselective elimination. Access to the allylic chloride would be possible by Riley oxidation of the more electron-rich olefin,[170] followed by Appel reaction. The use of geraniol (**226**) as the starting material for the chloride **225** would lead to 19 of the 20 carbon atoms of the later formed natural product being derived from terpene starting materials. The second approach to the ring system of the xenicanes started with hydroxy-directed epoxidation of **226** (Scheme 55). This reaction was performed on decagram scale, using a VO(acac)$_2$/*t*-BuOOH oxidation system,[189] to obtain **(±)-227** in 78% yield after distillation. Enantioselective formation of the new stereogenic centers was possible by employing Sharpless asymmetric epoxidation conditions to give **(*R*,*R*)-227** in 85% yield and 80% enantiomeric excess.[190]

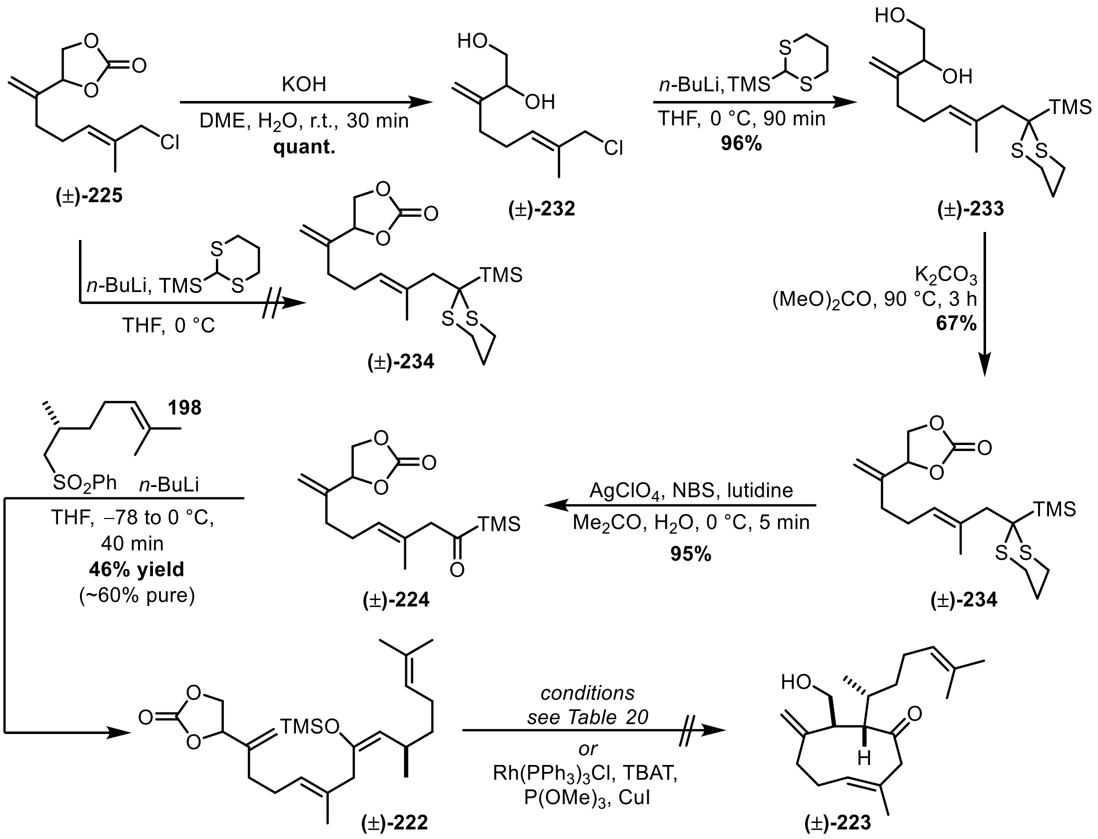


Scheme 55: Functionalization of geraniol (**226**) to allylic chloride **(±)-225** or bromide **(±)-231**.

Since residues in the crude product of the Sharpless epoxidation led to decomposition under elevated temperatures, column chromatography was necessary to obtain the product in the desired purity. Therefore, the racemate of epoxide **(±)-227** was used to develop the following reaction sequence, since it was readily available on a large scale.

Regioselective opening of the epoxide to the vicinal diol **(±)-228** was performed using stoichiometric amounts of Ti(O*i*-Pr)$_4$.[191] The reaction proceeds by coordination of the titanium alkoxide to the free hydroxy group, which allows one isopropoxy-ligand to regioselectively deprotonate the C-9 methyl group. **(±)-228** was obtained in nearly quantitative yield and could be used in the next step without purification. Cyclization of **(±)-228** under conditions developed by TROST and coworkers for the synthesis of *meso*-carbonates used in enantioselective allylic alkylations,[192] delivered carbonate **(±)-229** in 76% over two steps. Distillation was used to constantly remove methanol from the reaction and subsequently allowed to obtain pure carbonate **(±)-229** directly from the crude product mixture after full conversion. Chemoselective Riley-oxidation[170] of C-8 delivered a mixture of alcohol **(±)-230** and the corresponding aldehyde, which was reduced using NaBH$_4$ to obtain **(±)-230** in 57% yield over two steps. Appel reaction using either carbon tetrabromide[193] or hexachloroacetone[194] as the halogen sources, gave allylic bromide **(±)-231** and chloride **(±)-225** in 50% and 87% yield, respectively.

When subjecting **(±)-225** to Corey-Seebach reaction conditions,[168, 182] which were previously utilized for C$_1$-homologation of **202**, decomposition of **(±)-225** was observed, which was attributed to a preferred nucleophilic attack of the reagent on the carbonate (Scheme 56). Therefore, **(±)-225** was converted to the corresponding diol **(±)-232** by saponification with KOH in quantitative yield. The reaction with three equivalents of TMS-functionalized dithiane **201** then allowed homologation to **(±)-233** in near quantitative yield. Refunctionalization to the carbonate under the previously described conditions gave **(±)-234** in 67% yield, which could be converted to acylsilane **(±)-224** in 95% yield. The nucleophilic addition/Brook rearrangement of sulfone **198**, previously used in Scheme 52, successfully delivered the new cyclization precursor **222** in 46% yield. The product could not be obtained in pure form since excess sulfone **198**, necessary for full conversion of the starting material, was not separable from the product by standard column chromatography. Unfortunately, subjecting **222** to the conditions already used for the cyclization attempts of **197** did not lead to the desired product. Whereas no elimination was observed, the main outcome of the cyclization attempts was simple deprotection of the silyl enol ether to the corresponding ketone **245**. Additionally, a Rh-catalyzed reaction developed by EVANS and coworkers for the alkylation of comparable carbonates was employed for ring closure, which led to decomposition of the starting material.[195]

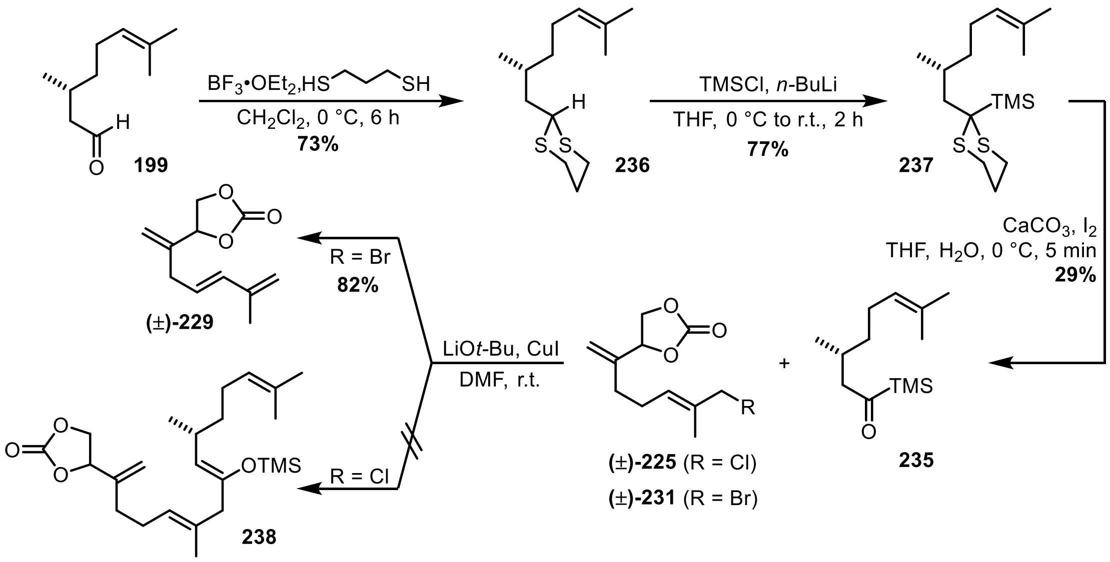


Scheme 56: Conversion of allylic chloride **(±)-225** to silyl enol ether **222** and attempted cyclization to **223**.

It was not clear if successful cyclization was hindered by the large amount of sulfone **198** remaining in the starting material, or again by the inability of **222** to undergo this challenging reaction. To avoid sulfone impurities in the starting material, a new strategy for silyl enol ether formation was envisioned. TAKEDA and TSUBOUCHI described a methodology, which allows direct regioselective synthesis of silyl enol ethers by substitution of an allylic chloride with a suitable acylsilane.[196] This new strategy would employ the already obtained allylic chloride **(±)-225** as one of the coupling partners, whereas the acylsilane **235** (Scheme 57) would be directly derived from (*R*)-citronellal **199**. This new strategy would also lower the amount of C–C bond formations needed to assemble the xenicane framework from previously four to two. No homologation with a dithiane would be necessary, and two functionalized monoterpenes could be used directly for the C–C bond formation, which would account for all carbon atoms of the natural product.

The synthesis of TMS-acylsilane **235** was planned by an umpolung strategy of the carbonyl functionality (Scheme 57). Reaction of 1,3-propanedithiol with **199** under Lewis-acidic conditions delivered the corresponding dithiane **236** in 73% yield.[197] Subsequent deprotonation with *n*-BuLi and functionalization with TMSCl build up the

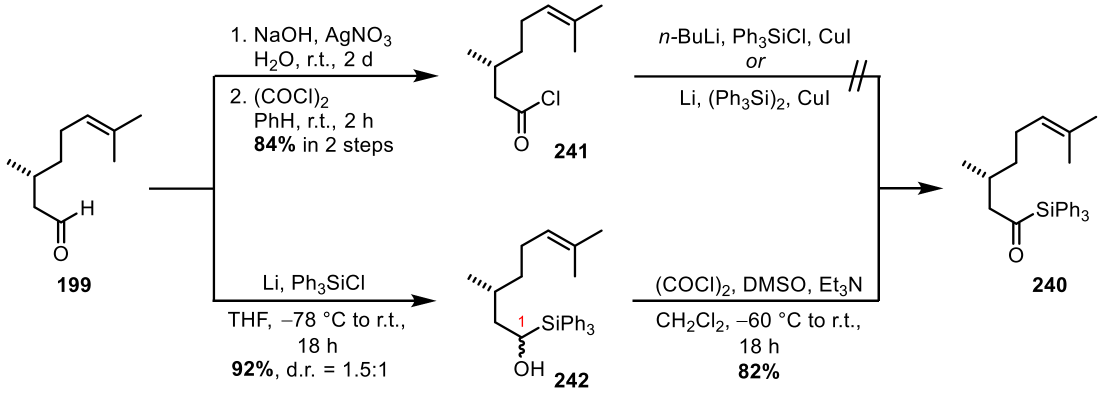
Si–C bond of **237** in 77% yield.[198] **237** was then converted to the corresponding acylsilane **235** in 29% yield. The low yield is attributed to unoptimized reaction conditions. The attempted C–C bond formation to silyl enol ether **238** did not lead to product formation for either allylic chloride **(±)-225** or the corresponding bromide **(±)-231**, which eliminated to conjugated diene **(±)-239** under the applied reaction conditions.



Scheme 57: Functionalization of (*R*)-citronellal (**199**) to the corresponding TMS acylsilane **235**, and attempted C–C bond formation to cyclization precursor **238**.

Since this reaction was previously described for triphenyl acylsilane derivatives, it was assumed that the TMS-group was not able to stabilize the positive charge on the silicon atom in the Brook rearrangement, due to the missing +M-effect of the phenyl groups. Therefore, the triphenyl substituted acylsilane **240** was prepared (Scheme 58). The umpolung strategy,[199] previously used to access the TMS derivative **235**, did not lead to any conversion of **236** with Ph_3SiCl. It was therefore planned to add the corresponding silyllithium reagent to a suitable carbonyl derivative.

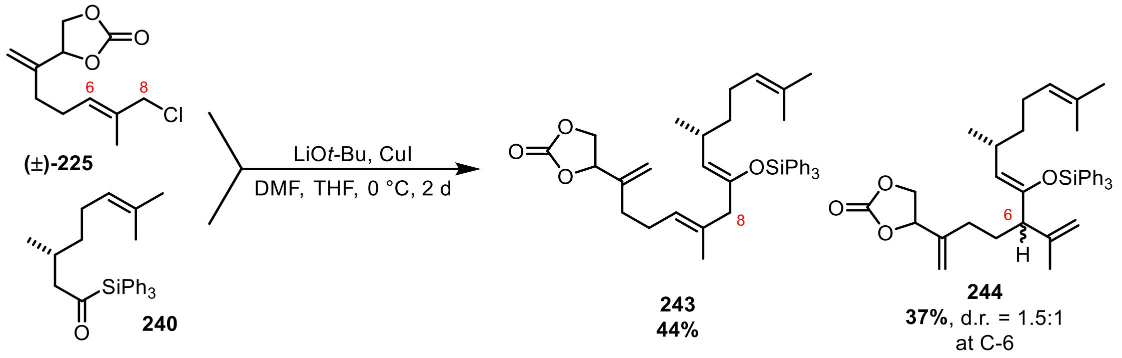
A first approach envisioned addition of Ph_3SiLi to the acid chloride **241**, which was obtained in two steps from **199**. Oxidation of the carbonyl functionality of **199** to the corresponding carboxylic acid with silver nitrate[200] was followed by reaction to **241** with oxalyl chloride, which was obtained in 84% yield in two steps. Addition of triphenylsilyl cuprate, generated from triphenylsilyl chloride by direct synthesis[201] or derived from reductive cleavage of hexaphenyldisilane,[202] led to decomposition of the starting material without detectable amounts of **240**. By reversing the reaction sequence the synthesis of **240** could be achieved. Addition of triphenylsilyl lithium to aldehyde **199** gave alcohol **242** as a mixture of C-1 epimers in 92% yield.[203] The resulting alcohol was oxidized to **240** using Swern oxidation conditions.[116b]



Scheme 58: Synthesis of triphenyl acylsilane **240** from (*R*)-citronellal (**199**).

At this point the coupling reaction of the two C$_{10}$-fragments **(±)-225** and **240** was investigated (Scheme 59). The reaction sequence consisting of deprotonation/rearrangement and subsequent substitution was initially performed at room temperature.[196] Under these conditions, silyl enol ether **243** was obtained as an inseparable mixture with the undesired (*E*)-configured product in 20% yield (not shown). Additionally, 52% of a complex mixture of other C–C bond formation products was observed. A second compound was identified as **244**, the product of the corresponding S$_N$2' reaction in which the new bond is formed at C-6 instead of C-8. By lowering the temperature to 0 °C, formation of the (*E*)-isomer of **243** could be suppressed, and at the same time undesired **244** was obtained in lower yields. This allowed the isolation of **243** in 44% yield, with additional 37% yield of the S$_N$2' product **244**, which were separable by column chromatography.

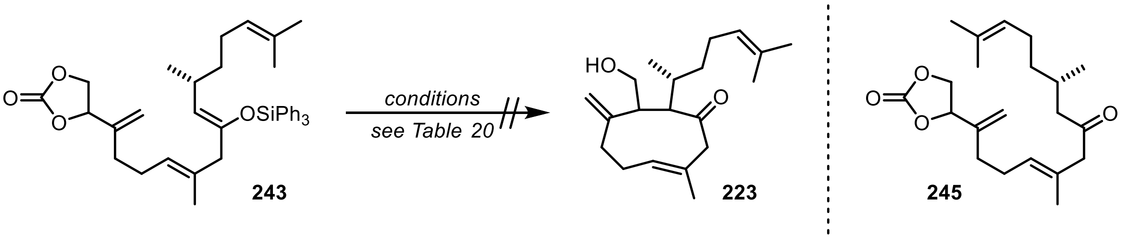
Judging by ^{1}H and ^{13}C NMR, the reaction product **243** obtained after optimization of the reaction conditions seemed isomerically pure, both in respect to the (*Z*)-selectivity of the newly formed double bond, as well as the two preexisting stereogenic centers, although a racemic mixture of allylic chloride **(±)-225** was employed. This stems most likely from the long distance between the two stereogenic centers at C-2 and C-11, which makes the obtained C-2 epimers of **243** indistinguishable by conventional NMR techniques.



Scheme 59: Coupling reaction of allylic chloride **225** and acylsilane **240**.

The reaction to **243** proceeds by initial formation of copper *tert*-butoxide from CuI and lithium *tert*-butoxide.[196] Acylsilane **240** is then deprotonated in α-position to the carbonyl functionality by the base, which leads to exclusive formation of the (*E*)-enolate, due to the high steric demand of the triphenylsilyl group. 1,2-Brook rearrangement gives the silylenol ether motif and simultaneously generates the reactive copper alkenyl species. This intermediate then reacts with the allylic chloride either at C-6 to give **244** or at C-8, which delivers the desired product **243**.

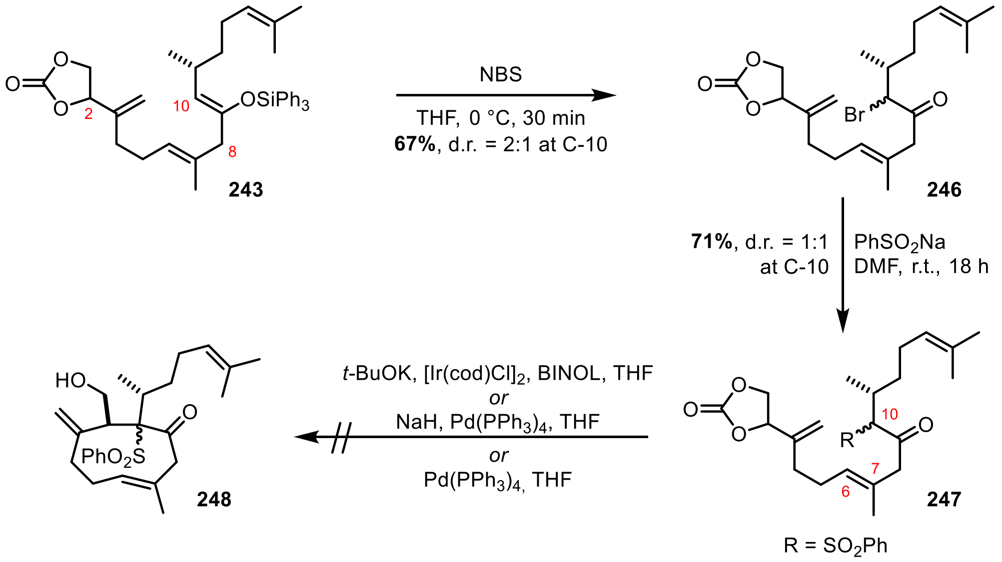
After optimization of the terpene coupling reaction, silyl enol ether **243** was subjected to the previously employed reaction conditions for the allylic alkylations to **223** (Scheme 60). Unfortunately, comparable reactivity to the previously tested cyclization precursors **197** and **222** was observed, so that no cyclization product could be obtained. When $Sc(OTf)_3$ was used in stoichiometric amounts, decomposition of the starting material was observed at elevated temperatures. When using catalytic amounts of Pd- or Ir-complexes, simple desilylation of the silyl enol ether to **245** was the main reaction product, with minor amounts of a structurally related compound stemming from activation of the allylic carbonate observable in ^1H NMR.



Scheme 60: Attempted cyclization of silyl enol ether **243** to form nine-membered carbocycle **223**.

A third strategy to facilitate the ring closure was based on introduction of a functional group that would stabilize the enolate anion. In all previous cyclization attempts fast formation of the enolate by TBAT could be observed by thin layer chromatography. If a competing protonation of the enolate followed by keto-enol tautomerism would be much faster than reaction with the transition-metal allyl complex, cyclization to the desired carbocycle **223** would be impossible. It was assumed that by introduction of a sulfone group at C-10, the corresponding proton would be more acidic than both protons at C-8. This would allow to reversibly form the C-9/C-10 enolate in a regioselective manner, which could be used for the 9-*exo*-trig cyclization under alkaline reaction conditions. By employing weak bases, the isomerization of the trisubstituted olefin to the corresponding enone could be suppressed. A similar strategy was previously employed for the total synthesis of the (*E*)-cyclononene motif in antheliolide A.[164] After successful cyclization, the sulfone could be removed under reductive conditions.[204]

Therefore, silyl enol ether **243** was converted to α-bromo ketone **246** under reaction conditions previously employed for selective bromination of multiply unsaturated polyketides.[205] **246** was obtained in 67% yield as an inseparable mixture of stereoisomers. Substitution with $NaSO_2Ph$ delivered sulfone **247** in 71% yield. The acidity of the α-proton was clearly indicated by the obtained 1:1 mixture of products, starting from a 2:1 mixture of **246**. Most likely, the initially formed 2:1 mixture was epimerized under the reaction conditions. Again, the C-2 diastereomers of **246** and **247** could not be observed in ^1H or ^{13}C NMR.

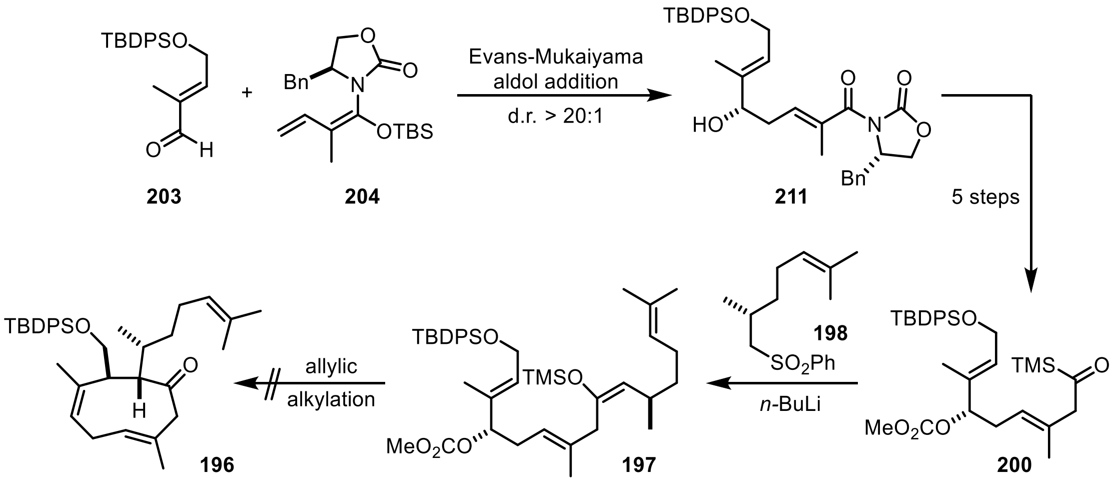


Scheme 61: Synthesis of sulfone **247** from silylenol ether **243** and attempted ring closure to **248**.

Three attempts for the ring closure of sulfone **247** to **248** were carried out. When employing *t*-BuOK as a base, following the standard reaction protocol for Ir-catalysis, the undesired isomerization of the C-6/C-7 olefin to the enone was observed in ^1H NMR of the crude product. Sodium hydride in combination with $Pd(PPh_3)_4$ as the catalyst led to a complex product mixture. When no base was applied, decomposition of the starting material was observed after 48 h at 50 °C. At this point, no more starting material was available to perform additional cyclization attempts with weaker bases. Since none of the reactions of any of the four cyclization precursors have shown reactivity towards the desired nine-membered carbocycle, further studies were stopped at this point.

3.3. Conclusion

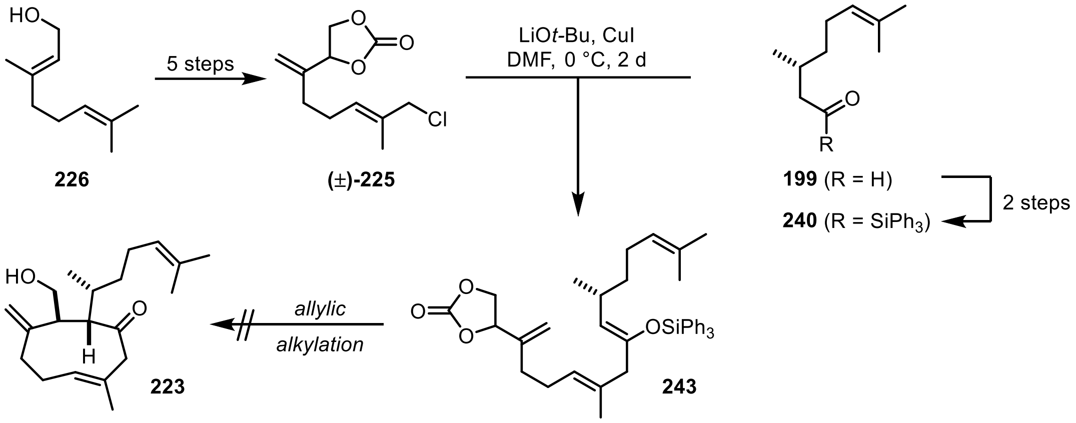
The study herein described was aimed to find a reliable and short access to the carbocyclic core structure of the xenicane diterpenes. The overall goal was the synthesis of 4-hydroxydictyolactone (**3**), a member of the xenicanes isolated in 1993 from the brown alga *Dictyota ciliolata*. This natural product class shows a range of promising biological activities, but a reliable strategy towards the strained carbocyclic system still needs to be developed. It was envisioned to obtain the (*E*)-cyclononene motif by a minimal amount of C–C bond formations, resembling the proposed biosynthesis from an acyclic diterpene pyrophosphate. Several cyclization precursors were synthesized from monoterpene starting materials, which contained an allylic carbonate that was intended to act as the electrophile in an intramolecular allylic alkylation. The nucleophile was initially envisaged as a silyl enol ether that undergoes *in-situ* transformation to the corresponding enolate. The first cyclization precursor **197** was assembled by a strategy, which employed an Evans-Mukaiyama aldol addition to build up the allylic alcohol **211** from aldehyde **203** and *N,O* silyl ketene acetal **204** (Scheme 62).



Scheme 62: First strategy to obtain the carbocyclic system of the xenicanes from silyl enol ether **197**.

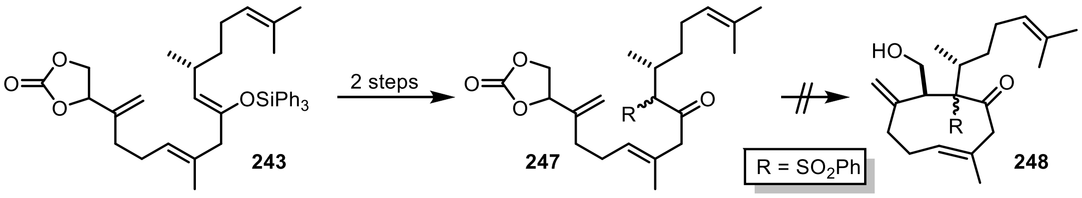
Corey-Seebach homologation was employed to obtain acylsilane **200** and nucleophilic addition/Brook rearrangement of sulfone **198** delivered silyl enol ether **197**. These three C–C bond formations delivered the cyclization precursor in ten steps in the longest linear sequence. Unfortunately, activation of **197** under a variety of conditions did not lead to product formation. Rather, undesired elimination and desilylation of the starting material was observed as the main reaction outcome.

A second approach was aimed at reducing the strain in the transition state of the key step, which was believed to be the reason for the unsuccessful cyclization (Scheme 63). By altering the cyclization mode from previously 9-*endo*-trig to 9-*exo*-trig it was hoped that a more facile conversion to the desired product **223** could be achieved. This second synthetic approach utilized two commercially available monoterpenes, geraniol (**226**) and (*R*)-citronellal (**199**), to obtain all carbon atoms of the cyclization precursor from the terpene pool. Furthermore, a single C–C bond formation was employed to connect the two fragments.



Scheme 63: Second strategy to obtain the carbocyclic system of the xenicanes from silyl enol ether **243**.

Key steps of the synthesis of the second cyclization precursor **243** consisted of an epoxidation/elimination sequence to obtain the vicinal diol in **(±)-225** and a one-pot substitution/Brook-rearrangement of **240** and **(±)-225** to obtain **243** in six steps in the longest linear sequence. The second cyclization precursor **243** was also unable to perform the envisaged cyclization. The main product of the attempted reaction was caused by desilylation of the silyl enol ether. To allow for a more stable enolate anion, silyl enol ether **243** was therefore converted to the corresponding sulfone **247** in two additional steps (Scheme 64). The stabilized enolate was envisaged to undergo reversible protonation/deprotonation to facilitate ring closure to **248** under alkaline conditions. Cyclization to the desired carbocycle was not successful. Since no more starting material was available for further ring closing attempts, the project was abandoned to focus on the promising results in the dichrocephone project described in the prior parts of this thesis.



Scheme 64: Further functionalization of silyl enol ether **243** to sulfone **247**, and attempted cyclization to carbocycle **248**.

In conclusion, a short access to acyclic diterpenes with regioselective incorporation of the required functional groups for ring closure by allylic alkylation could be accomplished in 8-18 overall steps. A minimal amount of C–C bond formations to obtain these compounds was necessary by employing readily available monoterpene starting materials. Mimicking the biosynthesis of the natural product class described by VAN DER HELM and coworkers could not be achieved. Apparently, the strain developed in the transition state of the cyclization, which was initially identified as the main synthetic challenge towards 4-hydroxydictyolactone, could not be overcome by the chosen allylic alkylation strategy. Future research into the synthesis of these compounds should either focus on cyclization towards a less strained carbocycle, with late implementation of the correctly configured olefins, or a strategy that utilizes a ring opening reaction in the formation of the carbocycle by starting from a bicyclic system.

4. Experimental Part

4.1. General Information

The analytical data was obtained with the help of the following equipment.

^{1}H and ^{13}C NMR spectra were acquired on a JEOL ECX 400 (400 MHz), JEOL ECP 500 (500 MHz) and a Bruker Avance 700 (700 MHZ) in $CDCl_3$ as a solvent. The chemical shifts were reported relative to $CDCl_3$ (δ = ^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm) and CD_3COCD_3 (δ = ^{1}H: 2.05 ppm, ^{13}C: 29.84 ppm). The multiplicities of the signals are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = quintuplet, br = broad.
The spectra were evaluated with the software MestReNova 7.1.2.

Mass spectra were obtained on a ESI-TOF-MS: Ionspec QFT-7 (Agilent/Varian), or a HR-EI-MS: Autospec Premier (Waters).

IR spectra were measured on a JASCO FT/IR-4100 Spectrometer. Characteristic absorption bands are displayed in wavelengths $\tilde{v}$ in cm-1 and were analyzed with the software Spectral Manager from JASCO.

Melting points were measured on a Thermovar from the company Reichert and are not corrected.

Chromatography Reaction progress was monitored by thin layer chromatography on aluminum backed silica gel plates (silica gel 60 F 254 from E. Merck), visualizing with UV light (λ = 254 nm). The plates were developed using anisaldehyde dip solution (135 mL ethanol, 5 ml conc. sulfuric acid, 1.5 mL glacial acetic acid and 3.7 mL *p*-anisaldehyde), $KMnO_4$ dip solution (3.0 g potassium permanganate, 5.0 mL NaOH-solution (5 w/w), 300 mL dest. water) or vanillin dip (15.0 g vanillin and 2.5 mL conc. sulfuric acid in 250 mL ethanol).

Flash chromatography was performed using silica gel M60 from Macherey & Nagel (particle size: 40 63 µm).

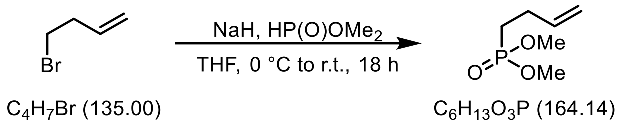
Reagents and Solvents Reactions with air or moisture-sensitive substances were, if not otherwise indicated, carried out under an argon atmosphere with the help of the Schlenk technique. All other reagents and solvents were used as purchased from commercial suppliers unless otherwise noted. Anhydrous solvents were purified with the solvent purification system MB-SPS-800 (Braun). Anhydrous DMF was purchased from Acros Organics in AcroSeal©-bottles under Argon atmosphere with molecular sieves (4 Å). THF was freshly distilled over Na/benzophenone prior to use. CuCN was purified following known procedures and thiophene was distilled and stored over MS.

The solvents (ethyl acetate, diethyl ether, pentane) used for column chromatography and work up were purified from commercially available technical grade solvents by distillation under reduced pressure with the help of rotatory evaporators (Heidolph or IKA) at 45 °C water bath temperature.

Compound names are derived from Chemdraw and are not necessarily identical with the IUPAC nomenclature.

4.2. To „Total Synthesis of the Dichrocephone Sesquiterpenes“

dimethyl but-3-en-1-ylphosphonate 85

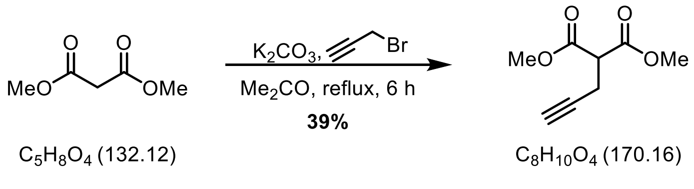


A suspension of NaH (60 wt% dispersion in mineral oil, 2.12 g, 53.2 mmol, 1.3 equiv.) in THF (64 mL) was treated dropwise with dimethyl phosphite (4.91 mL, 5.84 g, 53.1 mmol, 1.3 equiv.) at 0 °C and stirred for 30 min. The reaction mixture was refluxed for 2 h, cooled to 0 °C and treated with 1-bromo-but-3-en **86** (5.51 g, 40.8 mmol, 1 equiv.). The reaction mixture was stirred for 18 h at room temperature. Water (40 mL) and EtOAc (40 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3x 40 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Crude **85** was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 16.6, 10.1, 6.4 Hz, 1H), 5.06 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.00 (dq, *J* = 10.2, 1.5 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 2.40 – 2.27 (m, 2H), 1.91 – 1.80 (m, 1H), 1.83 – 1.78 (m, 1H).

The spectroscopic data agrees with previously published results.[206]

dimethyl 2-(prop-2-yn-1-yl)malonate 83

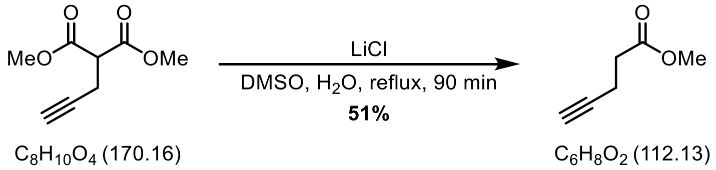


A mixture of dimethyl malonate **82** (8.69 mL, 10.0 g, 75.7 mmol, 1.5 equiv.), propargyl bromide (80% in toluene, 7.43 g, 50.0 mmol, 1 equiv.) and K_2CO_3 (21.0 g, 151 mmol, 3 equiv.) in acetone (250 mL) was refluxed for 6 h. The solvent was removed under reduced pressure and the crude product was dissolved in dichloromethane (150 mL) and water (150 mL). The phases were separated and the aqueous phase was extracted with dichloromethane (3x 100 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After distillation at reduced pressure (65 °C at 0.1 mbar) propargylated diester **83** (5.00 g, 29.5 mmol, 39%) was obtained as a colorless oil.

R_f = 0.5 (pentane/ethyl acetate = 25:1), $KMnO_4$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.77 (s, 6H), 3.61 (t, *J* = 7.7 Hz, 1H), 2.78 (dd, *J* = 7.7, 2.7 Hz, 2H), 2.02 (t, *J* = 2.7 Hz, 1H).

The spectroscopic data agrees with previously published results.[207]

methyl pent-4-ynoate 84

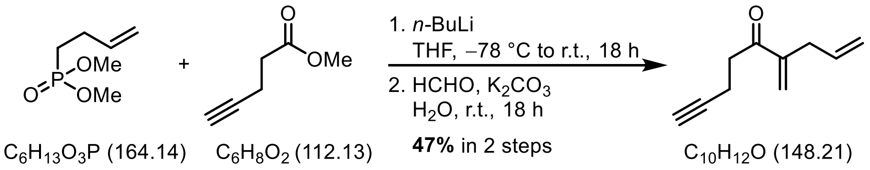


A solution of propargylated diester **83** (4.25 g, 25.0 mmol, 1 equiv.) and LiCl (5.29 g, 125 mmol, 5 equiv.) in water (0.9 mL) and DMSO (50 mL) was refluxed for 90 min. The reaction mixture was cooled to room temperature and acidified with aqueous HCl-solution (1 M, 25 mL). Et_2O (25 mL) was added, the phases were separated and the aqueous phase was extracted with Et_2O (2x 25 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 40:1) alkyne **84** (1.42 g, 12.8 mmol, 51%) was obtained as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 2.69 – 2.57 (m, 4H), 2.01 (t, *J* = 2.6 Hz, 1H).

The spectroscopic data agrees with previously published results.[208]

4-methylenenon-1-en-8-yn-5-one 80

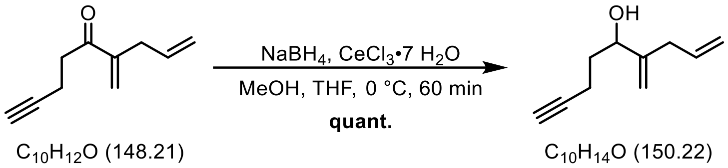


A solution of phosphonate **85** (1.00 g, 5.20 mmol, 1 equiv.) in THF (12 mL) was treated with *n*-BuLi (2.5 M in hexanes, 2.50 mL, 6.24 mmol, 1.2 equiv.) at –78 °C and stirred at the indicated temperature for 3 h. A solution of alkyne **84** (875 mg, 7.80 mmol, 1.5 equiv.) in THF (2.3 mL) was added and the reaction was warmed to r.t. over 18 h. Saturated aqueous NH_4Cl-solution (10 mL) and EtOAc (10 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was dissolved in water (20 mL) and K_2CO_3 (2.13 g, 15.4 mmol, 3 equiv.) and formaldehyde (37 wt% in water, 481 µL, 500 mg, 6.17 mmol, 1.2 equiv.) were added. The reaction mixture was stirred at room temperature for 18 h. Water (10 mL) and Et_2O (30 mL) were added, the phases were separated and the aqueous phase was extracted with Et_2O (3x 30 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 70:1) enone **80** (360 mg, 2.44 mmol, 47% in 2 steps) was obtained as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (s, 1H), 5.84 – 5.74 (m, 2H), 5.09 (t, *J* = 1.3 Hz, 1H), 5.10 – 5.00 (m, 1H), 3.03 (dqd, *J* = 6.8, 1.4, 0.8 Hz, 2H), 3.02 – 2.91 (m, 2H), 2.53 – 2.46 (m, 2H), 1.95 (t, *J* = 2.7 Hz, 1H).

The spectroscopic data agrees with previously published results.[75]

4-methylenenon-1-en-8-yn-5-ol (±)-87

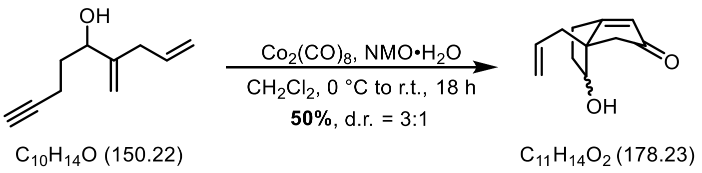


A solution of enone **80** (50 mg, 337 µmol, 1 equiv.) and $CeCl_3 \cdot 7\ H_2O$ (126 mg, 337 µmol, 1 equiv.) in MeOH (1 mL) and THF (2 mL) was treated with $NaBH_4$ (13 mg, 337 µmol, 1 equiv.) at 0 °C. The reaction mixture was stirred for 60 min at 0 °C and saturated aqueous NH_4Cl-solution (2 mL) and EtOAc (2 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 40:1) allylic alcohol **(±)-87** (50 mg, 337 µmol, quant.) was obtained as a colorless oil.

R$_f$ = 0.2 (pentane/ethyl acetate = 40:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 17.0, 10.0, 6.9 Hz, 1H), 5.11 – 5.06 (m, 3H), 4.91 (qd, *J* = 1.4, 0.6 Hz, 1H), 4.24 (dd, *J* = 8.3, 4.5 Hz, 1H), 2.86 (ddt, *J* = 16.1, 6.8, 1.1 Hz, 1H), 2.76 (ddt, *J* = 16.1, 7.1, 1.4 Hz, 1H), 2.34 – 2.25 (m, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.81 (dtd, *J* = 13.8, 7.6, 4.5 Hz, 1H), 1.78 (s, 1H), 1.74 (dddd, *J* = 13.7, 8.3, 7.4, 6.1 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 149.7, 136.2, 116.8, 111.5, 84.2, 73.8, 68.9, 36.4, 34.1, 15.1; **IR**: $\tilde{\nu}$ = 3420, 3303, 3077, 2926, 2118, 1734, 1431, 1054, 913 cm^{-1}.

Mass spectrometry of the compound was not successful.

6a-allyl-6-hydroxy-4,5,6,6a-tetrahydropentalen-2(1*H*)-one (±)-88



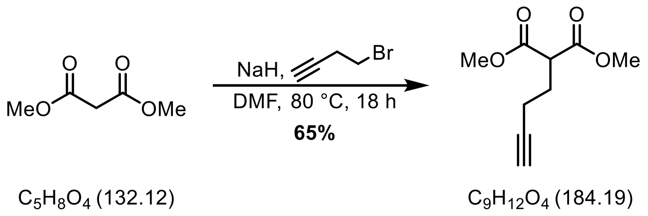
A solution of allylic alcohol **(±)-87** (50 mg, 328 µmol, 1 equiv.) and $Co_2(CO)_8$ (134 mg, 393 µmol, 1.2 equiv.) in dichloromethane (17 mL) was stirred for 2 h at room temperature.

The reaction mixture was cooled to 0 °C, treated with NMO·H_2O (443 mg, 3.28 mmol, 10 equiv.) and then warmed to room temperature over 18 h. The reaction mixture was filtered over a short pad of Celite®. Water (10 mL) and dichloromethane (10 mL) were added, the phases were separated and the aqueous phase was extracted with dichloromethane (3x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 2:1) enone **(±)-88** (29 mg, 164 µmol, 50%, 2 diastereomers, d.r. = 3:1) was obtained as a colorless oil.

^{1}H NMR (700 MHz, $CDCl_3$) δ 5.93 (s, 1H),* 5.89 (s, 1H), 5.69 – 5.57 (m, 1H), 5.15 – 5.07 (m, 2H), 4.17 – 4.00 (m, 1H), 2.80 – 2.72 (m, 1H), 2.69 – 2.54 (m, 3H), 2.30 – 2.18 (m, 2H), 2.07 – 1.95 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 211.0,* 209.7, 189.6,* 188.2, 132.8,* 132.7, 127.4, 126.3,* 119.4, 119.2,* 78.9, 73.6,* 59.6,* 56.5, 46.9, 41.7,* 40.6,* 34.8, 34.2,* 32.4, 24.4, 23.6*; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_2$, 201.0886; found: 201.0891; **IR**: $\tilde{\nu}$ = 3404, 2922, 1690, 1625, 1409, 1181, 1062, 920 cm^{-1}.

*Signals were unambiguously assigned to the major stereoisomer.

dimethyl 2-(but-3-yn-1-yl)malonate SI-1

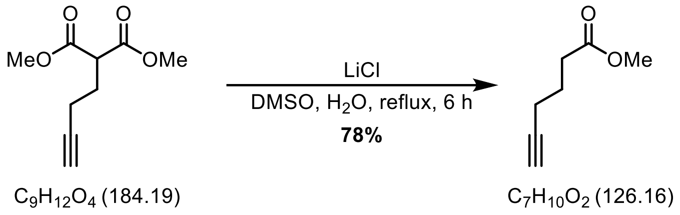


A mixture of NaH (60 wt% dispersion in mineral oil, 1.51 g, 37.8 mmol, 1 equiv.) in DMF (54 mL) was treated with dimethyl malonate (4.32 mL, 5.00 g, 37.8 mmol, 1 equiv.) at 0 °C and warmed to room temperature over 15 min. 1-Bromo but-3-yne (5.03 g, 37.8 mmol, 1 equiv.) was added and the reaction mixture was heated to 80 °C for 18 h. The solvent was removed under reduced pressure and the crude product was redissolved in dichloromethane (20 mL) and water (20 mL). the phases were separated and the aqueous phase was extracted with dichloromethane (3x 20 mL). After distillation at reduced pressure (65 °C at $3.5x10^{-2}$ mbar) diester **SI-1** (4.51 g, 24.6 mmol, 65%) was obtained as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 6H), 3.62 (t, *J* = 7.4 Hz, 1H), 2.29 (tdd, *J* = 6.9, 2.6, 0.6 Hz, 2H), 2.15 – 2.09 (m, 2H), 1.99 (t, *J* = 2.6 Hz, 1H).

The spectroscopic data agrees with previously published results.[209]

methyl hex-5-ynoate SI-2

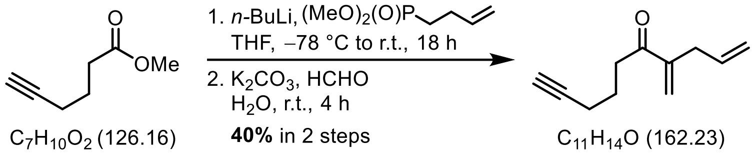


A solution of diester **SI-1** (4.51 g, 24.5 mmol, 1 equiv.) and LiCl (5.19 g, 122 mmol, 5 equiv.) in water (0.9 mL) and DMSO (50 mL) was refluxed for 6 h. The reaction was cooled to room temperature, Et_2O (25 mL) was added and the mixture was filtered over a short pad of Celite®. Water (100 mL) and Et_2O (100 mL) were added, the phases were separated and the aqueous phase was extracted with Et_2O (3x 100 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After distillation at reduced pressure (120 °C at 65 mbar) alkyne **SI-2** (2.4 g, 19.1 mmol, 78%) was obtained as a colorless liquid.

R_f = 0.5 (pentane/ethyl acetate = 40:1), $KMnO_4$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.67 (s, 3H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.26 (td, *J* = 6.9, 2.6 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.84 (p, *J* = 7.2 Hz, 2H).

The spectroscopic data agrees with previously published results.[210]

4-methylenedec-1-en-9-yn-5-one 90

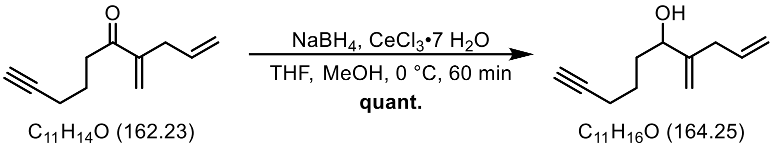


A solution of phosphonate **JDKZ** (1.38 g, 7.18 mmol, 1 equiv.) in THF (14 mL) was treated with *n*-BuLi (2.5 M in hexanes, 3.45 mL, 8.82 mmol, 1.2 equiv.) at –78 °C. After stirring for 60 min at –78 °C a solution of alkyne **SI-2** (1.36 g, 10.8 mmol, 1.5 equiv.) in THF (2.5 mL) was added and the reaction mixture was warmed to room temperature over 18 h. Saturated aqueous NH_4Cl-solution (20 mL) and EtOAc (20 mL) were added. the phases were separated and the aqueous phase was extracted with EtOAc (3x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was dissolved in water (32 mL), K_2CO_3 (2.97 g, 21.5 mmol, 3 equiv.) and formaldehyde (37% in water, 698 mg, 8.61 mmol, 1.2 equiv.) were added and the reaction mixture was stirred for 4 h at room temperature. Water (10 mL) and Et_2O (40 mL) were added. the phases were separated and the aqueous phase was extracted with Et_2O (3x 40 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 70:1) enone **90** (465 mg, 2.78 mmol, 40% in 2 steps) was obtained as a colorless oil.

R_f = 0.8 (pentane/ethyl acetate = 20:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.09 (s, 1H), 5.81 (ddt, *J* = 16.4, 10.8, 6.8 Hz, 1H), 5.77 (t, *J* = 1.5 Hz, 1H), 5.07 (t, *J* = 1.3 Hz, 1H), 5.06 – 5.05 (m, 1H), 3.03 (dt, *J* = 6.8, 1.1 Hz, 2H), 2.85 (t, *J* = 7.2 Hz, 2H), 2.26 (td, *J* = 6.8, 2.7 Hz, 2H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.85 (p, *J* = 7.1 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 200.8, 147.2, 135.6, 124.9, 116.9, 83.9, 69.1, 36.3, 35.1, 23.1, 18.0; **IR**: $\tilde{\nu}$ = 2917, 2850, 1735, 1466, 754 cm^{-1}.

Mass spectrometry of the compound was not successful.

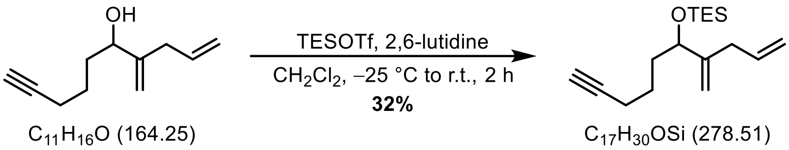
4-methylenedec-1-en-9-yn-5-ol (±)-91



A solution of enone **90** (580 mg, 3.58 mmol, 1 equiv.) and $CeCl_3\cdot 7\ H_2O$ (1.33 g, 3.58 mmol, 1 equiv.) in MeOH (11 mL) and THF (22 mL) was treated with $NaBH_4$ (135 mg, 3.58 mmol, 1 equiv.) at 0 °C. The reaction mixture was stirred for 60 min at 0 °C, saturated aqueous NH_4Cl-solution (20 mL) and EtOAc (20 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 40:1) allylic alcohol **(±)-91** (582 mg, 3.58 mmol, quant.) was obtained as a colorless oil.

R$_f$ = 0.5 (pentane/ethyl acetate = 10:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.84 (ddt, *J* = 17.0, 10.0, 6.9 Hz, 1H), 5.11 – 5.06 (m, 3H), 4.89 (d, *J* = 1.4 Hz, 1H), 4.13 (dd, *J* = 7.2, 4.9 Hz, 1H), 2.87 (dd, *J* = 16.1, 6.8 Hz, 1H), 2.76 (dd, *J* = 16.0, 7.1 Hz, 1H), 2.23 (tdd, *J* = 6.8, 2.7, 1.4 Hz, 2H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.76 – 1.70 (m, 1H), 1.68 – 1.60 (m, 2H), 1.59 – 1.53 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 150.2, 136.3, 116.7, 111.3, 84.4, 74.8, 68.7, 36.3, 34.3, 24.6, 18.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{16}NaO$, 187.1093; found: 187.1099; **IR**: $\tilde{\nu}$ = 3386, 3304, 3077, 2924, 2852, 2117, 1642, 1431, 1278, 997 cm^{-1}.

triethyl((4-methylenedec-1-en-9-yn-5-yl)oxy)silane (±)-93

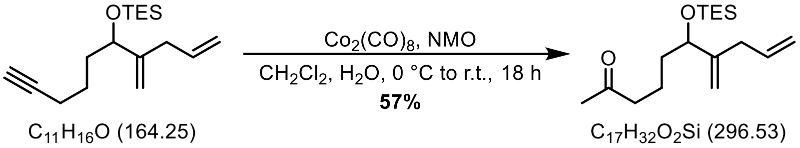


A solution of allylic alcohol **(±)-91** (130 mg, 792 µmol, 1 equiv.) in dichloromethane (16 mL) was treated with 2,6-lutidine (772 µL, 712 mg, 6.65 mmol, 8.4 equiv.) at –25 °C. After stirring for 5 min at –25 °C TESOTf (1.01 mL, 1.17 g, 4.43 mmol, 5.6 equiv.) was added dropwise and the reaction mixture was warmed to room temperature over 2 h.

Saturated aqueous NH_4Cl-solution (20 mL) and EtOAc (20 mL) were added. the phases were separated and the aqueous phase was extracted with EtOAc (3x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 100:1) silyl ether **(±)-93** (70 mg, 253 µmol, 32%) was obtained as a colorless oil.

R_f = 0.9 (pentane/ethyl acetate = 50:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 17.0, 10.3, 7.1 Hz, 1H), 5.07 (dd, *J* = 8.4, 1.6 Hz, 1H), 5.05 (s, 1H), 5.00 (s, 1H), 4.82 – 4.80 (m, 1H), 4.11 (t, *J* = 6.2 Hz, 1H), 2.85 (dd, *J* = 16.3, 6.6 Hz, 1H), 2.70 (dd, *J* = 16.4, 7.5 Hz, 1H), 2.19 (tt, *J* = 7.0, 2.5 Hz, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.62 (ddt, *J* = 10.7, 7.8, 4.0 Hz, 2H), 1.59 – 1.52 (m, 1H), 1.51 – 1.45 (m, 1H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.58 (q, *J* = 8.0 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 150.1, 136.5, 116.4, 110.9, 84.6, 75.7, 68.5, 35.5, 35.3, 24.5, 18.5, 7.0, 5.0; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{30}NaOSi$, 301.1959; found: 301.1970; **IR**: $\tilde{\nu}$ = 3312, 2953, 2876, 1643, 1239, 1078, 1003, 725 cm^{-1}.

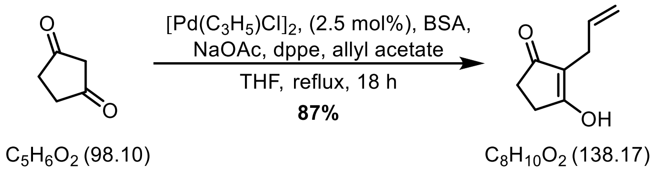
7-methylene-6-((triethylsilyl)oxy)dec-9-en-2-one (±)-95



A solution of silyl ether **(±)-93** (35 mg, 126 µmol, 1 equiv.) and $Co_2(CO)_8$ (52 mg, 151 µmol, 1.2 equiv.) in dichloromethane (6.3 mL) was stirred for 3 h at room temperature. The reaction mixture was cooled to 0 °C and water (22 µL, 22 mg, 1.26 mmol, 10 equiv.) and NMO (74 mg, 628 µmol, 5 equiv.) were added. The reaction mixture was warmed to room temperature over 18 h, filtered over a short pad of Celite® and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 15:1) ketone **(±)-95** (22 mg, 86 µmol, 57%) was obtained as a colorless oil.

R_f = 0.5 (pentane/ethyl acetate = 15:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.81 (ddt, *J* = 16.4, 10.7, 7.2 Hz, 1H), 5.08 – 5.05 (m, 1H), 5.04 (t, *J* = 1.3 Hz, 1H), 5.00 (s, 1H), 4.81 (q, *J* = 1.7 Hz, 1H), 4.09 (t, *J* = 6.0 Hz, 1H), 2.83 (dd, *J* = 16.3, 6.5 Hz, 1H), 2.68 (dd, *J* = 16.4, 7.5 Hz, 1H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.12 (s, 2H), 1.62 – 1.46 (m, 4H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.58 (q, *J* = 8.0 Hz, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.1, 150.0, 136.5, 116.5, 111.1, 76.0, 43.8, 35.9, 35.3, 30.0, 20.1, 7.0, 5.0; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{32}NaO_2Si$, 319.2064; found: 319.2074; **IR**: $\tilde{\nu}$ = 2954, 2915, 2876, 1720, 1365, 1083, 1003, 726 cm^{-1}.

2-allylcyclopentane-1,3-dione 109

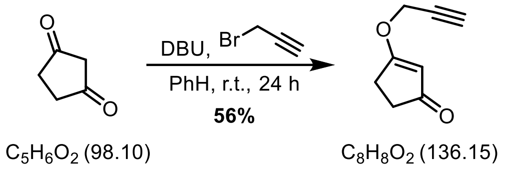


A solution of allylpalladium(II) chloride dimer (1.37 g, 3.75 mmol, 2.5 mol%) and dppe (5.97 g mg, 15 mmol, 10 mol%) in degassed THF (375 mL) was treated successively with allyl acetate (15.0 g, 16.1 mL, 150 mmol, 1 equiv.), 1,3-cyclopentanedione (**97**) (22.0 g, 225 mmol, 1.5 equiv.), BSA (45.7 g, 54.9 mL, 225 mmol, 1.5 equiv.) and sodium acetate (510 mg, 3.75 mmol, 2.5 mol%) at room temperature. After complete addition the reaction mixture was heated to reflux for 18 h. The solvent was removed under reduced pressure and the residue was taken up in dichloromethane (300 mL). The organic phase was washed with aqueous HCl (1 M, 3x 150 mL), the phases were separated and the aqueous phase was extracted with dichloromethane (3x 150 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product (yellow solid) was used for the next step without further purification. Analytically pure samples were obtained after column chromatography (silica gel, dichloromethane/methanol = 50:1). The pure product **109** was obtained as a colorless solid (yield after purification: 87%).

R_f = 0.3 (CH_2Cl_2/MeOH = 25:1), $KMnO_4$, UV-active; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.89 (ddt, *J* = 17.3, 9.9, 6.6 Hz, 1H), 5.18 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.12 (dt, *J* = 9.9, 1.5 Hz, 1H), 2.96 (d, *J* = 6.6 Hz, 2H), 2.53 (s, 4H).

Spectroscopic data agrees with previously published results.[94]

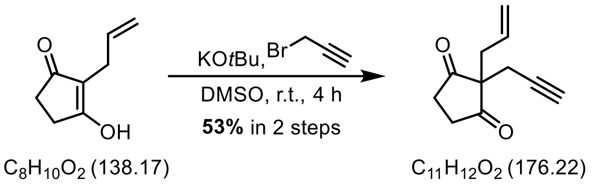
3-(prop-2-yn-1-yloxy)cyclopent-2-en-1-one 108



A solution of 1,3-cyclopentanedione (**97**) (500 mg, 5.10 mmol, 1 equiv.) and propargyl bromide (80 wt% in toluene, 773 mg, 5.20 mmol, 1.02 equiv.) in benzene (15.5 mL) was treated with DBU (776 µL, 792 mg, 5.2 mmol, 1.02 equiv.) at room temperature. The reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 15:1). Enol ether **108** was obtained as a colorless oil (388 mg, 2.86 mmol, 56%).

R$_f$ = 0.6 (pentane/ethyl acetate = 8:1), $KMnO_4$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.43 (q, *J* = 0.8 Hz, 1H), 4.66 (dd, *J* = 2.5, 0.7 Hz, 2H), 2.68 – 2.63 (m, 2H), 2.61 (td, *J* = 2.4, 0.7 Hz, 1H), 2.50 – 2.44 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.7, 188.6, 106.1, 77.4, 76.1, 59.1, 34.3, 28.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_8H_8NaO_2$, 159.0417; found: 159.0418; **IR**: $\tilde{\nu}$ = 3303, 2951, 2922, 1754, 1412, 980, 752 cm^{-1}.

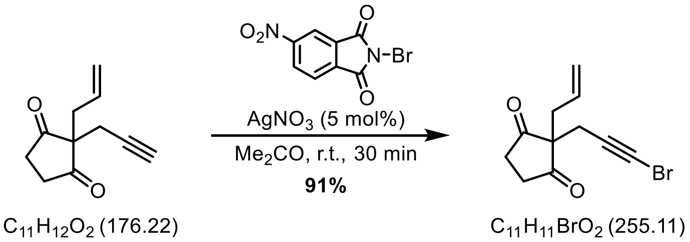
2-allyl-2-(prop-2-yn-1-yl)cyclopentane-1,3-dione 106



A solution of crude allylated dione **109** (<150 mmol, 1 equiv.) in DMSO (380 mL) was treated with potassium *tert*-butoxide (18.5 g, 165 mmol, 1.1 equiv.) in 3 portions at room temperature. After 15 min propargyl bromide (80 wt% in toluene, 26.8 g, 20.0 mL, 180 mmol, 1.2 equiv.) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. Brine (300 mL) and ethyl acetate (300 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (2x 150 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After recrystallization from ethyl acetate propargylated dione **106** (13.7 g, 79.5 mmol, 53% in 2 steps) was obtained as a colorless solid.

m.p.: 48 - 50 °C; **R$_f$** = 0.4 (pentane/ethyl acetate = 8:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.55 (dq, *J* = 17.1, 9.2, 8.7 Hz, 1H), 5.10 – 5.05 (m, 2H), 2.80 – 2.65 (m, 4H), 2.46 (s, 2H), 2.33 (d, *J* = 7.6 Hz, 2H), 1.96 (s, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 215.3, 130.8, 120.8, 78.8, 71.0, 59.8, 39.3, 36.8, 23.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{12}NaO_2$, 199.0730; found: 199.0734; **IR**: $\tilde{\nu}$ = 3300, 2955, 2917, 2849, 1726, 1416, 1215, 992, 928, 752 cm^{-1}.

2-allyl-2-(3-bromoprop-2-yn-1-yl)cyclopentane-1,3-dione 110



A solution of propargylated dione **106** (3.93 g, 22.1 mmol, 1 equiv.) in acetone (110 mL) was treated with $AgNO_3$ (188 mg, 1.11 mmol, 5 mol%) at room temperature. After 5 min stirring at room temperature 4-nitro-*N*-bromophthalimide (7.82 g, 28.8 mmol, 1.3 equiv.) was added in one portion. The reaction mixture was stirred for 30 min at room temperature, the solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1). Brominated alkyne **110** (5.13 g, 20.1 mmol, 91%) was obtained as a colorless solid.

m.p.: 46 °C; **R$_f$** = 0.6 (pentane/ethyl acetate = 6:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.54 (dq, *J* = 17.0, 8.4 Hz, 1H), 5.11 – 5.05 (m, 2H), 2.80 – 2.66 (m, 4H), 2.48 (s, 2H), 2.32 (d, *J* = 7.6 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 215.2, 130.7, 120.8, 74.8, 59.5, 41.6, 39.2, 36.7, 24.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{11}BrNaO_2$, 276.9835; found: 276.9834; **IR**: $\tilde{\nu}$ = 2955, 2916, 2849, 1726, 1416, 1216, 927, 751cm^{-1}.

PPh_3AuNTf_2

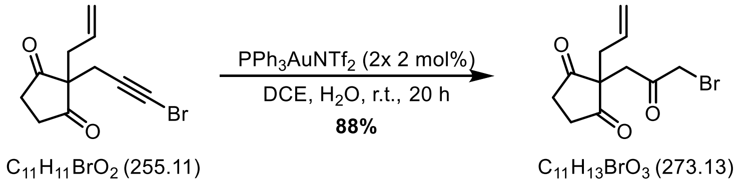
$$\underset{C_{18}H_{15}AuClP(494.71)}{PPh_3AuCl} \quad + \quad \underset{C_2AgF_6NO_4S_2\ (388.00)}{AgNTf_2} \xrightarrow[\substack{CH_2Cl_2,\ \text{r.t.},\ 30\ \text{min} \\ \textbf{quant.}}]{} \underset{C_{20}H_{15}AuF_6NO_4PS_2\ (739.39)}{PPh_3AuNTf_2}$$

PPh_3AuCl (172 mg, 348 µmol, 1 equiv.) and $AgNTf_2$ (135 mg, 348 µmol, 1 equiv.) were dissolved in dichloromethane (8.5 mL) at room temperature. The reaction mixture was stirred for 30 min until a grey suspension is formed. The reaction mixture was filtered over a short pad of Celite® and the solvent was removed under reduced pressure to give PPh_3AuNTf_2 (257 mg, 348 µmol, quant.) as a violet solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 3H), 7.54 – 7.47 (m, 12H).

The spectroscopic data matches reported values.[102]

2-allyl-2-(3-bromo-2-oxopropyl)cyclopentane-1,3-dione 81

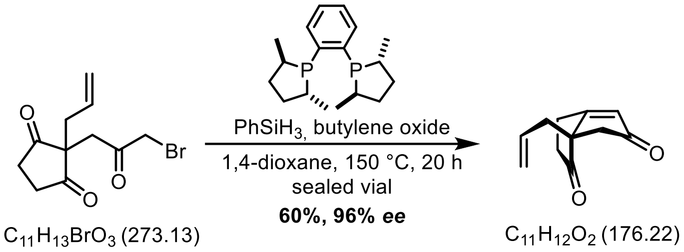


To a solution of bromoalkyne **110** (2.55 g, 10.0 mmol, 1 equiv.) in pre-dried 1,2-dichloroethane (100 mL) was added water (540 mg, 540 µL, 30 mmol, 3 equiv.) and freshly prepared PPh_3AuNTf_2 (148 mg, 201 µmol, 2 mol%). The reaction mixture was stirred at room temperature for 12 h before a second portion of catalyst (2 mol%) was added and stirred for additional 8 h. The reaction mixture was filtered over a short pad of Celite®, the solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane:ethyl acetate = 5:1) to give α-bromo ketone **81** as a nearly colorless solid (2.42 g, 8.80 mmol, 88%). Additional bulb-to-bulb distillation (170 °C at 3.6 x 10^{-2} mbar) gave the triketone **81** as a colorless solid with negligible loss of product mass, in sufficient purity for the next reaction.

M.P.: 76 °C; **R_f** = 0.3 (pentane/ethyl acetate = 6:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.59 (ddt, *J* = 17.5, 10.1, 7.6 Hz, 1H), 5.20 – 5.16 (m, 1H), 5.13 (dd, *J* = 16.9, 1.6 Hz, 1H), 3.84 (s, 2H), 3.33 (s, 2H), 2.97 – 2.91 (m, 2H), 2.77 – 2.70 (m, 2H), 2.23 (d, *J* = 7.6 Hz, 2H); **^{13}C NMR** (176 MHz, CDCl$_3$) δ 215.7, 200.5, 130.0, 121.1, 57.0, 47.1, 38.9, 35.9, 32.6; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for C$_{11}$H$_{13}$BrNaO$_3$, 294.9941; found: 294.9937; **IR**: $\tilde{\nu}$ = 2955, 2916, 2849, 1723, 1466, 1388, 1214, 1063, 750 cm^{-1}.

Crystals suitable for crystal structure analysis were grown by vapor diffusion technique from Et$_2$O/pentane.

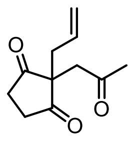
(*S*)-6a-allyl-2,3,6,6a-tetrahydropentalene-1,5-dione 79



A solution of tribromoketone **81** (1.60 g, 5.85 mmol, 1 equiv.) purified by bulb-to-bulb distillation, in 1,4-dioxane (78 mL) was treated with (*R*,*R*)-Me-DuPhos (180 mg, 585 µmol, 10 mol%), butylene oxide (845 mg, 11.7 mmol, 2 equiv.) and PhSiH$_3$ (3.25 mL, 2.85 g, 26.4 mmol, 4.5 equiv.) at room temperature. The flask was sealed and the reaction mixture was stirred for 20 h at 150 °C. After cooling the yellow solution to room temperature the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 3:1) bicyclic enone **79** (618 mg, 3.51 mmol, 60%, 96% *ee*) was obtained as a colorless oil.

R_f = 0.4 (pentane/ethyl acetate = 3:2), UV-active, KMnO$_4$; **^{1}H NMR** (700 MHz, CDCl$_3$) δ 6.03 (d, *J* = 1.5 Hz, 1H), 5.61 – 5.54 (m, 1H), 5.18 (ddt, *J* = 10.1, 1.7, 0.9 Hz, 1H), 5.14 (dq, *J* = 16.9, 1.4 Hz, 1H), 3.12 – 3.01 (m, 2H), 2.96 (ddd, *J* = 19.2, 10.9, 3.0 Hz, 1H), 2.52 – 2.46 (m, 2H), 2.46 – 2.43 (m, 1H), 2.41 (d, *J* = 18.1 Hz, 1H), 2.32 (ddt, *J* = 14.0, 7.2, 1.2 Hz, 1H); **^{13}C NMR** (176 MHz, CDCl$_3$) δ 211.6, 207.5, 182.6, 130.4, 127.6, 120.9, 60.7, 42.3, 39.3, 38.6, 24.8; **$[\alpha]_D^{26}$** = +27.99° (c = 0.89, CHCl$_3$); **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for C$_{12}$H$_{14}$NaO$_2$, 213.0886; found: 213.0883; **IR**: $\tilde{\nu}$ = 2922, 1742, 1703, 1627, 1408, 1320, 1195, 991, 926, 853, 703 cm^{-1}; **GC:** Hydrodex-β-TBDAc; isotherm 170 °C; 1.1 mL/min; Split 50:1; FID 200 °C: t_1 = 10.07 min. (minor), t_2 = 10.45 min. (major).

2-allyl-2-(2-oxopropyl)cyclopentane-1,3-dione 121

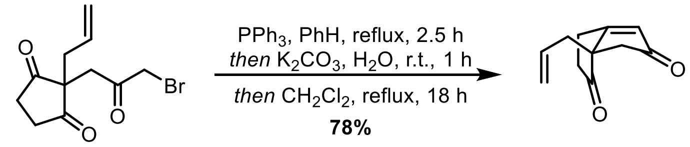


$C_{11}H_{14}O_3$ (194.23)

Debrominated triketone **121** was obtained in near quantitative yield, when the asymmetric Wittig reaction was performed without prior bulb-to-bulb distillation.

R$_f$ = 0.4 (pentane/ethyl acetate = 6:1), $KMnO_4$; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.57 (ddt, *J* = 17.5, 10.1, 7.6 Hz, 1H), 5.15 – 5.11 (m, 1H), 5.08 (dq, *J* = 16.8, 1.4 Hz, 1H), 3.14 (s, 2H), 2.97 – 2.88 (m, 2H), 2.71 – 2.62 (m, 2H), 2.18 (d, *J* = 7.7 Hz, 2H), 2.05 (s, 3H); **^{13}C NMR** (126 MHz, CDCl3) δ 216.3, 206.3, 130.4, 120.6, 56.8, 51.4, 38.8, 35.9, 28.4; ESI-TOF (*m/z*): [M + Na]$^+$ calcd for $C_{11}H_{14}NaO_3$, 217.0836; found: 217.0839; **IR**: ṽ = 2955, 2920, 1719, 1716, 1364, 1178, 995 cm^{-1}.

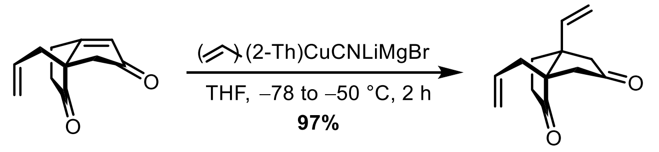
Procedure for the synthesis of **(±)-79**



$C_{11}H_{13}BrO_3$ (273.13) $C_{11}H_{12}O_2$ (176.22)

A solution of triketone **81** (100 mg, 366 µmol, 1 equiv.) and PPh_3 (192 mg, 732 µmol, 2 equiv.) in benzene (1.8 mL) was refluxed for 2.5 h. The reaction mixture was cooled to room temperature and saturated aqueous K_2CO_3 (1.2 mL) and dichloromethane (1 mL) were added. The mixture was stirred at room temperature until all solids were dissolved (ca. 1 h). The phases were separated, the aqueous phase was extracted with dichloromethane (3x 1 mL), the combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The remaining solid was redissolved in dichloromethane (2.2 mL) and refluxed for 18 h. The solvent was removed under reduced pressure and the obtained crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 3:1). Bicyclic enone **(±)-79** was obtained as a colorless oil (50 mg, 285 µmol, 78%).

(3a*R*,6a*S*)-6a-allyl-3a-vinylhexahydropentalene-1,5-dione 123

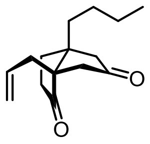


$C_{11}H_{12}O_2$ (176.22) $C_{13}H_{16}O_2$ (204.27)

A solution of thiophene (695 µL, 730 mg, 8.68 mmol, 3 equiv.) in THF (29 mL) was treated with *n*-BuLi (2.5 M in hexanes, 3.47 mL, 8.68 mmol, 3 equiv.) at –30 °C and stirred for 30 min at that temperature. In a second flask a mixture of CuCN (777 mg, 8.68 mmol, 3 equiv.) in THF (43 mL) was cooled to –78 °C, and the prepared solution of lithiated thiophene was added *via* transfer cannula. After 5 min vinylmagnesium bromide (0.7 M in THF, 12.4 mL, 8.68 mmol, 3 equiv.) was added and the cooling bath was removed. The mixture was warmed to room temperature over 20 min, and stirred for additional 40 min until a violet-grey mixture was formed. The mixture was cooled to –78 °C and a solution of diketone **79** (510 mg, 2.89 mmol, 1 equiv.) in THF (29 mL) was added dropwise. The reaction mixture was allowed to warm to –50 °C over the course of 2 h, saturated aqueous NH_4Cl solution (100 mL) was added and the mixture was warmed to room temperature. Water (ca. 25 mL) was added to form clear phases, the phases were separated and the aqueous phase was extracted with ethyl acetate (2x 100 mL). The combined organic phases were washed with brine (2x 100 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 8:1) the diene **123** was obtained as a colorless oil (576 mg, 2.80 mmol, 97%).

R_f = 0.3 (pentane/ethyl acetate = 5:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.99 (dd, *J* = 17.4, 10.9 Hz, 1H), 5.71 (ddt, *J* = 17.3, 10.2, 7.4 Hz, 1H), 5.26 (d, *J* = 10.9 Hz, 1H), 5.15 (d, *J* = 17.4 Hz, 1H), 5.09 – 5.05 (m, 2H), 2.61 – 2.57 (m, 1H), 2.56 – 2.46 (m, 3H), 2.32 (ddt, *J* = 14.2, 7.1, 1.2 Hz, 1H), 2.27 – 2.17 (m, 4H), 1.96 (ddd, *J* = 14.1, 9.2, 5.4 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 219.0, 214.2, 139.3, 132.6, 119.3, 115.5, 60.0, 52.6, 48.8, 44.0, 36.7, 34.7, 28.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{16}NaO_2$, 227.1043; found: 227.1059; **$[\alpha]_D^{26}$** = +10.65° (c = 1.25, $CHCl_3$); **IR**: ṽ = 2955, 2920, 2852, 1736, 1637, 1403, 1171, 999, 917, 752 cm^{-1}.

(3a*R*,6a*S*)-6a-allyl-3a-butylhexahydropentalene-1,5-dione SI-3

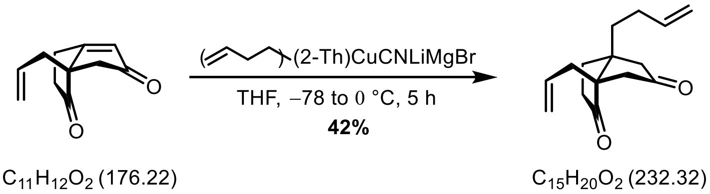


$C_{15}H_{22}O_2$ (234.34)

The 1,4 addition product **SI-3** was obtained as a minor product of the mixed cuprate addition in up to 7% yield.

R$_f$ = 0.33 (pentane/ethyl acetate = 5:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.77 – 5.71 (m, 1H), 5.10 (d, *J* = 1.6 Hz, 1H), 5.08 (dd, *J* = 8.2, 1.6 Hz, 1H), 2.59 (d, *J* = 19.4 Hz, 1H), 2.50 – 2.39 (m, 2H), 2.39 – 2.34 (m, 2H), 2.24 (dd, *J* = 14.2, 7.8 Hz, 1H), 2.17 (dd, *J* = 19.4, 1.9 Hz, 1H), 2.06 (d, *J* = 18.6 Hz, 1H), 1.97 (ddd, *J* = 13.7, 10.0, 7.4 Hz, 1H), 1.88 (ddd, *J* = 14.0, 9.2, 5.4 Hz, 1H), 1.55 (td, *J* = 12.8, 12.4, 3.9 Hz, 1H), 1.46 (ddd, *J* = 13.3, 11.6, 4.4 Hz, 1H), 1.37 – 1.29 (m, 3H), 1.27 – 1.23 (m, 1H), 0.93 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 220.1, 215.3, 133.0, 119.1, 59.6, 50.1, 48.9, 44.8, 35.9, 34.7, 34.4, 28.6, 26.9, 23.6, 14.1; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{22}NaO_2$, 257.1512; found: 257.1549; **IR**: ṽ = 2958, 2918, 2851, 1737, 1465, 1168, 918, 754 cm^{-1}.

(3a*R*,6a*S*)-6a-allyl-3a-(but-3-en-1-yl)hexahydropentalene-1,5-dione 124

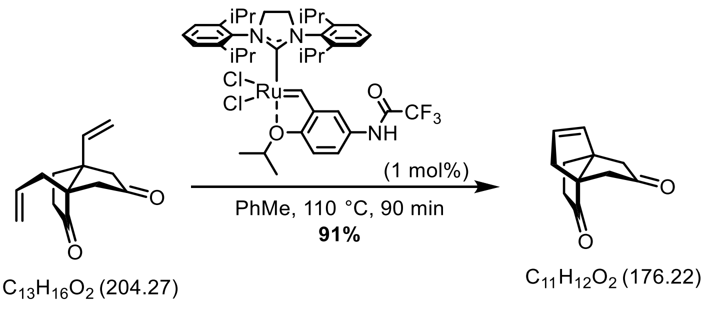


A solution of thiophene (113 µL, 119 mg, 1.42 mmol, 10 equiv.) in THF (4.7 mL) was treated with *n*-BuLi (2.5 M in hexanes, 0.56 mL, 1.42 mmol, 10 equiv.) at –30 °C and stirred for 30 min at that temperature. In a second flask a mixture of CuCN (127 mg, 1.42 mmol, 10 equiv.) in THF (7.1 mL) was cooled to –78 °C, and the prepared solution of lithiated thiophene was added *via* transfer cannula. After 5 min butenylmagnesium bromide (0.6 M in THF, 2.36 mL, 1.42 mmol, 10 equiv.), freshly prepared from butenylbromide, was added and the cooling bath was removed. The mixture was warmed to room temperature over 20 min, and stirred for additional 40 min until a violet-grey mixture was formed. The mixture was cooled to –78 °C and a solution of diketone **79**

(25 mg, 142 µmol, 1 equiv.) in THF (1.4 mL) was added dropwise. The reaction mixture was allowed to warm to 0 °C over 5 h, saturated aqueous NH_4Cl solution (20 mL) was added and the mixture was warmed to room temperature. Water (ca. 5 mL) was added to form clear phases, the phases were separated and the aqueous phase was extracted with ethyl acetate (2x 10 mL). The combined organic phases were washed with brine (2x 10 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 8:1) diene **124** was obtained as a colorless oil (33 mg, 60 µmol, 42%).

R_f = 0.3 (pentane/ethyl acetate = 9:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ = 5.82 (ddt, *J*=16.8, 10.2, 6.5, 1H), 5.80 – 5.67 (m, 1H), 5.11 – 5.04 (m, 3H), 5.00 (dq, *J*=10.2, 1.4, 1H), 2.60 (d, *J*=19.4, 1H), 2.48 (ddd, *J*=20.1, 10.1, 5.4, 1H), 2.45 – 2.38 (m, 2H), 2.38 – 2.34 (m, 1H), 2.24 (ddt, *J*=14.2, 7.8, 1.2, 1H), 2.18 (dd, *J*=19.4, 1.9, 1H), 2.15 – 2.02 (m, 3H), 2.00 (ddd, *J*=13.7, 10.1, 7.4, 1H), 1.90 (ddd, *J*=14.1, 9.2, 5.4, 1H), 1.66 (td, *J*=12.8, 12.4, 5.0, 1H), 1.56 (ddd, *J*=13.6, 11.8, 4.9, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 219.7, 214.9, 137.9, 132.8, 119.3, 115.4, 59.6, 50.0, 48.7, 44.7, 35.9, 34.6, 33.8, 29.0, 28.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{20}NaO_2$, 255.1356; found: 255.1372; **$[\alpha]_D^{26}$** = +8.02° (c = 0.55, $CHCl_3$); **IR:** ṽ = 3016, 2917, 2850, 1737, 1365, 1216, 1133, 996, 916, 753 cm^{-1}.

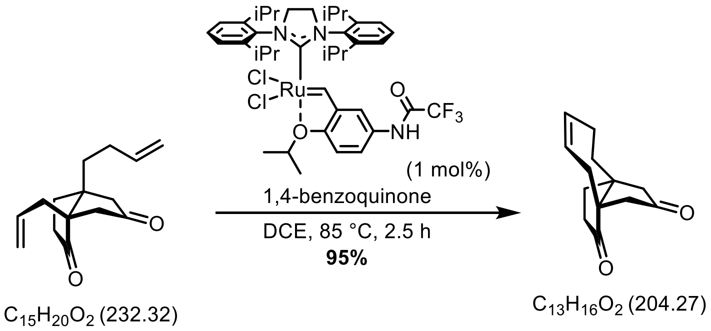
(3a*S*,6a*R*)-2,3-dihydro-3a,6a-propanopentalene-1,8(6*H*)-dione 78



A solution of diene **123** (1.87 g, 9.16 mmol, 1 equiv.) in degassed toluene (152 mL) was treated with Umicore M71SiPr (75.3 mg, 92 µmol, 1 mol%) at room temperature. The reaction mixture was heated to 110 °C in a closed flask. After 90 min the reaction was cooled to room temperature and the solvent was removed under reduced pressure. The obtained crude product was used without further purification. Analytically pure material was obtained after column chromatography (silica gel, pentane/ethyl acetate = 6:1), to give the tricyclic diketone **78** as a colorless solid (yield after purification: 91%).

M.P.: 82 - 85 °C; **R$_f$** = 0.45 (pentane/ethyl acetate = 3:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.76 (dt, *J* = 5.8, 2.2 Hz, 1H), 5.72 (dt, *J* = 5.3, 2.2 Hz, 1H), 2.89 (dt, *J* = 17.5, 2.2 Hz, 1H), 2.54 – 2.50 (m, 3H), 2.47 – 2.44 (m, 2H), 2.44 – 2.38 (m, 2H), 2.27 (ddd, *J* = 13.5, 8.1, 4.2 Hz, 1H), 1.81 (ddd, *J* = 13.4, 10.6, 8.8 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 220.8, 216.3, 136.7, 130.7, 60.9, 60.3, 50.4, 45.8, 44.6, 38.1, 32.1; **EI-TOF** (*m/z*): $[M]^+$ calcd for $C_{11}H_{12}O_2$, 176.0837; found: 176.0829; **$[\alpha]_D^{27}$** = +43.3° (c = 0.95, $CHCl_3$); **IR**: $\tilde{\nu}$ = 2952, 2918, 2850, 1733, 1457, 1403, 1165, 753 cm^{-1}.

(3a*S*,8a*R*)-2,3,4,5-tetrahydro-3a,8a-propanoazulene-1,10(8*H*)-dione 125



A solution of diene **124** (10 mg, 44 µmol, 1 equiv.), 1,4-benzoquinone (0.2 mg, 2 µmol, 5 mol%) and Umicore M71SIPr (0.4 mg, 0.4 µmol) in degassed DCE (0.75 mL) was heated to 85 °C. After 2.5 h the reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 5:1) to give propellane **125** (9 mg, 42 µmol, 95% yield) as a colorless oil.

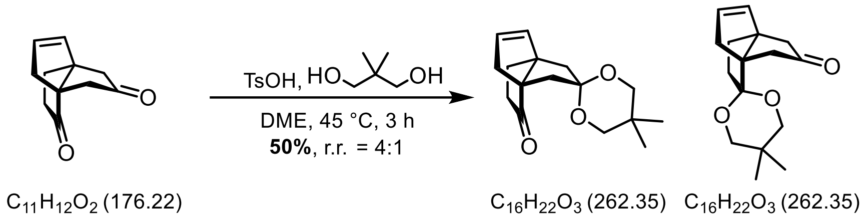
R$_f$ = 0.25 (pentane/ethyl acetate = 5:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.76 (dddd, *J* = 10.5, 6.0, 4.2, 2.1 Hz, 1H), 5.53 (dddd, *J* = 11.1, 9.3, 4.6, 2.9 Hz, 1H), 2.57 – 2.42 (m, 5H), 2.39 (dd, *J* = 19.0, 1.9 Hz, 1H), 2.28 (dd, *J* = 18.9, 1.3 Hz, 1H), 2.25 – 2.21 (m, 1H), 2.14 – 2.04 (m, 3H), 2.01 – 1.92 (m, 2H), 1.79 (ddd, *J* = 14.4, 8.7, 1.9 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 221.9, 216.2, 132.8, 125.4, 59.6, 50.7, 49.9, 45.8, 37.0, 35.2, 31.6, 29.5, 24.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{16}NaO_2$, 227.1043; found:

227.1054; **[α]$_D$^{26}** = -5.50° (c = 0.43, $CHCl_3$); **IR**: ṽ = 2954, 2916, 2850, 1735, 1464, 1401,1178, 752 cm^{-1}.

(3a*S*,6a*R*)-5',5'-dimethyl-3,4-dihydro-1*H*-spiro[3a,6a-propanopentalene-2,2'-[1,3]dioxan]-9-one 129a

and

(3a*R*,6a*S*)-5',5'-dimethyl-3,6-dihydro-2*H*-spiro[3a,6a-propanopentalene-1,2'-[1,3]dioxan]-8-one 129b

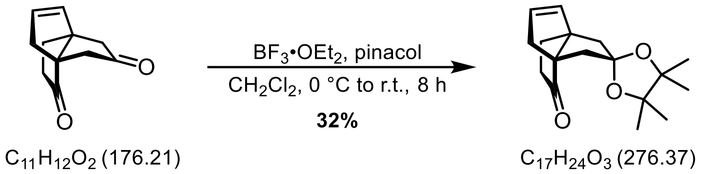


A solution of propellane **78** (13.3 mg, 75 μmol, 1 equiv.) and 2,2-dimethylpropane-1,3-diol (9.4 mg, 91 μmol, 1.2 equiv.) in DME (0.5 mL) was treated with TsOH (1.4 mg, 8 μmol, 10 mol%) at room temperature. The reaction mixture was heated to 45 °C for 3 h, the solvent was removed under reduced pressure and the obtained crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 15:1). Acetals **129a/b** were obtained as an inseparable mixture (9.9 mg, 38 μmol, 50%, r.r. = 4:1).

R_f = 0.4 (pentane/ethyl acetate = 10:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.73 (dt, *J* = 4.9, 2.3 Hz, 1H),* 5.64 – 5.57 (m, 1H), 5.58 – 5.51 (m, 1H), 5.50 (dt, *J* = 4.9, 2.2 Hz, 1H),* 3.60 (d, *J* = 11.3 Hz, 1H), 3.55 (d, *J* = 11.2 Hz, 1H), 3.46 (dd, *J* = 13.8, 11.4 Hz, 2H),* 3.43 (dd, *J* = 11.2, 2.7 Hz, 1H), 3.39 (dd, *J* = 11.1, 1.9 Hz, 1H),* 3.37 – 3.35 (m, 1H), 3.29 (dd, *J* = 11.5, 1.9 Hz, 1H),* 3.18 (d, *J* = 17.9 Hz, 1H), 3.06 (dd, *J* = 13.2, 2.2 Hz, 1H),* 2.81 (d, *J* = 17.8 Hz, 1H), 2.57 (dd, *J* = 12.9, 6.7 Hz, 1H), 2.47 – 2.35 (m, 3H), 2.33 – 2.21 (m, 2H), 2.04 – 1.91 (m, 2H), 1.87 (d, *J* = 13.1 Hz, 1H),* 1.62 (s, 1H), 1.57 (d, *J* = 13.3 Hz, 2H), 1.50 (dd, *J* = 12.8, 7.8 Hz, 1H), 1.18 (s, 3H), 1.04 (s, 3H),* 0.82 (s, 3H),* 0.72 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 221.2,* 219.8, 138.1,* 137.6, 128.7, 126.7,* 108.5, 108.4,* 73.2, 73.1,* 70.9, 70.7,* 61.8,* 61.7, 61.5,* 60.8, 51.0, 48.7,* 46.8, 44.5, 44.0,* 40.7,* 37.8, 37.7,* 33.0,* 30.1, 30.0,* 26.9, 23.2, 23.0,* 22.4,* 22.2A; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{16}H_{22}NaO_3$, 288.1461; found: 285.1463

*Signals unambiguously assigned to the major regioisomer. Due to the inseparable mixture of diastereomers, no IR spectrum was recorded.

(3a'S,6a'R)-4,4,5,5-tetramethyl-1'H,3'H,4'H-spiro[[1,3]dioxolane-2,2'-[3a,6a]propanopentalen]-9'-one 130

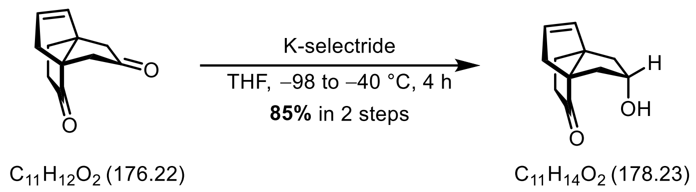


A solution of propellane **78** (16.3 mg, 93 µmol, 1 equiv.) and pinacol (16.3 mg, 140 µmol, 1.5 equiv.) in dichloromethane (0.4 mL) was treated with $BF_3·OEt_2$ (12.8 mg, 93 µmol, 1 equiv.) at 0 °C. The reaction mixture was warmed to room temperature over 4 h. Dichloromethane (2 mL) and saturated aqueous $NaHCO_3$-solution (2 mL) were added, the phases were separated and the aqueous phase was extracted with dichloromethane (2x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 15:1) ketone **130** was obtained as a colorless oil (8.2 mg, 30 µmol, 32%).

R_f = 0.4 (pentane/ethyl acetate = 8:1), vanillin; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.69 (dt, *J* = 4.9, 2.3 Hz, 1H), 5.55 – 5.51 (m, 1H), 2.55 (dt, *J* = 17.6, 2.3 Hz, 1H), 2.49 – 2.31 (m, 4H), 2.08 – 2.03 (m, 2H), 2.00 – 1.88 (m, 3H), 1.19 (s, 6H), 1.17 (s, 6H); **^{13}C NMR** (126 MHz, CDCl3) δ 209.1, 137.8, 127.5, 82.9, 82.3, 62.5, 61.3, 51.4, 48.8, 45.3, 38.2, 32.6, 29.9, 23.82,* 23.77, 23.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{24}NaO_3$, 299.1618; found: 299.1621; **IR**: ṽ = 3414, 2915, 2851, 1732, , 1054, 736 cm^{-1}.

*Signal with double intensity.

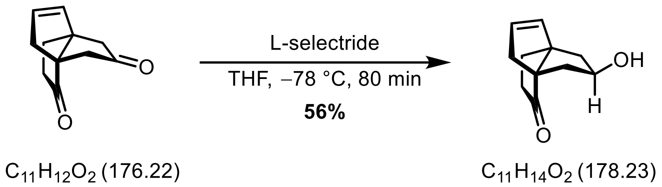
(3a*R*,6a*S*,8*S*)-8-hydroxy-2,3-dihydro-3a,6a-propanopentalen-1(6*H*)-one 131



A solution of crude diketone **78** (<9.16 mmol, 1 equiv.) in THF (183 mL) was treated dropwise with K-selectride (1 M in THF, 13.6 mL, 13.6 mmol, 1.5 equiv.) at –98 °C (methanol/liquid N_2 bath). The solution was slowly warmed to –40 °C over 4 h. Aqueous HCl solution (1 M, 100 mL) was added and the mixture was warmed to room temperature. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x 100 mL). The combined organic phases were washed with brine (200 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 4:1) alcohol **131** was obtained as a colorless oil (1.38 g, 7.79 mmol, 85% in 2 steps).

R_f = 0.4 (pentane/ethyl acetate = 2:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.70 (dt, *J* = 5.5, 2.3 Hz, 1H), 5.46 (dt, *J* = 5.5, 2.2 Hz, 1H), 4.39 (tt, *J* = 4.2, 3.1 Hz, 1H), 2.51 (ddd, *J* = 17.8, 2.7, 1.8 Hz, 1H), 2.49 – 2.46 (m, 1H), 2.43 (dt, *J* = 17.5, 9.6 Hz, 1H), 2.43 – 2.33 (m, 1H), 2.31 (ddd, *J* = 13.5, 3.2, 1.8 Hz, 1H), 2.05 (dt, *J* = 12.8, 9.1 Hz, 1H), 1.98 (ddd, *J* = 12.8, 9.7, 4.6 Hz, 1H), 1.94 (dt, *J* = 13.3, 2.4 Hz, 1H), 1.86 (dd, *J* = 13.3, 4.5 Hz, 1H), 1.75 (dd, *J* = 13.5, 3.9 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 222.4, 138.2, 126.6, 75.1, 65.0, 63.5, 48.2, 46.6, 44.5, 38.2, 33.9; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_2$, 201.0886; found: 201.0892; **$[\alpha]_D^{24}$** = -62.2° (c = 1.55, $CHCl_3$); **IR**: $\tilde{\nu}$ = 3406, 2919, 2850, 1732, 1457, 1054, 736 cm^{-1}.

(3a*R*,6a*S*,8*R*)-8-hydroxy-2,3-dihydro-3a,6a-propanopentalen-1(6*H*)-one 132

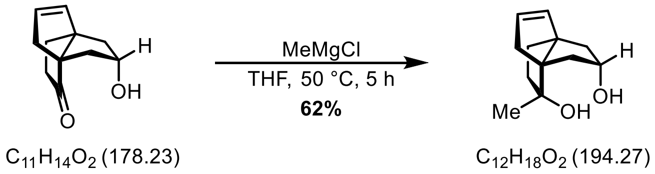


A solution of crude diketone **78** (13.7 mg, 78 µmol, 1 equiv.) in THF (1.5 mL) was treated with L-selectride (1 M in THF, 78 µL, 78 µmol, 1 equiv.) at –78 °C. The reaction mixture was stirred at this temperature for 80 min. MeOH (3 mL) was added and the reaction was allowed to warm to room temperature. Saturated aqueous NH_4Cl-solution (3 mL) and EtOAc (3 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (2x 3 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 2:1) the alcohol **132** was obtained as a colorless oil (7.8 mg, 44 µmol, 56% yield).

R_f = 0.3 (pentane/ethyl acetate = 2:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.75 (dt, *J* = 5.5, 2.3 Hz, 1H), 5.57 (dt, *J* = 5.5, 2.2 Hz, 1H), 4.20 (tt, *J* = 7.1, 5.7 Hz, 1H), 2.62 (dt, *J* = 17.9, 2.3 Hz, 1H), 2.58 (dt, *J* = 17.9, 2.2 Hz, 1H), 2.45 (ddd, *J* = 13.3, 5.8, 1.2 Hz, 1H), 2.38 (ddd, *J* = 17.1, 10.3, 9.3 Hz, 1H), 2.32 (ddd, *J* = 17.1, 8.2, 4.4 Hz, 1H), 2.12 (ddd, *J* = 12.8, 5.5, 1.2 Hz, 1H), 1.99 (ddd, *J* = 13.5, 9.4, 4.4 Hz, 1H), 1.79 (ddd, *J* = 12.8, 7.1, 0.8 Hz, 1H), 1.73 – 1.67 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 221.7, 137.8, 127.9, 74.6, 64.3, 62.3, 48.1, 45.7, 45.5, 38.3, 33.1; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_2$, 201.0886; found: 201.0881; **IR**: ṽ = 3408, 2919, 2851, 1729, 1463, 1054, 737 cm^{-1}.

(1*R*,3a*R*,6a*S*,8*S*)-1-methyl-1,2,3,6-tetrahydro-3a,6a-propanopentalene-1,8-diol

133

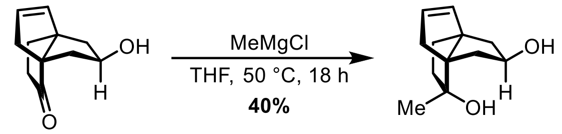


A solution of ketone **131** (553 mg, 3.10 mmol, 1 equiv.) in THF (9.0 mL) was treated dropwise with MeMgCl (3 M in THF, 4.13 mL, 12.4 mmol, 4 equiv.) at room temperature. The mixture was stirred at room temperature until gas evolution stopped (ca. 5 min), the flask was closed and heated to 50 °C for 18 h. The reaction mixture was quenched by adding it dropwise to a cold saturated NH_4Cl-solution (20 mL). After gas evolution stopped the aqueous phase was extracted with ethyl acetate (3x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 2:1) the diol **133** was obtained as a colorless solid (373 mg, 1.92 mmol, 62%, single diastereomer, 92% BRSM) along with remaining starting material.

m.p.: 115 °C; $\mathbf{R_f}$ = 0.3 (pentane/ethyl acetate = 1:2), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.47 (dt, *J* = 5.5, 2.3 Hz, 1H), 5.38 (dt, *J* = 5.5, 2.3 Hz, 1H), 4.33 (ddt, *J* = 7.1, 5.9, 2.8 Hz, 1H), 3.34 (s_{br}, 1H), 2.47 (dt, *J* = 17.6, 2.4 Hz, 1H), 2.31 (ddd, *J* = 14.3, 2.7, 1.7 Hz, 1H), 2.19 (dt, *J* = 17.6, 2.2 Hz, 1H), 1.93 (dd, *J* = 13.8, 6.0 Hz, 1H), 1.88 – 1.80 (m, 2H), 1.70 (dddd, *J* = 14.2, 12.3, 6.3, 1.7 Hz, 2H), 1.66 – 1.60 (m, 2H), 1.33 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 138.5, 126.2, 81.9, 75.8, 69.3, 67.1, 49.1, 46.4, 44.6, 41.7, 36.8, 24.9; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{18}NaO_2$, 217.1199; found: 217.1190; $[\alpha]_D^{24}$ = +19.7° (c = 1.00, $CHCl_3$); **IR**: ṽ = 3269, 3042, 2936, 2852, 1457, 1215, 1070, 737 cm^{-1}.

Crystals suitable for crystal structure analysis were grown by vapor diffusion technique from Et_2O/pentane.

(1*R*,3a*R*,6a*S*,8*R*)-1-methyl-1,2,3,6-tetrahydro-3a,6a-propanopentalene-1,8-diol 134

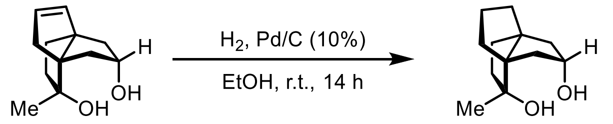


$C_{11}H_{14}O_2$ (178.23) $C_{12}H_{18}O_2$ (194.27)

A solution of ketone **132** (125 mg, 701 µmol, 1 equiv.) in THF (2.0 mL) was treated dropwise with MeMgCl (3M in THF, 0.93 mL, 2.81 mmol, 4 equiv.) at room temperature. The mixture was stirred at room temperature until gas evolution stopped (ca. 5 min), the flask was closed and heated to 50 °C for 18 h. The reaction mixture was quenched by adding it dropwise to a cold saturated NH_4Cl-solution (ca. 5 mL). After gas evolution stopped the aqueous phase was extracted with ethyl acetate (3x 5 mL). The combined organic phases were washed with brine (5 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 2:1) diol **134** was obtained as a colorless oil (55 mg, 280 µmol, 40%, 90% BRSM) along with recovered starting material.

R_f = 0.2 (pentane/ethyl acetate = 1:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.66 (dt, *J* = 4.9, 2.3 Hz, 1H), 5.49 (dt, *J* = 5.6, 2.2 Hz, 1H), 4.48 (ddd, *J* = 11.0, 6.0, 4.9 Hz, 1H), 2.56 (dd, *J* = 13.7, 6.0 Hz, 1H), 2.47 (dt, *J* = 17.6, 2.4 Hz, 1H), 2.36 (dt, *J* = 17.6, 2.3 Hz, 1H), 1.99 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.77 (dd, *J* = 13.1, 4.8 Hz, 1H), 1.74 – 1.71 (m, 1H), 1.66 – 1.59 (m, 5H), 1.41 (dd, *J* = 13.7, 5.1 Hz, 1H), 1.29 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 134.0, 127.1, 81.8, 77.2, 68.2, 65.6, 48.5, 46.0, 44.8, 41.1, 36.6, 24.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{18}NaO_2$, 217.1199; found: 217.1204; **IR**: ṽ = 3365, 2938, 2856, 2253, 1450, 1375, 1026, 918 cm^{-1}.

(1*R*,3a*R*,5*S*,6a*S*)-1-methylhexahydro-3a,6a-propanopentalene-1,5-diol 136



$C_{12}H_{18}O_2$ (194.27) $C_{12}H_{20}O_2$ (196.29)

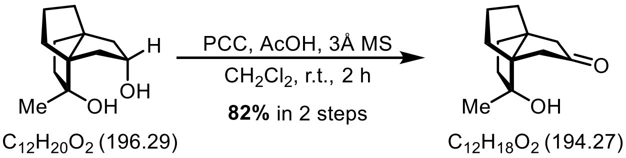
A mixture of palladium on charcoal (10% Pd, 133 mg) in EtOH (100 mL) was treated with a solution of diol **133** (370 mg, 1.93 mmol, 1 equiv.) in EtOH (10 mL) at room temperature.

