Development and Application of an Organocatalytic [3,3]-Sigmatropic Rearrangement

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Hiermit versichere ich, die vorliegende Dissertation selbstständig 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.

Caroline Apel, Berlin den 27.04.2020

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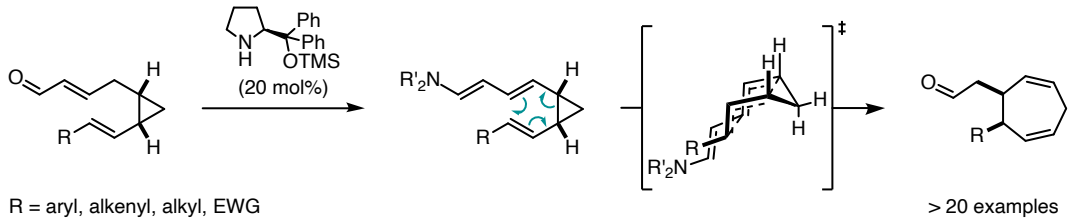
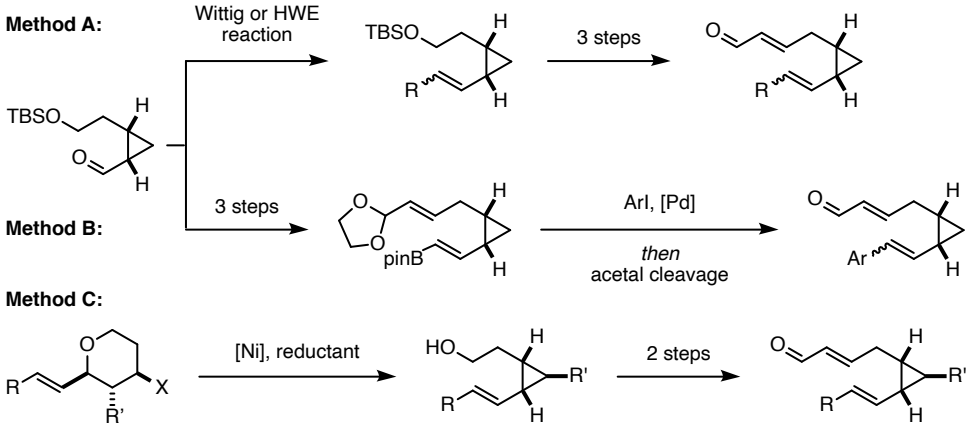
Abstract

This thesis deals with the development of an organocatalytic [3,3]-sigmatropic rearrangement of divinylcyclopropanes to cycloheptadienes. The reactive motif was formed *in situ* by condensation of α,β-unsaturated aldehydes with secondary amines. After optimisation of the reaction, a variety of cycloheptadienes with diverse substituents was obtained in high yields and with excellent diastereoselectivities. Furthermore, the reaction was demonstrated to be stereospecific and proceeded under mild conditions.

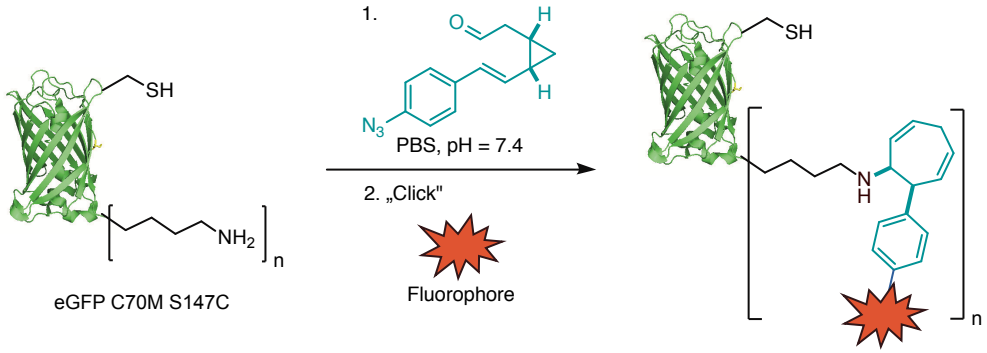


Hereby, the synthesis of a broad substrate library posed a formidable challenge. A synthetic strategy was devised in which the key transformation was the late-stage introduction of diversity in the final step by C–C cross coupling followed by one-pot deprotection. This strategy allowed most substrates to be derived from one common precursor. Individual substrates could be obtained by nickel catalysed reductive cross-coupling in a step efficient manner.



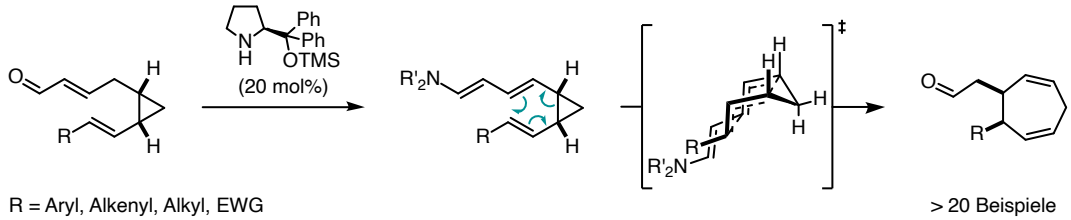
Intermediates of the substrate synthesis were applied to the selective modification of proteinogenic lysine residues. In coorporation with the group of Hackenberger, a protocol to modify the green fluorescent protein

was established. MS-MS results indicated that the aldehyde used is only attached to lysine. Subsequent functionalisation of the modified protein by ”click” reaction of an azide functionality was also possible.

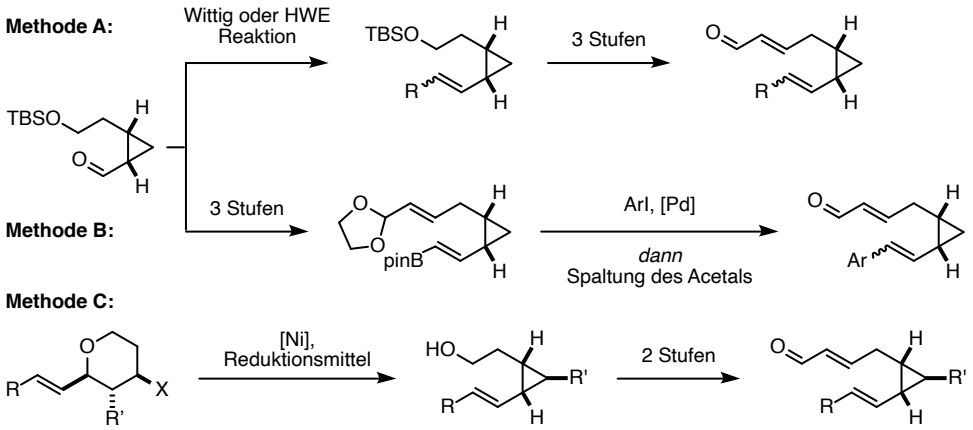


Zusammenfassung

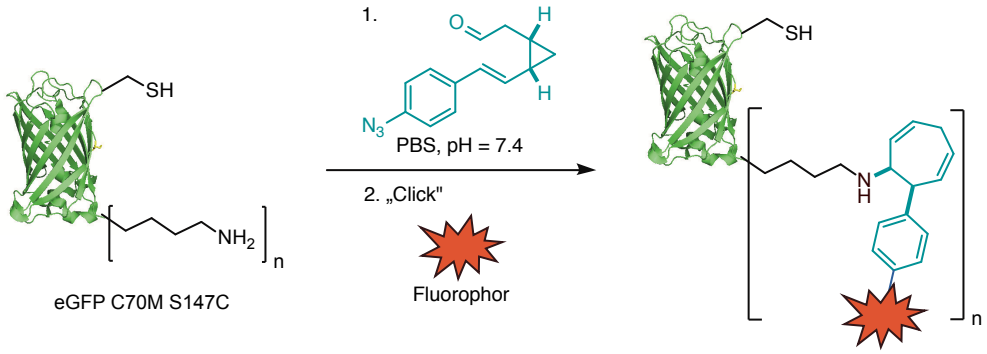
Das Ziel dieser Arbeit war die Entwicklung einer organokatalytischen [3,3]-sigmatropen Umlagerung von Divinylcyclopropanen zu Cycloheptadienen. Das reaktive Divinylcyclopropan wurde dabei *in situ* durch die Kondensation eines sekundären Amins mit einem α,β-ungesättigten Aldehyd erhalten. Nach der Optimierung der Reaktion konnten zahlreiche Cycloheptadiene mit unterschiedlichen Substituenten in guten Ausbeuten und mit exzellenter Diastereoselektivität erhalten werden. Die Reaktion war zudem stereospezifisch und verlief unter milden Bedingungen.



Die effiziente Entwicklung einer umfassenden Substratbibliothek stellte die größte Herausforderung dar. Es wurde eine Synthesestrategie entwickelt, bei der die Einführung verschiedener Substituenten im letzten Schritt durch C–C-Kreuzkupplung und anschließender Entschützung erfolgte. Dies ermöglichte die Darstellung der meisten Substrate ausgehend von einem gemeinsamen Vorläufer. Einzelne Substrate konnten durch eine Nickel-katalysierte reduktive Kreuzkupplung in wenigen Schritten erhalten werden.



Ausgewählte Syntheseintermediate wurden als Reagenzien verwendet, um proteinogene Lysinreste selektiv zu modifizieren. In Zusammenarbeit mit der Arbeitsgruppe Hackenberger wurde ein Protokoll entwickelt, um grün fluoreszierendes Protein zu modifizieren. MS-MS Messungen zeigten, dass der Aldehyd nur mit den Lysinresten des Proteins reagierte. Die Verwendung eines Azid-Derivats erlaubte zudem eine spätere Funktionalisierung des modifizierten Proteins mittels "Click"-Chemie.


SH
NH2
n
eGFP C70M S147C
1.
O
H
H
N3
PBS, pH = 7.4
2. „Click"
Fluorophor
SH
N
H
n

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1 Introduction

1.1 Cyclopropanes

Cyclopropanes are a versatile compound class whose reactivity excels that of other cyclic hydrocarbons. They are not only valuable synthetic intermediates[1–4] but also a structural motif in a variety of natural products with biological activity that ranges from anticancerous/antibacterial to neurotoxical effects.[5–7] For instance, *trans*-chrysanthemic acid (**1**), which was one of the first cyclopropanes isolated from plants, is a powerful insecticide (*Figure 1.1*).[8] The natural phytotoxin (+)-coronatine (**2**) possesses an interesting amide cyclopropyl moiety, and is involved in the jasmonic acid, ethylene, and auxin signalling pathways.[9] In medicinal chemistry, compounds bearing cyclopropane motifs are commonly used in structure-activity-relationship studies due to the ability to lock a certain conformation,[10] often leading to more stable or potent derivatives.[11–17]

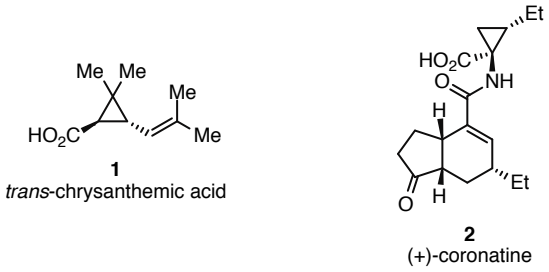


Figure 1.1: *trans*-Chrysanthemic acid (**1**) and (+)-coronatine (**2**) are representative examples for structures containing cyclopropanes in natural products.

1.1.1 Properties of Cyclopropanes

Cyclopropane represents the smallest possible carbocycle. It shows a high ring strain of 115.4 $\frac{\text{kJ}}{\text{mol}}$[18] composed of Baeyer strain, which describes the strain due to deviation of the bonding angles from the ideal tetrahedral angle and the Pitzer strain, a torsional strain due to ecliptic interactions of the hydrogen atoms. However, the reactivity of cyclopropanes resembles much more the reactivity of olefins than other cyclic hydrocarbons. This behaviour can be best explained by their bonding situation. It has been proposed that vinyl cyclopropane exhibits a conjugation similar to α,β-unsaturated systems as early as 1916[19] but the unique reactivity of cyclopropanes has been described later essentially by two models: In their valence bond model, Coulson and Moffit suggested that the central C–C bond of cyclopropanes is formed by an overlap of atomic sp^3-hybrid orbitals (*Figure 1.2a*).[20] The overlap is located outside of the C–C axis and leads to bent and shortened bonds. On the one hand, this assumption nicely explains the experimental observation that the density of

bonding electrons is indeed localised more off the C–C axis[21] but on the other hand it would result in an H–C–H angle of 113° which deviates from experimental values of 115°.[22] A model suggested by Walsh in 1949 takes the molecular orbitals of cyclopropane into account (*Figure 1.2b*).[23] In close analogy to ethylene, one can describe the bonding situation of cyclopropanes by three occupied molecular orbitals. The σ-orbital is formed by a linear combination of three sp^2-hybrid molecular orbitals resulting in a 6-electron-3-centre bond that shows σ-aromaticity (4+2 electrons).[24] The resulting ring current also provides a significant upfield shift of the protons in magnetic resonance spectra.[3] The orbitals of next higher energy, e_A and e_S, are degenerate and are formed by linear combinations of three atomic p-orbitals. Therefore, they are sometimes termed "quasi-π-orbitals". The participation of sp^2-hybrid orbitals suggests an H–C–H bond angle close to 120° and also results in shortened C–H bonds.[25]

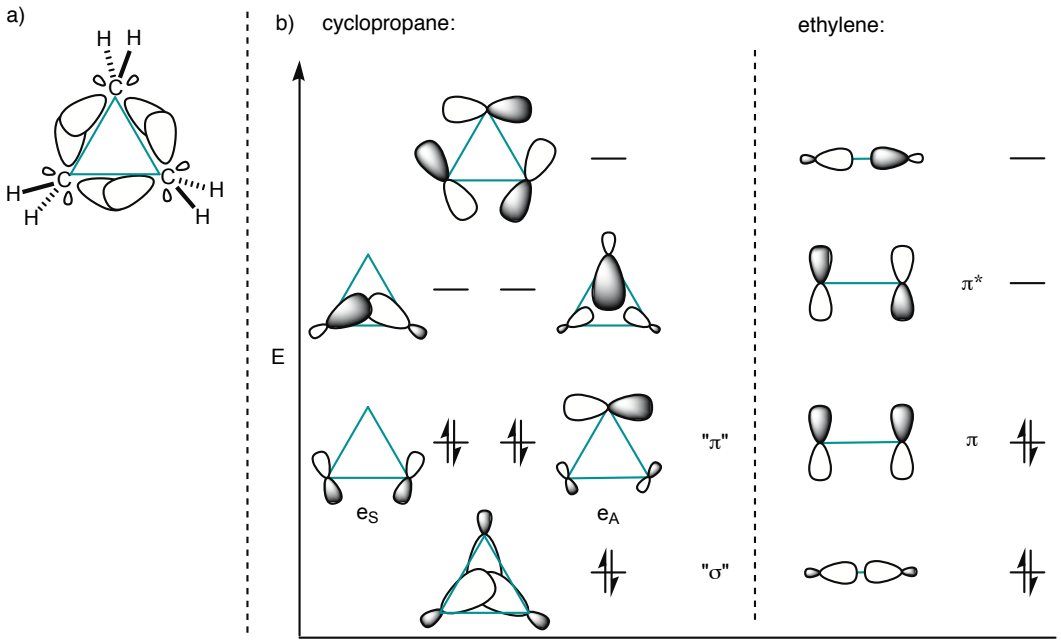


Figure 1.2: a) Bonding situation of cyclopropane in the Coulson-Moffit model. b) MO diagram of cyclopropane (Walsh model) in comparison to the MO diagram of ethylene.

The analogies in the bonding properties of ethylene and cyclopropanes help to understand the similarities in their reactivity. The regions of high electron density off the C–C axis for example determines the reactivity of cyclopropanes towards electrophiles.[26–30] Additionally, both ethylene and cyclopropanes, can undergo electronic interactions with π- or p-orbitals which in the case of ethylene becomes apparent in large conjugated systems. These interactions are greatest when the axes of the interacting orbitals are parallel to each other, for example resulting in the periplanar configuration of 1,3-butadiene. In analogy and due to the anisotropy of the electron density distribution of cyclopropanes, its interaction with a suitable neighbouring group is greatest when the p-orbital axis of the neighbouring group is parallel to the plane of the three membered ring.[18] This can be seen in the configuration of vinyl cyclopropane in which the antiperiplanar configuration is 4.6 $\frac{\text{kJ}}{\text{mol}}$ more stable than the synclinal configuration (*Figure 1.3*).[31–34] This effect is not as distinct as for 1,3-butadiene but still significant enough that also the stabilisation of the cyclopropyl methyl cation depends on the torsion angle.[35]

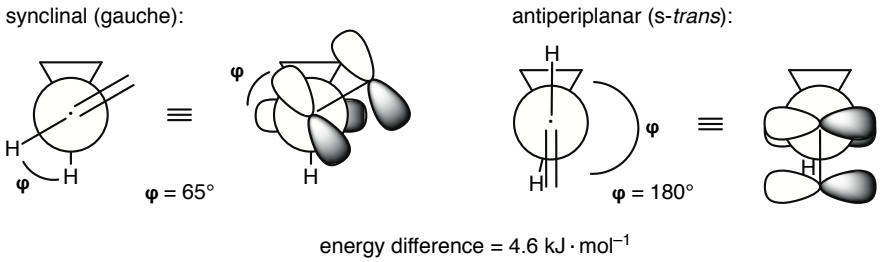
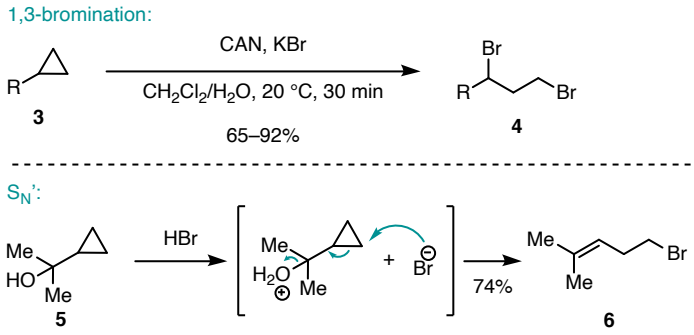


Figure 1.3: Newman projection of the conformations of vinyl cyclopropane.

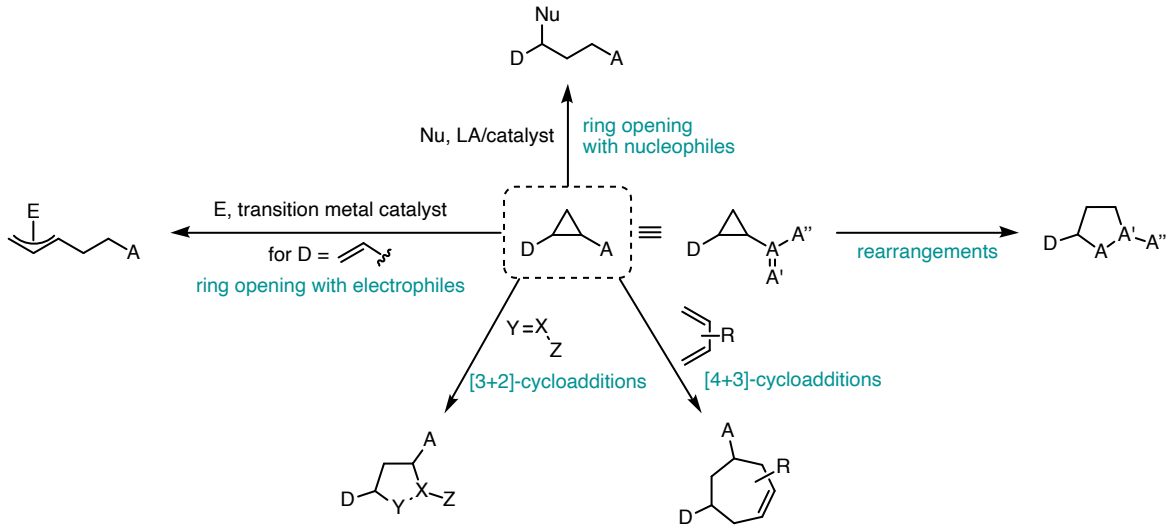
1.1.2 Reactivity of Cyclopropanes

Due to their specific bonding situation, the reactivity of cyclopropanes shows great similarity to that of olefins. Bromine radicals for instance, can add across the C–C bond of **3** in an analogue fashion as they would add across a double bond, leading to 1,3-dibrominated products **4** (*Scheme 1.1, top*).[36] This analogy between cyclopropanes and olefins has also been exploited by Julia and co-workers in an olefination reaction leading to 1,3-funtionalised products (*Scheme 1.1, bottom*).[37] The nucleophilic attack of bromide to protonated cyclopropyl alcohol **5** in a S_N'-like fashion leads to the cleavage of the leaving group and the formation of brominated olefin **6** which has been used in the synthesis of terpenes.



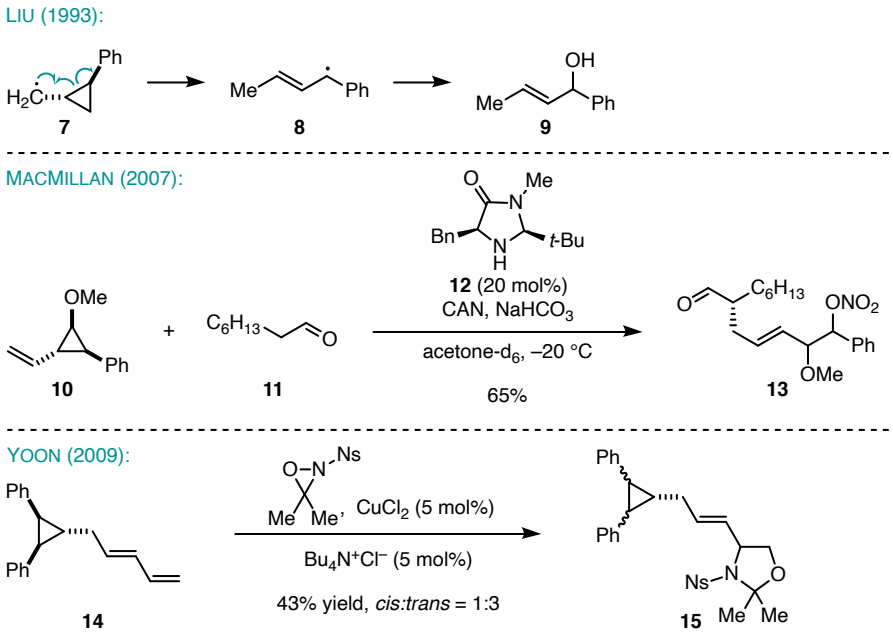
Scheme 1.1: 1,3-Bromination by bromine radicals (top) and S_N' reaction (bottom) of cyclopropanes.

In general, the C1–C2 bond of cyclopropanes has to be broken either in a heterolytic or a homolytic fashion to enable ring opening. Heterolytic cleavage formally generates a zwitterionic structure that can be stabilised by substitution with an electron withdrawing group on one side and an electron donating group on the other end of the cyclopropane moiety. These so called donor-acceptor substituted cyclopropanes readily undergo reactions with either nucleophiles (Nu) or electrophiles (E). Additionally, they engage in [3+2]- as well as [4+3]-cycloadditions[38] leading to five-membered and seven-membered products, respectively (*Scheme 1.2*). Donor-acceptor substituted cyclopropanes have been extensively studied and their reactivity has been exploited in the synthesis of complex organic molecules,[39–42] especially alkaloids[43] and terpenoids.[44–46]



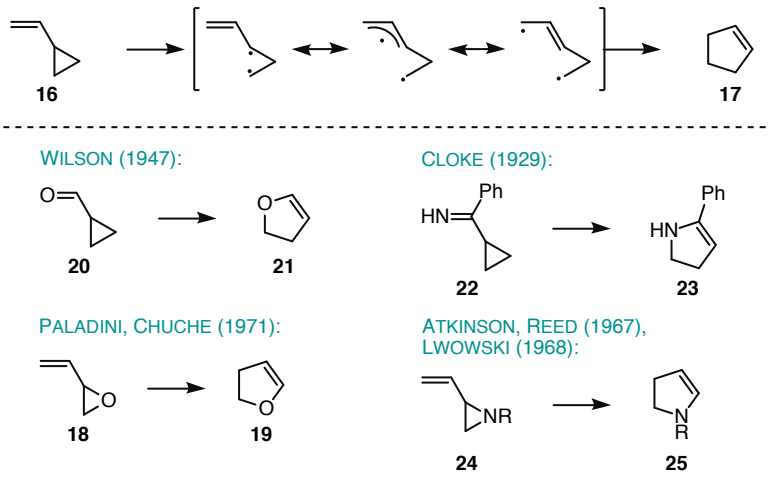
Scheme 1.2: Overview of the reactivity of donor-acceptor substituted cyclopropanes.

The homolytic cleavage of the C1–C2 bond leads to the formation of a diradical.[47] This reactivity is apparent in the 1,3-dibromination of **3** (*Scheme 1.1*) and finds broad application in so-called "radical clocks".[48,49] The high ring strain of cyclopropanes is a driving force in these kind of ring opening reactions. This reactivity is accelerated if a neighbouring radical is present and the compound can produce a more stable radical by rearrangement. The reaction rates for these reactions are known[50,51] and can be used either to indirectly measure the rate of another reaction or to generally indicate a radical mechanism of a given reaction. Common examples are the methyl cyclopropyl radical **7** used by Liu that arranges to the corresponding vinylic radical **8** (*Scheme 1.3, top*) or vinyl cyclopropane **10** used by MacMillan and co-workers to demonstrate that their α-alkylation of aldehyde **11** using organocatalyst **12** proceeds *via* a SOMO mechanism (*Scheme 1.3, middle*).[52] The generated radical cation reacts with the vinyl radical group of radical clock substrate **10**. By opening of the cyclopropane, a benzyl radical is formed that is trapped by a nitrate from the oxidant (ceric ammonium nitrate, CAN) leading to α-functionalised aldehyde **13**. A cationic mechanism would have led to ring-opening of the cyclopropane so that the resulting cation would be stabilised by the alkoxy-group and to the formation of a different open-chain aldehyde. However, the open-chain is not always preferred to the cyclopropane. In these cases, a *cis,trans*-isomerisation can indicate a radical mechanism. For instance, Yoon and co-workers showed that the oxaziridine-mediated amino hydroxylation of olefins most likely proceeds *via* a radical mechanism by isomerisation of **14** to the *trans*-product **15** upon functionalisation (*Scheme 1.3, bottom*).[53]



Scheme 1.3: Selected examples for the application of radical clocks.

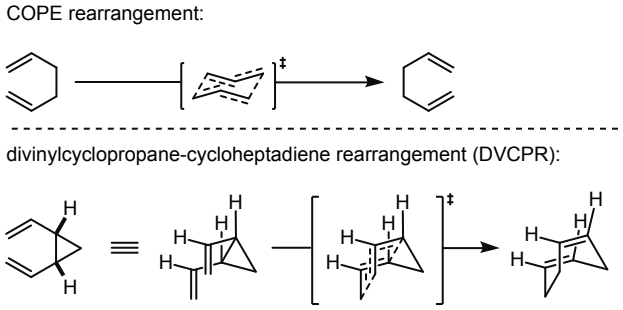
A biradical mechanism is also present in the rearrangement of vinylcyclopropane (**16**) to cyclopentene (**17**) (*Scheme 1.4, top*), although a concerted mechanism has long been discussed for related substrates.[2,54–57] Today, the mechanism of this rearrangement is thought to proceed *via* a biradical intermediate in most cases. Numerous applications of the vinylcyclopropane-cyclopentene rearrangement in the synthesis of complex natural products are known and modifications with heterocyclic substrates led for instance to the formation of hydrofuranes[58,59] or pyrrolines (*Scheme 1.4, bottom*).[60–62]



Scheme 1.4: The mechanism of the vinylcyclopropane-cyclopentene rearrangement (top) and heterocyclic variants of this reaction (bottom).

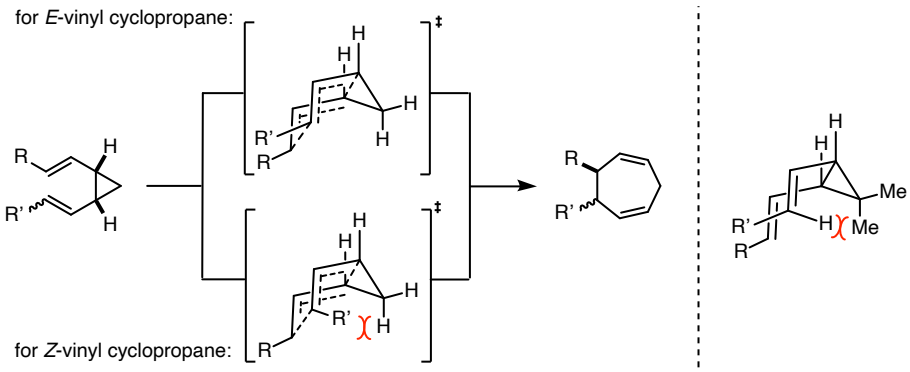
1.1.3 Divinylcyclopropane-Cycloheptadiene Rearrangement

An unique reactivity of divinylcyclopropanes is their [3,3]-sigmatropic rearrangement to cycloheptadienes. First observed in 1960 by Vogel,[63–65] the divinylcyclopropane-cycloheptadiene rearrangement (DVCPR) had become focus of numerous studies in the following years.[66–79] It could be demonstrated that the DVCPR proceeds *via* a concerted mechanism similar to the one of the Cope rearrangement. While the related Cope rearrangement passes through a chair-like transition state (*Scheme 1.5, top*),[80] the DVCPR proceeds *via* a boat-like transition state (*Scheme 1.5, bottom*).[68] Both vinyl groups are in *endo* configuration regarding the cyclopropyl moiety so that the double bonds of the resulting cycloheptadiene are *Z*-configurated.



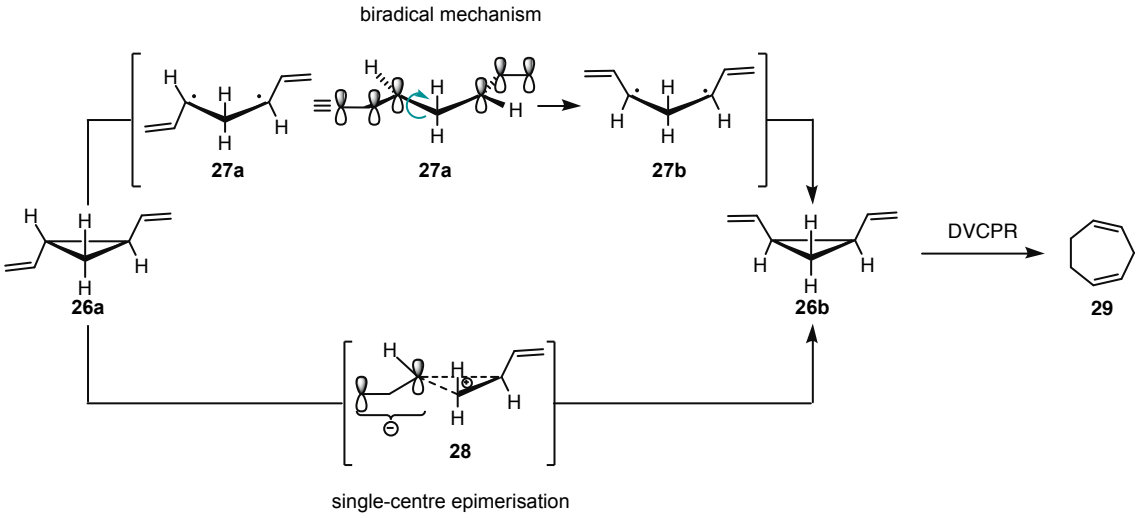
Scheme 1.5: Mechanistic considerations of the Cope rearrangement (top) and the DVCPR (bottom).

Substituents on the parent system have an influence on the kinetics as well as the stereochemical outcome of the reaction (*Scheme 1.6*).[70,72,81,82] If both vinyl groups are additionally substituted and *E*-configurated, the resulting cycloheptadiene shows a *cis*-configuration of the substituents. However, if one of the substituted vinyl moieties possesses a *Z*-configuration, the substituents are *trans* to each other in the cycloheptadiene. Steric interactions between the *Z*-substituent and the axial proton of the cyclopropyl moiety result in an increased activation barrier so that these reactions require a higher temperature. This effect becomes even more pronounced if the cyclopropane carries additional substituents. Here, steric interactions also occur with *E*-configurated vinyl groups and the activation barrier is increased to such an extent that the compounds might not undergo DVCPR at all.



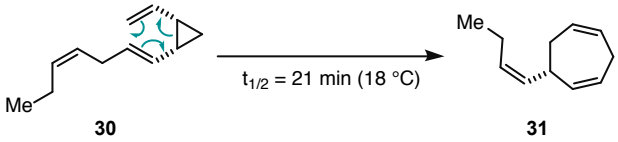
Scheme 1.6: Stereochemical considerations of the DVCPR (left) and steric interactions of substituted cyclopropane derivatives (right).

Following the mechanistic considerations (*Scheme 1.5*) it seems apparent that *trans*-cyclopropanes should not be able to undergo DVCPR. However, *trans*-cyclopropanes have been found to rearrange to the corresponding cycloheptadiene by *cis,trans*-isomerisation prior to the reaction. The parent compound *trans*-vinyl cyclopropane (**26a**) affords the corresponding cycloheptadiene at 190 °C.[63] Systems with a higher conjugation may show a decreased activation barrier. The *cis,trans*-isomerisation of divinyl cyclopropanes can proceed *via* two pathways (*Scheme 1.7*): The C1–C2 bond of **26a** can be cleaved homolytically resulting in the allylic biradical **27a**.[67,68,83,84] Rotation around the C–C axis and radical recombination forms the *cis*-cyclopropane **26b**. On the other hand, a single-centre epimerisation has also been considered.[69,70,85] By heterolytic cleavage of the C1–C2 bond, allylic anion **28** is formed. Inversion of **28** leads to the formation of *cis*-cyclopropane **26b**.



Scheme 1.7: The *cis,trans*-isomerisation of divinyl cyclopropanes can either proceed *via* formation of biradical **27** (top) or allylic anion **28** (bottom).

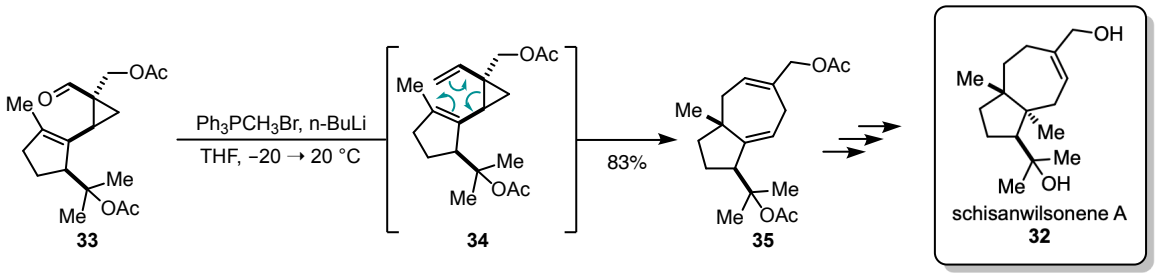
A prominent example for the appearance of the DVCPR in nature, is the deactivation of pheromone **30** (*Scheme 1.8*).[86] This hormone is excreted by the female marine brown algae *Ectocarpus siliculosus* as a sex attractant and has long been thought to possess the structure of cycloheptadiene ectocarpene **31**. However, the active structure could be eventually assigned to be that of divinyl cyclopropane **30** that arranges to its inactive form by DVCPR.[87] With a half-life $t_{1/2}$ of 21 min at 18 °C or 56 min at 8 °C,[88] this process allows the algae to signal receptiveness without saturating the environment with active pheromone.



Scheme 1.8: The pheromone **30** is deactivated by DVCPR.

The DVCPR has been used in numerous syntheses of complex organic molecules.[89] Recent examples include the total synthesis of schisanwilsonene A (**32**) by Echavarren and co-workers (*Scheme 1.9*).[90] Schisanwilsonene A (**32**) was isolated in 2009 from starvine *Schisandra wilsonia* and shows promising antiviral

activity inhibiting the hepatitis virus proteins HBsAg and HBeAg.[91] In the total synthesis of **32**, aldehyde **33** was converted to divinyl cyclopropane **34** by Wittig reaction. Divinyl cyclopropane **34** immediately rearranges to cycloheptadiene **35** which was converted to the natural product in 8 steps.

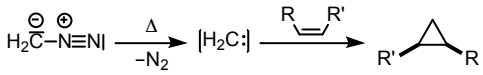


Scheme 1.9: The DVCPR of divinyl cyclopropane **34** enabled the total synthesis of schisanwilsonene A (**32**).

Other natural products have been prepared employing this rearrangement, including fatty acid metabolites,[92] terpenoids,[93–98] and alkaloids,[99–101] especially cyclohepta[*b*]indoles.[102] Additionally, heterocyclic variants of the DVCPR have been developed and well-studied.[103–106]

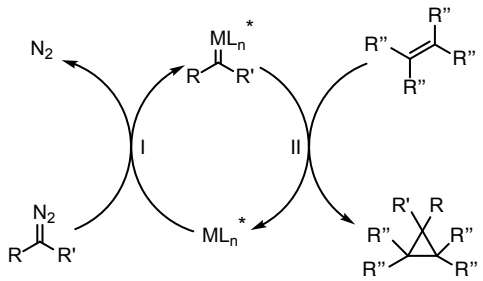
1.1.4 Synthesis of Cyclopropanes

Cyclopropanes are usually prepared either by the addition of carbenes or carbenoids to double bonds or by intramolecular substitution. Carbenes can for example be obtained *in situ* by thermolysis of diazomethane (*Scheme 1.10*).[107]



Scheme 1.10: Addition of methylene generated by thermolysis of diazomethane to an olefin results in cyclopropanation.

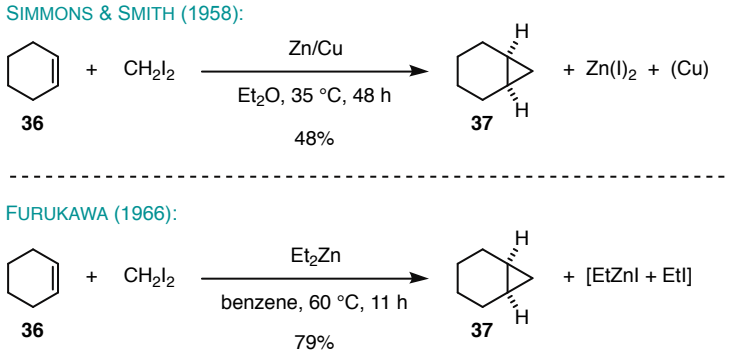
Instead of thermic energy, transition metal complexes are often used for the decomposition of diazoalkanes (*Scheme 1.11*, path **I**). The resulting carbene-metal complex shows a reactivity similar to that of free carbenes and can add to a double bond (path **II**), generating cyclopropanes.[108] Additionally, this method allows for asymmetric cyclopropanations by the use of chiral ligands.[109–115]



Scheme 1.11: Catalytic cycle of the transition metal catalysed cyclopropanation with diazoalkanes.

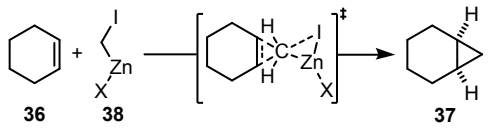
In most cases the carbene or carbenoid adds to the double bond in a *syn*-fashion so that the stereochemical outcome of the reaction is governed by the geometry of the double bond: An *E*-configurated double bond leads to the *trans*-cyclopropane while the *Z*-olefin affords a *cis*-cyclopropane.

However, diazomethane and other diazoalkanes are toxic and highly explosive. Therefore, surrogates and substitutes have been developed.[116–121] An alternative to take advantage of the reactivity of carbenoid species without the safety concern of diazoalkanes is the use of carbenoid species generated *via* a different route as for example in the Simmons-Smith reaction. In 1958, Simmons and Smith observed that the addition of diiodomethane to cyclohexene **36** in the presence of a zinc/copper couple led to the formation of cyclopropane **37** (*Scheme 1.12, top*).[122] However, the reaction was slow (up to 70 h were required for full conversion) and gave the cyclopropanes only in moderate yields. Modification of the reaction by use of diethyl zinc instead of the zinc/copper couple allowed for a more efficient conversion (*Scheme 1.12, bottom*).[123,124]



Scheme 1.12: Simmons-Smith reaction (top) and Furukawa modification thereof (bottom).

In the course of the reaction, the carbenoid zinc organyl **38** is generated from diiodomethane and the applied zinc source.[125] The carbenoid adds in a concerted [2+1]-cycloaddition to the double bond, passing through a so called ”butterfly-transition state” (*Scheme 1.13*).

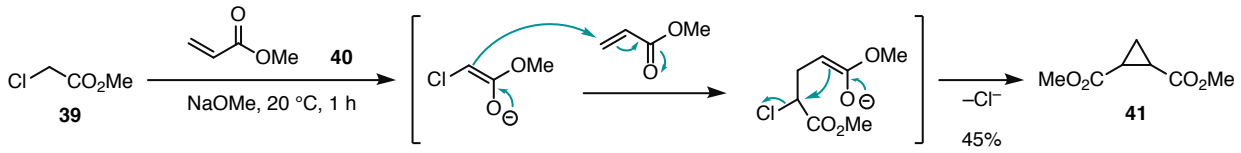


Scheme 1.13: The Simmons-Smith reaction proceeds *via* a concerted [2+1]-cycloaddition.

Allylic alcohols have been established as substrates for the Simmons-Smith reaction because the neighbouring oxygen atoms direct the zinc organyl and accelerate the reaction, allowing numerous regio- and enantioselective variants.[114]

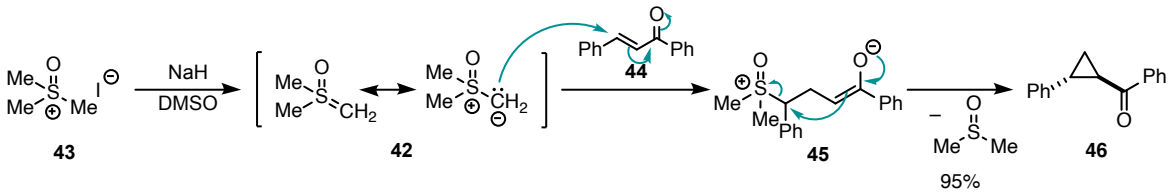
Another approach to cyclopropanes are intramolecular substitution reactions. Especially, irreversible Michael-initiated ring closures (MIRC) have become highly popular. The term MIRC was coined in 1980 by Little,[126] but the reaction has been used earlier, for instance by McCoy in 1958.[127] McCoy demonstrated that the reaction of α-chloroester **39** with methacrylate **40** delivers the cyclopropyl diester **41** (*Scheme 1.14*). The chloroester **39** is deprotonated and the enolate adds to the Michael-system of methacrylate in a 1,4-fashion.

The resulting enolate then adds intramolecularly in α-position to the ester, substituting the chloride. For a MIRC reaction to occur, either the nucleophile or the electrophile has to carry a leaving group that can be substituted by the intermediate enolate. Additionally, these reactions are only stereospecific when the ring-closure is faster than the rotation around the single bond in the second enolate.[114] Asymmetric variants have been developed in particular by the use of organocatalysts.[128–136]



Scheme 1.14: Synthesis of cyclopropanes by MIRC.

Ylides are common nucleophiles in the MIRC reactions, for example in the Corey-Chaykovsky reaction (*Scheme 1.15*).[137] In general, this reaction describes the addition of stabilised ylides **42** to different electrophiles. The ylide is formed by deprotonation of sulfonium **43**. If the ylide **42** adds to an α,β-unsaturated system **44** in a 1,4-addition, the resulting enolate **45** can undergo intramolecular nucleophilic substitution and release of DMSO delivers cyclopropane **46**. In open-chain systems, the more stable *trans*-product is favoured.

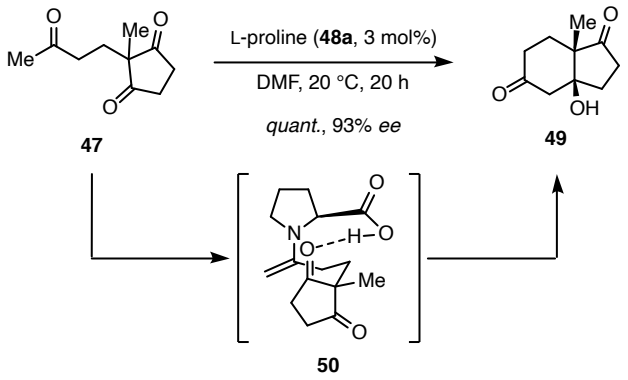


Scheme 1.15: Mechanism of the Corey-Chaykovsky reaction.

1.2 Asymmetric Aminocatalysis

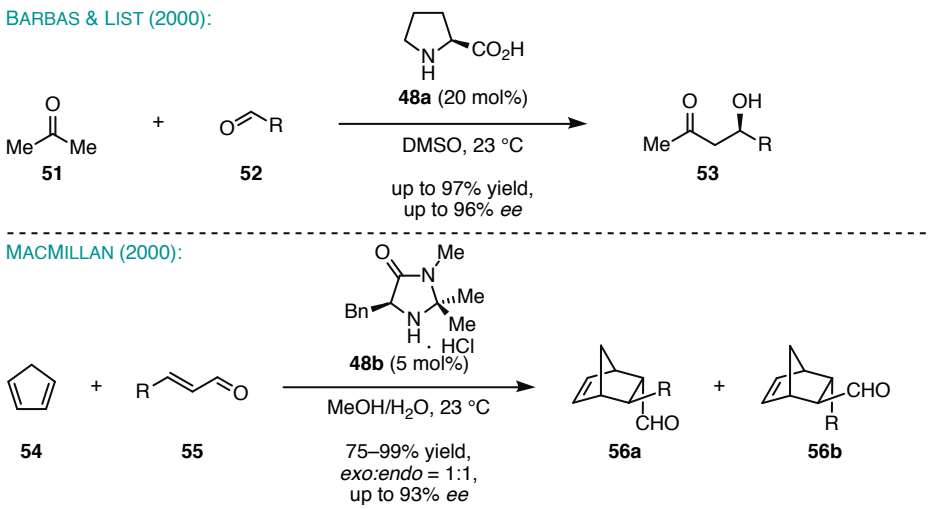
Asymmetric aminocatalysis has become a reliable and powerful tool for modern organic chemistry. It is one of the main activation modes of organocatalysis, which describes the catalysis by small organic molecules. It is used to complement enzyme and metal catalysed processes in the directed synthesis of chiral molecules. The catalysts employed are generally stable, fairly easy to design and to synthesise and are based on non-toxic compounds. Organocatalysis actually looks back on a long history as it is believed to have played a significant role in the formation of prebiotic building blocks, for instance sugars, and thereby allowed for the introduction and spread of homochirality in living organisms.[138] Enantiomerically enriched amino acids such as L-alanine or L-isovaline were present in carbonaceous meteorites with up to 15% *ee*. They can catalyse the dimerisation of glycal and aldol-type reactions between glycal and formaldehyde forming sugars with significant enantiomeric excess. In synthetic organic chemistry, the first proline-catalysed asymmetric aldol reaction was discovered independently by the groups of Hajos and Wiechert in the 1970's (*Scheme 1.16*).[139,140] The intramolecular aldol reaction of triketone **47** catalysed by L-proline (**48a**) delivered annulation product **49** in quantitative yield and 93% enantiomeric excess. Surprisingly, the reaction remained

a laboratory curiosity for a long time and was used only occasionally in syntheses.[141] The scope had not been explored and the mechanism was poorly understood, but is today believed to proceed *via* highly organised enamine **50**.[142–150]



Scheme 1.16: Hajos-Parrish-Eder-Sauer-Wiechert reaction.

The revival of organocatalysis began 30 years later, when the potential of small molecule catalysts for synthetic problems was demonstrated by the groups of Shi, Denmark, and Yang by asymmetric epoxidation of simple alkenes by enantiomerically pure ketones[151–153] and by the groups of Jacobsen and Corey by hydrogen-bonding catalysis.[154,155] However, organocatalysis as a concept was established by seminal works by Barbas, List and co-workers who developed an intermolecular aldol reaction of acetone and different aldol donors by enamine catalysis (*Scheme 1.17, top*)[156] and by MacMillan and co-workers who realised the first organocatalytic Diels-Alder reaction under iminium ion catalysis (*Scheme 1.17, bottom*).[157] These contributions resulted in an explosive growth of the field.[134,158–170]



Scheme 1.17: The first organocatalytic intermolecular aldol reaction (top) and the first organocatalytic Diels-Alder reaction (bottom).

Some of the most commonly used secondary amines for organocatalysis were developed by the groups of Jørgensen and MacMillan (*Figure 1.4*). Apart from aminocatalysis, also catalysis by hydrogen-bonding

donors, especially thioureas, by chiral bases and by phase-transfer agents as well as *N*-heterocyclic carbenes has been developed.

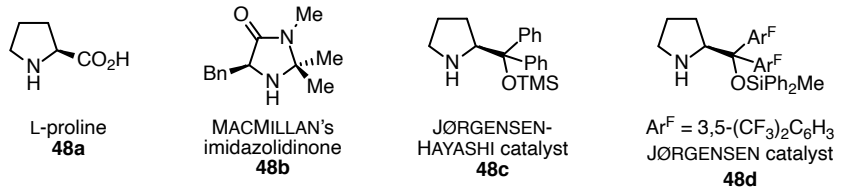
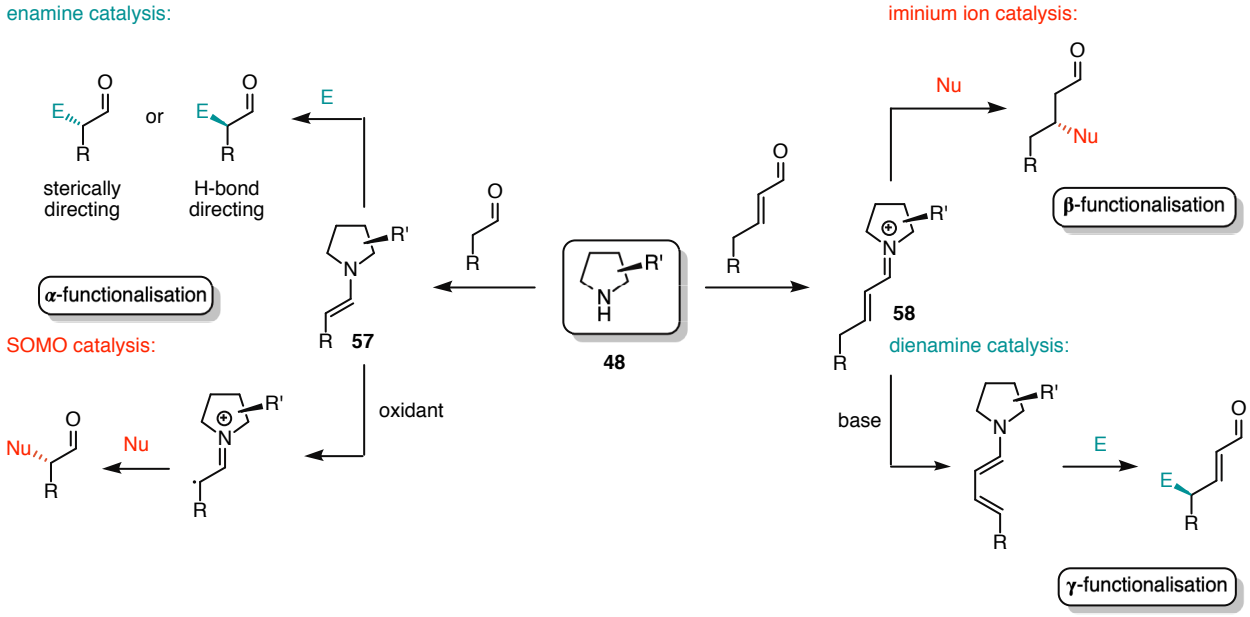


Figure 1.4: Selected examples of common aminocatalysts.

Today, several types of activation by aminocatalysis can be distinguished (*Scheme 1.18*). The reaction of secondary amines **48** with aldehydes typically delivers an intermediate enamine **57** that either attacks an electrophile E (enamine catalysis) or undergoes oxidation to form a radical cation which then reacts even with weak nucleophiles Nu (SOMO catalysis), both leading to α-functionalisation of the carbonyl compound. Additionally, reaction of the secondary amine with an α,β-unsaturated aldehyde leads to formation of an intermediate iminium ion **58** that can be attacked by nucleophiles in β-position (iminium ion catalysis). Alternatively, tautomerisation of iminium ion **58** delivers the corresponding dienamine, which incorporates electrophiles in γ-position (dienamine catalysis). Today, also various domino- and tandem reactions, pericyclic reactions and transformations *via* tri- and tetraenamine catalysis have been developed.[171–177]

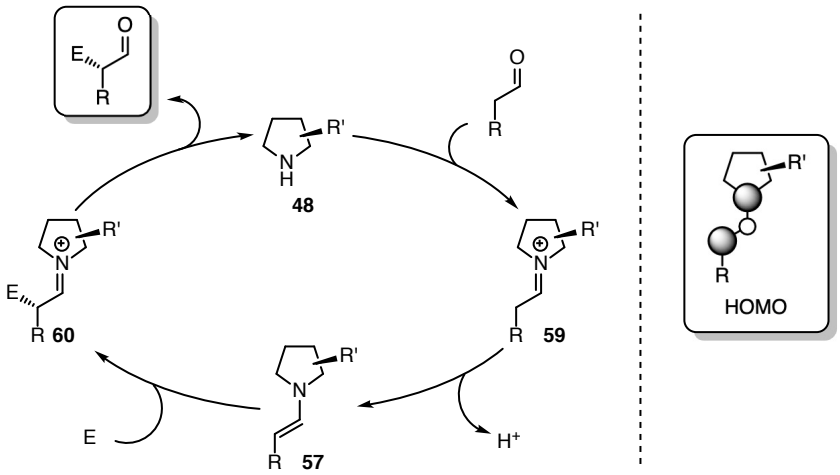


Scheme 1.18: Main aminocatalytic pathways for carbonyl functionalisation.

1.2.1 Enamine Catalysis

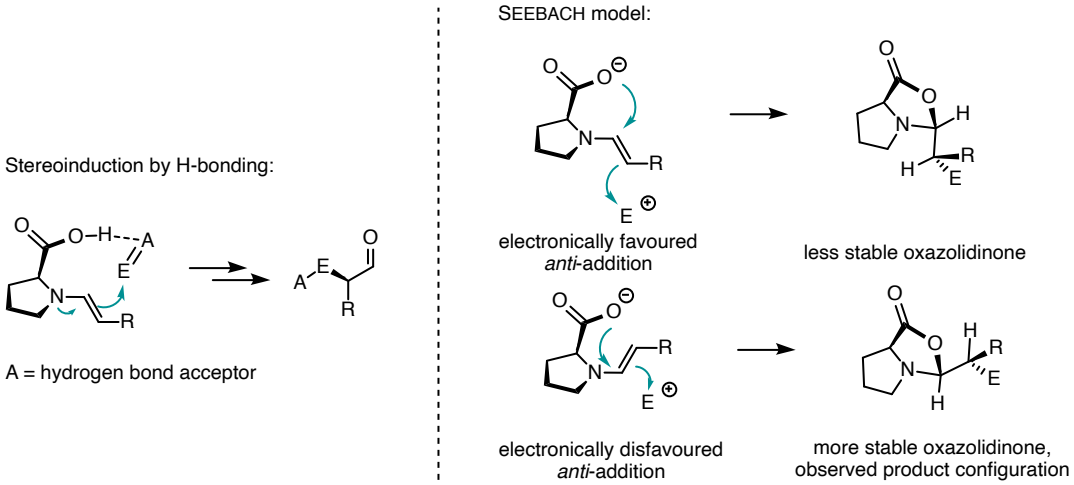
After pioneering work by the groups of Barbas and List, the mechanism of enamine catalysis has been extensively studied. The secondary amine **48** condenses with the carbonyl substrate to form an iminium ion **59** (*Scheme 1.19*). The LUMO energy of this iminium is decreased compared to the carbonyl which

also results in enhanced α-C–H acidity. Fast deprotonation of the iminium **59** leads to the formation of an enamine **57**. Since the nitrogen lone pair has a higher energy than the oxygen lone pair, the HOMO energy of the enamine is increased compared to an enol. Also, the tautomeric equilibrium is shifted: The keto/enol equilibrium strongly lies on the side of the keto form but the iminium/enamine equilibrium is shifted towards the enamine. Overall, this results in a high reactivity of the formed enamine which reacts in the stereoinducing step with an electrophile affording another iminium ion **60**. This iminium ion releases the α-functionalised carbonyl and liberates the catalyst upon hydrolysis.



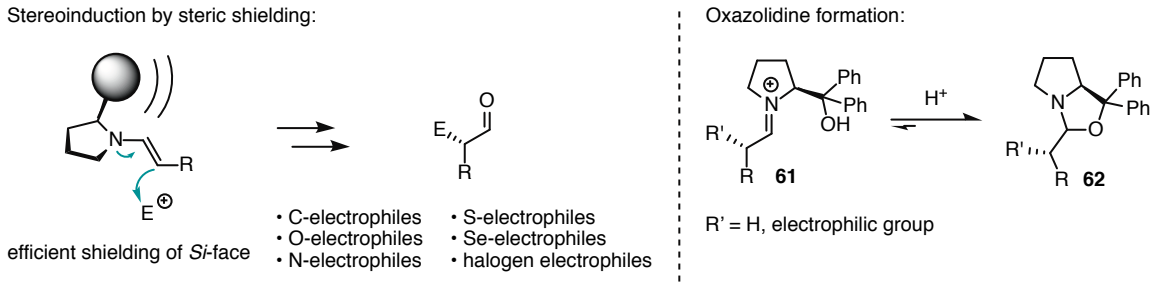
Scheme 1.19: Catalytic cycle of α-functionalisation of carbonyl compounds by enamine catalysis (left) and depiction of the HOMO of the enamine (right).

The enantioselectivity of these transformations arises from the highly organised transition state during the enamine addition to the electrophile. Calculations of the transition state geometry obtained from the reaction of trimethylsilyl diarylprolinol ethers and aldehydes indicated that the (*E-s-trans*)-configuration of the enamine is favoured.[178] For proline-derived catalysts carrying a free hydroxyl group, an accepted hypothesis proposes that the hydroxyl group activates and directs the electrophile to the "upper" side of the enamine by hydrogen bonding (*Scheme 1.20, left*).[146] Alternatively, Seebach and co-workers proposed that enamine formation and subsequent attack of the electrophile is potentially assisted by concerted oxazolidinone formation (*Scheme 1.20, right*).[179] The stereochemical outcome would then result from the formation of the more stable oxazolidinone even though this pathway would be electronically disfavoured.



Scheme 1.20: Origin of stereochemistry in proline-catalysed reactions by H-bond direction (left) and by the Seebach-model (right).

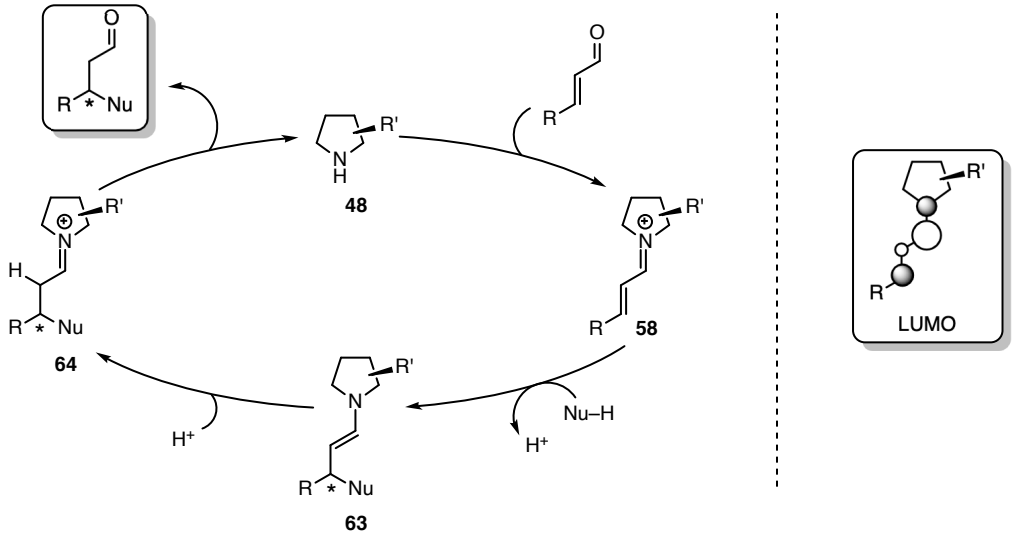
Modified proline derivatives have been developed in order to improve the solubility and the acidity of the directing proton.[166] They indeed resulted in major improvements in reactivity or selectivity in specific transformations but lacked the general applicability of proline. The direction of the electrophile by hydrogen bonding also requires the electrophile to have an electron lone pair which puts serious limitations to this methodology. Hence, the concept to induce stereoselectivity by shielding one side of the enamine by bulky substituents has emerged (*Scheme 1.21, left*). Especially, diarylprolinol silyl ethers employed by the groups of Jørgensen[180] and Hayashi[181] turned out to give outstanding enantiomeric excesses and consistent absolute configuration of the α-functionalised carbonyl independent of the nature of the electrophile. Today, a plethora of electrophiles and also nucleophiles when used in iminium catalysis, has been employed in catalysis with diarylprolinol silyl ethers.[166] Diphenylprolinol was first synthesised in 1934[182] and was used by Enders as a chiral auxiliary[183] and by Corey as a ligand in Lewis acid catalysed transformations[184] but rarely showed satisfying results in enamine catalysis. It was proposed that this is due to hemiaminal formation of the oxazolidine **62** as a parasitic equilibrium in the catalytic cycle (*Scheme 1.21, right*).[185] This problem was solved by protection of the free hydroxyl group which restored the catalytic activity.



Scheme 1.21: The origin of stereochemistry in reactions catalysed by diarylprolinol silyl ethers by steric shielding of the *Si*-face of the enamine (left). Catalyst deactivation by oxazolidine formation (right).

1.2.2 Iminium Catalysis

The condensation of α,β-unsaturated aldehydes with secondary amines **48** results in formation of a conjugated iminium ion **58** (*Scheme 1.22*). The electronic structure of this iminium closely resembles the π-orbitals in Lewis-acid catalysis and the energy of the LUMO is significantly lowered compared to the carbonyl, facilitating nucleophilic additions, conjugate additions, and pericyclic reactions. The conjugate addition of a nucleophile to the iminium in a stereoselective fashion results in the formation of an enamine **63** that after tautomerisation and hydrolysis delivers the β-functionalised carbonyl compound and liberates the catalyst.



Scheme 1.22: Catalytic cycle of β-functionalisation of carbonyl compounds by iminium activation (left) and depiction of the LUMO of the reactive iminium (right).

Determination of electrophilicity parameters (E_P) of different iminium ions **58** by kinetic measurements using nucleophiles with known nucleophilicity by Mayr and co-workers indicated that different iminium ions can show a significant variation in their electrophilicity (*Figure 1.5*).[186] In their studies, the simple pyrrolidine derived iminium **58a** showed the least electrophilicity while the electrophilicity of the iminium ion derived from trimethylsilyl-protected diphenylprolinol **58c** was 20-times higher. This was attributed to the electron withdrawing effects of the substituents. The iminium derived from imidazolidinones **58d** employed by MacMillan[157] showed the highest electrophilicity, explaining the variations in reactivity observed in the activation of enals with different aminocatalysts.

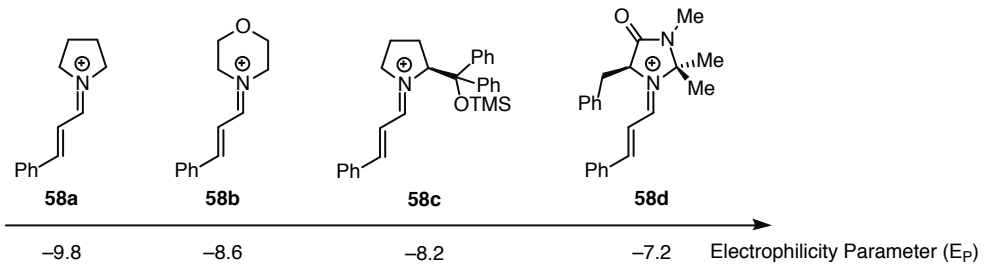
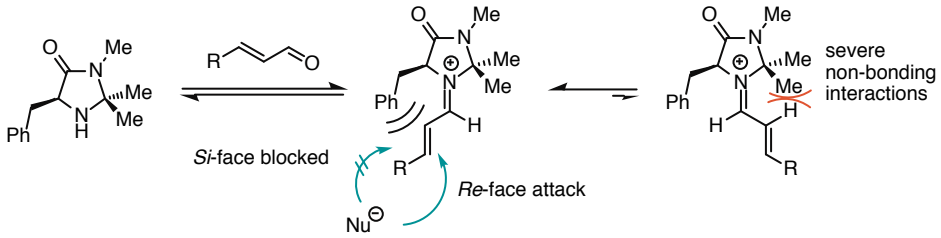


Figure 1.5: Relative electrophilicity of selected iminium ions.

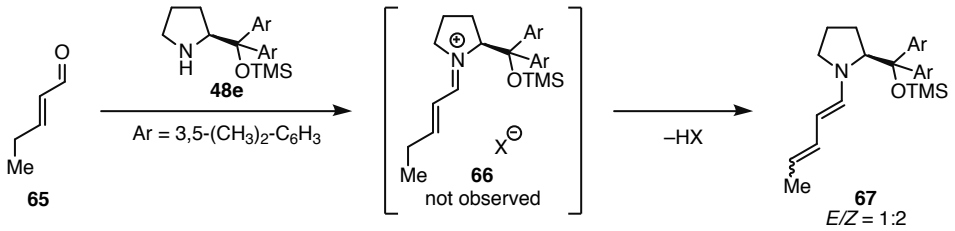
The iminium ions derived from imidazolidinones also show very high configurational stability and π-face discrimination leading to excellent enantiomeric excesses in these transformations (*Scheme 1.23*). Therefore, the imidazolidinones have been employed in numerous reactions proceeding under LUMO activation following the report by MacMillan and even show useful reactivity in enamine catalysis.[166]



Scheme 1.23: The configurational control of the C–N double bond in imidazolidinone derived iminiums only allows *Re*-face attack of nucleophiles, resulting in high stereocontrol.

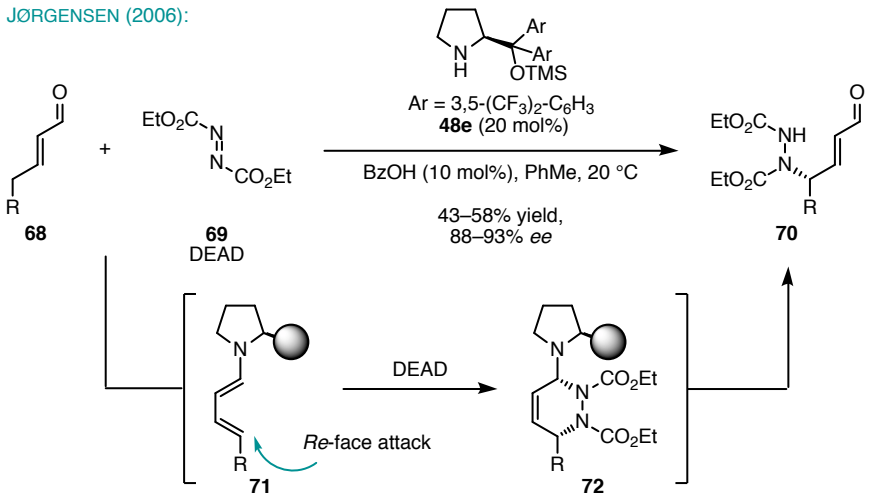
1.2.3 Dienamine Catalysis

In presence of a base, the iminium ion derived from α,β-unsaturated aldehydes and secondary amines can also tautomerise to the corresponding dienamine, which again shows nucleophilic character. During studies of the structure of iminium ions, dienamines were actually found to be the prevalent species in the reaction of trimethylsilyl diarylprolinol ether **48e** and *trans*-2-pentenal (**65**) (*Scheme 1.24*).[187]



Scheme 1.24: Deprotonation of the iminium ion leads to formation of a nucleophilic dienamine.

The resulting dienamine has been shown to be functionalised in α- or γ-position by diethyl azodicarboxylate (DEAD)[187–191] (*Scheme 1.25*) and to undergo intramolecular Diels-Alder cyclisations.[192]



Scheme 1.25: Organocatalytic γ-functionalisation of α,β-unsaturated aldehydes.

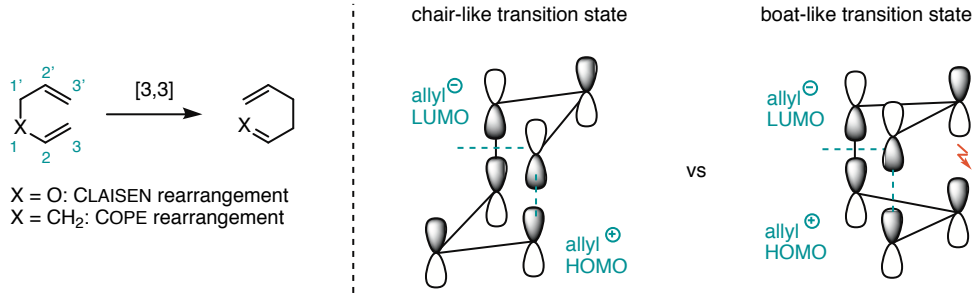
Overall, the popularity of catalysis with small organic molecules is based on their general stability compared to metal complexes so that processes become more operationally simple as the need to work under strict exclusion of air and water can be omitted. Furthermore, organocatalysts are based on non-toxic compounds making this approach attractive to pharmaceutical industry. In contrast to enzymes, organocatalysts are also easy to design and synthesise. The transformations are almost ideally step and atom economic, significantly enlarging the repertoire of the synthetic chemist.

1.3 Sigmatropic Rearrangements

Pericyclic reactions represent an efficient and reliable strategy in the synthesis of organic molecules.[193–195] They allow for straightforward construction of complex carbon frameworks. The stereochemical outcome can be easily predicted because bonds are broken and formed in a concerted, one-step mechanism *via* a cyclic transition state.[196] This has been described by three models: The Woodward-Hoffmann rules comprise a set of rules describing the feasability and stereochemistry by the consideration of the conservation of orbital symmetry.[197] Dewar and Zimmerman applied the concept of Hückel- and Möbius-aromaticity to predict the circumstances under which a reaction is possible.[198,199] Alternatively, Fukui demonstrated that also the frontier molecular orbitals can be used to describe pericyclic reactions.[200] Their contributions earned Hoffmann and Fukui the Nobel prize in 1981.

Pericyclic reactions include cycloadditions, cheletropic reactions, electrocyclisations and sigmatropic rearrangements. A sigmatropic rearrangement is a reaction where one σ-bond is intramolecularly converted into another. One substituent moves from one part of a π-system to another with simultaneous rearrangement of the π-system. Prominent examples of sigmatropic rearrangements are the Claisen rearrangement of allyl vinyl ethers to homoallyl carbonyl compounds[201–203] or the Cope rearrangement of 1,5-dienes (*Scheme 1.26*).[204] While the formation of a carbonyl moiety is the driving force for the Claisen rearrangement, the Cope rearrangement is virtually energy neutral. Both transformations are [3,3]-sigmatropic rearrangements

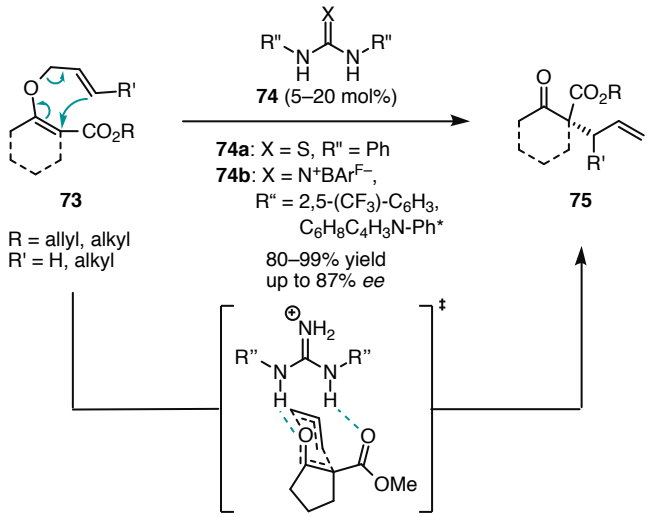
and therefore predicted by the Woodward-Hoffmann rules to proceed suprafacially. This means that the migrating group remains on the same side of the π-system. Especially the chair- and boat-like transition state have been extensively discussed.[205–208] Experiments indicated that the chair-like transition state is favoured, but the energy difference is small so that substrates that cannot adopt a chair-like transition state, undergo [3,3]-sigmatropic rearrangements *via* the boat-like transition state.[209]



Scheme 1.26: [3,3]-Sigmatropic rearrangements and their frontier molecular orbitals.

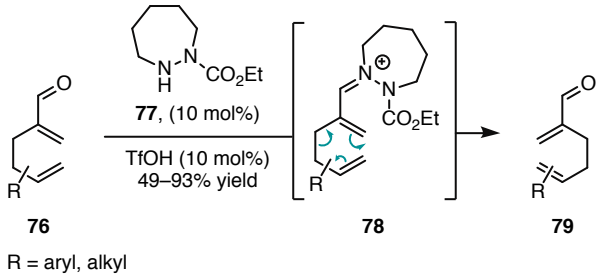
As for most pericyclic reactions, the concerted mechanism and the well-defined transition state allow for a high predictability of the stereochemical outcome of [3,3]-sigmatropic rearrangements. This led to a broad application in total synthesis,[210–214] especially of terpenes and terpenoids.[215] Furthermore, the accelerating effects of protic solvents and acids on the Claisen rearrangement has been observed[201,216–225] leading also to the development of numerous catalytic and asymmetric variants.[226,227]

For example, the groups of Hiersemann and Jacobsen independently developed organocatalytic Claisen rearrangements by hydrogen-bonding catalysis (*Scheme 1.27*).[228,229] The accelerating effect of either the thiourea catalyst **74a** employed by Hiersemann or the guanidine catalyst **74b** employed by Jacobsen is based on the stabilisation of developing charge on the oxygen atom by hydrogen-bonding.



Scheme 1.27: Organocatalytic Claisen rearrangement.

More recently, an organocatalytic Cope rearrangement was reported by Gleason and co-workers (*Scheme 1.28*).[230] They demonstrated that the rearrangement of 1,5-hexadiene-2-carboxyaldehydes **76** can be effectively catalysed by diazepane carboxylate (**77**). While they initially envisaged an accelerating effect in the Cope rearrangement by LUMO lowering upon formation of iminium **78**, preliminary calculations suggested that also a stepwise mechanism would be plausible.



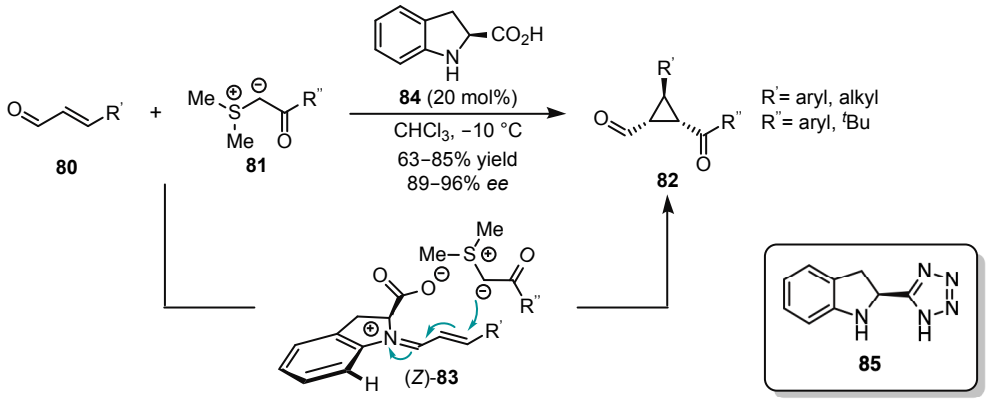
76 **78** **79**

Scheme 1.28: Organocatalytic Cope rearrangement developed by Gleason and co-workers.

1.4 Cyclopropanes in Aminocatalysis

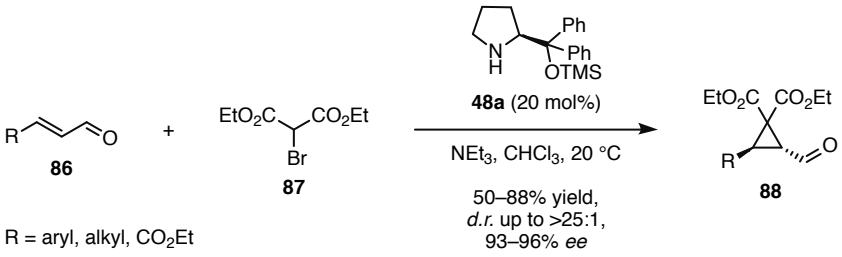
1.4.1 Organocatalytic Reactions Forming Cyclopropanes

Aminocatalysis has become a versatile tool in organic synthesis. However, exploiting the unique properties of cyclopropanes in this field has been limited to a few examples. The cyclopropyl motif has been utilised more often in the field of *N*-heterocyclic carbenes[231–234] and aminocatalysts have become more popular for the asymmetric synthesis of cyclopropanes by MIRC reactions (see section 1.1.4). Ylides are prominent nucleophiles, for instance in a Corey-Chaykovsky type cyclopropanation reported by MacMillan and Kunz in 2005 (*Scheme 1.29*).[235] The cyclopropanation of α,β-unsaturated aldehydes **80** with sulfonium ylides **81** delivered the corresponding cyclopropanes **82** in good yields and high enantiomeric excesses and proceeds *via* a (*Z*)–C=N iminium intermediate **83**. The corresponding *E*-iminium is disfavoured due to steric clash with the aryl C–H of the fused benzene ring. The approach of the ylid is thought to be governed by attractive electrostatic interactions with the carboxylate group in the catalyst **84**. A similar catalyst was later developed by Arvidsson, replacing the carboxylic group in **84** with a tetrazole. The catalyst **85** delivered somewhat improved diastereo- and enantioselectivities.[236] Also, peptides[237,238] and diamines[239] have been used as organocatalysts for the cyclopropanation of α,β-unsaturated aldehydes with stabilised sulphur ylides. Related cyclopropanations have also been reported employing for instance arsonium[129] or tertiary amine ylides.[240,241]



Scheme 1.29: Asymmetric cyclopropanation of α,β-unsaturated aldehydes with sulfonium ylides.

In addition to stabilised ylides, alkyl halides have become common amphiphiles in MICHAEL/alkylation cascades. The cyclopropanation of enals **86** with bromomalonate (**87**) yielding the corresponding cyclopropanes **88** has been developed independently by CÓRDOVA and co-workers and by WANG and co-workers (*Scheme 1.30*).[128,242–244] The only difference in their reactions was the utilised base. While WANG used 2,6-lutidine, CÓRDOVA and co-workers employed triethyl amine. VICARIO and co-workers later expanded the scope of the reaction using water as the solvent[245] and the reaction has also been realised in a flow set-up.[246] These results could be further improved by employing 2-bromo keto esters as amphiphiles.[247] A cyclopropanation of α-substituted α,β-unsaturated aldehydes with bromomalonate (**87**) was developed by CAMPAGNE and co-workers.[248]

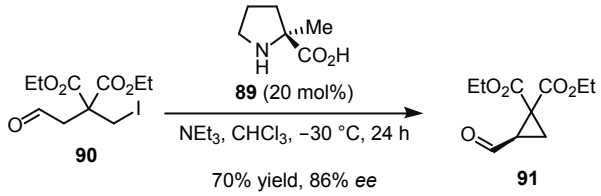


Scheme 1.30: Asymmetric cyclopropanation developed by CÓRDOVA and co-workers.

Other amphiphiles in MIRC cyclopropanations include bromonitromethane,[249–254] 3-chlorooxindole,[255] benzyl chloride,[256] α-alkyl-α-diazoesters,[257] or 4-alkenyl sulfamidates.[258] Furthermore, the organocatalytic cyclopropanation of nitroalkenes[259,260] and vinyl selenones[261] by addition of malonates as well as a MICHAEL addition following a 1,6-conjugate addition[262] have been reported.

Besides MIRC reactions other alkylation cascades have been employed to afford cyclopropanes. For example, the catalytic alkylation of enamines using proline derived catalysts had been a long-standing problem in organocatalysis until LIST and VIGNOLA achieved the first intramolecular asymmetric α-alkylation to form chiral cycloalkanes (*Scheme 1.31*).[263] The key to their success was the geminal disubstitution to accelerate the desired ring closure and to shut down undesired pathways. Using 20 mol% of 2-methylproline (**89**) as catalyst and alkyl iodide **90** as substrate, cyclopropane **91** could be obtained in high yield and high

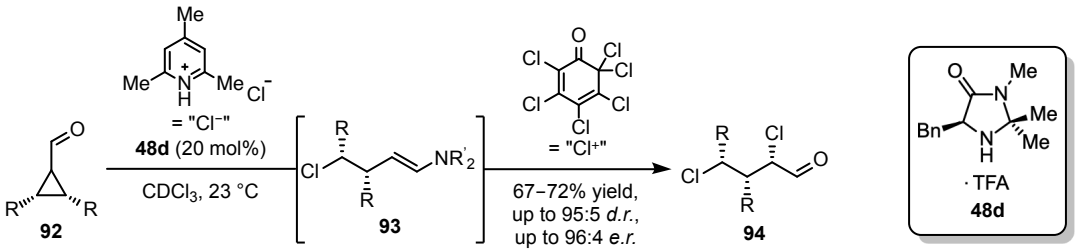
enantioselectivity. A similar method was employed by Huang and co-workers to obtain a variety of chiral bicyclo[3.1.0]hexanes by an α-iodination/double alkylation cascade.[264]



Scheme 1.31: List's intramolecular α-alkylation.

1.4.2 Organocatalytic Activation of Cyclopropanes

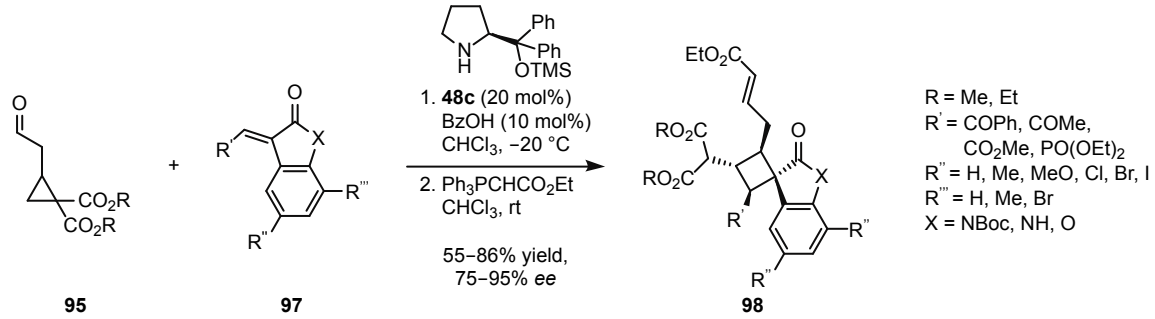
The spring-loaded character of cyclopropanes accounts for several reactivities. In the investigation of reaction mechanisms they are used as radical clocks to detect free radicals with their centre adjacent to the cyclopropane (see section 1.1.2). Despite their use as mechanistic tool, cyclopropylcarbaldehydes have been proven to be useful substrates for aminocatalysis in general. In 2009, Wang and co-workers were able to show that the reaction of cyclopropylcarbaldehydes with aryl thiols in the presence of proline leads to a ring-opening reaction.[265] Interestingly, even though a chiral catalyst was employed, the corresponding products were only obtained as racemic mixtures. Nevertheless, a similar concept was applied by the group of Gilmour to achieve the first asymmetric 1,3-dichlorination of symmetric cyclopropylcarbaldehydes **92** by cyclopropyl-iminium-activation (*Scheme 1.32*).[266] The cyclopropylcarbaldehydes **92** condense with an enantioenriched imidazolidinone **48d** to form chiral iminium ions. The attack of a chloride in β-position then leads to an opening of the cyclopropane moiety. Due to racemisation of the monochlorinated products **93** the intermediate enamines are intercepted by a chloronium electrophile. The corresponding dichlorinated aldehydes **94** can be obtained in good yields and with an enantiomeric ratio up to 96:4. Later, Reyes and Merino could show that also γ-acyloxy-substituted aldehydes can be obtained if the chiral iminium ion is attacked by carboxylic acids.[267]



Scheme 1.32: Asymmetric 1,3-dichlorination of symmetric aldehydes.

Recently, Jørgensen and co-workers developed a method that allows for the activation of cyclopropanes by enamine catalysis (*Scheme 1.33*).[268] The condensation of an acceptor substituted cyclopropyl substituted aldehyde **95** with a proline-based catalyst **48c** leads to the formation of a donor-acceptor substituted cyclopropane **96** *in situ* (not shown). Subsequent formal [2+2]-cycloaddition of **96** to suitable substrates **97**

results in the enantioselective formation of cyclobutanes **98** with good yields and high enantiomeric excesses. It has proven to be essential that the cyclopropylcarbaldehyde carries two identical acceptors, otherwise an additional stereogenic centre is generated without selectivity. A similar concept was applied by Reyes and Vicario who could show that dihydroquinolines can be obtained by domino reaction of aminobenzaldehydes with donor-acceptor substituted cyclopropanes formed *in situ*.[269]

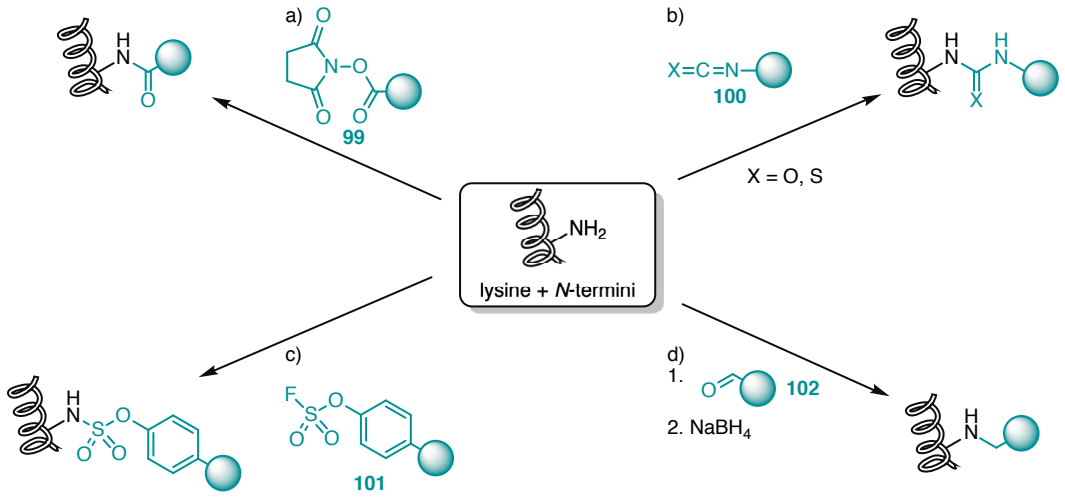


Scheme 1.33: Synthesis of enantioenriched cyclobutanes **98** *via* formal [2+2]-cycloaddition of **95** to **97**.

1.5 Covalent Modification of Lysine

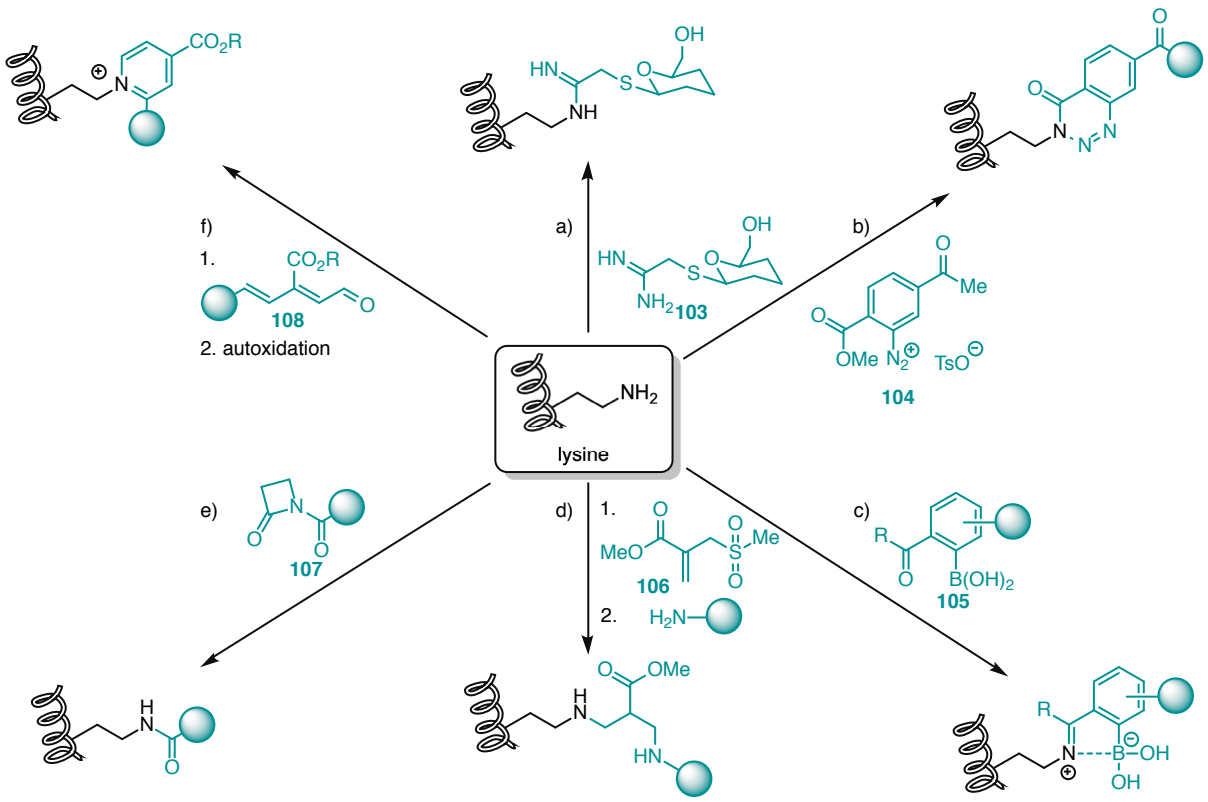
Covalent modifications of proteins are important for studying their function, developing targeted covalent inhibitors and for the synthesis of drug delivery constructs.[270,271] In general, protein modification can be achieved by incorporation of unnatural reactive entities, which yields homogeneously modified proteins but requires tedious biochemical processes.[272–275] On the other hand, the specific reactivity of proteinogenic amino acid residues can be exploited. The latter being a less complicated approach, especially when uniform or selective modification is not necessary.[276,277] Cysteine is an attractive target as its thiol group is usually the strongest nucleophile under physiologic conditions and off-target as well as non-specific tagging is minimised.[278–281] Unfortunately, cysteine constitutes only 2% of the human proteome and is found in only 15% of the protein pockets[282,283] which limits the applicability of this method. However, with 6% of the human proteome, lysine is three times more abundant and is typically found on protein surfaces, on interfaces mediating protein-protein interactions, and in binding cavities. Lysine plays an important role in catalysis, by acting either as a base or by activating substrates *via* hydrogen bonds. It is therefore often indispensable in protein active sites and resistance mutations as they occur for cysteine are much less likely.[270]

The most common covalent modification of lysine includes *N*-hydroxysuccinimide (NHS) esters **99** (*Scheme 1.34, a*),[284] isocyanates and isothiocyanates **100** (*b*)[270] or sulfonyl fluorides **101** (*c*)[285] but selectivity might be problematic when stronger nucleophiles are present. In general, the selectivity of the presented methods is governed by the fact that hard nucleophiles are used, reacting preferably with the harder amino group of lysine than with the softer sulfhydryl group of cysteine.[273] Aldehydes have also been used for the selective modification of lysine[286,287] but the reversibility of the formed Schiff base requires imine reductions which are often incompatible with the protein's function (*d*).[288,289]



Scheme 1.34: Classical methods for the modification of lysine.

Recently, more sophisticated examples of lysine modification have been reported (*Scheme 1.35*). The ε-amino group can be modified by either formation of amidines **103** (*a*)[290,291] or triazones from diazonium terephthalates **104** (*b*).[292] It was shown that the imine can be stabilised by an adjacent boronate (*c*).[293,294] Also, amine formation by a reaction with sulfonyl acrylates **106** (*d*)[295] and amide formation by a reaction with β-lactams **107** is possible (*e*).[296,297] In addition, the group of Tanaka developed an α,β,γ,δ-unsaturated aldehyde **108**. Upon condensation with lysine, an imine is formed that rapidly undergoes 6π-aza-electrocyclisation. Subsequent autoxidation then generates stable pyridinium salts (*f*).[298–300]



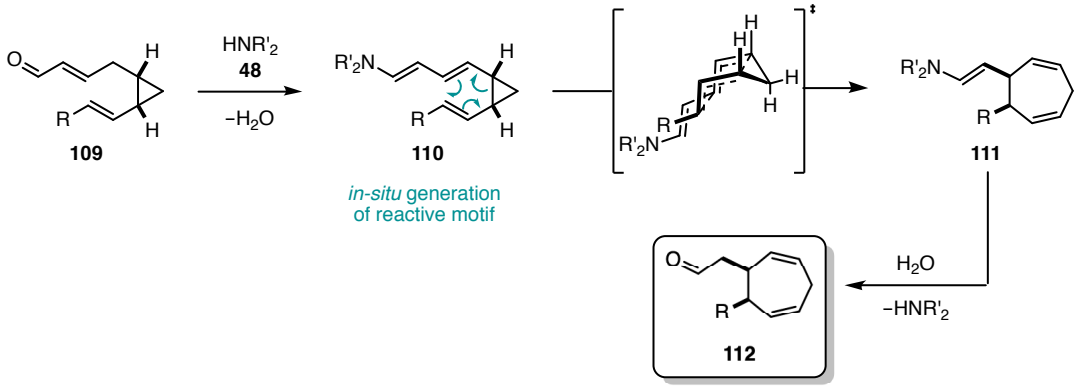
Scheme 1.35: Recent site-selective modifications of the ε-amino group of lysine.

These examples demonstrate that, even though there are numerous methods for covalent modification of proteins established, new reagents are still needed to extend the possibilities to study the function of different proteins.

2 Objectives

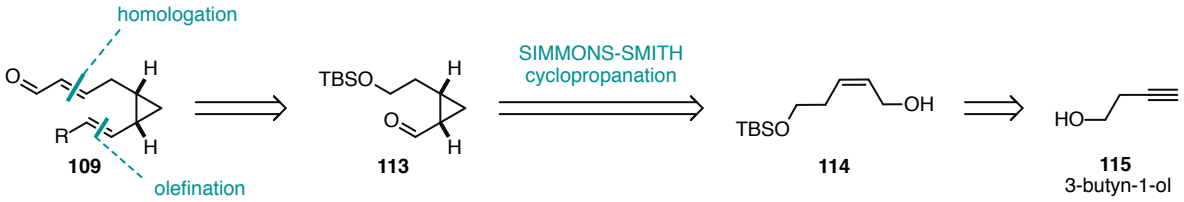
2.1 Development of a Dienamine-Induced DVCPR

Based on the organocatalytic Cope rearrangement developed by Gleason and co-workers (*Scheme 1.28*) a new approach for organocatalytic pericyclic reactions was pursued. Generating a 1,5-diene *in situ* by dienamine activation would constitute a mechanistically new approach for [3,3]-sigmatropic rearrangements. The Cope-like rearrangement of divinylcyclopropanes into cycloheptadienes was chosen as a model reaction as it also benefits from the additional driving force of ring-strain release (*Scheme 2.1*). It was anticipated that treatment of *cis*-4-(2-vinylcyclopropyl)but-2-enals **109** with secondary amine catalyst **48** would generate reactive *cis*-divinylcyclopropanes **110**. Their spontaneous [3,3]-sigmatropic rearrangement was expected to result in the formation of cycloheptadienes **111**. Hydrolysis of enamine **111** would then release the catalyst and the desired cycloheptadienals **112**.



Scheme 2.1: Planned transformation of *cis*-divinylcyclopropylcarbaldehydes to cycloheptadienals.

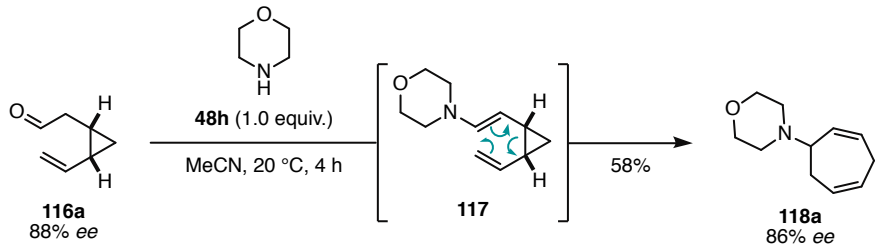
At the beginning of these studies, no general methodology was known for the synthesis of 4-(2-vinylcyclopropyl)but-2-enals **109**. Therefore, the development of an efficient synthetic strategy was a key challenge. Substrates for this transformation should be obtained from aldehyde **113** by olefination of the carbonyl moiety by either Wittig[301,302] or Horner-Wadsworth-Emmons[303] reaction and subsequent cleavage of the silyl ether (*Scheme 2.2*). The resulting alcohol could then be oxidised to the aldehyde and converted to the desired α,β-unsaturated system **109** by one-pot Wittig reaction/acetal cleavage.[304] Aldehyde **113** should be accessible from *Z*-olefin **114** by Simmons-Smith reaction and oxidation of the alcohol.[122,123] Olefin **114** would result from partial hydrogenation of the alkyne obtained from addition of protected 3-butyn-1-ol to formaldehyde.



Scheme 2.2: Retrosynthetic analysis of α,β-unsaturated aldehydes **109**.

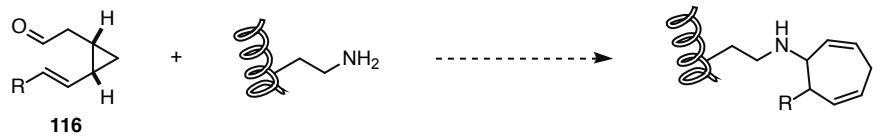
2.2 Application of the Developed Methodology to the Covalent Modification of Proteins

The synthesis of α,β-unsaturated aldehydes **109** delivered 2-(2-vinylcyclopropyl)ethanals **116** as intermediates. Previous studies demonstrated that these react with secondary amines in a condensation reaction (*Scheme 2.3*).[305] The resulting enamine **117** still underwent DVCPR but this time, a stable tertiary amine **118** was obtained. For example, the condensation of unsubstituted vinylcyclopropyl aldehyde **116a** with morpholine (**48h**) afforded tertiary amine **118a** in 58% yield and without erosion of the enantiomeric excess.



Scheme 2.3: Reaction of vinylcyclopropyl ethanal **116a** with morpholine (**48h**).

This concept should be utilised to selectively modify lysine residues in proteins in a similar fashion to the 6π-azaelectrocyclisation developed by Tanaka and co-workers (*Scheme 1.35, f*).[298–300] Unfortunately, previous studies showed that the unsubstituted vinylcyclopropyl aldehyde **116a** is extremely volatile and therefore not suited for such an application. Larger substituents on the double bond should raise the boiling point of the compounds and their addition to free lysine ε-amino groups should deliver stable adducts (*Scheme 2.4*).



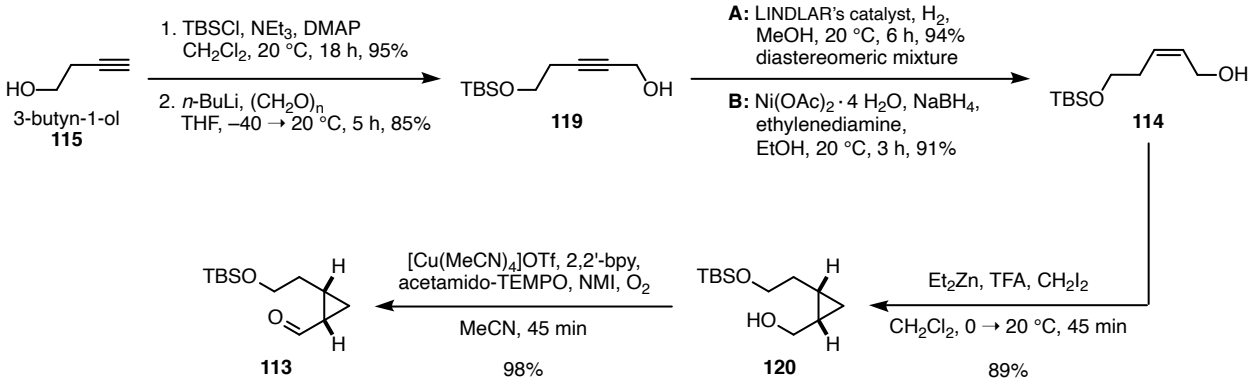
Scheme 2.4: Planned modification of proteinogenic lysine residues with cyclopropyl aldehydes.

3 Results

3.1 Dienamine-Induced Divinylcyclopropane-Cycloheptadiene Rearrangement

3.1.1 First Generation Synthesis of Substrates

A general approach to 4-(2-vinylcyclopropyl)but-2-enals **109** for the DVCPR was pursued starting from aldehyde **113**. The aldehyde **113** was synthesised from 3-butyn-1-ol (**115**, *Scheme 3.1*). Silylation of the hydroxyl group gave the silyl ether in 95% yield. The alkyne was deprotonated by *n*-butyllithium. Addition of the so generated carbanion to paraformaldehyde gave the desired propargylic alcohol **119** in 85% yield.[306] Partial hydrogenation of the alkyne gave olefin **114**. Although, excellent yields could be achieved using Lindlar's catalyst,[307] **114** was obtained as an inseparable mixture of *E*/*Z*-isomers. Hydration with Ni P2 complex[308] circumvented this problem and delivered solely the *Z*-olefin in an equally good yield. The allylic alcohol **114** was then converted to the cyclopropane **120** by Simmons-Smith reaction.[122,123] Stahl oxidation finally gave the desired aldehyde **113** in almost quantitative yield.[309]

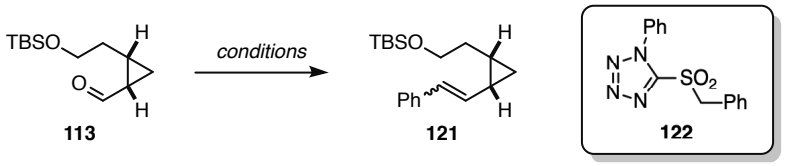


Scheme 3.1: Synthesis of aldehyde **113**.

Wittig-olefination[301,302] of aldehyde **113** gave the desired alkene **121** in excellent yield albeit with poor *E*/*Z*-selectivity (*Table 3.1*, entry 1). Since both isomers could possibly react in the desired rearrangement, it was attempted to improve the selectivity either towards the *E*- or the *Z*-isomer. The Schlosser modification[310] indeed enhanced the *E*/*Z*-selectivity to 4:1 but the yield dropped drastically (entry 2). In this reaction, addition of phenyllithium should result in the formation of a β-oxide ylide accounting for the stereoselectivity. However, conduction of the Gilman-test for detection of organolithium species[311] indicated that this transformation did not take place. Decreased yield and poor stereoselectivity could arise because of that. The Julia-Kocienski

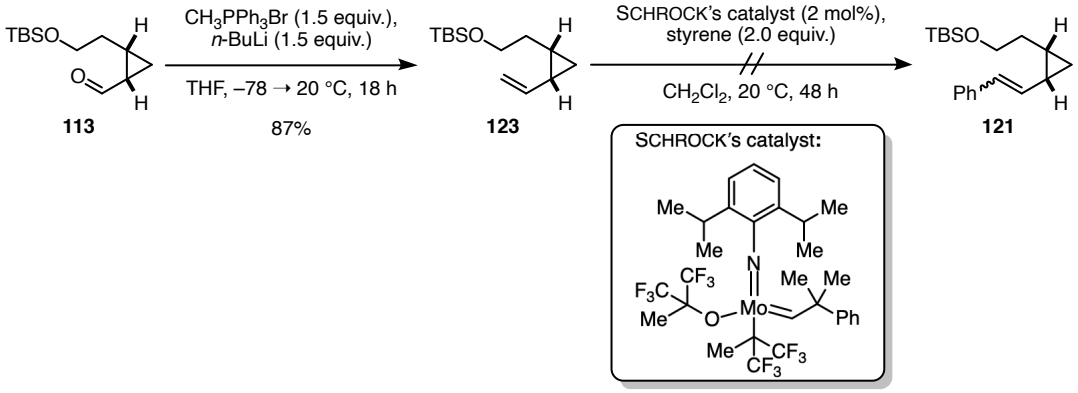
reaction with sulfone **122** led to an improved *E*/*Z*-selectivity of 3.5:1 but only in a moderate yield (entry 3).[312] By Julia olefination,[313] the *Z*-isomer of **121** could be obtained but only in 2% yield (entry 4).

Table 3.1: Conditions for the olefination of aldehyde **113**.



Entry	Reagents	Solvent	Temperature	Time	Yield	*E*/*Z*
1	$BnPPh_3Br$ (1.5 equiv.), *n*-BuLi (1.5 equiv.)	THF	−78→20 °C	3 h	93%	2:1
2	$BnPPh_3Br$ (1.0 equiv.), PhLi (1.5 equiv.), HCl (1.1 equiv.), KO*t*-Bu (1.5 equiv.)	THF/Et_2O	−78→20 °C	2 h	22%	4:1
3	**122** (1.0 equiv.), KHMDS (1.1 equiv.)	DME	−60→20 °C	18 h	57%	3.5:1
4	$PhCH_2SO_2py$ (1.0 equiv.), KHMDS (2.0 equiv.)	PhMe	20 °C	18 h	2%	1:2

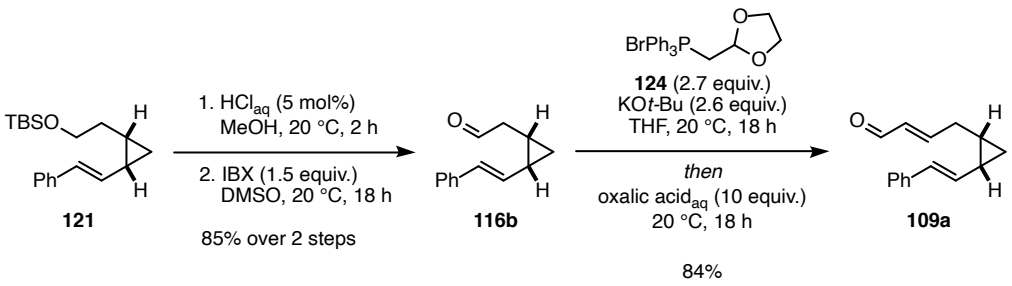
It was also attempted to obtain the desired olefin by a metathesis reaction (*Scheme 3.2*). Therefore, aldehyde **113** was converted to the terminal olefin **123** by Wittig olefination. However, reaction of **123** with styrene and Schrock's catalyst gave only traces of the desired product.[314]



Scheme 3.2: Synthesis of olefin **123** and attempted olefin metathesis.

Since the synthesis of **121** could not be optimised towards a single double bond isomer, the *E*/*Z*-mixture was separated by preparative HPLC. The silyl ether of *E*-**121** was cleaved, and the resulting alcohol was oxidised with 2-iodoxybenzoic acid (IBX) to deliver the aldehyde **116b** (*Scheme 3.3*). **116b** could then be converted

into the desired α,β-unsaturated aldehyde **109a** in a one-pot sequence consisting of Wittig reaction with the phosphonium salt **124** and subsequent cleavage of the acetal under acidic conditions.[304]

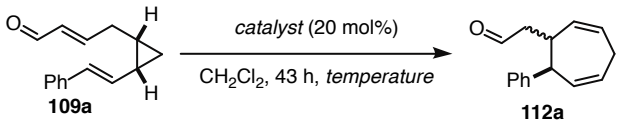


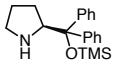
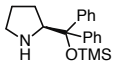
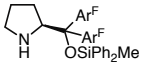
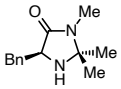
Scheme 3.3: Completion of the synthesis of **109a**.

3.1.2 Rearrangement of Enal 109a

With the α,β-unsaturated aldehyde **109a** in hand, the dienamine-induced DVCPR was investigated. Subjection of **109a** to different secondary amines led to moderate conversion to the desired cycloheptadiene **112a** (*Table 3.2*). Although a moderate conversion was achieved with pyrrolidine (**48f**) and piperidine (**48g**), *cis/trans*-selectivity was low (entries 1 and 2). When morpholine (**48h**) was used, the reaction rate was drastically reduced, and the selectivity did not improve (entry 3). Pleasantly, when the Jørgensen-Hayashi catalyst **48c** [185] was used, **112a** was obtained in an excellent yield of 96% and with high diastereoselectivity (entry 4). While the reaction rate could be increased by conducting the rearrangement at 40 °C the yield was decreased to 72% (entry 5). This might be due to the thermal instability of **48c**.[315] When the sterically more encumbered diaryl prolinol ether **48d** was used, the yield dropped to 60% (entry 6). Use of the MacMillan imidazolidinone **48b** [316] virtually gave no conversion.

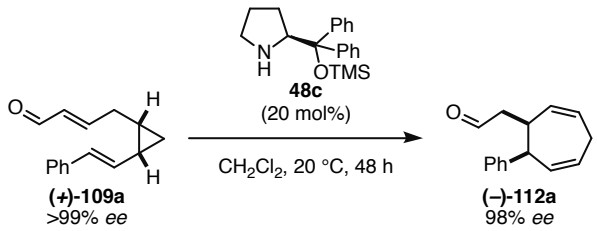
Table 3.2: Reaction of **109a** with different secondary amines.



Entry	Catalyst	Temperature	Yield[a]	*cis*/*trans*[a]
1	 **48f**	20 °C	31%	3:1
2	 **48g**	20 °C	38%	3:1
3	 **48h**	20 °C	7%	2:1
4	 **48c**	20 °C	96%	>20:1
5[b]	 **48c**	40 °C	72%	>20:1
6	 **48d**	20 °C	60%	>20:1
7	 **48b**	20 °C	2%	>20:1

Ar^F= 3,5-$(CF_3)_2$-C_6H_3
[a] Determined by GC-MS using methoxynaphthalene as standard.
[b] Conversion was complete after 24 h.

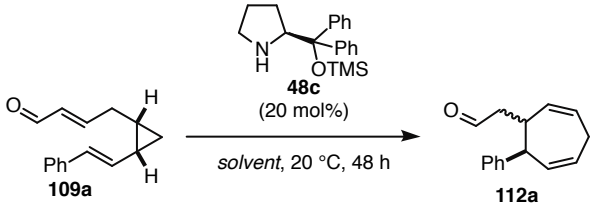
Although **48c** was used as a single enantiomer, no kinetic resolution was observed. However, it was possible to show that use of enantioenriched starting material leads to the formation of a likewise enantioenriched cycloheptadiene (*Scheme 3.4*). Enantioenriched **109a** was obtained by chiral HPLC from racemic **109a**.



Scheme 3.4: Conversion of enantiopure **109a**.

The yield of **112a** and the diastereoselectivity of the reaction proved to be highly solvent dependent (*Table 3.3*). The use of a very polar solvent led to decreased yield (DMSO, entry 1). In ethereal solvents as well as in ethyl acetate and acetonitrile, the reaction rate was significantly lowered (entries 2, 3, 5, and 8). It has been shown that cleavage of the silyl ether of **48c** is faster in these solvents[315] but this can only partly explain the poor yields as the use of unpolar solvents (cyclohexane and PhMe) also led to decreased yields (entries 10 and 11). The use of chlorinated solvents (1,2-dichloroethane and dichloromethane, entries 4 and 6) resulted in yields over 70%. Surprisingly, chloroform and chlorobenzene led again to moderate yields of **112a** (entries 7 and 9). In cyclohexane, diethyl ether, chlorobenzene, and 1,2-dichloroethane formation of polar side-products was observed but they could not be identified.

Table 3.3: Effect of different solvents on the DVCPR of **109a**.



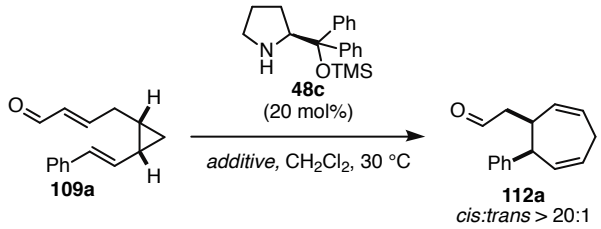
Entry	Solvent	Yield[a]	*cis*/*trans*[a]
1	DMSO	9%	>20:1
2	MeCN	47%	>20:1
3	EtOAc	31%	>20:1
4	1,2-DCE	78%	>20:1
5	THF	29%	>20:1
6	CH_2Cl_2	96%	>20:1
7	chlorobenzene	34%	5:1
8	Et_2O	41%	>20:1
9	$CHCl_3$	38%	>20:1
10	PhMe	34%	>20:1
11	cyclohexane	26%	3:1

[a] Determined by GC-MS using methoxynaphthalene as standard.

It has been shown that additives can have a significant effect on organocatalytic transformations, especially on the reaction rate.[317,318] Attempting shorter reaction times, different additives were surveyed (*Table 3.4*). The use of 1 mol% of acid proved to be beneficial for the reaction rate but the yield of **112a** dropped to about 70% (HCl, AcOH and BzOH, entries 1, 7 and 13). The yield further decreased when more acid was added or when the reaction time was prolonged (entries 2–4, 8–12 and 14–16), suggesting that one of the reagents or the product is not stable under these conditions. Furthermore, it was sufficient to use 0.1 mol% of acetic acid

to increase the reaction rate but the yield remained moderate (entries 5 and 6). The highest reaction rate was observed using 1 mol% of *m*-nitrobenzoic acid which showed complete conversion in 2 h with a yield of 72% (entry 17). Again, use of more equivalents of this acid or prolonged reaction time led to significant decomposition (entries 18–22). Methanol and potassium carbonate have also been reported to accelerate enamine formation.[319] Using these additives, it was possible to obtain complete conversion in 24 h with a yield of 71% and 81%, respectively (entries 23 and 24). As lower yields for **112a** were obtained in all cases, the use of additives was omitted.

Table 3.4: Effect of different additives on the DVCPR of **109a**.

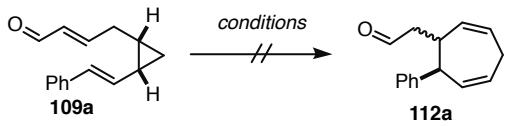


Entry	Additive	mol%	Time [h]	Yield[a]
1	HCl	1.0	24	65%
2	HCl	5.0	24	49%
3	HCl	10	24	34%
4	HCl	20	24	5%[b]
5	AcOH	0.1	8	68%
6	AcOH	0.1	24	71%
7	AcOH	1.0	8	68%
8	AcOH	5.0	8	61%
9	AcOH	10	4	83%
10	AcOH	10	8	50%
11	AcOH	20	4	64%
12	AcOH	20	8	45%
13	BzOH	1.0	8	71%
14	BzOH	5.0	8	50%
15	BzOH	10	8	32%
16	BzOH	20	8	28%
17	*m*-NO_2-BzOH	1.0	2	72%
18	*m*-NO_2-BzOH	5.0	2	54%
19	*m*-NO_2-BzOH	10	2	51%
20	*m*-NO_2-BzOH	10	7	44%
21	*m*-NO_2-BzOH	20	2	42%
22	*m*-NO_2-BzOH	20	7	41%
23	MeOH	20	24	71%
24	K_2CO_3	20	24	81%

[a] Determined by GC-MS using methoxynaphthalene as standard.
[b] *d.r.* 8:1.

Control reactions confirmed that the organocatalyst is vital in this transformation since no conversion was observed without the amine catalyst (*Table 3.5*). Also, under general acidic or basic conditions no conversion could be detected (entries 1,2 and 4). The DVCPR of silyl enol ethers was demonstrated by Piers and co-workers in 1986.[73] However, attempts to form the corresponding silyl enol ether of **109a** with potassium bis(trimethylsilyl)amide (KHMDS) and trimethylsilyl chloride were not successful (entry 3). When the *trans*-isomer of **109a** was used no conversion could be observed after 48 h at either 20 °C or 50 °C.

Table 3.5: Control reactions.



109a **112a**

Entry	Reagents (equiv.)	Conditions	Time [h]	Result
1	AcOH (1.0)	CH_2Cl_2, 20 °C	24	n.c.
2	KHMDS (1.0)	CH_2Cl_2, −78→20 °C	24	n.c.
3	KHMDS (1.0), TMSCl (1.0)	CH_2Cl_2, −78→20 °C	24	n.c.
4	Cs_2CO_3 (1.0)	CH_2Cl_2, 20 °C	24	n.c.
5[a]	**48c**	CH_2Cl_2, 20 °C	48	n.c.
6[a]	**48d**	CH_2Cl_2, 50 °C	48	n.c.

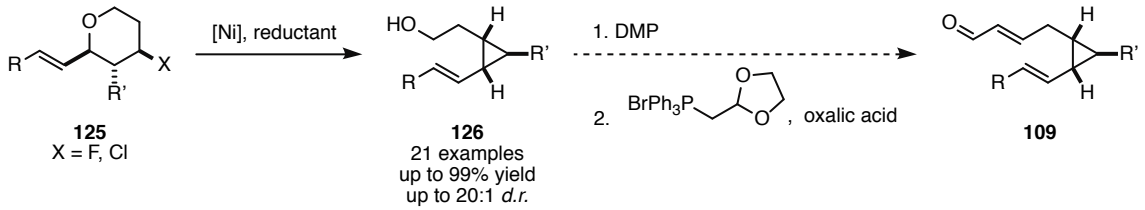
n.c.: no conversion; [a] The *trans*-cyclopropane was used instead of **109a**.

3.1.3 Synthesis of α,β-Unsaturated Aldehydes 109 by Nickel-Catalysed Reductive Coupling of Tetrahydropyrans

As described in section 3.1.1, the synthesis of **109a** was achieved in 9 steps from 3-butyn-1-ol (**115**) with an overall yield of 29%. In addition, the phenyl group was introduced in a relatively early stage of the synthesis, which would render the synthesis of a comprehensive substrate library tedious. Therefore, it was desirable to shorten the synthesis and to introduce the different substituents in the latest stage possible so that most derivatives of **109** would be accessible from one common precursor.

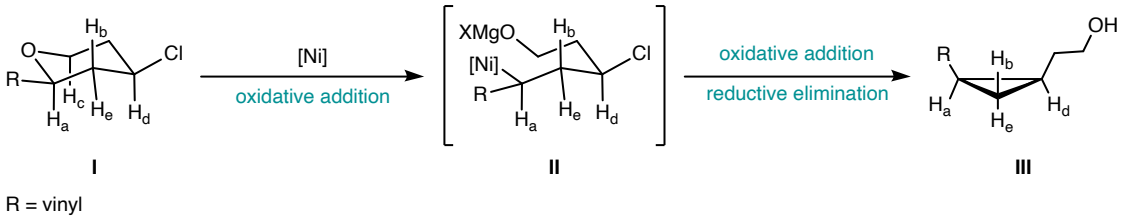
In 2016, the group of Jarvo developed a nickel-catalysed reductive cross-coupling reaction of 2-vinyl-4-halo-tetrahydropyrans **125** to vinylcyclopropanes **126**.[320] This transformation was reported to be stereospecific and to proceed with high yields. The resulting di- or trisubstituted vinylcyclopropyl alcohols could possibly be converted to the desired α,β-unsaturated aldehydes **109** in two already established steps (*Scheme 3.5*). Furthermore, by introduction of a substituent **R'** on the cyclopropane moiety the influence of this substitution pattern on the DVCPR could be studied as additional substituents at this position have been shown to have a major effect on the reaction kinetics of the DVCPR.[82]

JARVO 2016:



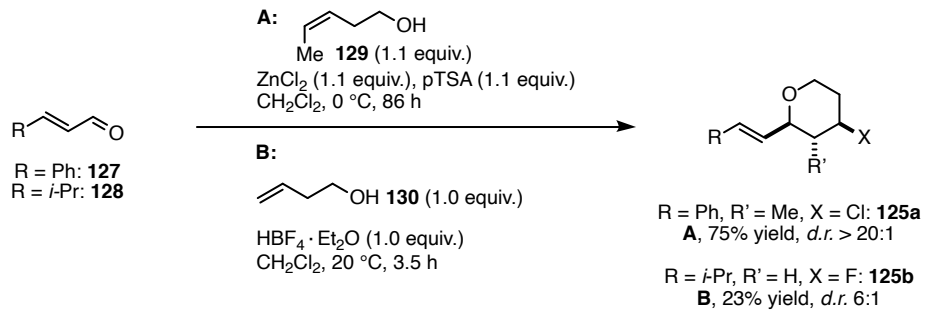
Scheme 3.5: The nickel-catalysed reductive cross-coupling of 2-vinyl-4-halotetrahydropyrans **125** for the synthesis of **109**.

It was proposed that the stereospecific outcome of the nickel-catalysed reductive coupling would be rationalised by an initial oxidative addition to the vinyl ether **I** with retention of the stereochemistry while the second oxidative addition to the halide and the reductive elimination would proceed under inversion of the configuration leading to the *cis*-configurated cyclopropane **III** (*Scheme 3.6*).[321]



Scheme 3.6: Proposed mechanism for the stereospecificity of the nickel-catalysed reductive cross-coupling.

The tetrahydropyrans **125** were obtained by PRINS cyclisation of the α,β-unsaturated aldehydes **127** and **128** with the homoallyl alcohols **129** and **130**, respectively (*Scheme 3.7*). While the PRINS reaction of cinnamaldehyde **127** with **129** delivered the desired ether **125a** in a good yield of 75%, the cyclisation of **128** with homoallyl alcohol **130** was attempted several times. The best yield was 23% with an *d.r.* of 6:1 but the tetrahydropyran **125b** showed significant impurities. However, purification of **125b** proved to be difficult and could not be achieved by column chromatography, bulb-to-bulb distillation or combinations thereof.

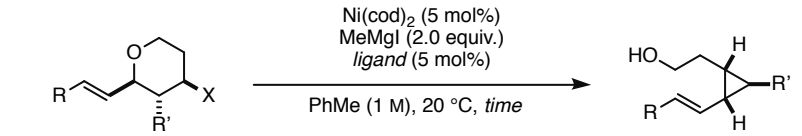


Scheme 3.7: Synthesis of tetrahydropyrans **125a** and **125b**.

The synthesis of **131** was described using XantPhos as a ligand. Attempts to reproduce the results of JARVO and co-workers delivered **131** only in a yield of 43% and with a *d.r.* of 7:1 (*Table 3.6*, entry 1). Methyl magnesium iodide which was used as a reductant in this reaction was freshly prepared by a procedure which

was also described by the authors but only when this reagent was filtered over celite instead of the described fritted Schlenk filter the yield could be increased to 67% (entry 2). The reductive coupling of **125b** to **132** was performed using BPhen as a ligand. The published procedure gave **132** on a 3.6 mmol scale in a yield of 6% as a diastereomeric mixture that was not further determined (entry 3). Running the reaction on a smaller scale and with a slightly prolonged reaction time gave **132** in 8% yield, but the product could not be purified by column chromatography (entry 4). By use of methyl magnesium iodide which was filtered over celite the yield of **132** could be increased to 12% but purification was still not possible (entry 5). On a larger scale, the yield dropped again to 9% (entry 6). However, when the reaction was run on a small scale of 0.3 mmol **132** was obtained in 34% yield albeit with a *d.r.* of 4:1 (entry 7). Running the cross-coupling at higher concentration or at elevated temperatures did not increase the yield (entries 8 and 9). Exhaustive degassing of the solvent made it possible to obtain a yield of 21% of **132** also on a larger scale (entry 10) but overall the results of Jarvo and co-workers could not be completely reproduced.

Table 3.6: Nickel-catalysed reductive coupling of tetrahydropyrans **125**.



R = Ph, R' = Me, X = Cl: **125a**
R = *i*-Pr, R' = H, X = F: **125b**

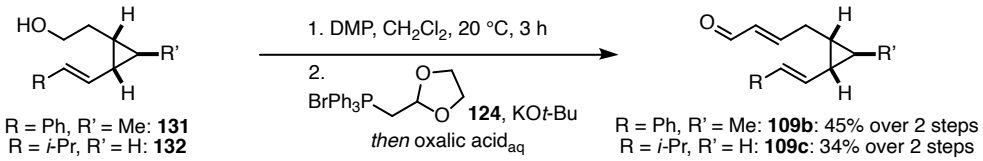
R = Ph, R' = Me: **131**
R = *i*-Pr, R' = H: **132**

Entry	R	R'	X	Ligand	Scale	Time	Result
1	Ph	Me	Cl	XantPhos	0.4 mmol	18 h	43% yield, *d.r.* 7:1
2[a]	Ph	Me	Cl	XantPhos	0.4 mmol	20 h	67% yield, *d.r.* > 20:1
3	*i*-Pr	H	F	BPhen	3.6 mmol	18 h	6% yield, diastereomeric mixture
4	*i*-Pr	H	F	BPhen	0.6 mmol	20 h	8% yield, impurities
5[a]	*i*-Pr	H	F	BPhen	0.6 mmol	20 h	12% yield, impurities
6[a]	*i*-Pr	H	F	BPhen	3.7 mmol	20 h	9% yield, impurities
7	*i*-Pr	H	F	BPhen	0.3 mmol	24 h	34% yield, *d.r.* 4:1
8[b]	*i*-Pr	H	F	BPhen	0.3 mmol	24 h	16% yield, *d.r.* 4:1
9[c]	*i*-Pr	H	F	BPhen	0.3 mmol	24 h	11% yield, *d.r.* 4:1
10[d]	*i*-Pr	H	F	BPhen	1.7 mmol	24 h	21% yield, *d.r.* 4:1

[a] MeMgI was filtered over Celite.
[b] 0.1 M instead of 1.0 M.
[c] The reaction was run at 30 °C.
[d] PhMe was degassed 3 times by freeze-pump-thaw.

Nevertheless, **132** was separated from the unwanted stereoisomer by means of preparative HPLC. Alcohols **131** and **132** could be converted to the desired cyclopropanes **109b** and **109c** by oxidation with Dess-Martin periodinane (DMP) and subsequent homologation in 45% and 34%, respectively (*Scheme 3.8*). It could be

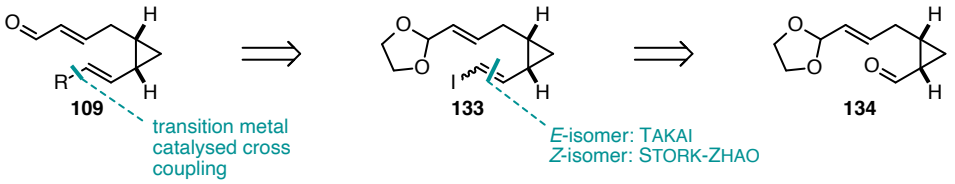
demonstrated that the nickel-catalysed cross-coupling described by Jarvo and co-workers is a viable method to shorten the synthesis of aryl vinyl cyclopropanes, since **109b** could be synthesised in 4 steps starting from cinnamic aldehyde. However, different substituents still would have to be introduced in the starting material, rendering this synthetic route unattractive for a large substrate library. Additionally, the results concerning the alkyl substituted compound **132** could not be reproduced so that a general route towards the vinyl substituted cyclopropanes is still sought after.



Scheme 3.8: Synthesis of **109b** and **109c**.

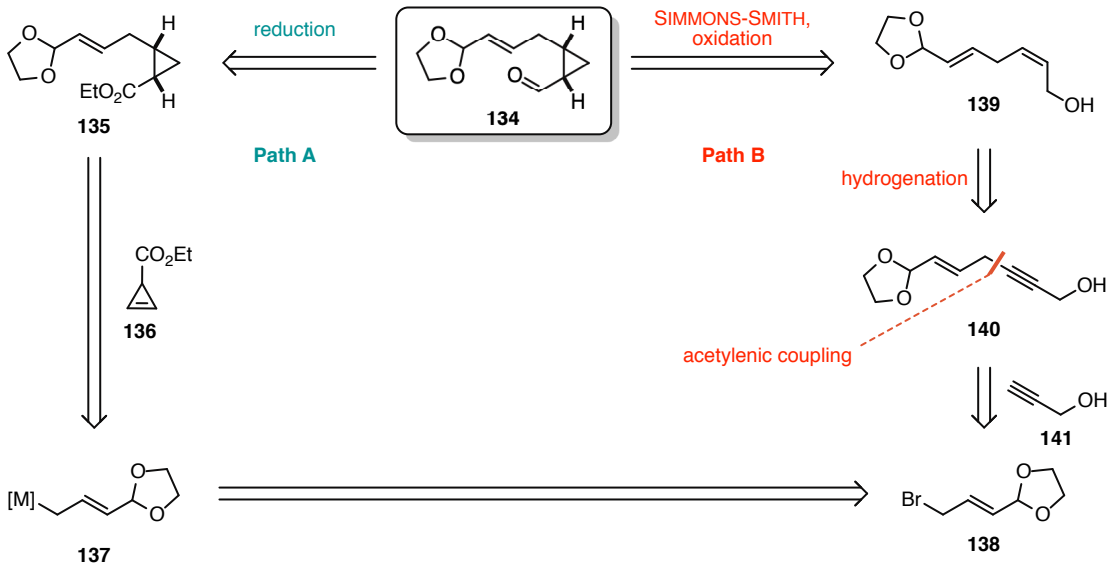
3.1.4 Improved Synthesis of α,β-Unsaturated Aldehydes 109

It was envisaged that the diversity of enals **109** could be introduced in the last step of the synthesis by transition metal catalysed cross coupling of iodide **133** and subsequent cleavage of the acetal (*Scheme 3.9*). Iodide **133** could be accessible from **134** either by Takai or by Stork-Zhao reaction, depending on the desired stereoisomer.[322]



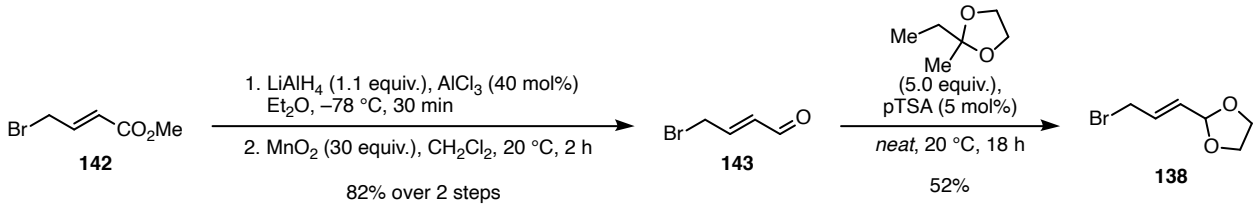
Scheme 3.9: Retrosynthetic analysis of **109**.

Aldehyde **134** could be prepared by reduction of the ester **135** which would be formed by carbometalation of cyclopropene **136** by metal organyl **137** (*Scheme 3.10*, path A).[323] **137** can be obtained by metal-halogen exchange of the bromide **138**. On the other hand, aldehyde **134** could also result from Simmons-Smith reaction and subsequent oxidation of the allylic alcohol **139** (path B). Alcohol **139** could be obtained by hydrogenation of the alkyne **140** which could be formed by coupling of bromide **138** and propargyl alcohol (**141**).[324,325]



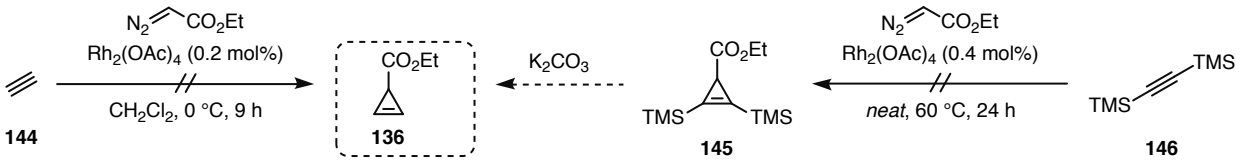
Scheme 3.10: Retrosynthetic analysis of aldehyde **134**.

The acetal **138** which was the starting point for both synthetic pathways was prepared from methyl-4-bromocrotonate (**142**, *Scheme 3.11*). Reduction with lithium aluminium hydride and oxidation of the resulting alcohol delivered the corresponding aldehyde **143** in 82% yield over 2 steps.[326] The aldehyde **143** was converted to the desired acetal **138** in 52% yield by transacetalisation.



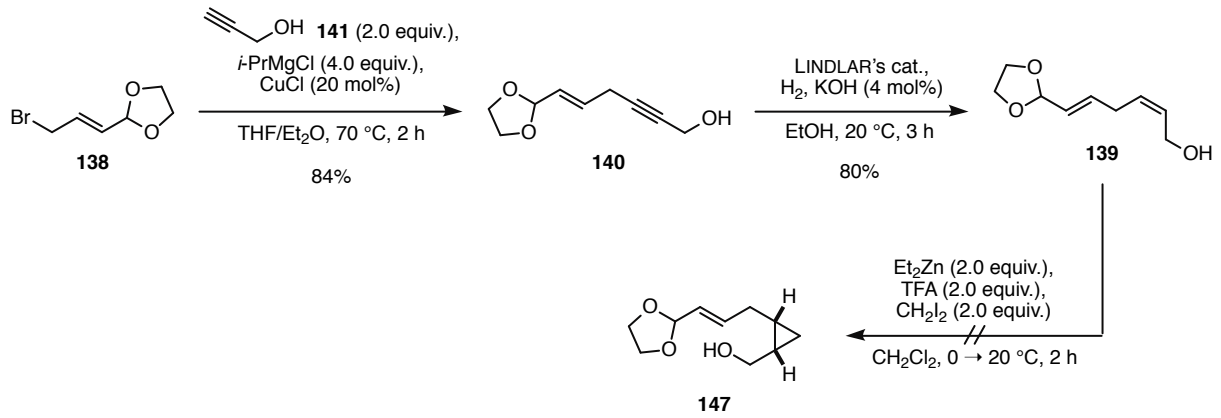
Scheme 3.11: Synthesis of acetal **138**.

It was attempted to prepare the cyclopropene ester **136** by cyclopropenation of acetylene (**144**) under rhodium catalysis (*Scheme 3.12*).[327,328] Unfortunately, exclusively the carbene dimer could be isolated and only traces of **136** were detected by GC-MS. Also, extremely slow addition of the carbene precursor to a saturated solution of acetylene did not result in the formation of **136**. It was reasoned, that **136** could further be obtained by desilylation of **145**.[329] But also the cyclopropenation of bis(trimethylsilyl)acetylene (**146**) by rhodium catalysed carbene addition delivered only traces of the desired cyclopropene. Due to these difficulties, path A in the synthesis of aldehyde **134** was abandoned.



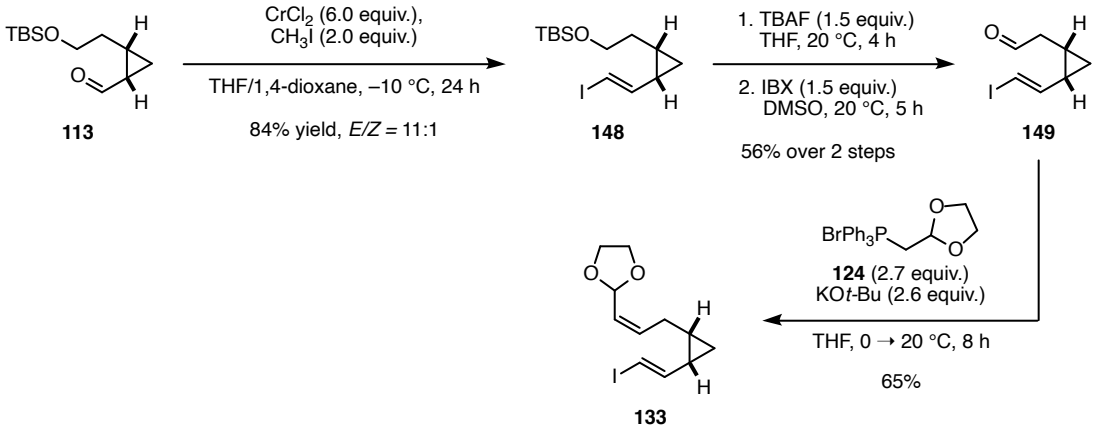
Scheme 3.12: Attempted synthesis of ester **136** by cyclopropanation of acetylene (**144**) or bis(trimethylsilyl)acetylene (**146**).

For the proposed pathway B, bromide **138** was coupled with propargyl alcohol (**141**) delivering the desired alkyne **140** in a good yield of 84% (*Scheme 3.13*). **140** could be converted to the corresponding alkene **139** by partial hydrogenation with Lindlar's catalyst in 80% yield. However, Simmons-Smith cyclopropanation of **139** only led to decomposition of the starting material. Also, when the Simmons-Smith reaction was performed without the addition of trifluoroacetic acid (TFA) or when a samarium catalysed cyclopropanation[330] was used only complex mixtures could be obtained. Cyclopropanation with trimethylsilyldiazomethane under palladium catalysis failed as well.



Scheme 3.13: Attempt to synthesise **147** by path B.

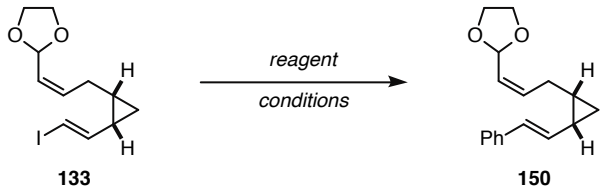
As the attempts of an efficient synthesis of iodide **133** were not successful, **133** was synthesised from the aldehyde **113** (*Scheme 3.14*). Aldehyde **113** was converted to the vinyl iodide **148** by *E*-selective Takai olefination in 84% yield and with a *d.r.* of 11:1.[331–333] Cleavage of the silyl ether and subsequent oxidation of the resulting alcohol delivered aldehyde **149**. Wittig reaction of aldehyde **149** with phosphonium salt **124** then resulted in the formation of iodide **133** in 4 steps from aldehyde **113** and an overall yield of 31%.



Scheme 3.14: Synthesis of **133** by Takai olefination.

With iodide **133** in hand, different conditions for the transition metal catalysed coupling were surveyed (*Table 3.7*). The addition of the Gilman cuprate, lithium diphenyl cuprate, to iodide **133** led to fast decomposition of the starting material (entry 1).[334,335] NMR analysis suggested that both the acetal and the cyclopropane moiety were cleaved and that a significant amount of biphenyl was formed. Conducting the experiment at a lower temperature and decreasing the amount of cuprate led to the same result (entry 2). $PhCuMgBr_2$ as a coupling partner produced a complex product mixture (entry 3) and when the reagent was formed *in situ* by lithium tetrachloro cuprate and phenyl magnesium bromide, only traces of **150** could be observed by GC-MS analysis (entry 4).[336–338] The Suzuki coupling of iodide **133** with phenylboronic acid delivered the desired product in 20% yield but with significant amounts of impurities that could not be separated (entry 5). Performing this reaction under modified conditions developed by Marsden and co-workers[339] with phenyl boronate **151** delivered the desired product in 32% yield (entry 6). The Negishi coupling of iodide **133** proved to be rather slow and was stopped when only low conversion was observed at 70 °C after 24 h (entry 7). In 2017, Feringa and co-workers developed an ultrafast cross-coupling of organolithium compounds that was reported to proceed under palladium nanoparticle catalysis.[340] Unfortunately, when their conditions were applied to the coupling of **133** with phenyllithium no conversion took place and the iodide **133** could be reisolated completely (entry 8).

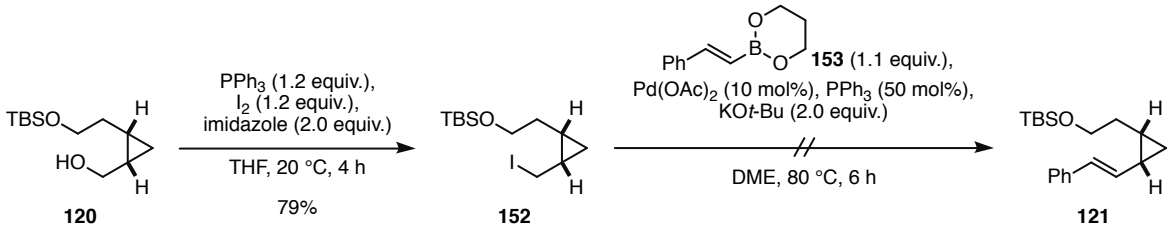
Table 3.7: Transition metal catalysed couplings of **133**.



Entry	Reagent (equiv.)	Conditions	Result
1	Ph_2CuLi (4.0)	Et_2O, −78 °C, 5 min	complex mixture
2	Ph_2CuLi (1.2)	Et_2O, −100 °C, 5 min	complex mixture
3	$PhCuMgBr_2$ (2.0)	THF, −78 °C, 5 min	complex mixture
4	$Li[CuCl_4]$ (1.0) + PhMgBr (2.0)	Et_2O, −100 °C, 5 min	traces
5	$PhB(OH)_2$ (2.0)	$Pd(dppf)Cl_2$ (10 mol%), NaOH (2.0 equiv.), THF, 4 → 80 °C, 48 h	20% yield[a]
6	 **151** (1.1)	$Pd(OAc)_2$ (10 mol%), PPh_3 (50 mol%), KO*t*-Bu (2.0 equiv.), DME, 80 °C, 2 h	32% yield
7	PhZnI·LiCl (1.1)	$Pd(amphos)Cl_2$ (2 mol%), TMEDA (1.1 equiv.), THF, 70 °C, 24 h	incomplete conversion
8	PhLi (1.5)	$Pd(P\textit{t}\text{-}Bu_3)_2$ (5 mol%), O_2, PhMe, 20 °C, 4 h	reisolation of **133**

[a] The product contained significant amounts of impurities.

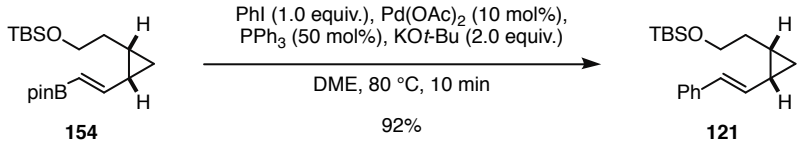
As the Suzuki coupling was the only reaction to produce olefin **150** in preferable amounts, the reaction was optimised. At first, iodide **152** was used as precursor (*Scheme 3.15*). Iodide **152** was synthesised by Appel reaction from **120** (*Scheme 3.15*). Unfortunately, Suzuki coupling of iodide **152** and boronate **153** under the conditions used above only resulted in decomposition of the starting materials.



Scheme 3.15: Attempted synthesis of olefin **121** from iodide **152**.

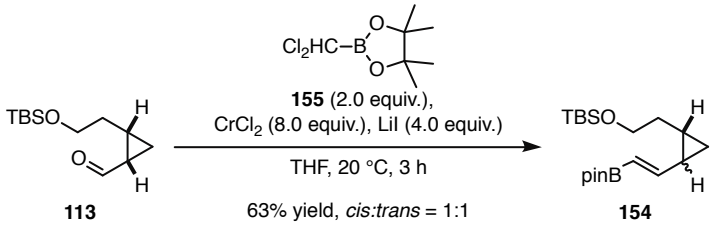
Since the previous attempts did not give the desired products in satisfying yields, an exchange of the polarities of the coupling partners was envisioned. In a model reaction, boronate **154** was reacted with iodobenzene

under the established reaction conditions (*Scheme 3.16*). Satisfyingly, the coupling product **121** could be obtained in only 10 min and a yield of 92%.



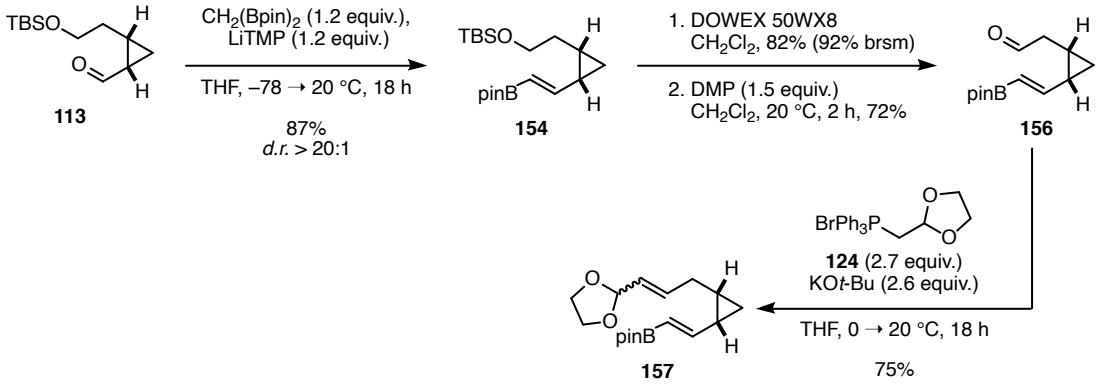
Scheme 3.16: Suzuki coupling of boronate **154** with iodobenzene.

The pinacol boronate **154** was synthesised by a chromium-mediated olefination developed by Takai and co-workers (*Scheme 3.17*).[341] However, boronate **154** was obtained as a mixture of the *cis*- and *trans*-cyclopropane. Subjecting the starting material to reaction conditions without the dichloromethylboronic ester **155** revealed that the aldehyde **113** isomerises when exposed to a mixture of lithium iodide and chromium dichloride.



Scheme 3.17: Synthesis of **154** by chromium-mediated olefination.

As a consequence, for further studies boronate **154** was obtained by an *E*-selective bora-Wittig reaction developed by Morken and co-workers (*Scheme 3.18*).[342] Subsequently, **154** was converted to the aldehyde **156** by silyl ether cleavage and oxidation of the resulting alcohol. Cleavage of the silyl ether with hydrochloric acid led to fast decomposition of the starting material, so an acidic proton exchange resin was used. Aldehyde **156** was then converted to the Suzuki precursor **157** by the previously established methods.

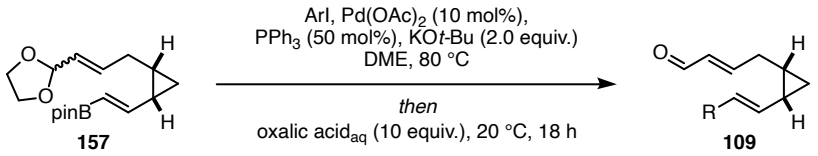


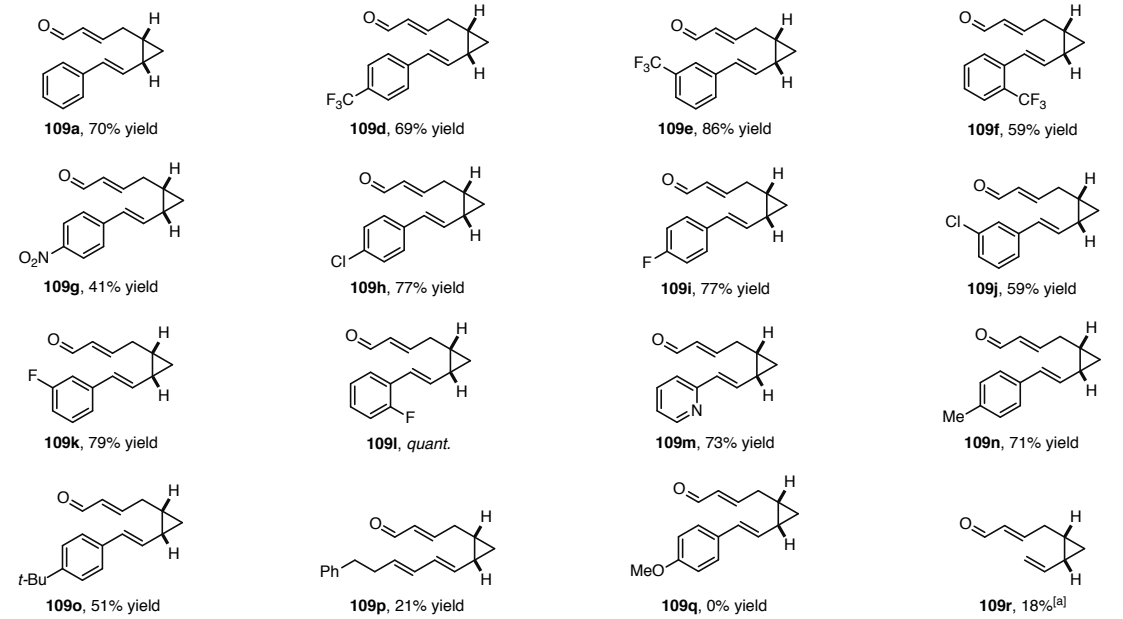
Scheme 3.18: Synthesis of the Suzuki precursor **157**.

With precursor **157** in hand, a variety of different aryl substituted enals could be synthesised (*Table 3.8*). Utilisation of aryl iodides with electron withdrawing substituents (EWG) in *ortho*, *meta*, and *para* position

gave the desired enals in good to excellent yields. Compounds **109i**, **109k**, **109l**, **109o**, and **109p** were obtained in cooperation with S. Hartmann as part of his bachelor thesis.[343] As exception, the nitro compound **109g** could only be obtained in 41% yield. Heteroaromatic **109m** was delivered in good yield as well as enal **109n** and **109o** bearing electron donating alkyl groups. The coupling of boronate **157** and (*E*)-(4-iodobut-3-en-1-yl)benzene, obtained from the Takai reaction of hydrocinnamaldehyde, only led to the formation of the desired enal **109p** in 21% yield. Serendipitously, the coupling of resorcinol iodide with boronate **157** delivered enal **109r** bearing a terminal vinyl group. The unsubstituted enal **109r** was probably formed by protonation of an intermediate. The actually desired enal bearing two hydroxyl groups could not be isolated.

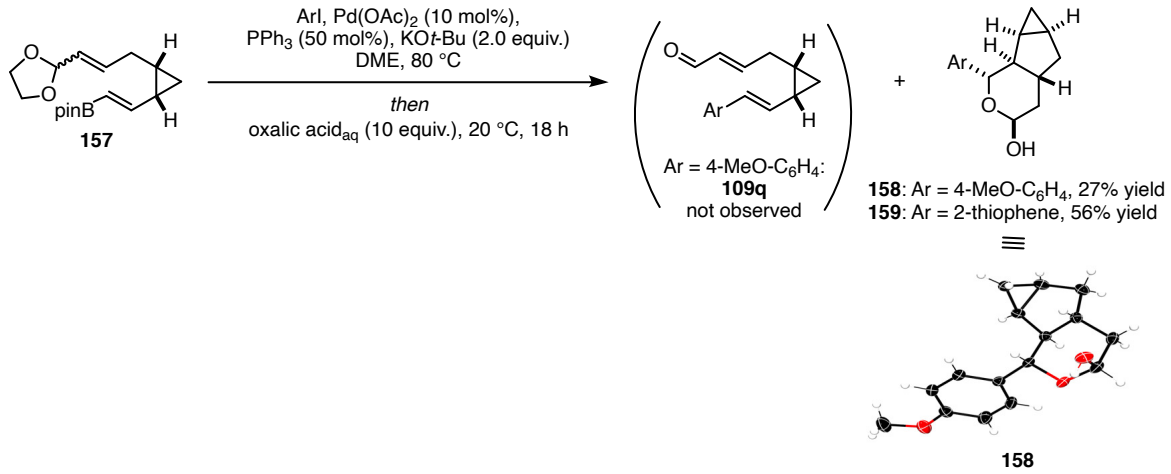
Table 3.8: Synthesis 4-(2-(*E*)-vinylcyclopropyl)but-2-enals **109** by Suzuki coupling.





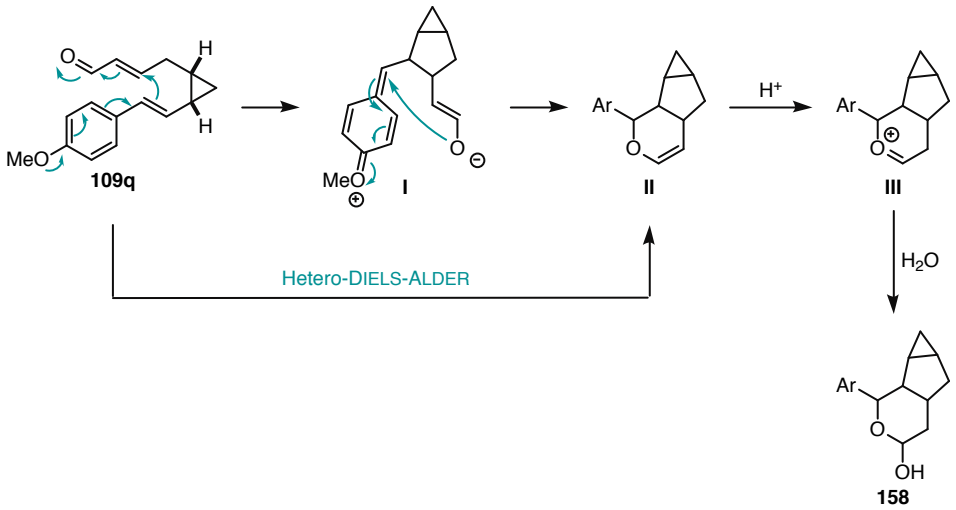
[a] Obtained with ArI = 2-iodobenzene-1,3-diol.

The methoxy substituted enal **109q** was not observed at all. Instead of enal **109q** lactol **158** was isolated from the Suzuki coupling of boronate **157** and 4-methoxyiodobenzene and subsequent reaction with oxalic acid (*Scheme 3.19*). The same happened when iodothiophene was used as coupling partner. The structure of lactol **158** was unambiguously confirmed by X-Ray analysis.



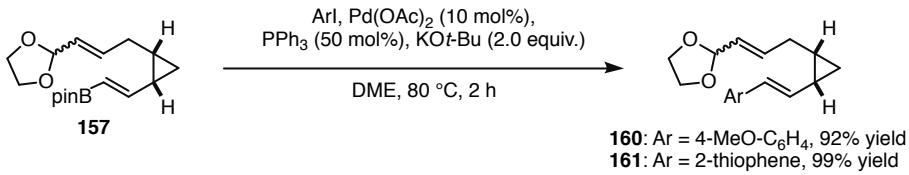
Scheme 3.19: Formation of lactols **158** and **159** from precursor **157**. Displacement ellipsoids of ORTEP of **158** set at 50% probability, hydrogens are calculated.

It is possible that the strong electron donating effect of the methoxy group in enal **109q** triggers an intramolecular MICHAEL addition of the styrene to the α,β-unsaturated aldehyde (*Scheme 3.20*). The anion in **I** would then add to the quinoid system to form ether **II**. Ether **II** could also be obtained from enal **109q** by hetero-DIELS-ALDER reaction. Under acidic conditions it is imaginable that **II** isomerises to the oxocarbenium ion **III** and addition of water would then result in the formation of lactol **158**.



Scheme 3.20: Proposed mechanism for the formation of lactols **158** and **159**.

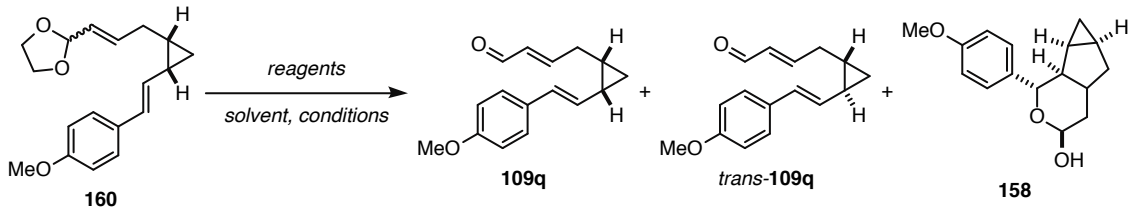
To support the hypothesis, that the enal **109q** is formed but undergoes subsequent cyclisation, acetal **160** was synthesised by SUZUKI coupling of boronate **157** with 4-methoxyiodobenzene in 92% yield and also the thiophene derivative **161** could be obtained under similar conditions in 99% yield (*Scheme 3.21*).



Scheme 3.21: Synthesis of acetals **160** and **161**.

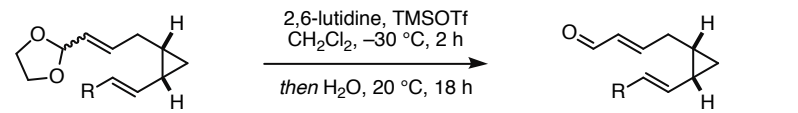
Different conditions were tested for the cleavage of the acetal in **160** (*Table 3.9*).[343] For this purpose, the reactions were performed on a small scale (75 µmol) and evaluated qualitatively by GC-MS analysis. Interestingly, when acetal **160** was subjected to oxalic acid at lower temperatures, only the *trans*-isomer of **109q** was detected and the lactol **158** could not be observed (entry 1). Attempts to cleave the acetal with *para*-toluenesulfonic acid (*p*TSA) or hydrochloric acid under literature known procedures led to the same result (entries 2 and 3).[344] When pyridinium *para*-toluenesulfonate (*p*PTS) was used the desired enal **109q** was formed together with lactol **158** (entry 4).[345] Reaction with perchloric acid or wet silica gel did not give any conversion (entries 5 and 6)[346,347] and with catalytic amounts of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) only lactol **158** was observed (entry 7).[348] Cleavage of acetal **160** with bis(acetonitrile)dichloropalladium(II) or tetrabromomethane led to the formation of a *cis*/*trans* mixture of enal **109q** with very low signal intensity (entries 8 and 10)[349,350] and the reaction with tetrabromomethane and triphenylphosphine again delivered only the *trans*-isomer of **109q** (entry 11).[351] However, promising results were made with wet DMSO which delivered **109q** as the only detectable product (entry 9)[352] and with a combination of 2,6-lutidine and trimethylsilyl trifluoromethanesulfonate which gave **109q** together with small amounts of its *trans*-isomer (entry 12).[353]

Table 3.9: Cleavage of acetal **160**.



Entry	Reagents (equiv.)	Solvent	Conditions	Result
1	oxalic acid (10.0)	THF	4 °C, 1.5 h	*trans*-**109q**
2	*p*TSA·H_2O (10 mol%)	acetone	70 °C, 48 h	*trans*-**109q**
3	HCl (30 mol%)	THF	20 °C, 2 h	*trans*-**109q**
4	*p*PTS (2 mol%)	acetone	70 °C, 2.5 h	**109q** + **158**
5	$HClO_4$ (10 mol%)	CH_2Cl_2	0 → 20 °C, 48 h	–
6	SiO_2 (3.0 equiv.)	CH_2Cl_2/H_2O	20 °C, 48 h	–
7	DDQ (3 mol%)	MeCN/H_2O	20 °C, 3.5 h	**158**
8	$PdCl_2(MeCN)_2$ (5 mol%)	acetone	20 °C, 2.5 h	**109q** + *trans*-**109q**
9	–	DMSO (wet)	180 °C, 3 h	**109q**
10	CBr_4 (5 mol%)	MeCN/H_2O	20 °C, 3.5 h	**109q** + *trans*-**109q**
11	CBr_4 (50 mol%), PPh_3 (50 mol%)	THF	0 → 20 °C, 1.5 h	*trans*-**109q**
12	2,6-lutidine (23 equiv.), TMSOTf (18 equiv.)	CH_2Cl_2/H_2O	−30 → 20 °C, 48 h	**109q** + *trans*-**109q**

The reactions with pyridinium *para*-toluenesulfonate, wet DMSO and with 2,6-lutidine and trimethylsilyl trifluoromethanesulfonate were repeated on a larger scale (0.5 mmol). At this scale, conversion with pyridinium *para*-toluenesulfonate and wet DMSO led to decomposition and the formation of complex mixtures. However, conversion with 2,6-lutidine and trimethylsilyl trifluoromethanesulfonate delivered the desired enal **109q** in 41% yield (*Scheme 3.22*). The *trans*-isomer of **109q** was not detected. Additionally, these conditions could be also applied to the acetal cleavage of thiophene **161** delivering enal **109s** in 42% yield.



160: R = 4-MeO-C_6H_4
161: R = 2-thiophene

109q: R = 4-MeO-C_6H_4, 41% yield
109s: R = 2-thiophene, 42% yield

Scheme 3.22: Cleavage of acetals **160** and **161** with a procedure developed by Inoue and co-workers.

3.1.5 Preparation of Substrates That Could Not Be Prepared by Suzuki Coupling

Some substrates like the *Z*-configurated vinyl cyclopropyl enals, the ester **109t**, the nitrile **109u** or the linear alkyl substrate **109y** where not suitable for a synthesis by nickel catalysed cross-coupling or by Suzuki reaction from boronate **157** (*Figure 3.1*). Their syntheses starting from aldehyde **113** shall be discussed in the following section.

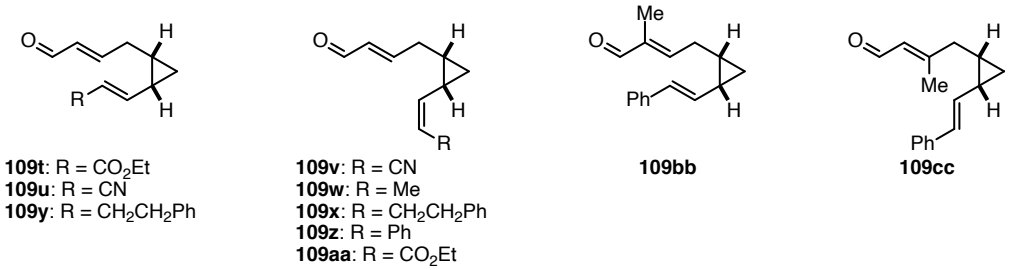
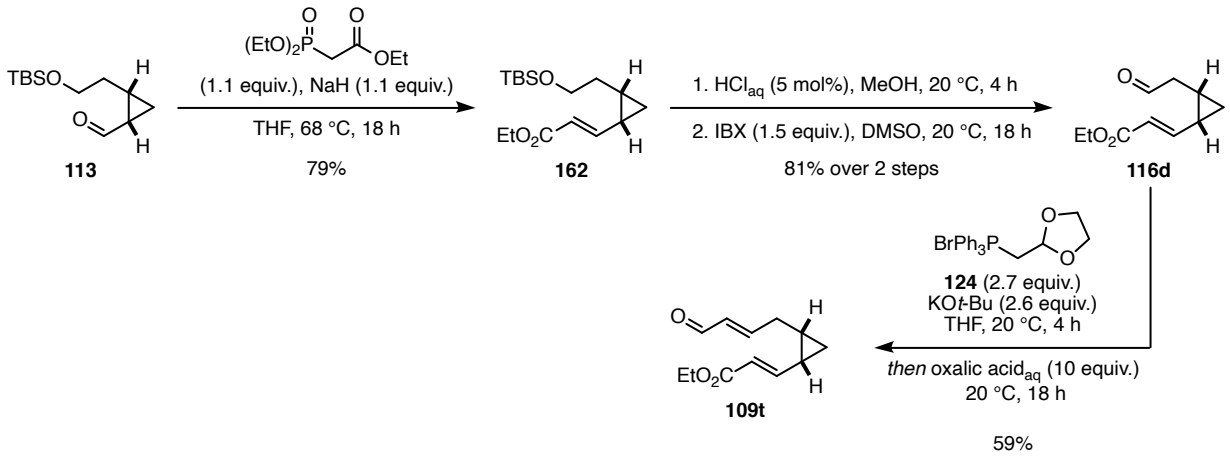


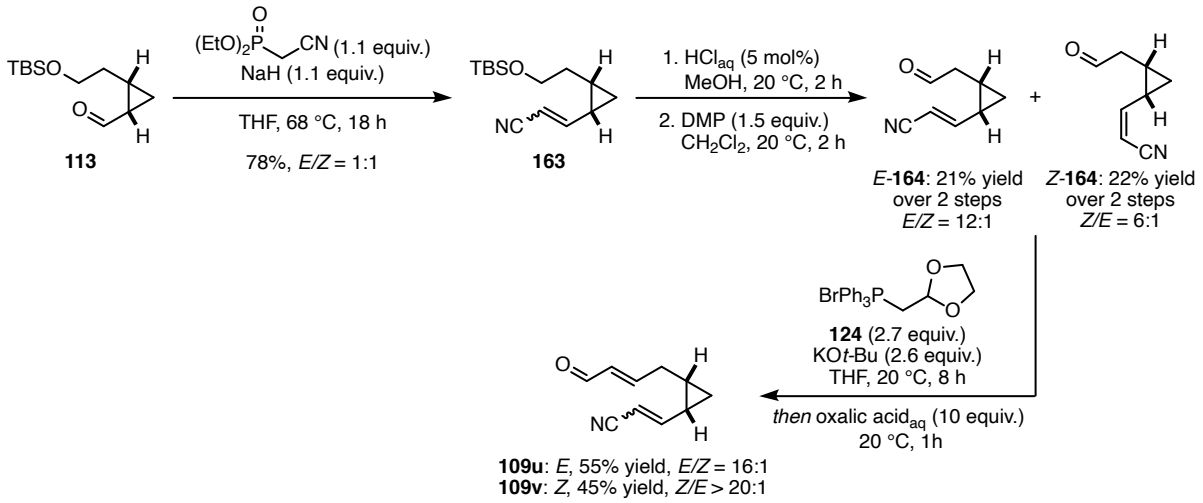
Figure 3.1: Substrates that could not be prepared by Suzuki-coupling or nickel-catalysed cross-coupling.

For the synthesis of ester **109t**, aldehyde **113** was converted to the *E*-configurated olefin **162** by Horner-Wadsworth-Emmons reaction with triphenylphosphonoacetate in 79% yield and isolated as a single diastereoisomer (*Scheme 3.23*).[303] The silyl ether **162** was cleaved under acidic conditions and the resulting alcohol was oxidised to deliver aldehyde **116d** in 81% yield over 2 steps. Subjection of aldehyde **116d** to established homologation conditions gave the enal **109t** in 59% yield and with an overall yield of 37% starting from aldehyde **113**.



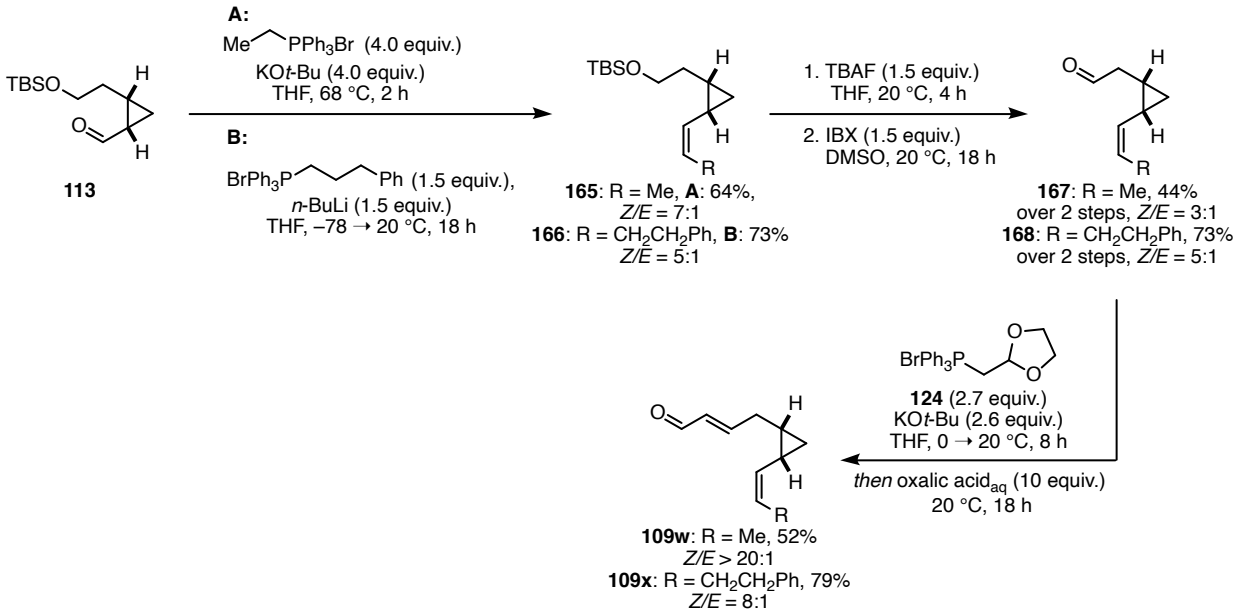
Scheme 3.23: Synthesis of ester substituted enal **109t**.

Horner-Wadsworth-Emmons reaction of aldehyde **113** with triethylphosphono acetonitrile led to the formation of nitrile **163** in an inseparable *E*/*Z*-mixture with a ratio of 1:1 (*Scheme 3.24*). After cleavage of the silyl ether and oxidation of the resulting alcohol the stereoisomers could be separated by column chromatography. *E*-**164** was obtained in 21% yield over 2 steps and *Z*-**164** in 22% yield. Both isomers were converted to the corresponding enals **109u** and **109v** in 55% and 45% yield, respectively.



Scheme 3.24: Synthesis of nitrile substituted enals **109u** and **109v**.

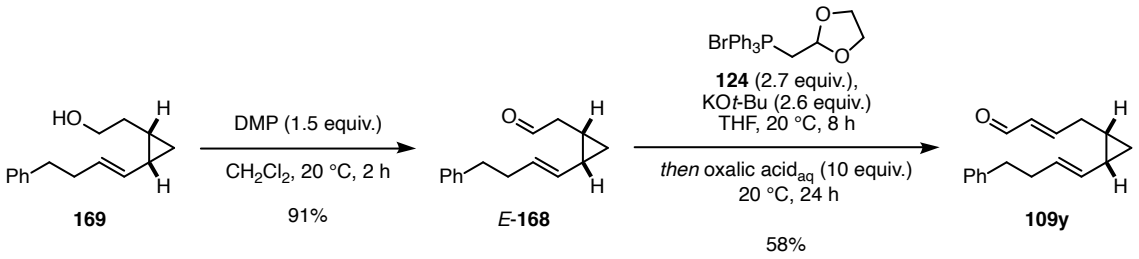
The *Z*-alkyl substituted enals **109w** and **109x** were synthesised from aldehyde **113** by Wittig reaction with the corresponding phosphonium salts (*Scheme 3.25*). The *Z*-configurated olefins **165** and **166** were obtained with good *Z/E* ratios. Cleavage of the silyl ether and subsequent oxidation delivered the aldehydes **167** and **168**. For the purification of aldehyde **167** by column chromatography some fractions of the *Z*-isomer had to be discarded due to significant impurities. Homologation of aldehydes **167** and **168** delivered enals **109w** and **109x** in 52% and 79% yield, respectively. Some fractions of the undesired *E*-isomers could be separated.



Scheme 3.25: Synthesis of *Z*-alkyl substituted enals **109w** and **109x**.

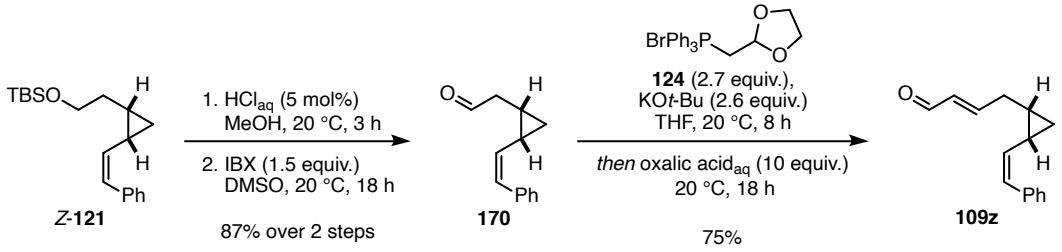
A fraction of the diastereomeric mixture of olefin **166** was deprotected under acidic conditions and the resulting alcohols separated by preparative HPLC delivering the *E*-alkyl substituted alcohol **169**. Alcohol

169 could be converted to the aldehyde *E*-**168** in 91% by oxidation with DMP (*Scheme 3.26*). The aldehyde was then subjected to homologation to deliver enal **109y** in 58% yield.



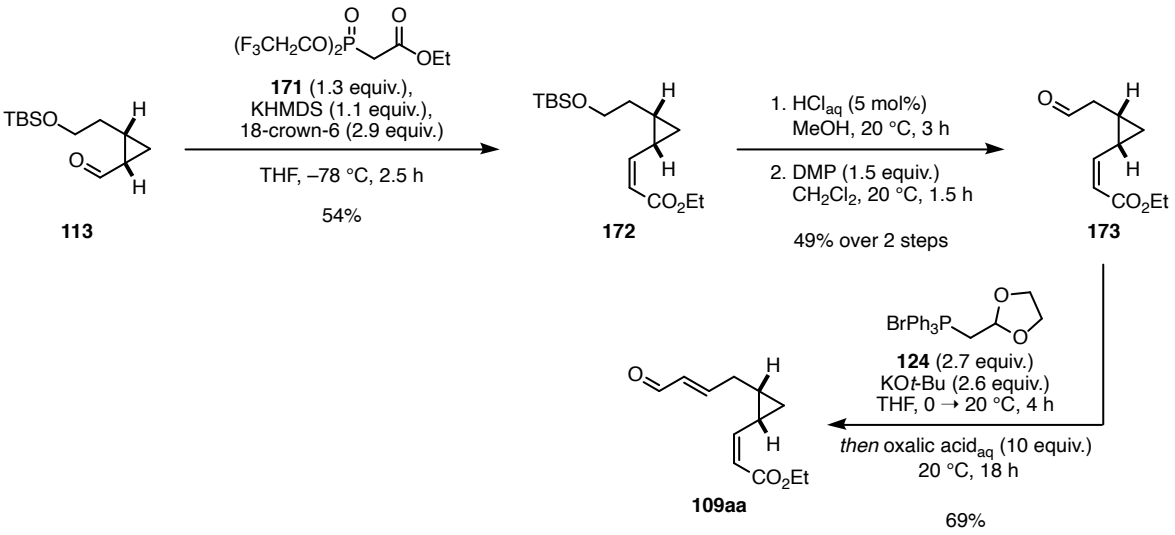
Scheme 3.26: Synthesis of *E*-alkyl substituted enal **109y**.

The *Z*-phenyl substituted olefin *Z*-**121** was obtained by separation of the double bond isomers by HPLC (see 3.1.1). It could be converted to the aldehyde **170** by cleavage of the silyl ether under acidic conditions and oxidation of the resulting alcohol by IBX in 87% yield over 2 steps (*Scheme 3.27*). Aldehyde **170** was then converted to the desired enal **109z** by homologation in 75% yield.



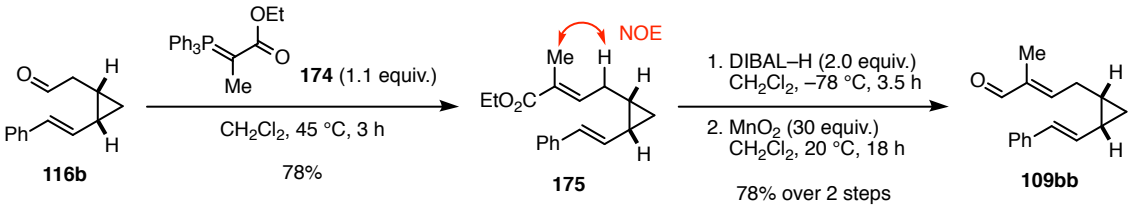
Scheme 3.27: Synthesis of *Z*-phenyl substituted enal **109z**.

The *Z*-ester substituted enal **109aa** was synthesised from aldehyde **113** by Still-Gennari reaction[82] with phosphonate **171** which was obtained *via* a procedure by Oberthür and co-workers.[354] The olefination delivered ester **172** in 54% yield as a single diastereoisomer (*Scheme 3.28*). The silyl ether of **172** was cleaved under acidic conditions and the resulting alcohol was oxidised using DMP to obtain the aldehyde **173** in 49% yield over 2 steps. Aldehyde **173** was then subjected to established homologation conditions and enal **109aa** was isolated in 69% yield.



Scheme 3.28: Synthesis of *Z*-ester substituted enal **109aa**.

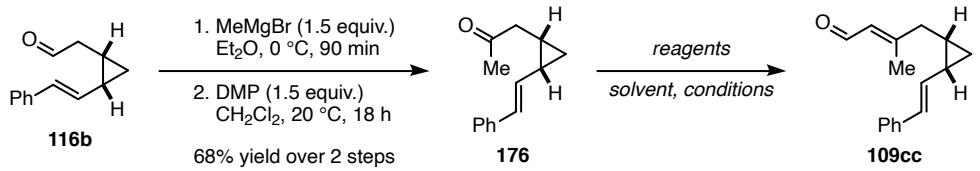
To study the influence of steric bulk on the enamine induced DVCPR enals **109bb** and **109cc**, bearing an additional substituent in α- and β-position of the unsaturated system were synthesised starting from aldehyde **116b**. Enal **109bb** was synthesised by Wittig reaction of aldehyde **116b** with ethyl methyltriphenylphosphoranylideneacetate (**174**)[355] which delivered ester **175** in 78% yield (*Scheme 3.29*). The *E*-configuration of the newly formed double bond could be confirmed by NOE experiments. Reduction of the ester with DIBAL–H and oxidation of the resulting allylic alcohol with manganese dioxide afforded enal **109bb** in 78% yield.

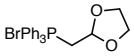
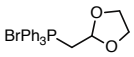
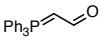
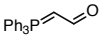
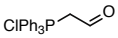
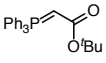
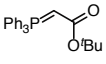
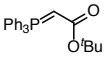
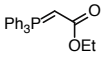
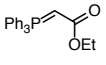
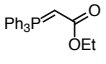
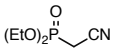


Scheme 3.29: Synthesis of α-branched enal **109bb**.

Enal **109cc** bearing the methyl substituent in β-position of the unsaturated system was attempted to be obtained from ketone **176**. Ketone **176** was delivered by methylation of aldehyde **116b** and subsequent oxidation of the resulting alcohols. When ketone **176** was subjected to the established homologation conditions only decomposition could be observed (*Table 3.10*, entry 1). Since lowering the reaction temperature did not change the outcome of the reaction (entry 2), different ylides were tested for the Wittig reaction to the corresponding C_2-elongated products. Unfortunately, conversion of ketone **176** with triphenyl(phosphoranylidene)acetaldehyde (**177**),[356] *tert*-butyl(triphenylphosphoranylidene)acetate (**178**),[357] or ethyl(triphenylphosphoranylidene)acetate (**179**)[358] gave either no conversion (entries 3, 5–7, 9, and 10) or led to decomposition of the starting materials at elevated temperature (entries 4, 8, and 11). In addition to that, reaction with diethyl(cyanomethyl)phosphonate **180** also only resulted in decomposition. Therefore, the synthesis of enal **109cc** was abandoned.

Table 3.10: Synthesis of ketone **176** and attempted synthesis of enal **109cc**.



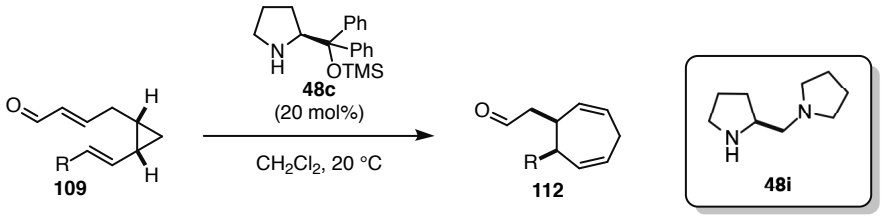
Entry	Reagents (equiv.)	Solvent	Conditions	Result
1	 **124** (2.7), KO*t*-Bu (2.6) *then* oxalic acid (10)	THF	0 → 20 °C, 24 h	decomposition
2	 **124** (2.7), KO*t*-Bu (2.6) *then* oxalic acid (10)	THF	−30 °C, 8 h *then* 20 °C, 18 h	decomposition
3	 **177** (1.1)	CH_2Cl_2	40 °C, 12 h	no conversion
4	 **177** (1.1)	PhMe	120 °C, 12 h	decomposition
5	 (1.1), KO*t*-Bu (1.0)	THF	70 °C, 1h h	no conversion
6	 **178** (1.1)	CH_2Cl_2	45 °C, 18 h	no conversion
7	 **178** (1.1)	THF	70 °C, 18 h	no conversion
8	 **179** (1.1)	PhMe	120 °C, 18 h	decomposition
9	 **179** (1.1)	CH_2Cl_2	45 °C, 18 h	no conversion
10	 **179** (1.1)	THF	70 °C, 18 h	no conversion
11	 **179** (1.1)	PhMe	120 °C, 18 h	decomposition
12	 **180** (1.1), NaH (1.1)	THF	0 → 20 °C, 18 h	decomposition

3.1.6 Scope and Limitations of the Dienamine-Induced DVCPR

With a variety of differently substituted enals **109** in hand, and the optimal reaction conditions being established (see 3.1.2) the scope of the dienamine-induced DVCPR was investigated (*Table 3.11*). The most 4-(2-(*E*)-vinylcyclopropyl)but-2-enals *E*-**109** were converted to the corresponding *cis*-disubstituted cycloheptadienes **112** in good to moderate yields with excellent diastereoselectivity. In case of the styrene derivatives, substitution at either position of the aryl system present in **109d**–**109o** is allowed and does not hinder the reaction. Both, electron donating and electron withdrawing groups are tolerated. Interestingly,

the thiophene substituted cycloheptadiene **112s** could be isolated in 66% yield whereas the corresponding pyridine derivative **112m** only showed rapid decomposition. The alkenyl substituted cycloheptadiene **112p** was obtained in a moderate yield of only 41%. Thus it was demonstrated, that an aryl group is not required for the rearrangement to proceed. Cycloheptadienes **112t** and **112u** bearing an ester and a nitrile group could be isolated in good yields as well. However, the nitrile **112u** could only be obtained as a 2:1 diastereomeric mixture. The monosubstituted cycloheptadiene **112r** could also be isolated, albeit in low yield due to its volatility. Compound **112y** bearing an alkyl substituent required a prolonged reaction time of 72 h but could be isolated in 62% yield. The cycloheptadiene **112c** with a branched alkyl substituent could not be obtained since only slow decomposition of the starting material was observed. The enal **109b** bearing an additional substituent on the cyclopropyl moiety did not show any conversion with catalyst **48c** and when the more reactive amine **48d** was used only slow decomposition could be observed with traces of the diene **112b** being detectable by GC-MS analysis. The additional methyl substituent in α-position of enal **109bb** probably hampers the condensation of the aminocatalyst with the enal, so that no conversion could be observed after 48 h. The same holds true when secondary amine catalysts **48d** or **48i** were employed. Compounds **112i**, **112k**, **112l**, and **112o** were obtained in cooperation with S. Hartmann as part of his bachelor thesis.[343]

Table 3.11: Scope and limitations of the DVCPR of 4-(2-(*E*)-vinylcyclopropyl)but-2-enals *E*-**109**.



112a, 48 h, 96%[a]
cis:trans > 20:1

112b, 48 h, traces[b]

112c, 24 h, 0%

112d, 24 h, 64%
cis:trans > 20:1

112e, 24 h, 75%
cis:trans > 20:1

112f, 24 h, 61%
cis:trans > 20:1

112g, 24 h, 58%
cis:trans > 20:1

112h, 24 h, 69%
cis:trans > 20:1

112i, 24 h, 87%
cis:trans > 20:1

112j, 24 h, 77%
cis:trans > 20:1

112k, 24 h, 61%
cis:trans > 20:1

112l, 24 h, 48%
cis:trans > 20:1

112m, 1 h
decomposition

112n, 24 h, 66%
cis:trans > 20:1

112o, 24 h, 61%
cis:trans > 20:1

112p, 24 h, 41%
cis:trans > 20:1

112q, 24 h, 50%
cis:trans > 20:1

112r, 48 h, 29%

112s, 48 h, 66%
cis:trans > 20:1

112t, 24 h, 86%
cis:trans > 20:1

112u, 24 h, 73%
cis:trans = 2:1

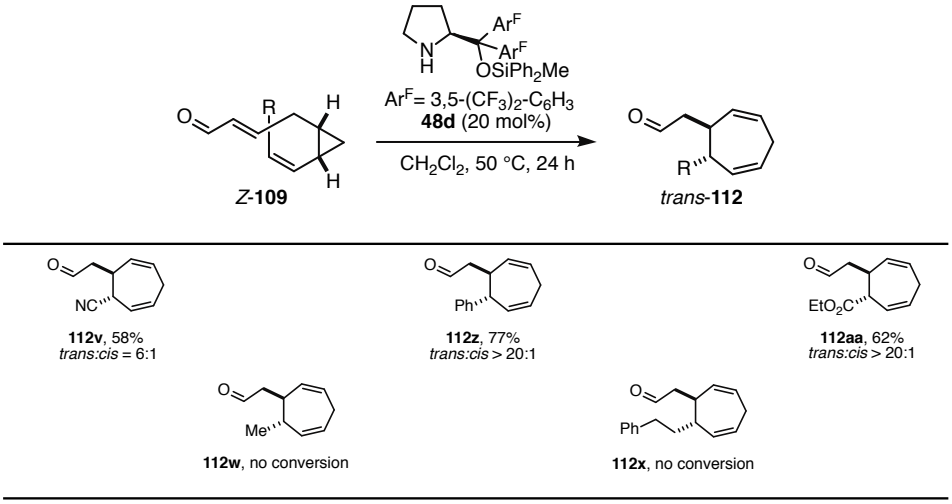
112y, 72 h, 63%

112bb, 48 h, no conversion

[a] Determined by GC-MS using methoxynaphthalene as standard.
[b] Catalyst **48i** was used instead of **48c**.

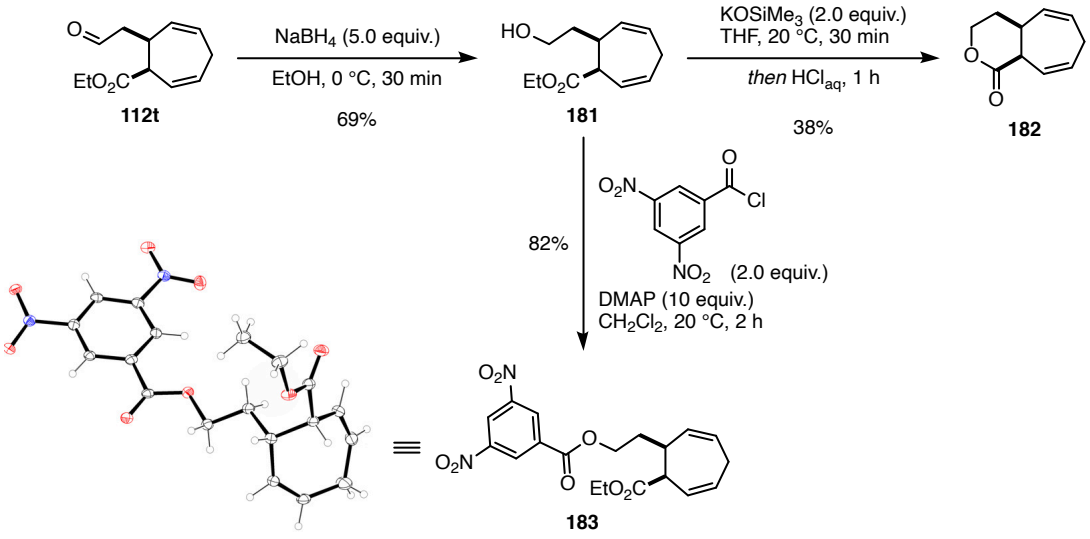
It had been demonstrated that a *Z*-configuration within the substrates can result in a significant increase in the activation barrier for the DVPCR.[70–72,81,359] These rearrangements usually require higher reaction temperatures not compatible with the temperature sensitive organocatalyst **48c**. Therefore, the more stable diarylprolinol silyl ether **48d** was used for the rearrangement of 4-(2-(*Z*)-vinylcyclopropyl)but-2-enals *Z*-**109** (*Table 3.12*). However, the alkylated cycloheptadienes **112w** and **112x** could not be obtained under these conditions. Nevertheless, utilisation of a electron withdrawing groups such as a nitrile or an ester or a phenyl group afforded the *trans*-cycloheptadienes **112v**, **112z**, and **112aa** in good to excellent yields and with high diastereoselectivity.

Table 3.12: DVCPR of 4-(2-(*Z*)-vinylcyclopropyl)but-2-enals *Z*-**109**.



3.1.7 Follow-Up Reactions

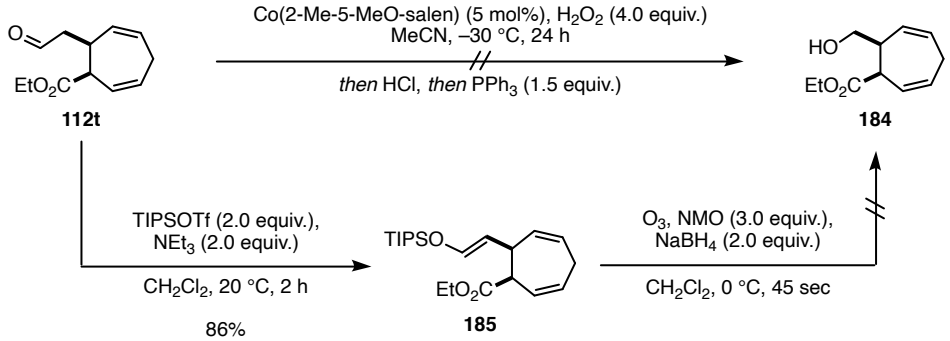
The aldehyde functionality represents a useful handle for further functionalisation of dienes **112**. As an example, the aldehyde **112t** was reduced to the corresponding alcohol **181** and could be either converted to the lactone **182** or to the benzoate **183** (*Scheme 3.30*). Diester **183** was a crystalline solid that formed crystals suitable for X-Ray analysis so that the structure and configuration of **112t** could be indirectly confirmed.



Scheme 3.30: Synthesis of lactone **182** and of benzoate **183** whose structure is depicted by the ORTEP drawing bottom left. Ellipsoids are drawn with 95% probability. Hydrogens are calculated.

The 6/7-fused lactone **182** is an interesting structure but 5/7-membered lactones are a more common structural motif in natural products, e.g. in tremulanes[360–362] or certain caryophyllane sesquiterpenes.[363] A recently developed method by Iwasawa and co-workers should deliver the precursor **184** for the 5-membered lactone from the aldehyde **112t** by oxidative deformylation and *in situ* reduction of the resulting hydroperoxide

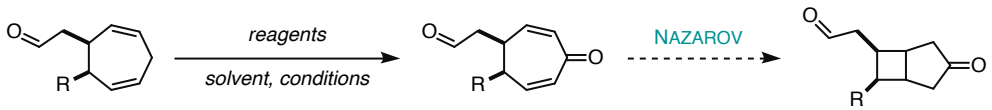
in one step (*Scheme 3.31*).[364] Subjecting aldehyde **112t** to the reported reaction conditions however, only led to decomposition. The corresponding hydroperoxide could also not be isolated. Therefore, aldehyde **112t** was converted to the corresponding silyl enol ether **185**. Unfortunately, ozonolysis of **185** led to rapid decomposition in under one minute even though *N*-methylmorpholine *N*-oxide (NMO) was used for immediate decomposition of the ozonide.[365] Due to these difficulties this path was abandoned.



Scheme 3.31: Attempted synthesis of alcohol **184**.

In an attempt to form a hardly accessible 4/5-membered bicyclic core from the cycloheptadienes by Nazarov cyclisation, the oxidation of dienes **112a** and **112t** at their double allylic position was surveyed (*Table 3.13*). Unfortunately, various oxidation methods using ruthenium, chromium, or manganese based reagents gave either no conversion or led to decomposition. Only pyridinium dichromate (PDC) gave traces of the oxidised ester (entry 4). But when the equivalents of PDC were doubled and the reaction time was prolonged again only decomposition was observed (entry 5).

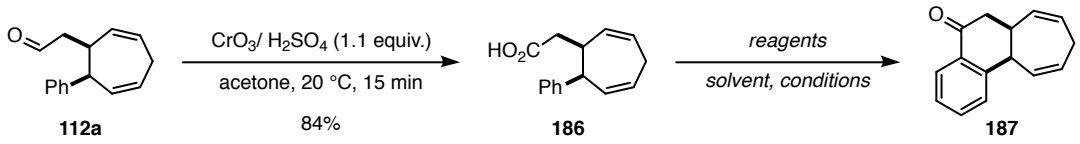
Table 3.13: Attempted allylic oxidation of dienes **112a** and **112t**.



Entry	R	Reagents (equiv.)	Solvent	Conditions	Result
1	Ph	TPAP (10 mol%), NMO (6.0), 4 Å MS	MeCN	20 °C, 18 h	no conversion
2	CO_2Et	TPAP (10 mol%), NMO (6.0), 4 Å MS	MeCN	20 °C, 18 h	no conversion
3	Ph	PDC (3.0)	$CHCl_3$	70 °C, 12 h	no conversion
4	CO_2Et	PDC (3.0)	$CHCl_3$	70 °C, 12 h	traces
5	CO_2Et	PDC (6.0)	$CHCl_3$	70 °C, 24 h	decomposition
6	Ph	PDC(4.0), *t*-BuOOH (4.0)	benzene	20 °C, 6 h	decomposition
7	CO_2Et	PDC(4.0), *t*-BuOOH (4.0)	benzene	20 °C, 6 h	decomposition
8	Ph	3,5-dimethylpyrazole (10), CrO_3 (10)	CH_2Cl_2	−20 °C, 30 min	decomposition
9	CO_2Et	3,5-dimethylpyrazole (10), CrO_3 (10)	CH_2Cl_2	−20 °C, 30 min	decomposition
10	Ph	$Mn(OAc)_3$ (1.0), TBHP (10)	EtOAc	40 °C, 4 h	decomposition + reisolated starting material

Finally, it was studied if the acid chloride of aldehyde **112a** could undergo an intramolecular Friedel-Crafts acylation (*Table 3.14*). Therefore, aldehyde **112a** was oxidised to the corresponding carboxylic acid **186** by Jones oxidation.[366] Acid **186** was converted to the acid chloride either with oxalyl chloride or by reaction with 1,1-dichloromethylether. However, upon subsequent reaction with aluminium trichloride only traces of the desired tricycle **187** could be observed by GC-MS (entries 1 and 2). If the acid chloride was synthesised in 1,1-dichloromethylether without another solvent and the following reaction with aluminium trichloride was performed in 1,2-dichloroethane (1,2-DCE) traces of the desired product were detected by GC-MS together with several signals suggesting the additional chlorination of the product (entry 3). The same could be observed when acid **186** was stirred in 1,1-dichloromethylether for a prolonged time at elevated temperature or when cyanuric chloride (TCT) was used as chlorinating agent (entries 5 and 6). If aluminium trichloride was added to the solvent free reaction of acid **186** with 1,1-dichloromethylether rapid decomposition was observed (entry 4). Overall, the intramolecular Friedel-Crafts acylation of **186** did not seem to be easily accessible and was therefore abandoned.

Table 3.14: Attempted intramolecular Friedel-Crafts reaction of **186**.

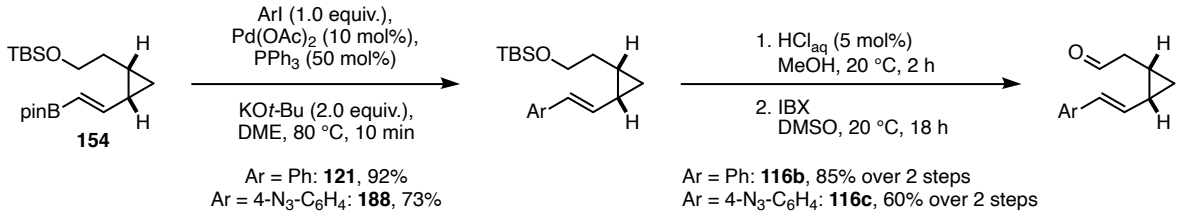


Entry	Reagents (equiv.)	Solvent	Conditions	Result
1	1. oxalyl chloride (1.1), DMF 2. $AlCl_3$ (3.0)	CH_2Cl_2	1. 20 °C, 1 h 2. 20 °C, 2 h	traces
2	1. 1,1-dichloromethyl ether (1.0) 2. $AlCl_3$ (3.0)	CH_2Cl_2	1. 60 °C, 1 h 2. 20 → 60 °C, 48 h	traces
3	1. 1,1-dichloromethyl ether 2. $AlCl_3$ (3.0)	1. neat 2. 1,2-DCE	1. 80 °C, 1 h 2. 80 °C, 2 h *then* 20 °C, 18 h	complex mixture
4	1. 1,1-dichloromethyl ether 2. $AlCl_3$ (3.0)	neat	1. 80 °C, 1 h 2. 80 °C, 5 min	decomposition
5	1,1-dichloromethyl ether	neat	80 °C, 18 h	complex mixture
6	TCT (1.6), py (1.0) *then* $AlCl_3$	CH_2Cl_2 *then* PhMe	20 °C, 15 min *then* 20 °C, 18 h	complex mixture

3.2 Selective Protein-Modification of Lysine with Cyclopropylaldehydes by Divinylcyclopropane-Cycloheptadiene Rearrangement

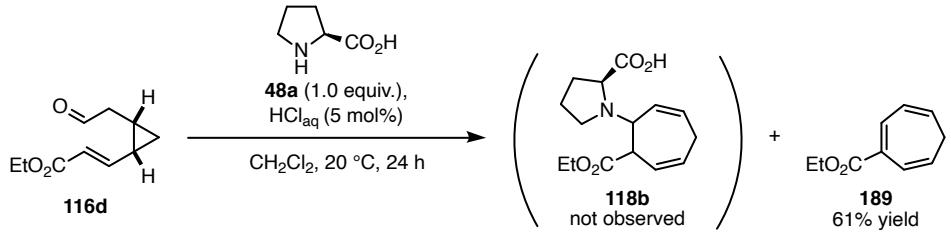
Due to their distinctive reactivity towards either amines or nucleophiles, selected intermediates of the former project were tested for their suitability as reagents to modify proteins selectively. Inspired by the procedure developed by Tanaka and co-workers (see section 1.5) who employed a 6π-aza-electrocyclisation for the formation of stable lysine-adducts, the DVCPR should be used in a similar fashion.

The model substrates were obtained from the boronate **154** by Suzuki coupling under established conditions delivering the styryl derivatives **121** and **188** in good and excellent yields (*Scheme 3.32*). In case of the azide **188**, preformation of the catalytic species was necessary to suppress the competing Staudinger reaction. After cleavage of the silyl ether and oxidation of the resulting alcohol, aldehydes **116b** and **116c** were obtained in 85% and 60% yield over 2 steps.



Scheme 3.32: Synthesis of model substrates **116b** and **116c**.

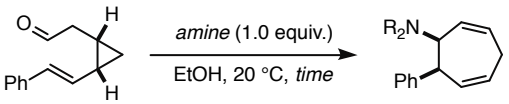
The synthesis of aldehyde **116d** has been described before (see 3.1.5). When the aldehyde **116d** was reacted with proline (**48a**) under acidic conditions, it was not possible to detect the desired adduct **118b**, instead the elimination product **189** was isolated in 61% yield (*Scheme 3.33*). Therefore, further studies were conducted with the phenyl substituted aldehyde **116b** which proved to be more stable.



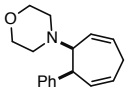
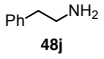
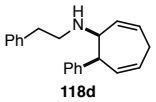
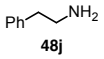
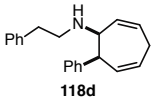
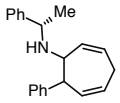
Scheme 3.33: Reaction of **116d** with proline (**48a**).

The model aldehyde **116b** bearing a phenyl substituent readily reacted with secondary and primary amines to form the amine substituted cycloheptadienes **118c** and **118d** in moderate to good yields (*Table 3.15*, entries 1 and 2). However, the yield decreases if the reaction was run in a mixture of ethanol and water, probably due to the low solubility of the starting materials (entry 3). Furthermore, the sterically encumbered benzylamine **118e** could be obtained as well, albeit with prolonged reaction time (entry 4).

Table 3.15: Conversion of aldehyde **116b** with different amines.

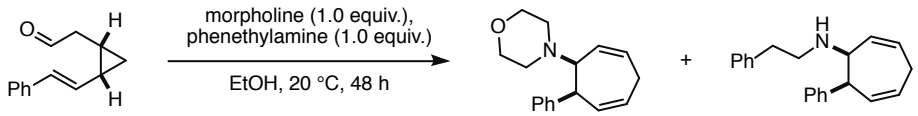


116b **118**

Entry	Amine	Time	Yield	Product
1	 **48h**	48 h	78%	 **118c**
2	 **48j**	48 h	54%	 **118d**
3[a]	 **48j**	48 h	29%	 **118d**
4	 **48k**	5 d	72%	 **118e**

[a] The reaction was run in EtOH/H_2O = 1:1.

A competition experiment between morpholine (**48h**) and phenethylamine (**48j**) with aldehyde **116b** showed the rearrangement to be significantly faster with the primary amine (*Scheme 3.34*). The tertiary amine **118c** was obtained in 17% yield while the secondary amine **118d** was formed in 50% yield.



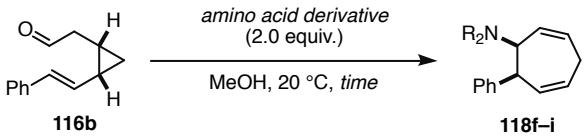
116b **118c** 17% **118d** 50%

Scheme 3.34: Competition experiment with morpholine and phenethylamine.

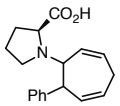
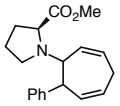
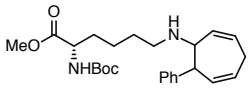
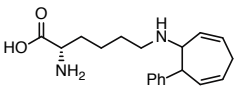
With these promising results in hand, the reactivity of aldehyde **116b** with different proteinogenic amino acid derivatives was investigated (*Table 3.16*). Initially, reaction at the α-amino group should be excluded. Therefore, the studies were performed with *N*-Boc-protected amino acids (entries 3–8). As shown in section 3.1.2, the DVCPR is quite sensitive towards acidic conditions. This behaviour could also be observed in the reaction of **116b** with proline which showed complete conversion in 2 h but was low yielding, and gave cycloheptadiene **118f** only in 32% yield (entry 1). In contrast, the adduct **118g** of aldehyde **116b** and proline methyl ester could be obtained in almost quantitative yield (entry 2). As a consequence, the methyl esters of the amino acids were used for further studies. No conversion of aldehyde **116b** was observed when Boc-Trp-OMe, Boc-His-OMe, Boc-Cys-OMe, Boc-Ser-OMe, and Boc-Tyr-OMe were used in the reaction (entries 3–7). Satisfyingly, the condensation product **118h** of **116b** and Boc-Lys-OMe could be obtained in

65% yield (entry 8). When unprotected lysine was used, rapid conversion was observed, but only a complex mixture could be obtained (entry 9). However, an adduct of aldehyde **116b** and lysine could be detected by high resolution mass spectrometry but it could not be resolved to be the desired ε-amino adduct **118i** or the corresponding α-amino adduct. When aldehyde **116b** was reacted with aspartic acid under neutral conditions in MeOH, no conversion could be observed due to low solubility of the reactant (entry 10). The same reaction in a mixture of methanol and water under basic conditions however, led to rapid decomposition (entry 11). These results indicate that the reaction of aldehyde **116b** is selective towards primary and secondary amines and shows no cross-reactivity with other nucleophilic amino acid derivatives.

Table 3.16: Conversion of aldehyde **116b** with different amino acid derivatives.



116b **118f–i**

Entry	Reagent	Time	Result	Product
1	H-Pro-OH	2 h	32%	 **118f**
2	H-Pro-OMe	24 h	99%	 **118g**
3	Boc-His-OMe	4 d	no conversion	–
4	Boc-Trp-OMe	4 d	no conversion	–
5[a]	Boc-Cys-OMe	24 h	no conversion	–
6	Boc-Ser-OMe	4 d	no conversion	–
7[b]	Boc-Tyr-OMe	4 d	no conversion	–
8	Boc-Lys-OMe	48 h	65%	 **118h**
9	H-Lys-OH	1 h	complex mixture	 **118i**
10	H-Asp-OH	24 h	no conversion	–
11[c]	H-Asp-OH	1 h	decomposition	–

[a] Boc-Cys-OMe was reisolated.
[b] Both starting materials were reisolated.
[c] The reaction was run in MeOH/H_2O = 1:1 and NaOH (2.0 equiv.).

After these promising initial results, the suitability of the amine-selective functionalisation as a general tool for the modification of lysine residues and the *N*-terminus on proteins was investigated by the group of Hackenberger.

As a model substrate, a previously established eGFP C70M S147C mutant,[367] carrying all nucleophilic amino acids, including a reactive cysteine residue, was selected. The Hackenberger group established a protocol for the modification of proteins by initially incubating eGFP with aldehyde **116b** at a concentration of 86 µM in phosphate-buffered saline (PBS) for 18 h at 20 °C over a range of 2–100 equivalents of the aldehyde (*Figure 3.2 a*). This resulted in a decent degree of 1.2 modifications per protein for 50 equivalents of aldehyde **116b** (*Figure 3.2 b,c*).

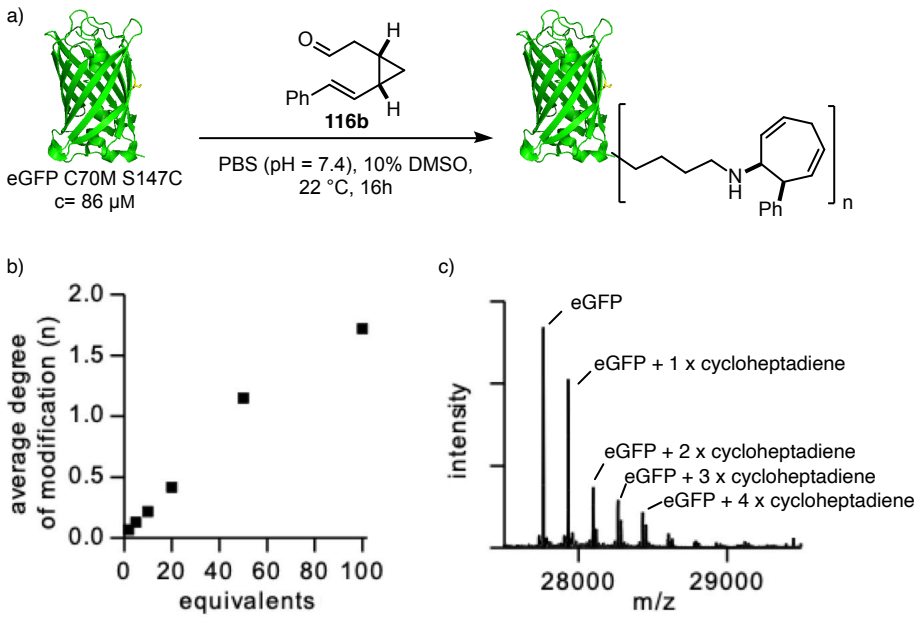


Figure 3.2: a) Reaction of eGFP with aldehyde **116b**. b) Average degree of modification after incubation with different equivalents of aldehyde **116b** estimated from MS analysis. c) Deconvoluted MS-spectrum after reaction with 50 equivalents aldehyde **116b**.

Due to decreased solubility under aqueous conditions at higher concentrations, the studies were continued with 50 equivalents of the aldehyde **116b**. Time resolved measurements revealed that the reaction does not significantly progress after 18 h of incubation (*Figure 3.3 a*). In line with the small molecule studies, it was observed that the protein modification is significantly less efficient under acidic conditions. In contrast to this, basic conditions could be applied and increased the conjugation efficiency, even though the reaction temperature had to be lowered to 4 °C to avoid protein precipitation (*Figure 3.3 b*).

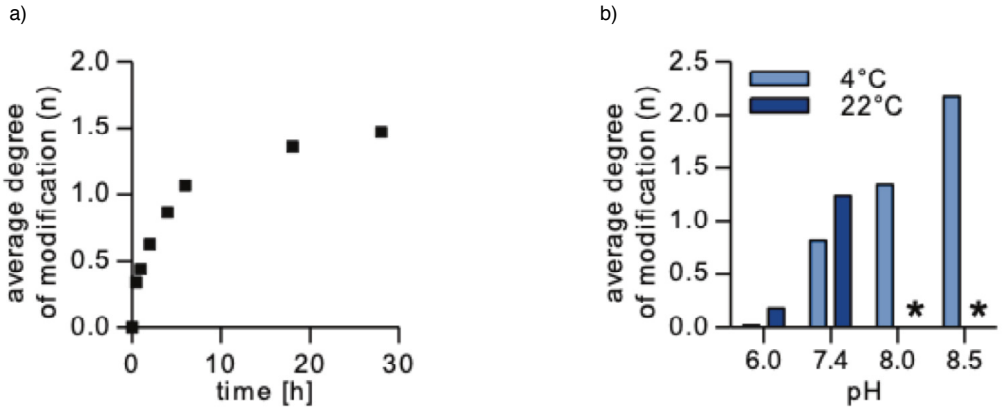


Figure 3.3: a) Time resolved monitoring of the reaction with 50 equivalents of aldehyde **116b** in PBS. b) pH-dependence of the reaction. *No protein masses detected at room temperature under basic conditions due to protein precipitation.

Fluorescence measurements of the eGFP before and after the reaction suggested that the protein structure is not affected by the labelling procedure (*Figure 3.4*).

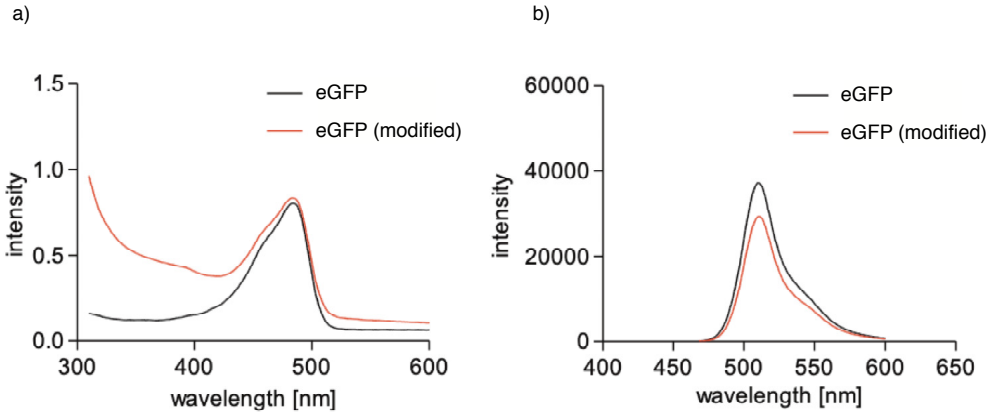
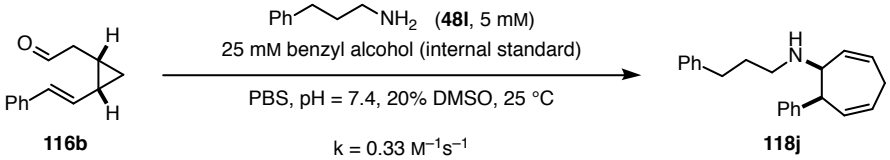


Figure 3.4: Spectra were recorded before and after the modification of eGFP with aldehyde **116b**. Measurements were performed in a 96-well plate (Corning 3615, black with clear, flat bottom) on a Tecan Safire plate reader. a) Absorption of 100 µL eGFP solutions with a concentration of 50 µM. b) Emission spectra of 100 µL eGFP solutions with a concentration of 5 µM. Excitation: 450 nm, bandwidth: 5 nm at 20 °C.

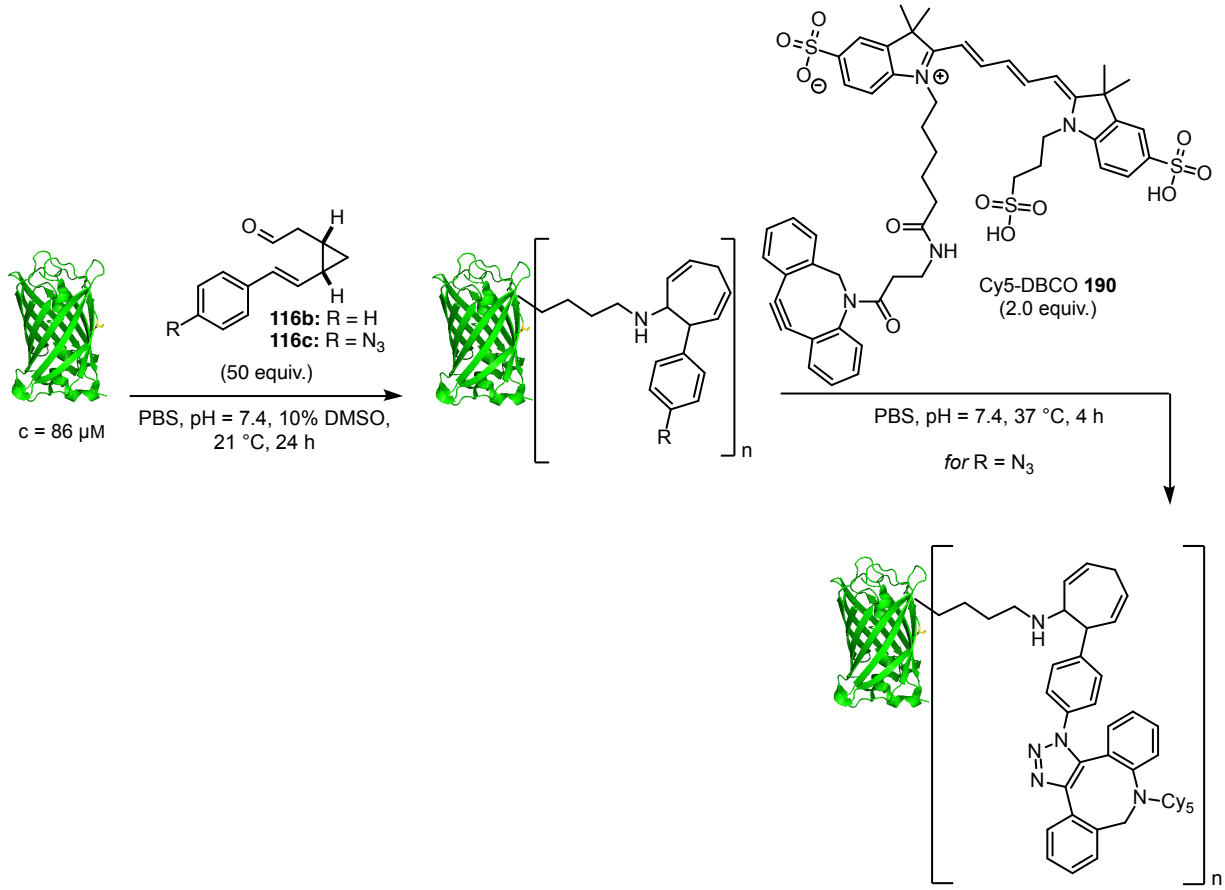
With a protocol for the modification of proteins in hand, the selectivity of the reaction for lysine residues was evaluated by mass spectrometry (LC-MS/MS) after trypsin ingestion of the modified eGFP. For peptide fragmentation during MS/MS electron transfer/higher energy collision dissociation had to be applied to preserve the modification during the fragmentation. Thus, modification sites could clearly be identified and in accordance with the small molecule studies, solely modified lysine residues were identified. Successful cysteine labelling with an ethynylphosphonamidate reagent[367] after modification with aldehyde **116b** confirmed that the reactivity of the sulfhydryl group of the eGFP mutant is retained.

To compare the developed strategy with other protein modification procedures, the reaction rate with a model amine **48l** was measured by the Hackenberger group under the optimised reaction conditions in PBS (*Scheme 3.35*). Even though, the measured second order rate constant of 0.33 $M^{-1}s^{-1}$ is slightly lower than that for instance for modification with NHS esters,[368] the reaction rate is still in the range of many other commonly applied protein labelling procedures.[369]



Scheme 3.35: The reaction of aldehyde **116b** with 3-phenyl-1-propylamine (**48l**) under buffered conditions in PBS was used to determine a second order rate constant to compare the developed labelling strategy with existing methods.

Additionally, the far red fluorescent Cy5 handle was incorporated to eGFP, following a two step modification protocol: First, optimised reaction conditions were used to modify eGFP with the azide substituted aldehyde **116c**. Subsequently, the resulting azide was selectively modified with a commercially available Cy5-dibenzocyclooctyne (**190**) *via* Strain-Promoted-Azide-Alkyne-Cycloaddition (SPAAC, *Scheme 3.36*).[370] Successful Cy5-labelling was confirmed by MS-analysis of the intact proteins and in gel fluorescence after SDS-PAGE separation showed selective Cy5-labelling of proteins modified with aldehyde **116c** over proteins modified with aldehyde **116b** or unmodified proteins.



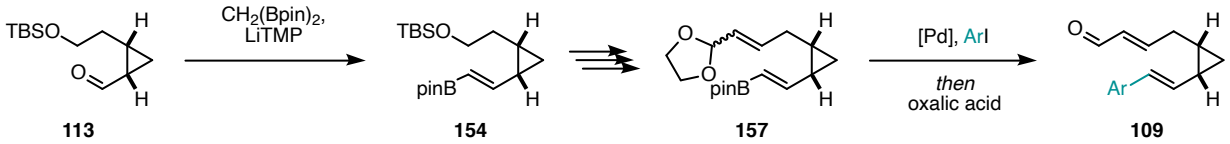
Scheme 3.36: Reaction of eGFP with aldehyde **116b** or **116c** followed by SPAAC with fluorescent dye **190**.

This clearly demonstrates that the lysine selective protein modification protocol is able to incorporate bioorthogonal azide-handles into proteins that can be subsequently modified with chemoselective SPAAC to incorporate highly functional modifications.

4 Conclusion and Outlook

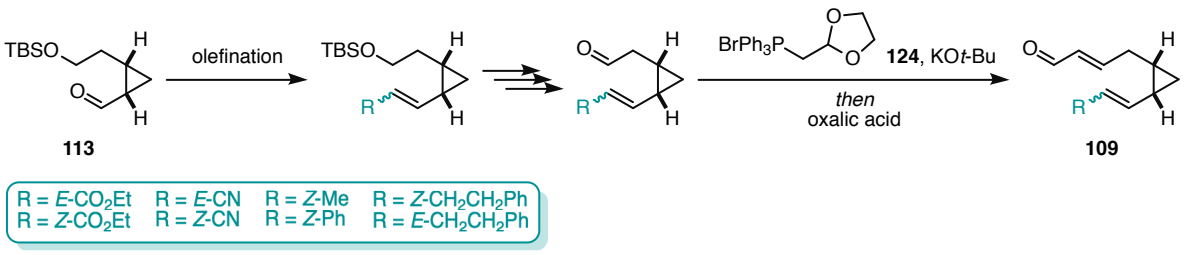
4.1 Conclusion

The dienamine-induced DVCPR represents a mechanistically new approach for 3,3-sigmatropic rearrangements. A general method for the synthesis of 4-(2-vinylcyclopropyl)but-2-enals **109** was not known at the beginning of these studies. Therefore, a synthetic strategy was developed and the substrates for the DVCPR could be obtained *via* three different pathways. A broad substrate library could be obtained from one common precursor **157** by Suzuki coupling with aryl iodides (*Scheme 4.1*). The boronate **157** was delivered by bora-Wittig-reaction of aldehyde **113**. Diversification in the last step of the synthesis makes this approach especially attractive for the creation of numerous substrates.



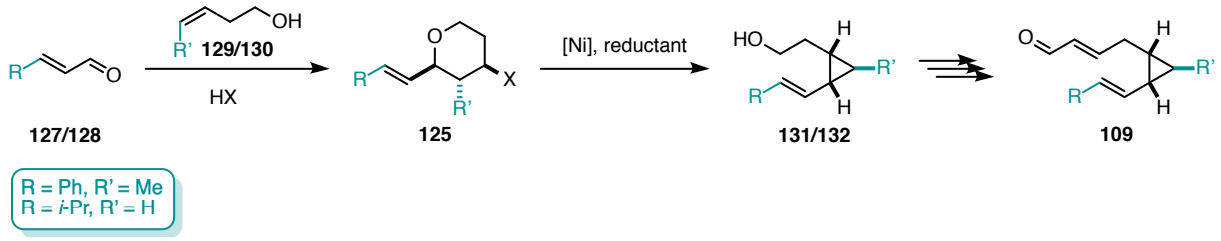
Scheme 4.1: Synthesis of α,β-unsaturated aldehydes **109** *via* Suzuki-coupling.

The substrates that could not be prepared *via* the Suzuki-coupling were obtained from aldehyde **113** by Wittig- or Horner-Wadsworth-Emmons reaction and subsequent homologation to the enal (*Scheme 4.2*).



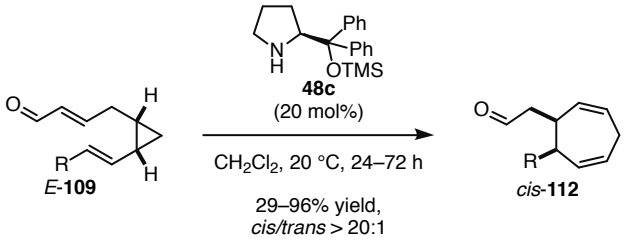
Scheme 4.2: Preparation of substrates by olefination of aldehyde **113**.

A step efficient synthesis of enals **109** was developed employing the nickel-catalysed reductive cross-coupling demonstrated by Jarvo and co-workers (*Scheme 4.3*). The tetrahydropyrans **125a** and **125b** were obtained by Prins cyclisation of the corresponding α,β-unsaturated aldehydes with homoallylic alcohols. The nickel-catalysed reductive cross coupling of the tetrahydropyrans then delivered the cyclopropyl alcohols **131** and **132** in good yields. The alcohols could be converted to the desired enals **109b** and **109c** by oxidation and homologation. As this approach relies on the diverse substituents being already contained in the starting material it is attractive especially in the synthesis of individual enals.



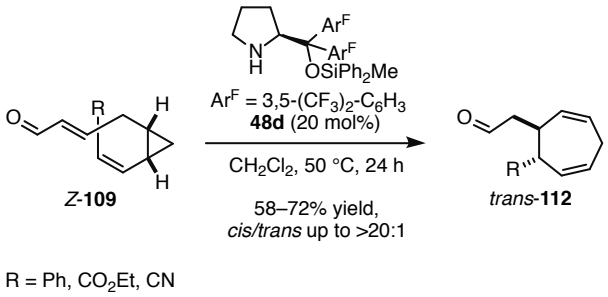
Scheme 4.3: Synthesis of substrates by nickel-catalysed reductive cross-coupling of tetrahydropyrans **125**.

With the substrates in hand, the reaction conditions for the dienamine-induced DVCPR were optimised and the *E*-vinyl enals *E*-**109** were converted to the *cis*-cycloheptadienes **112** in good yields and high stereoselectivity under catalysis using the JØRGENSEN-HAYASHI amine **48c** (*Scheme 4.4*). It was shown that different acids can be used as additives to shorten the reaction time but should be handled with care since the product decomposed under acidic conditions and prolonged reaction time. Therefore, the exploration of the reaction scope was conducted without additives.



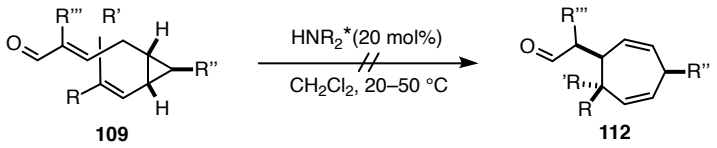
Scheme 4.4: DVCPR of *E*-vinyl enals **109**.

It could be also demonstrated that the reaction is sensitive to steric bulk on the substrates. The *Z*-vinyl enals **109** underwent cyclisation to the *trans*-cycloheptadienes **112** only if they carried an activating substituent (Ph, CO_2Et or CN) and at elevated reaction temperature (*Scheme 4.5*).



Scheme 4.5: DVCPR of *Z*-vinyl enals **109**.

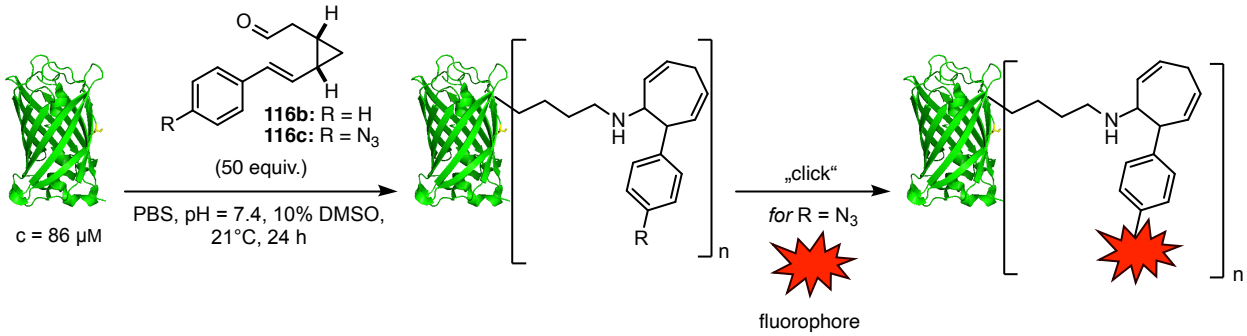
The influence of the steric bulk on the cyclisation becomes even more apparent when enals **109** were additionally substituted at the α-position or the cyclopropyl moiety. These substrates did not undergo the rearrangement under any conditions applied (*Scheme 4.6*).



b: R = Ph, R' = H, R'' = Me, R''' = H
c: R = Me, R' = Me, R'' = H, R''' = H
bb: R = Ph, R' = H, R'' = H, R''' = Me

Scheme 4.6: Attempted rearrangement of highly substituted enals **109**.

Aldehydes **116** that were obtained as intermediates in the synthesis of α,β-unsaturated aldehydes **109** were tested for their suitability as reagents for the covalent modification of proteinogenic lysine residues. In coorporation with the group of Hackenberger it was demonstrated that proteins can be modified selectively at the ε-amino group of lysine with the aldehydes **116b** and **116c**. A protocol for the modification of eGFP was established (*Scheme 4.7*). The azide functionality of **116c** also allowed for further modification with functional molecules. The fluorescent dye Cy5 was attached by SPAAC as an example.



Scheme 4.7: Modification of eGFP with aldehydes **116b** and **116c**.