The argon atmosphere was exchanged for a hydrogen atmosphere and the reaction mixture was stirred for 14 h at room temperature. The mixture was filtered over a short pad of Celite® and the solvent was removed under reduced pressure. The obtained crude product was used without further purification. Analytically pure samples were obtained after column chromatography (silica gel, pentane/ethyl acetate = 3:1). Pure diol **136** was obtained as a colorless solid (yield after purification: 96%).

M.P.: 177 °C; **R_f** = 0.25 (pentane/ethyl acetate = 2:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 4.32 (t, *J* = 5.1 Hz, 1H), 4.21 (s_{br}, 1H), 2.23 (dd, *J* = 14.8, 2.7 Hz, 1H), 1.94 (dd, *J* = 14.4, 2.7 Hz, 1H), 1.81 (ddd, *J* = 13.4, 11.8, 5.5 Hz, 1H), 1.80 – 1.69 (m, 1H), 1.67 – 1.58 (m, 4H), 1.52 – 1.46 (m, 2H), 1.35 – 1.28 (m, 2H), 1.27 (s, 3H), 1.26 – 1.22 (m, 2H), 1.19 (td, *J* = 12.6, 5.5 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 81.4, 76.1, 68.7, 62.0, 49.6, 42.6, 42.3, 40.7, 39.6, 37.1, 25.2, 24.0; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{20}NaO_2$, 219.1356; found: 219.1344; **$[\alpha]_D^{22}$** = +10.7° (c = 1.12, $CHCl_3$); **IR**: ṽ = 3220, 2937, 2859, 1457, 1080, 926, 755 cm^{-1}.

(3a*S*,4*R*,6a*R*)-4-hydroxy-4-methyltetrahydro-3a,6a-propanopentalen-2(1*H*)-one

135

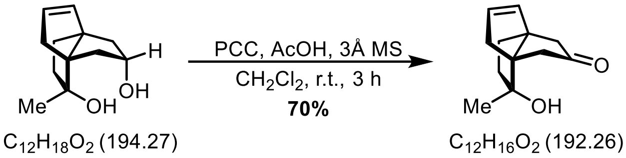


A mixture of PCC (494 mg, 2.28 mmol, 1.5 equiv.) and dry 3Å molecular sieve (366 mg) in dichloromethane (5 mL) was treated with a solution of diol **136** (300 mg, 1.53 mmol, 1 equiv.) in dichloromethane (6 mL) at room temperature. After 5 min acetic acid (10 drops) was added. The reaction mixture was stirred for 3 h at room temperature, filtered over Celite® and the solvent was removed under reduced pressure (45 °C, >150 mbar, product sublimates at lower pressure). After column chromatography (silica gel, pentane/diethyl ether = 2:3) ketone **135** was obtained as a yellowish solid (243 mg, 1.26 mmol, 82% in 2 steps).

m.p.: 142 °C; **R_f** = 0.2 (pentane/diethyl ether = 1:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 2.73 (dd, *J* = 18.1, 2.2 Hz, 1H), 2.45 (dd, *J* = 18.6, 2.2 Hz, 1H), 2.33 (dd, *J* = 18.5, 1.7

Hz, 1H), 1.91 (dd, *J* = 18.1, 1.7 Hz, 1H), 1.88 – 1.79 (m, 3H), 1.78 – 1.72 (m, 2H), 1.66 – 1.64 (m, 1H), 1.62 – 1.54 (m, 4H), 1.39 (ddd, *J* = 11.9, 10.4, 6.7 Hz, 1H), 1.28 (s, 3H); **^{13}C NMR** (176 MHz, CDCl$_3$) δ 220.0, 82.1, 64.3, 56.2, 55.1, 46.0, 44.0, 39.9, 39.6, 38.4, 26.2, 23.7; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{12}H_{18}NaO_2$, 217.1199; found: 217.1205; [M + K]$^+$ calcd for $C_{12}H_{18}KO_2$, 233.0939; found: 233.0933; **$[\alpha]_D^{22}$** = –22.3° (c = 1.0, CHCl$_3$); **IR**: ṽ = 3447, 2939, 2865, 1732, 1456, 1177, 922 cm^{-1}.

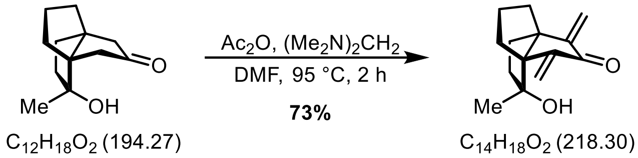
(3a*S*,6a*R*,9*R*)-9-hydroxy-9-methyl-3,4-dihydro-3a,6a-propanopentalen-2(1*H*)-one SI-8



A solution of diol **133** (50 mg, 257 µmol, 1 equiv.) in dichloromethane (1.12 mL) was treated with 3Å MS (61 mg) and PCC (83.2 mg, 386 µmol, 1.5 equiv.) at room temperature. AcOH was added (1 drop) and the reaction mixture was stirred at room temperature for 3 h. The mixture was filtered over a short pad of Celite® and the solvent was removed under reduced pressure (45 °C, >150 mbar, product sublimates at lower pressure). After column chromatography (silica gel, pentane/diethyl ether = 2:3) ketone **SI-8** was obtained as a yellow oil (35 mg, 180 µmol, 70%).

R$_f$ = 0.2 (pentane/diethyl ether = 1:2), vanillin; **^{1}H NMR** (500 MHz, CDCl$_3$) δ 5.61 (ddd, *J* = 5.6, 2.8, 1.6 Hz, 1H), 5.53 (dt, *J* = 5.6, 2.2 Hz, 1H), 2.81 (dd, *J* = 18.2, 1.7 Hz, 1H), 2.50 (dd, *J* = 18.8, 1.4 Hz, 1H), 2.41 (dd, *J* = 18.8, 1.7 Hz, 1H), 2.36 (ddd, *J* = 17.0, 2.7, 2.1 Hz, 1H), 2.25 (dt, *J* = 17.0, 2.1 Hz, 1H), 2.01 (dd, *J* = 18.1, 1.4 Hz, 1H), 1.93 – 1.88 (m, 2H), 1.83 (td, *J* = 12.4, 7.6 Hz, 1H), 1.71 (ddd, *J* = 12.9, 5.5, 2.2 Hz, 1H), 1.32 (s, 3H); **^{13}C NMR** (126 MHz, CDCl$_3$) δ 219.660, 138.8, 127.6, 82.6, 63.6, 63.6, 51.8, 47.1, 44.5, 40.6, 39.3, 23.5; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{12}H_{16}NaO_2$, 215.1043; found: 215.1045**;** **IR**: ṽ = 3445, 3045, 2941, 2865, 1733, 1458, 1177 cm^{-1}.

(3a*R*,4*R*,6a*S*)-4-hydroxy-4-methyl-1,3-dimethylenetetrahydro-3a,6a-propanopentalen-2(1*H*)-one 77

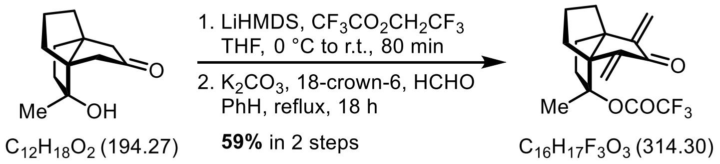


A solution of bis(dimethylamino)methane (1.68 mL, 1.26 g, 12.4 mmol, 30 equiv.) in DMF (1.2 mL) was treated with freshly distilled acetic acid anhydride (1.26 g, 1.17 mL, 12.4 mmol, 30 equiv.) at room temperature. The mixture was stirred at room temperature for 15 min, before a solution of ketone **135** (80 mg, 412 µmol, 1 equiv.) in DMF (0.5 mL) was added. The reaction mixture was stirred in a closed vial for 2 h at 95 °C. After cooling to room temperature water (5 mL) and EtOAc (5 mL) were added, and the aqueous phase was extracted with EtOAc (3x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 6:1) dienone **77** was obtained as a colorless solid (65 mg, 301 µmol, 73% yield).

R_f = 0.4 (pentane/ethyl acetate = 3:1), UV-active, vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.27 (s, 1H), 6.09 (s, 1H), 5.52 (s, 1H), 5.45 (s, 1H), 2.05 – 1.92 (m, 3H), 1.90 – 1.85 (m, 2H), 1.83 – 1.72 (m, 2H), 1.70 – 1.63 (m, 1H), 1.59 (ddd, *J* = 12.1, 5.8, 0.8 Hz, 1H), 1.35 (s, 3H), 1.32 – 1.18 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 196.0, 156.7, 151.0, 119.0*, 82.5, 67.5, 60.0, 45.3, 39.9, 39.4, 39.0, 26.9, 23.5; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{14}H_{18}NaO_2$, 241.1199; found: 241.1202**; $[\alpha]_D^{22}$** = –66.6° (c = 1.10, $CHCl_3$); **IR**: ṽ = 3478, 2949, 2865, 1704, 1630, 1456, 1061, 938 cm^{-1}.

*Signal appears as singlet with double intensity.
Crystals suitable for crystal structure analysis were grown by vapor diffusion technique from Et_2O/pentane.

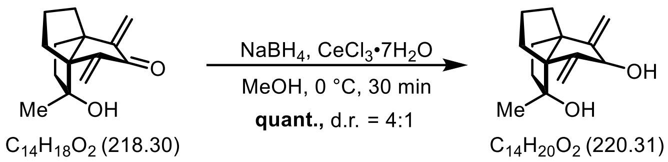
(1*R*,3a*S*,6a*R*)-1-methyl-4,6-dimethylene-5-oxohexahydro-3a,6a-propanopentalen-1-yl 2,2,2-trifluoroacetate 137



A solution of ketone **135** (30.0 mg, 154 µmol, 1 equiv.) in THF (1.5 mL) was treated with LiHMDS (1 M in THF, 925 µL, 925 µmol, 6 equiv.) at 0 °C and warmed to room temperature over 20 min. The reaction mixture war treated with 2,2,2-trifluoroethyl trifluoroacetate (182 mg, 927 µmol, 6 equiv.). The reaction mixture was stirred for 60 min, quenched with saturated aqueous NH_4Cl-solution (2.5 mL) and ethyl acetate (5 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was redissolved in benzene (8 mL) and treated with K_2CO_3 (66 mg, 479 µmol, 3.1 equiv.), 18-crown-6 (10 mg, 39 µmol, 25 mol%) and paraformaldehyde (162 mg, 5.41 mmol, 35 equiv.) at room temperature. The reaction mixture was refluxed for 18 h, quenched with saturated aqueous NH_4Cl-solution (8 mL) and ethyl acetate (15 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 20:1) ester **137** (17 mg, 91 µmol, 59%) was obtained as a yellow oil.

R_f = 0.7 (pentane/ethyl acetate = 10:1), UV-active, vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.28 (s, 1H), 6.14 (s, 1H), 5.51 (s, 1H), 5.45 (s, 1H), 2.72 (dd, *J* = 14.5, 6.2 Hz, 1H), 2.09 (dd, *J* = 12.9, 7.6 Hz, 1H), 2.06 – 1.98 (m, 2H), 1.96 (ddt, *J* = 12.4, 5.8, 1.9 Hz, 1H), 1.82 (td, *J* = 12.3, 6.1 Hz, 1H), 1.78 (dd, *J* = 13.0, 6.6 Hz, 1H), 1.75 (s, 3H), 1.72 (dddt, *J* = 12.1, 6.0, 4.2, 2.1 Hz, 1H), 1.65 (td, *J* = 12.0, 6.1 Hz, 1H), 1.41 – 1.33 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 194.8, 155.8 (q, *J* = 41.9 Hz), 155.7, 149.2, 119.7, 119.2, 114.3 (q, *J* = 287.1 Hz), 99.8, 67.2, 59.3, 45.4, 39.1, 38.5, 35.2, 26.4, 17.7; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –75.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{17}F_3NaO_3$, 337.1022; found: 337.1009; **IR**: ṽ = 2954, 2869, 1778, 1712, 1634, 1370, 1220, 1163 cm^{-1}.

(1R,3aR,6aR)-1-methyl-4,6-dimethylenetetrahydro-1H,4H-3a,6a-propanopentalene-1,5-diol 140

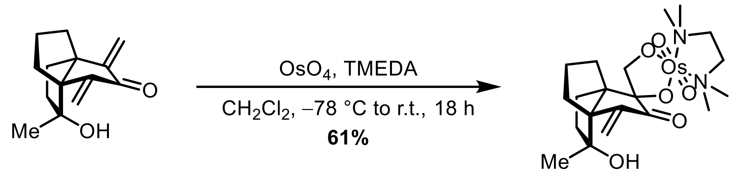


A solution of dienone **77** (5.0 mg, 23 µmol, 1 equiv.) and $CeCl_3$•7 H_2O (47 mg, 126 µmol, 5.5 equiv.) in MeOH (1.0 mL) was treated with $NaBH_4$ (5.2 mg, 137 µmol, 6 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and saturated aqueous NH_4Cl-solution (1 mL) and dichloromethane (1 mL) were added. The phases were separated and the aqueous phase was extracted with dichloromethane (2x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 3:1) bisallylic alcohol **140** (5.0 mg, 23 µmol, quant., d.r. = 4:1, inseparable mixture) was obtained as a colorless oil.

R_f = 0.4 (pentane/ethyl acetate = 3:2), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.43 – 5.41 (m, 1H),* 5.32 (d, *J* = 2.6 Hz, 1H), 5.23 – 5.22 (m, 1H),* 5.21 – 5.18 (m, 1H),* 5.11 (d, *J* = 2.7 Hz, 1H), 5.08 (d, *J* = 1.5 Hz, 1H),* 5.07 – 5.07 (m, 1H), 5.02 (d, *J* = 3.0 Hz, 1H), 4.65 – 4.64 (m, 1H), 2.03 (tt, *J* = 12.5, 6.2 Hz, 2H), 1.91 – 1.88 (m, 1H), 1.85 (td, *J* = 12.8, 6.8 Hz, 1H), 1.54 – 1.37 (m, 3H), 1.35 (s, 3H),* 1.29 (s, 3H), 1.23 – 1.15 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 162.3,* 160.8, 156.9, 156.4,* 111.8,* 109.3,* 105.5, 103.8, 82.5,* 82.1, 81.1,* 77.5, 72.4,* 69.0, 64.9,* 61.4, 43.7,* 41.5, 40.8,* 39.9,* 39.3, 38.7,* 38.2, 37.6, 26.7,* 26.4, 23.7, 23.5*; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{20}NaO_2$, 243.1356; found: 243.1351; **IR**: ṽ = 3030, 2952, 2872, 1456, 1063 cm^{-1}.

*Signals unambiguously assigned to the major stereoisomer.

Osmate ester 144



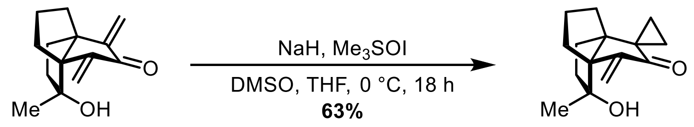
$C_{14}H_{18}O_2$ (218.30) $C_{20}H_{34}N_2O_6Os$ (588.73)

A solution of OsO_4 (24.5 mg, 96 µmol, 1.05 equiv.) in dichloromethane (7 mL) was treated with a solution of TMEDA (14.5 µL; 11.2 mg, 96 µmol, 1.05 equiv.) in dichloromethane (1 mL) at –78 °C. The reaction was stirred for 10 min at –78 °C before a solution of dienone **77** (20.0 mg, 92 µmol, 1 equiv.) in dichloromethane (1 mL) was added. The reaction mixture was warmed to r.t. overnight and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, dichloromethane/methanol = 10:1) osmate ester **144** (33 mg, 56 µmol, 61%) was obtained as a colorless oil.

R_f = 0.5 (CH_2Cl_2/MeOH = 10:1), UV-active, vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.19 (d, *J* = 0.8 Hz, 1H), 6.06 (d, *J* = 1.3 Hz, 1H), 5.52 (d, *J* = 0.8 Hz, 1H), 4.56 (d, *J* = 11.0 Hz, 1H), 4.40 (d, *J* = 11.0 Hz, 1H), 3.16 – 3.09 (m, 2H), 3.08 – 3.02 (m, 2H), 2.94 (s, 3H), 2.93 (s, 3H), 2.84 (s, 3H), 2.79 (s, 3H), 2.51 (ddd, *J* = 13.6, 12.2, 8.4 Hz, 1H), 2.00 (td, *J* = 12.4, 9.6 Hz, 1H), 1.95 (dt, *J* = 13.0, 7.3 Hz, 1H), 1.83 – 1.71 (m, 4H), 1.67 (dt, *J* = 13.7, 6.9 Hz, 1H), 1.54 (dt, *J* = 13.0, 6.8 Hz, 1H), 1.42 (d, *J* = 1.2 Hz, 3H), 1.29 (dd, *J* = 13.7, 9.5 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 202.7, 150.9, 120.1, 93.6, 81.8, 81.6, 68.1, 65.3, 64.0, 61.5, 52.7, 52.6, 52.6, 51.9, 42.5, 41.0, 40.2, 28.2, 26.6, 22.9; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{20}H_{35}N_2O_6Os$, 591.2105; found: 591.2092; $[M + Na]^+$ calcd for $C_{20}H_{34}N_2NaO_6Os$, 613.1924; found: 613.1922.

No IR spectrum was recorded.

(3a*R*,4*R*,6a*S*)-4-hydroxy-4-methyl-3-methylenetetrahydro-2*H*-spiro[3a,6a-propanopentalene-1,1'-cyclopropan]-2-one 150

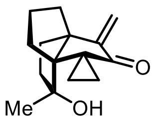


$C_{14}H_{18}O_2$ (218.30) $C_{15}H_{20}O_2$ (232.32)

A solution of trimethylsulfoxonium iodide (33.6 mg, 152 µmol, 1.05 equiv.) in DMSO (1.00 mL) was treated with NaH (60 wt% dispersion in mineral oil, 6.1 mg, 152 µmol, 1.05 equiv.) at room temperature and the resulting mixture was stirred for 60 min until a clear solution was formed. THF (1.00 mL) was added and the solution was cooled to 0 °C. Dienone **77** (31.7 mg, 145 µmol, 1 equiv.) was added as a solid and the reaction mixture was stirred for 18 h at 0 °C. Water (2 mL) and EtOAc (2 mL) were added and the aqueous phase was extracted with EtOAc (3x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 8:1) cyclopropanated enone **150** was obtained as a colorless oil (21.2 mg, 91 µmol, 63% yield).

R_f = 0.4 (pentane/ethyl acetate = 4:1), UV-active, vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.12 (d, *J* = 0.9 Hz, 1H), 5.36 (d, *J* = 0.9 Hz, 1H), 1.93 (td, *J* = 11.9, 6.8 Hz, 1H), 1.90 – 1.85 (m, 2H), 1.88 – 1.78 (m, 1H), 1.74 – 1.70 (m, 1H), 1.69 – 1.64 (m, 2H), 1.43 (dd, *J* = 12.2, 6.4 Hz, 1H), 1.38 (s, 3H), 1.36 – 1.32 (m, 2H), 1.28 – 1.23 (m, 2H), 1.12 (ddd, *J* = 9.6, 7.3, 3.3 Hz, 1H), 1.06 (ddd, *J* = 9.6, 7.2, 3.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 208.8, 150.6, 116.2, 82.1, 68.9, 57.6, 41.3, 40.7, 40.4, 39.1, 36.8, 26.53, 23.6, 20.8, 19.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{15}H_{21}O_2$, 233.1537; found: 233.1538; $[M + Na]^+$ calcd for $C_{15}H_{20}NaO_2$, 255.1356; found: 255.1362; $[M + K]^+$ calcd for $C_{15}H_{20}KO_2$, 271.1095; found: 271.1136; **$[\alpha]_D^{22}$** = –12.1° (c = 0.50, $CHCl_3$); **IR**: $\tilde{\nu}$ = 3406, 2949, 2858, 1695, 1631, 1456, 1375, 1064 cm^{-1}.

(3a*S*,6*R*,6a*R*)-6-hydroxy-6-methyl-3-methylenetetrahydro-2*H*-spiro[3a,6a-propanopentalene-1,1'-cyclopropan]-2-one 151

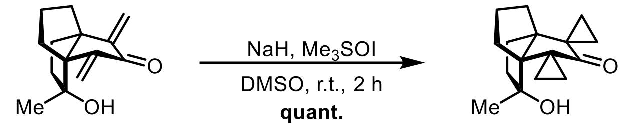


$C_{15}H_{20}O_2$ (232.32)

Cyclopropyl enone **151** was obtained as the minor product of the Corey-Chaykovsky cyclopropanation, and was separable from the main product by column chromatography (up to 30% yield).

R$_f$ = 0.45 (pentane/ethyl acetate = 4:1), UV active, vanillin; **^{1}H NMR** (700 MHz, Chloroform-d) δ 5.91 (s, 1H), 5.27 (s, 1H), 2.03 – 1.99 (m, 3H), 1.91 – 1.88 (m, 1H), 1.83 – 1.79 (m, 1H), 1.70 – 1.66 (m, 1H), 1.61 (ddd, *J* = 10.4, 7.1, 3.4 Hz, 1H), 1.51 (dq, *J* = 9.6, 3.5 Hz, 1H), 1.46 – 1.43 (m, 1H), 1.40 (dd, *J* = 7.0, 5.5 Hz, 1H), 1.36 – 1.33 (m, 2H), 1.28 (q, *J* = 3.1 Hz, 1H), 1.21 (s, 3H), 1.06 – 1.02 (m, 1H), 1.01 – 0.99 (m, 1H), 0.90 – 0.87 (m, 1H), 0.85 – 0.83 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 207.5, 156.5, 115.8, 82.5, 63.8, 61.8, 44.9, 39.9, 34.5, 33.6, 26.4, 24.1, 19.4, 13.0, 11.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{20}NaO_2$, 255.1356; found: 255.1364; **IR**: ṽ = 3503, 2948, 2868, 1703, 1456, 1332, 1060 cm^{-1}.

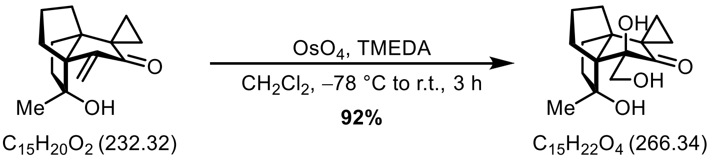
Bis-cyclopropane 149



A solution of sodium hydride (3.8 mg, 96 µmol, 2 equiv.) in DMSO (0.32 mL) was treated with trimethylsulfoxonium iodide (21.2 mg, 96 µmol, 2 equiv.) at room temperature. The mixture was stirred at room temperature for 90 min to form a colorless solution. Dienone **77** (10 mg, 48 µmol, 1 equiv.) was added at room temperature and the reaction mixture was stirred for 2 h. Water (1 mL) and ethyl acetate (1 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 7:1) bis-cyclopropyl ketone **149** was obtained as a colorless solid (10.6 mg, 48 µmol, quant.).

R$_f$ = 0.4 (pentane/ethyl acetate = 4:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 1.94 (td, *J* = 12.2, 6.8 Hz, 1H), 1.87 (td, *J* = 12.7, 6.8 Hz, 1H), 1.79 (q, *J* = 6.7 Hz, 1H), 1.75 (ddt, *J* = 12.7, 6.2, 1.9 Hz, 1H), 1.73 – 1.63 (m, 2H), 1.52 (ddd, *J* = 9.1, 8.1, 3.5 Hz, 1H), 1.47 – 1.42 (m, 2H), 1.38 (ddt, *J* = 12.8, 4.9, 1.5 Hz, 1H), 1.36 – 1.32 (m, 1H), 1.31 – 1.28 (m, 2H), 1.23 (s, 3H), 1.22 – 1.19 (m, 1H), 1.08 – 1.03 (m, 1H), 1.02 – 0.97 (m, 2H), 0.86 (dd, *J* = 9.0, 7.9 Hz, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 219.3, 82.6, 64.7, 59.1, 40.4, 40.1, 39.7, 37.4, 34.8, 32.7, 26.1, 24.3, 20.1, 18.1, 16.8, 11.4; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{16}H_{22}NaO_2$, 269.1512; found: 269.1217; [M + Na]$^+$ calcd for $C_{16}H_{22}NaO_2$, 269.1512; found: 269.1517; [M + K]$^+$ calcd for $C_{16}H_{22}KO_2$, 285.1252; found: 285.1217; **IR**: ṽ = 3502, 2948, 2867, 1705, 1455, 1334, 1060 cm^{-1}.

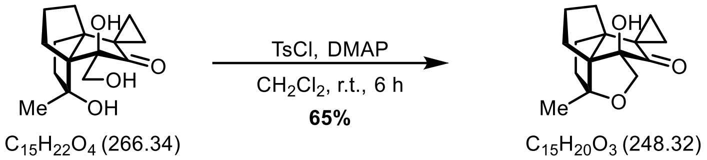
(3'R,3a'S,4'R,6a'S)-3',4'-dihydroxy-3'-(hydroxymethyl)-4'-methyldihydro-4'H-spiro[cyclopropane-1,1'-[3a,6a]propanopentalen]-2'(3'H)-one 155



A solution of OsO_4 (13 mg, 51 µmol, 1.05 equiv.) in dichloromethane (3 mL) was treated with a solution of TMEDA (77 µL, 5.9 mg, 51 µmol, 1.05 equiv.) in dichloromethane (0.5 mL) at –78 °C. After 10 min at –78 °C a solution of enone **150** (11.3 mg, 49 µmol, 1 equiv.) in dichloromethane (1.5 mL) was added and the reaction mixture was warmed to room temperature over 3 h. Ethylendiamine (16 µL, 14.7 mg, 245 µmol, 5 equiv.) was added and the reaction mixture was stirred at room temperature overnight. Water (5 mL) and dichloromethane (5 mL) were added, the phases were separated and the aqueous phase was extracted with dichloromethane (2x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 1:1) triol **155** (12 mg, 45 µmol, 92%, single diastereomer) was obtained as a colorless oil.

R_f = 0.6 (pentane/ethyl acetate = 1:2), vanillin; **^{1}H NMR** (400 MHz, CDCl3) δ 4.56 (d, J = 11.4 Hz, 1H), 3.60 (d, J = 11.3 Hz, 1H), 2.40 (dt, J = 13.9, 9.0 Hz, 1H), 2.00 – 1.86 (m, 4H), 1.70 – 1.56 (m, 3H), 1.48 (dd, *J* = 10.6, 6.5 Hz, 1H), 1.34 (s, 3H), 1.33 – 1.28 (m, 3H), 1.10 (ddd, *J* = 10.4, 5.1, 2.9 Hz, 1H), 1.07 – 1.01 (m, 2H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 221.0, 84.8, 78.1, 68.0, 64.2, 61.2, 44.0, 41.7, 39.3, 36.3, 27.3, 27.1, 24.7, 21.8, 14.9; **ESI-TOF** (*m/z*): [M + H]$^+$ calcd for $C_{16}H_{23}O_2$, 247.1693; found: 247.1681; [M + Na]$^+$ calcd for $C_{15}H_{22}NaO_4$, 289.1411; found: 289.1414; **IR**: ṽ = 3425, 2942, 2856, 2812, 1760, 1456, 1068 cm^{-1}.

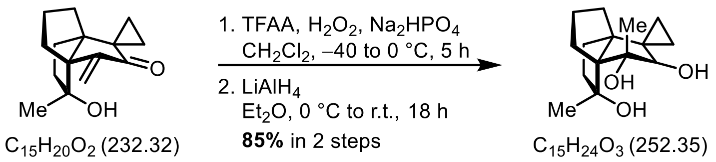
(1'R,3a'R,5a'S,8a'R)-1'-hydroxy-3a'-methylhexahydro-5'H,6'H-spiro[cyclopropane-1,9'-[1,5a]ethanopentaleno[1,6a-b]furan]-10'-one 154



A solution of triol **155** (4.0 mg, 15 µmol, 1 equiv.) in dichloromethane (0.15 mL) was treated with tosyl chloride (5.7 mg, 30 µmol, 2 equiv.) and DMAP (4.6 mg, 38 µmol, 2.5 equiv.) at room temperature. The reaction mixture was stirred for 6 h at room temperature. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1) to give furan **154** (2.4 mg, 10 µmol, 65%) as a colorless oil.

R_f = 0.8 (pentane/ethyl acetate = 1:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 4.09 (d, *J* = 10.1 Hz, 1H), 3.87 (d, *J* = 10.1 Hz, 1H), 2.84 (s, 1H), 2.25 – 2.15 (m, 1H), 2.05 – 1.96 (m, 1H), 1.82 – 1.73 (m, 2H), 1.74 – 1.63 (m, 1H), 1.66 – 1.56 (m, 1H), 1.44 – 1.40 (m, 2H), 1.39 – 1.33 (m, 1H), 1.33 (s, 3H), 1.32 – 1.23 (m, 2H), 1.22 (ddd, *J* = 10.3, 7.2, 3.5 Hz, 1H), 1.14 (ddd, *J* = 9.4, 7.6, 3.6 Hz, 1H), 1.08 (ddd, *J* = 9.6, 7.3, 3.7 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 221.2, 95.2, 87.7, 78.9, 72.6, 58.7, 40.3, 38.7, 37.7, 35.1, 28.9, 27.0, 21.6, 19.2, 16.9; **ESI-TOF** (*m/z*): [M + K]$^+$ calcd for $C_{15}H_{20}KO_3$, 287.1045; found: 289.1047; **IR**: ṽ = 3426, 2951, 2927, 2856, 1724, 1456, 1067,1041 cm^{-1}.

(3*S*,3a*S*,4*R*,6a*R*)-3,4-dimethyltetrahydro-2*H*-spiro[3a,6a-propanopentalene-1,1'-cyclopropane]-2,3,4-triol 158

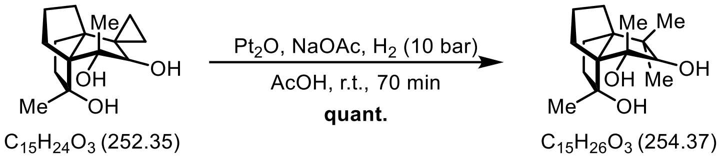


To a mixture of H_2O_2 (60 wt% in water, 122 mg, 102 µL, 2.15 mmol) in dichloromethane (0.5 mL) was slowly added trifluoracetic anhydride (1.07 g, 0.72 mL, 5.11 mmol) at 0 °C. The resulting solution was warmed to r.t. over 1 h. In a second flask a mixture of the enone **150** (19.0 mg, 82 µmol, 1 equiv.) and Na_2HPO_4 (58.1 mg, 410 µmol, 5 equiv.) in dichloromethane (8.2 mL) was cooled to –40 °C. A solution of the prepared oxidant (213 µL) was added in one portion and the reaction mixture was warmed to 0 °C over 5 h. Water (8 mL) and dichloromethane (8 mL) were added and the aqueous phase was extracted with dichloromethane (3x 8 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The obtained crude product was redissolved in diethyl ether (9.5 mL) and $LiAlH_4$ (32 mg, 820 µmol, 10 equiv.) was added in one portion at 0 °C. The reaction mixture was warmed to room temperature and after 18 h slowly quenched with cold saturated NH_4Cl-solution (15 mL). The aqueous phase was extracted with EtOAc (3x 10 mL), the combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 1:1) triol **158** was obtained as a colorless oil (17.5 mg, 70 µmol, 85% in 2 steps, single diastereomer).

R_f = 0.5 (pentane/ethyl acetate = 1:1), vanillin; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.99 (s_{br}, 1H), 3.30 (s, 1H), 3.22 (s_{br}, 1H), 1.84 – 1.80 (m, 1H), 1.78 – 1.71 (m, 2H), 1.72 – 1.62 (m, 2H), 1.52 (ddt, *J* = 13.1, 10.4, 5.3 Hz, 2H), 1.47 – 1.40 (m, 1H), 1.35 (s, 3H), 1.33 (s, 3H), 1.25 – 1.17 (m, 2H), 1.16 – 1.09 (m, 1H), 0.89 – 0.78 (m, 1H), 0.64 – 0.54 (m, 1H), 0.44 – 0.38 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 86.1, 85.5, 83.9, 69.0, 60.8, 41.0, 38.2, 35.1, 34.4, 30.3, 27.4, 24.3, 23.5, 9.9, 5.2; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{24}NaO_3$, 275.1618; found: 275.1630; **$[\alpha]_D^{23}$** = +23.6° (c = 0.42, $CHCl_3$); **IR**: $\tilde{v}$ = 3328, 2959, 2872, 1456, 1373, 1297, 1053 cm^{-1}.

(1*S*,3a*R*,6*R*,6a*S*)-1,3,3,6-tetramethylhexahydro-3a,6a-propanopentalene-1,2,6-triol

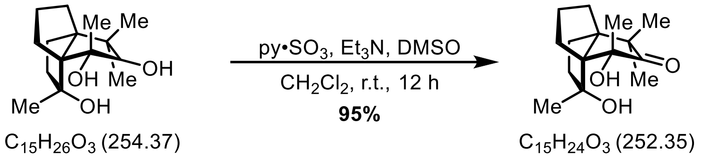
159



A mixture of cyclopropane **158** (8.1 mg, 32 µmol, 1 equiv.), NaOAc (8.0 mg, 97 µmol, 6 equiv.) and PtO_2 (24.4 mg, 107 µmol, 6.6 equiv.) in AcOH (0.81 mL) was stirred under 10 bar H_2-pressure for 70 min. The mixture was filtered over Celite® and quenched with saturated aqueous $NaHCO_3$-solution (5 mL). The aqueous phase was extracted with dichloromethane (3x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give triol **159** as a colorless oil (8.1 mg, 32 µmol, quant.), which was used without further purification. Analytically pure samples were obtained after column chromatography (silica gel, pentane/ethyl acetate = 4:1).

R_f = 0.5 (pentane/ethyl acetate = 1:1), vanillin; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.33 (s_{br}, 1H), 3.29 (s, 1H), 2.53 (s_{br}, 1H), 2.12 (dt, *J* = 13.0, 7.2 Hz, 1H), 1.95 (dt, *J* = 13.2, 6.5 Hz, 1H), 1.86 – 1.77 (m, 2H), 1.64 – 1.59 (m, 3H), 1.54 (dt, *J* = 12.6, 6.1 Hz, 1H), 1.38 (s, 3H), 1.35 – 1.32 (m, 1H), 1.29 (s, 3H), 1.28 – 1.25 (m, 1H), 1.11 (s, 3H), 1.07 (dt, *J* = 13.1, 6.6 Hz, 1H), 1.02 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 86.8, 85.5, 83.1, 68.4, 64.5, 44.2, 43.2, 39.0, 36.4, 33.1, 27.2, 27.0, 25.8, 24.9, 20.1; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{26}NaO_3$, 277.1775; found: 277.1778; **$[\alpha]_D^{22}$** = +34.9° (c = 0.35, $CHCl_3$); **IR**: $\tilde{v}$ = 3288, 2957, 2929, 2870, 1457, 1376, 1049 cm^{-1}.

reported structure of dichrocephone A (1)



A solution of triol **159** (2.5 mg, 10 µmol, 1 equiv.) in dichloromethane (55 µL), Et_3N (41 µL) and DMSO (41 µL) was treated with sulfur trioxide pyridine complex (28.2 mg, 177 µmol, 18 equiv.) at room temperature. The reaction mixture was stirred for 12 h at room temperature. Water (1 mL) and dichloromethane (1 mL) were added. The phases were separated and the aqueous phase was extracted with dichloromethane (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 5:1) ketone **1** was obtained as a colorless solid (2.4 mg, 9.5 µmol, 95% yield).

R_f = 0.5 (pentane/ethyl acetate = 2:1), vanillin; **^{1}H NMR** (700 MHz, CD_3COCD_3) δ 4.56 (s, 1H), 3.94 (s, 1H), 2.38 (ddd, *J* = 13.1, 11.6, 8.1 Hz, 1H), 2.07 – 1.96 (m, 2H), 1.81 – 1.73 (m, 2H), 1.73 – 1.60 (m, 1H), 1.59 (ddd, *J* = 13.1, 8.1, 1.4 Hz, 1H), 1.53 (ddd, *J* = 14.9, 8.8, 6.2 Hz, 1H), 1.48 (dt, *J* = 13.0, 6.5 Hz, 1H), 1.41 (s, 3H), 1.26 – 1.23 (m, 1H), 1.23 (s, 3H), 1.18 (s, 3H), 1.06 (s, 3H); **^{13}C NMR** (176 MHz, CD_3COCD_3) δ 225.8, 86.4, 82.0, 68.2, 63.5, 46.3, 40.9, 39.2, 35.7, 30.5, 27.9, 26.6, 25.5, 25.3, 25.2; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{24}NaO_3$, 275.1618; found: 275.1616; **$[\alpha]_D^{23}$** = +42.2° (c = 0.26, $CHCl_3$); **IR**: ṽ = 3462, 2952, 2925, 2854, 1735, 1457, 1376, 1022 cm^{-1}.

Crystals suitable for crystal structure analysis were grown by slow evaporation of Et_2O.

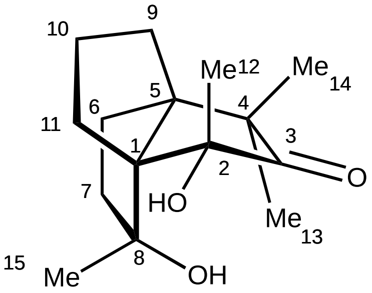
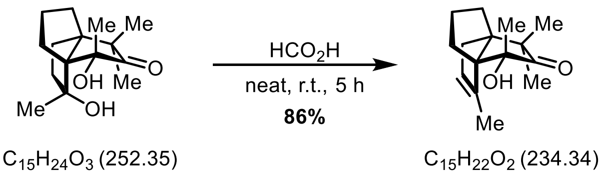


Table 16: Full comparison of NMR data of natural occurring dichrocephone A and the synthetic diol **1**. All data was obtained in CD_3COCD_3.

No.	**^{13}C NMR Isolation** 150 MHz [ppm]	**^{13}C NMR Synthetic** 176 MHz [ppm]	Δ [ppm]
1	70.5	68.3	2.2
2	80.2	82.0	1.8
3	222.7	225.8	3.1
4	48.3	46.4	1.9
5	65.6	63.5	2.1
6	33.8	35.8	2.0
7	44.5	41.0	3.5
8	83.4	86.5	3.1
9	31.9	30.3	1.6
10	28.4	27.9	0.5
11	38.6	39.2	0.6
12	20.0	25.6	5.6
13	24.4	25.4	1.0
14	27.1	26.7	0.4
15	26.4	25.3	1.1

No.	**^{1}H NMR Isolation** 600 MHz [ppm]	**^{1}H NMR Synthetic** 700 MHz [ppm]	Δ [ppm]
6	1.64 m, 2.17 m	1.24 m, 2.38 ddd	0.40/0.21
7	1.98 m, 2.21 m	1.59 ddd, 1.77 m	0.39/0.44
9	0.98 m, 2.03 m	1.53 ddd, 2.01 m	0.55/0.02
10	1.39 m, 1.91 m	1.66 m, 1.77 m	0.27/0.14
11	1.90 m, 2.02 m	1.49 dt, 2.01 m	0.41/0.01
12	1.27 s	1.23 s	0.04
13	0.99 s	1.06 s	0.07
14	1.18 s	1.18 s	0.00
15	1.52 s	1.41 s	0.09
2-OH	4.08 s	4.56 s	0.48
8-OH	3.21 s	3.94 s	0.73

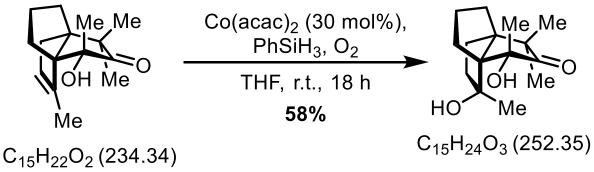
(1*R*,3a*S*,6a*R*)-1-hydroxy-1,3,3,6-tetramethyl-3,4-dihydro-3a,6a-propanopentalen-2(1*H*)-one 163



Diol **1** (2.5 mg, 10 µmol, 1 equiv.) was dissolved in formic acid (0.25 mL). The mixture was stirred for 5 h at room temperature and then slowly quenched with saturated aqueous $NaHCO_3$-solution (5 mL). The aqueous phase was extracted with dichloromethane (3x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 25:1) olefin **163** (2.0 mg, 8.6 µmol, 86%) was obtained as a colorless oil.

R_f = 0.3 (pentane/ethyl acetate = 20:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.58 (s, 1H), 2.55 (dt, *J* = 16.7, 4.2 Hz, 1H), 2.13 – 2.04 (m, 2H), 1.98 (dd, *J* = 13.0, 6.8 Hz, 1H), 1.95 – 1.84 (m, 1H), 1.79 – 1.72 (m, 3H), 1.55 – 1.44 (m, 2H), 1.38 (ddd, *J* = 13.4, 11.0, 8.1 Hz, 1H), 1.31 (s, 3H), 1.33 – 1.26 (m, 1H), 1.19 (s, 3H), 1.05 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 222.5, 140.2, 128.9, 76.9, 71.2, 61.7, 48.3, 42.7, 37.4, 32.6, 25.7, 25.25, 24.4, 21.6, 14.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{22}NaO_2$, 257.1512; found: 257.1542; **$[\alpha]_D^{23}$** = -17.1° (c = 0.24, $CHCl_3$); **IR**: ṽ = 3455, 2953, 2928, 2861, 1736, 1457, 1376, 1024 cm^{-1}.

Revised structure of dichrocephone A (160)



A solution of olefin **163** (4 mg, 17 µmol, 1 equiv.) in THF (0.36 mL) was treated with Co(acac)$_2$ (1.3 mg, 5.1 µmol, 30 mol%) and PhSiH$_3$ (36.9 mg, 42 µL, 341 µmol, 20 equiv.) at room temperature. The flask was purged three times with oxygen and then closed. After 18 h at room temperature the reaction was quenched with water (2 mL) and dichloromethane (2 mL). The phases were separated and the aqueous phase was extracted with dichloromethane (2x 2 mL). The combined organic phases were dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 5:1) dichrocephone A (**160**) was obtained as a colorless oil (2.5 mg, 10 µmol, 58% yield).

R$_f$ = 0.5 (pentane/ethyl acetate = 5:1), vanillin; **^{1}H NMR** (700 MHz, CD$_3$COCD$_3$) δ 4.10 (s, 1H), 3.24 (s, 1H), 2.22 (td, *J* = 12.2, 5.0 Hz, 1H), 2.17 – 2.12 (m, 1H), 2.04 – 1.92 (m, 3H), 1.95 – 1.86 (m, 2H), 1.63 (ddd, *J* = 12.5, 9.5, 4.9 Hz, 1H), 1.52 (s, 3H), 1.42 – 1.37 (m, 1H), 1.27 (s, 3H), 1.18 (s, 3H), 0.99 (s, 3H), 0.99 – 0.95 (m, 1H); **^{13}C NMR** (176 MHz, CD$_3$COCD$_3$) δ 222.5, 83.4, 80.2, 70.5, 65.6, 48.3, 44.6, 38.6, 33.7, 31.9, 28.4, 27.1, 26.4, 24.4, 20.4; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for C$_{15}$H$_{24}$NaO$_3$, 275.1618; found: 275.1617; **$[\alpha]_D^{26}$** = +59.1° (c = 0.22, MeOH); **IR**: ṽ = 3480, 2956, 2926, 2870, 1727, 1465, 1377, 1073 cm^{-1}.

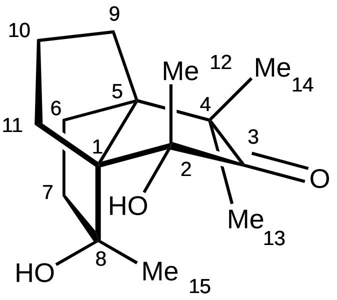
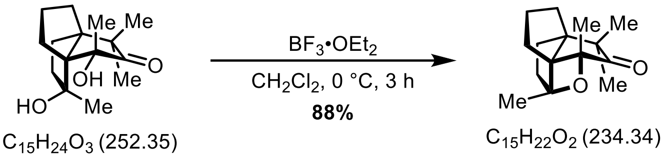


Table 17: Comparison of NMR data of isolated dichrocephone A and the corrected structure **160**. All data was obtained in CD_3COCD_3.

No.	**^{13}C NMR Isolation** 150 MHz [ppm]	**^{13}C NMR Synthetic** 176 MHz [ppm]	Δ [ppm]
1	70.5	70.5	0
2	80.2	80.2	0
3	222.7	222.5	0.2
4	48.3	48.3	0
5	65.6	65.6	0
6	33.8	33.7	0.1
7	44.5	44.6	0.1
8	83.4	83.4	0
9	31.9	31.9	0
10	28.4	28.4	0
11	38.6	38.6	0
12	20.0	20.1	0.1
13	24.4	24.4	0
14	27.1	27.1	0
15	26.4	26.4	0

No.	**^{1}H NMR Isolation** 600 MHz [ppm]	**^{1}H NMR Synthetic** 700 MHz [ppm]	Δ [ppm]
6	1.64 m, 2.17 m	1.63 ddd, 2.15 m	0.01/0.02
7	1.98 m, 2.21 m	1.98 m, 2.22 td	0/0.01
9	0.98 m, 2.03 m	0.97 m, 1.98 m	0.01/0.05
10	1.39 m, 1.91 m	1.39 m, 1.90 m	0/0.01
11	1.90 m, 2.02 m	1.90 m, 1.98 m	0/ 0.04
12	1.27 s	1.27 s	0
13	0.99 s	0.99 s	0
14	1.18 s	1.18 s	0
15	1.52 s	1.52 s	0
2-OH	4.08 s	4.10	0.02
8-OH	3.21 s	3.24	0.03

Dichrocephone B (2)



A solution of dichrocephone A (**160**) (2.2 mg, 9.0 µmol, 1 equiv.) in dichloromethane (50 µL) was treated with $BF_3 \cdot OEt_2$ (2.0 mg, 1.8 µL, 14 µmol, 1.65 equiv.) at 0 °C. After 3 h at 0 °C saturated aqueous $NaHCO_3$-solution (0.5 mL) was added and the aqueous phase was extracted with dichloromethane (3x 0.5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 30:1) dichrocephone B (**2**) was obtained as a colorless oil (1.8 mg, 8.0 µmol, 88%).

R_f = 0.3 (pentane/ethyl acetate = 18:1), vanillin; **^{1}H NMR** (700 MHz, CD_3COCD_3) δ 2.06 – 1.99 (m, 1H), 1.93 – 1.89 (m, 1H), 1.82 – 1.72 (m, 4H), 1.69 (dd, *J* = 13.0, 6.8 Hz, 1H), 1.62 (ddd, *J* = 13.9, 7.1, 0.7 Hz, 1H), 1.57 (ddd, *J* = 13.9, 12.6, 7.0 Hz, 1H), 1.48 (ddd, *J* = 14.2, 9.0, 6.9 Hz, 1H), 1.40 (s, 3H), 1.37 (s, 3H), 1.05 (s, 3H), 0.82 (s, 3H); **^{13}C NMR** (176 MHz, CD_3COCD_3) δ 218.8, 94.4, 84.8, 65.2, 64.4, 54.5, 39.4, 36.9, 32.3, 28.6, 26.8, 23.1, 22.3, 19.2, 18.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{22}NaO_2$, 257.1512; found: 257.1515; **$[\alpha]_D^{23}$** = +7.1° (c = 0.11, MeOH); **IR**: $\tilde{\nu}$ = 2955, 2925, 2854, 1733, 1275, 1261 cm^{-1}.

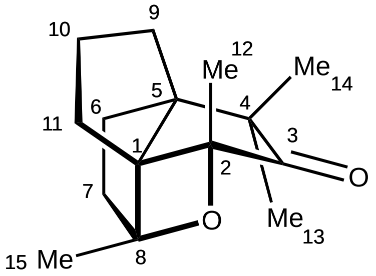
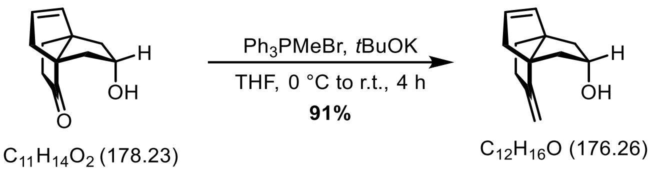


Table 18: Comparison of NMR data of isolated dichrocephone B and synthetic **2**.

No.	**^{13}C NMR Isolation** 150 MHz [ppm]	**^{13}C NMR Synthetic** 176 MHz [ppm]	**Δ** [ppm]
1	65.1	65.2	0.1
2	84.8	84.8	0
3	218.7	218.8	0.1
4	54.5	54.5	0
5	64.3	64.4	0.1
6	36.9	36.9	0
7	39.3	39.4	0.1
8	94.4	94.4	0
9	26.8	26.8	0
10	28.5	28.6	0.1
11	32.2	32.3	0.1
12	19.2	19.2	0
13	18.4	18.5	0.1
14	23.0	23.1	0.1
15	22.3	22.3	0

No.	**^{1}H NMR Isolation** 600 MHz [ppm]	**^{1}H NMR Synthetic** 700 MHz [ppm]	**Δ** [ppm]
6	1.70 m, 1.79 m	1.69 dd, 1.78 m	0.01/0.01
7	1.56 m, 1.61 m	1.57 ddd, 1.62 ddd	0.01/0.01
9	1.75 m, 1.92 m	1.76 m, 1.91 m	0.01/0.01
10	1.78 m	1.76 m	0.02
11	1.50 m, 2.02 m	1.48 ddd, 2.02 m	0.02/0
12	1.37 s	1.37 s	0
13	1.05 s	1.05 s	0
14	0.82 s	0.82 s	0
15	1.40 s	1.40 s	0

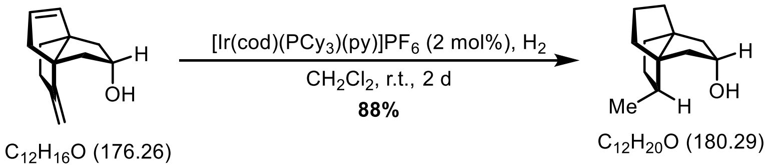
(2S,3aR,6aR)-9-methylene-2,3-dihydro-1H,4H-3a,6a-propanopentalen-2-ol 170



A solution of PPh_3MeBr (200 mg, 562 µmol, 2 equiv.) in THF (2.8 mL) was treated with KO*t*Bu (63 mg, 562 µmol, 2 equiv.) at room temperature and then refluxed in a closed vial for 2 h. The reaction mixture was cooled to room temperature and treated with a solution of ketone **131** (50 mg, 281 µmol, 1 equiv.) in THF (0.4 mL). The reaction mixture was warmed to room temperature over 4 h. Water (5 mL) and ethyl acetate (5 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (2x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 7:1) diene **170** (45 mg, 256 µmol, 91%) was obtained as a colorless solid.

m.p.: 77 °C; **R_f** = 0.7 (pentane/ethyl acetate = 2:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.53 – 5.46 (m, 2H), 4.82 (q, *J* = 1.5 Hz, 1H), 4.77 (q, *J* = 1.5 Hz, 1H), 4.25 – 4.18 (m, 1H), 2.52 (d, *J* = 17.3 Hz, 1H), 2.47 (dddt, *J* = 14.6, 7.3, 5.9, 1.5 Hz, 1H), 2.42 – 2.35 (m, 2H), 2.03 – 2.00 (m, 2H), 1.84 (dd, *J* = 12.6, 7.7 Hz, 1H), 1.75 – 1.66 (m, 2H), 1.63 (dd, *J* = 12.4, 7.6 Hz, 1H), 1.42 (d, *J* = 5.6 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 162.7, 137.5, 128.4, 103.2, 74.8, 67.2, 60.1, 49.2, 49.0, 47.8, 38.4, 34.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{18}NaO$, 201.1250; found: 201.1254; **IR**: ṽ = 3272, 2935, 2858, 1655, 1444, 1354, 1085, 1037, 880 cm^{-1}.

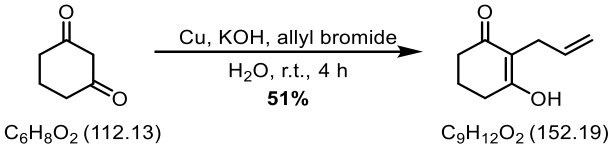
(2*S*,3a*R*,4*S*,6a*R*)-4-methylhexahydro-3a,6a-propanopentalen-2-ol 171



A solution of diene **170** (20 mg, 113 µmol, 1 equiv.) and Crabtree´s catalyst (2.3 mg, 3 µmol, 2 mol%) in degassed dichloromethane (5.7 mL) was stirred under hydrogen atmosphere for 2 d at room temperature. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 14:1). Alcohol **171** (18 mg, 99 µmol, 88%, single diastereomer) was obtained as a colorless oil.

R$_f$ = 0.65 (pentane/ethyl acetate = 5:1), vanillin; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 4.45 (tt, *J* = 4.9, 2.3 Hz, 1H), 2.07 (tt, *J* = 11.7, 6.9 Hz, 1H), 1.84 (dt, *J* = 13.8, 2.3 Hz, 1H), 1.81 (dt, *J* = 13.8, 2.3 Hz, 1H), 1.68 – 1.61 (m, 4H), 1.59 (dd, *J* = 13.7, 5.0 Hz, 1H), 1.57 – 1.53 (m, 1H), 1.46 (dd, *J* = 13.8, 4.9 Hz, 1H), 1.36 (td, *J* = 11.3, 5.8 Hz, 1H), 1.32 – 1.16 (m, 4H), 1.13 (s_{br}, 1H), 0.93 (d, *J* = 6.9 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 77.5, 63.6, 61.2, 50.2, 48.1, 45.1, 42.5, 40.5, 34.9, 33.9, 25.0, 14.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{20}NaO$, 203.1407; found: 203.1415; **IR**: ṽ = 2938, 1663, 1441, 1354, 1085, 1041 cm^{-1}.

2-allyl-3-hydroxycyclohex-2-enone 103

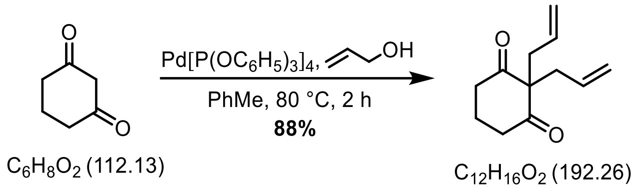


A solution of 1,3-cyclohexanedione (**99**) (5.00 g, 44.6 mmol, 1 equiv.), Cu powder (2.83 g, 44.6 mmol, 1 equiv.) and KOH (2.50 g, 44.6 mmol, 1 equiv.) in water (50 mL) was treated dropwise with allyl bromide (5.4 mL, 7.55 g, 62.4 mmol, 1.4 equiv.) at room temperature. The reaction mixture was stirred for 4 h, filtered over a short pad of Celite® and dichloromethane (50 mL) was added. The phases were separated and the aqueous phase was extracted with dichloromethane (3x 50 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give allylated dione **103** (3.46 g, 22.7 mmol, 51%) as a yellow solid, which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.78 (m, 1H), 5.10 (d, *J* = 17.3, 1H), 5.01 (d, *J* = 10.2 Hz, 1H), 3.05 (d, *J* = 6.4 Hz, 2H), 2.55 (d, *J* = 6.4 Hz, 2H), 2.43 (t, *J* = 6.4 Hz, 2H), 1.95 – 1.90 (m, 2H).

The spectroscopic data agrees with previously published results.[100]

2,2-diallylcyclohexane-1,3-dione 100

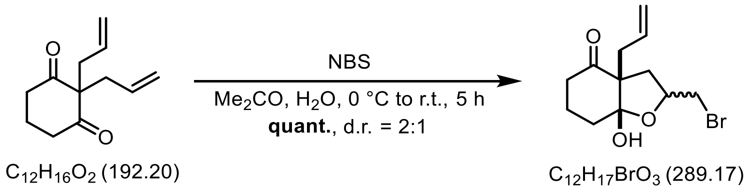


A solution of 1,3-cyclohexanedione (**99**) (280 mg, 2.50 mmol, 1 equiv.) and $Pd[P(OC_6H_5)_3]_4$ (13.9 mg, 10 µmol, 0.4 mol%) in toluene (2.5 mL) was treated with allyl alcohol (0.35 mL, 290 mg, 5.00 mmol, 2 equiv.) at room temperature. The reaction mixture was stirred for 2 h at 80 °C, cooled to room temperature and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 6:1) allylated dione **100** (423 mg, 2.20 mmol, 88%) was obtained as a colorless solid.

R_f = 0.7 (pentane/ethyl acetate = 4:1), $KMnO_4$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.64 – 5.46 (m, 2H), 5.07 – 5.01 (m, 4H), 2.55 (td, *J* = 6.7, 0.8 Hz, 4H), 2.52 (d, *J* = 7.5 Hz, 4H), 1.92 (p, *J* = 6.8 Hz, 2H).

The spectroscopic data agrees with previously published results.[211]

3a-allyl-2-(bromomethyl)-7a-hydroxyhexahydrobenzofuran-4(2*H*)-one (±)-101

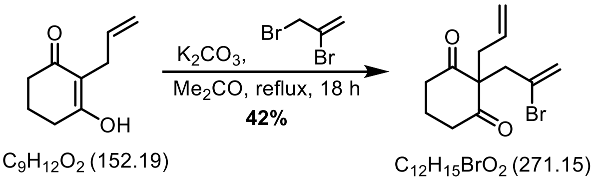


A solution of dione **100** (200 mg, 1.04 mmol, 1 equiv.) in acetone (4.3 mL) and water (6.7 mL) was treated with *N*-bromo succinimide (194 mg, 2.03 mmol, 1.95 equiv.) at 0 °C and warmed to room temperature over 5 h. Water (10 mL) and dichloromethane (10 mL) were added. the phases were separated and the aqueous phase was extracted with dichloromethane (3x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 7:1) the lactol **(±)-101** (300 mg, 1.04 mmol, quant., 2 diastereomers, d.r. = 2:1, inseparable mixture) was obtained as a colorless oil.

R_f = 0.3 (pentane/ethyl acetate = 4:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.55 (dtt, *J* = 17.4, 10.0, 7.4 Hz, 2H), 5.07 – 4.99 (m, 4H), 4.38 (dddd, *J* = 9.4, 7.3, 6.1, 3.4 Hz, 1H), 4.14 (ddt, *J* = 9.1, 6.5, 5.5 Hz, 1H), 3.50 – 3.45 (m, 2H), 3.26 – 3.19 (m, 2H), 2.92 (dd, *J* = 12.3, 6.6 Hz, 1H), 2.73 (dd, *J* = 12.9, 3.5 Hz, 1H), 2.56 – 2.41 (m, 2H), 2.17 – 2.01 (m, 3H), 1.89 – 1.81 (m, 1H), 1.71 (dd, *J* = 12.2, 9.2 Hz, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 210.2, 209.6,* 133.3, 133.2,* 118.3,* 117.98, 107.4, 107.3,* 77.0,* 76.3, 65.0,* 63.6, 38.5, 38.2,* 38.1, 37.6,* 37.2,* 35.0, 34.9, 34.6, 32.9, 32.7,* 20.3,* 20.0; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{17}BrNaO_3$, 311.0254; found: 311.0238; **IR**: ṽ = 3431, 2953, 2918, 1701, 1214, 1078, 1007 cm^{-1}.

*Signals unambiguously assigned to the major stereoisomer.

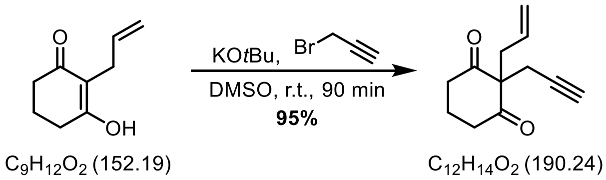
2-allyl-2-(2-bromoallyl)cyclohexane-1,3-dione 104



A solution of allylated dione **103** (200 mg, 1.31 mmol, 1 equiv.) and K_2CO_3 (182 mg, 1.31 mmol, 1 equiv.) in acetone (1.1 mL) was treated with 2,3-dibrom propene (324 mg, 1.38 mmol, 1.05 equiv.) at room temperature. The flask was closed and the reaction mixture was stirred for 18 h at 60 °C, cooled to room temperature and filtered over a short pad of Celite®. The organic phase was washed with saturated aqueous NH_4Cl-solution (3 mL) and water (3 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 10:1) dione **104** (150 mg, 42%) was obtained as a colorless oil.

R$_f$ = 0.3 (pentane/ethyl acetate = 6:1), KMnO$_4$; **^{1}H NMR** (700 MHz, CDCl$_3$) δ 5.56 (s, 1H), 5.55 – 5.49 (m, 1H), 5.45 (s, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.05 (d, *J* = 17.0 Hz, 1H), 3.04 (s, 1H), 2.72 (dt, *J* = 17.5, 5.8 Hz, 2H), 2.54 (ddd, *J* = 15.9, 8.8, 5.6 Hz, 2H), 2.47 (d, *J* = 7.6 Hz, 2H), 2.06 (td, *J* = 9.5, 4.8 Hz, 1H), 2.02 – 1.95 (m, 1H); **^{13}C NMR** (176 MHz, CDCl$_3$) δ 210.2, 131.6, 127.9, 121.9, 120.4, 67.2, 47.6, 43.8, 40.5, 16.6. **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{12}H_{15}BrNaO_2$, 293.0148; found: 293.0142; **IR**: ṽ = 2920, 2850, 1695, 1214, 900, 750 cm^{-1}.

2-allyl-2-(prop-2-yn-1-yl)cyclohexane-1,3-dione 111

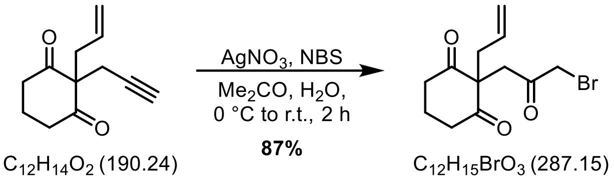


A solution of the allylated dione **103** (55 mg, 361 µmol, 1 equiv.) in DMSO (1 mL) was treated with potassium *tert*-butoxide (41 mg, 361 µmol, 1 equiv.) at room temperature. After 15 min propargyl bromide (80 wt% in toluene, 59 mg, 44 µL, 398 µmol, 1.1 equiv.) was added and the reaction mixture was stirred for 90 min at room temperature. Water (2 mL) and ethyl acetate (2 mL) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (2x 2 mL). The combined organic phases were dried over MgSO4, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane:ethyl acetate = 12:1) the propargylated dione **111** was obtained as a yellow oil (65 mg, 343 µmol, 95%).

R$_f$ = 0.4 (pentane:ethyl acetate = 9:1), KMnO$_4$; **^{1}H NMR** (700 MHz, CDCl$_3$) δ = 5.52 (ddt, *J* = 17.5, 10.1, 7.5, 1H), 5.09 (ddt, *J* = 10.3, 1.8, 0.8, 1H), 5.08 – 5.05 (m, 1H), 2.69 – 2.62 (m, 4H), 2.61 (d, *J* = 2.6, 2H), 2.49 (dt, *J* = 7.5, 1.0, 2H), 2.05 – 1.92 (m, 3H); **^{13}C NMR** (176 MHz, CDCl$_3$) δ 209.2, 131.4, 120.3, 80.6, 70.9, 67.6, 41.6, 39.8, 24.2, 16.7.

The spectroscopic data agrees with previously published results.[96]

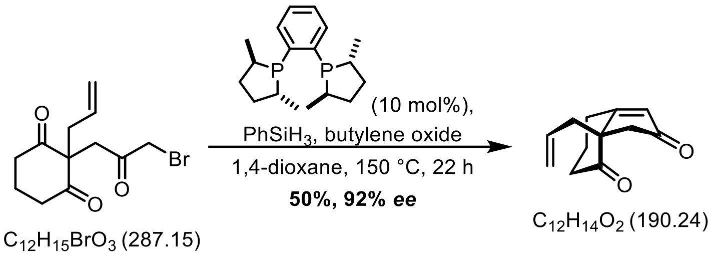
2-Allyl-2-(3-bromo-2-oxopropyl)cyclohexane-1,3-dione 102



A solution of the alkyne **111** (20 mg, 105 µmol, 1 equiv.) and water (5.7 mg, 5.7 µL, 315 µmol, 3 equiv.) in acetone (0.5 mL) was treated with $AgNO_3$ (18 mg, 105 µmol, 1 equiv.) at 0 °C. The reaction mixture was stirred for 5 minutes at 0 °C. N-bromo succinimide (19 mg, 105 µmol, 1 equiv.) was added and the reaction mixture was stirred for 90 min at 0 °C, before the cooling bath was removed. After 30 min the reaction mixture was filtered over Celite® and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane:ethyl acetate = 8:1) triketone **102** was obtained as a yellow oil (26 mg, 91 µmol, 87%).

R_f = 0.4 (pentane:ethyl acetate = 4:1), $KMnO_4$; **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 5.52 (ddt, *J* = 16.8, 10.0, 7.5, 1H), 5.16 (ddt, *J* = 10.1, 1.7, 0.9, 1H), 5.09 (dq, *J* = 16.9, 1.4, 1H), 3.90 (s, 2H), 3.35 (s, 2H), 2.76 – 2.70 (m, 2H), 2.68 – 2.60 (m, 2H), 2.37 (dt, *J* = 7.5, 1.1, 2H), 2.22 – 2.07 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 209.1, 200.4, 130.9, 120.4, 65.1, 44.6, 40.9, 38.5, 33.6, 17.4; **ESI-TOF** (m/z): $[M + Na]^+$ calcd for $C_{12}H_{15}BrNaO_3$ 309.0097; found: 309.0103; **IR**: ṽ = 2955, 2917, 2850, 1715, 1691, 1385, 1322, 1078, 923 cm^{-1}.

(R)-7a-allyl-5,6-dihydro-1*H*-indene-2,7(4*H*,7a*H*)-dione 89

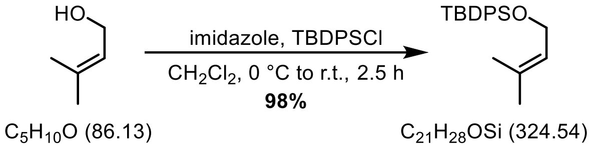


A solution of triketone **102** (27 mg, 100 µmol, 1 equiv.), $PhSiH_3$ (48 mg, 445 µmol, 4.5 equiv.), *rac*-1,2-butylene oxide (14 mg, 198 µmol, 2 equiv.) and (*R*,*R*)-Me-DuPhos (10 mg, 10 µmol, 10 mol%) in 1,4-dioxane (3 mL) was stirred at 150 °C in a sealed vial. After 24 h the reaction mixture was cooled to room temperature and saturated aqueous $NaHCO_3$-solution (3 mL) was added dropwise. Precipitated solids were removed by filtration over a short pad of Celite® and washed with ethyl acetate. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane:ethyl acetate = 3:1) the bicyclic diketone **89** was obtained as a colorless oil (9 mg, 50 µmol, 50%, 92% *ee*).

R_f = 0.4 (pentane/ethyl acetate = 3:2), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ = 5.85 (d, *J* = 1.7, 1H), 5.53 (ddt, *J* = 15.4, 10.8, 7.4, 1H), 5.15 (s, 1H), 5.14 – 5.12 (m, 1H), 3.07 (d, *J* = 18.9, 1H), 2.87 (dt, *J* = 14.3, 2.7, 1H), 2.78 – 2.64 (m, 3H), 2.51 – 2.46 (m, 2H), 2.29 (ddd, *J* = 13.5, 5.8, 3.0, 1H), 2.24 (d, *J* = 19.0, 1H), 1.75 (qt, *J* = 13.5, 4.5, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 208.5, 206.0, 179.9, 130.8, 128.8, 120.3, 41.838, 41.1, 37.6, 26.8, 25.2; **ESI-TOF** (m/z): $[M + Na]^+$ calcd for $C_{12}H_{14}NaO_2$, 213.0886; found: 213.0883; **$[\alpha]_D^{24}$** = –9.64° (c = 0.39, $CHCl_3$); **IR:** ṽ = 2955, 2916, 2850, 1733, 1715, 1464, 1377, 1214, 755 cm^{-1}; **GC** Hydrodex-β-TBDAc; isotherm 145 °C; 1.1 mL/min; Split 50:1; FID 200 °C: t_1 = 52.21 min. (minor), t_2 = 53.41 min. (major).

4.3. To „Synthetic Studies towards Xenicane Diterpenes“

tert-butyl((3-methylbut-2-en-1-yl)oxy)diphenylsilane SI-4

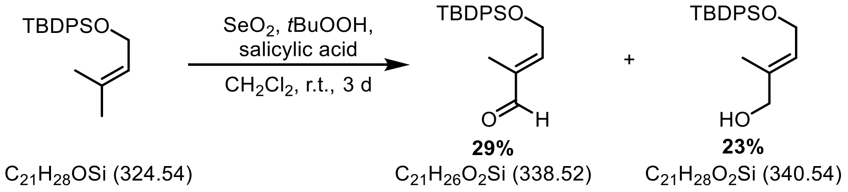


A solution of prenol **205** (25.0 g, 291 mmol, 1 equiv.) in dichloromethane (750 mL) was treated with imidazole (29.5 g, 433 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was treated dropwise with TBDPSCl (83.3 mL, 12.5 g, 319.8 mmol, 1.1 equiv.). After 30 min at 0 °C the reaction mixture was warmed to room temperature and stirred for additional 2 h. The reaction mixture was diluted with dichloromethane (250 mL) and washed with water (125 mL) and brine (125 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Distillation of the crude product (bath temp. 150 °C, bp. 108 °C at $3.5x10^{-3}$ mbar) afforded protected allylic alcohol **SI-4** (92.2 g, 285 mmol, 98%) as a colorless liquid. Smaller quantities were purified by column chromatography (silica gel, pentane/ethyl acetate = 1:0 to 50:1).

R_f = 0.45 (pentane), $KMnO_4$, UV-active; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.05 – 1.11 (m, 9H), 1.49 (s_{br}, 3H), 1.73 (s_{br}, 3H), 4.24 (d, *J* = 6.4 Hz, 2H), 5.42 (t, *J* = 6.4 Hz, 1H), 7.37 – 7.49 (m, 6H), 7.69 – 7.78 (m, 4H).

The spectroscopic data agrees with previously published results.[169]

(*E*)-4-((*tert*-butyldiphenylsilyl)oxy)-2-methylbut-2-enal 203



A solution of SeO_2 (582 mg, 5.25 mmol, 6 mol%), salicylic acid (1.45 g, 10.5 mmol) and *t*BuOOH (70% in H_2O, 48.4 g, 52 mL, 376 mmol, 4.3 equiv.) in dichloromethane (28 mL) were treated with protected allylic alcohol **SI-4** (28.4 g, 87.5 mmol, 1 equiv.) at room temperature and the reaction mixture was stirred for 72 h at room temperature. NaOH-solution (1 M, 2x 50 mL) and brine (1x 50 mL) were added and the phases were separated. The organic phase was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography aldehyde **203** (8.45 g, 25.4 mmol, 29%, R_f = 0.45, pentane/ethyl acetate = 35:1) was obtained as a yellow oil.

R_f = 0.45 (pentane/ethyl acetate = 35:1), $KMnO_4$, UV-active; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.75 – 7.63 (m, 5H), 7.51 – 7.34 (m, 6H), 6.59 (tq, *J* = 5.5, 1.4 Hz, 1H), 4.52 (dq, *J* = 5.4, 1.1 Hz, 2H), 1.58 – 1.51 (m, 3H), 1.07 (s, 9H).

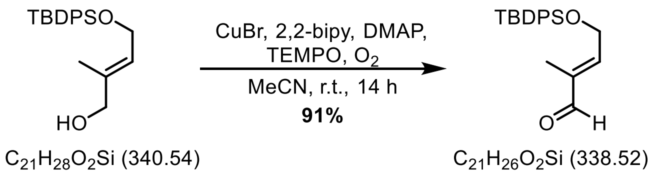
The spectroscopic data agrees with previously published results.[169]

Additionally, the corresponding alcohol **SI-8** (6.76 g, 20.1 mmol, 23%) was obtained as a yellow oil.

R_f = 0.65 (pentane/ethyl acetate = 3:1), $KMnO_4$, UV-active; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 – 7.66 (m, 4H), 7.44 – 7.36 (m, 6H), 5.62 (tq, *J* = 6.2, 1.4 Hz, 1H), 4.28 (dd, *J* = 6.2, 1.0 Hz, 2H), 4.02 – 3.85 (m, 2H), 1.57 – 1.40 (m, 3H), 1.05 (s, 9H).

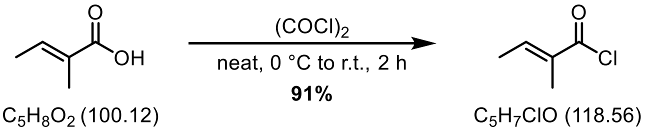
The spectroscopic data agrees witch previously published results.[212]

TEMPO oxidation to 203



A solution of allylic alcohol **ZBYR** (8.5 g, 25.0 mmol, 1 equiv.) in acetonitrile (33 mL) was at room temperature treated with DMAP (122 mg, 1.00 mmol, 4 mol%), 2,2'-bipyridine (78 mg, 500 µmol, 2 mol%), CuBr (72 mg, 500 µmol, 2 mol%) and TEMPO (78 mg, 500 µmol, 2 mol%). Air in the reaction flaks was exchanged for an O_2-atmosphere and stirred for 14 h at room temperature. Brine (30 ml) and ethyl acetate (30 ml) were added, the phases were separated and the aqueous phase was extracted with ethyl acetate (2x 30 ml). The combined organic phases wired dried over $MgSO_4$ and the solvent was removed under reduced pressure. Aldehyde **203** (7.65 g, 22.8 mmol, 91% yield) was obtained after bulb-to-bulb distillation (sublimation of impurities at 3x10^{-2} mbar, 190 °C, then distillation at 220 - 230 °C) as a yellowish oil.

(*E*)-2-methylbut-2-enoyl chloride SI-5

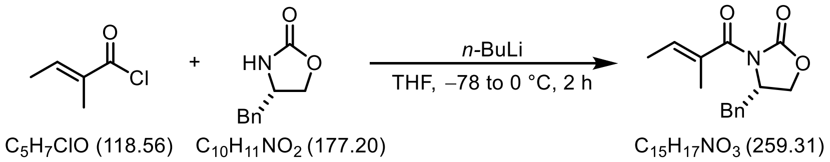


Oxalyl chloride (13.32 g, 9.0 mL, 105 mmol, 1.5 equiv.) was added dropwise to tiglic acid **207** (7.00 g, 70.0 mmol, 1 equiv.) at 0 °C. The reaction mixture was stirred for 60 min at 0 °C, warmed to room temperature and stirred for additional 60 min. Distillation yielded acid chloride **SI-5** (7.55 g, 95.6 mmol, 91%) as a colorless oil.

R$_f$ = 0.1 - 0.3 (pentane/ethyl acetate = 30:1), $KMnO_4$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 (qq, *J* = 7.1, 1.2 Hz, 1H), 1.91 (dq, *J* = 7.1, 1.2 Hz, 3H), 1.88 (p, *J* = 1.2 Hz, 3H).

The spectroscopic data agrees with previously published results.[213]

(*S*,*E*)-4-benzyl-3-(2-methylbut-2-enoyl)oxazolidin-2-one 209

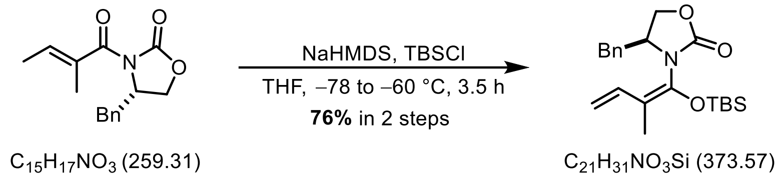


A solution of oxazolidinone **208** (4.34 g, 1 equiv.) in THF (29 mL) was treated dropwise with *n*-BuLi (2.5 M in hexane, 10.8 mL, 27.0 mmol, 1.1 equiv.) at –78 °C. After complete addition the reaction mixture was stirred for 15 min at –78 °C, followed by dropwise addition of acid chloride **SI-5** (3.19 g, 26.9 mmol, 1.1 equiv.). The reaction mixture was stirred for 45 min at –78 °C, slowly warmed to 0 °C and stirred for additional 30 min. Saturated aqueous NH_4Cl-solution (6 mL) was added, the phases were separated and the aqueous phase was extracted with ethyl acetate (3x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Oxazolidinone **209** (6.64 g, <24.5 mmol, quant., ~95% pure) was obtained as a yellowish solid, which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 3H), 7.22 – 7.18 (m, 2H), 6.21 (qq, *J* = 7.0, 1.4 Hz, 1H), 4.71 (dddd, *J* = 9.2, 8.1, 5.5, 3.5 Hz, 1H), 4.24 (dd, *J* = 9.0, 8.1 Hz, 1H), 4.14 (dd, *J* = 9.0, 5.5 Hz, 1H), 3.35 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.81 (dd, *J* = 13.5, 9.3 Hz, 1H), 1.91 (p, *J* = 1.2 Hz, 3H), 1.81 (dq, *J* = 7.0, 1.2 Hz, 3H); **$[\alpha]_D^{24}$** = –68.8° (c = 1.00, $CHCl_3$).

The spectroscopic data agrees with previously published results.[214]

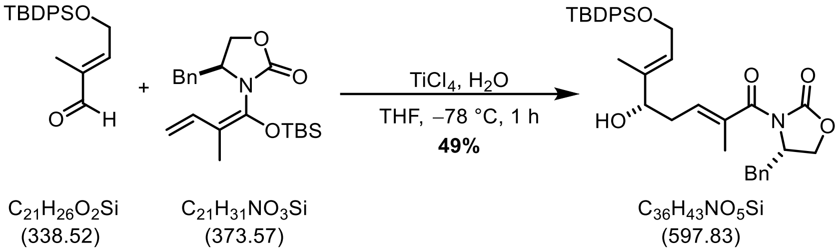
(*S*,*E*)-4-benzyl-3-(1-((*tert*-butyldimethylsilyl)oxy)-2-methylbuta-1,3-dien-1-yl)oxazolidin-2-one 204



A solution of oxazolidinone **209** (9.14 g, 35.3 mmol, 1 equiv.) in THF (230 mL) was treated dropwise with NaHMDS (2 M in THF, 26.4 mL, 52.8 mmol, 1.5 equiv.) at –78 °C. The reaction mixture was stirred for 2 h at –78 °C. A solution of TBSCl (15.9 g, 106 mmol, 3 equiv.) in THF (80 mL) was added dropwise and the reaction mixture was warmed to –60 °C over 1.5 h. MeOH (40 mL) and saturated aqueous NH_4Cl-solution (40 mL) were added, the phases were separated and the aqueous phase was extracted with diethyl ether (3x 200 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 20:1 to 18:1) silyl ketene acetal **204** (10.0 g, 26.8 mmol, 76%) was obtained as a colorless oil, which crystallized upon standing.

R_f = 0.35 (pentane/ethyl acetate = 15:1), $KMnO_4$, UV-active; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.26 – 7.22 (m, 1H), 7.14 – 7.10 (m, 2H), 6.50 (td, *J* = 11.4, 10.8, 5.4 Hz, 1H), 5.18 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.06 (dd, *J* = 10.9, 1.2 Hz, 1H), 4.28 – 4.23 (m, 2H), 4.13 – 4.08 (m, 1H), 3.15 – 3.07 (m, 1H), 2.61 (dd, *J* = 13.9, 8.7 Hz, 1H), 1.82 (s, 3H), 0.99 (s, 9H), 0.21 (s, 3H), 0.15 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.2, 135.6, 133.7, 129.0, 128.9, 127.2, 116.6, 113.0, 67.9, 56.3, 38.9, 25.7, 18.1, 11.5, -3.5, -4.2, -4.8; **ESI-TOF** (*m/z*): [M + H]$^+$ calcd for $C_{21}H_{32}NO_3Si$, 374.2146; found: 374.2158; [M + Na]$^+$ calcd for $C_{21}H_{31}NNaO_3Si$, 396.1966; found: 396.1989; [M + K]$^+$ calcd for $C_{21}H_{31}KNO_3Si$, 412.1705; found: 412.1745; **$[\alpha]_D^{24}$** = –59.3° (c = 1.00, $CHCl_3$); **IR**: ṽ = 2930, 1763, 1630, 1396, 1378, 1255, 1162, 1069, 830 cm^{-1}.

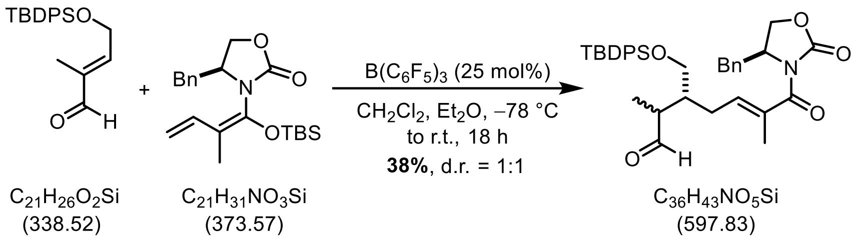
(*S*)-4-benzyl-3-((*S*,2*E*,6*E*)-8-((*tert*-butyldiphenylsilyl)oxy)-5-hydroxy-2,6-dimethylocta-2,6-dienoyl)oxazolidin-2-one 211



A solution of aldehyde **203** (1.69 g, 5.01 mmol, 2 equiv.) in dichloromethane (10 mL) and water (4 µl) was treated with $TiCl_4$ (1 M in dichloromethane, 2.51 mL, 2.51 mmol, 1 equiv.) at –78 °C. After 5 minutes a solution of silyl ketene acetal **204** (936 mg, 2.51 mmol, 1 equiv.) in dichloromethane (15 mL) was added dropwise. The reaction mixture was stirred for 1 h at –78 °C. Pyridine (3 mL) and a 1:1 mixture of Rochelle´s salt and saturated aqueous $NaHCO_3$-solution (20 mL) were added. The phases were separated and the aqueous phase was extracted with dichloromethane (3x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 7:1 to 4:1) allylic alcohol **211** (738 mg, 1.23 mmol, 49%, single diastereomer) was obtained as a yellow oil.

R_f = 0.6 (pentane/ethyl acetate = 2:1), $KMnO_4$, UV-active; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 4H), 7.43 – 7.28 (m, 9H), 7.23 – 7.16 (m, 2H), 5.98 (ddd, *J* = 8.5, 6.7, 1.6 Hz, 1H), 5.71 – 5.65 (m, 1H), 4.72 (dtd, *J* = 11.6, 5.5, 2.7 Hz, 1H), 4.29 – 4.10 (m, 5H), 3.35 (dd, *J* = 13.5, 3.6 Hz, 1H), 2.82 (dd, *J* = 13.5, 9.3 Hz, 1H), 2.58 (s_{br}, 1H), 2.47 (dd, *J* = 14.2, 8.8 Hz, 1H), 2.36 – 2.32 (m, 1H), 1.95 (s, 3H), 1.49 (s, 3H), 1.04 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.7, 153.7, 137.5, 135.7, 135.1, 134.4, 134.0, 133.3, 129.7, 129.5, 129.0, 127.9, 127.5, 125.6, 75.3, 66.5, 60.9, 55.4, 37.7, 34.6, 26.9, 19.2, 13.9, 12.5; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{36}H_{43}NNaO_5Si$ 620.2803; found: 620.2787; [M + K]$^+$ calcd for $C_{36}H_{43}KNO_5Si$, 636.2543; found: 636.2545; **[α]$_D$^{22}** = +0.32° (c = 3.27, $CHCl_3$); **IR**: ṽ = 3040, 2987, 2961, 1801, 1763, 1634, 1401, 1255, 1162, 830 cm^{-1}.

(3*R*,*E*)-7-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-3-(((*tert*-butyldiphenylsilyl)oxy)methyl)-2,6-dimethyl-7-oxohept-5-enal 210

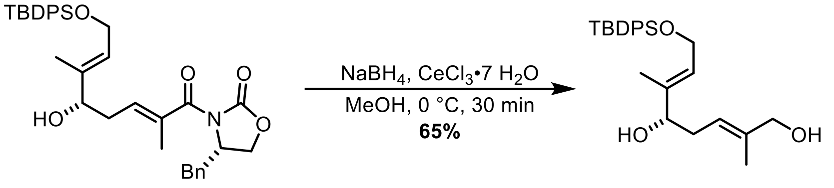


A solution of silyl ketene acetal **204** (50 mg, 134 µmol, 1 equiv.) and aldehyde **203** (91 mg, 268 µmol, 2 equiv.) in dichloromethane (1.2 mL) and Et_2O (0.13 mL) was treated with $B(C_6F_5)_3$ (17 mg, 33 µmol, 25 mol%) at –78 °C. The reaction mixture was warmed to room temperature over 18 h. The solvents were removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 6:1) aldehydes **210** (30 mg, 51 µmol, 38%, 2 diastereomers, d.r. = 1:1, inseparable mixture) were obtained as a colorless oil.

R$_f$ = 0.3 (pentane/ethyl acetate = 6:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.74 (d, *J* = 0.7 Hz, 1H), 9.72 (d, *J* = 1.5 Hz, 1H), 7.69 – 7.58 (m, 8H), 7.45 – 7.42 (m, 4H), 7.41 – 7.38 (m, 8H), 7.35 – 7.29 (m, 4H), 7.29 – 7.27 (m, 2H), 7.22 – 7.16 (m, 4H), 5.96 (dtd, *J* = 8.3, 6.8, 1.5 Hz, 1H), 5.96 – 5.87 (m, 1H), 4.73 – 4.64 (m, 1H), 4.26 – 4.20 (m, 2H), 4.18 – 4.10 (m, 2H), 3.77 – 3.72 (m, 1H), 3.61 – 3.49 (m, 3H), 3.33 (dtd, *J* = 12.8, 6.9, 6.4, 3.3 Hz, 2H), 2.87 – 2.72 (m, 2H), 2.72 – 2.65 (m, 1H), 2.51 (ddd, *J* = 18.5, 7.0, 3.8 Hz, 1H), 2.43 (tdd, *J* = 8.2, 6.0, 4.0 Hz, 1H), 2.30 – 2.10 (m, 5H), 1.87 (dt, *J* = 2.1, 1.1 Hz, 3H), 1.86 (dt, *J* = 4.5, 1.1 Hz, 3H), 1.06 (s, 9H), 1.05 – 1.04 (m, 6H), 1.03 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 204.9, 204.8, 171.57, 171.56, 153.2, 153.1, 136.5, 136.3, 135.8, 135.7, 135.3, 135.2, 133.4, 133.3, 133.22, 133.21, 132.6, 132.5, 129.92, 129.88, 129.6,* 127.9,* 127.52, 127.49, 66.6, 66.5, 64.1, 63.8, 55.53, 55.47, 47.0, 46.9, 42.0, 41.9, 41.5, 41.4, 27.8, 27.1, 27.0, 26.9, 19.4, 19.2, 13.9, 13.8, 10.0, 8.4; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{36}H_{43}NNaO_5Si$ 620.2803; found: 620.2798; [M + K]$^+$ calcd for $C_{36}H_{43}KNO_5Si$, 636.2543; found: 636.2532. *Signal with double intensity.

Due to inseparable product mixture no optical rotation value and IR spectrum was recorded.

(*S*,2*E*,6*E*)-8-((*tert*-butyldiphenylsilyl)oxy)-2,6-dimethylocta-2,6-diene-1,5-diol SI-6



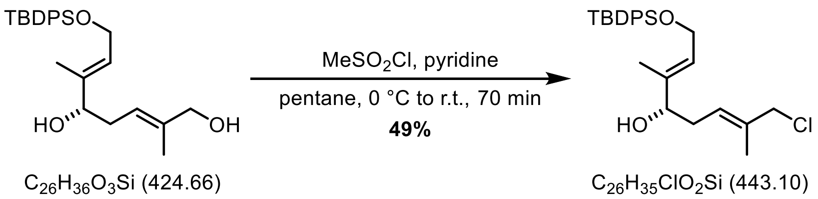
$C_{36}H_{43}NO_5Si$ (597.83) $C_{26}H_{36}O_3Si$ (424.66)

A solution of allylic alcohol **211** (6.56 g, 11.0 mmol, 1 equiv.) and $CeCl_3\cdot 7\,H_2O$ (2.04 g, 5.49 mmol, 50 mol%) in MeOH (150 mL) was treated with $NaBH_4$ (830 mg, 22.0 mmol, 2 equiv.) at 0 °C in 4 portions over 20 min. After complete addition the reaction mixture was stirred for additional 10 min. Saturated aqueous NH_4Cl-solution (100 mL) was added slowly and the reaction mixture was warmed to room temperature. The aqueous phase was extracted with dichloromethane (3x 200 mL), the combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 3:2) diol **SI-6** (3.04 g, 7.2 mmol, 65%) was obtained as a colorless oil.

R_f = 0.3 (pentane/ethyl acetate = 3:2), $KMnO_4$, UV-active; **^{1}H NMR** (500 MHz, CD_3COCD_3) δ 7.74 – 7.65 (m, 4H), 7.51 – 7.35 (m, 6H), 5.65 (tp, *J* = 6.2, 1.3 Hz, 1H), 5.44 (tdt, *J* = 7.1, 2.8, 1.4 Hz, 1H), 4.29 (ddd, *J* = 6.3, 1.8, 0.9 Hz, 2H), 4.02 – 3.95 (m, 1H), 3.91 (s, 2H), 3.73 (s_{br}, 1H), 2.89 (s_{br}, 1H), 2.23 (tq, *J* = 7.0, 1.1 Hz, 2H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.47 (d, *J* = 1.2 Hz, 3H), 1.03 (s, 9H); **^{13}C NMR** (126 MHz, CD_3COCD_3) δ 206.3, 140.3, 137.7, 136.3, 134.7, 130.6, 128.6, 125.1, 122.0, 76.9, 68.5, 61.6, 34.7, 27.2, 19.7, 14.7, 12.3; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{26}H_{36}NaO_3Si$, 447.2326; found: 447.2294; $[M + K]^+$ calcd for $C_{26}H_{36}KO_3Si$, 463.2066; found: 463.2104; **$[\alpha]_D^{24}$** = –4.20° (c = 0.52, $CHCl_3$); **IR**: ṽ = 3358, 2955, 2916, 2850, 1734, 1457, 1377, 1110, 701 cm^{-1}.

(*S*,2*E*,6*E*)-1-((*tert*-butyldiphenylsilyl)oxy)-8-chloro-3,7-dimethylocta-2,6-dien-4-ol

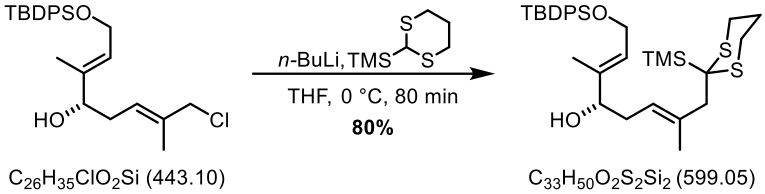
202



A mixture of diol **SI-6** (2.00 g, 4.71 mmol, 1 equiv.) in pentane (33 mL) was treated with pyridine (0.49 mL, 484 mg, 6.12 mmol, 1.3 equiv.) at room temperature. The mixture was cooled to 0 °C and after 5 min $MeSO_2Cl$ (0.47 mL, 701 mg, 6.12 mmol, 1.3 equiv.) was added. After 20 min at 0 °C the reaction mixture was warmed to room temperature. After 50 min saturated aqueous NH_4Cl-solution (30 ml) was added, the phases were separated and the aqueous phase was extracted with EtOAc (5x 50 ml). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate = 12:1 to 8:1) allylic chloride **202** (1.02 g, 2.31 mmol, 49%) was obtained as yellowish oil.

R_f = 0.45 (pentane/ethyl acetate = 8:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 5H), 7.45 – 7.41 (m, 2H), 7.41 – 7.36 (m, 4H), 5.61 (tt, *J* = 6.1, 1.2 Hz, 1H), 5.51 (td, *J* = 7.1, 1.1 Hz, 1H), 4.27 (tt, *J* = 5.1, 0.8 Hz, 2H), 4.02 – 3.98 (m, 3H), 2.26 (dtt, *J* = 21.3, 14.5, 6.8 Hz, 2H), 1.75 (dd, *J* = 1.4, 0.8 Hz, 3H), 1.44 (q, *J* = 1.0 Hz, 3H), 1.05 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 138.0, 135.8, 134.3, 134.0, 129.8, 127.8, 126.5, 126.2, 76.4, 60.9, 52.3, 33.8, 27.0, 19.3, 14.6, 12.1; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{26}H_{35}ClNaO_2Si$, 465.1988; found: 465.1991; $[M + K]^+$ calcd for $C_{26}H_{35}ClKO_2Si$, 481.1727; found: 481.1730; **$[\alpha]_D^{24}$** = –6.42° (c = 0.66, $CHCl_3$); **IR**: $\tilde{\nu}$ = 2955, 2917, 2851, 2364, 1110, 911, 735, 701 cm^{-1}.

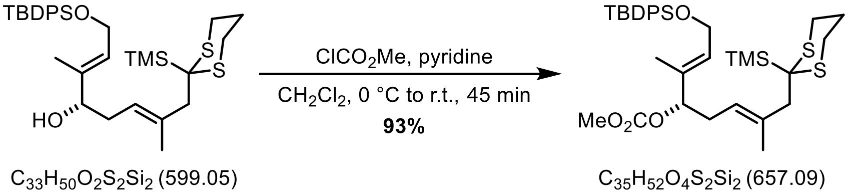
(*S*,2*E*,6*E*)-1-((*tert*-butyldiphenylsilyl)oxy)-3,7-dimethyl-8-(2-(trimethylsilyl)-1,3-dithian-2-yl)octa-2,6-dien-4-ol 213



A solution of dithiane **201** (62.6 µL, 65.1 mg, 339 µmol, 3 equiv.) in THF (1.1 mL) was treated with *n*-BuLi (2.5 M in hexanes, 126 µL, 316 µmol, 2.8 equiv.) at 0 °C. After 20 min at 0 °C a solution of allylic chloride **202** (50.0 mg, 113 µmol, 1 equiv.) in THF (0.34 mL) was added and the reaction mixture was stirred for additional 60 min. Saturated aqueous NH_4Cl-solution (1 mL), water (2 mL) and EtOAc (5 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 14:1) dithiane **213** (54 mg, 90 µmol, 80%) was obtained as a colorless oil.

R_f = 0.65 (pentane/ethyl acetate = 8:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.77 – 7.66 (m, 4H), 7.45 – 7.41 (m, 2H), 7.40 – 7.34 (m, 4H), 5.63 (tt, *J* = 6.1, 1.1 Hz, 2H), 5.35 (t, *J* = 7.1 Hz, 1H), 4.27 (t, *J* = 6.8 Hz, 2H), 4.01 (t, *J* = 6.4 Hz, 1H), 3.03 (ddt, *J* = 14.0, 11.6, 2.6 Hz, 2H), 2.94 (d, *J* = 14.2 Hz, 1H), 2.92 (d, *J* = 14.2 Hz, 1H), 2.52 (ddt, *J* = 14.0, 5.5, 3.3 Hz, 2H), 2.26 (dt, *J* = 15.1, 7.6 Hz, 1H), 2.26 – 2.15 (m, 1H), 2.01 (ddt, *J* = 10.6, 5.3, 2.6 Hz, 1H), 1.93 – 1.85 (m, 3H), 1.66 (d, *J* = 3.2 Hz, 1H), 1.46 (s, 3H), 1.05 (s, 9H), 0.19 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 138.1, 136.6, 135.8, 135.8, 134.1, 134.0, 129.7, 127.8, 126.1, 125.9, 76.5, 61.0, 47.1, 38.7, 34.2, 27.0, 25.0, 24.3, 19.3, 18.7, 12.2, -2.3; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{33}H_{50}NaO_2S_2Si_2$, 621.2683; found: 621.2679; $[M + K]^+$ calcd for $C_{33}H_{50}KO_2S_2Si_2$, 637.2423; found: 637.2423; **$[\alpha]_D^{24}$** = +26.2° (c = 1.12, $CHCl_3$); **IR**: $\tilde{\nu}$ = 2955, 2916, 2852, 1428, 1246, 1109, 1051, 845 cm^{-1}.

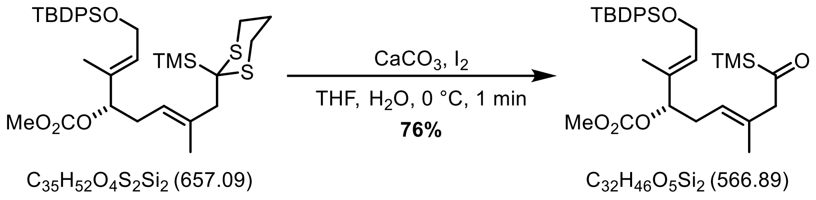
(*S*,2*E*,6*E*)-1-((*tert*-butyldiphenylsilyl)oxy)-3,7-dimethyl-8-(2-(trimethylsilyl)-1,3-dithian-2-yl)octa-2,6-dien-4-yl methyl carbonate 214



A solution of dithiane **213** (48 mg, 80 µmol, 1 equiv.) in dichloromethane (0.85 mL) was treated with pyridine (38.8 µL, 38 mg, 481 µmol, 6 equiv.) at 0 °C. The reaction mixture was stirred for 5 min, then methylchloro formate (168 µL, 205 mg, 12.8 mmol, 160 equiv.) was added and the reaction mixture was warmed to room temperature over 40 min. Saturated aqueous $NaHCO_3$-solution (2 mL) and dichloromethane (3 mL) were added. The phases were separated and the aqueous phase was extracted with dichloromethane (2x 3 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 25:1) carbonate **214** (49 mg, 74 µmol, 93%) was obtained as a colorless oil.

R_f = 0.5 (pentane/ethyl acetate = 15:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.71 – 7.57 (m, 4H), 7.44 – 7.40 (m, 2H), 7.40 – 7.37 (m, 4H), 5.72 (t, *J* = 5.7 Hz, 1H), 5.31 (t, *J* = 6.9 Hz, 1H), 4.97 (t, *J* = 7.0 Hz, 1H), 4.24 (t, *J* = 6.4 Hz, 2H), 3.76 (s, 3H), 3.06 (t, *J* = 13.2 Hz, 2H), 2.96 (s, 2H), 2.47 (dt, *J* = 14.1, 4.1 Hz, 2H), 2.48 – 2.37 (m, 1H), 2.35 – 2.24 (m, 1H), 2.03 (s, 1H), 1.89 (sbr, 4H), 1.45 (s, 3H), 1.04 (s, 9H), 0.17 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 155.3, 137.0, 135.7, 135.7, 133.9, 133.9, 133.6, 129.8, 128.8, 127.8, 127.8, 124.6, 82.4, 60.8, 54.7, 47.3, 38.5, 31.8, 26.9, 25.0, 24.0, 24.0, 19.3, 18.4, 12.4, -2.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{35}H_{52}NaO_4S_2Si_2$, 679.2738; found: 679.2774; $[M + K]^+$ calcd for $C_{35}H_{52}KO_4S_2Si_2$, 695.2478; found: 695.2522; **$[\alpha]_D^{24}$** = +11.2° (c = 0.89, $CHCl_3$); **IR**: ṽ = 2953, 2917, 2850, 1741, 1269, 1110, 845, 753, 702 cm^{-1}.

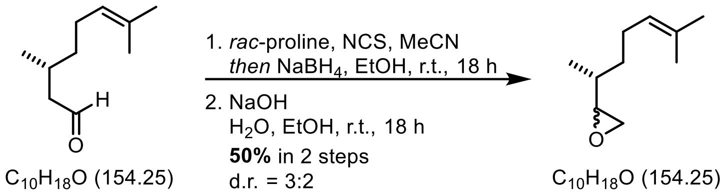
(*S*,2*E*,6*E*)-1-((*tert*-butyldiphenylsilyl)oxy)-3,7-dimethyl-9-oxo-9-(trimethylsilyl)nona-2,6-dien-4-yl methyl carbonate 200



A solution of carbonate **214** (19.8 mg, 30 µmol, 1 equiv.) in THF/H_2O (4:1, 0.2 mL) was treated with $CaCO_3$ (24 g, 241 µmol, 8 equiv.) and I_2 (23 mg, 90 µmol, 3 equiv.) at 0 °C. After 1 min water (1 mL), dichloromethane (1 mL) and $Na_2S_2O_3$-solution (1 M, 0.5 mL) were added. The mixture was filtered over a short pad of Celite®, the phases were separated and the aqueous phase was extracted with dichloromethane (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 40:1) acylsilane **200** (13 mg, 23 µmol, 76%) was obtained as a colorless oil.