4.2 Outlook

With the optimised conditions for the dienamine-induced DVCPR established and the influence of substituents on the reaction studied, further investigations could deal with the application of this rearrangement in natural product synthesis. The DVCPR has already been used to gain access to cycloheptadienes with a skipped diene moiety that are otherwise difficult to synthesise (see 1.1.3). This structural motif is contained in several natural products like the benzotropolone petradoriolone (**191**), isolated 2018 from *petradoria pumila*,[371] or in form of cyclohepta[*b*]indoles like exotine A (**192**) and exotine B (**193**) which has been synthesised for the first time in 2018 by Trauner and co-workers.[372] It is also imaginable that a cycloheptadiene obtained by the dienamine induced DVCPR could serve as an intermediate in the synthesis of chrysanthemulides (**194**) which have been isolated from *chrysanthemum indicum* the same flower, *trans*-chrysanthemic acid (**1**) has been isolated from.[373]

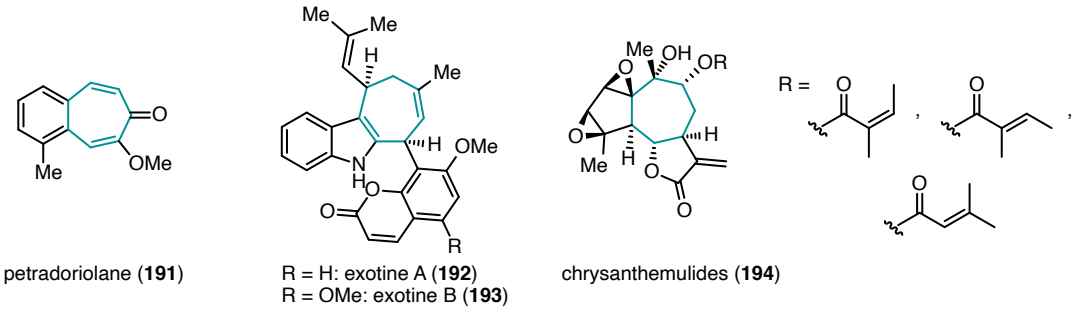
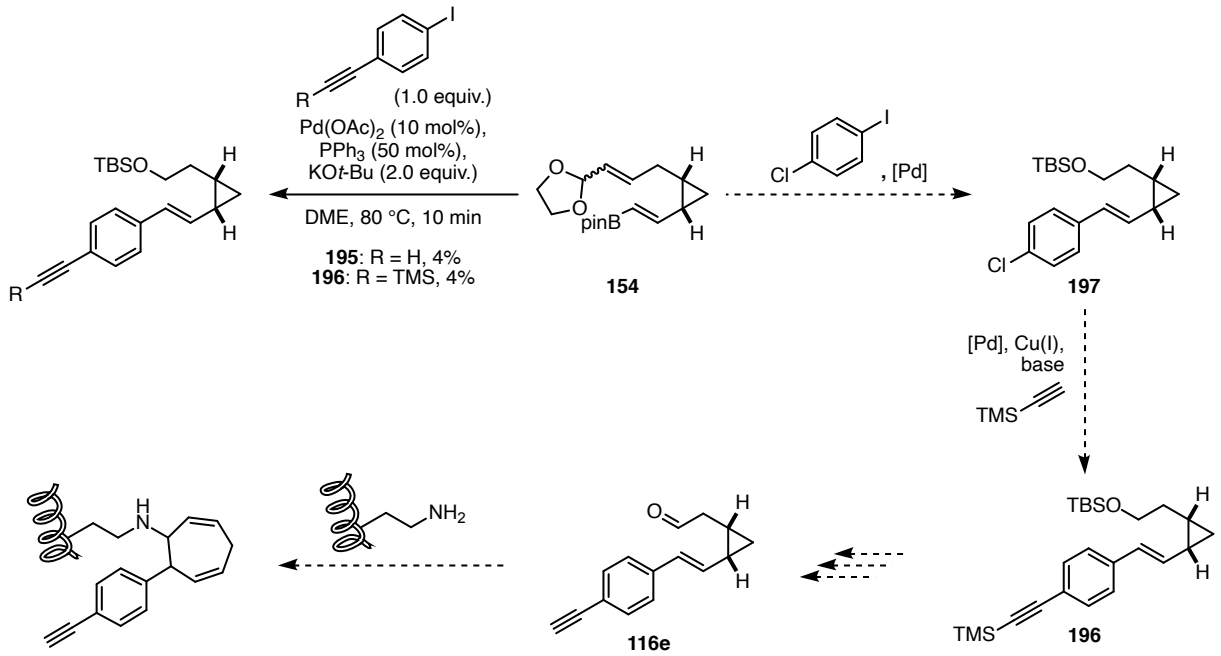


Figure 4.1: Selected examples for natural products containing a cycloheptadiene or derivatives thereof.

The covalent protein modification by aldehydes **116** discussed in 3.2 is another interesting starting point for further studies. The influence of different aryl substituents on the reaction still needs to be studied in order to increase the reaction rate and to lower the reagent loading. In coorporation with Hacker and co-workers, the synthesis of aldehyde **116e** carrying an alkyne is currently under investigation. Similar to the azide in **116c**, the alkyne shall serve as a handle for further functionalisation of modified proteins by cycloaddition chemistry. However, preliminary studies showed that the Suzuki coupling of boronate **154** with 4-iodophenylacetylene or 1-trimethylsilyl-2-(4-iodophenyl)acetylene gives very poor yields of the coupling products **195** and **196** (*Scheme 4.8*). For future studies, the synthesis should be conducted *via* Suzuki coupling of **154** with 4-chloroiodobenzene and subsequent Sonogashira coupling. The silylether **196** can then be converted to aldehyde **116e** whose application to different proteins is currently under investigation.



Scheme 4.8: Proposed synthesis of aldehyde **116e** and the reaction with proteinogenic lysine residues.

5 Experimental Section

5.1 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), Bruker Avance 500 (500 MHz), Varian Inova 600 (600 MHz) and a Bruker Avance 700 (700 MHz) in $CDCl_3$, C_6D_6, or CD_3OD as solvent. The chemical shifts were reported relative to $CDCl_3$ (δ = ^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm), C_6D_6 (δ = ^{1}H: 7.16 ppm, ^{13}C: 128.06 ppm), or CD_3OD (δ = ^{1}H: 3.31 ppm, ^{13}C: 49.00 ppm). The multiplicities of the signals are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, br = broad, m = multiplet, m_c = centred multiplet.

The spectra were evaluated with the software MestReNova 10.0.2.

High resolution mass spectra were obtained on an ESI-FTICR-MS: Ionspec QFT-7 (Agilent/Varian), or a HR-EI-MS: Autospec Premier (Waters). **Low resolution mass spectra (GC-MS)** were recorded on a GC system Agilent Technologies 7890-A series/Mass selective detector, Agilent Technologies 5975 C (Column: HP-5MS (J&W Scientific, Agilent); 30 m, 0.250 mm i.D., Film 0.25 µm).

Enantiomeric ratios were determined by chiral HPLC (Agilent Series 1200 with DAD) or by GC (Agilent 7890B) on a chiral column. The specific conditions are given in each case.

IR spectra were measured on a JASCO FT/IR-4100 spectrometer. Characteristic absorption bands are displayed in wavelength $\tilde{\nu}$ in cm^{-1} and were analysed with the software Spectral Manager from JASCO.

Optical rotations were measured on a JASCO P-2000 polarimeter at 589 nm using 100 mm cells. The solvent, temperature and concentration (g/100 mL) of the measurement are indicated.

Thin Layer Chromatography (TLC): Reaction progress was monitored by thin layer chromatography on aluminium 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 EtOH, 5 mL conc. H_2SO_4, 1.5 mL AcOH and 3.7 mL *p*-anisaldehyde).

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

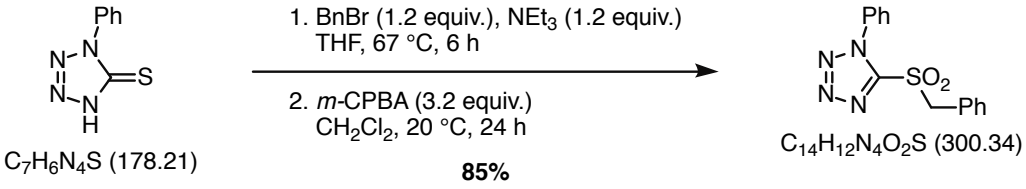
Automated Medium Pressure Liquid Chromatography (MPLC) was performed with a Teledyne ISCO Combiflash Rf.

Reagents and Solvents: Reactions with air or moisture-sensitive substances, if not otherwise indicated, were carried out under an argon atmosphere with the help of Schlenk technique. Anhydrous DMF and DMSO were purchased from Acros Organics in AcroSeal©-bottles under Argon atmosphere with molecular sieves (4 Å). $CHCl_3$ was filtrated over $NaHCO_3$ prior to use. THF was freshly distilled over Na/benzophenone prior to use. DME was dried over CaH_2, distilled and degassed three times by freeze-pump-thaw-technique prior to use. All other anhydrous solvents were purified by the solvent purification system MB-SPS-800 (Braun). Catalyst **48d** was synthesised by V. Schmiedel. Catalyst **48i** was synthesised by J. Dahl. All other reagents and solvents were used as purchased from commercial suppliers unless otherwise noted. 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 40 °C water bath temperature.

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

5.2 Preparation of Reagents

5.2.1 5-(Benzylsulfonyl)-1-phenyl-4,5-dihydro-1*H*-tetrazole (122)



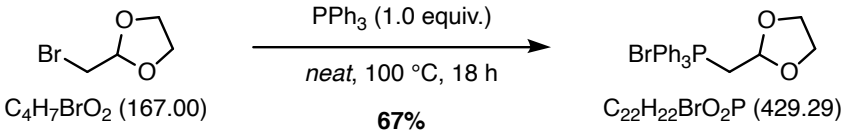
$C_7H_6N_4S$ (178.21) → $C_{14}H_{12}N_4O_2S$ (300.34)

A solution of 1-phenyl-1*H*-tetrazol-5-thiol (1.0 g, 5.6 mmol, 1.0 equiv.) in THF (20 mL, 0.3 M) was treated with NEt_3 (0.96 mL, 6.9 mmol, 1.2 equiv.). The reaction mixture was stirred for 40 min before benzyl bromide (0.80 mL, 6.7 mmol, 1.2 equiv.) was added. The mixture was stirred for 6 h at 67 °C. The reaction was quenched with H_2O (20 mL) and the resulting biphasic mixture was extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (38 mL, 0.15 M) and treated with *meta*-chloroperoxybenzoic acid (*m*-CPBA, 70%, 4.4 g, 18.0 mmol, 3.2 equiv.) at 0 °C. The resulting solution was allowed to reach 20 °C and was stirred for 24 h. The reaction was quenched with sat. aq. $NaHSO_4$ (100 mL). The phases were separated and the organic phase was washed with sat. aq. $NaHCO_3$ (3 x 100 mL), dried over $MgSO_4$, and filtrated. The solvent was removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 2:1) delivered the title compound **122** as a colourless solid (1.4 g, 4.8 mmol, 85%)

R_f (pentane/ethyl acetate = 2:1) = 0.5; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.93 (s, 2H, CH_2), 7.27–7.38 (m, 5H, *H*-Ar), 7.39–7.43 (m, 1H, *H*-Ar), 7.45–7.50 (m, 2H, *H-Ar*), 7.53–7.59 (m, 1H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 62.5, 124.9, 125.4 (2*C*), 129.3 (2*C*), 129.5 (2*C*), 129.9, 131.5, 131.8 (2*C*), 132.9, 153.0 ppm.

The spectroscopic data agree with previously published results.[374]

5.2.2 ((1,3-Dioxolan-2-yl)methyl)triphenyl-λ^5-phosphonium Bromide (124)

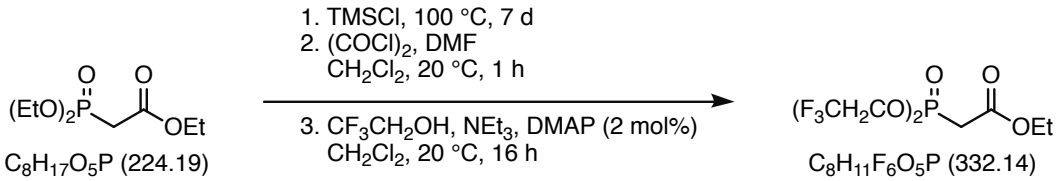


In a pressure tube, 2-bromomethyl-1,3-dioxolane (8.07 g, 48.3 mmol, 1.0 equiv.) and triphenylphosphine (12.7 g, 48.3 mmol, 1.0 equiv.) were stirred at 100 °C for 18 h. The reaction was cooled to 20 °C afterwards and the reaction mixture was diluted with CH_2Cl_2 (100 mL). The resulting clear solution was added to dry Et_2O (200 mL) at 0 °C and the precipitate was filtrated, washed with Et_2O, and dried *in vacuo*. The title compound **124** was obtained as a colourless solid (13.8 g, 32.2 mmol, 67%)

^{31}P NMR (162 MHz, $CDCl_3$): δ = 21.4 ppm; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 3.61–3.73 (m, 4H, OCH_2), 4.54 (dd, ^3J = 13.2 Hz, ^4J = 4.0 Hz, 1H, C*H*), 5.47 (dt, ^3J = 13.2 Hz, ^2J = 4.0 Hz, 1H, PCH_2), 7.62–7.69 (m, 6H, *H*-Ar), 7.72–7.78 (m, 3H *H*-Ar), 7.83–7.90 (m, 6H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 65.2 (2*C*), 112.4, 119.4 (d, *J* = 88 Hz, 3*C*), 130.2 (d, *J* = 13 Hz, 6*C*), 134.2 (d, *J* = 11 Hz, 6*C*), 134.8 (d, *J* = 3 Hz) ppm. The carbon adjacent to the phosphor atom could not be detected.

The spectroscopic data agree with previously published results.[375]

5.2.3 Ethyl 2-(Bis(2,2,2-trifluoroethoxy)phosphoryl)acetate (171)



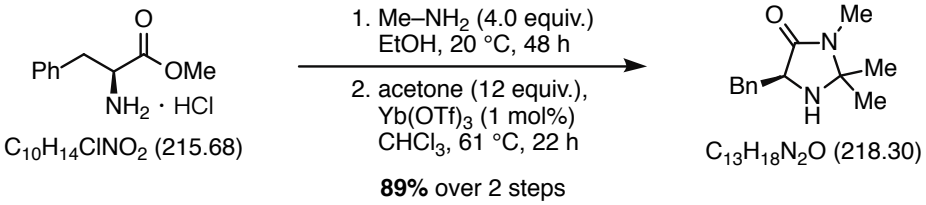
In a pressure tube, ethyl 2-(diethoxyphosphoryl)acetate (1.0 mL, 5.0 mmol, 1.0 equiv.) was added to chlorotrimethylsilane (3.2 mL, 25 mmol, 5.0 equiv.). The mixture was stirred at 100 °C for 7 d. The volatile components were removed under reduced pressure. The residue was dissolved in dry CH_2Cl_2 (12 mL, 0.4 M) and one drop of DMF was added. Oxalyl chloride (1.3 mL, 22 mmol, 4.3 equiv.) was added dropwise under vigorous gas evolution. The pale-yellow reaction mixture was stirred for 1 h at 20 °C. The solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (5 mL, 1.0 M). A solution of trifluoroethanol

(1.5 mL, 21 mmol, 4.0 equiv.) and triethylamine (4.2 mL, 30 mmol, 6.0 equiv.) in CH_2Cl_2 (5 mL, 4.0 M regarding the alcohol) was added dropwise at 0 °C. 4-Dimethylaminopyridine (DMAP, 12 mg, 98 µmol, 2 mol%) was added and the reaction mixture was stirred for 16 h at 20 °C. The solution was diluted with CH_2Cl_2 (100 mL), washed with brine (50 mL), and dried over $MgSO_4$. After filtration, the solvent of the filtrate was removed *in vacuo*. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 2:1) affording the title compound **171** (1.2 g, 3.5 mmol, 65% over 3 steps) as a pale-yellow oil.

R_f (pentane/ethyl acetate = 2:1) = 0.6; **^{31}P NMR** (161 MHz, $CDCl_3$): δ = 24.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −75.3 ppm; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.28 (t, ^3J = 7.1 Hz, 3H, CH_3), 3.14 (d, $^2J_{H,P}$ = 21.2 Hz, 2H, PCH_2), 4.21 (q, ^3J = 7.1 Hz, 2H, OCH_2CH$_3$), 4.50–4.40 (m, 4H, OCH_2CF$_3$) ppm.

The spectroscopic data agree with previously published results.[354]

5.2.4 (*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one (48b)

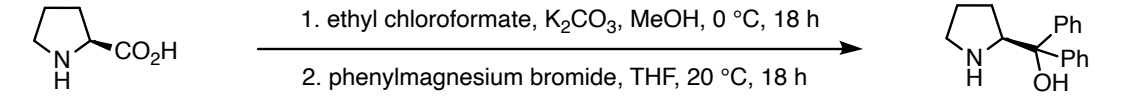


(*S*)-Phenylalanine methyl ester hydrochloride (5.00 g, 23.2 mmol, 1.0 equiv.) was added to a solution of methyl amine in EtOH (33%, 11.5 mL, 92.7 mmol, 4.0 equiv.) and the reaction mixture was stirred for 48 h. Volatile components were removed *in vacuo* and the residue was taken up in Et_2O. The solvent was evaporated under reduced pressure to remove remaining methyl amine. These steps were repeated until the residue formed a colourless solid which was dissolved in sat. aq. $NaHCO_3$ (48 mL). The aqueous phase was extracted with $CHCl_3$ (3 x 50 mL). The combined organic phases were dried over $MgSO_4$, filtrated, and the solvent was removed under reduced pressure. The residue was taken up in $CHCl_3$ (230 mL, 0.1 M) and treated with ytterbium(III) trifluoromethanesulfonate (137 mg, 220 µmol, 1 mol%) and acetone (20.0 mL, 272 mmol, 12 equiv.). The reaction mixture was stirred at 61 °C for 22 h. The solvents were removed under reduced pressure afterwards. Purification of the crude product by column chromatography (silica gel, ethyl acetate) delivered the title compound **48b** as yellow oil (4.50 g, 20.6 mmol, 89%).

R_f (ethyl acetate) = 0.3; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 1.14 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.72 (br s, 1H, NH), 2.73 (d, J = 0.7 Hz, 3H, NCH_3), 2.99 (dd, ^2J = 14.2 Hz, ^3J = 6.9 Hz, 1H, PhCH_2), 3.13 (dd, ^2J = 14.2 Hz, ^3J = 4.4 Hz, 1H, PhCH_2), 3.77 (dd, ^3J = 6.9, 4.4 Hz, 1H, NCH), 7.18–7.22 (m, 3H, *H*-Ar), 7.26–7.29 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 25.3, 25.4, 27.3, 37.4, 59.4, 75.6, 126.9, 128.7, 129.6, 137.3, 173.5 ppm.

The spectroscopic data agree with previously published results.[376]

5.2.5 (*S*)-Diphenyl(pyrrolidin-2-yl)methanol (61)



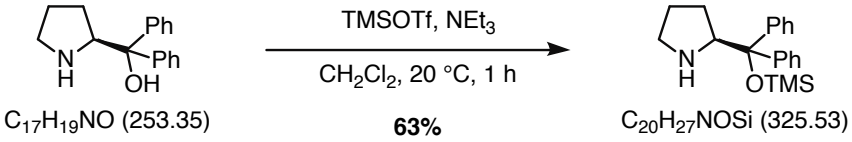
$C_5H_9NO_2$ (115.13) — **36%** — $C_{17}H_{19}NO$ (253.35)

A solution of L-proline (6.90 g, 60.0 mmol, 1.0 equiv.) and potassium carbonate (8.31 g, 60.0 mmol, 1.0 equiv.) in dry methanol (120 mL, 0.5 M) was carefully treated with ethyl chloroformate (12.5 mL, 132 mmol, 2.2 equiv.) at 0 °C. The reaction mixture was stirred at this temperature for 18 h before the solvent was removed under reduced pressure. The residue was taken up in H_2O (100 mL) and extracted with $CHCl_3$ (3 x 90 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The solvent was removed under reduced pressure to deliver the *N,O*-protected proline as crude product which was used in the next step without further purification (12.3 g, 60.0 mmol, *quant.*). Magnesium (11.7 g, 480 mmol, 8.0 equiv.) was flame-dried under an argon atmosphere. At 20 °C, THF (180 mL, 2.7 M) was added. To the resulting suspension, bromobenzene (25.1 mL, 240 mmol, 4.0 equiv.) in THF (90 mL, 2.7 M) was added dropwise. After complete addition, the reaction mixture was stirred at 20 °C for 18 h and added to a solution of the *N,O*-protected proline (12.3 g, 60.0 mmol, 1.0 equiv.) in THF (120 mL, 0.5 M) at 0 °C. The reaction mixture was stirred at this temperature for 18 h before the reaction was quenched with sat. aq. NH_4Cl (120 mL). The resulting precipitate was filtered off and the filtrate was extracted with $CHCl_3$ (2 x 90 mL). The combined organic phases were washed with brine (2 x 100 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed under reduced pressure. The residue was taken up in dry methanol (120 mL, 0.5 M) and treated with potassium hydroxide (33.7 g, 600 mmol, 10 equiv.). The reaction mixture was stirred at 65 °C for 6 h and the solvent was removed under reduced pressure afterwards. The residue was taken up in H_2O (60 mL) and extracted with CH_2Cl_2 (3 x 90 mL). The combined organic phases were dried over $MgSO_4$ and filtrated. The solvents of the filtrate were removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol/triethylamine = 20:1:0.1). The resulting yellow oil was recrystalised from hexane delivering the title compound **61** as colourless crystals (5.52 g, 21.8 mmol, 36%).

R_f (dichloromethane/methanol/triethylamine = 20:1:0.1) = 0.3; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.52–1.78 (m, 4H, C*H*$_2$), 2.88–3.01 (m, 1H, C*H*$_2$), 2.98–3.10 (m, 1H, C*H*$_2$), 4.26 (t, ^3J = 7.6 Hz, 1H, NC*H*), 7.11–7.23 (m, 2H, *H*-Ar), 7.23–7.33 (m, 4H, *H*-Ar), 7.47–7.53 (m, 2H, *H*-Ar), 7.55–7.60 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 25.6, 26.4, 46.9, 64.6, 77.2, 125.7 (2*C*), 126.0 (2*C*), 126.5, 126.6, 128.1 (2*C*), 128.4 (2*C*), 145.5, 148.3 ppm.

The spectroscopic data agree with previously published results.[377]

5.2.6 (*S*)-2-(Diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (48c)



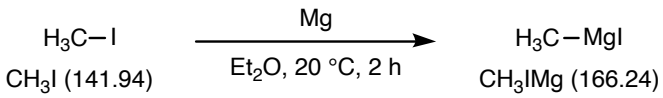
$C_{17}H_{19}NO$ (253.35) — **63%** — $C_{20}H_{27}NOSi$ (325.53)

A solution of **61** (3.77 g, 14.9 mmol, 1.0 equiv.) in CH_2Cl_2 (100 mL, 0.15 M) was treated with triethylamine (2.70 mL, 19.3 mmol, 1.3 equiv.) and trimethylsilyl trifluoromethanesulfonate (3.50 mL, 19.3 mmol, 1.3 equiv.) at 0 °C. The reaction mixture was stirred at 20 °C for 1 h before the reaction was quenched with H_2O (100 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 90 mL). The combined organic phases were washed with brine (150 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol = 9:1→4:1) affording the title compound **48c** as a colourless oil (3.06 g, 9.40 mmol, 63%).

R_f (dichloromethane/methanol = 9:1) = 0.3; $[\alpha]_D^{20}$ = +32.3 (c = 1.00, $CHCl_3$) **^{1}H NMR** (500 MHz, $CDCl_3$): δ = −0.09 (s, 9H, CH_3), 1.33–1.48 (m, 1H, NCH_2), 1.57–1.73 (m, 3H, $NCHCH_2$ + NCH_2), 2.71–2.83 (m, 1H, NCH_2CH_2), 2.85–2.97 (m, 1H, NCH_2CH_2), 3.47 (br s, 1H, NH), 4.16 (t, ^3J = 7.3 Hz, 1H, NCH), 7.18–7.35 (m, 6H, *H*-Ar), 7.34–7.38 (m, 2H, *H*-Ar), 7.43–7.47 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 2.2 (3*C*), 25.0, 27.6, 47.2, 65.8, 83.0, 127.2, 127.3, 127.8, (2*C*) 127.9 (2*C*), 127.9 (2*C*), 128.5 (2*C*), 145.2, 145.9. ppm.

The spectroscopic data agree with previously published results.[180]

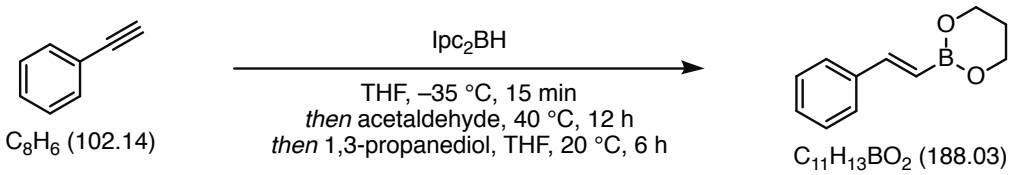
5.2.7 Methylmagnesium Iodide



CH_3I (141.94) — CH_3IMg (166.24)

To a suspension of flame-dried magnesium (2.30 g, 94.6 mmol, 1.5 equiv.) and iodine (2.0 mg, 7.9 µmol, cat.) in Et_2O (14 mL, 6.6 M) iodomethane (3.90 mL, 62.6 mmol, 1.0 equiv.) was added dropwise over a period of 30 min. The reaction mixture was stirred for 2 h at 20 °C. The solution was filtered over celite under an argon atmosphere, washed with Et_2O (3 x 1 mL), and stored under argon as a solution (1.73 M in Et_2O). The concentration of the solution was determined by Knochel's titration method.[378]

5.2.8 (*E*)-2-Styryl-1,3,2-dioxaborinane (153)

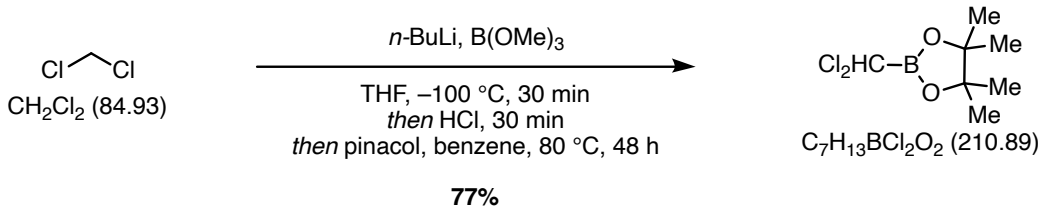


A solution of borane dimethylsulfide (10 M in THF, 0.49 mL, 4.9 mmol, 1.0 equiv.) in dry THF (4.9 mL, 1.0 M) was treated with α-pinene (1.6 mL, 9.8 mmol, 2.0 equiv.) at 0 °C. The solution was stirred for 2 h at 20 °C before it was cooled to −35 °C. Phenylacetylene (0.50 g, 4.9 mmol, 1.0 equiv.) in dry THF (4.9 mL, 1.0 M) was added dropwise over a period of 30 min and the reaction mixture was stirred at this temperature for 15 min. The reaction was allowed to warm to 20 °C and acetaldehyde (5.5 mL, 98 mmol, 20 equiv.) was added. The reaction mixture was heated at 78 °C for 12 h. The solvents were removed under reduced pressure afterwards, the residue was taken up in THF (4.9 mL, 1.0 M) and treated with 1,3-propanediol (1.8 mL, 25 mmol, 5.0 equiv.). The reaction mixture was stirred at 20 °C for 6 h, and the volatile components were removed under reduced pressure. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1→4:1→0:1) affording the title compound **153** as a colourless oil (0.22 g, 1.2 mmol, 24%).

^{11}B NMR (128 MHz, $CDCl_3$): δ = 25.9 ppm; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 1.96 (p, ^{3}J = 5.5 Hz, 2H, CH_2), 4.04 (t, ^{3}J = 5.6 Hz, 4H, OCH_2), 6.02 (d, $^{2}J_{B,H}$ = 18.3 Hz, 1H, BC*H*), 7.19–7.24 (m, 2H, *H*-Ar, BCHC*H*), 7.26–7.30 (m, 2H, *H*-Ar), 7.40–7.48 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 27.6, 62.0, 127.1, 128.6, 128.6, 138.0, 147.0 ppm. The olefinic carbons could not be detected due to line broadening

The spectroscopic data agree with previously published results.[379]

5.2.9 2-(Dichloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (155)



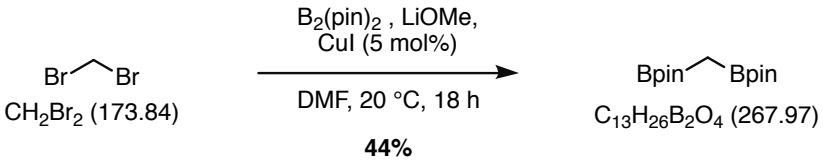
A solution of dichloromethane (0.35 mL, 5.5 mmol, 1.1 equiv.) in dry THF (10 mL, 0.5 M) was cooled to −100 °C and treated dropwise with *n*-BuLi (2.5 M in hexane, 2.0 mL, 5.0 mmol, 1.0 equiv.) over a period of 40 min. After complete addition the reaction mixture was stirred for 30 min at this temperature before trimethyl borate (0.63 mL, 5.5 mmol, 1.1 equiv.) was added. The reaction mixture was stirred again for 30 min, treated with hydrochloric acid (5 M in H_2O, 1.0 mL, 5.0 mmol, 1.0 equiv.), and allowed to reach room temperature. The mixture was extracted with Et_2O (3 x 100 mL) and the solvents of the extract were removed under reduced pressure. The residue was taken up in benzene (11.0 mL, 0.45 M) and treated with pinacol (0.65 g, 5.5 mmol,

1.1 equiv.). The mixture was heated at 80 °C for 48 h. The solvent was removed under reduced pressure and the residue was purified by bulb-to-bulb distillation (20 mbar, 110 °C) affording the title compound **155** as a colourless oil which solidified upon standing (0.89 g, 4.2 mmol, 77%).

^{11}B NMR (128 MHz, $CDCl_3$): δ = 28.1 ppm; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.33 (s, 12H, C*H*$_3$), 5.35 (s, 1H, Cl_2CH) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 24.6 (4*C*), 25.0 (2*C*), 85.9 ppm.

The spectroscopic data agree with previously published results.[380]

5.2.10 Bis((pinacolato)boryl)methane (197)



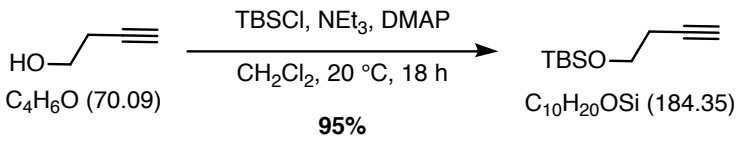
In a glovebox, pinacolborane (1.0 g, 3.9 mmol, 1.0 equiv.), copper(I) iodide (38 mg, 0.20 mmol, 5 mol%), and lithium methanolate (0.22 g, 5.9 mmol, 1.5 equiv.) were added to a Schlenk flask. The solids were dissolved in dry DMF (4.0 mL, 1.0 M) and the black solution was carefully treated with dibromomethane (0.27 mL, 3.9 mmol, 1.0 equiv.). The reaction mixture was stirred for 12 h at 20 °C before the solution was diluted with Et_2O (5.0 mL) and filtrated over silica gel. The solvents of the filtrate were removed under reduced pressure and the residue was taken up in hexane (50 mL). The organic phase was washed with H_2O (3 x 100 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed *in vacuo* affording the title compound **197** as a colourless oil which solidified upon standing (0.46 g, 1.7 mmol, 44%).

^{11}B NMR (128 MHz, $CDCl_3$): δ = 32.6 ppm; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.34 (s, 2H, C*H*$_2$), 1.22 (s, 24H, C*H*$_3$) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 24.8 (8*C*), 82.9 (d, $J_{C,B}$ = 7 Hz, 4*C*), 83.0 ppm.

The spectroscopic data agree with previously published results.[381]

5.3 First Generation Synthesis of Substrates

5.3.1 (But-3-yn-1-yloxy)(*tert*-butyl)dimethylsilane (198)



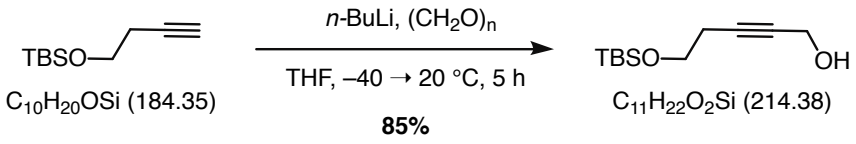
A solution of 3-butyn-1-ol (5.00 mL, 66.2 mmol, 1.0 equiv.) in dry CH_2Cl_2 (220 mL, 0.3 M) was treated successively with 4-dimethylaminopyridine (800 mg, 6.62 mmol, 10 mol%), triethylamine (11.0 mL, 79.4 mmol,

1.2 equiv.) and *t*-butyldimethylsilyl chloride (11.0 g, 72.7 mmol, 1.1 equiv.) at 0 °C. After complete addition the reaction mixture was stirred at 20 °C for 18 h. An aqueous solution of NH_4Cl (300 mL) was added and the phases were separated afterwards. The organic phase was washed with sat. aq. NH_4Cl (100 mL) and brine (100 mL), dried over $MgSO_4$, and filtrated. The solvent was removed under reduced pressure. The crude product was filtrated over a plug of silica gel eluting with pentane/ethyl acetate = 60:1 to obtain the silyl ether **198** as a colourless oil (11.6 g, 62.7 mmol, 95%).

R_f (pentane/ethyl acetate = 40:1) = 0.9; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.07 (s, 6H, CH_3), 0.90 (s, 9H, CH_3), 1.96 (t, ^4J = 2.7 Hz, 1H, CC*H*), 2.40 (td, ^3J = 7.1 Hz, ^4J = 2.7 Hz, 2H, CH_2CCH), 3.74 (t, ^3J = 7.1 Hz, 2H, OCH_2) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = −5.2 (2*C*), 18.4, 22.9, 26.0 (3*C*), 61.8, 69.4, 81.6 ppm.

The spectroscopic data agree with previously published results.[382]

5.3.2 5-((*tert*-Butyldimethylsilyl)oxy)pent-2-yn-1-ol (119)

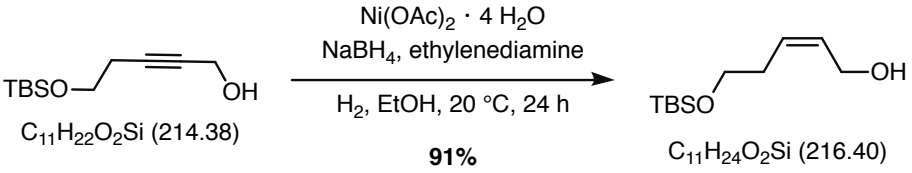


n-BuLi (2.5 M in hexanes, 21.6 mL, 54.1 mmol, 1.0 equiv.) was added dropwise to a solution of the silyl ether **198** (9.97 g, 54.1 mmol, 1.0 equiv.) in dry THF (100 mL, 0.5 M) at −40 °C. The reaction mixture was stirred for 15 min at this temperature and then transferred to a suspension of paraformaldehyde (4.80 g, 160 mmol, 3.0 equiv.) in dry THF (50 mL) at −45 °C *via* transfer cannula. After complete addition, the reaction mixture was stirred at 20 °C for 5 h. The reaction mixture was diluted with Et_2O (100 mL), washed with brine (200 mL), dried over $MgSO_4$, and filtrated. The solvents were evaporated under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1). The alkyne **119** was obtained as a colourless oil (9.68 g, 45.2 mmol, 85%).

R_f (pentane/ethyl acetate = 4:1) = 0.4; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.07 (s, 6H, CH_3), 0.89 (s, 9H, CH_3), 1.72 (t, ^3J = 6.0 Hz, 1H, O*H*), 2.43 (tt, ^3J = 7.2 Hz, ^5J = 2.2 Hz, 2H, CC-CH_2), 3.72 (t, ^3J = 7.2,Hz, 2H, SiOCH_2), 4.23 (dt, ^3J = 6.0 Hz, ^5J = 2.2 Hz, 2H, CH_2OH) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = −5.1 (2*C*), 18.5, 23.3, 26.0 (3*C*), 51.4, 62.0, 79.6, 83.5 ppm.

The spectroscopic data agree with previously published results.[382]

5.3.3 (*Z*)-5-((*tert*-Butyldimethylsilyl)oxy)pent-2-en-1-ol (114)

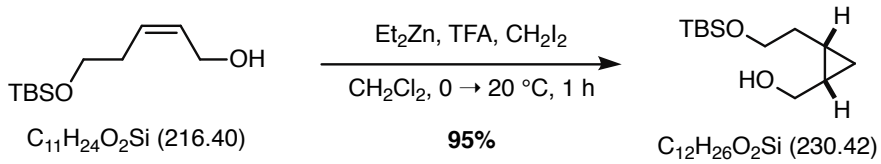


$Ni(OAc)_2 \cdot 4H_2O$ (1.13 g, 4.54 mmol, 10 mol%) was dissolved in EtOH (95%, 67 mL). H_2 was passed through the reaction mixture for 10 min before a solution of $NaBH_4$ (1 M in dry EtOH, 4.54 mL, 4.54 mmol, 10 mol%) was added dropwise. The reaction mixture immediately turned black and H_2 was passed through it again for 30 min. Ethylenediamine (683 mg, 11.4 mmol, 25 mol%) and a solution of alkyne **119** (9.74 g, 45.4 mmol, 1.0 equiv.) in dry EtOH (120 mL, 0.4 M) were added. The reaction mixture was stirred under an H_2-atmosphere for 3 h. The solvent was evaporated under reduced pressure and the residue was taken up in Et_2O (150 mL). The organic phase was washed with H_2O (200 mL) and the aqueous phase extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (200 mL), dried over $MgSO_4$, and filtrated. The solvent was removed under reduced pressure. The crude product was purified using column chromatography (silica gel, pentane/ethyl acetate = 4:1) yielding the allyl alcohol **114** as a colourless oil (8.89 g, 41.1 mmol, 91%).

R_f (pentane/ethyl acetate = 4:1) = 0.8; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.06 (s, 6H, CH_3), 0.89 (s, 9H, CH_3), 2.05–2.09 (m, 1H, O*H*), 2.34 (dtd, ^3J = 7.6, 6.1 Hz, ^4J = 1.4 Hz, 2H, CHCH_2), 3.64 (t, ^3J = 6.1 Hz, 2H, SiOCH_2), 4.14 (t, ^3J = 5.6 Hz, 2H, HOCH_2), 5.55–5.61 (m, 1H, C=C*H*), 5.78–5.84 (m, 1H, C=C*H*) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = –5.2 (2*C*), 18.6, 26.1 (3*C*), 31.1, 58.2, 62.4, 129.9, 131.0 ppm.

The spectroscopic data agree with previously published results.[306]

5.3.4 2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)methanol (120)

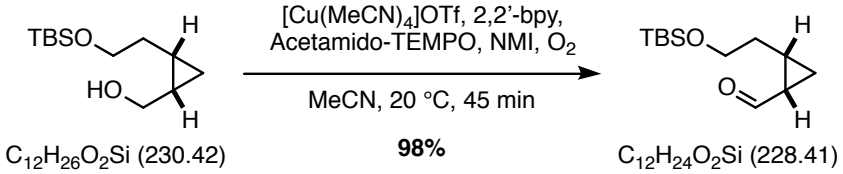


Diethylzinc (1.0 M in hexane, 100 mL, 100 mmol, 2.0 equiv.) in dry CH_2Cl_2 (100 mL) was cooled to 0 °C and a solution of TFA (7.70 mL, 100 mmol, 2.0 equiv.) in dry CH_2Cl_2 (50 mL, 2 M) was carefully added over a period of 30 min. The reaction mixture was stirred for 20 min at this temperature before a solution of CH_2I_2 (8.04 mL, 100 mmol, 2.0 equiv.) in dry CH_2Cl_2 (50 mL, 2 M) was added over a period of 20 min. The mixture was again stirred for 20 min at 0 °C and a solution of allyl alcohol **114** (10.8 g, 50.0 mmol, 1.0 equiv.) in dry CH_2Cl_2 (50 mL, 1 M) was added to the reaction mixture over a period of 20 min. The resulting clear solution was stirred for 45 min at 20 °C. HCl (0.1 M in H_2O, 180 mL) was added to the reaction mixture before the phases were separated. The aqueous phase was extracted with ethyl acetate (3 x 500 mL) and the combined organic phases were washed with brine (500 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under

reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 6:1) to yield the homocyclopropyl alcohol **120** as a colourless oil (10.9 g, 47.3 mmol, 89%).

R_f (pentane/ethyl acetate = 4:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{26}NaO_2Si$, 253.1600, found: 253.1615; **IR (ATR)**: $\tilde{\nu}$ = 3375, 3065, 2954, 2929, 2885, 2857, 1471, 1389, 1254, 1096, 1043, 1006, 835, 775 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = −0.08 (m_c, 1H, *H*-cyclopropyl), 0.11 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.66 (m_c, 1H, *H*-cyclopropyl), 0.75–0.80 (m, 1H, *H*-cyclopropyl), 0.93 (s, 9H, CH_3), 1.24 (m_c, 1H, *H*-cyclopropyl), 1.47 (m_c, 1H, $TBSOCH_2CH_2$), 1.82 (m_c, 1H, $TBSOCH_2CH_2$), 3.23 (m_c, 1H, $HOCH_2$), 3.47 (m_c, 1H, O*H*), 3.70 (m_c, 1H, $TBSOCH_2$), 3.83 (m_c, 1H, $HOCH_2$), 3.87 (m_c, 1H, $TBSOCH_2$) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.3, −5.2, 7.6, 13.8, 18.7, 18.8, 26.2 (3*C*), 30.8, 62.6, 64.6 ppm.

5.3.5 2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropane-1-carbaldehyde (113)

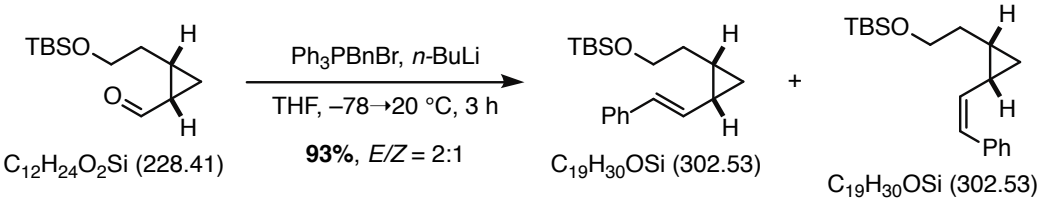


$C_{12}H_{26}O_2Si$ (230.42) → $C_{12}H_{24}O_2Si$ (228.41)

To a solution of homocyclopropyl alcohol **120** (9.07 g, 39.4 mmol, 1.0 equiv.) in MeCN (200 mL, 0.2 M) were added $[Cu(MeCN)_4]OTf$ (742 mg, 1.97 mmol, 5 mol%), 2,2'-bpy (308 mg, 1.97 mmol, 5 mol%), acetamido-TEMPO (420 mg, 1.97 mmol, 5 mol%) and NMI (310 µL, 3.94 mmol, 10 mol%). The resulting brown solution was stirred under an O_2-atmosphere for 45 min until it turned to dark green. H_2O (300 mL) was added and the reaction mixture was extracted with Et_2O (3 x 300 mL). The combined organic phases were washed with brine (300 mL), dried over $MgSO_4$, and filtrated. The solvent was evaporated under reduced pressure and the crude product filtrated through a plug of silica gel eluting with pentane/ethyl acetate = 10:1. The solution was washed with HCl (1 M in H_2O, 2 x 100 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure to yield the cyclopropylcarbaldehyde **113** as a colourless oil (8.79 g, 38.5 mmol, 98%).

R_f (pentane/ethyl acetate = 20:1) = 0.2; **ESI-TOF** *(m/z)*: $[M + Na]^+$ calcd for $C_{12}H_{24}NaO_2Si$, 251.1443, found: 251.1455; **IR (ATR)**: $\tilde{\nu}$ = 3003, 2953, 2928, 2886, 2857, 1704, 1471, 1463, 1443, 1390, 1254, 1101, 988, 835, 811, 776, 689 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.05 (s, 6H, CH_3), 0.89 (s, 9H, CH_3), 1.19 (m_c, 1H, *H*-cyclopropyl), 1.24 (m_c, 1H, *H*-cyclopropyl), 1.60 (m_c, 1H, *H*-cyclopropyl), 1.67–1.74 (m, 1H, $TBSOCH_2CH_2$), 1.82 (m_c, 1H, $TBSOCH_2CH_2$), 1.89–1.93 (m, 1H, *H*-cyclopropyl), 3.62–3.69 (m, 2H, $TBSOCH_2$), 9.42 (d, ^3J = 5.1 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −3.4 (2*C*) , 14.2, 21.8, 26.1 (3*C*), 27.4, 31.2, 63.1, 201.6 ppm.

5.3.6 *tert*-Butyldimethyl(2-(2-styrylcyclopropyl)ethoxy)silane (121)



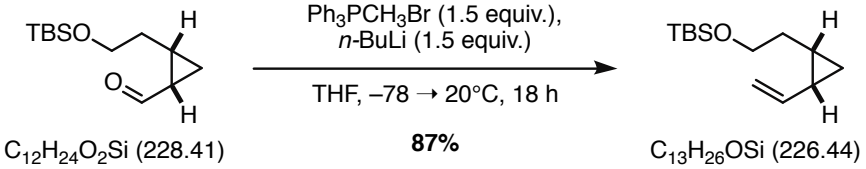
$C_{12}H_{24}O_2Si$ (228.41) $C_{19}H_{30}OSi$ (302.53) $C_{19}H_{30}OSi$ (302.53)

A suspension of benzyltriphenylphosphonium bromide (2.9 g, 6.6 mmol, 1.5 equiv.) in dry THF (21 mL, 0.2 M) was treated with *n*-BuLi (2.5 M in hexanes, 2.6 mL, 6.6 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and cooled to −78 °C, afterwards. A solution of aldehyde **113** (1.0 g, 4.4 mmol, 1.0 equiv.) in dry THF (7.0 mL, 0.6 M) was added dropwise over a period of 30 min. After complete addition the reaction mixture was allowed to reach 20 °C and stirred at this temperature for 3 h. The reaction was quenched with sat. aq. NH_4Cl (20 mL) and the phases were separated. The aqueous phase was extracted with pentane (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 100:1) delivered the silyl ether **121** as a colourless oil (1.2 g, 4.1 mmol, 93%, *E/Z* = 2:1). The diastereomers were separated by preparative HPLC (Nu 50-5, 32 x 50 mm, hexane, flow: 64 ml/min).

(*E*)-121: R_f (pentane/diethyl ether = 100:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{30}NaOSi$, 325.1964, found: 325.1958; **IR (ATR):** $\tilde{\nu}$ = 3063, 3024, 2953, 2926, 2855, 1737, 1645, 1602, 1494, 1470, 1463, 1449, 1381, 1361, 1254, 1216, 1159, 1096, 1030, 1006, 957, 908, 890, 834, 810, 774, 755, 692, 666 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.05 (s, 6H, SiCH_3), 0.39 (ddd, ^2J = 5.3 Hz, ^3J = 5.3, 5.3 Hz, 1H, *H*-cyclopropyl), 0.90 (s, 9H, SiCCH_3), 1.01 (m_c, 1H, *H*-cyclopropyl), 1.08–1.18 (m, 1H, *H*-cyclopropyl), 1.59–1.71 (m, 3H, CH_2, *H*-cyclopropyl), 3.69 (ddt, ^2J = 10.0 Hz, ^3J = 6.1 Hz, ^4J = 3.1 Hz, 2H, CH_2), 5.97 (dd, ^3J = 15.7, 9.0 Hz, 1H, C*H*), 6.50 (d, ^3J = 15.7 Hz, 1H, C*H*), 7.15–7.20 (m, 1H, *H*-Ar), 7.26–7.34 (m, 4H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = −5.1 (2*C*), 13.3, 16.3, 18.5, 19.3, 26.1 (3*C*), 32.9, 63.4, 125.8 (2*C*), 126.7, 128.6 (2*C*), 129.9, 130.8, 138.0 ppm.

(*Z*)-121: R_f (pentane/ethyl acetate = 100:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{30}NaOSi$, 325.1964, found: 325.1958; **IR (ATR):** $\tilde{\nu}$ = 3063, 3024, 2953, 2926, 2855, 1737, 1645, 1602, 1494, 1470, 1463, 1449, 1381, 1361, 1254, 1216, 1159, 1096, 1030, 1006, 957, 908, 890, 834, 810, 774, 755, 692, 666 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.05 (s, 6H, SiCH_3), 0.31 (ddd, ^2J = 5.3 Hz, ^3J = 5.3, 5.3 Hz, 1H, *H*-cyclopropyl), 0.90 (s, 9H, CCH_3), 1.03 (m_c, 1H, *H*-cyclopropyl), 1.07–1.20 (m, 1H, *H*-cyclopropyl), 1.64 (m_c, 2H, CH_2), 1.90 (dddt, ^3J = 9.3, 9.3, 8.9, 5.3 Hz, 1H, *H*-cyclopropyl), 3.72 (td, ^3J = 6.9 Hz, ^4J = 1.4 Hz, 2H, SiOCH_2), 5.37 (dd, ^3J = 11.6, 9.6 Hz, 1H, ArCH=C*H*), 6.46 (d, ^3J = 11.6 Hz, 1H, ArC*H*), 7.19–7.24 (m, 1H, *H*-Ar), 7.33 (dd, ^3J = 8.4, 7.0 Hz, 2H, *H*-Ar), 7.41–7.47 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.1 (2*C*), 15.3, 15.8, 16.6, 18.5, 26.1 (3*C*), 33.1, 63.3, 126.6, 128.3 (2*C*), 128.9 (2*C*), 129.6, 132.5, 138.0 ppm.

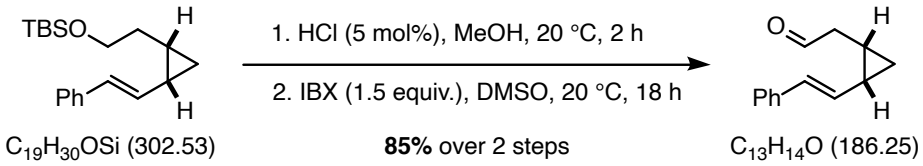
5.3.7 *tert*-Butyldimethyl(2-(2-vinylcyclopropyl)ethoxy)silane (123)



A suspension of methyltriphenylphosphonium bromide (16.2 g, 45.5 mmol, 1.5 equiv.) in dry THF (60.0 mL, 0.5 M) was treated with *n*-BuLi (2.5 M in hexanes, 18.2 mL, 45.5 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. The reaction was cooled to −78 °C and a solution of aldehyde **113** (6.92 g, 30.3 mmol, 1.0 equiv.) in dry THF (20.0 mL, 1.5 M) was added dropwise over a period of 30 min. After complete addition the reaction mixture was allowed to reach 20 °C and stirred at this temperature for 18 h. The reaction was quenched with sat. aq. NH_4Cl (200 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (3 x 200 mL). The combined organic phases were washed with brine (200 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 60:1) delivered the silyl ether **123** as a colourless oil (5.94 g, 26.2 mmol, 87%)

R_f (pentane/diethyl ether = 40:1) = 0.9; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{27}OSi$, 227.1826, found: 227.1825; **IR (ATR):** $\tilde{\nu}$ = 3082, 3068, 2998, 2954, 2928, 2895, 2857, 2361, 2342, 1634, 1471, 1463, 1433, 1389, 1361, 1319, 1294, 1254, 1185, 1159, 1140, 1097, 1062, 1030, 1006, 985, 964, 938, 894, 833, 810, 773, 737, 677, 661 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.05 (d, ^4J = 1.0 Hz, 6H, SiCH_3), 0.22–0.34 (m, 1H, *H*-cyclopropyl), 0.82–0.89 (m, 1H, *H*-cyclopropyl), 0.90 (s, 9H, CCH_3) 0.96–1.06 (m, 1H, *H*-cyclopropyl), 1.46–1.52 (m, 1H, *H*-cyclopropyl), 1.53–1.56 (m, 2H, CH_2), 3.60–3.72 (m, 2H, CH_2), 4.98 (ddd, ^2J = 2.0 Hz, ^3J = 10.3 Hz, ^4J = 0.6 Hz, 1H, C=CH_2), 5.11 (ddd, ^2J = 2.0 Hz, ^3J = 17.0 Hz, ^4J = 0.8 Hz, 1H, C=CH_2), 5.56 (ddd, ^3J = 17.0, 10.3, 8.8 Hz, 1H, C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ =−5.1 (2*C*), 12.4, 15.5, 18.5, 19.5, 26.1 (3*C*), 32.6, 63.4, 114.3, 138.4 ppm.

5.3.8 2-(2-((*E*)-Styryl)cyclopropyl)acetaldehyde (116b)

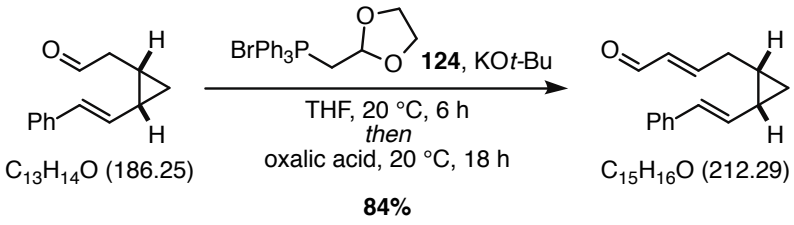


A solution of silyl ether **113** (2.2 g, 7.1 mmol, 1.0 equiv.) in MeOH (71 mL, 0.1 M) was treated with HCl (10 wt-% in H_2O, 0.12 mL, 0.36 mmol, 5 mol%) at 20 °C. The reaction mixture was stirred for 2 h and the reaction was quenched with sat. aq. $NaHCO_3$ (30 mL). The mixture was extracted with CH_2Cl_2 (3 x 100 mL) and the combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. The residue was taken up in DMSO (71 mL, 0.1 M) and treated with IBX (3.0 g, 11 mmol, 1.5 equiv.). The reaction mixture was stirred for 18 h and the reaction was quenched with H_2O (30 mL). The mixture was extracted with CH_2Cl_2 (3 x 100 mL) and the combined organic phases were washed with brine (3 x 100 mL) thoroughly. The organic phase was dried over $MgSO_4$, filtrated and

the solvents were removed *in vacuo*. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1→20:1) to deliver the aldehyde **116b** as a colourless oil (1.1 g, 6.1 mmol, 85% over 2 steps).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{14}NaO$, 209.0937, found: 209.0934; **IR (ATR):** $\tilde{\nu}$ = 3060, 3023, 2956, 2921, 2822, 2723, 1721, 1644, 1598, 1542, 1493, 1448, 1415, 1385, 1297, 1262, 1220, 1180,1156, 1142, 1074, 1029, 957, 915, 841, 795, 749, 69 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.50 (dt, ^2J = 5.4 Hz, ^3J = 5.4 Hz, 1H, *H*-cyclopropyl), 1.14 (td, ^2J = 5.4 Hz, ^3J = 8.3 Hz, 1H, *H*-cyclopropyl), 1.39 (m_c, 1H, *H*-cyclopropyl), 1.81 (m_c, 1H, *H*-cyclopropyl), 2.45 (ddd, ^2J = 17.6 Hz, ^3J = 7.4, 1.9 Hz, 1H, CH_2), 2.51 (ddd, ^2J = 17.6 Hz, ^3J = 7.2, 1.9 Hz, 1H, CH_2), 5.95 (dd, ^3J = 15.8, 8.1 Hz, 1H, C*H*), 6.51 (dd, ^3J = 15.8 Hz, ^4J = 0.8 Hz, 1H, C*H*), 7.18–7.22 (m, 1H, *H*-Ar), 7.27–7.33 (m, 4H, *H*-Ar), 9.81 (t, ^3J = 1.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 12.4, 12.5, 18.5, 43.7, 125.9 (2*C*), 127.2, 128.7 (2*C*), 128.8, 131.4, 137.5, 202.2 ppm.

5.3.9 (*E*)-4-(2-((*E*)-Styryl)cyclopropyl)but-2-enal (109a)

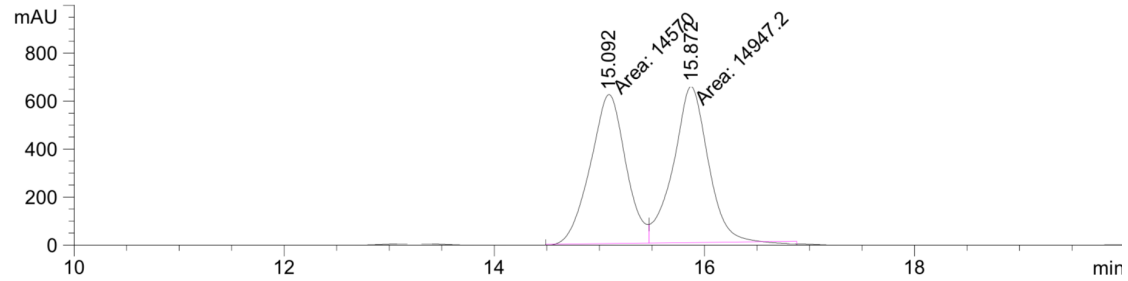


KO*t*-Bu (0.16 g, 1.4 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (0.63 g, 1.5 mmol, 2.7 equiv.) in dry THF (5.8 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **116b** (0.10 g, 0.54 mmol, 1.0 equiv.) in dry THF (1.4 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 6 h. Oxalic acid (0.9 M in H_2O, 6.0 mL, 5.4 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 60 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (60 mL) and brine (60 mL) subsequently, dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the title compound **109a** as a colourless oil (96 mg, 0.45 mmol, 84%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{16}NaO$, 235.1093, found: 235.1106; **IR (ATR):** $\tilde{\nu}$ = 3060, 3024, 2995, 2914, 2815, 2727, 1690, 1683, 1633, 1595, 1492, 1421, 1308, 1135, 1114, 1099, 1078, 1032, 1011, 968, 915, 880, 813, 795, 788, 749, 724, 692, 678 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.49 (m_c, 1H, *H*-cyclopropyl), 1.10 (ddd, ^2J = 5.0 Hz, ^3J = 8.3, 8.3 Hz, 1H, *H*-cyclopropyl), 1.16–1.23 (m, 1H, *H*-cyclopropyl), 1.79 (m_c, 1H, *H*-cyclopropyl), 2.34–2.47 (m, 2H, CH_2), 5.98 (dd, ^3J = 15.7, 8.3 Hz, 1H, ArCH=C*H*), 6.24 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.7 Hz, 1H, *H*CCHO), 6.52 (dd, ^3J = 15.7 Hz, ^4J = 0.8 Hz, 1H, ArC*H*), 6.91 (dt, ^3J = 15.7, 6.1 Hz, 1H, *H*C=CHCHO), 7.17–7.22 (m, 1H, *H*-Ar), 7.27–7.33 (m, 4H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.8, 17.2, 19.3, 32.4, 125.9 (2*C*), 127.1, 128.7 (2*C*), 128.9, 131.2, 133.1, 137.6, 157.8, 194.2 ppm.

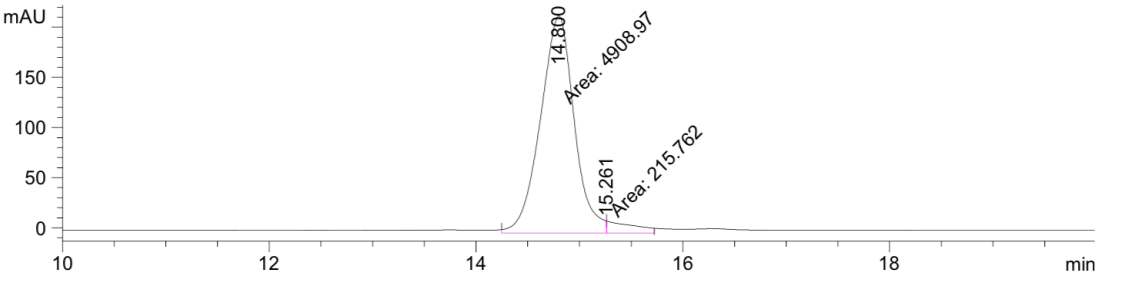
An enantiomerically pure sample was obtained by preparative HPLC. $[\alpha]_D^{20}$ = +0.99 (c = 1.13, $CHCl_3$)

HPLC: 0.55% EtOH/pentane, Chiralpak IA, 1 mL/min, 28 bar.



Signal 3: DAD1 E, Sig=270,4 Ref=360,100

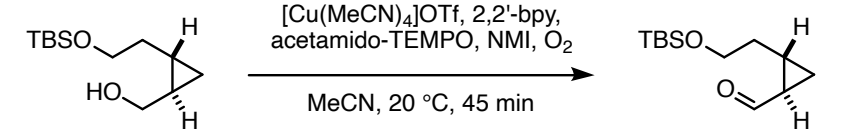
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.092	MF	0.3907	1.45700e4	621.55890	49.3612
2	15.872	FM	0.3824	1.49472e4	651.52979	50.6388
Totals :				2.95172e4	1273.08868	



Signal 3: DAD1 E, Sig=270,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.800	MF	0.3777	4908.96924	216.59328	95.7898
2	15.261	FM	0.2984	215.76155	12.04941	4.2102
Totals :				5124.73079	228.64268	

5.3.10 (*trans*-2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropane-1-carbaldehyde (200)



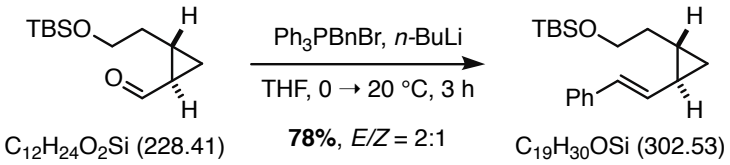
$C_{12}H_{26}O_2Si$ (230.42) $C_{12}H_{24}O_2Si$ (228.41)

To a solution of homocyclopropyl alcohol **199** (2.0 g, 8.7 mmol, 1.0 equiv.) in MeCN (43 mL, 0.2 M) were added $[Cu(MeCN)_4]OTf$ (0.16 g, 0.43 mmol, 5 mol%), 2,2'-bpy (67 mg, 0.43 mmol, 5 mol%), acetamido-TEMPO (92 mg, 0.43 mmol, 5 mol%) and NMI (69 µL, 0.87 mmol, 10 mol%). The resulting brown solution was stirred under an

O_2-atmosphere for 45 min until it turned to dark green. H_2O (20 mL) was added and the reaction mixture was extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The solvent was evaporated under reduced pressure and the crude product filtrated through a plug of silica gel eluting with pentane/ethyl acetate = 10:1. The solvents were removed under reduced pressure to yield the cyclopropylcarbaldehyde **200** as a colourless oil (1.9 g, 8.5 mmol, 98%).

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{25}O_2Si$, 229.1619, found: 229.1610; **IR (ATR):** $\tilde{\nu}$ = 2953, 2929, 2886, 2857, 2725, 1709, 1472, 1434, 1406, 1389, 1361, 1255, 1197, 1168, 1101, 1030, 1007, 939, 918, 836, 811, 776, 730 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = −0.01–0.11 (m, 6H, SiCH_3), 0.89–0.89 (m, 9H, SiCCH_3), 0.95–0.98 (m, 1H, *H*-cyclopropyl), 1.27–1.32 (m, 1H, *H*-cyclopropyl), 1.53–1.58 (m, 2H, cyclopropylCH_2), 1.59–1.61 (m, 1H, *H*-cyclopropyl), 1.64–1.69 (m, 1H, *H*-cyclopropyl), 3.66–3.70 (m, 2H, SiOCH_2), 9.00 (dd, ^3J = 5.6 Hz, ^4J = 0.7 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.2 (2*C*), 14.6, 18.4, 19.8, 26.1 (3*C*), 30.2, 35.9, 62.5, 201.1 ppm.

5.3.11 (*tert*-Butyldimethyl(2-(*trans*-2-((*E*)-styryl)cyclopropyl)ethoxy)silane (201)

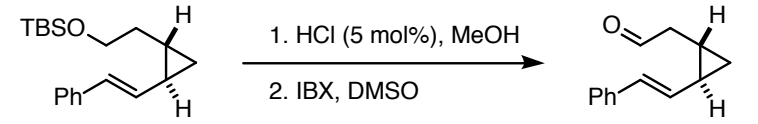


$C_{12}H_{24}O_2Si$ (228.41) — **78%**, *E/Z* = 2:1 — $C_{19}H_{30}OSi$ (302.53)

A suspension of benzyltriphenylphosphonium bromide (5.26 g, 12.2 mmol, 2.7 equiv.) in dry THF (27.0 mL, 0.2 M) was treated with *n*-BuLi (2.5 M in hexanes, 4.90 mL, 12.2 mmol, 2.7 equiv.) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. A solution of aldehyde **200** (1.10 g, 4.60 mmol, 1.0 equiv.) in dry THF (14.0 mL, 0.6 M) was added dropwise over a period of 30 min. After complete addition the reaction mixture was allowed to reach 20 °C and stirred at this temperature for 3 h. The reaction was quenched with sat. aq. NH_4Cl (20 mL) and the phases were separated. The aqueous phase was extracted with pentane (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 100:1) delivered the silyl ether **201** as a colourless oil (1.08 g, 3.56 mmol, 78%, *E/Z* = 2:1).

R_f (pentane/diethyl ether = 100:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{31}OSi$, 303.2139, found: 303.2138; **IR (ATR):** $\tilde{\nu}$ = 3062, 3024, 2998, 2953, 2927, 2897, 2856, 1650, 1598, 1493, 1471, 1463, 1448, 1388, 1361, 1254, 1099, 1045, 1027, 1007, 956, 938, 908, 888, 834, 810, 774, 741 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.07 (d, ^5J = 1.1 Hz, 6H, SiCH_3), 0.65 (dddd, ^2J = 4.7 Hz, ^3J = 9.7, 7.3 Hz, ^4J = 1.6 Hz, 1H, *H*-cyclopropyl), 0.70 (ddd, ^2J = 4.7 Hz, ^3J = 8.7, 4.7 Hz, 1H), 0.91 (s, 9H, SiCCH_3), 0.93–0.95 (m, 1H, *H*-cyclopropyl), 1.32–1.37 (m, 1H, *H*-cyclopropyl), 1.48–1.53 (m, 1H, SiOCH_2CH_2), 1.58 (dt, ^2J = 13.5 Hz, ^3J = 6.7 Hz, 1H, SiOCH_2CH_2), 3.71 (t, ^3J = 6.7 Hz, 2H, SiOCH_2CH_2), 5.78 (dd, ^3J = 15.8, 8.8 Hz, 1H, ArCH=C*H*), 6.42 (d, ^3J = 15.8 Hz, 1H, ArC*H*=CH), 7.13–7.18 (m, 1H, *H*-Ar), 7.24–7.31 (m, 4H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.1 (2*C*), 14.3, 18.6, 18.6, 22.1, 26.1 (3*C*), 37.3, 63.1, 125.7 (2*C*), 126.6, 127.2, 128.6 (2*C*), 134.6, 138.0 ppm.

5.3.12 2-(*trans*-2-((*E*)-Styryl)cyclopropyl)acetaldehyde (202)

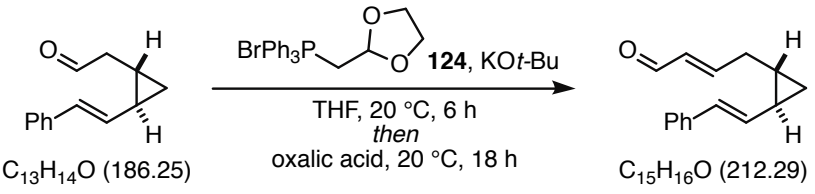


$C_{19}H_{30}OSi$ (302.53) — *E*: **62%**, *Z*: **20%** — $C_{13}H_{14}O$ (186.25)

A solution of the silyl ether **201** (906 mg, 2.99 mmol, *E:Z* = 2:1, 1.0 equiv.) in MeOH (30.0 mL, 0.1 M) was treated with HCl (10 wt-% in H_2O, 52.1 µL, 159 µmol, 5 mol%) at 20 °C. The reaction solution was stirred at this temperature for 3 h before the reaction was quenched with sat. aq. NH_4Cl (50 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The residue was dissolved in dry DMSO (30.0 mL, 0.1 M). IBX (1.26 g, 4.49 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred at 20 °C for 18 h. The reaction was quenched with sat. aq. $NaHCO_3$ (50 mL) and the resulting mixture was extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The solvents were removed *in vacuo* and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1→20:1) to obtain the aldehyde **202** as a colourless oil (346 mg, 1.86 mmol, 62%, *E/Z* > 20:1) and the *Z*-isomer of **202** (114 mg, 0.61 mmol, 20%, *Z/E* > 20:1).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{14}NaO$, 209.0937, found: 209.0944; **IR (ATR):** $\tilde{\nu}$ = 3073, 3060, 3024, 2924, 2717, 1722, 1649, 1596, 1492, 1448, 1392, 1072, 1038, 959, 913, 746 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.75 (m_c, 1H, *H*-cyclopropyl), 0.88 (m_c, 1H, *H*-cyclopropyl), 1.14–1.23 (m, 1H, *H*-cyclopropyl), 1.44 (dddd, ^3J = 8.7, 8.7, 4.6, 4.6 Hz, 1H, *H*-cyclopropyl), 2.36 (ddd, ^2J = 17.1 Hz, ^3J = 7.3, 2.1 Hz, 1H, CHOCH_2), 2.50 (ddd, ^2J = 17.1 Hz, ^3J = 6.7, 2.1 Hz, 1H, CHOCH_2), 5.81 (dd, ^3J = 15.8, 8.7 Hz, 1H, ArCH=C*H*), 6.46 (d, ^3J = 15.8 Hz, 1H, ArC*H*=CH), 7.15–7.20 (m, 1H, *H*-Ar), 7.26–7.31 (m, 4H, *H*-Ar), 9.82 (t, ^3J = 2.1 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.0, 14.6, 21.8, 47.9, 125.8, 126.9 (2*C*), 128.4, 128.6 (2*C*), 132.7, 137.6, 201.7 ppm.

5.3.13 (*E*)-4-(*trans*-2-((*E*)-Styryl)cyclopropyl)but-2-enal (203)



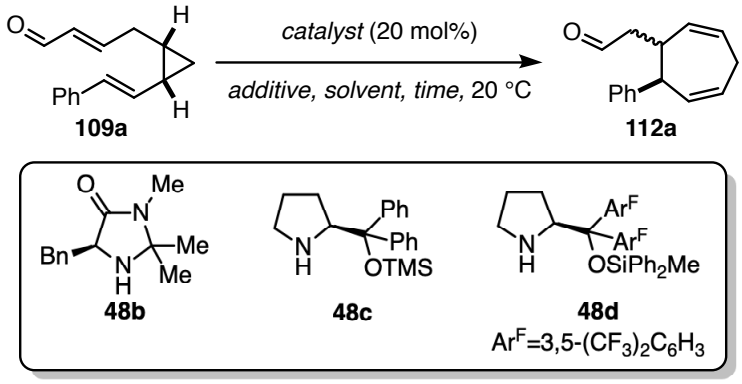
$C_{13}H_{14}O$ (186.25) — **83%** — $C_{15}H_{16}O$ (212.29)

KO*t*-Bu (525 mg, 4.68 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (2.09 g, 4.87 mmol, 2.7 equiv.) in dry THF (20 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **202** (335 mg, 1.80 mmol, 1.0 equiv.) in dry THF (4.5 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 6 h. Oxalic acid (0.9 M

in H_2O, 20.0 mL, 18.0 mmol, 10.0 equiv.) was added and the mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 50 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the title compound **203** as a pale yellow oil (318 mg, 1.50 mmol, 83%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{15}H_{17}O$, 213.1274, found: 213.1285; **IR (ATR):** $\tilde{\nu}$ = 3024, 2998, 2817, 2732, 1685, 1636, 1598, 1492, 1448, 1415, 1306, 1140, 1117, 1096, 1075, 1025, 958, 872, 821, 745 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.64–0.71 (m, 1H, *H*-cyclopropyl), 0.76–0.79 (m, 1H, *H*-cyclopropyl), 0.96–1.00 (m, 1H, *H*-cyclopropyl), 1.36 (dddd, ^3J = 8.7, 8.6, 4.6, 4.6 Hz, 1H, *H*-cyclopropyl), 2.27–2-35 (m, 2H, CH_2), 5.74 (ddd, ^3J = 15.7, 8.7 Hz, ^4J = 1.6 Hz, 1H, Ar-CH=C*H*), 6.18 (ddd, ^3J = 15.3, 7.9 Hz, ^4J = 1.8 Hz, 1H, CHOC*H*=CH), 6.40 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.85 (dt, ^3J = 15.3, 5.9 Hz, 1H, CHOCH=C*H*), 7.11–7.14 (m, 1H, *H*-Ar), 7.19–7.26 (m, 4H, *H*-Ar), 9.49 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.3, 19.1, 22.2, 36.7, 125.8 (2*C*), 126.9, 128.2, 128.7 (2*C*), 132.9, 133.3, 137.6, 157.0, 194.1 ppm.

5.4 Optimisation of Reaction Conditions for the DVCPR of α,β-Unsaturated Aldehydes



A solution of aldehyde **109a** (10.6 mg, 50.0 µmol, 1.0 equiv.) in the indicated solvent (0.1 M) was treated with the corresponding catalyst (10.0 µmol, 20 mol%) and additive. The reaction was stirred at 20 °C. An aliquot (10.0 µL) was taken at the indicated reaction times, diluted with CH_2Cl_2 to yield a volume of 190 µL, and treated with a solution of 2-methoxynaphthalene (10.0 µL, 0.025 M in CH_2Cl_2). The conversion as well as the diastereomeric ratio were determined via GC-MS with 2-methoxynaphthalene as standard.

Entry	Catalyst	Additive	Solvent	Time [h]	Conv. [%]	*d.r.*
1	pyrrolidine (**48f**)	–	CH_2Cl_2	20	30	3:1
2	pyrrolidine (**48f**)	–	CH_2Cl_2	43	31	3:1
3	piperidine (**48g**)	–	CH_2Cl_2	20	20	3:1

*The reaction was run at 40 °C

Entry	Catalyst	Additive	Solvent	Time [h]	Conv. [%]	*d.r.*
4	piperidine (**48g**)	–	CH_2Cl_2	43	38	3:1
5	morpholine (**48h**)	–	CH_2Cl_2	20	2	4:1
6	morpholine (**48h**)	–	CH_2Cl_2	43	7	2:1
7	**48c**	–	CH_2Cl_2	20	75	>20:1
8	**48c**	–	CH_2Cl_2	43	96	>20:1
9*	**48c**	–	CH_2Cl_2	4	43	>20:1
10*	**48c**	–	CH_2Cl_2	8	62	>20:1
11*	**48c**	–	CH_2Cl_2	24	72	>20:1
12	**48d**	–	CH_2Cl_2	20	32	>20:1
13	**48d**	–	CH_2Cl_2	43	60	>20:1
14	**48b**	–	CH_2Cl_2	20	2	>20:1
15	**48b**	–	CH_2Cl_2	43	2	>20:1
16*	**48c**	–	$CHCl_3$	4	16	>20:1
17*	**48c**	–	$CHCl_3$	23	38	>20:1
18*	**48c**	–	$CHCl_3$	51	26	>20:1
19	**48c**	–	$CHCl_3$	4	19	>20:1
20	**48c**	–	$CHCl_3$	8	38	>20:1
21	**48c**	–	$CHCl_3$	29	21	>20:1
22	**48c**	–	1,2-DCE	4	43	>20:1
23	**48c**	–	1,2-DCE	20	68	>20:1
24	**48c**	–	1,2-DCE	44	78	>20:1
25	**48c**	–	MeCN	4	16	>20:1
26	**48c**	–	MeCN	20	33	>20:1
27	**48c**	–	MeCN	44	47	>20:1
28	**48c**	–	PhMe	4	19	>20:1
29	**48c**	–	PhMe	20	25	>20:1
30	**48c**	–	PhMe	44	34	>20:1
31	**48c**	–	cyclohexane	4	18	8:1
32	**48c**	–	cyclohexane	20	26	4:1
33	**48c**	–	cyclohexane	44	23	3:1
34	**48c**	–	Et_2O	4	12	>20:1
35	**48c**	–	Et_2O	20	31	>20:1

*The reaction was run at 40 °C

Entry	Catalyst	Additive	Solvent	Time [h]	Conv. [%]	*d.r.*
36	**48c**	–	Et_2O	44	41	>20:1
37	**48c**	–	EtOAc	4	11	>20:1
38	**48c**	–	EtOAc	20	24	>20:1
39	**48c**	–	EtOAc	44	31	>20:1
40	**48c**	–	DMSO	4	5	12:1
41	**48c**	–	DMSO	20	4	>20:1
42	**48c**	–	DMSO	44	7	>20:1
43	**48c**	–	THF	4	9	>20:1
44	**48c**	–	THF	20	20	>20:1
45	**48c**	–	THF	44	29	>20:1
46	**48c**	–	chlorobenzene	4	11	12:1
47	**48c**	–	chlorobenzene	23	25	6:1
48	**48c**	–	chlorobenzene	51	35	5:1
49	**48c**	HCl (1 mol%)	CH_2Cl_2	4	62	>20:1
50	**48c**	HCl (1 mol%)	CH_2Cl_2	8	60	>20:1
51	**48c**	HCl (1 mol%)	CH_2Cl_2	24	65	>20:1
52	**48c**	HCl (5 mol%)	CH_2Cl_2	4	36	>20:1
53	**48c**	HCl (5 mol%)	CH_2Cl_2	8	45	>20:1
54	**48c**	HCl (5 mol%)	CH_2Cl_2	24	49	>20:1
55	**48c**	HCl (10 mol%)	CH_2Cl_2	4	25	>20:1
56	**48c**	HCl (10 mol%)	CH_2Cl_2	8	31	>20:1
57	**48c**	HCl (10 mol%)	CH_2Cl_2	24	34	>20:1
58	**48c**	HCl (20 mol%)	CH_2Cl_2	4	5	10:1
59	**48c**	HCl (20 mol%)	CH_2Cl_2	8	5	9:1

*The reaction was run at 40 °C

Entry	Catalyst	Additive	Solvent	Time [h]	Conv. [%]	*d.r.*
60	**48c**	HCl (20 mol%)	CH_2Cl_2	24	5	8:1
61	**48c**	AcOH (0.1 mol%)	CH_2Cl_2	1	24	>20:1
62	**48c**	AcOH (0.1 mol%)	CH_2Cl_2	2	49	>20:1
63	**48c**	AcOH (0.1 mol%)	CH_2Cl_2	4	63	>20:1
64	**48c**	AcOH (0.1 mol%)	CH_2Cl_2	8	68	>20:1
65	**48c**	AcOH (0.1 mol%)	CH_2Cl_2	24	71	>20:1
66	**48c**	AcOH (1 mol%)	CH_2Cl_2	4	73	>20:1
67	**48c**	AcOH (1 mol%)	CH_2Cl_2	8	68	>20:1
68	**48c**	AcOH (5 mol%)	CH_2Cl_2	4	48	>20:1
69	**48c**	AcOH (5 mol%)	CH_2Cl_2	8	61	>20:1
70	**48c**	AcOH (10 mol%)	CH_2Cl_2	4	83	>20:1
71	**48c**	AcOH (10 mol%)	CH_2Cl_2	8	50	>20:1
72	**48c**	AcOH (20 mol%)	CH_2Cl_2	4	64	>20:1
73	**48c**	AcOH (20 mol%)	CH_2Cl_2	8	45	>20:1
74	**48c**	BzOH (1 mol%)	CH_2Cl_2	4	70	>20:1
75	**48c**	BzOH (1 mol%)	CH_2Cl_2	8	71	>20:1
76	**48c**	BzOH (5 mol%)	CH_2Cl_2	4	45	>20:1
77	**48c**	BzOH (5 mol%)	CH_2Cl_2	8	50	>20:1
78	**48c**	BzOH (10 mol%)	CH_2Cl_2	4	33	>20:1

*The reaction was run at 40 °C

Entry	Catalyst	Additive	Solvent	Time [h]	Conv. [%]	*d.r.*
79	**48c**	BzOH (10 mol%)	CH_2Cl_2	8	32	>20:1
80	**48c**	BzOH (20 mol%)	CH_2Cl_2	4	29	>20:1
81	**48c**	BzOH (20 mol%)	CH_2Cl_2	8	28	>20:1
82	**48c**	3-NO_2-BzOH (1 mol%)	CH_2Cl_2	2	72	>20:1
83	**48c**	3-NO_2-BzOH (5 mol%)	CH_2Cl_2	2	54	>20:1
84	**48c**	3-NO_2-BzOH (10 mol%)	CH_2Cl_2	2	51	>20:1
85	**48c**	3-NO_2-BzOH (10 mol%)	CH_2Cl_2	7	44	>20:1
86	**48c**	3-NO_2-BzOH (20 mol%)	CH_2Cl_2	2	42	>20:1
87	**48c**	3-NO_2-BzOH (20 mol%)	CH_2Cl_2	7	41	>20:1
88	**48c**	MeOH (20 mol%)	CH_2Cl_2	4	55	>20:1
89	**48c**	MeOH (20 mol%)	CH_2Cl_2	8	69	>20:1
90	**48c**	MeOH (20 mol%)	CH_2Cl_2	24	71	>20:1
91	**48c**	K_2CO_3 (20 mol%)	CH_2Cl_2	4	71	>20:1
92	**48c**	K_2CO_3 (20 mol%)	CH_2Cl_2	8	74	>20:1
93	**48c**	K_2CO_3 (20 mol%)	CH_2Cl_2	24	81	>20:1
94	–	AcOH (0.1 mol%)	CH_2Cl_2	4	no conversion	–

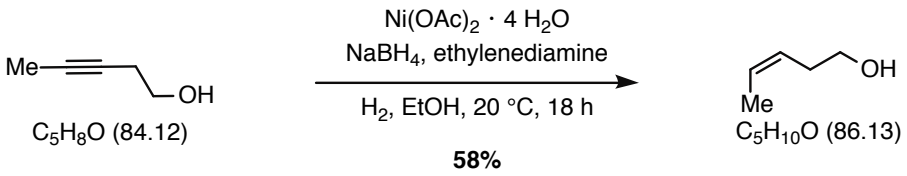
*The reaction was run at 40 °C

Entry	Catalyst	Additive	Solvent	Time [h]	Conv. [%]	*d.r.*
95	–	AcOH (0.1 mol%)	CH_2Cl_2	8	no conversion	–
96	–	AcOH (0.1 mol%)	CH_2Cl_2	24	no conversion	–

*The reaction was run at 40 °C

5.5 Nickel-catalysed Reductive Coupling of Tetrahydropyrans

5.5.1 (*Z*)-3-Pentene-1-ol (129)

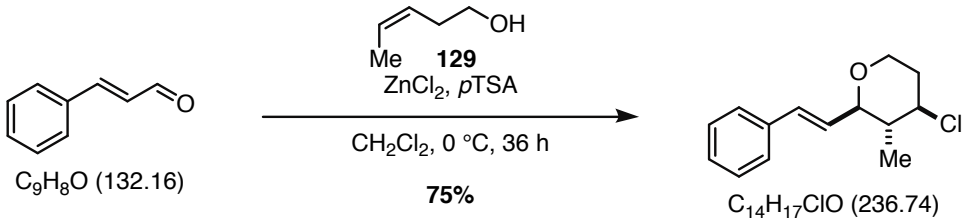


$Ni(OAc)_2 \cdot 4H_2O$ (0.30 g, 1.1 mmol, 10 mol%) was dissolved in EtOH (95%, 11 mL). H_2 was passed through the reaction mixture for 10 min before a solution of $NaBH_4$ (1 M in dry EtOH, 1.1 mL, 1.1 mmol, 10 mol%) was added dropwise. The reaction mixture immediately turned black and H_2 was passed through it again for 30 min. Ethylenediamine (0.18 mL, 2.7 mmol, 25 mol%) and a solution of alkyne 3-pentyne-1-ol (1.0 mL, 11 mmol, 1.0 equiv.) in dry EtOH (22 mL, 0.4 M) were added. The reaction mixture was stirred under an H_2-atmosphere for 18 h. The solution was diluted with Et_2O (50 mL) and filtrated over celite. The solvent was removed under reduced pressure (150 mbar). The organic phase was washed with H_2O (50 mL) and the aqueous phase extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The filtrate was purified by fractioned distillation (bp = 134 °C, 1 bar) to afford the title compound as a colourless oil (0.54 g, 6.3 mmol, 58%).

R_f (pentane/diethyl ether = 5:1) = 0.3; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.57(br s, 1H, O*H*), 1.64 (m_c, 3H, CH_3), 2.33 (m_c, 2H, CH_2CH$_2$OH), 3.64 (t, ^3J = 6.5 Hz, 1H, CH_2OH), 5.39 (dtq, ^3J = 11.0, 7.4 Hz, ^4J = 1.8 Hz, 1H, C*H*CH$_3$), 5.58–5.68 (m, 1H, C*H*CH$_2$) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 13.1, 30.6, 62.4, 126.2, 127.4 ppm.

The spectroscopic data agree with previously published results.[383]

5.5.2 4-Chloro-3-methyl-2((*E*)-styryl)tetrahydro-2*H*-pyran (125a)

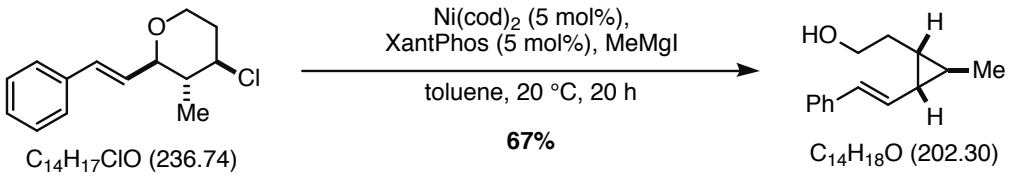


Zinc chloride (158 mg, 1.16 mmol, 1.1 equiv.), was flame-dried at 240 °C and treated with *p*-toluenesulfonic acid monohydrate (221 mg, 1.16 mmol, 1.1 equiv.) in dry CH_2Cl_2 (5 mL, 0.23 M). At 0 °C, a solution of freshly distilled cinnamaldehyde (130 µL, 1.05 mmol, 1.0 equiv.) and alcohol **129** (100 mg, 1.16 mmol, 1.1 equiv.) in dry CH_2Cl_2 (5 mL, 0.23 M) was added dropwise over 10 min. The reaction mixture was stirred for 36 h at 0 °C afterwards. The reaction was quenched with sat. aq. $NaHCO_3$ (10 mL). The phases were separated, the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and filtrated. The solvent was removed *in vacuo* and purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 40:1) afforded the title compound **125a** as a pale-yellow oil (196 mg, 0.820 mmol, 75%, *d.r.* > 20:1).

R_f (pentane/diethyl ether = 20:1) = 0.7; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.11 (d, ^3J = 7.0 Hz, 3H, CH_3), 1.85 (ddd, ^3J = 12.7, 4.4, 2.6 Hz, 1H, OCH$_2$CH_2), 2.08–2.24 (m, 2H, OCH$_2$CH_2, CHCH$_3$), 3.55 (td, ^3J = 12.7, 2.6 Hz, 1H, OCH_2), 4.08–4.13 (m, 2H, OCH_2, OCH), 4.34 (dt, ^3J = 12.3, 4.4 Hz, 1H, CHCl), 6.16 (dd, ^3J = 16.1, 5.1 Hz, 1H, OCHCH), 6.62 (dd, ^3J = 16.1 H, ^4J = 1.7 Hz, 1H, PhCH), 7.23–7.43 (m, 5H, *H*-Ar) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 6.9, 31.4, 40.9, 61.3, 67.5, 80.6, 126.6 (2*C*), 127.8, 128.2, 128.7 (2*C*), 130.6, 136.9 ppm.

The spectroscopic data agree with previously published results.[320]

5.5.3 2-(2-Methyl-3-((*E*)-styryl)cyclopropyl)ethan-1-ol (131)



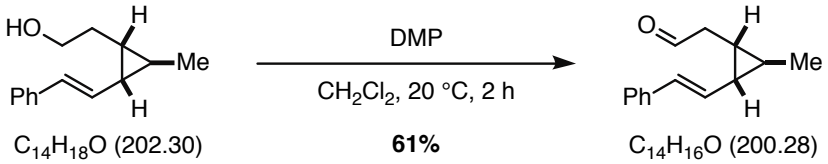
The pyran **125a** (0.67 g, 2.8 mmol, 1.0 equiv.) was added to a solution of bis(1,5-cyclooctadiene)nickel(0) (39 mg, 0.14 mmol, 5 mol%) and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (81 mg, 0.14 mmol, 5 mol%) in dry PhMe (2.8 mL, 1 M). The reaction mixture was treated dropwise with methyl magnesium iodide (1.67 M in Et_2O, 3.4 mL, 5.6 mmol, 2.0 equiv.) over a period of 15 min. The solution was stirred for 20 h afterwards before the reaction was quenched with *i*-PrOH (5.0 mL), diluted with Et_2O (20 mL), and filtered over silica gel. The solvents were removed under reduced pressure and purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the title compound as a yellow oil (0.38 g,

1.9 mmol, 67%).

R_f (pentane/diethyl ether = 4:1) = 0.4; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.08–1.17 (m, 4H, CH_3, *H*-cyclopropyl), 1.21–1.30 (m, 1H, *H*-cyclopropyl), 1.40 (br s, 1H, O*H*), 1.63–1.80 (m, 3H, *H*-cyclopropyl, HOCH_2CH_2), 3.73 (t, ^3J = 6.9 Hz, 2H, HOCH_2), 6.01 (dd, ^3J = 15.7, 9.9 Hz, 1H, PhCHC*H*), 6.58 (d, ^3J = 15.7 Hz, 1H, PhC*H*), 7.18 (t, ^3J = 7.0 Hz, 1H, *H*-Ar), 7.23–7.39 (m, 4H, *H*-Ar) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 8.8, 16.0, 19.3, 22.2, 27.4, 63.3, 125.8, 126.8, 127.1, 128.6 (2*C*), 128.6 (2*C*), 131.5 ppm.

The spectroscopic data agree with previously published results.[320]

5.5.4 2-(2-Methyl-3-((*E*)-styryl)cyclopropyl)acetaldehyde (204)

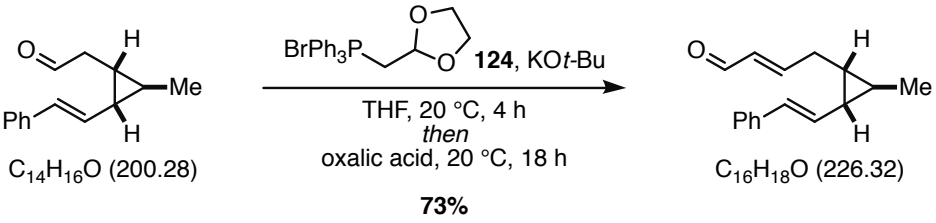


$C_{14}H_{18}O$ (202.30) → $C_{14}H_{16}O$ (200.28)

The primary alcohol **131** (47 mg, 0.23 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (2.3 mL, 0.1 M) and treated with DMP (0.15 g, 0.35 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at this temperature for 15 min, allowed to warm to 20 °C, and stirred for 2 h. H_2O (40 mL) was added and the reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure and the residue was filtrated over celite. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1) to afford the aldehyde **204** as a colourless oil (29 mg, 0.14 mmol, 61%).

R_f (pentane/ethyl acetate = 20:1) = 0.2; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{16}NaO$, 223.1093, found: 223.1097; **IR (ATR):** $\tilde{\nu}$ = 3024, 2955, 2931, 2879, 2821, 2721, 2360, 1722, 1646, 1599, 1494, 1450, 1389, 1074, 965, 751, 694 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.11 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.36 (m_c, 1H, *H*-cyclopropyl), 1.42–1.48 (m, 1H, *H*-cyclopropyl), 1.83 (m_c, 1H, *H*-cyclopropyl), 2.48–2.58 (m, 2H, CH_2), 5.92 (dd, ^3J = 15.7, 9.5 Hz, 1H, PhCHC*H*), 6.61 (d, ^3J = 15.7 Hz, 1H, PhC*H*), 7.18–7.21 (m, 1H, *H*-Ar), 7.28–7.33 (m, 4H, *H*-Ar), 9.84 (t, ^3J = 1.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 8.9, 15.6, 15.8, 21.8, 39.0, 125.6, 125.9 (2*C*), 127.1, 128.7 (2*C*), 132.7, 137.8, 202.2 ppm.

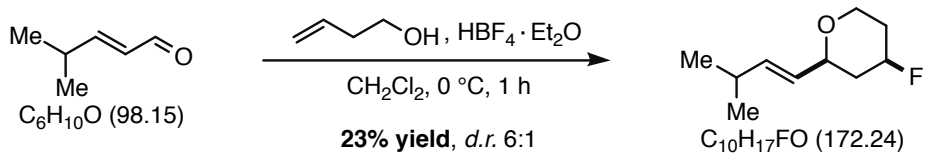
5.5.5 (*E*)-4-(2-Methyl-3-((*E*)-styryl)cyclopropyl)but-2-enal (109b)



KO*t*-Bu (210 mg, 1.87 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (837 g, 1.95 mmol, 2.7 equiv.) in dry THF (7.8 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **204** (145 mg, 0.720 mmol, 1.0 equiv.) in dry THF (1.8 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 6 h. Oxalic acid (0.9 M in H_2O, 1.50 mL, 1.70 mmol, 2.4 equiv.) was added and the mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the title compound **109b** as a pale yellow oil (119 mg, 0.530 mmol, 73%).

R_f (pentane/ethyl acetate = 20:1) = 0.2; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{19}O$, 227.1430, found: 227.1430; **IR (ATR):** $\tilde{\nu}$ = 3024, 3001, 2927, 2815, 2732, 1685, 1635, 1143, 1119, 968, 752 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 1.13 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.21–1.26 (m, 1H, *H*-cyclopropyl), 1.33 (td, ^3J = 8.9, 6.6 Hz, 1H, *H*-cyclopropyl), 1.77–1.83 (m, 1H, *H*-cyclopropyl), 2.46–2.49 (m, 2H, CH_2), 5.98 (dd, ^3J = 15.6, 9.6 Hz, 1H, PhCHC*H*), 6.26 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.7 Hz, 1H, C*H*CHO), 6.61 (d, ^3J = 15.6 Hz, 1H, PhC*H*), 6.94 (dt, ^3J = 15.7, 6.1 Hz, 1H, C*H*CHCHO), 7.14–7.25 (m, 1H, *H*-Ar), 7.27–7.34 (m, 4H, *H*-Ar), 9.53 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 8.6, 16.0, 20.3, 22.2, 27.5, 125.8, 125.8 (2*C*), 127.0, 128.7 (2*C*), 132.5, 133.2, 137.9, 158.1, 194.2 ppm.

5.5.6 4-Fluoro2-((*E*)-3-methylbut-1-en-1-yl)tetrahydro-2*H*-pyran (125b)



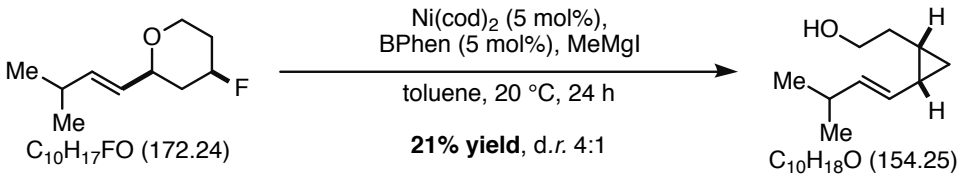
To a solution of 4-methyl-2-pentene-1-al (1.50 mL, 18.2 mmol, 1.0 equiv.) and 3-butene-1-ol (1.60 mL, 18.2 mmol, 1.0 equiv.) in dry CH_2Cl_2 (73 mL, 0.25 M) at 0 °C tetrafluoroboronic acid diethyl ether complex (2.50 mL, 18.2 mmol, 1.0 equiv.) was added dropwise over a period of 20 min. The reaction mixture was stirred for 1 h before the reaction was quenched with sat. aq. $NaHCO_3$ (50 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (100 mL) and brine (100 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/diethyl ether = 40:1) afforded the title

compound **125b** as yellow oil (715 mg, 4.15 mmol, 23%, *d.r.* 6:1)

R_f (pentane/ethyl acetate = 40:1) = 0.5; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −170.1 (d, $^2J_{H,F}$ = 50 Hz) ppm. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.99 (d, ^3J = 6.9 Hz, 3H, CH_3), 0.99 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.46–1.61 (m, 1H, CHCH_2), 1.65–1.81 (m, 1H, OCH$_2$CH_2), 1.99–2.05 (m, 1H, OCH$_2$CH_2), 2.10–2.15 (m, 1H, CHCH_2), 2.22–2.36 (m, 1H, CH(CH$_3$)$_2$), 3.42 (tt, ^3J = 12.1 Hz, ^4J = 1.9 Hz, 1H, OCH_2), 3.69–3.79 (m, 1H, OCH), 4.01–4.13 (m, 1H, OCH_2), 4.68 (dddd, $^2J_{H,F}$ = 50 Hz, ^3J = 16.0, 10.9, 4.9 Hz, 1H, CHF), 5.44 (ddd, ^3J = 15.6, 6.3 Hz, ^4J = 1.1 Hz, 1H, (CH$_3$)$_2$CHCHCH), 5.69 (ddd, ^3J = 15.6, 6.5 Hz, ^4J = 1.1 Hz, 1H, (CH$_3$)$_2$CHCH) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 22.3 (2*C*), 30.8, 33.0 (d, $^2J_{C,F}$ = 18 Hz), 39.1 (d, $^2J_{C,F}$ = 17 Hz), 65.1 (d, $^3J_{C,F}$ = 12 Hz), 76.4 (d, $^3J_{C,F}$ = 12 Hz), 89.3 (d, $^1J_{C,F}$ = 176 Hz), 126.7, 140.1 ppm.

The spectroscopic data agree with previously published results.[320]

5.5.7 2-(2-((*E*)-3-Methylbut-1-en-1-yl)cyclopropyl)ethan-1-ol (132)

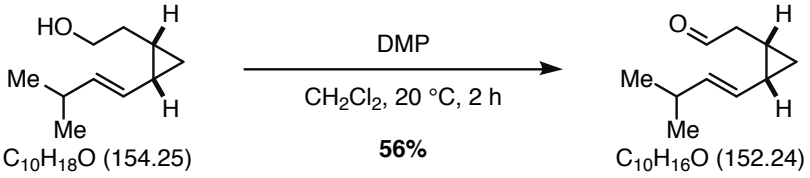


The pyran **125b** (0.29 g, 1.7 mmol, 1.0 equiv.) was added to a solution of bis(1,5-cyclooctadiene)nickel(0) (24 mg, 87 µmol, 5 mol%) and bathophenanthroline (30 mg, 87 µmol, 5 mol%) in dry, degassed PhMe (1.7 mL, 1 M). The reaction mixture was treated dropwise with methyl magnesium iodide (1.80 M in Et_2O, 1.9 mL, 3.4 mmol, 2.0 equiv.) over a period of 15 min. The solution was stirred for 24 h afterwards before the reaction was quenched with *i*-PrOH (5.0 mL), diluted with Et_2O (20 mL), and filtered over silica gel. The solvents were removed under reduced pressure and purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the title compound as a yellow oil (55 mg, 0.35 mmol, 21%, *d.r.* 4:1). An analytically pure sample was obtained by preparative TLC.

R_f (pentane/ethyl acetate = 4:1) = 0.5; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.20 (m_c, 1H, *H*-cyclopropyl), 0.86 (m_c, 1H, *H*-cyclopropyl), 0.91–0.95 (m, 1H, *H*-cyclopropyl), 0.97 (d, ^3J = 6.8 Hz, 6H, CH_3), 1.39 (br s, 1H, O*H*), 1.45 (m_c, 1H, *H*-cyclopropyl), 1.59 (m_c, 2H, HOCH$_2$CH_2), 2.27 (m_c, 1H, C*H*), 3.70 (t, ^3J = 6.5 Hz, 2H, HOCH_2), 5.13 (ddd, ^3J = 15.4, 8.5 Hz, ^4J = 1.3 Hz, 1H, C*H*CHCH(CH$_3$)$_2$), 5.53 (ddd, ^3J = 15.4, 6.8 Hz, ^4J = 0.8 Hz, 1H, C*H*CH(CH$_3$)$_2$) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.9, 15.1, 18.0, 22.9 (2*C*), 31.4, 32.3, 63.4, 126.1, 138.8 ppm.

The spectroscopic data agree with previously published results.[320]

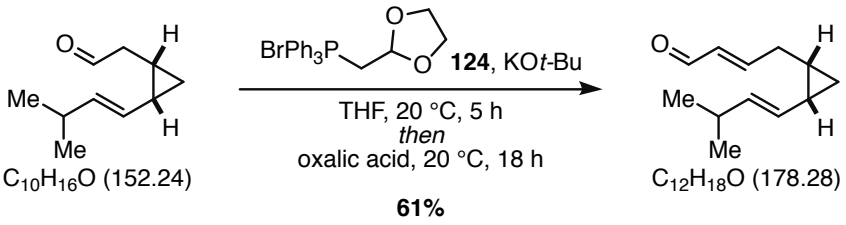
5.5.8 2-(2-((*E*)-3-Methylbut-1-en-1-yl)cyclopropyl)acetaldehyde (205)



The primary alcohol **132** (42 mg, 0.27 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (2.7 mL, 0.1 M) and treated with DMP (0.17 g, 0.41 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at this temperature for 15 min, allowed to warm to 20 °C, and stirred for 2 h. H_2O (40 mL) was added and the reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure and the residue was filtrated over celite. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1) to afford the aldehyde **205** as a colourless oil (23 mg, 0.15 mmol, 56%).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{16}NaO$, 175.1093, found: 175.1096; **IR (ATR):** $\tilde{\nu}$ = 3070, 3003, 2958, 2869, 2817, 2719, 2359, 2342, 1725, 1466, 1416, 1383, 1333, 1300, 1261, 1212, 1141, 1100, 1036, 966, 916, 836, 810, 734, 667 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.30 (m_c, 1H, *H*-cyclopropyl), 0.96 (d, ^3J = 6.8 Hz, 7H, *H*-cyclopropyl, CH_3), 1.13–1.26 (m, 1H, *H*-cyclopropyl), 1.52–1.63 (m, 1H, *H*-cyclopropyl), 2.25 (dtd, ^3J = 13.6, 6.8 Hz, ^4J = 1.3 Hz, 1H, C*H*), 2.30–2.44 (m, 2H, CH_2), 5.13 (ddd, ^3J = 15.4, 7.6 Hz, ^4J = 1.3 Hz, 1H, C*H*CHCH$(CH_3)_2$), 5.52 (dd, ^3J = 15.4, 6.8 Hz, 1H, C*H*CH$(CH_3)_2$), 9.78 (t, ^3J = 2.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 11.4, 17.5, 22.8 (3*C*), 31.3, 43.4, 77.2, 124.8, 140.0, 202.8 ppm.

5.5.9 (*E*)-4-(2-((*E*)-3-Methylbut-1-en-1-yl)cyclopropyl)but-2-enal (109c)

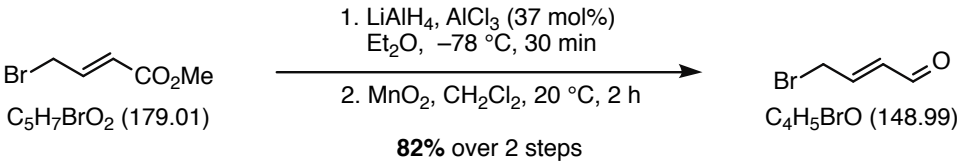


KO*t*-Bu (40 mg, 0.31 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (0.14 mg, 0.32 mmol, 2.7 equiv.) in dry THF (1.3 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **205** (19 mg, 0.12 mmol, 1.0 equiv.) in dry THF (0.30 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 5 h. Oxalic acid (0.9 M in H_2O, 1.3 mL, 1.2 mmol, 10 equiv.) was added and the mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the title compound **109c** as a pale yellow oil (13 mg, 73 µmol, 61%).

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{19}O$, 179.1431, found: 179.1429; **IR (ATR):** $\tilde{\nu}$ = 3070, 3003, 2958, 2868, 2809, 2727, 1690, 1636, 1465, 1382, 1362, 1306, 1142, 1116, 1032, 972, 831 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.28 (m_c, 1H, *H*-cyclopropyl), 0.91 (m_c, 1H, *H*-cyclopropyl), 0.96 (d, ^3J = 6.8 Hz, 6H, CH_3), 0.99–1.05 (m, 1H, *H*-cyclopropyl), 1.51–1.57 (m, 1H, *H*-cyclopropyl), 2.23–2.30 (m, 2H, C*H*, CH_2), 2.35 (dddd, ^2J = 16.9 Hz, ^3J = 7.0, 6.2 Hz, ^4J = 1.6 Hz, 1H, CH_2), 5.15 (ddd, ^3J = 15.3, 7.8 Hz, ^4J = 1.3 Hz, 1H, C*H*CHCH$(CH_3)_2$), 5.53 (ddd, ^3J = 15.3, 6.8 Hz, ^4J = 0.9 Hz, 1H, C*H*CH$(CH_3)_2$), 6.21 (ddt, ^3J = 15.6, 7.9 Hz, ^4J = 1.6 Hz, 1H, CHOC*H*), 6.90 (dt, ^3J = 15.6, 6.1 Hz, 1H, CHOCHC*H*), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.7, 16.0, 18.3, 22.8 (2*C*), 31.3, 32.2, 124.9, 133.1, 139.7, 158.4, 194.3 ppm.

5.6 Improved Synthesis of Substrates

5.6.1 (*E*)-4-Bromobut-2-enal (143)

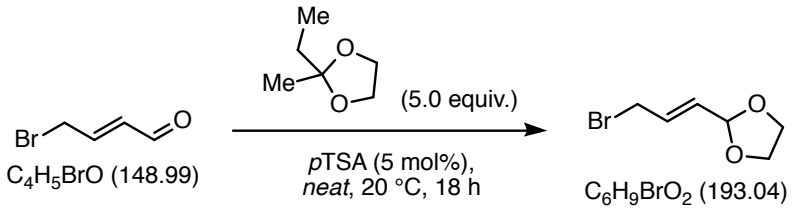


Lithium aluminium hydride (466 mg, 12.3 mmol, 1.1 equiv.) was suspended in Et_2O (20 mL, 0.6 M), cooled to −50 °C, and treated with aluminium trichloride (551 mg, 4.13 mmol, 37 mol%). The slurry was stirred for 30 min at 20 °C and cooled to −78 °C afterwards. A solution of methyl (*E*)-4-bromobut-2-enoate (2.00 g, 11.2 mmol, 1.0 equiv.) in Et_2O (8.0 mL, 1.4 M) was added dropwise over a period of 20 min and the resulting reaction mixture was stirred for 3 h at −78 °C. The reaction was quenched with H_2SO_4 (1 M in H_2O, 10 mL) at −78 °C and the mixture was allowed to reach 20 °C. The phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 100 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (100 mL) and brine (100 mL), dried over $MgSO_4$, and filtrated. The solvents of the filtrate were removed *in vacuo* and the residue was taken up in CH_2Cl_2 (150 mL, 0.07 M). MnO_2 (29.0 g, 335 mmol, 30 equiv.) was added and the slurry was stirred for 2 h before it was filtrated over celite. The filter cake was washed with CH_2Cl_2 and the solvent of the filtrate was carefully removed under reduced pressure to afford the aldehyde **143** as a yellow oil (1.37 g, 9.20 mmol, 82% over 2 steps).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.11 (d, ^3J = 8.9 Hz, 2H, CH_2), 6.26 (dd, ^3J = 15.7, 7.9 Hz, 1H, CHOC*H*), 6.83–6.93 (m, 1H, CHOCHC*H*), 9.61 (d, ^3J,=,7.9,Hz, 1H, C*H*O) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 28.7, 134.3, 149.5, 192.8 ppm.

The spectroscopic data agree with previously published results.[384]

5.6.2 (*E*)-2-(3-Bromoprop-1-en-1-yl)-1,3-dioxolane (138)

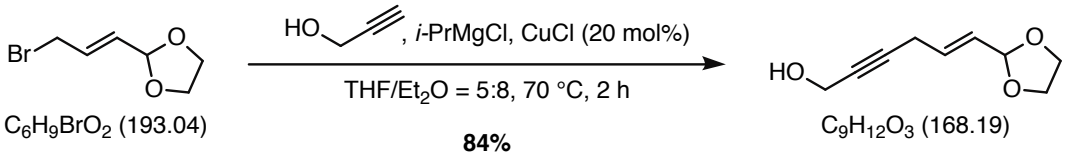


The aldehyde **143** (1.37 g, 9.20 mmol, 1.0 equiv.), 2-ethyl-2-methyl-1,3-dioxolane (5.70 mL, 46.0 mmol, 5.0 equiv.) and *p*-toluene sulfonic acid monohydrate (87.0 mg, 0.46 mmol, 5 mol%) were stirred at 20 °C for 18 h. The reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed *in vacuo* and the residue was purified by column chromatography (aluminium oxide, pentane/ethyl acetate = 20:1) affording the acetal **138** as a colourless oil (925 mg, 4.80 mmol, 52%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **IR (ATR):** $\tilde{\nu}$ = 2961, 2886, 1665, 1473, 1436, 1395, 1345, 1300, 1268, 1207, 1131, 1054, 1031, 962, 937, 877, 804 cm^{-1}; **^{1}H NMR** (500 MHz, C_6D_6): δ = 3.29–3.35 (m, 4H, BrCH_2, OCH_2), 3.42–3.48 (m, 2H, OCH_2), 5.09 (d, ^3J = 5.4 Hz, 1H, OCH), 5.52 (ddt, ^3J = 15.3, 5.4 Hz, ^4J = 1.1 Hz, 1H, CH_2CHCH), 5.81 (dtd, ^3J = 15.3, 7.4 Hz, ^4J = 0.9 Hz, 1H, CH_2CH) ppm; **^{13}C NMR** (126 MHz, C_6D_6): δ = 30.8, 64.8 (2*C*), 102.5, 130.8, 131.5 ppm.

Mass spectrometry of the compound was not successful.

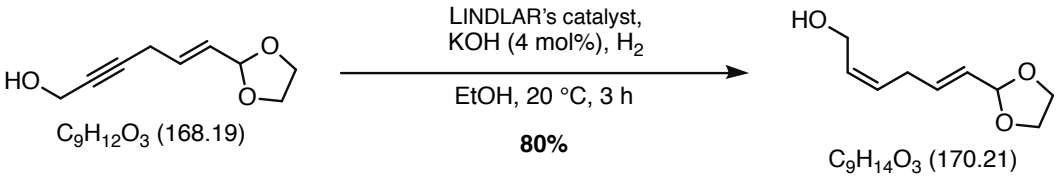
5.6.3 (*E*)-6-(1,3-Dioxolan-2-yl)hex-5-en-2-yn-1-ol (140)



i-Propylmagnesium chloride (2 M in THF, 20.0 mL, 38.6 mmol, 4.0 equiv.) was added dropwise to a solution of freshly distilled propargylic alcohol (1.10 mL, 19.3 mmol, 2.0 equiv.) in freshly distilled dry THF (10 mL, 2 M) over a period of 20 min at 0 °C. The reaction mixture was stirred for 30 min at 70 °C before it was cooled to 0 °C and treated with copper(I) chloride (191 mg, 1.93 mmol, 20 mol%). The acetal **138** (1.86 g, 9.64 mmol, 1.0 equiv.) in Et_2O (10 mL, 1 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 70 °C for 2 h. The reaction was quenched with sat. aq. NH_4Cl (50 mL), the phases separated and the aqueous phase was extracted with ethyl acetate (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, and filtrated. The solvents of the filtrate were removed and the residue was purified by column chromatography (silica gel, deactivated with 1% NEt_3, pentane/ethyl acetate = 1:1) affording the title compound **140** as a colourless oil (1.37 g, 8.15 mmol, 84%).

R_f (pentane/ethyl acetate = 1:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_9H_{13}O_3$ 169.0859, found: 169.0859; **IR (ATR):** $\tilde{\nu}$ = 3430, 2923, 2853, 1683, 1507, 1457, 1417, 1397, 1222, 1151, 1067, 1019, 966, 758 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.74 (br s, 1H, O*H*), 3.03 (dt, ^3J = 5.9 Hz, ^4J = 2.1 Hz, 2H, CH_2), 3.85–3.92 (m, 2H, OCH_2), 3.98–4.02 (m, 2H, OCH_2), 4.26 (br s, 2H, CH_2), 5.25 (d, ^3J = 5.9 Hz, 1H, C*H*), 5.79 (ddt, ^3J = 15.4, 6.1 Hz, ^4J = 1.8 Hz, 1H, CH_2CHCH), 5.91 (dtd, ^3J = 15.4, 5.3 Hz, ^4J = 0.7 Hz, 1H, CH_2CH) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 21.7, 51.4, 65.1 (2*C*), 81.2, 82.3, 103.4, 128.4, 130.8 ppm.

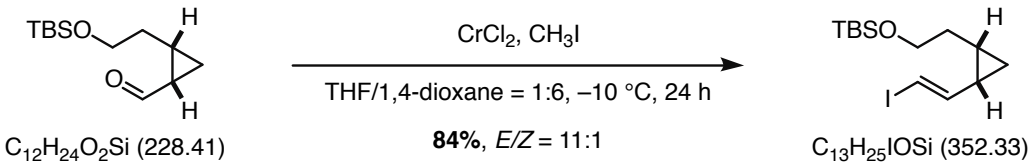
5.6.4 (2*Z*,5*E*)-6-(1,3-Dioxolan-2-yl)hexa-2,5-dien-1-ol (139)



A solution of the alkyne **140** (1.60 g, 9.51 mmol, 1.0 equiv.) in EtOH (9.5 mL, 1 M) was treated with potassium hydroxide (21.0 mg, 380 µmol, 4 mol%) and LINDLAR's catalyst (380 mg, 40 mg/mmol) at 20 °C. The reaction mixture was stirred for 3 h under an H_2-atmosphere and was filtrated over celite afterwards. The solvent of the filtrate was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, deactivated with 1% NEt_3, pentane/ethyl acetate = 1:1) delivering the title compound **139** as a colourless oil (1.29 g, 7.58 mmol, 80%).

R_f (pentane/ethyl acetate = 1:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_9H_{15}O_3$ 171.0943, found: 171.1025; **IR (ATR):** $\tilde{\nu}$ = 3397, 3017, 2952, 2920, 2883, 1718, 1676, 1473, 1397, 1346, 1303, 1260, 1212, 1144, 1033, 946, 802, 735 cm^{-1}; **^{1}H NMR** (700 MHz, C_6D_6): δ = 1.22–1.51 (m, 1H, O*H*), 2.56 (dd, ^3J = 6.8, 6.8 Hz, 2H, CH_2), 3.38–3.41 (m, 2H, OCH_2), 3.54–3.57 (m, 2H, OCH_2), 3.92 (d, ^3J = 6.2 Hz, 2H, HOCH_2), 5.18–5.21 (m, 1H, C*H*), 5.29–5.34 (m, 1H, C*H*), 5.53–5.60 (m, 1H, C*H*), 5.61–5.66 (m, 1H, C*H*), 5.73–5.78 (m, 1H, C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 30.1, 58.4, 64.9 (2*C*), 104.3, 127.9 (2*C*), 131.4, 134.4 ppm.

5.6.5 *tert*-Butyl(2-(-2-((*E*)-2-iodovinyl)cyclopropyl)ethoxy)dimethylsilane (148)

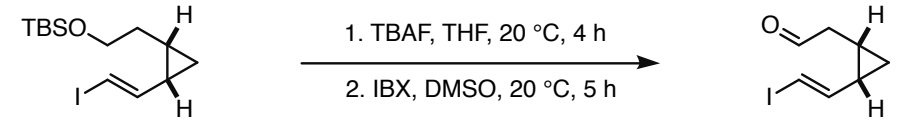


Chromium(II) chloride (3.22 g, 26.3 mmol, 6.0 equiv.) was flame dried at 200 °C for 30 min and suspended in dry THF/1,4-dioxane (6:1, 84 mL, 0.3 M). The mixture was sonicated for 10 min and then cooled to −10 °C. A solution of the aldehyde **113** (1.00 g, 4.38 mmol, 1.0 equiv.) and iodoform (3.45 g, 8.76 mmol, 2.0 equiv.) in dry

THF/1,4-dioxane (6:1, 70 mL, 0.06 M) was added dropwise over a period of 1 h and the mixture was stirred for 24 h afterwards. The reaction was quenched with sat. aq. $Na_2S_2O_3$ (100 mL) and extracted with pentane (3 x 250 mL). The combined organic phases were washed with brine (250 mL), dried over $MgSO_4$, and filtrated. The solvents of the filtrate were removed under reduced pressure and the residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 100:1) affording the iodide **148** as a yellow oil (1.30 g, 3.69 mmol, 84%, *E*/*Z* = 11:1).