R_f = 0.4 (pentane/ethyl acetate = 15:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.68 – 7.65 (m, 4H), 7.43 – 7.40 (m, 2H), 7.39 – 7.35 (m, 4H), 5.71 (tt, *J* = 6.0, 1.0 Hz, 1H), 5.15 (td, *J* = 7.2, 1.3 Hz, 1H), 4.96 (t, *J* = 6.9 Hz, 1H), 4.24 (t, *J* = 5.2 Hz, 2H), 3.76 (s, 3H), 3.24 (dd, *J* = 2.1, 1.1 Hz, 2H), 2.47 (dt, *J* = 15.0, 7.4 Hz, 1H), 2.33 (dt, *J* = 14.3, 6.6 Hz, 1H), 1.57 (q, *J* = 0.9 Hz, 3H), 1.45 (q, *J* = 1.0 Hz, 3H), 1.03 (s, 9H), 0.17 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 246.0, 155.3, 135.7, 135.7, 133.9, 133.9, 133.6, 131.6, 129.8, 128.6, 127.8, 124.2, 82.4, 60.8, 59.4, 54.8, 31.8, 26.9, 19.3, 17.1, 12.4, -2.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{32}H_{46}NaO_5Si_2$, 589.2776; found: 589.2803; $[M + K]^+$ calcd for $C_{32}H_{46}KO_5Si_2$, 605.2516; found: 605.2545; **$[\alpha]_D^{24}$** = +15.6° (c = 1.11, $CHCl_3$); **IR**: ṽ = 2955, 2929, 2857, 1748, 1265, 1110, 843, 702 cm^{-1}.

2-((R)-6-methylhept-5-en-2-yl)oxirane 215

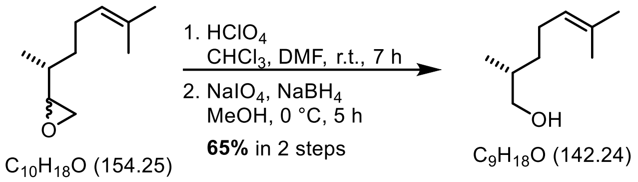


A solution of (*R*)-citronellal **199** (3.00 g, 19.5 mmol, 1 equiv.), *N*-chloro succinimide (3.11 g, 23.3 mmol, 1.2 equiv.) and *rac*-proline (448 mg, 3.89 mmol, 20 mol%) in acetonitrile (40 ml) was stirred for 16 h at room temperature. The reaction mixture was treated with EtOH (17 mL) and $NaBH_4$ (1.84 g, 48.6 mmol, 2.5 equiv.) was added in 5 portions. After 2 h at room temperature saturated aqueous NH_4Cl-solution (40 mL) was added. After 10 min at room temperature water (100 mL) and EtOAc (100 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3x 100 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was redissolved in EtOH (30 mL) and a solution of NaOH (17.34 g, 434 mmol, ca. 23 equiv.) in water (63 mL) was added. The reaction mixture was stirred for 18 h at room temperature. Dichloromethane (100 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (2x 100 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 50:1) epoxide **215** (1.50 g, 9.75 mmol, 50%, 2 diastereomers, d.r. = 3:2, inseparable mixture) was obtained as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 – 5.02 (m, 2H), 2.76 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.74 – 2.67 (m, 3H), 2.53 (dd, *J* = 5.0, 2.8 Hz, 1H), 2.48 (dd, *J* = 4.8, 2.9 Hz, 1H), 2.04 (dq, *J* = 14.5, 7.2 Hz, 4H), 1.68 (s, 6H), 1.61 (s, 3H), 1.60 (s, 3H), 1.47 – 1.39 (m, 1H), 1.38 – 1.25 (m, 4H), 1.03 (d, *J* = 6.3 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H).

The spectroscopic data agrees with previously published results.[215]

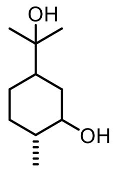
(*R*)-2,6-dimethylhept-5-en-1-ol 216



A solution of epoxide **215** (150 mg, 972 µmol, 1 equiv.) in chloroform (0.65 mL) was treated with a solution of perchloric acid (70% in water, 42 µL, 70 mg, 486 µmol, 50 mol%) in DMF (1.45 mL) at room temperature and the reaction mixture was stirred for 20 h at that temperature. Saturated aqueous $NaHCO_3$-solution (2 mL) and dichloromethane (2 mL) were added. The phases were separated and the aqueous phase was extracted with dichloromethane (3x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was redissolved in MeOH (1 mL) and K_2CO_3 (156 mg, 1.12 mmol, 1.15 equiv.) was added. The reaction mixture was stirred for 5 h at room temperature. Saturated aqueous NH_4Cl-solution (2 mL) and dichloromethane (2 mL) were added. the phases were separated and the aqueous phase was extracted with dichloromethane (2x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was redissolved in acetone/water (5:1, 1.1 mL), cooled to 0 °C, treated with $NaIO_4$ (223 mg, 1.05 mmol, 1.2 equiv.) and stirred for 3.5 h at 0 °C. The solvent was removed under reduced pressure and the crude product was redissolved in MeOH (1.5 mL) and treated with $NaBH_4$ (47 mg, 1.24 mmol, 1.45 equiv.) at 0 °C. The reaction mixture was warmed to room temperature over 90 min. Saturated aqueous NH_4Cl-solution (1 mL) and dichloromethane (2 mL) were added, the phases were separated and the aqueous phase was extracted with dichloromethane (3x 2 mL). The combined organic phases were dried over MgSO4, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 5:1) alcohol **216** (80 mg, 632 µmol, 65% in 2 steps) was obtained as a colorless oil.

R_f = 0.65 (pentane/ethyl acetate = 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.12 (ddt, *J* = 8.5, 5.7, 1.5 Hz, 1H), 3.53 (dd, *J* = 10.5, 5.7 Hz, 1H), 3.43 (dd, *J* = 10.5, 6.6 Hz, 1H), 2.13 – 1.92 (m, 2H), 1.70 (s, 1H), 1.67 – 1.63 (m, 1H), 1.62 (s, 1H), 1.45 (dddd, *J* = 13.3, 9.4, 6.7, 5.4 Hz, 1H), 1.16 (dddd, *J* = 13.7, 9.3, 8.1, 5.9 Hz, 1H), 0.95 (d, *J* = 6.7 Hz, 2H); **$[\alpha]_D^{23}$** = +24.1° (c = 1.05, $CHCl_3$). The spectroscopic data agrees with previously published results.[216]

Diol **217** was obtained as a single diastereomer when performing the hydrolysis of **215** in an aqueous medium. No conclusion about the configuration of the new stereocenters was made.

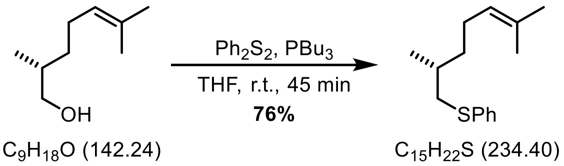


$C_{10}H_{20}O_2$ (172.27)

^{1}H NMR (700 MHz, $CDCl_3$) δ 3.15 (td, *J* = 10.5, 4.3 Hz, 1H), 2.09 – 2.05 (m, 1H), 1.80 – 1.71 (m, 2H), 1.63 (s, 1H), 1.39 (tt, *J* = 12.0, 3.2 Hz, 1H), 1.32 (s, 1H), 1.25 (ddq, *J* = 13.6, 6.4, 3.9, 3.2 Hz, 1H), 1.17 (s, 6H), 1.06 (td, *J* = 12.2, 10.8 Hz, 2H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.99 – 0.90 (m, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 76.7, 72.6, 48.1, 40.2, 36.8, 33.2, 27.3, 27.2, 26.8, 18.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{20}NaO_2$, 195.1356; found: 195.1350; **IR**: ṽ =2965, 2912, , 1451, 1341, 1064, 735 cm^{-1}.

No optical rotation value was recorded.

(*R*)-(2,6-dimethylhept-5-en-1-yl)(phenyl)sulfane 218

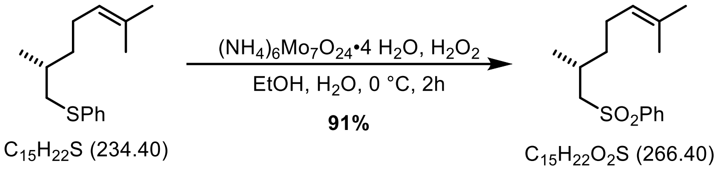


A solution of alcohol **216** (150 mg, 1.06 mmol, 1 equiv.) and diphenyl sulfide (230 mg, 1.06 mmol, 1 equiv.) in THF (1.3 mL) was treated with PBu_3 (333 µL, 270 mg, 1.27 mmol, 1.2 equiv.) at room temperature. The reaction mixture was stirred at room temperature for 45 min before the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane) sulfide **218** (188 mg, 806 µmol, 76%) was obtained as a colorless oil.

R_f = 0.5 (pentane), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.35 – 7.32 (m, 2H), 7.29 – 7.24 (m, 2H), 7.18 – 7.13 (m, 1H), 5.10 (ddp, *J* = 8.5, 5.7, 1.4 Hz, 1H), 2.97 (dd, *J* = 12.5, 5.7 Hz, 1H), 2.77 (dd, *J* = 12.5, 7.6 Hz, 1H), 2.04 (dt, *J* = 15.1, 7.4 Hz, 1H), 1.98

(dq, *J* = 14.7, 7.4 Hz, 1H), 1.80 – 1.73 (m, 1H), 1.69 (q, *J* = 1.3 Hz, 3H), 1.61 (d, *J* = 1.3 Hz, 3H), 1.61 – 1.49 (m, 1H), 1.29 (dddd, *J* = 13.5, 9.3, 7.8, 5.9 Hz, 1H), 1.05 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 137.6, 131.7, 129.0, 128.9, 125.7, 124.5, 41.2, 36.4, 32.7, 25.8, 25.5, 19.5, 17.8; **EI-TOF** (*m/z*): [M - H]$^+$ calcd for $C_{15}H_{22}NaS$, 233.1359; found: 233.1443; **[α]$_D$^{29}** = –2.93° (c = 1.03, $CHCl_3$); **IR**: ṽ = 2961, 2912, 2852, 2362, 1584, 1479, 1437, 1375, 1089, 1024, 735, 689 cm^{-1}.

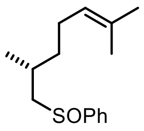
(*R*)-((2,6-dimethylhept-5-en-1-yl)sulfonyl)benzene 198



A solution of $(NH_4)_6Mo_7O_{24}\cdot 4\ H_2O$ (169 mg, 137 µmol, 40 mol%) in EtOH (2 mL) was treated with H_2O_2 (35% in H_2O, 233 µL, 265 mg, 2.73 mmol, 8 equiv) at 0 °C. After 10 min a solution of sulfide **218** (80 mg, 341 µmol, 1 equiv.) in EtOH (1.3 mL) was added dropwise and the reaction mixture was stirred for 2 h at 0 °C. EtOAc (10 mL) was added and the organic phase was washed with water (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 15:1) sulfone **198** (85 mg, 310 µmol, 91%) was obtained as a colorless oil.

R$_f$ = 0.4 (pentane/ethyl acetate = 10:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.92 – 7.85 (m, 2H), 7.66 – 7.60 (m, 1H), 7.59 – 7.51 (m, 2H), 4.96 (ddp, *J* = 8.5, 5.7, 1.5 Hz, 1H), 3.08 (dd, *J* = 14.2, 4.6 Hz, 1H), 2.92 (dd, *J* = 14.2, 7.9 Hz, 1H), 2.07 (tddd, *J* = 7.7, 6.6, 5.6, 4.5 Hz, 1H), 1.99 – 1.79 (m, 2H), 1.63 (q, *J* = 1.3 Hz, 3H), 1.54 (d, *J* = 1.4 Hz, 3H), 1.43 (dddd, *J* = 13.5, 8.9, 6.8, 5.7 Hz, 1H), 1.27 (dddd, *J* = 13.7, 8.7, 7.8, 6.3 Hz, 1H), 1.06 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 140.3, 133.6, 132.2, 129.3, 128.0, 123.6, 62.6, 36.8, 28.3, 25.8, 25.0, 19.9, 17.8; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{15}H_{22}NaO_2S$, 289.1233; found: 289.1281; [M + K]$^+$ calcd for $C_{15}H_{22}KO_2S$, 305.0973; found: 305.1028; **[α]$_D$^{26}** = –7.09° (c = 1.0, $CHCl_3$); **IR**: ṽ = 2963, 2919, 1446, 1303, 1144, 1084, 735 cm^{-1}.

With shorter reaction times, up to 42% of the corresponding sulfoxide **219** was isolated as an inseparable mixture of diastereomers (d.r. = 1:1).



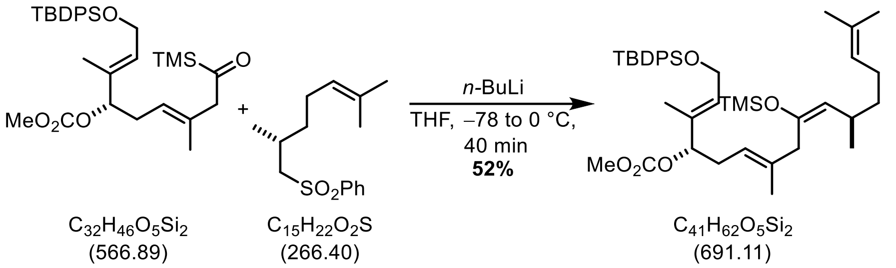
$C_{15}H_{22}OS$ (250.40)

R$_f$ = 0.25 (pentane/ethyl acetate = 5:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.64 (dt, *J* = 8.0, 1.7 Hz, 4H), 7.56 – 7.44 (m, 6H), 5.09 – 5.01 (m, 2H), 2.88 (dd, *J* = 13.0, 4.0 Hz, 1H), 2.80 (dd, *J* = 13.1, 6.2 Hz, 1H), 2.64 (dd, *J* = 13.1, 7.6 Hz, 1H), 2.44 (dd, *J* = 13.0, 10.0 Hz, 1H), 2.17 – 2.11 (m, 1H), 2.08 – 1.95 (m, 5H), 1.72 – 1.64 (m, 7H), 1.59 (s, 6H), 1.46 – 1.40 (m, 1H), 1.37 – 1.29 (m, 2H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 144.9, 144.9, 132.1, 132.0, 131.1, 131.0, 129.3, 124.1, 124.0, 123.9, 123.9, 66.6, 66.4, 37.1, 36.1, 28.8, 28.4, 25.8, 25.3, 25.1, 20.0, 19.0, 17.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{22}NaOS$, 273.1284; found: 273.1334; $[M + K]^+$ calcd for $C_{15}H_{22}KOS$, 289.1023; found: 289.1080; **IR**: ṽ = 2960, 2917, 2852, 1734, 1443, 1377, 1086, 1037, 746, 690 cm^{-1}.

No optical rotation value was recorded.

(*S*,4*E*,6*E*,10*E*)-4-((*R*)-2,6-dimethylhept-5-en-1-ylidene)-2,2,6,10,15,15-hexamethyl-14,14-diphenyl-3,13-dioxa-2,14-disilahexadeca-6,10-dien-9-yl methyl carbonate

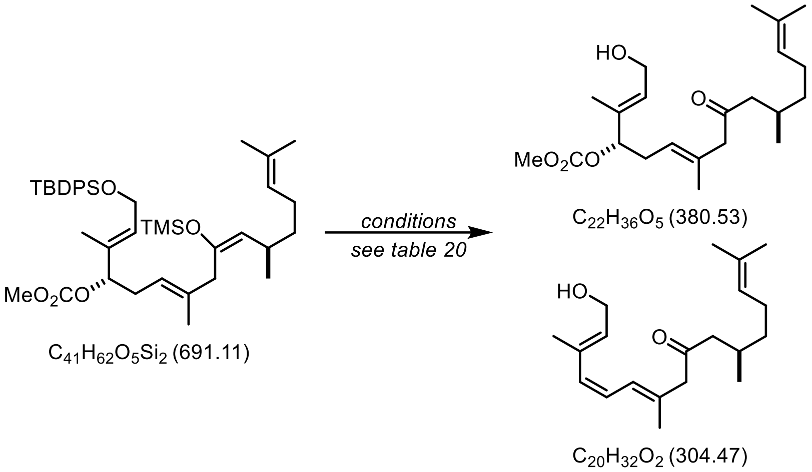
197



A solution of sulfone **198** (20 mg, 75 µmol, 1 equiv.) in THF (0.18 mL) and Et_2O (0.18 mL) was treated with *n*-BuLi (2.5 M in hexanes, 32 µL, 79 µmol, 1.05 equiv.) at –78 °C. After 10 min a solution of acylsilane **200** (43 mg, 75 µmol, 1 equiv.) in THF (0.1 mL) and Et_2O (0.1 mL) was added. The reaction mixture was warmed to 0 °C and after 30 min saturated aqueous NH_4Cl-solution (1 mL) and Et_2O (1 mL) were added. the phases were separated and the aqueous phase was extracted with Et_2O (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 15:1) silylenol ether **197** (22 mg, 39 µmol, 52%, single isomer) was obtained as a colorless oil.

R_f = 0.6 (pentane/ethyl acetate = 30:1), $KMnO_4$, UV-active; **^{1}H NMR** (400 MHz, CD_3COCD_3) δ 7.73 – 7.67 (m, 4H), 7.47 – 7.40 (m, 6H), 5.71 (ddt, *J* = 7.2, 6.1, 1.2 Hz, 1H), 5.17 (ddq, *J* = 8.4, 7.1, 1.3 Hz, 1H), 5.11 (dddd, *J* = 8.5, 5.7, 2.9, 1.4 Hz, 1H), 4.93 (t, *J* = 6.8 Hz, 1H), 4.47 (d, *J* = 10.0 Hz, 1H), 4.30 (ddd, *J* = 5.9, 2.2, 1.1 Hz, 2H), 3.71 (s, 3H), 2.83 (d, *J* = 14.9 Hz, 1H), 2.68 (d, *J* = 15.1 Hz, 1H), 2.43 (dt, *J* = 14.6, 7.4 Hz, 1H), 2.38 – 2.20 (m, 2H), 2.03 – 1.88 (m, 2H), 1.66 – 1.62 (m, 6H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.47 (q, *J* = 1.0 Hz, 3H), 1.36 – 1.26 (m, 1H), 1.25 – 1.15 (m, 1H), 1.03 (s, 9H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.15 (s, 9H); **^{13}C NMR** (176 MHz, CD_3COCD_3) δ 155.8, 149.2, 136.3, 135.8, 135.1, 134.5, 131.5, 130.6, 128.6, 128.4, 125.7, 121.3, 116.2, 82.8, 61.4, 54.8, 42.5, 39.8, 39.2, 32.5, 32.3, 29.8, 27.2, 26.8, 26.4, 25.9, 24.1, 22.5, 19.7, 17.8, 16.5, 14.4, 12.6, 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{41}H_{62}NaO_5Si_2$, 713.4028; found: 713.4035; $[M + K]^+$ calcd for $C_{41}H_{62}KO_5Si_2$, 729.3768; found: 729.3776; **$[\alpha]_D^{24}$** = -21.6° (c = 0.55, $CHCl_3$); **IR**: $\tilde{\nu}$ = 3042, 2925, 2857, 1748, 1266, 1110, 846, 701 cm^{-1}.

Main product of the cyclization attempts of **197** was an inseparable 3:1 mixture of deprotected carbonate **220** and its corresponding elimination product, conjugated triene **221**.

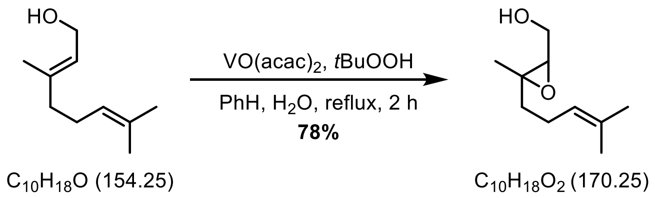


^{1}H NMR (700 MHz, $CDCl_3$) δ 6.05 (s, 1H), 5.72 (t, *J* = 7.0 Hz, 1H), 5.67 (t, *J* = 6.8 Hz, 1H),* 5.15 (t, *J* = 7.5 Hz, 1H), 5.08 (d, *J* = 7.1 Hz, 1H), 5.00 – 4.93 (m, 2H), 4.25 – 4.15 (m, 4H), 3.77 (s, 3H),* 3.06 – 3.04 (m, 2H),* 2.70 (td, *J* = 11.4, 5.0 Hz, 1H), 2.52 – 2.34 (m, 4H), 2.22 (ddd, *J* = 16.0, 8.2, 1.8 Hz, 1H), 2.19 – 2.14 (m, 1H), 2.02 – 1.91 (m, 3H), 1.88 (s, 3H), 1.81 – 1.75 (m, 1H), 1.73 (s, 3H), 1.69 (s, 3H), 1.68 (s, 6H), 1.62 (s, 3H), 1.59 (s, 6H), 1.34 – 1.27 (m, 4H), 1.22 – 1.14 (m, 2H), 0.93 – 0.80 (m, 6H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.6,* 201.1, 157.7, 155.3,* 135.9, 135.2,* 132.5, 131.7,* 131.6, 128.0,* 127.7, 124.8, 124.6,* 124.4,* 123.6,* 82.6, 82.2,* 59.1,* 59.0, 54.82,* 54.80, 54.3,* 52.1, 49.8,* 37.3, 37.1,* 31.5,* 30.9, 29.9, 29.0,* 25.9,* 25.7, 25.6,* 25.5, 19.9, 19.8,* 17.8,* 17.0,* 14.3, 12.3,* 12.2; **ESI-TOF** (*m/z*): Carbonate: $[M + Na]^+$ calcd for $C_{22}H_{36}NaO_5$, 403.2455; found: 403.2469; Triene $[M + Na]^+$ calcd for $C_{20}H_{32}KO_2$, 327.2295; found: 327.2304.

*Signals unambiguously assigned to the main product.

Due to the inseparable mixture of products, no optical rotation value and IR spectrum was recorded.

(3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methanol 227

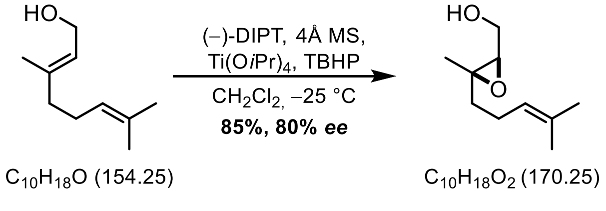


A solution of geraniol **226** (40.0 g, 259 mmol) in benzene (300 ml) was treated with VO(acac)$_2$ (1.03 g, 3.89 mmol) at room temperature. *t*BuOOH (70 wt% in water, 39 ml, 37 g, 285 mmol) was added dropwise over 10 min. After additional 10 min at room temperature the reaction was heated for 2 h to 90 °C, to form a deeply green suspension. The reaction mixture was washed with saturated aqueous $Na_2S_2O_3$-solution (2x 150 ml), water (2x 300 ml) and brine (2x 100 ml). The organic phase was filtered over Celite® and the solvent was removed under reduced pressure. The crude product was distilled under reduced pressure to give epoxygeraniol **227** (34.6 g, 78%) as a colorless liquid.

R$_f$ = 0.4 (pentane/ethyl acetate = 3:1), $KMnO_4$; **b.p.:** 75 °C at 3.7x10^{-3} mbar; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.07 (ddq, *J* = 8.5, 5.7, 1.4 Hz, 1H), 3.87 – 3.76 (m, 1H), 3.67 (dd, *J* = 12.1, 6.8 Hz, 1H), 2.97 (dd, *J* = 6.8, 4.2 Hz, 1H), 2.11 – 1.99 (m, 3H), 1.71 – 1.63 (m, 4H), 1.60 (s, 3H), 1.46 (ddd, *J* = 13.7, 9.0, 7.5 Hz, 1H), 1.29 (s, 3H).

The spectroscopic data agrees with previously published results.[217]

enantioenriched
((2R,3R)-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methanol 227

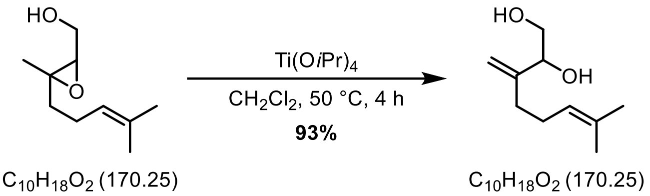


A mixture of 4Å molecular sieves (11.2 g) and (–)-diisopropyl tartrate (1.66 mL, 1.85 g, 7.88 mmol, 7.5 mol%) in dichloromethane (160 mL) was treated with Ti(O*i*Pr)$_4$ (1.86 mL, 1.79 g, 6.30 mmol, 6 mol%) and TBHP (5-6 M in decane, 31.2 mL, 171 mmol, 1.63 equiv.) at –10 °C. After 20 min at –10 °C the mixture was cooled to –25 °C. Geraniol **226**

(18.4 mL, 16.2 g, 105 mmol, 1 equiv.) was added and the reaction was stirred for 60 min at -25 °C. Water (40 mL) was added and the reaction mixture was warmed to room temperature. Aqueous NaOH solution (1 M, 40 mL) was added and the mixture was stirred for 30 min at room temperature. The reaction mixture was filtered over Celite®, the phases were separated and the aqueous phase was extracted with dichloromethane (3x 100 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 5:1) *(R)*-epoxygeraniol **227** (15.2 g, 89 mmol, 85%, 80% *ee*) was obtained as a colorless oil.

$[\alpha]_D^{26}$ = +4.21° (c = 1.0, $CHCl_3$);

7-methyl-3-methyleneoct-6-ene-1,2-diol 228

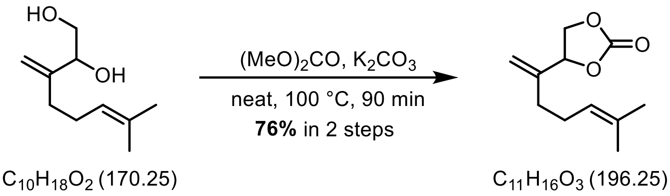


A solution of epoxygeraniol **227** (34.6 g, 203 mmol, 1 equiv.) in dichloromethane (750 ml) was treated with a solution of $Ti(OiPr)_4$ (60.1 ml, 57.7 g, 203 mmol, 1 equiv.) in dichloromethane (250 ml) at room temperature. The reaction mixture was heated to 50 °C for 4 h, cooled to room temperature and treated with NaOH (175 g, 4.37 mol) in water (800 ml). The reaction was vigorously stirred overnight, and then filtered over Celite® (2 cm). The phases were separated and the aqueous phase was extracted with dichloromethane (2x 300 ml). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Diol **228** (32.1 g, 189 mmol, 93%) was obtained as a pink liquid and was used without further purification.

R_f = 0.25 (pentane/ethyl acetate = 2:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.15 (t, *J* = 1.2 Hz, 1H), 5.11 (dddd, *J* = 7.0, 5.5, 2.9, 1.4 Hz, 1H), 4.99 (d, *J* = 1.5 Hz, 1H), 4.20 (dd, *J* = 7.3, 3.3 Hz, 1H), 3.70 (dd, *J* = 11.2, 3.4 Hz, 1H), 3.54 (dd, *J* = 11.3, 7.2 Hz, 1H), 2.19 – 2.14 (m, 2H), 2.12 – 2.07 (m, 1H), 2.01 (dt, *J* = 15.4, 7.6 Hz, 1H), 1.69 (q, *J* = 1.3 Hz, 3H), 1.61 (d, *J* = 1.3 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 148.4, 132.4, 123.8, 111.1, 75.2, 65.7, 32.7, 26.8, 25.8, 17.9; **IR**: ṽ = 3358, 2924, 1648, 1446, 1376, 1066, 905, 731 cm^{-1}.

Mass spectrometry of the compound was not successful.

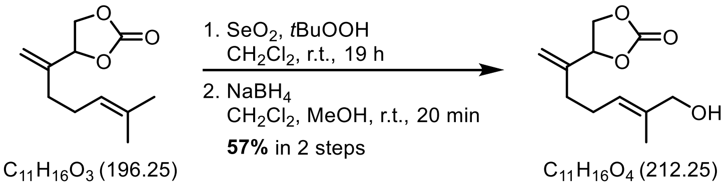
4-(6-methylhepta-1,5-dien-2-yl)-1,3-dioxolan-2-one 229



A solution of diol **228** (32.1 g, 188 mmol, 1 equiv.) in dimethyl carbonate (19.8 mL, 21.2 g, 235 mmol, 1.25 equiv.) was treated with K_2CO_3 (260 mg, 1.88 mmol, 1 mol%) at room temperature. The reaction mixture was heated to 100 °C while constantly removing MeOH via distillation. After 2 h at 100 °C the reaction was cooled to room temperature and remaining dimethyl carbonate was removed under reduced pressure. The crude product was distilled under reduced pressure to give carbonate **229** (30.4 g, 143 mmol, 76% in 2 steps) as a colorless liquid.

b.p.: 96 °C at 1.8x10^{-3} mbar, 145 °C bath temperature; **R$_f$** = 0.6 (pentane/ethyl acetate = 5:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.21 (d, *J* = 1.1 Hz, 1H), 5.14 – 5.01 (m, 3H), 4.56 (t, *J* = 8.5 Hz, 1H), 4.18 (dd, *J* = 8.5, 7.5 Hz, 1H), 2.19 (tt, *J* = 14.8, 7.5 Hz, 2H), 2.11 (dt, *J* = 15.2, 7.4 Hz, 1H), 2.06 – 1.99 (m, 1H), 1.69 (t, *J* = 1.4 Hz, 3H), 1.61 (d, *J* = 1.3 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 155.0, 143.4, 133.0, 123.0, 114.0, 79.0, 68.7, 30.550, 26.1, 25.8, 17.9; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{11}H_{16}NaO_3$, 219.0992; found: 219.1004; **IR**: ṽ = 2967, 2916, 1790, 1378, 1159, 1073, 912, 770 cm^{-1}.

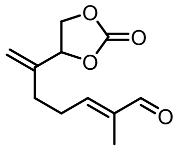
(*E*)-4-(7-hydroxy-6-methylhepta-1,5-dien-2-yl)-1,3-dioxolan-2-one 230



A solution of carbonate **229** (6.71 g, 34.2 mmol, 1 equiv.) in dichloromethane (11.4 mL) was treated with SeO_2 (379 mg, 3.42 mmol, 10 mol%). *t*BuOOH (70 wt% in water, 14.0 mL, 13.2 g, 103 mmol, 3 equiv.) was added dropwise while cooling the reaction mixture in a water bath. After 30 min at room temperature the reaction mixture was refluxed for 18 h. After cooling to room temperature, dichloromethane (30 mL) and saturated aqueous $NaHCO_3$-solution (30 mL) were added, the phases were separated and the aqueous phase was extracted with dichloromethane (3x 30 mL). The combined organic phases were dried over MgSO4, filtered and the solvent was removed under reduced pressure. The crude mixture was redissolved in MeOH (175 mL) and dichloromethane (175 mL). $NaBH_4$ (657 mg, 50 mol%) was added in 3 portions over 10 min and the reaction mixture was stirred for additional 10 min. Saturated aqueous NH_4Cl-solution (150 mL) was added at 0 °C, the phases were separated and the aqueous phase was extracted with dichloromethane (3x 75 mL). The combined organic phases were dried over MgSO4, filtered and the solvent was removed under reduced pressure. The crude product was purified by bulb-to-bulb distillation ($3.5x10^{-3}$ mbar, 210 °C) to give allylic alcohol **230** (4.14 g, 19.5 mmol, 57% in 2 steps) as a colorless oil.

R_f = 0.3 (pentane/ethyl acetate = 1:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.40 (tq, *J* = 7.0, 1.4 Hz, 1H), 5.27 – 5.20 (m, 1H), 5.16 – 5.02 (m, 2H), 4.58 (t, *J* = 8.5 Hz, 1H), 4.19 (dd, *J* = 8.5, 7.4 Hz, 1H), 4.01 (s, 2H), 2.31 – 2.23 (m, *J* = 7.3 Hz, 2H), 2.18 – 2.13 (m, 1H), 2.09 (dt, *J* = 15.7, 7.8 Hz, 1H), 1.67 (d, *J* = 1.2 Hz, 3H), 1.42 (s, 1H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.9, 143.2, 136.3, 124.1, 114.5, 79.0, 68.7, 68.6, 30.1, 25.7, 13.9; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{16}NaO_4$, 235.0941; found: 235.0946; $[M + K]^+$ calcd for $C_{11}H_{16}KO_4$, 251.0681; found: 251.0702; **IR**: ṽ = 3362, 2917, 2850, 1786, 1381 cm^{-1}.

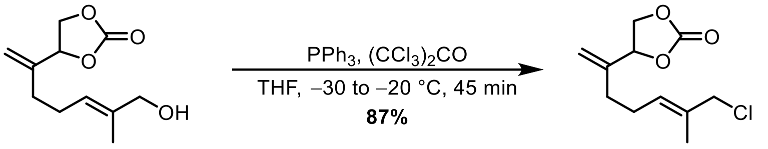
The intermediate aldehyde **SI-7** could be obtained after the Riley oxidation by column chromatography (25% yield)



$C_{11}H_{14}O_4$ (210.23)

R$_f$ = 0.5 (pentane/ethyl acetate = 1:1), UV-active, $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 9.39 (s, 1H), 6.44 (t, *J* = 7.1 Hz, 1H), 5.27 (s, 1H), 5.15 (t, *J* = 8.0 Hz, 1H), 5.13 (s, 1H), 4.60 (t, *J* = 8.5 Hz, 1H), 4.20 (t, *J* = 8.0 Hz, 1H), 2.64 – 2.46 (m, *J* = 7.6 Hz, 2H), 2.31 (dt, *J* = 15.4, 7.5 Hz, 1H), 2.25 (dt, *J* = 16.0, 7.8 Hz, 1H), 1.75 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 195.0, 154.7, 152.0, 142.2, 140.3, 115.3, 78.8, 68.5, 28.8, 26.8, 9.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_4$, 233.0785; found: 233.0790; **IR**: ṽ = 3430, 2917, 2850, 1788, 1167, 1074 cm^{-1}.

(*E*)-4-(7-chloro-6-methylhepta-1,5-dien-2-yl)-1,3-dioxolan-2-one 225

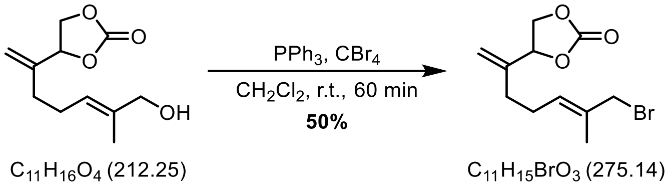


$C_{11}H_{16}O_4$ (212.25) $C_{11}H_{15}ClO_3$ (230.69)

A solution of allylic alcohol **230** (18.0 mg, 85 µmol, 1 equiv.) in THF (0.2 mL) was treated with PPh_3 (33.4 mg, 127 µmol, 1.5 equiv.) at –30 °C. After 10 min at –30 °C hexachloro acetone (19.3 µL, 33.7 mg, 127 µmol, 1.5 equiv.) was added dropwise and the solution was warmed to –20 °C over 45 min. Saturated aqueous NH_4Cl-solution (1 mL) and EtOAc (1 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 5:1) allylic chloride **225** (17.1 mg, 74 µmol, 87%) was obtained as a colorless oil.

b.p.: 200 °C at $6x10^{-3}$ mbar; **R$_f$** = 0.4 (pentane/ethyl acetate = 4:1), $KMnO_4$; **^{1}H NMR** (700 MHz, Chloroform-d) δ 5.53 – 5.46 (m, 1H), 5.24 (q, *J* = 1.0 Hz, 1H), 5.13 – 5.08 (m, 2H), 4.58 (t, *J* = 8.5 Hz, 1H), 4.18 (dd, *J* = 8.6, 7.5 Hz, 1H), 4.00 (d, *J* = 0.9 Hz, 2H), 2.27 (tq, *J* = 15.2, 7.6 Hz, 2H), 2.19 – 2.13 (m, 1H), 2.09 (dt, *J* = 15.7, 7.7 Hz, 1H), 1.75 (q, *J* = 1.0 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.9, 142.8, 133.3, 128.9, 114.6, 78.9, 68.6, 52.1, 29.7, 26.0, 14.4; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{11}H_{15}ClNaO_3$, 253.0602; found: 253.0610; [M + K]$^+$ calcd for $C_{11}H_{15}ClKO_3$, 269.0342; found: 269.0420; **IR**: ṽ = 2919, 1792, 1163, 1074, 916, 750 cm^{-1}.

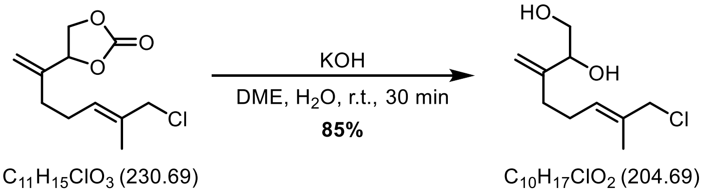
(*E*)-4-(7-bromo-6-methylhepta-1,5-dien-2-yl)-1,3-dioxolan-2-one 231



A solution of allylic alcohol **230** (200 mg, 942 µmol, 1 equiv.) in dichloromethane (3 mL) was treated with PPh_3 (297 mg, 1.13 mmol, 1.2 equiv.) at 0 °C. After 5 min at room temperature CBr_4 (375 mg, 1.13 mmol, 1.2 equiv.) was added and the reaction mixture was stirred for 60 min. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 5:1) to give allylic bromide **231** (130 mg, 471 µmol, 50%) as a colorless oil.

R_f = 0.4 (pentane/ethyl acetate = 4:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.57 (t, *J* = 7.1 Hz, 1H), 5.24 (d, *J* = 1.1 Hz, 1H), 5.13 – 5.10 (m, 2H), 4.58 (t, *J* = 8.5 Hz, 1H), 4.19 (dd, *J* = 8.6, 7.4 Hz, 1H), 3.95 (s, 2H), 2.31 – 2.21 (m, 2H), 2.17 (dt, *J* = 15.1, 7.5 Hz, 1H), 2.09 (dt, *J* = 15.6, 7.7 Hz, 1H), 1.78 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.8, 142.8, 133.6, 129.4, 114.7, 78.9, 68.6, 41.2, 29.6, 26.3, 15.0; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{11}H_{15}BrNaO_3$, 297.0097; found: 297.0114; **IR**: ṽ = 2919, 1791, 1379, 1161, 1073, 749 cm^{-1}.

(*E*)-8-chloro-7-methyl-3-methyleneoct-6-ene-1,2-diol 232

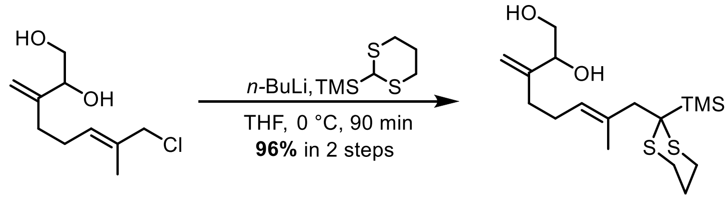


A solution of allylic chloride **225** (180 mg, 780 µmol, 1 equiv.) in 1,2-dimethoxyethane (15.6 mL) was treated with aqueous KOH-solution (2 M, 10.4 mL) at room temperature and the reaction mixture was stirred for 30 min. Dichloromethane (30 mL) and water (20 mL) were added, the phases were separated and the aqueous phase was extracted with dichloromethane (2x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. Diol **232** was obtained as a yellow oil (135 mg, 663 µmol, 85%). The crude product was used without further purification.

R_f = 0.3 (pentane/ethyl acetate = 1:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.53 (t, *J* = 7.1 Hz, 1H), 5.17 (s, 1H), 4.99 (s, 1H), 4.20 (dd, *J* = 7.5, 3.3 Hz, 1H), 4.01 (s, 2H), 3.70 (dd, *J* = 11.2, 3.4 Hz, 1H), 3.54 (dd, *J* = 11.2, 7.3 Hz, 1H), 2.24 (q, *J* = 7.7 Hz, 2H), 2.15 (dt, *J* = 15.5, 7.7 Hz, 1H), 2.06 (dt, *J* = 15.5, 7.7 Hz, 1H), 1.75 (s, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 147.8, 132.6, 130.0, 111.5, 75.1, 65.7, 52.4, 31.9, 26.7, 14.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{17}ClNaO_2$, 227.0810; found: 221.1530; **IR**: ṽ = 3372, 2924, 2358, 1648, 1439, 1263, 1066, 904 cm^{-1}.

(*E*)-7-methyl-3-methylene-8-(2-(trimethylsilyl)-1,3-dithian-2-yl)oct-6-ene-1,2-diol

233



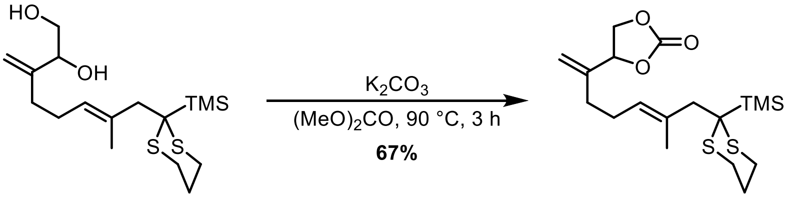
$C_{10}H_{17}ClO_2$ (204.69)

$C_{17}H_{32}O_2S_2Si$ (360.65)

A solution of dithiane **201** (470 mg, 2.44 mmol, 4. equiv) in THF (8 mL) was treated with *n*-BuLi (2.5 M in hexanes, 806 µL, 2.02 mmol, 3.3 equiv.) at 0 °C. After 30 min at 0 °C a solution of crude diol **232** (125 mg, 611 µmol, 1 equiv.) in THF (1.8 mL) was added. After stirring for 60 min at 0 °C, saturated aqueous NH_4Cl-solution (10 mL) and EtOAc (10 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 2:1) dithiane **233** (212 mg, 587 µmol, 96% in 2 steps) was obtained as a colorless oil.

R_f = 0.4 (pentane/ethyl acetate = 1:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.38 (t, *J* = 6.9 Hz, 1H), 5.16 (s, 1H), 5.00 (s, 1H), 4.21 (dd, *J* = 7.6, 2.9 Hz, 1H), 3.70 (dd, *J* = 11.2, 3.4 Hz, 1H), 3.54 (dd, *J* = 11.3, 7.3 Hz, 1H), 3.17 – 2.99 (m, 2H), 2.95 (s, 2H), 2.49 (dt, *J* = 14.1, 4.1 Hz, 2H), 2.23 – 2.09 (m, 3H), 2.08 – 2.02 (m, 2H), 1.92 – 1.85 (m, 4H), 0.19 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 148.3, 134.7, 129.5, 111.2, 75.1, 65.8, 47.2, 38.7, 32.1, 26.9, 25.0, 24.1, 18.2, -2.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{32}NaO_2S_2Si$, 383.1506; found: 383.1529; $[M + K]^+$ calcd for $C_{17}H_{32}KO_2S_2Si$, 399.1245; found: 399.3041; **IR**: $\tilde{\nu}$ = 3373, 2904, 1648, 1423, 1246, 842 cm^{-1}.

(*E*)-4-(6-methyl-7-(2-(trimethylsilyl)-1,3-dithian-2-yl)hepta-1,5-dien-2-yl)-1,3-dioxolan-2-one 234

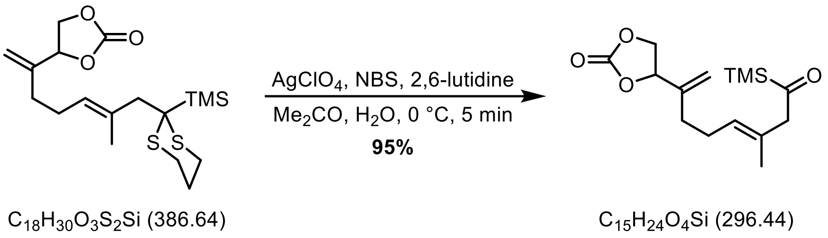


$C_{17}H_{32}O_2S_2Si$ (360.65) $C_{18}H_{30}O_3S_2Si$ (386.64)

A solution of dithiane **233** (50 mg, 139 µmol, 1 equiv.) in dimethyl carbonate (0.4 mL) was treated with K_2CO_3 (260 mg, 1.88 mmol) at room temperature. The reaction mixture was heated to 90 °C for 3 h. The reaction was cooled to room temperature and remaining dimethyl carbonate was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 8:1) carbonate **234** (36 mg, 93 µmol, 67%) was obtained as a colorless oil.

R$_f$ = 0.25 (pentane/ethyl acetate = 8:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.37 (td, *J* = 6.8, 1.0 Hz, 1H), 5.23 (d, *J* = 1.0 Hz, 1H), 5.15 – 5.04 (m, 2H), 4.58 (t, *J* = 8.5 Hz, 1H), 4.19 (dd, *J* = 8.5, 7.4 Hz, 1H), 3.07 (dddd, *J* = 14.9, 12.2, 2.8, 1.0 Hz, 2H), 2.95 (s, 2H), 2.50 (ddd, *J* = 14.3, 4.6, 3.3 Hz, 2H), 2.22 (td, *J* = 15.7, 15.0, 7.4 Hz, 2H), 2.15 (q, *J* = 8.0 Hz, 1H), 2.10 – 2.03 (m, 2H), 1.93 – 1.85 (m, 4H), 0.19 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.9, 143.3, 135.4, 128.5, 114.2, 78.9, 68.7, 47.2, 38.6, 30.0, 26.2, 25.0, 24.1, 18.3, -2.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{18}H_{30}NaO_3S_2Si$, 409.1298; found: 409.1312; $[M + K]^+$ calcd for $C_{18}H_{30}KO_3S_2Si$, 425.1038; found: 425.2171; **IR**: ṽ = 2900, 1797, 1423, 1245, 1073, 839 cm^{-1}.

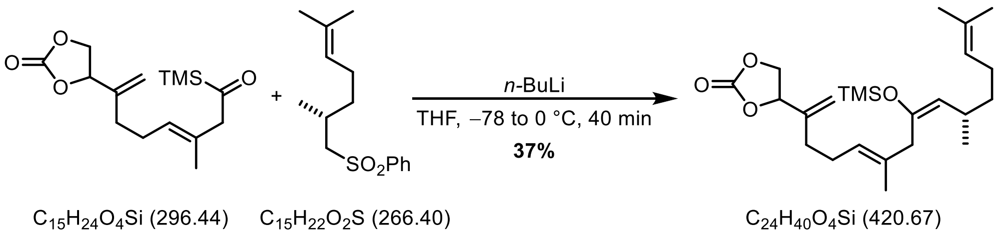
(*E*)-4-(6-methyl-8-oxo-8-(trimethylsilyl)octa-1,5-dien-2-yl)-1,3-dioxolan-2-one 224



A solution of *N*-bromo succinimide (81 mg, 453 µmol, 2 equiv.), 2,6-lutidine (158 µL, 146 mg, 1.34 mmol, 6 equiv.) and $AgClO_4$ (112 mg, 498 µmol, 2.2 equiv.) in acetone (26 mL) and water (2.8 mL) was treated with a solution of carbonate **234** (71 mg, 227 µmol, 1 equiv.) in acetone (2 mL) at 0 °C. After 10 min at 0 °C saturated aqueous $NaHCO_3$-solution (20 mL) was added. The mixture was filtered over a short pad of Celite®, and dichloromethane (20 mL) and water (20 mL) were added. The phases were separated and the aqueous phase was extracted with dichloromethane (2x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 7:1) acylsilane **224** (48 mg, 216 µmol, 95%) was obtained as a colorless oil.

R_f = 0.4 (pentane/ethyl acetate = 5:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.23 (s, 1H), 5.17 (t, *J* = 7.1 Hz, 1H), 5.14 – 5.11 (m, 2H), 4.58 (t, *J* = 8.5 Hz, 1H), 4.19 (dd, *J* = 8.5, 7.4 Hz, 1H), 3.25 (s, 2H), 2.32 – 2.21 (m, 2H), 2.15 (dt, *J* = 15.3, 6.8 Hz, 1H), 2.07 (dt, *J* = 15.7, 7.8 Hz, 1H), 1.57 (s, 3H), 0.19 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 246.0, 154.9, 143.1, 129.9, 128.1, 114.3, 78.9, 68.7, 59.0, 30.2, 26.2, 17.1, -2.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{24}NaO_4Si$, 319.1337; found: 319.1344; $[M + K]^+$ calcd for $C_{15}H_{24}KO_4Si$, 335.1076; found: 335.1113; **IR**: ṽ = 2917, 2850, 1793, 1629, 844, 751 cm^{-1}.

4-((R,5E,8E)-6,10,14-trimethyl-8-((trimethylsilyl)oxy)pentadeca-1,5,8,13-tetraen-2-yl)-1,3-dioxolan-2-one 222



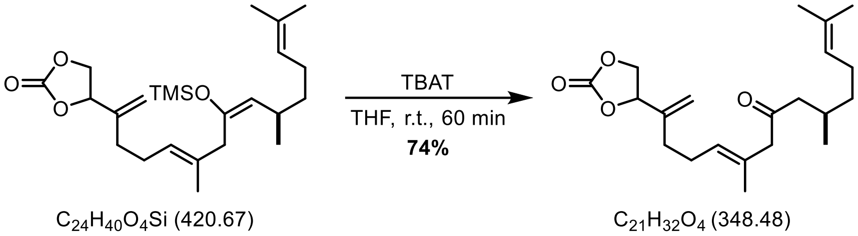
A solution of sulfone **198** (71.0 mg, 267 µmol, 1 equiv.) in Et_2O/THF (1:1, 0.8 mL) was at –78 °C treated with *n*-BuLi (2.5 M in hexanes, 112 µL, 280 µmol, 1.05 equiv.). The reaction mixture was stirred for 10 min at –78 °C. A solution of acylsilane **224** (60 mg, 267 µmol, 1 equiv.) in Et_2O/THF (0.5 mL) was added, the reaction mixture was stirred for 20 min at –78 °C and then warmed to 0 °C over 20 min. Saturated aqueous NH_4Cl (1 mL) and EtOAc (1 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 13:1) silyl enol ether **222** was obtained as a yellow oil (4.1 mg, 88 µmol, 37%, ca. 60% pure).

R_f = 0.7 (pentane/ethyl acetate = 5:1), vanillin; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.22 (s, 1H), 5.20 – 5.14 (m, 1H), 5.14 – 5.07 (m, 3H), 4.56 (t, *J* = 8.5 Hz, 1H), 4.48 (d, *J* = 10.0 Hz, 1H), 4.18 (t, *J* = 8.0 Hz, 1H), 2.79 (d, *J* = 14.5 Hz, 1H), 2.64 (d, *J* = 14.3 Hz, 1H), 2.17 – 2.00 (m, 4H), 1.68 (s, 3H), 1.62 (s, 3H), 1.59 (s, 3H), 1.48 – 1.39 (m, 1H), 1.32 – 1.17 (m, 4H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.15 (s, 9H); **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{24}H_{40}NaO_4Si$, 443.2588; found: 443.2591; $[M + K]^+$ calcd for $C_{15}H_{24}KO_4Si$, 335.1076; found: 335.1113.

Due to the impurity of the obtained product, no ^{13}C NMR and IR spectra were recorded.

4-((*R*,*E*)-6,10,14-trimethyl-8-oxopentadeca-1,5,13-trien-2-yl)-1,3-dioxolan-2-one

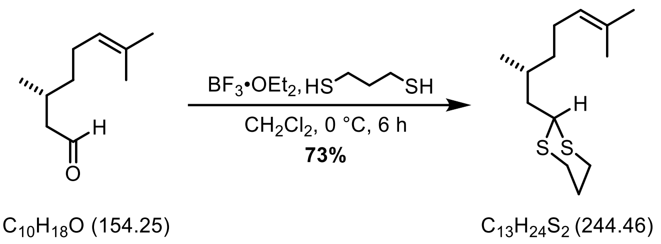
245



A solution of silylenol ether **245** (22 mg, 52 µmol, 1 equiv.) in THF (0.1 mL) was treated with TBAT (28.2 mg, 52 µmol, 1 equiv.) at room temperature. The reaction mixture was stirred for 60 min at room temperature. Saturated aqueous $NaHCO_3$-solution (1 mL) and EtOAc (1 mL) were added. the phases were separated and the aqueous phase was extracted with EtOAc (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 5:1) ketone **245** (13 mg, 38 µmol, 74%) was obtained as a colorless oil.

R_f = 0.5 (pentane/ethyl acetate = 3:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.23 – 5.20 (m, 2H), 5.14 – 5.11 (m, 2H), 5.08 (tt, *J* = 7.0, 1.4 Hz, 1H), 4.58 (t, *J* = 8.4 Hz, 1H), 4.19 (dd, *J* = 8.6, 7.5 Hz, 1H), 3.04 (s, 2H), 2.39 (dd, *J* = 16.1, 5.6 Hz, 1H), 2.27 (p, *J* = 7.5 Hz, 2H), 2.23 (dd, *J* = 16.0, 8.1 Hz, 1H), 2.16 (dt, *J* = 15.2, 7.4 Hz, 1H), 2.08 (dt, *J* = 15.7, 7.7 Hz, 1H), 2.03 – 1.90 (m, 3H), 1.68 (s, 3H), 1.63 (s, 3H), 1.59 (s, 3H), 1.30 (ddt, *J* = 13.4, 9.6, 6.1 Hz, 1H), 1.18 (dddd, *J* = 13.5, 9.4, 7.8, 5.8 Hz, 1H), 0.88 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 209.3, 154.9, 143.1, 131.7, 130.7, 127.9, 124.5, 114.3, 78.9, 68.7, 54.2, 49.6, 37.1, 30.2, 29.0, 26.2, 25.9, 25.6, 19.9, 17.8, 16.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{32}NaO_4$, 371.2193; found: 371.2193; $[M + K]^+$ calcd for $C_{21}H_{32}KO_4$, 387.1933; found: 387.1923; **IR**: ṽ = 2917, 2851, 2359, 2314, 1793, 1162, 1073, 753 cm^{-1}.

(*R*)-2-(2,6-dimethylhept-5-en-1-yl)-1,3-dithiane 236

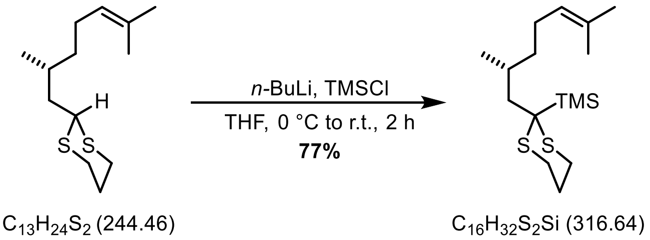


A solution of (*R*)-citronellal **199** (1.00 g, 6.48 mmol, 1 equiv.) and 1,3-propanedithiol (1.95 mL, 2.11 g, 19.4 mmol, 3 equiv.) in dichloromethane (65 mL) was treated with $BF_3·OEt_2$ (4.86 mL, 5.47 g, 38.5 mmol, 6 equiv.) at 0 °C. The reaction mixture was stirred for 6 h at 0 °C, aqueous NaOH-solution (1 M, 30 mL) was added and the phases were separated. The aqueous phase was extracted with dichloromethane (2x 30 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 70:1) the dithiane **236** (1.16 mg, 4.73 mmol, 73%) was obtained as a colorless oil.

R_f = 0.8 (pentane), $KMnO_4$; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.09 (tt, *J* = 7.1, 1.4 Hz, 1H), 4.09 (dd, *J* = 8.5, 6.1 Hz, 1H), 2.93 – 2.77 (m, 3H), 2.69 – 2.57 (m, 1H), 2.11 (dtt, *J* = 14.5, 4.9, 2.3 Hz, 1H), 1.93 – 1.70 (m, 4H), 1.67 (s, 3H), 1.60 (s, 3H), 1.54 – 1.45 (m, 1H), 1.40 – 1.29 (m, 2H), 1.21 – 1.10 (m, 1H), 0.91 (d, *J* = 6.6 Hz, 3H).

The spectroscopic data agrees with previously published results.[197]

(*R*)-(2-(2,6-dimethylhept-5-en-1-yl)-1,3-dithian-2-yl)trimethylsilane 237

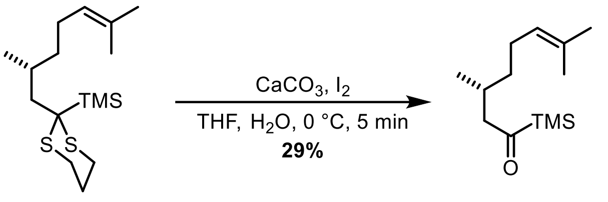


A solution of dithiane **236** (175 mg, 716 µmol, 1 equiv.) in THF (0.72 mL) was treated with *n*-BuLi (2.5 M in hexanes, 315 µL, 787 µmol, 1.1 equiv.) at 0 °C and stirred for 30 min. TMSCl (100 µL, 86 mg, 787 µmol, 1.1 equiv.) was added and the reaction mixture was warmed to room temperature over 90 min. Saturated aqueous NH_4Cl-solution (2 mL) and EtOAc (2 mL) were added. the phases were separated and the aqueous phase was extracted with EtOAc (3x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 80:1) dithiane **237** (175 mg, 551 µmol, 77%, ca. 90% pure) was obtained as a yellow oil.

R_f = 0.3 (pentane), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.12 (tt, *J* = 7.3, 1.4 Hz, 1H), 3.05 – 2.98 (m, 2H), 2.51 – 2.44 (m, 2H), 2.15 (dd, *J* = 14.9, 4.0 Hz, 1H), 2.11 (dd, *J* = 14.9, 5.5 Hz, 1H), 2.05 – 2.00 (m, 2H), 1.97 – 1.93 (m, 1H), 1.93 – 1.88 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.58 – 1.56 (m, 1H), 1.22 (ddd, *J* = 14.1, 9.2, 4.9 Hz, 1H), 1.06 (d, *J* = 6.6 Hz, 3H), 0.21 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 131.5, 124.9, 44.7, 39.4, 39.1, 31.5, 25.9, 25.7, 25.2, 24.1, 24.0, 21.4, 17.8, -2.1; **IR**: ṽ = 2951, 2921, 1450, 1375, 1247, 840 cm^{-1}.

Mass spectrometry of the compound was not successful.

(*R*)-3,7-dimethyl-1-(trimethylsilyl)oct-6-en-1-one 235

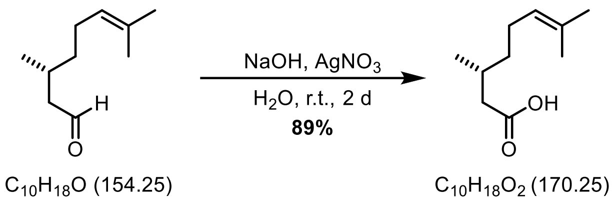


$C_{16}H_{32}S_2Si$ (316.64) $C_{13}H_{26}OSi$ (226.44)

A solution of dithiane **237** (58 mg, 183 µmol, 1 equiv.) and $CaCO_3$ (147 mg, 1.47 mmol, 8 equiv.) in THF/H_2O (4:1, 0.6 mL) was treated with a solution of I_2 (279 mg, 1.10 mmol, 6 equiv.) in THF/H_2O (4:1, 0.6 mL) at 0 °C. After 5 min saturated aqueous $Na_2S_2O_3$-solution (1 mL) and EtOAc (1 mL) were added. The phases were separated and the aqueous phase was extracted with EtOAc (3x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 25:1) the acylsilane **235** (12 mg, 5 µmol, 29%) was obtained as a colorless oil.

R_f = 0.3 (pentane/ethyl acetate = 25:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.17 – 5.02 (m, 1H), 2.56 (dd, *J* = 16.1, 5.5 Hz, 1H), 2.42 (dd, *J* = 16.1, 7.9 Hz, 1H), 2.08 (h, *J* = 6.9 Hz, 1H), 2.02 – 1.89 (m, 2H), 1.68 – 1.66 (m, 3H), 1.59 (d, *J* = 1.5 Hz, 3H), 1.27 – 1.21 (m, 1H), 1.20 – 1.04 (m, 1H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.19 (s, 9H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 249.2, 131.6, 124.6, 56.1, 37.3, 27.4, 25.8, 25.7, 20.1, 17.8, -3.0; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{26}NaOSi$, 249.1646; found: 249.1649; **IR**: ṽ = 2919, 2851, 1731, 1456, 1214, 843, 754 cm^{-1}.

(R)-citronellic acid 182

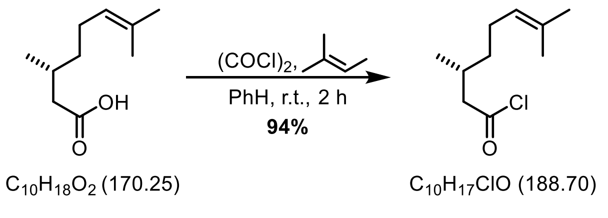


A solution of NaOH (1.04 g, 25.9 mmol, 4 equiv.) in H_2O (4.5 mL) was treated with $AgNO_3$ (1.99 g, 11.7 mmol, 1.8 equiv.) at room temperature. After 30 min at room temperature (*R*)-citronellal **199** (1.00 g, 6.48 mmol, 1 equiv.) was added dropwise. The reaction mixture was stirred for 2 d at room temperature, solids were removed by filtration and the remaining solution was acidified with concentrated HCl (37%) and dichloromethane (20 mL). the phases were separated and the aqueous phase was extracted with dichloromethane (3x 20 mL). The crude product was purified by distillation under reduced pressure to give (*R*)-citronellic acid **182** (980 mg, 5.77 mmol, 89%) as a colorless oil.

Bp.: 86 °C at 2.3x10^{-2} mbar; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.95 (s$_{br}$, 1H), 5.09 (dddd, *J* = 7.1, 5.6, 2.9, 1.5 Hz, 1H), 2.37 (dd, *J* = 15.0, 5.8 Hz, 1H), 2.15 (dd, *J* = 15.0, 8.3 Hz, 1H), 2.05 – 1.93 (m, 3H), 1.68 (s, 3H), 1.60 (s, 3H), 1.44 – 1.33 (m, 1H), 1.30 – 1.21 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H); **$[\alpha]_D^{22}$** = +6.76° (neat).

The spectroscopic data agrees with previously published results.[218]

(*R*)-3,7-dimethyloct-6-enoyl chloride 241

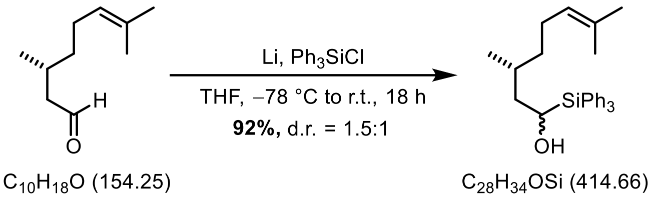


A solution of citronellic acid **182** (500 mg, 2.94 mol, 1 equiv.) in 2-methyl-2-butene (0.85 mL) and benzene (2.5 mL) was treated dropwise with thionyl chloride (277 µL, 410 mg, 3.23 mmol, 1.1 equiv.) at room temperature and stirred for 2 h. The solvent was removed under reduced pressure to give acid chloride **241** (520 mg, 2.76 mol, 94%) as a yellow liquid, which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (tt, *J* = 7.0, 1.4 Hz, 1H), 2.89 (dd, *J* = 16.1, 5.7 Hz, 1H), 2.68 (ddd, *J* = 16.1, 8.1, 0.6 Hz, 1H), 2.12 – 2.05 (m, 1H), 2.05 – 1.95 (m, 2H), 1.69 (t, *J* = 1.4 Hz, 3H), 1.61 (d, *J* = 1.2 Hz, 3H), 1.43 – 1.33 (m, 1H), 1.32 – 1.23 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H).

The spectroscopic data agrees with previous published results.[200]

(3*R*)-3,7-dimethyl-1-(triphenylsilyl)oct-6-en-1-ol 242

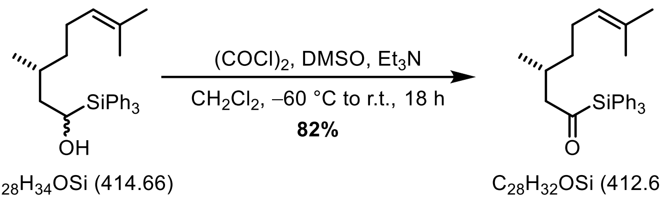


A mixture of freshly cut lithium (2.98 g, 430 mmol, 8.5 equiv.) in THF (250 mL) was treated with Ph_3SiCl (22.4 g, 75.8 mmol, 1.5 equiv.). The reaction mixture was refluxed for 3 h, to form a brown suspension and then cooled to room temperature. In a separate flask a solution of (*R*)-citronellal **199** (7.80 g, 50.5 mmol, 1 equiv) in THF (140 mL) was cooled to –78 °C and the freshly formed Li-reagent was added *via* transfer cannula over 30 min. The reaction mixture was warmed over night to room temperature and then quenched with saturated aqueous NH_4Cl-solution (200 mL) and EtOAc (200 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3x 200 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 90:1) alcohol **242** (19.3 g, 46.5 mmol, 92%, 2 diastereomers, inseparable mixture, d.r. = 1.5:1) was obtained as a colorless oil.

R_f = 0.3 (pentane/ethyl acetate = ca. 60:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.63 – 7.60 (m, 6H), 7.45 – 7.42 (m, 3H), 7.40 – 7.37 (m, 6H), 5.10 – 5.04 (m, 1H), 4.39 – 4.35 (m, 1H), 1.98 (s, 1H), 1.90 (s, 1H), 1.84 – 1.73 (m, 1H), 1.72 – 1.60 (m, 4H), 1.57 (d, *J* = 1.2 Hz, 3H), 1.56 – 1.48 (m, 4H), 1.45 – 1.39 (m, 1H), 1.30 – 1.24 (m, 1H), 1.16 (dd, *J* = 35.6, 5.6 Hz, 1H), 1.04 (dtd, *J* = 14.0, 9.3, 5.3 Hz, 1H), 0.93 – 0.90 (m, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 136.3,* 133.3,* 131.4, 131.3, 129.9,* 128.2,* 125.0, 124.9, 62.3, 61.9, 41.3, 41.1, 38.2, 35.4, 29.6, 28.9, 25.9, 25.84, 25.78, 25.5, 20.8, 18.5, 17.81, 17.76; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{28}H_{34}NaOSi$, 437.2272; found: 437.2257; $[M + K]^+$ calcd for $C_{28}H_{34}KOSi$, 453.2011; found: 453.1999; **IR**: ṽ = 2918, 2850, 1428, 1215, 1109, 753 cm^{-1}.

*Signals with double intensity.

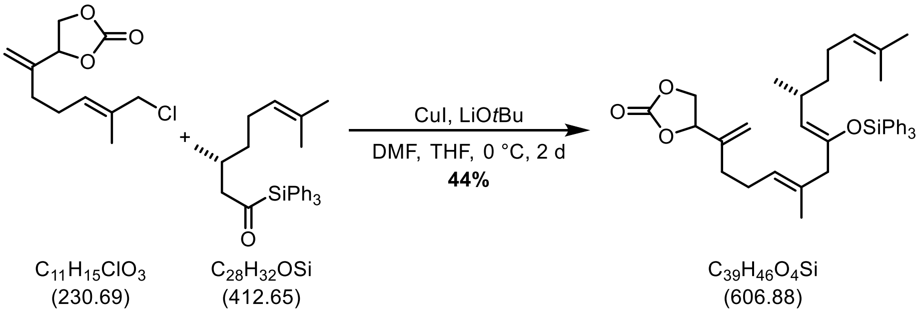
(*R*)-3,7-dimethyl-1-(triphenylsilyl)oct-6-en-1-one 240



A solution of oxalyl chloride (244 µL, 361 mg, 2.85 mmol, 2 equiv.) in dichloromethane (6.3 mL) was treated with DMSO (404 µL, 445 mg, 5.69 mmol, 4 equiv.) at –60 °C. The reaction mixture was stirred for 10 min and treated with a solution of alcohol **242** (590 mg, 1.42 mmol, 1 equiv.) in dichloromethane (1.8 mL). The reaction mixture was stirred for additional 30 min at –60 °C, treated with Et_3N (986 µL, 720 mg, 7.11 mmol, 5 equiv.) and was warmed over night to room temperature. Aqueous HCl-solution (1 M, 10 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (10 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 100:1) acylsilane **240** (480 mg, 1.16 mmol, 82%) was obtained as a colorless oil.

$\mathbf{R_f}$ = 0.5 (pentane/ethyl acetate = 60:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 6H), 7.50 – 7.46 (m, 3H), 7.42 – 7.36 (m, 6H), 4.99 (ddd, *J* = 8.3, 5.1, 1.6 Hz, 1H), 2.72 (dd, *J* = 16.8, 5.2 Hz, 1H), 2.58 (dd, *J* = 16.8, 7.8 Hz, 1H), 2.09 – 2.00 (m, 1H), 1.89 – 1.77 (m, 2H), 1.65 (d, *J* = 1.5 Hz, 3H), 1.53 (d, *J* = 1.3 Hz, 3H), 1.19 (ddt, *J* = 12.3, 9.5, 6.2 Hz, 1H), 1.07 (dddd, *J* = 13.5, 9.4, 7.9, 5.7 Hz, 1H), 0.79 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 243.5, 136.3, 131.6, 131.4, 130.4, 128.3, 124.6, 58.2, 37.1, 27.3, 25.8, 25.6, 19.9, 17.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{28}H_{32}NaOSi$, 435.2115; found: 435.2093; $[M + K]^+$ calcd for $C_{28}H_{32}KOSi$, 451.1854; found: 451.1951; $\mathbf{[\alpha]_D^{22}}$ = +18.7° (c = 1.00); **IR**: ṽ = 2960, 2911, 1642, 1428, 1109, 754, 698 cm^{-1}.

4-((*R*,5*E*,8*Z*)-6,10,14-trimethyl-8-((triphenylsilyl)oxy)pentadeca-1,5,8,13-tetraen-2-yl)-1,3-dioxolan-2-one 243

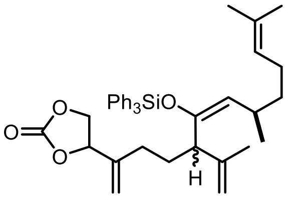


A suspension of CuI (1.32 g, 6.93 mmol, 5 equiv.) in DMF (10.5 mL) was treated with LiO*t*Bu (1 M in THF, 3.47 mL, 3.47 mmol, 2.5 equiv.) at room temperature and stirred for 30 min. The reaction mixture was cooled to 0 °C and treated dropwise with a solution of acylsilane **240** (1.43 g, 3.47 mmol, 2 equiv.) in DMF (11.6 mL). After stirring for 22 h at 0 °C allyl chloride **225** (320 mg, 1.39 mmol, 1 equiv.) was added and the reaction mixture was stirred for additional 24 h at 0 °C. The solvent was removed under reduced pressure and the crude product was redissolved in dichloromethane. The resulting suspension was filtered over silica gel, using Et_2O as eluent and the solvent was removed under reduced pressure. After column chromatography (silica gel, pentane/ethyl acetate 30:1, then 14:1) silylenol ether **243** (371 mg, 312 µmol, 44%) was obtained as a colorless oil.

R$_f$ = 0.45 (pentane/ethyl acetate = 6:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 6H), 7.49 – 7.44 (m, 3H), 7.42 – 7.37 (m, 6H), 5.20 (s, 1H), 5.10 – 5.05 (m, 3H), 4.97 (t, *J* = 7.1 Hz, 1H), 4.51 (t, *J* = 8.5 Hz, 1H), 4.27 (d, *J* = 9.5 Hz, 1H), 4.13 (t, *J* = 8.0 Hz, 1H), 2.61 (s, 2H), 2.57 (p, *J* = 7.3 Hz, 1H), 2.16 (q, *J* = 7.1 Hz, 1H), 2.05 (dt, *J* = 15.3, 7.5 Hz, 1H), 1.95 (dd, *J* = 15.8, 8.0 Hz, 1H), 1.89 – 1.81 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.47 (s, 3H), 1.21 – 1.10 (m, 3H), 0.73 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.9, 146.9, 143.3, 135.6, 134.6, 133.2, 131.0, 130.2, 127.9, 125.4, 125.2, 117.7, 114.0, 78.9, 68.7, 46.6, 38.0, 30.3, 30.1, 26.3, 26.1, 25.9, 20.9, 17.8, 16.1; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{39}H_{46}NaO_4Si$, 629.3058; found: 629.3073; $[M + K]^+$ calcd for $C_{39}H_{46}KO_4Si$, 645.2797; found: 645.3011; **IR:** ṽ = 2917, 2850, 1799, 1162, 1115, 1075, 754 cm^{-1}.

4-((8*R,E*)-8,12-dimethyl-5-(prop-1-en-2-yl)-6-((triphenylsilyl)oxy)trideca-1,6,11-trien-2-yl)-1,3-dioxolan-2-one 244

Additionally, up to 37% of the corresponding S_N2' product was obtained as an inseparable mixture of diastereomers (d.r. = 3:2).



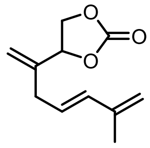
$C_{39}H_{46}O_4Si$ (606.88)

R$_f$ = 0.55 (pentane/ethyl acetate = 6:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 6H), 7.44 (t, *J* = 7.4 Hz, 3H), 7.39 – 7.35 (m, 6H), 5.10 (d, *J* = 14.1 Hz, 1H), 5.05 – 4.94 (m, 1H), 4.94 – 4.87 (m, 2H), 4.81 (d, *J* = 6.2 Hz, 1H), 4.59 – 4.50 (m, 1H), 4.43 (tdd, *J* = 8.3, 5.7, 2.7 Hz, 1H), 4.35 – 4.25 (m, 1H), 4.05 – 3.93 (m, 1H), 2.51 – 2.43 (m, 2H), 1.86 – 1.74 (m, 2H), 1.73 – 1.67 (m, 2H), 1.65 – 1.61 (m, 3H), 1.57 (s, 3H), 1.55 (s, 3H), 1.51 (dq, *J* = 20.4, 8.2, 7.4 Hz, 1H), 1.19 – 1.08 (m, 2H), 1.05 (ddd, *J* = 11.7, 6.8, 3.1 Hz, 1H), 0.76 – 0.53 (m, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 154.9, 154.8, 149.40, 149.38, 144.48, 144.46, 143.4, 143.3, 135.7,* 134.5,* 131.1, 130.0, 130.3,* 127.9,* 125.07, 125.06, 116.4, 116.3, 113.5, 113.3, 113.2, 113.1, 78.8, 78.6, 68.7, 68.6, 52.9, 52.8, 34.0, 37.8, 30.2,* 29.0, 28.8, 28.5, 28.3, 26.1,* 25.8,* 20.6, 20.54, 20.45, 20.1, 17.8*; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{39}H_{46}NaO_4Si$, 629.3058; found: 629.3071.

*Signals with double intensity.
Due to the inseparable mixture of diastereomers, no IR spectrum was recorded.

(*E*)-4-(6-methylhepta-1,4,6-trien-2-yl)-1,3-dioxolan-2-one 239

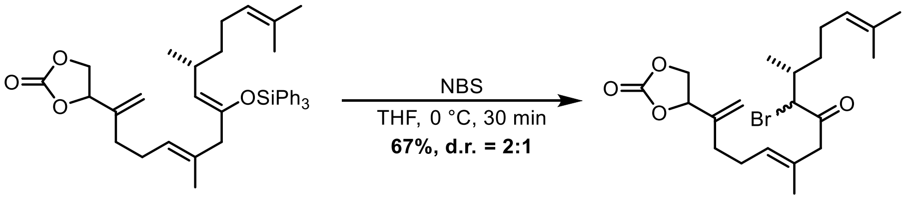
Triene **239** was obtained in quantitative yield when using allylic bromide **231** in the terpene coupling reaction.



$C_{11}H_{14}O_3$ (194.23)

R$_f$ = 0.4 (pentane/ethyl acetate = 4:1), $KMnO_4$; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.21 (d, *J* = 15.6 Hz, 1H), 5.59 (dt, *J* = 15.5, 7.1 Hz, 1H), 5.26 (d, *J* = 1.1 Hz, 1H), 5.15 – 5.11 (m, 2H), 4.96 (t, *J* = 1.7 Hz, 1H), 4.95 – 4.92 (m, 1H), 4.56 (t, *J* = 8.4 Hz, 1H), 4.21 (dd, *J* = 8.6, 7.6 Hz, 1H), 2.94 (dd, *J* = 16.2, 7.0 Hz, 1H), 2.87 (dd, *J* = 16.2, 7.2 Hz, 1H), 1.85 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.9, 142.3, 141.4, 136.3, 135.6, 127.9, 125.3, 116.5, 115.3, 78.4, 68.7, 34.7, 18.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_3$, 217.0836; found: 217.0867; $[M + K]^+$ calcd for $C_{11}H_{14}KO_3$, 233.0575; found: 233.0667, **IR**: ṽ = 3080, 3021, 1746, 1289, 1216, 841, 757 cm^{-1}.

4-((10*R*,*E*)-9-bromo-6,10,14-trimethyl-8-oxopentadeca-1,5,13-trien-2-yl)-1,3-dioxolan-2-one 246



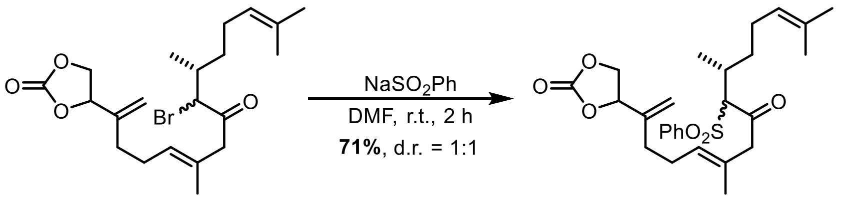
$C_{39}H_{46}O_4Si$ (606.88) $C_{21}H_{31}BrO_4$ (427.38)

A solution of silylenol ether **243** (290 mg, 478 µmol, 1 equiv.) in THF (21 mL) was treated with NBS (94 mg, 526 µmol, 1.1 equiv.) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, saturated aqueous $NaHCO_3$-solution (20 mL) and EtOAc (20 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3x 20 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 10:1) bromoketone **246** (137 mg, 320 µmol, 67%, d.r. = 2:1) was obtained as a colorless oil (80% pure).

R$_f$ = 0.4 (pentane/ethyl acetate = 5:1), $KMnO_4$; **^{1}H NMR** (700 MHz, $CDCl_3$) δ 5.30 – 5.20 (m, 3H), 5.17 – 5.03 (m, 5H), 4.58 (t, *J* = 8.5 Hz, 1H), 4.28 (d, *J* = 6.9 Hz, 1H), 4.23 – 4.13 (m, 2H), 3.39 (ddd, *J* = 16.3, 9.2, 3.0 Hz, 1H),* 3.26 (ddd, *J* = 15.8, 8.3, 3.2 Hz, 1H),* 3.00 – 2.88 (m, 1H), 2.73 – 2.64 (m, 1H), 2.31 – 2.14 (m, 6H), 2.11 – 1.95 (m, 7H), 1.68 (s, 3H), 1.66 (s, 3H), 1.60 (s, 3H), 1.05 (d, *J* = 6.5 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 202.5, 202.2, 154.97, 154.92, 143.1,* 135.6, 132.5, 132.3, 130.1, 123.0, 128.8, 128.7, 123.9, 123.6, 114.49, 114.45, 78.94, 78.92, 68.7, 61.4, 60.33, 60.32, 50.5,* 35.1, 35.0, 34.6, 34.0, 30.12, 30.08, 29.9, 26.2, 25.9,* 25.5, 24.9, 17.9, 17.1, 17.0, 16.74, 16.68; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{31}BrNaO_4$, 449.1298; found: 449.1297; **IR**: ṽ = 2917, 2850, 1794, 1716, 1165, 1074, 754 cm^{-1}.

*Signals with double intensity.

4-((9*R*,10*R*,*E*)-6,10,14-trimethyl-8-oxo-9-((phenylperoxy)thio)pentadeca-1,5,13-trien-2-yl)-1,3-dioxolan-2-one 247



$C_{21}H_{31}BrO_4$ (427.38)

$C_{27}H_{36}O_6S$ (488.64)

A solution of bromoketone **246** (130 mg, 304 µmol, 1 equiv.) in DMF (1.3 mL) was treated with $NaSO_2Ph$ (100 mg, 608 µmol, 2 equiv.) at room temperature. The reaction mixture was stirred over night at room temperature. Water (2 mL) and EtOAc (2 mL) were added, the phases were separated and the aqueous phase was extracted with EtOAc (3x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After purification by column chromatography (silica gel, pentane/ethyl acetate = 4:1) sulfone **247** (106 mg, 216 µmol, 71%, d.r. = 1:1, inseparable mixture) was obtained as a colorless oil.

R$_f$ = 0.5 (pentane/ethyl acetate = 2:1), $KMnO_4$, UV-active; **^{1}H NMR** (700 MHz, Chloroform-d) δ 7.87 – 7.82 (m, 4H), 7.69 – 7.66 (m, 2H), 7.58 – 7.54 (m, 4H), 5.24 –

5.21 (m, 2H), 5.17 – 5.08 (m, 8H), 4.99 – 4.95 (m, 1H), 4.96 – 4.92 (m, 1H), 4.61 – 4.54 (m, 2H), 4.22 – 4.16 (m, 2H), 4.13 (dd, *J* = 7.4, 1.4 Hz, 1H), 4.07 (d, *J* = 8.6 Hz, 1H), 3.25 – 3.14 (m, 5H), 2.99 – 2.86 (m, 2H), 2.74 – 2.64 (m, 2H), 2.27 – 2.22 (m, 2H), 2.21 – 2.12 (m, 3H), 1.92 – 1.84 (m, 2H), 1.77 (tdd, *J* = 11.0, 6.0, 3.5 Hz, 1H), 1.67 – 1.65 (m, 3H), 1.65 – 1.64 (m, 3H), 1.58 (s, 3H), 1.57 (s, 3H), 1.54 (s, 6H), 1.38 – 1.34 (m, 1H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.08 (dtt, *J* = 14.1, 9.6, 5.1 Hz, 2H), 0.91 (dd, *J* = 6.8, 3.1 Hz, 3H); **^{13}C NMR** (176 MHz, $CDCl_3$) δ 206.3, 201.2, 154.9,* 143.1, 138.3, 138.0, 134.27, 134.27, 132.60, 132.58, 130.4, 129.7, 129.6,* 129.33, 129.27, 129.25, 123.3, 123.2, 120.7,* 114.5, 114.4, 79.8, 78.92, 78.86, 78.2, 68.7,* 57.0, 56.3, 38.8, 35.9, 34.7, 34.0, 33.0, 32.8, 26.2, 26.1, 25.9, 25.8, 25.1, 24.9, 17.84, 17.83, 17.7, 16.8, 16.7, 16.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{27}H_{36}NaO_6S$, 511.2125; found: 511.2122; $[M + K]^+$ calcd for $C_{27}H_{36}KO_6S$, 527.1865; found: 527.1868; **IR**: ṽ = 3017, 2922, 1737, 1365, 1216, 749 cm^{-1}.

*Signals with double intensity.

5. Literature

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6. Appendix

6.1. Abbreviations

2D	two dimensional
acac	acetylacetonate
bpy	bipyridine
Bu	butyl
d.r.	diastereomeric ratio
DMAP	*N,N*-dimethylaminopyridine
DMP	Dess-Martin periodinane
dpm	dipivaloylmethanato
ee	enantiomeric excess
ent	enantiomer
et al.	and others
equiv.	equivalents
GC	gas chromatography
h	hour
HMDS	hexamethyl disilazan
HRMS	high resolution mass spectrometry
IC50	half maximal inhibitory concentration
IR	infrared spectroscopy
L	liter
LDA	lithiumdiisopropyl amide
m	multiplett

Ac	acetyl
Bn	benzyl
BTMSA	bis(trimethylsilyl)acetylene
d	duplett
DCE	1,2-dichloroethane
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
ECD	electronic circular dichroism
EI	electron impact ionization
epi	epimer
HeLa	Henrietta Lacks
ESI	electrospray ionization
GOESY	gradient enhanced nuclear Overhauser effect spectroscopy
HMBC	heteronuclear multiple-bond correlation spectroscopy
HMQC	heteronuclear multiple-quantum correlation spectroscopy
Hz	Hertz (s^{-1})
IMS	ion mobility spectroscopy
J	coupling constant
L	ligand

Me	methyl
min	minute
mmol	millimol (10^{-3} mol)
m.p.	melting point
n.d.	not determined
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance
Pd/C	palladium on charcoal
PG	protecting group
PDC	pyridinium dichromate
PtnM	a cytochrome P450 enzyme
quant.	quantitative
rac	racemic
ROESY	rotating frame nuclear Overhauser effect spectroscopy
s	singulett
t	tert
TBAF	tetrabutylammoniumfluoride
TBDPS	*tert*-butyl diphenylsilyl
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
Tf	trifluoromethanesulfonyl
TFAA	trifluoroacetic anhydride
TMS	trimethylsilyl
UV	ultraviolet
VCD	vibrational circular dichroism
m	molar (mol/L)
m-CPBA	*meta*-chloroperoxybenzoic acid
mg	milligram (10^{-3} g)
mL	milliliter (10^{-3} L)
MS	molecular sieves
NBS	*N*-bromosuccinimide
NMO	*N*-morpholine oxide
nOe	nuclear Overhauser effect
Ph	phenyl
PCC	pyridinium chlorochromate
ppm	parts per million
q	quartett
r.t.	room temperature
RCM	ring-closing metathesis
R_f	retardation factor
T	temperature
t	triplett
TBAT	tetrabutylammonium difluorotriphenyl silicate
TBS	*tert*-butyl dimethylsilyl
TES	triethylsilyl
tfa	trifluoroacetic acid
THF	tetrahydrofuran
TOF	time-of-flight
$\tilde{\nu}$	wavenumber

6.2. InChI-Codes of synthesized compounds

1	YMBQNIPNEQSRMW-CVSAEHQPSA-N InChI=1S/C15H24O3/c1-11(2)10(16)13(4,18)15-7-5-6-14(11,15)9-8-12(15,3)17/h17-18H,5-9H2,1-4H3/t12?,13?,14-,15+/m1/s1
2	NSXMOWMCCRWLTD-CVSAEHQPSA-N InChI=1S/C15H22O2/c1-11(2)10(16)13(4)15-7-5-6-14(11,15)9-8-12(15,3)17-13/h5-9H2,1-4H3/t12?,13?,14-,15+/m1/s1
77	QCMLNCNWPVIBPY-ILMHWDKJSA-N InChI=1S/C14H18O2/c1-9-11(15)10(2)14-6-4-5-13(9,14)8-7-12(14,3)16/h16H,1-2,4-8H2,3H3/t12?,13-,14-/m1/s1
78	QHNKAUVXQJBNPE-GHMZBOCLSA-N InChI=1S/C11H12O2/c12-8-6-10-3-1-4-11(10,7-8)9(13)2-5-10/h1,3H,2,4-7H2/t10-,11-/m1/s1
79	MVBMBIFYEIRPCF-NSHDSACASA-N InChI=1S/C11H12O2/c1-2-5-11-7-9(12)6-8(11)3-4-10(11)13/h2,6H,1,3-5,7H2/t11-/m0/s1
80	ZFAJLQHDVQVNFJ-UHFFFAOYSA-N InChI=1S/C10H12O/c1-4-6-8-10(11)9(3)7-5-2/h1,5H,2-3,6-8H2
81	GXKSEDGUIYSVHZ-UHFFFAOYSA-N InChI=1S/C11H13BrO3/c1-2-5-11(6-8(13)7-12)9(14)3-4-10(11)15/h2H,1,3-7H2
83	83XFWWMXTVFT-UHFFFAOYSA-N InChI=1S/C8H10O4/c1-4-5-6(7(9)11-2)8(10)12-3/h1,6H,5H2,2-3H3
84	WCSNOLUUFIWIHY-UHFFFAOYSA-N InChI=1S/C6H8O2/c1-3-4-5-6(7)8-2/h1H,4-5H2,2H3
85	JDKZQOKQRZLXNC-UHFFFAOYSA-N InChI=1S/C6H13O3P/c1-4-5-6-10(7,8-2)9-3/h4H,1,5-6H2,2-3H3
87	ILNREZHCHRHERT-UHFFFAOYSA-N InChI=1S/C10H14O/c1-4-6-8-10(11)9(3)7-5-2/h1,5,10-11H,2-3,6-8H2
88	UCSSXNWJGIMACB-DTIOYNMSSA-N InChI=1S/C11H14O2/c1-2-5-11-7-9(12)6-8(11)3-4-10(11)13/h2,6,10,13H,1,3-5,7H2/t10?,11-/m0/s1
SI-1	YUWCTPBJANQNJF-UHFFFAOYSA-N InChI=1S/C9H12O4/c1-4-5-6-7(8(10)12-2)9(11)13-3/h1,7H,5-6H2,2-3H3
SI-2	LZULAZTXJLWELL-UHFFFAOYSA-N InChI=1S/C7H10O2/c1-3-4-5-6-7(8)9-2/h1H,4-6H2,2H3
90	IFJVPDPDXKZTON-UHFFFAOYSA-N InChI=1S/C11H14O/c1-4-6-7-9-11(12)10(3)8-5-2/h1,5H,2-3,6-9H2
91	AIWHUJIMWUWJTI-UHFFFAOYSA-N InChI=1S/C11H16O/c1-4-6-7-9-11(12)10(3)8-5-2/h1,5,11-12H,2-3,6-9H2
93	URILIXGTLACVBO-UHFFFAOYSA-N InChI=1S/C17H30OSi/c1-7-12-13-15-17(16(6)14-8-2)18-19(9-3,10-4)11-5/h1,8,17H,2,6,9-15H2,3-5H3
89	BQZKMIARBWHOIH-LBPRGKRZSA-N InChI=1S/C12H14O2/c1-2-6-12-8-10(13)7-9(12)4-3-5-11(12)14/h2,7H,1,3-6,8H2/t12-/m0/s1
95	VLUUTDRAXUIOOJ-UHFFFAOYSA-N InChI=1S/C17H32O2Si/c1-7-12-15(5)17(14-11-13-16(6)18)19-20(8-2,9-3)10-4/h7,17H,1,5,8-14H2,2-4,6H3
96	PVQFSSGBSSPTSR-UHFFFAOYSA-N

	InChI=1S/C11H14O2/c1-3-7-11(8-4-2)9(12)5-6-10(11)13/h3-4H,1-2,5-8H2
101	ZRPAXRFPNPSAIQ-UHFFFAOYSA-N
	InChI=1S/C12H17BrO3/c1-2-5-11-7-9(8-13)16-12(11,15)6-3-4-10(11)14/h2,9,15H,1,3-8H2
102	GAHJTOMCUNDIMV-UHFFFAOYSA-N
	InChI=1S/C12H15BrO3/c1-2-6-12(7-9(14)8-13)10(15)4-3-5-11(12)16/h2H,1,3-8H2
104	QYVBFRMUZSEBNL-UHFFFAOYSA-N
	InChI=1S/C12H15BrO2/c1-3-7-12(8-9(2)13)10(14)5-4-6-11(12)15/h3H,1-2,4-8H2
108	MZCPHRQTAQRXGU-UHFFFAOYSA-N
	InChI=1S/C8H8O2/c1-2-5-10-8-4-3-7(9)6-8/h1,6H,3-5H2
106	BAZGPCVRZIKXCA-UHFFFAOYSA-N
	InChI=1S/C11H12O2/c1-3-7-11(8-4-2)9(12)5-6-10(11)13/h1,4H,2,5-8H2
110	WYAZWHHZLIXKFB-UHFFFAOYSA-N
	InChI=1S/C11H11BrO2/c1-2-6-11(7-3-8-12)9(13)4-5-10(11)14/h2H,1,4-7H2
111	ISYCNZUEFPIBQS-UHFFFAOYSA-N
	InChI=1S/C12H14O2/c1-3-8-12(9-4-2)10(13)6-5-7-11(12)14/h1,4H,2,5-9H2
121	ASTXOUZSWGACMK-UHFFFAOYSA-N
	InChI=1S/C11H14O3/c1-3-6-11(7-8(2)12)9(13)4-5-10(11)14/h3H,1,4-7H2,2H3
123	YLRXMHAHNKZNBW-CHWSQXEVSA-N
	InChI=1S/C13H16O2/c1-3-6-13-9-10(14)8-12(13,4-2)7-5-11(13)15/h3-4H,1-2,5-9H2/t12-,13-/m1/s1
124	FIBSEQYPTRRMCL-HUUCEWRRSA-N
	InChI=1S/C15H20O2/c1-3-5-8-14-9-6-13(17)15(14,7-4-2)11-12(16)10-14/h3-4H,1-2,5-11H2/t14-,15-/m1/s1
SI-3	ZSUKEJOJSRJRFU-HUUCEWRRSA-N
	InChI=1S/C15H22O2/c1-3-5-8-14-9-6-13(17)15(14,7-4-2)11-12(16)10-14/h4H,2-3,5-11H2,1H3/t14-,15-/m1/s1
125	GPBPXOFSKUDLKJ-ZGTCLIOFSA-N
	InChI=1S/C13H16O2/c14-10-8-12-5-2-1-3-6-13(12,9-10)11(15)4-7-12/h1,3H,2,4-9H2/t12?,13-/m1/s1
130	PGEIUYTUQDNDIH-HZPDHXFCSA-N
	InChI=1S/C17H24O3/c1-13(2)14(3,4)20-17(19-13)10-15-7-5-8-16(15,11-17)12(18)6-9-15/h5,7H,6,8-11H2,1-4H3/t15-,16-/m1/s1
131	MQWOUHUUSQJFIV-JMJZKYOTSA-N
	InChI=1S/C11H14O2/c12-8-6-10-3-1-4-11(10,7-8)9(13)2-5-10/h1,3,8,12H,2,4-7H2/t8-,10+,11+/m0/s1
132	MQWOUHUUSQJFIV-FBIMIBRVSA-N
	InChI=1S/C11H14O2/c12-8-6-10-3-1-4-11(10,7-8)9(13)2-5-10/h1,3,8,12H,2,4-7H2/t8-,10-,11-/m1/s1
133	UNYAGRLXOYPDMM-DYXFLFRNSA-N
	InChI=1S/C12H18O2/c1-10(14)5-6-11-3-2-4-12(10,11)8-9(13)7-11/h2-3,9,13-14H,4-8H2,1H3/t9-,10?,11+,12+/m0/s1
134	UNYAGRLXOYPDMM-DBPBRPCRSA-N
	InChI=1S/C12H18O2/c1-10(14)5-6-11-3-2-4-12(10,11)8-9(13)7-11/h2-3,9,13-14H,4-8H2,1H3/t9-,10?,11-,12-/m1/s1
135	IPDQQRQCJLQGIW-PQDIPPBSSA-N
	InChI=1S/C12H18O2/c1-10(14)5-6-11-3-2-4-12(10,11)8-9(13)7-11/h14H,2-8H2,1H3/t10?,11-,12-/m1/s1
136	DQZFBSAUFAJAEE-DYXFLFRNSA-N
	InChI=1S/C12H20O2/c1-10(14)5-6-11-3-2-4-12(10,11)8-9(13)7-11/h9,13-14H,2-8H2,1H3/t9-,10?,11+,12+/m0/s1

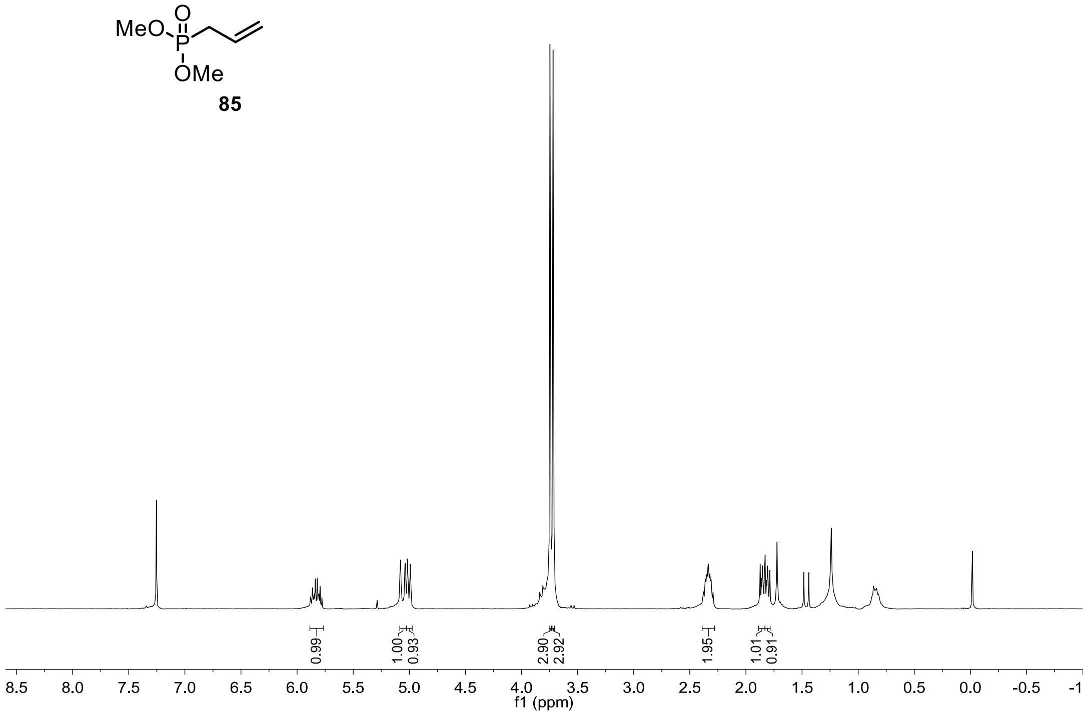
137	BTEGVCWVZBJOSD-JVIGXAJISA-N InChI=1S/C16H17F3O3/c1-9-11(20)10(2)15-6-4-5-14(9,15)8-7-13(15,3)22-12(21)16(17,18)19/h1-2,4-8H2,3H3/t13?,14-,15-/m1/s1
140	BGJJHDAECNNDJU-ZXCYLUJYSA-N InChI=1S/C14H20O2/c1-9-11(15)10(2)14-6-4-5-13(9,14)8-7-12(14,3)16/h11,15-16H,1-2,4-8H2,3H3/t11-,12?,13-,14-/m1/s1
144	ZDRHRBPKGLEPRQ-BXCZTXNRSA-N InChI=1S/C14H18O4.C6H16N2.2O.Os/c1-9-10(16)14(18,8-15)12-4-3-5-13(9,12)11(2,17)6-7-12;1-7(2)5-6-8(3)4;;;/h17H,1,3-8H2,2H3;5-6H2,1-4H3;;;/q-2;;;;+4/t11?,12-,13+,14+;;;;/m0..../s1
150	BTVZNOBJIVGQPV-JENMUQSASA-N InChI=1S/C15H20O2/c1-10-11(16)13(7-8-13)14-4-3-5-15(10,14)12(2,17)6-9-14/h17H,1,3-9H2,2H3/t12?,14-,15-/m1/s1
149	PJKMPHQWOJYYGH-AGIABQAESA-N InChI=1S/C16H22O2/c1-12(18)5-10-15-3-2-4-16(12,15)14(8-9-14)11(17)13(15)6-7-13/h18H,2-10H2,1H3/t12?,15-,16+/m1/s1
151	CCOYGOOTZIZXPO-JYRZLJSNSA-N InChI=1S/C15H20O2/c1-10-11(16)14(8-9-14)15-5-3-4-13(10,15)7-6-12(15,2)17/h17H,1,3-9H2,2H3/t12?,13-,15-/m1/s1
154	RNVTXSUGNKDCOQ-YKYOPCIESA-N InChI=1S/C15H20O3/c1-11-5-8-13-3-2-4-15(11,13)14(17,9-18-11)10(16)12(13)6-7-12/h17H,2-9H2,1H3/t11?,13-,14-,15-/m1/s1
155	UFUWCKUPLGICBO-YKYOPCIESA-N InChI=1S/C15H22O4/c1-11(18)5-8-13-3-2-4-15(11,13)14(19,9-16)10(17)12(13)6-7-12/h16,18-19H,2-9H2,1H3/t11?,13-,14-,15-/m1/s1
158	POMGPYYUXDYQJI-UIWQZIKGSA-N InChI=1S/C15H24O3/c1-11(17)6-9-14-4-3-5-15(11,14)12(2,18)10(16)13(14)7-8-13/h10,16-18H,3-9H2,1-2H3/t10-,11?,12?,14-,15+/m1/s1
159	LZTGVVKXSHPJPO-FPNUHLBXSA-N InChI=1S/C15H26O3/c1-11(2)10(16)13(4,18)15-7-5-6-14(11,15)9-8-12(15,3)17/h10,16-18H,5-9H2,1-4H3/t10?,12?,13?,14-,15+/m1/s1
160	YMBQNIPNEQSRMW-CVSAEHQPSA-N InChI=1S/C15H24O3/c1-11(2)10(16)13(4,18)15-7-5-6-14(11,15)9-8-12(15,3)17/h17-18H,5-9H2,1-4H3/t12?,13?,14-,15+/m1/s1
163	DFVXYXVXXGFZCZ-DMJDIKPUSA-N InChI=1S/C15H22O2/c1-10-6-9-14-7-5-8-15(10,14)13(4,17)11(16)12(14,2)3/h6,17H,5,7-9H2,1-4H3/t13?,14-,15+/m1/s1
170	BASDRCHVBDIWOE-QJPTWQEYSA-N InChI=1S/C12H16O/c1-9-3-6-11-4-2-5-12(9,11)8-10(13)7-11/h2,4,10,13H,1,3,5-8H2/t10-,11+,12+/m0/s1
171	HTRVMUJNVMTYHW-FGHRXAJISA-N InChI=1S/C12H20O/c1-9-3-6-11-4-2-5-12(9,11)8-10(13)7-11/h9-10,13H,2-8H2,1H3/t9?,10-,11+,12+/m0/s1
182	GJWSUKYXUMVMGX-SECBINFHSA-N InChI=1S/C10H18O2/c1-8(2)5-4-6-9(3)7-10(11)12/h5,9H,4,6-7H2,1-3H3,(H,11,12)/t9-/m1/s1
197	XDSVNMOMIKLDRG-SVEZIJJLSA-N InChI=1S/C41H62O5Si2/c1-32(2)20-19-21-33(3)30-36(46-47(10,11)12)31-34(4)26-27-39(45-40(42)43-9)35(5)28-29-44-48(41(6,7)8,37-22-15-13-16-23-37)38-24-17-14-18-25-38/h13-18,20,22-26,28,30,33,39H,19,21,27,29,31H2,1-12H3/b34-26+,35-28+,36-30+/t33-,39?/m1/s1
198	YWVJDXRVHMYMEL-CQSZACIVSA-N