R_f (pentane/diethyl ether = 100:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{25}NaIOSi$ 375.0611, found: 375.0631; **IR (ATR):** $\tilde{\nu}$ = 3064, 2997, 2952, 2929, 2890, 2857, 2359, 2338, 1700, 1603, 1540, 1469, 1389, 1360, 1320, 1254, 1189, 1099, 1065, 1034, 1006, 943, 888, 834, 776, 733 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.06 (s, 6H, $SiCH_3$), 0.34 (m_c, 1H, *H*-cyclopropyl), 0.90 (s, 9H, $CHCH_3$), 0.92–0.95 (m, 1H, *H*-cyclopropyl), 1.04–1.12 (m, 1H, *H*-cyclopropyl), 1.50–1.58 (m, 3H, *H*-cyclopropyl, CH_2), 3.66 (td, ^3J = 6.7 Hz, ^4J = 2.1 Hz, 2H, OCH_2), 5.99 (d, ^3J = 14.3 Hz, 1H, ICH), 6.23 (dd, ^3J = 14.3, 9.1 Hz, 1H, ICHCH) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = −5.1 (2*C*), 12.6, 15.8, 18.5, 22.0, 26.1 (3*C*), 32.8, 63.1, 72.4, 146.2 ppm.

5.6.6 2-(2-((*E*)-2-Iodovinyl)cyclopropyl)acetaldehyde (149)

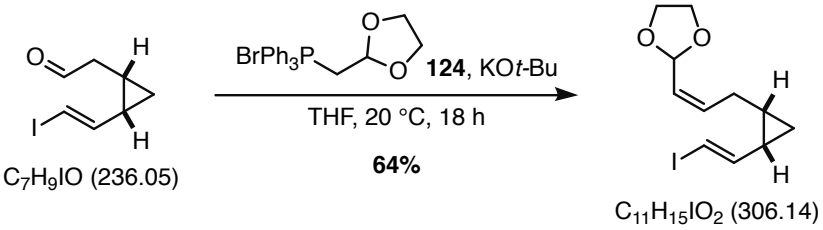


$C_{13}H_{25}IOSi$ (352.33) — **56%** over 2 steps — C_7H_9IO (236.05)

A solution of the silyl ether **148** (391 mg, 1.11 mmol, 1.0 equiv.) in THF (7.4 mL, 0.15 M) was treated with TBAF (1.0 M in THF, 1.67 mL, 1.67 mmol, 1.5 equiv.) at 20 °C. The reaction mixture was stirred at this temperature for 4 h. The solvents were removed under reduced pressure and the residue was filtrated over silica gel (pentane/ethyl acetate = 4:1) delivering the crude alcohol as a colourless oil (249 mg, 1.04 mmol, 94%) which was used in the next step without further purification. The alcohol (249 mg, 1.04 mmol, 1.0 equiv.) was dissolved in DMSO (10 mL, 0.1 M). The solution was treated with IBX (437 mg, 1.56 mmol, 1.5 equiv.) at 20 °C. The reaction mixture was stirred at this temperature for 5 h before the reaction was quenched with sat. aq. $NaHCO_3$ (20 mL). The mixture was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed *in vacuo* and the residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1) affording the aldehyde **149** as a colourless oil (148 mg, 630 µmol, 60%).

R_f (pentane/ethyl acetate = 20:1) = 0.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_7H_9NaIOSi$ 258.9590, found: 258.9586; **IR (ATR):** $\tilde{\nu}$ = 3055, 2998, 2883, 2817, 2720, 2359, 2342, 1869, 1720, 1653, 1635, 1599, 1558, 1541, 1522, 1507, 1472, 1446, 1416, 1385, 1288, 1220, 1191, 1127, 1104, 1040, 944, 915, 860, 829, 785, 764, 741, 722, 712 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.43 (m_c, 1H, *H*-cyclopropyl), 1.07 (ddd, ^2J = 8.3 Hz, ^3J = 8.3, 5.3 Hz, 1H. *H*-cyclopropyl), 1.33 (m_c, 1H, *H*-cyclopropyl), 1.68 (m_c, 1H, *H*-cyclopropyl), 2.37–2.53 (m, 2H, CH_2), 6.09 (dd, ^3J = 14.4 Hz, ^4J = 0.8 Hz, 1H, IC*H*), 6.23 (dd, ^3J = 14.4, 8.2 Hz, 1H, ICHC*H*), 9.79 (t, ^3J = 1.7 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.8, 11.9, 21.3, 43.6, 74.8, 144.5, 201.4 ppm.

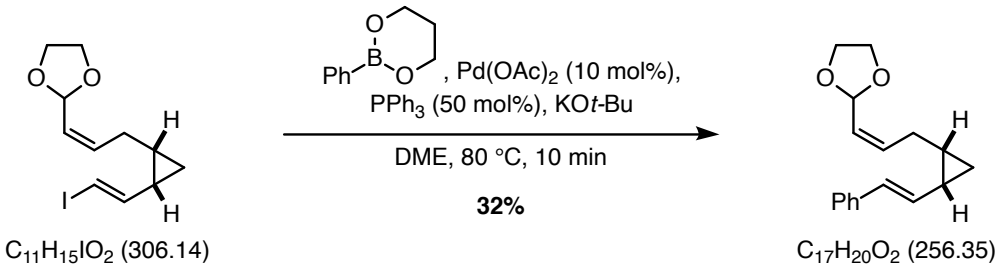
5.6.7 2-((*E*)-3-(2-((*E*)-2-Iodovinyl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (133)



KO*t*-Bu (155 mg, 1.38 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (617 mg, 1.43 mmol, 2.7 equiv.) in dry THF (6.0 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **149** (125 mg, 0.530 mmol, 1.0 equiv.) in dry THF (1.3 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 18 h. Oxalic acid (0.9 M in H_2O, 30.0 mL, 27.1 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h before the reaction was quenched with sat. aq. NH_4Cl (20 mL). The solution was extracted with Et_2O (3 x 50 mL) and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the title compound **133** as a colourless oil (104 mg, 0.340 mmol, 64%). A clean fraction of the *E*-acetal was used for analysis.

R_f (pentane/ethyl acetate = 20:1) = 0.7; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{11}H_{16}IO_2$, 307.0190, found: 307.0189; **IR (ATR)**: $\tilde{\nu}$ = 3062, 2994, 2948, 2881, 1665, 1473, 1423, 1346, 1288, 1215, 1190, 1131, 1115, 1066, 1008, 944, 827, 802, 750, 735 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.39 (m_c, 1H, *H*-cyclopropyl), 0.94 (m_c, 1H, *H*-cyclopropyl), 1.07 (m_c, 1H, *H*-cyclopropyl), 1.53–1.64 (m, 1H, *H*-cyclopropyl), 2.20 (td, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 2H, CH_2), 3.86–3.94 (m, 2H, OCH_2), 3.98–4.06 (m, 2H, OCH_2), 5.44–5.53 (m, 2H, OC*H*, OCHC*H*), 5.81 (dt, ^3J = 9.7, 7.6 Hz, 1H, CH_2C*H*), 6.02 (dd, ^3J = 14.3 Hz, ^4J = 0.7 Hz, 1H, IC*H*), 6.28 (dd, ^3J = 14.3, 8.7 Hz, 1H, ICHC*H*) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 12.3, 18.6, 22.3, 27.6, 65.1, 65.1, 73.3, 99.3, 126.5, 136.0, 145.5 ppm.

5.6.8 2-((*E*)-3-(2-((*E*)-Styryl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (150)

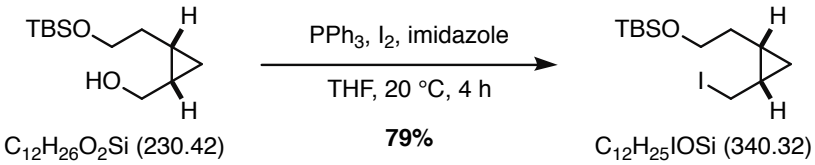


The iodide **133** (50 mg, 0.16 mmol, 1.0 equiv.) and 2-phenyl-2-bora-1,3-dioxane (29 mg, 0.18 mmol, 1.1 equiv.) were dissolved in degassed DME (2.00 mL, 0.08 M) and treated with $Pd(OAc)_2$ (4.0 mg, 16 µmol, 10 mol%) and PPh_3 (21 mg, 80 µmol, 50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature,

KO*t*-Bu (1 M in *t*-BuOH, 0.32 mL, 0.32 mmol, 2.0 equiv.) was added dropwise over a period of 15 min. After complete addition, the reaction mixture was stirred at 80 °C for 10 min. After cooling to 20 °C, the reaction mixture was diluted with pentane (20 mL) and filtrated over silica gel. The solvents of the filtrate were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) afforded the title compound **150** as colourless oil (13 mg, 51 µmol, 32%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + K]^+$ calcd for $C_{17}H_{20}KO_2$, 295.1110, found: 295.1157; **IR (ATR)**: $\tilde{\nu}$ = 3069, 2997, 2883, 2360, 2342, 1734, 1716, 1666, 1633, 1558, 1542, 1508, 1474, 1423, 1346, 1281, 1221, 1119, 1073, 1030, 1006, 990, 956, 897, 797, 785, 695, 669, 608 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.45 (m_c, 1H, *H*-cyclopropyl), 1.01 (m_c, 1H, *H*-cyclopropyl), 1.13 (dddd, ^3J = 15.8, 8.5, 7.4, 5.8 Hz, 1H, *H*-cyclopropyl), 1.65–1.77 (m, 1H, *H*-cyclopropyl), 2.23–2.32 (m, 2H, CH_2), 3.75–3.87 (m, 2H, OCH_2), 3.93–4.03 (m, 2H, OCH_2), 5.41–5.53 (m, 2H, OC*H*, OCHC*H*), 5.87 (dt, ^3J = 10.5, 7.6 Hz, 1H, OCHCHC*H*), 6.01 (dd, ^3J = 15.7, 8.6 Hz, 1H, PhCHC*H*), 6.50 (d, ^3J = 15.7 Hz, 1H, PhC*H*), 7.15–7.21 (m, 1H, *H*-Ar), 7.27–7.37 (m, 4H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.0, 19.3, 19.6, 27.8, 65.1, 99.4, 125.9 (2*C*), 126.1, 126.9, 128.6 (2*C*), 130.1, 130.4, 136.7, 137.9 ppm.

5.6.9 *tert*-Butyl(2-(2-(iodomethyl)cyclopropyl)ethoxy)dimethylsilane (152)

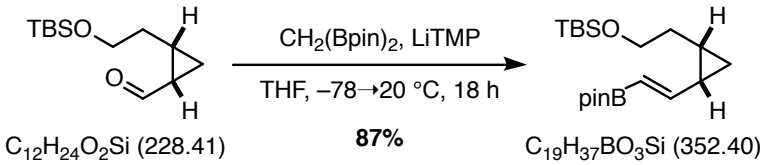


$C_{12}H_{26}O_2Si$ (230.42) → $C_{12}H_{25}IOSi$ (340.32)

A solution of the alcohol **120** (0.10 g, 0.43 mmol, 1.0 equiv.) in dry THF (7.2 mL, 0.06 M) was treated with triphenylphosphine (0.14 g, 0.52 mmol, 1.2 equiv.), iodine (132 mg, 0.52 mmol, 1.2 equiv.), and imidazole (59 mg, 0.86 mmol, 2.0 equiv.) at 20°C. The reaction mixture was stirred at this temperature for 4 h before the reaction was quenched with sat. aq. $Na_2S_2O_3$ (20 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents of the filtrate were removed *in vacuo* and the residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 100:1) affording the title compound **152** as a colourless oil (0.12 g, 0.34 mmol, 79%).

R_f (pentane/diethyl ether = 100:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{26}IOSi$ 341.0792, found: 341.0787; **IR (ATR):** $\tilde{\nu}$ = 3066, 2994, 2953, 2928, 2886, 2856, 1471, 1463, 1387, 1361, 1254, 1172, 1140, 1100, 1024, 1006, 989, 967, 938, 893, 834, 810, 775, 735, 684, 664 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = −0.02–0.04 (m, 1H, *H*-cyclopropyl), 0.07 (s, 6H, $SiCH_3$), 0.86–0.92 (m, 1H, *H*-cyclopropyl), 0.90 (s, 9H, CCH_3), 1.13 (m_c, 1H, *H*-cyclopropyl), 1.33–1.46 (m, 2H, CH_2), 1.79 (m_c, 1H, *H*-cyclopropyl), 3.17 (dd, ^2J = 9.9 Hz, ^3J = 8.5 Hz, 1H, ICH_2), 3.32 (dd, ^2J = 9.9 Hz, ^3J = 7.9 Hz, 1H, ICH_2), 3.73 (t, ^3J = 6.6 Hz, 2H, OCH_2) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = −5.1 (2*C*), 9.4, 15.9, 18.5, 18.6, 20.3, 26.1 (3*C*), 31.0, 63.6 ppm.

5.6.10 (*tert*-Butyldimethyl(2-(2-((*E*)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl-cyclopropyl)ethoxy)silane (154)

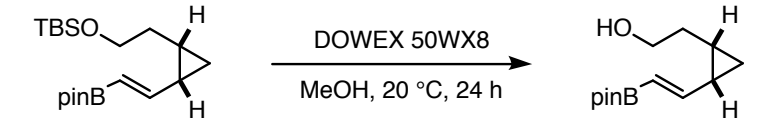


$C_{12}H_{24}O_2Si$ (228.41) — $C_{19}H_{37}BO_3Si$ (352.40)

At 0 °C, a solution of LiTMP (3.75 g, 25.5 mmol, 1.2 equiv.) in dry THF (25 mL, 1 M) was treated with a solution of $CH_2(Bpin)_2$ (**197**, 6.83 g, 25.5 mmol, 1.2 equiv.) in dry THF (50 mL, 0.5 M). The resulting mixture was stirred at 0 °C for 5 min and then cooled to −78 °C. A solution of aldehyde **113** (4.85 g, 21.2 mmol, 1.0 equiv.) in dry THF (25 mL, 0.8 M) was added dropwise over a period of 30 min. After complete addition, the reaction mixture was allowed to warm to 20 °C over 18 h. Silica gel (10 g) was added, the solvent removed under reduced pressure and the crude product purified by column chromatography (silica gel, pentane/ethyl acetate = 80:1→20:1). The vinyl borane **154** was obtained as a colourless oil (6.48 g, 18.4 mmol, 87%, *d.r.* > 20:1).

R_f (pentane/ethyl acetate = 80:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{38}BO_3Si$, 353.2678, found: 353.2696; **IR (ATR)**: $\tilde{\nu}$ = 2995, 2978, 2954, 2929, 2857, 1631, 1471, 1409, 1370, 1320, 1255, 1214, 1146, 1101, 1044, 1005, 990, 972, 889, 835, 775, 660 cm^{-1}; **^{11}B NMR** (128 MHz, $CDCl_3$): δ = 28.1 ppm; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.03–0.07 (m, 6H, SiCH_3), 0.43 (m_c, 1H, *H*-cyclopropyl), 0.85–0.89 (m, 9H, SiCCH_3), 0.97 (m_c, 1H, *H*-cyclopropyl), 1.07–1.16 (m, 1H, *H*-cyclopropyl), 1.25 (s, 12H, CH_3-Bpin), 1.53–1.68 (m, 3H, TBSOCH$_2$CH_2, *H*-cyclopropyl), 3.64 (t, ^3J = 6.9 Hz, 2H, TBSOCH_2), 5.54 (dt, ^3J = 17.7 Hz, ^4J = 0.7 Hz, 1H, BC*H*=CH), 6.32 (dd, ^3J = 17.7, 9.5 Hz, 1H, BCH=C*H*) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = −5.1, −5.1, 14.1, 17.4, 18.5, 22.0, 24.9 (2*C*), 24.9 (2*C*), 26.1 (3*C*), 32.7, 63.3, 83.0 (2*C*), 120.1, 154.7 ppm.

5.6.11 2-(2-((*E*)-2-(4,4,5,5-Tetramethyl-1,3,2-dioxa-borolan-2-yl)-vinyl)-cyclo-propyl)-ethan-1-ol (206)

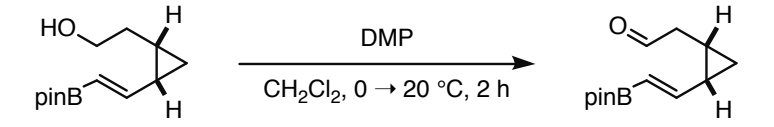


$C_{19}H_{37}BO_3Si$ (352.40) — $C_{13}H_{23}BO_3$ (238.13)

The vinyl borane **154** (5.98 g, 17.0 mmol, 1.0 equiv.) was dissolved in dry MeOH (19 mL, 0.9 M) and treated with DOWEX 50WX8 (proton form, 1.60 g, 94.0 mg/mmol). The reaction mixture was stirred at 20 °C for 24 h. The resin was filtered off and washed with CH_2Cl_2. The solvents of the combined organic phases were removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 2:1) to obtain the primary alcohol **206** as a colourless oil (3.33 g, 14.0 mmol, 82%, 92% brsm) together with recovered starting material (632 mg, 1.79 mmol).

R_f (pentane/ethyl acetate = 2:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{24}BO_3$, 239.1812, found: 239.1815; **IR (ATR)**: $\tilde{\nu}$ = 3425, 3073, 2979, 2929, 2361, 2341, 1631, 1455, 1368, 1320, 1273, 1215, 1144, 1107, 1034, 991, 970, 899, 849, 745, 695, 669 cm^{-1}; **^{11}B NMR** (128 MHz, $CDCl_3$): δ = 28.4 ppm; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.45 (ddd, ^2J = 5.4 Hz, ^3J = 5.4, 5.4 Hz, 1H, *H*-cyclopropyl), 1.01 (m_c, 1H, *H*-cyclopropyl), 1.12–1.16 (m_c, 1H, *H*-cyclopropyl), 1.25 (s, 12H, CH_3), 1.60–1.69 (m, 4H, CH_2, *H*-cyclopropyl, *OH*), 3.70 (t, ^3J = 6.6 Hz, 2H, HOCH_2), 5.56 (d, ^3J = 17.6 Hz, 1H, BC*H*), 6.31 (dd, ^3J = 17.6, 9.5 Hz, 1H, BCH=C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.9, 17.3, 21.8, 24.7, 24.9 (4*C*), 32.4, 63.2, 83.1 (2*C*), 154.2 ppm.

5.6.12 2-(2-((*E*)-2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)cyclopropyl)acetaldehyde (156)

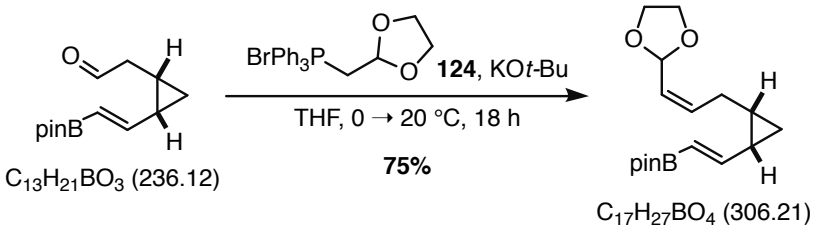


$C_{13}H_{23}BO_3$ (238.13) — $C_{13}H_{21}BO_3$ (236.12)

The primary alcohol **206** (1.46 g, 6.13 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (62 mL, 0.1 M) and treated with DMP (3.91 g, 9.22 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at this temperature for 15 min, allowed to warm to 20 °C, and stirred for 2 h. H_2O (40 mL) was added and the reaction mixture extracted with Et_2O (3 x 150 mL). The combined organic phases were washed with brine (150 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1) to yield the aldehyde **156** as a colourless oil (1.04 g, 4.40 mmol, 72%).

R_f (pentane/ethyl acetate = 10:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{21}BNaO_3$, 259.1476, found: 259.1489; **IR (ATR)**: $\tilde{\nu}$ = 3073, 2978, 2929, 2724, 1725, 1631, 1447, 1407, 1389, 1371, 1353, 1328, 1317, 1300, 1272, 1205, 1165, 1144, 1108, 1046, 996, 971, 926, 894, 871, 849, 835, 792, 776, 735, 720, 700, 691, 679, 665, 652 cm^{-1}; **^{11}B NMR** (128 MHz, $CDCl_3$): δ = 28.3 ppm; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.51 (m_c, 1H, *H*-cyclopropyl), 1.12 (m_c, 1H, *H*-cyclopropyl), 1.25 (s, 12H, CH_3-Bpin), 1.38 (m_c, 1H, *H*-cyclopropyl), 1.69–1.79 (m, 1H, *H*-cyclopropyl), 2.43 (ddd, ^2J = 17.7 Hz, ^3J = 7.7, 1.3 Hz, 1H, H_2CCHO), 2.54 (dd, ^2J = 17.7 Hz, ^3J = 7.0 Hz, 1H, H_2CCHO), 5.56 (d, ^3J = 17.8 Hz, 1H, BC*H*=CH), 6.28 (dd, ^3J = 17.8, 8.9 Hz, 1H, BCH=C*H*), 9.78 (br s, 1H, C*H*O) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 13.3, 13.5, 21.1, 24.9 (4*C*), 43.5, 83.2 (2*C*), 120.1, 152.5, 202.1 ppm.

5.6.13 2-((*E*)-2-(-2-((*Z*)-3-(1,3-Dioxolan-2-yl)allylcyclopropyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (157)



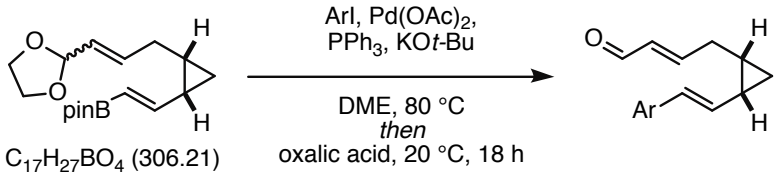
$C_{13}H_{21}BO_3$ (236.12) → $C_{17}H_{27}BO_4$ (306.21)

KO*t*-Bu (790 mg, 7.05 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (3.16 g, 7.33 mmol, 2.7 equiv.) in dry THF (30 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of aldehyde **156** (640 mg, 2.71 mmol, 1.0 equiv.) in dry THF (7.0 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 18 h. H_2O (15 mL) was added and the resulting biphasic system was separated. The aqueous phase was extracted with Et_2O (3 x 50 mL) and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1). The acetal **157** was obtained as a colourless oil (626 mg, 2.04 mmol, 75%) in an inconsequential *E/Z*-mixture at the acetal part of the molecule. A clean fraction of the *Z*-configured acetal was used for analytical purpose.

R_f (pentane/ethyl acetate = 10:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{28}BO_4$, 307.2075, found: 307.2062; **IR (ATR):** $\tilde{\nu}$ = 2976, 2926, 2886, 1628, 1469, 1408, 1389, 1370, 1329, 1315, 1299, 1272, 1210, 1142, 1069, 1029, 995, 970, 899, 870, 850, 832, 821, 731, 710, 691, 678, 669, 659 cm^{-1}; **^{11}B NMR** (128 MHz, $CDCl_3$): δ = 28.4 ppm; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.47 (m_c, 1H, *H*-cyclopropyl), 1.00 (m_c, 1H, *H*-cyclopropyl), 1.11 (m_c, 1H, *H*-cyclopropyl), 1.25 (s, 12H, CH_3-Bpin), 1.59–1.69 (m, 1H, *H*-cyclopropyl), 2.25 (m_c, 2H, CH_2), 3.84–3.92 (m, 2H, CH_2), 3.96–4.04 (m, 2H, CH_2), 5.45 (ddt, ^3J = 10.6, 7.0 Hz, ^4J = 1.4 Hz, 1H, HC=C*H*CHO$_2$), 5.51–5.53 (m, 1H, C*H*O$_2$), 5.55 (d, ^3J = 17.7 Hz, 1H, BpinC*H*=CH), 5.82 (dt, ^3J = 10.6, 7.8 Hz, 1H, *H*C=CHCHO2), 6.33 (dd, ^3J = 17.7, 9.4 Hz, 1H, BpinCH=C*H*) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 14.0, 20.3, 22.3, 24.9 (2*C*), 24.9(2*C*), 27.7, 65.1, 83.1(2*C*), 99.4 (2C), 120.1, 126.1, 136.6, 153.9 ppm.

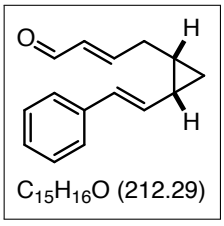
5.6.14 Preparation of Substrates by Suzuki Coupling

General Procedure for the Coupling of 157 with Different Aryl Iodides (GP1)



The pinacolborane **157** (1.1 equiv.) and the corresponding iodide (1.0 equiv.) were dissolved in degassed DME (0.08 M) and treated with $Pd(OAc)_2$ (10 mol%) and PPh_3 (50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 2.0 equiv.) was added dropwise over a period of 15 min. After complete addition, the reaction mixture was stirred at 80 °C until TLC showed complete conversion of the starting materials. The mixture was cooled to 20 °C, treated with oxalic acid (0.9 M in H_2O, 10 equiv.), and stirred for 18 h. The reaction mixture was then extracted with Et_2O (3 x) and the combined organic phases were washed with sat. aq. $NaHCO_3$ and brine. The organic phases were dried over $MgSO_4$, filtrated, and the solvents were removed under reduced pressure. The crude products were purified by column chromatography.

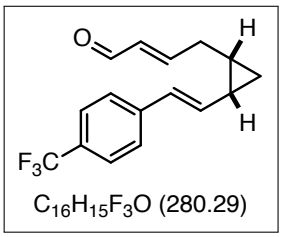
(*E*)-4-(2-((*E*)-Styryl)cyclopropyl)but-2-enal (109a)



The title compound was derived from **157** (1.01 g, 3.30 mmol) and iodobenzene (340 µL, 3.00 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109a** as a colourless oil (492 mg, 2.32 mmol, 70%).

The spectroscopic data agree with the ones mentioned in 5.3.9.

(*E*)-4-(2-((*E*)-4-(Trifluoromethyl)styryl)cyclopropyl)but-2-enal (109d)

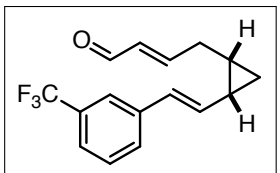


The title compound was derived from **157** (0.10 g, 0.33 mmol) and 4-iodobenzotrifluoride (82 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the aldehyde **109d** as a yellow oil (58 mg, 0.21 mmol, 69%).

R_f (pentane/ethyl acetate = 10:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{15}F_3NaO$, 303.0967, found: 303.0959; **IR (ATR):** $\tilde{\nu}$ = 3001, 2953, 2924, 2851, 2733, 2360, 2342, 1686, 1644, 1614, 1587, 1507, 1456, 1436, 1417, 1376, 1322, 1261, 1185, 1161, 1107, 1065, 1014, 970, 952, 904, 879, 860, 820, 751, 693 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −62.7 ppm; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.53 (m_c, 1H, *H*-cyclopropyl), 1.15 (m_c, 1H, *H*-cyclopropyl), 1.20–1.33 (m, 1H, *H*-cyclopropyl), 1.73–2.02 (m, 1H, *H*-cyclopropyl), 2.32–2.53 (m, 2H, C*H*$_2$), 6.06 (dd, ^3J = 15.7, 8.6 Hz, 1H, ArCH=C*H*), 6.24 (ddt, ^3J = 15.6, 7.9 Hz, ^4J = 1.6 Hz, 1H,

C*H*=CHCHO), 6.55 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.6, 6.0 Hz, 1H, CH=C*H*CHO), 7.39 (d, ^3J = 8.1 Hz, 2H, *H*-Ar), 7.53 (d, ^3J = 8.1 Hz, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.2, 17.5, 19.5, 32.4, 124.4 (q, $^1J_{C,F}$ = 272 Hz),125.7 (2*C*), 126.0 (2*C*), 128.9 (q, $^2J_{C,F}$ = 33.0 Hz), 129.9, 132.1, 133.2, 141.0, 157.3, 194.1 ppm.

(*E*)-4-(2-((*E*)-3-(Trifluoromethyl)styryl)cyclopropyl)but-2-enal (109e)

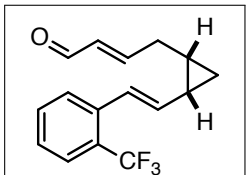


$C_{16}H_{15}F_3O$ (280.29)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 3-iodobenzotrifluoride (82 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the aldehyde **109e** as a brown oil (72 mg, 0.26 mmol, 86%).

R_f (pentane/ethyl acetate = 10:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{15}F_3NaO$, 303.0967, found: 303.0972; **IR (ATR):** $\tilde{\nu}$ = 3001, 2924, 2816, 2736, 2362, 2335, 1686, 1637, 1591, 1489, 1438, 1365, 1328, 1258, 1199, 1161, 1119, 1095, 1070, 1040, 1011, 966, 901, 830, 794, 751, 727, 696, 661 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −62.3 ppm; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.53 (m_c, 1H, *H*-cyclopropyl), 1.14 (m_c, 1H, *H*-cyclopropyl), 1.21–1.29 (m_c, 1H, *H*-cyclopropyl), 1.81 (m_c, 1H, *H*-cyclopropyl), 2.37–2.48 (m, 2H, CH_2), 6.04 (dd, ^3J = 15.8, 8.6 Hz, 1H, ArCH=C*H*), 6.25 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.55 (dd, ^3J = 15.8 Hz, ^4J = 0.7 Hz, 1H, ArC*H*=CH), 6.92 (dt, ^3J = 15.7, 6.0 Hz, 1H, HC=C*H*CHO), 7.38–7.41 (m, 1H, *H*-Ar), 7.43–7.48 (m, 2H, *H*-Ar), 7.53–7.54 (m, 1H, *H*-Ar), 9.53 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.1, 17.5, 19.4, 32.4, 122.4, 123.6, 124.3 (q, $^1J_{C,F}$ = 272 Hz), 129.0, 129.1, 129.8, 131.1 (q, $^2J_{C,F}$ = 32 Hz), 131.2, 133.2, 138.3, 157.4, 194.1 ppm.

(*E*)-4-(2-((*E*)-2-(Trifluoromethyl)styryl)cyclopropyl)but-2-enal (109f)

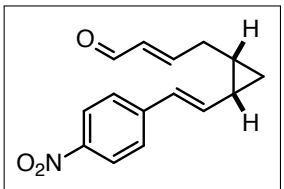


$C_{16}H_{15}F_3O$ (280.29)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 2-iodobenzotrifluoride (82 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the aldehyde **109f** as a yellow oil (50 mg, 0.18 mmol, 59%).

R_f (pentane/ethyl acetate = 10:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{15}F_3NaO$, 303.0967, found: 303.0973; **IR (ATR):** $\tilde{\nu}$ = 3069, 3001, 2923, 2815, 2733, 1686, 1638, 1604, 1575, 1487, 1454, 1436, 1312, 1282, 1266, 1152, 1105, 1059, 1035, 1011, 968, 903, 880, 849, 819, 763, 745, 725, 693, 655 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −59.6 ppm; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.54 (m_c, 1H, *H*-cyclopropyl), 1.14 (m_c, 1H, *H*-cyclopropyl), 1.18–1.30 (m, 1H, *H*-cyclopropyl), 1.84 (m_c, 1H, *H*-cyclopropyl), 2.37 (dddd, ^2J = 17.0 Hz, ^3J = 7.7, 5.9 Hz, ^4J = 1.7 Hz, 1H, CH_2), 2.46 (dddd, ^2J = 17.0 Hz, ^3J=7.1, 6.3 Hz, ^4J = 1.6 Hz, 1H, CH_2), 5.95 (dd, ^3J = 15.5, 8.3 Hz, 1H, ArCH=C*H*), 6.23 (ddt, ^3J = 15.6, 7.9 Hz, ^4J = 1.6 Hz, 1H, C*H*=CHCHO), 6.84–6.94 (m, 2H, ArC*H*=CH, HC=C*H*CHO), 7.28–7.32 (m, 1H, *H*-Ar), 7.44–7.52 (m, 2H, *H*-Ar), 7.59–7.62 (m, 1H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.0, 17.6, 19.5, 32.3, 124.5 (q, $^1J_{C,F}$ = 273 Hz), 125.9, 126.6–126.9 (m, 2*C*), 127.2, 131.9, 133.2, 133.5, 135.1, 136.7, 157.5, 194.1 ppm.

(*E*)-4-(-2-((*E*)-4-Nitrostyryl)cyclopropyl)but-2-enal (109g)

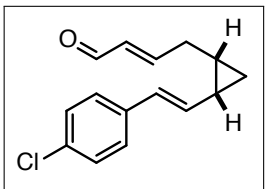


$C_{15}H_{15}NO_3$ (257.29)

The title compound was derived from **157** (70 mg, 0.23 mmol) and 4-nitroiodobenzene (52 mg, 0.21 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the aldehyde **109g** as a yellow oil (22 mg, 86 µmol, 41%).

R_f (pentane/ethyl acetate = 4:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}NNaO_3$, 280.0944, found: 280.0951; **IR (ATR):** $\tilde{\nu}$ = 3069, 2998, 2926, 2819, 2734, 2446, 2360, 2342, 1683, 1637, 1592, 1508, 1446, 1335, 1181, 1142, 1109, 1037, 1011, 969, 860, 841, 748, 691, 658 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.58 (m_c, 1H, *H*-cyclopropyl), 1.18–1.22 (m, 1H, *H*-cyclopropyl), 1.32 (dddd, ^3J = 15.7, 8.4, 7.3, 5.9 Hz, 1H, *H*-cyclopropyl), 1.81–1.88 (m, 1H, *H*-cyclopropyl), 2.29–2.63 (m, 2H, CH_2), 6.15 (dd, ^3J,=,15.7, 8.9,Hz, 1H, ArCH=C*H*), 6.24 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, C*H*=CHCHO), 6.59 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.7, 6.0 Hz, 1H, CH=C*H*CHO), 7.36–7.50 (m, 2H, *H*-Ar), 8.10–8.22 (m, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.8, 18.0, 19.9, 32.4, 124.2 (2*C*), 126.2 (2*C*), 129.2, 133.3, 134.9, 143.9, 146.6, 157.0, 194.0 ppm.

(*E*)-4-(2-((*E*)-4-Chlorostyryl)cyclopropyl)but-2-enal (109h)

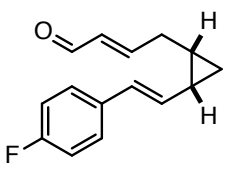


$C_{15}H_{15}ClO$ (246.73)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 4-chloroiodobenzene (72 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109h** as a yellow oil (57 mg, 0.23 mmol, 77%).

R_f (pentane/ethyl acetate = 10:1) = 0.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}ClNaO$, 269.0703, found: 269.0716; **IR (ATR):** $\tilde{\nu}$ = 3070, 3020, 2997, 2924, 2814, 2732, 2360, 2342, 1685, 1641, 1592, 1490, 1435, 1408, 1366, 1308, 1258, 1197, 1178, 1141, 1115, 1088, 1030, 1011, 968, 905, 877, 852, 810, 745, 726, 702, 691, 672 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.49 (m_c, 1H, *H*-cyclopropyl), 1.11 (m_c, 1H, *H*-cyclopropyl), 1.18–1.24 (m, 1H, *H*-cyclopropyl), 1.78 (dddd, ^3J = 8.4, 8.3, 8.3, 5.6 Hz, 1H, *H*-cyclopropyl), 2.33–2.49 (m, 2H, CH_2), 5.94 (dd, ^3J = 15.7, 8.4 Hz, 1H, ArCH=C*H*), 6.24 (ddd, ^3J = 15.7, 8.0 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.47 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.7, 6.0 Hz, 1H, HC=C*H*CHO), 7.22 (d, ^3J = 8.5 Hz, 2H, *H*-Ar), 7.25 (d, ^3J = 8.5 Hz, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.9, 17.3, 19.4, 32.4, 127.1, 128.8 (2*C*), 129.8 (2*C*), 130.0, 132.6, 133.2, 136.0, 157.6, 194.1 ppm.

(*E*)-4-(-2-((*E*)-4-Fluorostyryl)cyclopropyl)but-2-enal (109i)

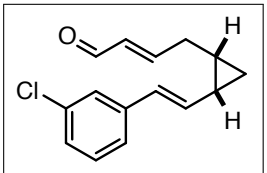


$C_{15}H_{15}FO$ (230.28)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 4-fluoroiodobenzene (66 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 0:1) delivered the aldehyde **109i** as a yellow oil (54 mg, 0.23 mmol, 77%).

R_f (pentane/ethyl acetate = 10:1) = 0.3; **ESI-TOF** (*m/z*) $[M + Na]^+$ calcd for $C_{15}H_{15}FNaO$, 253.1005, found: 253.1010; **IR (ATR):** $\tilde{\nu}$ = 3070, 2998, 2918, 2814, 2734, 1685, 1507, 1226, 968, 819,cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −115.3 ppm; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.36–0.52 (m, 1H, *H*-cyclopropyl), 1.10 (m_c, 1H, *H*-cyclopropyl), 1.20 (m_c, 1H, *H*-cyclopropyl), 1.77 (m_c, 1H, *H*-cyclopropyl), 2.36–2.44 (m, 2H, CH_2), 5.88 (dd, ^3J = 15.6, 8.2 Hz, 1H, ArCH=C*H*), 6.24 (dd, ^3J = 15.3, 7.8 Hz, 1H, *H*C=CHCHO), 6.48 (d, ^3J = 15.6 Hz, 1H, ArC*H*=CH), 6.89–6.93 (m, 1H, HC=C*H*CHO), 6.95–7.01 (m, 2H, *H*-Ar), 7.16–7.37 (m, 2H, *H*-Ar), 9.52 (d, ^3J = 7.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.7, 17.1, 19.3, 32.4, 115.6 (d, $^2J_{C,F}$ = 22 Hz, 2*C*), 127.3 (d, $^3J_{C,F}$ = 8 Hz, 2*C*), 128.7, 130.0, 133.2, 133.7, 157.7, 162.1 (d, $^1J_{C,F}$ = 245 Hz), 194.2 ppm.

(*E*)-4-(2-((*E*)-3-Chlorostyryl)cyclopropyl)but-2-enal (109j)

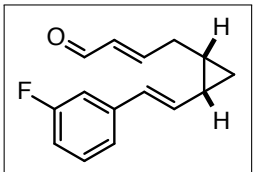


$C_{15}H_{15}ClO$ (246.73)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 3-chloroiodobenzene (72 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109j** as a yellow oil (44 mg, 0.18 mmol, 59%).

R_f (pentane/ethyl acetate = 20:1) = 0.3; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{15}H_{15}ClO$, 247.0884, found: 247.0882; **IR (ATR):** $\tilde{\nu}$ = 3065, 2998, 2915, 2815, 2733, 2360, 2342, 1684, 1643, 1592, 1562, 1474, 1447, 1425, 1365, 1307, 1254, 1201, 1140, 1115, 1094, 1077, 1035, 1009, 970, 876, 826, 777, 722, 685 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl^3$): δ = 0.50 (m_c, 1H, *H*-cyclopropyl), 1.12 (m_c, 1H, *H*-cyclopropyl), 1.23 (dddd, ^3J = 15.9, 8.5, 7.3, 5.9 Hz, 1H, *H*-cyclopropyl), 1.79 (m_c, 1H, *H*-cyclopropyl), 2.36–2.48 (m, 2H, CH_2), 5.97 (dd, ^3J = 15.7, 8.5 Hz, 1H, ArCH=C*H*), 6.24 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.46 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.7, 6.0 Hz, 1H, HC=C*H*CHO), 7.15–7.17 (m, 2H, *H*-Ar), 7.19–7.23 (m, 1H, *H*-Ar), 7.29 (t, ^4J = 1.9 Hz, 1H, *H*-Ar), 9.53 (d, ^3J = 7.9 Hz, 1H, C*HO*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.1, 17.4, 19.4, 32.4, 124.2, 125.7, 127.0, 129.8, 129.9, 130.8, 133.2, 134.6, 139.4, 157.5, 194.1 ppm.

(*E*)-4-(2-((*E*)-3-Fluorostyryl)cyclopropyl)but-2-enal (109k)

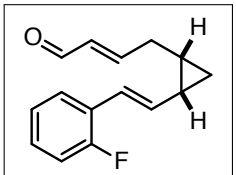


$C_{15}H_{15}FO$ (230.28)

The title compound was derived from **157** (0.13 g, 0.42 mmol) and 3-fluoroiodobenzene (86 mg, 0.39 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109k** as a yellow oil (71 mg, 0.31 mmol, 79%).

R_f (pentane/ethyl acetate = 20:1) = 0.2; **ESI-TOF** (*m/z*) $[M + Na]^+$ calcd for $C_{15}H_{15}FNaO$, 253.1005, found: 253.1000; **IR (ATR):** $\tilde{\nu}$ = 3067, 2998, 2923, 2820, 2734, 1684, 1644, 1610, 1580, 1445, 1265, 1244, 1142, 972, 778, 753 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −113.6 ppm, **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.50 (m_c, 1H, *H*-cyclopropyl), 1.12 (m_c, 1H, *H*-cyclopropyl), 1.23 (m_c, 1H, *H*-cyclopropyl), 1.78 (dddd, ^3J = 8.5, 8.5, 8.4, 5.6 Hz, 1H, *H*-cyclopropyl), 2.36–2.45 (m, 2H, CH_2), 5.97 (dd, ^3J = 15.7, 8.5 Hz, 1H, ArCH=C*H*), 6.24 (ddd, ^3J = 15.7, 8.0 Hz, ^4J = 1.9 Hz, 1H, *H*C=CHCHO), 6.48 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.85–6.95 (m, 2H, HC=C*H*CHO, *H*-Ar), 6.97–7.02 (m, 1H, *H*-Ar), 7.05–7.06 (m, 1H, *H*-Ar), 7.22–7.26 (m, 1H, *H*-Ar), 9.52 (d, ^3J = 8.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.0, 17.4, 19.3, 32.3, 112.2 (d, $^2J_{C,F}$ = 22 Hz), 113.8 (d, $^2J_{C,F}$ = 21 Hz), 121.7, 130.1, 130.1, 130.6, 133.2, 139.9 (d, $^3J_{C,F}$ = 8 Hz), 157.5, 162.6 (d, $^1J_{C,F}$ = 245 Hz), 194.1 ppm.

(*E*)-4-(2-((*E*)-2-Fluorostyryl)cyclopropyl)but-2-enal (109l)

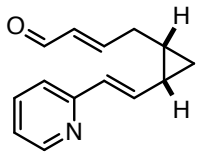


$C_{15}H_{15}FO$ (230.28)

The title compound was derived from **157** (0.13 g, 0.42 mmol) and 2-fluoroiodobenzene (86 mg, 0.39 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109l** as a yellow oil (90 mg, 0.39 mmol, *quant.*).

R_f (pentane/ethyl acetate = 20:1) = 0.2; **ESI-TOF** (*m/z*) $[M + Na]^+$ calcd for $C_{15}H_{15}FNaO$, 253.1005, found: 253.1003; **IR (ATR):** $\tilde{\nu}$ = 3001, 2916, 2816, 2733, 1685, 1636, 1487, 1229, 967, 750 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −118.5 ppm; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.51 (m_c, 1H, *H*-cyclopropyl), 1.11 (m_c, 1H, *H*-cyclopropyl), 1.17–1.28 (m, 1H, *H*-cyclopropyl), 1.81 (dddd, ^3J = 8.5, 8.5, 8.4, 4.3 Hz, 1H, *H*-cyclopropyl), 2.34–2.50 (m, 2H, CH_2), 6.06 (dd, ^3J = 15.9, 8.5 Hz, 1H, ArCH=C*H*), 6.23 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.64 (d, ^3J = 15.9 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.7, 6.1 Hz, 1H, HC=C*H*CHO), 6.99–7.02 (m, 1H, *H*-Ar), 7.05–7.07 (m, 1H, *H*-Ar), 7.13–7.19 (m, 1H, *H*-Ar), 7.34–7.36 (m, 1H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.0, 17.4, 19.8, 32.4, 115.8 (d, $^2J_{C,F}$ = 22 Hz), 123.6 (d, $^3J_{C,F}$ = 3 Hz), 124.2 (d, $^3J_{C,F}$ = 3 Hz), 125.3 (d, $^2J_{C,F}$ = 12 Hz), 127.1 (d, $^3J_{C,F}$ = 4 Hz), 128.2 (d, $^3J_{C,F}$ = 8 Hz), 132.0 (d, $^3J_{C,F}$ = 5 Hz), 133.1, 157.7, 160.0 (d, $^1J_{C,F}$ = 248 Hz), 194.2 ppm.

(*E*)-4-(2-((*E*)-2-(Pyridin-2-yl)vinyl)cyclopropyl)but-2-enal (109m)

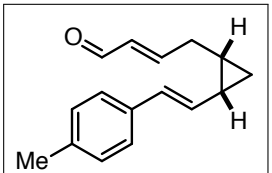


$C_{14}H_{15}NO$ (213.28)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 2-iodopyridine (62 mg, 0.30 mmol) according to **GP1**. The aqueous phase was neutralised with HCl (10 wt% in H_2O, pH = 7) before extraction. Column chromatography (silica gel, pentane/ethyl acetate = 1:1) delivered the aldehyde **109m** as a yellow oil (47 mg, 0.22 mmol, 73%).

R_f (pentane/ethyl acetate = 2:1) = 0.2; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{15}NNaO$, 236.1046, found: 236.1058; **IR (ATR):** $\tilde{\nu}$ = 3066, 3001, 2924, 2816, 2734, 2358, 2342, 1684, 1645, 1584, 1561, 1470, 1432, 1367, 1302, 1265, 1227, 1197, 1145, 1116, 1093, 1048, 1010, 970, 881, 854, 818, 769, 743, 722, 699, 675 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.57 (m_c, 1H, *H*-cyclopropyl), 1.15 (m_c, 1H, *H*-cyclopropyl), 1.24–1.29 (m, 1H, *H*-cyclopropyl), 1.83 (dddd, ^3J = 8.6, 8.6, 8.6, 5.3 Hz, 1H, *H*-cyclopropyl), 2.46 (m_c, 2H, CH_2), 6.23 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.53 (dd, ^3J = 15.4, 9.0 Hz, 1H, ArCH=C*H*), 6.60 (d, ^3J = 15.4 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.7, 6.1 Hz, 1H, HC=C*H*CHO), 7.06–7.08 (m, 1H, *H*-Ar), 7.14–7.16 (m, 1H, *H*-Ar), 7.57–7.60 (m, 1H, *H*-Ar), 8.49–8.51 (m, 1H, *H*-Ar), 9.50 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.6, 17.9, 19.5, 32.4, 121.3, 121.7, 130.7, 133.1, 134.3, 136.6, 149.6, 155.5, 157.7, 194.2 ppm.

(*E*)-4-(2-((*E*)-4-Methylstyryl)cyclopropyl)but-2-enal (109n)

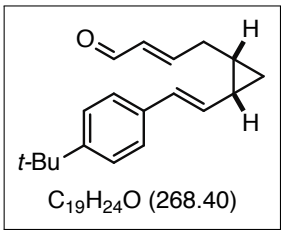


$C_{16}H_{18}O$ (226.32)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 4-iodotoluene (65 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the carbaldehyde **109n** as a yellow oil (48 mg, 0.21 mmol, 71%).

R_f (pentane/ethyl acetate = 10:1) = 0.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{18}NaO$, 249.1250, found: 249.1243; **IR (ATR):** $\tilde{\nu}$ = 3019, 2996, 2920, 2813, 2733, 2361, 2337, 1685, 1635, 1513, 1447, 1417, 1386, 1306, 1260, 1200, 1181, 1140, 1113, 1034, 1010, 966, 903, 877, 850, 801, 772, 750, 732, 722, 710, 696, 684, 661, 652 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.48 (m_c, 1H, *H*-cyclopropyl), 1.08 (m_c, 1H, *H*-cyclopropyl), 1.19 (m_c, 1H, *H*-cyclopropyl), 1.77 (m_c, 1H, *H*-cyclopropyl), 2.33 (s, 3H, CH_3), 2.35–2.45 (m, 2H, CH_2), 5.93 (dd, ^3J = 15.7, 8.3 Hz, 1H, ArCH=C*H*), 6.24 (ddt, ^3J = 15.6, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.49 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.91 (dt, ^3J = 15.6, 6.1 Hz, 1H, HC=C*H*CHO), 7.07–7.13 (m, 2H, *H*-Ar), 7.17–7.23 (m, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.7, 17.1, 19.3, 21.3, 32.4, 125.8 (2*C*), 127.8, 129.4 (2*C*), 131.1, 133.1, 134.8, 136.9, 158.0, 194.2 ppm.

(*E*)-4-(2-((*E*)-4-(*tert*-Butyl)styryl)cyclopropyl)but-2-enal (109o)

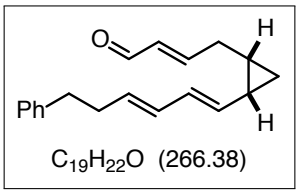


$C_{19}H_{24}O$ (268.40)

The title compound was derived from **157** (0.10 g, 0.33 mmol) and 4-(*tert*-butyl)-iodobenzene (78 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109o** as a yellow oil (41 mg, 0.15 mmol, 51%).

R_f (pentane/ethyl acetate = 10:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{24}NaO$, 291.1725, found: 291.1733; **IR (ATR):** $\tilde{\nu}$ = 2961, 2901, 2866, 2811, 2730, 1686, 1637, 1269, 1140, 1111, 968, 817 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.48 (m_c, 1H, *H*-cyclopropyl), 1.08 (m_c, 1H, *H*-cyclopropyl), 1.14–1.20 (m, 1H, *H*-cyclopropyl), 1.31 (s, 9H, CH_3), 1.75–1.80 (m, 1H, *H*-cyclopropyl), 2.34–2.45 (m, 2H, CH_2), 5.95 (dd, ^3J = 15.7, 8.2 Hz, 1H, ArCH=C*H*), 6.24 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.5 Hz, 1H, *H*C=CHCHO), 6.49 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.91 (ddd, ^3J = 15.7, 6.6, 5.6 Hz, 1H, HC=C*H*CHO), 7.23–7.29 (m, 2H, *H*-Ar), 7.30–7.35 (m, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.6, 17.1, 19.3, 31.4 (3*C*), 32.4, 34.7, 125.6 (4*C*), 128.0, 131.0, 133.1, 134.8, 150.2, 158.0, 194.2 ppm.

(*E*)-4-(2-((1*E*,3*E*)-6-Phenylhexa-1,3-dien-1-yl)cyclopropyl)but-2-enal (109p)

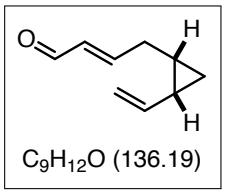


$C_{19}H_{22}O$ (266.38)

The title compound was derived from **157** (77 mg, 0.33 mmol) and (*E*)-(4-iodobut-3-en-1-yl)benzene (77 mg, 0.30 mmol) according to **GP1**. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **109p** as a yellow oil (17 mg, 0.06 mmol, 21%). An analytically pure sample was obtained by preparative HPLC (Chiralpak IA 5 µm, 4.6 x 250 mm , hexane/EtOAc = 96:4, flow: 1.0 mL/min).

R_f (pentane/ethyl acetate = 20:1) = 0.3; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{22}NaO$, 289.1569, found: 289.1571; **IR (ATR):** $\tilde{\nu}$ = 3062, 3023, 3002, 2923, 2852, 2730, 1686, 1636, 1604, 1496, 1454, 1416, 1306, 1199, 1142, 1115, 1075, 1030, 1009, 977, 944, 903, 876, 843, 733 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 0.36 (ddd, ^2J = 5.5 Hz, ^3J = 5.5, 5.5 Hz, 1H, *H*-cyclopropyl), 1.03 (m_c, 1H, *H*-cyclopropyl), 1.13 (m_c, 1H, *H*-cyclopropyl), 1.65 (m_c, 1H, *H*-cyclopropyl), 2.28–2.38 (m, 2H, cyclopropylCH_2), 2.51 (dtd, ^3J = 9.0, 7.4 Hz, ^4J = 1.5 Hz, 2H, ArCH_2CH_2), 2.70 (td, ^3J = 7.4 Hz, ^4J = 1.9 Hz, 2H, ArCH_2), 5.32–5.36 (m, 1H, ArCH_2CH_2C*H*), 5.41 (dd, ^3J = 15.0, 8.5 Hz, 1H, cyclopropylC*H*), 5.93–5.99 (m, 1H, ArCH_2CH_2CH=C*H*), 6.21 (ddt, ^3J = 15.6, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*CCHO), 6.40 (ddt, ^3J = 15.0, 11.1 Hz, ^4J = 1.0 Hz, 1H, cyclopropylCH=C*H*), 6.89 (dt, ^3J = 15.6, 6.1 Hz, 1H, HC=C*H*CHO), 7.17–7.22 (m, 3H, *H*-Ar), 7.27–7.30 (m, 2H, *H*-Ar), 9.53 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 12.9, 17.2, 19.1, 29.7, 32.3, 36.0, 126.0, 127.0, 128.5 (2*C*), 128.6 (2*C*), 128.9, 129.0, 132.7, 133.1, 142.0, 157.9, 194.3 ppm.

(*E*)-4-(2-Vinylcyclopropyl)but-2-enal (109r)

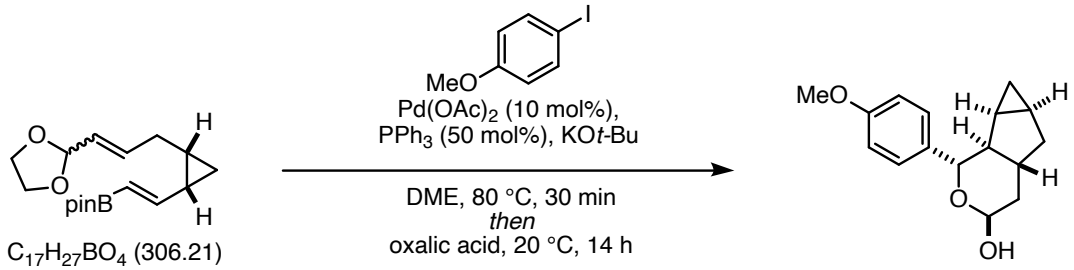


$C_9H_{12}O$ (136.19)

The title compound was derived from **157** (0.20 g, 0.66 mmol) and 2-iodobenzene-1,3-diol (0.14 g, 0.60 mmol). Column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the aldehyde **109r** as a yellow oil (15 mg, 0.11 mmol, 18%).

R_f (pentane/ethyl acetate = 20:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_9H_{12}NaO$, 159.0780, found: 159.0792; **IR (ATR):** $\tilde{\nu}$ = 3014, 2924, 2857, 1732, 1644, 1596, 1441, 1370, 1208, 1124, 971, 831, 765 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.37 (m_c, 1H, *H*-cyclopropyl), 0.98 (m_c, 1H, *H*-cyclopropyl), 1.10 (m_c, 1H, *H*-cyclopropyl), 1.63 (m_c, 1H, *H*-cyclopropyl), 2.30 (ddd, ^2J = 17.0 Hz, ^3J = 6.8, 6.8 Hz, 1H, CH_2), 2.38 (ddd, ^2J = 17.0 Hz, ^3J = 6.6 Hz, 1H, CH_2), 5.04 (d, ^3J = 10.2 Hz, 1H, C=CH_2), 5.14 (d, ^3J = 17.3 Hz, 1H, C=CH_2), 5.59 (ddd, ^3J = 17.3, 10.2, 8.4 Hz, 1H, *H*C=CH_2), 6.22 (dd, ^3J = 15.6, 7.9 Hz, 1H, *H*C=CHCHO), 6.90 (dt, ^3J = 15.6, 6.1 Hz, 1H, HC=C*H*CHO), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.9, 16.4, 19.6, 32.1, 115.7, 133.1, 136.8, 158.0, 194.3 ppm.

5.6.15 1-(4-Methoxyphenyl)octahydro-1*H*-cyclopropa[4,5]cyclopenta[1,2-*c*]pyran-3-ol (158)



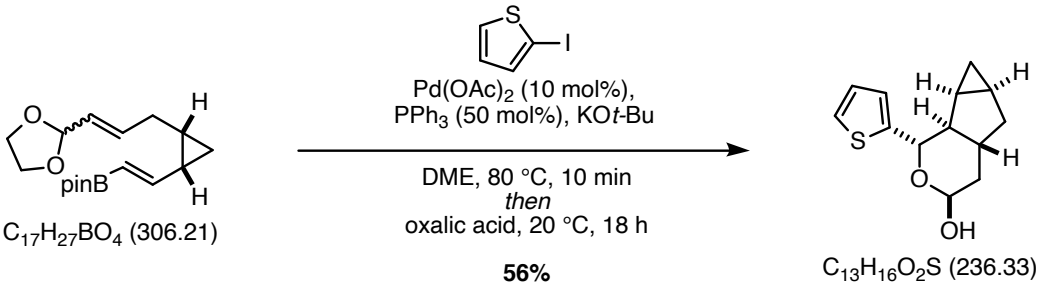
$C_{17}H_{27}BO_4$ (306.21) → $C_{16}H_{20}O_3$ (260.33)

The pinacolborane **157** (0.10 g, 0.33 mmol, 1.1 equiv.) and 4-iodoanisole (69 mg, 0.30 mmol, 1.0 equiv.) were dissolved in degassed DME (3.75 mL, 0.08 M) and treated with $Pd(OAc)_2$ (7.0 mg, 30 µmol, 10 mol%) and PPh_3 (39 mg, 0.15 mmol, 50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 0.60 mL, 0.60 mmol, 2.0 equiv.) was added dropwise over a period of 15 min. After complete addition the reaction mixture was stirred at 80 °C for 30 min. The mixture was cooled to 20 °C, treated with oxalic acid (0.9 M in H_2O, 3.3 mL, 3.0 mmol, 10 equiv.), and stirred for 14 h. The reaction mixture was extracted with Et_2O (3 x 15 mL) and the combined organic phases were washed with sat. aq. $NaHCO_3$ (15 mL) and brine (15 mL). The organic phases were dried over $MgSO_4$, filtrated and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1) affording the title compound **158** as a colourless oil (21 mg, 80 µmol, 27%). Single crystals suitable for diffraction analysis were obtained by diffusion of pentane into a solution of **158** in ethyl acetate.

R_f (pentane/ethyl acetate = 4:1) = 0.3; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{20}NaO_3$, 283.1304, found: 283.1312; **IR (ATR):** $\tilde{\nu}$ = 3390, 3064, 3031, 3002, 2927, 2854, 2360, 2341, 1718, 1613, 1586, 1513, 1450, 1378, 1302,

1243, 1174, 1124, 1108, 1093, 1070, 1054, 1023, 975, 936, 910, 892, 880, 859, 825, 811, 792, 769, 736, 702, 675 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 0.12–0.23 (m, 1H, CH_2-cyclopropyl), 0.59–0.66 (m, 1H, CH_2-cyclopropyl), 0.83–0.86 (m, 1H, *H*-cyclopropyl), 1.07–1.14 (m, 1H, *H*-cyclopropyl), 1.37–1.41 (m, 1H, CH_2), 1.46–1.54 (m, 1H, CH_2), 1.67–1.78 (m, 2H, C*H*), 1.82–1.90 (m, 1H, CH_2), 2.00–2.02 (m, 1H, CH_2), 3.81 (s, 3H, CH_3), 4.73 (d, ^3J = 9.6 Hz, 1H, OC*H*), 5.45 (br s, 1H, HOC*H*), 6.90 (d, ^3J = 8.7 Hz, 2H, *H*-Ar), 7.30–7.37 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 4.0, 12.9, 16.1, 28.8, 32.2, 36.3, 51.9, 55.4, 81.1, 92.7, 113.8 (2*C*), 127.9 (2*C*), 134.0, 159.2 ppm. Only the signals of the major diastereoisomer are indicated.

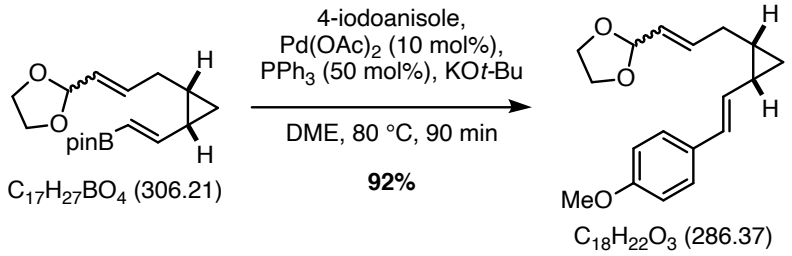
5.6.16 1-(Thiophen-2-yl)octahydro-1*H*-cyclopropa-[4,5]cyclopenta[1,2-*c*]pyran-3-ol (159)



The pinacolborane **157** (0.10 g, 0.33 mmol, 1.1 equiv.) and 2-iodothiophene (63 mg, 0.30 mmol, 1.0 equiv.) were dissolved in degassed DME (3.75 mL, 0.08 M) and treated with $Pd(OAc)_2$ (7.0 mg, 30 µmol, 10 mol%) and PPh_3 (39 mg, 0.15 mmol, 50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 0.60 mL, 0.60 mmol, 2.0 equiv.) was added dropwise over a period of 15 min. After complete addition the reaction mixture was stirred at 80 °C for 10 min. The mixture was cooled to 20 °C, treated with oxalic acid (0.9 M in H_2O, 3.3 mL, 3.0 mmol, 10 equiv.), and stirred for 18 h. The reaction mixture was extracted with Et_2O (3 x 15 mL) and the combined organic phases were washed with sat. aq. $NaHCO_3$ (15 mL) and brine (15 mL). The organic phases were dried over $MgSO_4$, filtrated and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 20:1→10:1) affording the title compound **159** as a colourless oil (40 mg, 0.17 mmol, 56%).

R_f (pentane/ethyl acetate = 10:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{16}NaO_2S$, 259.0763, found: 259.0765; **IR (ATR):** $\tilde{\nu}$ = 3384, 3067, 3031, 3004, 2926, 2855, 2360, 2342, 1717, 1448, 1314, 1278, 1239, 1201, 1123, 1093, 1066, 1054, 1035, 1019, 975, 933, 911, 850, 825, 812, 774, 697, 669 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.17–0.30 (m, 1H, CH_2-cyclopropyl), 0.61–0.70 (m, 1H, CH_2-cyclopropyl), 1.03–1.05 (m, 1H, *H*-cyclopropyl), 1.15–1.18 (m, 1H, *H*-cyclopropyl), 1.19–1.26 (m, 1H, CH_2), 1.39–1.44 (m, 1H, CH_2), 1.50–1.54 (m, 1H, CH_2), 1.64 (s, 1H, O*H*), 1.80–1.84 (m, 1H, C*H*), 1.88 (dd, ^2J = 11.8 Hz, ^3J = 6.1 Hz, 1H, CH_2), 1.98–2.01 (m, 1H, C*H*), 5.06 (d, ^3J = 10.3 Hz, 1H, OC*H*), 5.43–5.44 (m, 1H, HOC*H*), 6.95–7.02 (m, 1H, *H*-Ar), 7.08–7.09 (m, 1H, *H*-Ar), 7.26–7.27 (m, 1H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 4.1, 13.0, 16.2, 28.7, 32.1, 36.1, 52.5, 73.5, 92.7, 124.6, 124.7, 126.6, 145.2 ppm. Only the signals of the major diastereoisomer are indicated.

5.6.17 2-((*E*)-3-(2-((*E*)-4-Methoxystyryl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (160)



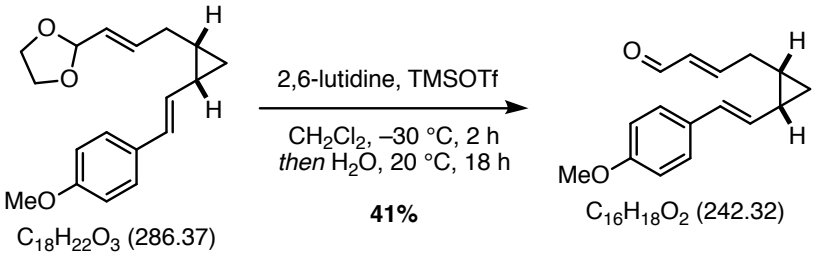
$C_{17}H_{27}BO_4$ (306.21)

$C_{18}H_{22}O_3$ (286.37)

The pinacolborane **157** (500 mg, 1.64 mmol, 1.1 equiv.) and 4-iodoanisole (390 mg, 1.49 mmol, 1.0 equiv.) were dissolved in degassed DME (19.5 mL, 0.08 M) and treated with $Pd(OAc)_2$ (34.0 mg, 150 µmol, 10 mol%) and PPh_3 (195 mg, 0.750 mmol, 50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 3.00 mL, 3.00 mmol, 2.0 equiv.) was added dropwise over a period of 15 min. After complete addition the reaction mixture was stirred at 80 °C for 90 min. The mixture was cooled to 20 °C and sat. aq. NH_4Cl (10 mL) was added. The reaction mixture was extracted with Et_2O (3 x 50 mL) and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1) to deliver the acetal coupling product **160** as a red oil (466 mg, 1.37 mmol, 92%) as an inconsequential *E/Z*-mixture on the acetal part of the molecule.

R_f (pentane/ethyl acetate = 5:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{18}H_{22}NaO_3$, 309.1467, found: 309.1468; **IR (ATR):** $\tilde{\nu}$ = 3066, 2999, 2952, 2886, 2364, 1606, 1509, 1242, 955, 819 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.44 (m_c, 1H, *H*-cyclopropyl), 1.01 (m_c, 1H, *H*-cyclopropyl), 1.12 (dddd, ^3J = 13.0, 8.5, 7.3, 7.3 Hz, 1H, *H*-cyclopropyl), 1.65–1.75 (m, 1H, *H*-cyclopropyl), 2.21–2.33 (m, 2H, CH_2), 3.82 (s, 3H, CH_3), 3.84–3.93 (m, 2H, CH_2), 3.96–4.06 (m, 2H, CH_2), 5.42–5.57 (m, 2H, C*H*), 5.84–5.95 (m, 2H, C*H*), 6.47 (d, ^3J = 15.7 Hz, 1H, C*H*), 6.78–6.98 (m, 2H, *H*-Ar), 7.16–7.43 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 12.8, 19.0, 19.5, 27.7, 55.4, 65.1 (2*C*), 99.4, 114.0 (2*C*), 126.0 (2*C*), 127.0, 127.7, 129.9, 130.8, 136.8, 158.7 ppm.

5.6.18 (*E*)-4-(2-((*E*)-4-Methoxystyryl)cyclopropyl)but-2-enal (109q)



$C_{18}H_{22}O_3$ (286.37)

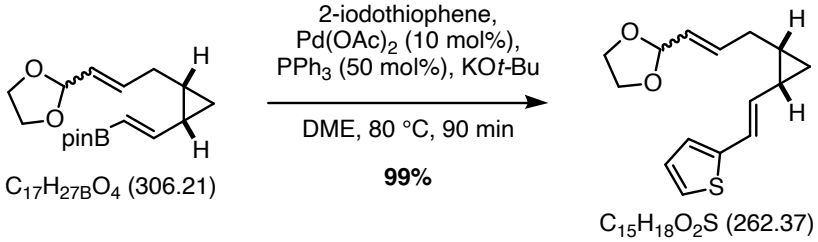
$C_{16}H_{18}O_2$ (242.32)

A solution of acetal **160** (0.13 g, 0.46 mmol, 1.0 equiv.) and 2,6-lutidine (1.4 mL, 11 mmol, 23 equiv.) in dry CH_2Cl_2 (46 mL, 0.01 M) was treated with TMSOTf (1.8 mL, 8.4 mmol, 18 equiv.) at –30 °C. The reaction mixture was stirred for 2 h at this temperature. H_2O (10 mL) was added and the resulting biphasic system was stirred at 20 °C for 18 h. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL).

The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1) to deliver the aldehyde **109q** as a colourless oil (46 mg, 0.19 mmol, 41%).

R_f (pentane/ethyl acetate = 10:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{18}NaO_2$, 265.1205, found: 265.1207; **IR (ATR):** $\tilde{\nu}$ = 3062, 2997, 2933, 2835, 2733, 2360, 1684, 1606, 1509, 1241, 818 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.46 (m_c, 1H, *H*-cyclopropyl), 1.06 (m_c, 1H, *H*-cyclopropyl), 1.17 (m_c, 1H, *H*-cyclopropyl), 1.76 (m_c, 1H, *H*-cyclopropyl), 2.39 (m_c, 2H, CH_2), 3.80 (s, 3H, CH_3), 5.84 (dd, ^3J = 15.7, 8.1 Hz, 1H, ArCH=C*H*), 6.24 (dd, ^3J = 15.6, 7.9 Hz, 1H, HC=C*H*CHO), 6.46 (d, ^3J = 15.7 Hz, 1H, ArC*H*=CH), 6.83 (d, ^3J = 7.5 Hz, 2H, *H*-Ar), 6.91 (dt, ^3J = 15.6, 6.0 Hz, 1H, *H*C=CHCHO), 7.23–7.26 (m, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.5, 17.0, 19.2, 32.4, 55.5, 114.1 (2*C*), 126.6, 127.0 (2*C*), 130.5, 130.7, 133.1, 158.0, 158.9, 194.2 ppm.

5.6.19 2-((*E*)-3-(2-((*E*)-2-(Thiophen-2-yl)vinyl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (161)

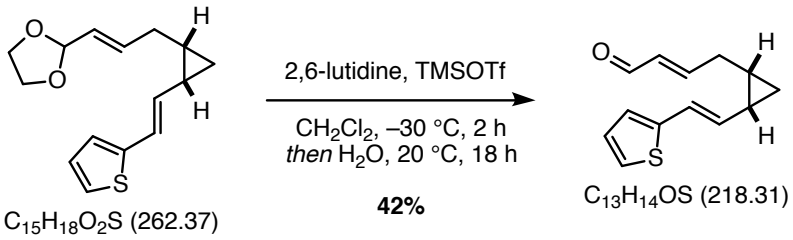


The pinacolborane **157** (0.20 g, 0.66 mmol, 1.1 equiv.) and 2-iodothiophene (0.26 g, 0.60 mmol, 1.0 equiv.) were dissolved in degassed DME (7.5 mL, 0.08 M) and treated with $Pd(OAc)_2$ (14 mg, 60 µmol, 10 mol%) and PPh_3 (78 mg, 0.30 mmol, 50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 1.2 mL, 1.2 mmol, 2.0 equiv.) was added dropwise over a period of 15 min. After complete addition the reaction mixture was stirred at 80 °C for 18 h. The mixture was cooled to 20 °C and sat. aq. NH_4Cl (3 mL) was added. The reaction mixture was extracted with Et_2O (3 x 10 mL) and the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 20:1) to deliver the acetal **161** as a red oil (0.16 g, 0.59 mmol, 99%) in an inconsequential *E/Z*-mixture on the acetal part of the molecule.

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{15}H_{19}O_2S$, 263.1101, found: 263.1106; **IR (ATR):** $\tilde{\nu}$ = 3106, 3070, 2992, 2882, 2360, 2342, 1670, 1636, 1473, 1425, 1396, 1346, 1281, 1263, 1205, 1116, 1067, 1040, 1028, 1006, 946, 873, 852, 828, 810, 777, 746, 691, 617 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.42 (m_c, 1H, *H*-cyclopropyl), 1.01 (m_c, 1H, *H*-cyclopropyl), 1.07–1.16 (m, 1H, *H*-cyclopropyl), 1.65 (dddd, ^3J = 8.5, 8.5, 8.5, 5.4 Hz, 1H, *H*-cyclopropyl), 2.24–2.27 (m, 2H, CH_2), 3.79–3.91 (m, 2H, CH_2), 3.94–4.03 (m, 2H, CH_2), 5.41–5.49 (m, 1H, O_2CHC*H*=CH), 5.51 (d, ^3J = 7.1 Hz, 1H, C*H*O_2), 5.79–5.92 (m, 2H, O_2CHCH=C*H*, ArCH=C*H*), 6.62 (d, ^3J = 15.5 Hz, 1H, ArC*H*=CH), 6.85 (dd, ^3J = 8.0 Hz, ^4J = 3.5 Hz, 1H, *H*-Ar), 6.93 (dd, ^3J = 5.2 Hz, ^4J = 3.5 Hz, 1H, *H*-Ar), 7.04–7.09 (m, 1H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.0, 19.4, 19.4, 27.7, 65.1

(2*C*), 99.4, 123.0, 123.7, 124.0, 126.2, 127.4, 130.0, 136.6, 143.1 ppm. Only the signals of the major diastereomer are indicated.

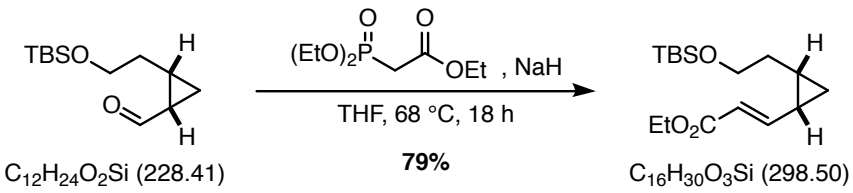
5.6.20 2-(*E*)-4-(2-((*E*)-2-(Thiophen-2-yl)vinyl)cyclopropyl)but-2-enal (109s)



A solution of acetal **161** (0.14 g, 0.55 mmol, 1.0 equiv.) and 2,6-lutidine (1.5 mL, 13 mmol, 23 equiv.) in dry CH_2Cl_2 (5.5 mL, 0.1 M) was treated with TMSOTf (2.3 mL, 13 mmol, 23 equiv.) at −30 °C. The reaction mixture was stirred for 2 h at this temperature. H_2O (5 mL) was added and the resulting biphasic system was stirred at 20 °C for 18 h. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 20:1) to deliver the aldehyde **109s** as a colourless oil (51 mg, 0.23 mmol, 42%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{15}OS$, 219.0838, found: 219.0844; **IR (ATR):** $\tilde{\nu}$ = 3106, 3068, 2995, 2917, 2815, 2733, 2360, 1683, 1635, 1520, 1447, 1434, 1389, 1306, 1262, 1202, 1141, 1116, 1040, 1010, 972, 951, 902, 876, 852, 814, 747, 694 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.47 (m_c, 1H, *H*-cyclopropyl), 1.08 (m_c, 1H, *H*-cyclopropyl), 1.19 (dddd, ^3J = 15.9, 8.6, 7.4, 5.8 Hz, 1H, *H*-cyclopropyl), 1.69–1.79 (m, 1H, *H*-cyclopropyl), 2.36–2.42 (m, 2H, CH_2), 5.82 (dd, ^3J = 15.6, 8.3 Hz, 1H, ArCH=C*H*), 6.23 (ddt, ^3J = 15.6, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*C=CHCHO), 6.63 (dd, ^3J = 15.6 Hz, ^4J = 1.0 Hz, 1H, ArC*H*=CH), 6.86 (d, ^3J = 3.1 Hz, 1H, *H*-Ar), 6.89–6.91 (m, 1H, CH=C*H*CHO), 6.91–6.94 (m, 1H, *H*-Ar), 7.07 (d, ^3J = 5.1 Hz, 1H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.8, 17.3, 19.2, 32.4, 123.3, 124.4, 124.4, 127.5, 128.8, 133.2, 142.8, 157.7, 194.2 ppm.

5.6.21 Ethyl (*E*)-3-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)acrylate (162)

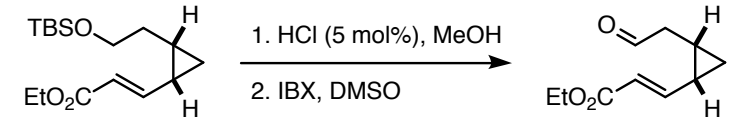


Triethyl phosphonoacetate (460 µL, 2.30 mmol, 1.05 equiv.) was added dropwise to a suspension of NaH (60% in mineral oil, 93.0 mg, 2.32 mmol, 1.06 equiv.) in dry THF (3.0 mL, 0.75 M) at 0 °C over a period of 15 min. The resulting solution was stirred for 1 h at 0 °C and warmed to 20 °C over 1 h. The mixture was treated

with aldehyde **113** (500 mg, 2.19 mmol, 1.00 equiv.) and stirred at 68 °C for 18 h. The reaction mixture was diluted with pentane (6 mL) and sat. aq. $NaHCO_3$ (3 mL) was added. The phases were separated and the aqueous phase was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, pentane/ethyl acetate = 100:1) delivered the silyl ether **162** as a colourless oil (518 mg, 1.74 mmol, 79%).

R_f (pentane/ethyl acetate = 40:1) = 0.6; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{31}O_3Si$, 299.2037, found: 299.2042; **IR (ATR)**: $\tilde{\nu}$ = 3071, 2953, 2929, 2896, 2857, 2362, 2341, 1716, 1644, 1471, 1464, 1447, 1389, 1375, 1362, 1308, 1261, 1186, 1142, 1098, 1039, 1006, 978, 950, 921, 894, 834, 810, 775, 741, 705, 678, 661 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.04 (s, 6H, SiCH_3), 0.53 (ddd, ^2J = 4.9 Hz, ^3J = 6.4, 5.0 Hz, 1H, *H*-cyclopropyl), 0.89 (s, 9H, SiCCH_3), 1.12 (ddd, ^2J = 4.9 Hz, ^3J = 8.1, 8.1 Hz, 1H, *H*-cyclopropyl), 1.28 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.28–1.32 (m, 1H, *H*-cyclopropyl), 1.57–1.68 (m, 3H, CH_3-CH_2, *H*-cyclopropyl), 3.62–3.68 (m, 2H, CH_2), 4.14–4.20 (m, 2H, CH_2), 5.92 (dd, ^3J = 15.3 Hz, ^4J = 0.5 Hz, 1H, C*H*), 6.67 (dd, ^3J = 15.3, 10.4 Hz, 1H, C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.2 (2*C*), 14.5, 15.2, 18.4, 18.5, 19.2, 26.1 (3*C*), 32.8, 60.1, 63.0, 120.3, 150.6, 166.7 ppm.

5.6.22 Ethyl (*E*)-3-(2-(2-Oxoethyl)cyclopropyl)acrylate (116d)

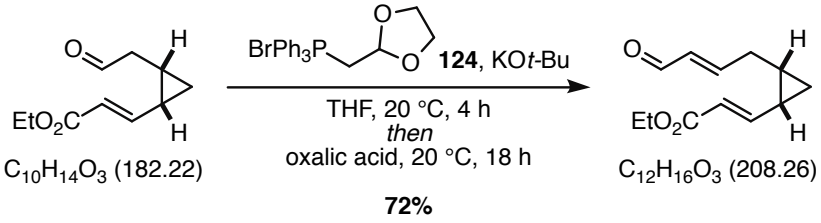


$C_{16}H_{30}O_3Si$ (298.50) **81%** $C_{10}H_{14}O_3$ (182.22)

A solution of the silyl ether **162** (471 mg, 1.58 mmol, 1.0 equiv.) in MeOH (16.0 mL, 0.1 M) was treated with HCl (10 wt-% in H_2O, 25.5 µL, 80.0 µmol, 5 mol%) at 20 °C. The reaction solution was stirred at this temperature for 4 h before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed *in vacuo* and the residue was dissolved in dry DMSO (16.0 mL, 0.1 M). IBX (664 mg, 2.37 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred at 20 °C for 18 h. The reaction was quenched with H_2O (10 mL) and the resulting mixture was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed *in vacuo* and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1) to obtain the aldehyde **116d** as a colourless oil (234 mg, 1.28 mmol, 81%).

R_f (pentane/ethyl acetate = 4:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{14}NaO_3$, 205.0835, found: 205.0839; **IR (ATR)**: $\tilde{\nu}$ = 2982, 2937, 2903, 2825, 2726, 2359, 2341, 1706, 1643, 1465, 1447, 1418, 1387, 1374, 1308, 1262, 1226, 1187, 1149, 1136, 1095, 1035, 980, 915, 884, 856, 831, 807, 790, 734, 704, 668 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.58 (m_c, 1H, *H*-cyclopropyl), 1.22–1.27 (m, 1H, *H*-cyclopropyl), 1.27 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.52 (m_c, 1H, *H*-cyclopropyl), 1.75–1.81 (m, 1H, *H*-cyclopropyl), 2.48–2.59 (m, 2H, CH_3CH_2), 4.16 (m_c, 2H, CH_2), 5.94 (dd, ^3J = 15.4 Hz, ^4J = 0.7 Hz, 1H, C*H*), 6.59 (dd, ^3J = 15.4, 9.9 Hz, 1H, C*H*), 9.78 (t, ^3J = 1.5 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.2, 14.4 (2*C*), 18.4, 43.6, 60.3, 121.7, 148.4, 166.4, 201.0 ppm.

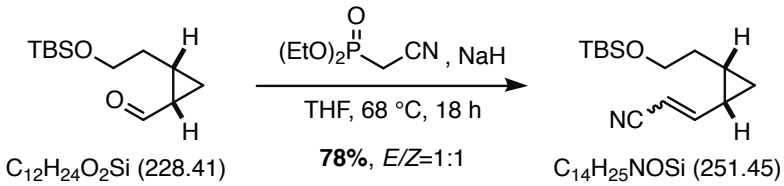
5.6.23 Ethyl (*E*)-3-(2-((*E*)-4-Oxobut-2-en-1-yl)cyclopropyl)acrylate (109t)



KO*t*-Bu (466 mg, 4.15 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (1.86 g, 4.32 mmol, 2.7 equiv.) in dry THF (17 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **116d** (292 mg, 1.6 mmol, 1.0 equiv.) in dry THF (4.0 mL, 0.4 M) was added dropwise over a period of 20 min. The reaction mixture was stirred at 20 °C for 4 h. Oxalic acid (0.9 M in H_2O, 30.0 mL, 27.1 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 60 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (60 mL) and brine (60 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the title compound **109t** as a colourless oil (221 mg, 0.940 mmol, 59%).

R_f (pentane/ethyl acetate = 4:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{16}NaO_3$, 231.0991, found: 231.1008; **IR (ATR)**: $\tilde{\nu}$ = 2982, 2932, 2905, 2817, 2733, 2359, 2341, 2252, 1708, 1686, 1641, 1464, 1446, 1420, 1394, 1373, 1307, 1263, 1186, 1146, 1115, 1095, 1035, 978, 913, 881, 852, 832, 816, 730, 692, 667 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.61 (m_c, 1H, *H*-cyclopropyl), 1.22 (m_c, 1H, *H*-cyclopropyl), 1.27 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.35 (m_c, 1H, *H*-cyclopropyl), 1.77 (m_c, 1H, *H*-cyclopropyl), 2.40 (dddd, ^2J = 17.2 Hz, ^3J = 7.6, 6.0 Hz, ^4J = 1.7 Hz, 1H, CH_2), 2.48 (dddd, ^2J = 17.2 Hz, ^3J = 7.6, 6.0 Hz, ^4J = 1.7 Hz, 1H, CH_2), 4.17 (qd, ^3J = 7.2 Hz, ^4J = 0.5 Hz, 2H, CH_3CH_2), 5.95 (dd, ^3J = 15.3 Hz, ^4J = 0.6 Hz, 1H, CO_2EtCH), 6.21 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*CCHO), 6.64 (dd, ^3J = 15.3, 10.1 Hz, 1H, CO_2EtCH=C*H*), 6.86 (dt, ^3J = 15.7, 6.0 Hz, 1H, CH_2CH), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.4, 14.8, 18.9, 19.2, 32.3, 60.3, 121.6, 133.3, 148.6, 156.6, 166.5, 194.0 ppm.

5.6.24 3-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)acrylonitrile (163)

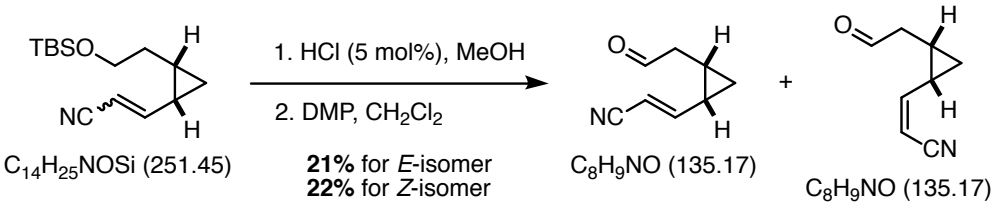


A suspension of NaH (60% in mineral oil, 93.0 mg, 2.32 mmol, 1.06 equiv.) in dry THF (3.0 mL, 0.75 M) was treated with triethylphosphono acetonitrile (370 µL, 2.30 mmol, 1.05 equiv.) at 0 °C. The resulting solution was stirred at 20 °C for 1 h and cooled again to 0 °C. The aldehyde **113** (500 mg, 2.19 mmol, 1.00 equiv.) was added dropwise. After complete addition, the reaction mixture was heated to 68 °C for 18 h. The mixture

was diluted with pentane (5 mL) and sat. aq. $NaHCO_3$ (5 mL) was added. The mixture was extracted with Et_2O (3 x 15 mL) and the combined organic phases washed were with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the silyl ether **163** as a colourless oil (431 mg, 1.71 mmol, 78%, *E*/*Z* = 1:1).

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{14}H_{26}NOSi$, 252.1778, found: 252.1791; **IR (ATR)**: $\tilde{\nu}$ = 2999, 2953, 2928, 2857, 2218, 1624, 1471, 1389, 1362, 1254, 1098, 1006, 960, 917, 885, 833, 811, 775, 751, 728, 717, 682, 666 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.05 (s, 2 x 6H, $SiCH_3$, $SiCH_3$*), 0.57 (dddd, ^2J = 9.9 Hz, ^3J = 6.5, 5.0, 5.0 Hz, 2 x 1H, *H*-cyclopropyl, *H*-cyclopropyl*), 0.89 (s, 9H, CCH_3*), 0.90 (s, 9H, CCH_3), 1.19 (m_c, 1H, *H*-cyclopropyl), 1.27 (m_c, 1H, *H*-cyclopropyl*), 1.34–1.44 (m, 2 x 1H, *H*-cyclopropyl, *H*-cyclopropyl*), 1.52–1.67 (m, 3H + 2H, $SiCH_2CH_2$, *H*-cyclopropyl, $SiCH_2CH_2$*), 2.06 (dtd, ^3J = 10.9, 8.3, 5.0 Hz, 1H, *H*-cyclopropyl*), 3.54–3.72 (m, 2 x 2H, $SiCH_2$, $SiCH_2$*), 5.25 (d, ^3J = 10.9 Hz, 1H, NCC*H**), 5.38 (d, ^3J = 16.0 Hz, 1H, NCC*H*), 6.11 (dd, ^3J = 10.9, 10.9 Hz, 1H, NCCH=C*H**), 6.38 (dd, ^3J = 16.0, 10.2 Hz, 1H, NCCH=C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.2 (2*C*, 2*C**), 15.6*, 16.1, 18.5*, 19.0, 19.1, 19.4*, 20.4 (*C*, *C**), 26.1 (3*C*, 3*C**), 32.7*, 33.0, 62.8*, 62.8, 97.4*, 97.8, 117.0*, 118.1, 156.2*, 157.0 ppm. *The signals of the *Z*-isomer are indicated.

5.6.25 3-(2-(2-Oxoethyl)cyclopropyl)acrylonitrile (164)



$C_{14}H_{25}NOSi$ (251.45) — C_8H_9NO (135.17) — C_8H_9NO (135.17)

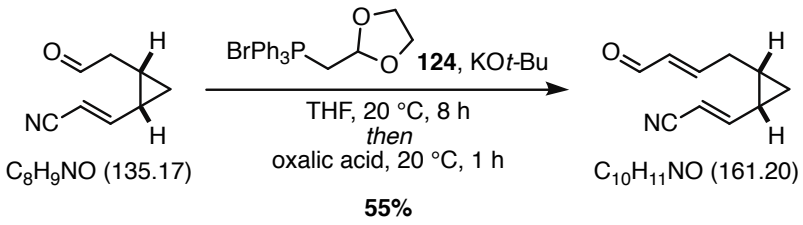
A solution of the silyl ether **163** (0.42 g, 1.7 mmol, 1.0 equiv.) in MeOH (17.0 mL, 0.1 M) was treated with HCl (10 wt% in H_2O, 29 µL, 90 µmol, 5 mol%) at 20 °C. The reaction mixture was stirred at this temperature for 2 h before the reaction was quenched with sat. aq. $NaHCO_3$ (15 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The residue was dissolved in dry CH_2Cl_2 (17.0 mL, 0.1 M) and DMP (1.1 g, 2.5 mmol, 1.5 equiv.) was added at 0 °C. The reaction mixture was stirred at 20 °C for 2 h before the reaction was quenched with H_2O (20 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 2:1) delivered the *E*-isomer of the aldehyde **164** (47 mg, 0.35 mmol, 21%, *E*/*Z* = 12:1) as well as the *Z*-isomer (50 mg, 0.37 mmol, 22%, *Z*/*E* = 6:1) as colourless oils.

***E*-164: R_f** (pentane/ethyl acetate = 2:1) = 0.8; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_8H_{10}NO$, 136.0757, found: 136.0751; **IR (ATR)**: $\tilde{\nu}$ = 3060, 3016, 2903, 2825, 2727, 2218, 1720, 1625, 1389, 1254, 1169, 1054, 969, 922, 830, 711, 683 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.58–0.64 (m, 1H, *H*-cyclopropyl), 1.30 (ddd, ^2J = 8.3 Hz, ^3J = 8.3, 5.4 Hz, 1H, *H*-cyclopropyl), 1.53–1.63 (m, 1H, *H*-cyclopropyl), 1.77–1.83 (m, 1H, *H*-cyclopropyl), 2.43–2.57 (m,

2H, CH_2), 5.42 (d, ^3J = 16.0 Hz, 1H, NCC*H*), 6.30 (dd, ^3J = 16.0, 9.9 Hz, 1H, NCCH=C*H*), 9.78 (t, ^3J = 1.3 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.7, 14.7, 19.6, 43.5, 99.4, 117.6, 155.0, 200.2 ppm.

***Z*-164: R_f** (pentane/ethyl acetate = 2:1) = 0.7; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for C_8H_9NaNO, 158.0576, found: 158.0576; **IR (ATR)**: $\tilde{\nu}$ = 3077, 3005, 2916, 2830, 2731, 2214, 1720, 1611, 1447, 1385, 1323, 1302, 1247, 1136, 1101, 1050, 1016, 965, 919, 872, 855, 822, 748, 704, 694, 667, 659 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.65 (ddd, ^2J = 5.3 Hz, ^3J = 6.6, 5.3 Hz, 1H, *H*-cyclopropyl), 1.41 (ddd, ^2J = 5.3 Hz, ^3J = 8.3, 8.3 Hz, 1H, *H*-cyclopropyl), 1.64–1.71 (m, 1H, *H*-cyclopropyl), 2.13–2.23 (m, 1H, *H*-cyclopropyl), 2.45–2.56 (m, 2H, CH_2), 5.32 (dd, ^3J = 10.8 Hz, ^4J = 0.8 Hz, 1H, NCC*H*), 6.02 (dd, ^3J = 10.8, 10.8 Hz, 1H, NCCH=C*H*), 9.78 (t, ^3J = 1.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.7, 15.5, 18.7, 43.6, 99.1, 116.5, 154.1, 200.3 ppm.

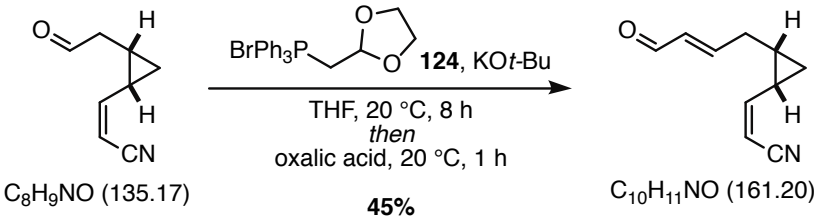
5.6.26 (*E*)-3-(2-((*E*)-4-Oxobut-2-en-1-yl)cyclopropyl)acrylonitrile (109u)



KO*t*-Bu (0.10 g, 0.91 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (0.41 g, 0.95 mmol, 2.7 equiv.) in dry THF (3.8 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 30 min at 0 °C before a solution of the *E*-isomer of aldehyde **164** (47 mg, 0.35 mmol, 1.0 equiv.) in dry THF (0.9 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 8 h. Oxalic acid (0.9 M in H_2O, 3.9 mL, 3.5 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 1 h. The reaction mixture was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the α,β-unsaturated aldehyde **109u** as a colourless oil (31 mg, 0.19 mmol, 55%, *E*/*Z* = 16:1).

R_f (pentane/ethyl acetate = 2:1) = 0.7; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{10}H_{11}NNaO_3$, 184.0733, found: 184.0737; **IR (ATR)**: $\tilde{\nu}$ = 2952, 2920, 2848, 2724, 2306, 2217, 2179, 2136, 2094, 2053, 1979, 1683, 1624, 1419, 1308, 1144, 1115, 1008, 966, 927, 904, 897, 874, 845, 827, 817, 800, 786, 775, 766, 756, 733, 723, 707, 695, 681, 669, 658 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.64 (ddd, ^2J = 5.3 Hz, ^3J = 6.4, 5.3 Hz, 1H, *H*-cyclopropyl), 1.29 (ddd, ^2J = 5.3 Hz, ^3J = 8.2, 8.2 Hz, 1H, *H*-cyclopropyl), 1.41 (m_c, 1H, *H*-cyclopropyl), 1.78 (m_c, 1H, *H*-cyclopropyl), 2.36 (dddd, ^2J = 17.4 Hz, ^3J = 7.5, 5.8 Hz, ^4J = 1.7 Hz, 1H, CH_2), 2.45 (dddd, ^2J = 17.4 Hz, ^3J = 7.5, 6.0 Hz, ^4J = 1.8 Hz, 1H, CH_2), 5.44 (dd, ^3J = 16.0 Hz, ^4J = 0.6 Hz, 1H, NCC*H*), 6.20 (ddt, ^3J = 15.8, 7.8 Hz, ^4J = 1.7 Hz, 1H, *H*CCHO), 6.35 (dd, ^3J = 16.0, 10.0 Hz, 1H, NCCH=C*H*), 6.85 (dt, ^3J = 15.8, 5.9 Hz, 1H, HC=C*H*CHO), 9.53 (d, ^3J = 7.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 15.1, 19.3, 20.3, 32.1, 99.3, 117.6, 133.4, 155.1, 155.6, 193.7 ppm.

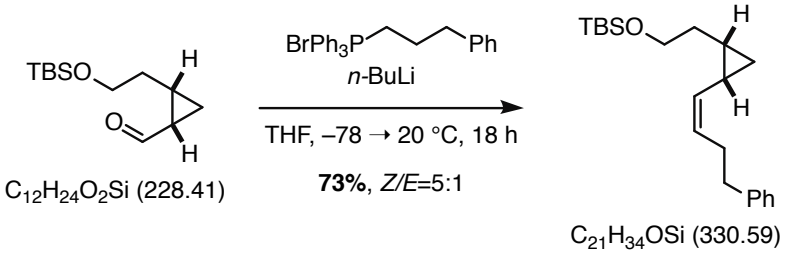
5.6.27 (*Z*)-3-(2-((*E*)-4-Oxobut-2-en-1-yl)cyclopropyl)acrylonitrile (109v)



KO*t*-Bu (0.11 g, 0.96 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (0.43 g, 1.0 mmol, 2.7 equiv.) in dry THF (4.0 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 30 min at 0 °C before a solution of the *Z*-isomer of aldehyde **164** (50 mg, 0.37 mmol, 1.0 equiv.) in dry THF (1.0 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 8 h. Oxalic acid (0.9 M in H_2O, 4.1 mL, 3.7 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 1 h. The reaction mixture was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the α,β-unsaturated aldehyde **109v** as a colourless oil (27 mg, 0.17 mmol, 45%, *Z*/*E* = 6:1).

R_f (pentane/ethyl acetate = 2:1) = 0.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{11}NNaO_3$, 184.0733, found: 184.0739; **IR (ATR)**: $\tilde{\nu}$ = 3006, 2918, 2818, 2730, 2253, 2215, 1684, 1634, 1611, 1558, 1507, 1425, 1308, 1247, 1140, 1115, 1094, 1042, 1011, 972, 909, 873, 824, 727, 682, 668 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.66 (ddd, ^2J = 5.2 Hz, ^3J = 6.5, 5.2 Hz, 1H, *H*-cyclopropyl), 1.38 (ddd, ^2J = 5.2 Hz, ^3J = 8.2, 8.2 Hz, 1H, *H*-cyclopropyl), 1.50 (m_c, 1H, *H*-cyclopropyl), 2.18 (m_c, 1H, *H*-cyclopropyl), 2.39 (dddd, ^2J = 17.0 Hz, ^3J = 7.7, 6.2 Hz, ^4J = 1.7 Hz, 1H, CH_2), 2.46 (dddd, ^2J = 17.0 Hz, ^3J = 7.6, 6.1 Hz, ^4J = 1.7 Hz, 1H, CH_2), 5.32 (dd, ^3J = 10.8 Hz, ^4J = 0.7 Hz, 1H, NCC*H*), 6.08 (dd, ^3J = 10.8, 10.8 Hz, 1H, NCCH=C*H*), 6.19 (ddt, ^3J = 15.7, 7.8 Hz, ^4J = 1.7 Hz, 1H, *H*CCHO), 6.84 (dt, ^3J = 15.7, 6.2 Hz, 1H, *H*C=CHCHO), 9.53 (d, ^3J = 7.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 15.8, 19.4 (2*C*), 32.5, 98.9, 116.6, 133.5, 154.3, 155.5, 193.7 ppm.

5.6.28 *tert*-Butyldimethyl(2-(2-(4-phenylbut-1-en-1-yl)cyclopropyl)ethoxy)silane (166)

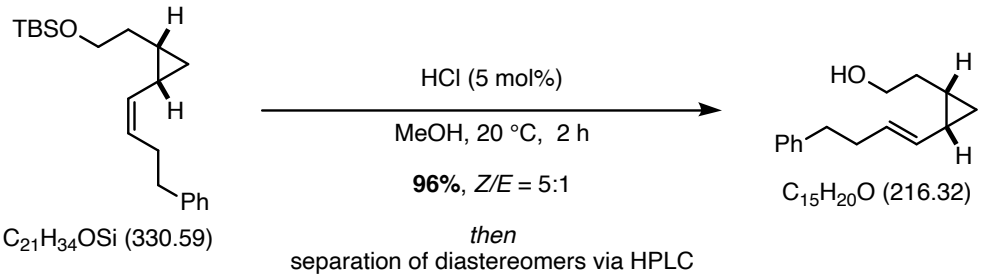


A solution of triphenyl(3-phenylpropyl) phosphonium bromide (1.52 g, 3.29 mmol, 1.5 equiv.) in dry THF (17.0 mL, 0.2 M) was treated with *n*-BuLi (2.5 M in hexanes, 1.30 mL, 3.29 mmol, 1.5 equiv.) at 0 °C. The reaction

mixture was stirred at 0 °C for 1 h and cooled to −78 °C afterwards. A solution of the aldehyde **113** (500 mg, 2.19 mmol, 1.0 equiv.) in dry THF (3.5 mL, 0.6 M) was added dropwise over a period of 30 min. After complete addition the reaction mixture was allowed to reach 20 °C and stirred for 18 h. The reaction was quenched with sat. aq. NH_4Cl (10 mL) and the phases separated. The aqueous phase was extracted with pentane (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 100:1) delivered the silyl ether **166** as a colourless oil (525 mg, 1.59 mmol, 73%, *Z/E* = 5:1).

R_f (pentane/ethyl acetate = 100:1) = 0.5; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{35}OSi$, 331.2452, found: 331.2454; **IR (ATR):** $\tilde{\nu}$ = 3060, 2954, 2927, 2856, 2359, 2342, 1734, 1470, 1463, 1436, 1379, 1362, 1264, 1210, 1160, 1094, 1062, 1029, 1006, 962, 938, 908, 835, 811, 776, 735, 703, 662 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.06 (s, 6H, SiCH_3, SiCH_3*), 0.14 (ddd, ^2J = 5.4 Hz, ^3J = 5.5, 5.4 Hz, 1H, *H*-cyclopropyl), 0.17 (ddd, ^2J = 5.4 Hz, ^3J = 5.5, 5.4 Hz, 1H, *H*-cyclopropyl*), 0.80–0.83 (m, 1H, *H*-cyclopropyl*), 0.90 (s, 10H, CCH_3, *H*-cyclopropyl, CCH_3*, *H*-cyclopropyl*), 0.95–1.01 (m, 1H, *H*-cyclopropyl), 1.40–1.44 (m, 3H, CH_2*, *H*-cyclopropyl*), 1.47–1.58 (m, 3H, CH_2, *H*-cyclopropyl), 2.32–2.35 (m, 2H, ArCH_2CH_2*), 2.46–2.51 (m, 2H, ArCH_2CH_2), 2.67 (t, ^3J = 7.9 Hz, 2H, ArCH_2*), 2.71 (t, ^3J = 7.9 Hz, 2H, ArCH_2), 3.61–3.69 (m, 2H, SiOCH_2, SiOCH_2*), 5.07 (ddt, ^3J = 11.0, 9.5 Hz, ^4J = 1.5 Hz, 1H, CH_2CH=C*H*), 5.22 (dd, ^3J = 14.8, 8.4 Hz, 1H, CH_2CH=C*H**), 5.47 (dtd, ^3J = 11.0, 7.3 Hz, ^4J = 1.1 Hz, 1H, CH_2C*H*CH), 5.57 (dt, ^3J = 14.8, 6.8 Hz, 1H, CH_2C*H*=CH*), 7.18–7.20 (m, 1H, *H*-Ar, *H*-Ar*), 7.21–7.23 (m, 2H, *H*-Ar, *H*-Ar*), 7.27–7.31 (m, 2H, *H*-Ar, *H*-Ar*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = −5.1 (2*C*, 2*C**), 12.1*, 13.7 (*C*, *C**), 14.0, 14.9*, 15.1, 18.2*, 18.6, 26.2 (3*C*, 3*C**), 29.6, 32.7*, 32.9, 34.7*, 36.1, 36.4*, 63.4, 63.5*, 125.9*, 125.9, 128.4 (2*C*, 2*C**), 128.6 (2*C*, 2*C**), 129.5, 129.9*, 130.1, 130.2*, 142.3*, 142.3 ppm. *The signals of the *E*-isomer are indicated.

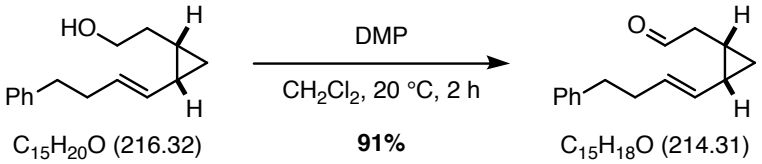
5.6.29 2-(2-((*E*)-4-Phenylbut-1-en-1-yl)cyclopropyl)ethan-1-ol (169)



A solution of **166** (4.32 g, 14.0 mmol, 1.0 equiv.) in MeOH (65.0 mL, 0.2 M) was treated with HCl (3 M in H_2O, 220 µL, 0.650 mmol, 5 mol%) at 20 °C. The reaction mixture was stirred at this temperature for 2 h before the reaction was quenched with sat. aq. $NaHCO_3$ (35 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (100 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The crude product was purified by column chromatography (silica gel, pentane/ ethyl acetate = 6:1) to deliver the alcohol **169** as a colourless oil (2.73 g, 12.6 mmol, 96%, *E/Z* = 1:5). A fraction of **169** was subjected to preparative HPLC (Nu 50-5, 32 x 50 mm, hexane/*i*-PrOH = 95:5, flow: 64 ml min) to deliver the pure *E*-isomer of **169**.

R_f (pentane/ethyl acetate = 4:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{20}NaO$, 239.1406, found: 239.1416; **IR (ATR):** $\tilde{\nu}$ = 3322, 3062, 3024, 2996, 2927, 2855, 1665, 1603, 1496, 1453, 1393, 1335, 1201, 1132, 1043, 959, 824, 745 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.19 (ddd, ^2J = 4.7 Hz, ^3J = 5.6, 5.7 Hz, 1H, *H*-cyclopropyl), 0.86 (ddd, ^2J = 4.7 Hz, ^3J = 8.3, 8.3 Hz, 1H, *H*-cyclopropyl), 0.88–0.97 (m, 1H, *H*-cyclopropyl), 1.41–1.52 (m, 3H, *H*-cyclopropyl, $HOCH_2CH_2$, O*H*), 1.53–1.60 (m, 1H, $HOCH_2CH_2$), 2.32–2.45 (m, 2H, $ArCH_2CH_2$), 2.66–2.73 (m, 2H, $ArCH_2$), 3.64 (td, ^3J = 6.6 Hz, ^4J = 1.0 Hz, 2H, $HOCH_2$), 5.21 (ddt, ^3J = 15.2, 8.4 Hz, ^4J = 1.4 Hz, 1H, cyclopropylC*H*=CH), 5.59 (dtd, ^3J = 15.2, 6.8 Hz, ^4J = 0.8 Hz, 1H, cyclopropylCH=C*H*), 7.15–7.20 (m, 3H, *H*-Ar), 7.26–7.30 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.9, 15.0, 18.0, 32.2, 34.5, 36.2, 63.3, 77.2, 125.8, 128.4 (2*C*), 128.6 (2*C*), 130.0, 130.3, 142.1 ppm.

5.6.30 2-(2-((*E*)-4-Phenylbut-1-en-1-yl)cyclopropyl)acetaldehyde ((*E*)-168)

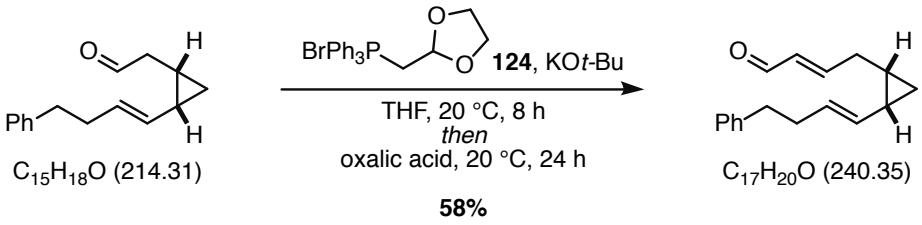


$C_{15}H_{20}O$ (216.32) — $C_{15}H_{18}O$ (214.31)

The alcohol **(*E*)-169** (0.11 g, 0.52 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (2.6 mL, 0.1 M) and treated with DMP (0.33 g, 0.78 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at 20 °C for 2 h before the reaction was quenched with H_2O (5 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the aldehyde **(*E*)-168** (0.10 g, 0.47 mmol, 91%) as a colourless oil.

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{18}NaO$, 237.1250, found: 237.1257; **IR (ATR):** $\tilde{\nu}$ = 3063, 3025, 2925, 2853, 2720, 1820, 1724, 1603, 1496, 1454, 1414, 1388, 1308, 1182, 1133, 1031, 1002, 966, 914, 827, 746 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ =0.26–0.28 (m, 1H, *H*-cyclopropyl), 0.95 (ddd, ^2J = 5.0 Hz, ^3J = 8.3, 8.4 Hz, 1H, *H*-cyclopropyl), 1.12–1.21 (m, 1H, *H*-cyclopropyl), 1.55–1.59 (m, 1H, *H*-cyclopropyl), 2.25–2.27 (m, 2H, $CHOCH_2$), 2.33–2.27 (m, 2H, $ArCH_2CH_2$), 2.68 (td, ^3J = 7.5 Hz, ^4J = 2.2 Hz, 2H, $ArCH_2$), 5.19 (ddt, ^3J = 15.3, 7.5 Hz, ^4J = 1.5 Hz, 1H, cyclopropylC*H*=CH), 5.57 (dtd, ^3J = 15.3, 6.8 Hz, ^4J = 1.0 Hz, 1H, cyclopropylCH=C*H*), 7.13–7.20 (m, 3H, *H*-Ar), 7.26–7.30 (m, 2H, *H*-Ar), 9.69 (t, ^3J = 1.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.4, 11.4, 17.6, 34.4, 36.1, 43.4, 125.9, 128.4 (2*C*), 128.6 (2*C*), 128.8, 131.6, 141.9, 202.6 ppm.

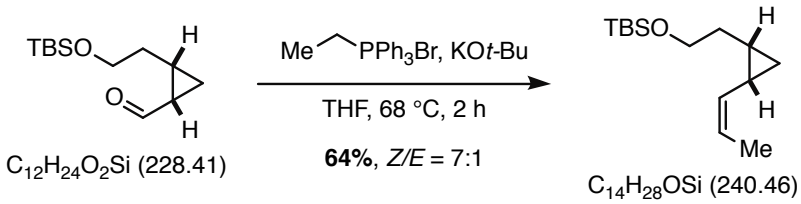
5.6.31 (*E*)-4-(2-((*E*)-4-Phenylbut-1-en-1-yl)cyclopropyl)but-2-enal (109y)



KO*t*-Bu (0.12 g, 1.1 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (0.49 g, 1.2 mmol, 2.7 equiv.) in dry THF (4.60 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of **(*E*)-168** (91 mg, 0.42 mmol, 1.0 equiv.) in dry THF (1.05 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 8 h. Oxalic acid (0.9 M in H_2O, 4.6 mL, 4.2 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 24 h. The reaction mixture was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the α,β-unsaturated aldehyde **109y** as a colourless oil (59 mg, 0.25 mmol, 58%).

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{20}NaO$, 263.1406, found: 263.1417; **IR (ATR):** $\tilde{\nu}$ = 3063, 3025, 2921, 2850, 2730, 1686, 1635, 1604, 1496, 1454, 1307, 1142, 1116, 1030, 970, 912, 822, 747 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl^3$): δ = 0.24–0.27 (m, 1H, *H*-cyclopropyl), 0.89–0.92 (m, 1H, *H*-cyclopropyl), 1.00 (ttd, ^3J = 8.5, 7.4, 5.6 Hz, 1H, *H*-cyclopropyl), 1.50–1.56 (m, 1H, *H*-cyclopropyl), 2.18 (dddd, ^2J = 17.0 Hz, ^3J = 7.4, 6.1 Hz, ^4J = 1.6 Hz, 1H, CHOCH=CHCH_2), 2.25 (dddd, ^2J = 17.0 Hz, ^3J = 7.4, 6.1 Hz, ^4J = 1.6 Hz, 1H, CHOCH=CHCH_2), 2.33–2.38 (m, 2H, ArCH_2CH_2), 2.65–2.70 (m, 2H, ArCH_2CH_2), 5.22 (ddt, ^3J = 15.3, 7.7 Hz, ^4J = 1.4 Hz, 1H, ArCH_2CH_2CH=C*H*), 5.58 (dtd, ^3J = 15.3, 6.8 Hz, ^4J = 1.0 Hz, 1H, ArCH_2CH_2C*H*=CH), 6.18 (ddt, ^3J = 15.6, 8.0 Hz, ^4J = 1.6 Hz, 1H, *H*CCHO), 6.82 (dt, ^3J = 15.6, 6.1 Hz, 1H, *H*=CHCHO), 7.14–7.20 (m, 3H, *H*-Ar), 7.24–7.29 (m, 2H, *H*-Ar), 9.51 (d, ^3J = 8.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.7, 16.0, 18.3, 32.1, 34.4, 36.1, 125.9, 128.4 (2*C*), 128.6 (2*C*), 128.8, 131.3, 133.0, 141.9, 158.4, 194.3 ppm.

5.6.32 *tert*-Butyldimethyl(2-(2-((*Z*)-prop-1-en-1-yl)cyclopropyl)ethoxy)silane (165)

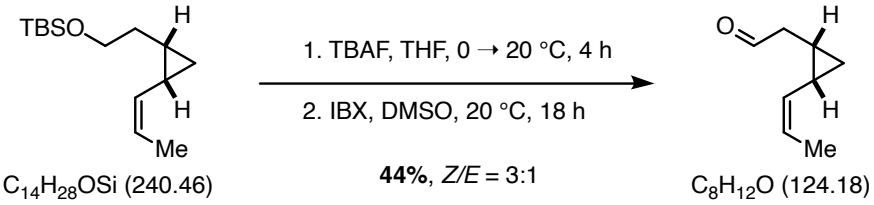


A suspension of ethyltriphenylphosphonium bromide (3.26 g, 8.76 mmol, 4.0 equiv.) in dry THF (10.0 mL, 0.9 M) was treated with KO*t*-Bu (983 mg, 8.76 mmol, 4.0 equiv.) and stirred at 20 °C for 1 h. The aldehyde **113** (500 mg, 2.19 mmol, 1.0 equiv.) was added and the reaction mixture was stirred at 68 °C for 2 h. The reaction

was quenched with sat. aq. NH_4Cl (10 mL). The reaction mixture was extracted with pentane (3 x 50 mL) and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was taken up in pentane/ethyl acetate (20:1, 30 mL) and the precipitate was filtered off. The mother liquor was concentrated *in vacuo* and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 100:1) to obtain the silyl ether **165** as a pale yellow oil (336 mg, 1.40 mmol, 64%, *Z*/*E* = 7:1).

R_f (pentane/ethyl acetate = 100:1) = 0.4; **ESI-TOF** (*m*/*z*): $[M + H]^+$ calcd for $C_{14}H_{29}OSi$, 241.1982, found: 241.1983; **IR (ATR):** $\tilde{\nu}$ = 3065, 3020, 2994, 2953, 2928, 2886, 2857, 2360, 2341, 1652, 1471, 1463, 1448, 1436, 1417, 1389, 1361, 1311, 1254, 1187, 1159, 1096, 1062, 1029, 1006, 983, 962, 938, 884, 833, 810, 773, 732, 679, 661 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.05 (s, 6H, SiCH_3), 0.12–0.18 (m, 1H, *H*-cyclopropyl), 0.89–0.90 (m, 10H, CCH_3, *H*-cyclopropyl), 0.91–0.94 (m, 1H, *H*-cyclopropyl), 0.97–1.04 (m, 1H, *H*-cyclopropyl), 1.51–1.56 (m, 2H, CH_2), 1.72 (dd, ^3J = 6.8 Hz, ^4J = 1.8 Hz, 3H, CH_3), 3.61–3.70 (m, 2H, SiOCH_2), 5.06 (ddt, ^3J = 9.5, 9.5 Hz, ^4J = 1.8 Hz, 1H, CH_3CH=C*H*), 5.48–5.51 (m, 1H, CH_3C*H*) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = −5.1, −5.1, 13.3, 13.6, 13.7, 15.0, 18.6, 26.1 (3*C*), 33.0, 63.4, 124.6, 130.2 ppm.