	InChI=1S/C15H22O2S/c1-13(2)8-7-9-14(3)12-18(16,17)15-10-5-4-6-11-15/h4-6,8,10-11,14H,7,9,12H2,1-3H3/t14-/m1/s1
200	XVHNHIQEZPGYBY-UDMRSLNFSA-N InChI=1S/C32H46O5Si2/c1-25(24-30(33)38(7,8)9)20-21-29(37-31(34)35-6)26(2)22-23-36-39(32(3,4)5,27-16-12-10-13-17-27)28-18-14-11-15-19-28/h10-20,22,29H,21,23-24H2,1-9H3/b25-20+,26-22+
202	QEMQLLPBGCJKBX-CAWNPKITSA-N InChI=1S/C26H35ClO2Si/c1-21(20-27)16-17-25(28)22(2)18-19-29-30(26(3,4)5,23-12-8-6-9-13-23)24-14-10-7-11-15-24/h6-16,18,25,28H,17,19-20H2,1-5H3/b21-16+,22-18+/t25-/m0/s1
203	OIQIWCKKGXWYIW-OBGWFSINSA-N InChI=1S/C21H26O2Si/c1-18(17-22)15-16-23-24(21(2,3)4,19-11-7-5-8-12-19)20-13-9-6-10-14-20/h5-15,17H,16H2,1-4H3/b18-15+
204	LDAUNFGJLKHFDP-KNTRCKAVSA-N InChI=1S/C21H31NO3Si/c1-8-16(2)19(25-26(6,7)21(3,4)5)22-18(15-24-20(22)23)14-17-12-10-9-11-13-17/h8-13,18H,1,14-15H2,2-7H3/b19-16+
SI-4	PTQHYYRGDQETQD-UHFFFAOYSA-N InChI=1S/C21H28OSi/c1-18(2)16-17-22-23(21(3,4)5,19-12-8-6-9-13-19)20-14-10-7-11-15-20/h6-16H,17H2,1-5H3
SI-8	ZBYRDZYXAKWLKT-OBGWFSINSA-N InChI=1S/C21H28O2Si/c1-18(17-22)15-16-23-24(21(2,3)4,19-11-7-5-8-12-19)20-13-9-6-10-14-20/h5-15,22H,16-17H2,1-4H3/b18-15+
209	OYXDZMIBTDSEQU-QDEBKDIKSA-N InChI=1S/C15H17NO3/c1-3-11(2)14(17)16-13(10-19-15(16)18)9-12-7-5-4-6-8-12/h3-8,13H,9-10H2,1-2H3/b11-3+
210	DVTHXTXIAATJEA-NZCSQEIHSA-N InChI=1S/C36H43NO5Si/c1-27(34(39)37-31(26-41-35(37)40)23-29-15-9-6-10-16-29)21-22-30(28(2)24-38)25-42-43(36(3,4)5,32-17-11-7-12-18-32)33-19-13-8-14-20-33/h6-21,24,28,30-31H,22-23,25-26H2,1-5H3/b27-21+/t28?,30-,31?/m0/s1
211	BXEPPDIEZJBZEW-QUNSEZJESA-N InChI=1S/C36H43NO5Si/c1-27(23-24-42-43(36(3,4)5,31-17-11-7-12-18-31)32-19-13-8-14-20-32)33(38)22-21-28(2)34(39)37-30(26-41-35(37)40)25-29-15-9-6-10-16-29/h6-21,23,30,33,38H,22,24-26H2,1-5H3/b27-23+,28-21+/t30?,33-/m0/s1
SI-6	QTLZIHUNCOBIDF-CAWNPKITSA-N InChI=1S/C26H36O3Si/c1-21(20-27)16-17-25(28)22(2)18-19-29-30(26(3,4)5,23-12-8-6-9-13-23)24-14-10-7-11-15-24/h6-16,18,25,27-28H,17,19-20H2,1-5H3/b21-16+,22-18+/t25-/m0/s1
213	AWCFSYJBLMXQQO-IFJYVERXSA-N InChI=1S/C33H50O2S2Si2/c1-27(26-33(38(6,7)8)36-24-15-25-37-33)20-21-31(34)28(2)22-23-35-39(32(3,4)5,29-16-11-9-12-17-29)30-18-13-10-14-19-30/h9-14,16-20,22,31,34H,15,21,23-26H2,1-8H3/b27-20+,28-22+/t31-/m0/s1
214	MIKFYWMJDRNGIO-RCXPEZBOSA-N InChI=1S/C35H52O4S2Si2/c1-28(27-35(42(7,8)9)40-25-16-26-41-35)21-22-32(39-33(36)37-6)29(2)23-24-38-43(34(3,4)5,30-17-12-10-13-18-30)31-19-14-11-15-20-31/h10-15,17-21,23,32H,16,22,24-27H2,1-9H3/b28-21+,29-23+
215	GLYYRWADVSGYMW-YHMJZVADSA-N InChI=1S/C10H18O/c1-8(2)5-4-6-9(3)10-7-11-10/h5,9-10H,4,6-7H2,1-3H3/t9-,10?/m1/s1
216	WFZFXUZFKAOTRR-SECBINFHSA-N InChI=1S/C9H18O/c1-8(2)5-4-6-9(3)7-10/h5,9-10H,4,6-7H2,1-3H3/t9-/m1/s1
217	QTJUHINKPNOAEU-IWSPIJDZSA-N InChI=1S/C10H20O2/c1-7-4-5-8(6-9(7)11)10(2,3)12/h7-9,11-12H,4-6H2,1-3H3/t7-,8-,9-/m1/s1

218	FBYNCBIZLWVQNF-CQSZACIVSA-N InChI=1S/C15H22S/c1-13(2)8-7-9-14(3)12-16-15-10-5-4-6-11-15/h4-6,8,10-11,14H,7,9,12H2,1-3H3/t14-/m1/s1
219	BXZXQNAQYTXCIU-XPCCGILXSA-N InChI=1S/C15H22OS/c1-13(2)8-7-9-14(3)12-17(16)15-10-5-4-6-11-15/h4-6,8,10-11,14H,7,9,12H2,1-3H3/t14-,17?/m1/s1
220	VWCQPAALTUECSP-NJFXARDXSA-N InChI=1S/C22H36O5/c1-16(2)8-7-9-17(3)14-20(24)15-18(4)10-11-21(19(5)12-13-23)27-22(25)26-6/h8,10,12,17,21,23H,7,9,11,13-15H2,1-6H3/b18-10+,19-12+/t17-,21?/m1/s1
221	ZCHCMPVVPPUSJE-BADXOGKISA-N InChI=1S/C20H32O2/c1-16(2)8-6-10-18(4)14-20(22)15-19(5)11-7-9-17(3)12-13-21/h7-9,11-12,18,21H,6,10,13-15H2,1-5H3/b9-7-,17-12+,19-11+/t18-/m1/s1
222	XUFXFOMJFDPSOB-AZGNXENWSA-N InChI=1S/C24H40O4Si/c1-18(2)11-9-12-19(3)15-22(28-29(6,7)8)16-20(4)13-10-14-21(5)23-17-26-24(25)27-23/h11,13,15,19,23H,5,9-10,12,14,16-17H2,1-4,6-8H3/b20-13+,22-15+/t19-,23-/m1/s1
224	MZIRAORPOHHBRQ-SVTZGKHISA-N InChI=1S/C15H24O4Si/c1-11(9-14(16)20(3,4)5)7-6-8-12(2)13-10-18-15(17)19-13/h7,13H,2,6,8-10H2,1,3-5H3/b11-7+/t13-/m1/s1
225	OZWGSIKBQUBAKN-VMKBVTSJSA-N InChI=1S/C11H15ClO3/c1-8(6-12)4-3-5-9(2)10-7-14-11(13)15-10/h4,10H,2-3,5-7H2,1H3/b8-4+/t10-/m1/s1
227	HQEMRNWKAVWSOY-GHMZBOCLSA-N InChI=1S/C11H21O2/c1-9(2)6-5-7-11(3)10(8-12)13(11)4/h6,10,12H,5,7-8H2,1-4H3/t10-,11-/m1/s1
228	CSRABKKYPRURRM-UHFFFAOYSA-N InChI=1S/C10H18O2/c1-8(2)5-4-6-9(3)10(12)7-11/h5,10-12H,3-4,6-7H2,1-2H3
229	FNBZSECDFRGXPN-UHFFFAOYSA-N InChI=1S/C11H16O3/c1-8(2)5-4-6-9(3)10-7-13-11(12)14-10/h5,10H,3-4,6-7H2,1-2H3
230	IZMVUNLUEQUPRK-XBXARRHUSA-N InChI=1S/C11H16O4/c1-8(6-12)4-3-5-9(2)10-7-14-11(13)15-10/h4,10,12H,2-3,5-7H2,1H3/b8-4+
SI-7	MRNSHVDTELZAKJ-XBXARRHUSA-N InChI=1S/C11H14O4/c1-8(6-12)4-3-5-9(2)10-7-14-11(13)15-10/h4,6,10H,2-3,5,7H2,1H3/b8-4+
231	ILVOTDNMCPZJON-XBXARRHUSA-N InChI=1S/C11H15BrO3/c1-8(6-12)4-3-5-9(2)10-7-14-11(13)15-10/h4,10H,2-3,5-7H2,1H3/b8-4+
232	IRMFHAHWUDQYDM-XBXARRHUSA-N InChI=1S/C10H17ClO2/c1-8(6-11)4-3-5-9(2)10(13)7-12/h4,10,12-13H,2-3,5-7H2,1H3/b8-4+
233	GCRCXVPJNZSPRU-RIYZIHGNSA-N InChI=1S/C17H32O2S2Si/c1-14(8-6-9-15(2)16(19)13-18)12-17(22(3,4)5)20-10-7-11-21-17/h8,16,18-19H,2,6-7,9-13H2,1,3-5H3/b14-8+
234	QSURZHRNMGODOO-RIYZIHGNSA-N InChI=1S/C18H30O3S2Si/c1-14(8-6-9-15(2)16-13-20-17(19)21-16)12-18(24(3,4)5)22-10-7-11-23-18/h8,16H,2,6-7,9-13H2,1,3-5H3/b14-8+
235	BIRHULMPMOWQGL-GFCCVEGCSA-N InChI=1S/C13H26OSi/c1-11(2)8-7-9-12(3)10-13(14)15(4,5)6/h8,12H,7,9-10H2,1-6H3/t12-/m1/s1
236	ODRGRTPDKPMVOZ-GFCCVEGCSA-N InChI=1S/C13H24S2/c1-11(2)6-4-7-12(3)10-13-14-8-5-9-15-13/h6,12-13H,4-5,7-10H2,1-3H3/t12-/m1/s1
237	DUKLBDIEIRRZEI-OAHLLOKOSA-N InChI=1S/C16H32S2Si/c1-14(2)9-7-10-15(3)13-16(19(4,5)6)17-11-8-12-18-16/h9,15H,7-8,10-13H2,1-6H3/t15-/m1/s1

239	QXEQXWMVDFMWGX-SNAWJCMRSA-N InChI=1S/C11H14O3/c1-8(2)5-4-6-9(3)10-7-13-11(12)14-10/h4-5,10H,1,3,6-7H2,2H3/b5-4+
240	GUOLOJVZMMZFCC-XMMPIXPASA-N InChI=1S/C28H32OSi/c1-23(2)14-13-15-24(3)22-28(29)30(25-16-7-4-8-17-25,26-18-9-5-10-19-26)27-20-11-6-12-21-27/h4-12,14,16-21,24H,13,15,22H2,1-3H3/t24-/m1/s1
242	UHNUAEMMVKSABZ-RIBGEGAISA-N InChI=1S/C28H34OSi/c1-23(2)14-13-15-24(3)22-28(29)30(25-16-7-4-8-17-25,26-18-9-5-10-19-26)27-20-11-6-12-21-27/h4-12,14,16-21,24,28-29H,13,15,22H2,1-3H3/t24-,28?/m1/s1
243	HMELAMIESXSBES-CDEUPQFYSA-N InChI=1S/C39H46O4Si/c1-30(2)17-15-18-31(3)27-34(28-32(4)19-16-20-33(5)38-29-41-39(40)42-38)43-44(35-21-9-6-10-22-35,36-23-11-7-12-24-36)37-25-13-8-14-26-37/h6-14,17,19,21-27,31,38H,5,15-16,18,20,28-29H2,1-4H3/b32-19+,34-27-/t31-,38?/m1/s1
244	BXLURCJZMWTFOI-HCXHUKTLSA-N InChI=1S/C39H46O4Si/c1-29(2)17-16-18-31(5)27-37(36(30(3)4)26-25-32(6)38-28-41-39(40)42-38)43-44(33-19-10-7-11-20-33,34-21-12-8-13-22-34)35-23-14-9-15-24-35/h7-15,17,19-24,27,31,36,38H,3,6,16,18,25-26,28H2,1-2,4-5H3/b37-27-/t31-,36?,38?/m1/s1
246	RLMWWQRXOAWPRF-CKRSJRDASA-N InChI=1S/C21H31BrO4/c1-14(2)8-6-11-17(5)20(22)18(23)12-15(3)9-7-10-16(4)19-13-25-21(24)26-19/h8-9,17,19-20H,4,6-7,10-13H2,1-3,5H3/b15-9+/t17-,19?,20?/m1/s1
24	LYQYKGSLPWCCAR-FWGOWYOCSA-N InChI=1S/C27H36O6S/c1-19(2)11-9-14-22(5)26(34(30,31)23-15-7-6-8-16-23)24(28)17-20(3)12-10-13-21(4)25-18-32-27(29)33-25/h6-8,11-12,15-16,22,25-26H,4,9-10,13-14,17-18H2,1-3,5H3/b20-12+/t22-,25?,26?/m1/s1

6.3. NMR-Spectra



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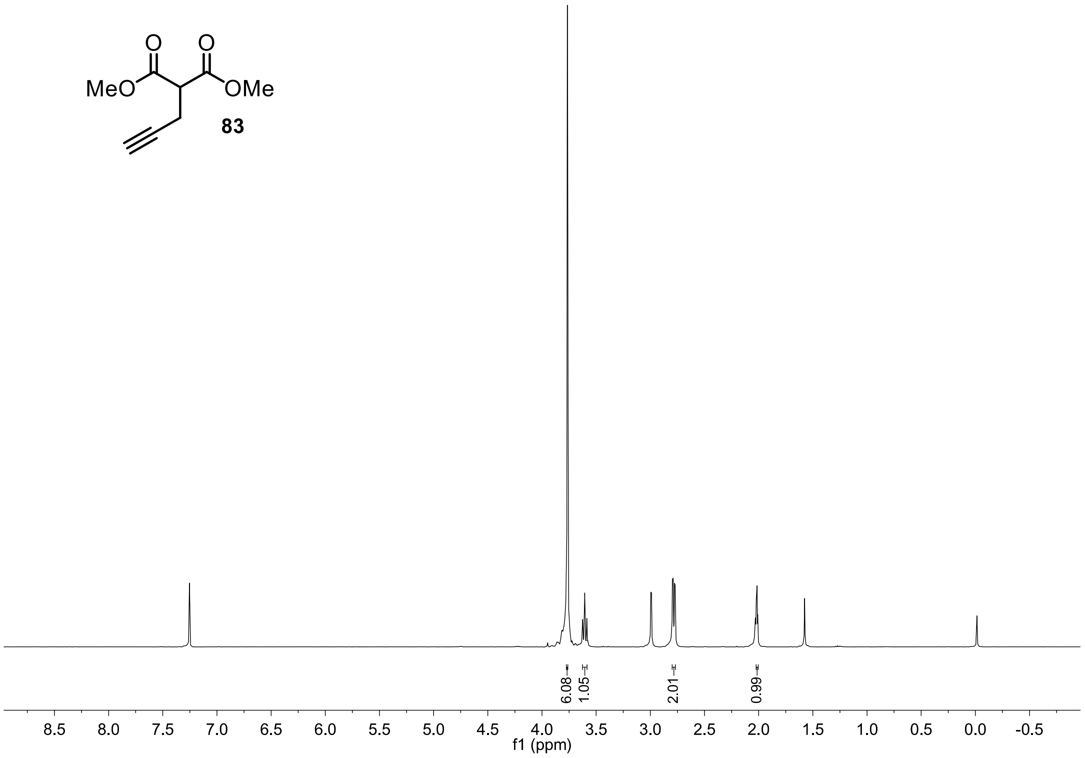

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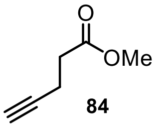
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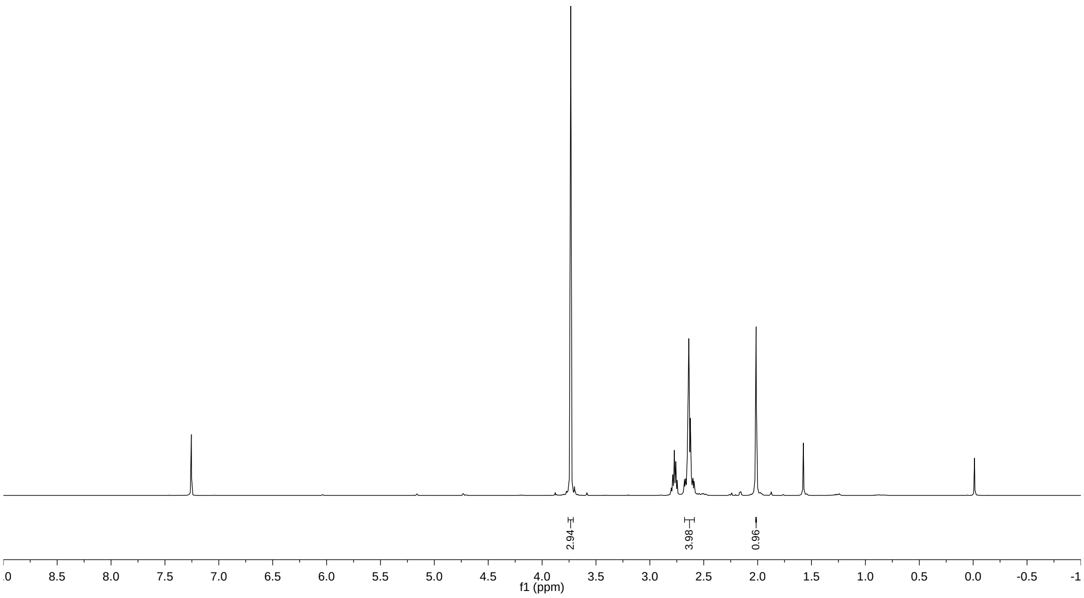
OMe

84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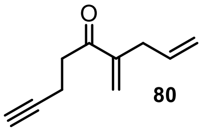
f1 (ppm)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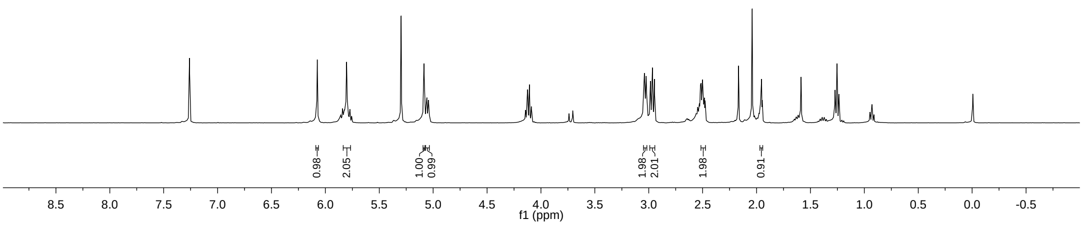
80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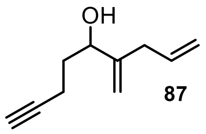
f1 (ppm)



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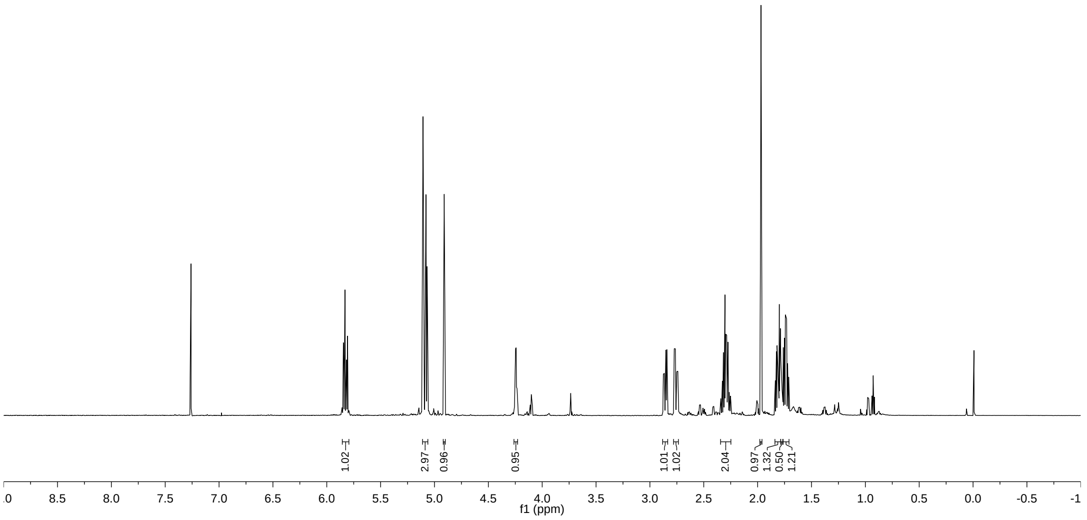
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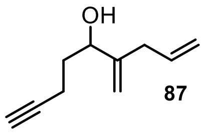
f1 (ppm)



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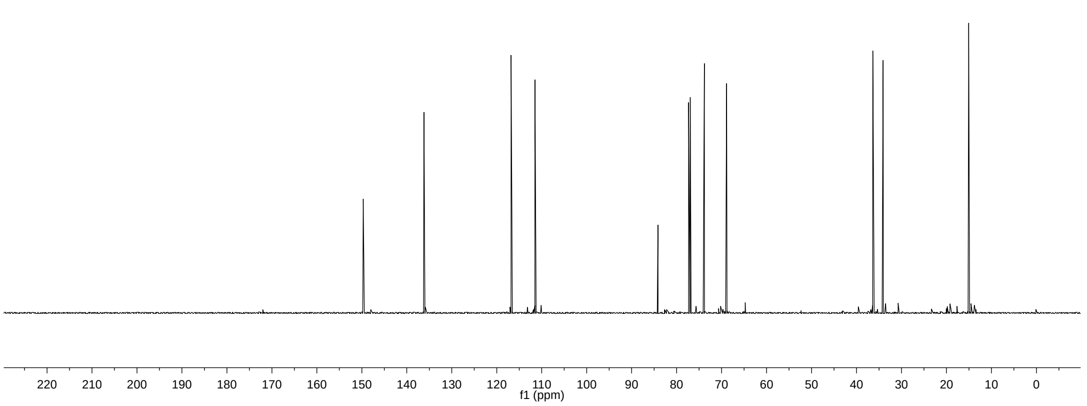
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200
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180
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160
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140
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120
110
100
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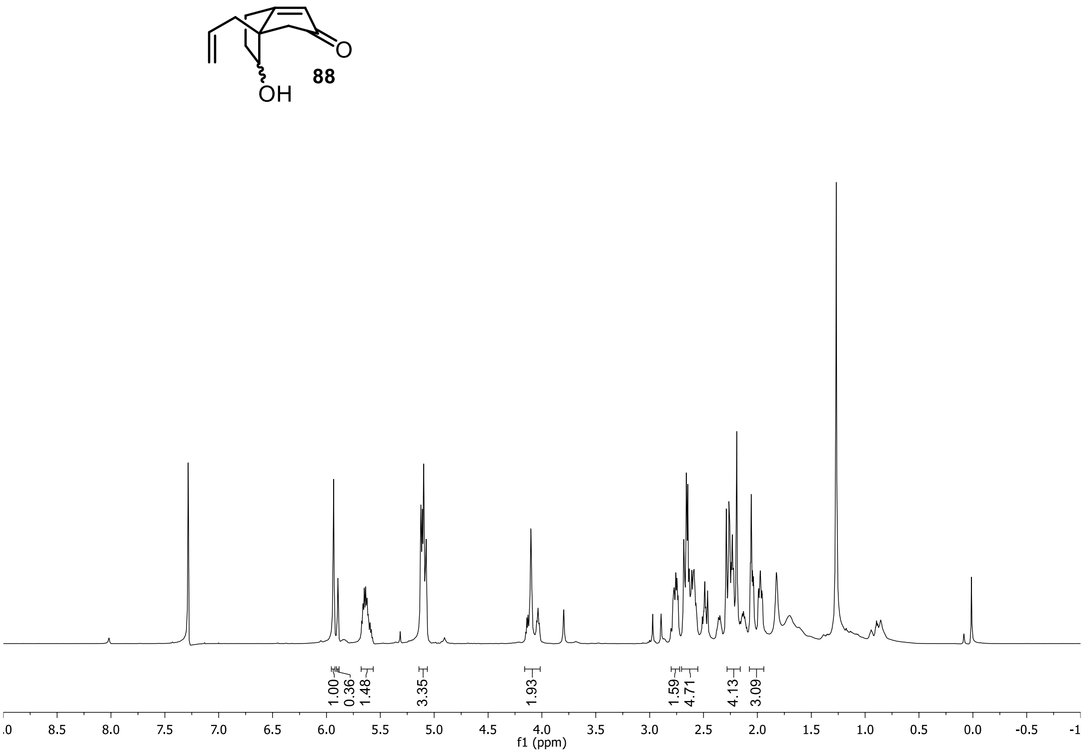
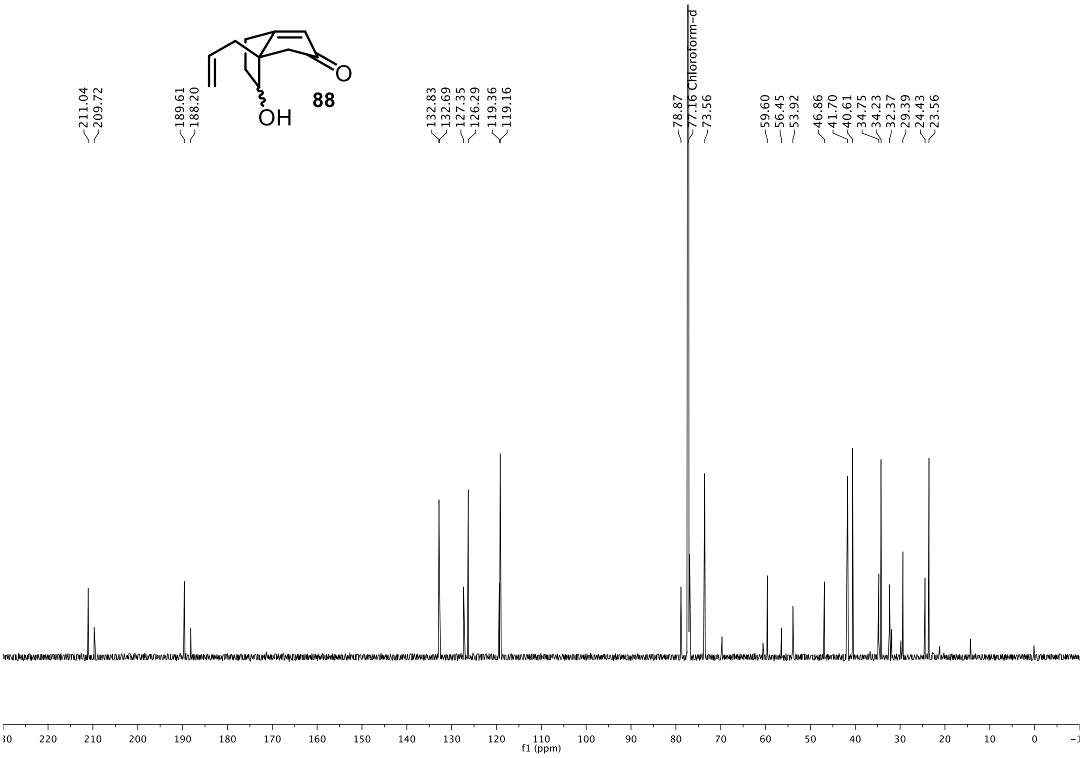
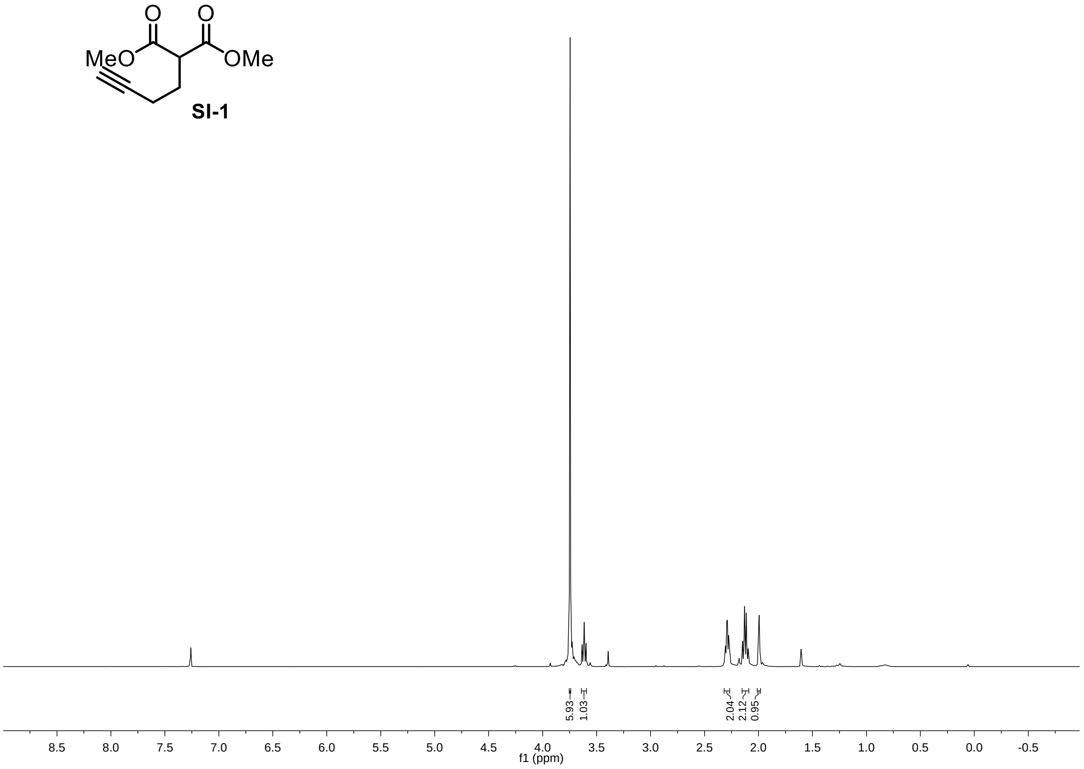
80
70
60
50
40
30
20
10
0
f1 (ppm)

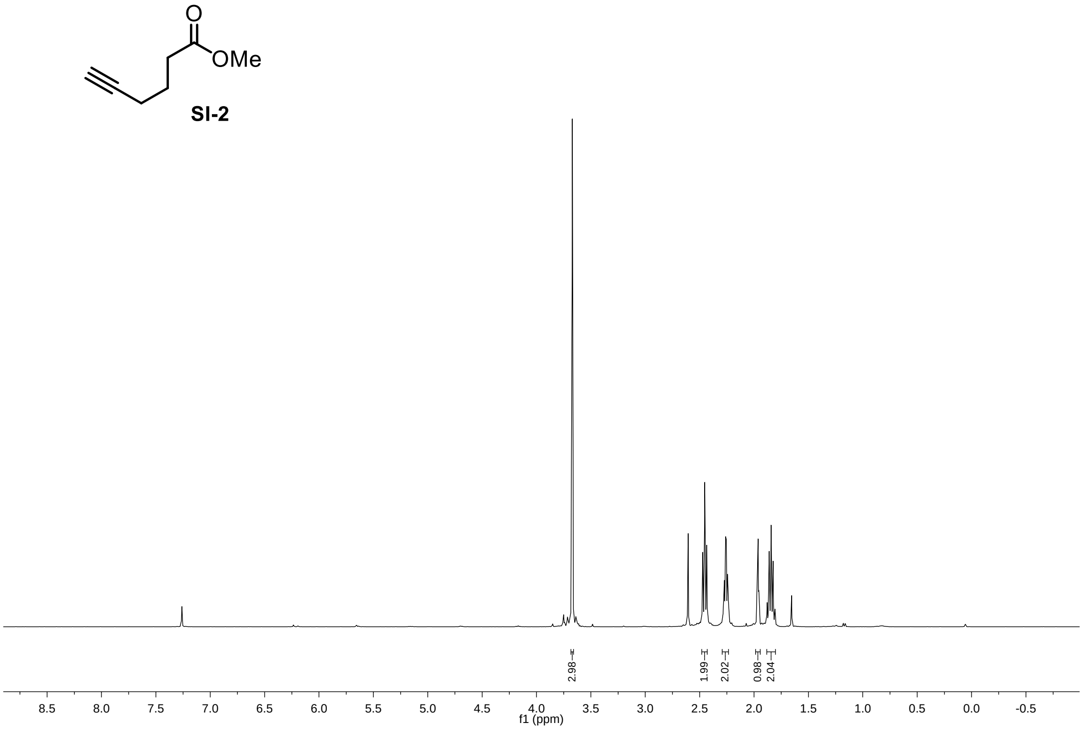

O
OH
88
1.00
0.36
1.48
3.35
1.93
1.59
4.71
4.13
3.09
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


O
OH
88
211.04
209.72
189.61
188.20
132.83
132.69
127.35
126.29
119.36
119.16
78.87
77.16 Chloroform-d
73.56
59.60
56.45
53.92
46.86
41.70
40.61
34.75
34.23
32.37
29.39
24.43
23.56
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



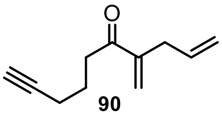
SI-1

MeO
OMe
O
O
5.93
1.03
2.04
2.12
0.95
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

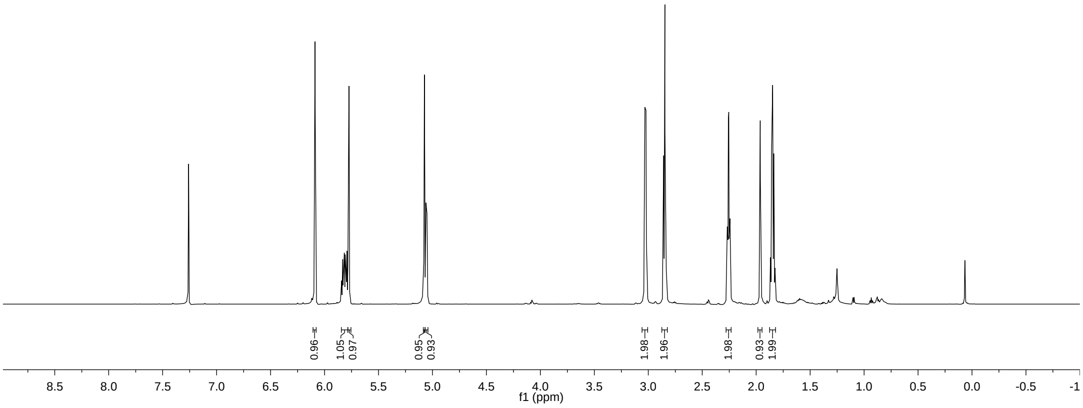


SI-2

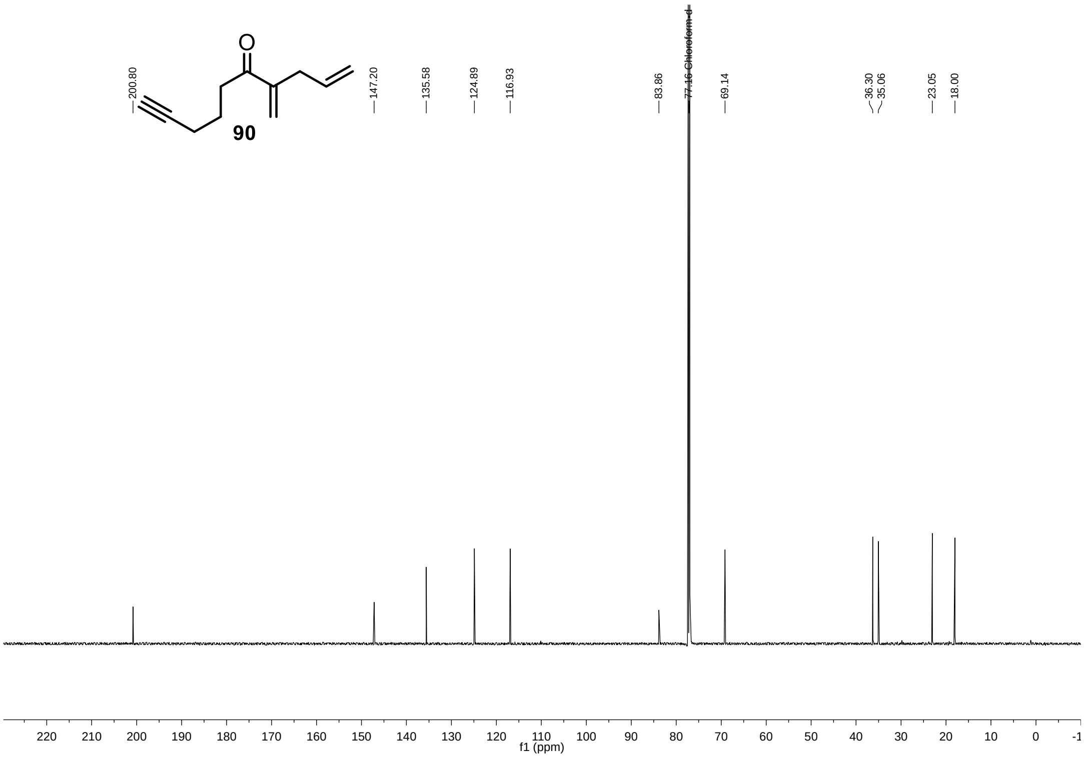
O
OMe
2.98
1.99
2.02
0.98
2.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



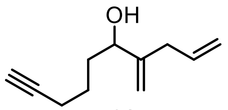
90



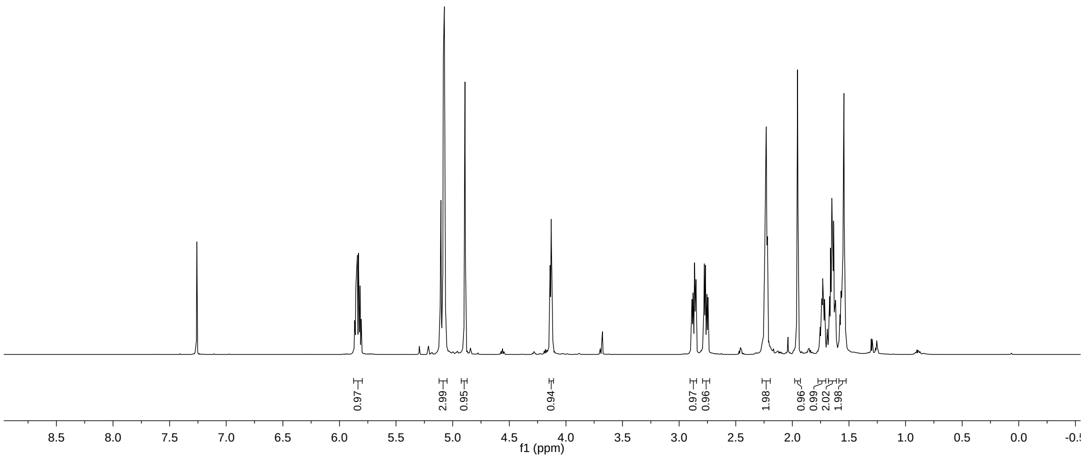
0.96
1.05
0.97
0.95
0.93
1.98
1.96
1.98
0.93
1.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

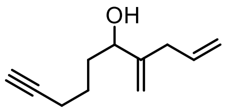


200.80
147.20
135.58
124.89
116.93
83.86
77.16 Chloroform-d
69.14
36.30
35.06
23.05
18.00
90
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

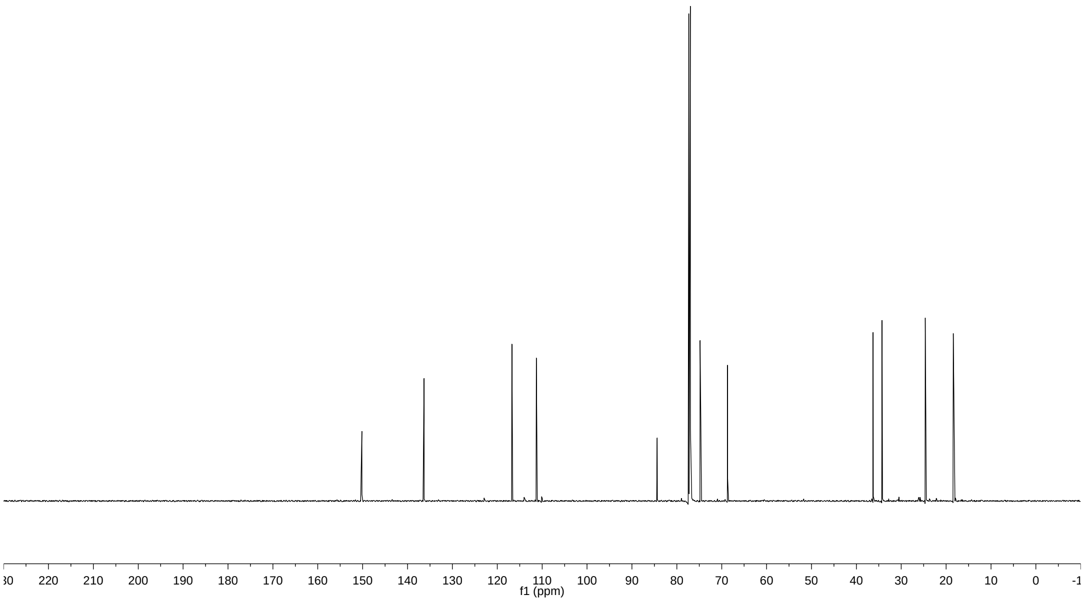

OH

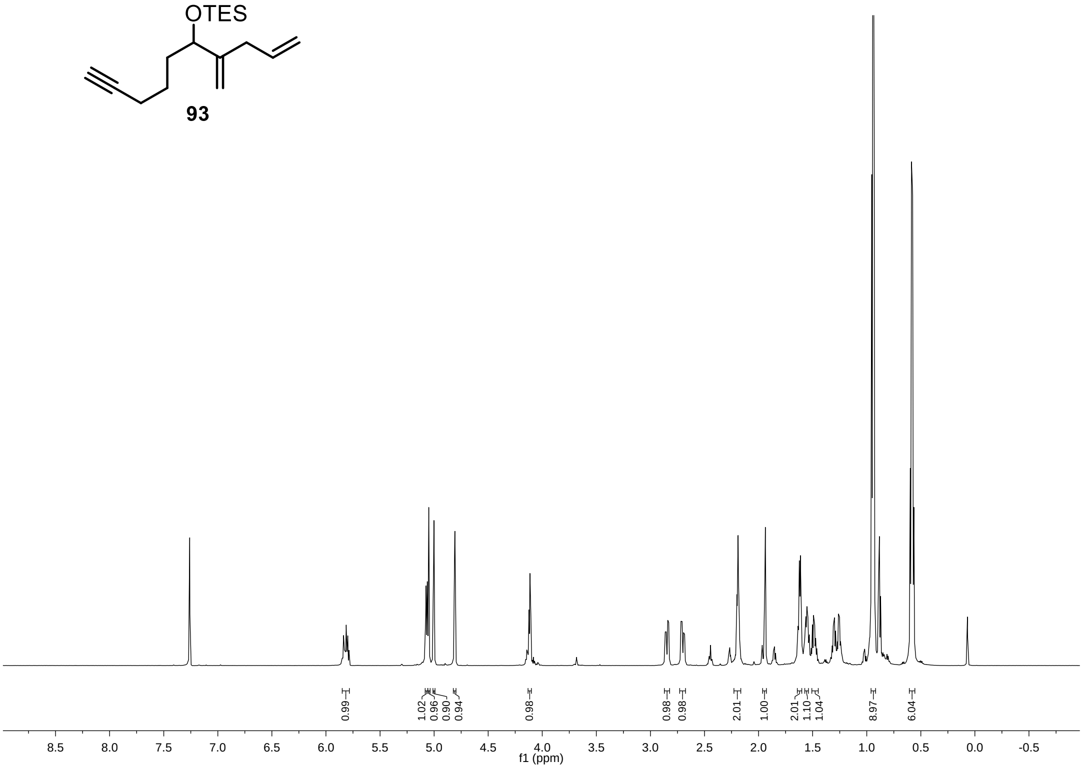
91


0.97
2.99
0.95
0.94
0.97
0.96
1.98
0.96
0.99
2.02
1.98
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


OH

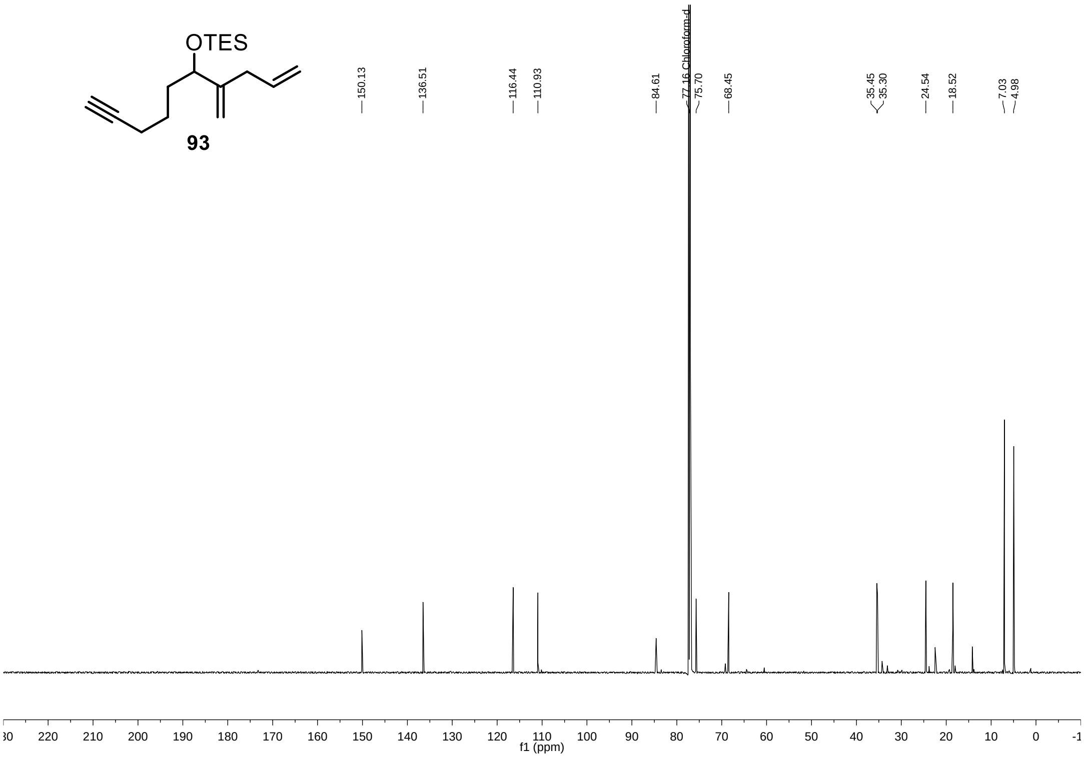
91


150.18
136.32
116.74
111.30
84.38
77.16 Chloroform-d
74.82
68.70
36.27
34.28
24.64
18.40
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



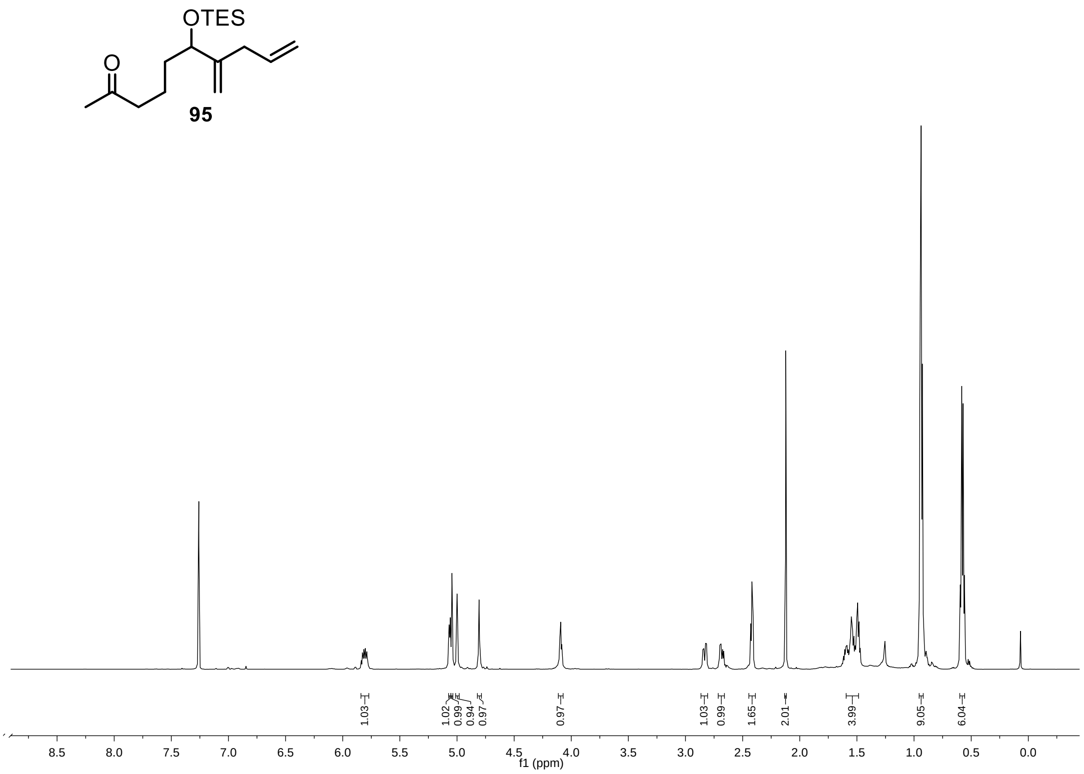
93

OTES
0.99
1.02
0.96
0.90
0.94
0.98
0.98
0.98
2.01
1.00
2.01
1.10
1.04
8.97
6.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

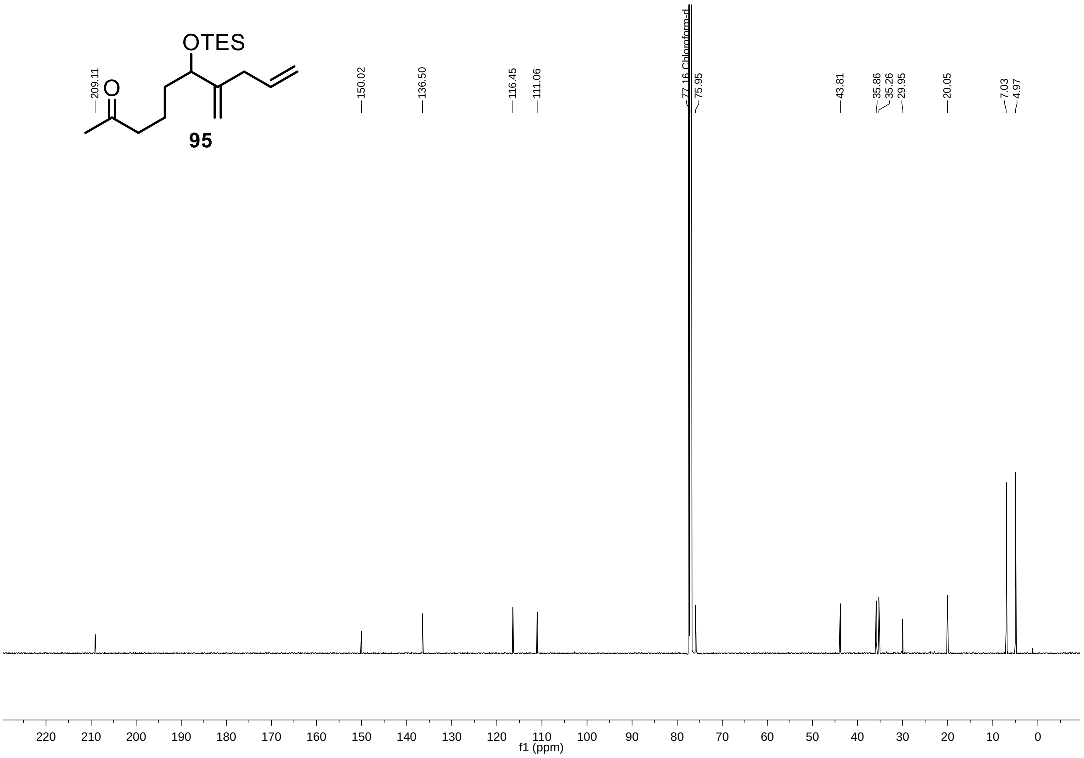


93

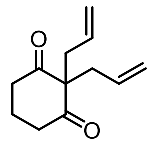
OTES
150.13
136.51
116.44
110.93
84.61
77.16 Chloroform-d
75.70
68.45
35.45
35.30
24.54
18.52
7.03
4.98
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OTES
O
1.03
1.02
0.99
0.94
0.97
0.97
1.03
0.99
1.65
2.01
3.99
9.05
6.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

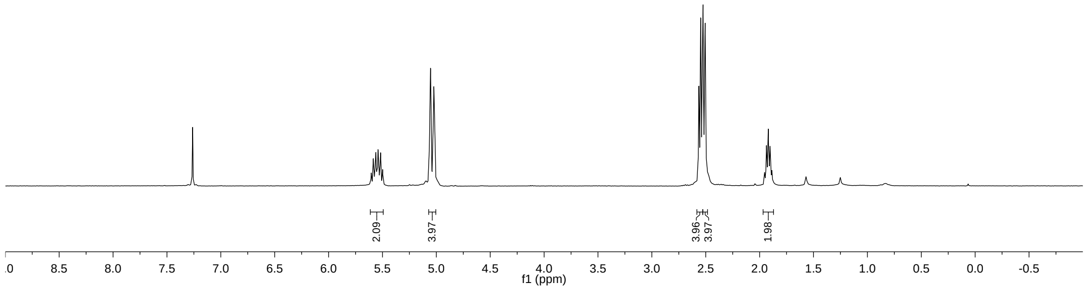
95

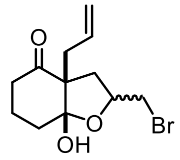

OTES
O
209.11
150.02
136.50
116.45
111.06
77.16 Chloroform-d
75.95
43.81
35.86
35.26
29.95
20.05
7.03
4.97
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

95

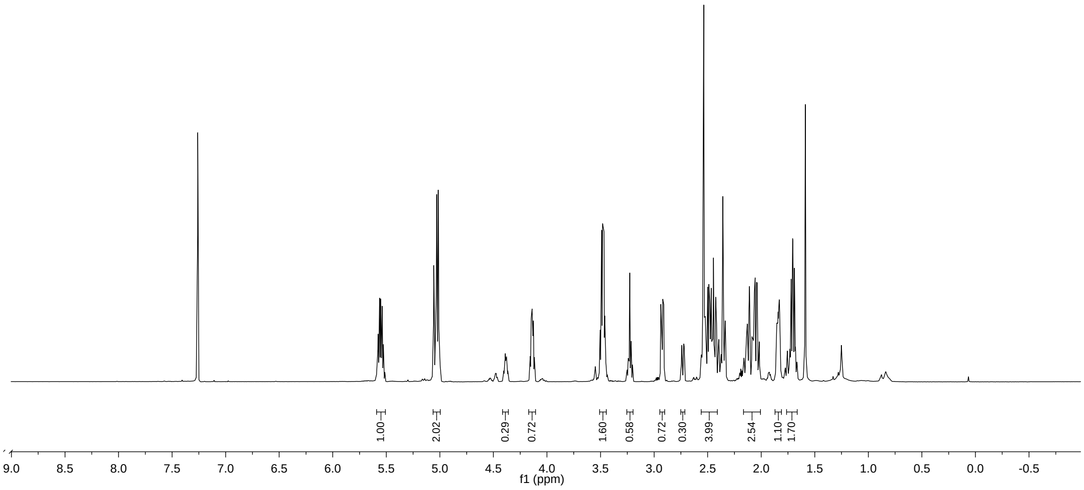

O
O

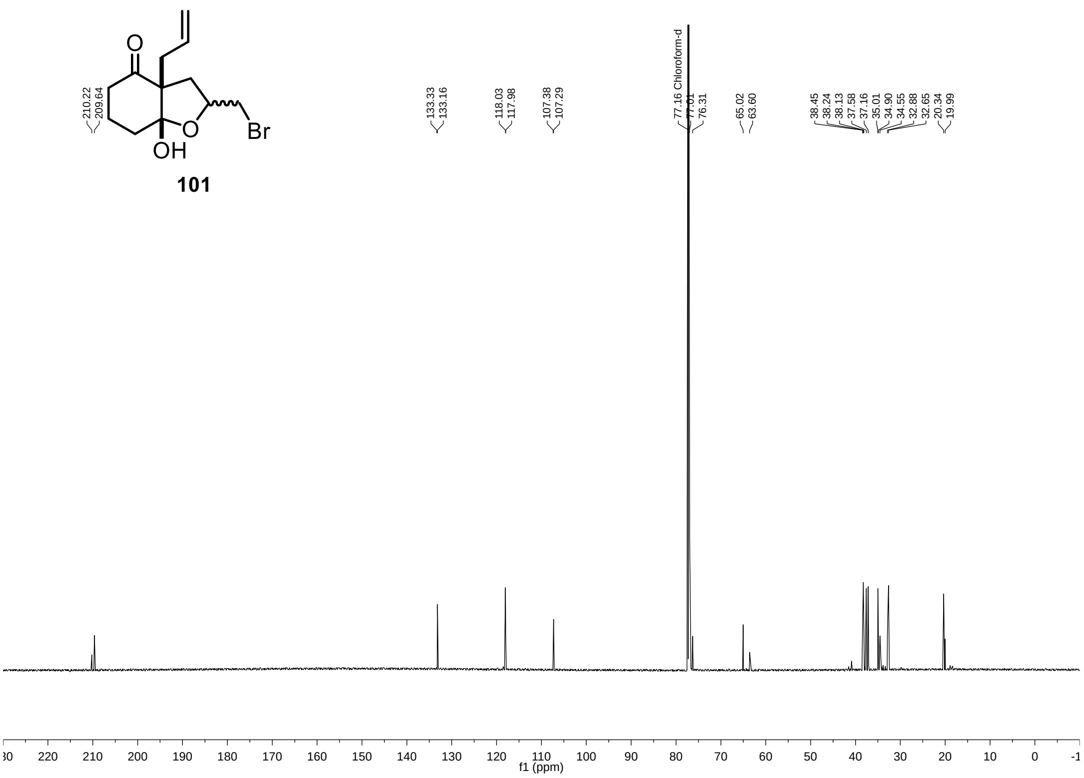
100


2.09
3.97
3.96
3.97
1.98
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

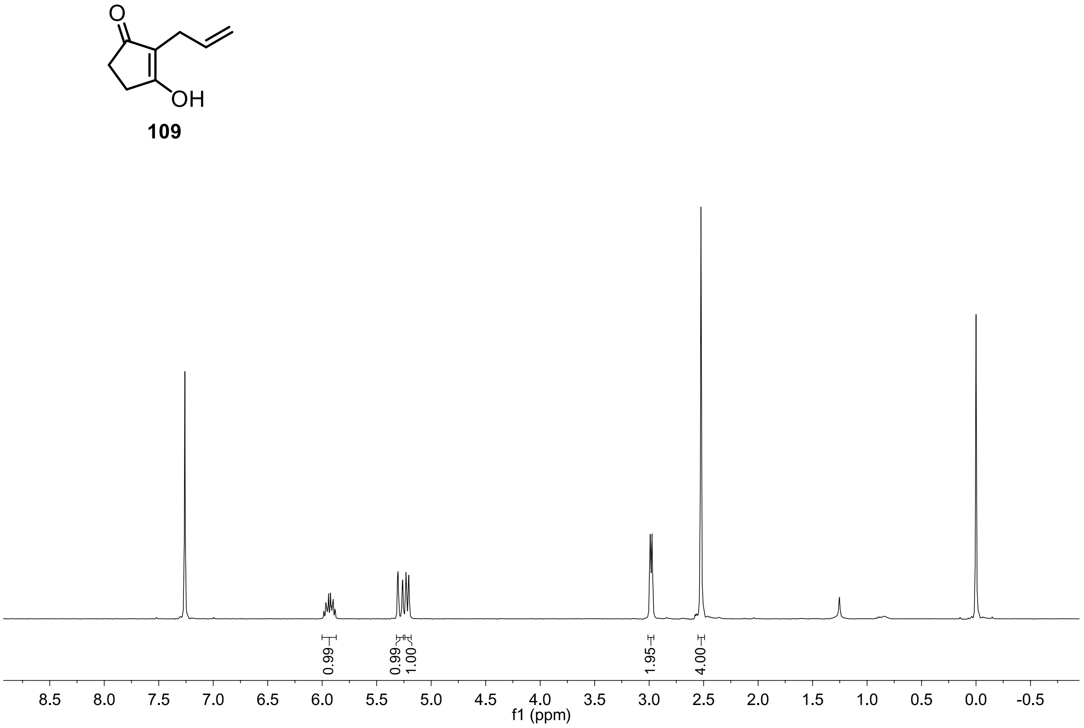

O
O
OH
Br

101

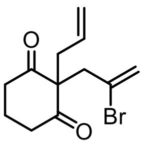

1.00
2.02
0.29
0.72
1.60
0.58
0.72
0.30
3.99
2.54
1.10
1.70
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


O
OH
O
Br
210.22
209.64
133.33
133.16
118.03
117.98
107.38
107.29
77.16 Chloroform-d
77.01
76.31
65.02
63.60
38.45
38.24
38.13
37.58
37.16
35.01
34.90
34.55
32.88
32.65
20.34
19.99
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

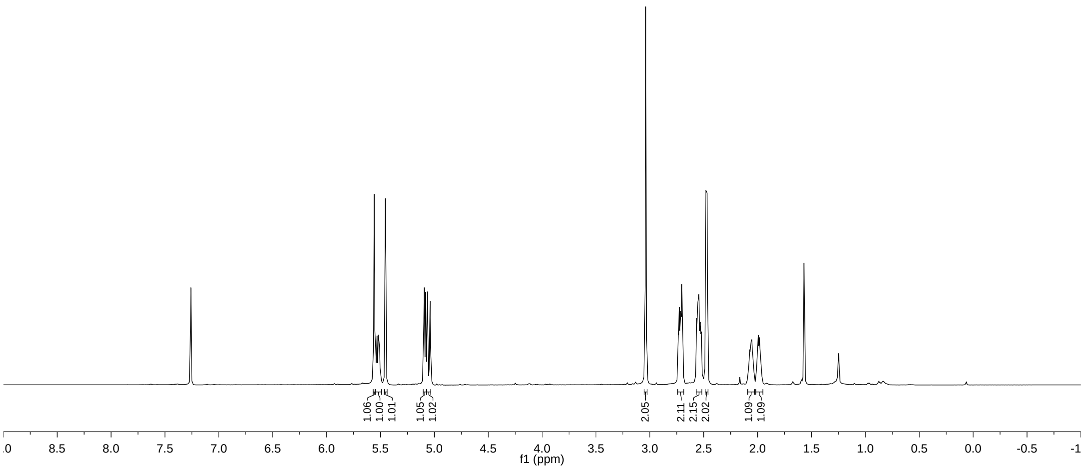
101

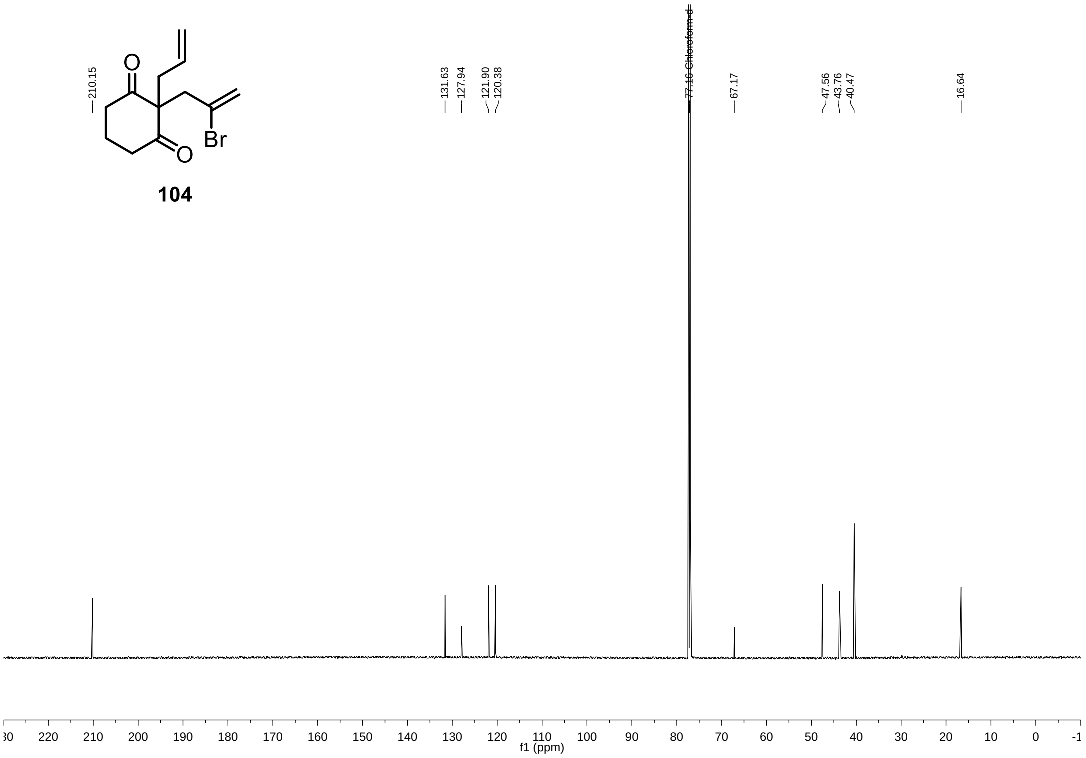

O
OH
0.99
0.99
1.00
1.95
4.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

109

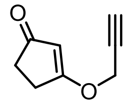

O
O
Br

104

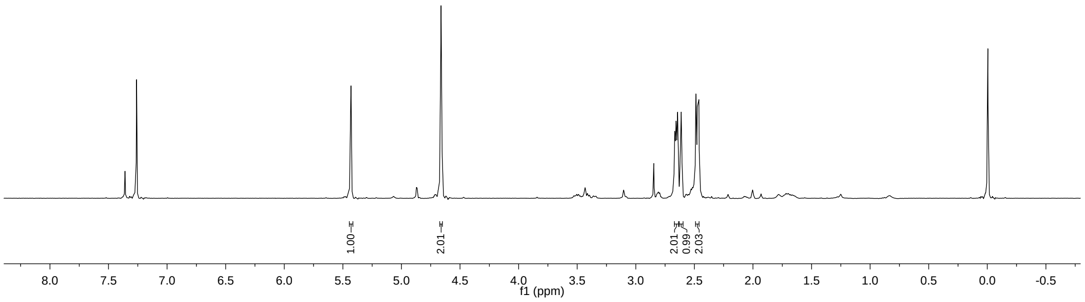

1.06
1.00
1.01
1.05
1.02
2.05
2.11
2.15
2.02
1.09
1.09
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

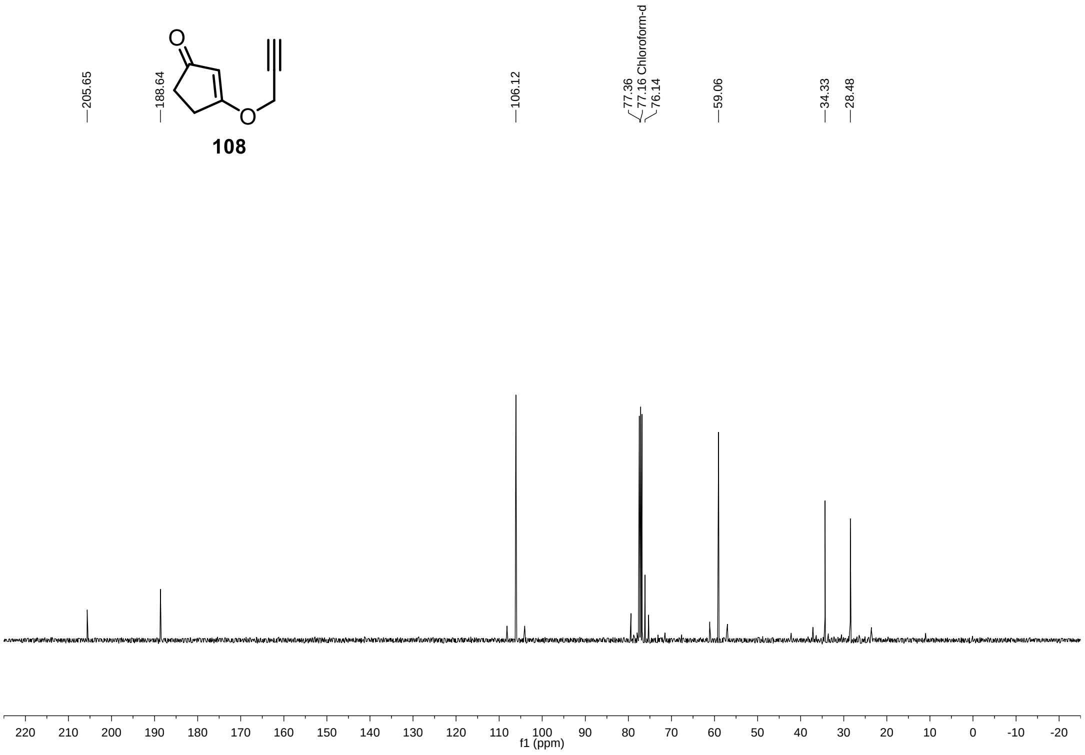

210.15
131.63
127.94
121.90
120.38
77.16 Chloroform-d
67.17
47.56
43.76
40.47
16.64
O
O
Br
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

104

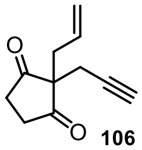


108

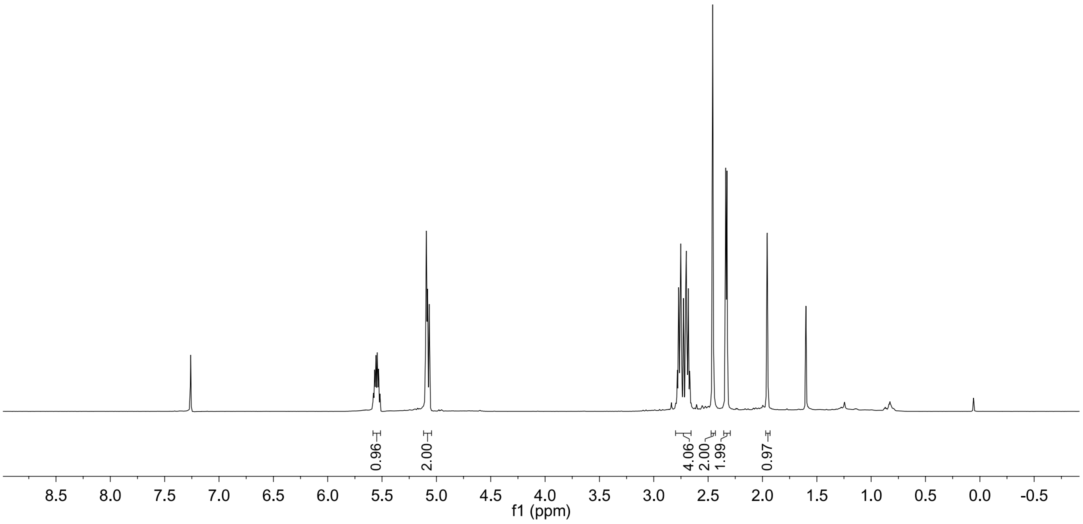

1.00
2.01
2.01
0.99
2.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

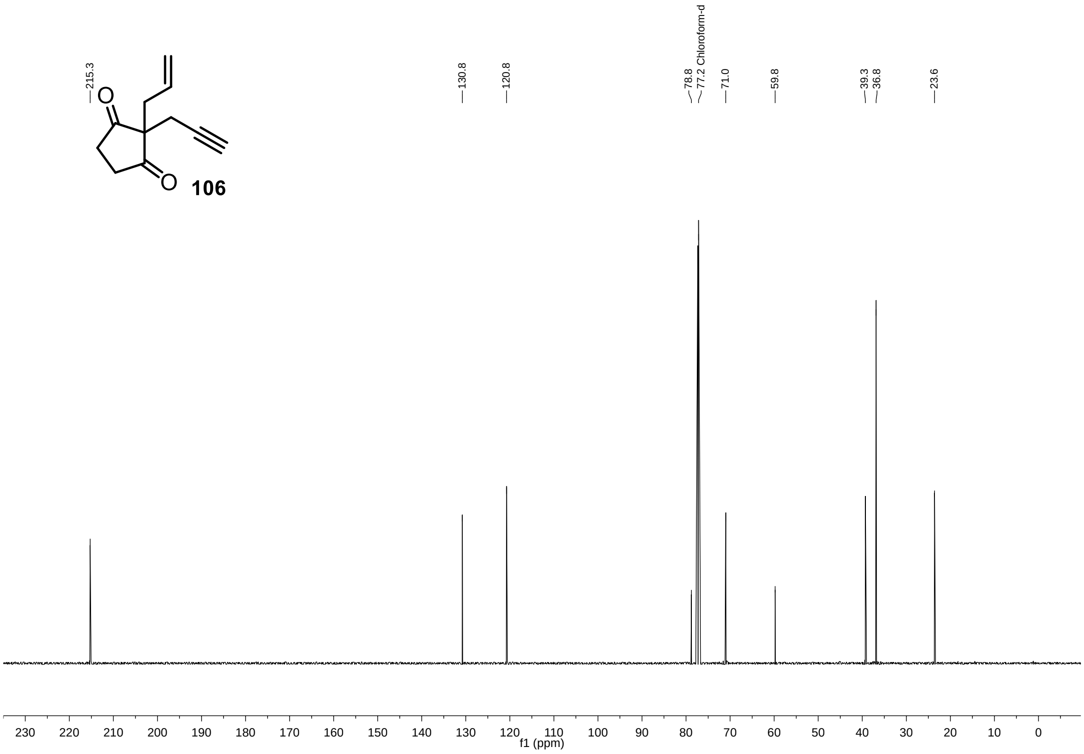

205.65
188.64
106.12
77.36
77.16 Chloroform-d
76.14
59.06
34.33
28.48
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

108



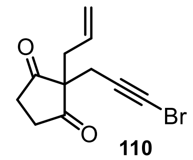
106


0.96
2.00
4.06
2.00
1.99
0.97
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

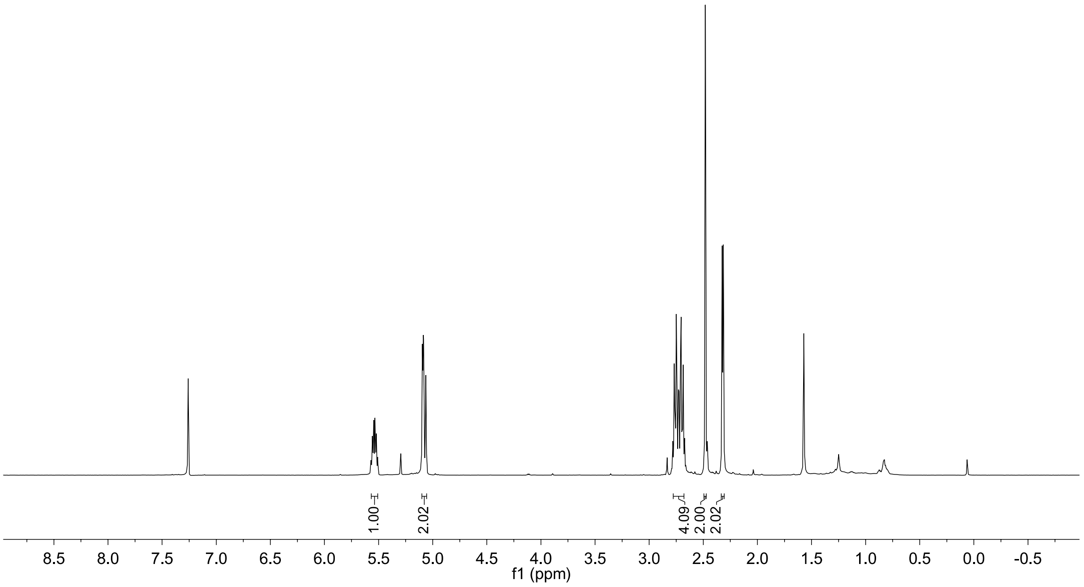


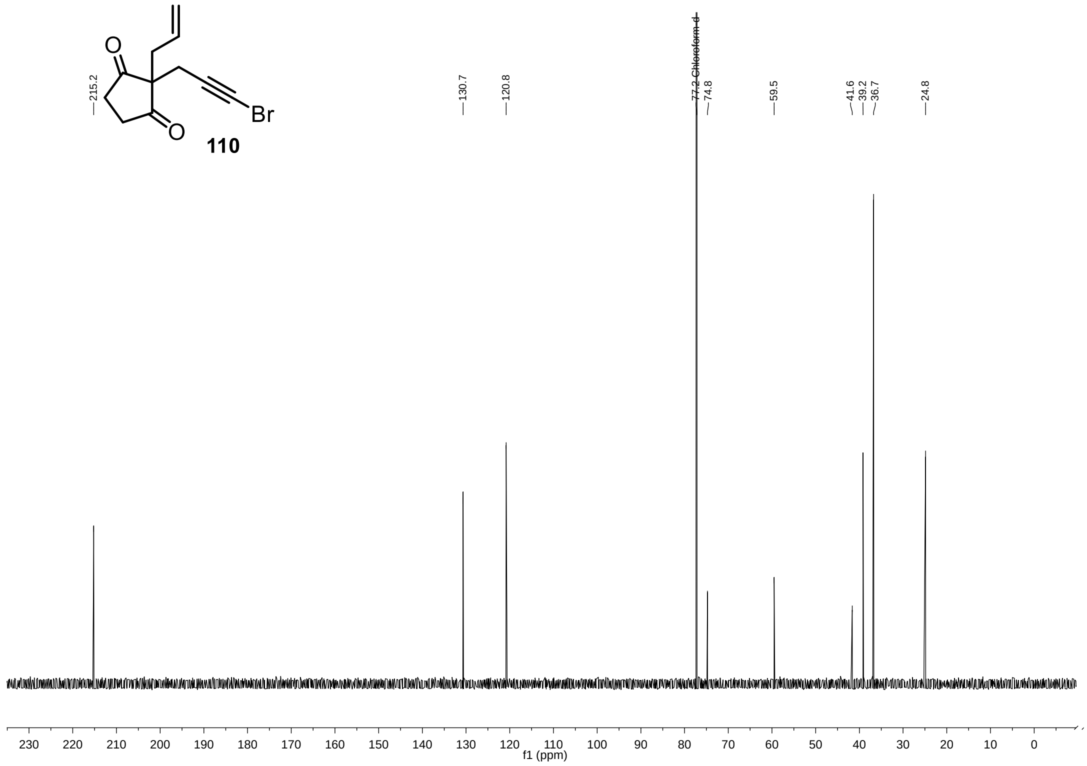
106

215.3
130.8
120.8
78.8
77.2 Chloroform-d
71.0
59.8
39.3
36.8
23.6
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



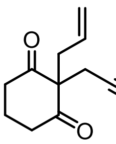
110


1.00
2.02
4.09
2.00
2.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

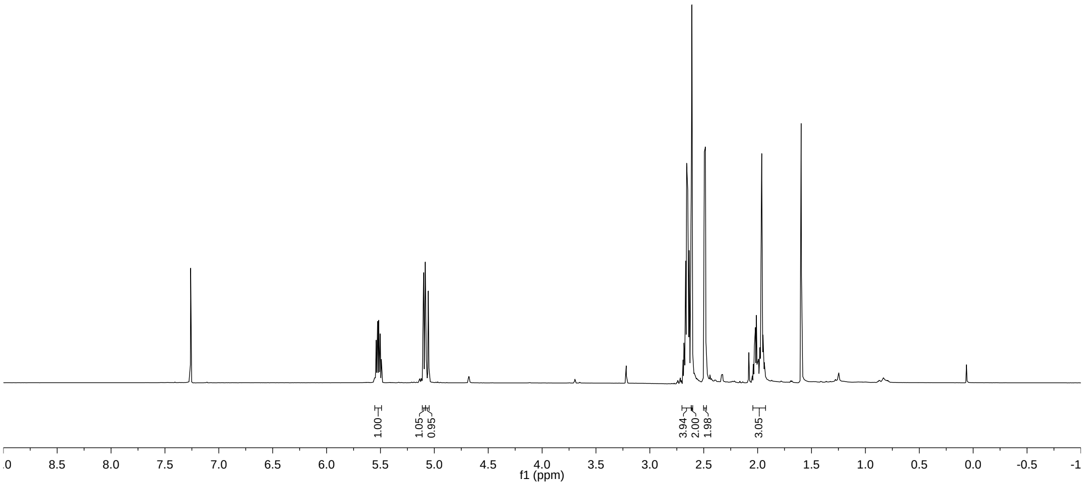


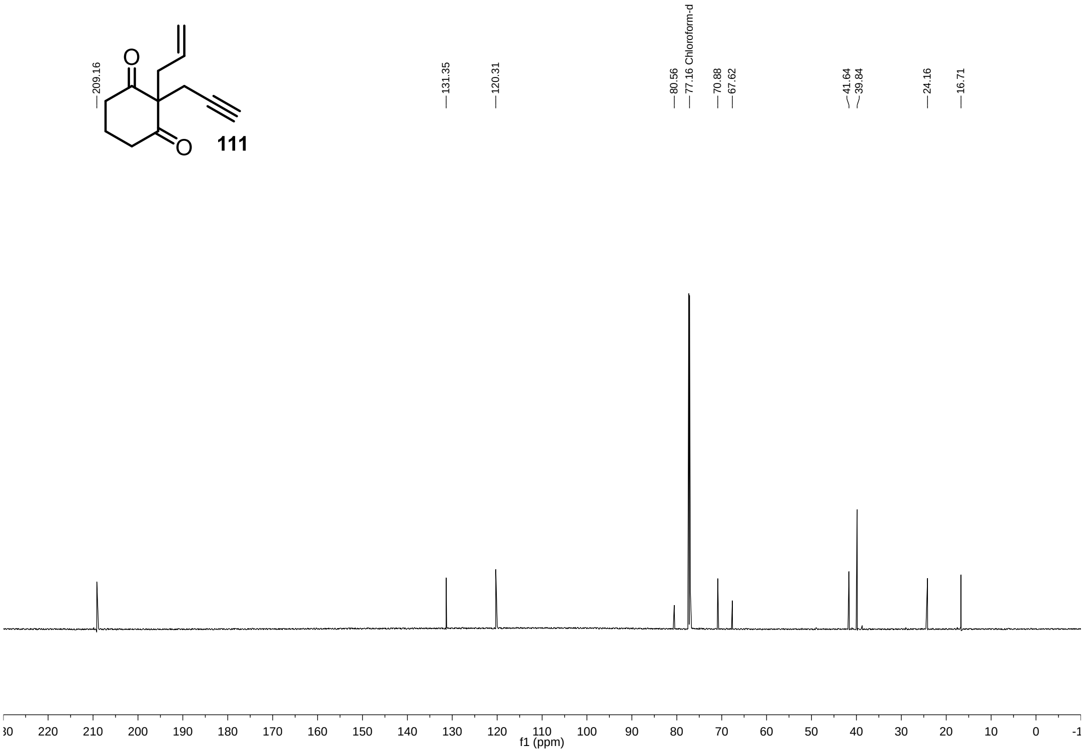
110

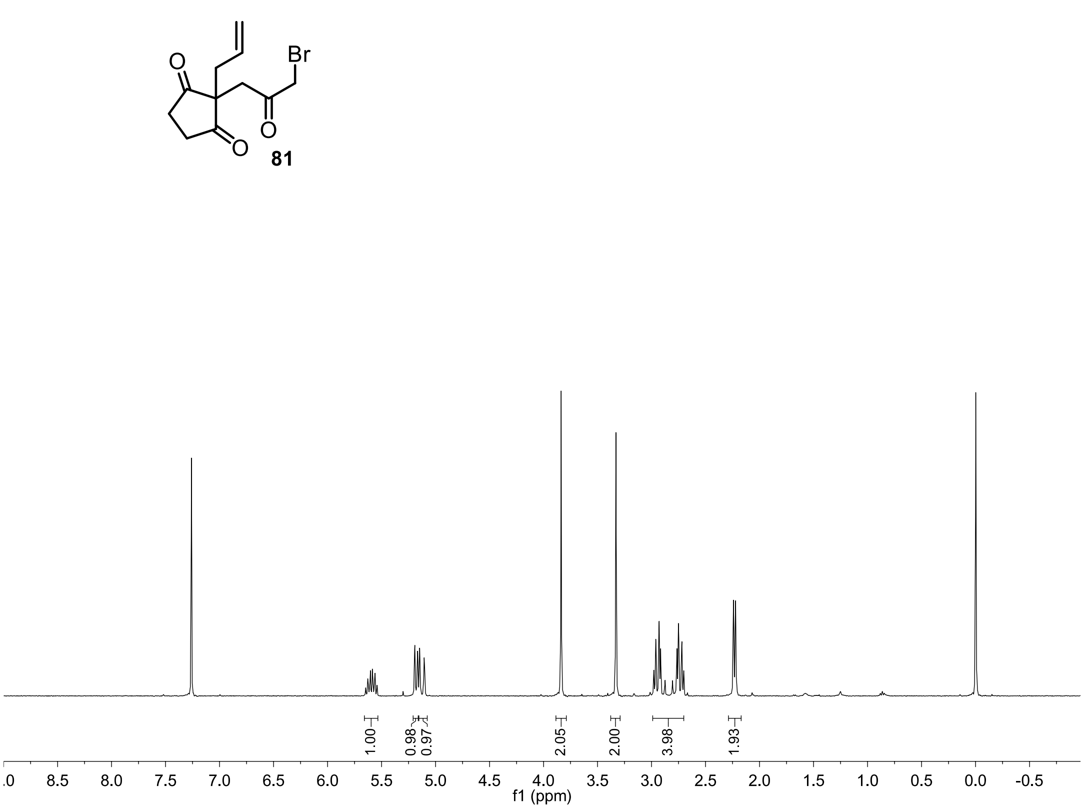
215.2
O
O
Br
130.7
120.8
77.2 Chloroform-d
74.8
59.5
41.6
39.2
36.7
24.8
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

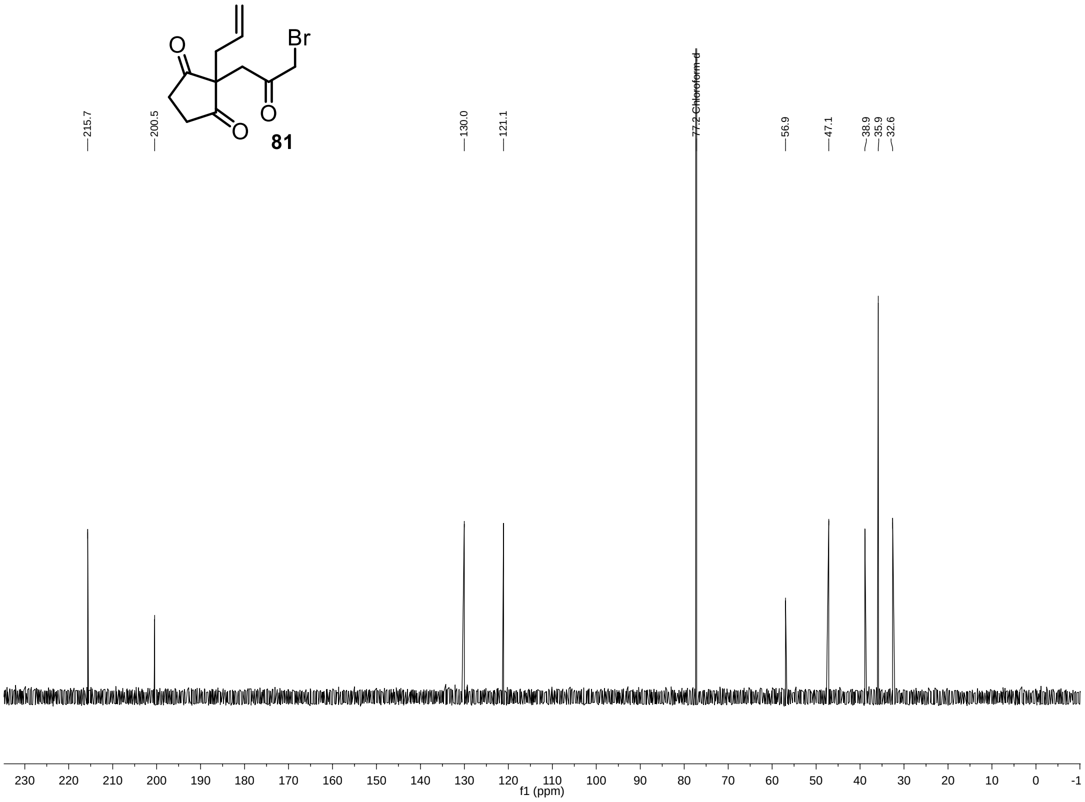


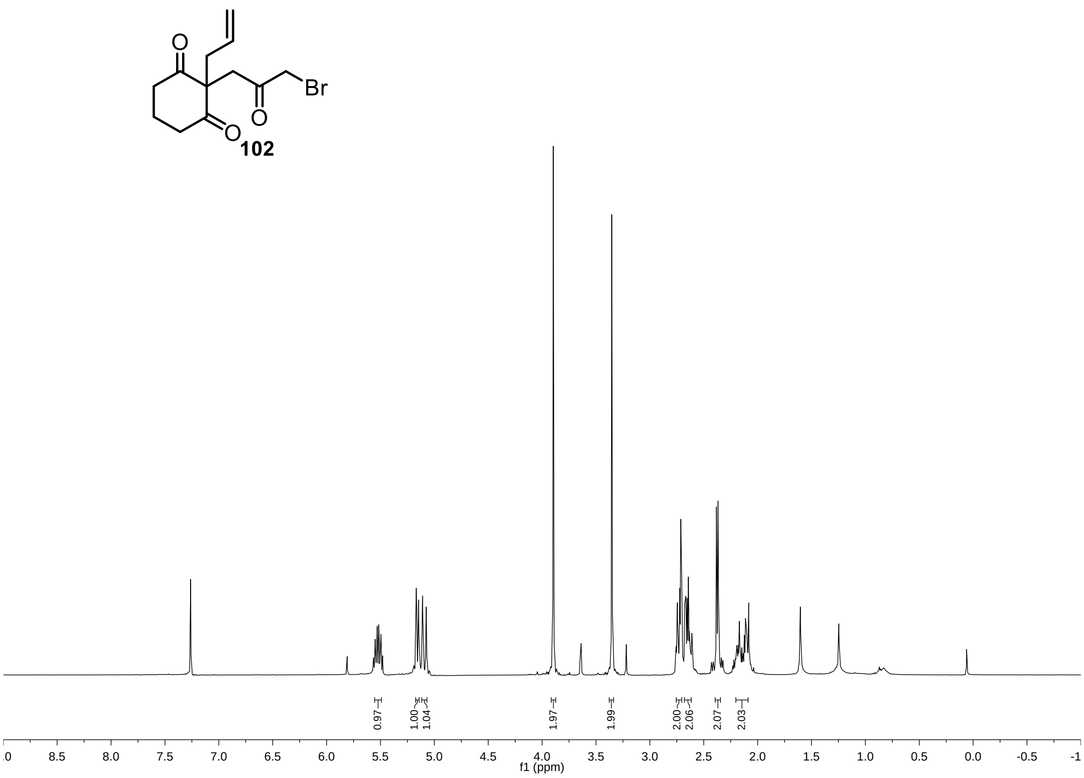
111


1.00
1.05
0.95
3.94
2.00
1.98
3.05
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


111
209.16
131.35
120.31
80.56
77.16 Chloroform-d
70.88
67.62
41.64
39.84
24.16
16.71
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

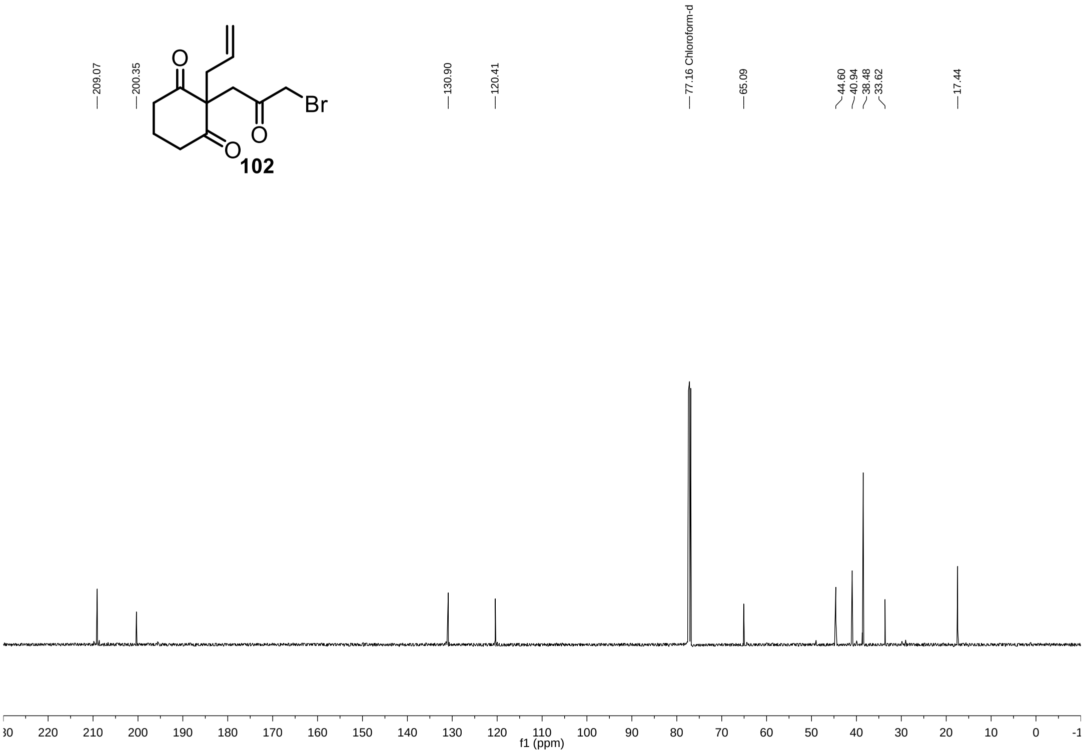

Br
O
O
O
81
1.00
0.98
0.97
2.05
2.00
3.98
1.93
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Br
O
O
O
81
215.7
200.5
130.0
121.1
77.2 Chloroform-d
56.9
47.1
38.9
35.9
32.6
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



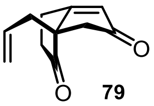
102

O
O
O
Br
0.97
1.00
1.04
1.97
1.99
2.00
2.06
2.07
2.03
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

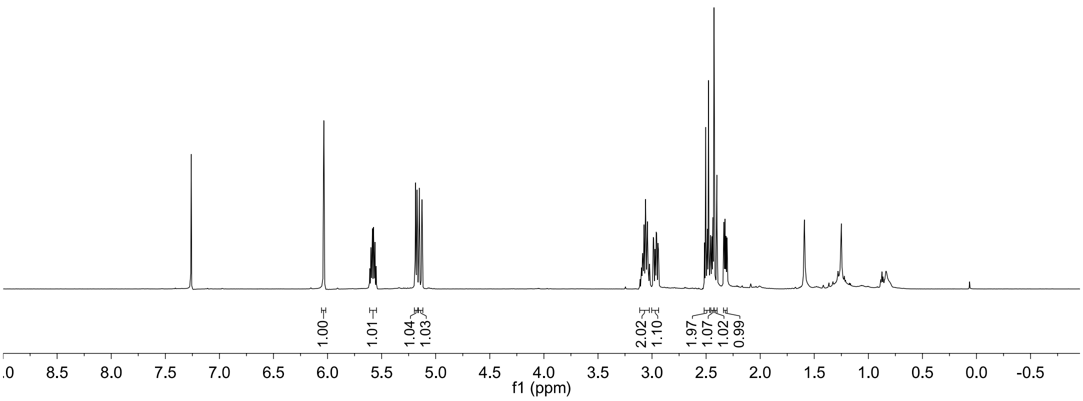


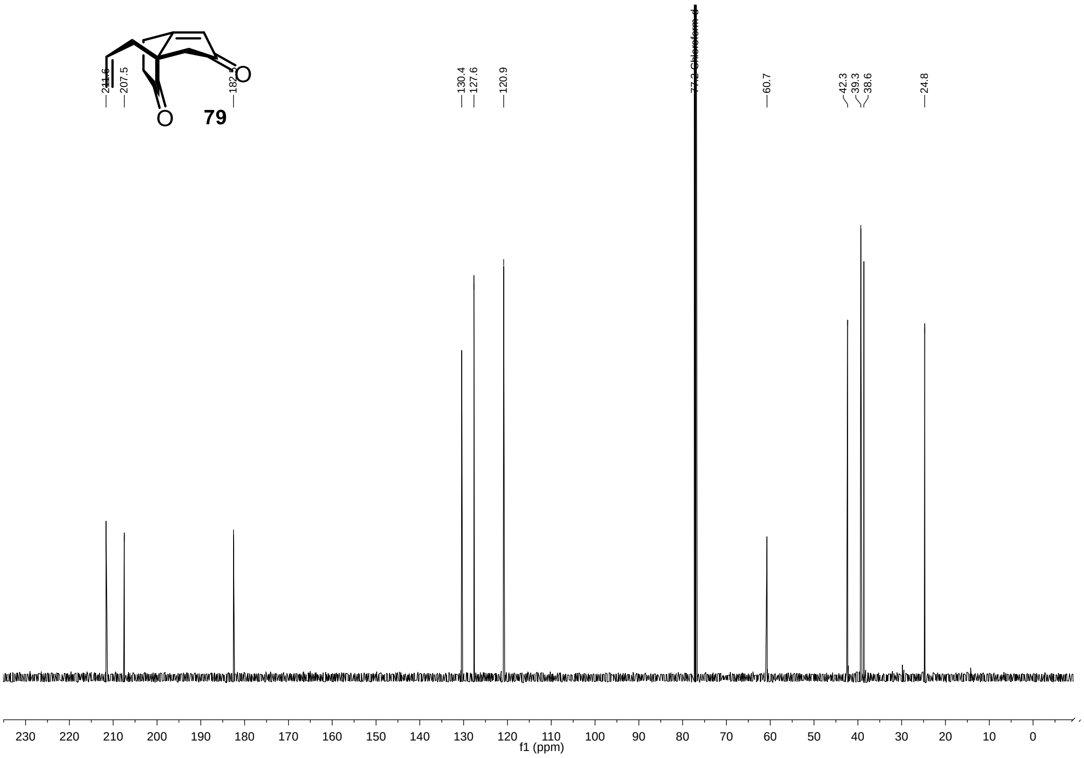
102

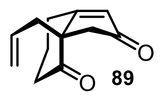
209.07
200.35
130.90
120.41
77.16 Chloroform-d
65.09
44.60
40.94
38.48
33.62
17.44
O
O
O
Br
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



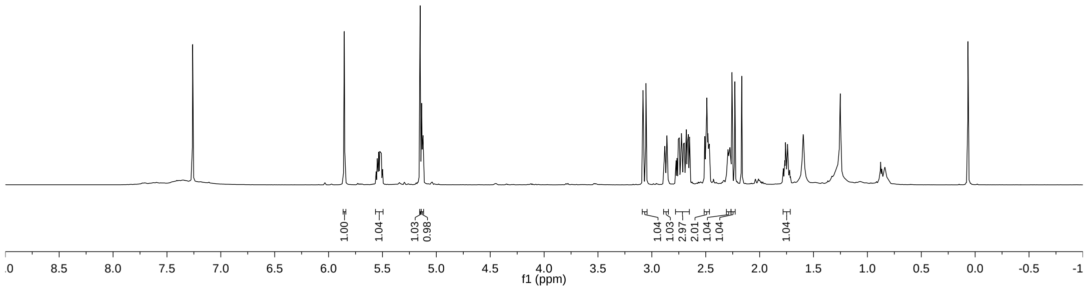
79

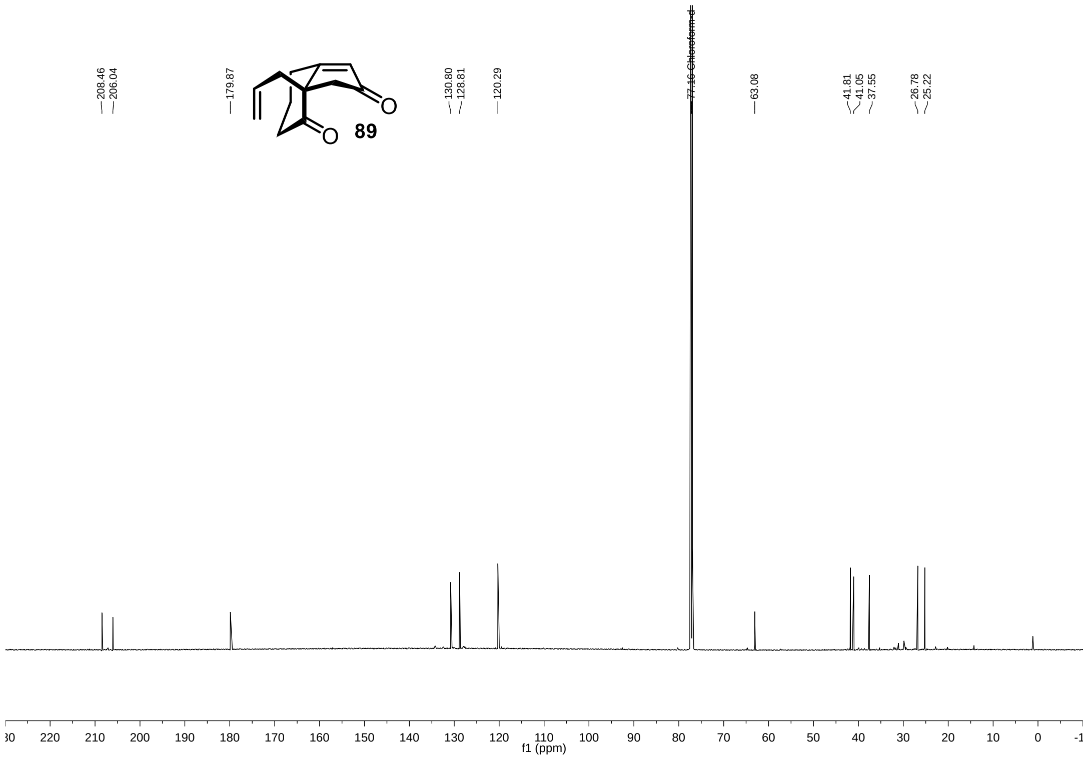

1.00
1.01
1.04
1.03
2.02
1.10
1.97
1.07
1.02
0.99
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

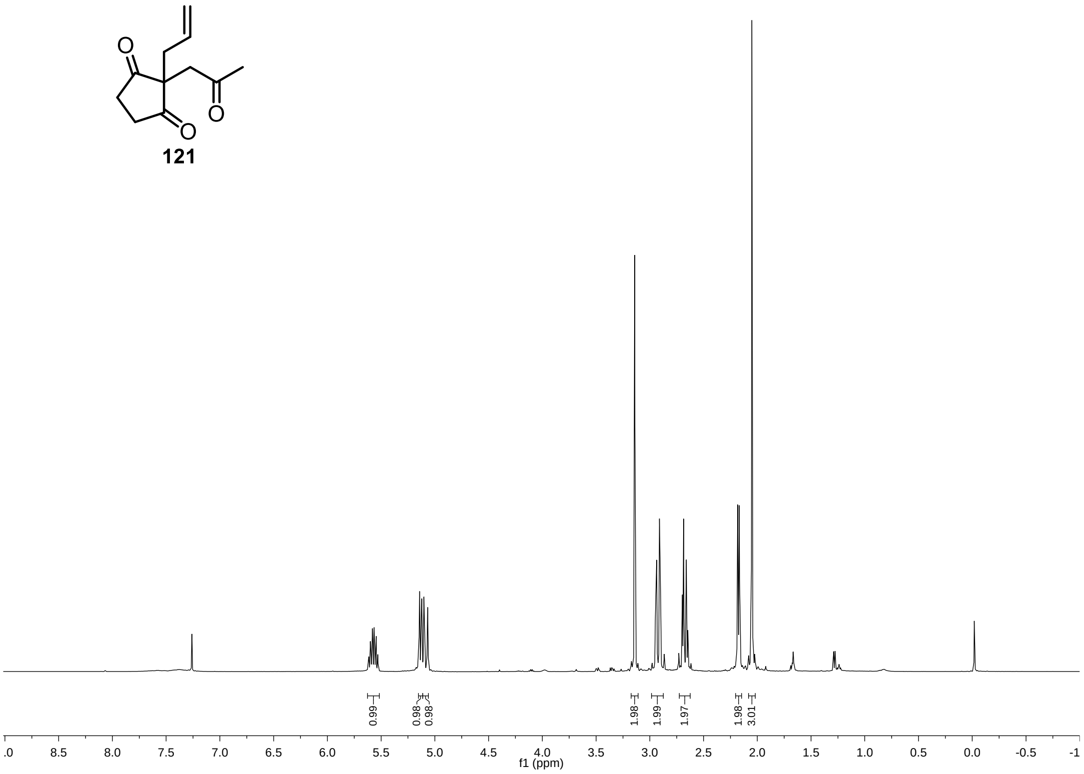

211.6
207.5
182.5
130.4
127.6
120.9
77.2 Chloroform-d
60.7
42.3
39.3
38.6
24.8
79
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

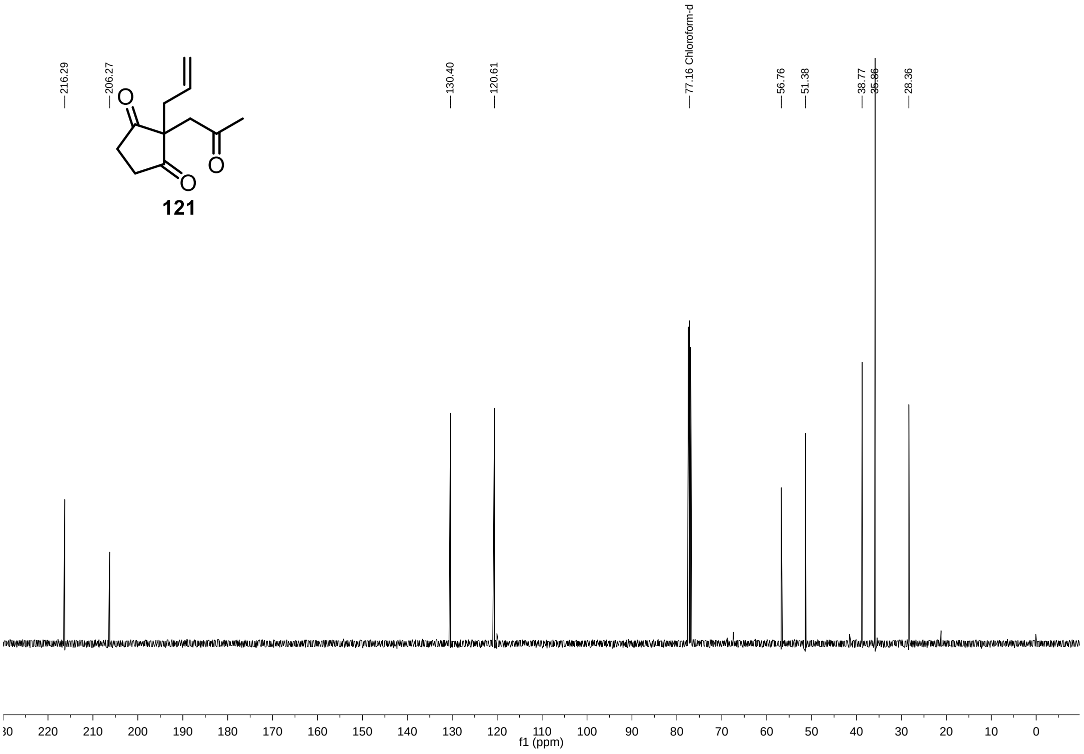


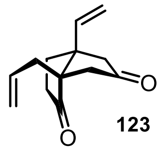
89


1.00
1.04
1.03
0.98
1.04
1.03
2.97
2.01
1.04
1.04
1.04
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

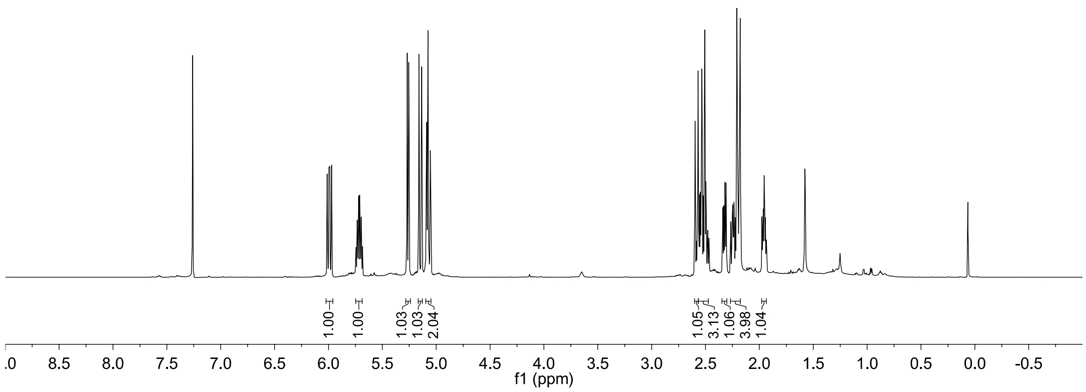

208.46
206.04
179.87
89
130.80
128.81
120.29
77.16 Chloroform-d
63.08
41.81
41.05
37.55
26.78
25.22
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

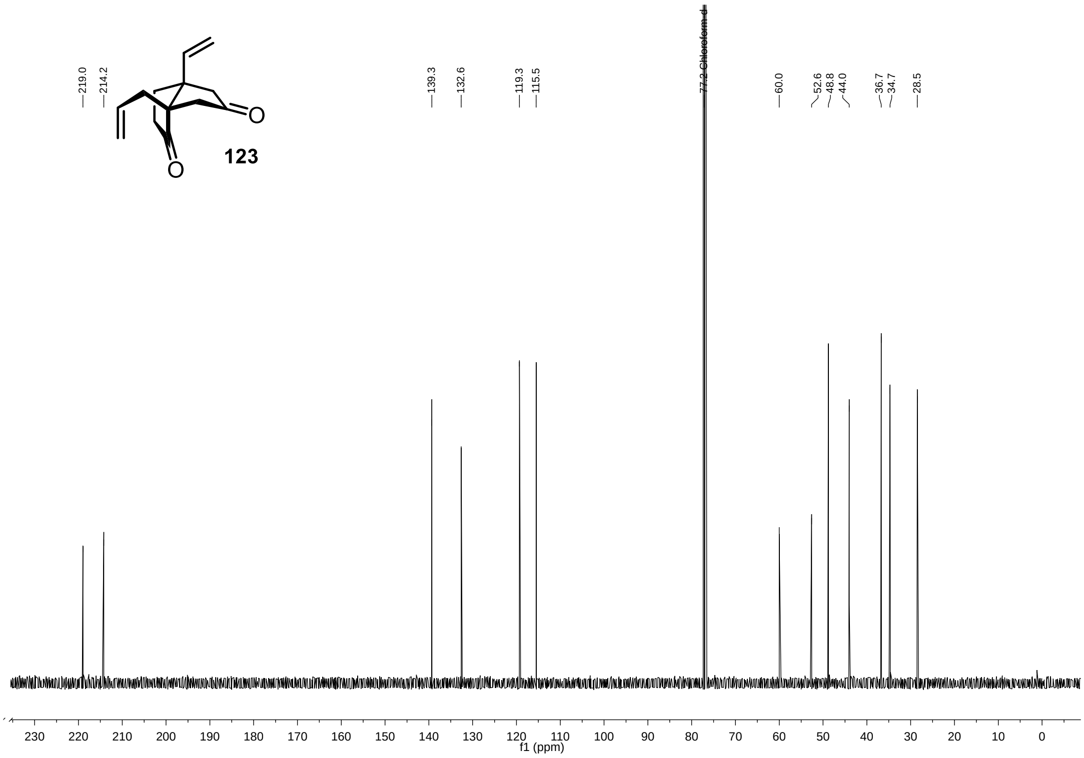

121
0.99
0.98
0.98
1.98
1.99
1.97
1.98
3.01
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


216.29
206.27
130.40
120.61
77.16 Chloroform-d
56.76
51.38
38.77
35.86
28.36
121
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



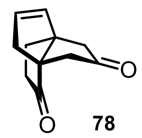
123


1.00
1.00
1.03
1.03
2.04
1.05
3.13
1.06
3.98
1.04
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

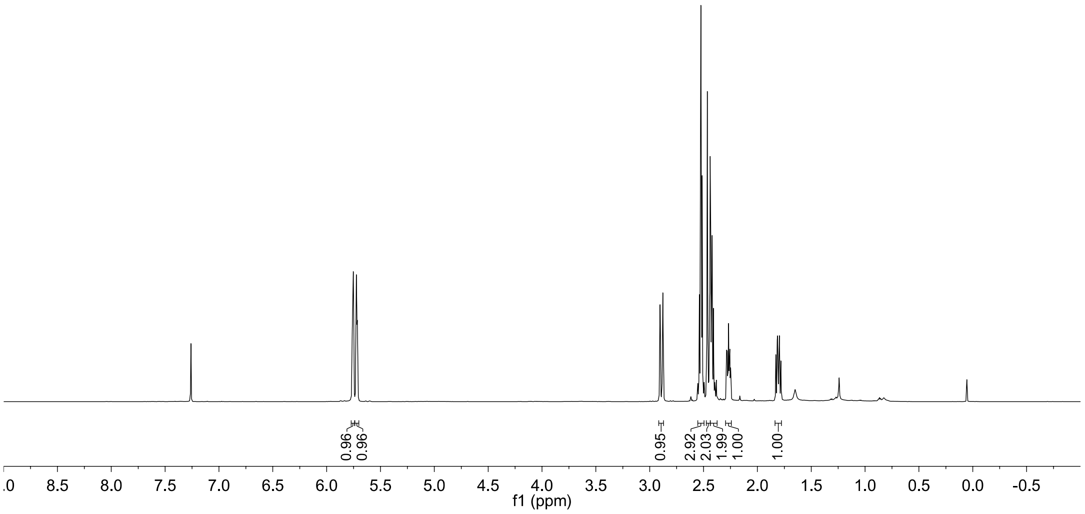


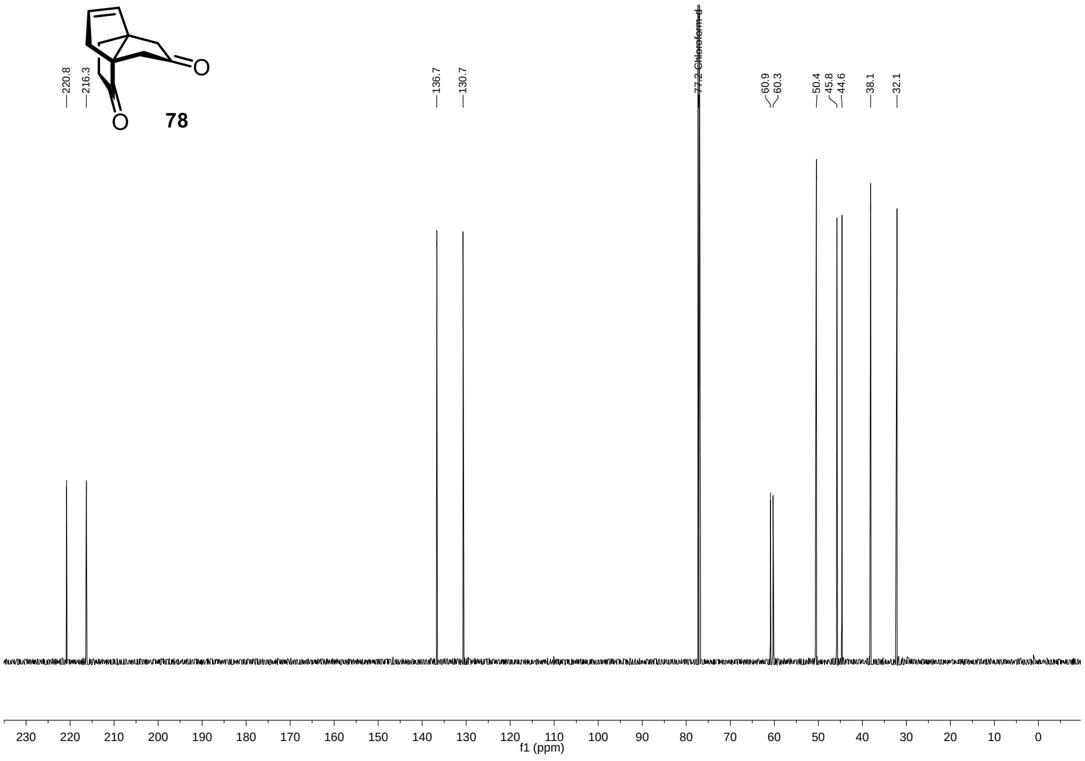
123

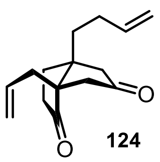
219.0
214.2
139.3
132.6
119.3
115.5
77.2 Chloroform-d
60.0
52.6
48.8
44.0
36.7
34.7
28.5
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



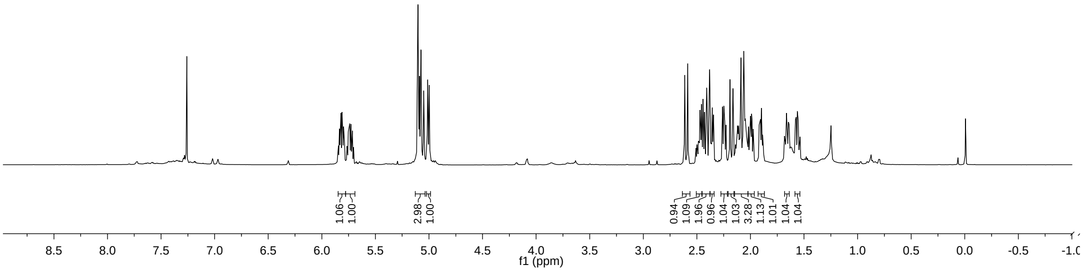
78

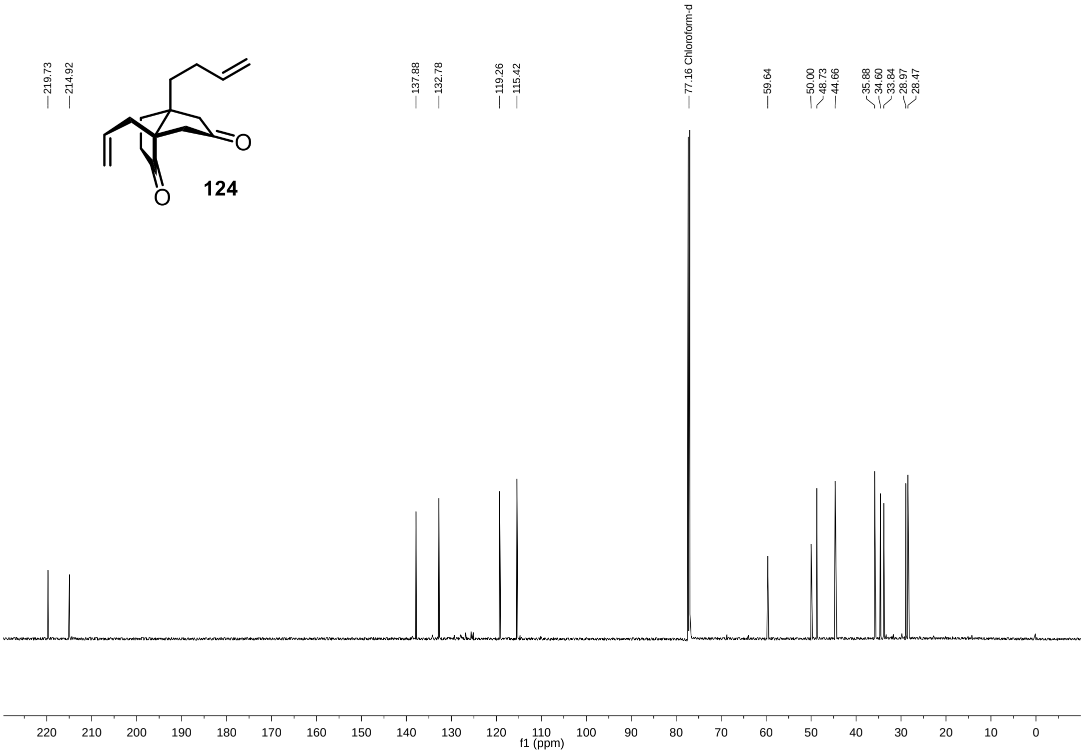

0.96
0.96
0.95
2.92
2.03
1.99
1.00
1.00
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

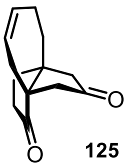

78
220.8
216.3
136.7
130.7
77.2 Chloroform-d
60.9
60.3
50.4
45.8
44.6
38.1
32.1
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



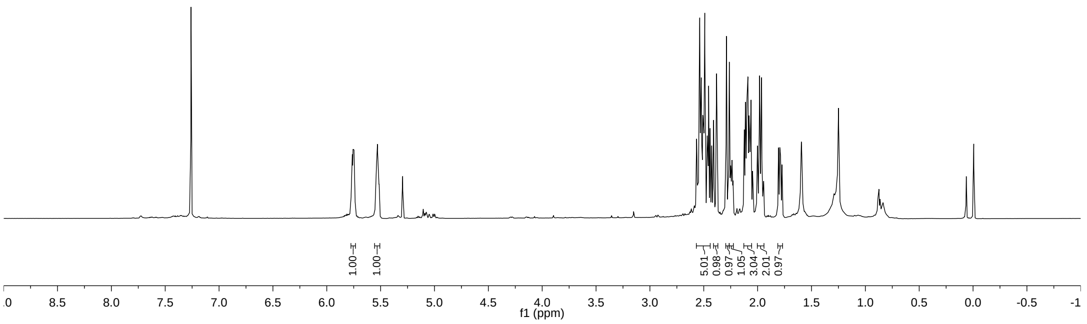
124

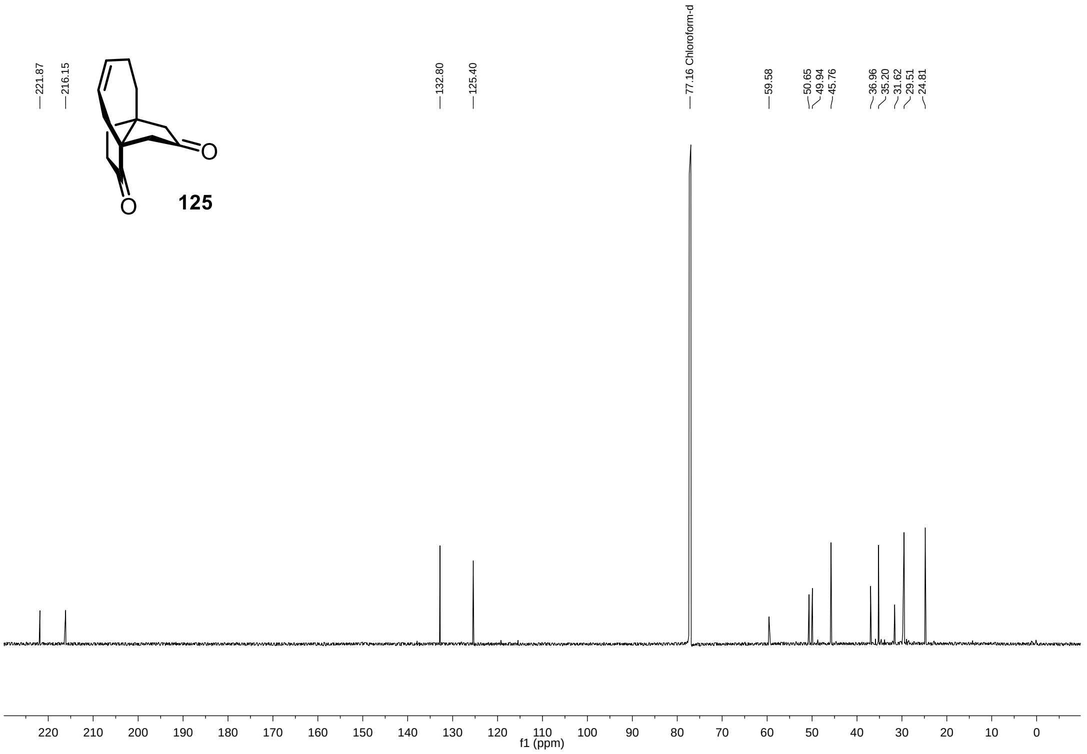

1.06
1.00
2.98
1.00
0.94
1.09
1.96
0.96
1.04
1.03
3.28
1.13
1.01
1.04
1.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

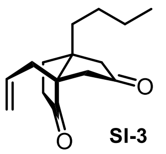

219.73
214.92
137.88
132.78
119.26
115.42
77.16 Chloroform-d
59.64
50.00
48.73
44.66
35.88
34.60
33.84
28.97
28.47
124
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



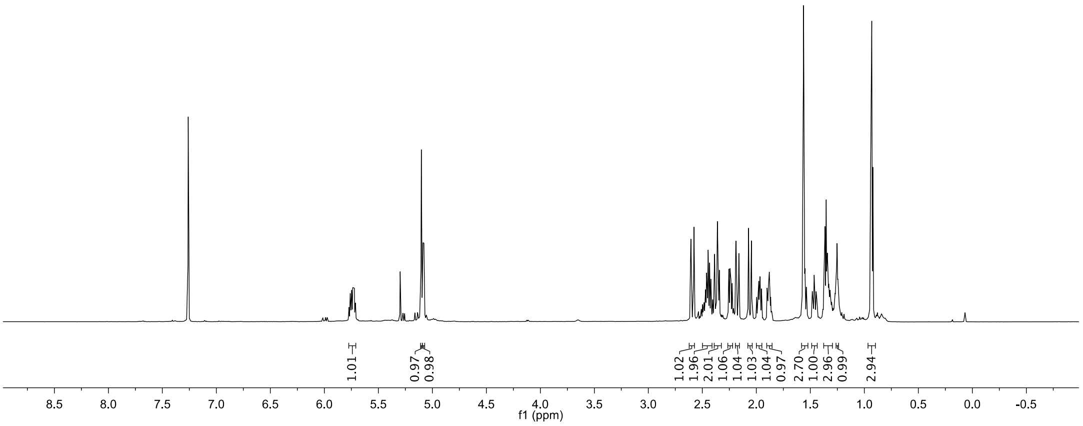
125

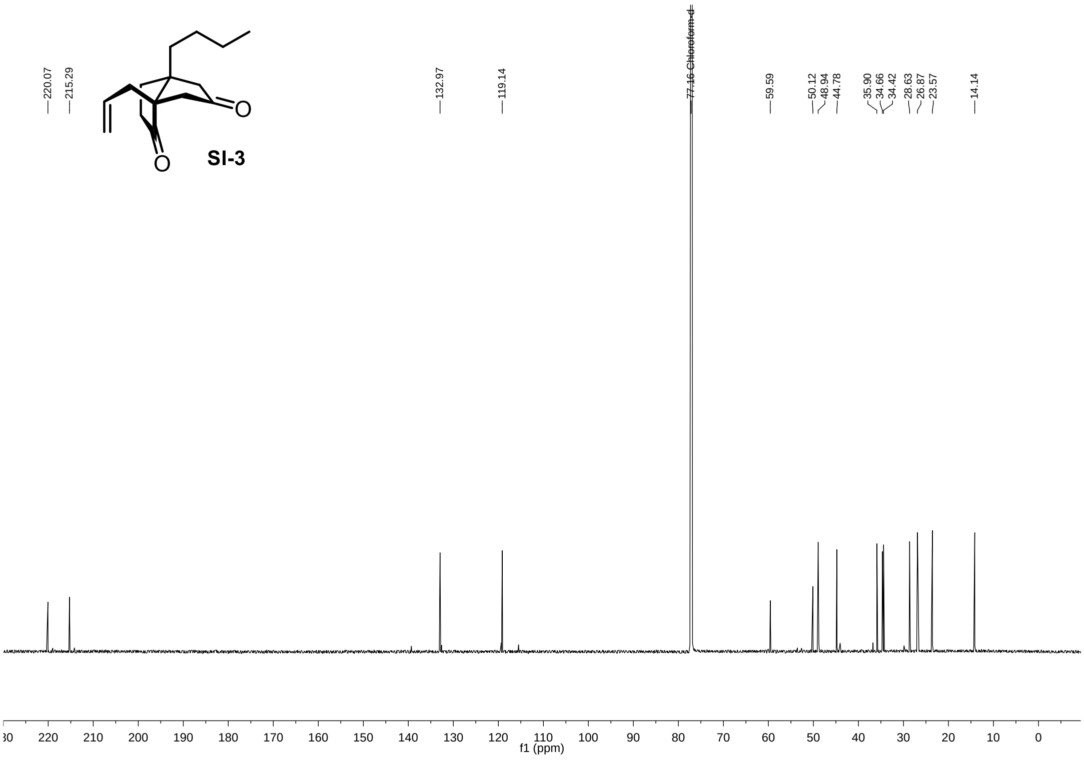

1.00
1.00
5.01
0.98
0.97
1.05
3.04
2.01
0.97
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

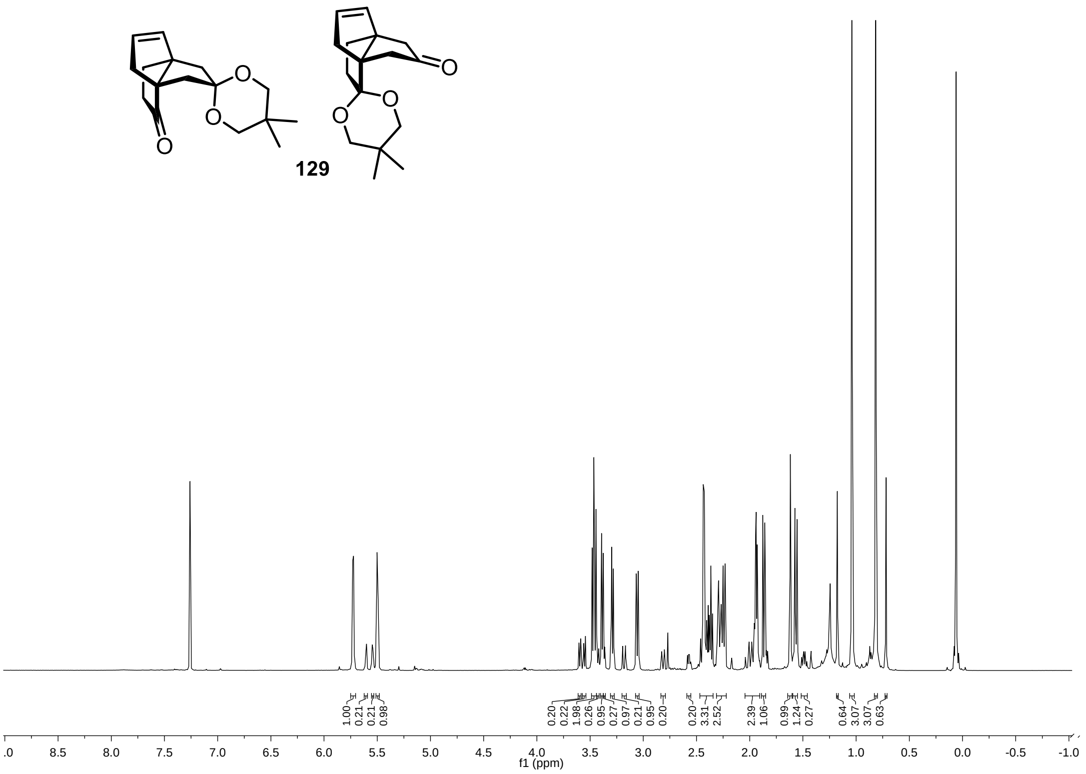

221.87
216.15
132.80
125.40
77.16 Chloroform-d
59.58
50.65
49.94
45.76
36.96
35.20
31.62
29.51
24.81
125
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



SI-3

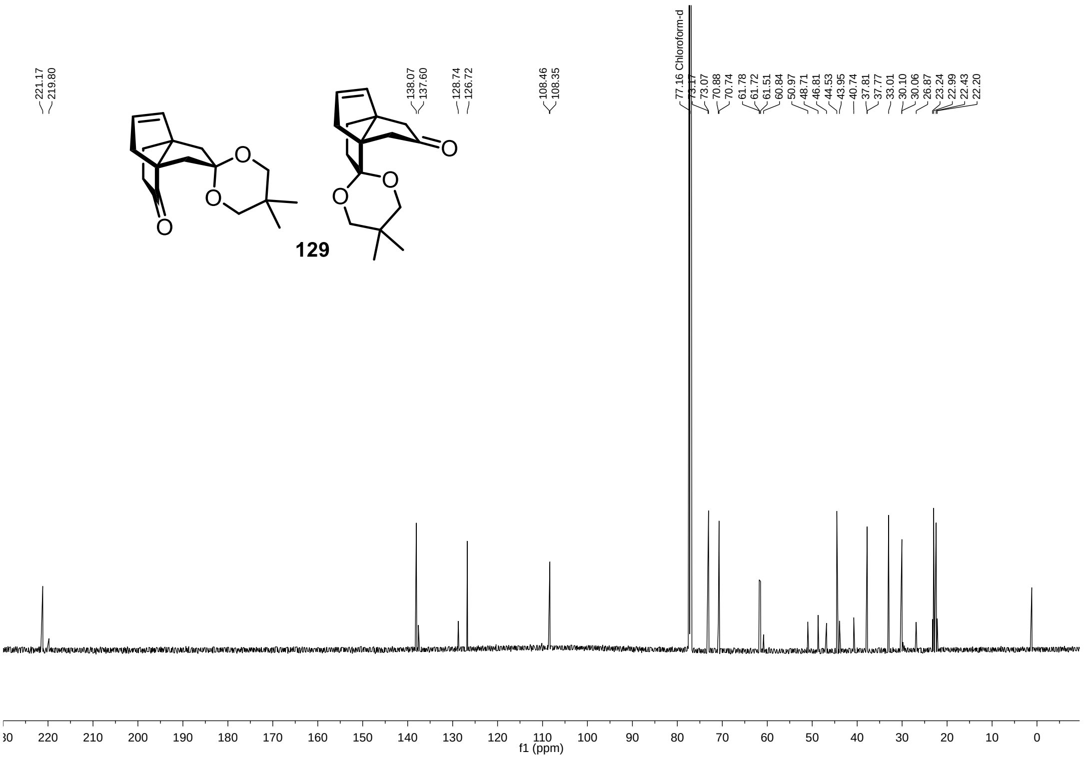

1.01
0.97
0.98
1.02
1.96
2.01
1.06
1.04
1.03
1.04
0.97
2.70
1.00
2.96
0.99
2.94
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


220.07
215.29
132.97
119.14
77.16 Chloroform-d
59.59
50.12
48.94
44.78
35.90
34.66
34.42
28.63
26.87
23.57
14.14
SI-3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



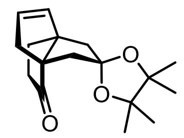
129

1.00
0.21
0.21
0.98
0.20
0.22
1.98
0.26
0.95
0.27
0.97
0.21
0.95
0.20
0.20
3.31
2.52
2.39
1.06
0.99
1.24
0.27
0.64
3.07
3.07
0.63
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)
O
O
O
O
O
O

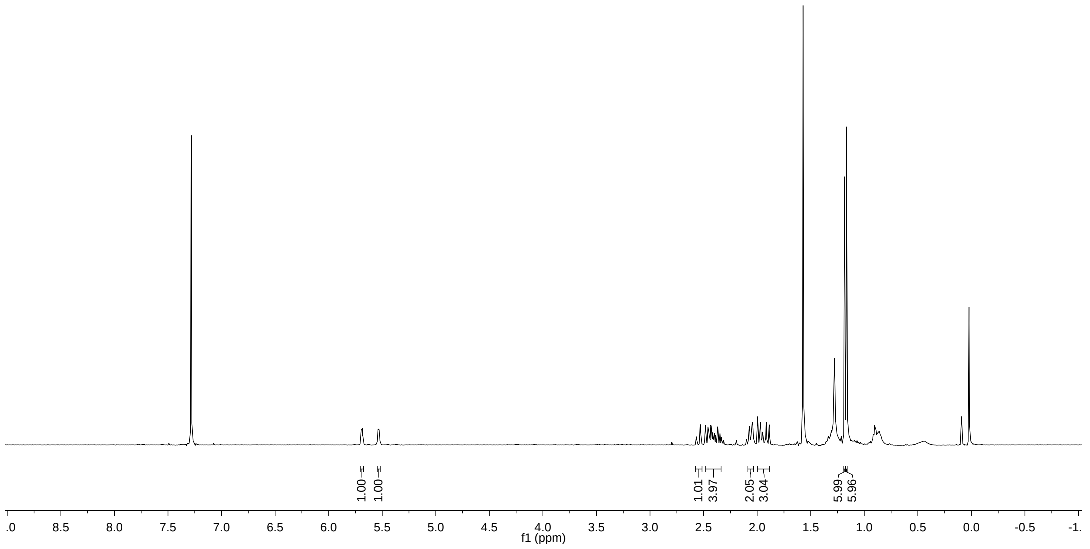


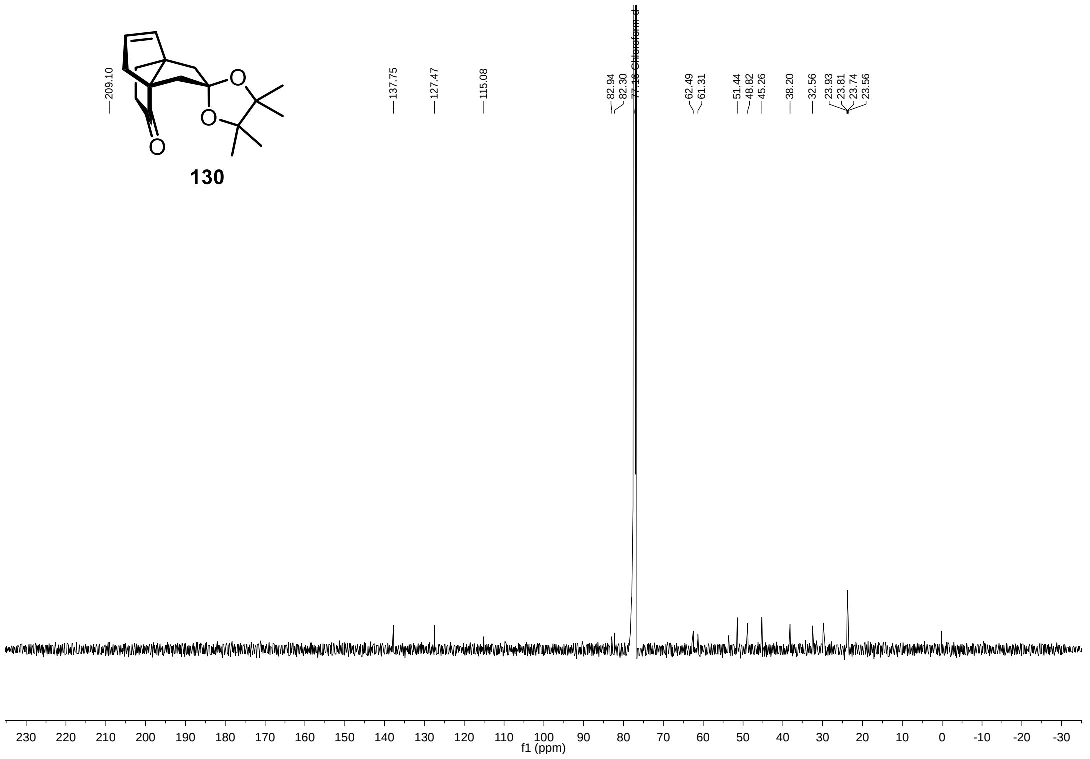
129

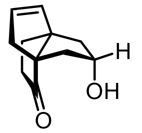
221.17
219.80
138.07
137.60
128.74
126.72
108.46
108.35
77.16 Chloroform-d
73.17
73.07
70.88
70.74
61.78
61.72
61.51
60.84
50.97
48.71
46.81
44.53
43.95
40.74
37.81
37.77
33.01
30.10
30.06
26.87
23.24
22.99
22.43
22.20
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
O
O
O
O
O
O



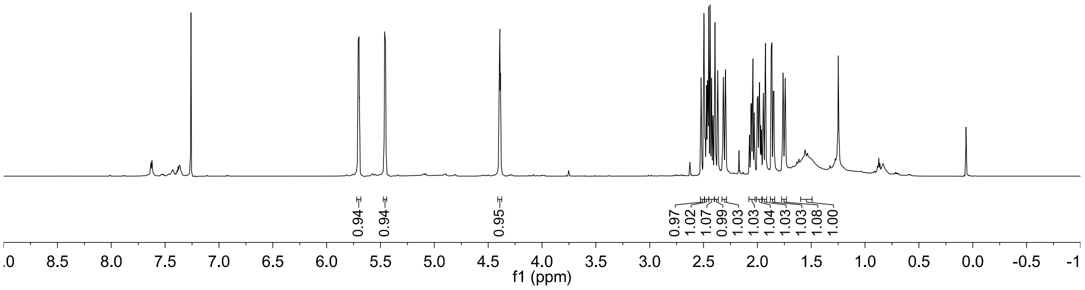
130

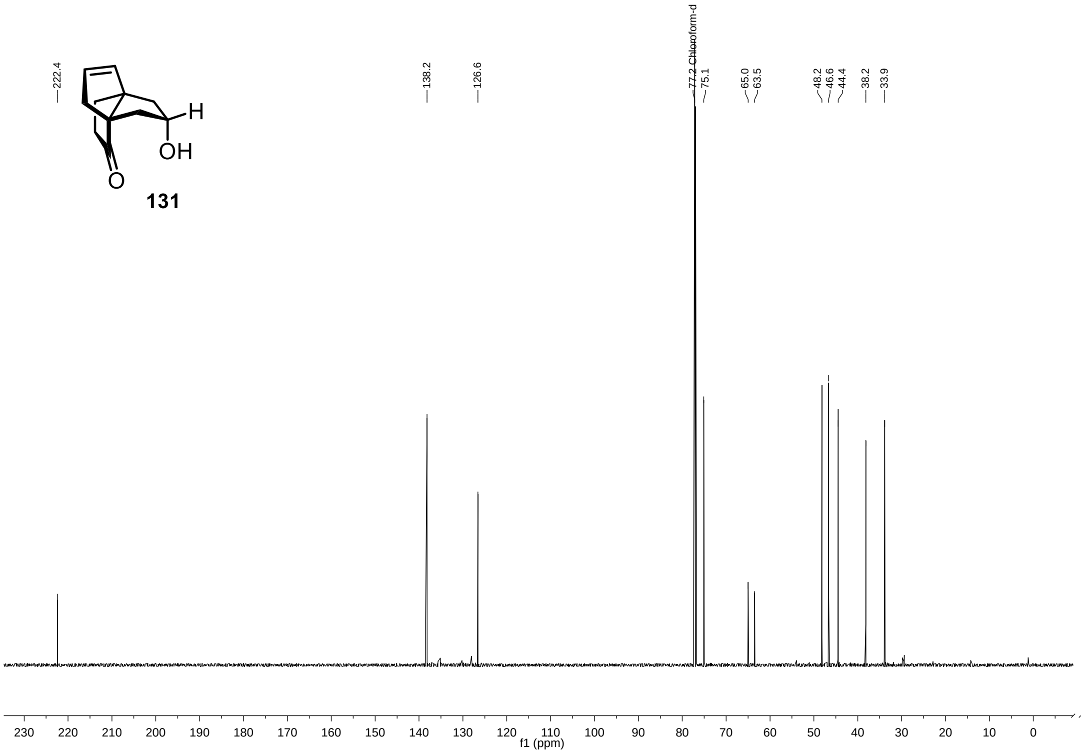

1.00
1.00
1.01
3.97
2.05
3.04
5.99
5.96
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


209.10
137.75
127.47
115.08
82.94
82.30
77.16 Chloroform-d
62.49
61.31
51.44
48.82
45.26
38.20
32.56
23.93
23.81
23.74
23.56
130
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
f1 (ppm)

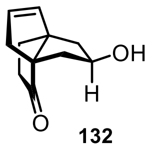

H
OH
O

131

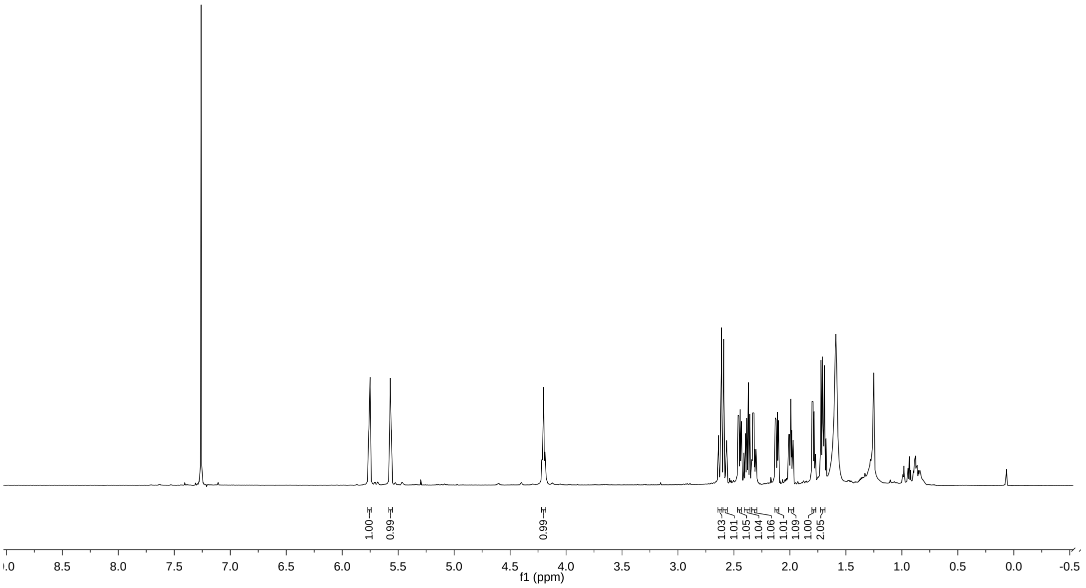

0.94
0.94
0.95
0.97
1.02
1.07
0.99
1.03
1.03
1.04
1.03
1.03
1.08
1.00
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

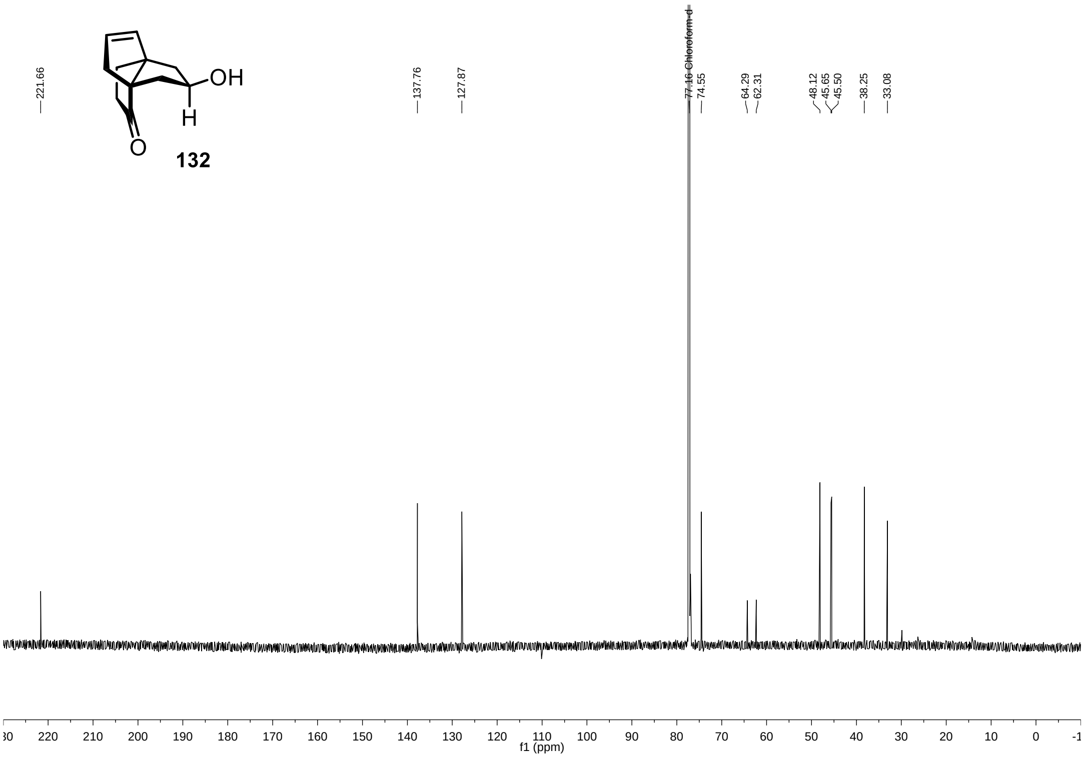

222.4
138.2
126.6
77.2 Chloroform-d
75.1
65.0
63.5
48.2
46.6
44.4
38.2
33.9
H
OH
O
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

131



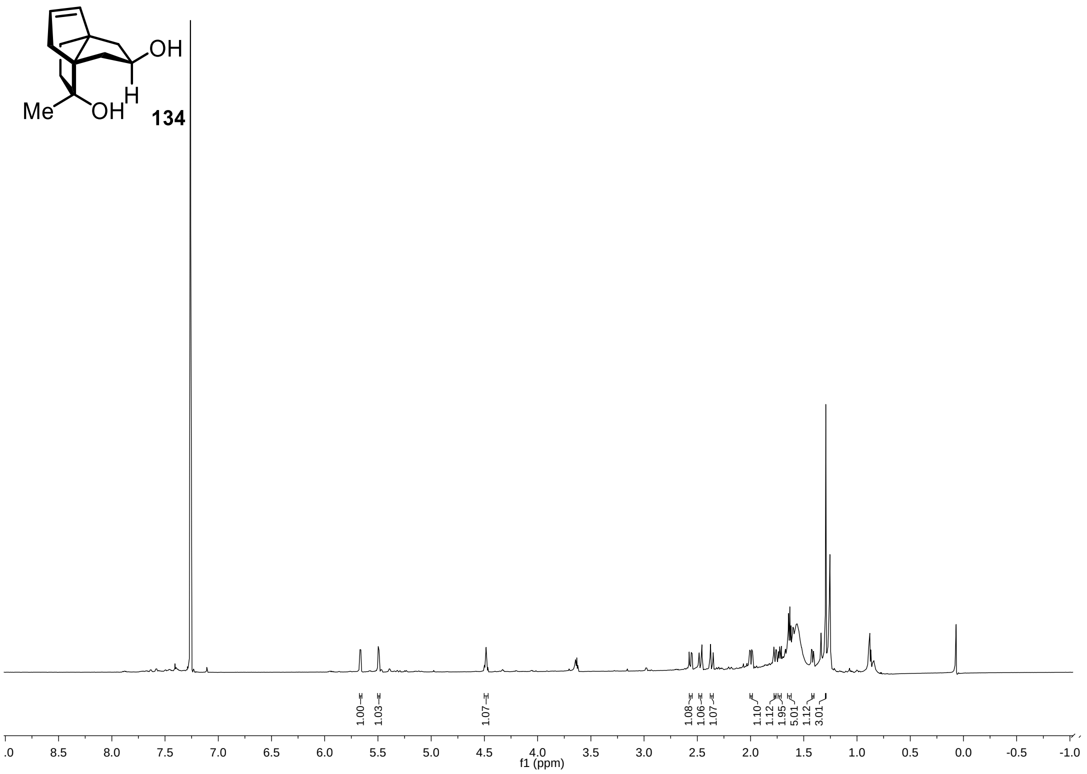
132

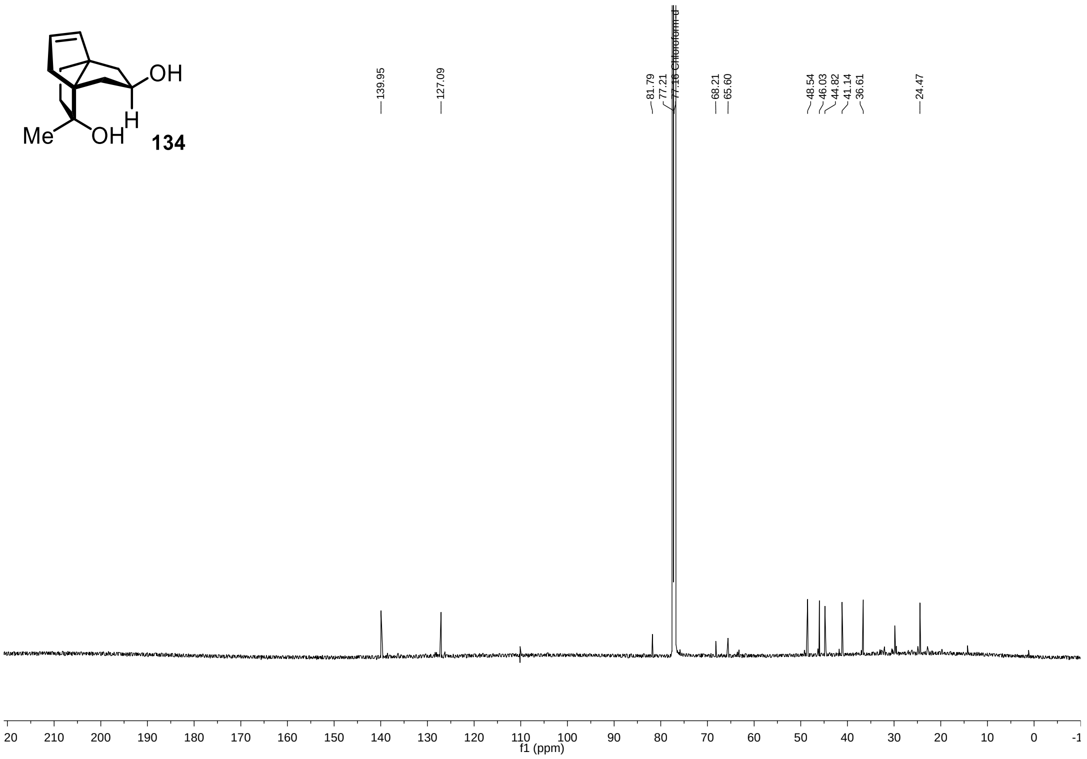

1.00
0.99
0.99
1.03
1.01
1.05
1.04
1.06
1.01
1.09
1.00
2.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

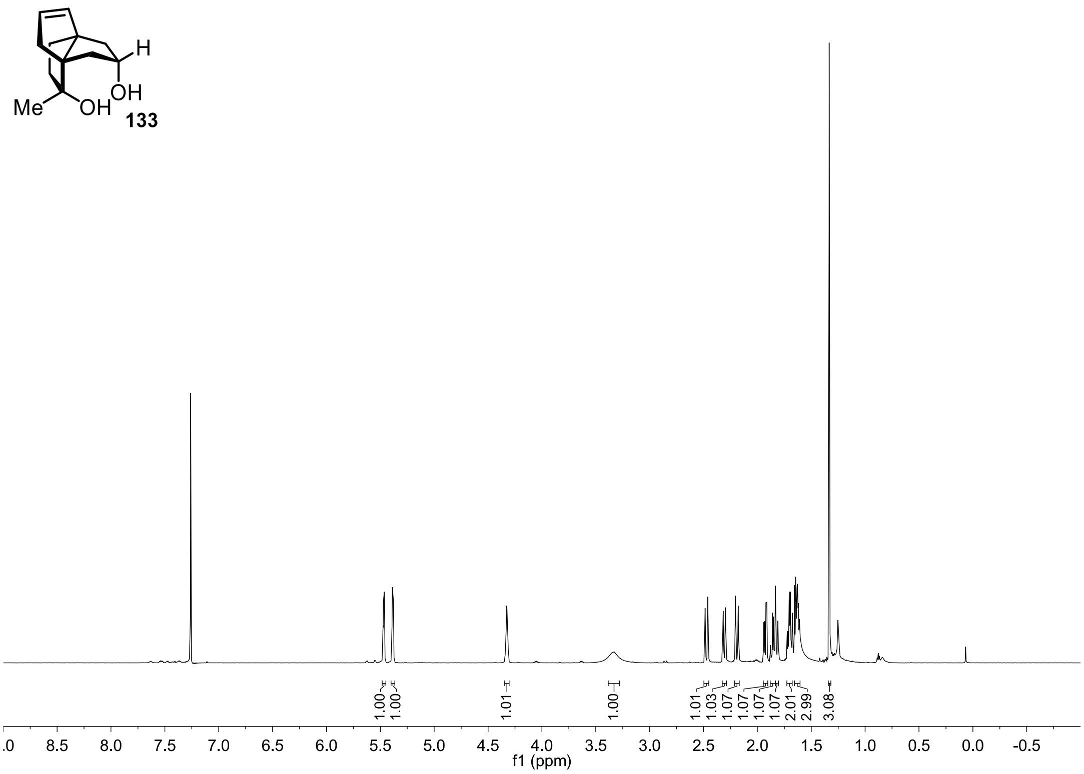


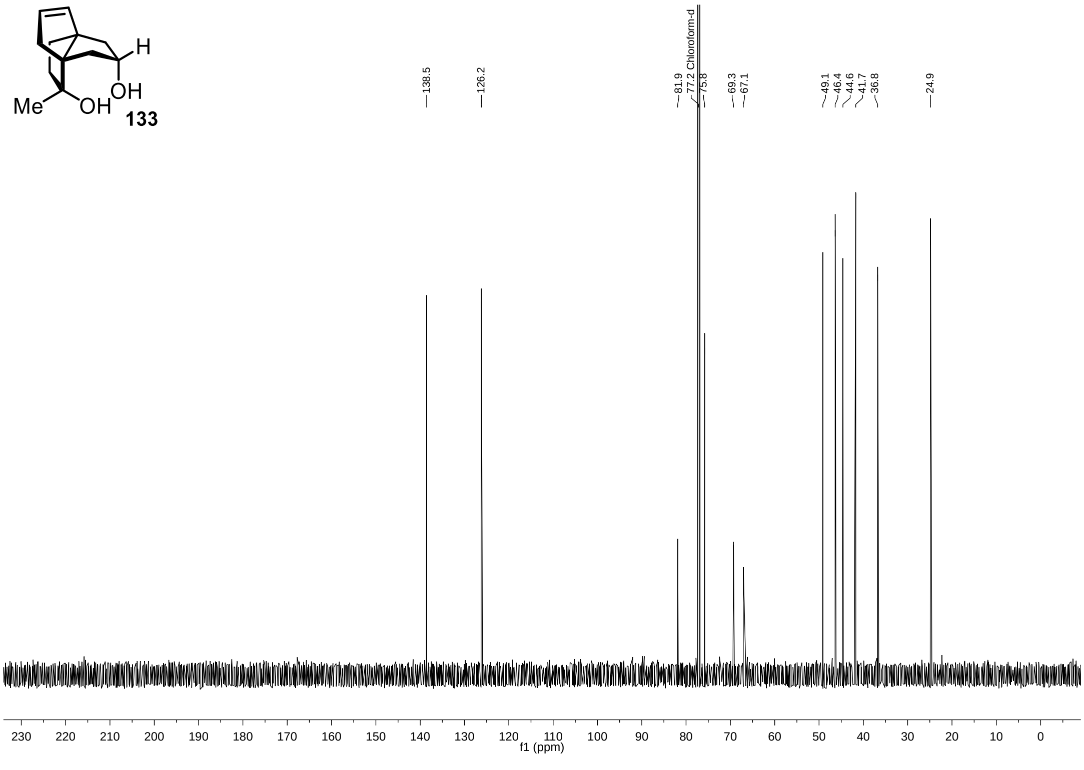
132

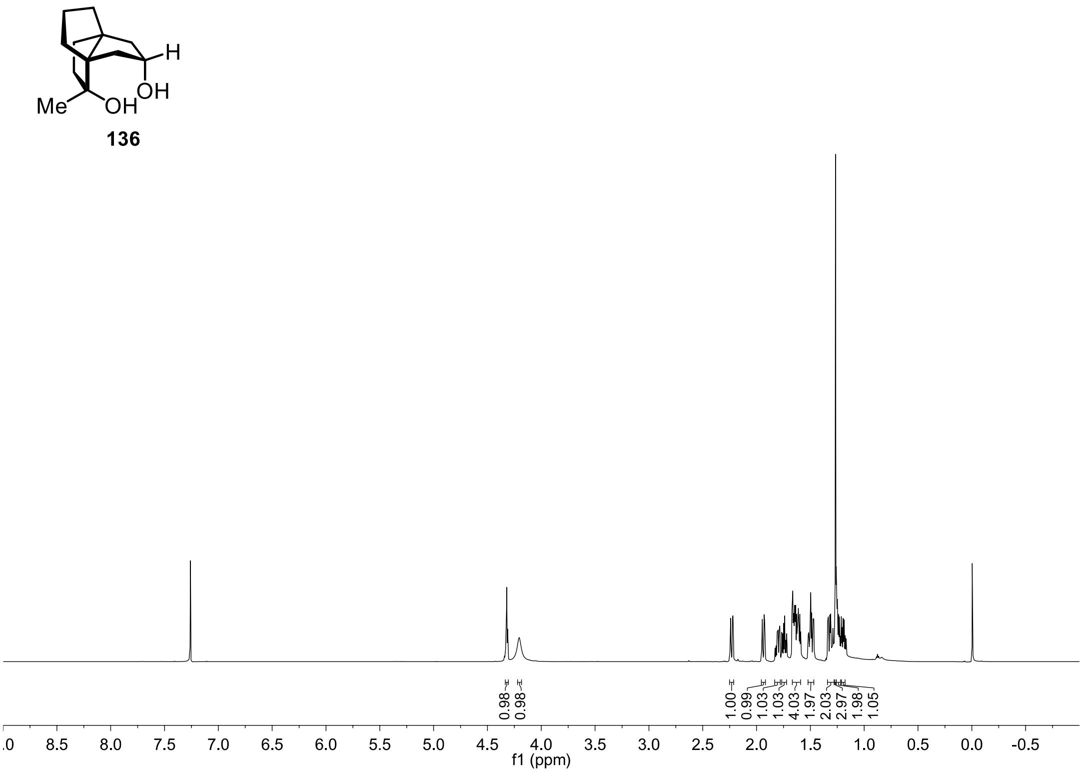
221.66
137.76
127.87
77.16 Chloroform-d
74.55
64.29
62.31
48.12
45.65
45.50
38.25
33.08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OH
H
Me
OH
134
1.00
1.03
1.07
1.08
1.06
1.07
1.10
1.12
1.95
5.01
1.12
3.01
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


OH
H
Me
OH
134
139.95
127.09
81.79
77.21
77.16 Chloroform-d
68.21
65.60
48.54
46.03
44.82
41.14
36.61
24.47
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

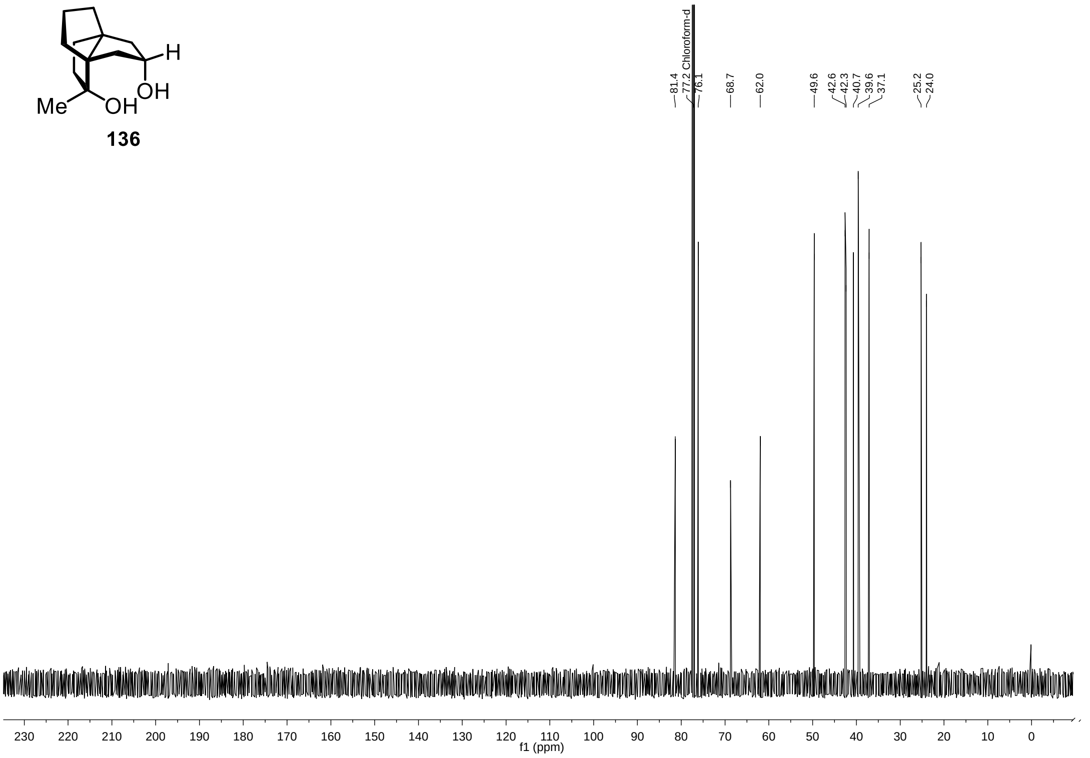

133
H
OH
Me
OH
1.00
1.00
1.01
1.00
1.01
1.03
1.07
1.07
1.07
1.07
2.01
2.99
3.08
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


133
H
OH
Me
OH
138.5
126.2
81.9
77.2 Chloroform-d
75.8
69.3
67.1
49.1
46.4
44.6
41.7
36.8
24.9
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



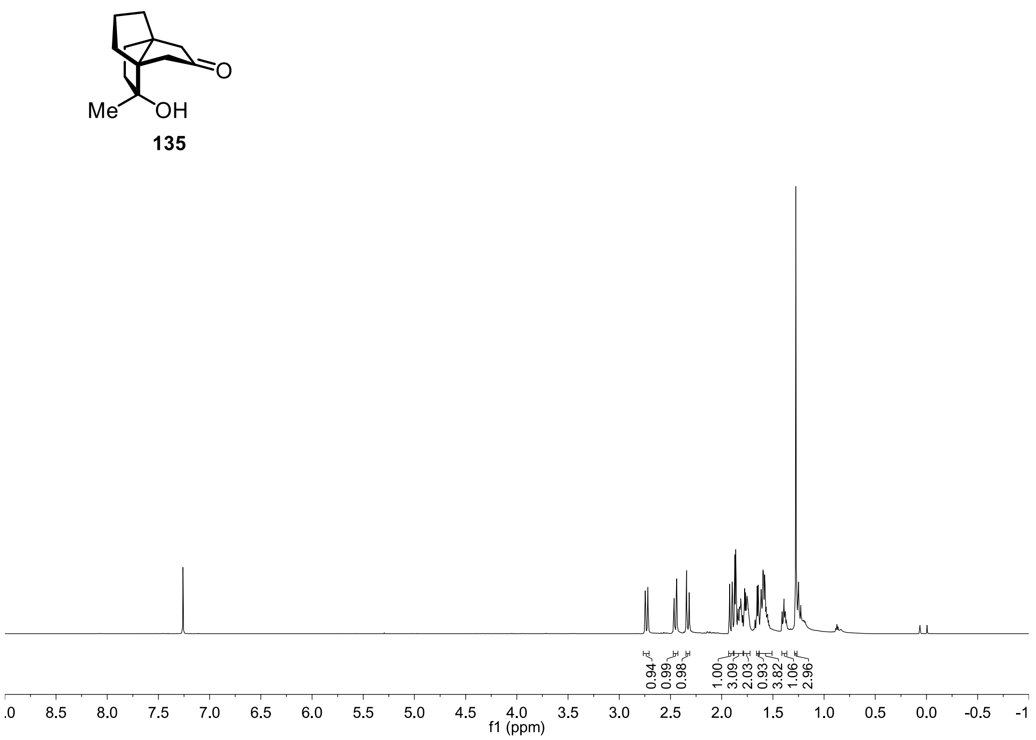
136

Me
OH
OH
H
0.98
0.98
1.00
0.99
1.03
1.03
4.03
1.97
2.03
2.97
1.98
1.05
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



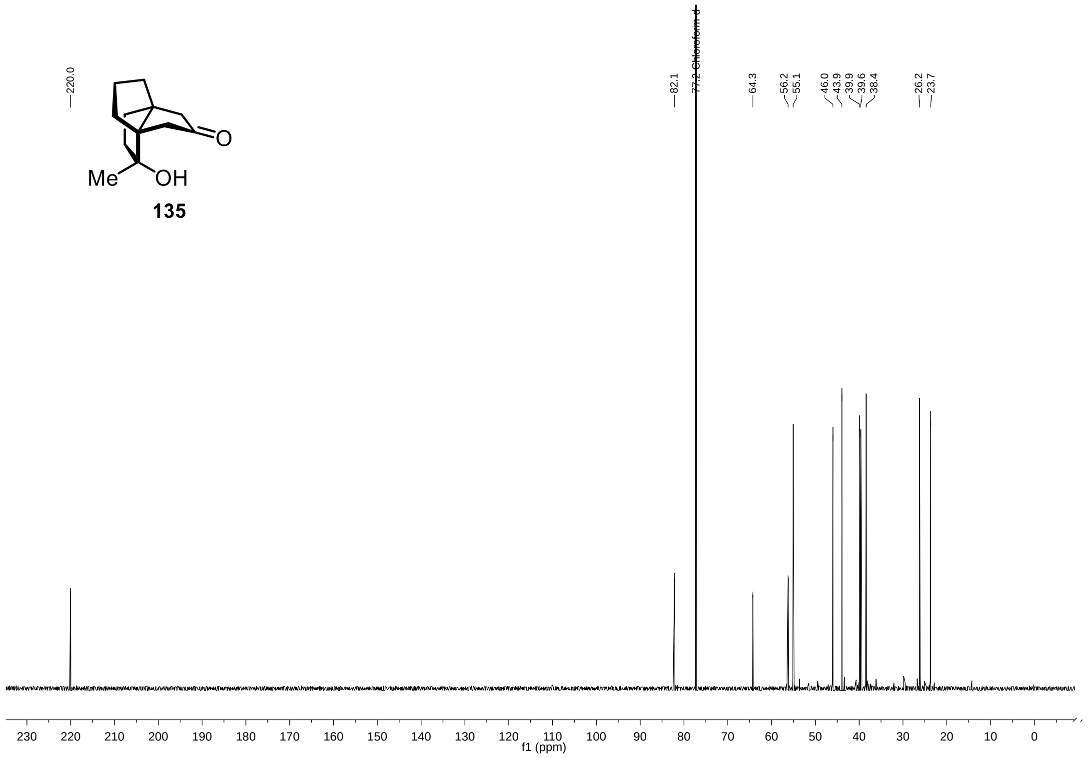
136

Me
OH
OH
H
81.4
77.2 Chloroform-d
76.1
68.7
62.0
49.6
42.6
42.3
40.7
39.6
37.1
25.2
24.0
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



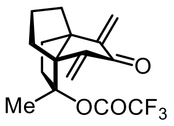
135

Me
OH
O
0.94
0.99
0.98
1.00
3.09
2.03
0.93
3.82
1.06
2.96
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

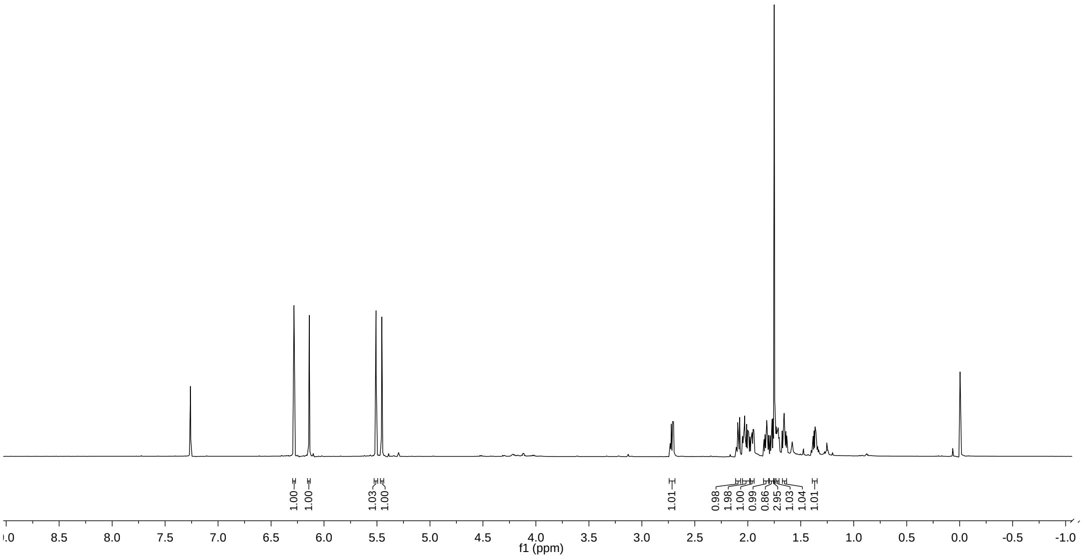


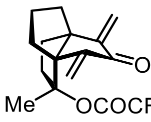
135

Me
OH
O
220.0
82.1
77.2 Chloroform-d
64.3
56.2
55.1
46.0
43.9
39.9
39.6
38.4
26.2
23.7
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

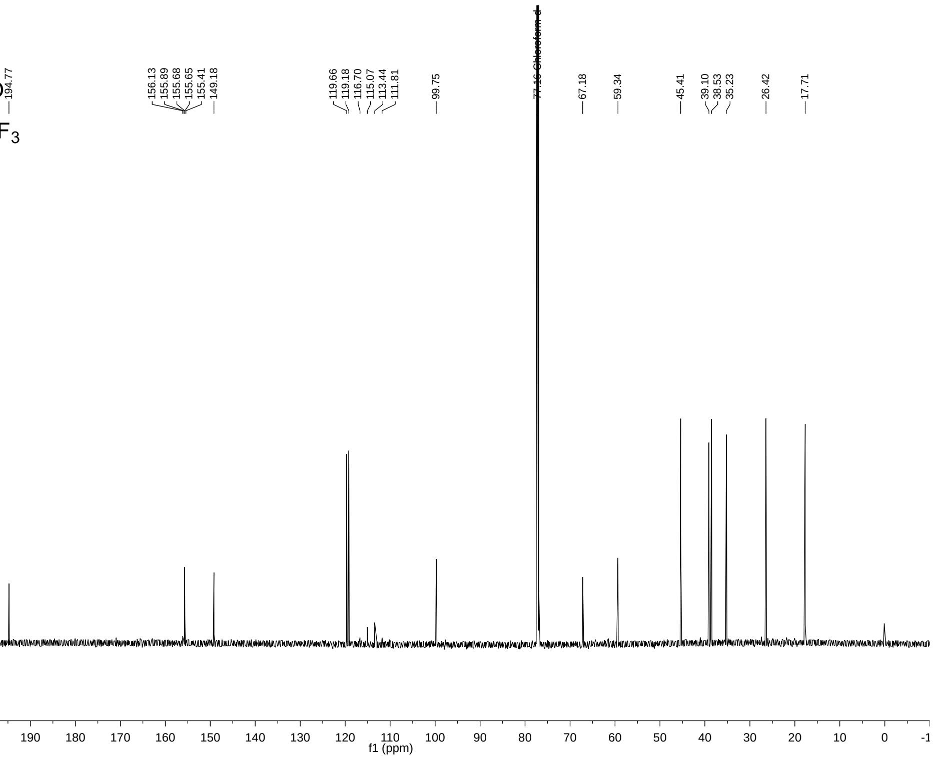

O
Me
OCOCF3

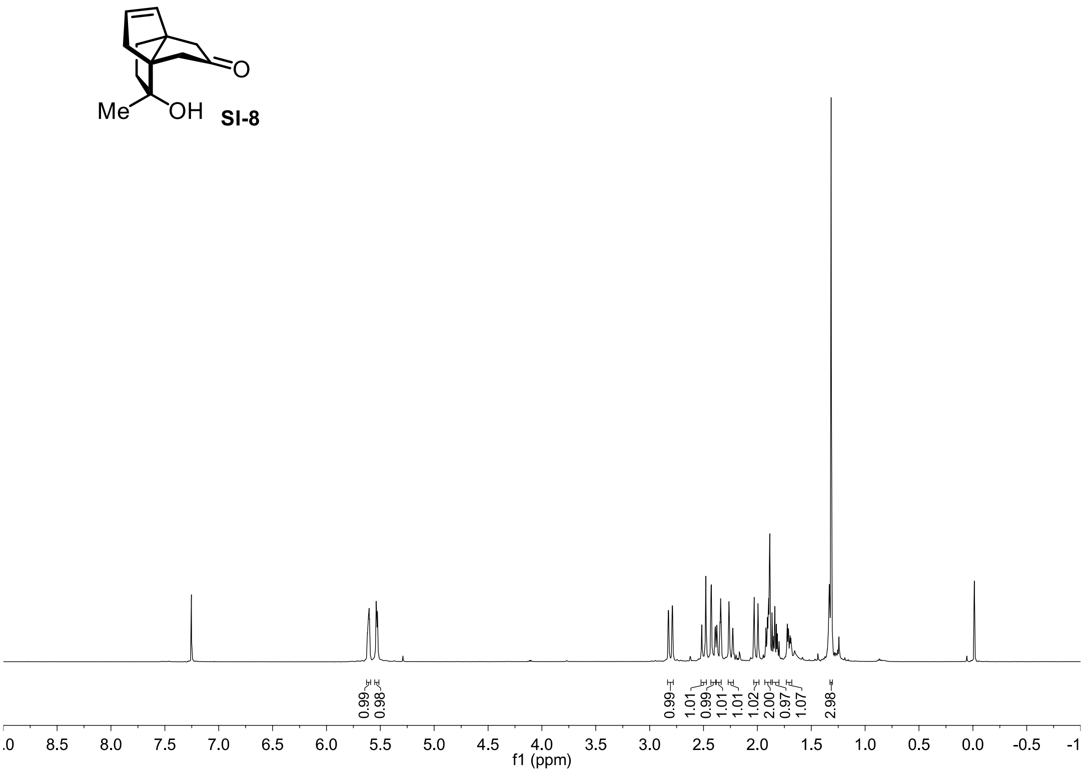
137


1.00
1.00
1.03
1.00
1.01
0.98
1.98
1.00
0.99
0.86
2.95
1.03
1.04
1.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

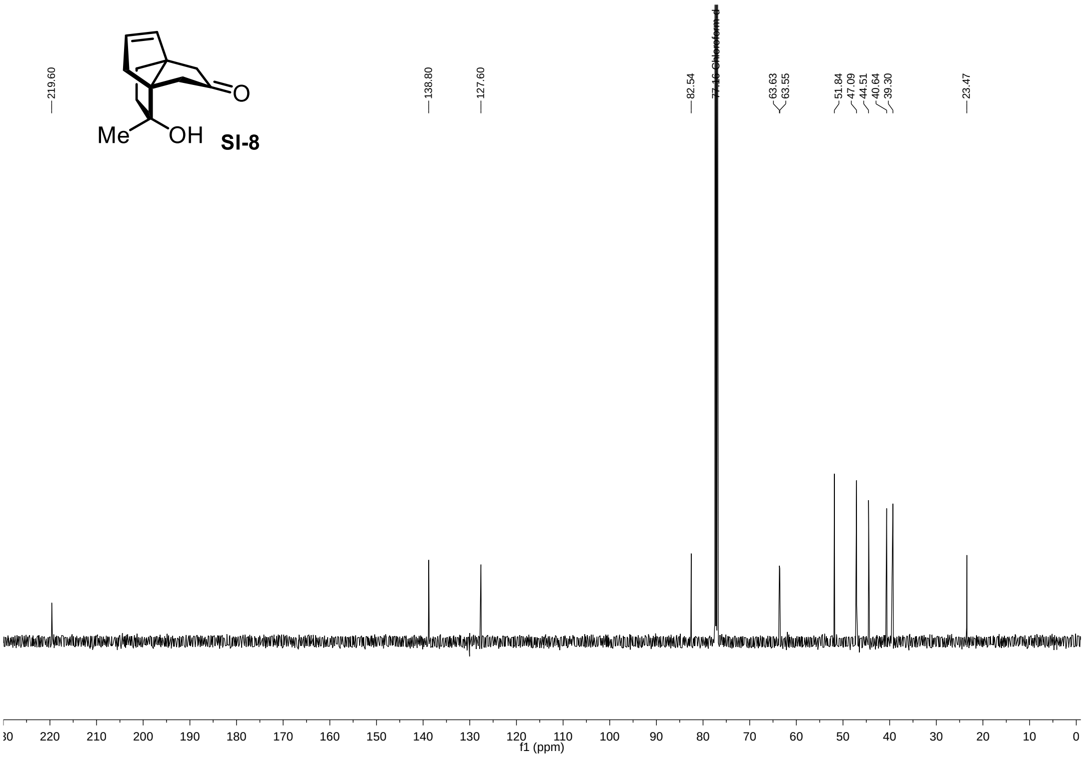

O
Me
OCOCF3

137

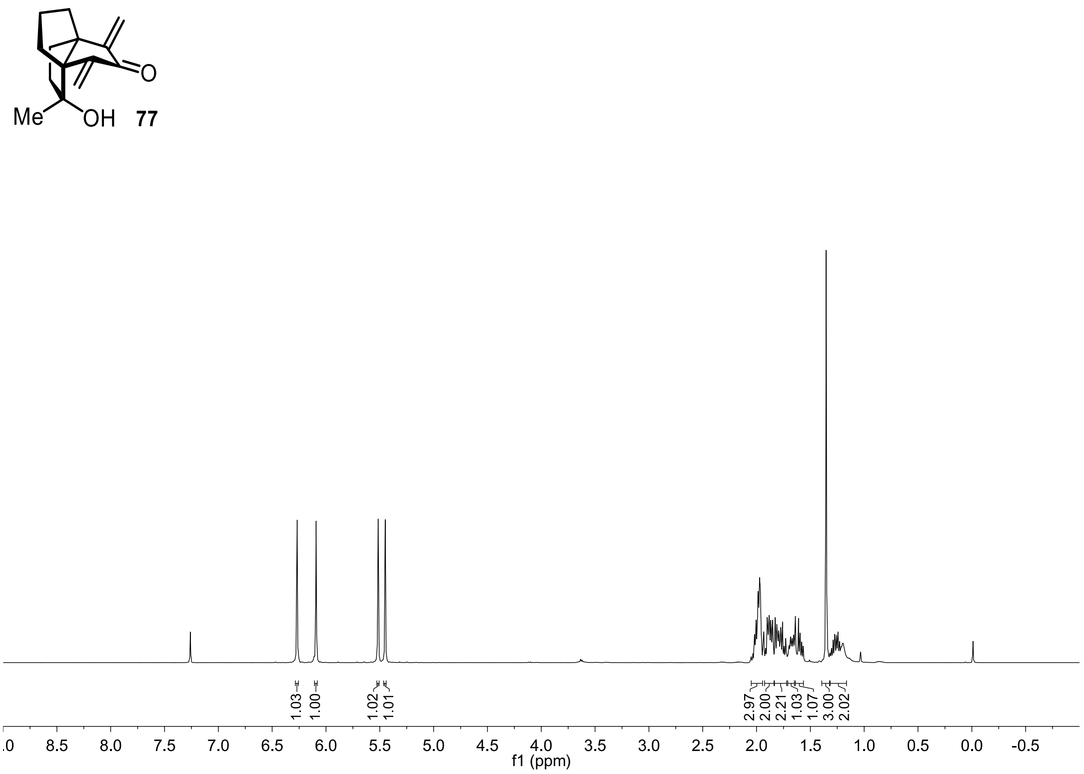

194.77
156.13
155.89
155.68
155.65
155.41
149.18
119.66
119.18
116.70
115.07
113.44
111.81
99.75
77.16 Chloroform-d
67.18
59.34
45.41
39.10
38.53
35.23
26.42
17.71
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

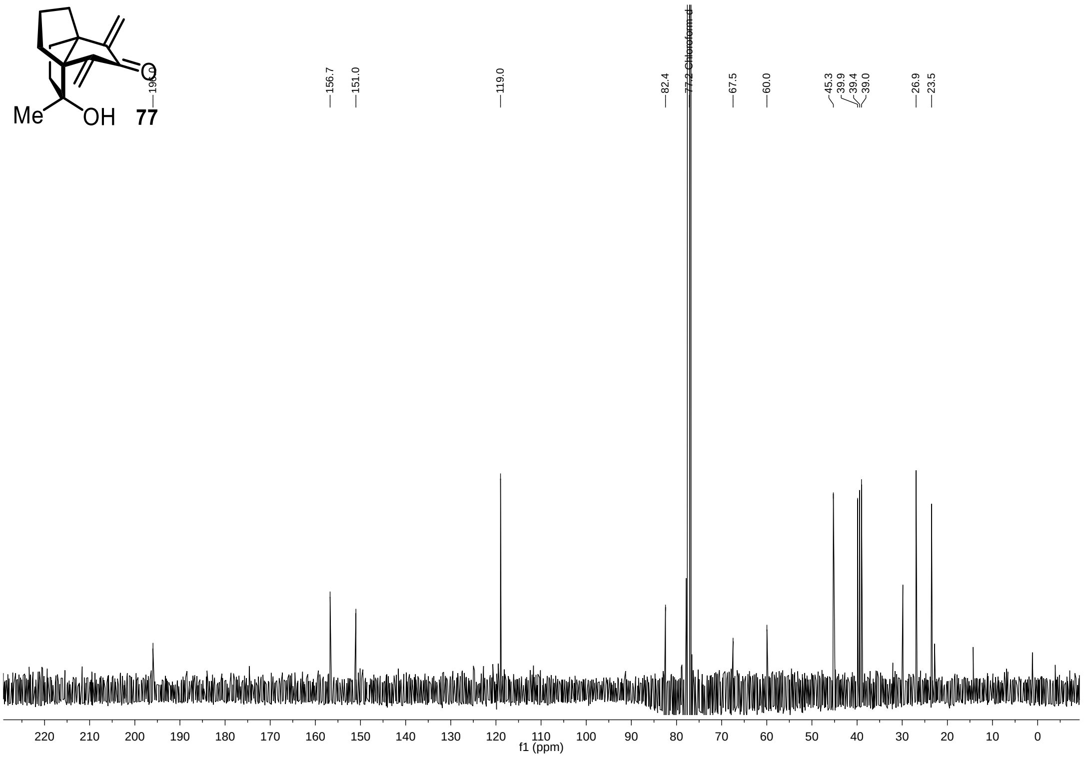

Me
OH
0.99
0.98
0.99
1.01
0.99
1.01
1.01
1.02
2.00
0.97
1.07
2.98
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

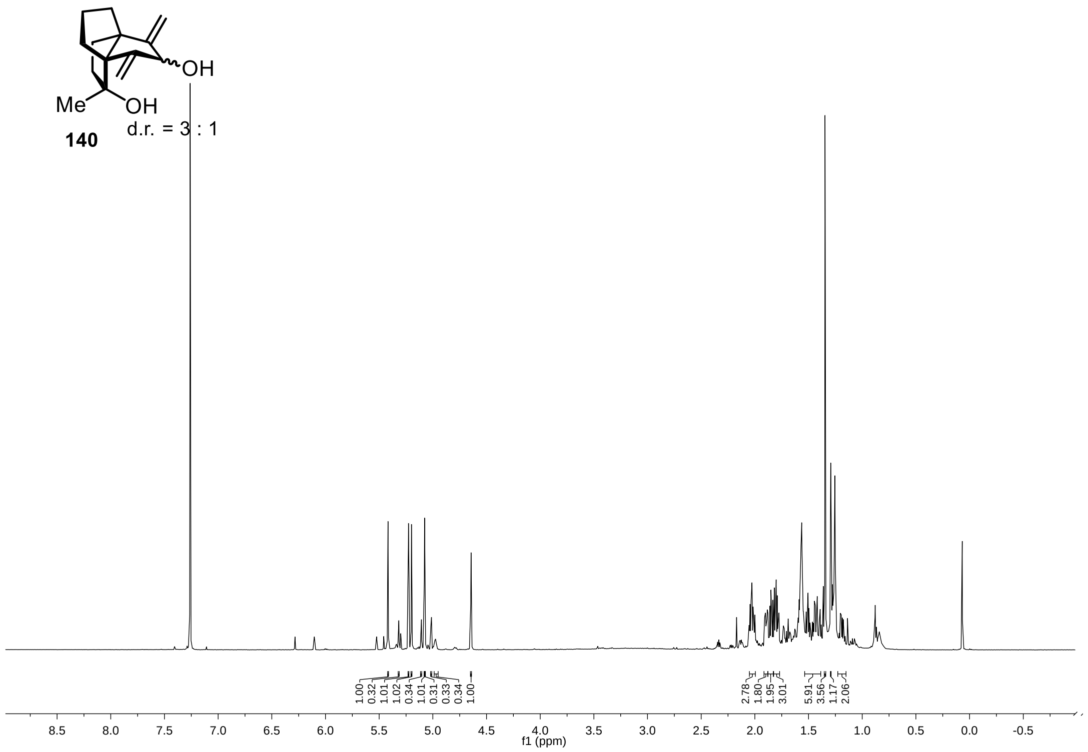
SI-8

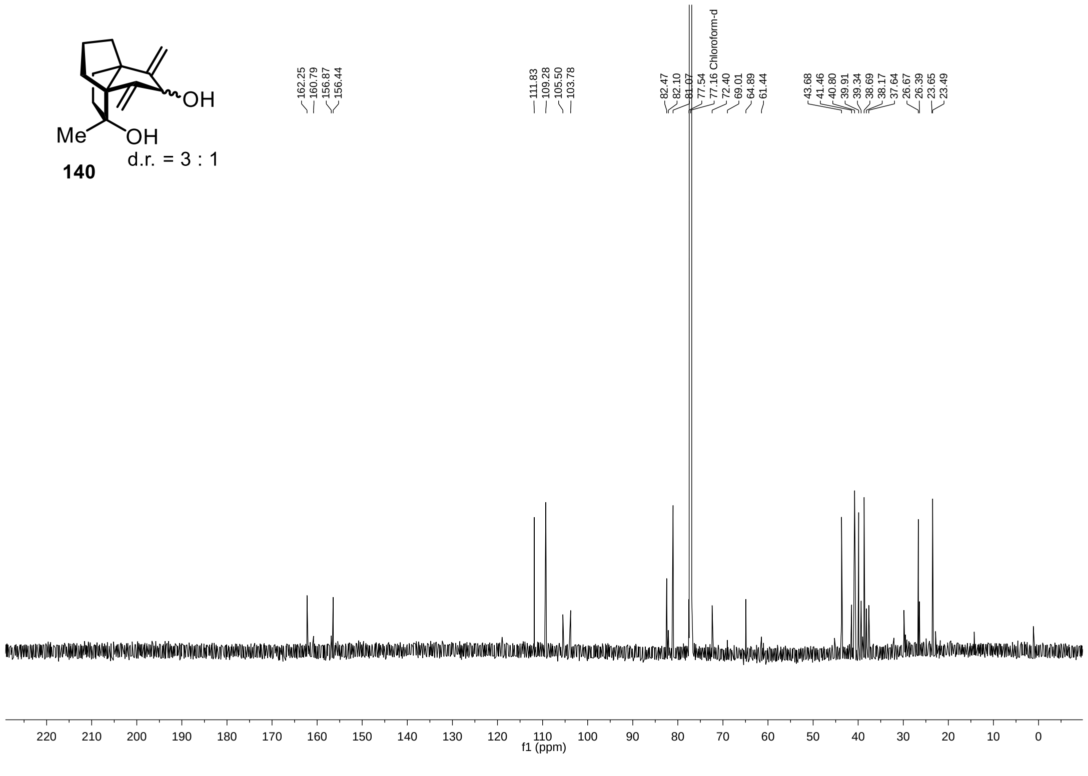

Me
OH
219.60
138.80
127.60
82.54
77.16 Chloroform-d
63.63
63.55
51.84
47.09
44.51
40.64
39.30
23.47
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

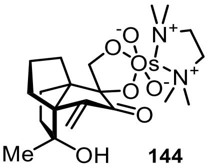
SI-8


Me
OH
O
77
1.03
1.00
1.02
1.01
2.97
2.00
2.21
1.03
1.07
3.00
2.02
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

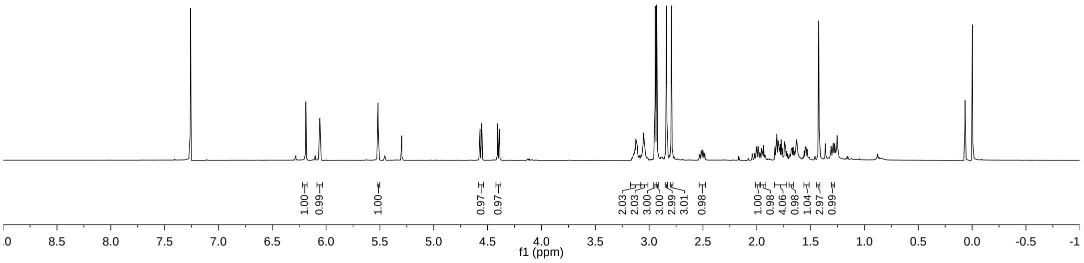

Me
OH
O
77
196.0
156.7
151.0
119.0
82.4
77.2 Chloroform-d
67.5
60.0
45.3
39.9
39.4
39.0
26.9
23.5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

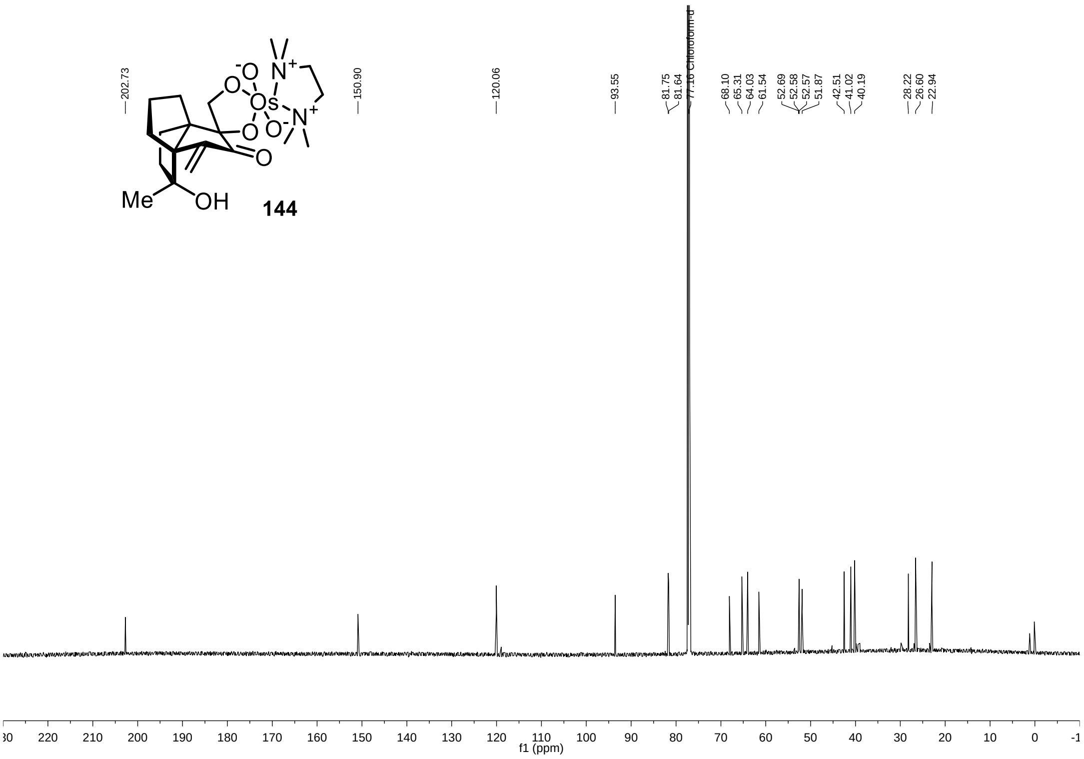

OH
Me
OH
140
d.r. = 3 : 1
1.00
0.32
1.01
1.02
0.34
1.01
0.31
0.33
0.34
1.00
2.78
1.80
1.95
3.01
5.91
3.56
1.17
2.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

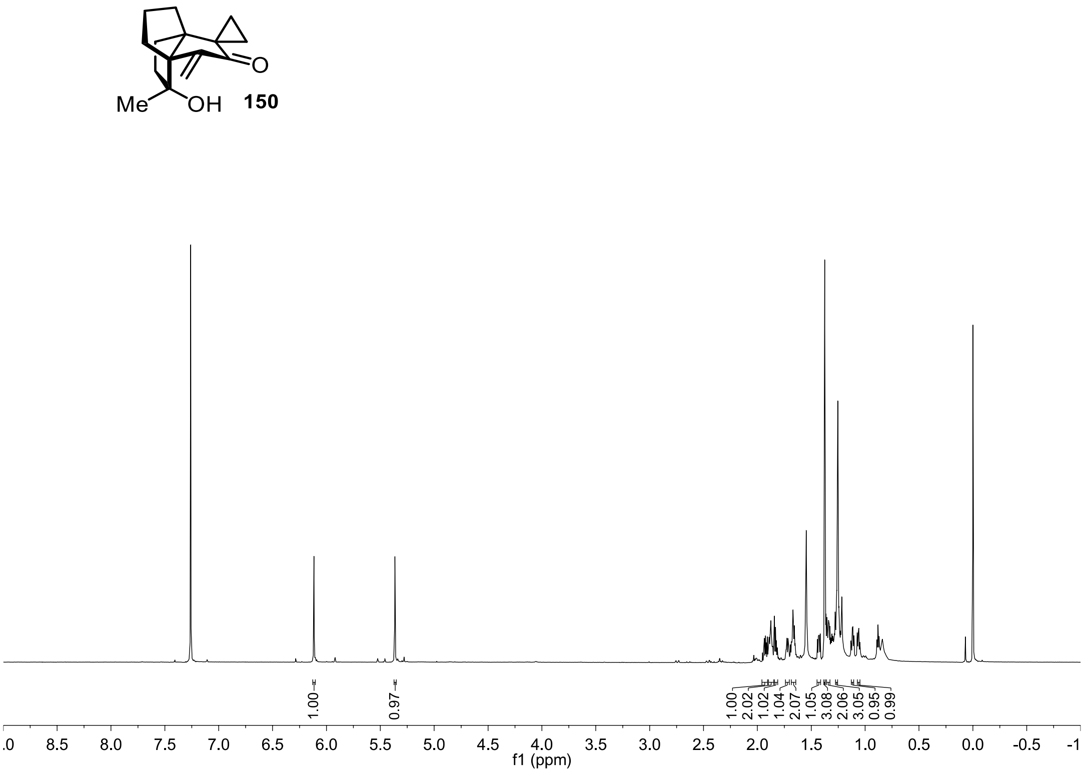

OH
Me
OH
140
d.r. = 3 : 1
162.25
160.79
156.87
156.44
111.83
109.28
105.50
103.78
82.47
82.10
81.07
77.54
77.16 Chloroform-d
72.40
69.01
64.89
61.44
43.68
41.46
40.80
39.91
39.34
38.69
38.17
37.64
26.67
26.39
23.65
23.49
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
-O
N+
Os
O
O
O-
N+
O
Me
OH