5.6.33 2-(2-((*Z*)-Prop-1-en-1-yl)cyclopropyl)acetaldehyde (167)



$C_{14}H_{28}OSi$ (240.46)

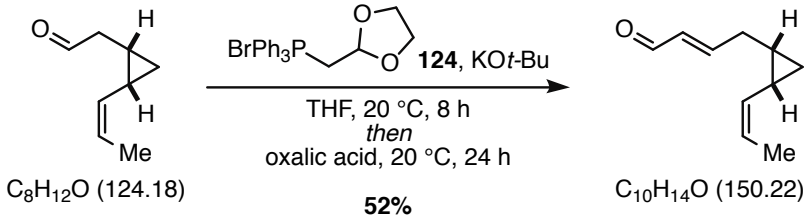
44%, *Z*/*E* = 3:1

$C_8H_{12}O$ (124.18)

The silyl ether **165** (512 mg, 2.13 mmol, 1.0 equiv.) was dissolved in dry THF (14.0 mL, 0.15 M) and treated with TBAF (1.0 M in THF, 3.20 mL, 3.20 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at 20 °C for 4 h before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The mixture was extracted with Et_2O (3 x 20 mL) and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in dry DMSO (11.0 mL, 0.2 M) and IBX (896 mg, 3.20 mmol, 1.5 equiv.) was added. The resulting solution was stirred at 20 °C for 18 h and the reaction was quenched with H_2O (11 mL), subsequently. The mixture was extracted with Et_2O (3 x 20 mL) and the combined organic phases were washed thoroughly with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the aldehyde **167** as a pale yellow oil (117 mg, 0.940 mmol, 44%, *Z*/*E* = 3:1).

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m*/*z*): $[M + Na]^+$ calcd for $C_8H_{12}NaO$, 147.0780, found: 147.0782; **IR (ATR):** $\tilde{\nu}$ = 3069, 3019, 2999, 2959, 2916, 2884, 2818, 2721, 2363, 2342, 2329, 1723, 1651, 1445, 1416, 1386, 1318, 1297, 1267, 1162, 1142, 1037, 962, 942, 912, 852, 820, 788, 773, 734, 697, 686, 676, 661 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.25 (ddd, ^2J = 5.5 Hz, ^3J = 5.5, 5.5 Hz, 1H, *H*-cyclopropyl), 1.09 (m_c, 1H, *H*-cyclopropyl), 1.24–1.34 (m, 1H, *H*-cyclopropyl), 1.66–1.74 (m, 3H, CH_3), 1.73–1.77 (m, 1H, *H*-cyclopropyl), 2.25–2.45 (m, 2H, CH_2), 4.99 (ddq, ^3J = 10.7, 8.9 Hz, ^4J = 1.8 Hz, 1H, CH_3CH=C*H*), 5.52–5.60 (m, 1H, CH_3C*H*), 9.78 (t, ^3J = 2.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 11.5, 13.3, 13.4, 17.6, 43.9, 126.7, 128.9, 202.6 ppm.

5.6.34 (*E*)-4-(2-((*Z*)-Prop-1-en-1-yl)cyclopropyl)but-2-enal (109w)

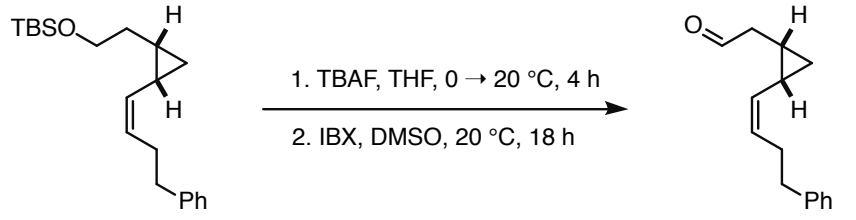


$C_8H_{12}O$ (124.18) $C_{10}H_{14}O$ (150.22)

KO*t*-Bu (0.23 g, 2.1 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (0.92 g, 2.1 mmol, 2.7 equiv.) in dry THF (8.5 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 30 min at 0 °C before a solution of aldehyde **167** (98 mg, 0.79 mmol, 1.0 equiv.) in dry THF (2.0 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 8 h. Oxalic acid (0.9 M in H_2O, 8.8 mL, 7.9 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 30 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (30 mL) and brine (30 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the title compound **109w** as a colourless oil (61 mg, 0.41 mmol, 52%, the compound was isolated as a single diastereomer).

R_f (pentane/ethyl acetate = 4:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{14}NaO$, 173.0937, found: 173.0946; **IR (ATR):** $\tilde{\nu}$ = 3073, 3019, 2997, 2917, 2816, 2734, 2360, 2338, 2252, 1685, 1636, 1418, 1375, 1306, 1141, 1115, 1098, 1033, 1010, 974, 909, 866, 819, 729 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.24 (ddd, ^2J = 5.3 Hz, ^3J = 5.5, 5.3 Hz, 1H, *H*-cyclopropyl), 1.04 (m_c, 1H, *H*-cyclopropyl), 1.10 (dddd, ^3J = 15.7, 8.5, 7.2, 5.5 Hz, 1H, *H*-cyclopropyl), 1.68–1.76 (m, 1H, *H*-cyclopropyl), 1.72 (dd, ^3J = 6.8 Hz, ^4J = 1.8 Hz, 3H, CH_3), 2.28–2.33 (m, 1H, CH_2), 2.36 (m, 1H, CH_2), 5.04 (ddq, ^3J = 10.8, 8.9 Hz, ^4J = 1.8 Hz, 1H, CH_3CH=C*H*), 5.55 (dqd, ^3J = 10.8, 6.8 Hz, ^4J = 1.3 Hz, 1H, CH_3CH), 6.21 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*CCHO), 6.90 (dt, ^3J = 15.7, 6.1 Hz, 1H, HC=C*H*CHO), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 3.4, 13.5, 14.0, 16.1, 32.6, 126.2, 128.9, 133.0, 158.2, 194.3 ppm.

5.6.35 2-(2-((*Z*)-4-Phenylbut-1-en-1-yl)cyclopropyl)acetaldehyde ((*Z*)-168)



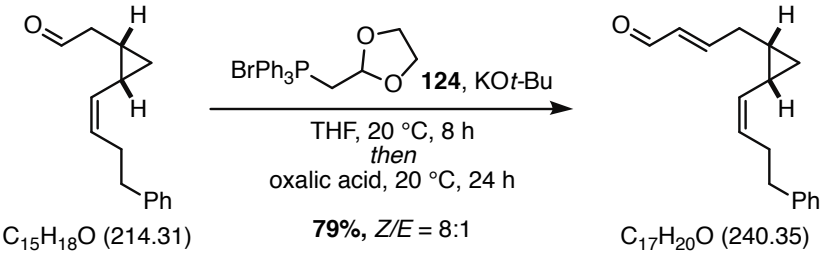
$C_{21}H_{34}OSi$ (330.59) **73%**, *Z*/*E* = 7:1 $C_{15}H_{18}O$ (214.31)

The silyl ether **169** (517 mg, 1.56 mmol, 1.0 equiv.) was dissolved in dry THF (11.0 mL, 0.15 M) and treated with TBAF (1.0 M in THF, 2.34 mL, 2.34 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at 20 °C

for 4 h before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The mixture was extracted with Et_2O (3 x 20 mL) and the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in dry DMSO (8.0 mL, 0.2 M) and at 20 °C, IBX (655 mg, 2.34 mmol, 1.5 equiv.) was added. The resulting solution was stirred at this temperature for 18 h and the reaction was quenched with H_2O (8 mL), subsequently. The mixture was extracted with Et_2O (3 x 15 mL) and the combined organic phases were washed thoroughly with brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the aldehyde **(*Z*)-168** as a pale yellow oil (244 mg, 1.13 mmol, 73%, *Z*/*E* = 5:1).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{18}NaO$, 237.1250, found: 237.1261; **IR (ATR):** $\tilde{\nu}$ = 3063, 3025, 2923, 2854, 2821, 2719, 2359, 2341, 1723, 1651, 1603, 1496, 1454, 1415, 1384, 1317, 1302, 1266, 1211, 1177, 1142, 1126, 1108, 1076, 1031, 963, 914, 841, 815, 768, 741, 698, 667, 657 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.22 (ddd, ^2J = 5.5 Hz, ^3J = 5.5, 5.5 Hz, 1H, *H*-cyclopropyl), 1.06 (m_c, 1H, *H*-cyclopropyl), 1.24 (m_c, 1H, *H*-cyclopropyl), 1.67 (ddddd, ^3J,=,8.6, 8.6, 8.6, 5.5,Hz, ^4J = 1.2 Hz, 1H, *H*-cyclopropyl), 2.29–2.40 (m, 2H, H_2CCHO), 2.47–2.51 (m, 2H, ArCH$_2$CH_2), 2.69-2.73 (m, 2H, ArCH_2), 4.99 (ddt, ^3J = 10.7, 9.0 Hz, ^4J = 1.6 Hz, 1H, CH$_2$CH=C*H*), 5.53 (dtd, ^3J = 10.7, 7.3 Hz, ^4J = 1.2 Hz, 1H, CH$_2$C*H*), 7.15–7.23 (m, 3H, *H*-Ar), 7.27–7.32 (m, 2H, *H*-Ar), 9.74 (t, ^3J = 1.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 11.6, 13.5, 13.6, 29.7, 35.9, 43.8 , 126.0, 128.4 (2*C*), 128.6 (2*C*), 128.8, 131.4, 142.0, 202.5 ppm.

5.6.36 (*E*)-4-(2-((*Z*)-4-Phenylbut-1-en-1-yl)cyclopropyl)but-2-enal (109x)



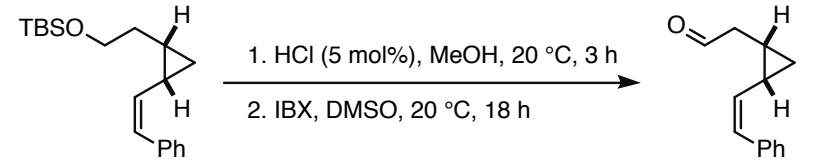
$C_{15}H_{18}O$ (214.31) — $C_{17}H_{20}O$ (240.35)

KO*t*-Bu (315 mg, 2.81 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (1.26 g, 2.92 mmol, 2.7 equiv.) in dry THF (12.0 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 30 min at 0 °C before a solution of aldehyde **(*Z*)-168** (232 mg, 1.08 mmol, 1.0 equiv.) in dry THF (2.7 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 8 h. Oxalic acid (0.9 M in H_2O, 12.0 mL, 10.8 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 25 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the title compound **109x** as a colourless oil (205 mg, 0.852 mmol, 79%, *Z*/*E* = 8:1).

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{20}NaO$, 263.1406, found: 263.1405; **IR (ATR):** $\tilde{\nu}$ = 3062, 3025, 2996, 2918, 2854, 2735, 1716, 1686, 1635, 1603, 1541, 1496, 1453, 1304, 1262, 1141, 1114, 1094, 1077, 1030, 1009, 972, 907, 872, 845, 814, 770, 741 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$):

δ = 0.21 (ddd, ^2J = 5.5 Hz, ^3J = 5.3, 5.3 Hz, 1H, *H*-cyclopropyl), 0.98–1.08 (m, 2H, *H*-cyclopropyl), 1.66 (dddd, ^3J = 8.7, 8.6, 8.6, 5.5 Hz, 1H, *H*-cyclopropyl), 2.25–2.32 (m, 2H, CH_2HC=CHCHO), 2.50 (m_c, 2H, ArCH$_2$CH_2), 2.71 (t, ^3J = 7.3 Hz, 2H, ArCH_2), 5.04 (dd, ^3J = 10.5, 10.0 Hz, 1H, cyclopropylC*H*), 5.52 (dt, ^3J = 10.5, 7.3 Hz, 1H, ArCH$_2$CH$_2$C*H*), 6.20 (dd, ^3J = 15.8, 7.9 Hz, 1H, *H*CCHO), 6.87 (dt, ^3J = 15.8, 6.2 Hz, 1H, HC=C*H*CHO), 7.11–7.23 (m, 3H, *H*-Ar), 7.26–7.30 (m, 2H, *H*-Ar), 9.52 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.7, 14.2, 16.2, 29.7, 32.5, 36.0, 126.0, 128.4 (2*C*), 128.6 (2*C*), 128.8, 131.0, 133.0, 142.1, 158.1, 194.3 ppm.

5.6.37 2-(2-((*Z*)-Styryl)cyclopropyl)acetaldehyde (170)

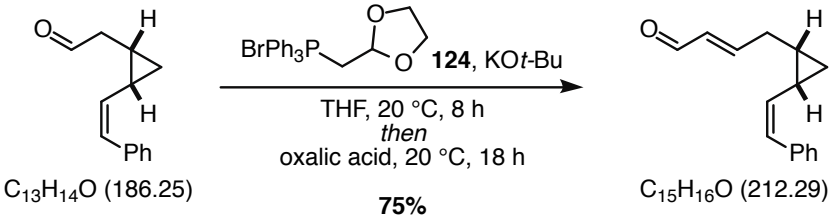


$C_{19}H_{30}OSi$ (302.53) **87%**, *Z*/*E* = 14:1 $C_{13}H_{14}O$ (186.25)

A solution of the silyl ether **121** (412 mg, 1.36 mmol, 1.0 equiv.) in MeOH (14.0 mL, 0.1 M) was treated with HCl (10 wt-% in H_2O, 23.7 µL, 68.0 µmol, 5 mol%) at 20 °C. The reaction mixture was stirred at this temperature for 3 h before the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtrated, and concentrated *in vacuo*. The residue was filtered over silica gel before it was used in the next step without further purification. The alcohol (230 mg, 1.22 mmol, 1.0 equiv.) was dissolved in dry DMSO (12.0 mL, 0.1 M). IBX (512 mg, 1.83 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred at 20 °C for 18 h. The reaction was quenched with sat. aq. $NaHCO_3$ (12 mL) and the resulting mixture was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed *in vacuo* and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 20:1) to obtain the aldehyde **170** as a colourless oil (197 mg, 1.06 mmol, 87%, *Z*/*E* = 14:1).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{14}NaO$, 209.0943, found: 209.0934; **IR (ATR):** $\tilde{\nu}$ = 3062, 3023, 2922, 2820, 2721, 1721, 1645, 1600, 1576, 1541, 1493, 1448, 1417, 1385, 1299, 1262, 1216, 1180, 1155, 1071, 1029, 957, 915, 877, 838, 795, 749, 715, 694, 672, 663 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.39 (m_c, 1H, *H*-cyclopropyl), 1.19 (m_c, 1H, *H*-cyclopropyl), 1.44 (m_c, 1H, *H*-cyclopropyl), 2.04 (m_c, 1H, *H*-cyclopropyl), 2.41–2.61 (m, 2H, CH_2), 5.29 (dd, ^3J = 11.5, 9.1 Hz, 1H, ArCH=C*H*), 6.51 (d, ^3J = 11.5 Hz, 1H, ArC*H*), 7.21–7.27 (m, 1H, *H*-Ar), 7.33–7.37 (m, 2H, *H*-Ar), 7.41–7.46 (m, 2H, *H*-Ar), 9.83 (t, ^3J = 1.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 13.0, 15.1, 15.5, 44.0, 126.9, 128.3 (2*C*), 128.9 (2*C*), 130.7, 131.3, 137.5, 202.1 ppm.

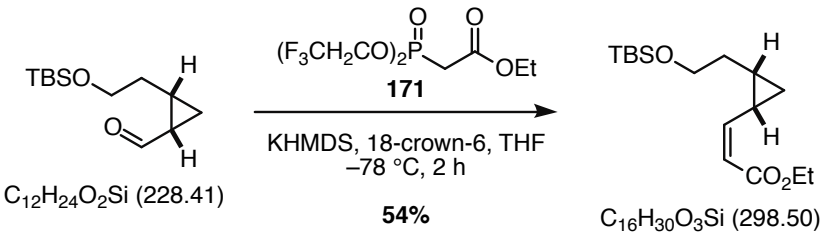
5.6.38 (*E*)-4-(2-((*Z*)-Styryl)cyclopropyl)but-2-enal (109z)



KO*t*-Bu (166 mg, 1.48 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (660 mg, 1.54 mmol, 2.7 equiv.) in dry THF (6.2 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 30 min at 0 °C before a solution of aldehyde **170** (106 mg, 56.9 µmol, 1.0 equiv.) in dry THF (1.4 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 8 h. Oxalic acid (0.9 M in H_2O, 6.30 mL, 5.69 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 12 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 40:1→20:1) delivered the title compound **109z** as a colourless oil (91.0 mg, 0.429 mmol, 75%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{16}NaO$, 235.1093, found: 235.1106; **IR (ATR):** $\tilde{\nu}$ = 3057, 3017, 2995, 2915, 2815, 2734, 2358, 2342, 1685, 1634, 1599, 1574, 1558, 1541, 1493, 1448, 1419, 1396, 1306, 1254, 1181, 1145, 1127, 1094, 1076, 1029, 1010, 973, 916, 874, 845, 796, 785, 764, 697, 669, 654 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.38 (m_c, 1H, *H*-cyclopropyl), 1.15 (m_c, 1H, *H*-cyclopropyl), 1.23 (m_c, 1H, *H*-cyclopropyl), 2.02 (m_c, 1H, *H*-cyclopropyl), 2.36–2.47 (m, 2H, C*H*$_2$), 5.36 (dd, ^3J = 11.5, 9.2 Hz, 1H, ArCH=C*H*), 6.23 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*CCHO), 6.51 (d, ^3J = 11.5 Hz, 1H, ArC*H*), 6.92 (dt, ^3J = 15.7, 6.3 Hz, 1H, *H*C=CHCHO), 7.21–7.26 (m, 1H, *H*-Ar), 7.32–7.38 (m, 2H, *H*-Ar), 7.42–7.44 (m, 2H, *H*-Ar), 9.51 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 15.2, 16.1, 17.7, 32.7, 126.9, 128.4 (2*C*), 128.9 (2*C*), 130.8, 131.0, 133.2, 137.6, 157.7, 194.2 ppm.

5.6.39 Ethyl (*Z*)-3-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)acrylate (172)

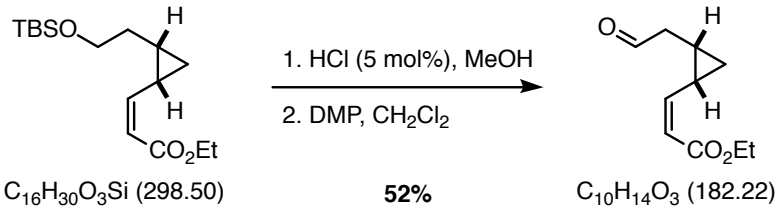


Aldehyde **113** (605 mg, 2.65 mmol, 1.0 equiv.) in THF (24 mL, 0.1 M) was added slowly to a mixture of phosphonate **171** (1.15 g, 3.45 mmol, 1.3 equiv.), KHMDS (0.7 M in PhMe, 4.20 mL, 2.92 mmol, 1.1 equiv.), and 18-crown-6 (2.00 g, 7.70 mmol, 2.9 equiv.) at −78 °C. After complete addition, the reaction mixture was stirred

for 2.5 h at this temperature before sat. aq. NH_4Cl (20 mL) was added. The reaction mixture was extracted with Et_2O (3 x 50 mL) and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the silyl ether **172** as a colourless oil (424 mg, 1.42 mmol, 54%).

R_f (pentane/ethyl acetate = 40:1) = 0.6; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{31}O_3Si$, 299.2037, found: 299.2046; **IR (ATR):** $\tilde{\nu}$ = 2953, 2929, 2857, 1715, 1631, 1471, 1434, 1388, 1254, 1180, 1097, 1034, 954, 833, 775 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.04 (s, 3H, SiCH_3), 0.04 (s, 3H, SiCH_3), 0.45 (m_c, 1H, *H*-cyclopropyl), 0.88 (s, 9H, SiCCH_3), 1.19 (m_c, 1H, *H*-cyclopropyl), 1.29 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.23–1.36 (m, 1H, *H*-cyclopropyl), 1.61–1.66 (m, 2H, CH_2), 2.91 (dtd, ^3J = 10.6, 8.4, 5.2 Hz, 1H, *H*-cyclopropyl), 3.66 (t, ^3J = 6.8 Hz, 2H, SiOCH_2), 4.18 (q, ^3J = 7.1 Hz, 2H, H_3CCH_2), 5.72–5.85 (m, 2H, C*H*) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = –5.2 (2*C*), 14.5, 16.5, 16.5, 18.5, 18.5, 26.1 (3*C*), 32.9, 59.8, 63.1, 118.8, 151.7, 167.2 ppm.

5.6.40 Ethyl (*Z*)-3-(2-(2-Oxoethyl)cyclopropyl)acrylate (173)

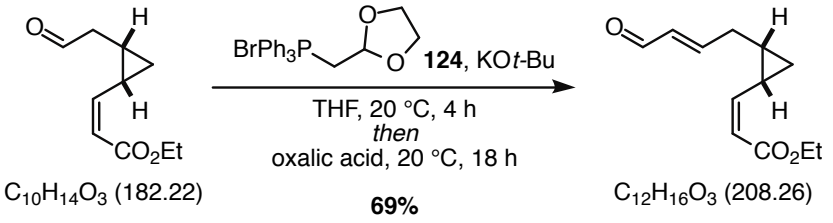


$C_{16}H_{30}O_3Si$ (298.50) **52%** $C_{10}H_{14}O_3$ (182.22)

A solution of the silyl ether **172** (372 mg, 1.24 mmol, 1.0 equiv.) in MeOH (12.0 mL, 0.1 M) was treated with HCl (10 wt-%, 20.3 µL, 62.0 µmol, 5 mol%) at 20 °C. The reaction solution was stirred at this temperature for 3 h before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed *in vacuo* and the residue was dissolved in dry CH_2Cl_2 (12.0 mL, 0.1 M). DMP (789 mg, 1.86 mmol, 1.5 equiv.) was added to the solution and the reaction mixture was stirred at 20 °C for 1.5 h. The reaction was quenched with H_2O (12 mL) and the resulting mixture was extracted with Et_2O (3 x 15 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed *in vacuo* and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1) to obtain the aldehyde **173** as a pale yellow oil (110 mg, 0.604 mmol, 49%).

R_f (pentane/ethyl acetate = 4:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{14}NaO_3$, 205.0835, found: 205.0841; **IR (ATR):** $\tilde{\nu}$ = 2984, 2822, 2725, 1711, 1632, 1437, 1386, 1183, 1031, 826 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.50 (m_c, 1H, *H*-cyclopropyl), 1.28 (t, ^3J = 7.2 Hz, 3H, CH_3), 1.33 (m_c, 1H, *H*-cyclopropyl), 1.57 (m_c, 1H, *H*-cyclopropyl), 2.44 (ddd, ^2J = 17.4 Hz, ^3J = 8.0, 2.0 Hz, 1H, H_2CCHO), 2.52 (ddd, ^2J = 17.4 Hz, ^3J = 7.0, 2.0 Hz, 1H, OHCCH_2), 3.03 (dtdd, ^3J = 10.8, 8.6, 5.5 Hz, ^4J = 0.9 Hz, 1H, *H*-cyclopropyl), 4.17 (q, ^3J = 7.1 Hz, 2H, H_3CCH_2), 5.70 (dd, ^3J = 11.4, 10.8 Hz, 1H, Et_2OCCH=C*H*), 5.81 (dd, ^3J = 11.4 Hz, ^4J = 0.9 Hz, 1H, Et_2OCC*H*=CH), 9.77 (t, ^3J = 2.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.4, 14.4, 15.8, 16.0, 43.6, 60.0, 120.3, 149.5, 166.8, 201.3 ppm.

5.6.41 Ethyl (*Z*)-3-(2-((*E*)-4-Oxo-but-2-en-1-yl)-cyclo-propyl)-acrylate (109aa)

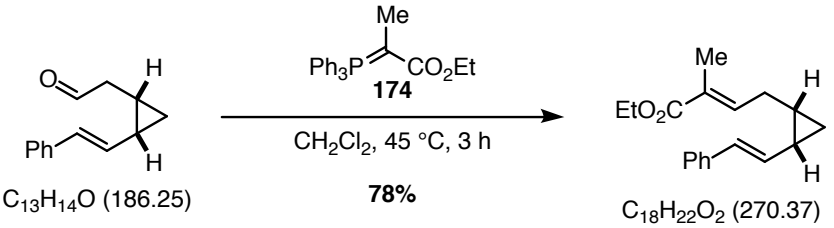


$C_{10}H_{14}O_3$ (182.22) — **69%** — $C_{12}H_{16}O_3$ (208.26)

KO*t*-Bu (175 mg, 1.56 mmol, 2.6 equiv.) was added to a suspension of the phosphonium salt **124** (699 mg, 1.62 mmol, 2.7 equiv.) in dry THF (6.5 mL, 0.25 M) at 0 °C. The resulting slurry was stirred for 1 h at 0 °C before a solution of the aldehyde **173** (110 mg, 0.604 mmol, 1.0 equiv.) in dry THF (1.5 mL, 0.4 M) was added dropwise at this temperature over a period of 20 min. The reaction mixture was stirred at 20 °C for 4 h. Oxalic acid (0.9 M in H_2O, 6.7 mL, 6.40 mmol, 10.0 equiv.) was added and the biphasic mixture was stirred at 20 °C for 18 h. The reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the title compound **109aa** as a pale yellow oil (86.0 mg, 0.413 mmol, 69%).

R_f (pentane/ethyl acetate = 4:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{12}H_{16}NaO_3$, 231.0992, found: 231.1002; **IR (ATR):** $\tilde{\nu}$ = 2979, 1711, 1687, 1633, 1436, 1183, 1135, 1031, 972, 822 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.52 (dt, ^3J = 6.2, 5.1 Hz, 1H, *H*-cyclopropyl), 1.25–1.32 (m, 1H, *H*-cyclopropyl), 1.29 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.35–1.43 (m, 1H, *H*-cyclopropyl), 2.38 (dddd, ^2J = 17.1 Hz, ^3J = 7.7, 6.1 Hz, ^4J = 1.6 Hz, 1H, cyclopropylCH_2), 2.48 (dddd, ^2J = 17.1 Hz, ^3J = 7.5, 6.1 Hz, ^4J = 1.6 Hz, 1H, cyclopropylCH_2), 2.99–3.06 (m, 1H, *H*-cyclopropyl), 4.18 (q, ^3J = 7.1 Hz, 2H, H_2CCH_3), 5.76 (dd, ^3J = 11.5, 10.5 Hz, 1H, EtO_2CCH), 5.81 (dd, ^3J = 11.5 Hz, ^4J = 0.6 Hz, 1H, EtO_2CCH=C*H*), 6.21 (ddt, ^3J = 15.7, 7.9 Hz, ^4J = 1.6 Hz, 1H, *H*CCHO), 6.86 (dt, ^3J = 15.7, 6.1 Hz, 1H, HC=C*H*CHO), 9.51 (d, ^3J = 7.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.3, 16.1, 16.5, 19.0, 32.3, 59.9, 120.0, 133.2, 149.6, 156.5, 166.7, 193.9 ppm.

5.6.42 Ethyl (*E*)-2-Methyl-4-(2-((*E*)-styryl)cyclopropyl)but-2-enoate (175)



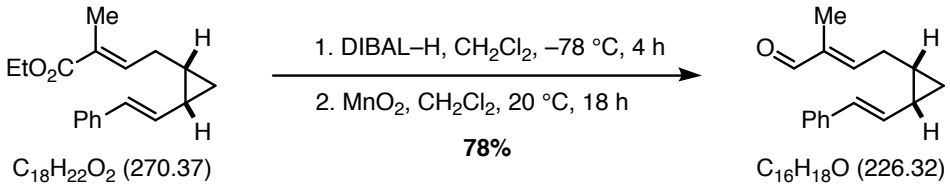
$C_{13}H_{14}O$ (186.25) — **78%** — $C_{18}H_{22}O_2$ (270.37)

A solution of the aldehyde **116b** (50 mg, 0.27 mmol, 1.0 equiv.) and ethyl methyltriphenylphosphoranylidene-acetate (**174**, 0.10 g, 0.28 mmol, 1.1 equiv.) in dry CH_2Cl_2 (1.4 mL, 0.15 M) was heated to 45 °C for 3 h. The solvent was removed under reduced pressure and purification of the crude product by column chromato-

graphy (silica gel, pentane/ethyl acetate = 40:1) delivered the title compound **175** as a colourless oil (57 mg, 0.21 mmol, 78%).

R_f (pentane/ethyl acetate = 40:1) = 0.8; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{23}O_2$, 271.1693, found: 271.1695; **IR (ATR):** $\tilde{\nu}$ = 3062, 3024, 2986, 2938, 2904, 1707, 1649, 1601, 1493, 1447, 1389, 1366, 1285, 1256, 1217, 1143, 1096, 1073, 1031, 960, 911, 768, 747 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.47 (m_c, 1H, *H*-cyclopropyl), 1.04 (m_c, 1H, *H*-cyclopropyl), 1.16 (m_c, 1H, *H*-cyclopropyl), 1.29 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 1.73 (m_c, 1H, *H*-cyclopropyl), 1.82 (q, ^4J = 1.2 Hz, 3H, CH_3), 2.19–2.24 (m, 1H, cyclopropylCH_2), 2.26–2.31 (m, 1H, cyclopropylCH_2), 4.19 (q, ^3J = 7.1 Hz, 2H, OCH_2), 6.00 (dd, ^3J = 15.7, 8.5 Hz, 1H, PhCHC*H*), 6.52 (d, ^3J = 15.7 Hz, 1H, PhC*H*), 6.84 (tq, ^3J = 7.4 Hz, ^4J = 1.2 Hz, 1H, CH_2CH), 7.16–7.21 (m, 1H, *H*-Ar), 7.27–7.30 (m, 2H, *H*-Ar), 7.31–7.33 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.6, 13.1, 14.4, 18.5, 19.5, 28.6, 60.6, 125.8 (2*C*), 126.9, 128.0, 128.6 (2*C*), 129.8, 130.7, 137.8, 141.3, 168.3 ppm.

5.6.43 (*E*)-2-Methyl-4-(2-((*E*)-styryl)cyclopropyl)but-2-enal (109bb)

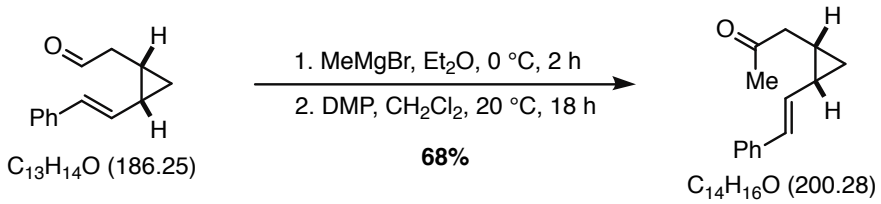


$C_{18}H_{22}O_2$ (270.37) → $C_{16}H_{18}O$ (226.32)

A solution of the ester **175** (57 mg, 0.21 mmol, 1.0 equiv.) in dry CH_2Cl_2 (2.1 mL, 0.1 M) was treated with DIBAL–H (1.0 M in hexanes, 0.42 mL, 0.42 mmol, 2.0 equiv.) at −78 °C and the reaction was stirred at this temperature for 4 h. The reaction was quenched with sat. aq. potassium sodium tartrate (20 mL) and stirred for 30 min at 20 °C. The phases were separated and the aqueous phase was extracted with ethyl acetate (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents of the filtrate were removed *in vacuo* and the residue was taken up in CH_2Cl_2 (1.1 mL, 0.2 M). The resulting solution was treated with MnO_2 (0.55 g, 6.3 mmol, 30 equiv.) and stirred for 18 h at 20 °C. The reaction mixture was filtrated over celite and the solvent of the filtrate was removed *in vacuo*. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the title compound **109bb** as a colourless oil (37 mg, 0.16 mmol, 78%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{19}O$, 227.1431, found: 227.1430; **IR (ATR):** $\tilde{\nu}$ = 3062, 3023, 3000, 2969, 2926, 2818, 2710, 1683, 1644, 1601, 1493, 1448, 1411, 1357, 1282, 1198, 1073, 961, 849, 805, 749 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.51 (m_c, 1H, *H*-cyclopropyl), 1.08 (m_c, 1H, *H*-cyclopropyl), 1.20 (dddd, ^3J = 15.9, 8.4, 7.4, 5.8 Hz, 1H, *H*-cyclopropyl), 1.73 (dd, ^4J = 1.4, 0.8 Hz, 3H, CH_3), 1.77 (m_c, 1H, *H*-cyclopropyl), 2.34–2.49 (m, 2H, CH_2), 6.00 (dd, ^3J = 15.7, 8.5 Hz, 1H, PhCHC*H*), 6.54 (d, ^3J = 15.7 Hz, 1H, PhC*H*), 6.57 (tq, ^3J = 7.2 Hz, ^4J = 1.4 Hz, 1H, CH_2CH), 7.13–7.22 (m, 1H, *H*-Ar), 7.27–7.34 (m, 4H, *H*-Ar), 9.41 (s, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 9.5, 13.0, 18.2, 19.4, 28.9, 125.8 (2*C*), 127.1, 128.7 (2*C*), 129.3, 131.0, 137.6, 139.3, 153.7, 195.4 ppm.

5.6.44 1-(2-((*E*)-Styryl)cyclopropyl)propan-2-one (176)



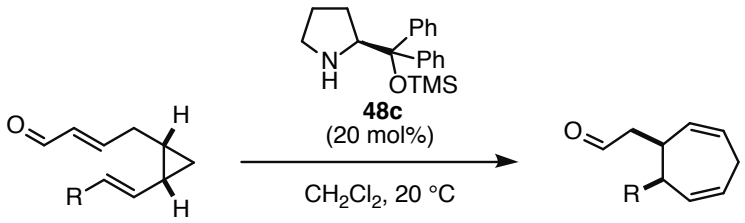
$C_{13}H_{14}O$ (186.25) → $C_{14}H_{16}O$ (200.28)

A solution of the aldehyde **116b** (200 mg, 1.07 mmol, 1.0 equiv.) in Et_2O (5.40 mL, 0.2 M) was treated dropwise with methyl magnesiumbromide (3.0 M in Et_2O, 540 µL, 1.61 mmol, 1.5 equiv.) at 0 °C over a period of 30 min. The reaction mixture was stirred at this temperature for 90 min before the reaction was quenched with sat. aq. NH_4Cl (10 mL). The phases were separated and the aqueous phase was extracted with Et_2O (3 x 50 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvent of the filtrate was removed under reduced pressure and the residue was taken up in CH_2Cl_2 (5.40 mL, 0.2 M). The solution was treated with DMP (683 mg, 1.61 mmol. 1.5 equiv.) and stirred for 18 h at 20 °C. The reaction was quenched with H_2O (10 mL) and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were dried over $MgSO_4$ and filtrated. The solvent of the filtrate was removed *in vacuo* and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1→10:1) affording the title compound **176** as a colourless oil (145 mg, 0.724 mmol, 68%).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{14}H_{16}NaO$, 223.1093, found: 223.1103; **IR (ATR):** $\tilde{\nu}$ = 3020, 2920, 2368, 2339, 2185, 2155, 2027, 1961, 1713, 1645, 1601, 1492, 1448, 1419, 1355, 1166, 1128, 1029, 958, 898, 859, 784, 746, 719 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 0.45 (m_c, 1H, *H*-cyclopropyl), 1.11 (m_c, 1H, *H*-cyclopropyl), 1.39 (m_c, 1H, *H*-cyclopropyl), 1.72–1.91 (m, 1H, *H*-cyclopropyl), 2.16 (s, 3H, C*H*$_3$), 2.43 (dd, ^2J = 17.2 Hz, ^3J = 7.3 Hz, 1H, C*H*$_2$), 2.52 (dd, ^2J = 17.2 Hz, ^3J = 7.0 Hz, 1H, C*H*$_2$), 5.94 (dd, ^3J = 15.7, 8.2 Hz, 1H, PhCHC*H*), 6.49 (d, ^3J = 15.7 Hz, 1H, PhC*H*), 7.18–7.21 (m, 1H, *H*-Ar), 7.27–7.33 (m, 4H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 12.8, 14.5, 18.9, 29.9, 43.7, 125.9 (2*C*), 127.1, 128.7 (2*C*), 129.2, 131.1, 137.6, 208.7 ppm.

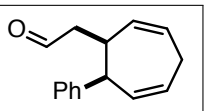
5.7 DVCPR of α,β-Unsaturated Cyclopropylcarbaldehydes

5.7.1 General Procedure for Enamine-Induced DCVPR of *E*-Vinyl Cyclopropylcarbaldehydes (GP2)



A solution of the corresponding α,β-unsaturated cyclopropylcarbaldehyde **109** (1.0 equiv.) in CH_2Cl_2 (0.1 M) was treated with diphenylprolinol trimethylsilyl ether (**48c**, 20 mol%). The reaction mixture was stirred at 20 °C until TLC or GC-MS showed complete conversion. The reaction was quenched with sat. aq. NH_4Cl (0.5 mL) and the resulting mixture was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic phases were washed with brine (10 mL), dried over $MgSO_4$, and filtrated. The solvent was removed *in vacuo* and the crude products were purified by column chromatography.

2-((1,7-*cis*)-7-Phenylcyclohepta-2,5-dien-1-yl)acetaldehyde (112a)



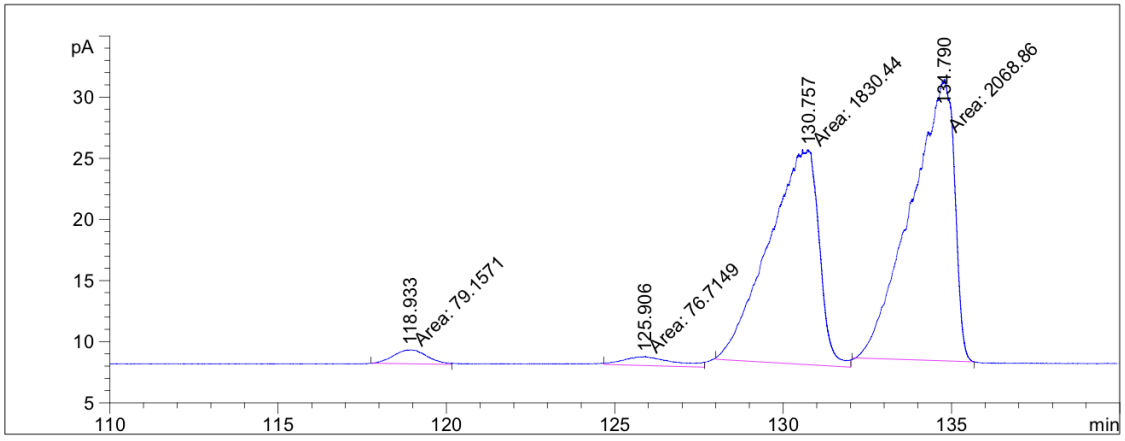
$C_{15}H_{16}O$ (212.29)

Derived from **109a** (386 mg, 1.77 mmol, 1.0 equiv.) and **48c** (115 mg, 353 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 48 h. Column Chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the cycloheptadiene **112a** as a pale yellow oil (296 mg, 1.39 mmol, 79%).

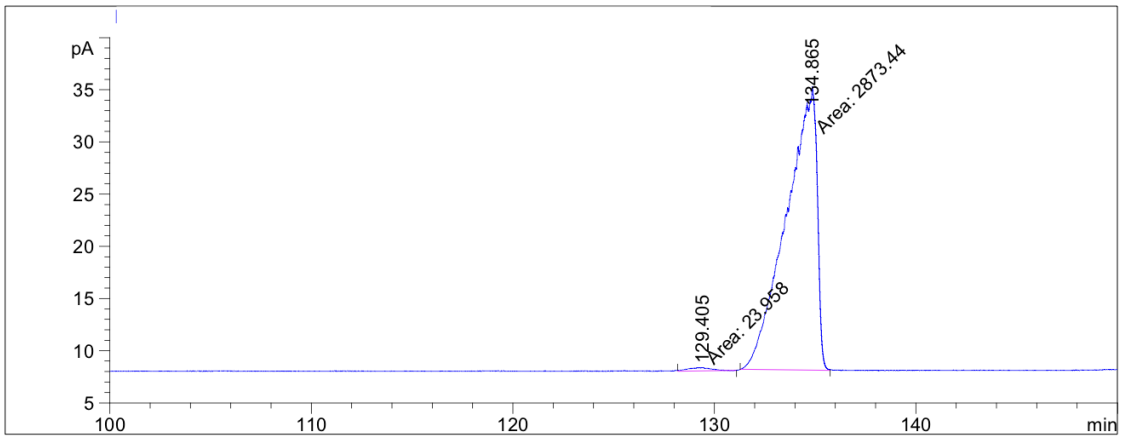
R_f (pentane/ethyl acetate = 10:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{16}NaO$, 235.1093, found: 235.1095; **IR (ATR):** $\tilde{\nu}$ = 3421, 3082, 3059, 3022, 2955, 2857, 2818, 2719, 2362, 1950, 1879, 1720, 1650, 1601, 1582, 1492, 1451, 1426, 1389, 1348, 1304, 1279, 1238, 1182, 1156, 1112, 1078, 1058, 1032, 1001, 960, 938, 914, 868, 797, 765, 724, 702, 670 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.32–2.57 (m, 2H, H_2CCHO), 2.75 (ddd, ^2J = 20.1 Hz, ^3J = 7.2, 7.2 Hz, 1H, CH_2), 3.15–3.33 (s, 1H, CH_2), 3.55 (br s, 1H, *H*CCH$_2$CHO), 3.72 (br s, 1H, PhC*H*), 5.35–5.40 (m, 1H, C*H*), 5.73–5.75 (m, 1H, C*H*), 5.77–5.80 (m, 1H, C*H*), 5.86–5.92 (m, 1H, C*H*), 7.21–7.25 (m, 3H, *H*-Ar), 7.28–7.30 (m, 2H, *H*-Ar), 9.72 (t, ^3J = 1.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.4, 37.1, 47.4, 47.6, 126.9, 127.3, 128.1 (2*C*), 129.7 (2*C*), 130.2, 132.3, 133.2, 141.1, 202.3 ppm. Chiral chromatography showed that the substrate is racemic.

Reaction of enantiopure **(+)-109a** (5.00 mg, 23.6 µmol, 1.0 equiv.) with **48c** (1.5 mg, 4.71 µmol, 20 mol%) delivered the cycloheptadiene **(−)-112a** (4.00 mg, 18.8 µmol, 80%) with 98% *ee*. $[\alpha]_D^{20}$ = −0.43 (c = 0.33, $CHCl_3$).

GC: Hydrodex-β-6TBDAc, 120 °C, 1.5 ml/min He, FID300°, Split 50:1.

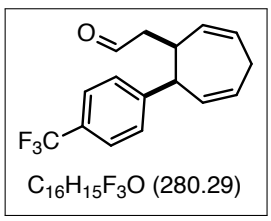


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	118.933	MM	1.1439	79.15709	1.15337	1.95200
2	125.906	MM	1.7138	76.71494	7.46057e-1	1.89178
3	130.757	MM	1.7327	1830.44092	17.60715	45.13842
4	134.790	MM	1.4955	2068.85962	23.05683	51.01779



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	129.405	MM	1.3992	23.95804	2.85384e-1	0.82688
2	134.865	MM	1.7629	2873.43530	27.16606	99.17312

2-((1,7-*cis*)-7-(4-(Trifluoromethyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112d)



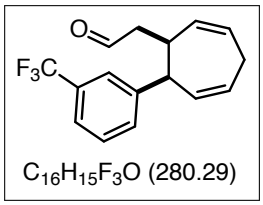
$C_{16}H_{15}F_3O$ (280.29)

Derived from **109d** (28 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112d** as a yellow oil (18 mg, 64 µmol, 64%).

R_f (pentane/ethyl acetate = 10:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{15}F_3NaO$, 303.0967, found: 303.0976; **IR (ATR):** $\tilde{\nu}$ = 3016, 2823, 2723, 1921, 1723, 1651, 1617, 1582, 1418,

1389, 1322, 1243, 1161, 1109, 1067, 1017, 958, 914, 841, 823, 802, 775, 755, 714, 673 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_{3)}$: δ = −62.3 ppm, **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.35–2.47 (m, 2H, H_2CCHO), 2.77 (ddd, ^2J = 20.0 Hz, ^3J = 7.3, 7.3 Hz, 1H, CH_2), 3.18–3.37 (m, 1H, CH_2), 3.62 (br s, 1H, HCCH$_2$CHO), 3.75 (br s, 1H, ArCH), 5.31 (dd, ^3J = 8.5, 8.5 Hz, 1H, CH), 5.69 (ddd, ^3J = 11.7, 5.6 Hz, ^4J = 2.9 Hz, 1H, CH), 5.80–5.84 (m, 1H, CH), 5.88–5.94 (m, 1H, CH), 7.36 (d, ^3J = 8.0 Hz, 2H, *H*-Ar), 7.54 (d, ^3J = 8.0 Hz, 2H, *H*-Ar), 9.74 (t, ^3J = 1.9 Hz, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.6, 47.4, 47.5, 124.4 (q, $^1J_{C,F}$ = 272 Hz), 125.0 (q, $^3J_{C,F}$ = 4 Hz, 2*C*), 127.9, 129.2 (q, $^2J_{C,F}$ = 32 Hz), 130.1 (2*C*), 130.7, 131.4, 132.9, 145.0, 201.7 ppm.

2-((1,7-*cis*)-7-(3-(Trifluoromethyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112e)

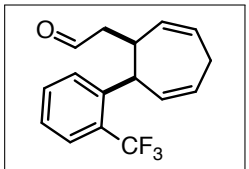


$C_{16}H_{15}F_3O$ (280.29)

Derived from **109e** (28 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the cycloheptadiene **112e** as a yellow oil (21 mg, 75 µmol, 75%).

Rf (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{16}H_{15}F_3NaO$, 303.0967, found: 303.0978, **IR (ATR):** $\tilde{\nu}$ = 3018, 2821, 2721, 1723, 1652, 1613, 1595, 1490, 1443, 1390, 1323, 1266, 1160, 1119, 1095, 1073, 1035, 1003, 922, 907, 868, 848, 835, 802, 777, 742, 706 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −62.7 ppm, **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.33–2.48 (m, 2H, H_2CCHO), 2.78 (ddd, ^2J = 19.8 Hz, ^3J = 7.3, 7.3 Hz, 1H, CH_2), 3.26 (d, ^2J = 19.8 Hz, 1H, CH_2), 3.61 (br s, 1H, HCCH$_2$CHO), 3.75 (br s, 1H, ArCH), 5.29–5.32 (m, 1H, CH), 5.68–5.71 (m, 1H, CH), 5.78–5.87 (m, 1H, CH), 5.91–5.94 (m, 1H, CH), 7.39–7.43 (m, 2H, *H*-Ar), 7.49–7.50 (m, 2H, *H*-Ar), 9.74 (t, ^3J = 2.0 Hz, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.6, 47.4, 123.8, 123.6–125.1 (m) 126.4, 128.0, 128.5, 130.2–130.7 (m) 130.7, 130.8, 131.4, 132.8, 133.2, 141.9, 201.7 ppm.

2-((1,7-*cis*)-7-(2-(Trifluoromethyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112f)



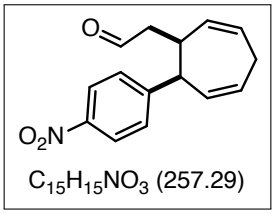
$C_{16}H_{15}F_3O$ (280.29)

Derived from **109f** (28 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112f** as a yellow oil (17 mg, 61 µmol, 61%).

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): [M + Na]$^+$ calcd for $C_{16}H_{15}F_3NaO$, 303.0967, found: 303.0982; **IR (ATR):** $\tilde{\nu}$ = 3077, 3018, 2925, 2822, 2722, 1724, 1653, 1606, 1580, 1490, 1454, 1413, 1389, 1352, 1308, 1155, 1112, 1061, 1036, 957, 937, 914, 883, 866, 817, 802, 771, 722, 708, 696, 673 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −57.7 ppm, **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.42 (ddd, ^2J = 17.0 Hz, ^3J = 9.6, 2.7 Hz, 1H, H_2CCHO), 2.50 (dd, ^2J = 17.0 Hz, ^3J = 4.9 Hz, 1H, H_2CCHO), 2.80 (ddd, ^2J = 20.4 Hz, ^3J = 6.6, 6.6 Hz, 1H, CH_2), 3.14–3.31 (m, 1H, CH_2), 3.44 (br s, 1H, HCCH$_2$CHO), 4.29 (br s, 1H, ArCH), 5.68 (ddd, ^3J = 11.8, 4.5 Hz, ^4J = 2.8 Hz, 1H, CH), 5.72 (ddd, ^3J = 10.8, 6.5 Hz, ^4J = 2.1 Hz, 1H, CH), 5.76 (dddd, ^3J = 11.8, 5.9 Hz, ^4J = 2.6, 2.6 Hz, 1H, CH), 5.87–5.92 (m, 1H, CH), 7.33 (t, ^3J = 7.6 Hz, 1H, *H*-Ar), 7.49 (t, ^3J = 7.6 Hz, 1H, *H*-Ar), 7.65 (d, ^3J = 7.6 Hz, 1H, *H*-Ar), 7.71 (d, ^3J = 7.6 Hz, 1H, *H*-Ar), 9.38–9.91 (m, 1H, CHO) ppm; **^{13}C NMR**

(176 MHz, $CDCl_3$): δ = 28.6, 37.0, 42.4, 46.2, 124.5 (q, $^1J_{C,F}$ = 274 Hz), 126.1 (q, $^3J_{C,F}$ = 7 Hz), 126.7, 127.3, 128.7 (q, $^2J_{C,F}$ = 29 Hz), 130.2, 131.0, 131.5, 131.9, 133.4, 141.5, 201.8 ppm.

2-((1,7-*cis*)-7-(4-Nitrophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112g)

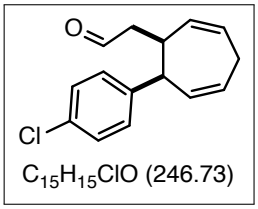


$C_{15}H_{15}NO_3$ (257.29)

Derived from **109g** (19 mg, 74 µmol, 1.0 equiv.) and **48c** (4.8 mg, 15 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 6:1) delivered the cycloheptadiene **112g** (11 mg, 43 µmol, 58%) as a yellow oil.

R_f (pentane/ethyl acetate = 4:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}NNaO_3$, 280.0944, found: 280.0955; **IR (ATR):** $\tilde{\nu}$ = 3108, 3077, 3015, 2923, 2851, 2820, 2724, 2452, 1934, 1720, 1651, 1596, 1515, 1416, 1389, 1342, 1314, 1180, 1108, 1060, 1014, 962, 916, 852, 824, 798, 737, 704, 676 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 2.31–2.57 (m, 2H, H_2CCHO), 2.73–2.90 (m, 1H, CH_2), 3.13–3.35 (m, 1H, CH_2), 3.67 (br s, 1H, *H*CCH_2CHO), 3.79 (br s, 1H, ArC*H*), 5.24–5.29 (m, 1H, C*H*), 5.67 (dddd, ^3J = 11.7, 5.6 Hz, ^4J = 2.9, 0.8 Hz, 1H, C*H*), 5.79–5.87 (m, 1H, C*H*), 5.88–6.00 (m, 1H, C*H*), 7.36–7.45 (m, 2H, *H*-Ar), 8.09–8.19 (m, 2H, *H*-Ar), 9.74 (t, ^3J = 1.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.2, 36.3, 47.2, 47.3, 123.1 (2*C*), 128.2, 130.5 (2*C*), 130.6, 130.9, 132.4, 147.0, 148.4, 201.1 ppm.

2-((1,7-*cis*)-7-(4-Chlorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112h)

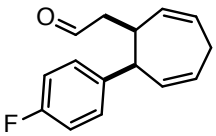


$C_{15}H_{15}ClO$ (246.73)

Derived from **109h** (25 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112h** (17 mg, 69 µmol, 69%) as a yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}ClNaO$, 269.0703, found: 269.0710; **IR (ATR):** $\tilde{\nu}$ = 3420, 3014, 2957, 2925, 2858, 2819, 2724, 1904, 1720, 1650, 1593, 1574, 1489, 1409, 1388, 1352, 1294, 1262, 1229, 1215, 1180, 1091, 1014, 961, 938, 925, 872, 816, 800, 768, 746, 722 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.33–2.49 (m, 2H, H_2CCHO), 2.74 (ddd, ^2J = 19.9 Hz, ^3J = 7.3, 7.3 Hz, 1H, CH_2), 3.18–3.30 (m, 1H, CH_2), 3.47–3.60 (m, 1H, *H*CCH_2CHO), 3.59–3.72 (m, 1H, ArC*H*), 5.19–5.34 (m, 1H, C*H*), 5.67 (ddd, ^3J = 11.8, 5.4 Hz, ^4J = 2.9 Hz, 1H, C*H*), 5.77–5.80 (m, 1H, C*H*), 5.88–5.91 (m, 1H, C*H*), 7.17 (d, ^3J = 8.4 Hz, 2H, *H*-Ar), 7.25 (d, ^3J = 8.4 Hz, 2H, *H*-Ar), 9.72 (t, ^3J = 1.9 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.7, 46.9, 47.5, 127.5, 128.2 (2*C*), 130.6, 131.1 (2*C*), 131.8, 132.8, 133.0, 139.3, 201.9 ppm.

2-((1,7-*cis*)-7-(4-Fluorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112i)

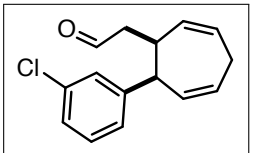


$C_{15}H_{15}FO$ (230.28)

Derived from **109i** (23 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112i** (20 mg, 87 µmol, 87%) as a yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.2; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}FNaO$, 253.1005, found: 253.1007; **IR (ATR):** $\tilde{\nu}$ = 3014, 2958, 2924, 1723, 1602, 1507, 1438, 1222, 840, 754 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −115.0 ppm, **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 2.33–2.48 (m, 2H, H_2CCHO), 2.74 (ddd, ^2J = 19.9 Hz, ^3J = 7.2, 7.2 Hz, 1H, CH_2), 3.20–3.27 (m, 1H, CH_2), 3.56 (br s, 1H, HCCH$_2$CHO), 3.66 (br s, 1H, ArCH), 5.31 (ddd, ^3J = 9.9, 6.0 Hz, ^4J = 2.7 Hz, 1H, CH), 5.68 (ddd, ^3J = 11.7, 5.4 Hz, ^4J = 2.8 Hz, 1H, CH), 5.77 (dddd, ^3J = 11.7, 5.4 Hz, ^4J = 3.1, 1.4 Hz, 1H, CH), 5.86–5.95 (m, 1H, CH), 6.93–7.00 (m, 2H, *H*-Ar), 7.16–7.23 (m, 2H, *H*-Ar), 9.72 (t, ^3J = 2.0 Hz, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.8, 46.8, 47.5, 114.9 (d, $^2J_{C,F}$ = 21 Hz, 2*C*), 127.2, 130.5, 131.2 (d, $^2J_{C,F}$ = 8 Hz, 2*C*), 132.2, 133.1, 136.5, 162.0 (d, $^1J_{C,F}$ = 245 Hz), 202.0 ppm.

2-((1,7-*cis*)-7-(3-Chlorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112j)

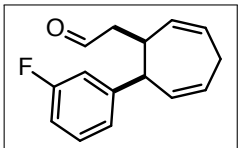


$C_{15}H_{15}ClO$ (246.73)

Derived from **109j** (25 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112j** (19 mg, 77 µmol, 77%) as a yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}ClNaO$, 269.0703, found: 269.0708; **IR (ATR):** $\tilde{\nu}$ = 3432, 3014, 2956, 2854, 2818, 2720, 1939, 1720, 1650, 1593, 1570, 1474, 1428, 1389, 1350, 1298, 1263, 1240, 1183, 1166, 1081, 1060, 1032, 999, 946, 889, 867, 836, 788, 761, 738, 706 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.35–2.50 (m, 2H, H_2CCHO), 2.76 (ddd, ^2J = 19.9 Hz, ^3J = 7.3, 7.3 Hz, 1H, CH_2), 3.19–3.30 (m, 1H, CH_2), 3.57 (br s, 1H, HCCH$_2$CHO), 3.67 (br s, 1H, ArCH), 5.33–5.36 (m, 1H, CH), 5.68 (ddd, ^3J = 11.7, 5.5 Hz, ^4J = 2.9 Hz, 1H, CH), 5.76–5.86 (m, 1H, CH), 5.87–5.94 (m, 1H, CH), 7.10–7.11 (m, 1H, *H*-Ar), 7.19–7.22 (m, 2H, *H*-Ar), 7.23–7.24 (m, 1H, *H*-Ar), 9.73 (t, ^3J = 1.9 Hz, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.7, 47.3, 47.5, 127.1, 127.7, 128.0, 129.3, 129.8, 130.6, 131.6, 132.9, 134.0, 143.1, 201.9 ppm.

2-((1,7-*cis*)-7-(3-Fluorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112k)

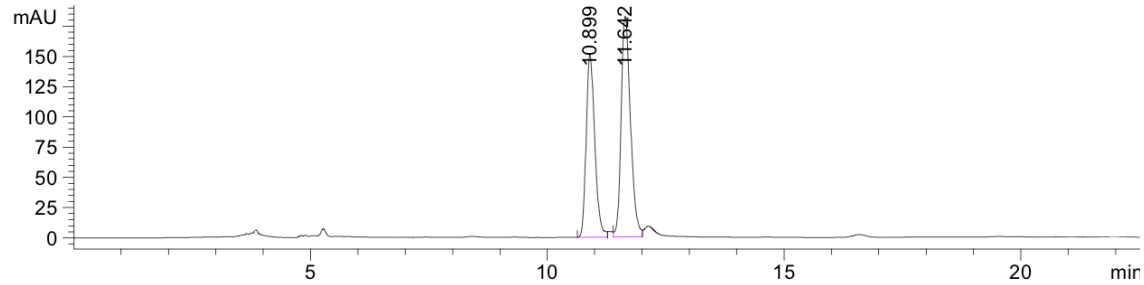


$C_{15}H_{15}FO$ (230.28)

Derived from **109k** (23 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112k** (11 mg, 48 µmol, 48%) as a yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.3; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}FNaO$, 253.1005, found: 253.1011; **IR (ATR):** $\tilde{\nu}$ = 3016, 2923, 2856, 2820, 2724, 1721, 1612, 1586, 1240, 780 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = −113.4 ppm, **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.28–2.57 (m, 2H, CH_2CHO), 2.75 (ddd, ^2J = 20.0 Hz, ^3J = 7.3, 7.3 Hz, 1H, CH_2), 3.10–3.36 (m, 1H, CH_2), 3.57 (br s, 1H, *H*CCH$_2$CHO), 3.69 (br s, 1H, ArC*H*), 5.34–7.36 (m, 1H, C*H*), 5.69 (ddd, ^3J = 11.9, 5.1 Hz, ^4J = 2.8 Hz, 1H, C*H*), 5.74–5.81 (m, 1H, C*H*), 5.86–5.92 (m, 1H, C*H*), 6.78–6.96 (m, 1H, *H*-Ar), 6.95–7.02 (m, 2H, *H*-Ar), 7.15–7.32 (m, 1H, *H*-Ar), 9.73 (t, ^3J = 1.7 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.7, 47.3, 47.5, 113.8 (d, $^2J_{C,F}$ = 21 Hz), 116.6 (d, $^2J_{C,F}$ = 21 Hz), 125.4, 127.7, 129.4 (d, $^3J_{C,F}$ = 8 Hz), 130.5, 131.7, 133.0, 143.7, 162.3 (d, $^1J_{C,F}$ = 245 Hz), 201.9 ppm. Chiral chromatography showed that the substance is racemic.

HPLC: 5% ethyl acetate/hexane, Chiralpak IC, 1 mL/min, 34 bar

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   2  11.642 VV    0.2122 2504.38550  182.40547  56.6674

Totals :                  4419.44629  333.23296
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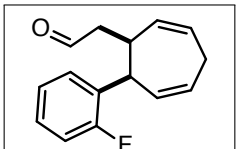
2-((1,7-*cis*)-7-(2-Fluorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112l)



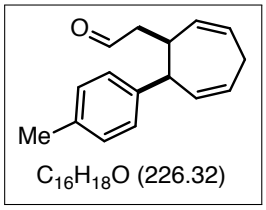
$C_{15}H_{15}FO$ (230.28)

Derived from **109l** (23 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112l** (11 mg, 48 µmol, 48%) as a yellow oil.

R_f (pentane/ethyl acetate = 10:1) = 0.5; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{15}H_{15}FNaO$, 253.1005, found: 253.1012; **IR (ATR):** $\tilde{\nu}$ = 3018, 2922, 2853, 1723, 1486, 1454, 1228, 1093, 755 cm^{-1};

^{19}F NMR (376 MHz, $CDCl_3$): δ = −117.7 ppm, **^{1}H NMR** (700 MHz, $CDCl^3$): δ = 2.37 (dd, ^2J = 17.3 Hz, ^3J = 8.6 Hz, 1H, H_2CCHO), 2.56 (dd, ^2J = 17.3 Hz, ^3J = 6.1 Hz, 1H, H_2CCHO), 2.75 (ddd, ^2J = 19.9 Hz, ^3J = 7.3, 7.3 Hz, 1H, CH_2), 3.19–3.36 (m, 1H, CH_2), 3.63 (br s, 1H, HCCH$_2$CHO), 4.16 (br s, 1H, ArCH), 5.26–5.35 (m, 1H, CH), 5.64 (ddd, ^3J = 11.8, 5.5 Hz, ^4J = 2.8 Hz, 1H, CH), 5.74–5.84 (m, 1H, CH), 5.85–5.93 (m, 1H, CH), 7.02 (dd, ^3J = 10.2 Hz, ^4J = 8.3 Hz, 1H, H-Ar), 7.07 (dd, ^3J = 7.5, 7.5 Hz, 1H, H-Ar), 7.18–7.22 (m, 1H, H-Ar), 7.36 (dd, ^3J = 7.6 Hz, ^4J = 7.6 Hz, 1H, H-Ar), 9.73 (s, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 36.3, 38.8, 47.2, 115.1 (d, $^2J_{C,F}$ = 23 Hz), 123.8 (d, $^4J_{C,F}$ = 4 Hz), 127.9, 128.4 (d, $^3J_{C,F}$ = 8 Hz), 128.6 (d, $^2J_{C,F}$ = 12 Hz), 130.5, 131.3, 131.9, 133.2, 160.9 (d, $^1J_{C,F}$ = 244 Hz), 201.9 ppm.

2-((1,7-*cis*)-7-(*p*-Tolyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112n)

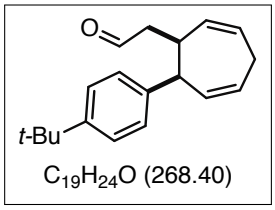


$C_{16}H_{18}O$ (226.32)

Derived from **109n** (23 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112n** as a pale yellow oil (15 mg, 66 µmol, 66%).

R_f (pentane/ethyl acetate = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{16}H_{18}NaO$, 249.1250, found: 249.1243; **IR (ATR):** $\tilde{\nu}$ = 3012, 2922, 2860, 2817, 2719, 1903, 1721, 1650, 1510, 1451, 1422, 1388, 1349, 1301, 1238, 1213, 1186, 1112, 1082, 1059, 1022, 961, 936, 915, 869, 811, 781, 746, 727 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.32 (s, 3H, CH_3), 2.37–2.50 (m, 2H, H_2CCHO), 2.74 (ddd, ^2J = 20.0 Hz, ^3J = 7.1, 7.1 Hz, 1H, CH_2), 3.17–3.27 (m, 1H, CH_2), 3.52 (br s, 1H, HCCH$_2$CHO), 3.68 (br s, 1H, ArCH), 5.34–5.40 (m, 1H, CH), 5.71–5.74 (m, 1H, CH), 5.75–5.80 (m, 1H, CH), 5.86–5.89 (m, 1H, CH), 7.09 (d, ^3J = 7.9 Hz, 2H, H-Ar), 7.13 (d, ^3J = 7.9 Hz, 2H, H-Ar), 9.71 (t, ^3J = 1.8 Hz, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 21.1, 28.4, 37.1, 47.2, 47.5, 127.1, 128.8 (2*C*), 129.6 (2*C*), 130.2, 132.5, 133.3, 136.4, 138.0, 202.4 ppm.

2-((1,7-*cis*)-7-(4-(*tert*-Butyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112o)

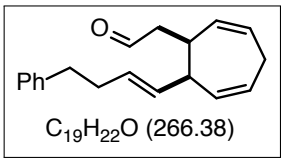


$C_{19}H_{24}O$ (268.40)

Derived from **109o** (27 mg, 0.10 mg, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112o** (17 mg, 63 µmol, 63%) as a yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{24}NaO$, 291.1725, found: 291.1734; **IR (ATR):** $\tilde{\nu}$ = 3013, 2959, 2868, 2713, 1724, 1363, 837 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 1.31 (s, 9H, CH_3), 2.37–2.53 (m, 2H, H_2CCHO), 2.70–2.79 (m, 1H, CH_2), 3.19–3.26 (m, 1H, CH_2), 3.52 (br s, 1H, HCCH$_2$CHO), 3.70 (br s, 1H, ArCH), 5.39–5.42 (m, 1H, CH), 5.69–5.80 (m, 2H, CH), 5.83–5.93 (m, 1H, CH), 7.15–7.17 (m, 2H, H-Ar), 7.29–7.31 (m, 2H, H-Ar), 9.72 (t, ^3J = 2.0 Hz, 1H, CHO) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.4, 31.5 (3*C*), 34.5, 37.2, 47.1, 47.5, 125.0 (2*C*), 127.1, 129.3 (2*C*), 130.1, 132.6, 133.3, 138.0, 149.6, 202.5 ppm.

(2-((1,7-*cis*)-7-((*E*)-4-Phenylbut-1-en-1-yl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112p)

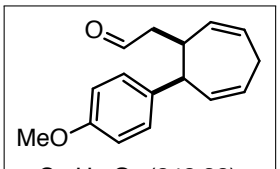


$C_{19}H_{22}O$ (266.38)

Derived from **109p** (6.0 mg, 22 µmol, 1.0 equiv.) and **48c** (1.4 mg, 4.5 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the cycloheptadiene **112p** as a colourless oil (2.5 mg, 9.4 µmol, 42%).

R_f (pentane/ethyl acetate = 20:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{22}NaO$, 289.1563, found: 289.1559; **IR (ATR):** $\tilde{\nu}$ = 3010, 2954, 2924, 2852, 2822, 2714, 1724, 1655, 1603, 1496, 1455, 1387, 1261, 1188, 1084, 1030 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.28–2.46 (m, 4H, CH_2, H_2CCHO), 2.58–2.77 (m, 3H, ArCH_2, CH_2), 3.05–3.12 (m, 1H, CH_2), 3.18 (br s, 1H, *H*CCH$_2$CHO), 3.26 (br s, 1H, C*H*), 5.33–5.36 (m, 1H, C*H*), 5.36–5.40 (m, 1H, C*H*), 5.43–5.47 (m, 1H, C*H*), 5.49 (dtd, ^3J = 10.9, 7.4 Hz, ^4J = 1.0 Hz, 1H, C*H*), 5.53–5.56 (m, 1H, C*H*), 5.68–5.75 (m, 1H, C*H*), 7.16–7.20 (m, 3H, *H*-Ar), 7.26–7.30 (m, 2H, *H*-Ar), 9.68 (t, ^3J = 2.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl^3$): δ = 29.0, 29.7, 36.1, 36.2, 40.6, 48.0, 126.0, 126.8, 128.5 (2*C*), 128.7 (2*C*), 129.6, 130.1, 130.5, 132.6, 133.0, 141.9, 202.4 ppm.

2-((1,7-*cis*)-7-(4-Methoxyphenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112q)

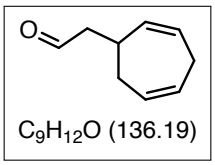


$C_{16}H_{18}O_2$ (242.32)

Derived from **109q** (16 mg, 66 µmol, 1.0 equiv.) and **48c** (4.3 mg, 13 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112q** (8.0 mg, 33 µmol, 50%) as a yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{16}H_{19}O_2$, 243.1380, found: 243.1385; **IR (ATR):** $\tilde{\nu}$ = 009, 2953, 2928, 2834, 2719, 2360, 2342, 1720, 1650, 1608, 1580, 1508, 1463, 1442, 1422, 1389, 1347, 1302 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.39 (dd, ^2J = 16.8 Hz, ^3J = 8.4 Hz, 1H, H_2CCHO), 2.45 (dd, ^2J = 16.8 Hz, ^3J = 6.1 Hz, 1H, H_2CCHO), 2.73 (ddd, ^2J = 19.8 Hz, ^3J = 7.2, 7.2 Hz, 1H, CH_2), 3.16–3.27 (m, 1H, CH_2), 3.53 (br s, 1H, *H*CCH$_2$CHO), 3.64 (br s, 1H, ArC*H*), 3.79 (m, 3H, CH_3), 5.35 (dd, ^3J = 8.2, 8.2 Hz, 1H, C*H*), 5.71 (ddd, ^3J = 9.8, 5.1 Hz, ^4J = 2.3 Hz, 1H, C*H*), 5.73–5.78 (m, 1H, C*H*), 5.87–5.90 (m, 1H, C*H*), 6.82 (d, ^3J = 7.9 Hz, 2H, *H*-Ar), 7.15 (d, ^3J = 7.9 Hz, 2H, *H*-Ar), 9.72 (br s, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.3, 37.1, 46.8, 47.6, 55.4, 113.5 (2*C*), 126.9, 130.3, 130.7 (2*C*), 132.7, 133.0, 133.3, 158.6, 202.4 ppm.

2-(Cyclohepta-2,5-dien-1-yl)acetaldehyde (112r)

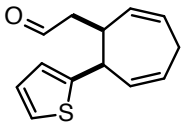


$C_9H_{12}O$ (136.19)

Derived from **109r** (14 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 48 h. Column chromatography (silica gel, pentane/ethyl acetate = 80:1) delivered the cycloheptadiene **112r** (4.0 mg, 29 µmol, 29%) as a colourless oil. The product seemed to form azeotropic mixtures with the solvents used.

R_f (pentane/ethyl acetate = 20:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_9H_{12}NaO$, 159.0780, found: 159.0788; **IR (ATR):** $\tilde{\nu}$ = 3015, 2960, 2925, 2854, 2822, 2720, 2360, 2342, 1724, 1658, 1447, 1428, 1404, 1389, 1315, 1277, 1258, 1177, 1106, 1082, 1031, 792, 705, 669 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.18–2.23 (m, 1H, CH_2), 2.30–2.34 (m, 1H, CH_2), 2.51 (m_c, 2H, H_2CCHO), 2.75–2.79 (m, 1H, CH_2), 2.96–3.00 (m, 1H, CH_2), 3.04–3.07 (m, 1H, *H*CCH$_2$CHO), 5.55–5.60 (m, 1H, C*H*), 5.63–5.68 (m, 1H, C*H*), 5.70–5.71 (m, 2H, C*H*), 9.78 (t, ^3J = 2.1 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.7, 32.4, 32.7, 50.1, 128.7, 129.0, 129.4, 134.1, 202.3 ppm.

2-((1,7-*cis*)-7-(Thiophen-2-yl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112s)

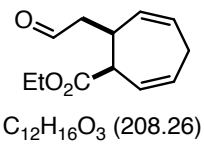


$C_{13}H_{14}OS$ (218.31)

Derived from **109s** (25 mg, 0.11 mmol, 1.0 equiv.) and **48c** (7.4 mg, 22 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 48 h. Column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the cycloheptadiene **112s** (17 mg, 78 µmol, 66%) as a pale yellow oil.

R_f (pentane/ethyl acetate = 20:1) = 0.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{13}H_{14}NaOS$, 241.0657, found: 241.0667; **IR (ATR):** $\tilde{\nu}$ = 3104, 3068, 3013, 2958, 2852, 2818, 2720, 2359, 2342, 1719, 1651, 1528, 1433, 1404, 1389, 1351, 1295, 1239, 1203, 1150, 1100, 1078, 1061, 1040, 915, 866, 849, 825, 781, 698 cm_{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.46–2.58 (m, 2H, H_2CCHO), 2.73 (ddd, ^2J = 20.1 Hz, ^3J = 7.1, 7.1 Hz, 1H, CH_2), 3.20 (m_c, 1H, CH_2), 3.52 (br s, 1H, *H*CCH$_2$CHO), 4.06 (br s, 1H, ArC*H*), 5.50–5.52 (m, 1H, C*H*), 5.72–5.78 (m, 1H, C*H*), 5.81 (ddd, ^3J = 11.4, 5.5 Hz, ^4J = 2.7 Hz, 1H, C*H*), 5.87–5.89 (m, 1H, C*H*), 6.85 (d, ^3J = 3.3 Hz, 1H, *H*-Ar), 6.93–6.94 (m, 1H, *H*-Ar), 7.17 (d, ^3J = 5.1 Hz, 1H, *H*-Ar), 9.73 (t, ^3J = 1.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.5, 37.2, 43.3, 47.7, 124.4, 125.9, 126.5, 127.8, 130.5, 132.5, 133.1, 144.9, 201.9 ppm.

Ethyl (1,7-*cis*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carboxylate (112t)

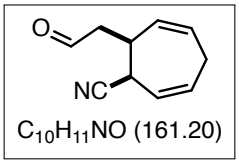


$C_{12}H_{16}O_3$ (208.26)

Derived from **109t** (0.22 g, 0.94 mmol, 1.0 equiv.) and **48c** (61 mg, 0.19 mmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the cycloheptadiene **112t** as a colourless oil (0.17 g, 0.81 mmol, 86%).

R_f (pentane/ethyl acetate = 20:1) = 0.3; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{17}O_3$, 209.1172, found: 209.1179; **IR (ATR):** $\tilde{\nu}$ = 3429, 3018, 2980, 2918, 2848, 2820, 2723, 2363, 2338, 1722, 1655, 1465, 1446, 1390, 1367, 1317, 1303, 1287, 1178, 1124, 1096, 1066, 1030, 979, 951, 926, 863, 812, 790, 777, 768, 756, 740, 727 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.2 Hz, 3H, CH_3), 2.54–2.78 (m, 3H, H_2CCHO, CH_2), 2.97–3.19 (m, 1H, CH_2), 3.35–3.38 (m, 1H, *H*CCH$_2$CHO), 3.71–3.73 (m, 1H, EtO$_2$CC*H*), 4.15 (q, ^3J = 7.2 Hz, 2H, CH$_3$CH_2), 5.58–5.63 (m, 1H, C*H*), 5.75 (dddd, ^3J = 11.5, 6.5 Hz, ^4J = 2.6, 1.2 Hz, 1H, C*H*), 5.81–5.85 (m, 1H, C*H*), 5.92 (dddd, ^3J = 11.1, 5.6 Hz, ^4J = 2.9, 0.8 Hz, 1H, C*H*), 9.75 (t, ^3J = 1.6 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.3, 29.0, 34.4, 47.0, 47.2, 61.0, 127.4, 127.7, 130.3, 132.2, 173.0, 201.4 ppm.

(1,7-*cis*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carbonitrile (112u)

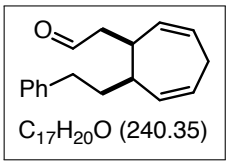


$C_{10}H_{11}NO$ (161.20)

Derived from **109u** (30 mg, 0.19 mmol, 1.0 equiv., *E/Z* = 16:1) and **48c** (12 mg, 38 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the cycloheptadiene **112u** as yellow oil (22 mg, 0.14 mmol, 72%, *cis/trans* = 2:1).

R_f (pentane/ethyl acetate = 2:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{10}H_{11}NNaO$, 184.0733, found: 184.0741; **IR (ATR):** $\tilde{\nu}$ = 3034, 2953, 2923, 2851, 2733, 2367, 2236, 1719, 1460, 1377, 1192, 1082, 1037, 969, 914, 849, 838, 806, 776, 745, 722, 692, 670, 653 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.79–2.86 (m, 2H, H_2CCHO), 2.88–2.97 (m, 1H, CH_2), 3.06 (ddddd, ^2J = 21.1 Hz, ^3J = 4.3, 4.3 Hz, ^4J = 2.4, 1.8 Hz, 1H, CH_2), 3.35–3.38 (m, 1H, *H*CCH$_2$CHO), 3.57–3.64 (m, 1H, NCC*H*), 5.56 (ddd, ^3J = 11.3, 5.1 Hz, ^4J = 2.4 Hz, 1H, C*H*), 5.68 (ddd, ^3J = 8.2, 4.0 Hz, ^4J = 1.8 Hz, 1H, C*H*), 5.76–5.81 (m, 1H, C*H*), 5.87–5.92 (m, 1H, C*H*), 9.81 (s, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.9, 34.0, 34.3, 47.9, 119.1, 123.4, 129.9, 130.9, 132.9, 199.8 ppm. Only the signals of the major diastereomer are indicated.

2-((1,7-*cis*)-7-Phenethylcyclohepta-2,5-dien-1-yl)acetaldehyde (112y)

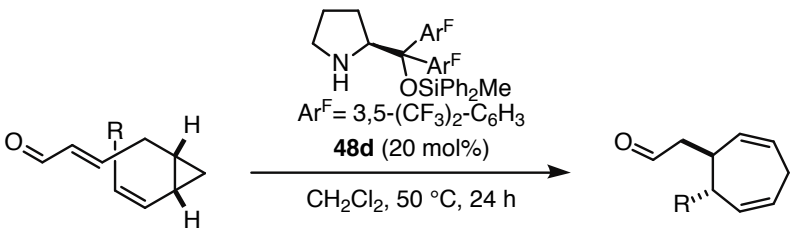


$C_{17}H_{20}O$ (240.35)

Derived from **109y** (24 mg, 0.10 mmol, 1.0 equiv.) and **48c** (6.6 mg, 20 µmol, 20 mol%) according to **GP2**. The reaction was stirred for 72 h. Column chromatography (silica gel, pentane/ethyl acetate = 40:1) delivered the cycloheptadiene **112y** (15 mg, 62 µmol, 62%) as a colourless oil.

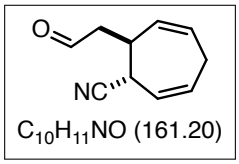
R_f (pentane/ethyl acetate = 20:1) = 0.7; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{17}H_{20}NaO$, 263.1406, found: 263.1415; **IR (ATR):** $\tilde{\nu}$ = 3021, 2923, 2857, 2717, 1721, 1653, 1603, 1496, 1454, 1390, 1340, 1191, 1081, 1030, 910, 856, 801, 749 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.63 (dddd, ^2J = 13.2 Hz, ^3J = 10.0, 6.8 Hz, ^4J = 4.7 Hz, 1H, ArCH_2), 1.74 (dtd, ^2J = 13.2 Hz, ^3J = 9.9 Hz, ^4J = 5.2 Hz, 1H, ArCH_2), 2.48 (ddd, ^2J = 16.5 Hz, ^3J = 5.1, 2.0 Hz, 1H, CHOCH_2), 2.51–2.61 (m, 2H, CHOCH_2, CH=CHCH_2), 2.62–2.75 (m, 2H, CH=CHCH_2, ArCH$_2$CH_2), 2.98 (br s, 1H, CHOCH$_2$C*H*), 3.07 (ddt, ^3J = 20.6, 5.3, 2.9 Hz, 1H, ArCH$_2$CH$_2$C*H*), 5.56–5.69 (m, 3H, 3 x C*H*), 5.74–5.77 (m, 1H, C*H*), 7.15–7.21 (m, 3H, *H*-Ar), 7.27–7.30 (m, 2H, *H*-Ar), 9.78 (t, ^3J = 2.0 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 29.4, 34.1, 35.6, 37.0, 40.7, 46.6, 126.0, 127.8, 128.5 (2*C*), 128.5 (2*C*), 129.1, 133.0, 134.3, 142.3, 202.6 ppm.

5.7.2 General Procedure for Enamine-Induced DCVPR of *Z*-Vinyl Cyclopropylcarbaldehydes (GP3)



A solution of the corresponding α,β-unsaturated cyclopropylcarbaldehyde (1.0 equiv.) in CH_2Cl_2 (0.1 M) was treated with (*S*)-2-(bis(3,5-bis(trifluoromethyl)phenyl)((methyldiphenylsilyl)oxy)methyl)pyrrolidine (**48d**, 20 mol%). The reaction mixture was stirred at 50 °C until TLC or GC-MS showed complete conversion. The reaction was quenched with sat. aq. NH_4Cl and the resulting mixture was extracted with CH_2Cl_2 (3 x). The combined organic phases were washed with brine, dried over $MgSO_4$, and filtrated. The solvent was removed *in vacuo* and the crude products were purified by column chromatography.

(1,7-*trans*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carbonitrile (112v)

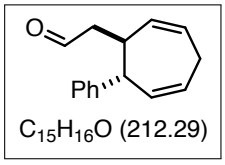


$C_{10}H_{11}NO$ (161.20)

Derived from **109v** (26 mg, 0.16 mmol, 1.0 equiv., *Z*/*E* = 6:1) and **48d** (23 mg, 32 µmol, 20 mol%) according to **GP3**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the cycloheptadiene **112v** (15 mg, 93 µmol, 58%, *trans*/*cis* = 6:1) as a yellow oil.

R_f (pentane/ethyl acetate = 2:1) = 0.8; **ESI-TOF** (*m*/*z*): $[M + Na]^+$ calcd for $C_{10}H_{11}NNaO$, 184.0733, found: 184.0741; **IR (ATR):** $\tilde{\nu}$ = 3034, 2953, 2923, 2851, 2733, 2367, 2236, 1719, 1460, 1377, 1192, 1082, 1037, 969, 914, 849, 838, 806, 776, 745, 722, 692, 670, 653 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.64–2.82 (m, 2H, H_2CCHO), 2.88–2.95 (m, 1H, CH_2), 3.14 (ddddd, ^2J = 21.6 Hz, ^3J = 4.2, 4.2 Hz, ^4J = 2.1, 2.1 Hz, 1H, CH_2), 3.24 (m_c, 1H, *H*CCH$_2$CHO), 3.61 (dd, ^3J = 6.9, 6.9 Hz, 1H, NCC*H*), 5.61–5.67 (m, 2H, C*H*), 5.69–5.75 (m, 1H, C*H*), 5.87–5.99 (m, 1H, C*H*), 9.77 (t, ^3J = 1.1 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 29.4, 33.3, 34.9, 47.8, 119.7, 122.9, 129.2, 130.2, 134.0, 199.7 ppm.

2-((1,7-*trans*)-7-Phenylcyclohepta-2,5-dien-1-yl)acetaldehyde (112z)

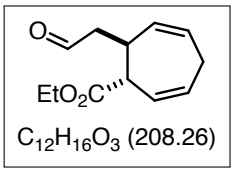


$C_{15}H_{16}O$ (212.29)

Derived from **109z** (21 mg, 0.10 mmol, 1.0 equiv.) and **48d** (14 mg, 20 µmol, 20 mol%) according to **GP3**. The reaction was stirred for 24 h. Column chromatography (silica gel, pentane/ethyl acetate = 20:1) delivered the cycloheptadiene **112z** (15 mg, 71 µmol, 71%) as a pale yellow oil.

R_f (pentane/ethyl acetate = 10:1) = 0.7; **ESI-TOF** (*m*/*z*): $[M + Na]^+$ calcd for $C_{15}H_{16}NaO$, 235.1093, found: 235.1095; **IR (ATR):** $\tilde{\nu}$ = 3022, 2954, 2925, 2854, 2717, 2317, 1722, 1689, 1652, 1491, 1454, 1279, 1141, 773 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.35–2.45 (m, 2H, H_2CCHO), 2.89 (ddddd, ^2J = 20.1 Hz, ^3J = 5.3, 5.3 Hz, ^4J = 1.4, 1.4 Hz, 1H, CH_2), 3.02–3.10 (m, 1H, CH_2), 3.25–3.32 (m, 1H, *H*CCH$_2$CHO), 3.53 (ddd, ^3J = 8.9, 4.5 Hz, ^4J = 2.1 Hz, 1H, ArC*H*), 5.55 (dddd, ^3J = 10.9, 5.8 Hz, ^4J = 1.8, 1.4 Hz, 1H, C*H*), 5.66 (dddd, ^3J = 11.6, 4.7 Hz, ^4J = 2.1, 1.6 Hz, 1H, C*H*), 5.75–5.80 (m, 1H, C*H*), 5.83 (m_c, 1H, C*H*), 7.21–7.24 (m, 2H, *H*-Ar), 7.29–7.32 (m, 3H, *H*-Ar), 9.59 (dd, ^3J = 2.2, 1.6 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.8, 38.8, 49.0, 49.1, 126.8, 127.9, 128.5 (2*C*), 128.7 (2*C*), 130.3, 132.9, 133.1, 144.1, 201.9 ppm.

Ethyl (1,7-*trans*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carboxylate (112aa)

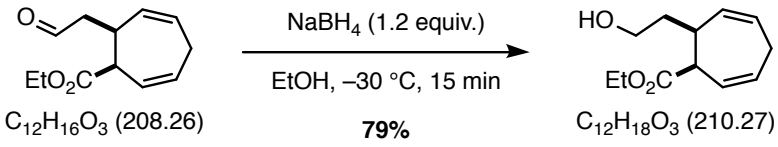


Derived from **109aa** (49 mg, 0.24 mmol, 1.0 equiv.) and **48d** (34 mg, 47 µmol, 20 mol%) according to **GP3**. The reaction was stirred for 48 h. Column chromatography (silica gel, pentane/ethyl acetate = 10:1) delivered the cycloheptadiene **112aa** (31 mg, 0.15 mmol, 62%) as a yellow oil.

R_f (pentane/ethyl acetate = 4:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]_+$ calcd for $C_{10}H_{11}NNaO$, 184.0733, found: 184.0741; **IR (ATR):** $\tilde{\nu}$ = 3019 , 2980, 2927, 2850, 1724, 1367, 1174, 1031 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.26 (t, ^3J = 7.1 Hz, 3H, CH_3), 2.52–2.62 (m, 2H, H_2CCHO), 2.82–2.90 (m, 1H, CH_2), 2.91–3.01 (m, 1H, CH_2), 3.33–3.41 (m, 2H, *H*CCH_2CHO, EtO_2C*H*), 4.15 (qd, ^3J = 7.1 Hz, ^5J = 1.2 Hz, 2H, CH_2), 5.59–5.69 (m, 3H, C*H*), 5.79–5.89 (m, 1H, C*H*), 9.75 (t, ^3J = 1.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.3, 29.7, 34.5, 48.5, 48.7, 61.0, 126.0, 129.1, 131.3, 131.5, 172.9, 201.3 ppm.

5.8 Follow-Up Reactions

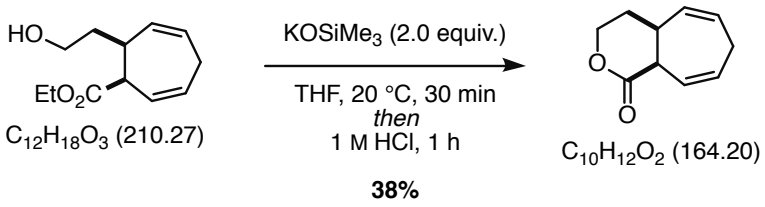
5.8.1 Ethyl (1,7-*cis*)-7-(2-Hydroxyethyl)cyclohepta-2,5-diene-1-carboxylate (181)



A solution of **112t** (0.15 g, 0.72 mmol, 1.0 equiv.) in EtOH (7.2 mL, 0.1 M) was cooled to −30 °C and treated with $NaBH_4$ (33 mg, 0.86 mmol, 1.2 equiv.). The reaction was stirred at this temperature for 15 min before sat. aq. NH_4Cl (5 mL) was added. The mixture was extracted with CH_2Cl_2 (3 x 10 mL) and the organic phases were washed with brine (10 mL), dried over $MgSO_4$, and filtrated. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivering the title compound **181** as a colourless oil (0.12 g, 0.57 mmol, 79%).

R_f (pentane/ethyl acetate = 4:1) = 0.3; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{12}H_{19}O_3$, 211.1329, found: 211.1334; **IR (ATR):** $\tilde{\nu}$ = 3419, 3014, 2979, 2931, 2874, 2818, 2360, 2338, 1729, 1654, 1392, 1367, 1300, 1177, 1124, 1093, 1055, 1028, 914, 862, 811, 746 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.54 (br s, 1H, O*H*), 1.70 (dddd, ^2J = 13.7 Hz, ^3J = 7.2, 6.5, 5.5 Hz, 1H, HOCH_2CH_2), 1.77 (dddd, ^2J = 13.7 Hz, ^3J = 9.0, 6.1, 6.1 Hz, 1H, HOCH_2CH_2), 2.71 (ddd, ^2J = 20.6 Hz, ^3J = 6.6, 6.6 Hz, 1H, CH_2), 3.00 (m_c, 1H, HOCH_2CH$_2$C*H*), 3.03–3.09 (m, 1H, CH_2), 3.62–3.69 (m, 3H, HOCH_2, EtO_2CC*H*), 4.17 (q, ^3J = 7.1 Hz, 2H, CH_3CH_2), 5.60–5.63 (m, 1H, C*H*), 5.74–5.77 (m, 1H, C*H*), 5.78–5.81 (m, 1H, C*H*), 5.94–5.97 (m, 1H, C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.4, 29.2, 36.0, 36.4, 47.6, 60.9, 61.2, 127.4, 127.6, 129.6, 133.3, 173.6 ppm.

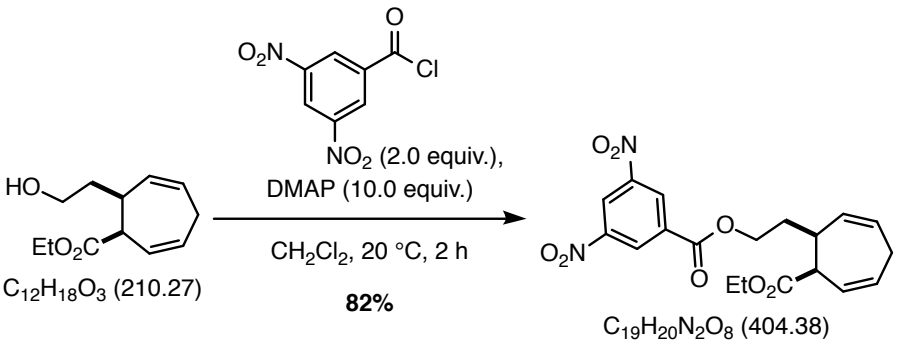
5.8.2 4,4a,7,9a-Tetrahydrocyclohepta[*c*]pyran-1(3*H*)-one (182)



A solution of alcohol **181** (33 mg, 0.16 mmol, 1.0 equiv.) in THF (1.6 mL, 0.1 M) was treated with potassium trimethylsilanolate (41 mg, 0.32 mmol, 2.0 equiv.) at 20 °C. The reaction mixture was stirred at this temperature for 30 min before HCl (1 M in H_2O, 3.0 mL) was added. The mixture was stirred again for 1 h at 20 °C and extracted with Et_2O (3 x 5 mL) afterwards. The combined organic phases were washed with brine (10 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, pentane/ethyl acetate = 4:1) delivered the title compound **182** as colourless oil (10 mg, 61 µmol, 38%).

R_f (pentane/ethyl acetate = 4:1) = 0.6; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{10}H_{13}O_2$, 165.0910, found: 165.0918; **IR (ATR):** $\tilde{\nu}$ = 3016, 2918, 2851, 1721, 1652, 1477, 1402, 1296, 1267, 1188, 1158, 1101, 1072, 1031, 992, 955, 917, 892, 877, 869, 852, 845, 809, 798, 787, 770, 759, 744, 724, 711, 695, 683, 653 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.79–1.87 (m, 1H, CH_2), 1.99–2.05 (m, 1H, CH_2), 2.73–3.02 (m, 3H, CH_2CH, CH_2), 3.29–3.47 (m, 1H, O=CC*H*), 4.31 (ddd, ^2J = 11.4 Hz, ^3J = 10.1, 3.6 Hz, 1H, OCH_2), 4.42 (ddd, ^2J = 11.4 Hz, ^3J = 4.5, 4.5 Hz, 1H, OCH_2), 5.49–5.53 (m, 1H, C*H*), 5.65–5.71 (m, 1H, C*H*), 5.75–5.83 (m, 1H, C*H*), 6.14–6.18 (m, 1H, C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.4, 30.4, 36.5, 45.4, 68.3, 128.6, 128.8, 129.1, 133.7, 172.5 ppm.

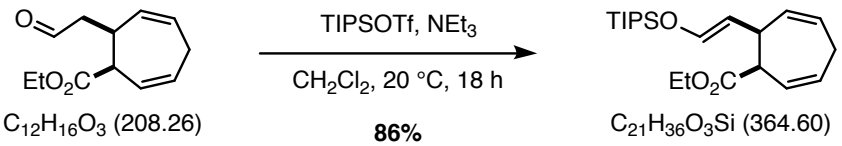
5.8.3 Ethyl 7-(2-((3,5-Dinitrobenzoyl)oxy)ethyl)cyclohepta-2,5-diene-1-carboxylate (183)



A solution of alcohol **181** (38 mg, 0.18 mmol, 1.0 equiv.) in dry CH_2Cl_2 (9.0 mL, 0.02 M) was treated with 4-dimethylaminopyridine (0.22 g, 1.8 mmol, 10 equiv.) and 3,5-dinitrobenzoylchloride (83 mg, 0.36 mg, 2.0 equiv.). The reaction mixture was stirred at 20 °C for 2 h. The solvent was removed *in vacuo* and the residue was purified by column chromatography (silica gel, pentane/ethyl acetate = 10:1) to deliver the title compound **183** as colourless oil which turned solid at −30 °C (60 mg, 0.15 mmol, 82%). Single crystals suitable for diffraction analysis were obtained by diffusion of pentane into a solution of **183** in ethyl acetate **(CCDC: 1877358)**.

R_f (pentane/ethyl acetate = 10:1) = 0.6; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{19}H_{20}N_2NaO_8$, 427.1112, found: 427.110; **IR (ATR):** $\tilde{\nu}$ = 3099, 3017, 2970, 2937, 2906, 1729, 1629, 1598, 1545, 1463, 1345, 1278, 1218, 1167, 1076, 1030, 974, 922, 863, 827, 774, 721 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 1.27 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.94–2.09 (m, 2H, OCH_2CH_2), 2.78 (ddd, ^2J = 21.0 Hz, ^3J = 6.6, 6.6 Hz, 1H, CH_2), 3.00–3.04 (m, 1H, CH_2CH), 3.05–3.12 (m, 1H, CH_2), 3.72 (br s, 1H, EtO_2CCH), 4.19 (q, ^3J = 7.1 Hz, 2H, CH_3CH_2), 4.49 (dd, ^3J = 7.3, 6.3 Hz, 2H, OCH_2), 5.67–5.71 (m, 1H, CH), 5.78–5.85 (m, 2H, 2 x CH), 5.99 (ddd, ^3J = 11.2, 5.4 Hz, ^4J = 2.9 Hz, 1H, CH), 9.16 (d, ^4J = 2.2 Hz, 2H, *H*-Ar), 9.23 (t, ^4J = 2.2 Hz, 1H, *H*-Ar) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 14.4, 29.4, 31.8, 37.0, 47.7, 61.0, 65.7, 122.5, 127.3, 128.4, 129.6 (2*C*), 129.8, 132.0, 134.2 (2*C*), 148.8, 162.6, 173.0 ppm.

5.8.4 Ethyl 7-((*E*)-2-((tri*iso*-propylsilyl)oxy)vinyl)cyclohepta-2,5-diene-1-carboxylate (185)

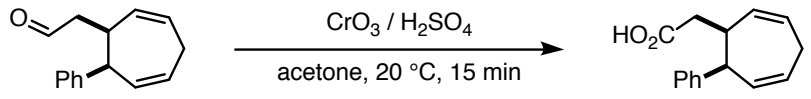


$C_{12}H_{16}O_3$ (208.26) → $C_{21}H_{36}O_3Si$ (364.60)

A solution of triisopropylsilyl trifluoromethanesulfonate (0.15 g, 0.48 mmol, 2.0 equiv.) and triethylamine (49 mg, 0.48 mmol, 2.0 equiv.) in dry CH_2Cl_2 (1.6 mL, 0.15 M) was treated with the aldehyde **109t** (50 mg, 0.24 mmol, 1.0 equiv.). The reaction mixture was stirred at 20 °C for 18 h before the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were dried over $MgSO_4$ and filtrated. The solvent of the filtrate was removed under reduced pressure, the residue was taken up in pentane/ethyl acetate (40:1, 20 mL), and filtrated over silica gel. The solvents of the filtrate were removed *in vacuo* affording the title compound **185** as a colourless oil, that was used in the next step without further purification (75 mg, 0.21 mmol, 86%).

R_f (pentane/ethyl acetate = 40:1) = 0.7; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.99–1.16 (m, 21H, SiC*H*, SiCH_3), 1.27 (t, ^3J = 7.2 Hz, 3H, CH_3), 2.58–2.68 (m, 1H, CH_2), 2.94–3.16 (m, 1H, CH_2), 3.34–3.37 (m, 1H, OCHCHC*H*), 3.75–3.78 (m, 1H, EtO_2CH), 4.15 (q, ^3J = 7.2 Hz, 2H, CH_3CH_2), 4.99 (dd, ^3J = 11.9, 9.2 Hz, 1H, OCHC*H*), 5.52–5.59 (m, 2H, CH), 5.81–5.87 (m, 1H, CH), 6.00–6.05 (m, 1H, CH), 6.32 (d, ^3J = 11.9 Hz, 1H, OC*H*) ppm. The compound decomposed readily so that further analysis could not be obtained. The signals were assigned in analogy to the other cycloheptadienes.

5.8.5 2-(7-Phenylcyclohepta-2,5-dien-1-yl)acetic Acid (186)



$C_{15}H_{16}O$ (212.29) → $C_{15}H_{16}O_2$ (228.29)

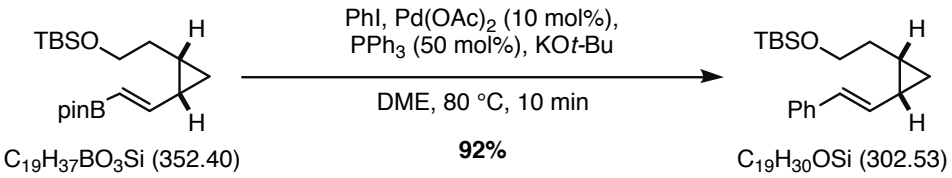
A solution of the aldehyde **109a** (55 mg, 0.26 mmol, 1.0 equiv.) in acetone (0.70 mL, 0.4 M) was treated with Jones reagent (2.5 M in H_2O, 0.10 mL, 0.27 mmol, 1.1 equiv.) at 20 °C and was stirred at this temperature

for 15 min. The reaction was quenched with *i*-PrOH (10 mL) and diluted with H_2O (10 mL). The mixture was extracted with CH_2Cl_2 (3 x 20 mL), the combined organic phases were dried over $MgSO_4$, and filtrated. The solvents of the filtrate were removed under reduced pressure and the residue was purified by column chromatography (silica gel, pentane/ethyl acetate/acetic acid = 100:10:1) affording the title compound **186** as a colourless oil (40 mg, 0.18 mmol, 69%).

R_f (pentane/ethyl acetate = 4:1) = 0.7; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{15}H_{17}O_2$, 229.1223, found: 229.1221; **IR (ATR):** $\tilde{\nu}$ = 3023, 2924, 2818, 2668, 1703, 1653, 1601, 1492, 1451, 1413, 1288, 1227, 1167, 1078, 1031, 933, 878, 826, 795, 762, 702 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 2.29 (dd, ^2J = 15.7 Hz, ^3J = 8.8 Hz, 1H, HO_2CH_2), 2.40 (dd, ^2J = 15.7 Hz, ^3J = 6.6 Hz, 1H, HO_2CH_2), 2.73 (ddd, ^2J = 20.1 Hz, ^3J = 7.0, 7.0 Hz, 1H, CH_2), 3.18–3.26 (m, 1H, CH_2), 3.45–3.51 (m, 1H, $CHCH_2$), 3.69–3.73 (m, 1H, PhC*H*), 5.34 (ddd, ^3J = 9.5, 6.1 Hz, ^4J = 2.3 Hz, 1H, C*H*), 5.71 (ddd, ^3J = 11.7, 5.1 Hz, ^4J = 2.5 Hz, 1H, C*H*), 5.74–5.79 (m, 1H, C*H*), 5.84–5.90 (m, 1H, C*H*), 7.17–7.30 (m, 4H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 28.3, 37.8, 38.7, 47.4, 126.8 (2*C*), 127.1, 128.0 (2*C*), 129.9, 130.1, 132.2, 133.2, 140.9, 179.2 ppm.

5.9 Selective Modification of Lysine

5.9.1 *tert*-Butyldimethyl(2-(2-styrylcyclopropyl)ethoxy)silane (121)

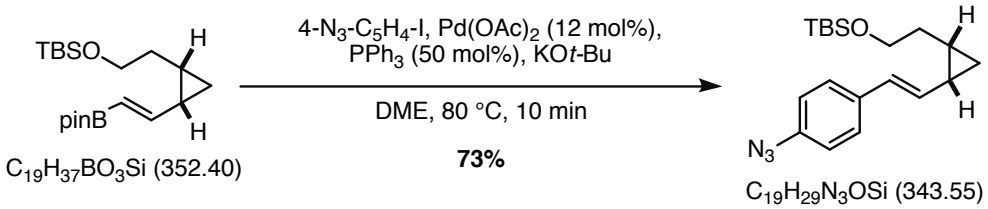


$C_{19}H_{37}BO_3Si$ (352.40) → $C_{19}H_{30}OSi$ (302.53)

A solution of pinacol boronate **157** (50 mg, 0.14 mmol, 1.1 equiv.) and phenyl iodide (26 mg, 0.13 mmol, 1.0 equiv.) in degassed DME (1.60 mL, 0.08 M) was treated with $Pd(OAc)_2$ (3.0 mg, 13 µmol, 10 mol%) and PPh_3 (17 mg, 65 µmol, 50 mol%). The resulting solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 0.26 mL, 0.26 mmol, 2.0 equiv.) was added dropwise over a period of 5 min. After complete addition, the reaction mixture was stirred at 80 °C for 5 min. The mixture was cooled to 20 °C, the reaction was quenched with sat. aq. NH_4Cl (5.0 mL), and extracted with pentane (3 x 15 mL). The combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 200:1). The silyl ether **121** was obtained as a colourless oil (36 mg, 0.12 mmol, 92%).

The spectroscopic data agree with those described in 5.3.6.

5.9.2 ((2-(2-((*E*)-4-Azidostyryl)cyclopropyl)ethoxy)(*tert*-butyl)dimethylsilane (188)

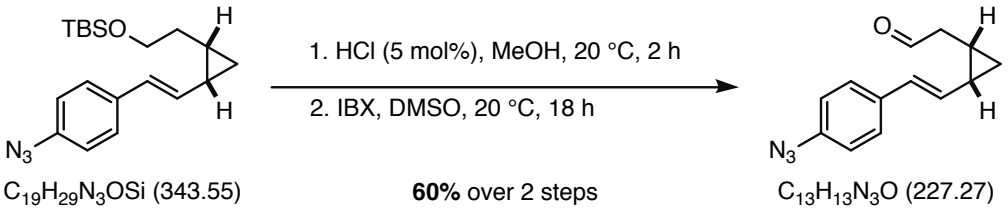


$C_{19}H_{37}BO_3Si$ (352.40) → $C_{19}H_{29}N_3OSi$ (343.55)

A solution of pinacol boronate **157** (0.20 g, 0.57 mmol, 1.1 equiv.) in degassed DME (6.5 mL, 0.08 M) was treated with $Pd(OAc)_2$ (14 mg, 62 µmol, 12 mol%) and PPh_3 (75 mg, 0.29 mmol, 50 mol%). 4-Iodophenylazide (0.13 mg, 0.52 mmol, 1.0 equiv.) was added. The solution was degassed and heated to 80 °C. At this temperature, KO*t*-Bu (1 M in *t*-BuOH, 1.0 mL, 1.0 mmol, 2.0 equiv.) was added dropwise over a period of 5 min. After complete addition, the reaction mixture was stirred at 80 °C for 5 min. The mixture was cooled to 20 °C, the reaction was quenched with sat. aq. NH_4Cl (10 mL), and extracted with pentane (3 x 20 mL). The combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure and the crude product purified by column chromatography (silica gel, pentane/ethyl acetate = 100:1). The silyl ether **188** was obtained as a colourless oil (36 mg, 0.12 mmol, 73%).

R_f (pentane/diethyl ether = 100:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{30}N_3OSi$, 344.2153, found: 344.2157; **IR (ATR):** $\tilde{\nu}$ = 3066, 3021, 2996, 2953, 2928, 2885, 2856, 2413, 2256, 2110, 1645, 1603, 1573, 1505, 1471, 1388, 1361, 1285, 1254, 1181, 1157, 1128, 1097, 1031, 1006, 957, 938, 892, 834, 809, 775, 734 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.04 (s, 6H, SiCH_3), 0.38 (dt, ^2J = 5.3 Hz, ^3J = 5.3 Hz, 1H, *H*-cyclopropyl), 0.89 (s, 9H, CCH_3), 0.97–1.03 (m, 1H, *H*-cyclopropyl), 1.09–1.16 (m, 1H, *H*-cyclopropyl), 1.55–1.70 (m, 3H, CH_2, *H*-cyclopropyl), 3.68 (td, ^3J = 7.0 Hz, ^4J = 1.7 Hz, 2H, OCH_2), 5.92 (dd, ^3J = 15.7, 9.0 Hz, 1H, C*H*), 6.45 (d, ^3J = 15.7 Hz, 1H, C*H*), 6.89–6.99 (m, 2H, *H*-Ar), 7.24–7.33 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = −5.1 (2*C*), 13.4, 16.4, 18.5, 19.3, 26.1 (3*C*), 32.9, 63.4, 119.3 (3*C*), 127.1 (2*C*), 128.9, 130.8, 135.0, 138.1 ppm.

5.9.3 2-(2-((*E*)-4-Azidostyryl)cyclopropyl)acetaldehyde (116c)



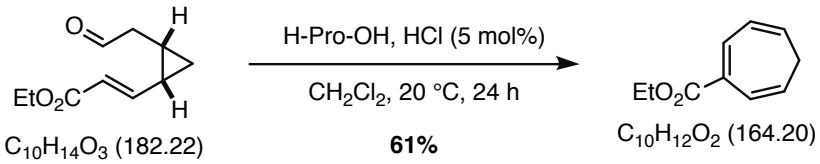
$C_{19}H_{29}N_3OSi$ (343.55) → **60%** over 2 steps → $C_{13}H_{13}N_3O$ (227.27)

A solution of silyl ether **188** (0.27 g, 0.79 mmol, 1.0 equiv.) in MeOH (7.9 mL, 0.1 M) was treated with HCl (10 wt-% in H_2O, 14 µL, 0.36 mmol, 5 mol%) at 20 °C. The reaction mixture was stirred for 2 h and the reaction quenched with sat. aq. $NaHCO_3$ (10 mL). The mixture was extracted with CH_2Cl_2 (3 x 20 mL), and the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and filtrated. The solvents were removed under reduced pressure. The residue was taken up in DMSO (7.9 mL, 0.1 M) and treated with IBX (0.33 g, 1.1 mmol, 1.5 equiv.) at 20 °C. The reaction mixture was stirred for 18 h and the reaction was quenched

with sat. aq. $NaHCO_3$ (10 mL). The mixture was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic phases were washed with brine (3 x 20 mL) thoroughly. The organic phase was dried over $MgSO_4$, filtrated, and the solvents were removed *in vacuo*. The crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1→20:1) to deliver the aldehyde **116c** as a colourless oil (0.11 g, 0.48 mmol, 60% over 2 steps).

R_f (pentane/ethyl acetate = 20:1) = 0.3; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{13}H_{14}N_3O$, 228.1132, found: 228.1138; **IR (ATR):** $\tilde{\nu}$ = 3034, 2999, 2875, 2818, 2719, 2415, 2259, 2109, 1721, 1646, 1601, 1572, 1504, 1449, 1421, 1387, 1284, 1216, 1177, 1128, 1038, 957, 919, 850, 808, 781, 717, 688, 655 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 0.49 (dt, ^2J = 5.4 Hz, ^3J = 5.4 Hz, 1H, *H*-cyclopropyl), 1.14 (td, ^2J = 5.4 Hz, ^3J = 8.3 Hz, 1H, *H*-cyclopropyl), 1.39 (m_c, 1H, *H*-cyclopropyl), 1.74–1.84 (m, 1H, *H*-cyclopropyl), 2.42–2.53 (m, 2H, CH_2), 5.89 (dd, ^3J = 15.7, 8.2 Hz, 1H, C*H*), 6.46 (d, ^3J = 15.7 Hz, 1H, C*H*), 6.93–6.96 (m, 2H, *H*-Ar), 7.27–7.30 (m, 2H, *H*-Ar), 9.80 (t, ^3J = 1.8 Hz, 1H, C*H*O) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 12.5, 12.6, 18.6, 43.7, 119.3 (2*C*), 127.2 (2*C*), 128.8, 130.4, 134.5, 138.6, 202.0 ppm.

5.9.4 Ethyl Cyclohepta-1,3,6-triene-1-carboxylate (207)



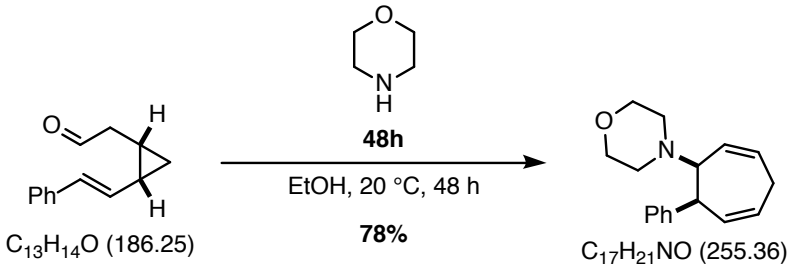
$C_{10}H_{14}O_3$ (182.22) — $C_{10}H_{12}O_2$ (164.20)

A solution of aldehyde **116d** (18 mg, 99 µmol, 1.0 equiv.), L-proline (12 mg, 99 µmol, 1.0 equiv.) in CH_2Cl_2 (1.0 mL, 0.1 M) was treated with HCl (3 M in H_2O, 1.7 uL, 5.0 µmol, 5 mol%) and stirred for 24 h at 20 °C. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, dichloromethane/methanol = 10:1) affording the title compound **207** as a colourless oil (10 mg, 61 µmol, 61%).

R_f (dichloromethane/methanol = 10:1) = 0.4; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.35 (t, ^3J = 7.2 Hz, 3H, CH_3), 2.30 (dd, ^3J = 6.8, 6.8 Hz, 2H, CHCH_2), 4.29 (q, ^3J = 7.2 Hz, 2H, OCH_2), 5.45–5.49 (m, 1H, C*H*), 5.61–5.72 (m, 1H, C*H*), 6.21–6.39 (m, 1H, C*H*), 6.72 (ddd, ^3J = 9.5 Hz, ^4J = 1.1, 0.6 Hz, 1H, C*H*), 7.64–7.80 (m, 1H, C*H*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 14.4, 28.1, 61.1, 121.2, 125.2, 126.1, 126.9, 133.1, 137.2, 167.8 ppm.

The spectroscopic data agree with previously published results.[385]

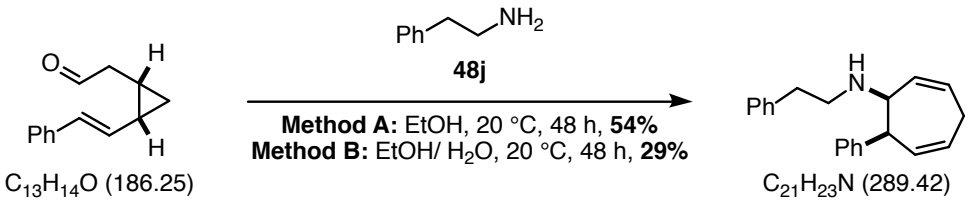
5.9.5 4-(7-Phenylcyclohepta-2,5-dien-1-yl)morpholine (118c)



A solution of aldehyde **116b** (37 mg, 0.20 mmol, 1.0 equiv.) and morpholine (**48h**, 17.4 µL, 0.20 mmol, 1.0 equiv.) in EtOH (2.0 mL, 0.1 M) was stirred for 48 h at 20 °C. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol = 60:1) to deliver the tertiary amine **118c** as a colourless oil (40 mg, 0.16 mmol, 78%).

R_f (dichloromethane/methanol = 40:1) = 0.6; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{22}NO$, 256.1696, found: 256.1689; **IR (ATR):** $\tilde{\nu}$ = 3087, 3056, 3024, 3008, 2955, 2889, 2850, 2807, 1647, 1601, 1494, 1450, 1407, 1392, 1347, 1326, 1265, 1206, 1133, 1117, 1070, 1032, 1017, 955, 921, 881, 795, 763, 725 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 2.54–2.57 (m, 4H, NCH_2), 2.64–2.69 (m, 1H, HCCH_2), 3.15–3.19 (m, 1H, HCCH_2), 3.59 (br s, 1H, NC*H*), 3.64–3.70 (m, 4H, OCH_2), 4.00–4.01 (m, 1H, ArC*H*), 5.55 (ddd, ^3J = 10.9, 6.1 Hz, ^4J = 3.0 Hz, 1H, C*H*), 5.73–5.78 (m, 2H, 2 x C*H*), 5.89–5.93 (m, 1H, C*H*), 7.19–7.22 (m, 1H, *H*-Ar), 7.25–7.27 (m, 2H, *H*-Ar), 7.35–7.36 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 27.8, 45.0, 52.2 (2*C*), 66.7, 67.4 (2*C*), 126.5, 127.2, 127.7 (2*C*), 128.6, 130.1 (2*C*), 132.1, 132.7, 141.3 ppm.