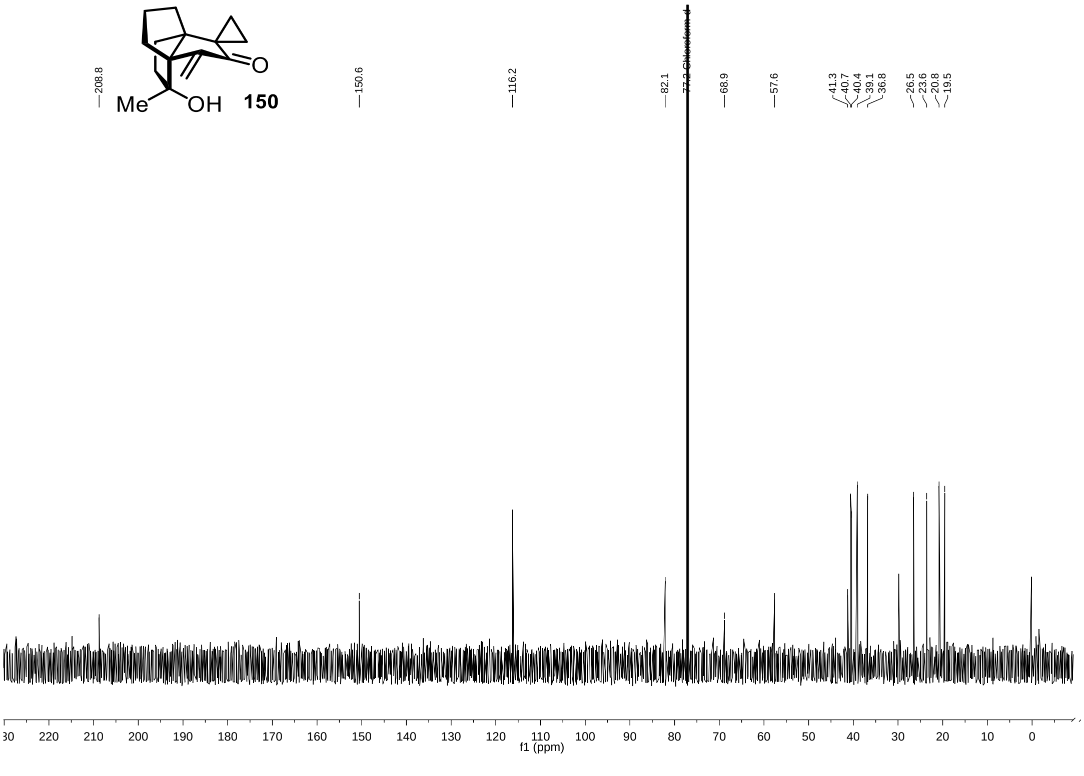
144


1.00
0.99
1.00
0.97
0.97
2.03
2.03
3.00
3.00
2.99
3.01
0.98
1.00
0.98
4.06
0.98
1.04
2.97
0.99
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

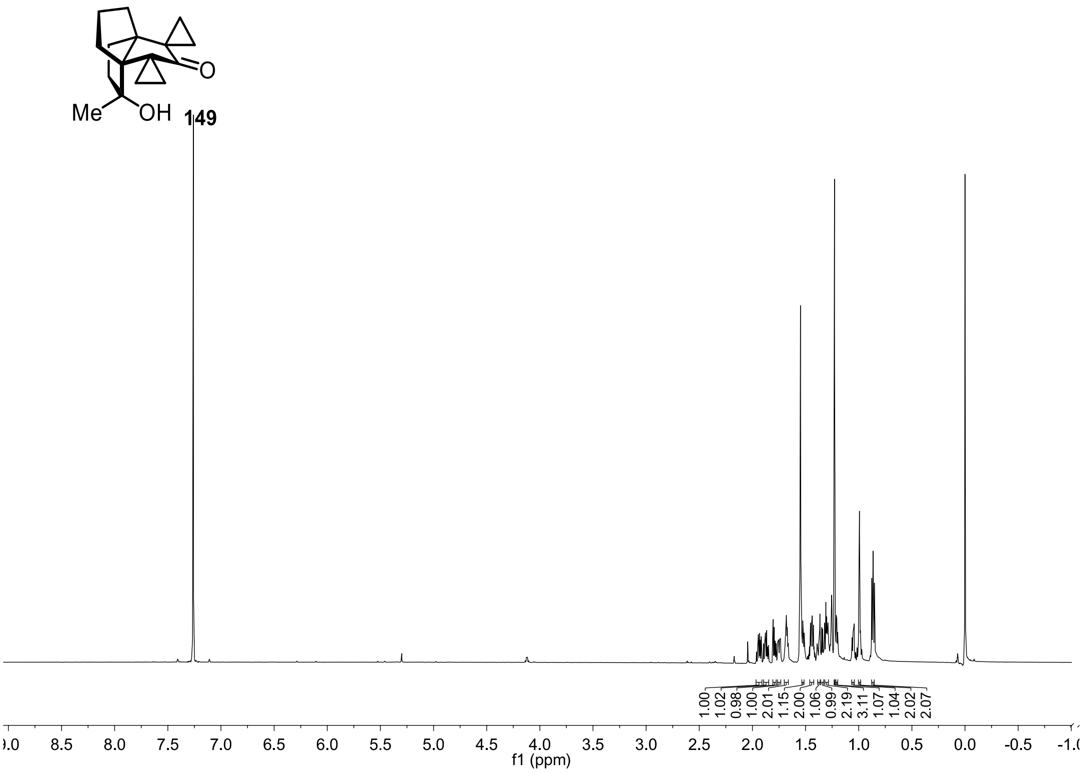

202.73
150.90
120.06
93.55
81.75
81.64
77.16 Chloroform-d
68.10
65.31
64.03
61.54
52.69
52.58
52.57
51.87
42.51
41.02
40.19
28.22
26.60
22.94
Me
OH
144
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

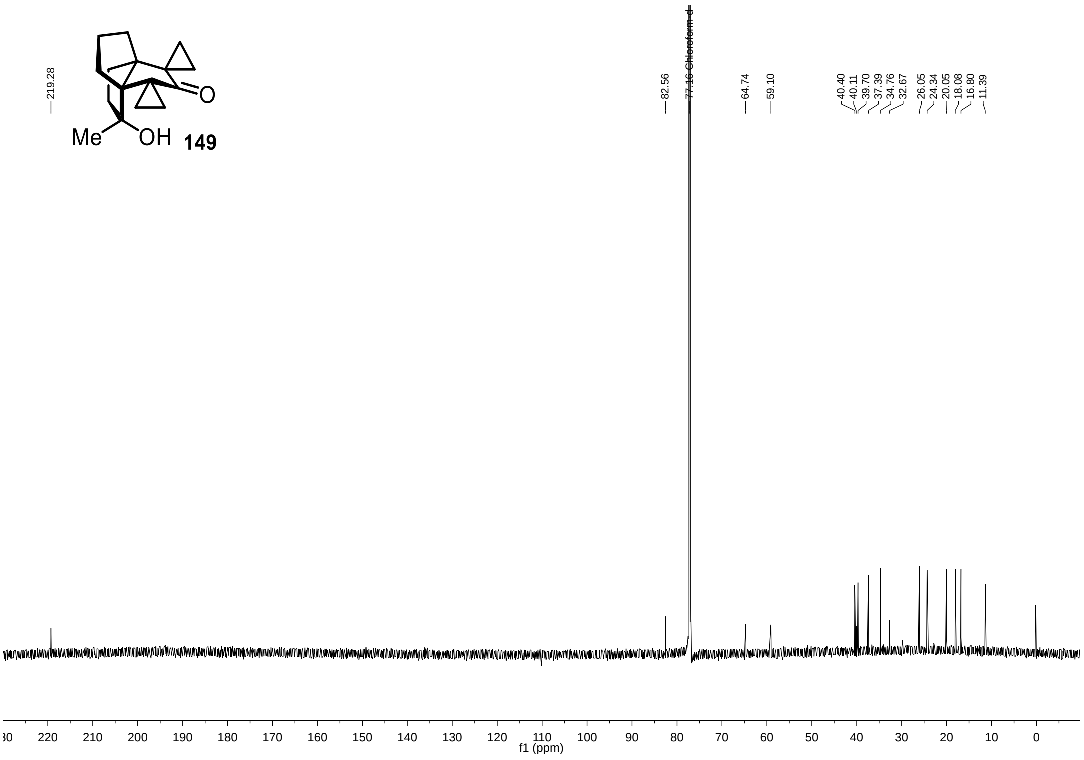

Me
OH
O
1.00
0.97
1.00
2.02
1.02
1.04
2.07
1.05
3.08
2.06
3.05
0.95
0.99
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

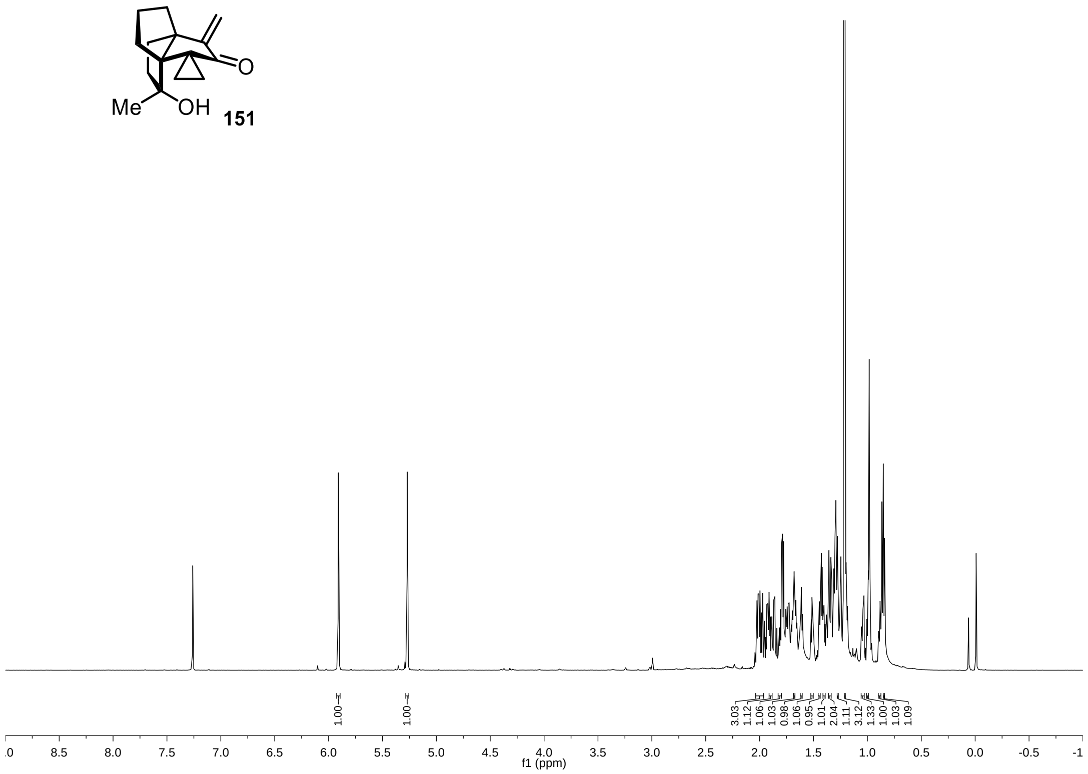
150

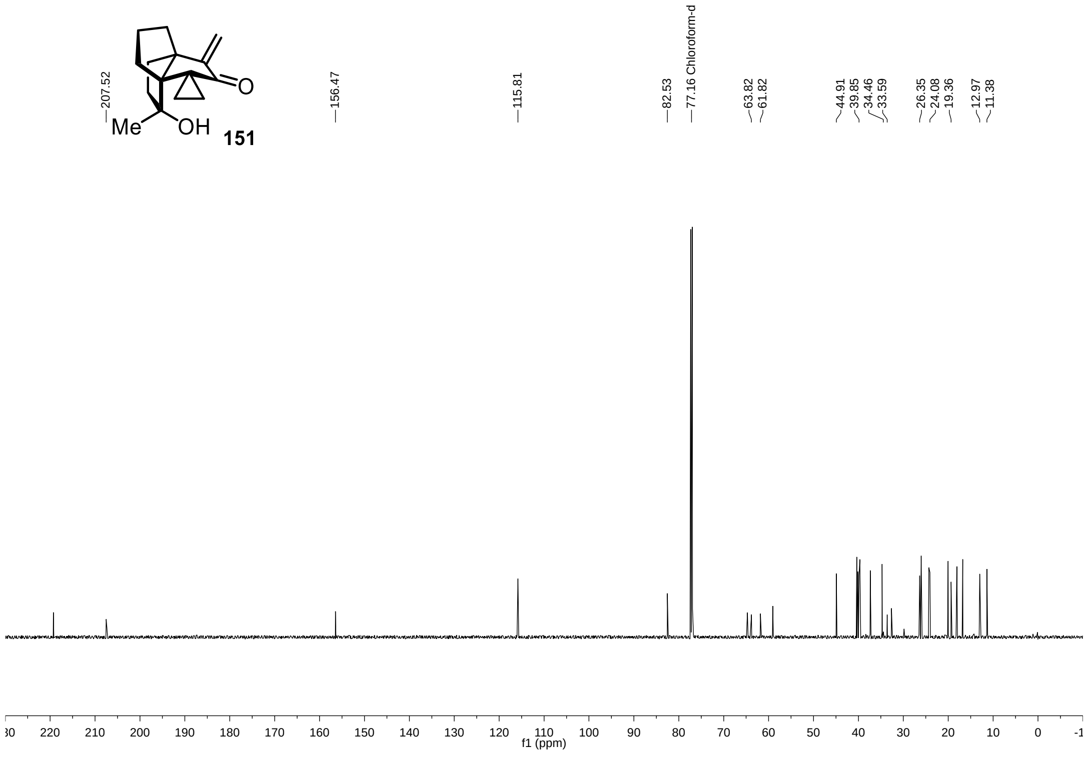

Me
OH
O
208.8
150.6
116.2
82.1
77.2 Chloroform-d
68.9
57.6
41.3
40.7
40.4
39.1
36.8
26.5
23.6
20.8
19.5
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

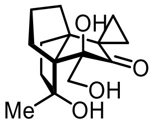
150


Me
OH
O
149
1.00
1.02
0.98
1.00
2.01
1.15
2.00
1.06
0.99
2.19
3.11
1.07
1.04
2.02
2.07
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

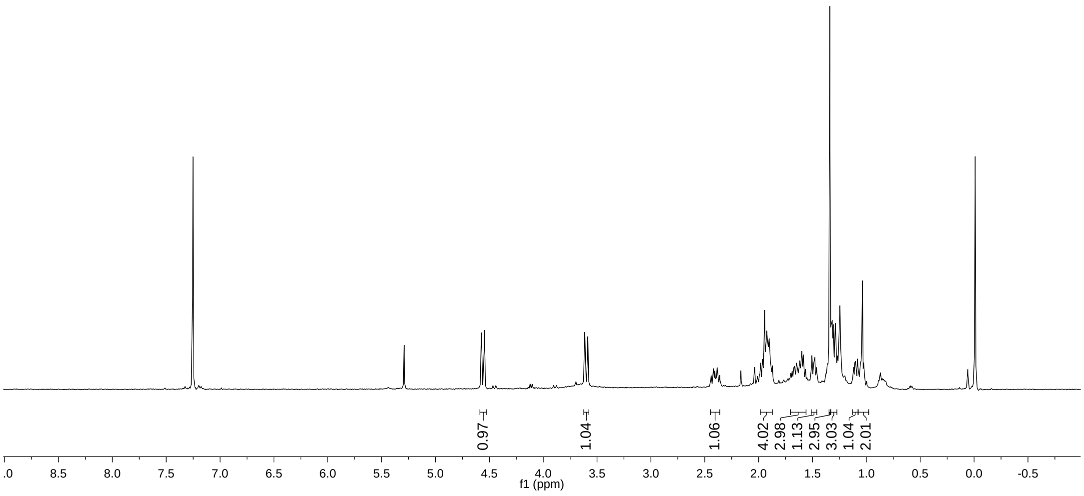

219.28
Me
OH
O
149
82.56
77.16 Chloroform-d
64.74
59.10
40.40
40.11
39.70
37.39
34.76
32.67
26.05
24.34
20.05
18.08
16.80
11.39
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

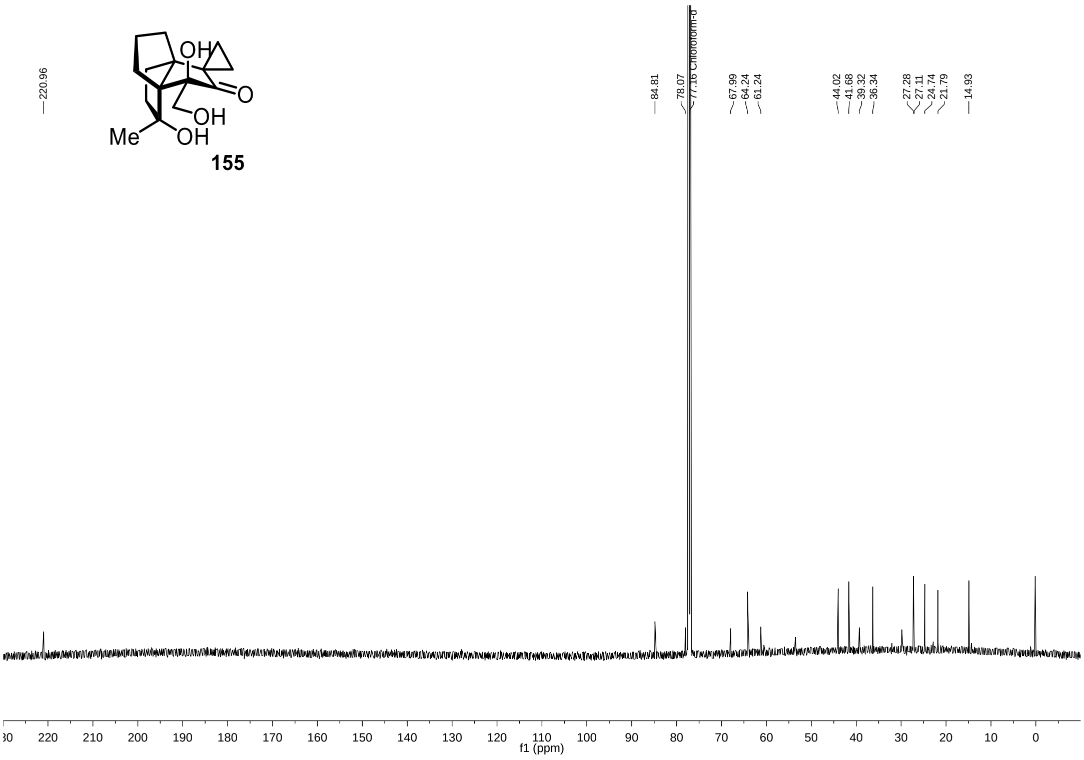

Me
OH
O
151
1.00
1.00
3.03
1.12
1.06
1.03
0.98
1.06
0.95
1.01
2.04
1.11
3.12
1.33
1.00
1.03
1.09
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

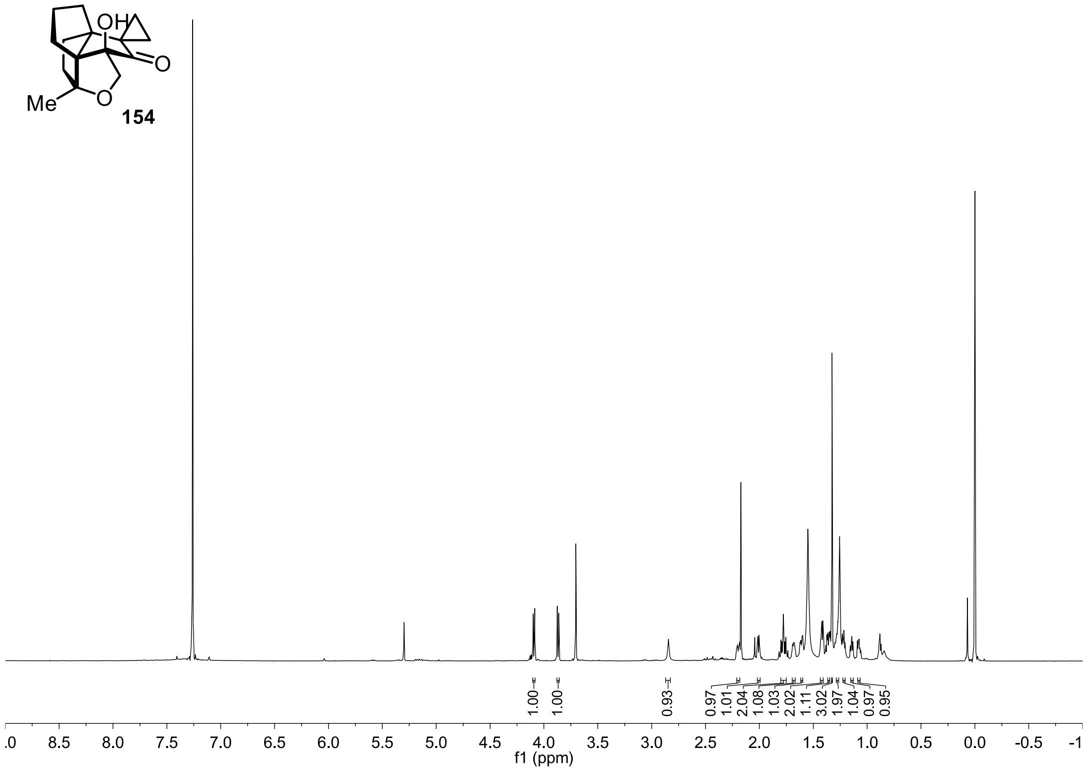

Me
OH
O
151
207.52
156.47
115.81
82.53
77.16 Chloroform-d
63.82
61.82
44.91
39.85
34.46
33.59
26.35
24.08
19.36
12.97
11.38
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

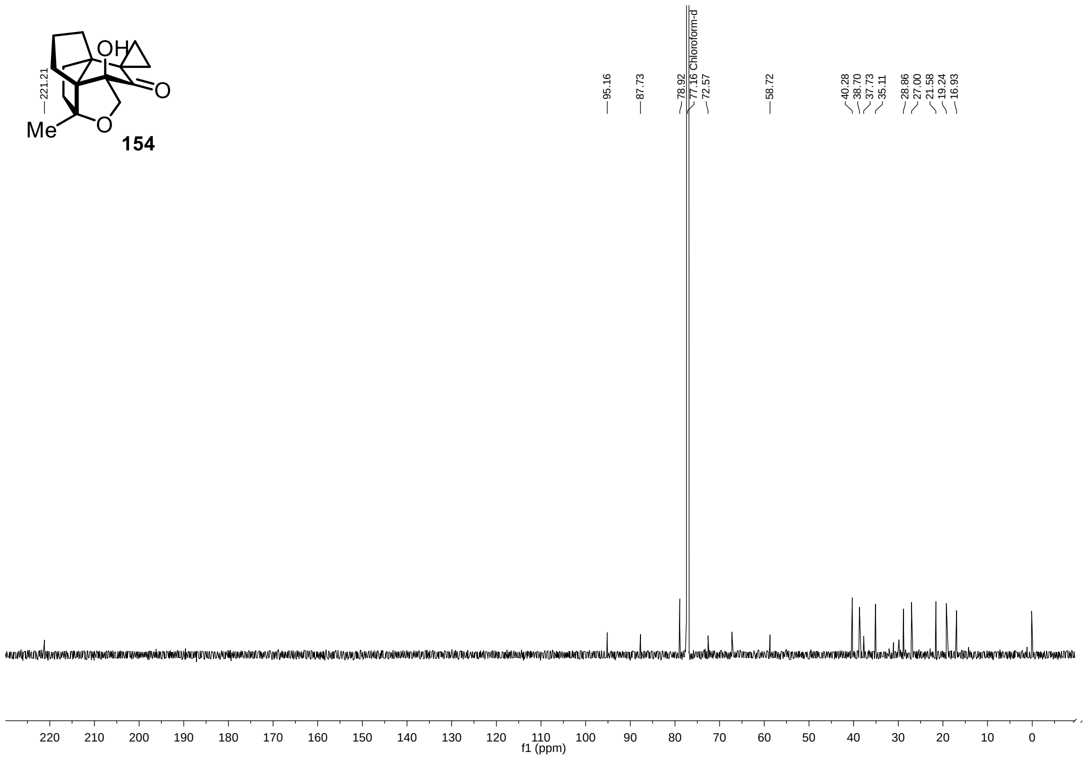

OH
O
OH
Me
OH

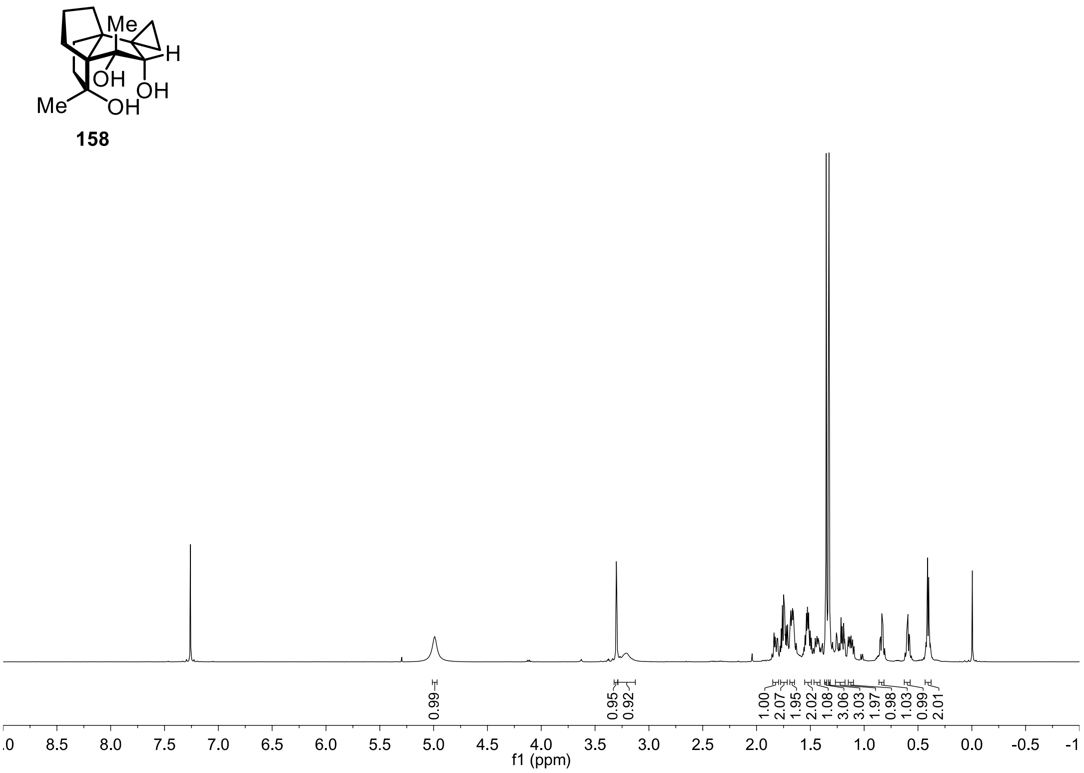
155

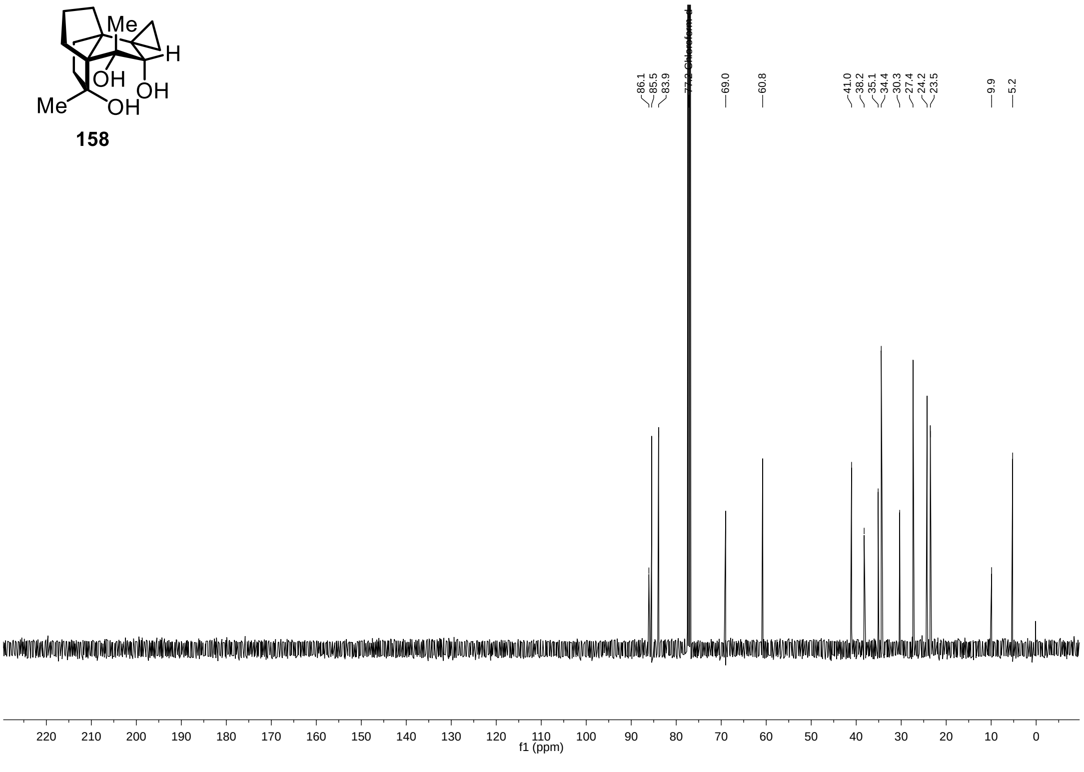

0.97
1.04
1.06
4.02
2.98
1.13
2.95
3.03
1.04
2.01
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

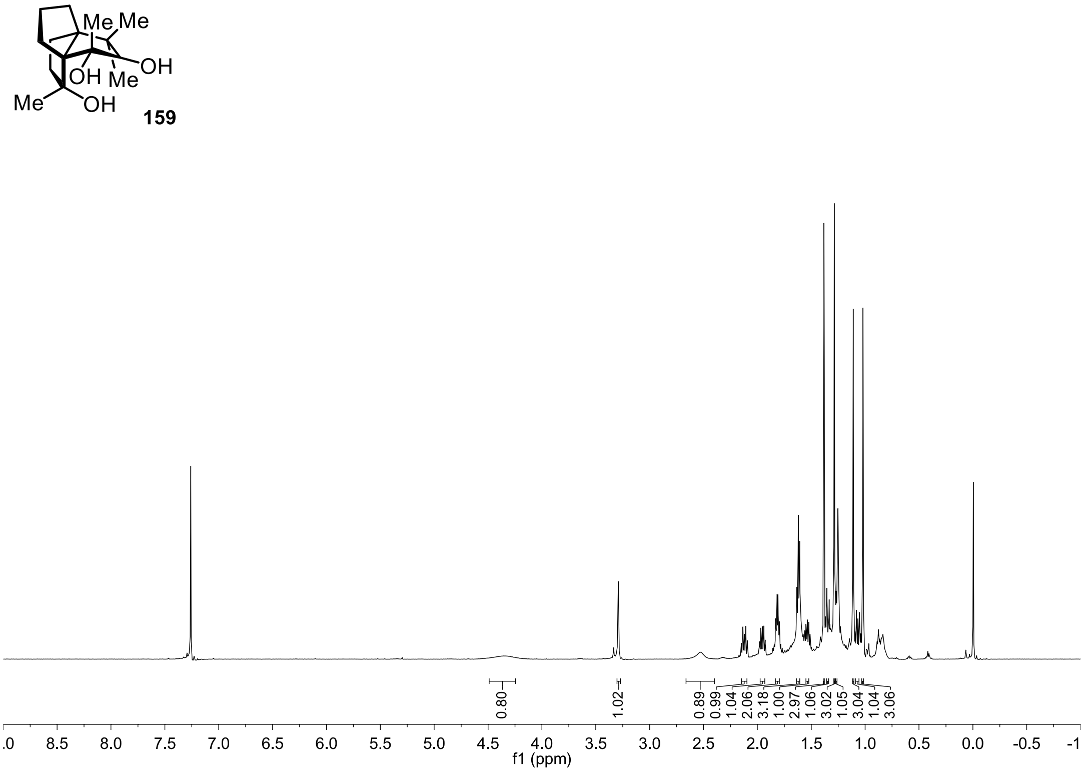

220.96
OH
O
OH
Me
OH
155
84.81
78.07
77.16 Chloroform-d
67.99
64.24
61.24
44.02
41.68
39.32
36.34
27.28
27.11
24.74
21.79
14.93
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


OH
O
Me
O
154
1.00
1.00
0.93
0.97
1.01
2.04
1.08
1.03
2.02
1.11
3.02
1.97
1.04
0.97
0.95
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

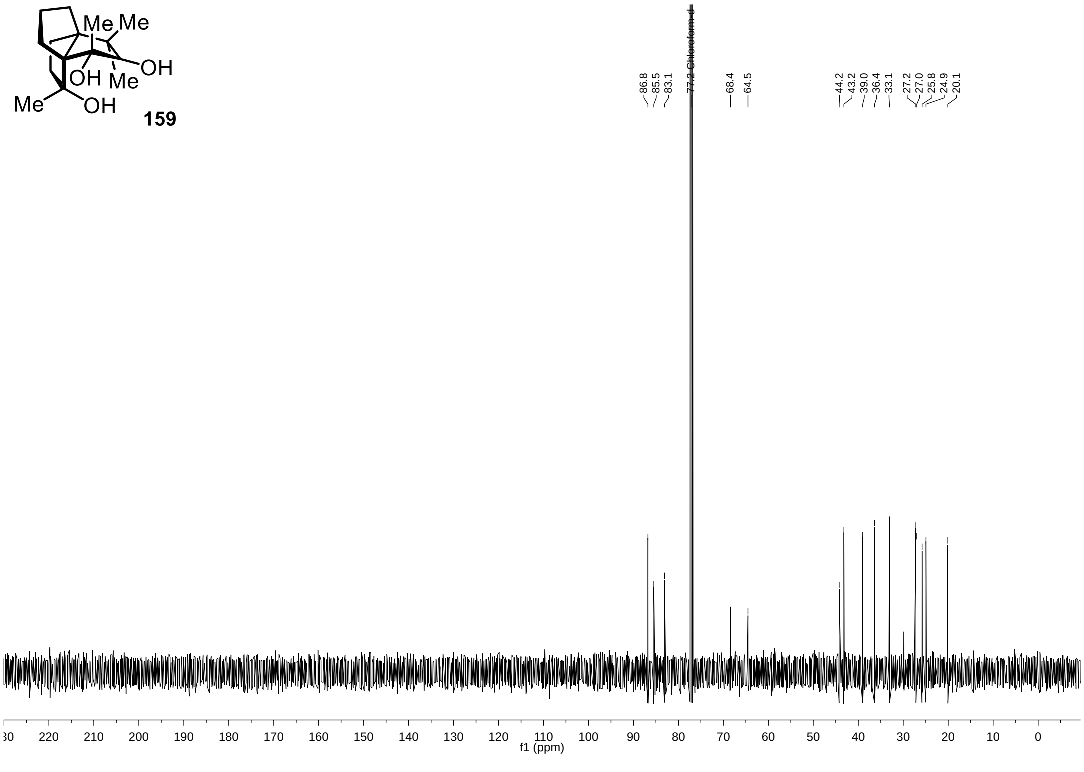

OH
O
Me
O
154
221.21
95.16
87.73
78.92
77.16 Chloroform-d
72.57
58.72
40.28
38.70
37.73
35.11
28.86
27.00
21.58
19.24
16.93
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Me
H
OH
OH
Me
OH
158
0.99
0.95
0.92
1.00
2.07
1.95
2.02
1.08
3.06
3.03
1.97
0.98
1.03
0.99
2.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

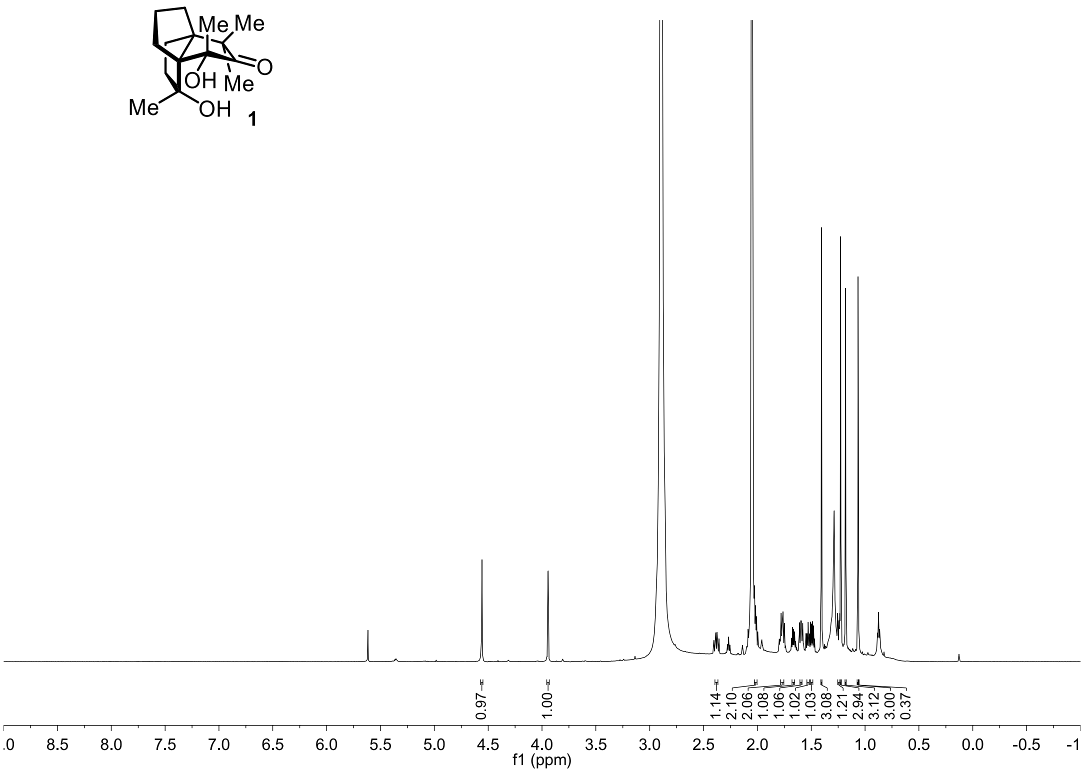

Me
H
OH
OH
Me
OH
158
86.1
85.5
83.9
77.2 Chloroform-d
69.0
60.8
41.0
38.2
35.1
34.4
30.3
27.4
24.2
23.5
9.9
5.2
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

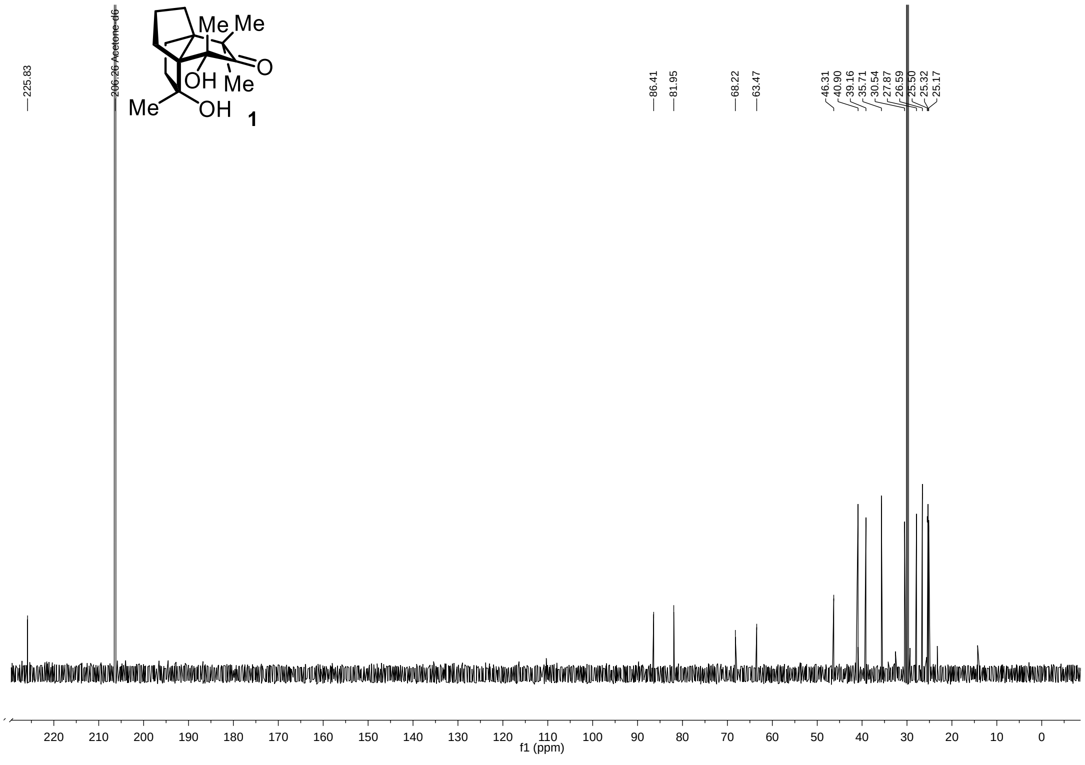

Me
Me
OH
OH
Me
Me
OH
0.80
1.02
0.89
0.99
1.04
2.06
3.18
1.00
2.97
1.06
3.02
1.05
3.04
1.04
3.06
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

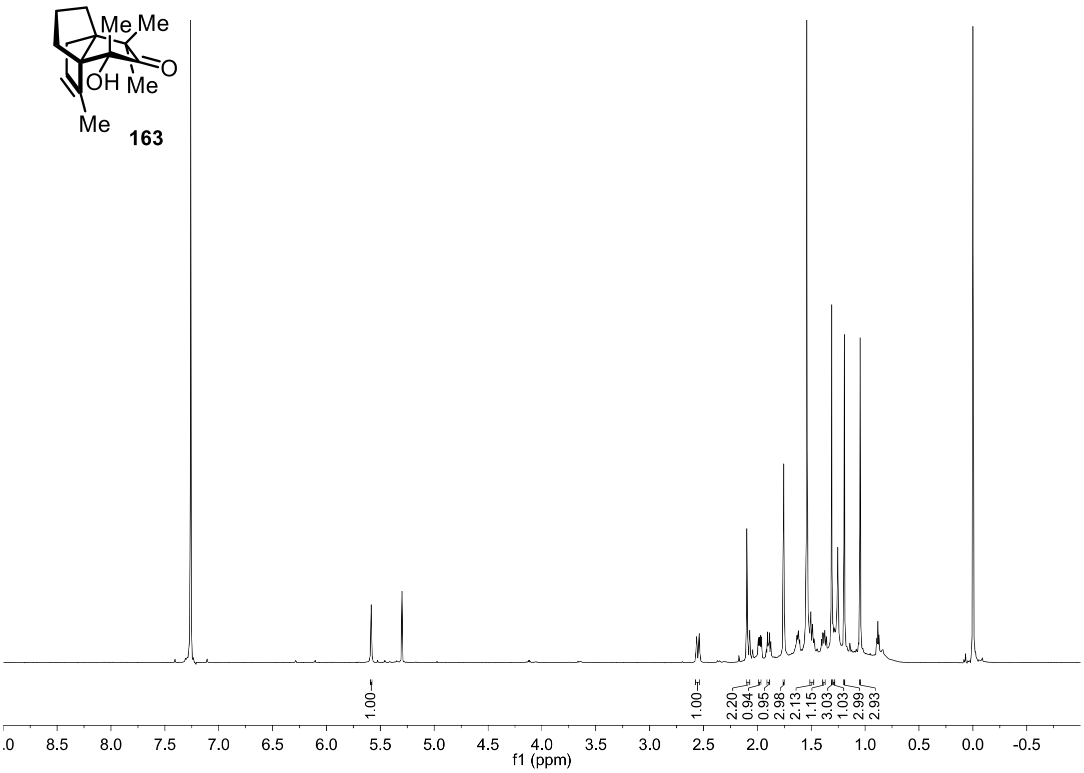
159

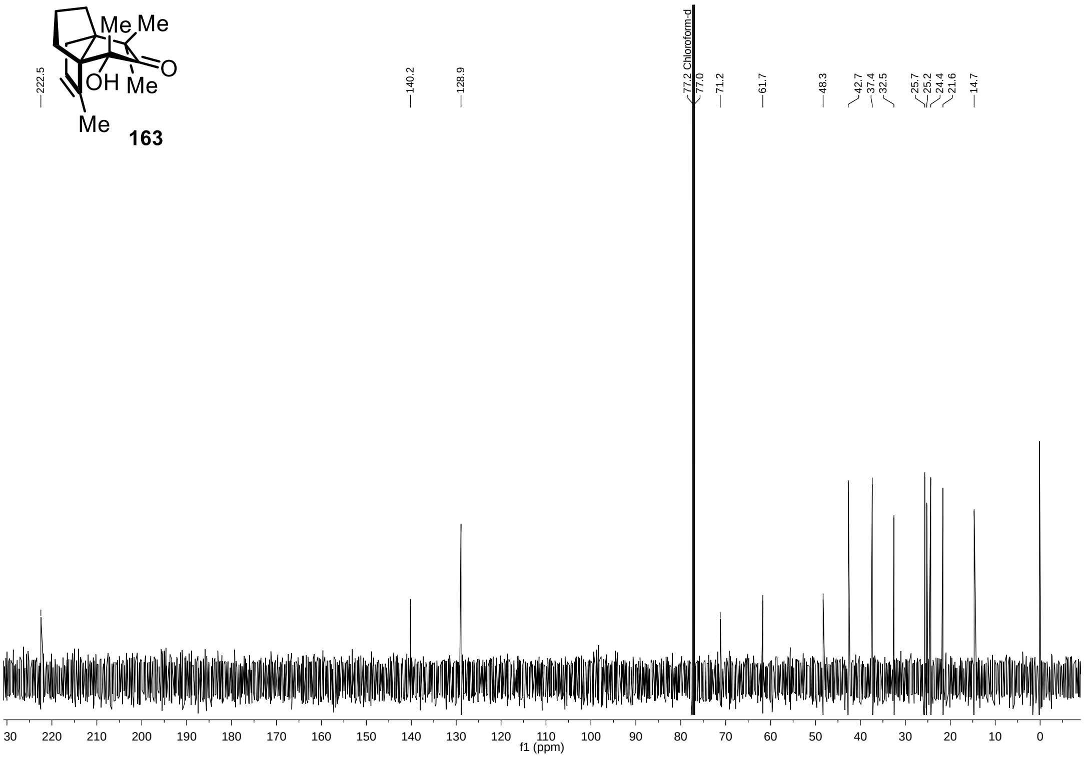

Me
Me
OH
OH
Me
Me
OH
86.8
85.5
83.1
77.2 Chloroform-d
68.4
64.5
44.2
43.2
39.0
36.4
33.1
27.2
27.0
25.8
24.9
20.1
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

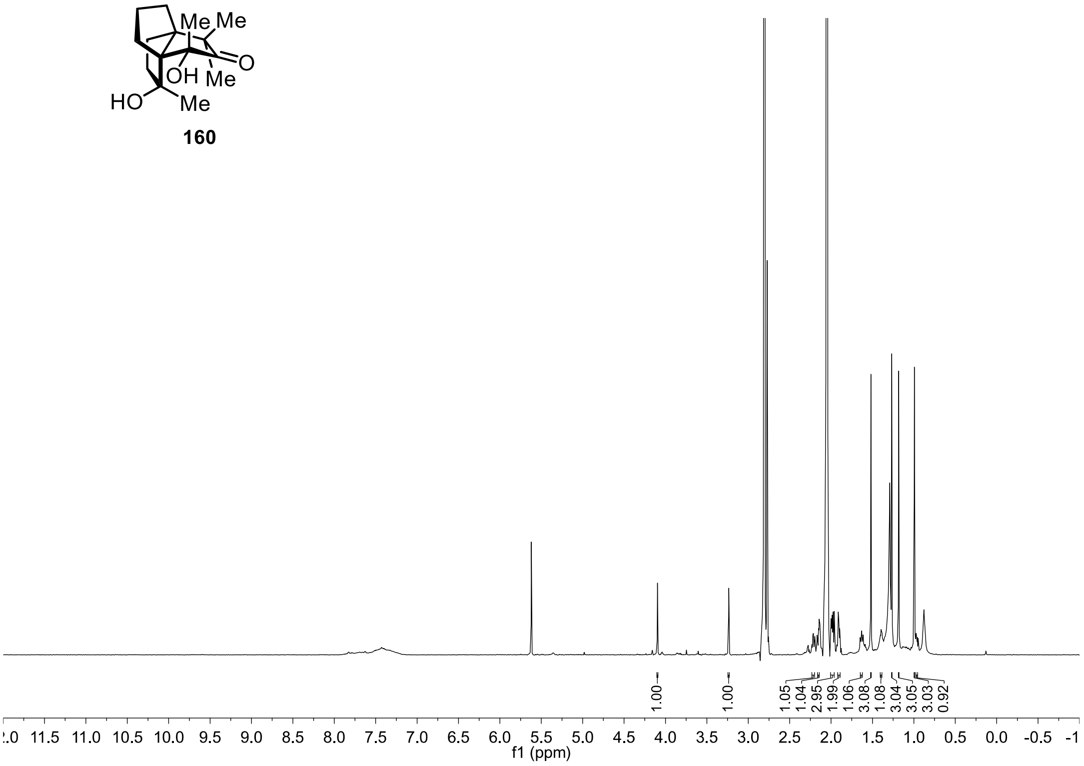
159


Me
Me
O
OH
Me
Me
OH
1
0.97
1.00
1.14
2.10
2.06
1.08
1.06
1.02
1.03
3.08
1.21
2.94
3.12
3.00
0.37
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


225.83
206.26 Acetone-d6
Me
Me
O
OH
Me
Me
OH
1
86.41
81.95
68.22
63.47
46.31
40.90
39.16
35.71
30.54
27.87
26.59
25.50
25.32
25.17
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

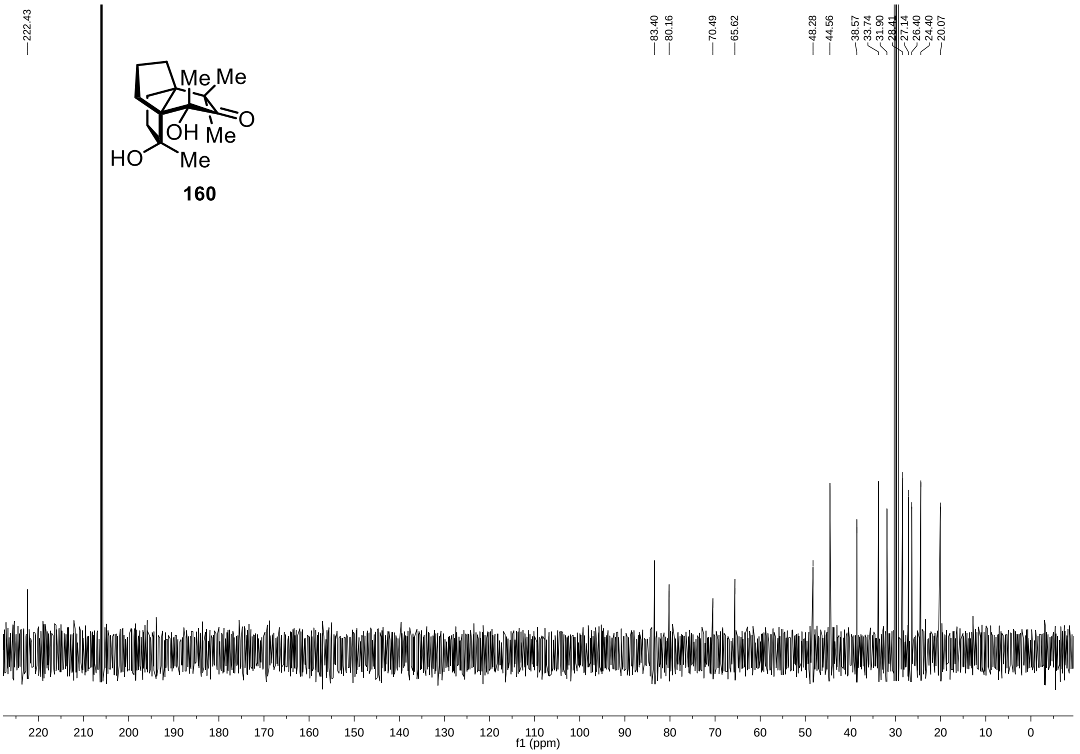

Me
Me
OH
Me
O
Me
163
1.00
1.00
2.20
0.94
0.95
2.98
2.13
1.15
3.03
1.03
2.99
2.93
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Me
Me
OH
Me
O
Me
163
222.5
140.2
128.9
77.2 Chloroform-d
77.0
71.2
61.7
48.3
42.7
37.4
32.5
25.7
25.2
24.4
21.6
14.7
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



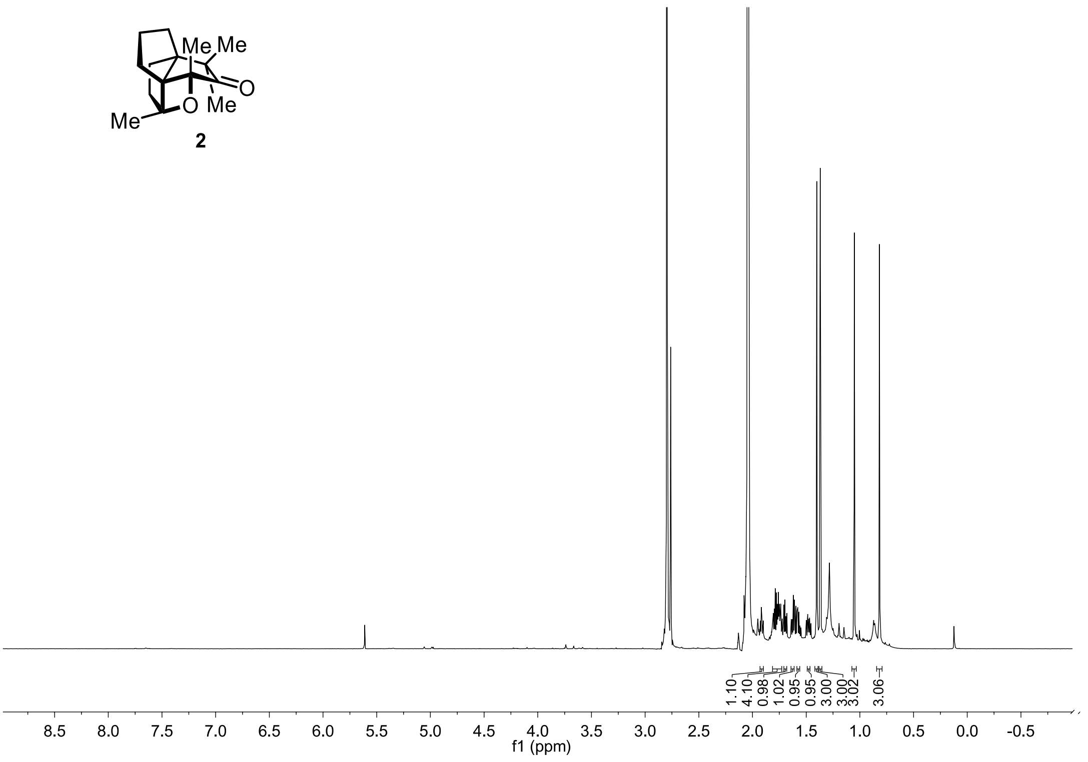
160

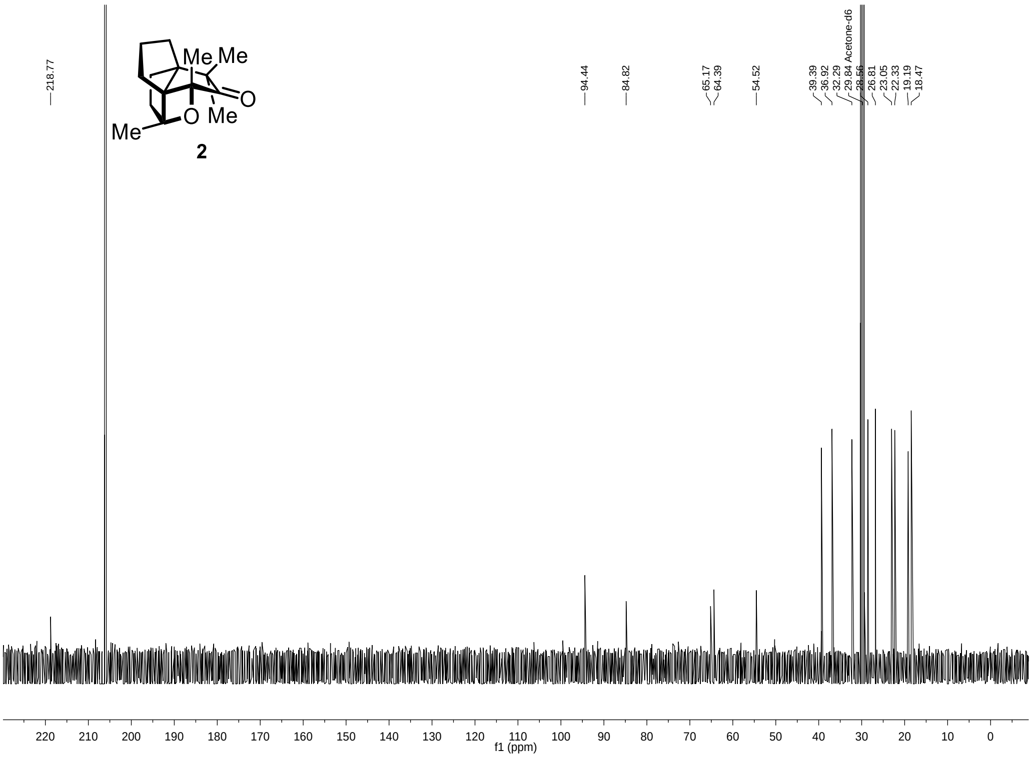
Me
Me
O
OH
Me
HO
Me
1.00
1.00
1.05
1.04
2.95
1.99
1.06
3.08
1.08
3.04
3.05
3.03
0.92
.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

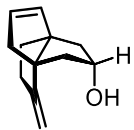


160

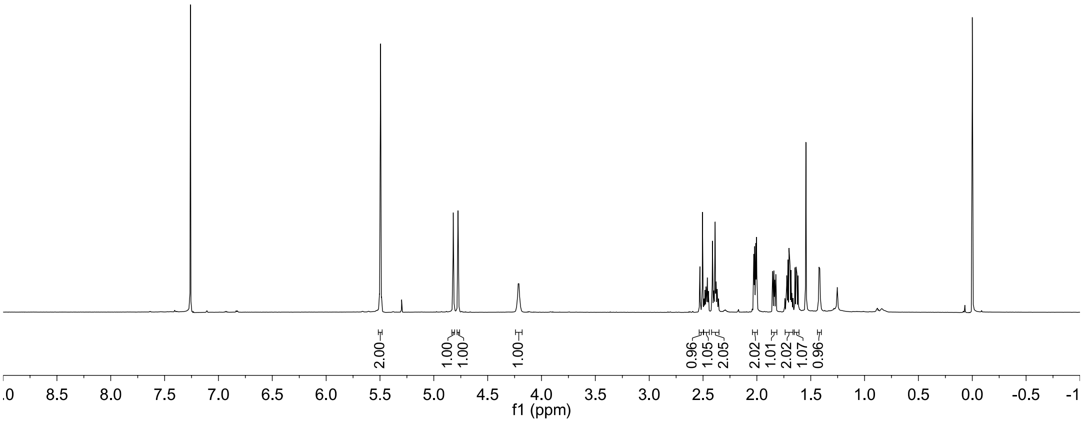
222.43
83.40
80.16
70.49
65.62
48.28
44.56
38.57
33.74
31.90
28.41
27.14
26.40
24.40
20.07
Me
Me
O
OH
Me
HO
Me
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

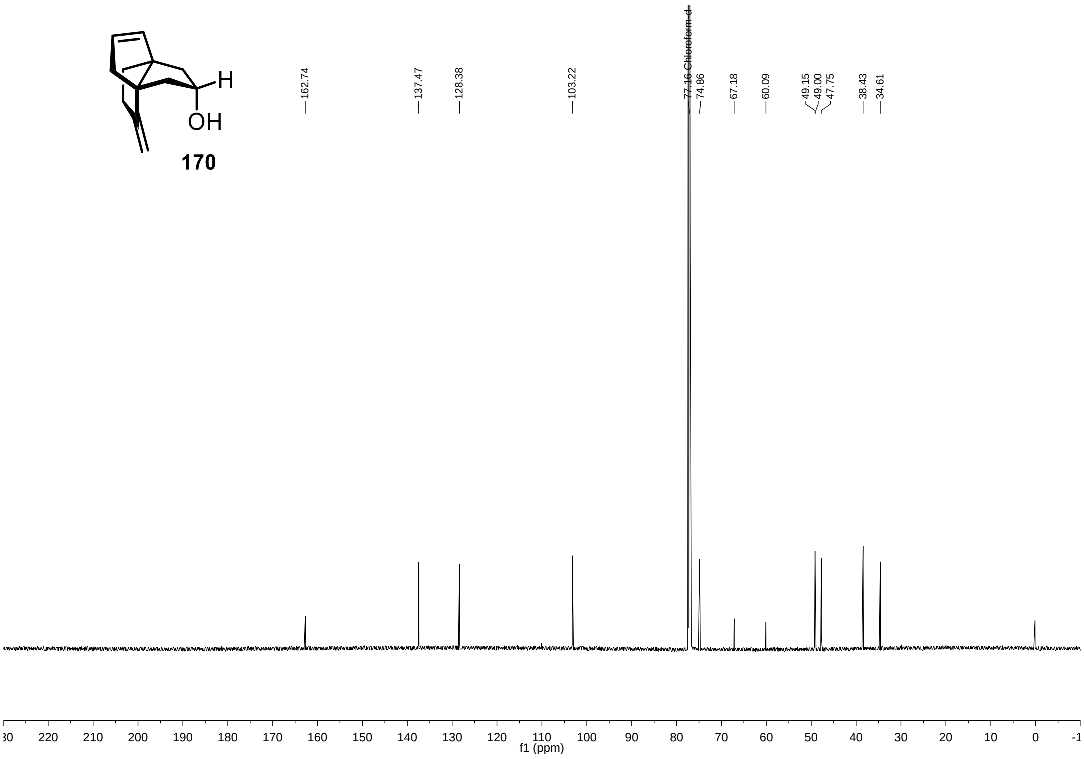

Me
Me
O
O
Me
Me
2
1.10
4.10
0.98
1.02
0.95
0.95
3.00
3.02
3.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


218.77
Me
Me
O
O
Me
Me
2
94.44
84.82
65.17
64.39
54.52
39.39
36.92
32.29
29.84 Acetone-d6
28.56
26.81
23.05
22.33
19.19
18.47
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

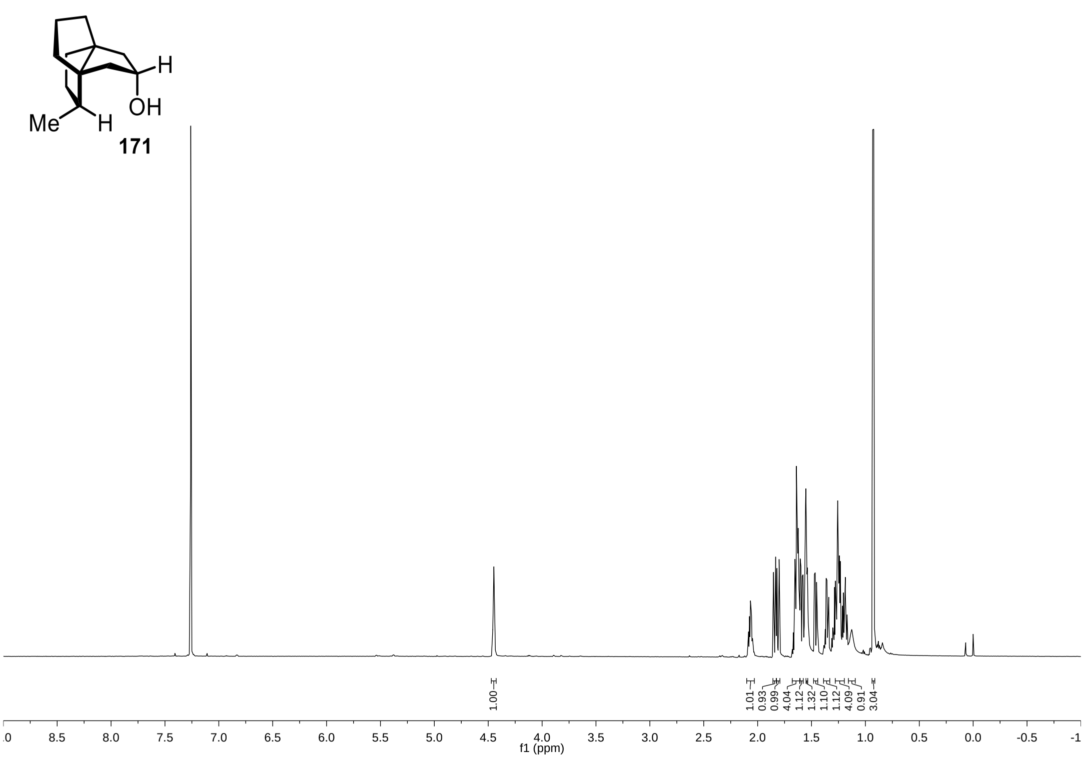


170

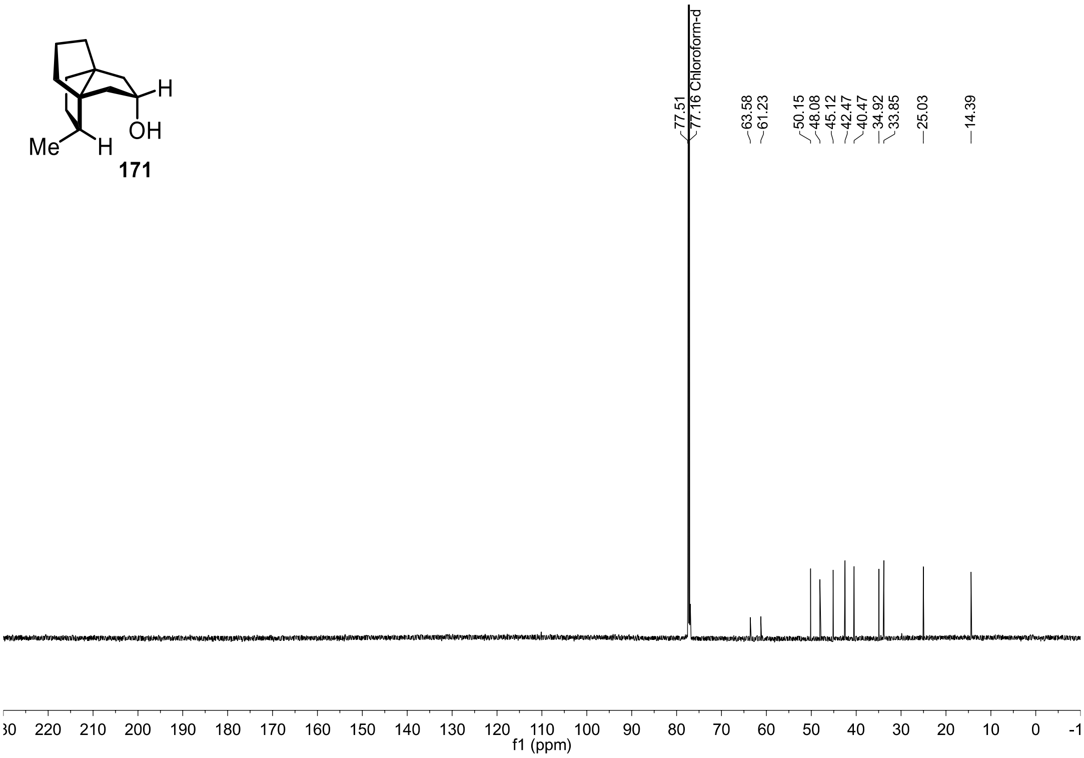

2.00
1.00
1.00
1.00
0.96
1.05
2.05
2.02
1.01
2.02
1.07
0.96
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


162.74
137.47
128.38
103.22
77.16 Chloroform-d
74.86
67.18
60.09
49.15
49.00
47.75
38.43
34.61
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

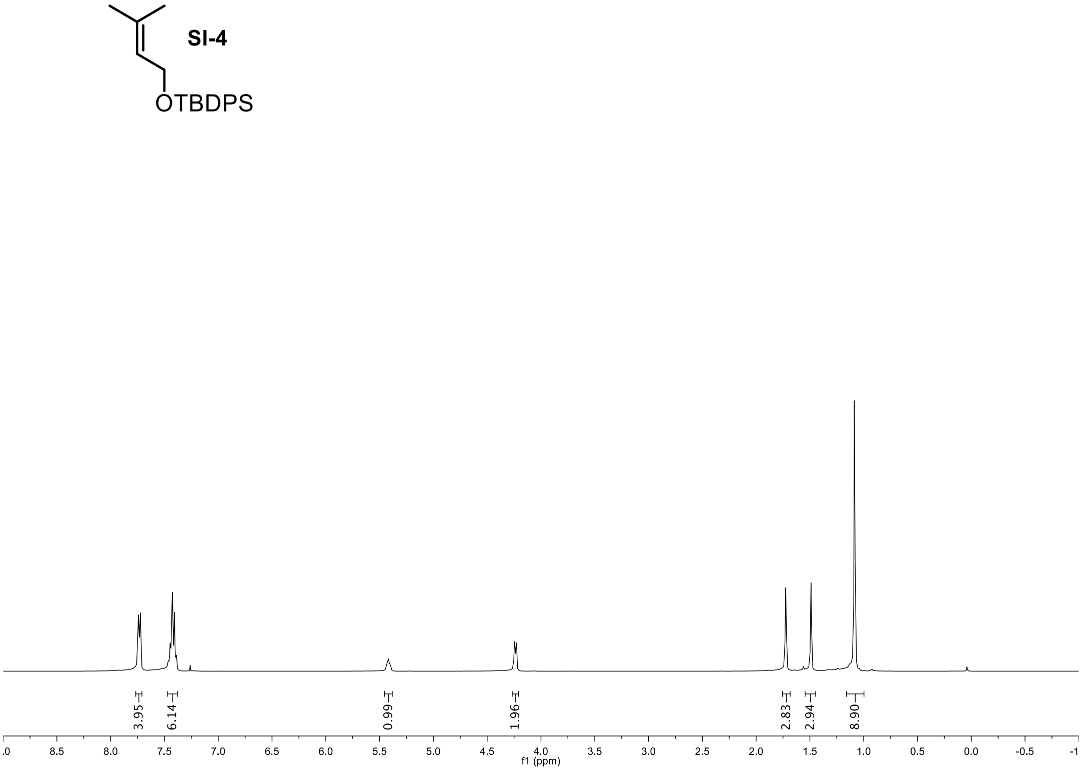
170

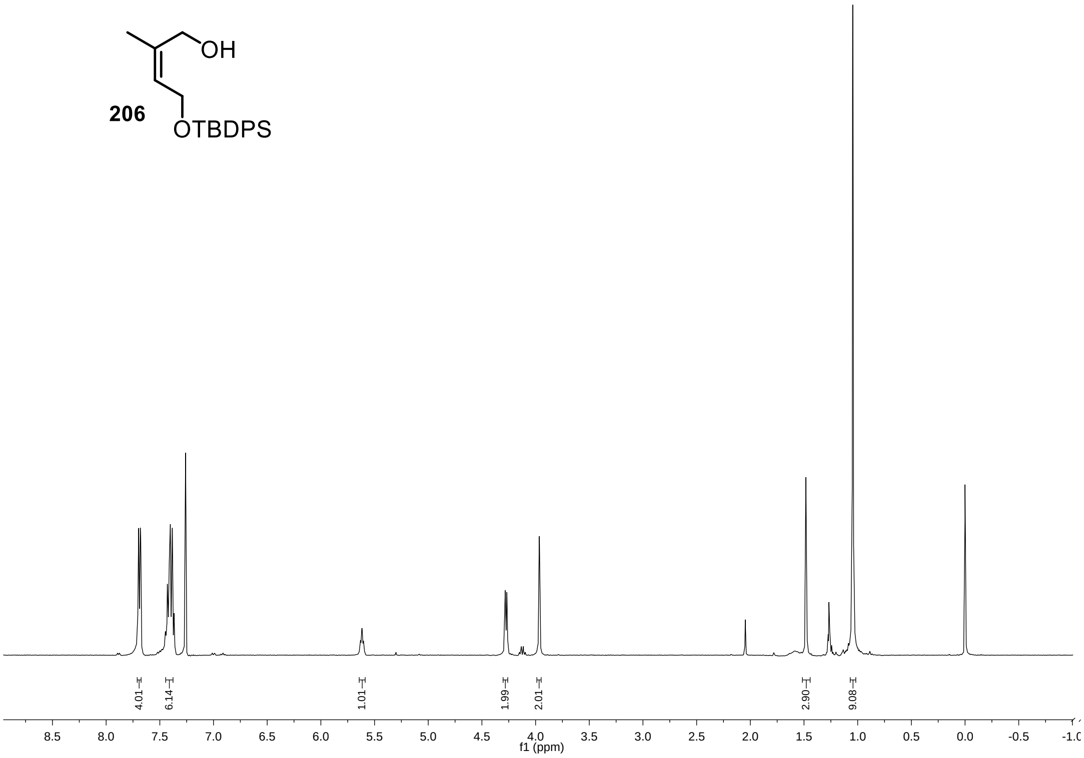

Me
H
H
OH
1.00
1.01
0.93
0.99
4.04
1.12
1.32
1.10
1.12
4.09
0.91
3.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

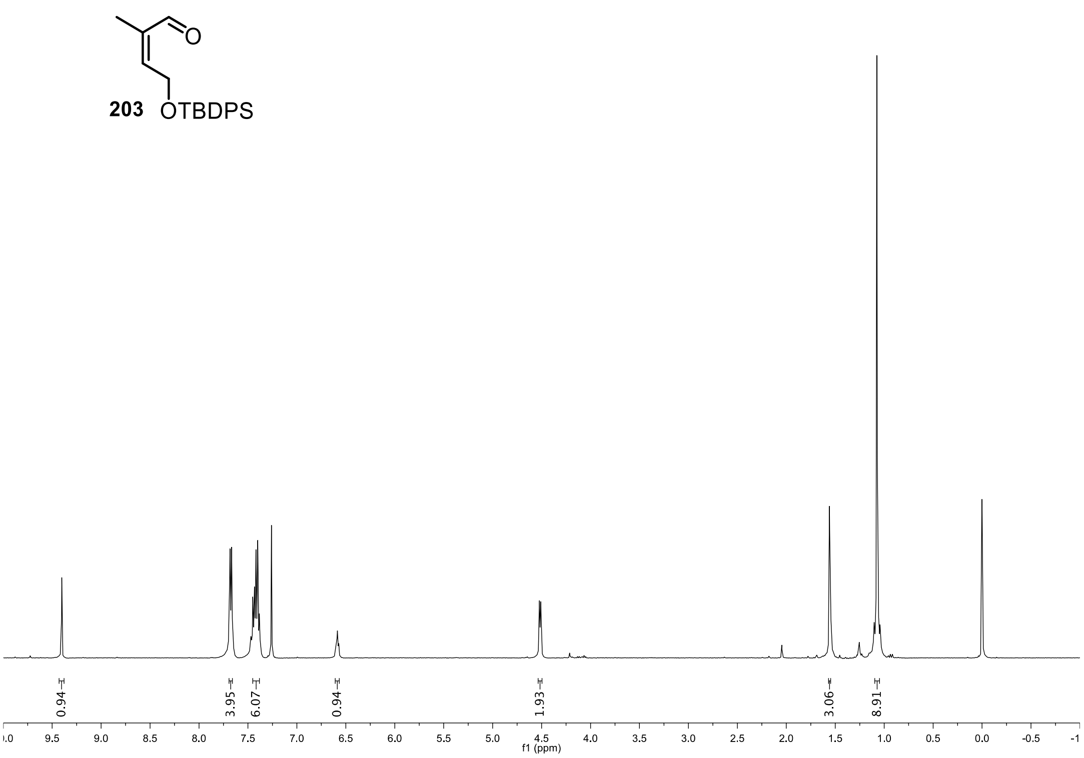
171


Me
H
H
OH
77.51
77.16 Chloroform-d
63.58
61.23
50.15
48.08
45.12
42.47
40.47
34.92
33.85
25.03
14.39
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

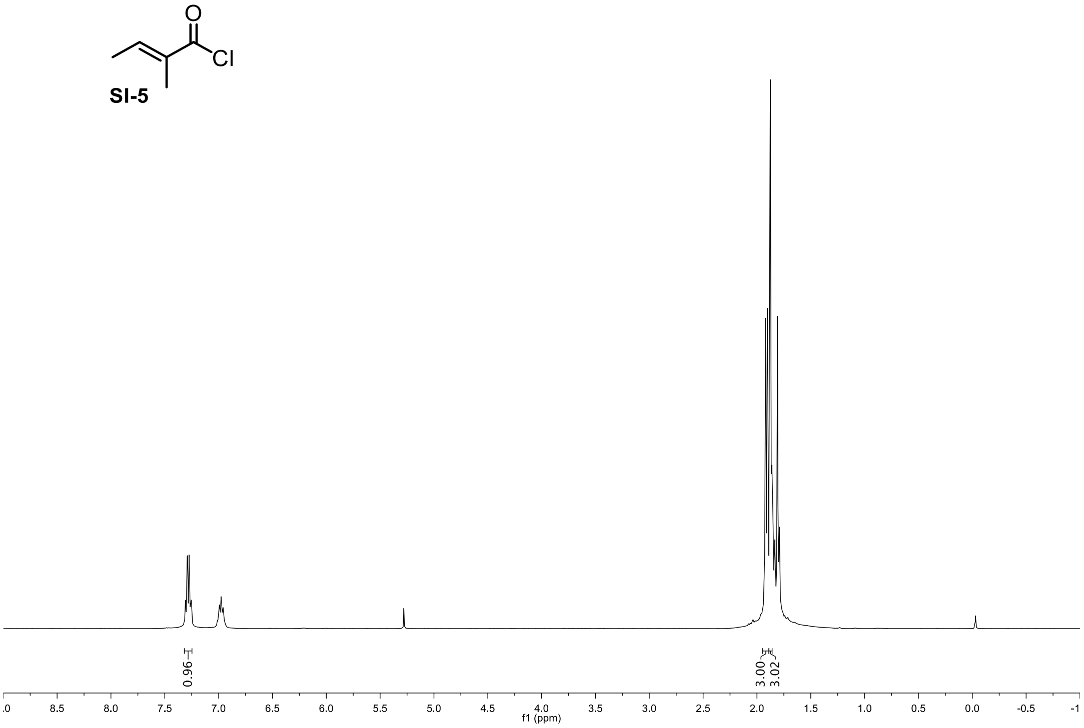
171


SI-4
OTBDPS
3.95
6.14
0.99
1.96
2.83
2.94
8.90
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

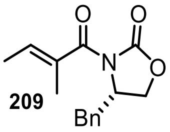

206
OH
OTBDPS
4.01
6.14
1.01
1.99
2.01
2.90
9.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


203

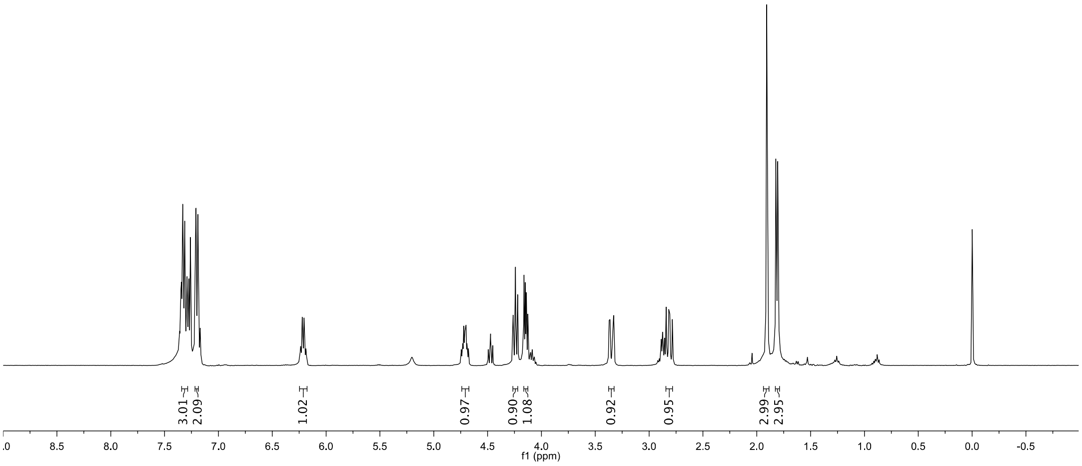
OTBDPS
O
0.94
3.95
6.07
0.94
1.93
3.06
8.91
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

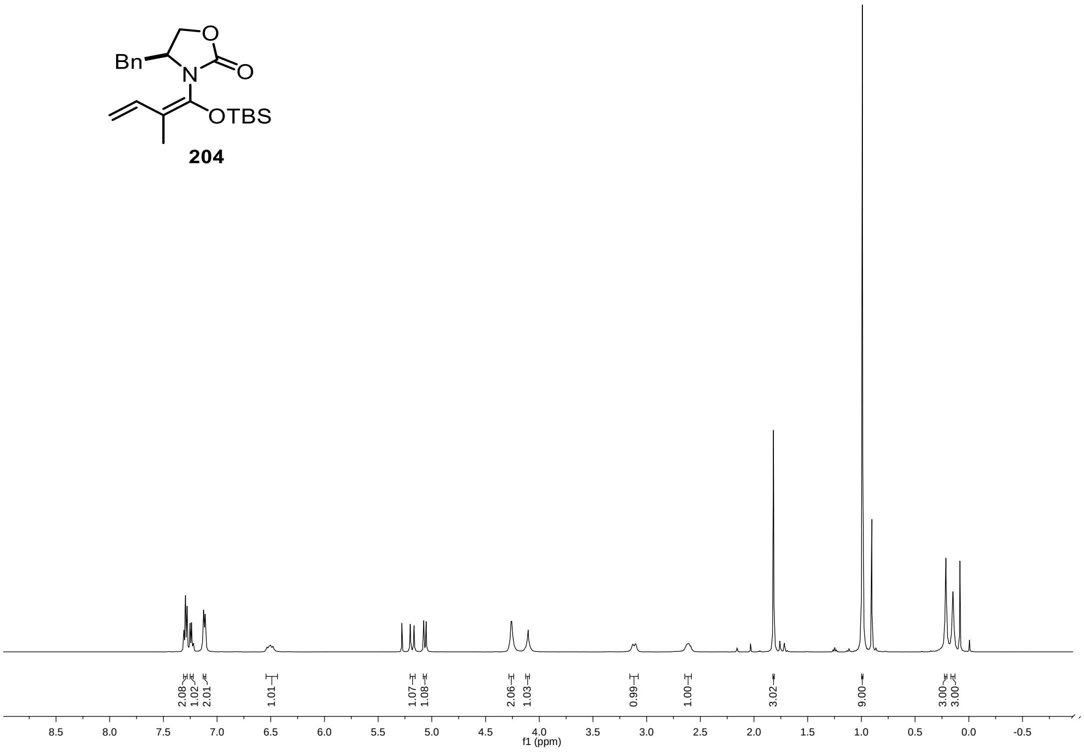

SI-5

O
Cl
0.96
3.00
3.02
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


O
O
N
O
Bn

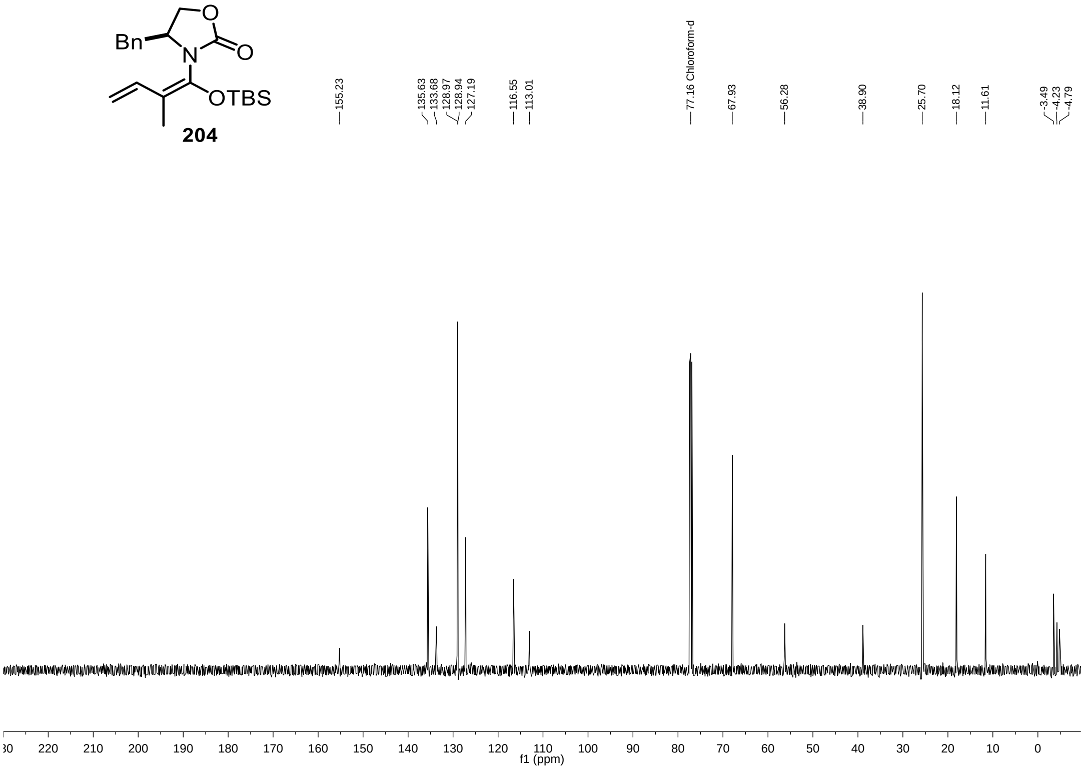
209


3.01
2.09
1.02
0.97
0.90
1.08
0.92
0.95
2.99
2.95
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Bn
O
N
O
OTBS

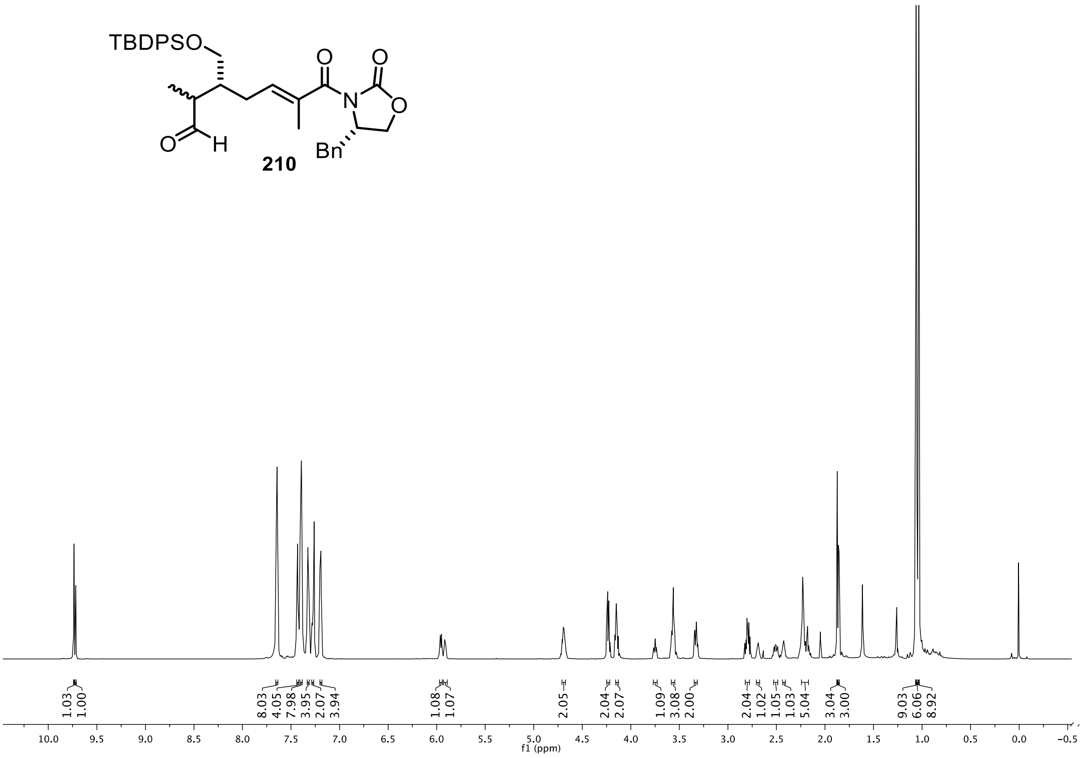
204

2.08
1.02
2.01
1.01
1.07
1.08
2.06
1.03
0.99
1.00
3.02
9.00
3.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



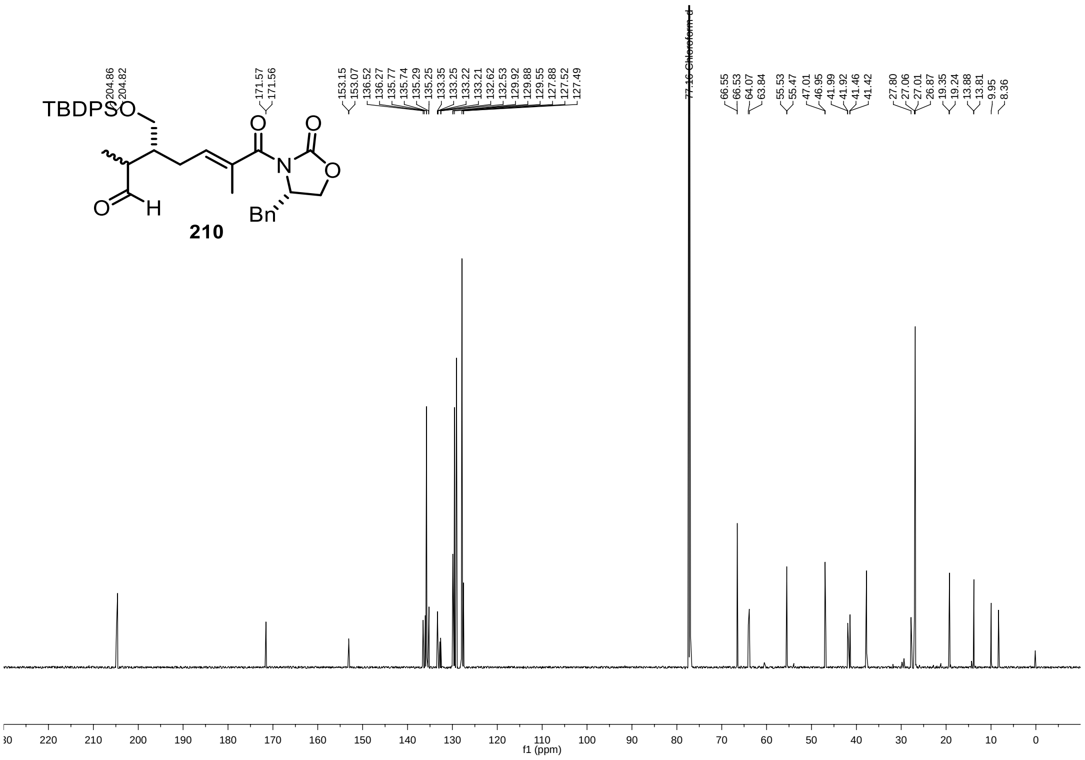
204

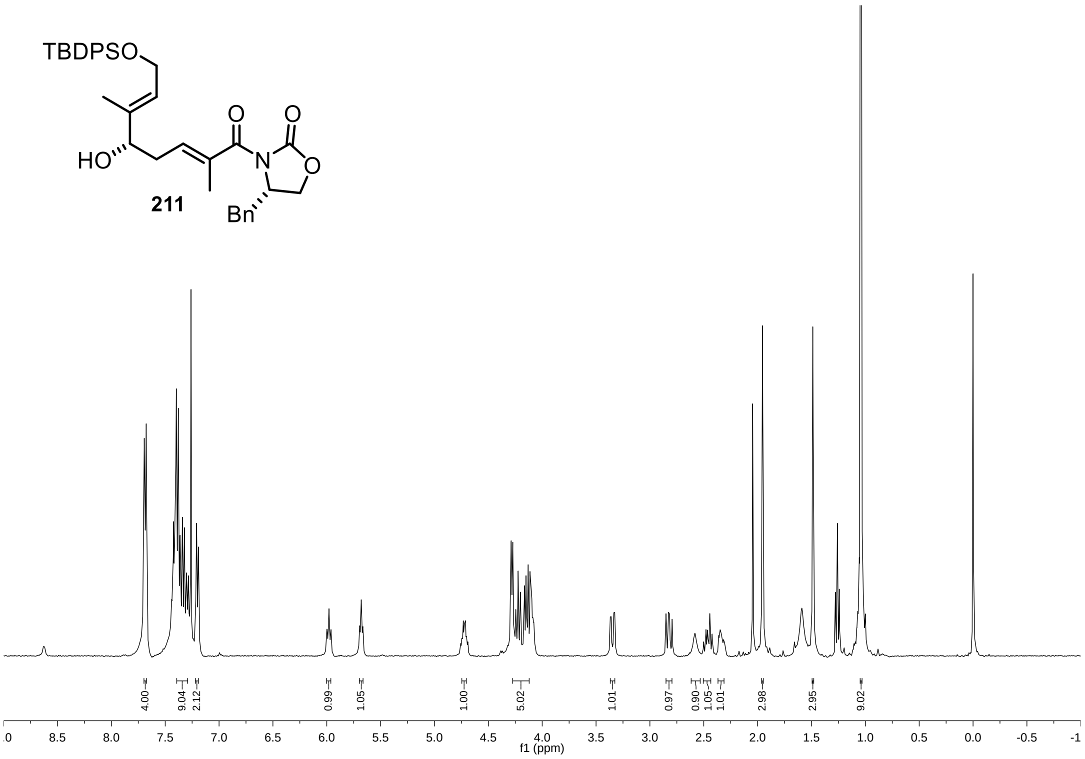
Bn
O
N
O
OTBS
155.23
135.63
133.68
128.97
128.94
127.19
116.55
113.01
77.16 Chloroform-d
67.93
56.28
38.90
25.70
18.12
11.61
-3.49
-4.23
-4.79
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

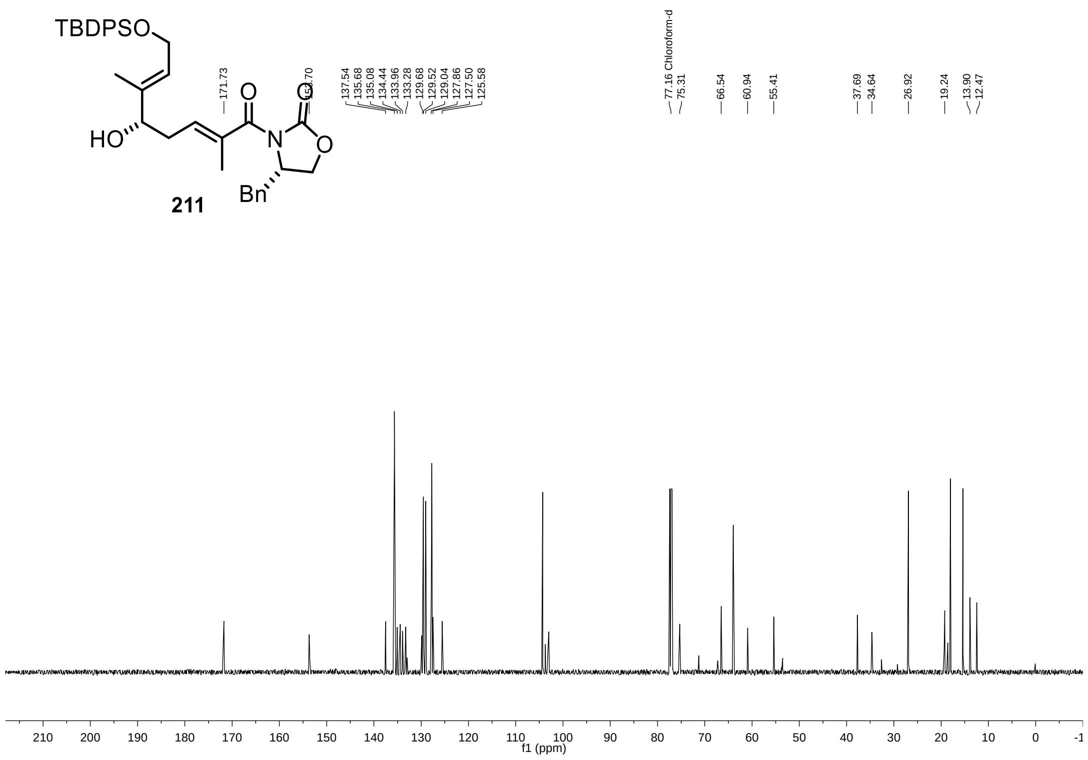


210

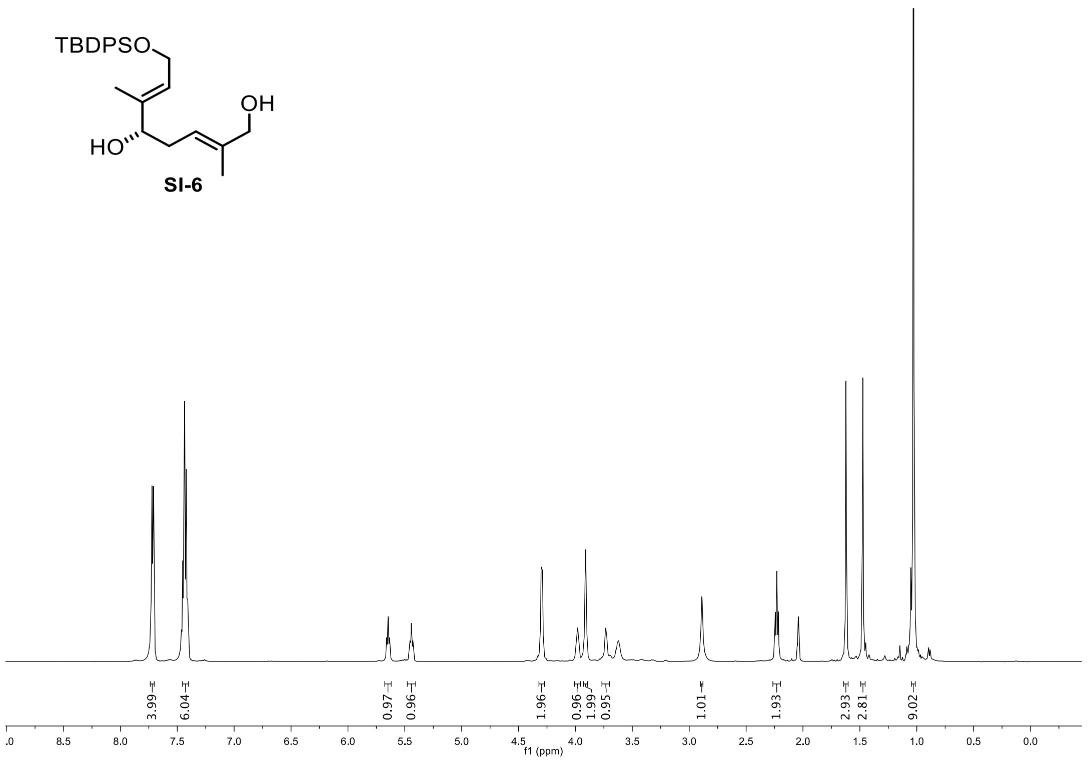
TBDPSO
O
O
N
O
O
H
Bn
1.03
1.00
8.03
4.05
7.98
3.95
2.07
3.94
1.08
1.07
2.05
2.04
2.07
1.09
3.08
2.00
2.04
1.02
1.05
1.03
5.04
3.04
3.00
9.03
6.06
8.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


TBDPSO
O
H
O
O
N
O
Bn
210
204.86
204.82
171.57
171.56
153.15
153.07
136.52
136.27
135.77
135.74
135.29
135.25
133.35
133.25
133.22
133.21
132.62
132.53
129.92
129.88
129.55
127.88
127.52
127.49
77.16 Chloroform-d
66.55
66.53
64.07
63.84
55.53
55.47
47.01
46.95
41.99
41.92
41.46
41.42
27.80
27.06
27.01
26.87
19.35
19.24
13.88
13.81
9.95
8.36
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

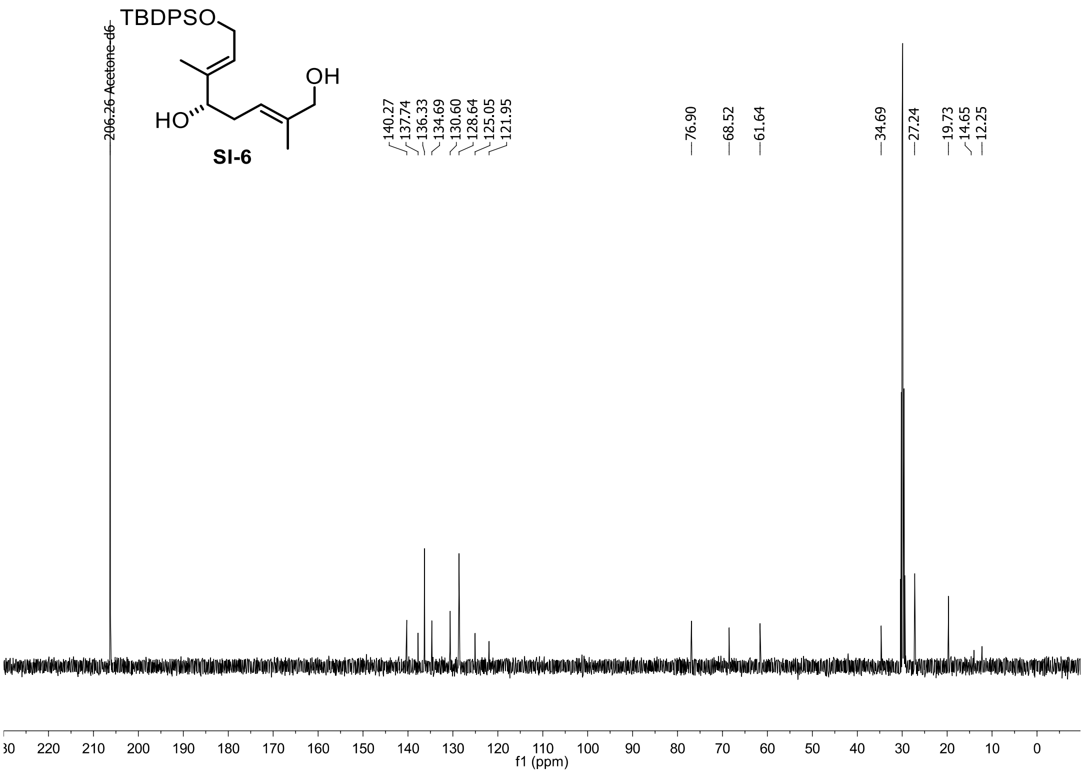

TBDPSO
HO
O
O
N
O
Bn
211
4.00
9.04
2.12
0.99
1.05
1.00
5.02
1.01
0.97
0.90
1.05
1.01
2.98
2.95
9.02
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

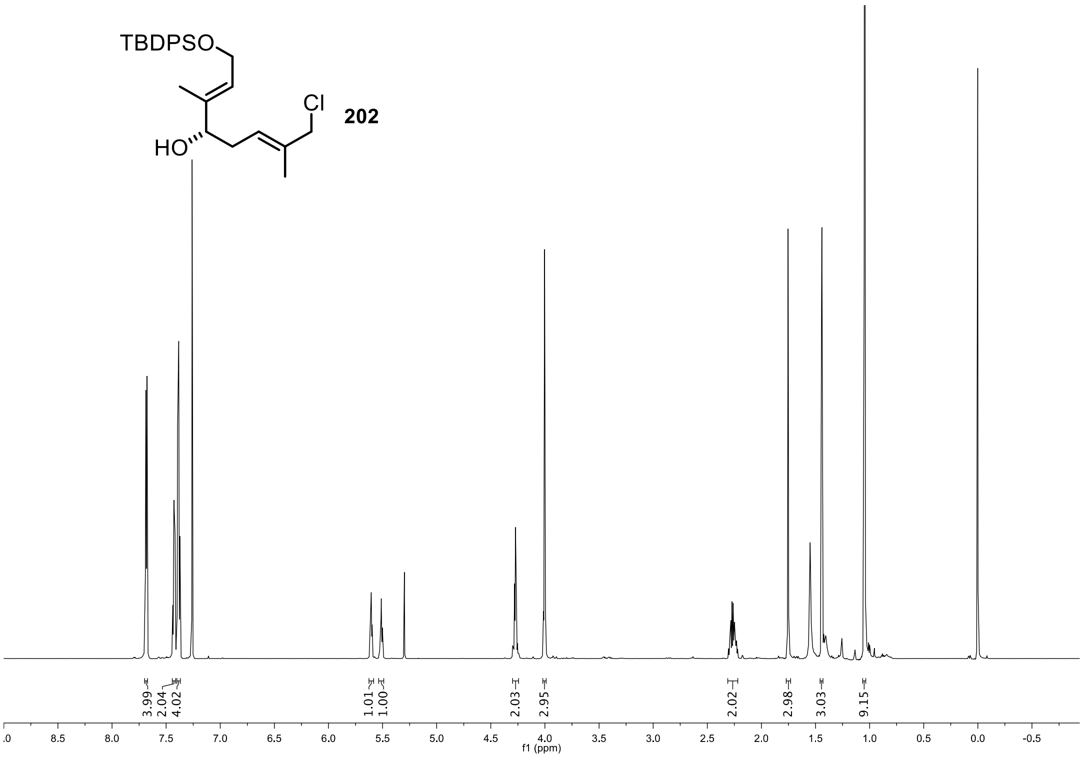

TBDPSO
HO
O
O
N
O
Bn
171.73
153.70
137.54
135.68
135.08
134.44
133.96
133.28
129.68
129.52
129.04
127.86
127.50
125.58
77.16 Chloroform-d
75.31
66.54
60.94
55.41
37.69
34.64
26.92
19.24
13.90
12.47
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

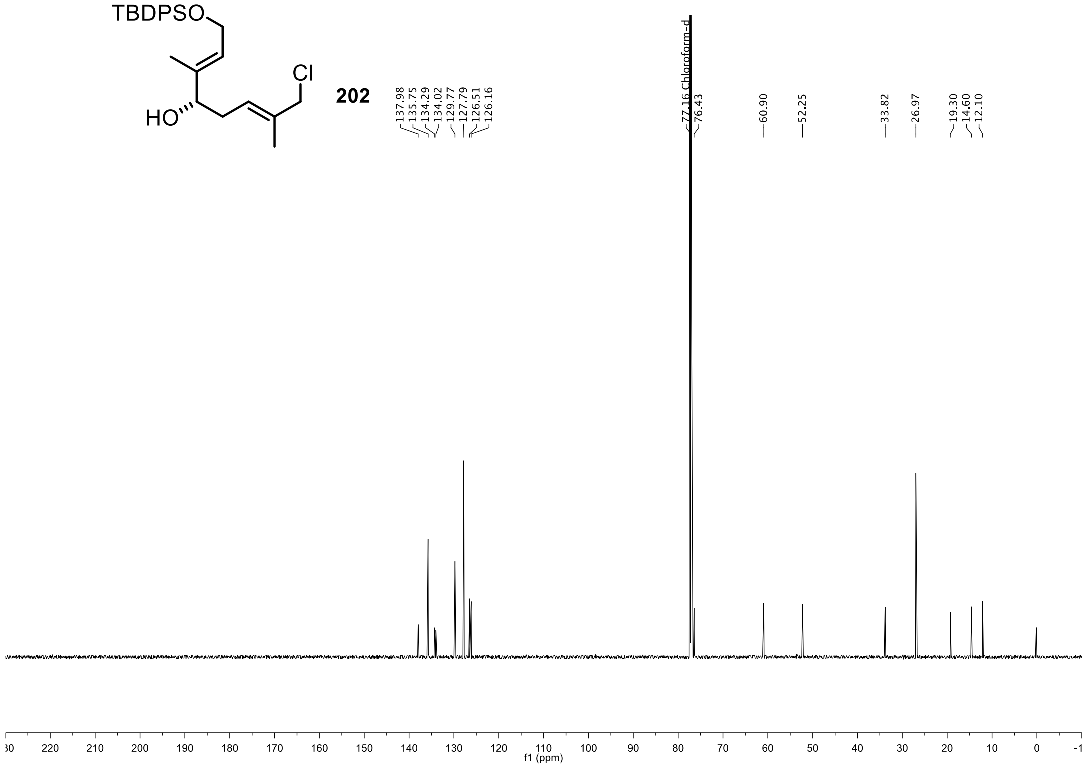
211

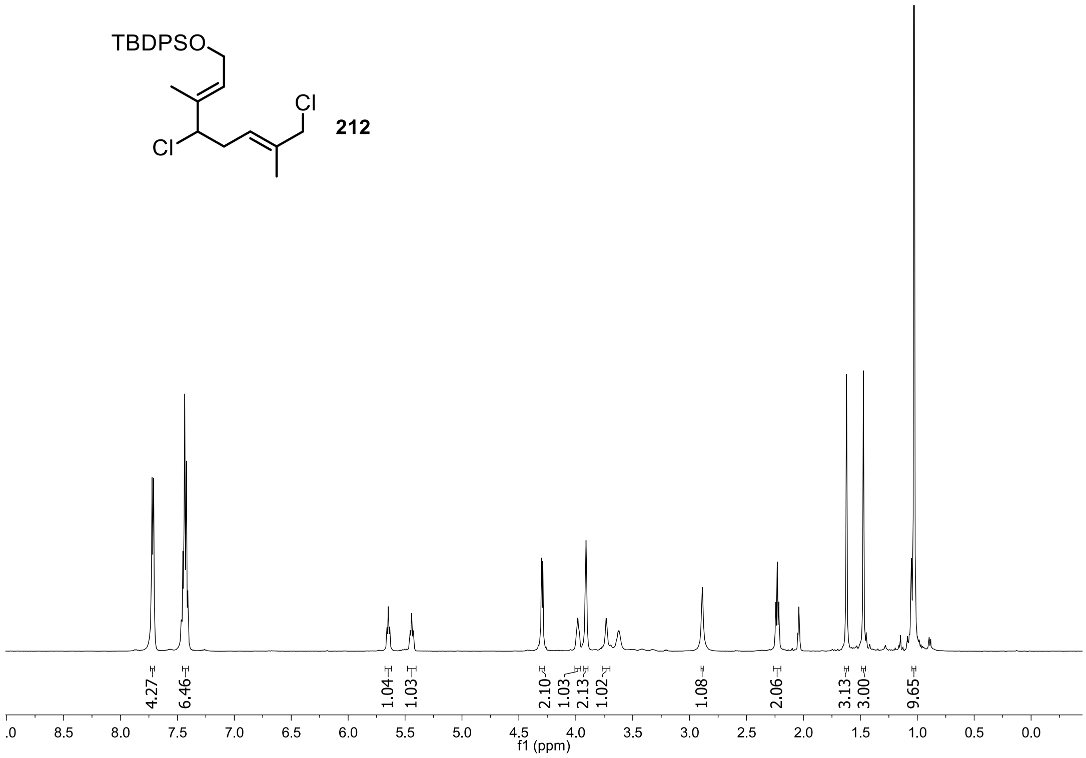

TBDPSO
OH
HO
3.99
6.04
0.97
0.96
1.96
0.96
1.99
0.95
1.01
1.93
2.93
2.81
9.02
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

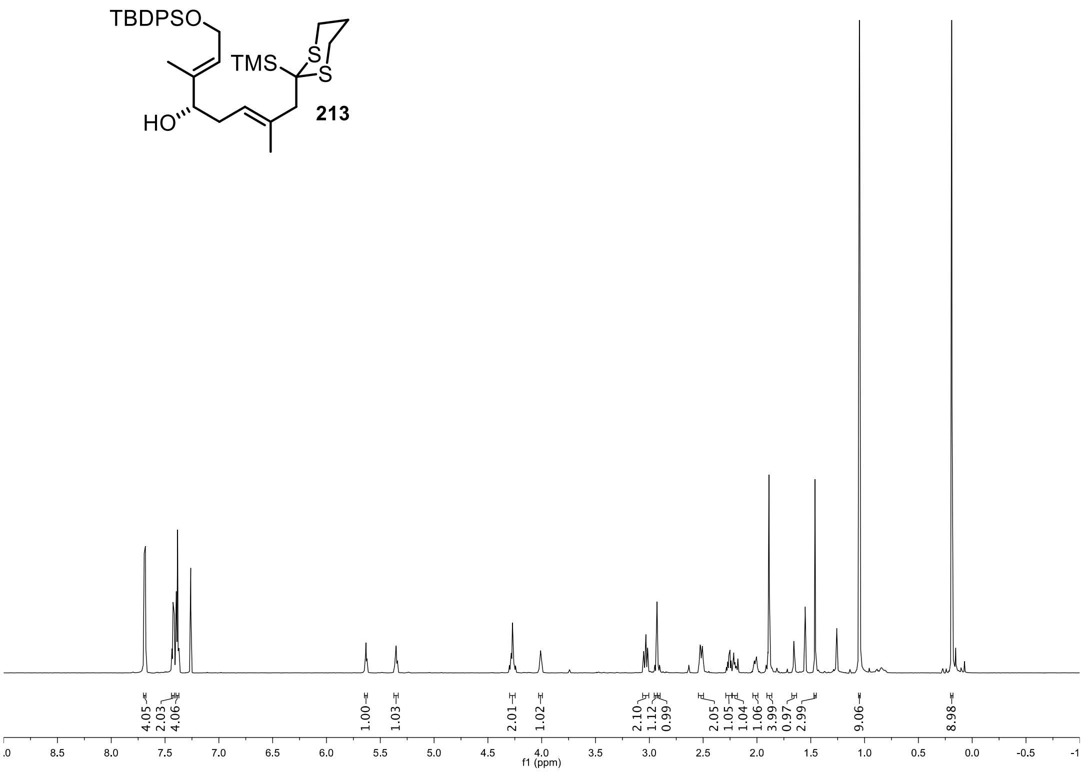
SI-6

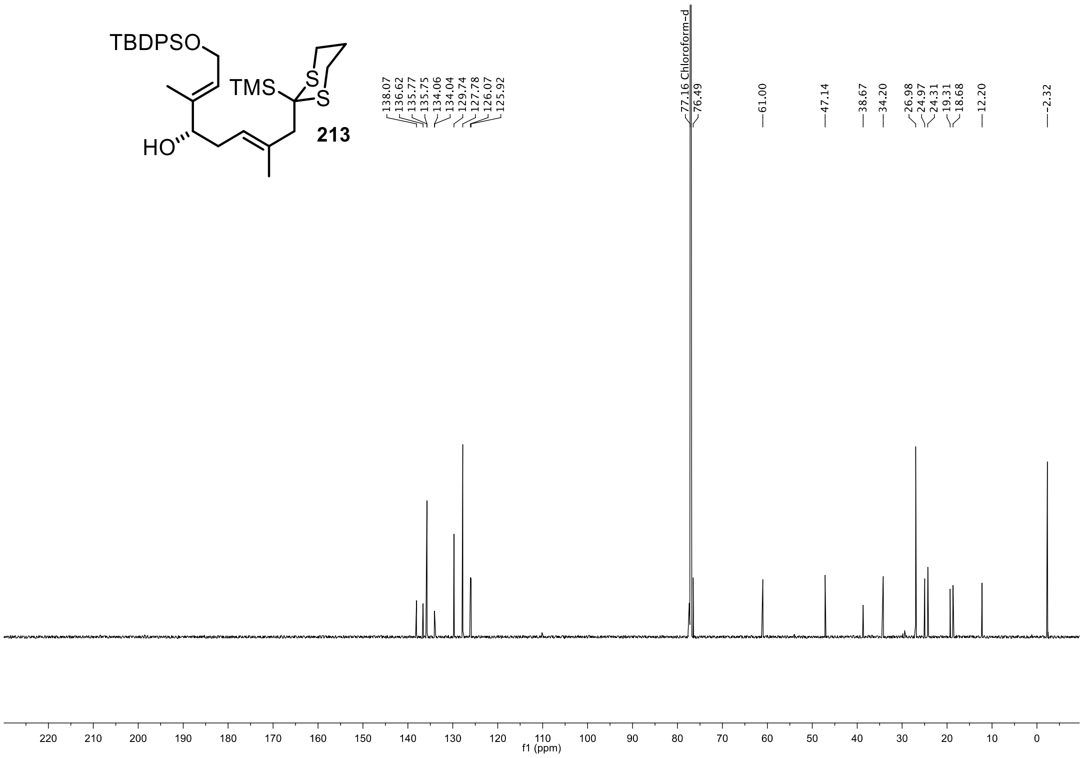

TBDPSO
OH
HO
SI-6
206.26 Acetone-d6
140.27
137.74
136.33
134.69
130.60
128.64
125.05
121.95
76.90
68.52
61.64
34.69
27.24
19.73
14.65
12.25
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

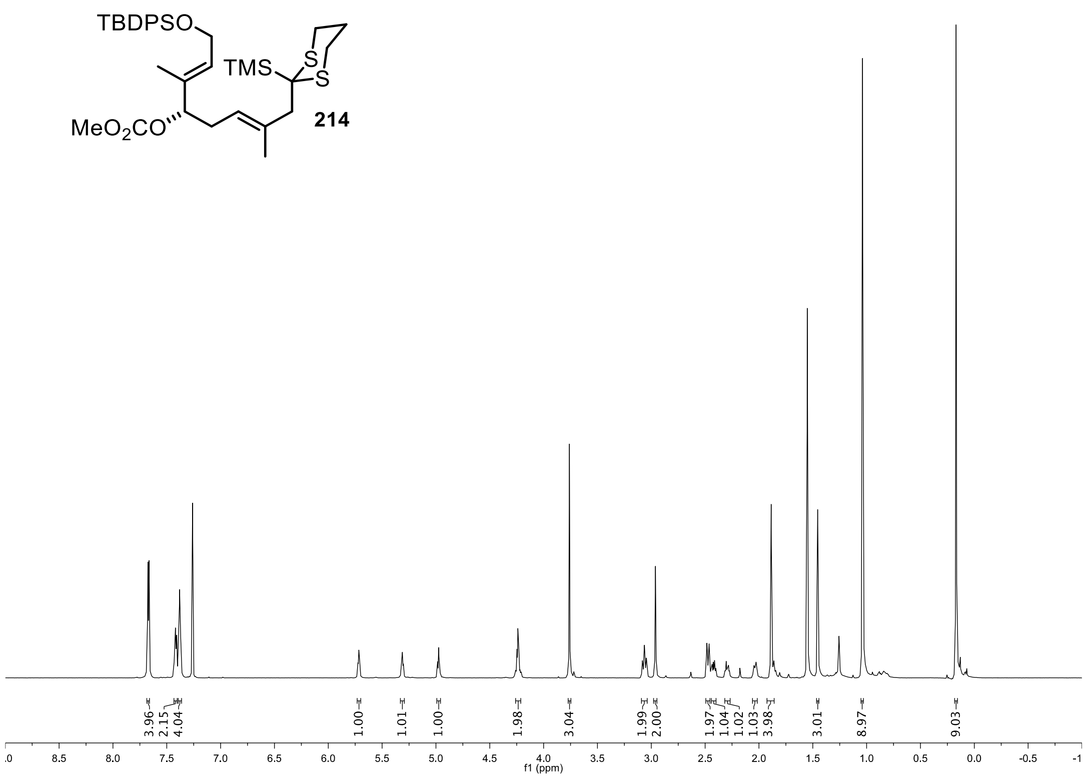

TBDPSO
Cl
HO
202
3.99
2.04
4.02
1.01
1.00
2.03
2.95
2.02
2.98
3.03
9.15
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

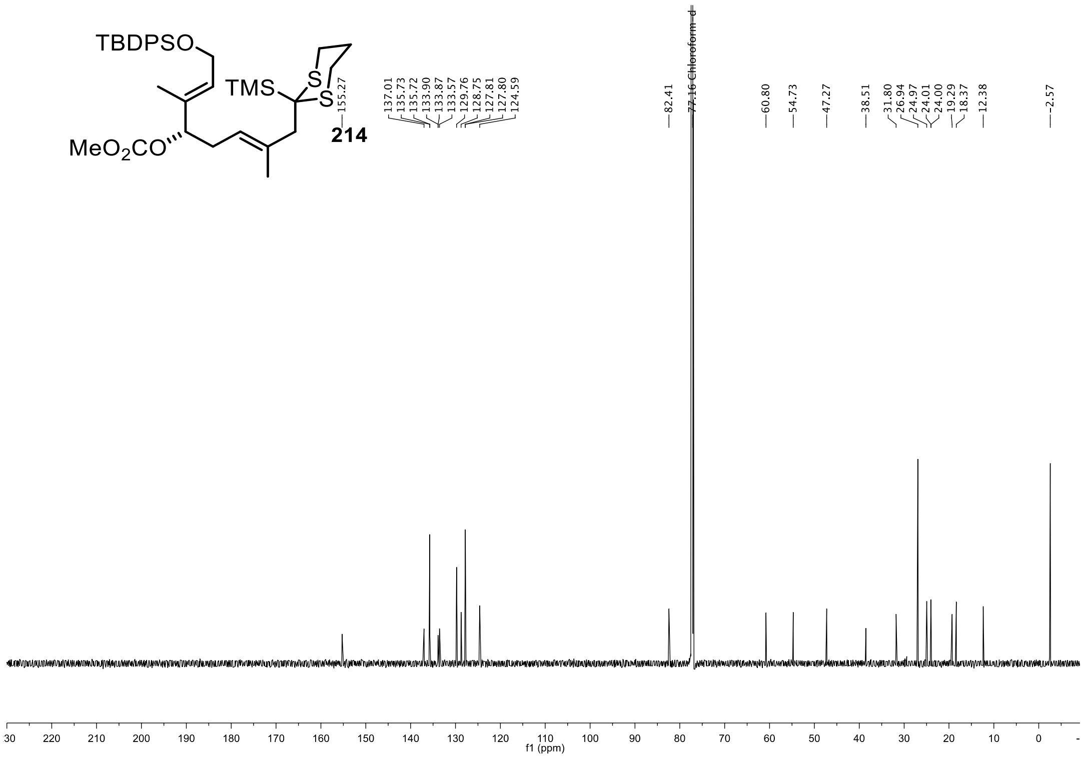

TBDPSO
Cl
HO
202
137.98
135.75
134.29
134.02
129.77
127.79
126.51
126.16
77.16 Chloroform-d
76.43
60.90
52.25
33.82
26.97
19.30
14.60
12.10
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

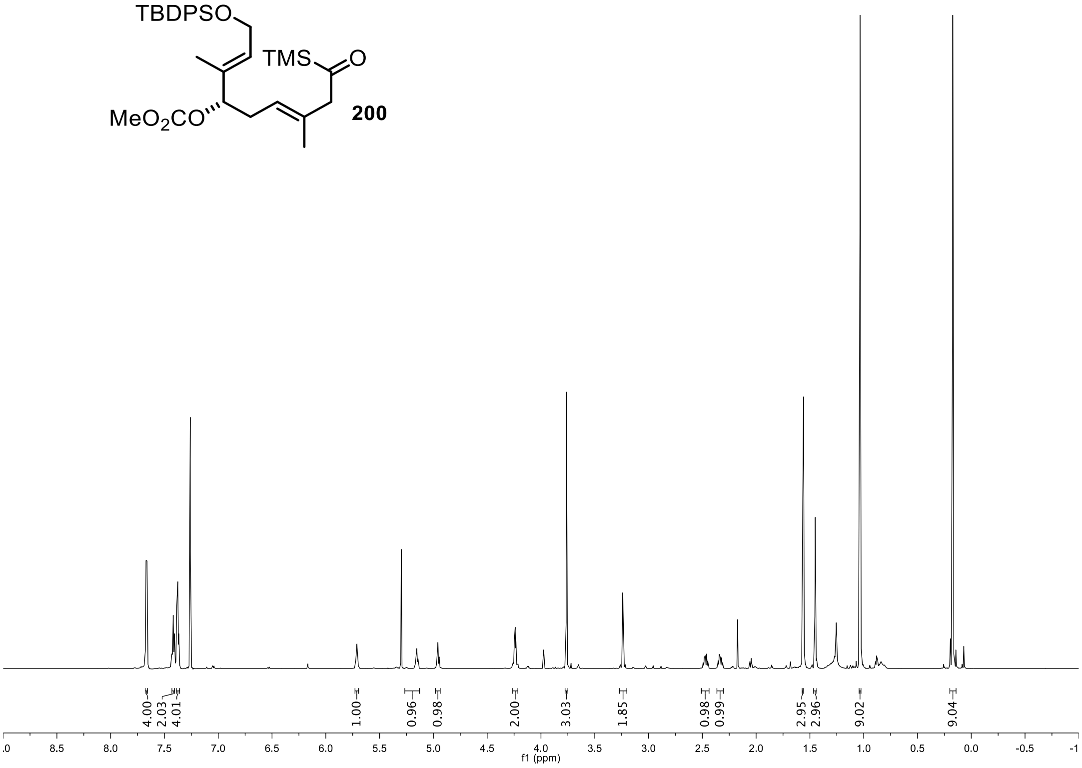

TBDPSO
Cl
Cl
212
4.27
6.46
1.04
1.03
2.10
1.03
2.13
1.02
1.08
2.06
3.13
3.00
9.65
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

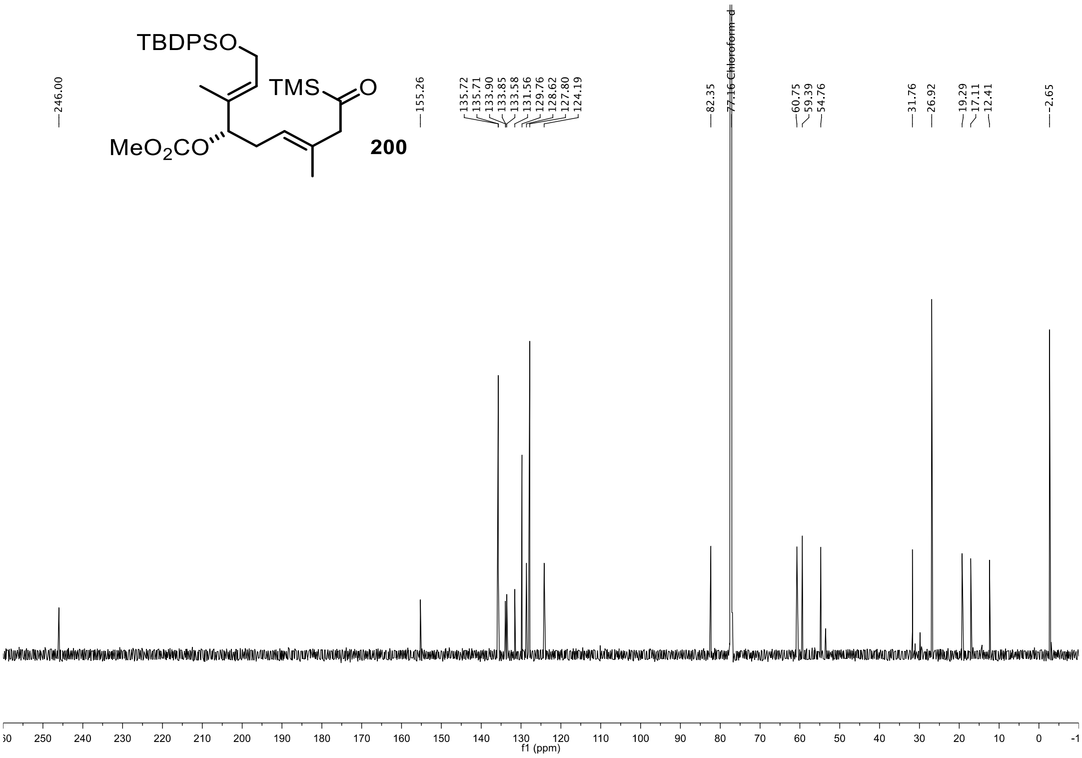

TBDPSO
TMS
S
S
HO
213
4.05
2.03
4.06
1.00
1.03
2.01
1.02
2.10
1.12
0.99
2.05
1.05
1.04
1.06
3.99
0.97
2.99
9.06
8.98
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

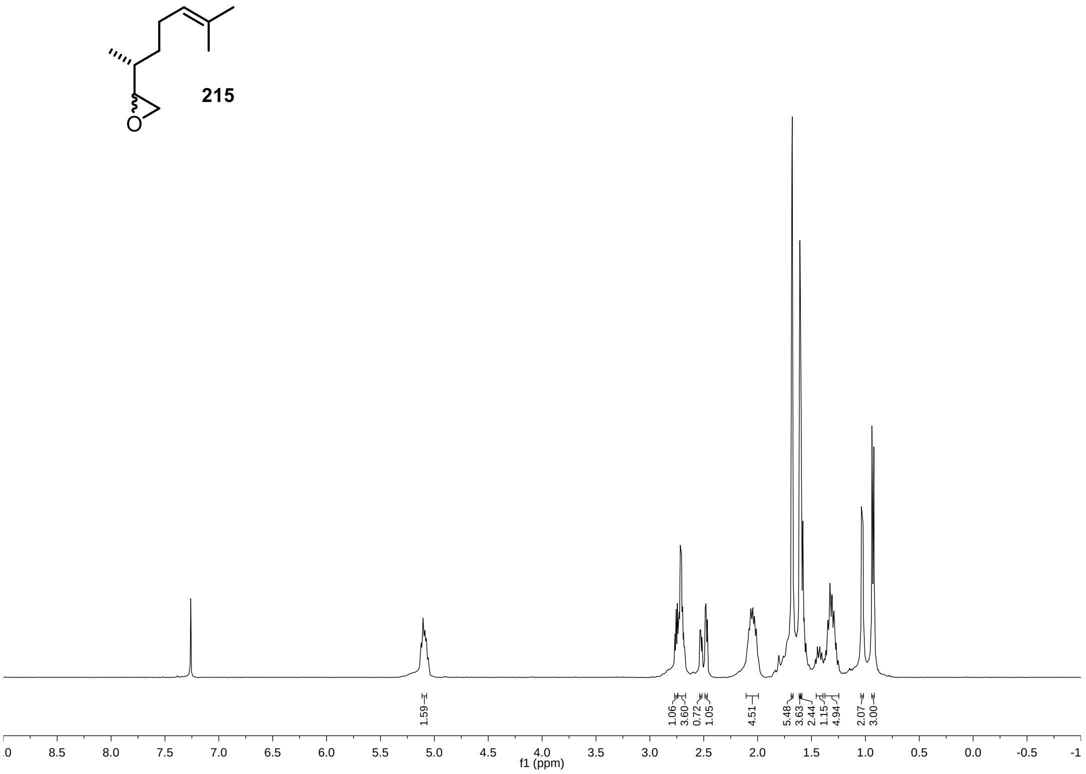

TBDPSO
TMS
S
S
HO
213
138.07
136.62
135.77
135.75
134.06
134.04
129.74
127.78
126.07
125.92
77.16 Chloroform-d
76.49
61.00
47.14
38.67
34.20
26.98
24.97
24.31
19.31
18.68
12.20
-2.32
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


TBDPSO
TMS
S
S
MeO$_2$CO
214
3.96
2.15
4.04
1.00
1.01
1.00
1.98
3.04
1.99
2.00
1.97
1.04
1.02
1.03
3.98
3.01
8.97
9.03
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


TBDPSO
TMS
S
S
MeO$_2$CO
214
155.27
137.01
135.73
135.72
133.90
133.87
133.57
129.76
128.75
127.81
127.80
124.59
82.41
77.16 Chloroform-d
60.80
54.73
47.27
38.51
31.80
26.94
24.97
24.01
24.00
19.29
18.37
12.38
-2.57
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-
f1 (ppm)

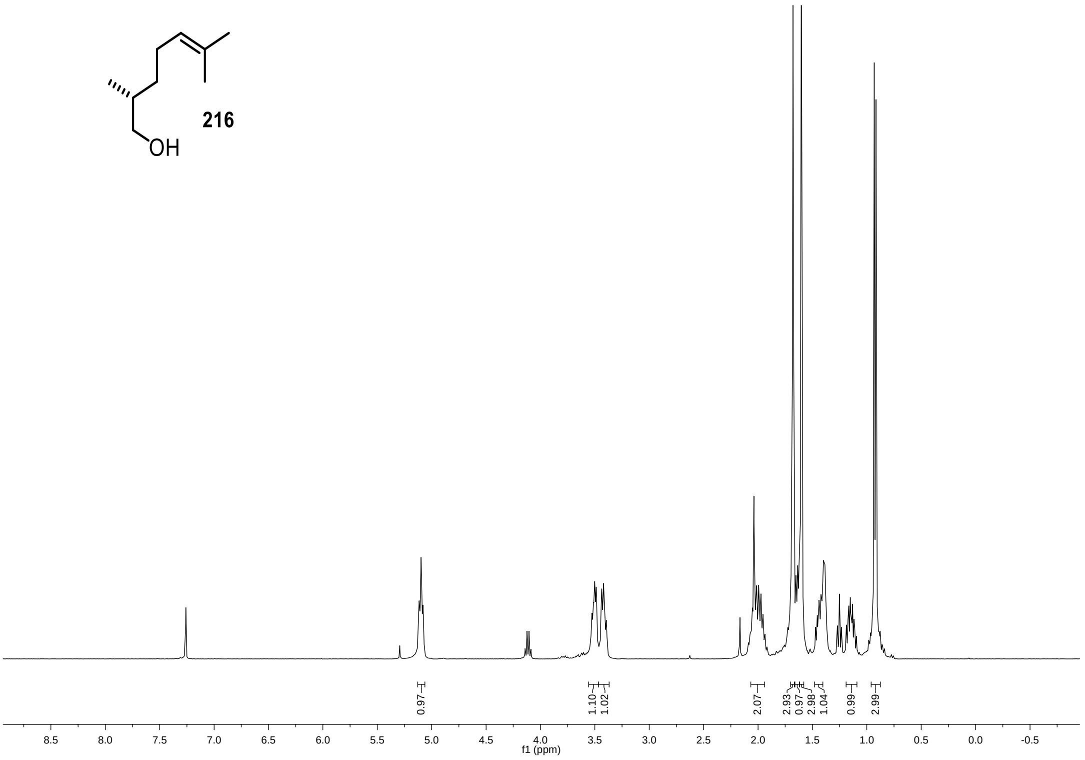

TBDPSO
TMS
O
MeO2CO
200
4.00
2.03
4.01
1.00
0.96
0.98
2.00
3.03
1.85
0.98
0.99
2.95
2.96
9.02
9.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


TBDPSO
TMS
O
MeO2CO
200
246.00
155.26
135.72
135.71
133.90
133.85
133.58
131.56
129.76
128.62
127.80
124.19
82.35
77.16 Chloroform-d
60.75
59.39
54.76
31.76
26.92
19.29
17.11
12.41
-2.65
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



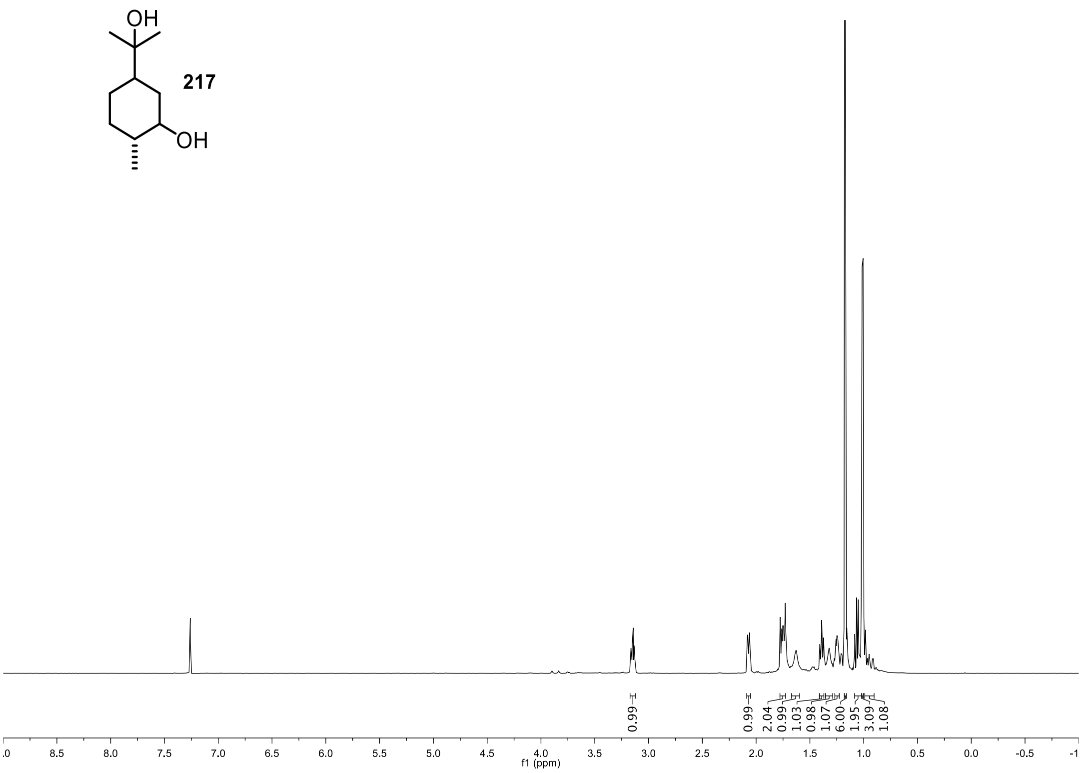
215

O
1.59
1.06
3.60
0.72
1.05
4.51
5.48
3.63
2.44
1.15
4.94
2.07
3.00
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



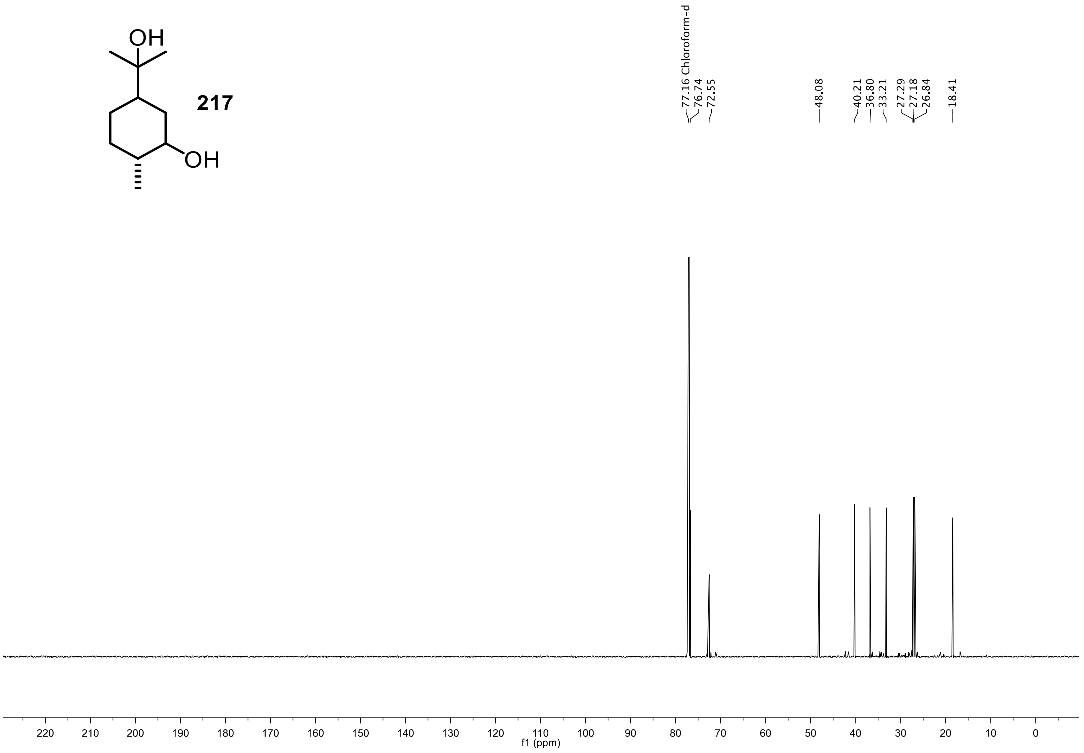
216

OH
0.97
1.10
1.02
2.07
2.93
0.97
2.98
1.04
0.99
2.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



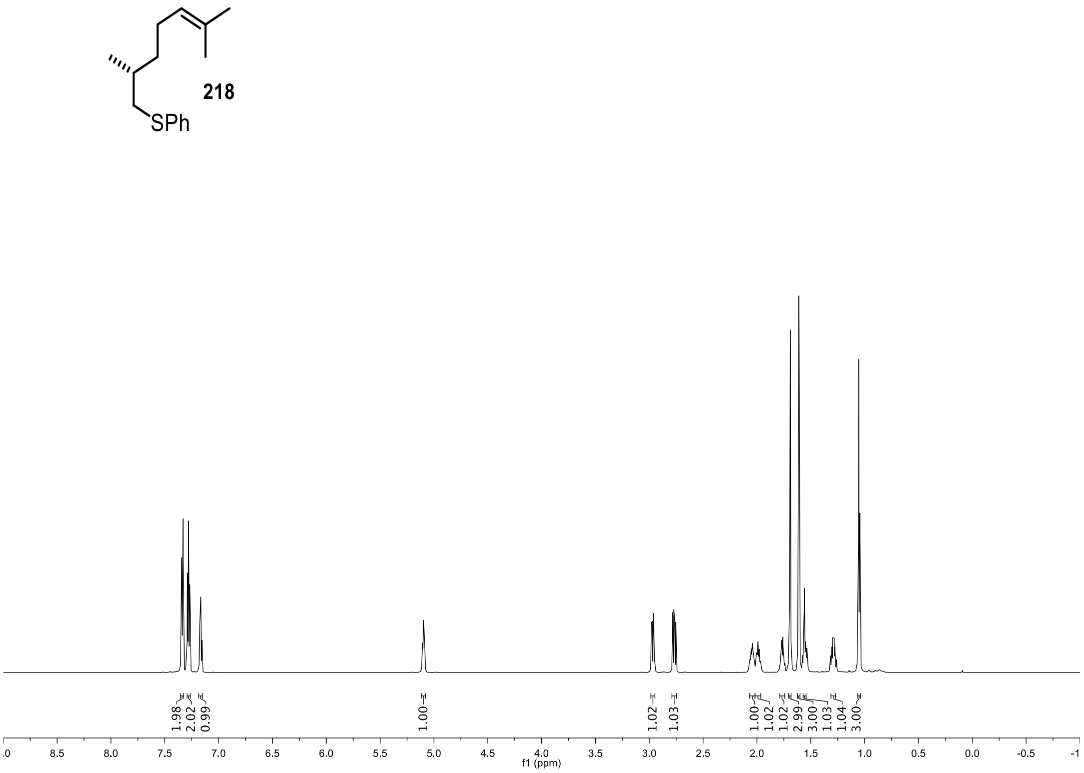
217

OH
OH
0.99
0.99
2.04
0.99
1.03
0.98
1.07
6.00
1.95
3.09
1.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

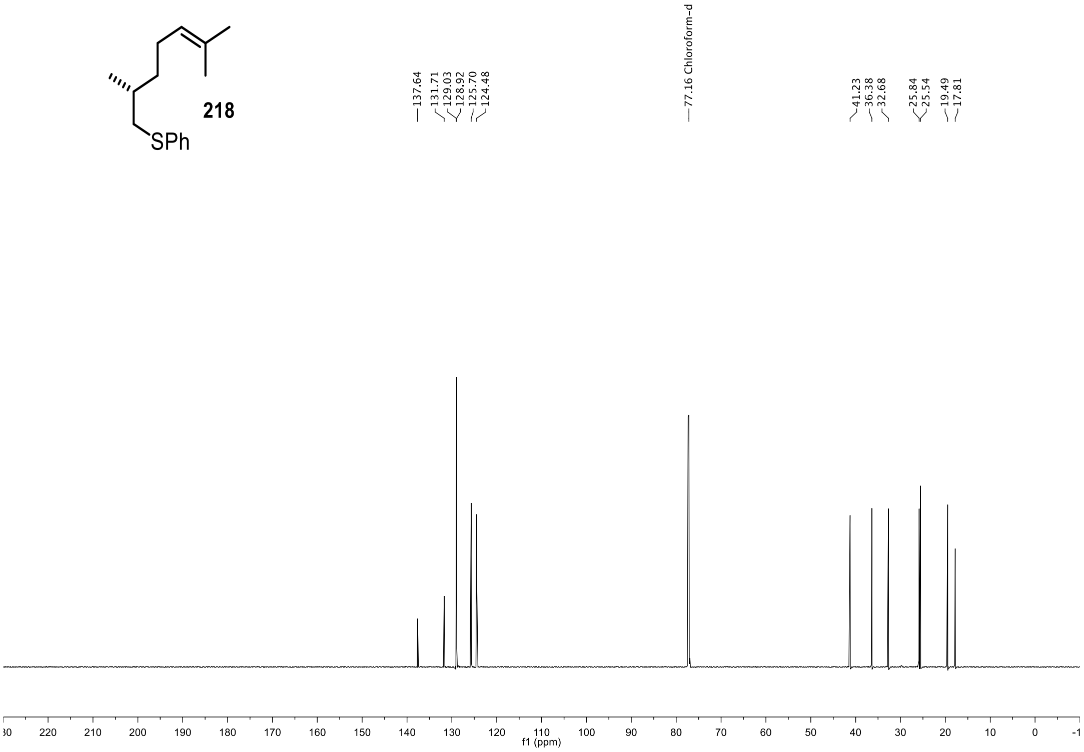


217

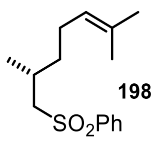
OH
OH
77.16 Chloroform-d
76.74
72.55
48.08
40.21
36.80
33.21
27.29
27.18
26.84
18.41
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


218

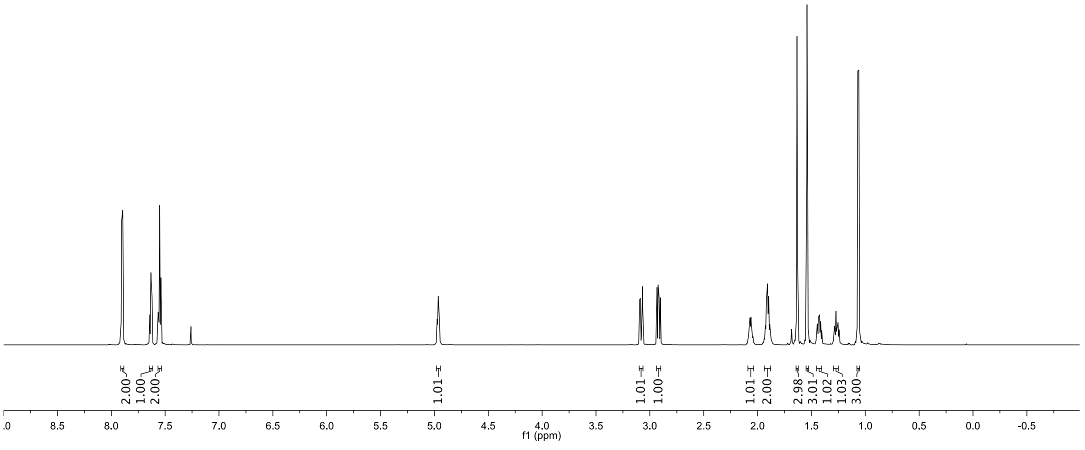
SPh
1.98
2.02
0.99
1.00
1.02
1.03
1.00
1.02
1.02
2.99
3.00
1.03
1.04
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

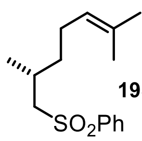

218

SPh
137.64
131.71
129.03
128.92
125.70
124.48
77.16 Chloroform-d
41.23
36.38
32.68
25.84
25.54
19.49
17.81
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

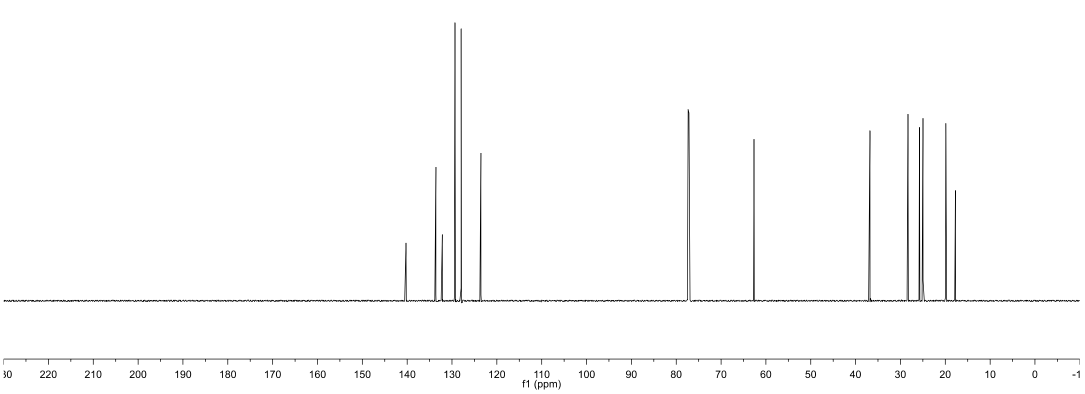

SO2Ph

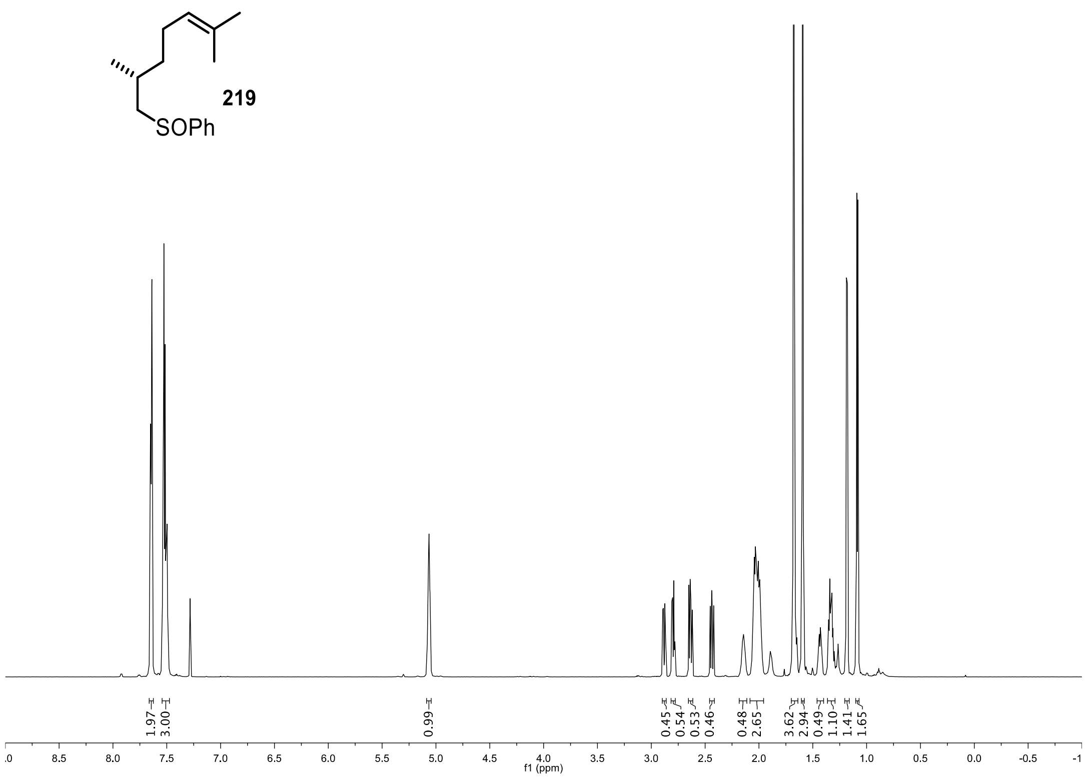
198

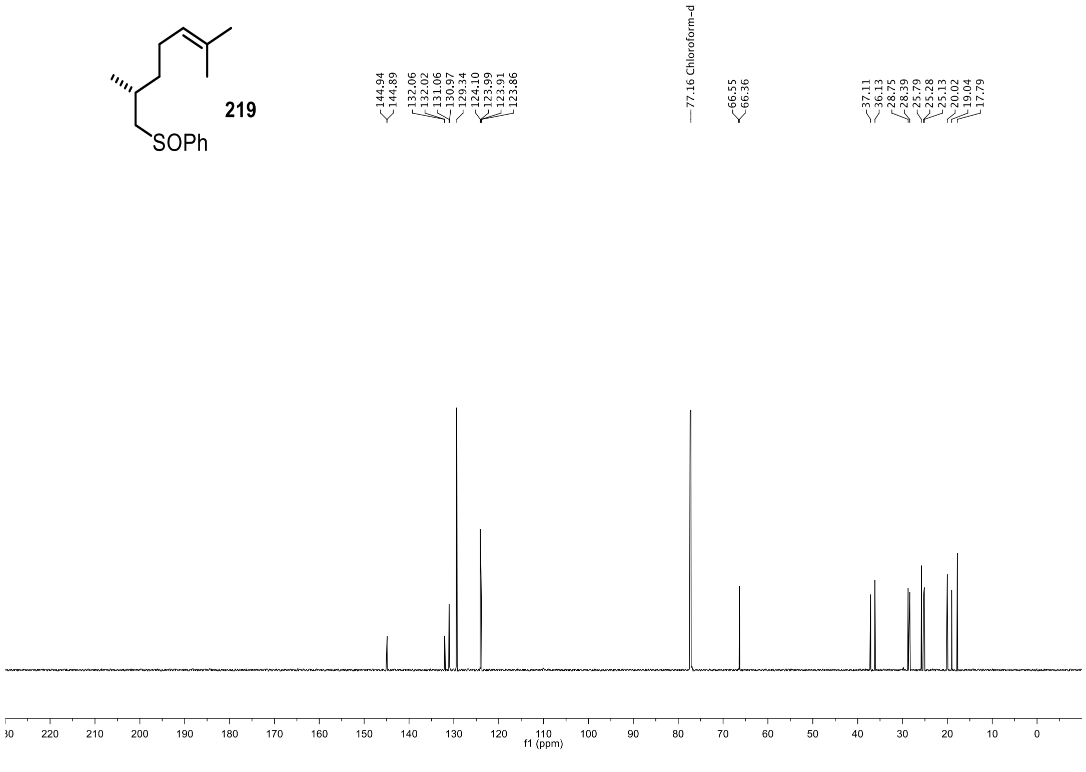

2.00
1.00
2.00
1.01
1.01
1.00
1.01
2.00
2.98
3.01
1.02
1.03
3.00
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

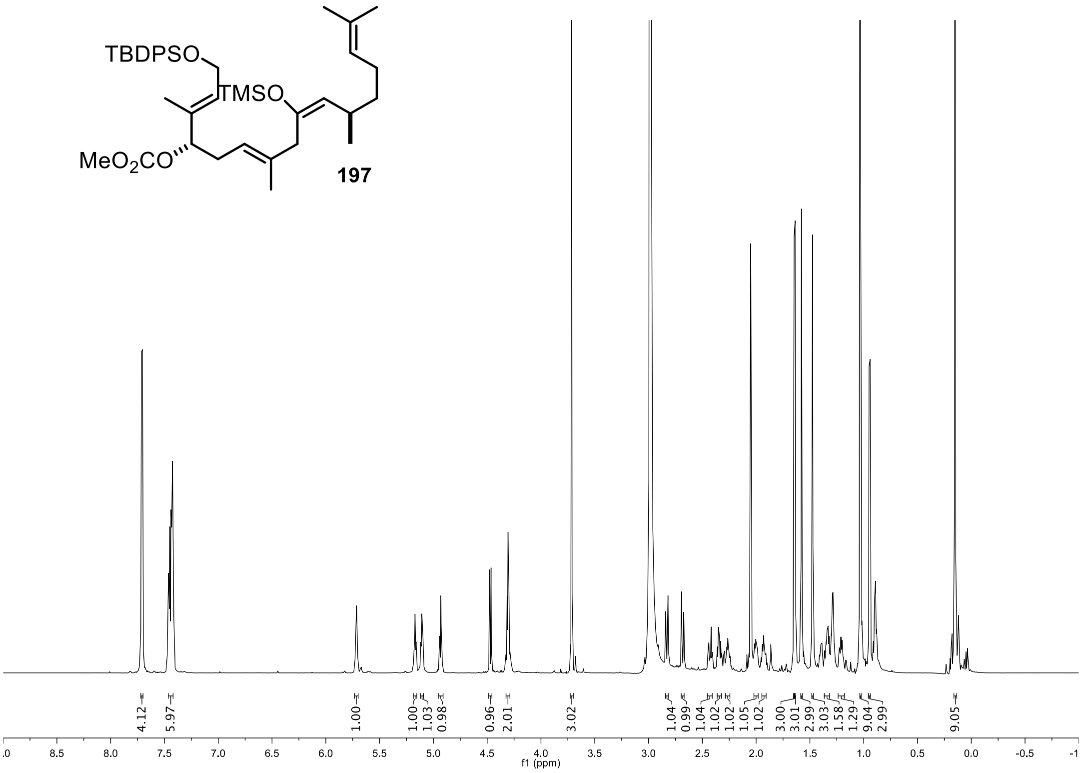

SO2Ph

198


140.26
133.61
132.15
129.34
127.95
123.57
77.16 Chloroform-d
62.64
36.81
28.32
25.76
24.97
19.88
17.75
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


219
SOPh
1.97
3.00
0.99
0.45
0.54
0.53
0.46
0.48
2.65
3.62
2.94
0.49
1.10
1.41
1.65
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

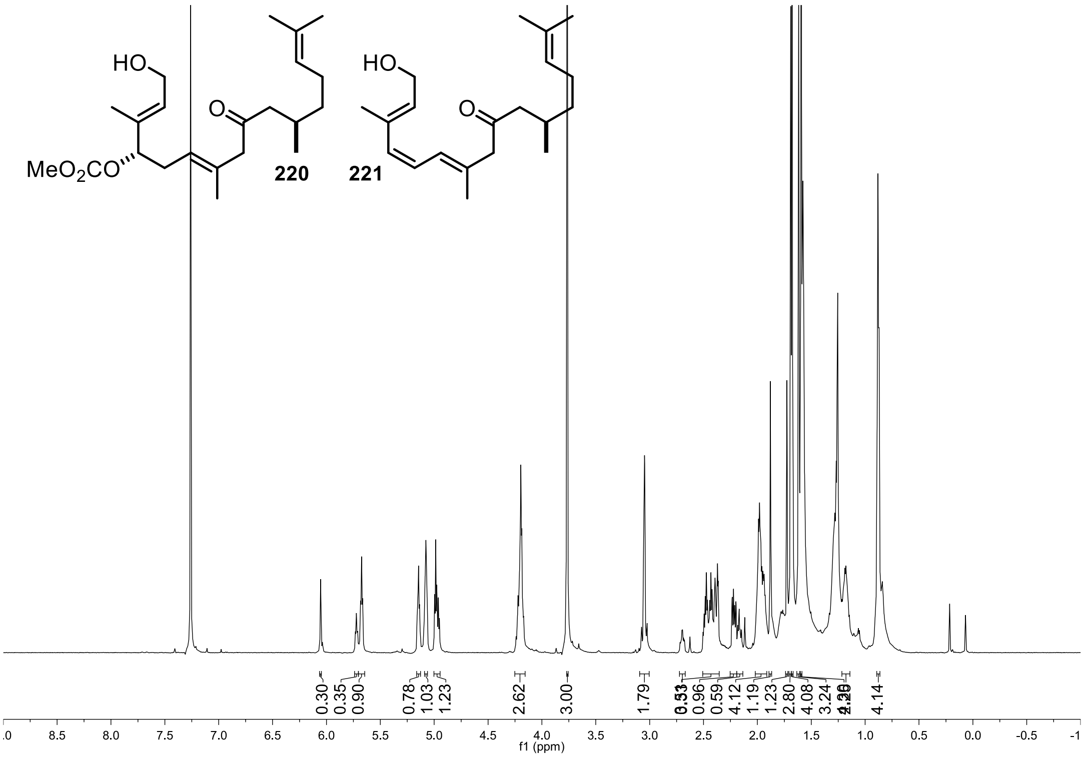

219
SOPh
144.94
144.89
132.06
132.02
131.06
130.97
129.34
124.10
123.99
123.91
123.86
77.16 Chloroform-d
66.55
66.36
37.11
36.13
28.75
28.39
25.79
25.28
25.13
20.02
19.04
17.79
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

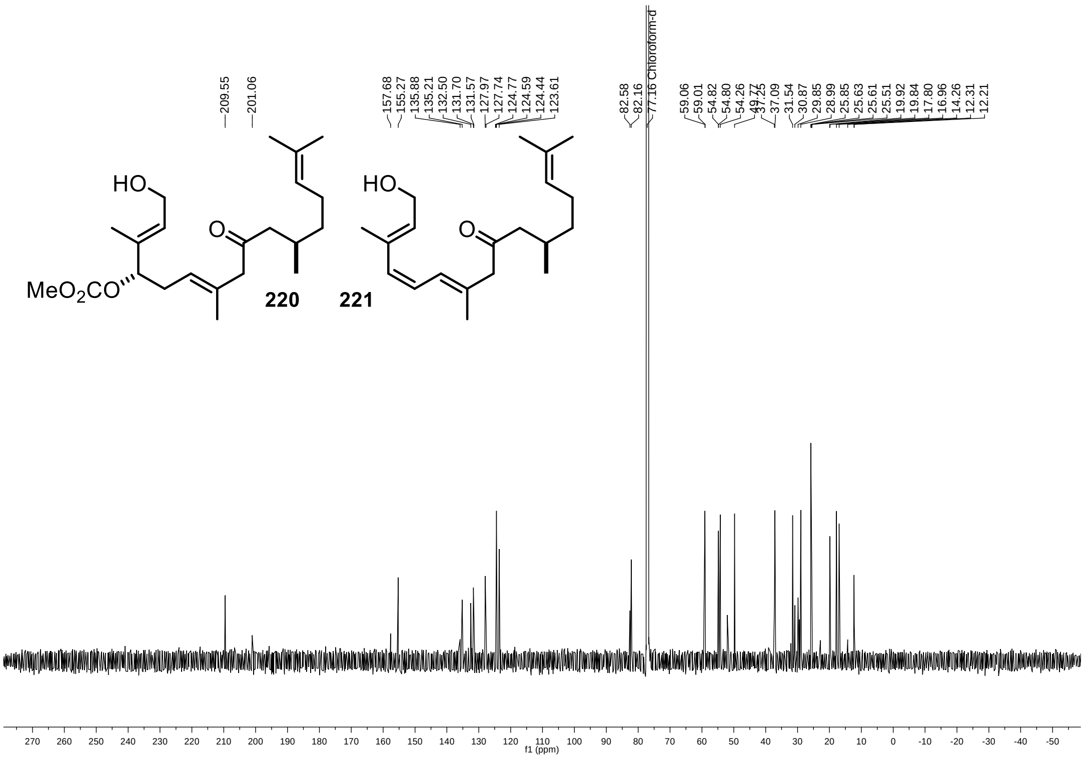

TBDPSO
TMSO
MeO$_2$CO
4.12
5.97
1.00
1.00
1.03
0.98
0.96
2.01
3.02
1.04
0.99
1.04
1.02
1.02
1.05
1.02
3.00
3.01
2.99
3.03
1.58
1.29
9.04
2.99
9.05
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

197

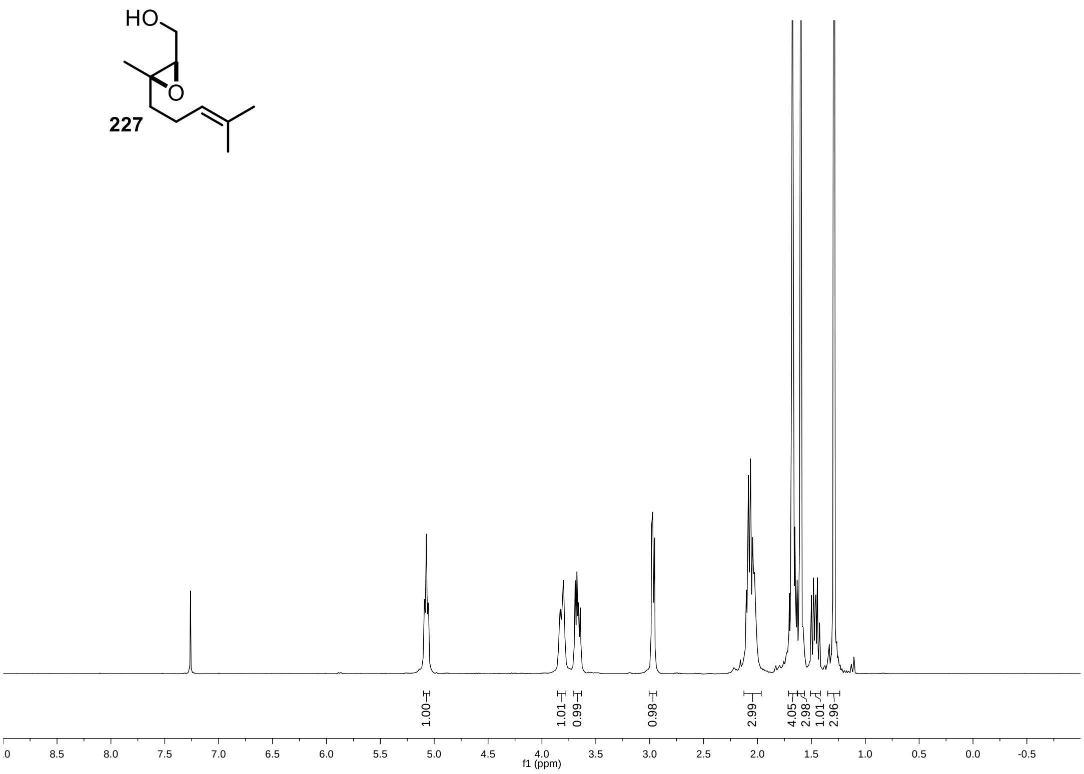

TBDPSO
TMSO
MeO$_2$CO
155.83
149.15
136.28
135.75
135.06
134.48
131.52
130.61
128.62
128.43
125.65
121.31
116.20
82.80
61.35
54.80
42.49
39.82
39.19
32.53
32.26
29.84 Acetone-d6
27.15
26.84
26.44
25.85
24.10
22.54
19.67
17.78
16.53
14.44
12.59
0.49
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

197

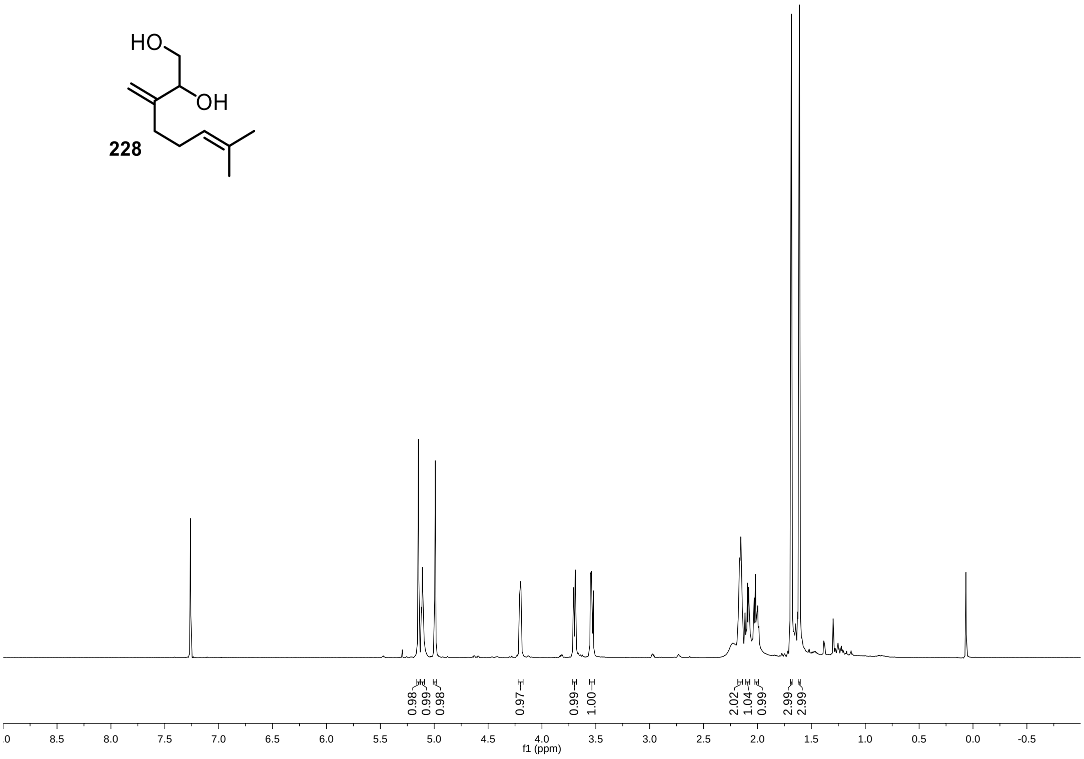

HO
MeO$_2$CO
O
220
221
HO
O
0.30
0.35
0.90
0.78
1.03
1.23
2.62
3.00
1.79
0.53
0.96
0.59
4.12
1.19
1.23
2.80
4.08
3.24
4.20
4.14
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

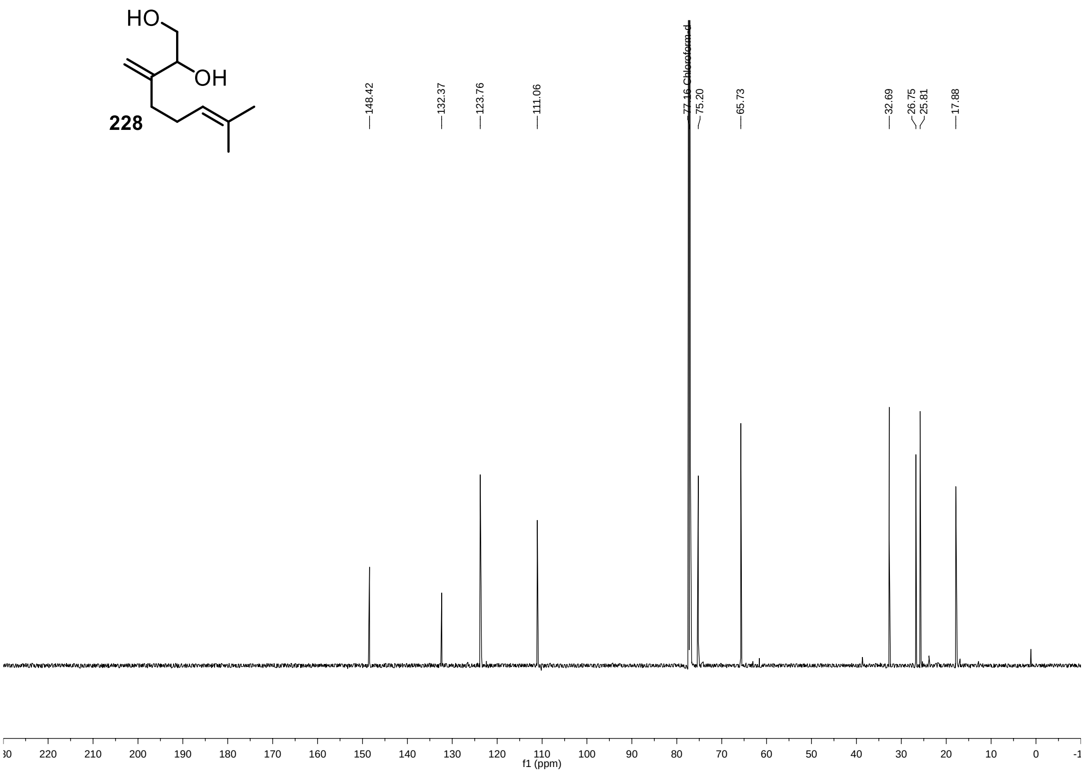

209.55
201.06
157.68
155.27
135.88
135.21
132.50
131.70
131.57
127.97
127.74
124.77
124.59
124.44
123.61
82.58
82.16
77.16 Chloroform-d
59.06
59.01
54.82
54.80
54.26
49.77
37.25
37.09
31.54
30.87
29.85
28.99
25.85
25.63
25.61
25.51
19.92
19.84
17.80
16.96
14.26
12.31
12.21
HO
MeO$_2$CO
O
220
221
HO
O
270
260
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
f1 (ppm)

227

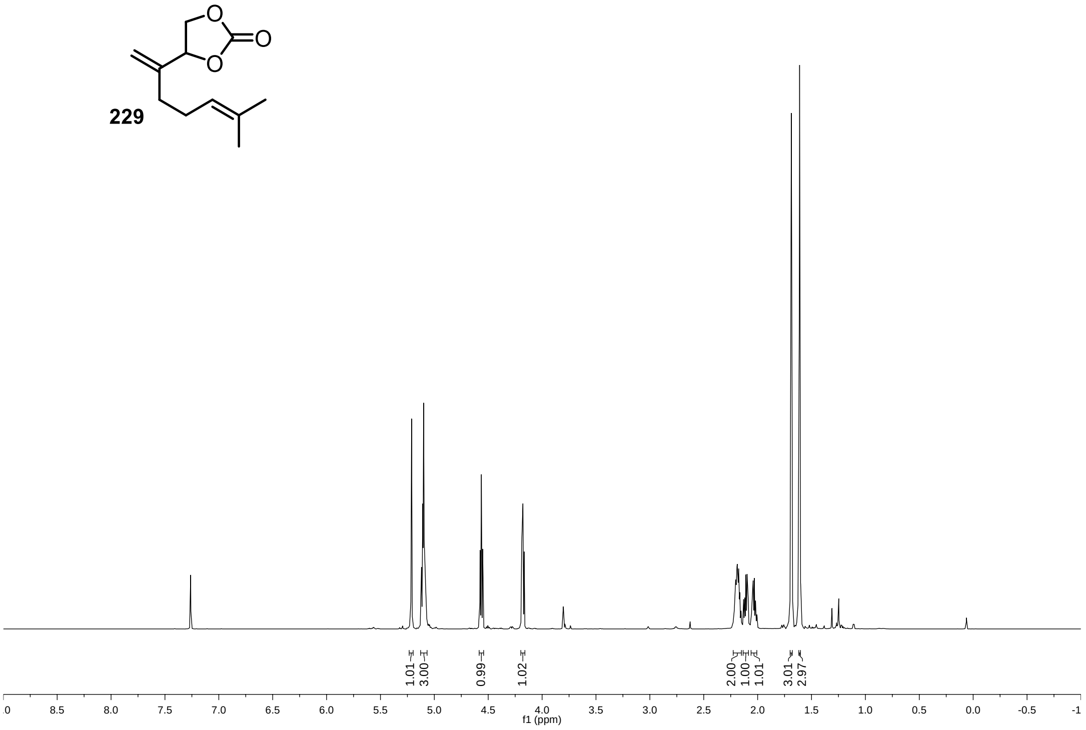

HO
O
1.00
1.01
0.99
0.98
2.99
4.05
2.98
1.01
2.96
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

228

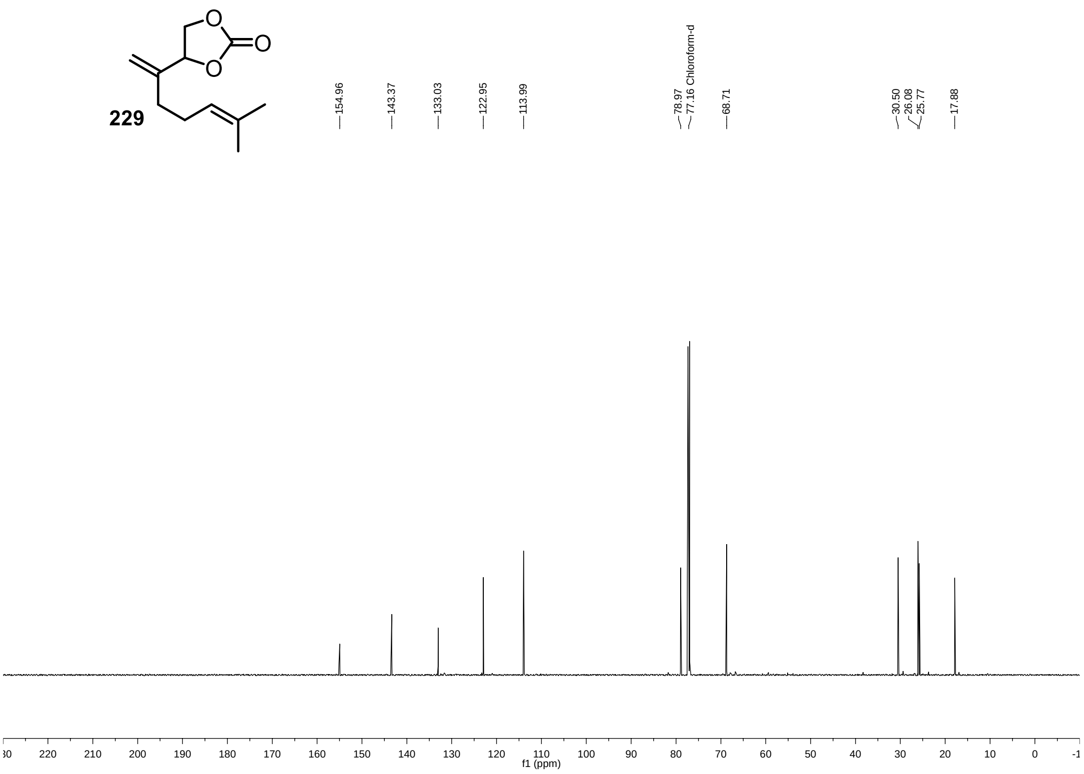

HO
OH
0.98
0.99
0.98
0.97
0.99
1.00
2.02
1.04
0.99
2.99
2.99
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


HO
OH
148.42
132.37
123.76
111.06
77.16 Chloroform-d
75.20
65.73
32.69
26.75
25.81
17.88
f1 (ppm)

228

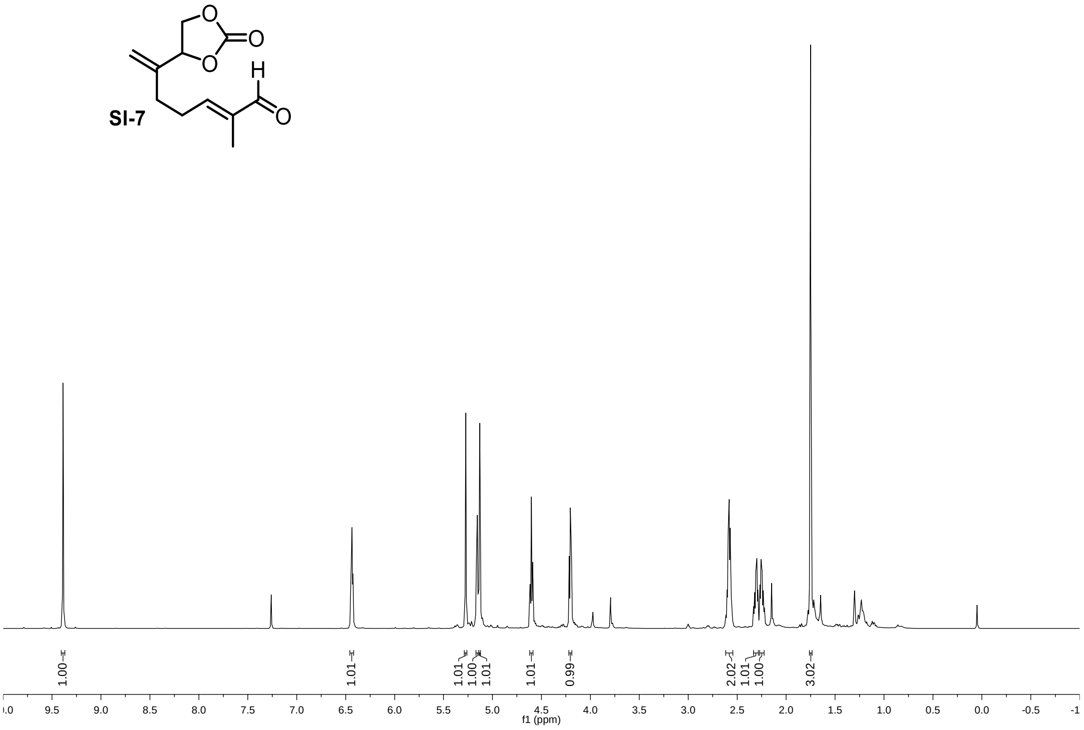

O
O
O
1.01
3.00
0.99
1.02
2.00
1.00
1.01
3.01
2.97
f1 (ppm)

229



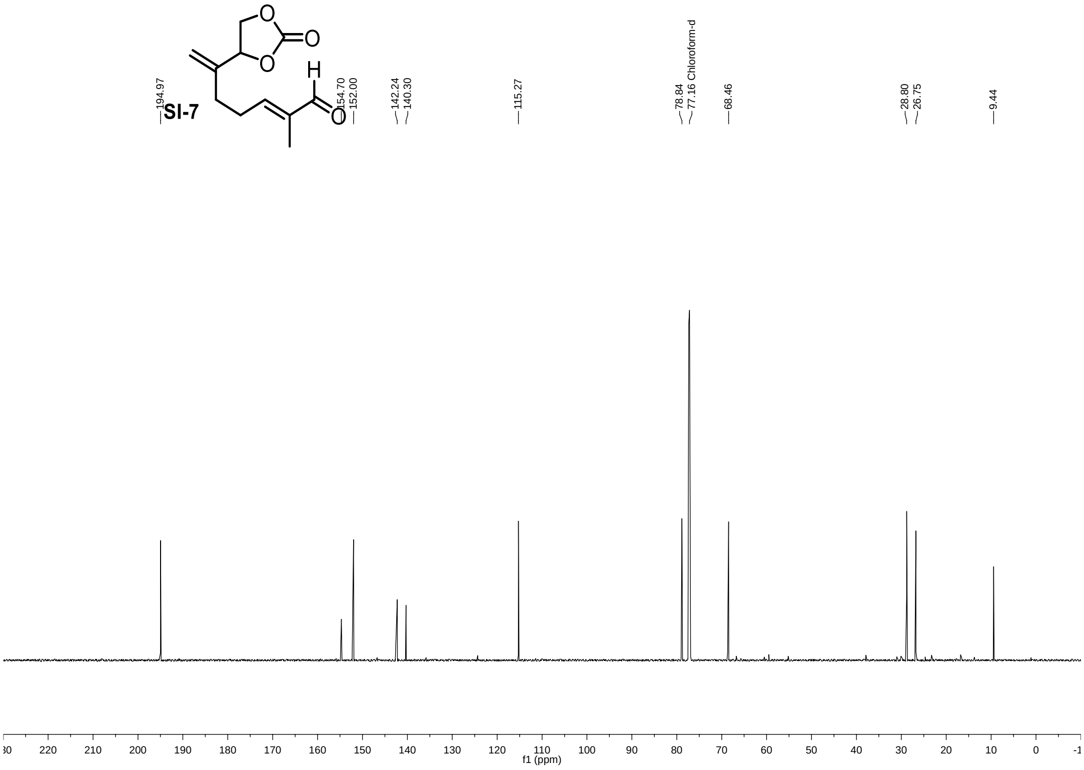
229

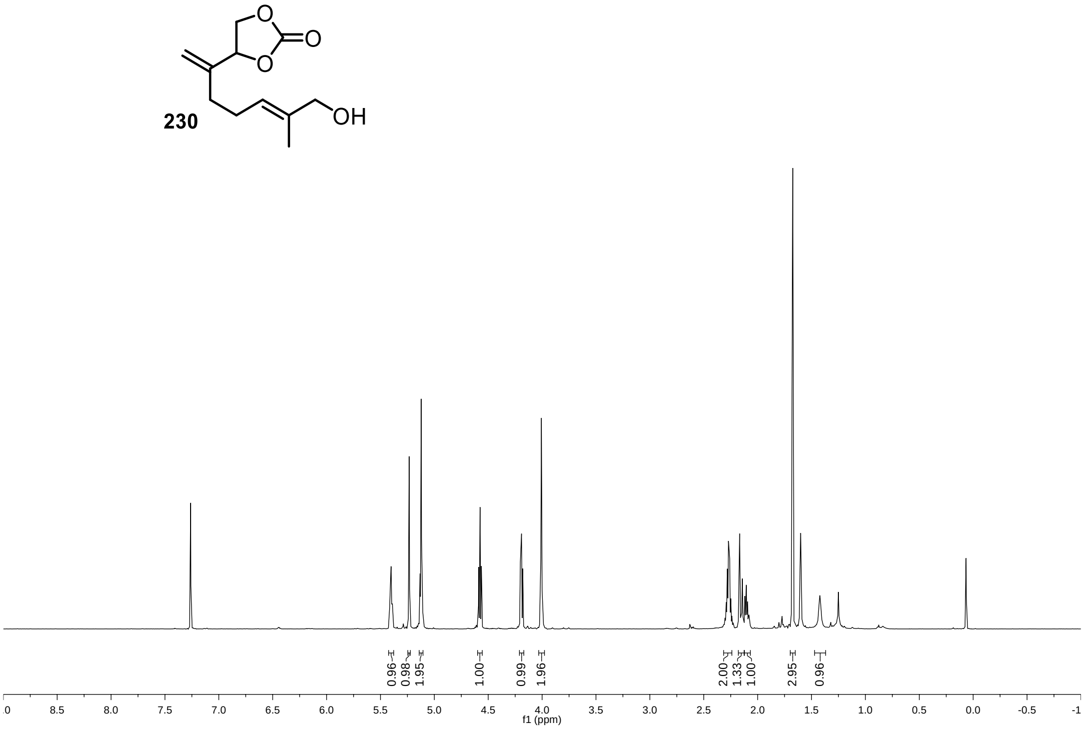
O
O
O
154.96
143.37
133.03
122.95
113.99
78.97
77.16 Chloroform-d
68.71
30.50
26.08
25.77
17.88
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

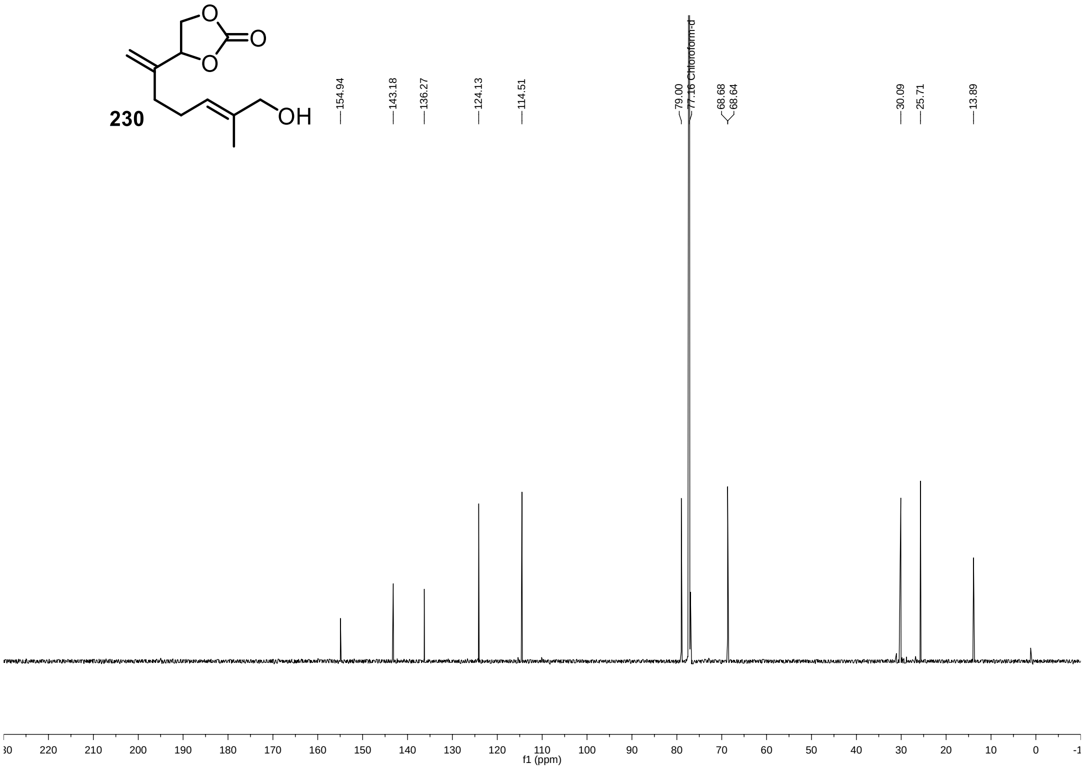


SI-7

O
O
O
H
O
1.00
1.01
1.01
1.00
1.01
1.01
0.99
2.02
1.01
1.00
3.02
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

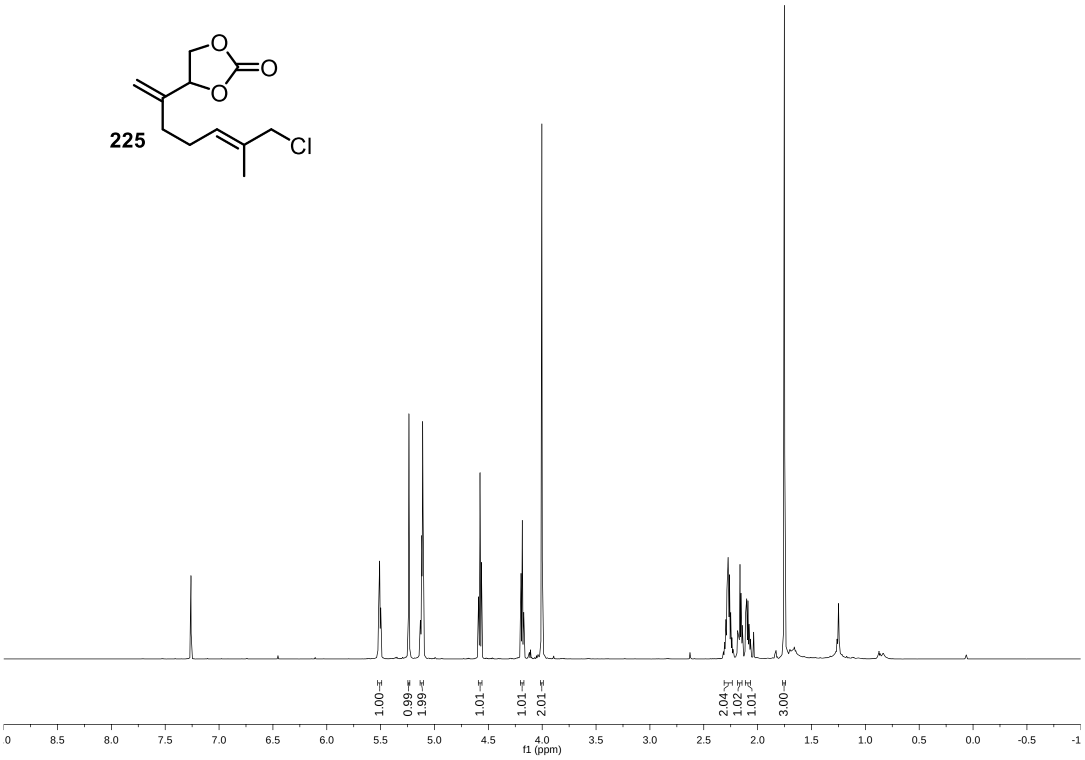

SI-7
H
O
O
O
O
194.97
154.70
152.00
142.24
140.30
115.27
78.84
77.16 Chloroform-d
68.46
28.80
26.75
9.44
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


230
O
O
O
OH
0.96
0.98
1.95
1.00
0.99
1.96
2.00
1.33
1.00
2.95
0.96
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



230

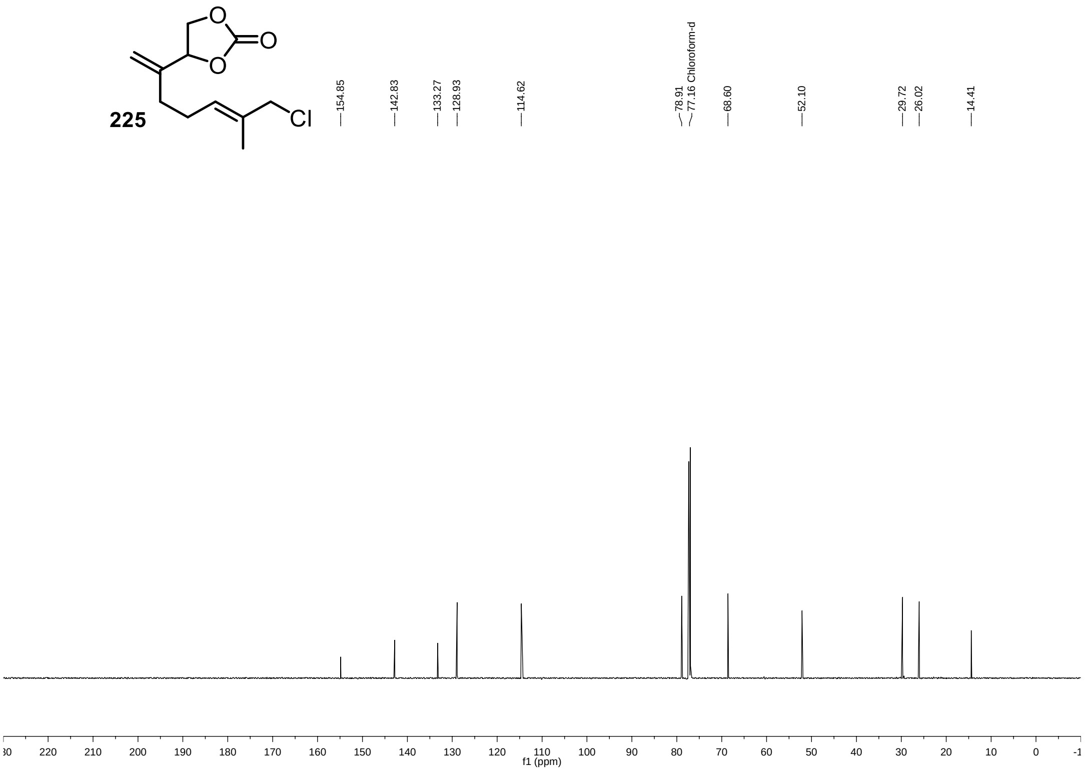
OH
154.94
143.18
136.27
124.13
114.51
79.00
77.16 Chloroform-d
68.68
68.64
30.09
25.71
13.89
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



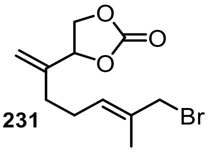
225

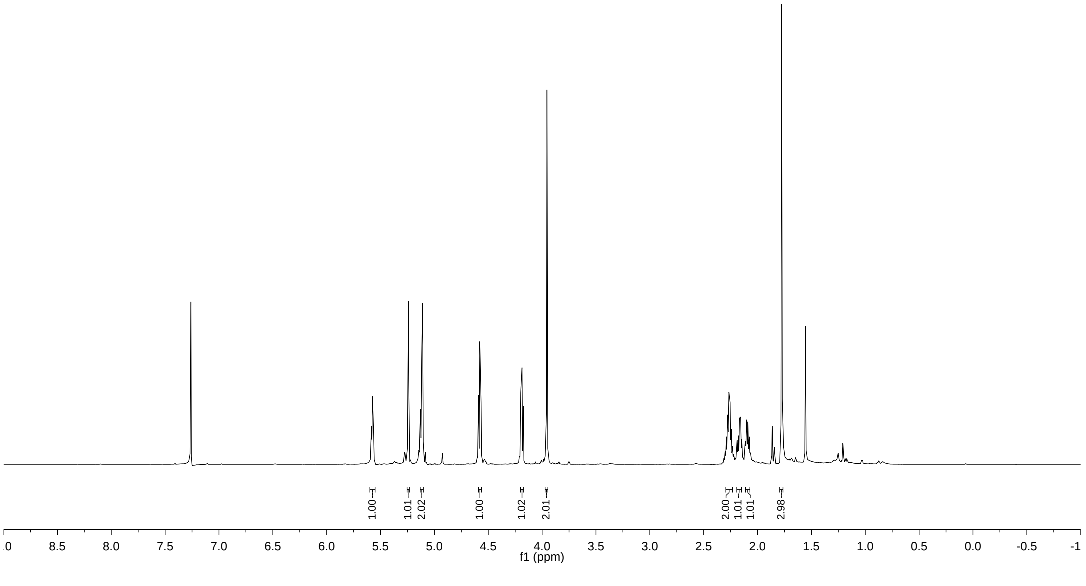
Cl
1.00
0.99
1.99
1.01
1.01
2.01
2.04
1.02
1.01
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

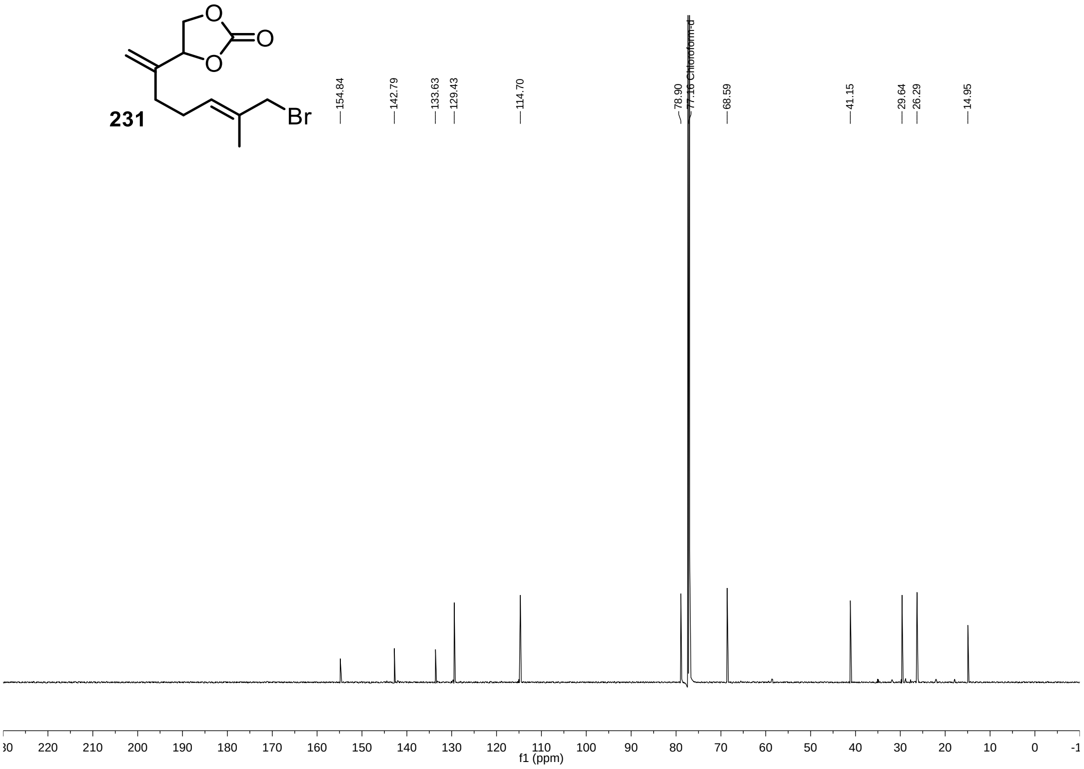
225


154.85
142.83
133.27
128.93
114.62
78.91
77.16 Chloroform-d
68.60
52.10
29.72
26.02
14.41
O
O
O
Cl
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