5.9.6 *N*-Phenethyl-7-phenylcyclohepta-2,5-dien-1-amine (118d)



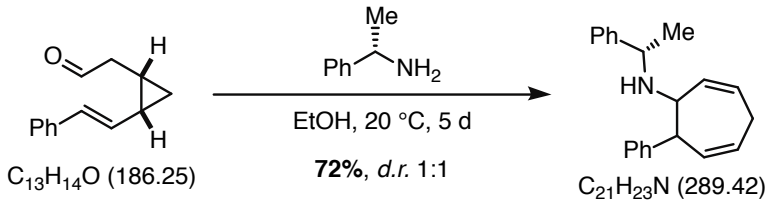
Method A (*Table 3.15*, entry 2): A solution of aldehyde **116b** (37 mg, 0.20 mmol, 1.0 equiv.) and phenethylamine (**48j**, 25 µL, 0.20 mmol, 1.0 equiv.) in EtOH (2.0 mL, 0.1 M) was stirred for 48 h at 20 °C. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol = 40:1) to deliver the secondary amine **118d** as a colourless oil (31 mg, 0.11 mmol, 54%).

Method B (*Table 3.15*, entry 3): A solution of aldehyde **116b** (37 mg, 0.20 mmol, 1.0 equiv.) and phenethylamine (**48j**, 25 uL, 0.20 mmol, 1.0 equiv.) in EtOH/H_2O (1:1, 2.0 mL, 0.1 M) was stirred for 48 h at 20 °C. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol = 40:1) to deliver the secondary amine **118d** as a colourless oil (17 mg,

59 µmol, 29%).

R_f (dichloromethane/methanol = 20:1) = 0.8; **ESI-TOF** (*m/z*): $[M + Na]^+$ calcd for $C_{21}H_{23}NNa$, 312.1722, found: 312.1732; **IR (ATR):** $\tilde{\nu}$ = 3734, 3709, 3648, 3627, 3310, 3082, 3060, 3024, 2924, 2854, 2815, 2359, 2341, 1944, 1648, 1601, 1582, 1541, 1493, 1452, 1385, 1365, 1309, 1180, 1155, 1123, 1079, 1051, 1030, 1003, 961, 930, 910, 866, 795, 747, 724, 697, 667 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.40 (br s, 1H, N*H*), 2.65–2.74 (m, 1H, HCCH_2), 2.79 (t, ^3J = 7.6 Hz, 2H, PhCH_2), 2.92 (ddd, ^2J = 11.4 Hz, ^3J = 7.6, 6.5 Hz, 1H, PhCH_2CH_2), 2.98 (dt, ^2J = 11.4 Hz, ^3J = 7.6 Hz, 1H, PhCH_2CH_2), 3.10–3.17 (m, 1H, HCCH_2), 3.78 (d, ^3J = 5.3 Hz, 1H, NC*H*), 4.01 (br s, 1H, PhC*H*), 5.25 (br s, 1H, C*H*), 5.68 (dddd, ^3J = 11.7, 6.0 Hz, ^4J = 2.9, 0.7 Hz, 1H, C*H*), 5.73–5.78 (m, 1H, C*H*), 5.79–5.84 (m, 1H, C*H*), 7.15–7.23 (m, 8H, *H*-Ar), 7.25–7.30 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 28.2, 36.8, 47.4, 49.1, 58.9, 126.3 (2*C*), 126.7 (2*C*), 127.1 (2*C*), 127.8, 128.0, 128.6 (2*C*), 128.9 (2*C*), 130.0, 131.5, 135.9, 140.3 ppm.

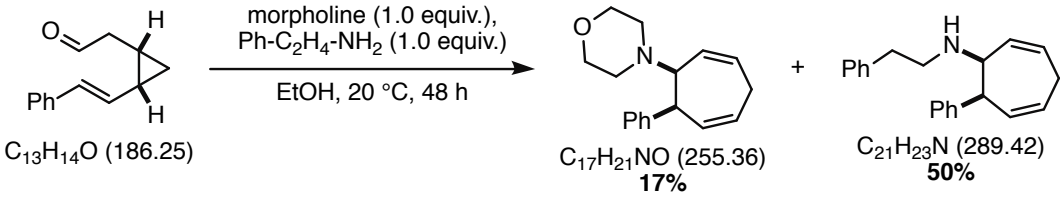
5.9.7 7-Phenyl-*N*-(1-phenylethyl)cyclohepta-2,5-dien-1-amine (118e)



A solution of aldehyde **116b** (75 mg, 0.40 mmol, 1.0 equiv.) and L-α-methyl-benzylamine (52 µL, 0.40 mmol, 1.0 equiv.) in EtOH (4.0 mL, 0.1 M) was stirred for 5 d at 20 °C. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, pentane/ethyl acetate = 40:1) to deliver the title compound **118e** as a colourless oil (83 mg, 0.29 mmol, 72%, *d.r.* 1:1).

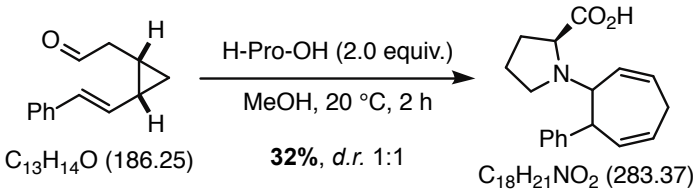
R_f (pentane/ethyl acetate = 40:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{21}H_{24}N$, 290.1903, found: 290.1915; **IR (ATR):** $\tilde{\nu}$ = 3734, 3709, 3675, 3648, 3627, 3329, 3082, 3060, 3023, 2958, 2922, 2868, 2817, 2602, 2359, 2341, 1945, 1877, 1809, 1749, 1685, 1648, 1601, 1583, 1541, 1491, 1465, 1450, 1385, 1368, 1354, 1326, 1308, 1269, 1243, 1202, 1181, 1123, 1078, 1055, 1029, 1006, 956, 938, 911, 866, 829, 796, 759, 743, 721, 698, 666 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.25 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.29 (d, ^3J = 6.5 Hz, 3H, CH_3*), 1.42 (br s, 2H, N*H*, N*H**), 2.63–2.71 (m, 2H, CH_2, CH_2*), 2.95–3.00 (m, 1H, CH_2), 3.00–3.04 (m, 1H, CH_2*), 3.68 (br s, 1H, PhC*H*), 3.71 (br s, 1H, PhC*H**), 3.86–3.93 (m, 3H, NC*H*, NC*H**, NC*H*CH$_3$), 4.02 (q, ^3J = 6.5 Hz, 1H, NC*H*CH$_3$*), 5.24–5.27 (m, 1H, C*H*), 5.48 (br s, 1H, C*H**), 5.64–5.70 (m, 2H, C*H*, C*H**), 5.70–5.73 (m, 2H, C*H*, C*H**), 5.73–5.77 (m, 1H, C*H*), 5.82–5.88 (m, 1H, C*H**), 7.21–7.35 (m, 20H, *H*-Ar, *H*-Ar*) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 24.5, 25.2*, 28.3, 28.4*, 46.7, 49.0*, 54.7, 55.0*, 55.8, 56.0*, 126.6, 126.7 (2*C*), 126.8 (2*C*)*, 126.8*, 126.9 (2*C*), 127.0 (2*C*)*, 127.3, 127.3*, 127.8 (2*C*), 127.9 (2*C*)*, 128.4, 128.5*, 128.5 (2*C*), 128.5, 130.1 (2*C*)*, 131.5*, 131.8, 136.2 (*C*, *C**), 136.3, 140.6*, 145.9, 146.2* ppm. *The signals of the diastereoisomers are indicated. Signals might be exchanged.

5.9.8 Comparison Between the Reaction of Aldehyde 116b With a Primary and a Secondary Amine



A solution of aldehyde **116b** (37 mg, 0.20 mmol, 1.0 equiv.), morpholine (**48h**, 17 µL, 0.20 mmol, 1.0 equiv.), and phenethylamine (**48j**, 25 µL, 0.2 mmol, 1.0 equiv.) in EtOH (2.0 mL, 0.1 M) was stirred for 48 h at 20 °C. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol = 60:1) to deliver a mixed fraction of the amines **118c** and **118d** (30 mg, **118c**:**118d** = 1:3), the amine **118c** (2.0 mg, combined: 9.0 mg, 35 µmol, 17%) and the amine **118d** (6.0 mg, combined: 29 mg, 0.10 mmol, 50%).

5.9.9 (7-Phenylcyclohepta-2,5-dien-1-yl)-L-proline (118f)

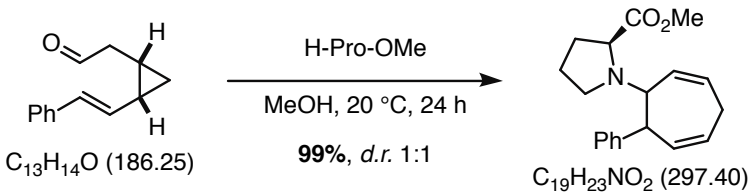


A solution of aldehyde **116b** (37 mg, 0.20 mmol, 1.0 equiv.) and L-proline (46 mg, 0.40 mmol, 2.0 equiv.) in MeOH (2.0 mL, 0.1 M) was stirred for 2 h at 20 °C. The solvents were removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane/methanol/ammonia 7 N in MeOH = 40:3:1) to deliver the title compound **118f** as a yellow oil (18 mg, 64 µmol, 32%, *d.r.* 1:1). **118f** was found to decompose under air for longer than two days and was therefore stored under an argon atmosphere.

R_f (dichloromethane/methanol/ 7 N ammonia in MeOH = 40:3:1) = 0.4; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{22}NO_2$, 284.1645, found: 284.1652; **IR (ATR):** $\tilde{\nu}$ = 3388, 3062, 2952, 2920, 2885, 2853, 1769, 1727, 1491, 1440, 1366 1341, 1268, 1178, 1117, 1056, 1033, 986, 920, 849, 798, 734 cm^{-1}; **^{1}H NMR** (700 MHz, CD_3OD): δ = 1.74–1.87 (m, 2H, pyrrolidine-CH_2, pyrrolidine-CH_2*), 1.92–1.99 (m, 1H, pyrrolidine-CH_2*), 2.07–2.11 (m, 2H, pyrrolidine-CH_2, pyrrolidine-CH_2*), 2.19–2.30 (m, 3H, 2 x pyrrolidine-CH_2, pyrrolidine-CH_2*), 2.83–2.94 (m, 2H, CH_2, CH_2*), 2.96–3.00 (m, 1H, NCH_2*), 3.24–3.29 (m, 3H, N-CH_2, CH_2, CH_2*), 3.38–3.46 (m, 1H, NCH_2*), 3.83 (br s, 1H, CHCO_2H*), 4.01–4.03 (m, 2H, NCH_2, CHCO_2H), 4.17 (br s, 1H, NCH*), 4.24 (br s, 1H, NCH), 4.84 (br s under H_2O signal, 1H, PhCH*), 4.90 (br s, 1H, PhCH), 5.55 (br s, 1H, CH*), 5.74 (br s, 1H, CH), 5.75–5.80 (m, 1H, CH), 5.81–5.91 (m, 3H, CH, 2 x CH*), 6.24–6.27 (m, 1H, CH*), 6.29–6.36 (m, 1H, CH), 7.29–7.35 (m, 2H, *H*-Ar, *H*-Ar*), 7.33–7.40 (m, 4H, *H*-Ar, *H*-Ar*), 7.43–7.49 (m, 4H, *H*-Ar, *H*-Ar*) ppm; **^{13}C NMR** (176 MHz, CD_3OD): δ = 25.1, 25.5*, 28.0*, 28.7, 29.9*, 30.8, 46.1*, 47.4, 53.4*, 56.4, 66.5, 67.2*, 69.2*,

71.0, 124.1, 126.1*, 128.7*, 129.2 (2*C*)*, 129.3 (2*C*), 129.9 (2*C*)*, 129.9 (2*C*), 130.7, 130.9 (*C*, *C**), 131.1, 131.2*, 135.4*, 136.4, 137.7*, 139.0, 172.8, 173.6* ppm. *The signals of the diastereoisomers are indicated. Signals might be exchanged.

5.9.10 Methyl-(7-phenylcyclohepta-2,5-dien-1-yl)-L-prolinate (118g)

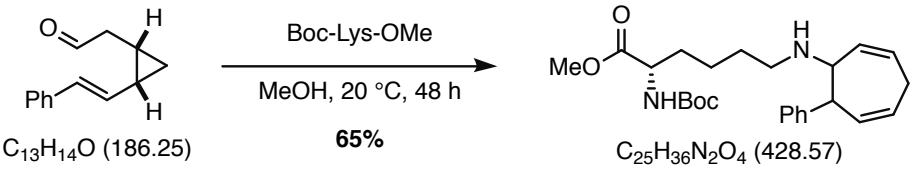


$C_{13}H_{14}O$ (186.25) → $C_{19}H_{23}NO_2$ (297.40)

A solution of aldehyde **116b** (75 mg, 0.40 mmol, 1.0 equiv.) and L-proline methyl ester (0.10 g, 0.80 mmol, 2.0 equiv.) in MeOH (4.0 mL, 0.1 M) was stirred for 24 h at 20 °C. The solvents were removed under reduced pressure and the crude product was purified by MPLC (silica gel, NP4, cyclohexane/ethyl acetate = 95:5→90:10) to deliver the title compound **118g** as a yellow oil (118 mg, 0.40 mmol, 99%, *d.r.* 1:1).

R_f (pentane/ethyl acetate = 20:1) = 0.3; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{24}NO_2$, 298.1802, found: 298.1814; **IR (ATR):** $\tilde{\nu}$ = 3066, 3024, 3008, 2950, 2871, 1734, 1647, 1601, 1550, 1492, 1452, 1434, 1365, 1277, 1196, 1166, 1088, 1032, 1002, 869, 797, 758, 721 cm^{-1}; **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 1.71–1.78 (m, 2H, NCH_2CH_2, NCH_2CH_2*), 1.81–1.87 (m, 3H, $NCHCH_2$, $NCHCH_2$*, NCH_2CH_2*), 1.88–2.01 (m, 3H, $NCHCH_2$, $NCHCH_2$*, NCH_2CH_2*), 2.61–2.70 (m, 2H, C=C*H*, C=C*H**), 2.75–2.78 (m, 1H, NCH_2*), 2.86–2.93 (m, 2H, NCH_2), 3.07–3.11 (m, 1H, NCH_2*), 3.12–3.15 (m, 1H, C=C*H*), 3.15–3.18 (m, 1H, C=C*H**), 3.48 (s, 3H, CH_3*), 3.57 (dd, ^3J = 8.1, 4.0 Hz, 1H, NC*H*), 3.62 (s, 3H, CH_3), 3.63–3.66 (m, 1H, NC*H**), 3.88–3.90 (m, 1H, NC*H*), 3.93–3.94 (m, 1H, NC*H**), 4.00 (br s, 1H, PhC*H*), 4.14 (br s, 1H, PhC*H**), 5.54–5.61 (m, 2H, C*H*, C*H**), 5.68–5.73 (m, 4H, 2 x C*H*, 2 x C*H**), 5.83–5.92 (m, 1H, C*H*, C*H**), 7.15–7.21 (m, 2H, *H*-Ar, *H*-Ar*), 7.21–7.28 (m, 4H, 2 x *H*-Ar, 2 x *H*-Ar*), 7.31–7.35 (m, 2H, *H*-Ar*), 7.39–7.43 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 23.8*, 24.5, 27.9*, 28.0, 29.4*, 30.7, 47.8, 48.0*, 49.9, 51.4, 51.5*, 52.3*, 62.5*, 62.6*, 63.4, 63.9, 126.3*, 126.4, 126.9*, 127.1, 127.6 (2*C**), 127.8 (2*C*), 128.5*, 129.2, 129.8 (2*C*), 130.1 (2*C**), 130.7, 132.2*, 133.1, 133.3*, 141.8, 141.9*, 175.2, 176.0* ppm. *The signals of the diastereoisomers are indicated. Signals might be exchanged.

5.9.11 Methyl-N^2-(*tert*-butoxycarbonyl)-N^6-(7-phenylcyclohepta-2,5-dien-1-yl)-L-lysinate (118h)



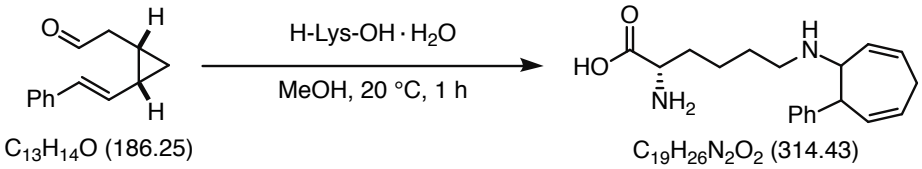
$C_{13}H_{14}O$ (186.25) → $C_{25}H_{36}N_2O_4$ (428.57)

A solution of aldehyde **116b** (37 mg, 0.20 mmol, 1.0 equiv.) and Boc-Lys-OMe (0.10 g, 0.40 mmol, 2.0 equiv.) in MeOH (2.0 mL, 0.1 M) was stirred for 48 h at 20 °C. The solvent was removed under reduced pressure and

the crude product was purified by column chromatography (silica gel, dichloromethane/methanol = 20:1) to deliver the title compound **118h** as a yellow oil (56 mg, 0.13 mmol, 65%, *d.r.* could not be determined since there are no isolated signals in the proton spectrum available).

R_f (dichloromethane/methanol = 20:1) = 0.6; **ESI-TOF** (*m/z*): $[M + H]^+$ calcd for $C_{25}H_{37}N_2O_4$, 429.2748, found: 429.2764; **IR (ATR):** $\tilde{\nu}$ = 3331, 3014, 2977, 2931, 2865, 1745, 1697, 1603, 1495, 1470, 1454, 1436, 1418, 1390, 1365, 1335, 1297, 1249, 1216, 1162, 1095, 1054, 1019, 941, 905, 867, 826, 753, 703 cm^{-1}; **^{1}H NMR** (700 MHz, CD_3OD): δ = 1.32–1.39 (m, 2H, CH_2), 1.43 (s, 9H, CH_3), 1.47–1.54 (m, 2H, CH_2), 1.59–1.67 (m, 1H, CH_2), 1.74–1.78 (m, 1H, CH_2), 2.61–2.69 (m, 2H, HNCH_2), 2.73 (ddd, ^2J = 19.6 Hz, ^3J = 7.7, 7.7 Hz, 1H, HCCH_2), 3.16–3.20 (m, 1H, HCCH_2), 3.69 (s, 3H, OCH_3), 3.83 (br s, 1H, ArC*H*), 4.07–4.09 (m, 2H, HNC*H*,HNC*H*), 5.30–5.33 (m, 1H, C*H*), 5.65 (ddd, ^3J = 11.9, 6.0 Hz, ^4J = 2.9 Hz, 1H, C*H*), 5.73–5.80 (m, 1H, C*H*), 5.91–5.95 (m, 1H, C*H*), 7.19–7.24 (m, 1H, *H*-Ar), 7.25–7.28 (m, 2H, *H*-Ar), 7.29–7.31 (m, 2H, *H*-Ar) ppm; **^{13}C NMR** (176 MHz, CD_3OD): δ = 24.7, 28.6, 28.7 (3*C*), 29.7, 32.4, 32.4, 47.9, 52.6, 54.9, 59.9, 80.5, 127.8, 128.0, 128.9 (2*C*), 130.1, 131.2 (2*C*), 132.3, 135.4, 140.6, 158.1, 174.9 ppm. Only the signals of the major diastereoisomer are indicated.

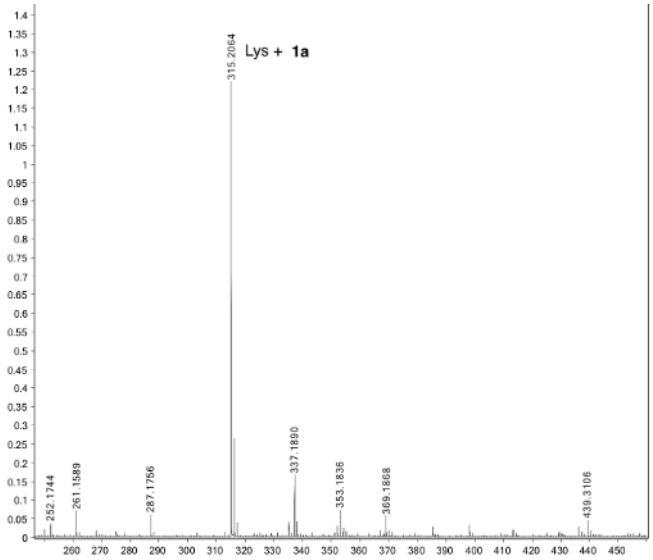
5.9.12 N^6-(7-Phenylcyclohepta-2,5-dien-1-yl)-L-lysine (118i)



$C_{13}H_{14}O$ (186.25) → $C_{19}H_{26}N_2O_2$ (314.43)

A solution of aldehyde **116b** (5 mg, 27 µmol, 1.0 equiv.) and H-Lys-OH·H_2O (8.8 mg, 54 µmol, 2.0 equiv.) in MeOH (0.3 mL, 0.1 M) was stirred for 1 h at 20 °C. TLC and GC-MS showed complete conversion but only a complex mixture could be obtained.

ESI-TOF (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{26}N_2O_2$, 315.2067, found: 315.2064.



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Appendix

List of Abbreviations

d.r.	diastereomeric ratio
*p*PTS	pyridinium *para*-toluenesulfonate
*p*TSA	*para*-toluenesulfonic acid
1,2-DCE	1,2-dichloroethane
AcOH	acetic acid
aq.	aqueous
Asp	aspartic acid
ATR	attenuated total reflection
bp	boiling point
BPhen	bathophenanthroline
bpy	bipyridine
br	broad
brsm	based on recovered starting material
BzOH	benzoic acid
calcd	calculated
CAN	cer ammonium nitrate
CCDC	Cambridge Crystallographic Data Centre
Cys	cysteine

d	doublet
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicarboxylate
DIBAL–H	diisobutylaluminium hydride
DMAP	4-dimethylaminopyridine
DME	dimethoxyethane
DMF	dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethylsulfoxide
DVCPR	divinylcyclopropane-cycloheptadiene rearrangement
E	electrophile(s)
E_P	electrophilicity parameter(s)
ee	enantiomeric excess
eGFP	enhanced green fluorescent protein
equiv.	equivalent(s)
ESI	electrospray ionisation
EtOAc	ethyl acetate
EWG	electron withdrawing group(s)
GC-MS	gas chromatography/ mass spectrometry
GP	general procedure
h	hour(s)
HBeAg	hepatitis B viral protein
HBsAg	hepatitis B virus surface antigen
His	histidine
HOMO	highest occupied molecular orbital
HPLC	high-performance liquid chromatography

IBX	2-iodoxybenzoic acid
IR	infrared
KHMDS	potassium bis(trimethylsilyl)amide
LC-MS/MS	liquid chromatography-mass spectrometry/mass spectrometry
LUMO	lowest unoccupied molecular orbital
Lys	lysine
m	multiplet
m_c	centred multiplet
min	minute(s)
MIRC	Michael-initiated ring closure
MPLC	medium pressure liquid chromatography
NHS	*N*-hydroxysuccinimide
NMI	*N*-methyl imidazole
NMO	*N*-methylmorpholine *N*-oxide
NOE	nuclear Oberhauser effect
NP	normal phase
Nu	nucleophile(s)
p	quintet
PBS	phosphate-buffered saline
PDC	pyridinium dichromate
ppm	parts per milion
Pro	proline
q	quartet
quant.	quantitative
R_f	retention factor
s	singlet

S_N	nucleophilic substitution
sat.	saturated
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
Ser	serine
SOMO	single occupied molecular orbital
SPAAC	strain-promoted-azide-alkyne-cycloaddition
t	triplett
$t_{1/2}$	half-life
TBAF	tetrabutyl ammonium fluoride
TCT	cyanuric chloride
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
TFA	trifluoroacetic acid
THF	tetrahydrofurane
TLC	thin layer chromatography
TMP	2,2,6,6-tetramethylpiperidine
TOF	time of flight
Trp	tryptophan
Tyr	tyrosine
wt-%	weight-%
XantPhos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

InChI codes of synthesised compounds

Compound	InChI code
122	OSGGKOOYEDWDJN-UHFFFAOYSA-N InChI=1S/C14H12N4O2S/c19-21(20,11-12-7-3-1-4-8-12)14-15-16-17-18(14)13-9-5-2-6-10-13/h1-10H,11H2
124	LYDCXLSTPOXWLS-UHFFFAOYSA-N InChI=1S/C22H22BrO2P/c23-26(18-22-24-16-17-25-22,19-10-4-1-5-11-19,20-12-6-2-7-13-20)21-14-8-3-9-15-21/h1-15,22H,16-18H2
171	HBYHPBCAZBLFTD-UHFFFAOYSA-N InChI=1S/C8H11F6O5P/c1-2-17-6(15)3-20(16,18-4-7(9,10)11)19-5-8(12,13)14/h2-5H2,1H3
61	OGCGXUGBDJGFFY-INIZCTEOSA-N InChI=1S/C17H19NO/c19-17(16-12-7-13-18-16,14-8-3-1-4-9-14)15-10-5-2-6-11-15/h1-6,8-11,16,18-19H,7,12-13H2/t16-/m0/s1
48c	RSUHWMSTWSSNOW-IBGZPJMESA-N InChI=1S/C20H27NOSi/c1-23(2,3)22-20(19-15-10-16-21-19,17-11-6-4-7-12-17)18-13-8-5-9-14-18/h4-9,11-14,19,21H,10,15-16H2,1-3H3/t19-/m0/s1
48d	UJBVRSVKZAQAMP-LJAQVGFWSA-N InChI=1S/C34H27F12NOSi/c1-49(27-9-4-2-5-10-27,28-11-6-3-7-12-28)48-30(29-13-8-14-47-29,21-15-23(31(35,36)37)19-24(16-21)32(38,39)40)22-17-25(33(41,42)43)20-26(18-22)34(44,45)46/h2-7,9-12,15-20,29,47H,8,13-14H2,1H3/t29-/m0/s1
48b	UACYWOJLWBDSHG-UHFFFAOYSA-N InChI=1S/C13H18N2O/c1-13(2)14-11(12(16)15(13)3)9-10-7-5-4-6-8-10/h4-8,11,14H,9H2,1-3H3
48b	YLBWRMSQRFEIEB-VIFPVBQESA-N InChI=1S/C9H18N2/c1-2-7-11(6-1)8-9-4-3-5-10-9/h9-10H,1-8H2/t9-/m0/s1
153	BYLXGCMSNMEIEM-BQYQJAHWSA-N InChI=1S/C11H13BO2/c1-2-5-11(6-3-1)7-8-12-13-9-4-10-14-12/h1-3,5-8H,4,9-10H2/b8-7+
155	GQFQFYFLABSDDS-UHFFFAOYSA-N InChI=1S/C7H13BCl2O2/c1-6(2)7(3,4)12-8(11-6)5(9)10/h5H,1-4H3
197	MQYZGGWWHUGYDR-UHFFFAOYSA-N InChI=1S/C13H26B2O4/c1-10(2)11(3,4)17-14(16-10)9-15-18-12(5,6)13(7,8)19-15/h9H2,1-8H3
198	NUZBJLXXTAOBPH-UHFFFAOYSA-N InChI=1S/C10H20OSi/c1-7-8-9-11-12(5,6)10(2,3)4/h1H,8-9H2,2-6H3
119	HHKHLMZEHVBXRG-UHFFFAOYSA-N InChI=1S/C11H22O2Si/c1-11(2,3)14(4,5)13-10-8-6-7-9-12/h12H,8-10H2,1-5H3
114	XPMXAAGISRJZIU-SREVYHEPSA-N InChI=1S/C11H24O2Si/c1-11(2,3)14(4,5)13-10-8-6-7-9-12/h6-7,12H,8-10H2,1-5H3/b7-6-

Compound	InChI code
120	RYCABMPYBHYKIB-GHMZBOCLSA-N InChI=1S/C12H26O2Si/c1-12(2,3)15(4,5)14-7-6-10-8-11(10)9-13/h10-11,13H,6-9H2,1-5H3/t10-,11-/m1/s1
113	NOOWXHOKVIQAFQ-GHMZBOCLSA-N InChI=1S/C12H24O2Si/c1-12(2,3)15(4,5)14-7-6-10-8-11(10)9-13/h9-11H,6-8H2,1-5H3/t10-,11-/m1/s1
(*E*)-121	RZOWPXOVPDFYRL-AAIOHFERSA-N InChI=1S/C19H30OSi/c1-19(2,3)21(4,5)20-14-13-18-15-17(18)12-11-16-9-7-6-8-10-16/h6-12,17-18H,13-15H2,1-5H3/b12-11+/t17-,18+/m0/s1
(*Z*)-121	RZOWPXOVPDFYRL-IXTIOBCPSA-N InChI=1S/C19H30OSi/c1-19(2,3)21(4,5)20-14-13-18-15-17(18)12-11-16-9-7-6-8-10-16/h6-12,17-18H,13-15H2,1-5H3/b12-11-/t17-,18+/m0/s1
123	MDCNDVKFCLXITF-NWDGAFQWSA-N InChI=1S/C13H26OSi/c1-7-11-10-12(11)8-9-14-15(5,6)13(2,3)4/h7,11-12H,1,8-10H2,2-6H3/t11-,12+/m0/s1
116b	HFHBKGZYQSGLIK-VFZNBBLXSA-N InChI=1S/C13H14O/c14-9-8-13-10-12(13)7-6-11-4-2-1-3-5-11/h1-7,9,12-13H,8,10H2/b7-6+/t12-,13+/m0/s1
109a	ZGQZRVUKTQCRGP-RHPSVNQBSA-N InChI=1S/C15H16O/c16-11-5-4-8-14-12-15(14)10-9-13-6-2-1-3-7-13/h1-7,9-11,14-15H,8,12H2/b5-4+,10-9+/t14-,15+/m1/s1
200	NOOWXHOKVIQAFQ-MNOVXSKESA-N InChI=1S/C12H24O2Si/c1-12(2,3)15(4,5)14-7-6-10-8-11(10)9-13/h9-11H,6-8H2,1-5H3/t10-,11+/m1/s1
201	WUSYOXMBHSPDCG-QJPMGVOCSA-N InChI=1S/C19H30OSi.C12H24O2Si/c1-19(2,3)21(4,5)20-14-13-18-15-17(18)12-11-16-9-7-6-8-10-16;1-12(2,3)15(4,5)14-7-6-10-8-11(10)9-13/h6-12,17-18H,13-15H2,1-5H3;9-11H,6-8H2,1-5H3/b12-11+;/t17-,18-;10-,11+/m11/s1
202	HFHBKGZYQSGLIK-AMRKSYTLSA-N InChI=1S/C13H14O/c14-9-8-13-10-12(13)7-6-11-4-2-1-3-5-11/h1-7,9,12-13H,8,10H2/b7-6+/t12-,13-/m1/s1
203	LDCVUAPPMDTKOY-BHRPGFAJSA-N InChI=1S/C15H16O.C13H14O/c16-11-5-4-8-14-12-15(14)10-9-13-6-2-1-3-7-13;14-9-8-13-10-12(13)7-6-11-4-2-1-3-5-11/h1-7,9-11,14-15H,8,12H2;1-7,9,12-13H,8,10H2/b5-4+,10-9+;7-6+/t14-,15-;12-,13-/m11/s1
129	FSUXYWPILZJGCC-IHWYPQMZSA-N InChI=1S/C5H10O/c1-2-3-4-5-6/h2-3,6H,4-5H2,1H3/b3-2-
125a	OFDXEXATDZHVGU-VPNLLINDSA-N InChI=1S/C14H17ClO/c1-11-13(15)9-10-16-14(11)8-7-12-5-3-2-4-6-12/h2-8,11,13-14H,9-10H2,1H3/b8-7+/t11-,13+,14+/m0/s1

Compound	InChI code
131	RIQSBRCEMVBEJE-NEDDKPEDSA-N InChI=1S/C14H18O/c1-11-13(14(11)9-10-15)8-7-12-5-3-2-4-6-12/h2-8,11,13-15H,9-10H2,1H3/b8-7+/t11-,13-,14+/m0/s1
204	UVXYZMRNCYQWAV-NEDDKPEDSA-N InChI=1S/C14H16O/c1-11-13(14(11)9-10-15)8-7-12-5-3-2-4-6-12/h2-8,10-11,13-14H,9H2,1H3/b8-7+/t11-,13-,14+/m0/s1
109b	BWUJIWJFFNFJIU-ZWWFZDCKSA-N InChI=1S/C16H18O.C14H16O/c1-13-15(9-5-6-12-17)16(13)11-10-14-7-3-2-4-8-14;1-11-13(14(11)9-10-15)8-7-12-5-3-2-4-6-12/h2-8,10-13,15-16H,9H2,1H3;2-8,10-11,13-14H,9H2,1H3/b6-5+,11-10+;8-7+/t13-,15-,16+;11-,13-,14+/m10/s1
125b	FGFYGXJZMVNWPB-HIHHVFROSA-N InChI=1S/C10H17FO/c1-8(2)3-4-10-7-9(11)5-6-12-10/h3-4,8-10H,5-7H2,1-2H3/b4-3+/t9-,10-/m1/s1
132	QPIUCMITGZBTKC-FCVPOFOPSA-N InChI=1S/C10H18O/c1-8(2)3-4-9-7-10(9)5-6-11/h3-4,8-11H,5-7H2,1-2H3/b4-3+/t9-,10+/m0/s1
205	HHCCMEBKRXQUBA-FCVPOFOPSA-N InChI=1S/C10H16O/c1-8(2)3-4-9-7-10(9)5-6-11/h3-4,6,8-10H,5,7H2,1-2H3/b4-3+/t9-,10+/m0/s1
109c	KQFCCAORUSPXAY-MXYKJOAXSA-N InChI=1S/C12H18O.C10H16O/c1-10(2)6-7-12-9-11(12)5-3-4-8-13;1-8(2)3-4-9-7-10(9)5-6-11/h3-4,6-8,10-12H,5,9H2,1-2H3;3-4,6,8-10H,5,7H2,1-2H3/b4-3+,7-6+;4-3+/t11-,12+;9-,10+/m10/s1
143	JDTSGIGHGUYHME-OWOJBTEDSA-N InChI=1S/C4H5BrO/c5-3-1-2-4-6/h1-2,4H,3H2/b2-1+
138	WKOCFKKBWSKFCI-OWOJBTEDSA-N InChI=1S/C6H9BrO2/c7-3-1-2-6-8-4-5-9-6/h1-2,6H,3-5H2/b2-1+
140	WBZVZQXZHVPZPT-VLFPEWDESA-N InChI=1S/C9H12O3.C6H9BrO2/c10-6-4-2-1-3-5-9-11-7-8-12-9;7-3-1-2-6-8-4-5-9-6/h3,5,9-10H,1,6-8H2;1-2,6H,3-5H2/b5-3+;2-1+
139	PDSHOEHTTNOYDA-VOERYJCWSA-N InChI=1S/C9H14O3/c10-6-4-2-1-3-5-9-11-7-8-12-9/h2-5,9-10H,1,6-8H2/b4-2-,5-3+
148	MYPANVIEHPLGMQ-TXBNAWBVSA-N InChI=1S/C13H25IOSi/c1-13(2,3)16(4,5)15-9-7-12-10-11(12)6-8-14/h6,8,11-12H,7,9-10H2,1-5H3/b8-6+/t11-,12+/m0/s1
149	VHPHMQOCEQNLKC-YPIXSHMWSA-N InChI=1S/C7H9IO/c8-3-1-6-5-7(6)2-4-9/h1,3-4,6-7H,2,5H2/b3-1+/t6-,7+/m0/s1
133	WRCPDPNORKHQGI-GXKCBUAXSA-N InChI=1S/C11H15IO2/c12-5-4-10-8-9(10)2-1-3-11-13-6-7-14-11/h1,3-5,9-11H,2,6-8H2/b3-1-,5-4+/t9-,10+/m1/s1
150	JSNBBWDLAWZBMX-PICDLYDTSA-N InChI=1S/C17H20O2/c1-2-5-14(6-3-1)9-10-16-13-15(16)7-4-8-17-18-11-12-19-17/h1-6,8-10,15-17H,7,11-13H2/b8-4-,10-9+/t15-,16+/m1/s1

Compound	InChI code
152	BVFIWFJYUCGITP-GHMZBOCLSA-N InChI=1S/C12H25IOSi/c1-12(2,3)15(4,5)14-7-6-10-8-11(10)9-13/h10-11H,6-9H2,1-5H3/t10-,11-/m1/s1
154	KCEVQRYEXFSRSO-AOOXPWSASA-N InChI=1S/C19H37BO3Si/c1-17(2,3)24(8,9)21-13-11-16-14-15(16)10-12-20-22-18(4,5)19(6,7)23-20/h10,12,15-16H,11,13-14H2,1-9H3/b12-10+/t15-,16+/m0/s1
206	SLXRMHKPUWDXEH-KKSDUGGKSA-N InChI=1S/C13H23BO3/c1-12(2)13(3,4)17-14(16-12)7-5-10-9-11(10)6-8-15/h5,7,10-11,15H,6,8-9H2,1-4H3/b7-5+/t10-,11+/m0/s1
156	FUFIVTNXFJJOSC-KKSDUGGKSA-N InChI=1S/C13H21BO3/c1-12(2)13(3,4)17-14(16-12)7-5-10-9-11(10)6-8-15/h5,7-8,10-11H,6,9H2,1-4H3/b7-5+/t10-,11+/m0/s1
157	FMJIBKSDKVQMNR-HUEKLUQDSA-N InChI=1S/C17H27BO4/c1-16(2)17(3,4)22-18(21-16)9-8-14-12-13(14)6-5-7-15-19-10-11-20-15/h5,7-9,13-15H,6,10-12H2,1-4H3/b7-5-,9-8+/t13-,14+/m1/s1
109d	QYHQXZFFFWSDMT-JXCUUXDUSA-N InChI=1S/C16H15F3O/c17-16(18,19)15-8-5-12(6-9-15)4-7-14-11-13(14)3-1-2-10-20/h1-2,4-10,13-14H,3,11H2/b2-1+,7-4+/t13-,14+/m1/s1
109e	GSHVDXRIYIOINO-FLECDUFJSA-N InChI=1S/C16H15F3O/c17-16(18,19)15-6-3-4-12(10-15)7-8-14-11-13(14)5-1-2-9-20/h1-4,6-10,13-14H,5,11H2/b2-1+,8-7+/t13-,14+/m1/s1
109f	NMJXPLNQHAUWSM-MLBWORRFSA-N InChI=1S/C16H15F3O/c17-16(18,19)15-7-2-1-5-12(15)8-9-14-11-13(14)6-3-4-10-20/h1-5,7-10,13-14H,6,11H2/b4-3+,9-8+/t13-,14+/m1/s1
109g	LRMNGRSOCOFMHE-JXCUUXDUSA-N InChI=1S/C15H15NO3/c17-10-2-1-3-13-11-14(13)7-4-12-5-8-15(9-6-12)16(18)19/h1-2,4-10,13-14H,3,11H2/b2-1+,7-4+/t13-,14+/m1/s1
109h	FFVZYDXPAFMNDW-JXCUUXDUSA-N InChI=1S/C15H15ClO/c16-15-8-5-12(6-9-15)4-7-14-11-13(14)3-1-2-10-17/h1-2,4-10,13-14H,3,11H2/b2-1+,7-4+/t13-,14+/m1/s1
109i	ZFHOBWJCQJYAPU-JXCUUXDUSA-N InChI=1S/C15H15FO/c16-15-8-5-12(6-9-15)4-7-14-11-13(14)3-1-2-10-17/h1-2,4-10,13-14H,3,11H2/b2-1+,7-4+/t13-,14+/m1/s1
109j	JYHFODNDPDGNLK-FLECDUFJSA-N InChI=1S/C15H15ClO/c16-15-6-3-4-12(10-15)7-8-14-11-13(14)5-1-2-9-17/h1-4,6-10,13-14H,5,11H2/b2-1+,8-7+/t13-,14+/m1/s1
109k	KGHJKRHYJSNMED-FLECDUFJSA-N InChI=1S/C15H15FO/c16-15-6-3-4-12(10-15)7-8-14-11-13(14)5-1-2-9-17/h1-4,6-10,13-14H,5,11H2/b2-1+,8-7+/t13-,14+/m1/s1

Compound	InChI code
109l	IYMSIEMEBBVKIH-MLBWORRFSA-N InChI=1S/C15H15FO/c16-15-7-2-1-5-12(15)8-9-14-11-13(14)6-3-4-10-17/h1-5,7-10,13-14H,6,11H2/b4-3+,9-8+/t13-,14+/m1/s1
109m	JXESFZYQSBJWRS-BGZYEUMYSA-N InChI=1S/C14H15NO/c16-10-4-2-5-12-11-13(12)7-8-14-6-1-3-9-15-14/h1-4,6-10,12-13H,5,11H2/b4-2+,8-7+/t12-,13+/m1/s1
109n	LMEIRPXYVUSXCK-IHFQYPRESA-N InChI=1S/C16H18O/c1-13-5-7-14(8-6-13)9-10-16-12-15(16)4-2-3-11-17/h2-3,5-11,15-16H,4,12H2,1H3/b3-2+,10-9+/t15-,16+/m1/s1
109o	QTGLKUMVMFQTND-CVDYVIDOSA-N InChI=1S/C19H24O/c1-19(2,3)18-11-8-15(9-12-18)7-10-17-14-16(17)6-4-5-13-20/h4-5,7-13,16-17H,6,14H2,1-3H3/b5-4+,10-7+/t16-,17+/m1/s1
109p	VKLYNBSLAKMLPR-OYYCDXOVSA-N InChI=1S/C19H22O/c20-15-9-8-14-19-16-18(19)13-7-2-1-4-10-17-11-5-3-6-12-17/h1-3,5-9,11-13,15,18-19H,4,10,14,16H2/b2-1+,9-8+,13-7+/t18-,19+/m0/s1
109r	TWVJULVMIZUUHV-DXMIZCBPSA-N InChI=1S/C9H12O/c1-2-8-7-9(8)5-3-4-6-10/h2-4,6,8-9H,1,5,7H2/b4-3+/t8-,9+/m0/s1
158	MYMSNUXRUXQMEK-MXWNMBBBSA-N InChI=1S/C16H20O3/c1-18-12-4-2-9(3-5-12)16-15-11(8-14(17)19-16)6-10-7-13(10)15/h2-5,10-11,13-17H,6-8H2,1H3/t10-,11-,13+,14+,15-,16-/m1/s1
159	MOQVCKPKTFZTSK-ITXLKETKSA-N InChI=1S/C13H16O2S/c14-11-6-8-4-7-5-9(7)12(8)13(15-11)10-2-1-3-16-10/h1-3,7-9,11-14H,4-6H2/t7-,8-,9+,11+,12-,13-/m1/s1
160	ZLNGRJBUELDXED-MFXKQFABSA-N InChI=1S/C18H22O3/c1-19-17-9-6-14(7-10-17)5-8-16-13-15(16)3-2-4-18-20-11-12-21-18/h2,4-10,15-16,18H,3,11-13H2,1H3/b4-2+,8-5+/t15-,16+/m1/s1
109q	XTOAPEMAYBETND-UAGGOGPXSA-N InChI=1S/C16H18O2/c1-18-16-9-6-13(7-10-16)5-8-15-12-14(15)4-2-3-11-17/h2-3,5-11,14-15H,4,12H2,1H3/b3-2+,8-5+/t14-,15+/m1/s1
161	KGTOAMVJSPTWEL-XNOXLNHLSA-N InChI=1S/C15H18O2S/c1(5-15-16-8-9-17-15)3-12-11-13(12)6-7-14-4-2-10-18-14/h1-2,4-7,10,12-13,15H,3,8-9,11H2/b5-1+,7-6+/t12-,13+/m1/s1
109s	BRJYFXCQJDAERC-XYSARSPMSA-N InChI=1S/C13H14OS/c14-8-2-1-4-11-10-12(11)6-7-13-5-3-9-15-13/h1-3,5-9,11-12H,4,10H2/b2-1+,7-6+/t11-,12+/m1/s1
162	GVYNXASBLDMNPA-NYCDYWJRSA-N InChI=1S/C16H30O3Si/c1-7-18-15(17)9-8-13-12-14(13)10-11-19-20(5,6)16(2,3)4/h8-9,13-14H,7,10-12H2,1-6H3/b9-8+/t13-,14+/m0/s1

Compound	InChI code
116d	OPQXFAQBYBCUHX-DXMIZCBPSA-N InChI=1S/C10H14O3/c1-2-13-10(12)4-3-8-7-9(8)5-6-11/h3-4,6,8-9H,2,5,7H2,1H3/b4-3+/t8-,9+/m0/s1
109t	HXLLQTJUOQFIGP-DWENZHRASA-N InChI=1S/C12H16O3.C10H14O3/c1-2-15-12(14)7-6-11-9-10(11)5-3-4-8-13;1-2-13-10(12)4-3-8-7-9(8)5-6-11/h3-4,6-8,10-11H,2,5,9H2,1H3;3-4,6,8-9H,2,5,7H2,1H3/b4-3+,7-6+;4-3+/t10-,11+;8-,9+/m10/s1
163	LSUABYNHBZSUJN-VFZNBBLXSA-N InChI=1S/C14H25NOSi/c1-14(2,3)17(4,5)16-10-8-13-11-12(13)7-6-9-15/h6-7,12-13H,8,10-11H2,1-5H3/b7-6+/t12-,13+/m0/s1
(*E*)-164	AHAIGWXQYODCFZ-PPYPBTKYSA-N InChI=1S/C8H9NO/c9-4-1-2-7-6-8(7)3-5-10/h1-2,5,7-8H,3,6H2/b2-1+/t7-,8+/m0/s1
(*Z*)-164	AHAIGWXQYODCFZ-WFWQCHFMSA-N InChI=1S/C8H9NO/c9-4-1-2-7-6-8(7)3-5-10/h1-2,5,7-8H,3,6H2/b2-1-/t7-,8+/m0/s1
109u	FQJBYLWIMXMFIT-XUQXPODJSA-N InChI=1S/C10H11NO.C8H9NO/c11-6-3-5-10-8-9(10)4-1-2-7-12;9-4-1-2-7-6-8(7)3-5-10/h1-3,5,7,9-10H,4,8H2;1-2,5,7-8H,3,6H2/b2-1+,5-3+;2-1+/t9-,10+;7-,8+/m10/s1
109v	FQJBYLWIMXMFIT-AVUDQOLYSA-N InChI=1S/C10H11NO.C8H9NO/c11-6-3-5-10-8-9(10)4-1-2-7-12;9-4-1-2-7-6-8(7)3-5-10/h1-3,5,7,9-10H,4,8H2;1-2,5,7-8H,3,6H2/b2-1+,5-3-;2-1-/t9-,10+;7-,8+/m10/s1
166	OUXRLSLKUKVTDR-OEUBYQANSA-N InChI=1S/C21H34OSi/c1-21(2,3)23(4,5)22-16-15-20-17-19(20)14-10-9-13-18-11-7-6-8-12-18/h6-8,10-12,14,19-20H,9,13,15-17H2,1-5H3/b14-10-/t19-,20+/m0/s1
169	FYHIQEHDYRQHEA-KOMYPQRHSA-N InChI=1S/C15H20O/c16-11-10-15-12-14(15)9-5-4-8-13-6-2-1-3-7-13/h1-3,5-7,9,14-16H,4,8,10-12H2/b9-5+/t14-,15+/m0/s1
(*E*)-168	FKNCXNISLCOOIK-KOMYPQRHSA-N InChI=1S/C15H18O/c16-11-10-15-12-14(15)9-5-4-8-13-6-2-1-3-7-13/h1-3,5-7,9,11,14-15H,4,8,10,12H2/b9-5+/t14-,15+/m0/s1
109y	GDRNLCCZHKZILH-DFDWCSKVSA-N InChI=1S/C17H20O.C15H18O/c18-13-7-6-12-17-14-16(17)11-5-4-10-15-8-2-1-3-9-15;16-11-10-15-12-14(15)9-5-4-8-13-6-2-1-3-7-13/h1-3,5-9,11,13,16-17H,4,10,12,14H2;1-3,5-7,9,11,14-15H,4,8,10,12H2/b7-6+,11-5+;9-5+/t16-,17+;14-,15+/m00/s1
165	BVIMVPDFGDULQN-PFKSKYCVSA-N InChI=1S/C14H28OSi.C12H24O2Si/c1-7-8-12-11-13(12)9-10-15-16(5,6)14(2,3)4;1-12(2,3)15(4,5)14-7-6-10-8-11(10)9-13/h7-8,12-13H,9-11H2,1-6H3;9-11H,6-8H2,1-5H3/b8-7-;/t12-,13+;10-,11-/m01/s1
167	OSIQMBWCPRFAKF-HZHJCBGQSA-N InChI=1S/C8H12O/c1-2-3-7-6-8(7)4-5-9/h2-3,5,7-8H,4,6H2,1H3/b3-2-/t7-,8+/m0/s1
109w	QMVPTWWPNAEATM-OHFISBHESA-N InChI=1S/C10H14O.C8H12O/c1-2-5-9-8-10(9)6-3-4-7-11;1-2-3-7-6-8(7)4-5-9/h2-5,7,9-10H,6,8H2,1H3;2-3,5,7-8H,4,6H2,1H3/b4-3+,5-2-;3-2-/t9-,10+;7-,8+/m00/s1

Compound	InChI code
(*Z*)-168	FKNCXNISLCOOIK-HBXAWUERSA-N InChI=1S/C15H18O/c16-11-10-15-12-14(15)9-5-4-8-13-6-2-1-3-7-13/h1-3,5-7,9,11,14-15H,4,8,10,12H2/b9-5-/t14-,15+/m0/s1
109x	GDRNLCCZHKZILH-XNACPBBMSA-N InChI=1S/C17H20O.C15H18O/c18-13-7-6-12-17-14-16(17)11-5-4-10-15-8-2-1-3-9-15;16-11-10-15-12-14(15)9-5-4-8-13-6-2-1-3-7-13/h1-3,5-9,11,13,16-17H,4,10,12,14H2;1-3,5-7,9,11,14-15H,4,8,10,12H2/b7-6+,11-5-;9-5-/t16-,17+;14-,15+/m00/s1
170	HFHBKGZYQSGLIK-ASOISWSRSA-N InChI=1S/C13H14O/c14-9-8-13-10-12(13)7-6-11-4-2-1-3-5-11/h1-7,9,12-13H,8,10H2/b7-6-/t12-,13+/m0/s1
109z	LDCVUAPPMDTKOY-ILRFDMCGSA-N InChI=1S/C15H16O.C13H14O/c16-11-5-4-8-14-12-15(14)10-9-13-6-2-1-3-7-13;14-9-8-13-10-12(13)7-6-11-4-2-1-3-5-11/h1-7,9-11,14-15H,8,12H2;1-7,9,12-13H,8,10H2/b5-4+,10-9-;7-6-/t14-,15+;12-,13+/m10/s1
172	GVYNXASBLDMNPA-WFNIXHHISA-N InChI=1S/C16H30O3Si/c1-7-18-15(17)9-8-13-12-14(13)10-11-19-20(5,6)16(2,3)4/h8-9,13-14H,7,10-12H2,1-6H3/b9-8-/t13-,14+/m0/s1
173	OPQXFAQBYBCUHX-HNRDENNGSA-N InChI=1S/C10H14O3/c1-2-13-10(12)4-3-8-7-9(8)5-6-11/h3-4,6,8-9H,2,5,7H2,1H3/b4-3-/t8-,9+/m0/s1
109aa	HXLLQTJUOQFIGP-JNGYUHHRSA-N InChI=1S/C12H16O3.C10H14O3/c1-2-15-12(14)7-6-11-9-10(11)5-3-4-8-13;1-2-13-10(12)4-3-8-7-9(8)5-6-11/h3-4,6-8,10-11H,2,5,9H2,1H3;3-4,6,8-9H,2,5,7H2,1H3/b4-3+,7-6-;4-3-/t10-,11+;8-,9+/m10/s1
175	SNTOIXAVNTYWLF-NVIXSHDYSA-N InChI=1S/C18H22O2/c1-3-20-18(19)14(2)9-11-16-13-17(16)12-10-15-7-5-4-6-8-15/h4-10,12,16-17H,3,11,13H2,1-2H3/b12-10+,14-9+/t16-,17+/m1/s1
109bb	YKDKUPLILCTUJO-QNIYXLKKSA-N InChI=1S/C16H18O/c1-13(12-17)7-9-15-11-16(15)10-8-14-5-3-2-4-6-14/h2-8,10,12,15-16H,9,11H2,1H3/b10-8+,13-7+/t15-,16+/m1/s1
176	XIQITUVJTIGMBQ-JYASZMECSA-N InChI=1S/C14H16O/c1-11(15)9-14-10-13(14)8-7-12-5-3-2-4-6-12/h2-8,13-14H,9-10H2,1H3/b8-7+/t13-,14+/m0/s1
112a	UPMQTQAGRJIFCC-GICMACPYSA-N InChI=1S/C15H16O/c16-12-11-14-9-5-2-6-10-15(14)13-7-3-1-4-8-13/h1,3-10,12,14-15H,2,11H2/t14-,15?/m1/s1
112d	LUBOHGMMYDCKAI-IUODEOHRSA-N InChI=1S/C16H15F3O/c17-16(18,19)14-8-6-13(7-9-14)15-5-3-1-2-4-12(15)10-11-20/h2-9,11-12,15H,1,10H2/t12-,15-/m1/s1
112e	JODZBZDHTXWDRH-IUODEOHRSA-N InChI=1S/C16H15F3O/c17-16(18,19)14-7-4-6-13(11-14)15-8-3-1-2-5-12(15)9-10-20/h2-8,10-12,15H,1,9H2/t12-,15-/m1/s1

Compound	InChI code
112f	LBYNGMZUZXIIGC-CHWSQXEVSA-N InChI=1S/C16H15F3O/c17-16(18,19)15-9-5-4-8-14(15)13-7-3-1-2-6-12(13)10-11-20/h2-9,11-13H,1,10H2/t12-,13-/m1/s1
112g	GIXCNKPPGPXEBE-IUODEOHRSA-N InChI=1S/C15H15NO3/c17-11-10-12-4-2-1-3-5-15(12)13-6-8-14(9-7-13)16(18)19/h2-9,11-12,15H,1,10H2/t12-,15-/m1/s1
112h	GROUNJHCHJNWQT-IUODEOHRSA-N InChI=1S/C15H15ClO/c16-14-8-6-13(7-9-14)15-5-3-1-2-4-12(15)10-11-17/h2-9,11-12,15H,1,10H2/t12-,15-/m1/s1
112i	NRIPLSVMQFLBEQ-IUODEOHRSA-N InChI=1S/C15H15FO/c16-14-8-6-13(7-9-14)15-5-3-1-2-4-12(15)10-11-17/h2-9,11-12,15H,1,10H2/t12-,15-/m1/s1
112j	LGHCTIPVGPWQGI-IUODEOHRSA-N InChI=1S/C15H15ClO/c16-14-7-4-6-13(11-14)15-8-3-1-2-5-12(15)9-10-17/h2-8,10-12,15H,1,9H2/t12-,15-/m1/s1
112k	QQTKQEXVGLDVPS-IUODEOHRSA-N InChI=1S/C15H15FO/c16-14-7-4-6-13(11-14)15-8-3-1-2-5-12(15)9-10-17/h2-8,10-12,15H,1,9H2/t12-,15-/m1/s1
112l	MXYNOMKVVQPJKR-CHWSQXEVSA-N InChI=1S/C15H15FO/c16-15-9-5-4-8-14(15)13-7-3-1-2-6-12(13)10-11-17/h2-9,11-13H,1,10H2/t12-,13-/m1/s1
112n	ZRCQSZDQVBSKPG-GDBMZVCRSA-N InChI=1S/C16H18O/c1-13-7-9-15(10-8-13)16-6-4-2-3-5-14(16)11-12-17/h3-10,12,14,16H,2,11H2,1H3/t14-,16-/m1/s1
112o	ALBMNFMKHIGLTJ-CRAIPNDOSA-N InChI=1S/C19H24O/c1-19(2,3)17-11-9-16(10-12-17)18-8-6-4-5-7-15(18)13-14-20/h5-12,14-15,18H,4,13H2,1-3H3/t15-,18-/m1/s1
112q	PYNIAALGWQOWSW-CZUORRHYSA-N InChI=1S/C16H18O2/c1-18-15-9-7-14(8-10-15)16-6-4-2-3-5-13(16)11-12-17/h3-10,12-13,16H,2,11H2,1H3/t13-,16-/m1/s1
112s	RYZPKPDXGOEKRC-VXGBXAGGSA-N InChI=1S/C13H14OS/c14-9-8-11-5-2-1-3-6-12(11)13-7-4-10-15-13/h2-7,9-12H,1,8H2/t11-,12-/m1/s1
112t	FAPAVCJKSZVROX-NFJWQWPMSA-N InChI=1S/C12H16O3/c1-2-15-12(14)11-7-5-3-4-6-10(11)8-9-13/h4-7,9-11H,2-3,8H2,1H3/t10-,11?/m1/s1
112u	GVKYFKGTMKBIEF-YHMJZVADSA-N InChI=1S/C10H11NO/c11-8-10-5-3-1-2-4-9(10)6-7-12/h2-5,7,9-10H,1,6H2/t9-,10?/m1/s1

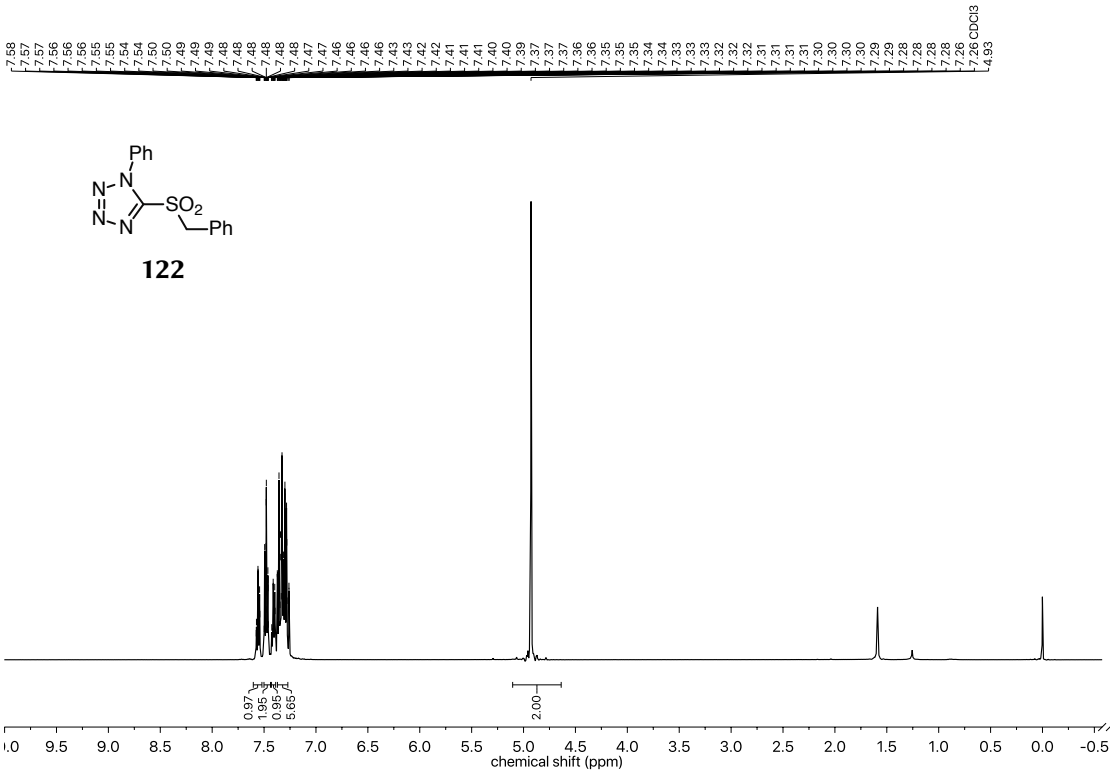
Compound	InChI code
112p	ZTDVHBBYXKMVIP-YMJMCWPSSA-N InChI=1S/C19H22O/c20-16-15-19-13-6-2-5-12-18(19)14-8-7-11-17-9-3-1-4-10-17/h1,3-6,8-10,12-14,16,18-19H,2,7,11,15H2/b14-8+/t18-,19+/m0/s1
112r	LENZLCRVBFRBCB-UHFFFAOYSA-N InChI=1S/C9H12O/c10-8-7-9-5-3-1-2-4-6-9/h1,3-4,6,8-9H,2,5,7H2
112y	UFEQQFZJNFNUIG-DLBZAZTESA-N InChI=1S/C17H20O/c18-14-13-17-10-6-2-5-9-16(17)12-11-15-7-3-1-4-8-15/h1,3-10,14,16-17H,2,11-13H2/t16-,17+/m0/s1
112z	UPMQTQAGRJIFCC-GICMACPYSA-N InChI=1S/C15H16O/c16-12-11-14-9-5-2-6-10-15(14)13-7-3-1-4-8-13/h1,3-10,12,14-15H,2,11H2/t14-,15?/m1/s1
112aa	FAPAVCJKSZVROX-NFJWQWPMSA-N InChI=1S/C12H16O3/c1-2-15-12(14)11-7-5-3-4-6-10(11)8-9-13/h4-7,9-11H,2-3,8H2,1H3/t10-,11?/m1/s1
112v	GVKYFKGTMKBIEF-YHMJZVADSA-N InChI=1S/C10H11NO/c11-8-10-5-3-1-2-4-9(10)6-7-12/h2-5,7,9-10H,1,6H2/t9-,10?/m1/s1
181	QOQOMBWYCQXPPU-NFJWQWPMSA-N InChI=1S/C12H18O3/c1-2-15-12(14)11-7-5-3-4-6-10(11)8-9-13/h4-7,10-11,13H,2-3,8-9H2,1H3/t10-,11?/m1/s1
182	MIMXUKPQZOAILY-RKDXNWHRSA-N InChI=1S/C10H12O2/c11-10-9-5-3-1-2-4-8(9)6-7-12-10/h2-5,8-9H,1,6-7H2/t8-,9-/m1/s1
183	KTWYJMDTHZWSPL-FWJOYPJLSA-N InChI=1S/C19H20N2O8/c1-2-28-19(23)17-7-5-3-4-6-13(17)8-9-29-18(22)14-10-15(20(24)25)12-16(11-14)21(26)27/h4-7,10-13,17H,2-3,8-9H2,1H3/t13-,17?/m1/s1
185	PSTJGTBMPBFOEJ-RKUIQBLJSA-N InChI=1S/C21H36O3Si/c1-8-23-21(22)20-13-11-9-10-12-19(20)14-15-24-25(16(2)3,17(4)5)18(6)7/h10-20H,8-9H2,1-7H3/b15-14+/t19-,20?/m1/s1
186	HGNPMUWSLMLJEU-KWCCSABGSA-N InChI=1S/C15H16O2/c16-15(17)11-13-9-5-2-6-10-14(13)12-7-3-1-4-8-12/h1,3-10,13-14H,2,11H2,(H,16,17)/t13-,14?/m1/s1
188	FQCBAZYBNYHKKF-RUZMYDRRSA-N InChI=1S/C19H29N3OSi/c1-19(2,3)24(4,5)23-13-12-17-14-16(17)9-6-15-7-10-18(11-8-15)21-22-20/h6-11,16-17H,12-14H2,1-5H3/b9-6+/t16-,17+/m0/s1
116c	KFGHAHPHSYYPHL-URUUNZHMSA-N InChI=1S/C13H13N3O/c14-16-15-13-5-2-10(3-6-13)1-4-11-9-12(11)7-8-17/h1-6,8,11-12H,7,9H2/b4-1+/t11-,12+/m0/s1
207	UFEDSIGHACMCAJ-UHFFFAOYSA-N InChI=1S/C10H12O2/c1-2-12-10(11)9-7-5-3-4-6-8-9/h3,5-8H,2,4H2,1H3

Compound	InChI code
118c	LNKMABXRYGEWME-DJNXLDHESA-N InChI=1S/C17H21NO/c1-3-7-15(8-4-1)16-9-5-2-6-10-17(16)18-11-13-19-14-12-18/h1,3-10,16-17H,2,11-14H2/t16?,17-/m0/s1
118d	ITMWSCXNKRZFJH-LBAQZLPGSA-N InChI=1S/C21H23N/c1-4-10-18(11-5-1)16-17-22-21-15-9-3-8-14-20(21)19-12-6-2-7-13-19/h1-2,4-15,20-22H,3,16-17H2/t20?,21-/m0/s1
118e	HLWWSEBCRORLQV-UHFFFAOYSA-N InChI=1S/C21H23N/c1-17(18-11-5-2-6-12-18)22-21-16-10-4-9-15-20(21)19-13-7-3-8-14-19/h2-3,5-17,20-22H,4H2,1H3
118f	BHFFUMIEACOCGZ-AEHNDQHQSA-N InChI=1S/C18H21NO2.C13H14O/c20-18(21)17-12-7-13-19(17)16-11-6-2-5-10-15(16)14-8-3-1-4-9-14;14-9-8-13-10-12(13)7-6-11-4-2-1-3-5-11/h1,3-6,8-11,15-17H,2,7,12-13H2,(H,20,21);1-7,9,12-13H,8,10H2/b;7-6+/t;12-,13+/m.0/s1
118g	HBEPIEWNIZIMJA-UHFFFAOYSA-N InChI=1S/C19H23NO2/c1-22-19(21)18-13-8-14-20(18)17-12-7-3-6-11-16(17)15-9-4-2-5-10-15/h2,4-7,9-12,16-18H,3,8,13-14H2,1H3
118h	TYXXUCYFNNKHGO-UHFFFAOYSA-N InChI=1S/C25H36N2O4/c1-25(2,3)31-24(29)27-22(23(28)30-4)17-11-12-18-26-21-16-10-6-9-15-20(21)19-13-7-5-8-14-19/h5,7-10,13-16,20-22,26H,6,11-12,17-18H2,1-4H3,(H,27,29)
118i	NSWKANZMOYHJQG-ADKAHSJRSA-N InChI=1S/C19H26N2O2/c20-17(19(22)23)12-7-8-14-21-18-13-6-2-5-11-16(18)15-9-3-1-4-10-15/h1,3-6,9-11,13,16-18,21H,2,7-8,12,14,20H2,(H,22,23)/t16?,17-,18?/m0/s1

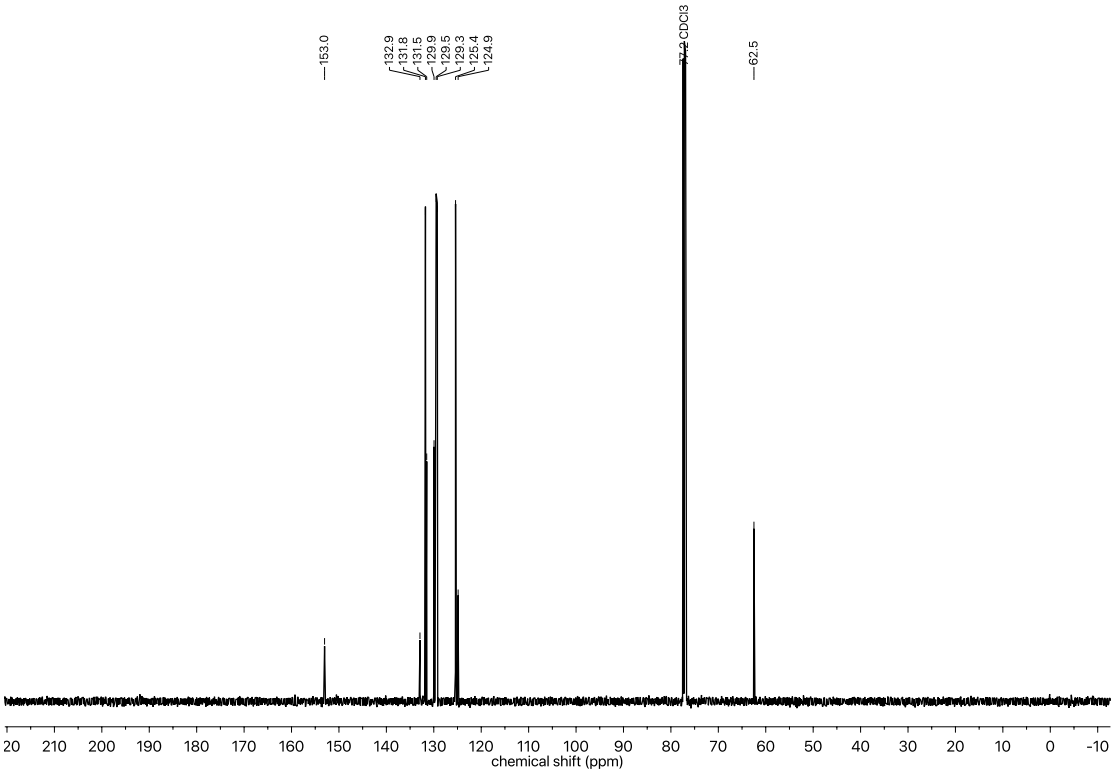
NMR Spectra of All Compounds

5-(Benzylsulfonyl)-1-phenyl-4,5-dihydro-1*H*-tetrazole (122)

^{1}H NMR:

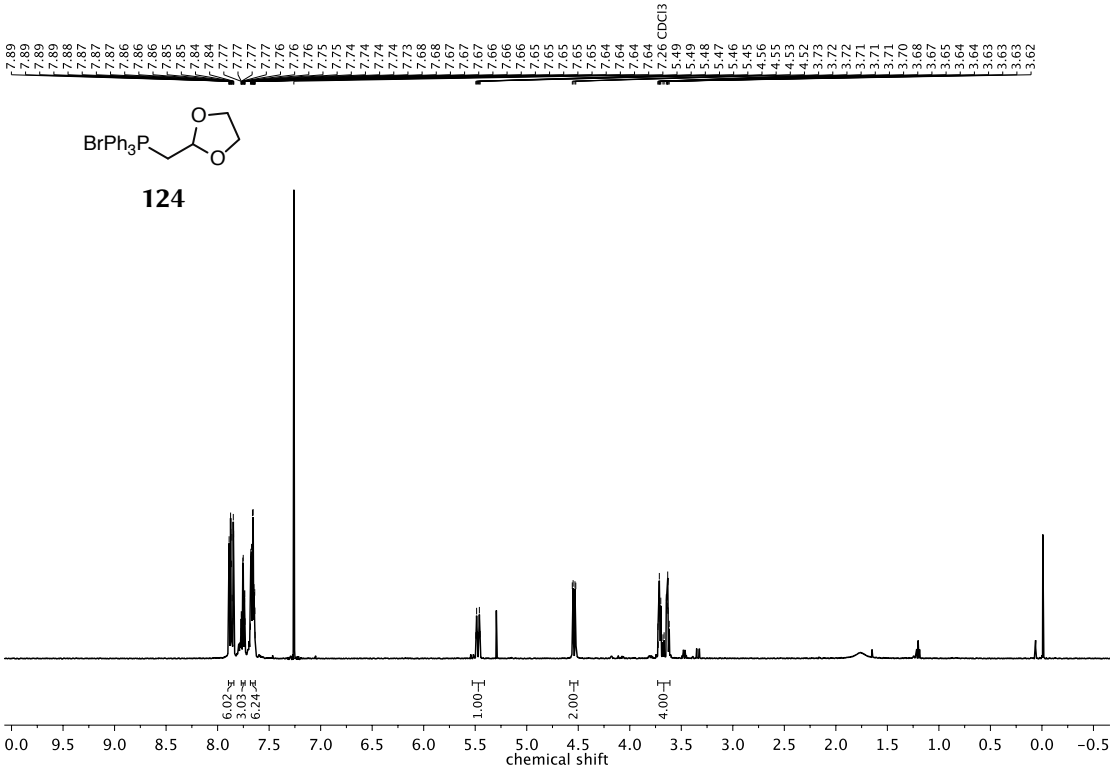


^{13}C NMR:

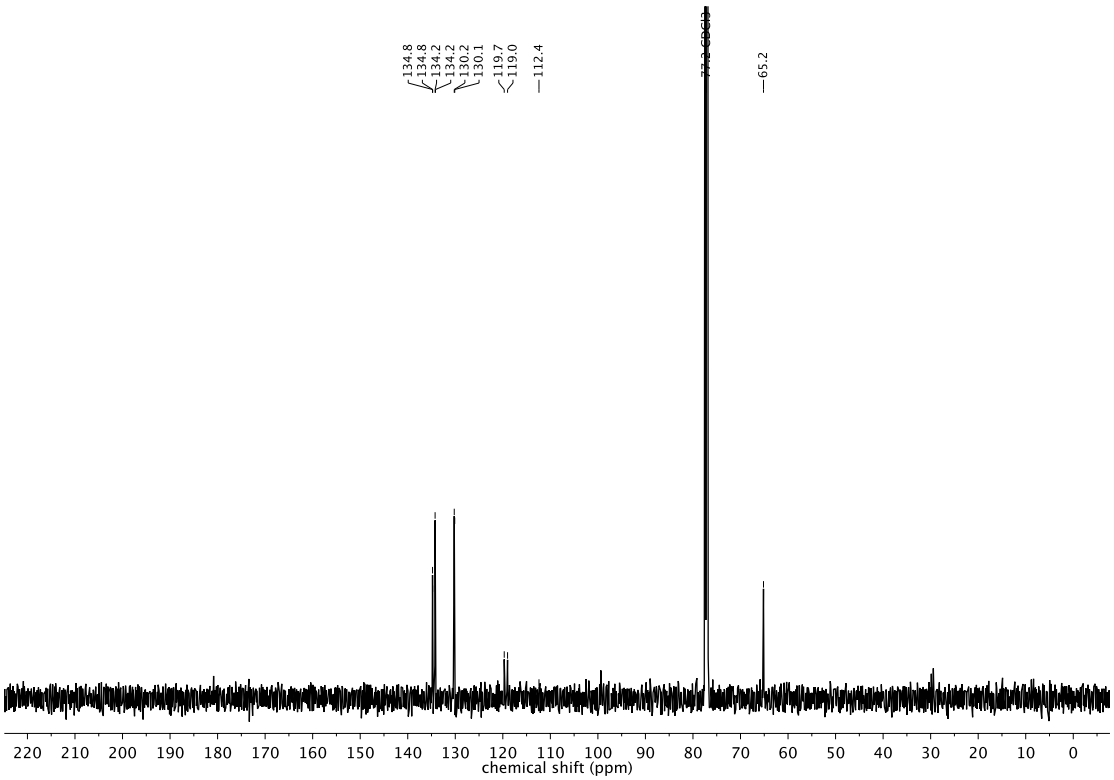

153.0
132.9
131.8
131.5
129.9
129.5
129.3
125.4
124.9
77.2 CDCl3
62.5
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift (ppm)

((1,3-Dioxolan-2-yl)methyl)triphenyl-λ^5-phosphonium Bromide (124)

^{1}H NMR:

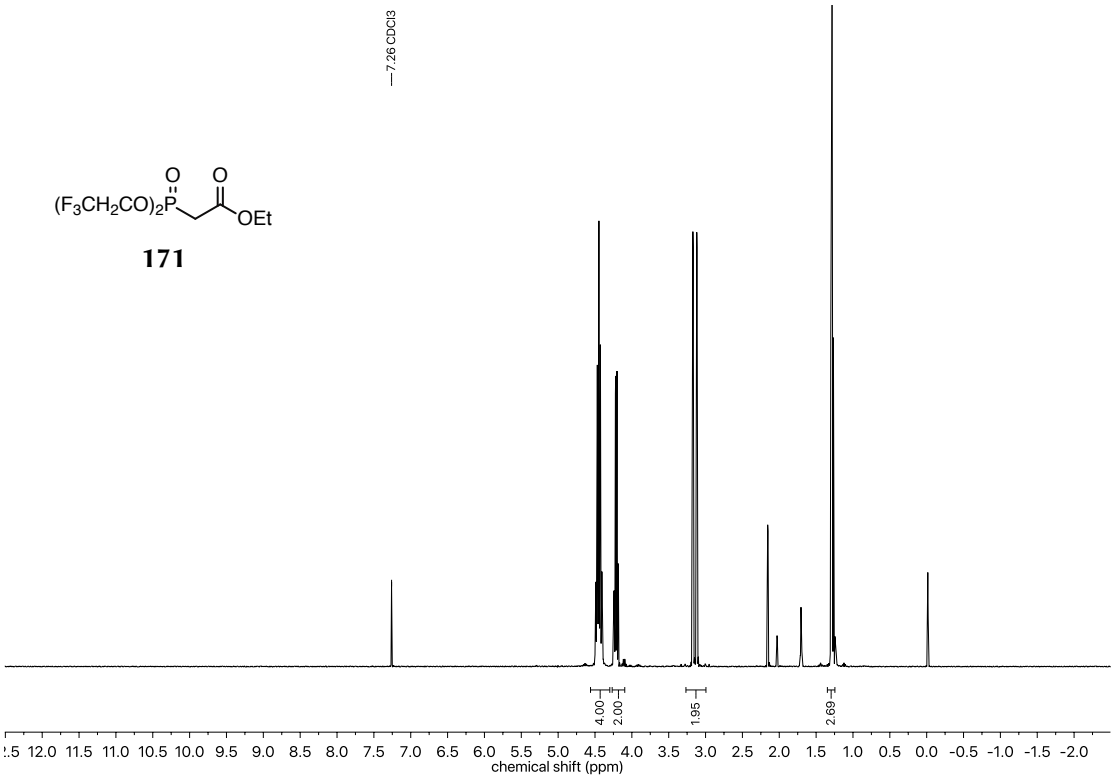


^{13}C NMR:

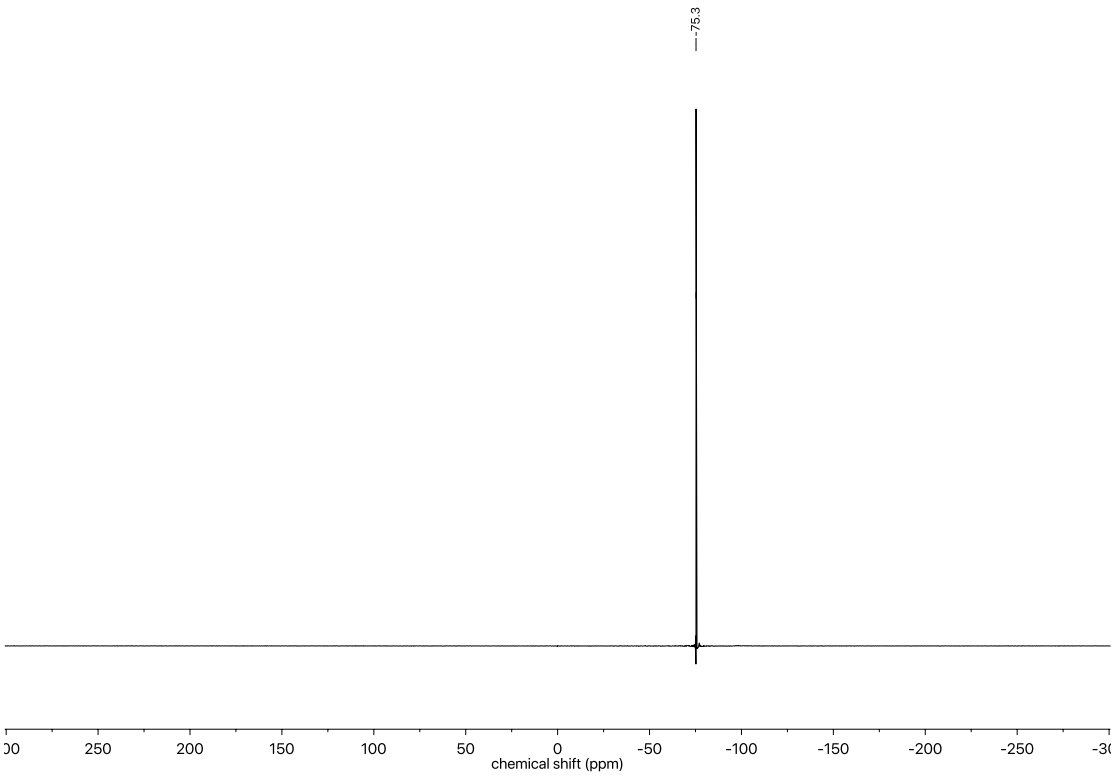


Ethyl 2-(Bis(2,2,2-trifluoroethoxy)phosphoryl)acetate (171)

^{1}H NMR:

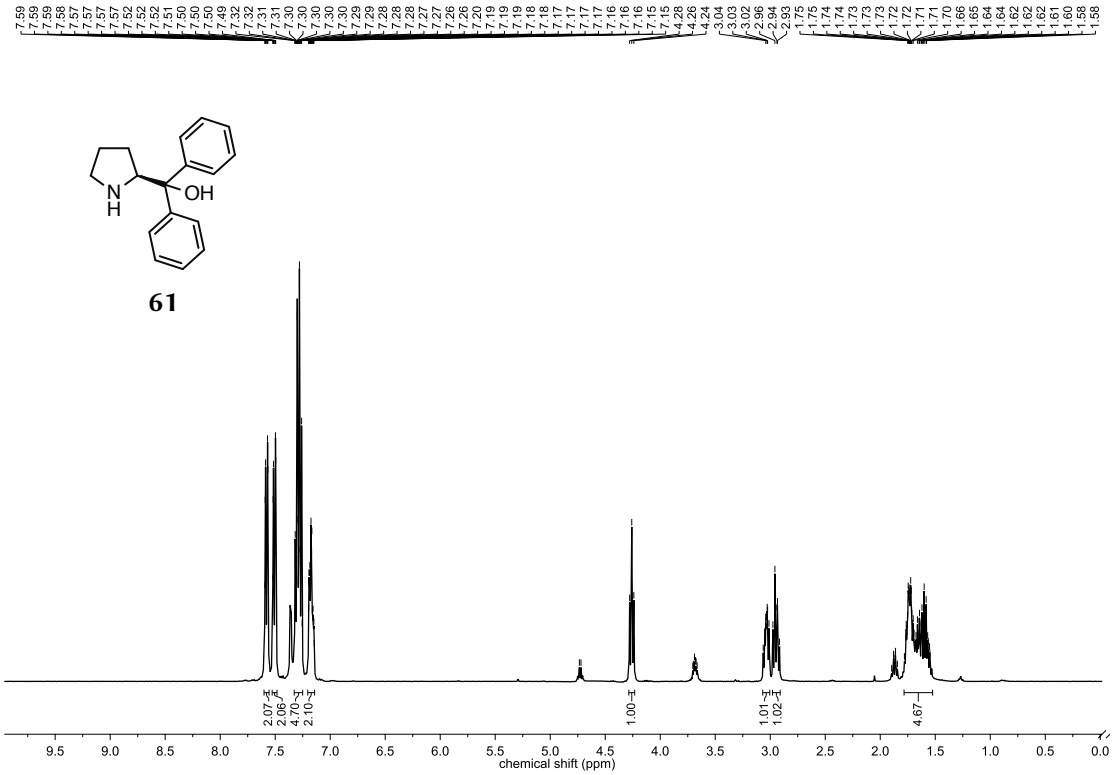


^{19}F NMR:

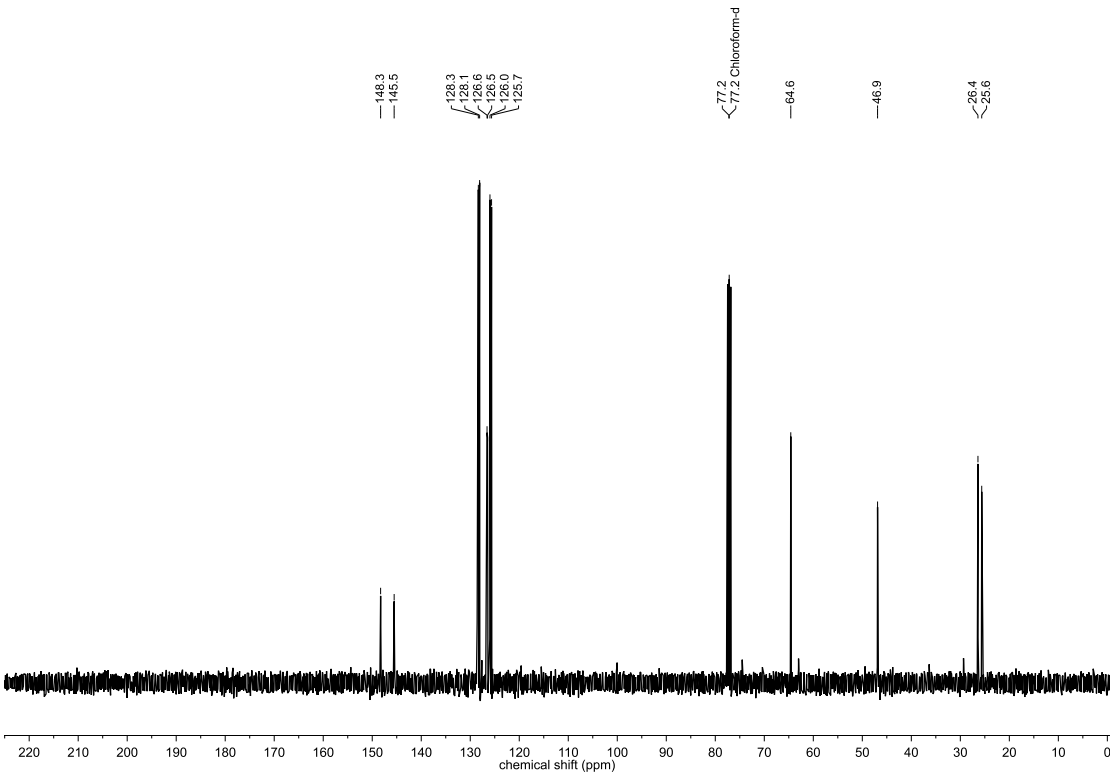


(*S*)-Diphenyl(pyrrolidin-2-yl)methanol (61)

^{1}H NMR:

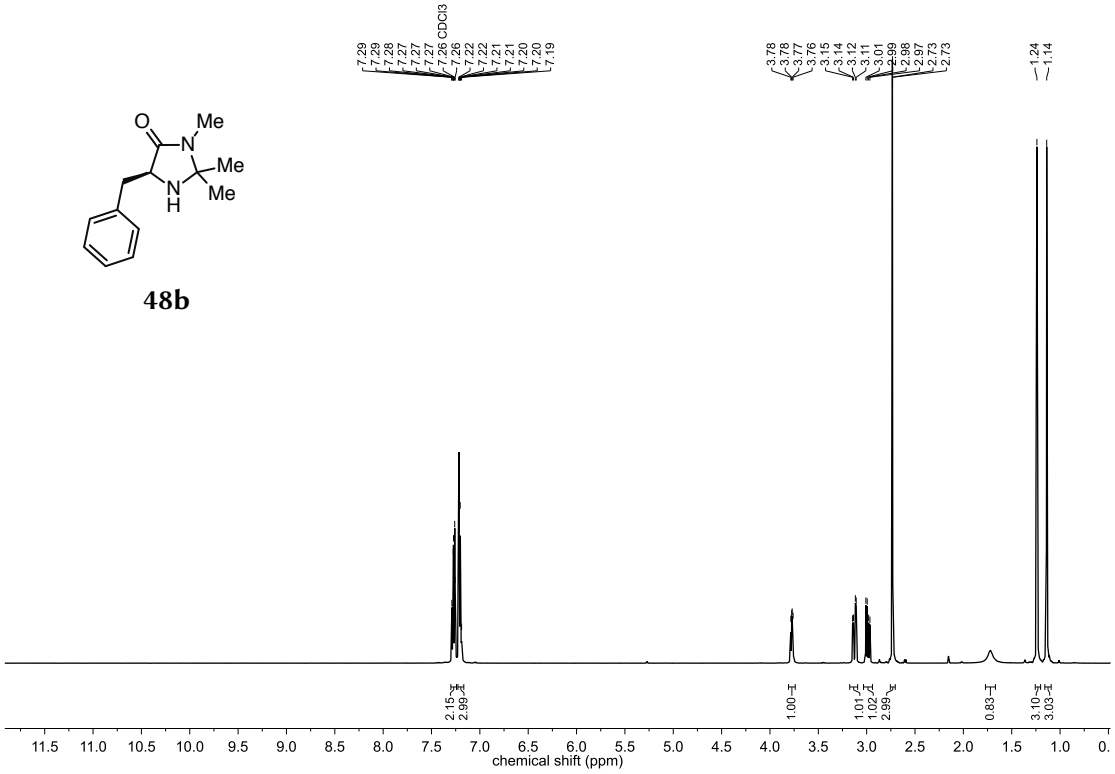


^{13}C NMR:



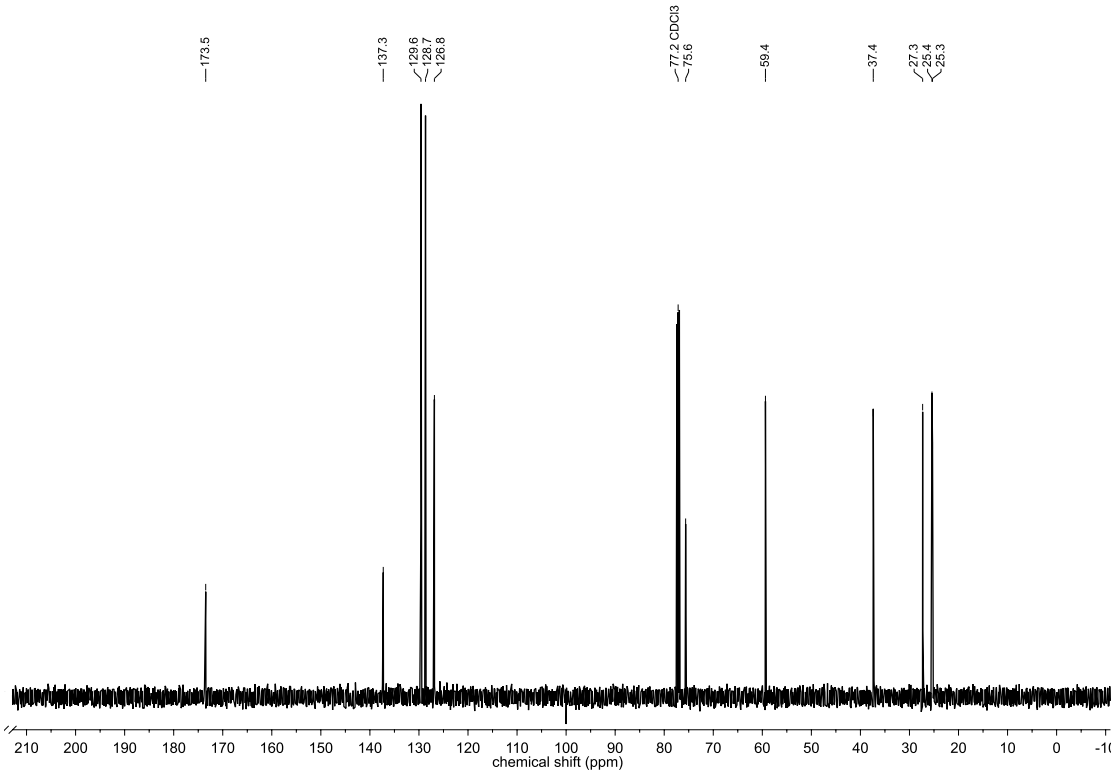
(S)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one (48b)

^{1}H NMR:



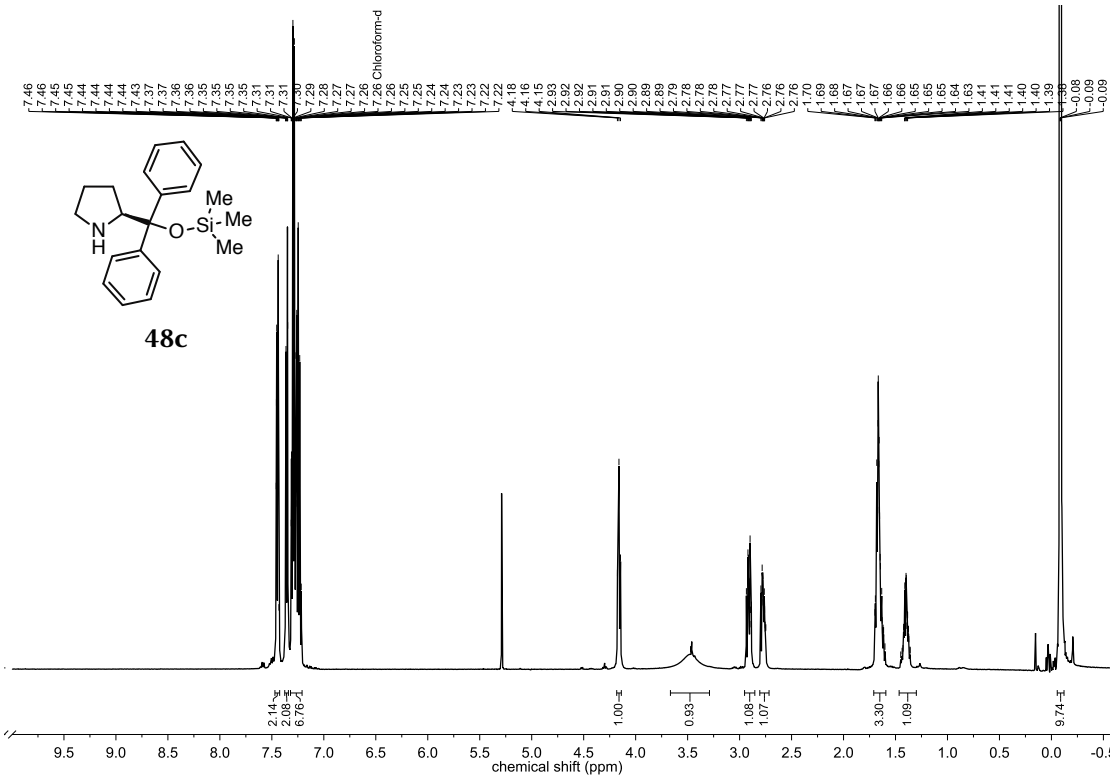
48b

^{13}C NMR:

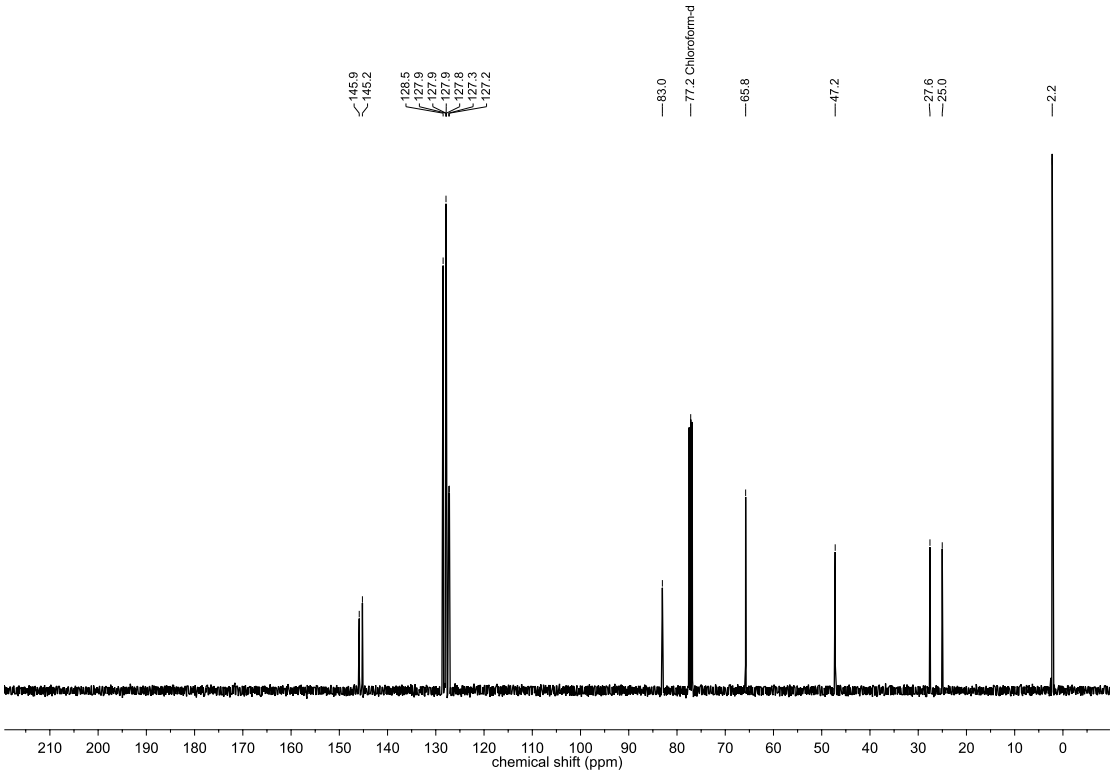


(*S*)-2-(Diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (48c)

^{1}H NMR:

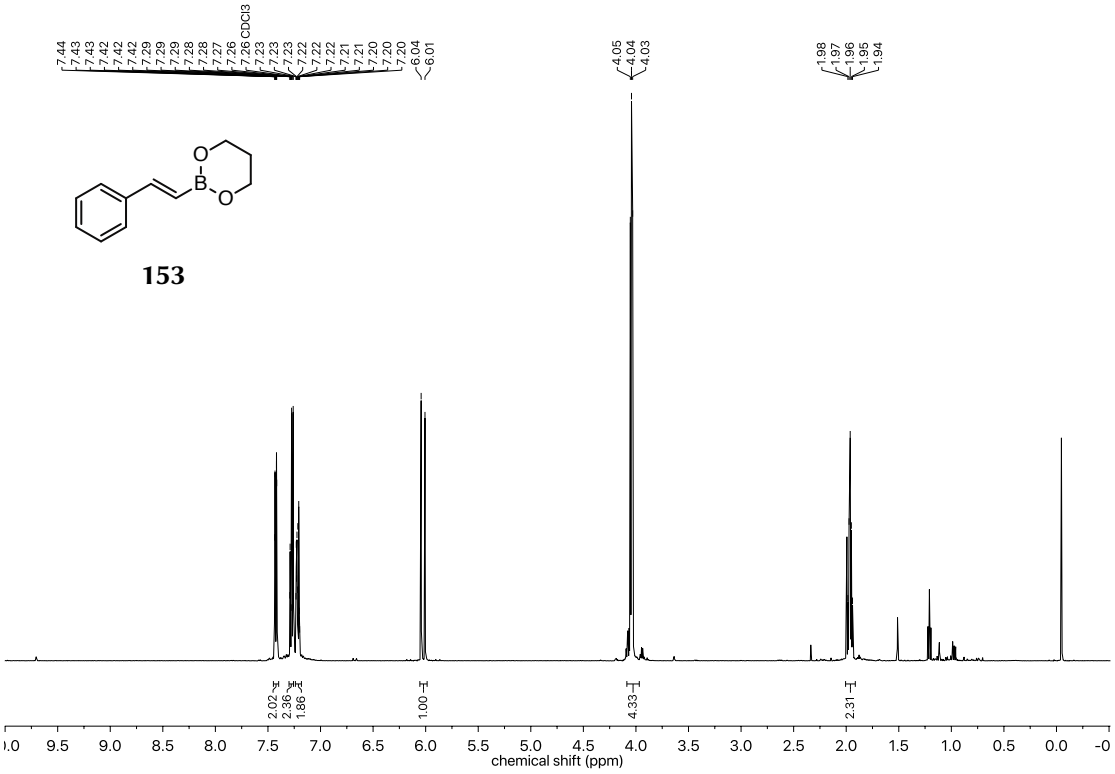


^{13}C NMR:

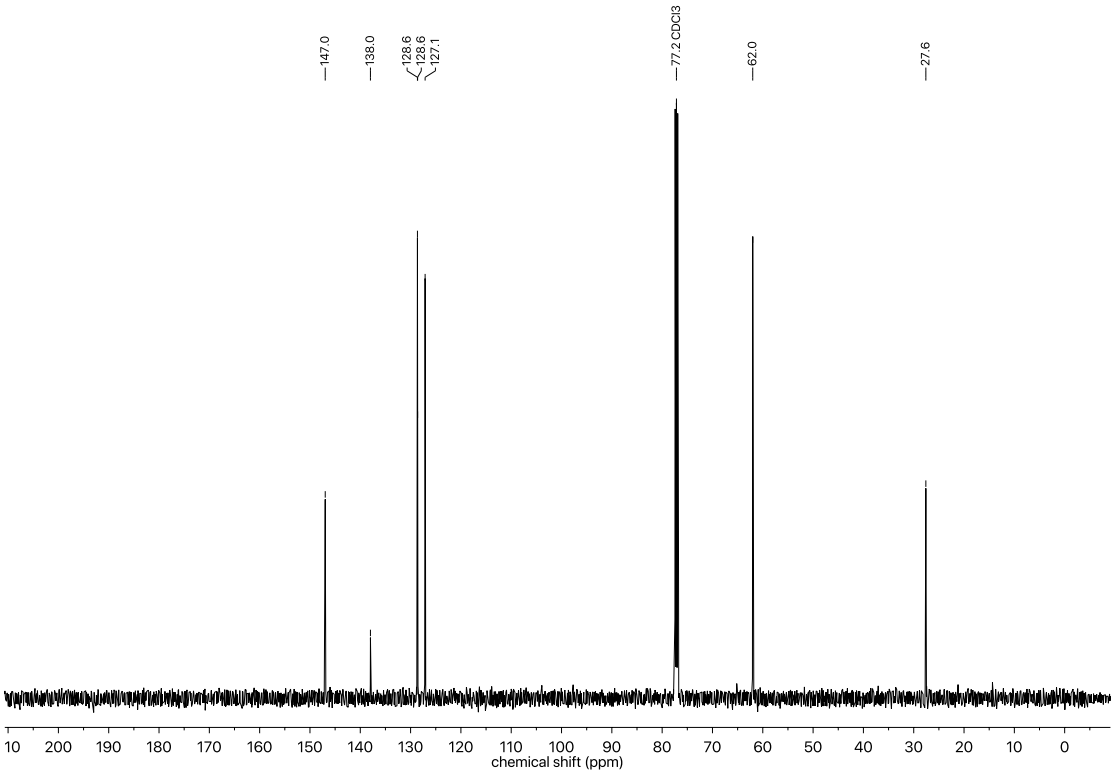


(*E*)-2-Styryl-1,3,2-dioxaborinane (153)

^{1}H NMR:

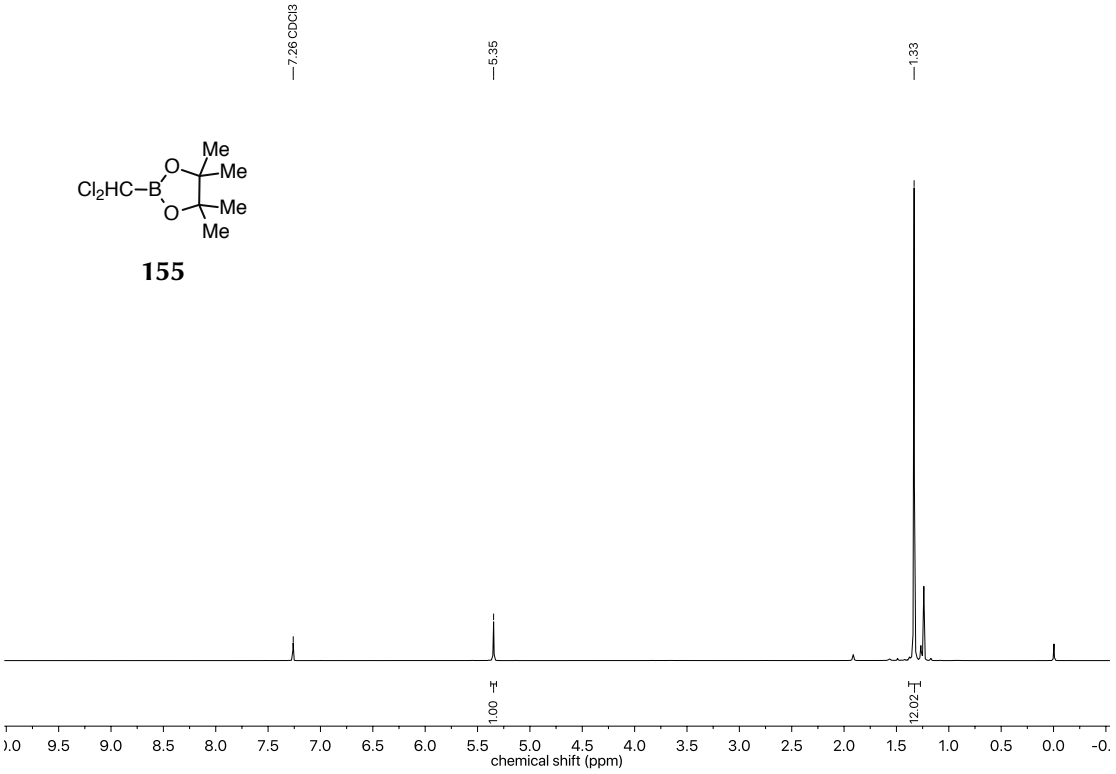


^{13}C NMR:



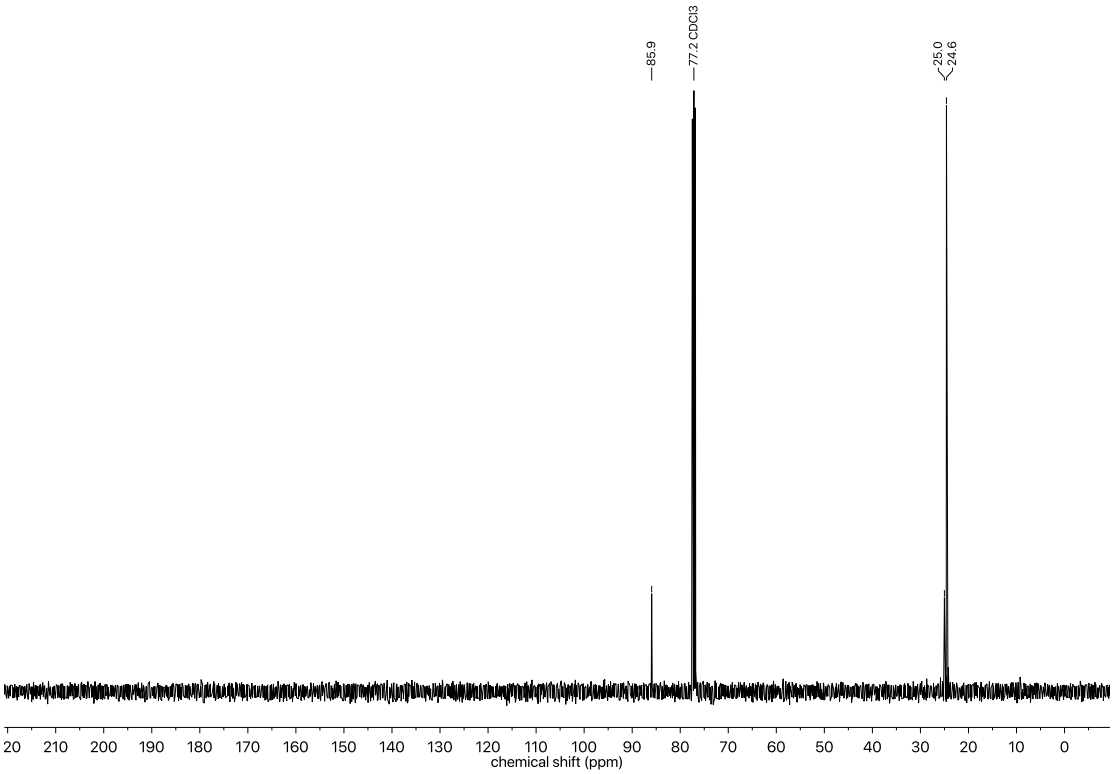
2-(Dichloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (155)

^{1}H NMR:



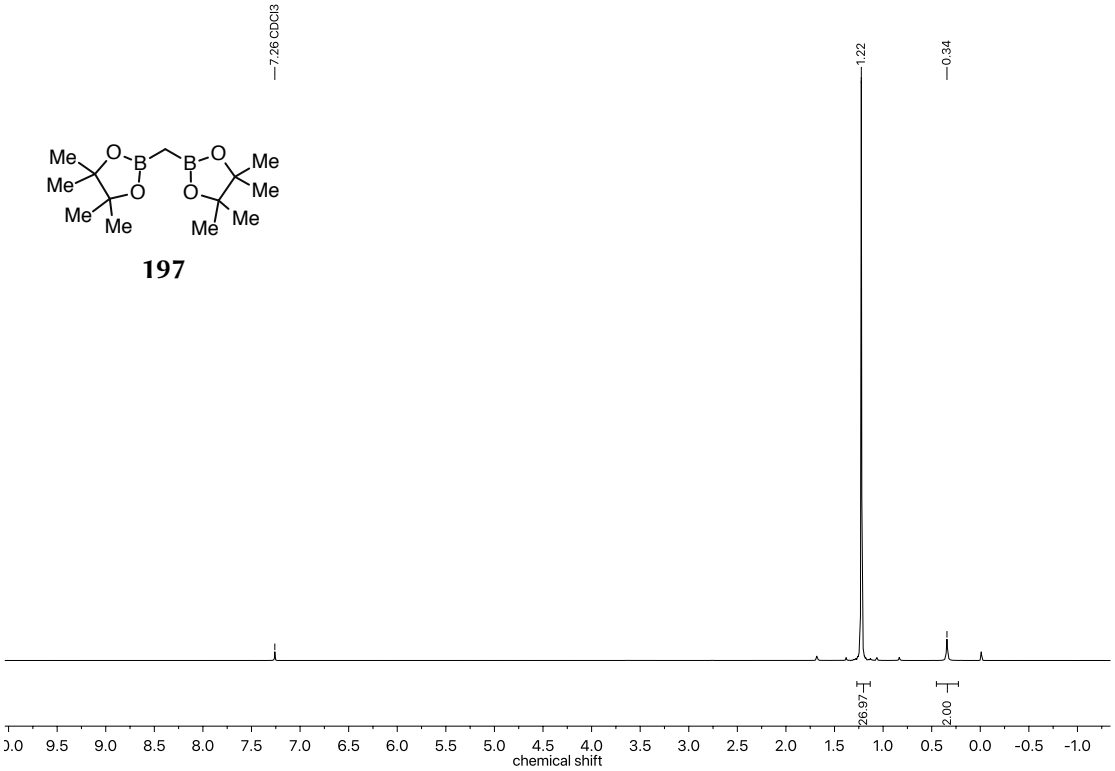
155

^{13}C NMR:



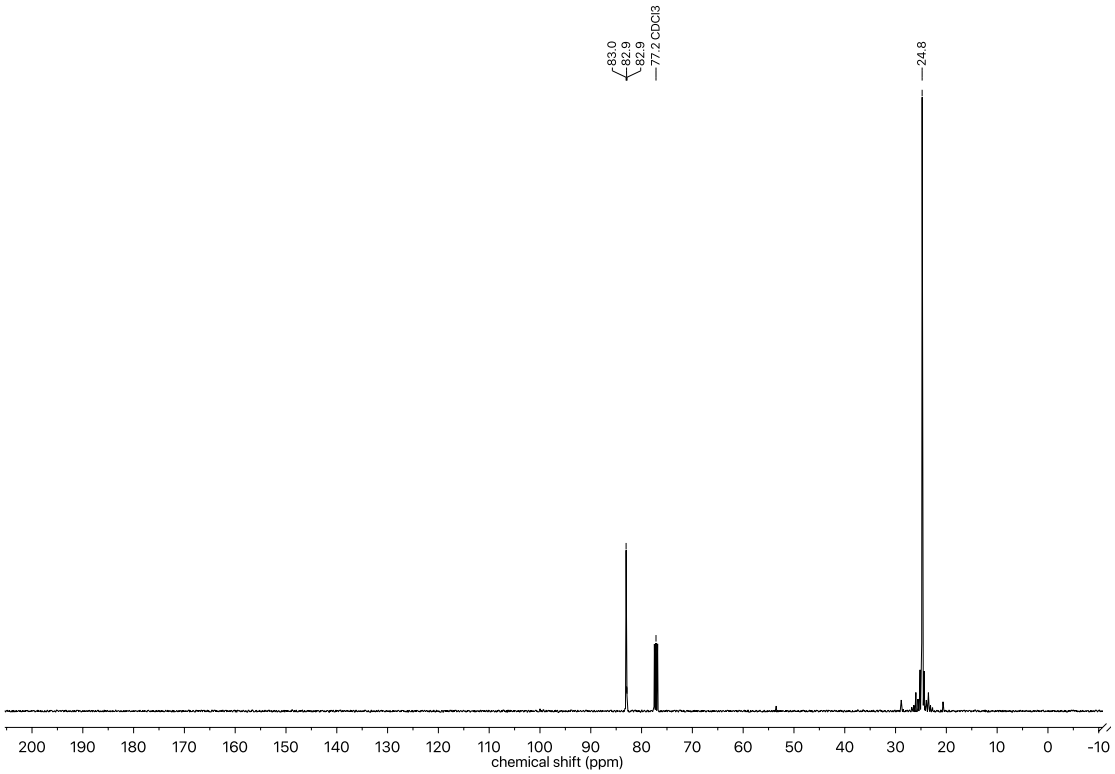
Bis((pinacolato)boryl)methane (197)

^{1}H NMR:



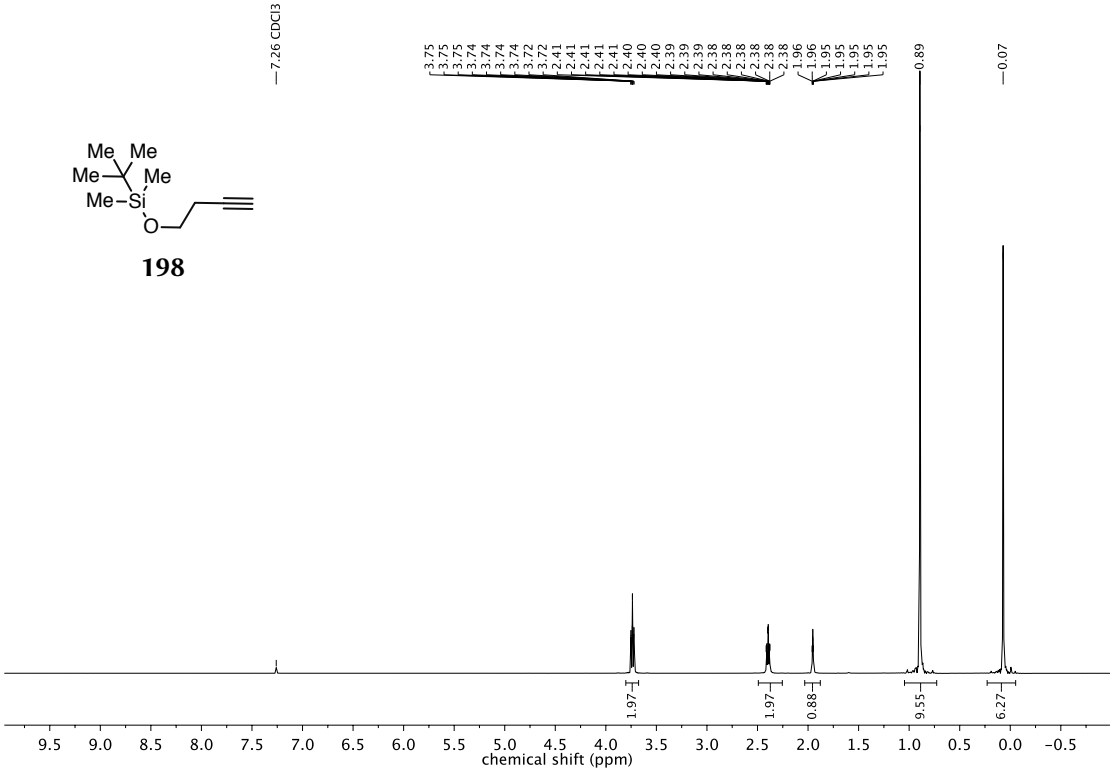
197

^{13}C NMR:

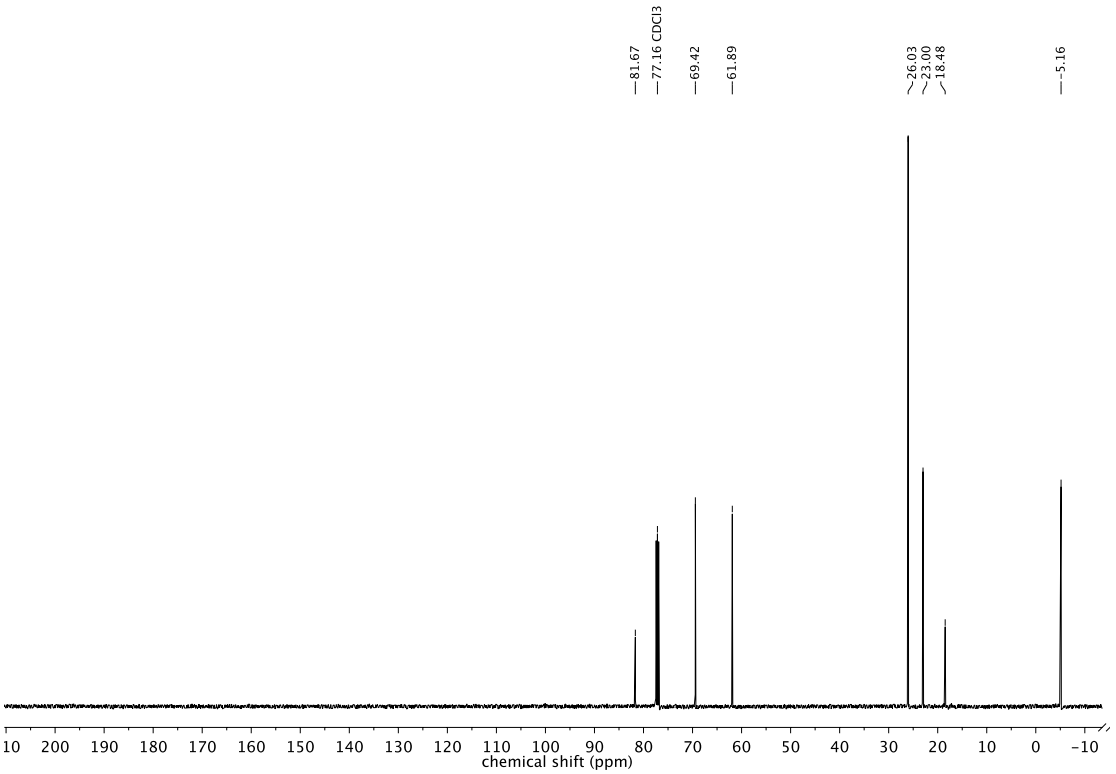


(But-3-yn-1-yloxy)(*tert*-butyl)dimethylsilane (198)

^{1}H NMR:

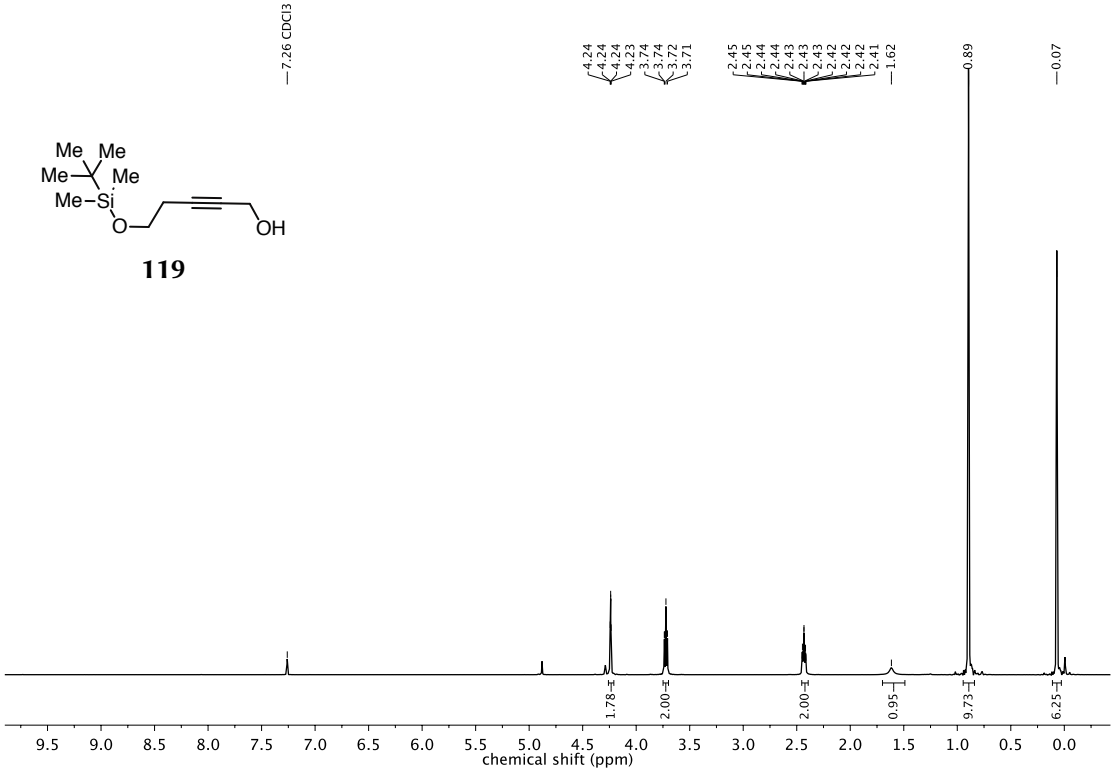


^{13}C NMR:

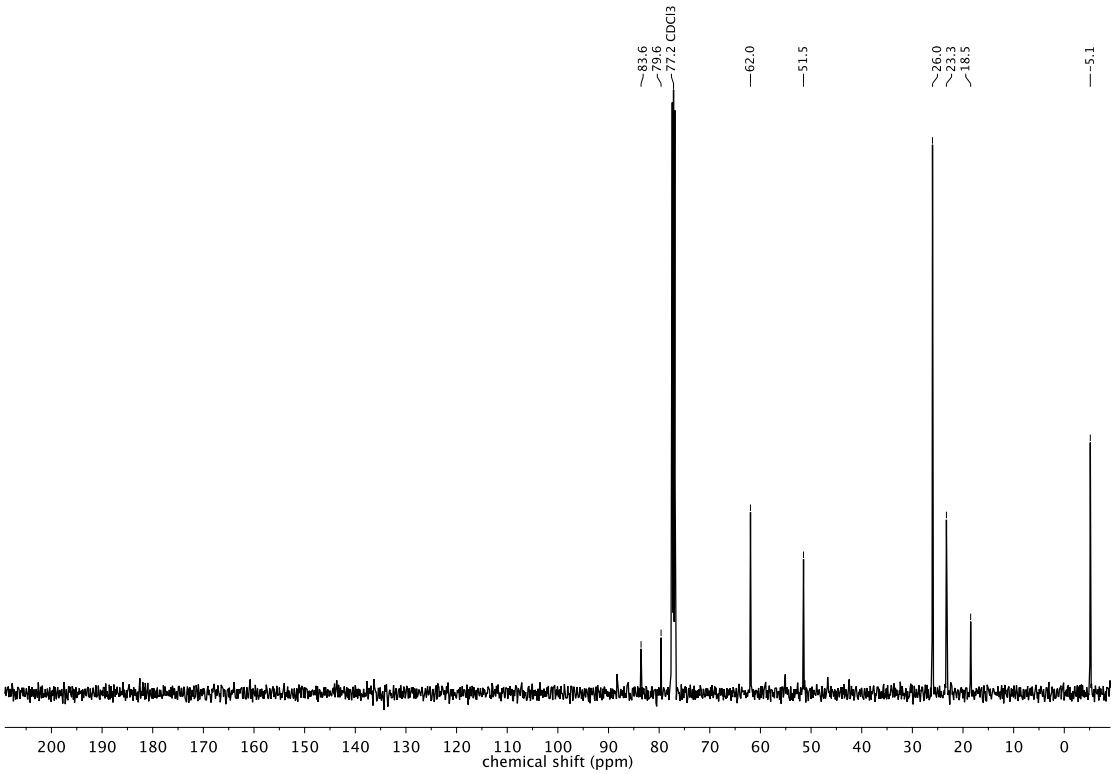


5-((*tert*-Butyldimethylsilyl)oxy)pent-2-yn-1-ol (119)

^{1}H NMR:

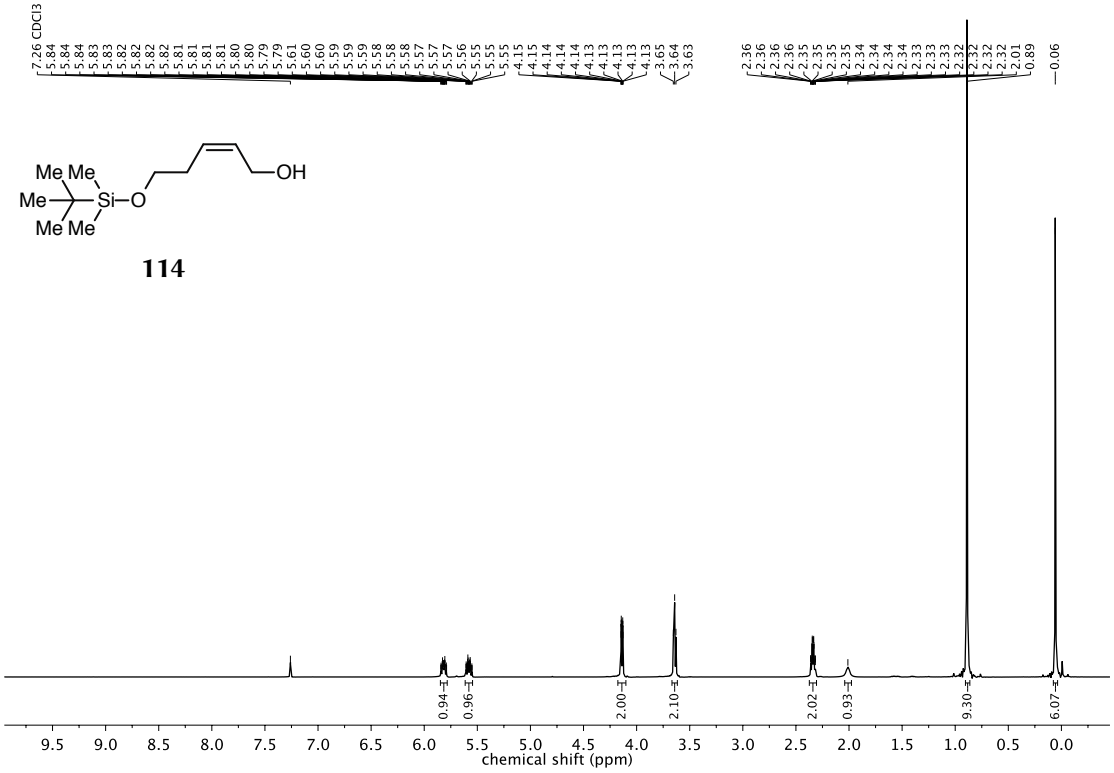


^{13}C NMR:

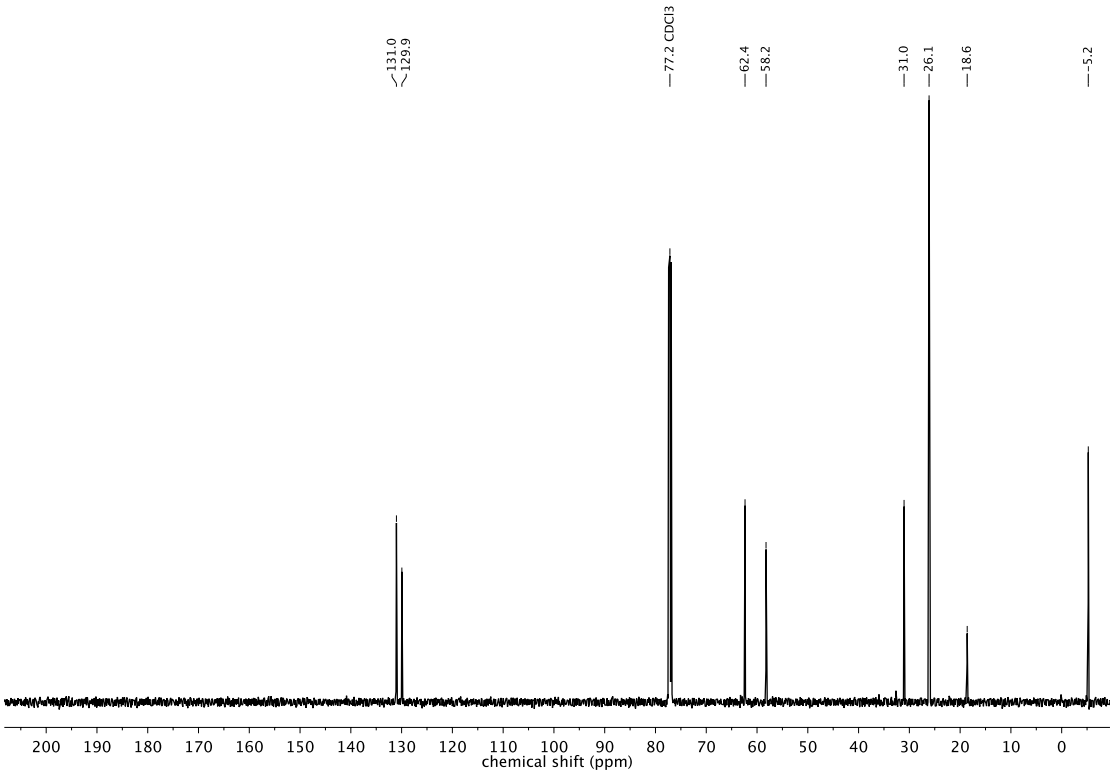


(*Z*)-5-((*tert*-Butyldimethylsilyl)oxy)pent-2-en-1-ol (114)

^{1}H NMR:

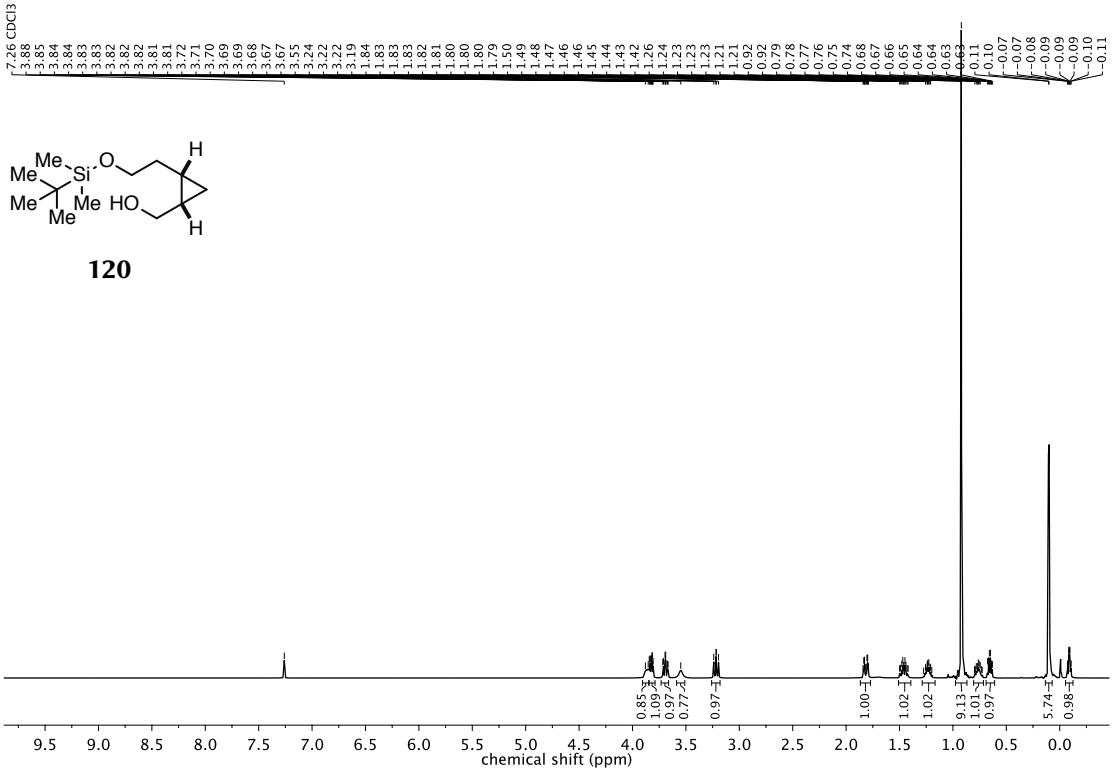


^{13}C NMR:



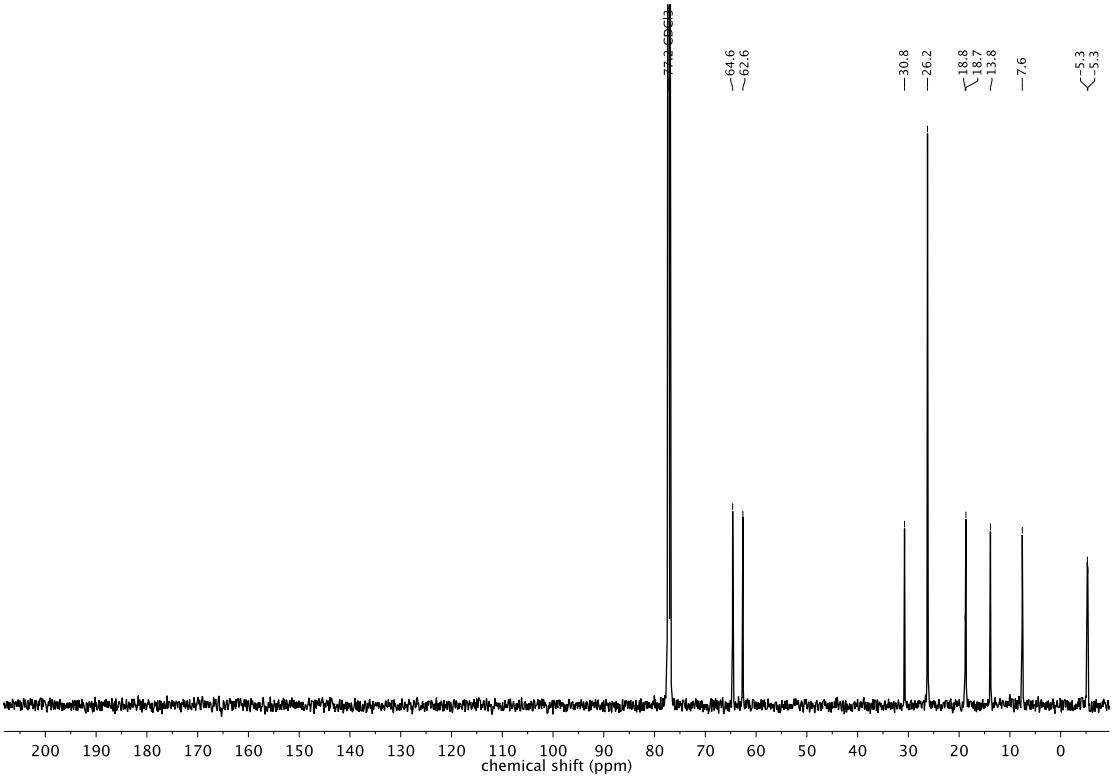
2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)methanol (120)

^{1}H NMR:



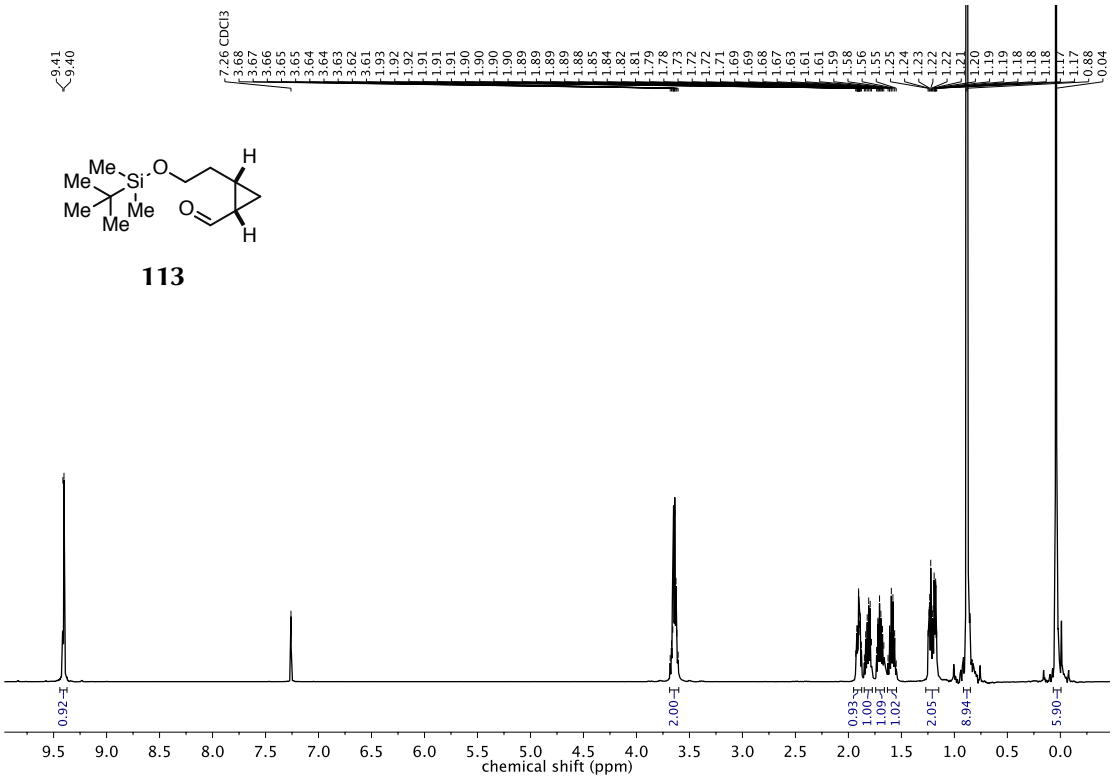
120

^{13}C NMR:



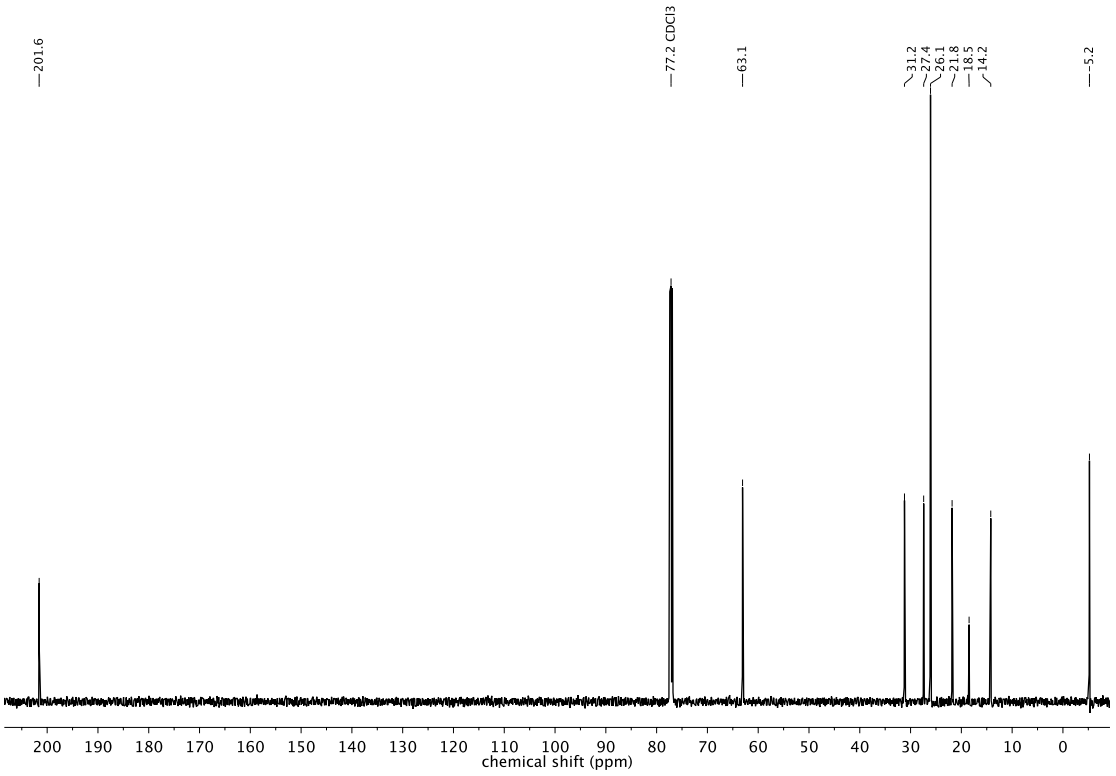
2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropane-1-carbaldehyde (113)

^{1}H NMR:



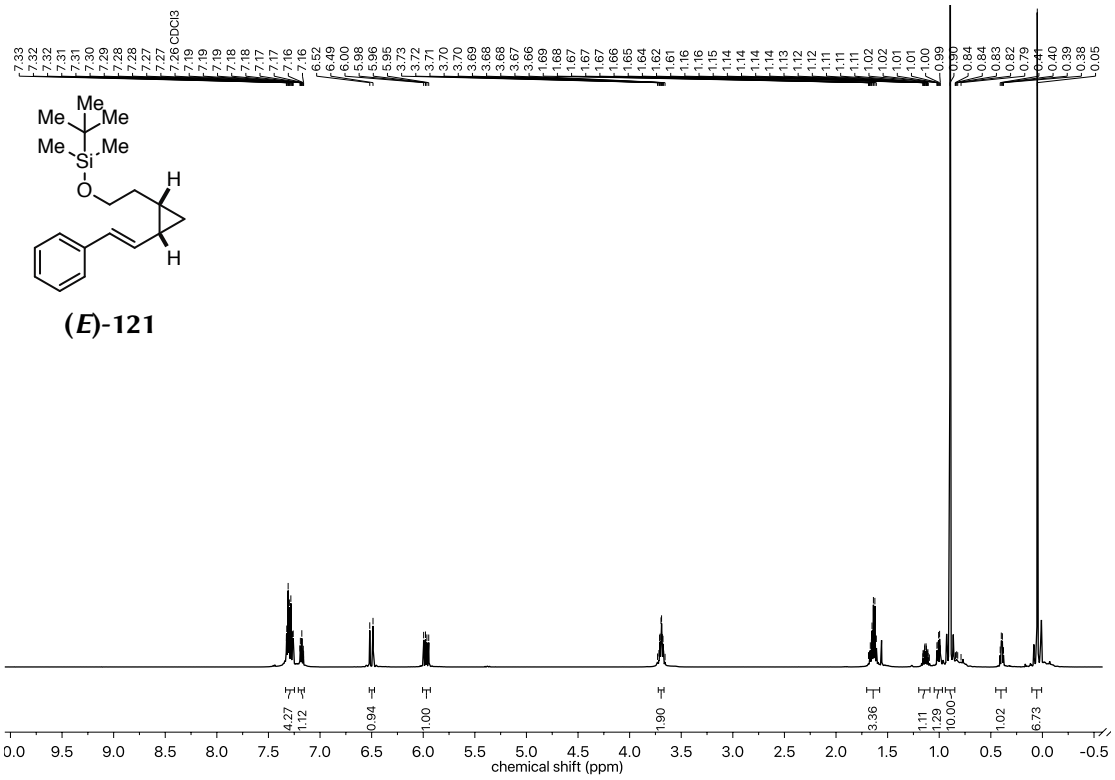
113

^{13}C NMR:

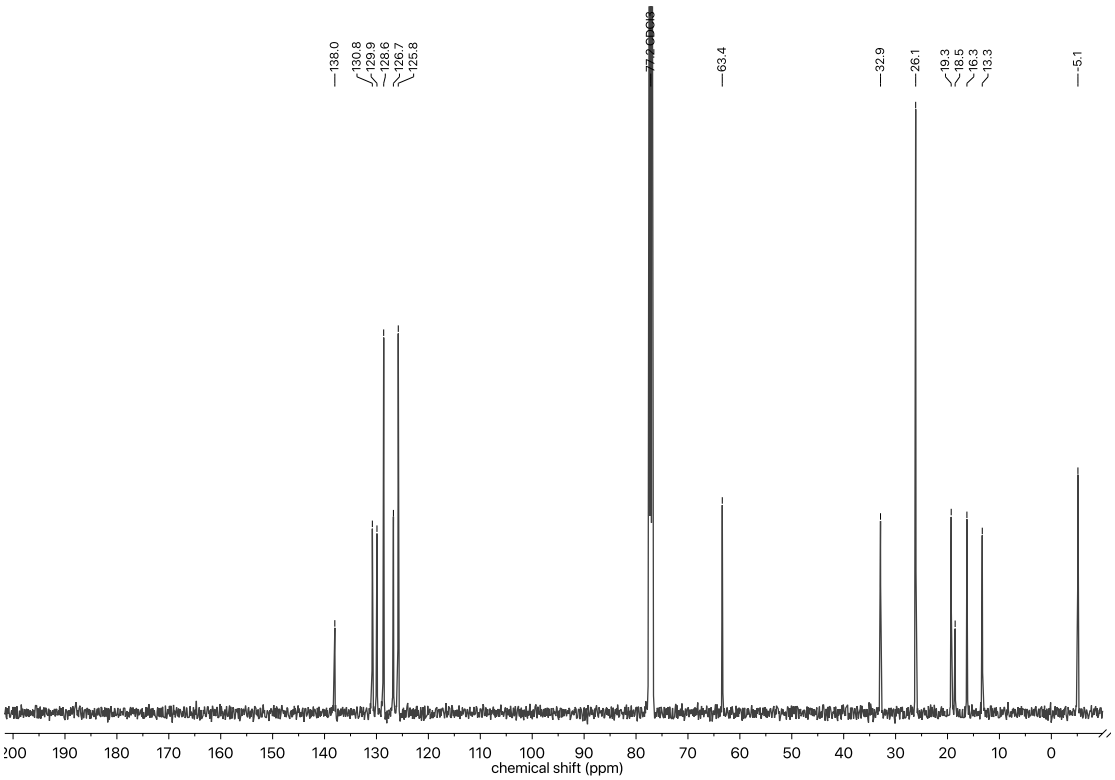


(*E*)-*tert*-Butyldimethyl(2-(2-styrylcyclopropyl)ethoxy)silane ((*E*)-121)

^{1}H NMR:

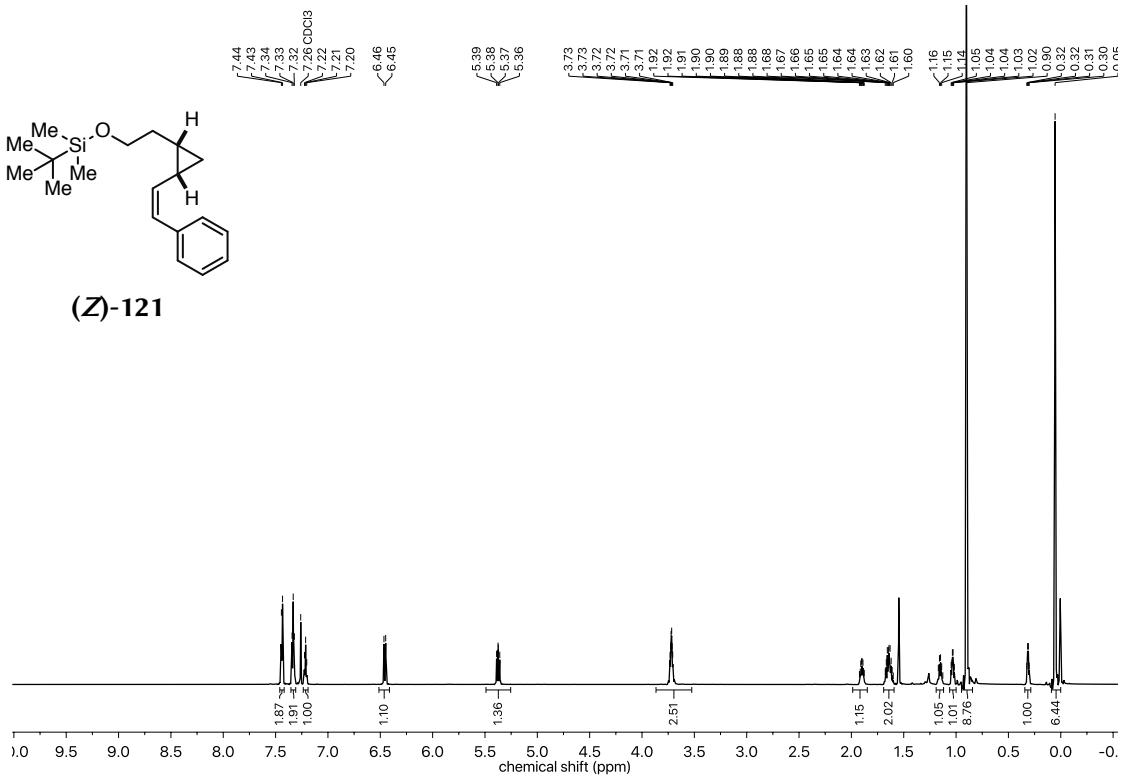


^{13}C NMR:

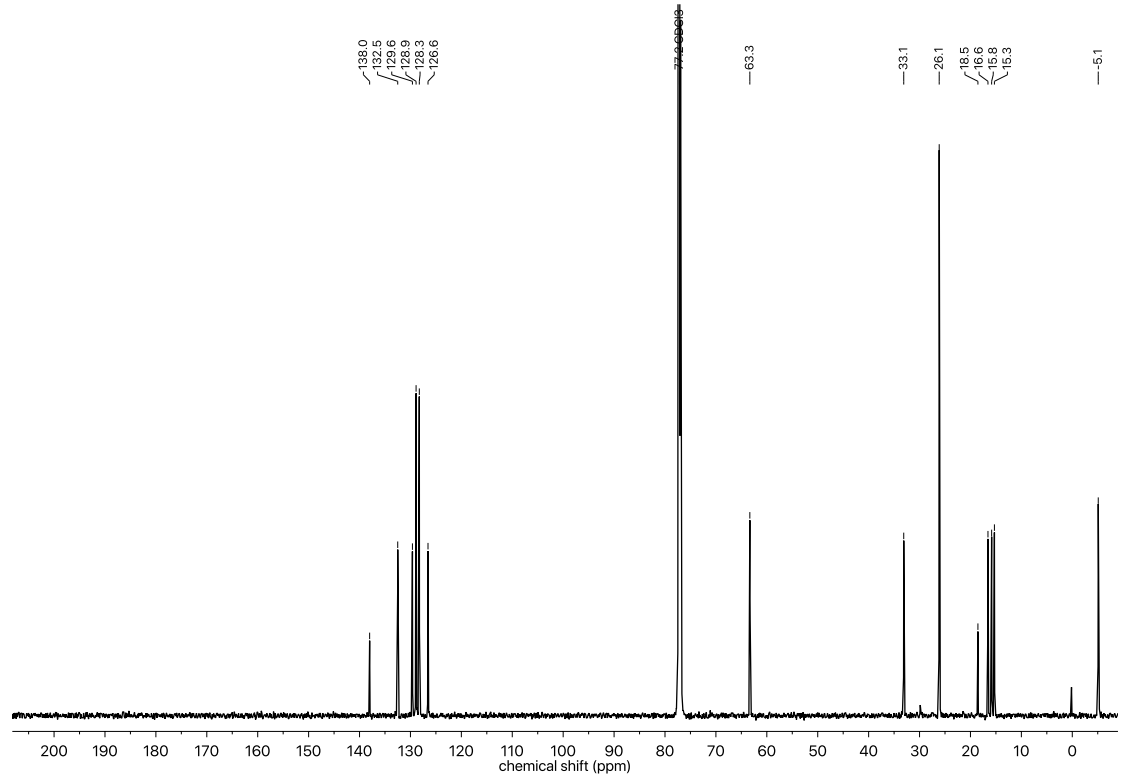


(*Z*)-*tert*-Butyldimethyl(2-(2-styrylcyclopropyl)ethoxy)silane ((*Z*)-121)

^{1}H NMR:

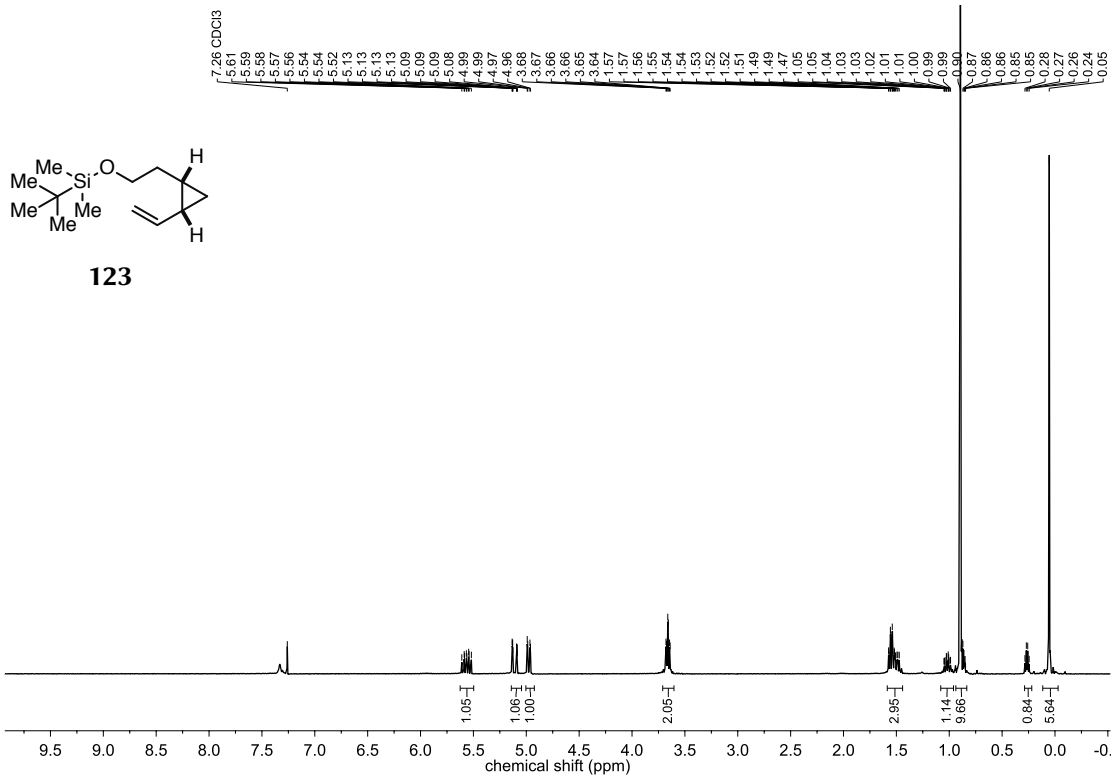


^{13}C NMR:



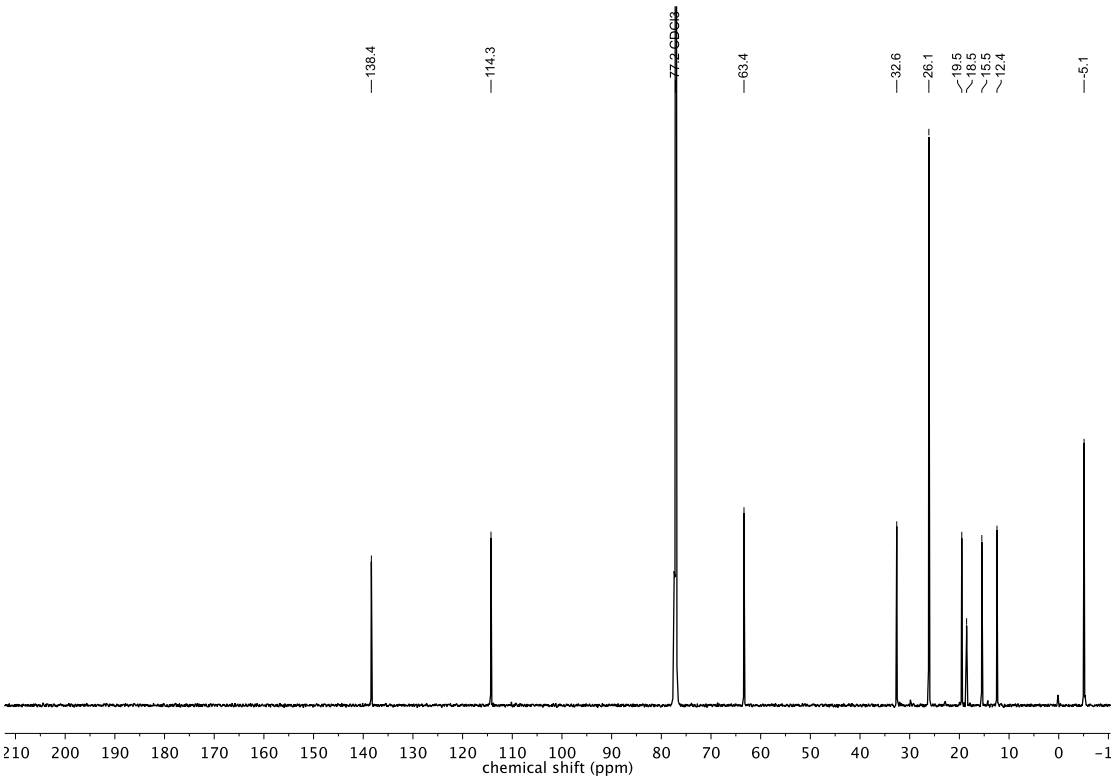
tert-Butyldimethyl(2-(2-vinylcyclopropyl)ethoxy)silane (123)

^{1}H NMR:



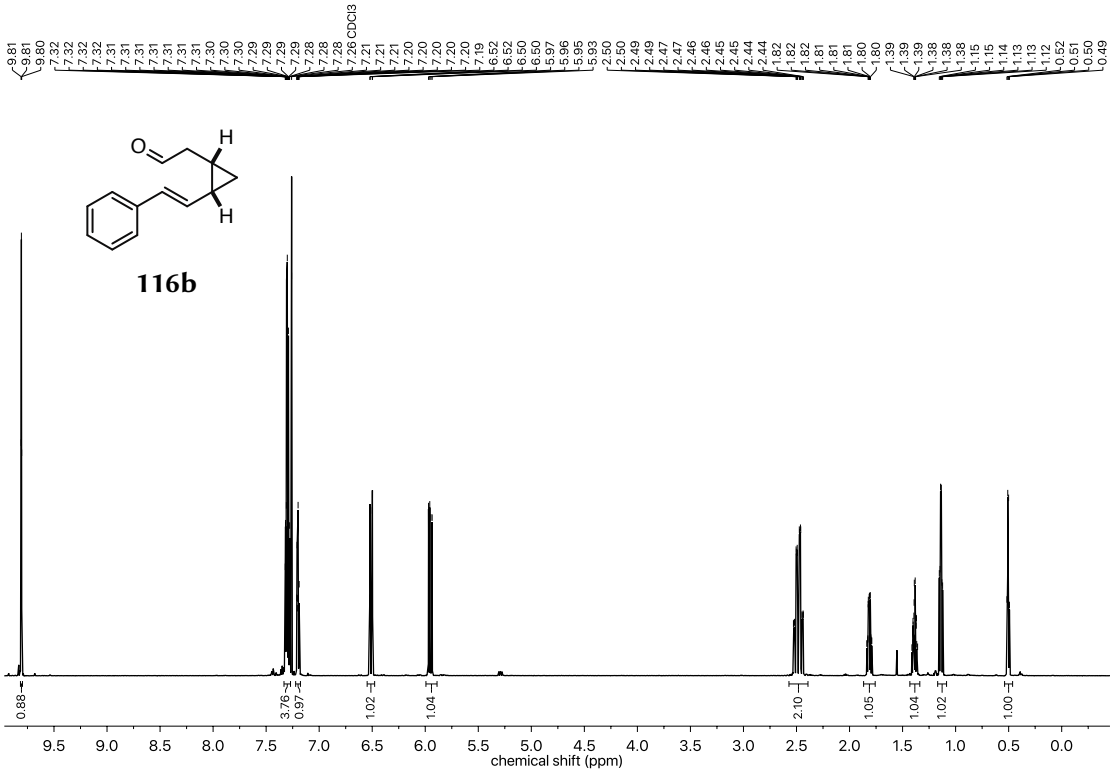
123

^{13}C NMR:

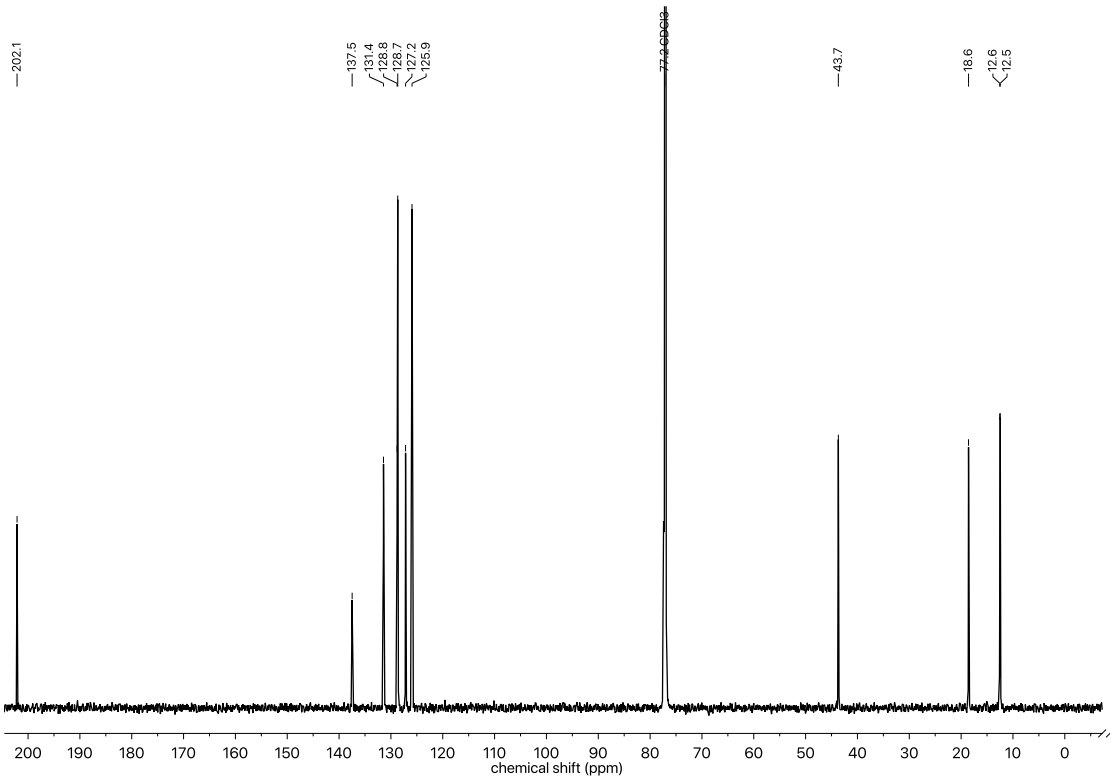


2-(2-((*E*)-Styryl)cyclopropyl)acetaldehyde (116b)

^{1}H NMR:

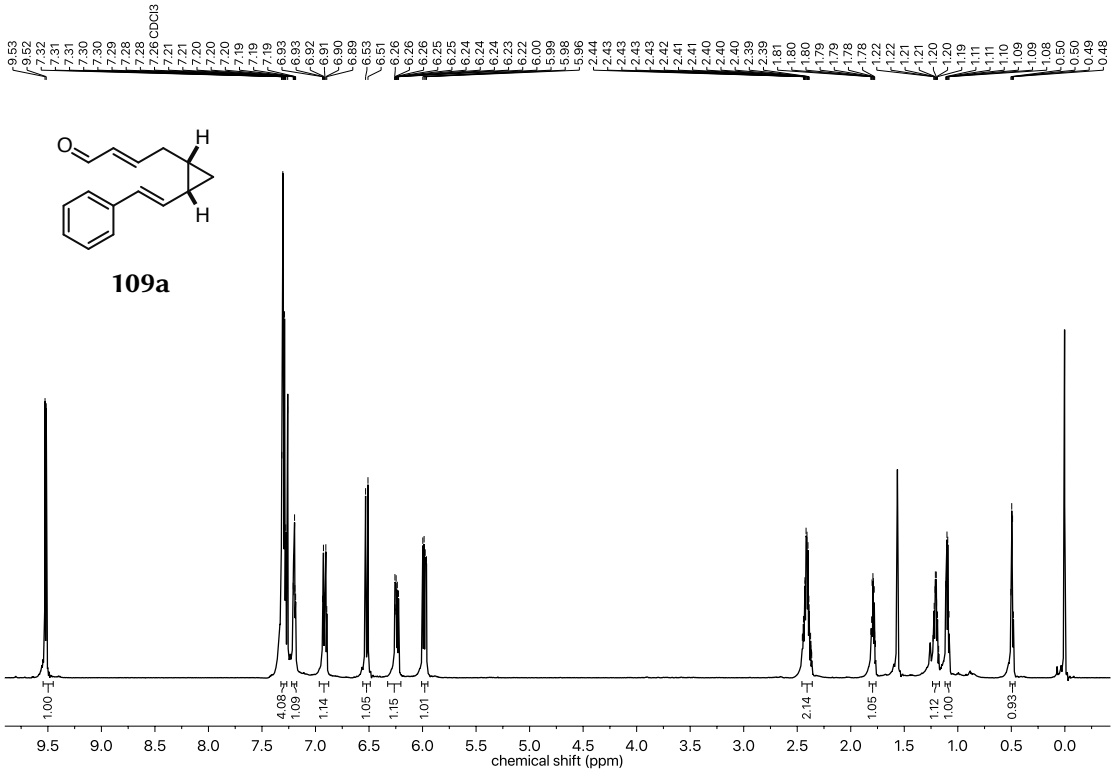


^{13}C NMR:

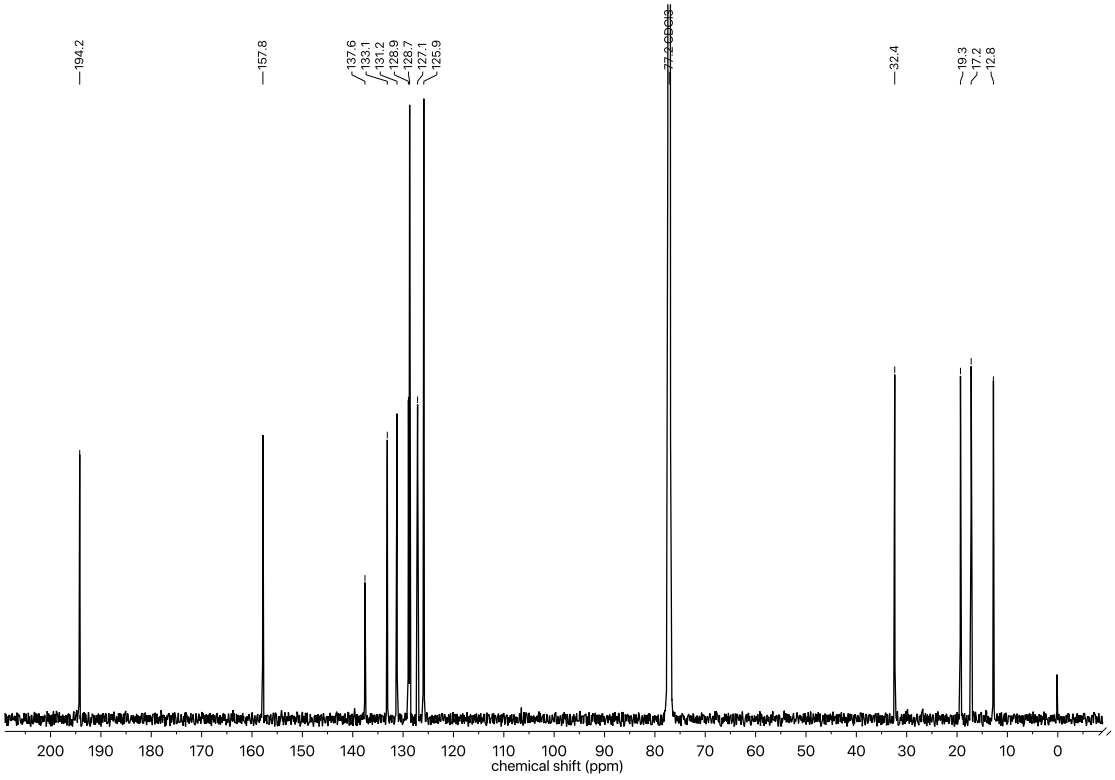


(*E*)-4-(2-((*E*)-Styryl)cyclopropyl)but-2-enal (109a)

^{1}H NMR:

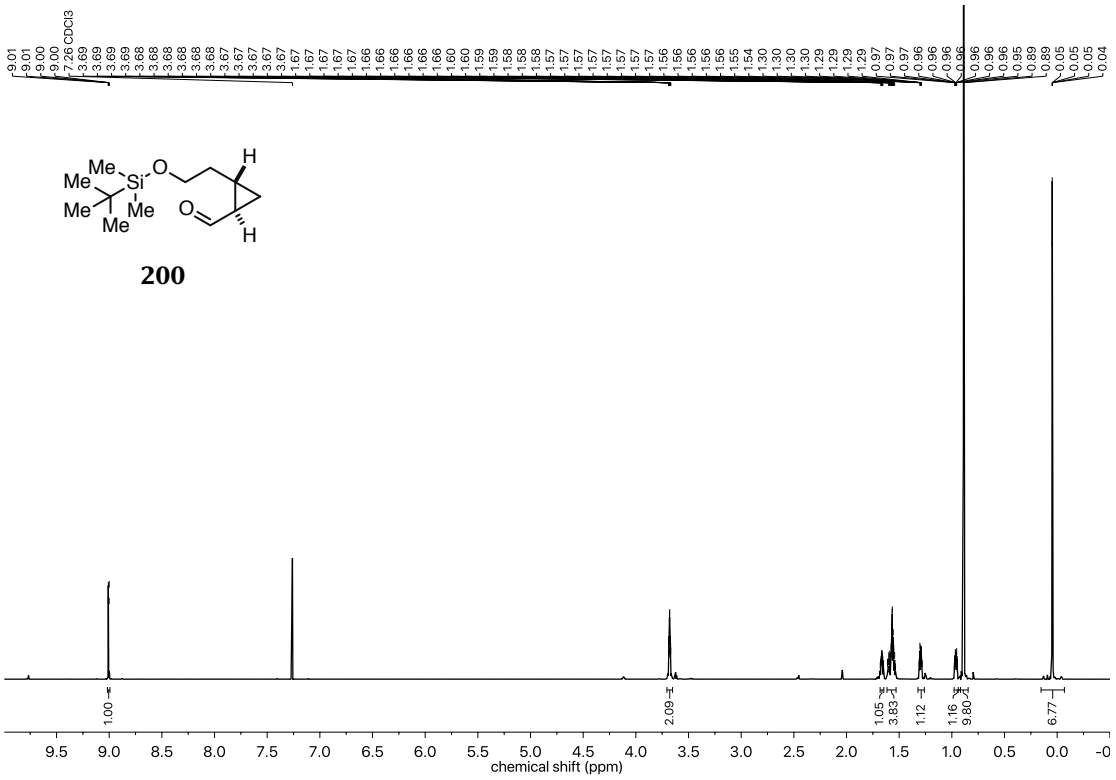


^{13}C NMR:



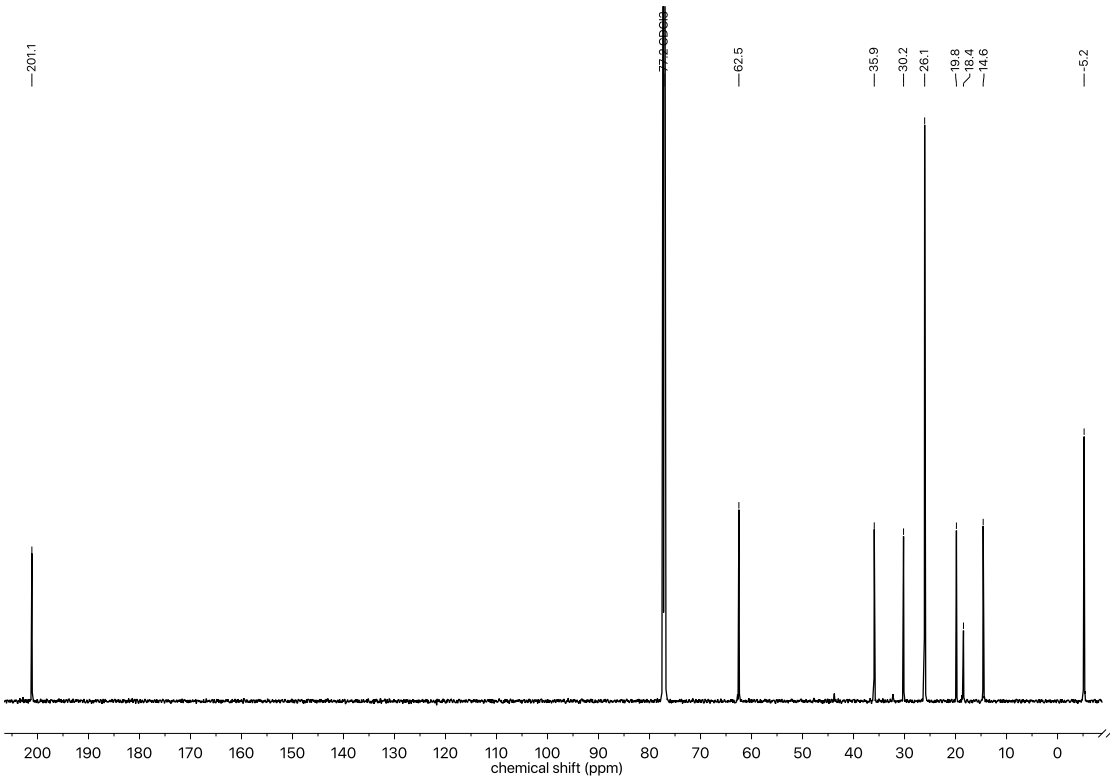
(*trans*-2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropane-1-carbaldehyde (200)

^{1}H NMR:



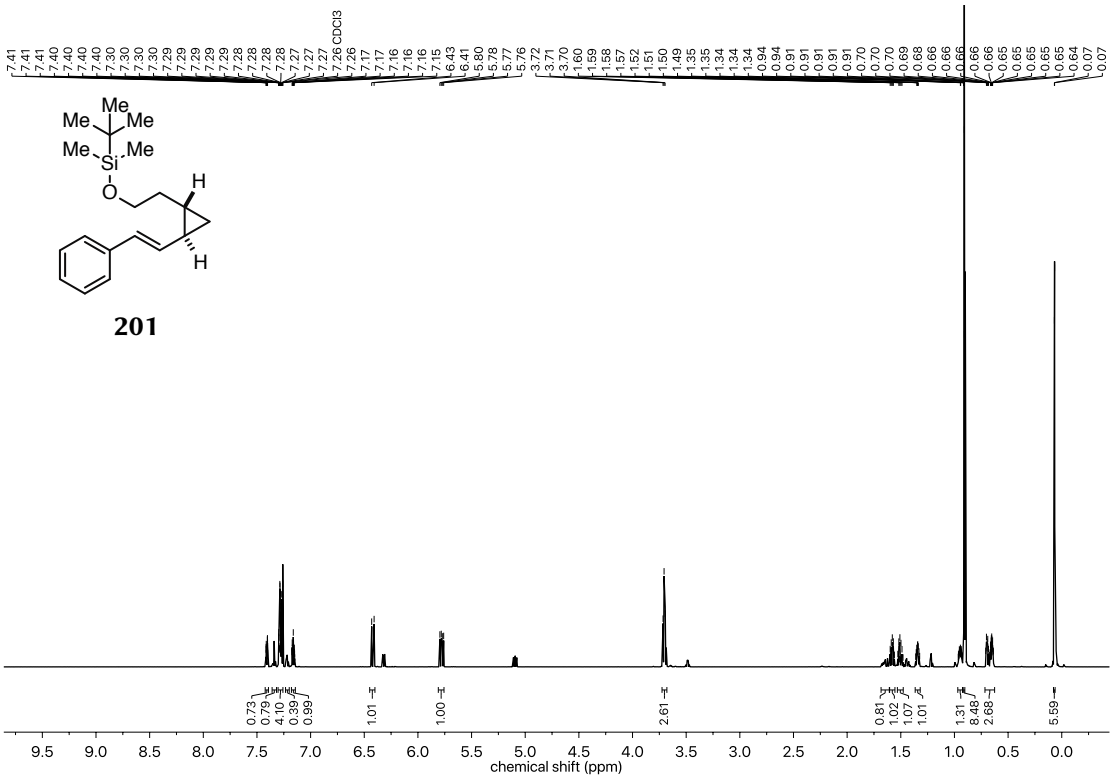
200

^{13}C NMR:



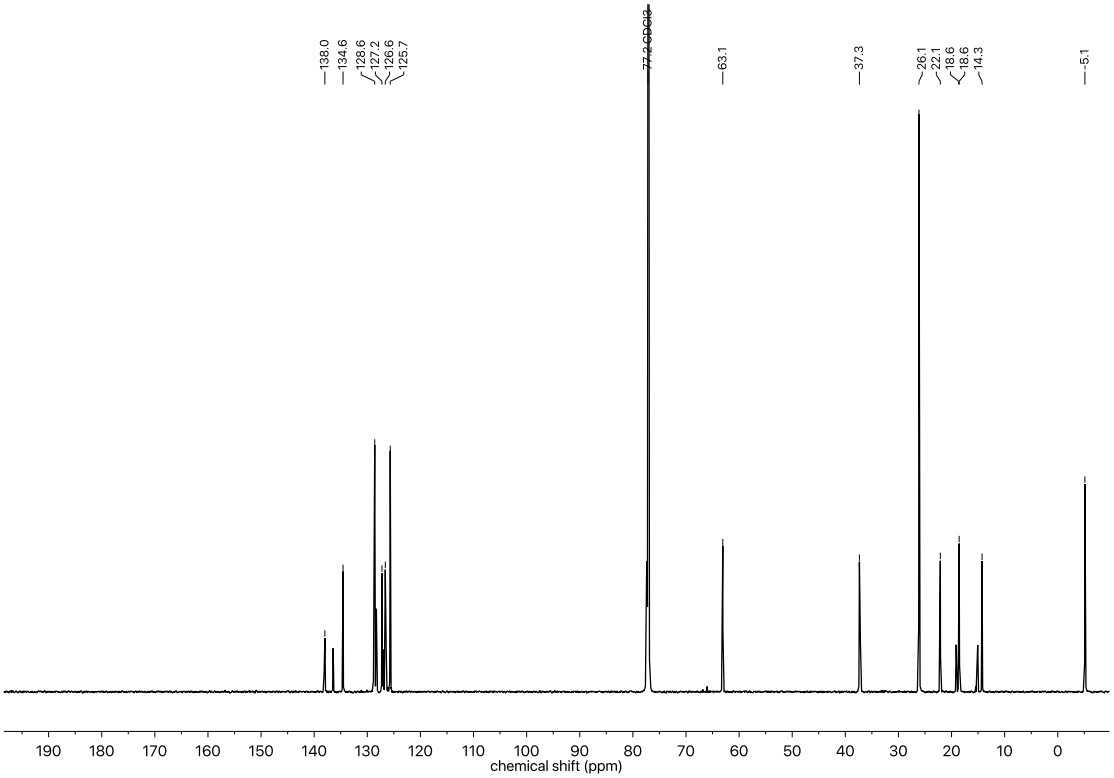
(*tert*-Butyldimethyl(2-(*trans*-2-((*E*)-styryl)cyclopropyl)ethoxy)silane (201)

^{1}H NMR:



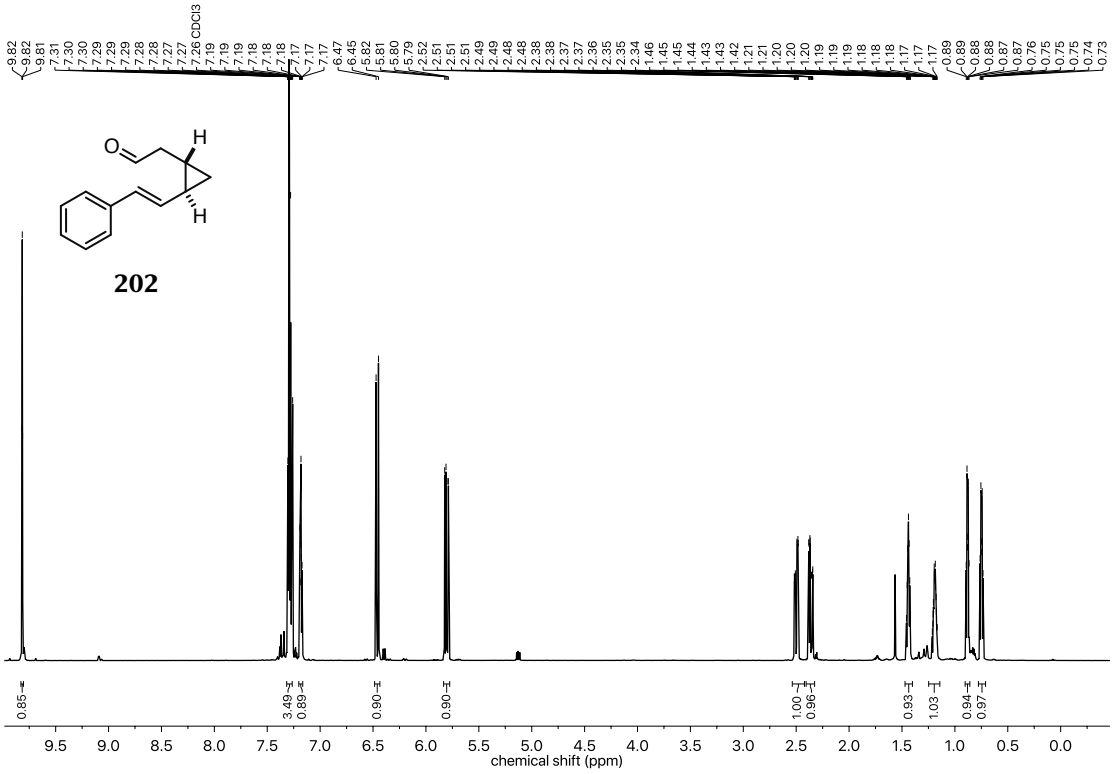
201

^{13}C NMR:

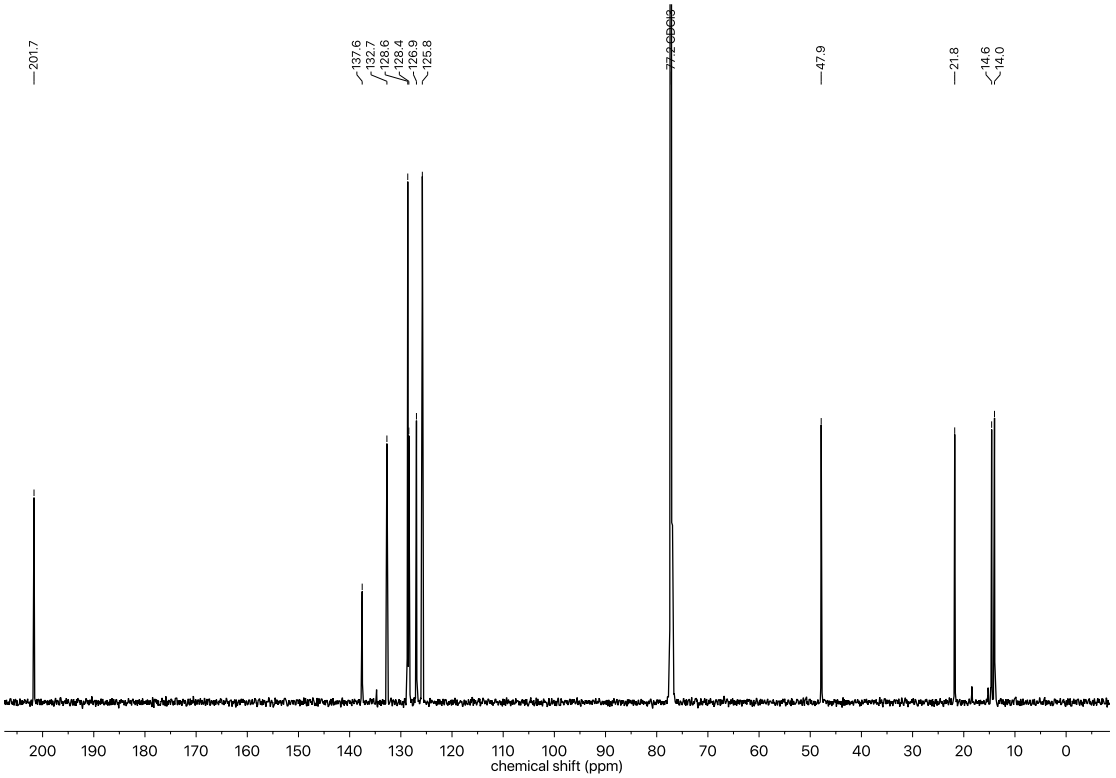


2-(*trans*-2-((*E*)-Styryl)cyclopropyl)acetaldehyde (202)

^{1}H NMR:

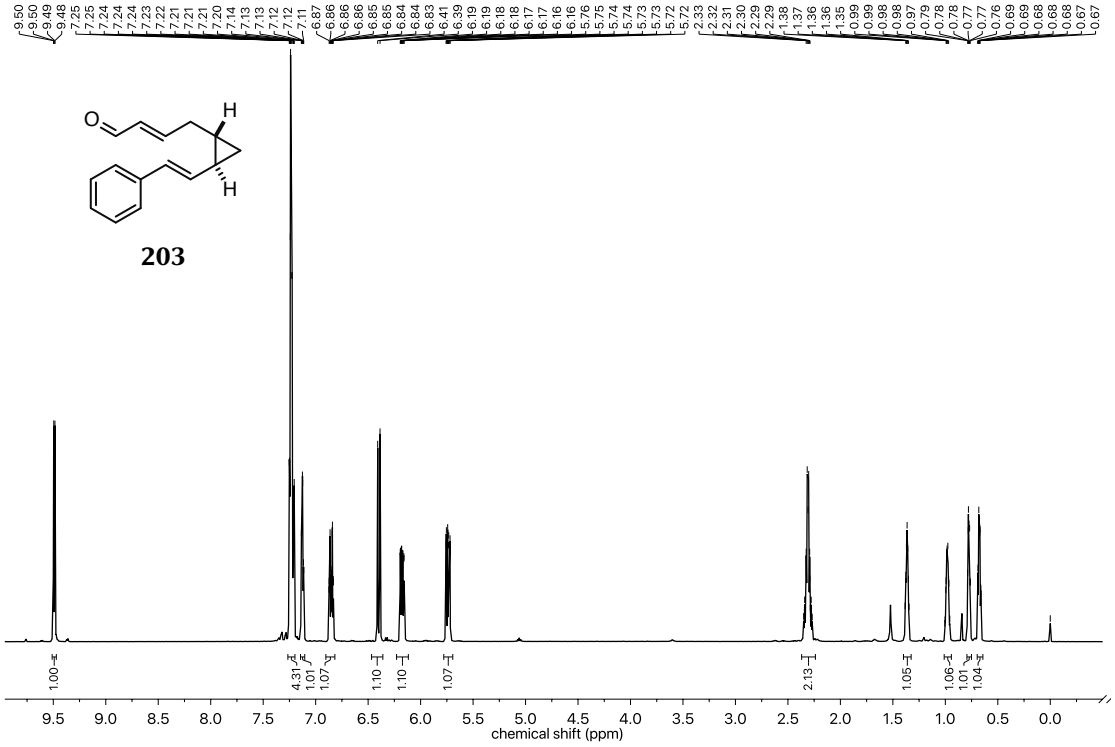


^{13}C NMR:

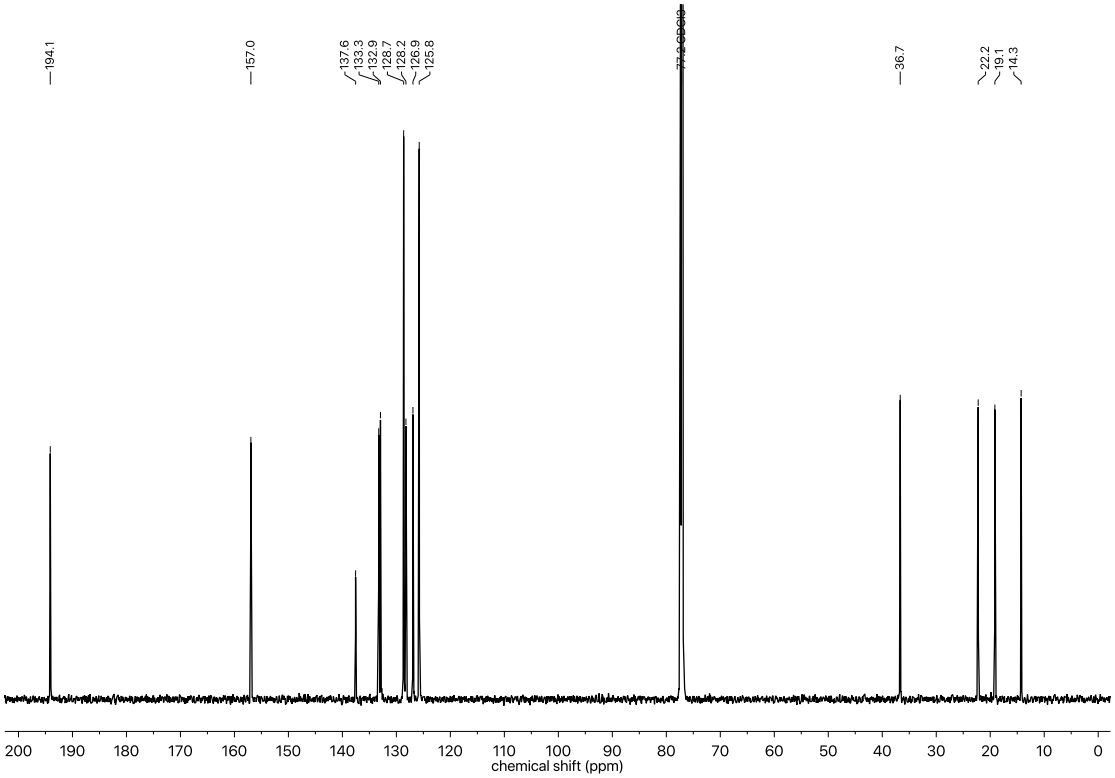


(*E*)-4-(*trans*-2-((*E*)-Styryl)cyclopropyl)but-2-enal (203)

^{1}H NMR:

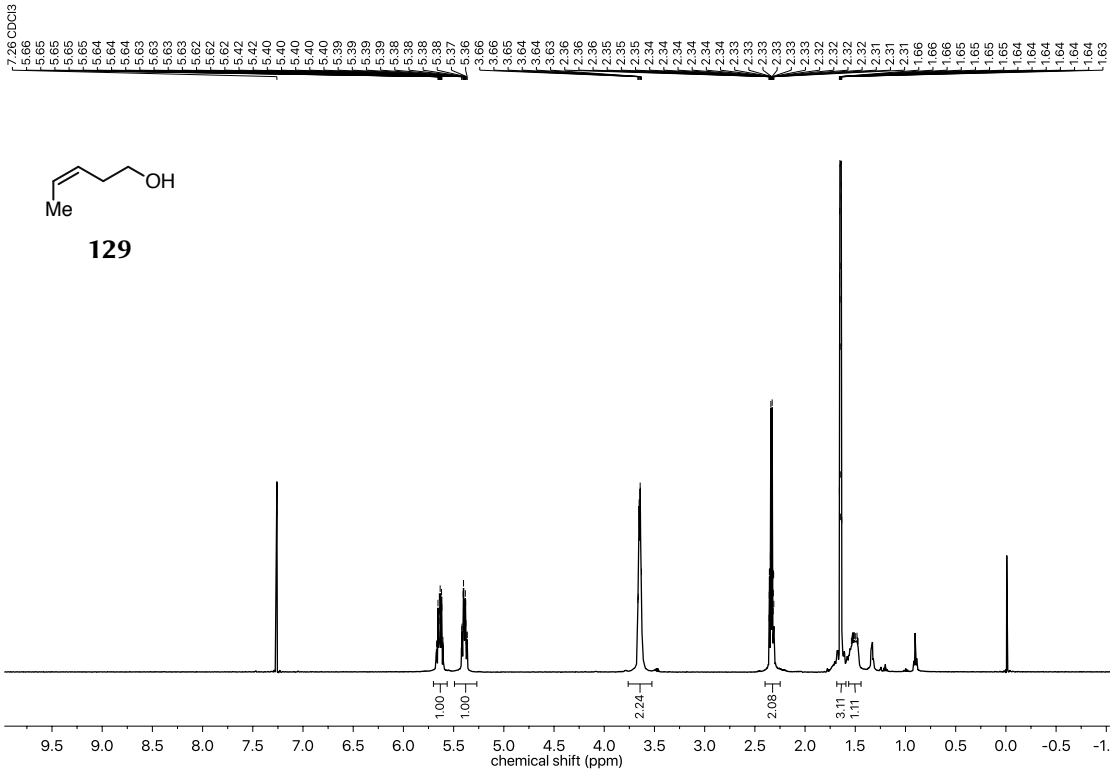


^{13}C NMR:

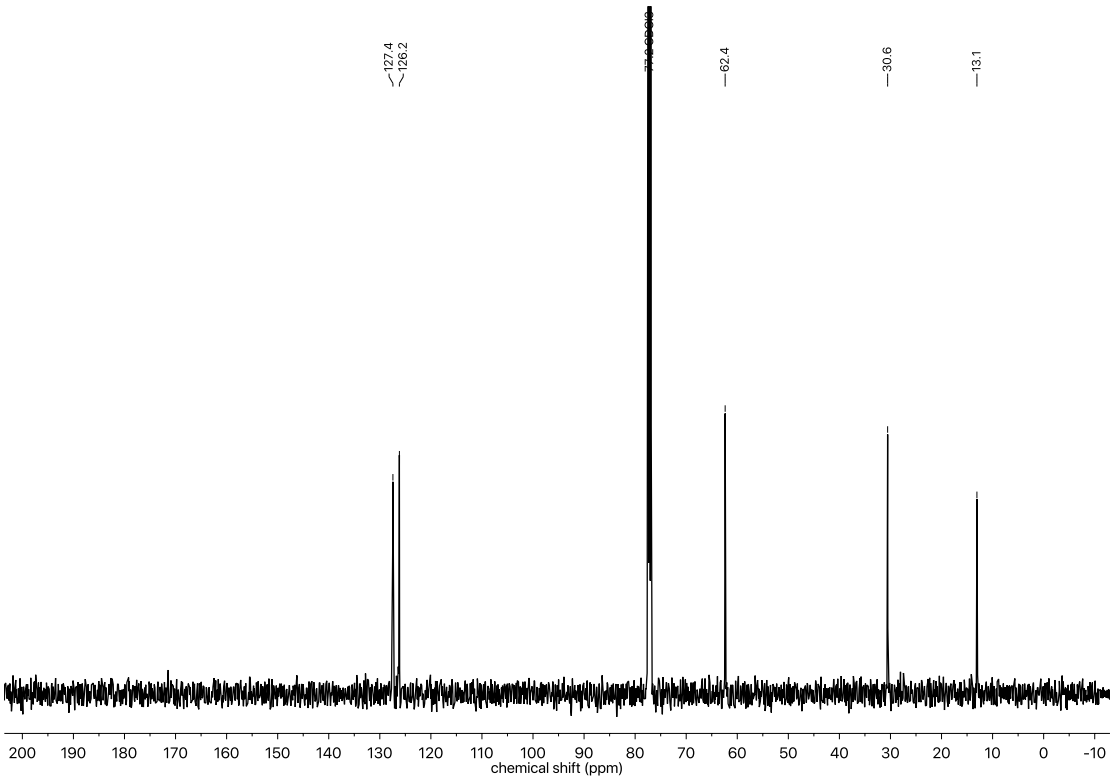


(*Z*)-3-Pentene-1-ol (129)

^{1}H NMR:

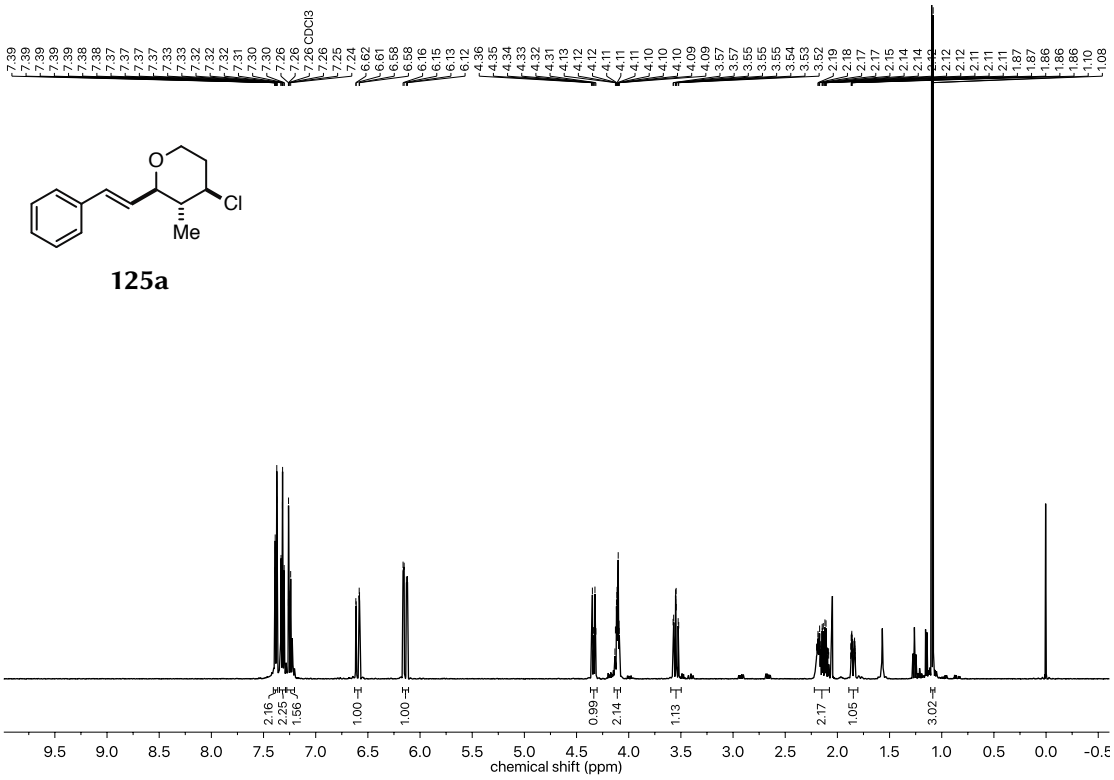


^{13}C NMR:



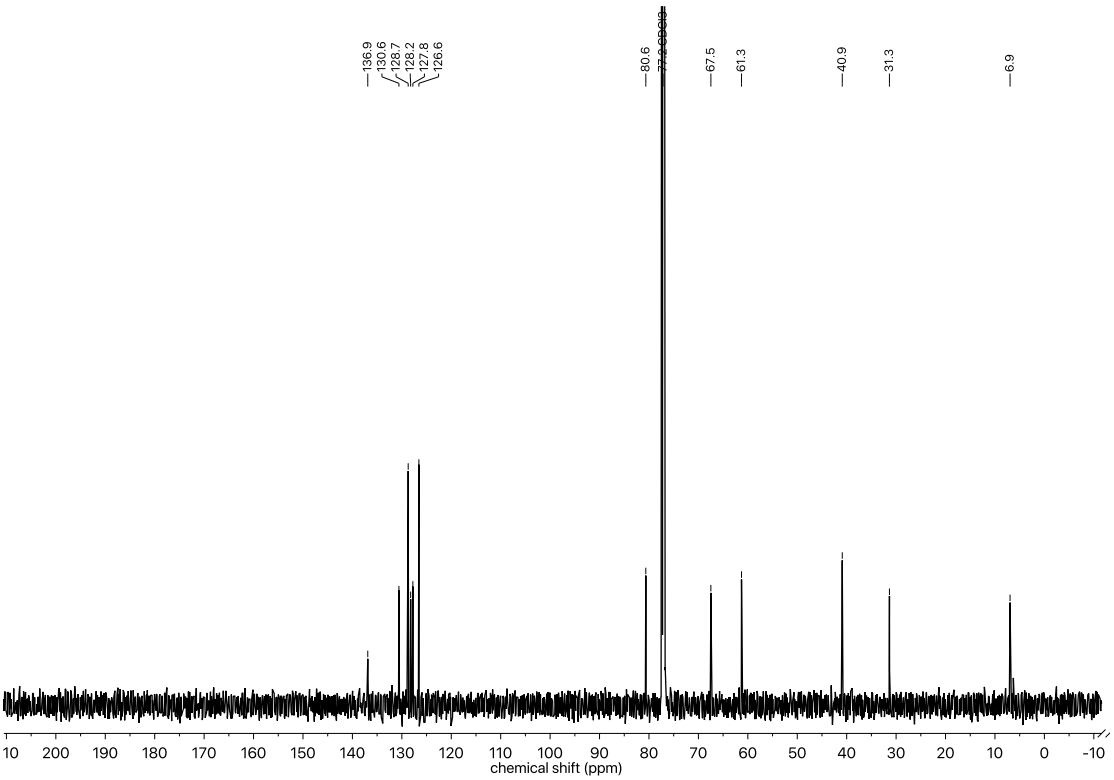
4-Chloro-3-methyl-2((*E*)-styryl)tetrahydro-2*H*-pyran (125a)

^{1}H NMR:



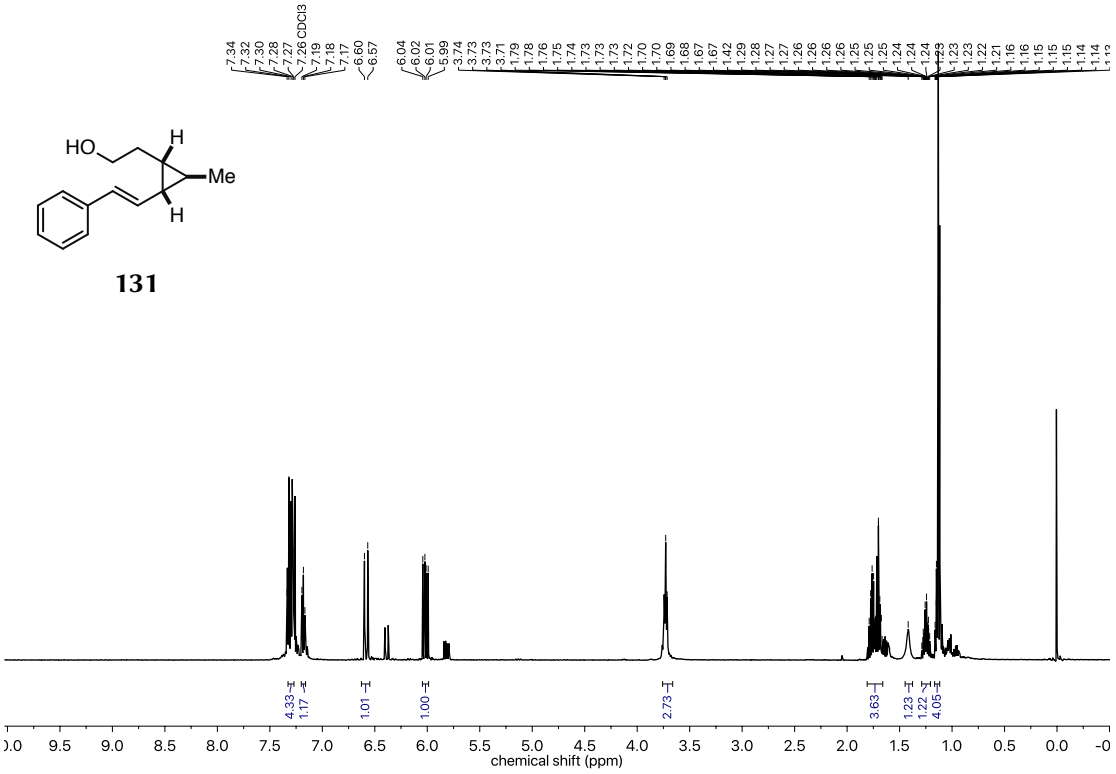
125a

^{13}C NMR:

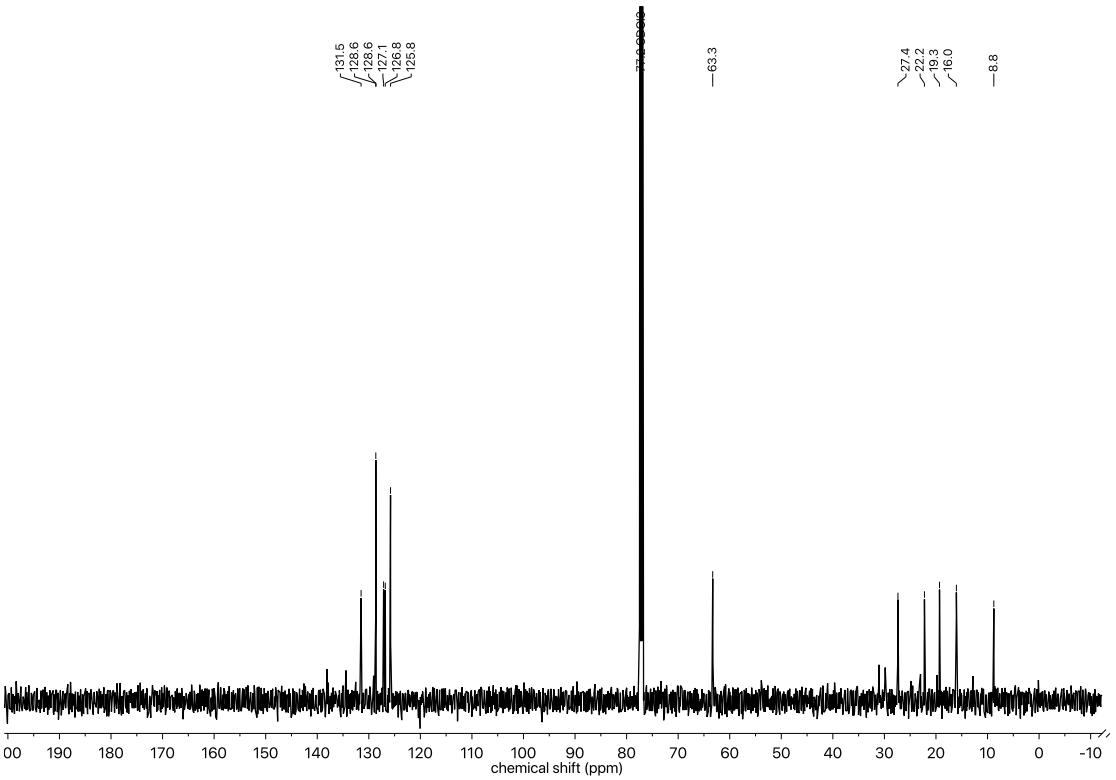


2-(2-Methyl-3-((*E*)-styryl)cyclopropyl)ethan-1-ol (131)

^{1}H NMR:

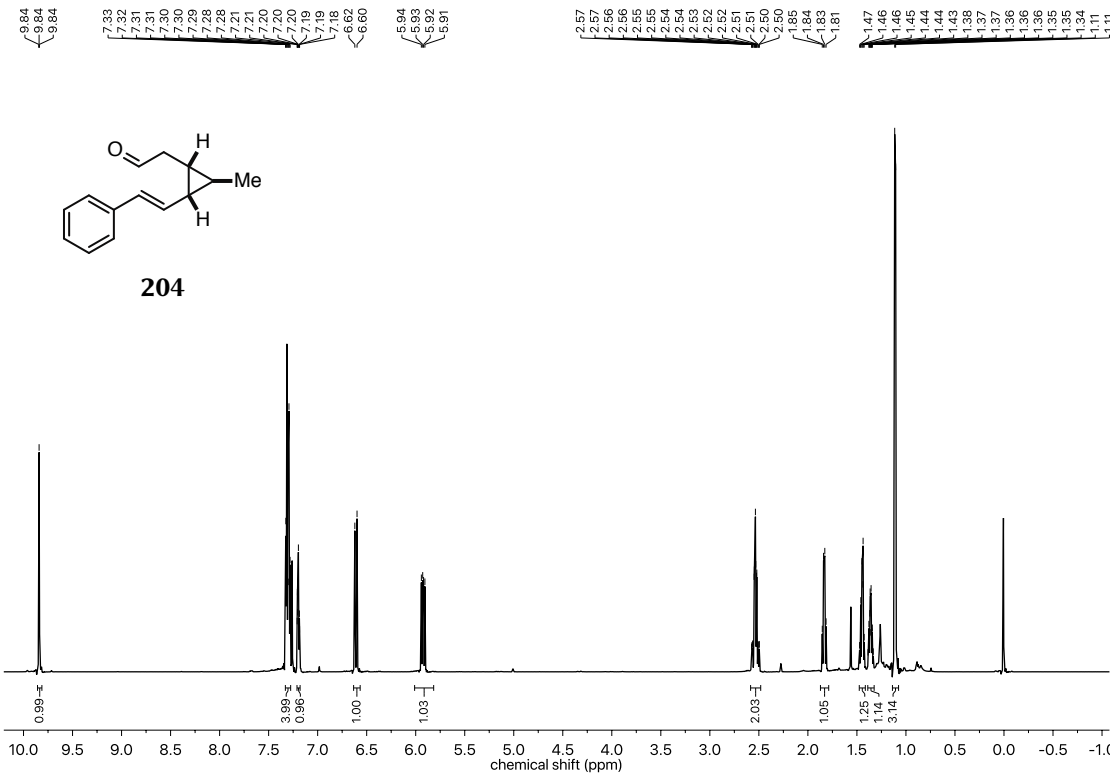


^{13}C NMR:

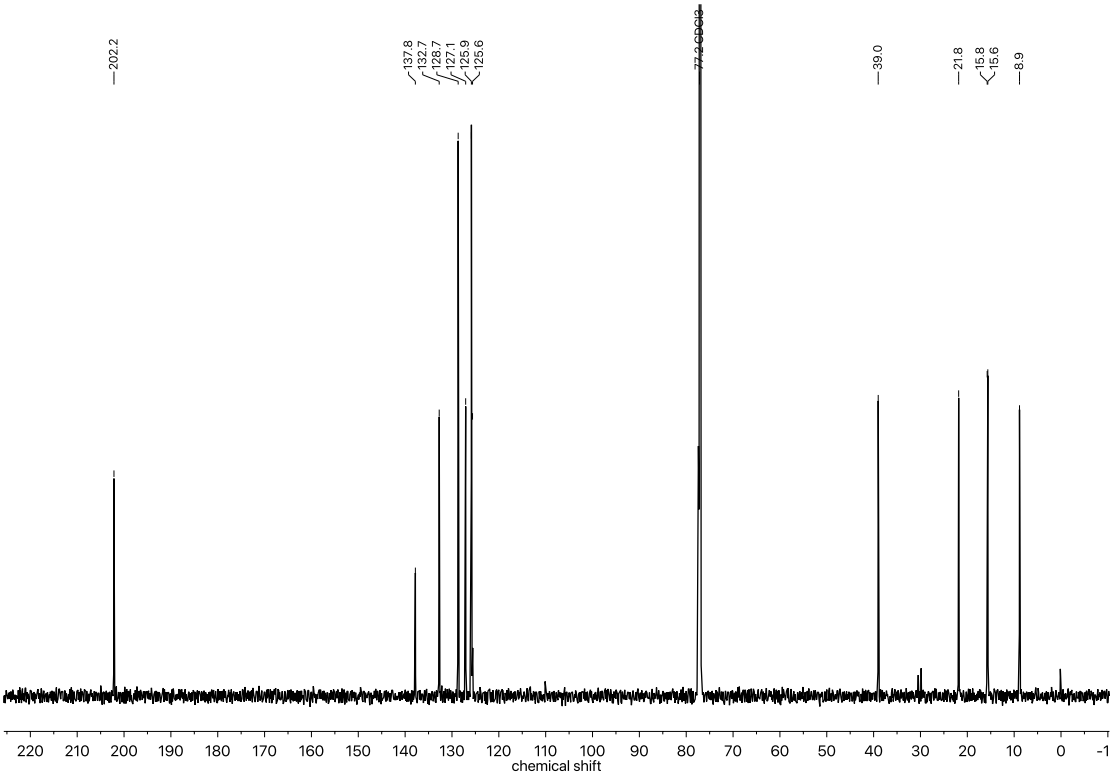


2-(2-Methyl-3-((*E*)-styryl)cyclopropyl)acetaldehyde (204)

^{1}H NMR:

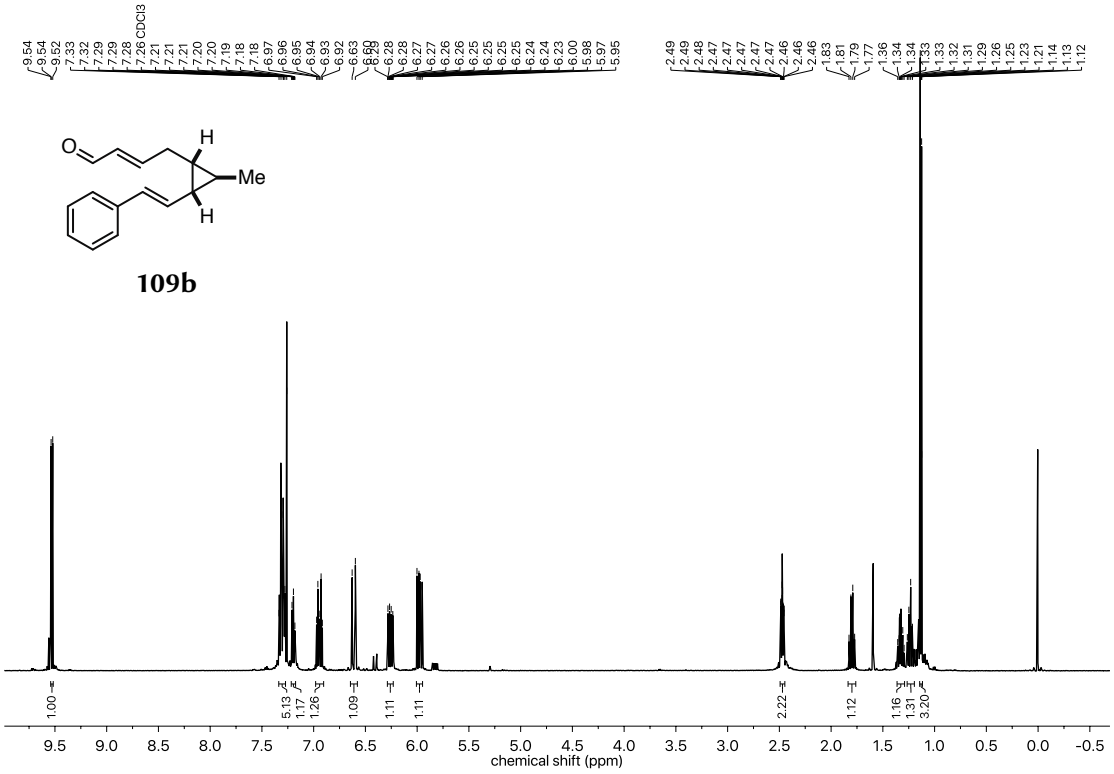


^{13}C NMR:

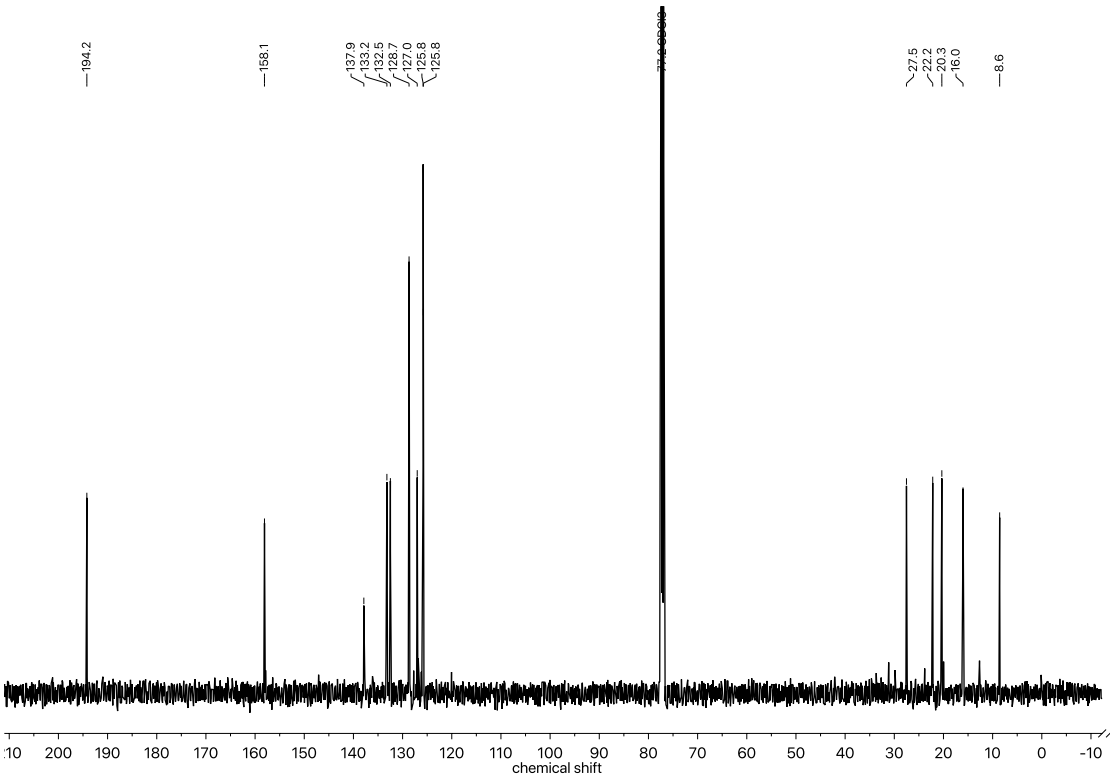


(*E*)-4-(2-Methyl-3-((*E*)-styryl)cyclopropyl)but-2-enal (109b)

^{1}H NMR:

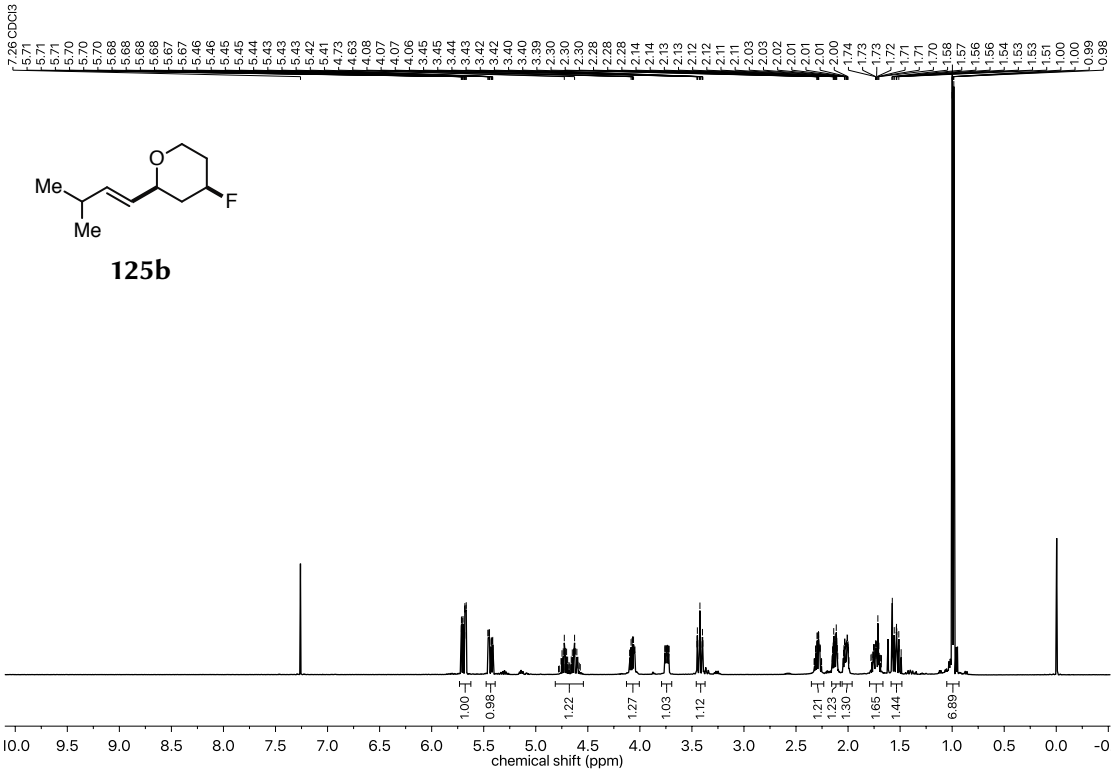


^{13}C NMR:



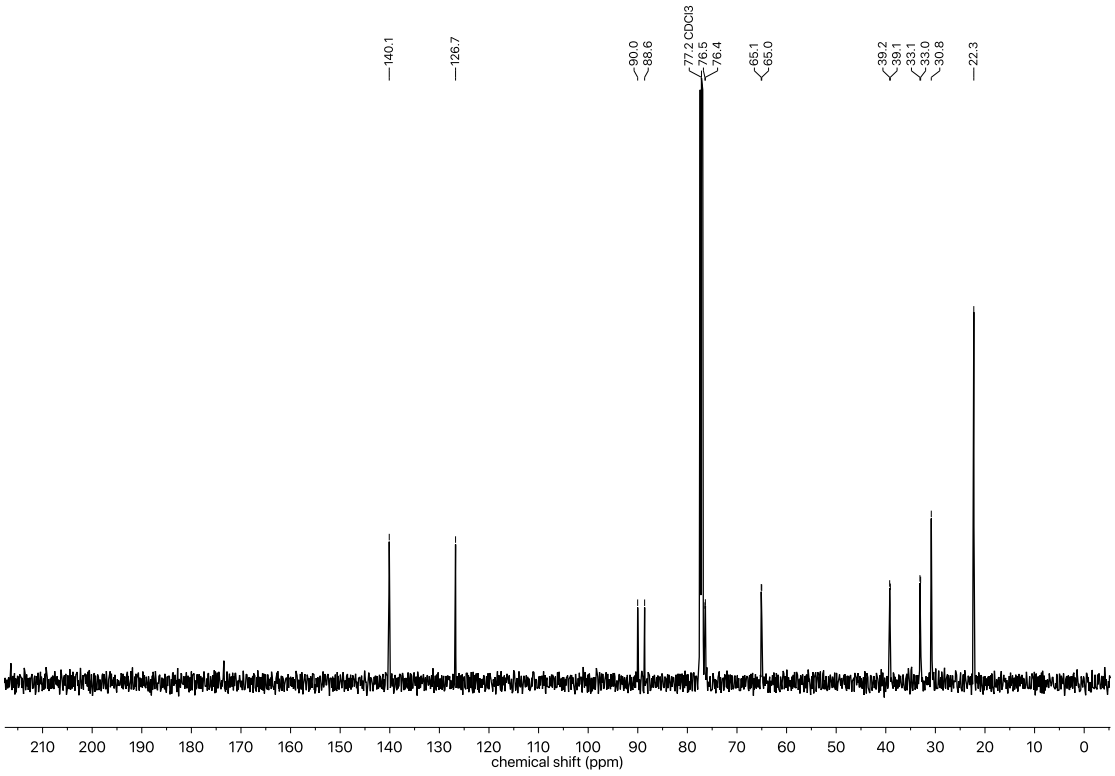
4-Fluoro2-((*E*)-3-methylbut-1-en-1-yl)tetrahydro-2*H*-pyran (125b)

^{1}H NMR:



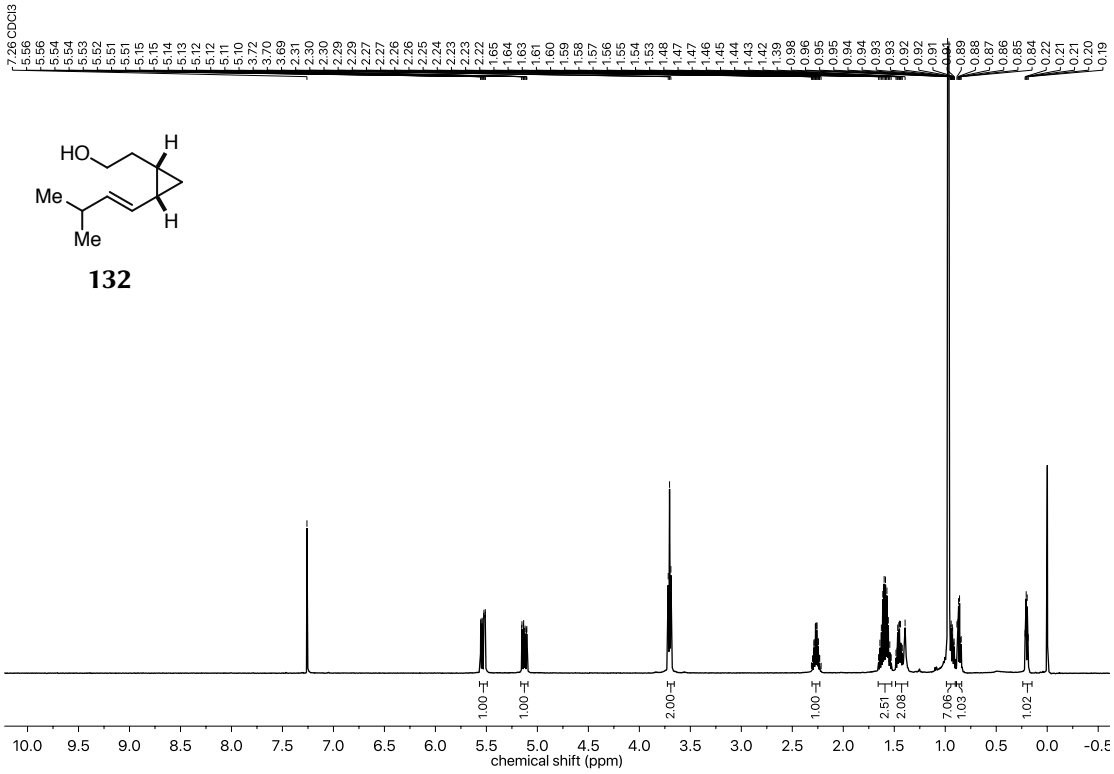
125b

^{13}C NMR:



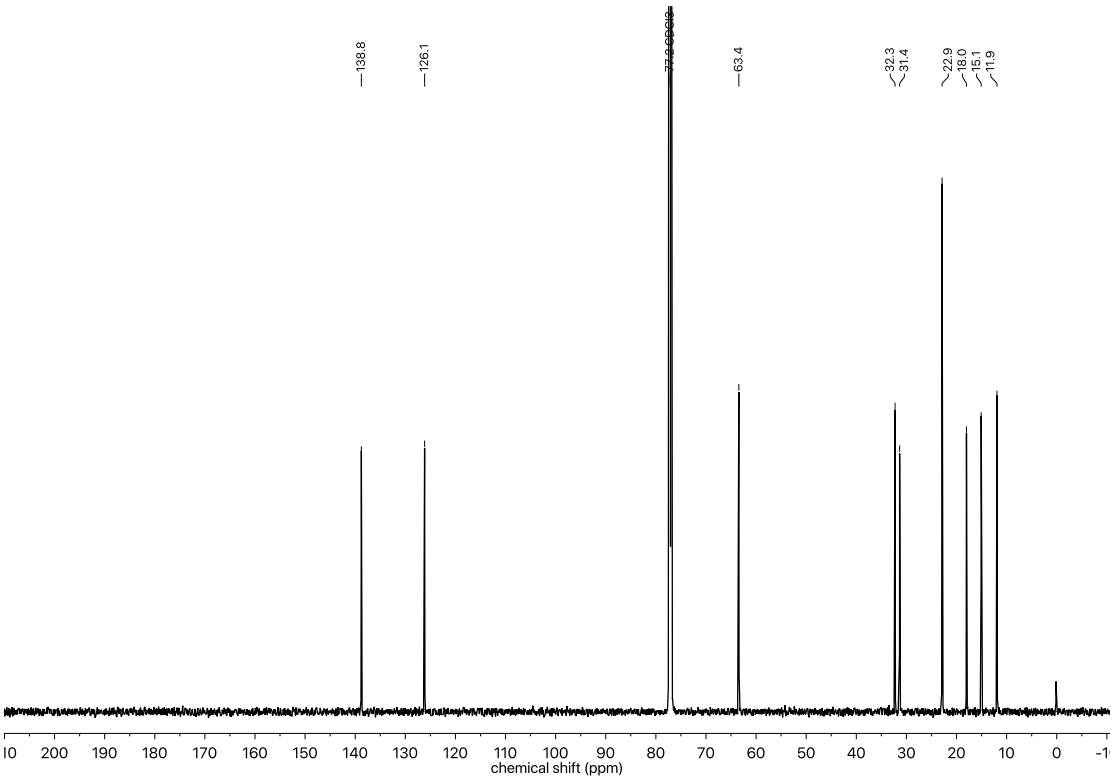
2-(2-((*E*)-3-Methylbut-1-en-1-yl)cyclopropyl)ethan-1-ol (132)