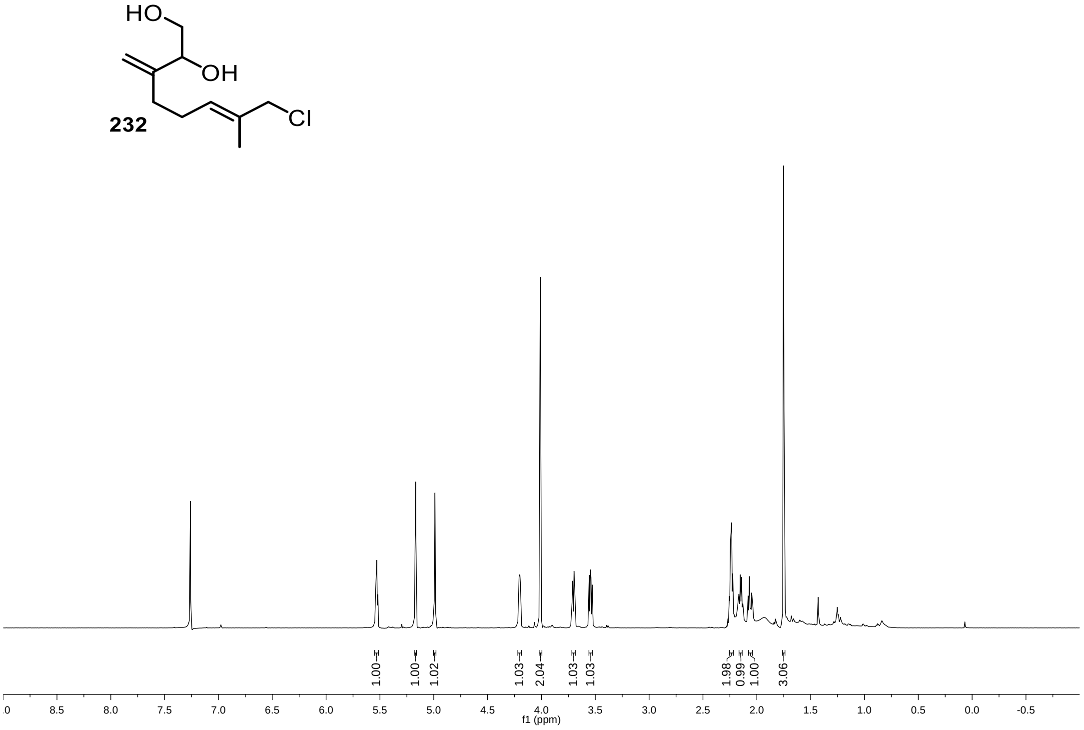
231


O
O
O
Br

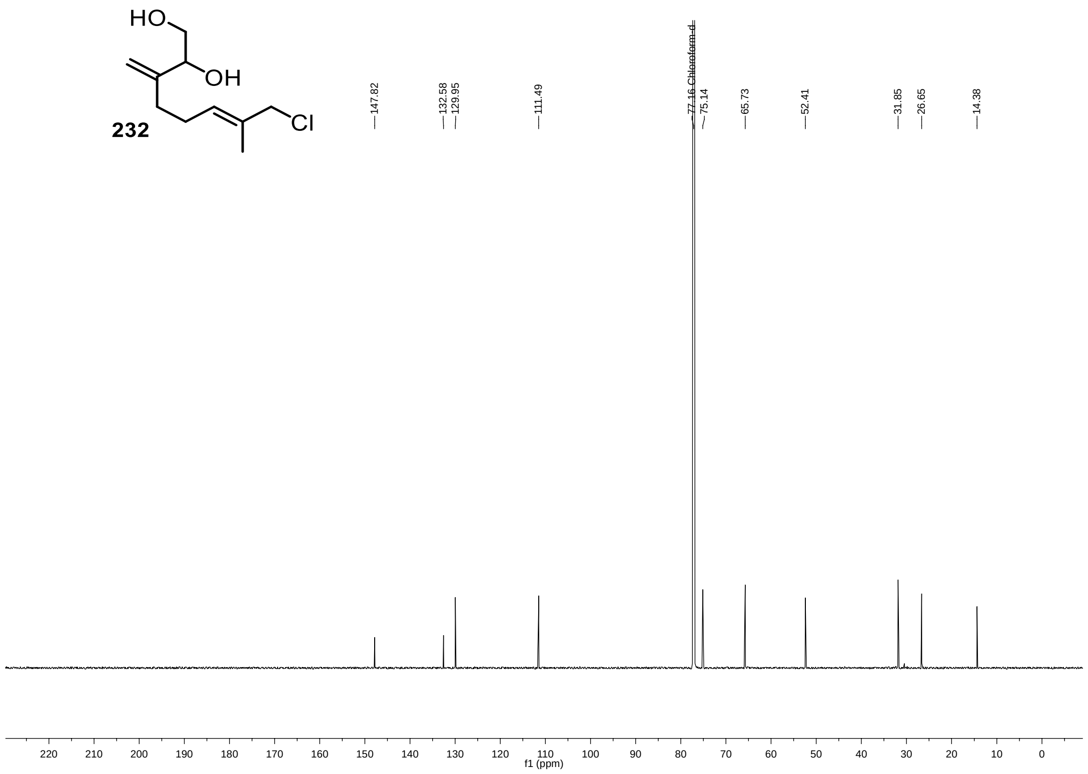

1.00
1.01
2.02
1.00
1.02
2.01
2.00
1.01
1.01
2.98
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

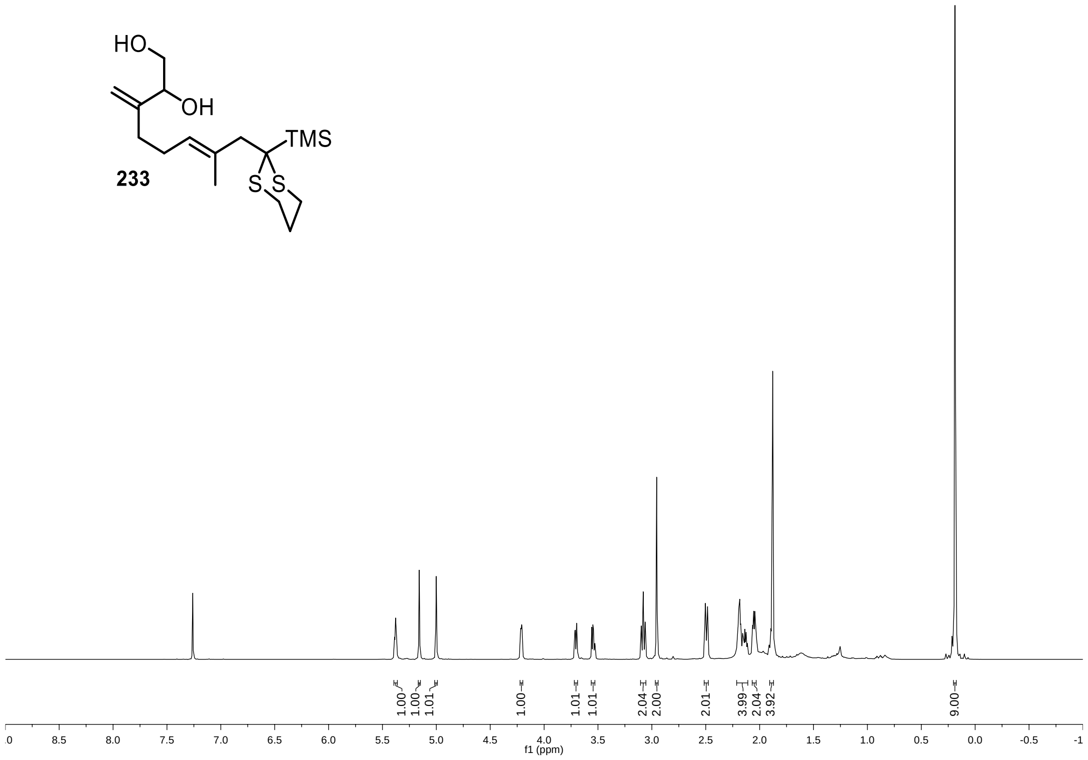

O
O
O
Br
154.84
142.79
133.63
129.43
114.70
78.90
77.16 Chloroform-d
68.59
41.15
29.64
26.29
14.95
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

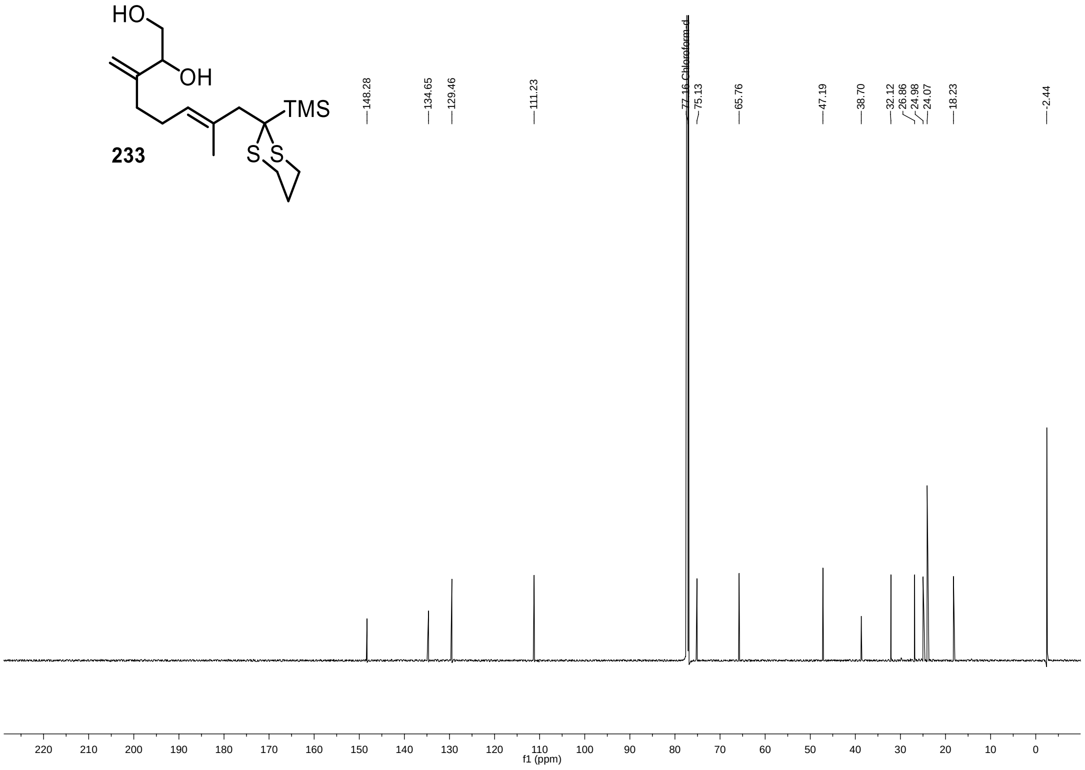
231


HO
OH
Cl
1.00
1.00
1.02
1.03
2.04
1.03
1.03
1.98
0.99
1.00
3.06
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

232

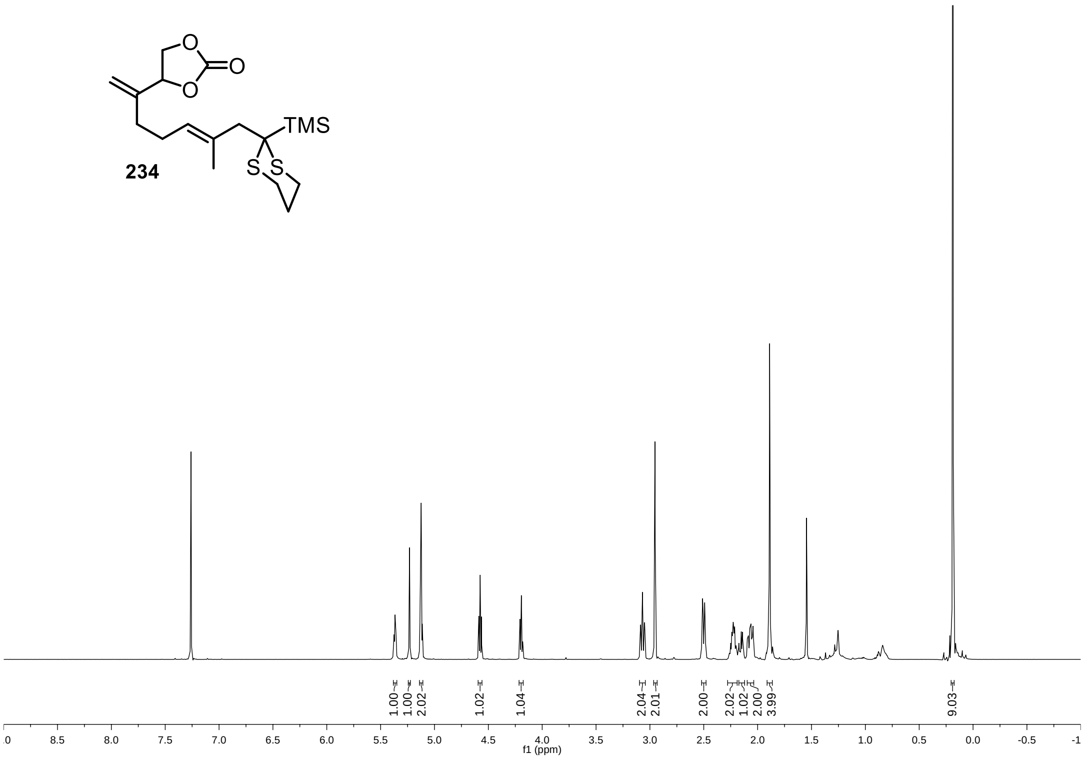

HO
OH
Cl
232
147.82
132.58
129.95
111.49
77.16 Chloroform-d
75.14
65.73
52.41
31.85
26.65
14.38
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HO
OH
TMS
S
S
233
1.00
1.00
1.01
1.00
1.01
1.01
2.04
2.00
2.01
3.99
2.04
3.92
9.00
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



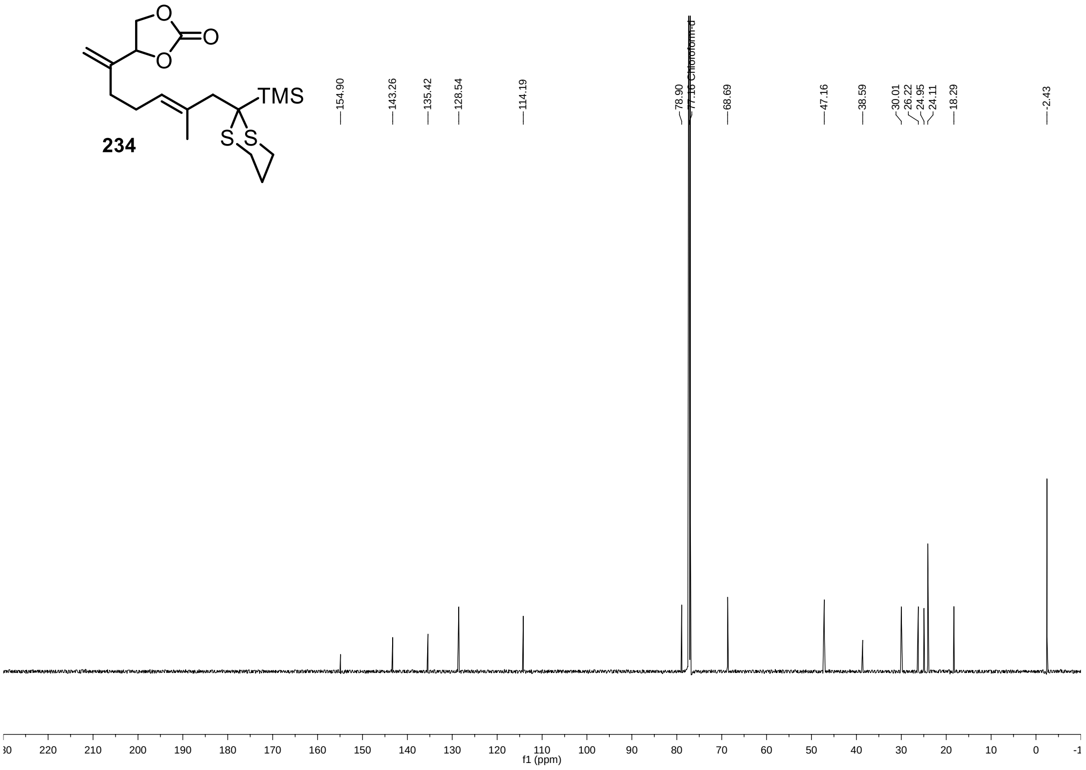
233

HO
OH
TMS
S
S
148.28
134.65
129.46
111.23
77.16 Chloroform-d
75.13
65.76
47.19
38.70
32.12
26.86
24.98
24.07
18.23
-2.44
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



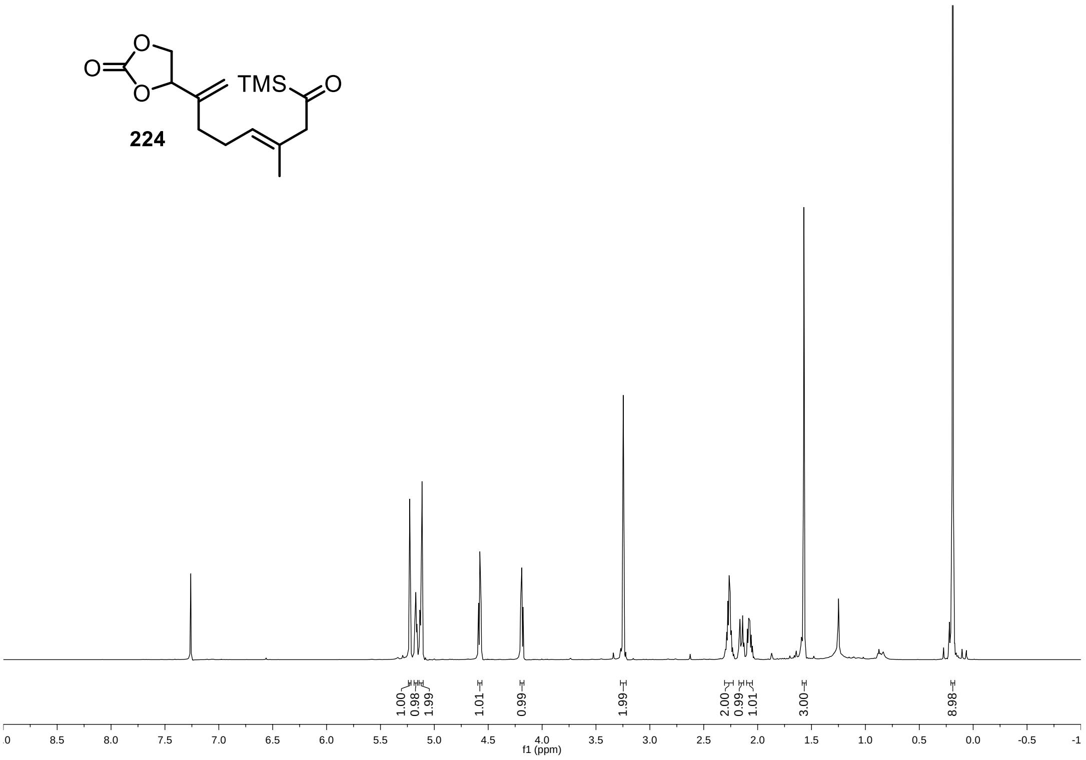
234

O
O
O
TMS
S
S
1.00
1.00
2.02
1.02
1.04
2.04
2.01
2.00
2.02
1.02
2.00
3.99
9.03
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



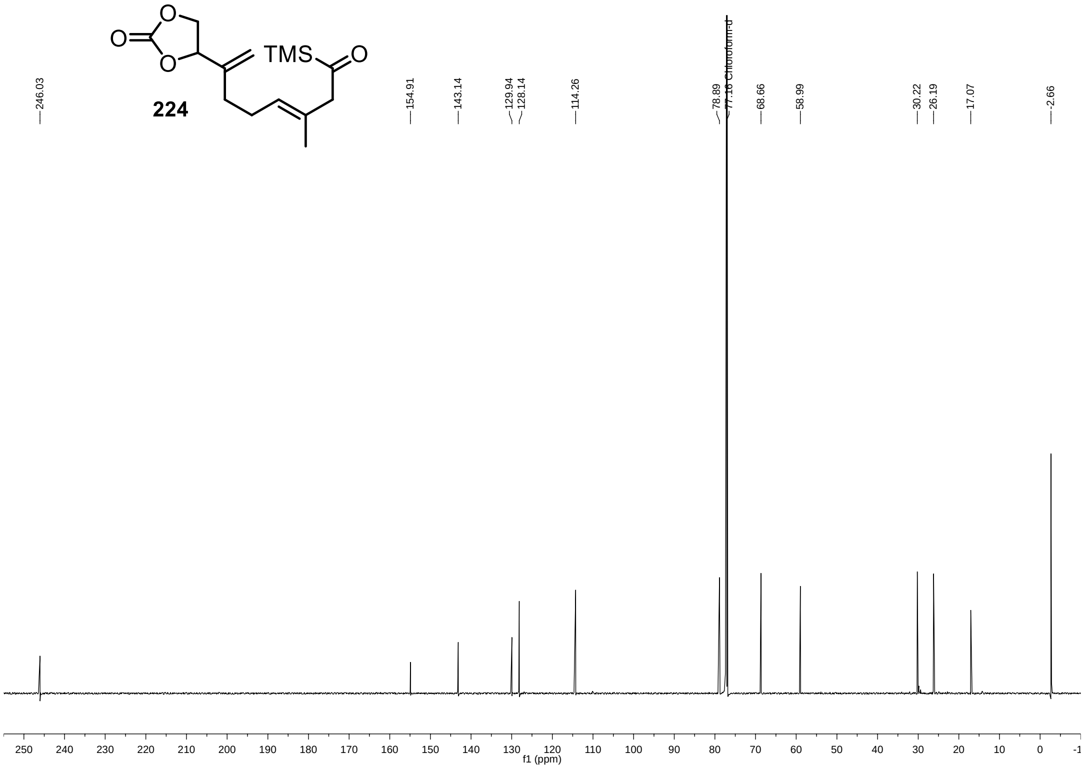
234

O
O
O
TMS
S
S
154.90
143.26
135.42
128.54
114.19
78.90
77.16 Chloroform-d
68.69
47.16
38.59
30.01
26.22
24.95
24.11
18.29
-2.43
f1 (ppm)

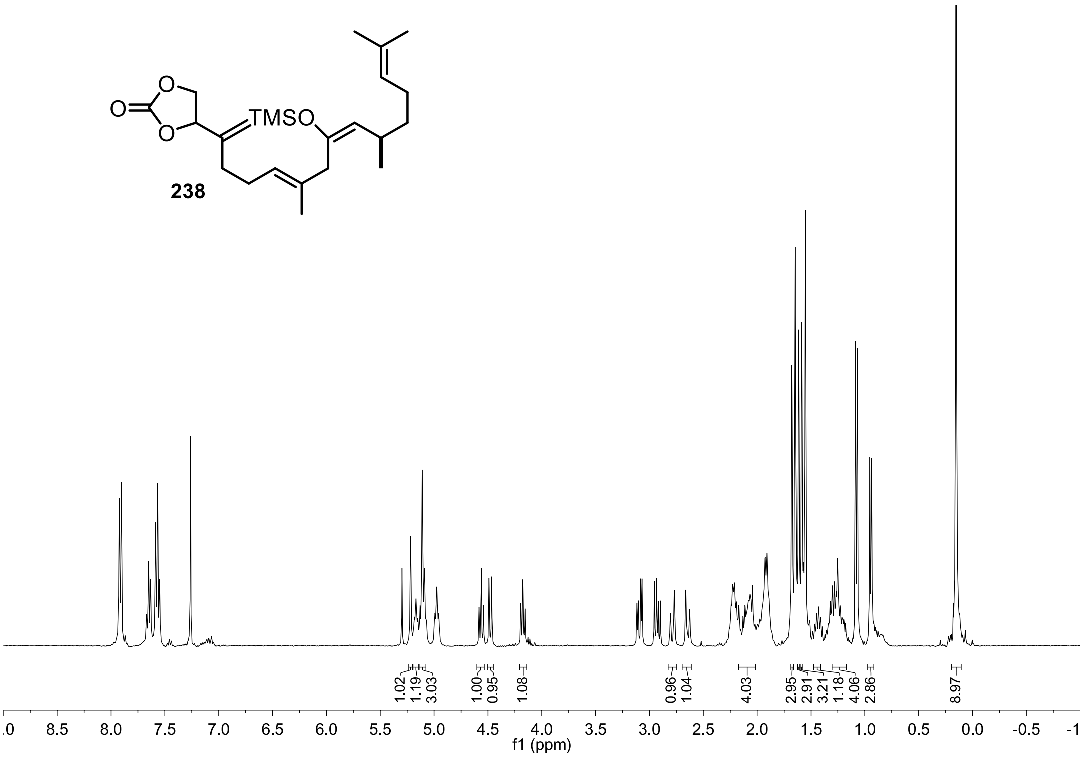


224

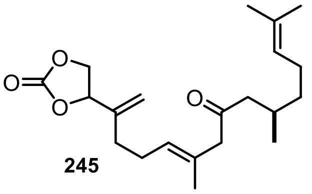
O
O
O
TMS
O
1.00
0.98
1.99
1.01
0.99
1.99
2.00
0.99
1.01
3.00
8.98
f1 (ppm)


O
O
O
TMS
O
—246.03
—154.91
—143.14
129.94
128.14
—114.26
78.89
77.16 Chloroform-d
—68.66
—58.99
—30.22
—26.19
—17.07
—-2.66
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

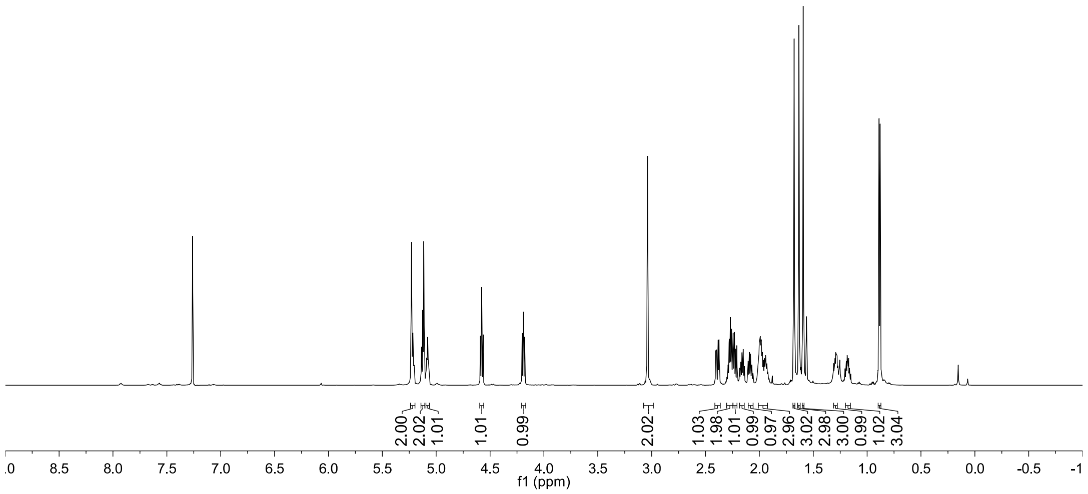
224


O
O
O
TMS
O
1.02
1.19
3.03
1.00
0.95
1.08
0.96
1.04
4.03
2.95
2.91
3.21
1.18
4.06
2.86
8.97
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

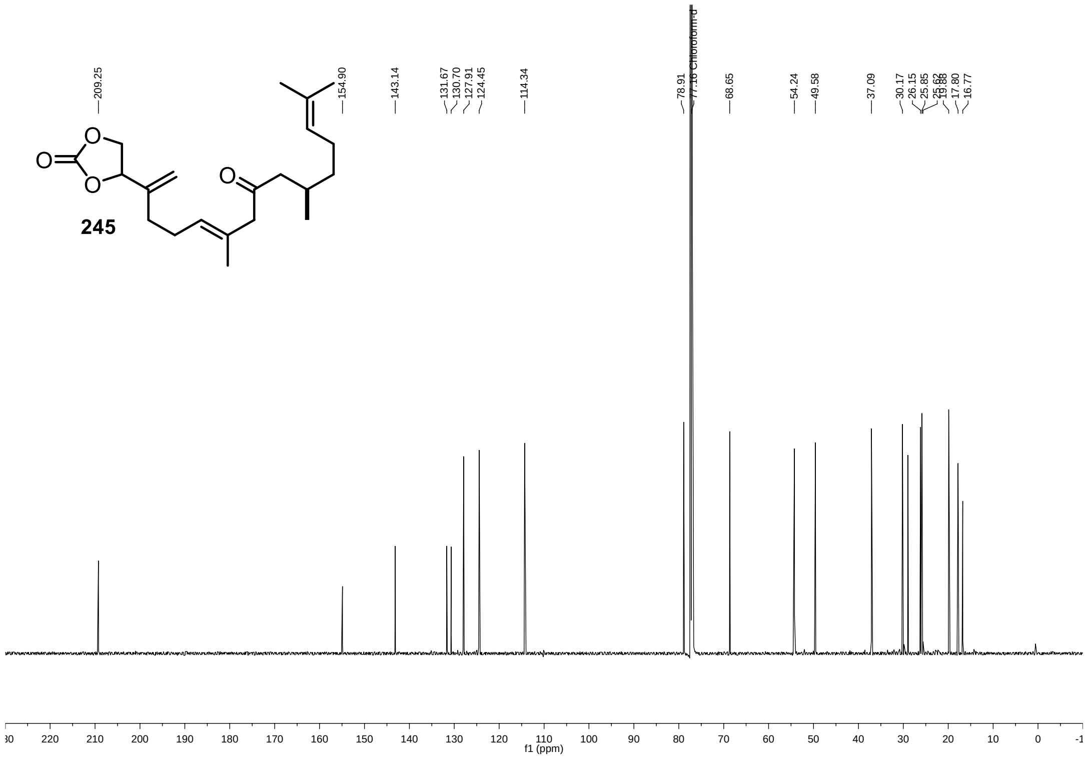
238



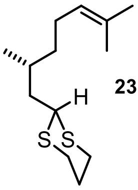
245



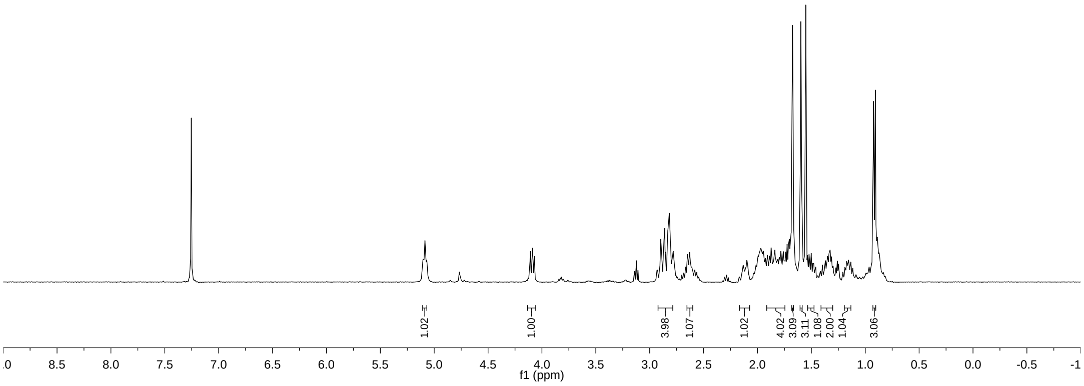
2.00
2.02
1.01
1.01
0.99
2.02
1.03
1.98
1.01
0.99
0.97
2.96
3.02
2.98
3.00
0.99
1.02
3.04
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

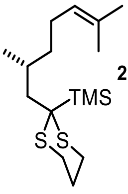


245
209.25
154.90
143.14
131.67
130.70
127.91
124.45
114.34
78.91
77.16 Chloroform-d
68.65
54.24
49.58
37.09
30.17
26.15
25.85
25.62
19.88
17.80
16.77
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

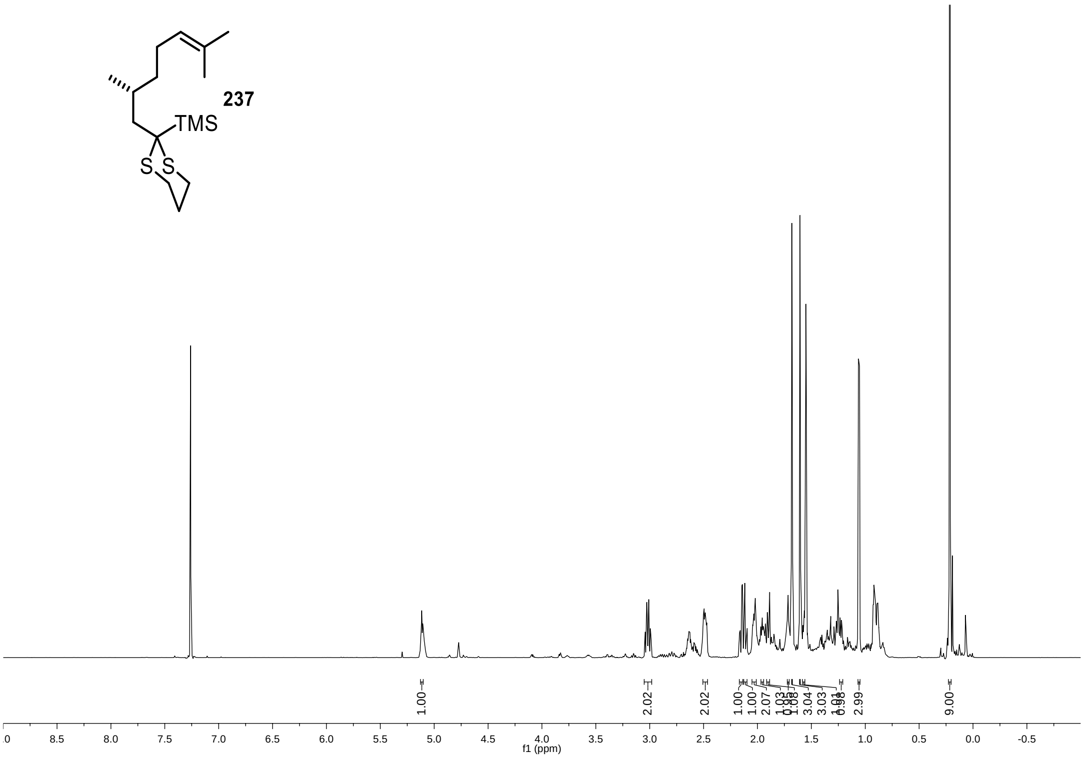

H
S
S

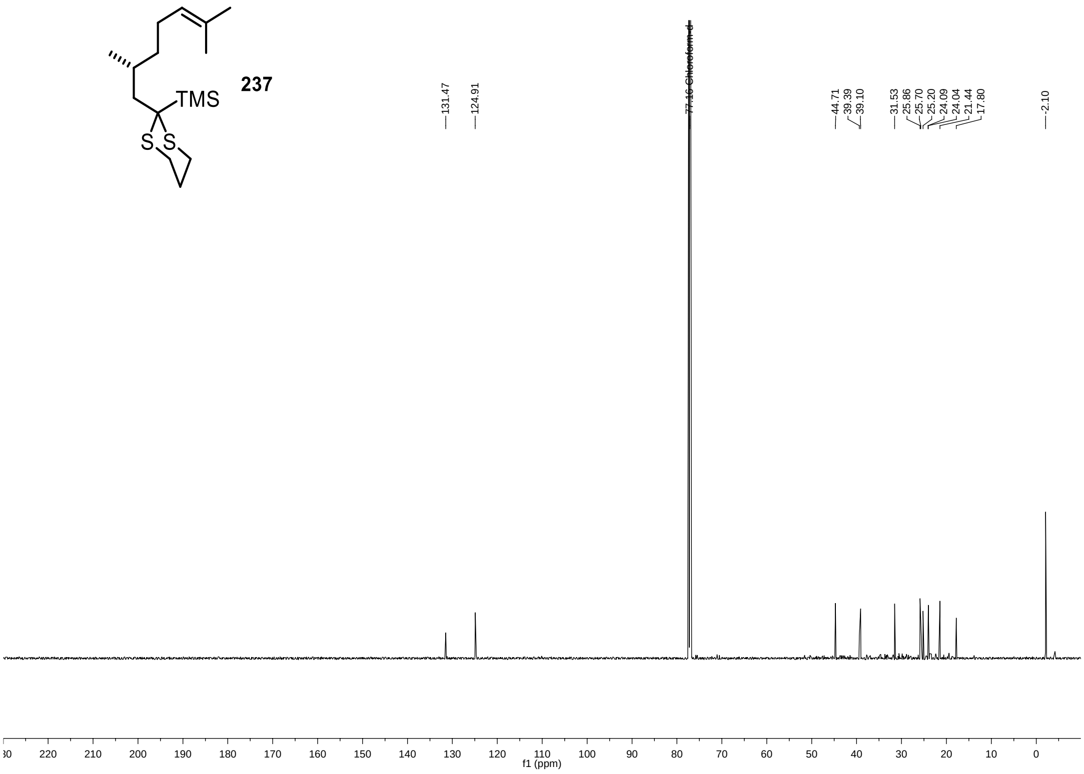
236


1.02
1.00
3.98
1.07
1.02
4.02
3.09
3.11
1.08
2.00
1.04
3.06
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


TMS
S
S

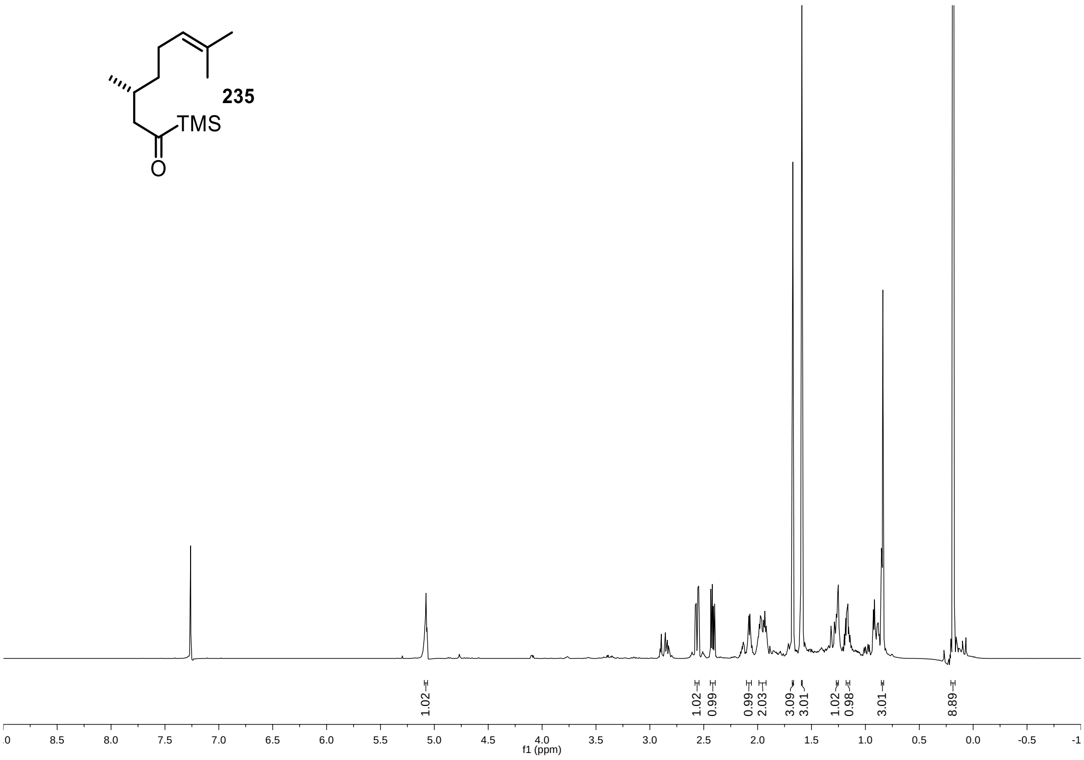
237


1.00
2.02
2.02
1.00
1.00
2.07
1.03
0.95
1.08
3.04
3.03
1.01
0.98
2.99
9.00
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



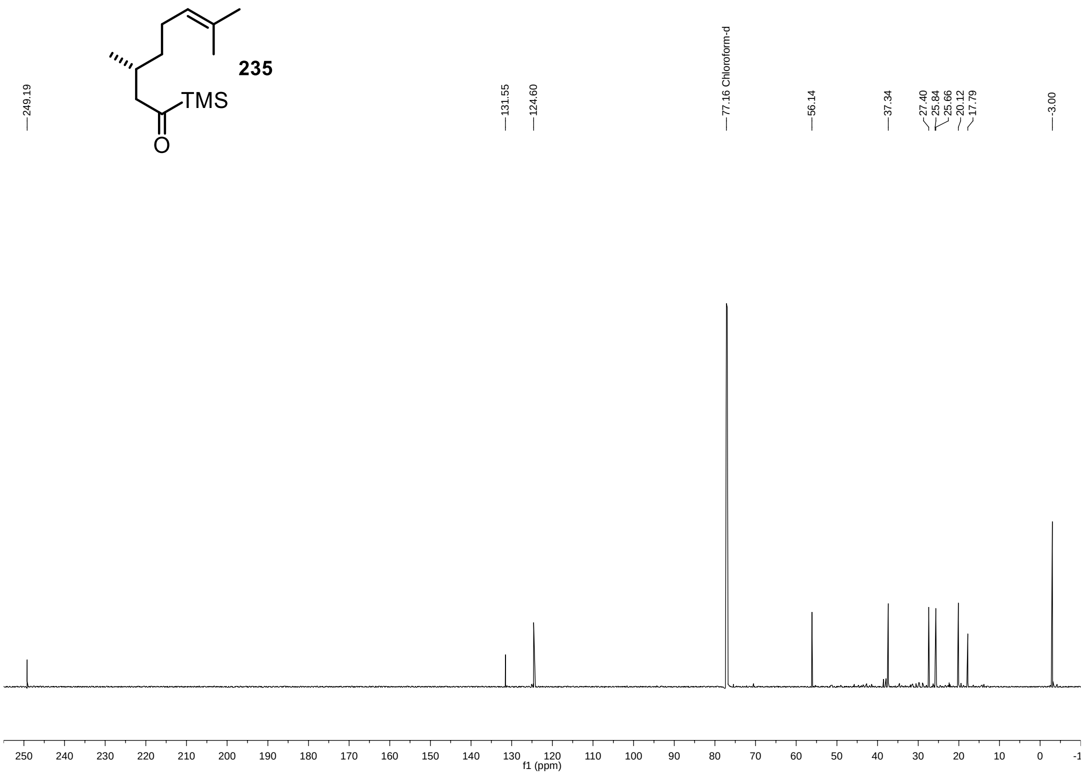
237

TMS
S
S
131.47
124.91
77.16 Chloroform-d
44.71
39.39
39.10
31.53
25.86
25.70
25.20
24.09
24.04
21.44
17.80
-2.10
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0



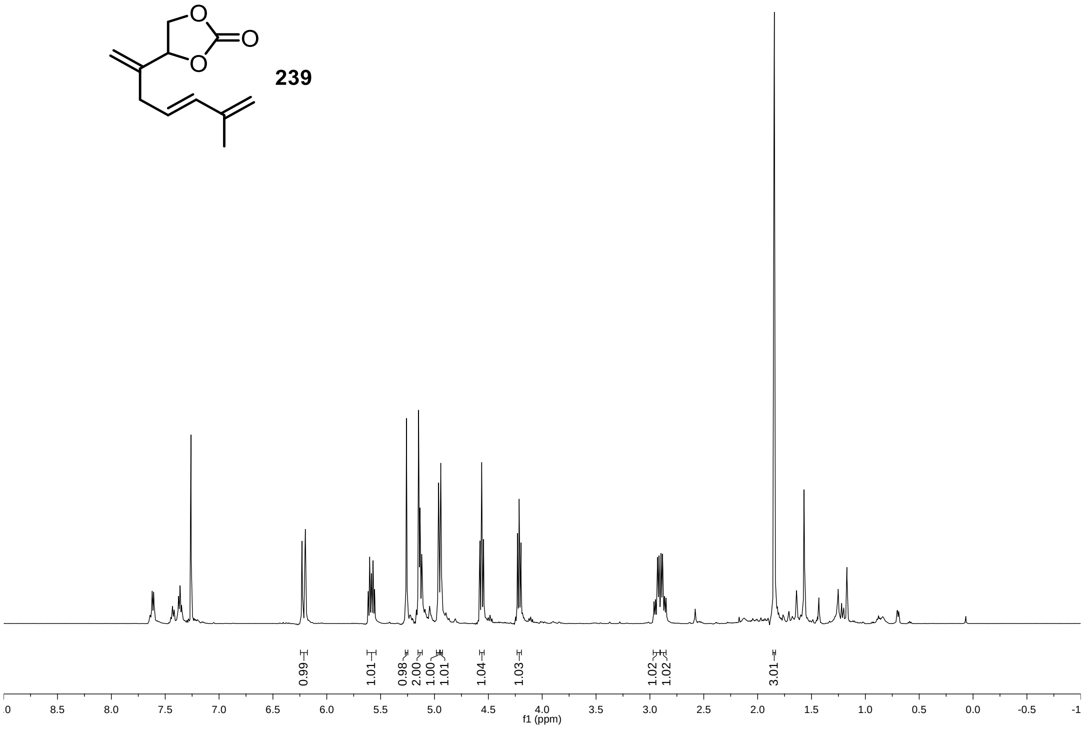
235

TMS
O
1.02
1.02
0.99
0.99
2.03
3.09
3.01
1.02
0.98
3.01
8.89
f1 (ppm)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1



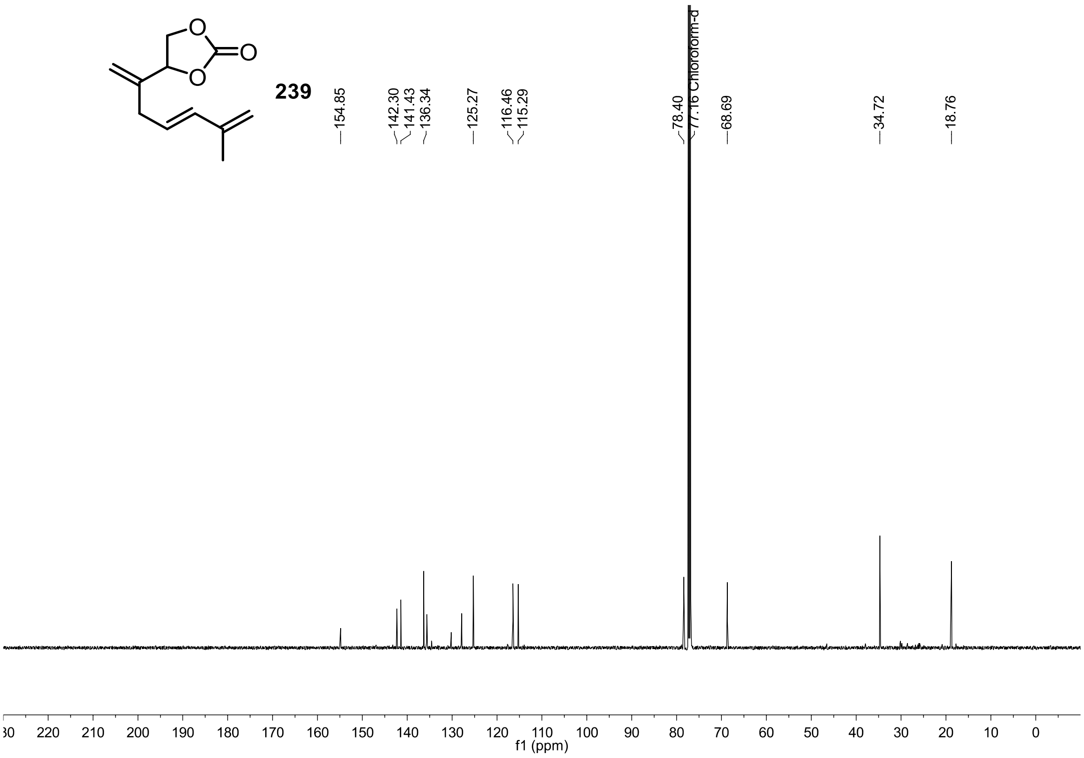
235

TMS
O
249.19
131.55
124.60
77.16 Chloroform-d
56.14
37.34
27.40
25.84
25.66
20.12
17.79
-3.00
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)



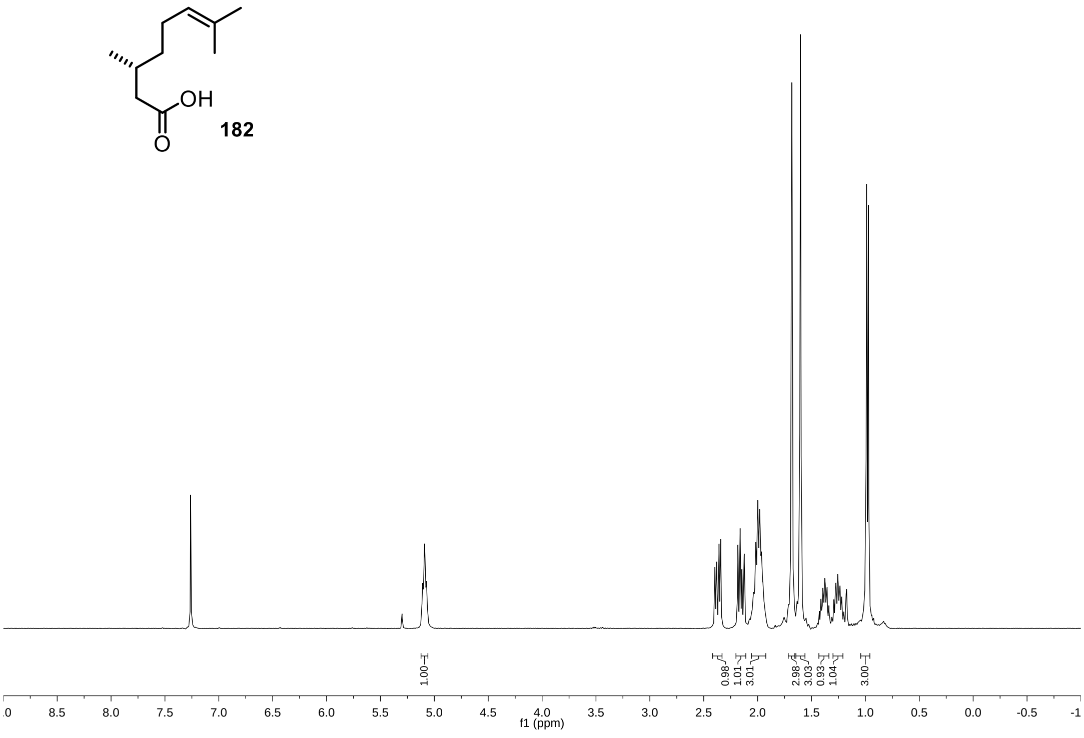
239

O
O
O
0.99
1.01
0.98
2.00
1.00
1.01
1.04
1.03
1.02
1.02
3.01
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



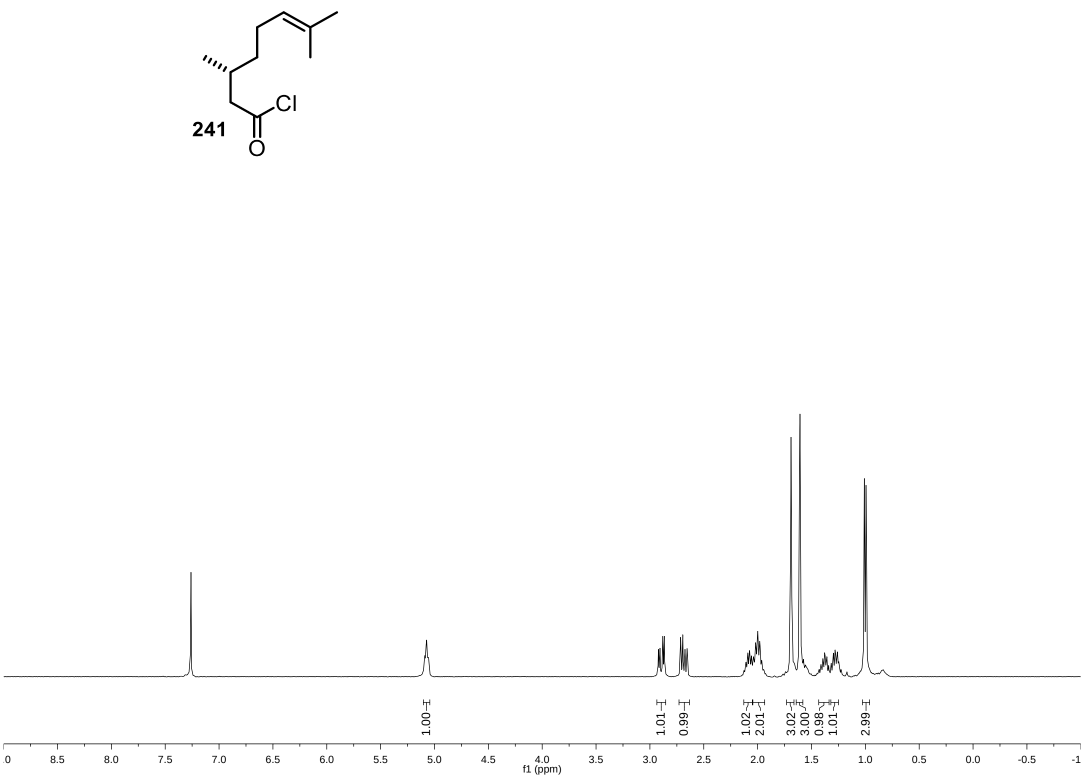
239

154.85
142.30
141.43
136.34
125.27
116.46
115.29
78.40
77.16 Chloroform-d
68.69
34.72
18.76
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



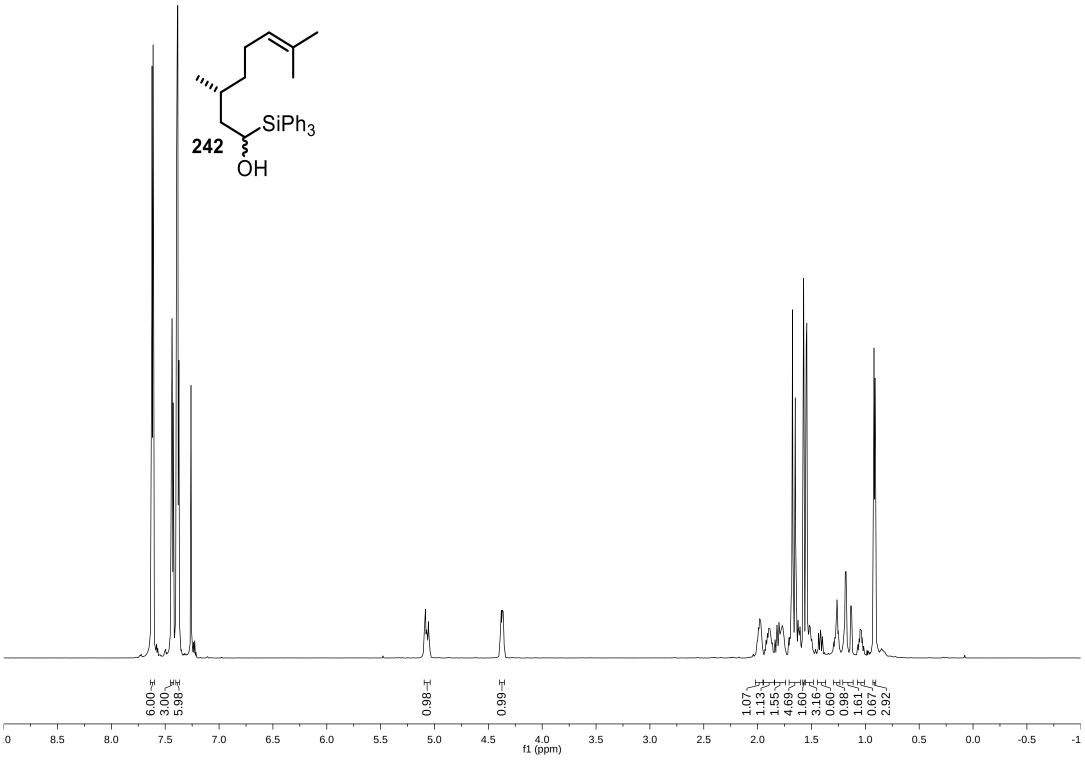
182

OH
O
1.00
0.98
1.01
3.01
2.98
3.03
0.93
1.04
3.00
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)



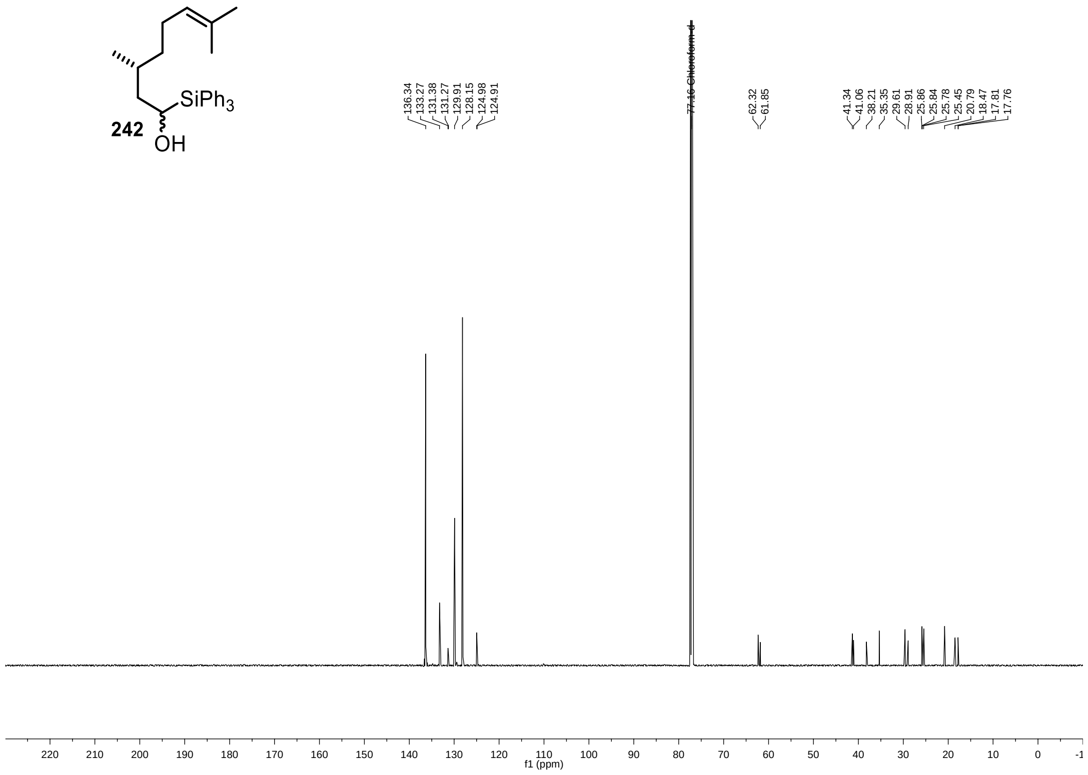
241

Cl
O
1.00
1.01
0.99
1.02
2.01
3.02
3.00
0.98
1.01
2.99
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1



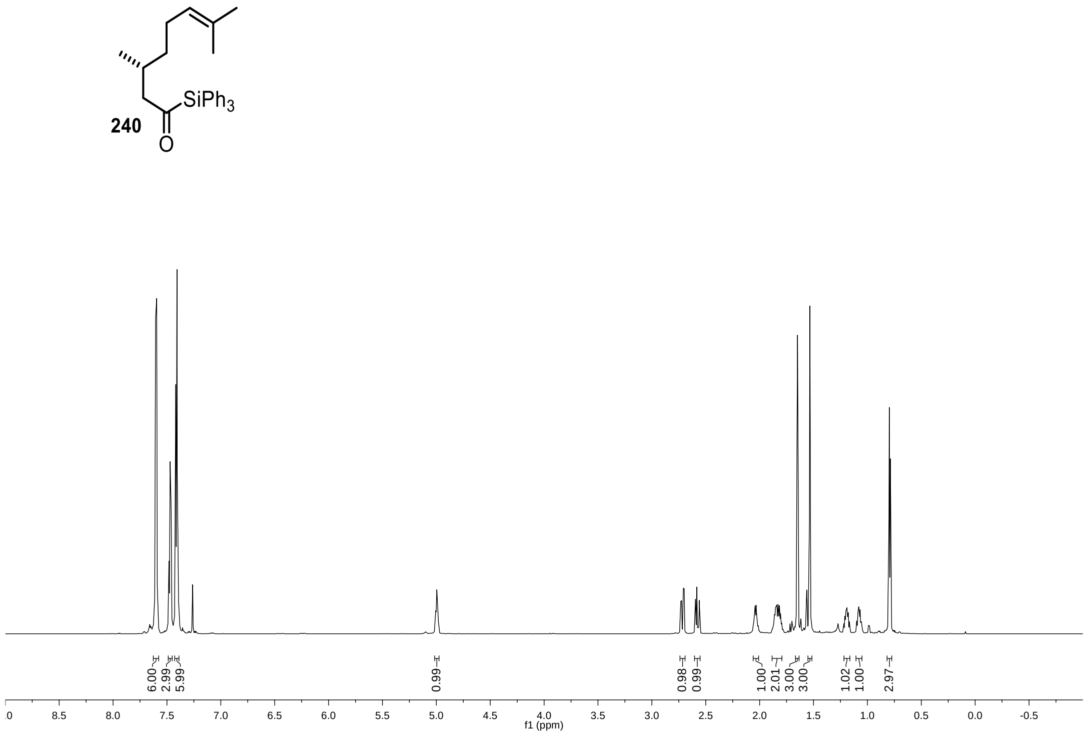
242

SiPh3
OH
6.00
3.00
5.98
0.98
0.99
1.07
1.13
1.55
4.69
1.60
3.16
0.60
0.98
1.61
0.67
2.92
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
f1 (ppm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1



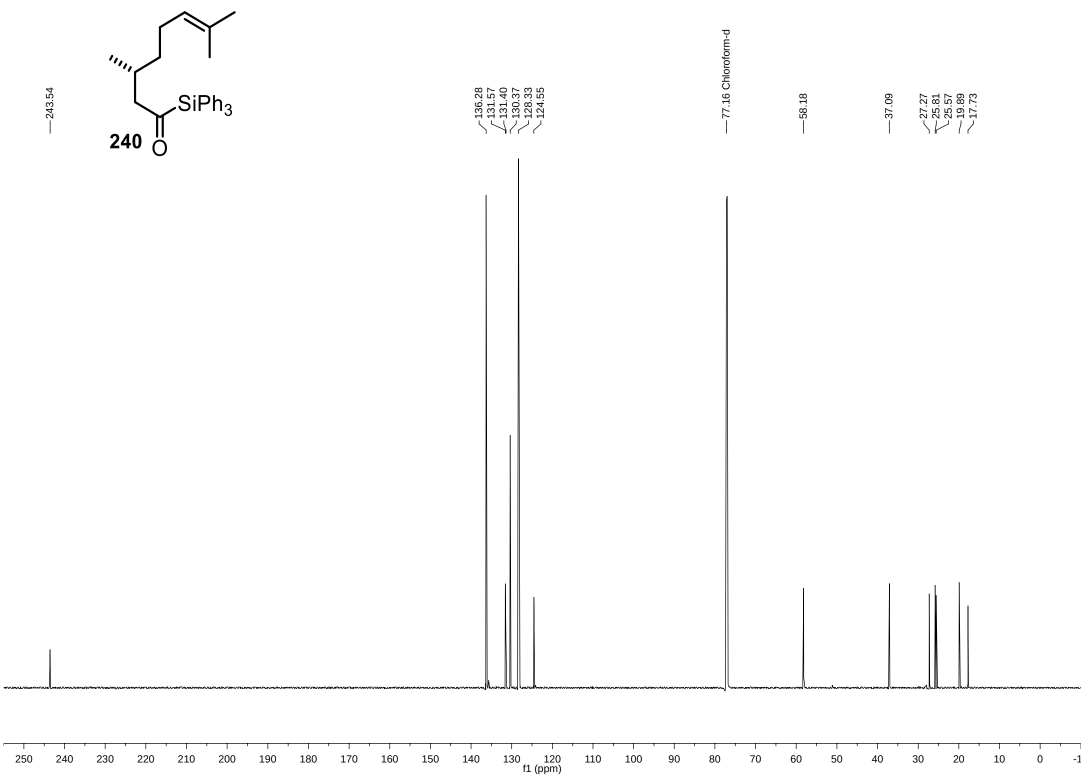
242

SiPh3
OH
136.34
133.27
131.38
131.27
129.91
128.15
124.98
124.91
77.16 Chloroform-d
62.32
61.85
41.34
41.06
38.21
35.35
29.61
28.91
25.86
25.84
25.78
25.45
20.79
18.47
17.81
17.76
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



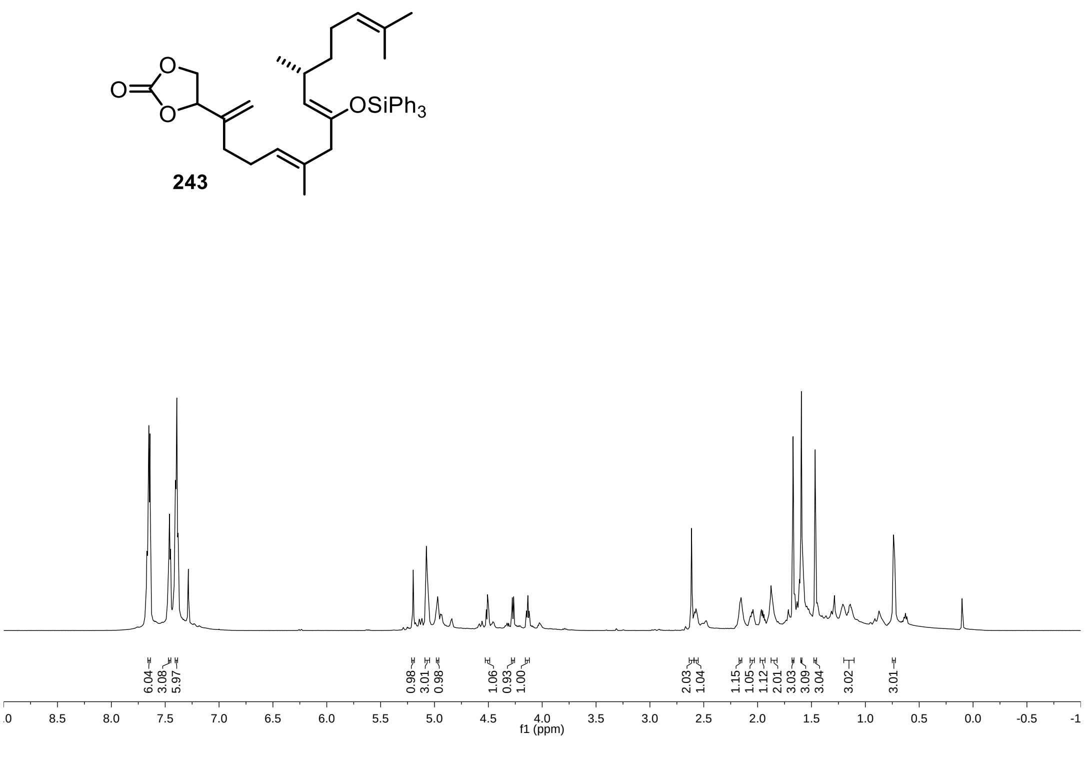
240

SiPh3
O
6.00
2.99
5.99
0.99
0.98
0.99
1.00
2.01
3.00
3.00
1.02
1.00
2.97
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



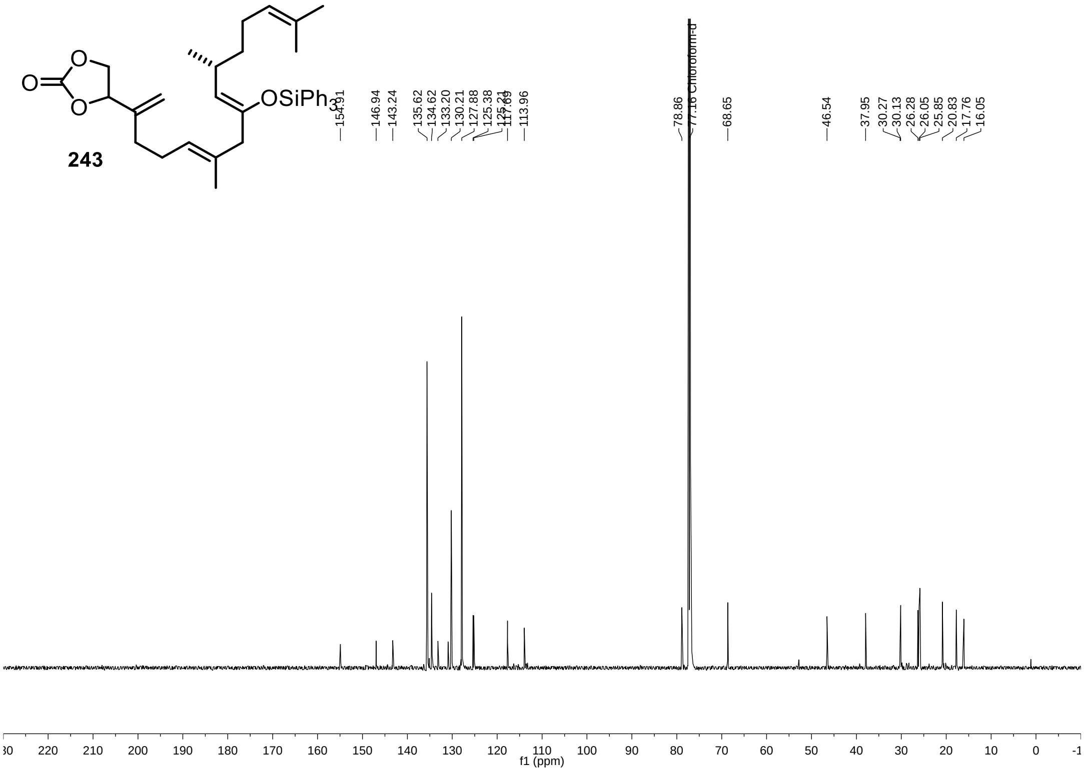
240

SiPh3
O
243.54
136.28
131.57
131.40
130.37
128.33
124.55
77.16 Chloroform-d
58.18
37.09
27.27
25.81
25.57
19.89
17.73
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

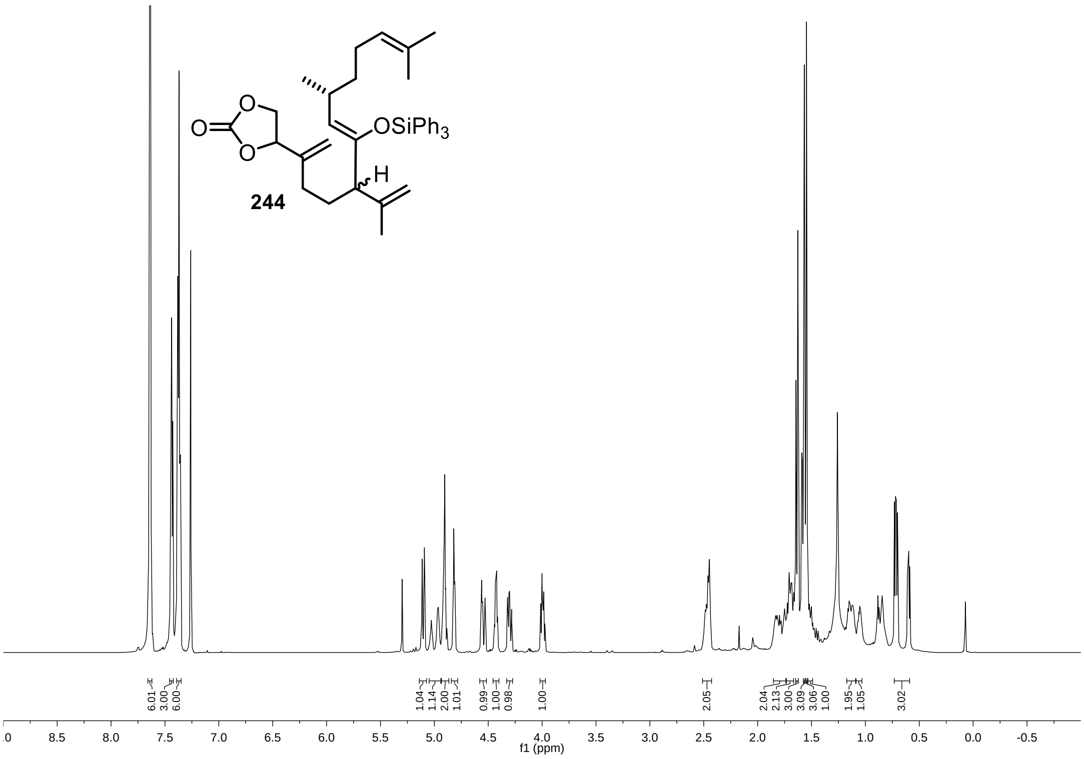


243

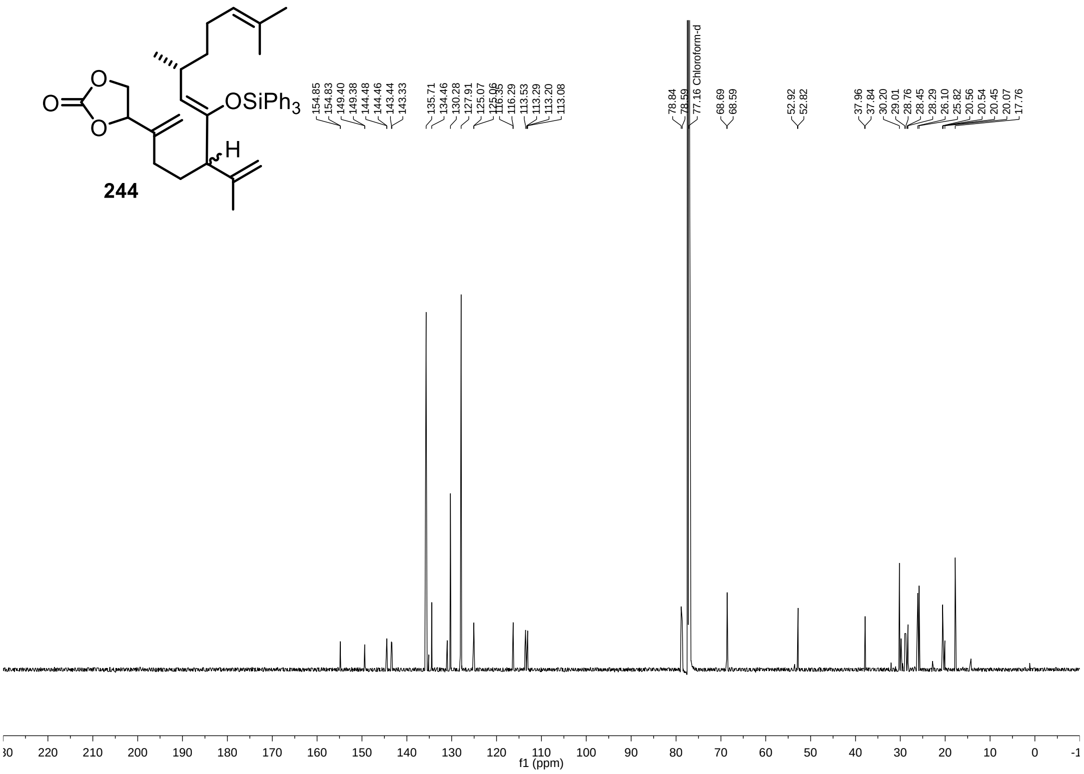
O
O
O
OSiPh3
6.04
3.08
5.97
0.98
3.01
0.98
1.06
0.93
1.00
2.03
1.04
1.15
1.05
1.12
2.01
3.03
3.09
3.04
3.02
3.01
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


O
O
O
OSiPh3
154.91
146.94
143.24
135.62
134.62
133.20
130.21
127.88
125.38
125.21
117.69
113.96
78.86
77.16 Chloroform-d
68.65
46.54
37.95
30.27
30.13
26.28
26.05
25.85
20.83
17.76
16.05
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

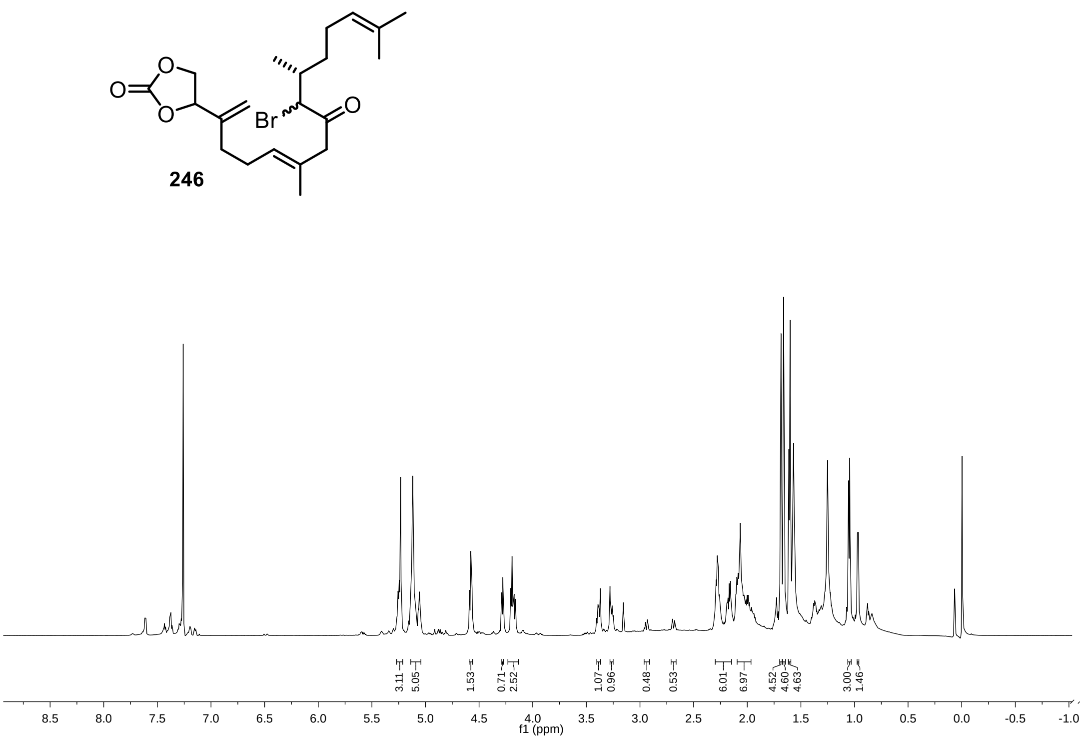
243


O
O
O
OSiPh3
H
6.01
3.00
6.00
1.04
1.14
2.00
1.01
0.99
1.00
0.98
1.00
2.05
2.04
2.13
3.00
3.09
3.06
1.00
1.95
1.05
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

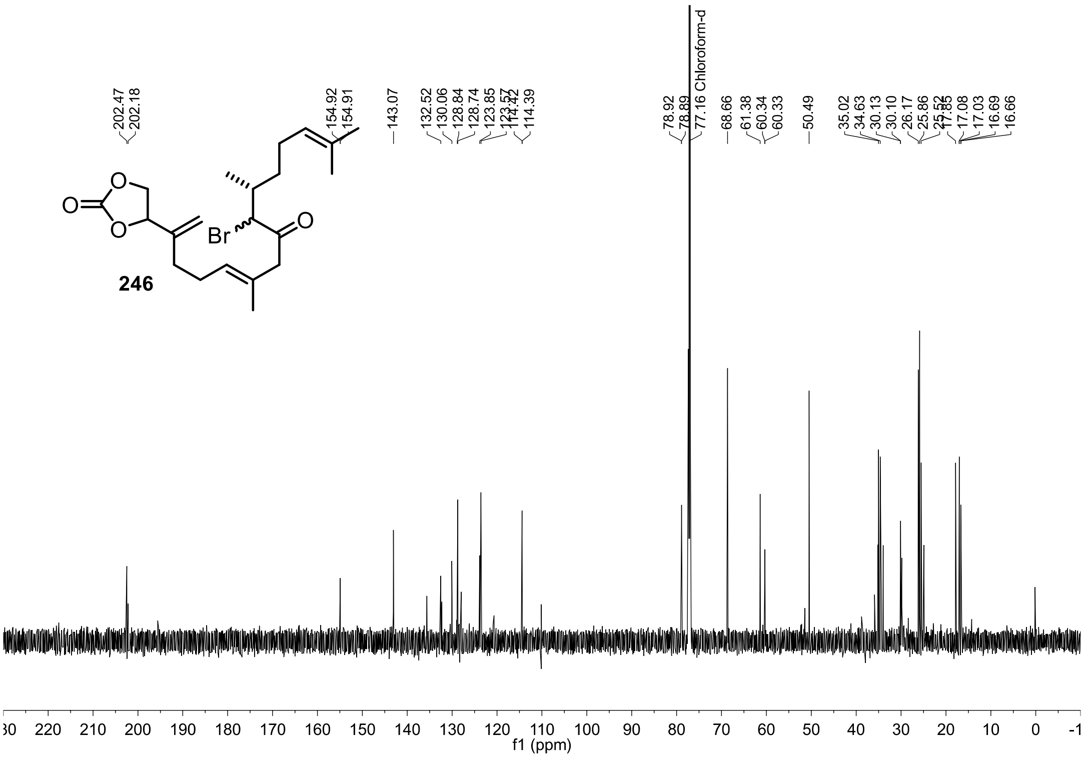
244


244

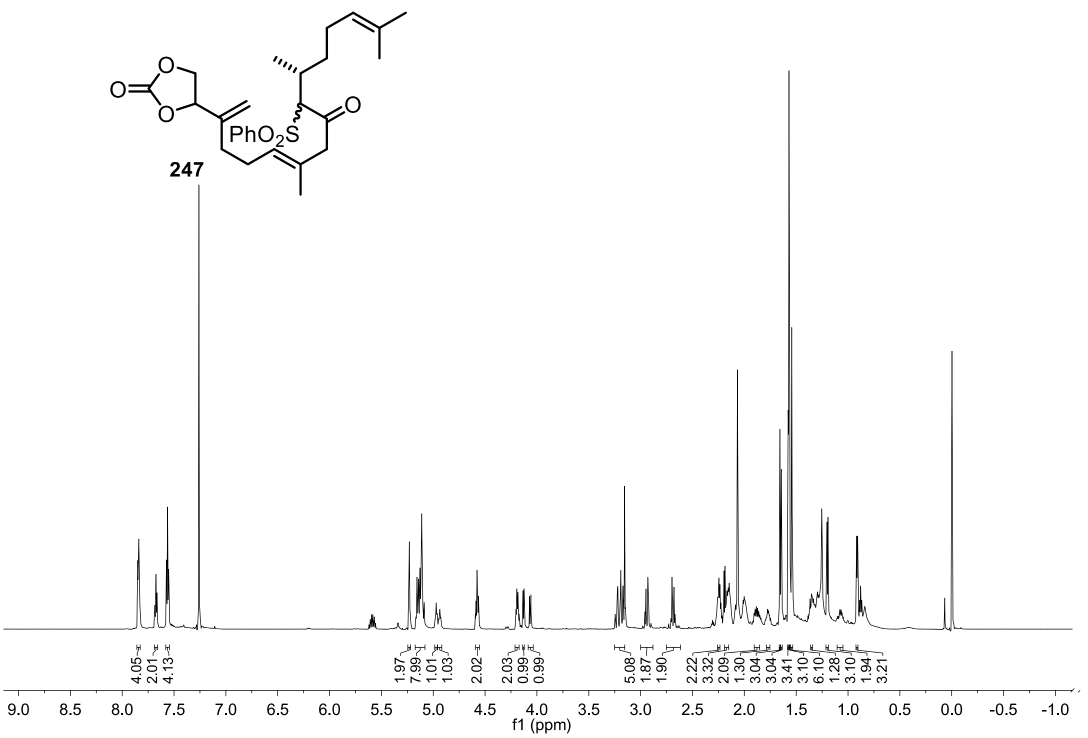
OSiPh3
H
O
O
O
154.85
154.83
149.40
149.38
144.48
144.46
143.44
143.33
135.71
134.46
130.28
127.91
125.07
125.06
116.35
116.29
113.53
113.29
113.20
113.08
78.84
78.59
77.16 Chloroform-d
68.69
68.59
52.92
52.82
37.96
37.84
30.20
29.01
28.76
28.45
28.29
26.10
25.82
20.56
20.54
20.45
20.07
17.76
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


246

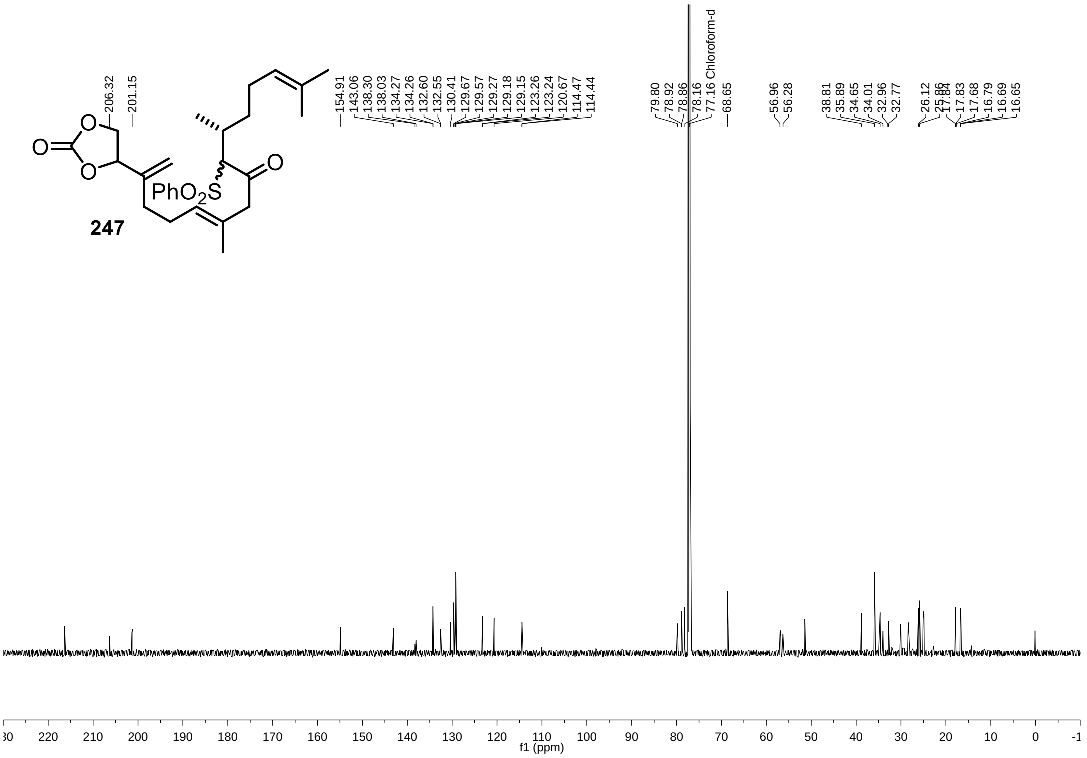
O
O
O
Br
O
3.11
5.05
1.53
0.71
2.52
1.07
0.96
0.48
0.53
6.01
6.97
4.52
4.60
4.63
3.00
1.46
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


202.47
202.18
154.92
154.91
143.07
132.52
130.06
128.84
128.74
123.85
123.57
114.42
114.39
78.92
78.89
77.16 Chloroform-d
68.66
61.38
60.34
60.33
50.49
35.02
34.63
30.13
30.10
26.17
25.86
25.52
17.85
17.08
17.03
16.69
16.66
O
O
O
Br
O
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

246


O
O
O
PhO2S
O
4.05
2.01
4.13
1.97
7.99
1.01
1.03
2.02
2.03
0.99
0.99
5.08
1.87
1.90
2.22
3.32
2.09
1.30
3.04
3.04
3.41
3.10
6.10
1.28
3.10
1.94
3.21
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

247



247

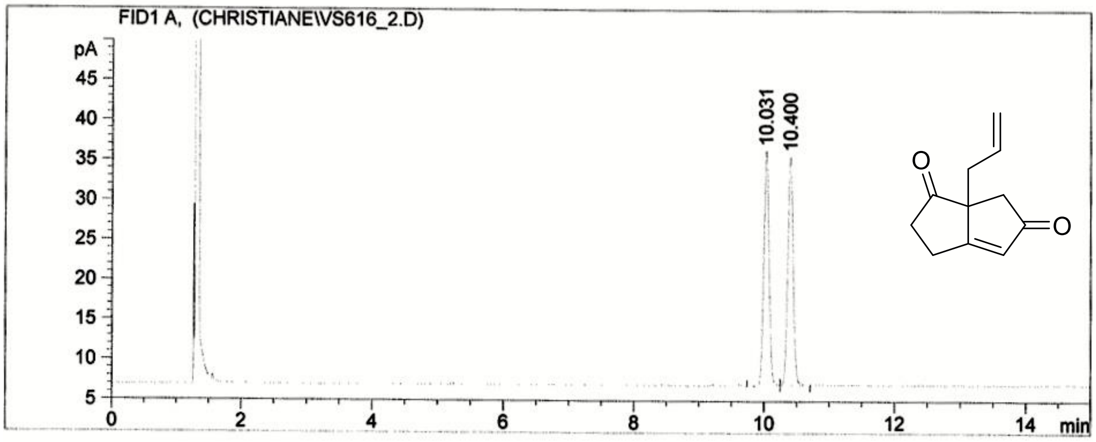
206.32
201.15
154.91
143.06
138.30
138.03
134.27
134.26
132.60
132.55
130.41
129.67
129.57
129.27
129.18
129.15
123.26
123.24
120.67
114.47
114.44
79.80
78.92
78.86
78.16
77.16 Chloroform-d
68.65
56.96
56.28
38.81
35.89
34.65
34.01
32.96
32.77
26.12
25.86
17.84
17.83
17.68
16.79
16.69
16.65
O
O
O
PhO$_2$S
O
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

6.4. GC-Spectra

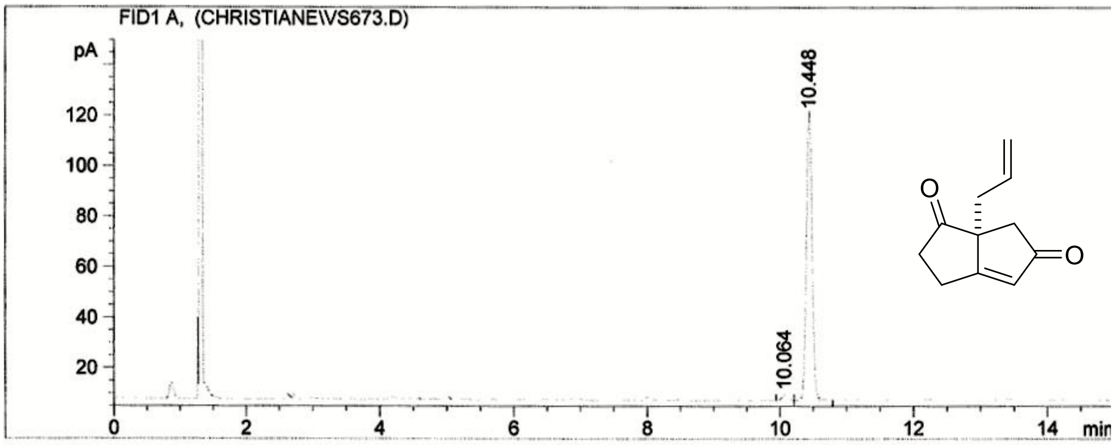
6a-allyl-2,3,6,6a-tetrahydropentalene-1,5-dione

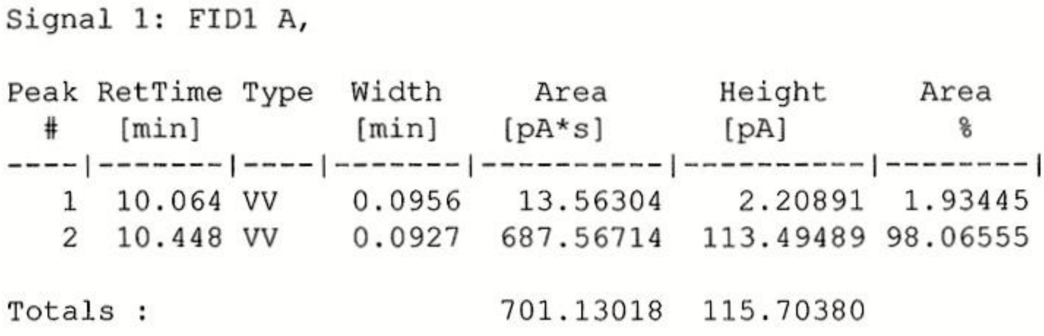
Hydrodex-β-TBDAc: isotherm 170 °C; 1.1 mL/min; Split 50:1; FID 200 °C

Racemic mixture



Enantioenriched

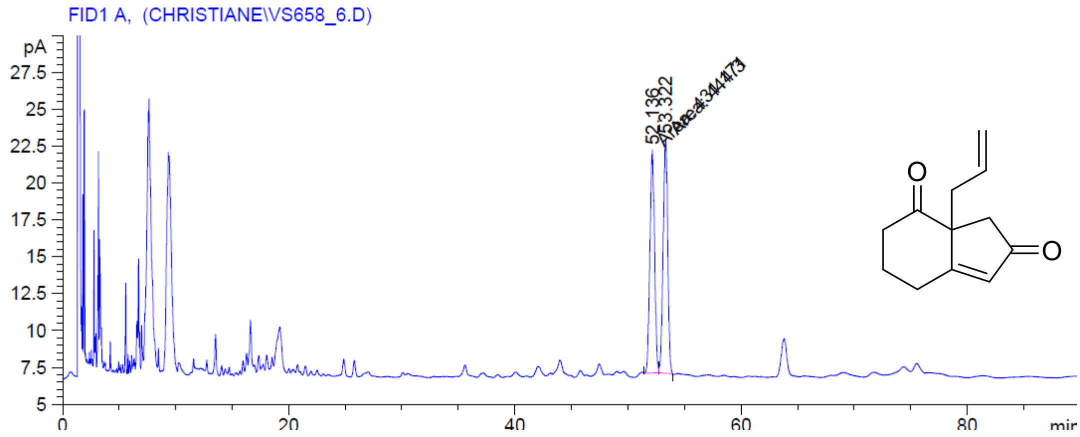




```
Signal 1: FID1 A,

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [pA*s]      [pA]         %
----|-------|----|-------|----------|----------|--------|
   1  10.064 VV    0.0956   13.56304    2.20891  1.93445
   2  10.448 VV    0.0927  687.56714  113.49489 98.06555

Totals :                   701.13018  115.70380
```

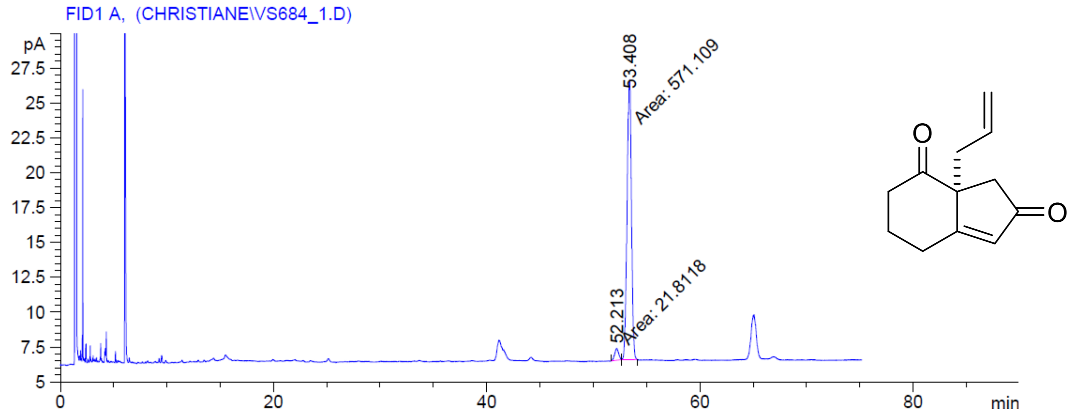
3a-allyl-3,3a,6,7-tetrahydro-2H-indene-2,4(5H)-dione

Racemic mixture



```
Signal 1: FID1 A,

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [pA*s]       [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  52.136 MM    0.4759  431.17053   15.10022 49.25016
   2  53.322 MM    0.4651  444.29987   15.92011 50.74984
```

Enantioenriched



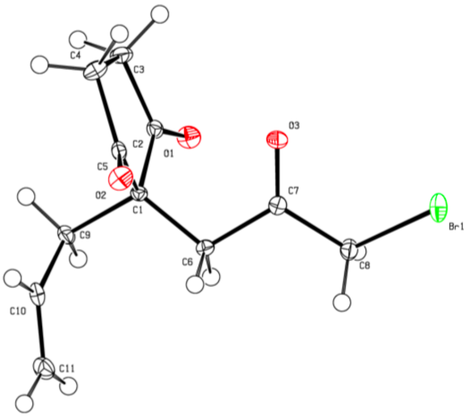
```
Signal 1: FID1 A,

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [pA*s]       [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  52.213 MM    0.4254   21.81184 8.54538e-1  3.67871
   2  53.408 MM    0.4735  571.10919   20.10239 96.32129
```

6.5. Crystallographic Data

Triketone **7**

Formula: $C_{11}H_{13}BrO_3$

Unit Cell Parameters: a 14.2324(9) b 8.8841(5) c 17.5119(10) P bca

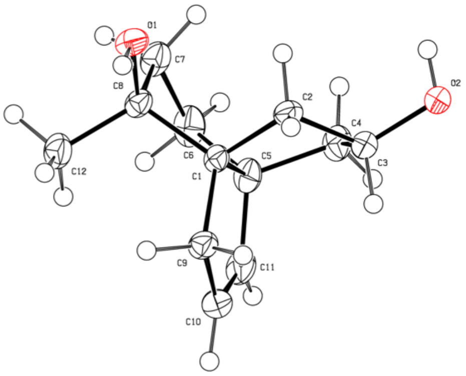


CCDC 1580415 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/structures.

Diol **12**

Formula: $C_{12}H_{18}O_2$

Unit Cell Parameters: a 10.4884(19) b 12.022(2) c 8.4697(14) P 21/c

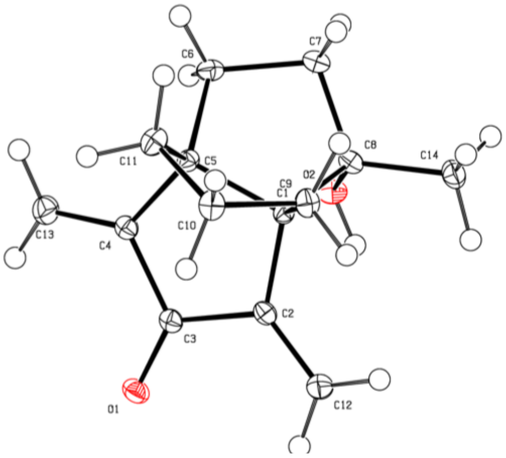


CCDC 1580414 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/structures.

Dienone **5**

Formula: $C_{14}H_{18}O_2$

Unit Cell Parameters: a 8.4455(4) b 11.0073(5) c 12.1692(7) P 21/n

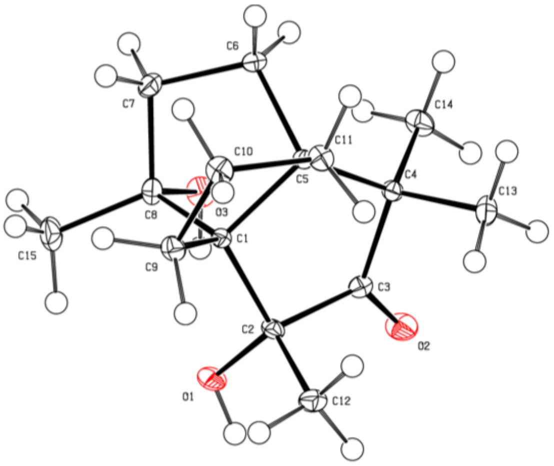


CCDC 1580412 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/structures.

α-Hydroxy ketone **1**

Formula: $C_{15}H_{24}O_3$

Unit Cell Parameters: a 6.999(3) b 8.200(5) c 12.895(8) P -1



CCDC 1580413 contains the supplementary crystallographic data for this structure. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/structures.