^{1}H NMR:



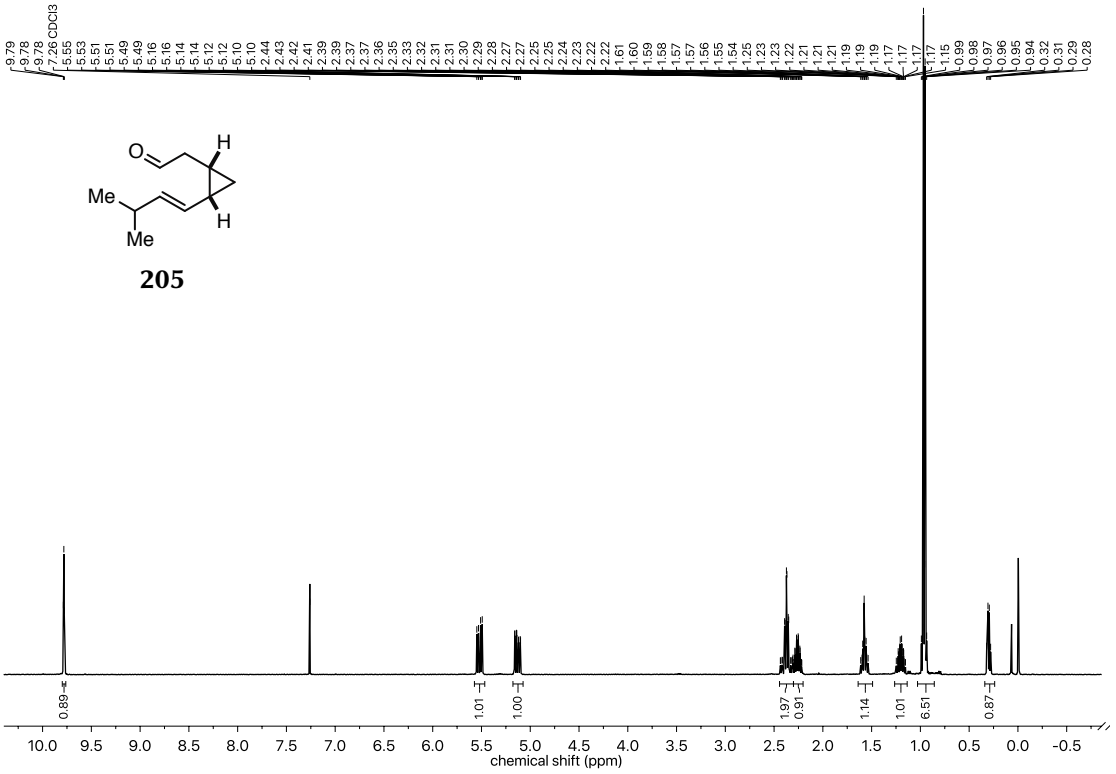
132

^{13}C NMR:



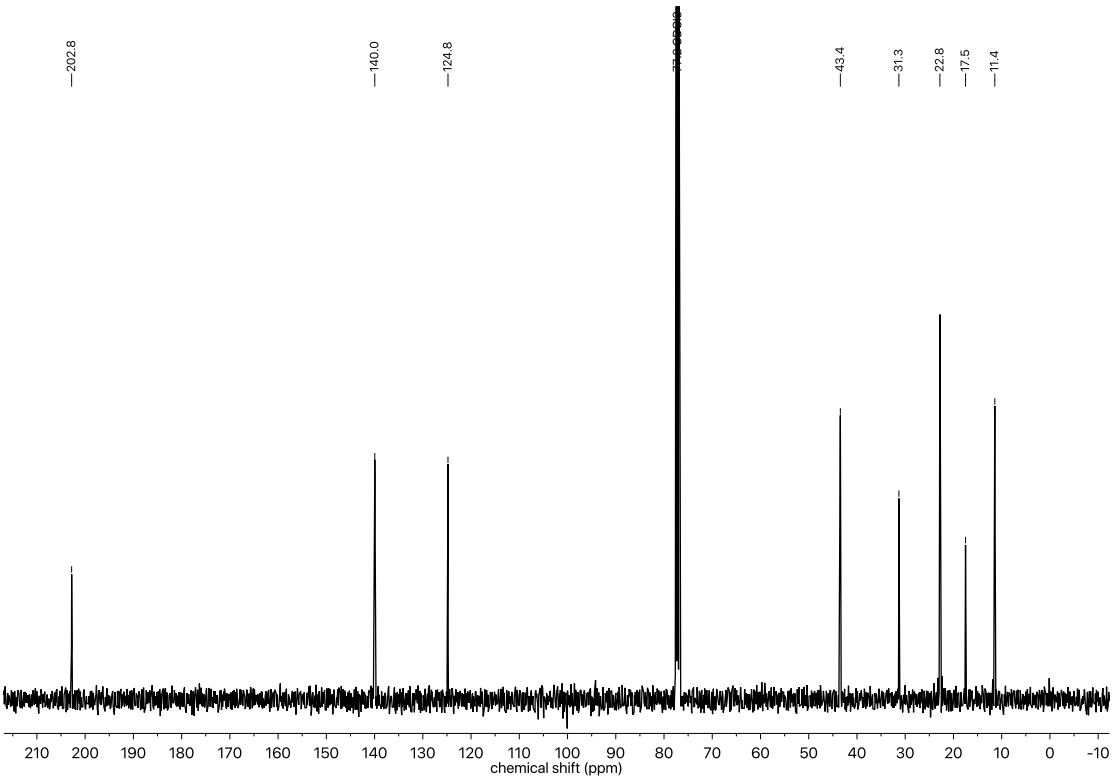
2-(2-((*E*)-3-Methylbut-1-en-1-yl)cyclopropyl)acetaldehyde (205)

^{1}H NMR:



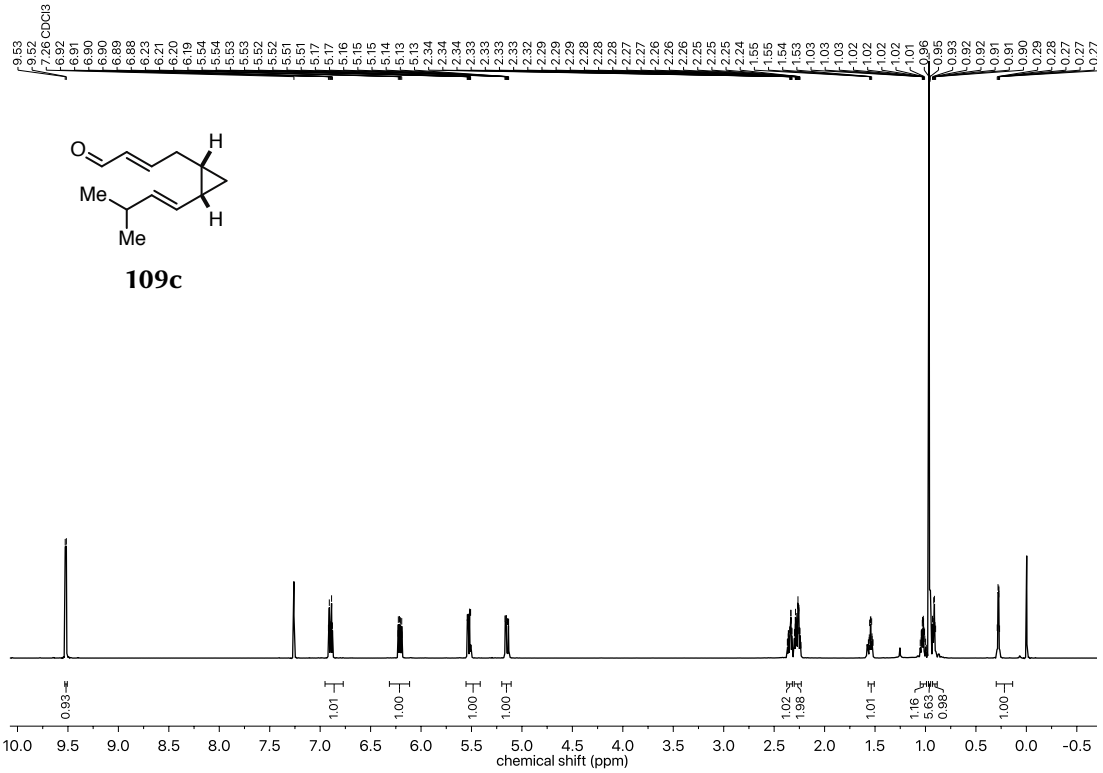
205

^{13}C NMR:

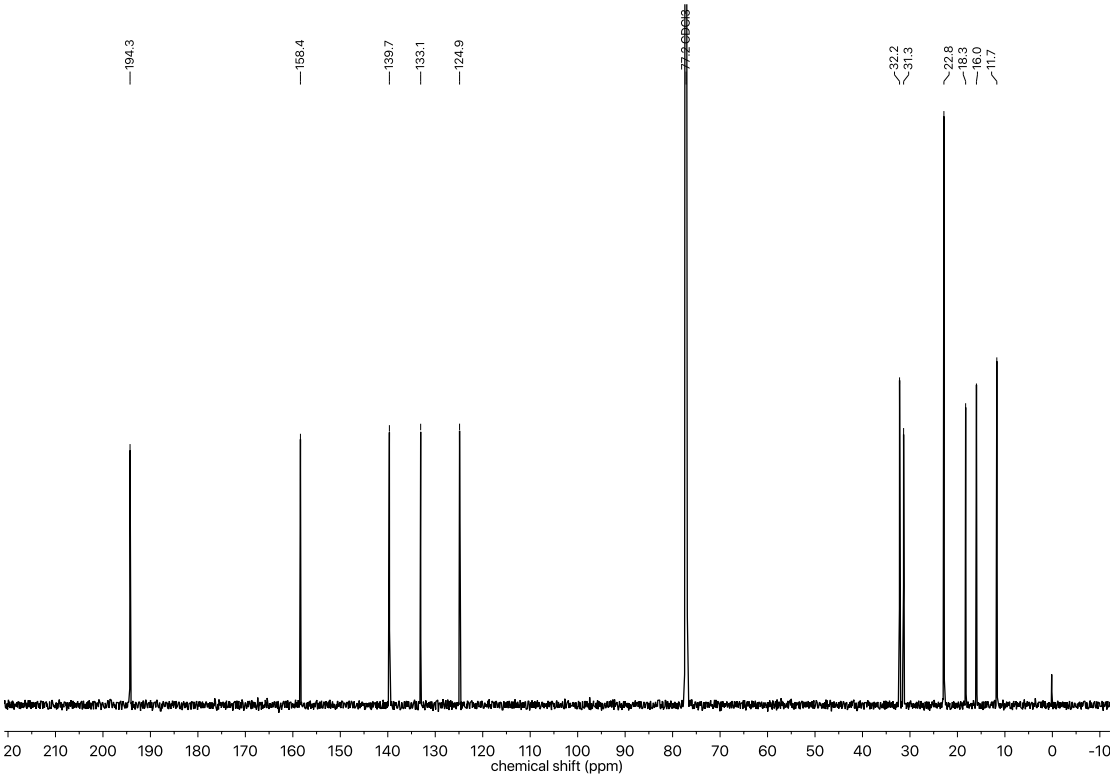


(*E*)-4-(2-((*E*)-3-Methylbut-1-en-1-yl)cyclopropyl)but-2-enal (109c)

^{1}H NMR:

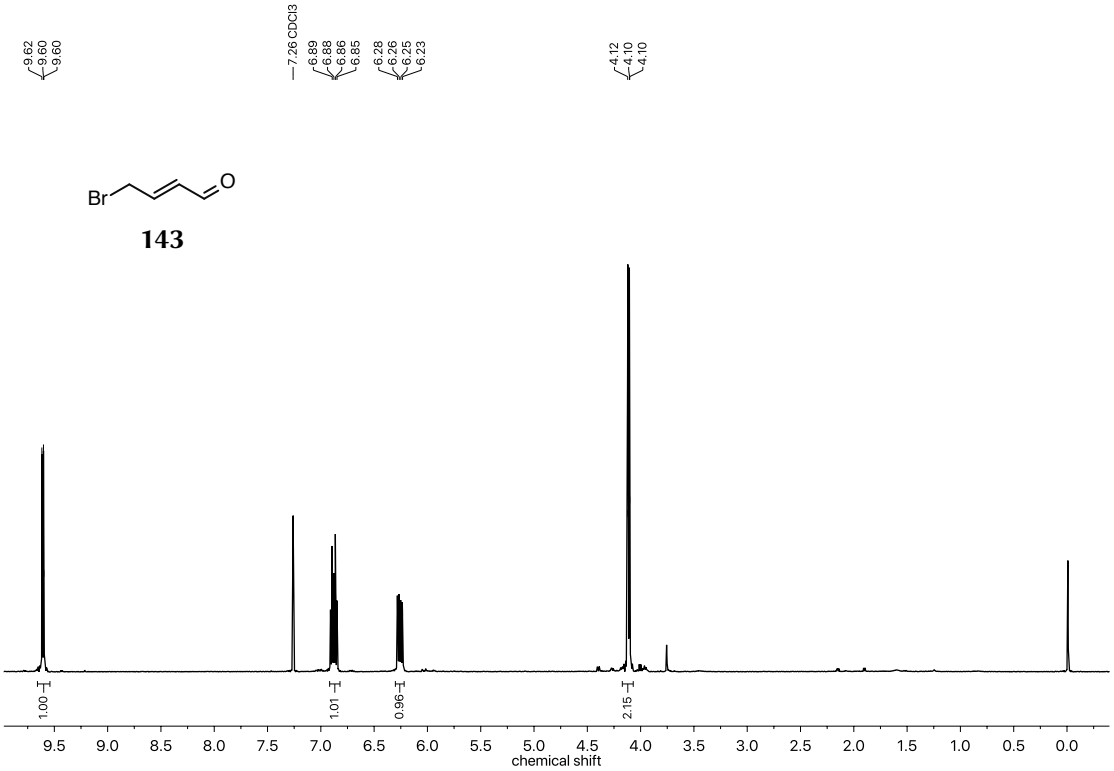


^{13}C NMR:

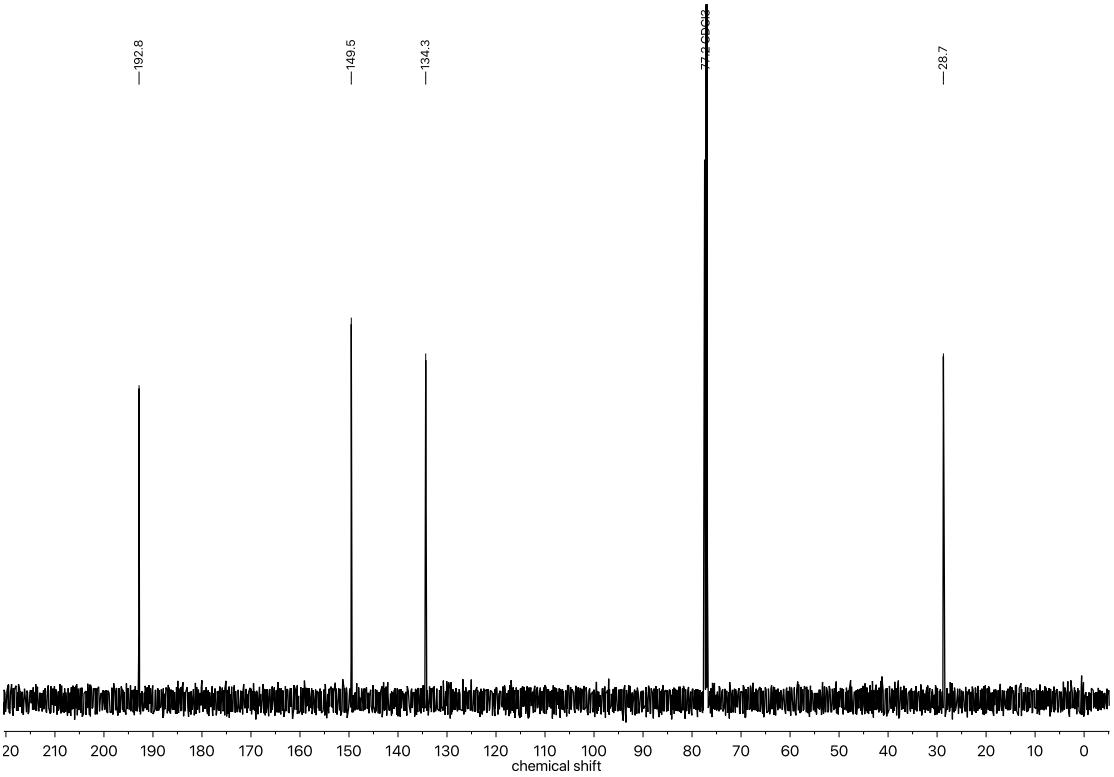


(*E*)-4-Bromobut-2-enal (143)

^{1}H NMR:

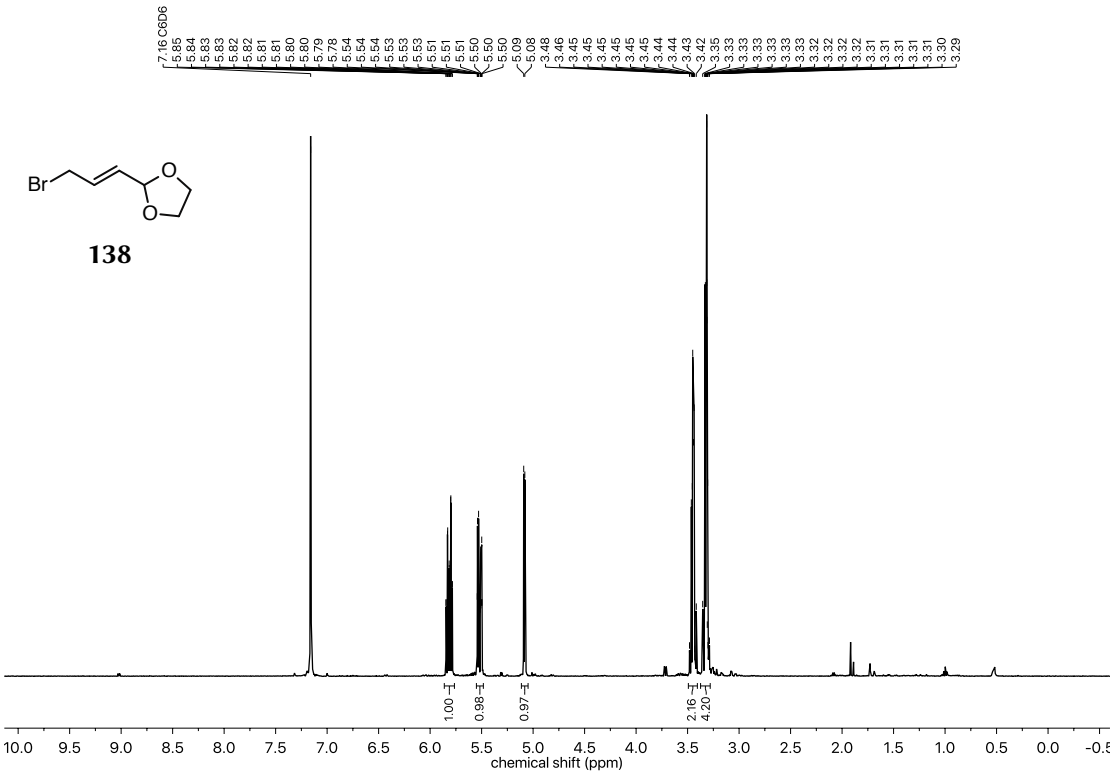


^{13}C NMR:

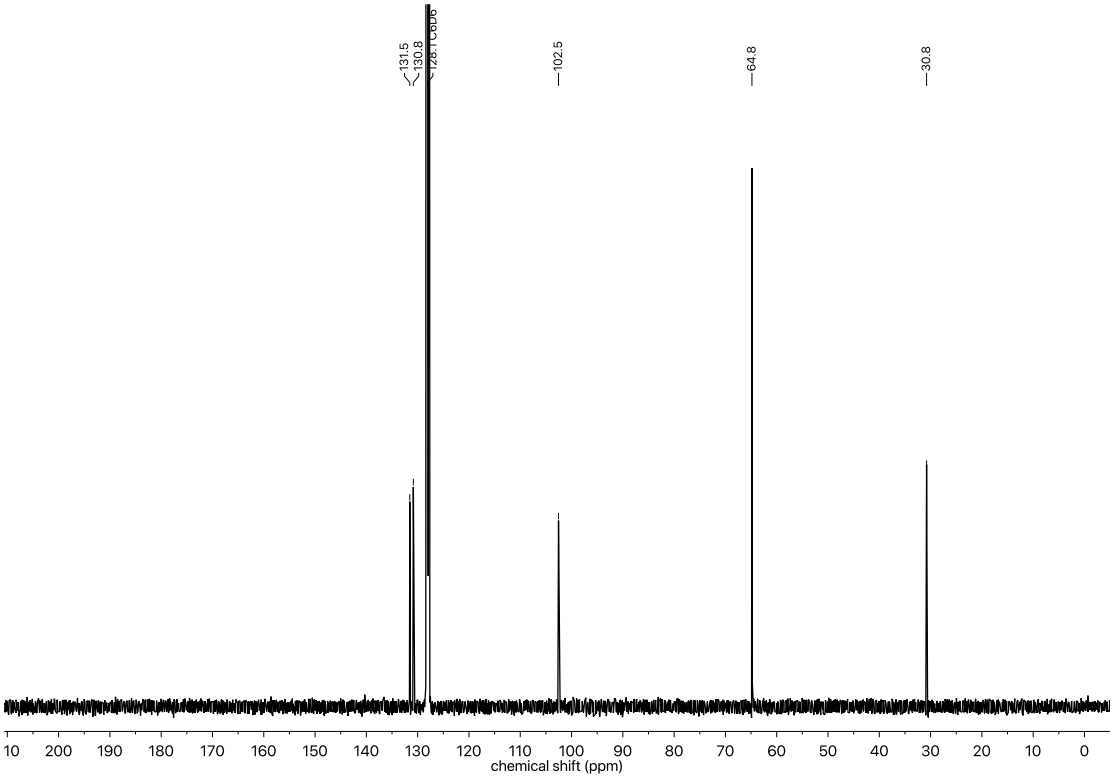


(*E*)-2-(3-Bromoprop-1-en-1-yl)-1,3-dioxolane (138)

^{1}H NMR:

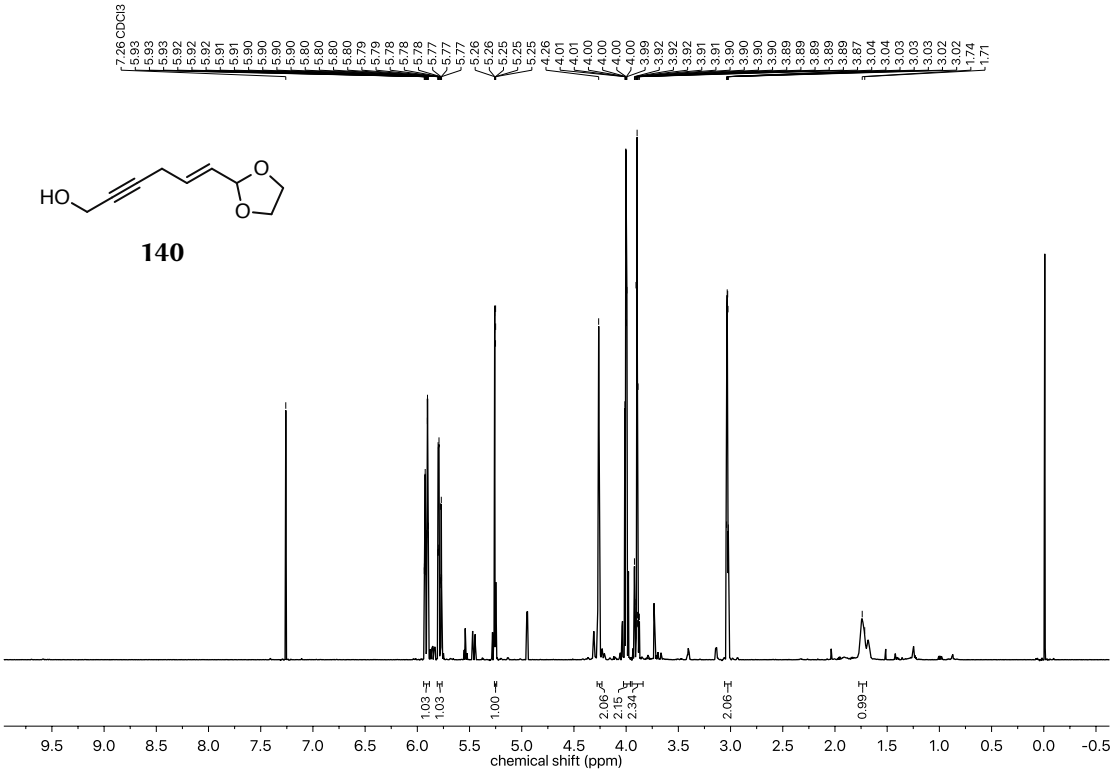


^{13}C NMR:

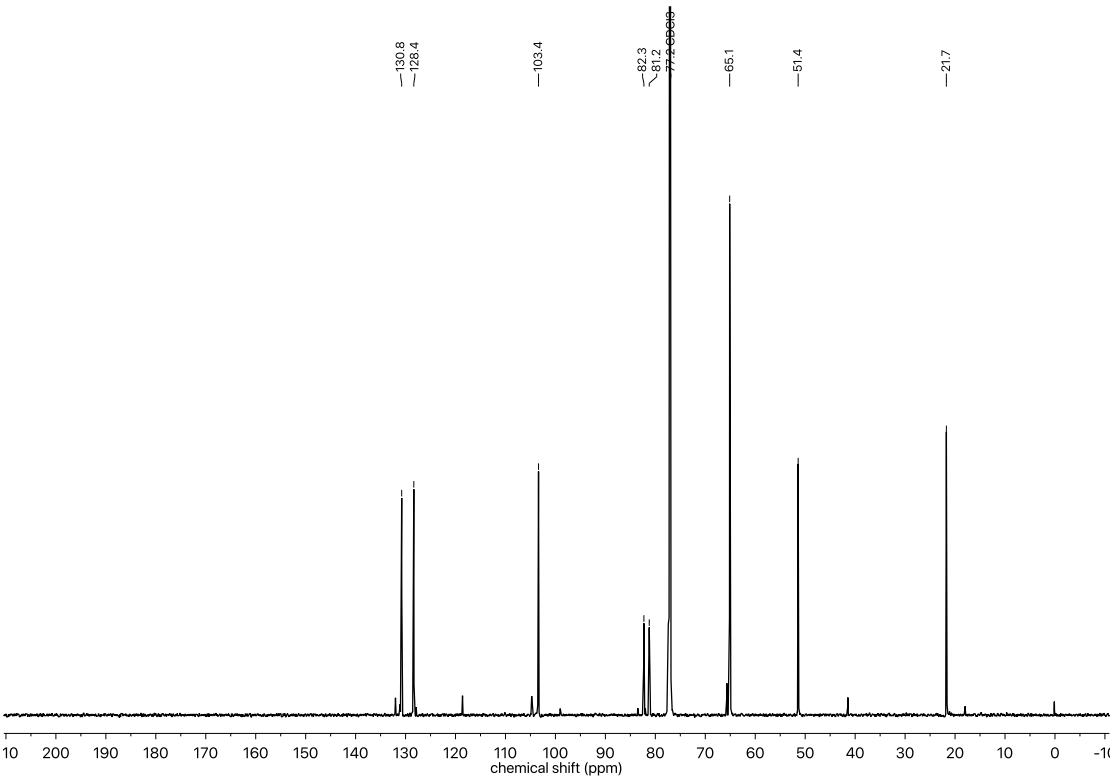


(*E*)-6-(1,3-Dioxolan-2-yl)hex-5-en-2-yn-1-ol (140)

^{1}H NMR:

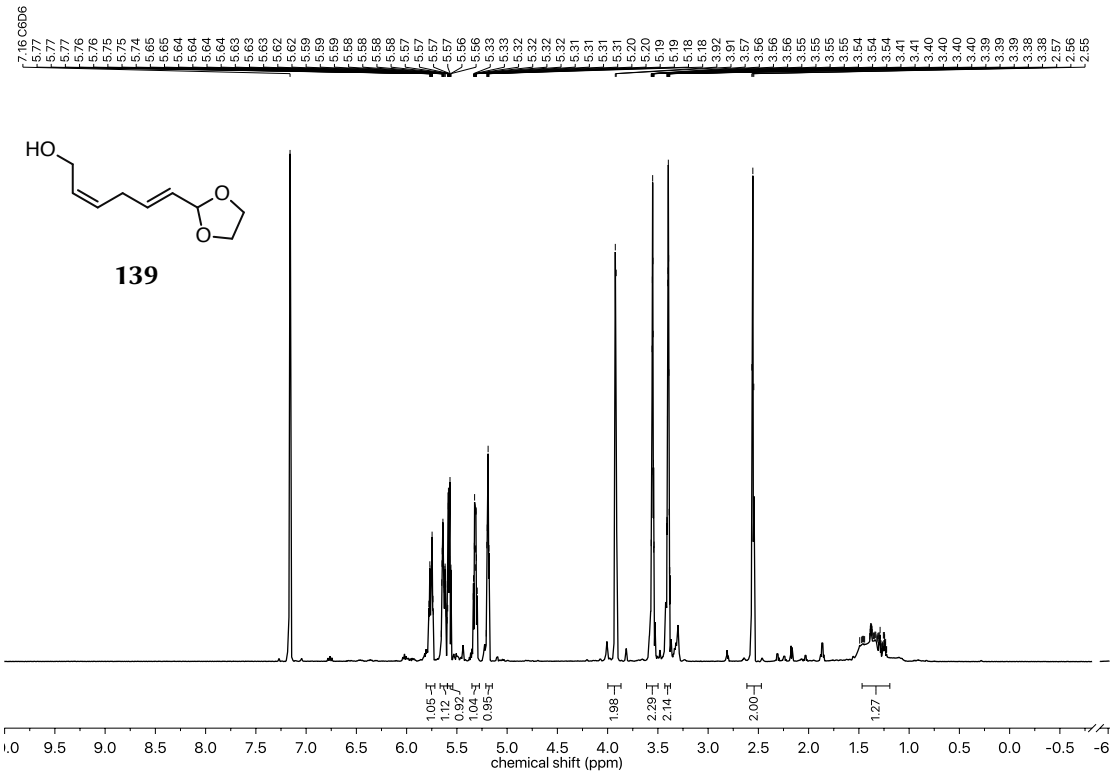


^{13}C NMR:

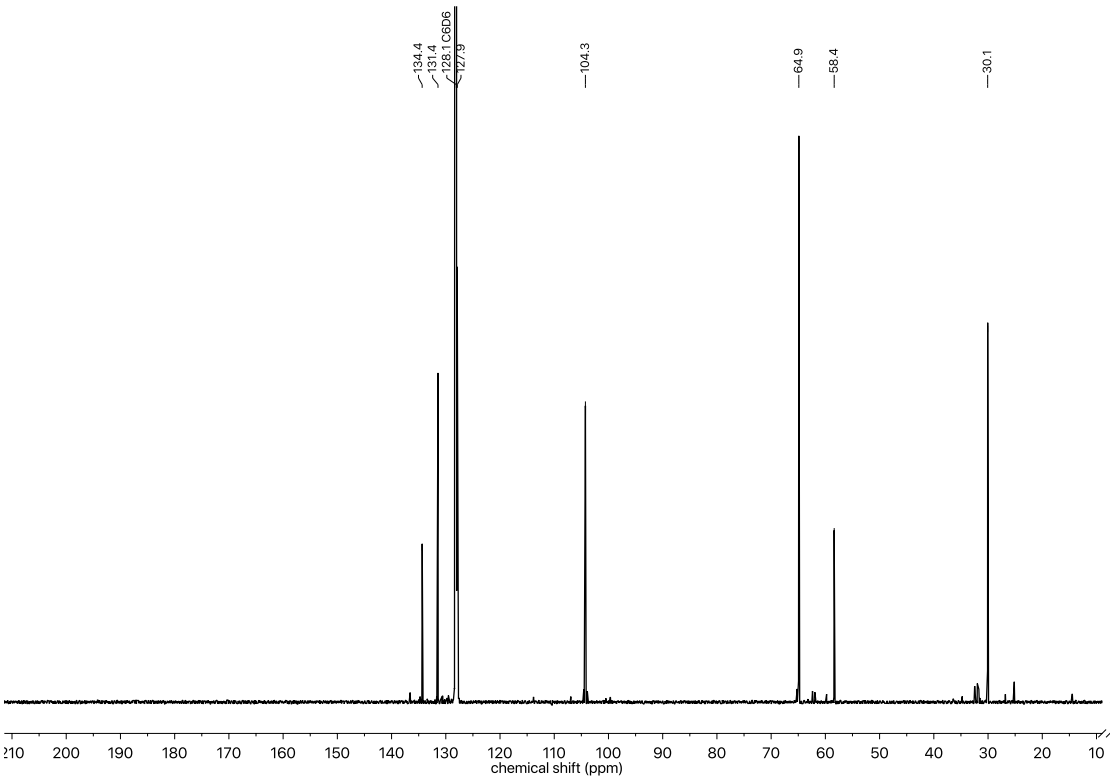


(2*Z*,5*E*)-6-(1,3-Dioxolan-2-yl)hexa-2,5-dien-1-ol (139)

^{1}H NMR:

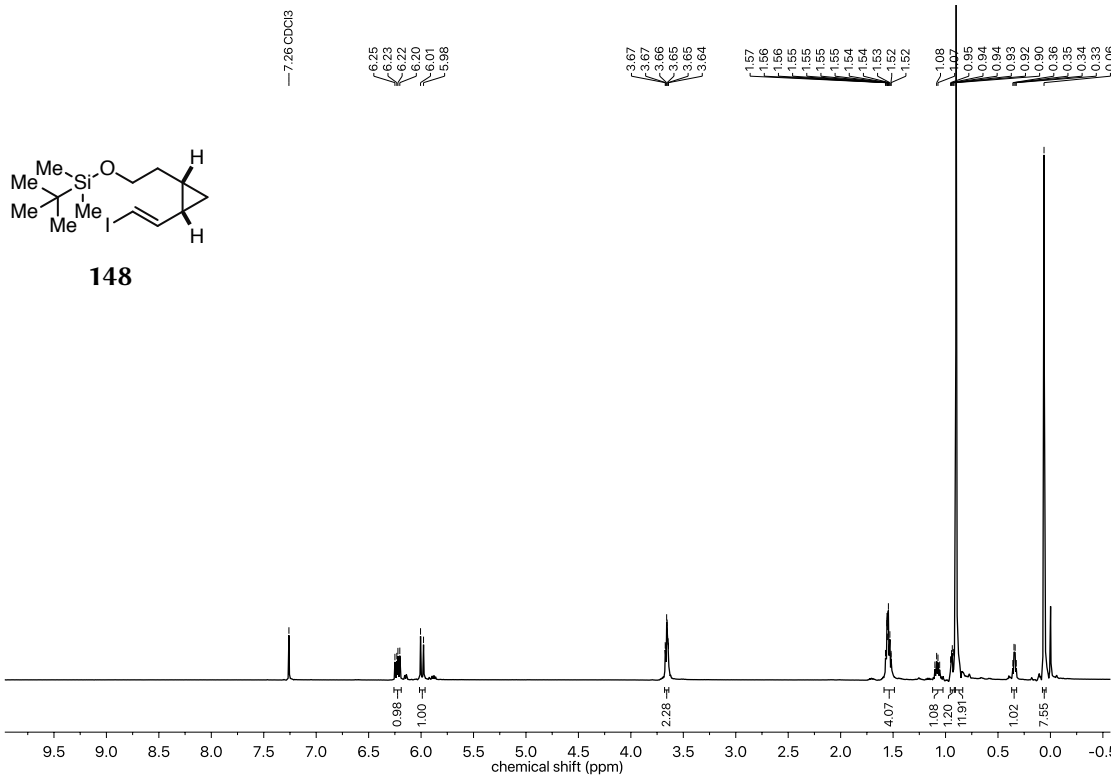


^{13}C NMR:



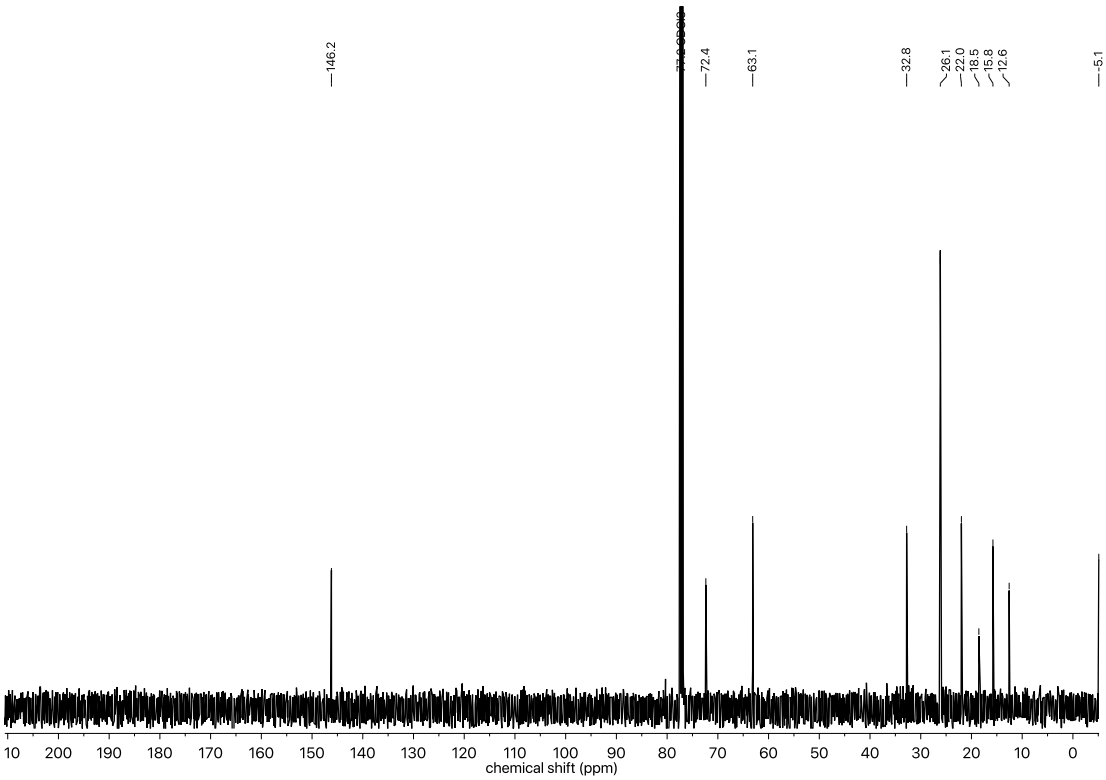
tert-Butyl(2-(-2-((*E*)-2-iodovinyl)cyclopropyl)ethoxy)dimethylsilane (148)

^{1}H NMR:



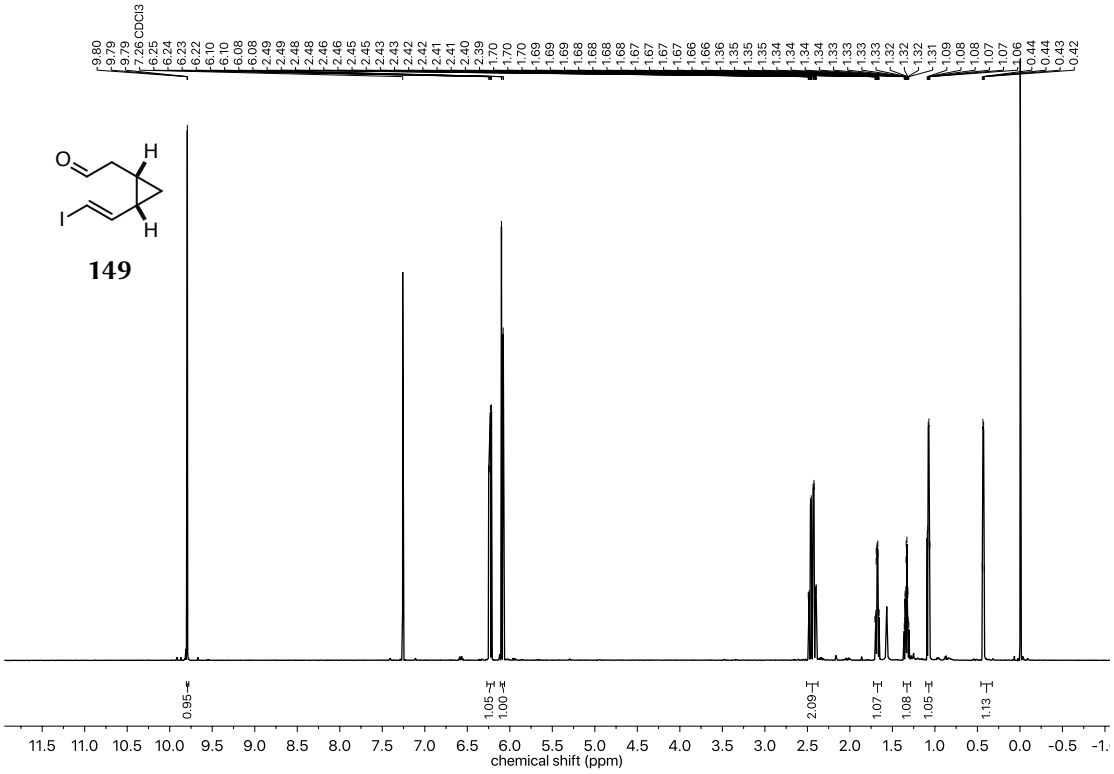
148

^{13}C NMR:

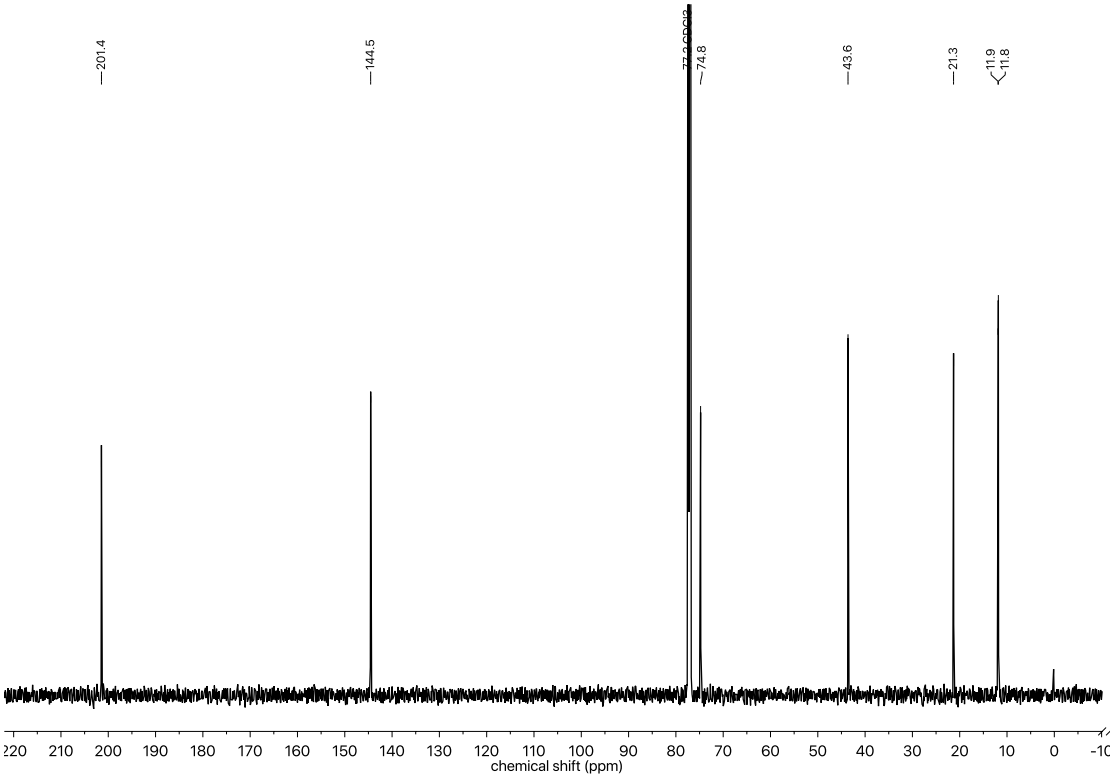


2-(2-((*E*)-2-Iodovinyl)cyclopropyl)acetaldehyde (149)

^{1}H NMR:

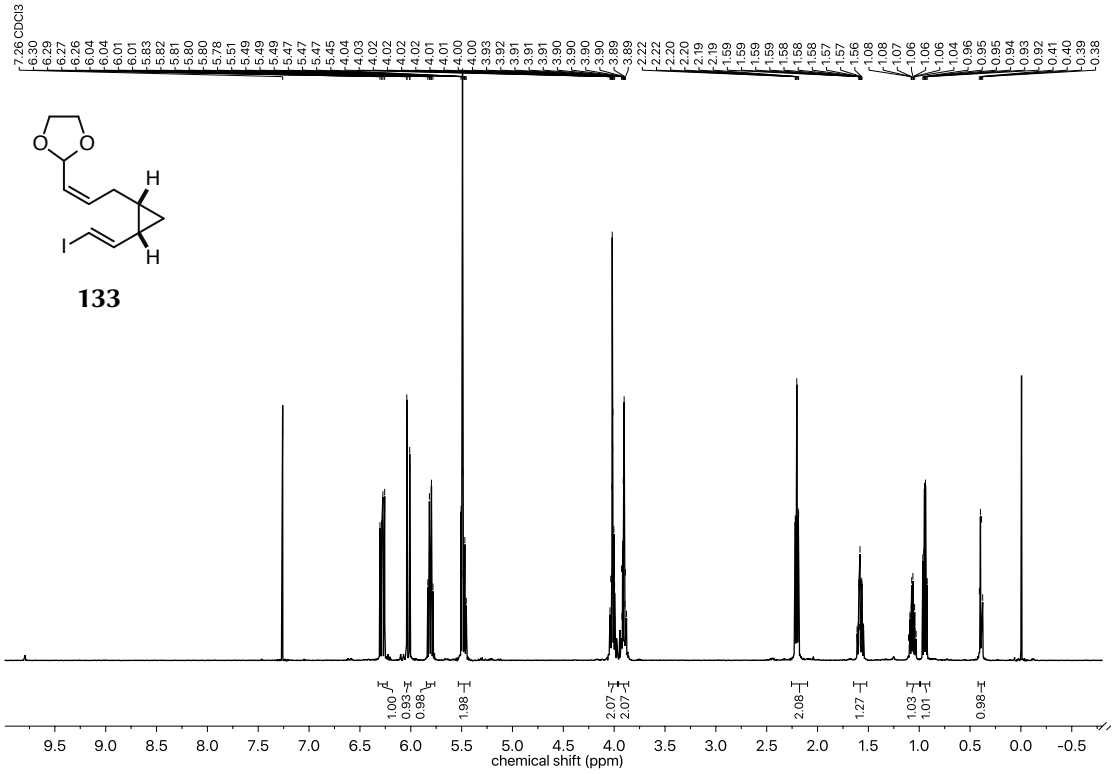


^{13}C NMR:



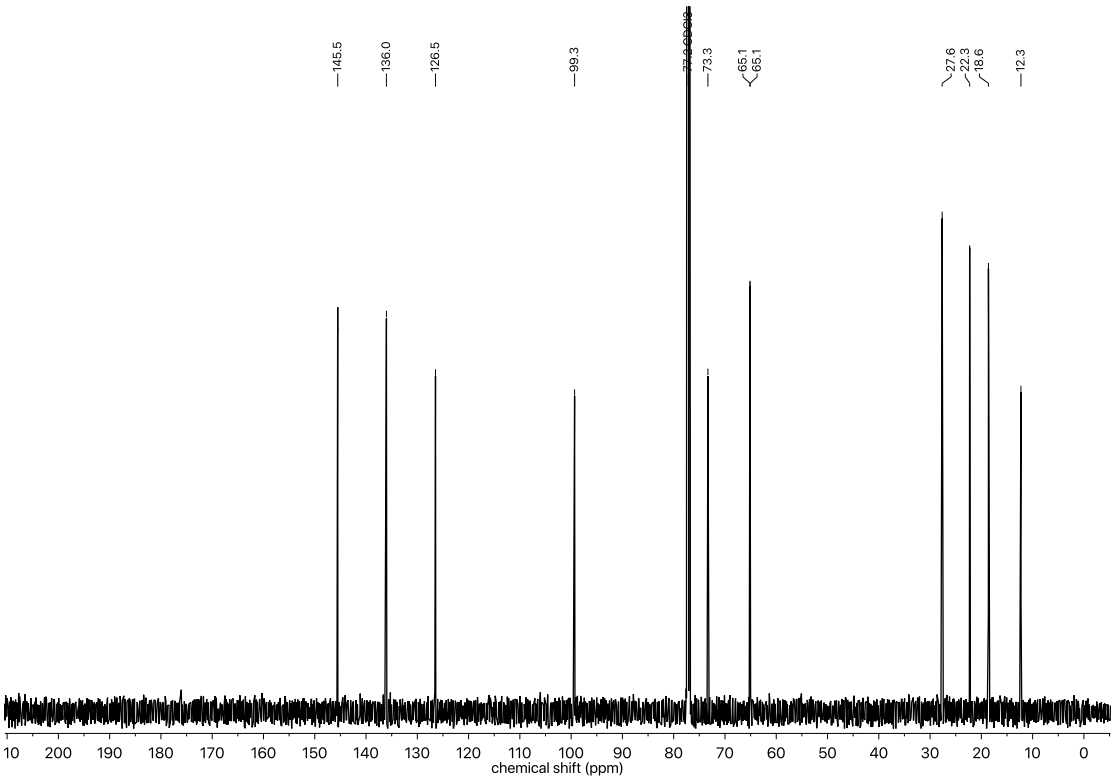
2-((*E*)-3-(2-((*E*)-2-Iodovinyl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (133)

^{1}H NMR:



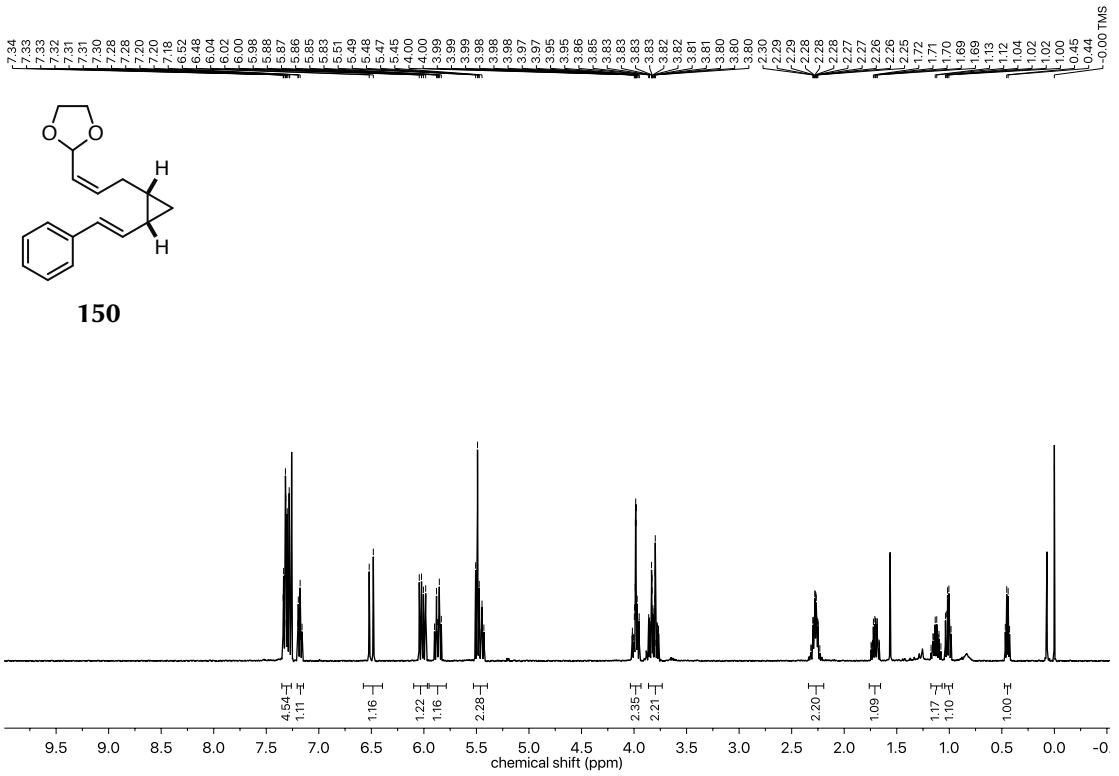
133

^{13}C NMR:



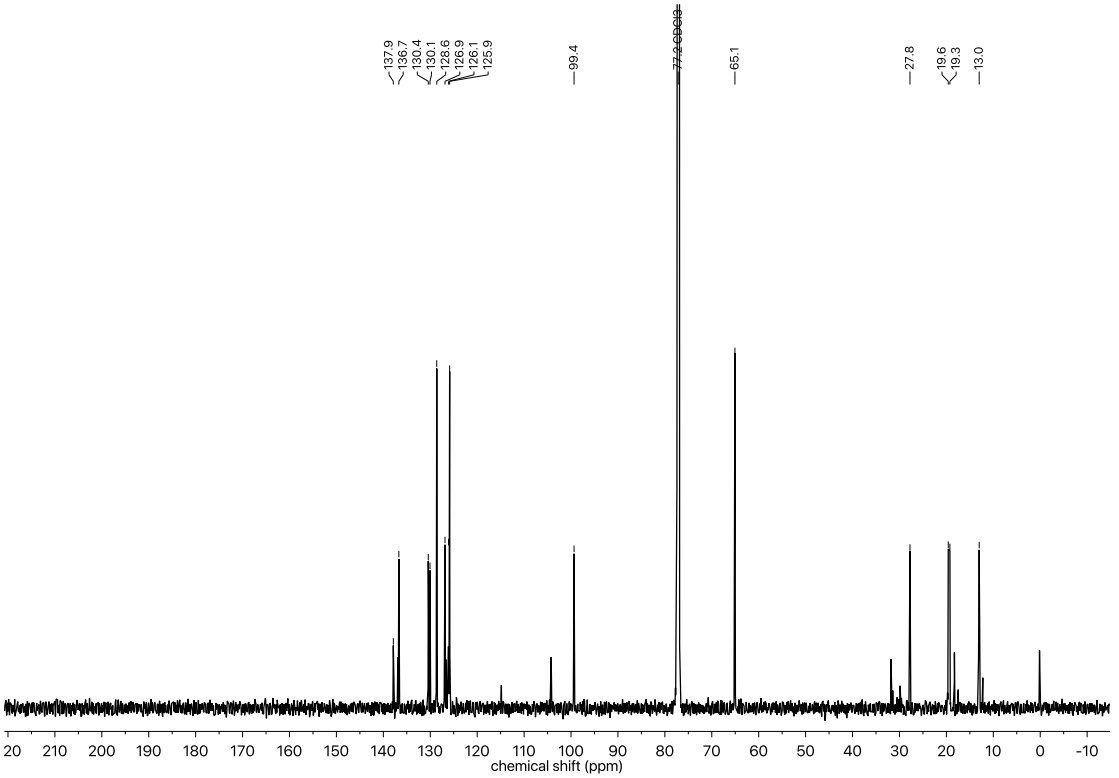
2-((*E*)-3-(2-((*E*)-Styryl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (150)

^{1}H NMR:



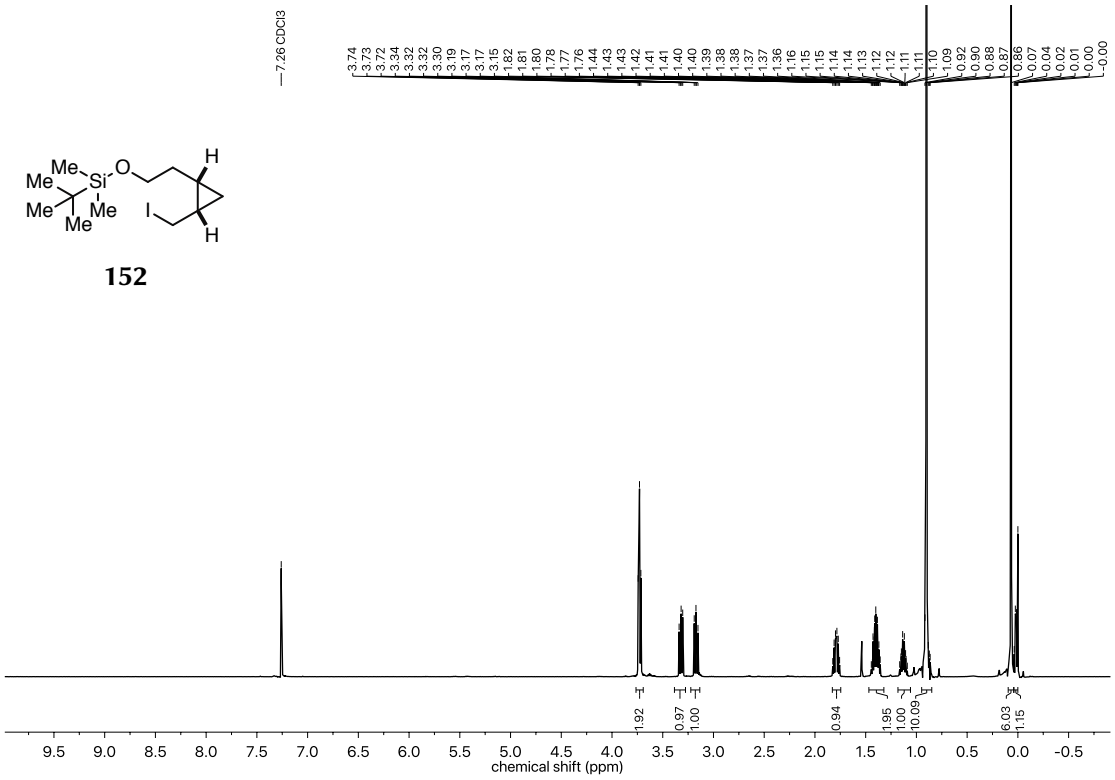
150

^{13}C NMR:



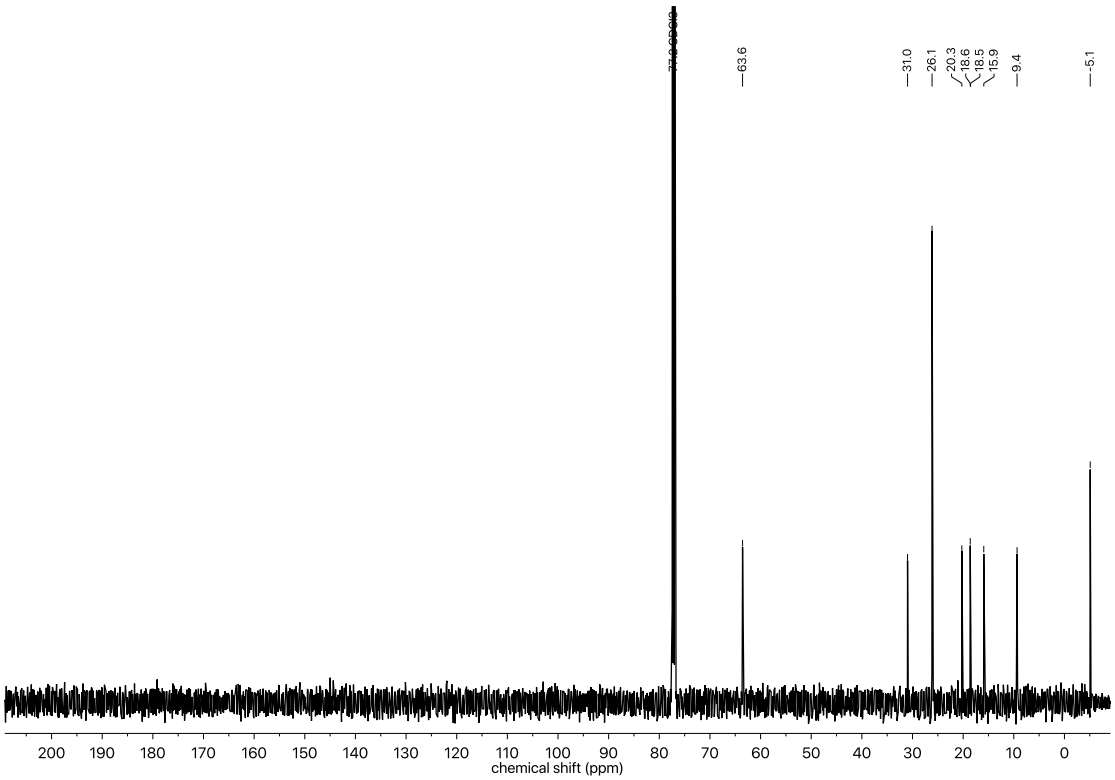
tert-Butyl(2-(2-(iodomethyl)cyclopropyl)ethoxy)dimethylsilane (152)

^{1}H NMR:



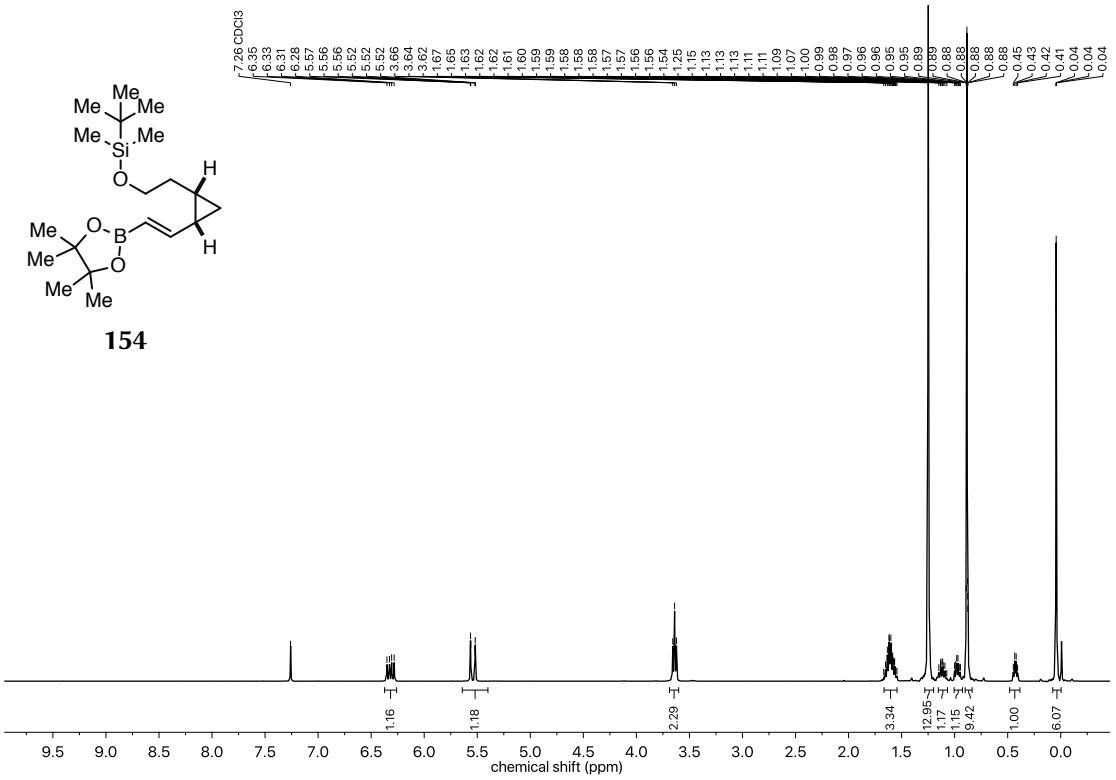
152

^{13}C NMR:



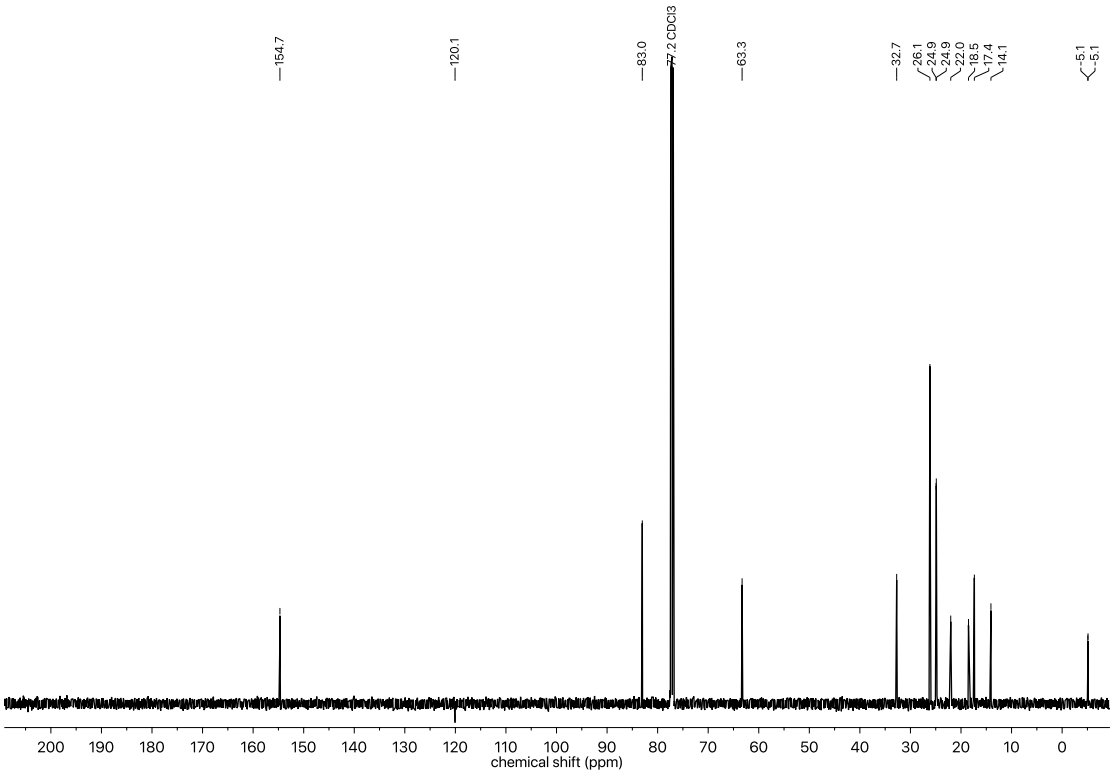
(*tert*-Butyldimethyl(2-(2-((*E*)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinylcyclopropyl)-ethoxy)silane (154)

^{1}H NMR:



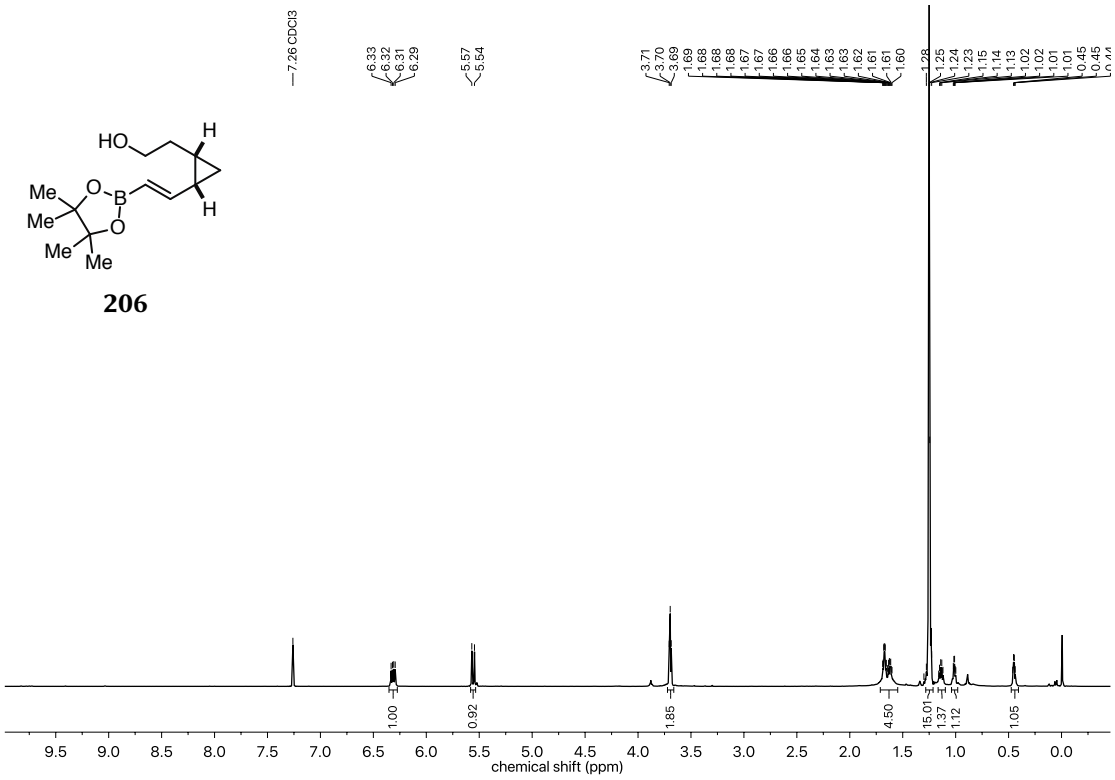
154

^{13}C NMR:



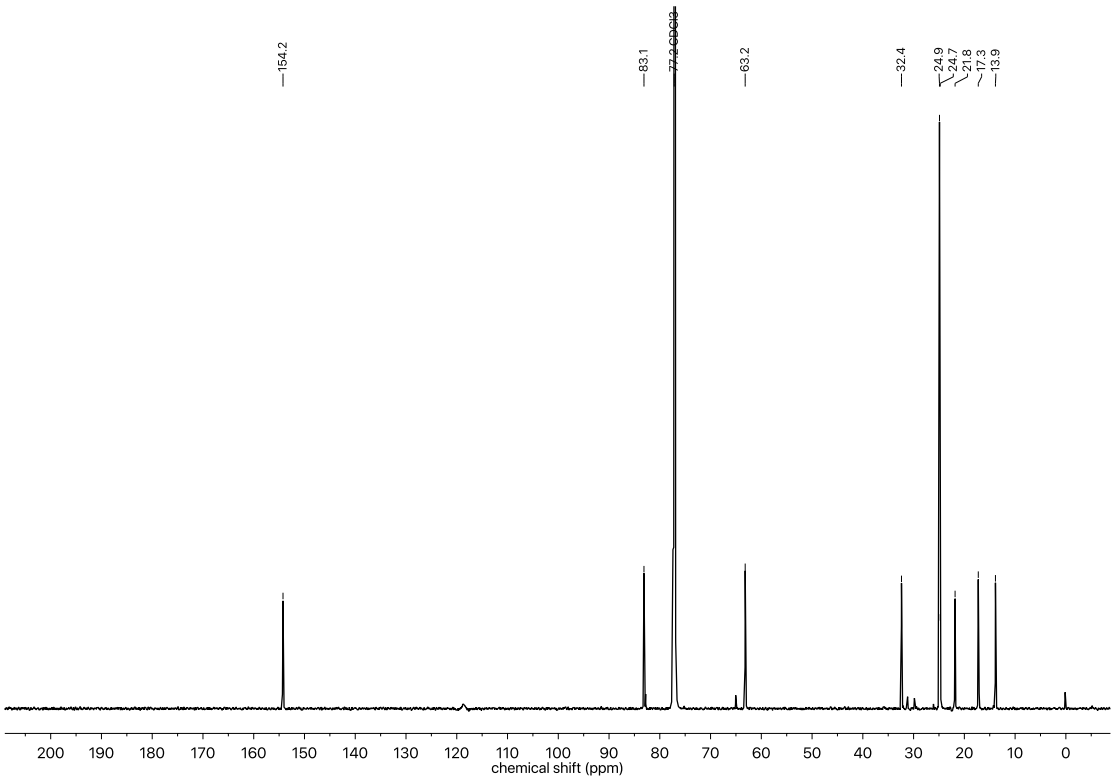
2-(2-((*E*)-2-(4,4,5,5-Tetramethyl-1,3,2-dioxa-borolan-2-yl)-vinyl)-cyclo-propyl)-ethan-1-ol (206)

^{1}H NMR:



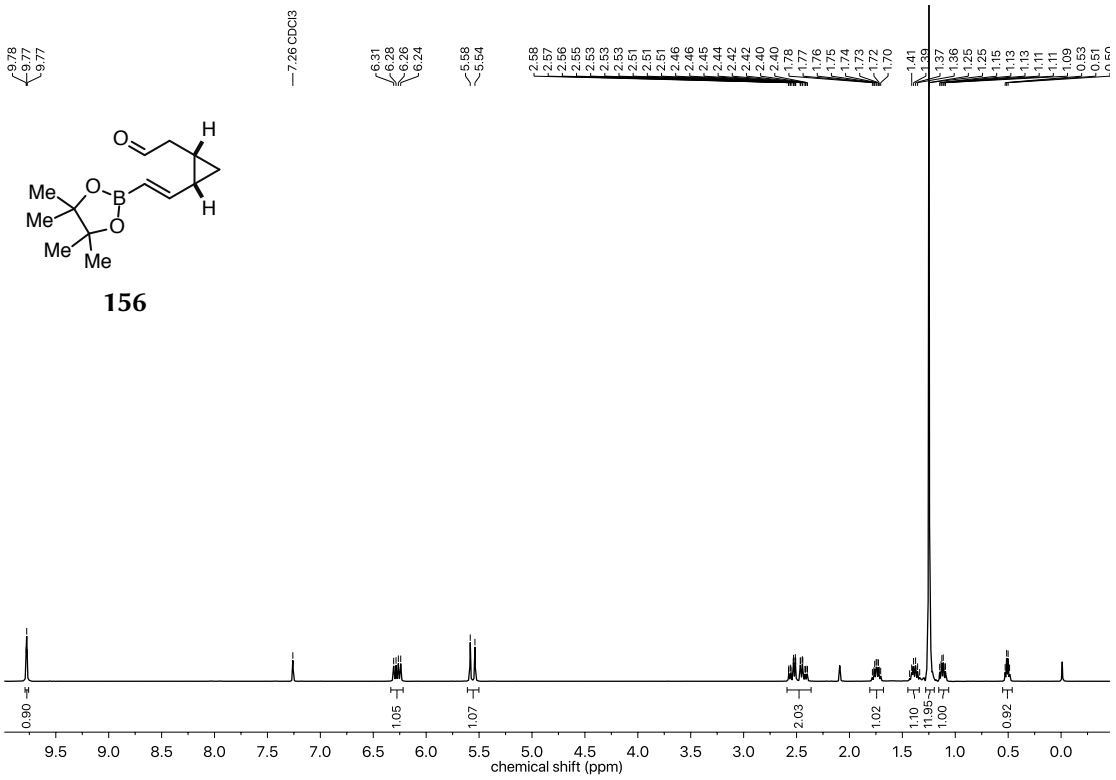
206

^{13}C NMR:



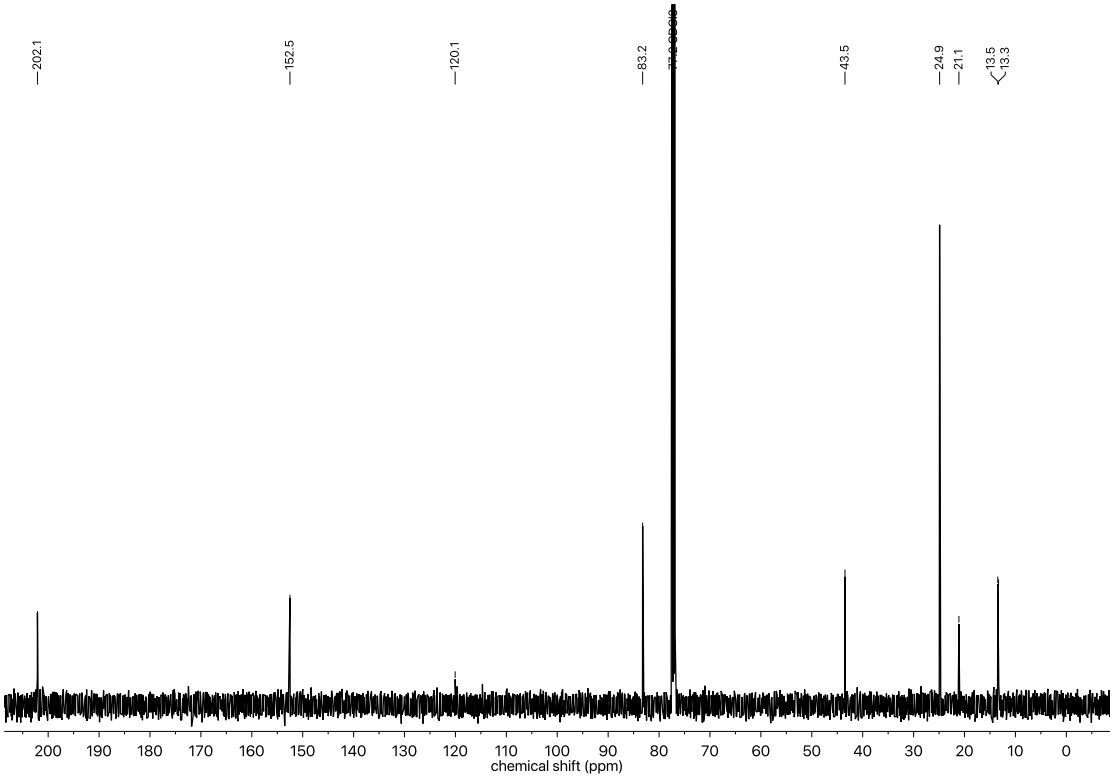
2-(2-((*E*)-2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)cyclopropyl)acetaldehyde (156)

^{1}H NMR:



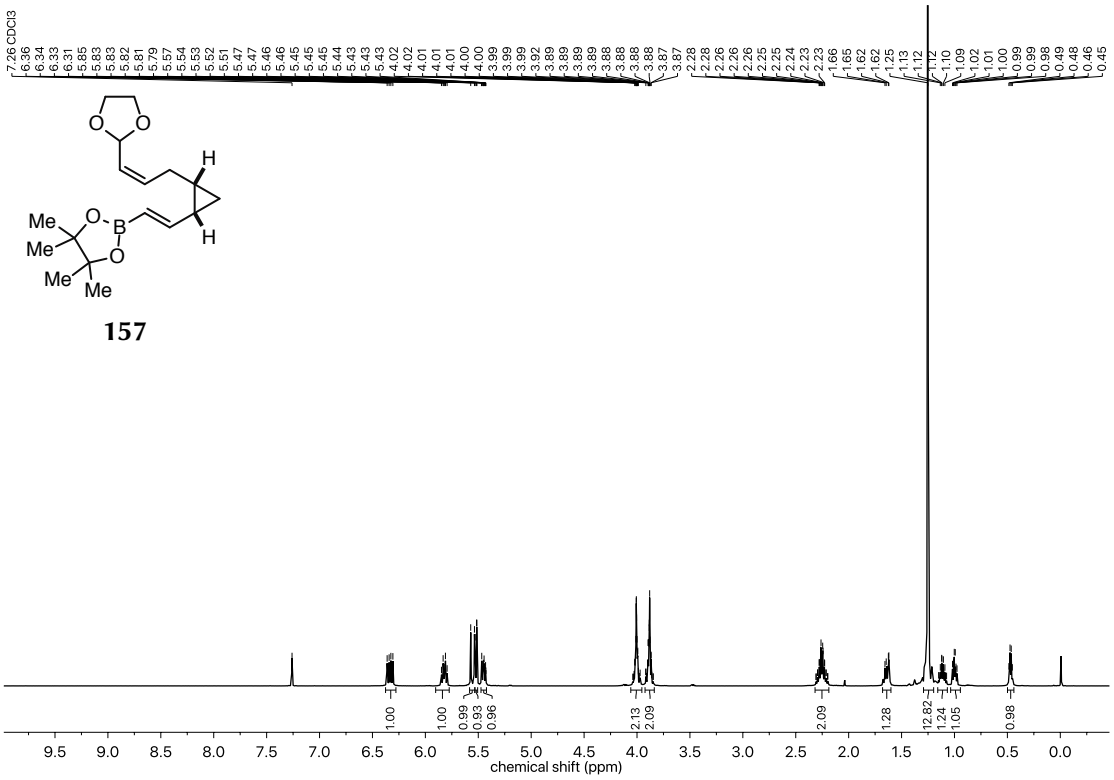
156

^{13}C NMR:



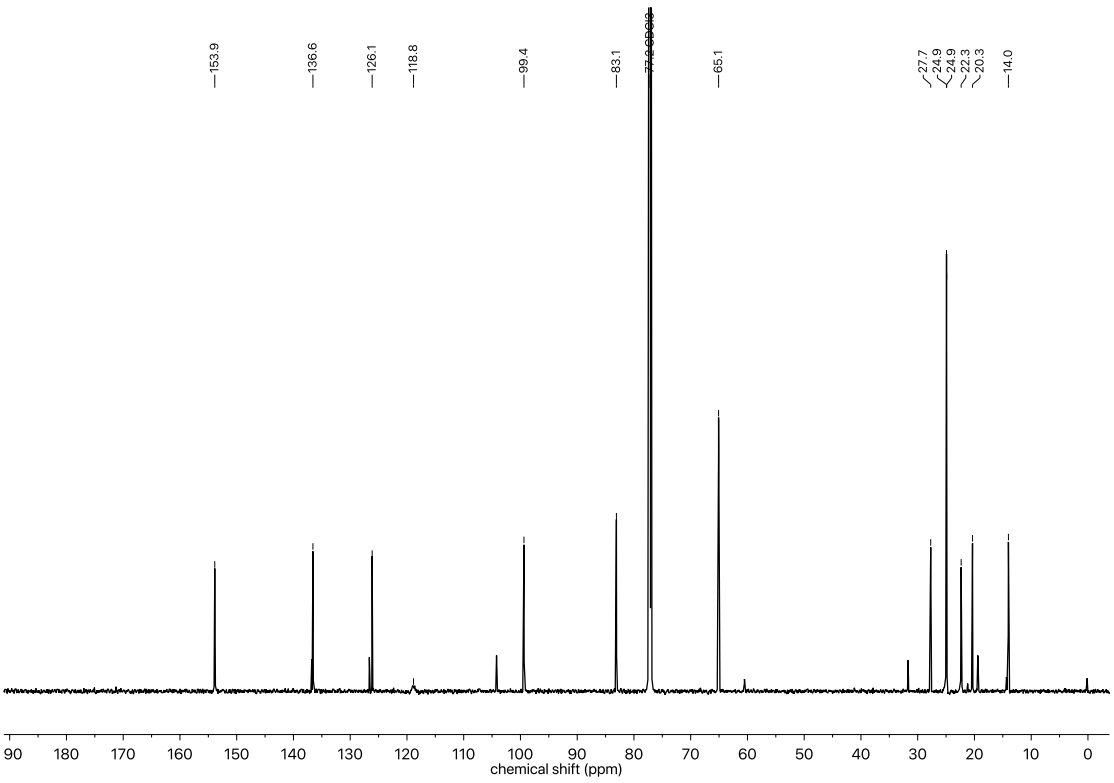
2-((*E*)-2-(-2-((*Z*)-3-(1,3-dioxolan-2-yl)allylcyclopropyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (157)

^{1}H NMR:



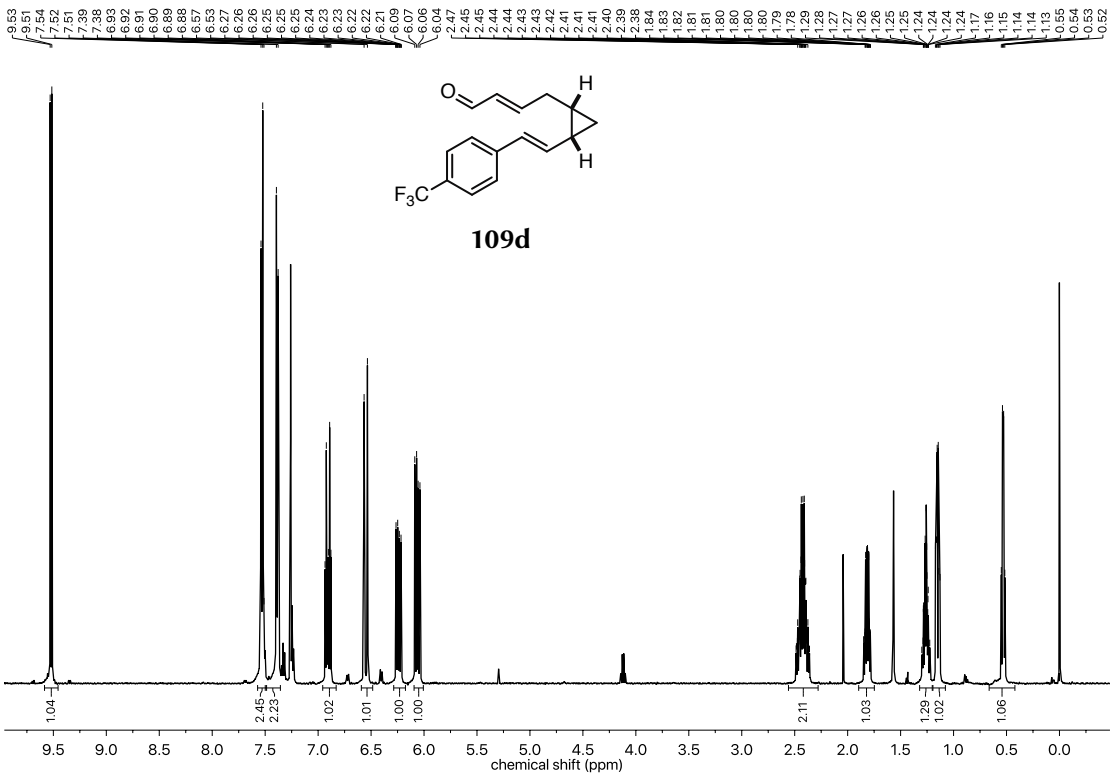
157

^{13}C NMR:

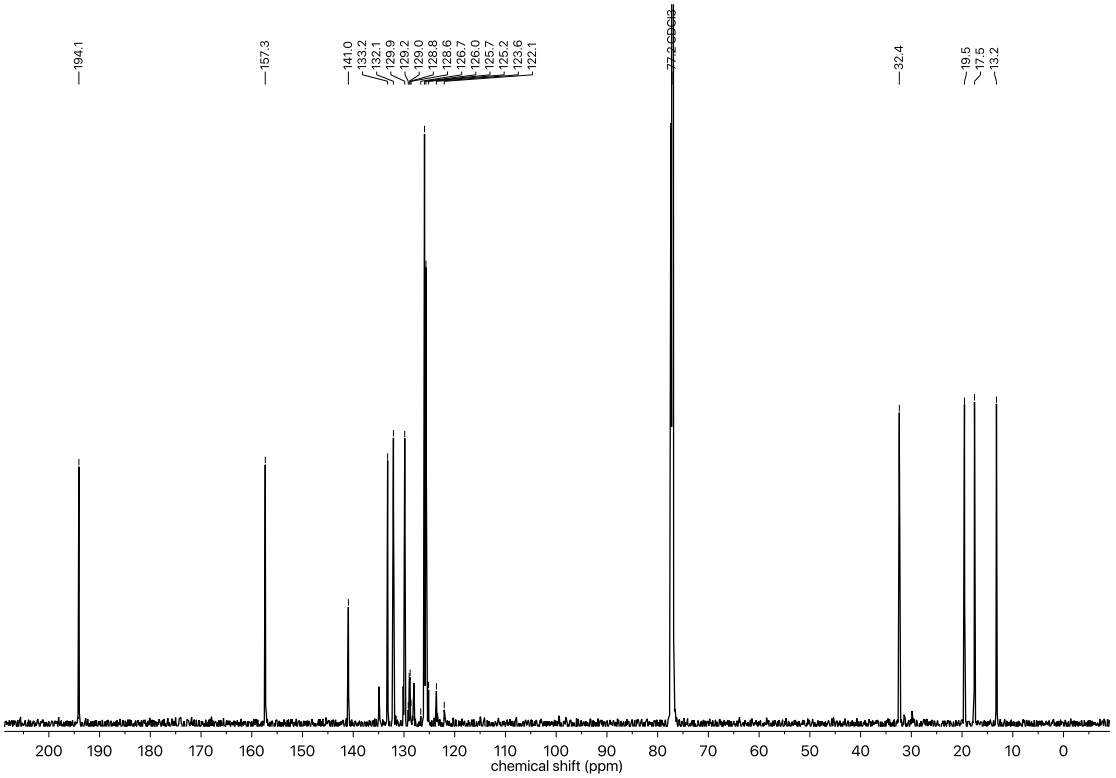


(*E*)-4-(2-((*E*)-4-(Trifluoromethyl)styryl)cyclopropyl)but-2-enal (109d)

^{1}H NMR:

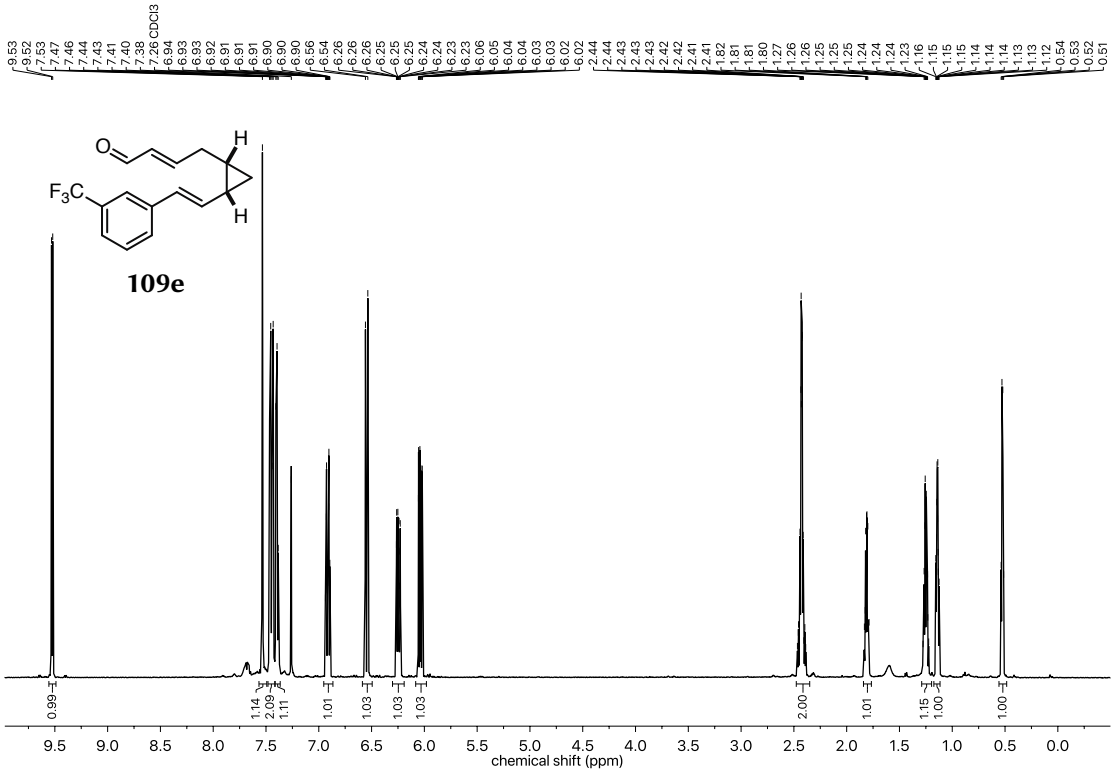


^{13}C NMR:

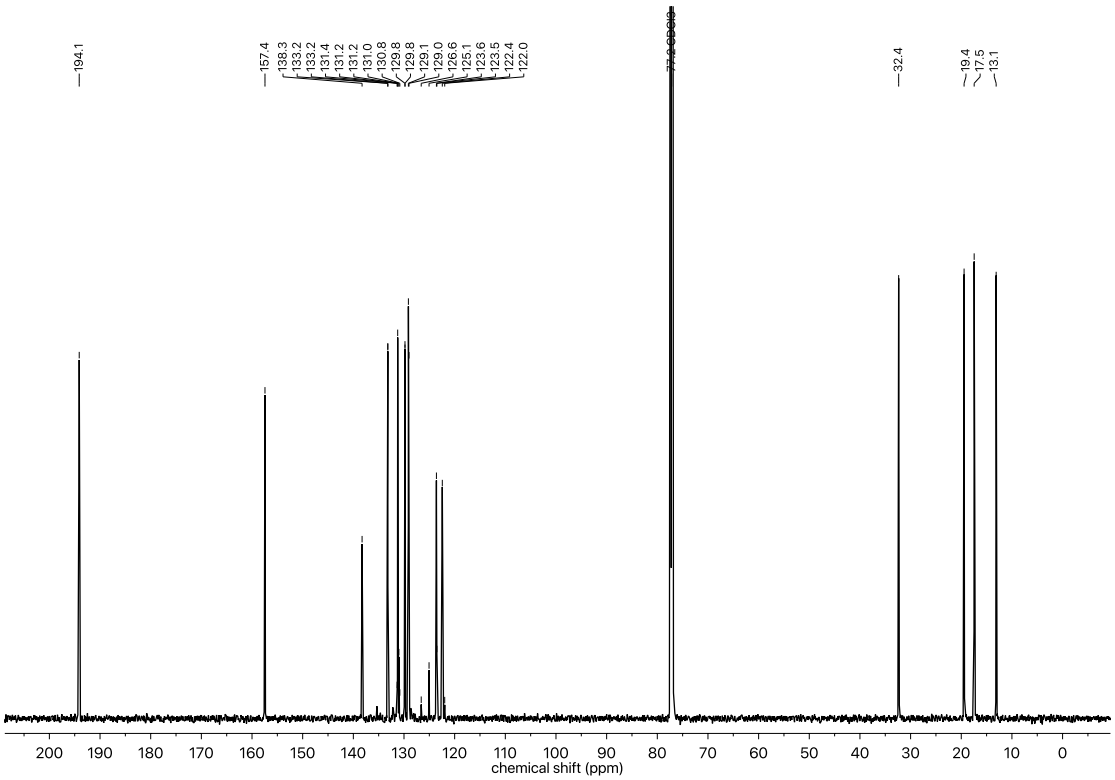


(*E*)-4-(2-((*E*)-3-(Trifluoromethyl)styryl)cyclopropyl)but-2-enal (109e)

^{1}H NMR:

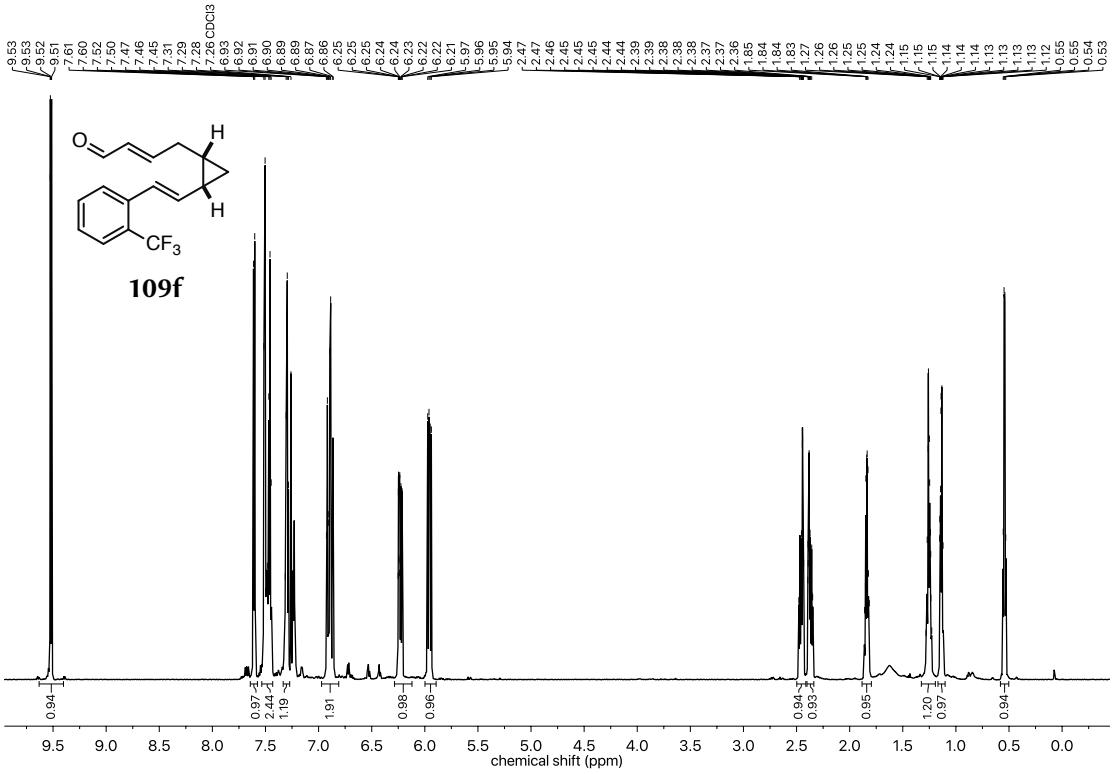


^{13}C NMR:

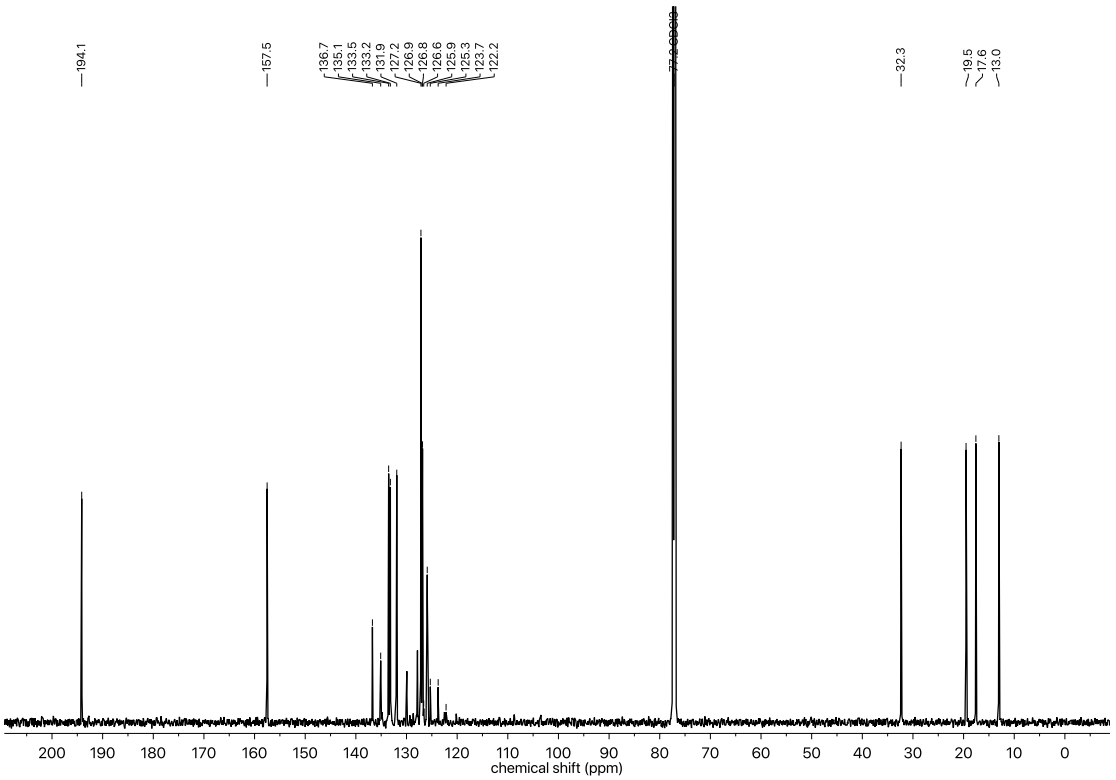


(*E*)-4-(2-((*E*)-2-(Trifluoromethyl)styryl)cyclopropyl)but-2-enal (109f)

^{1}H NMR:

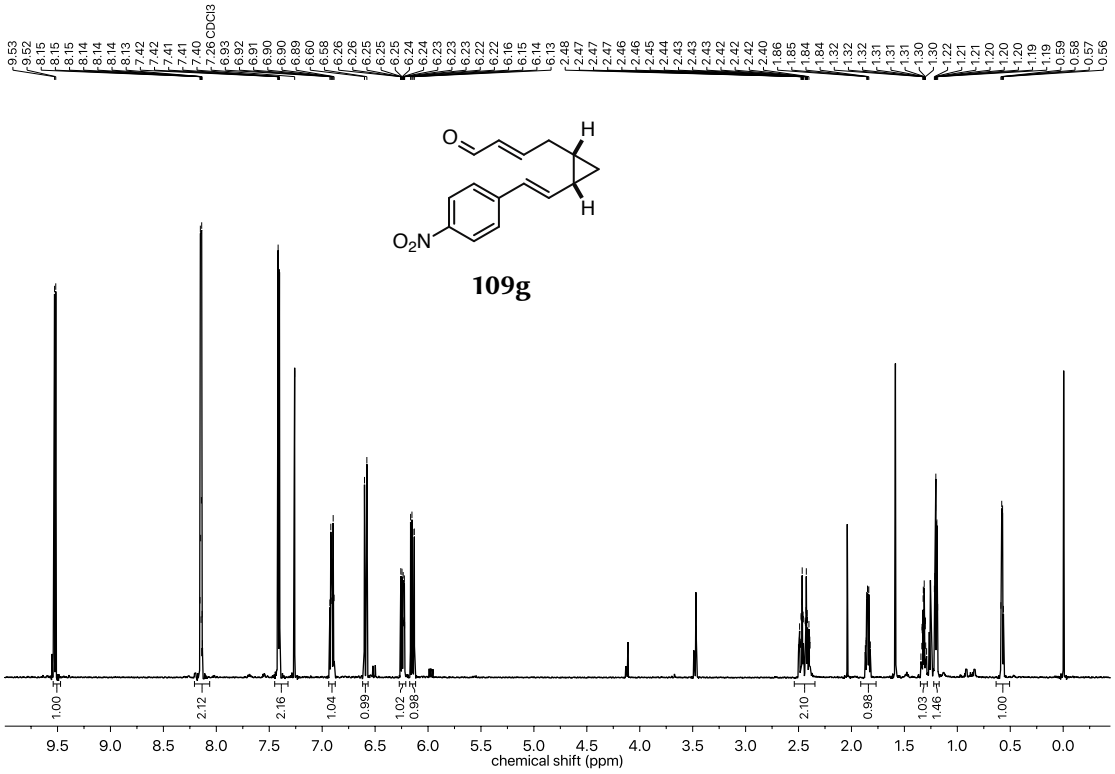


^{13}C NMR:

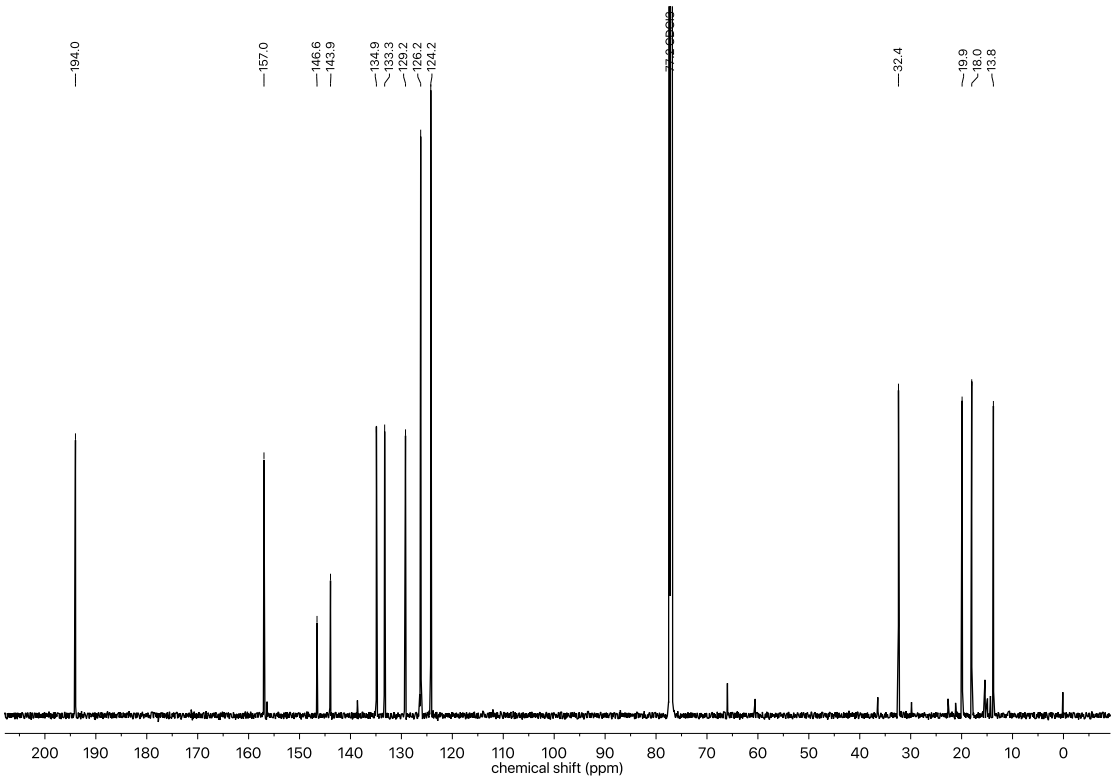


(*E*)-4-(-2-((*E*)-4-Nitrostyryl)cyclopropyl)but-2-enal (109g)

^{1}H NMR:

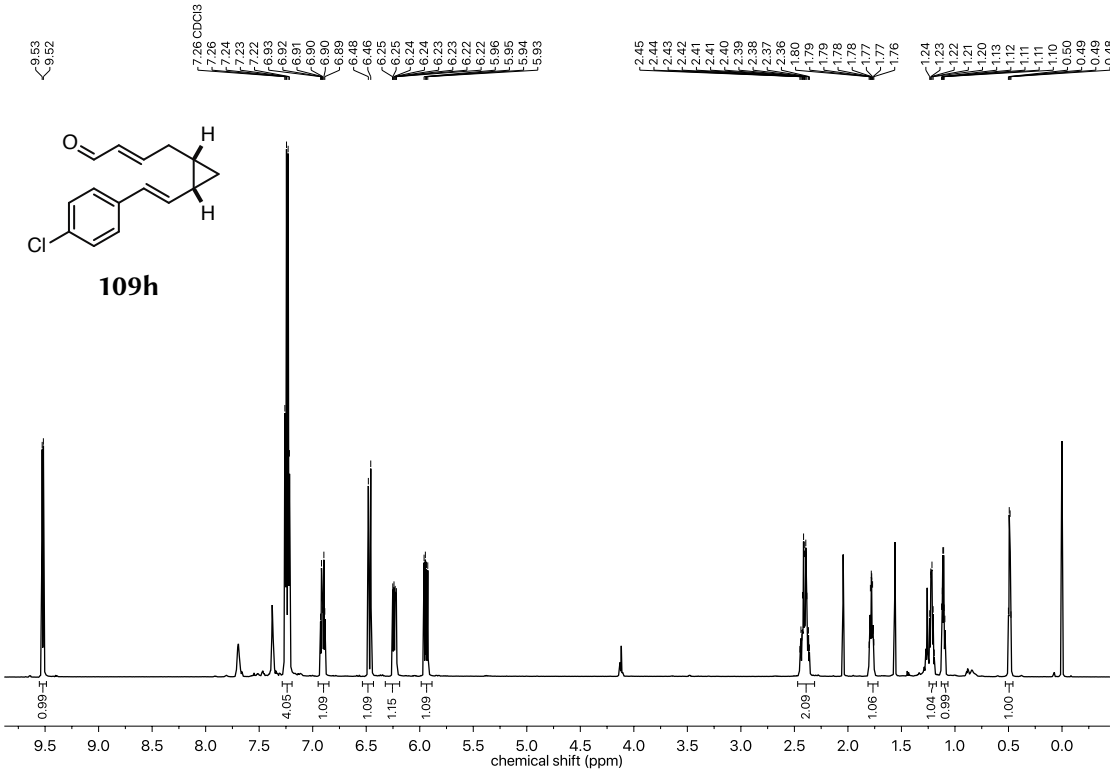


^{13}C NMR:

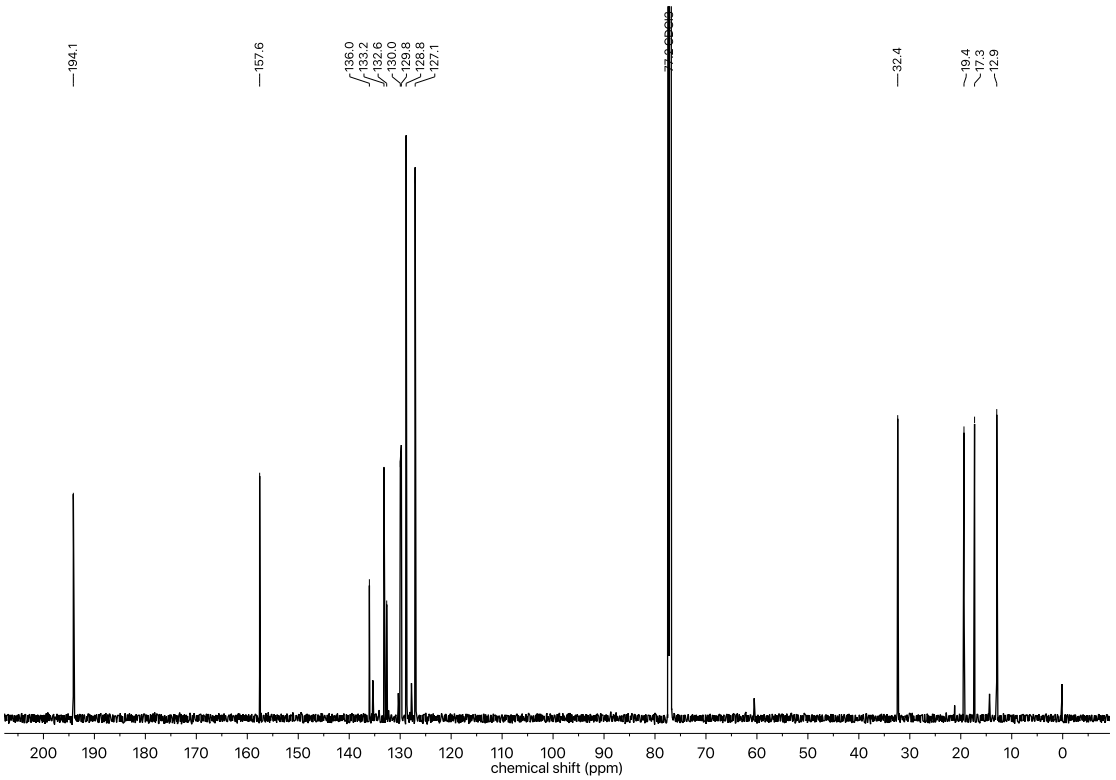


(*E*)-4-(2-((*E*)-4-Chlorostyryl)cyclopropyl)but-2-enal (109h)

^{1}H NMR:

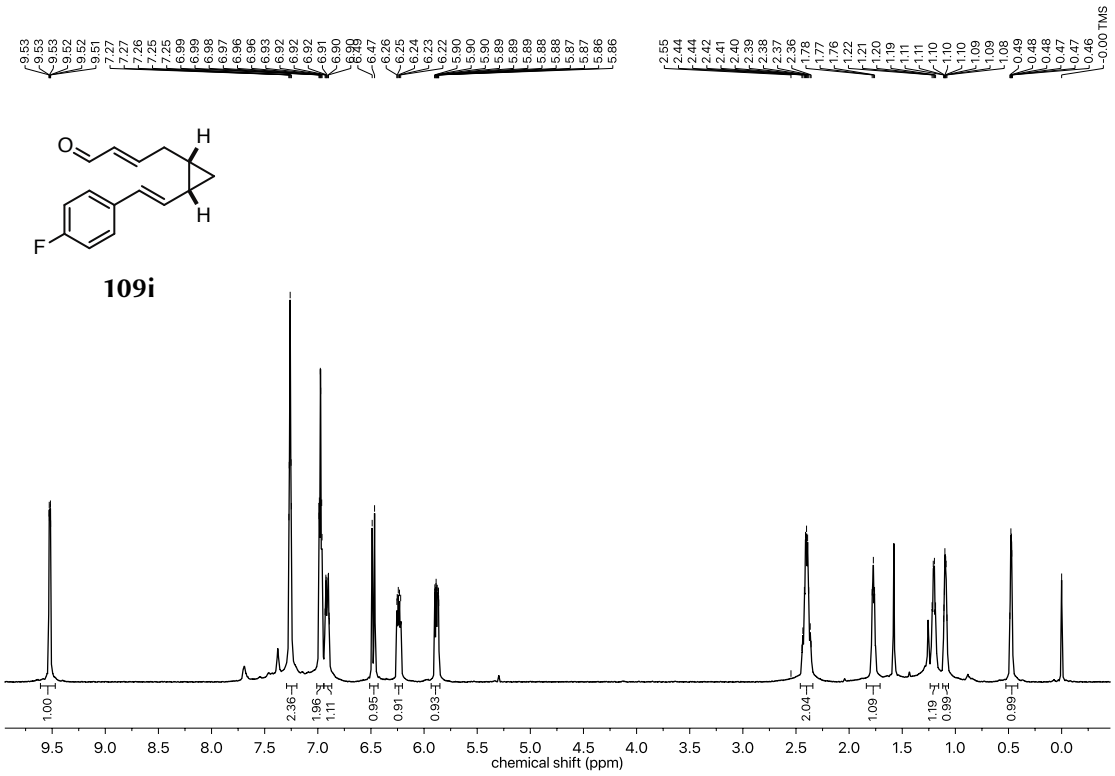


^{13}C NMR:

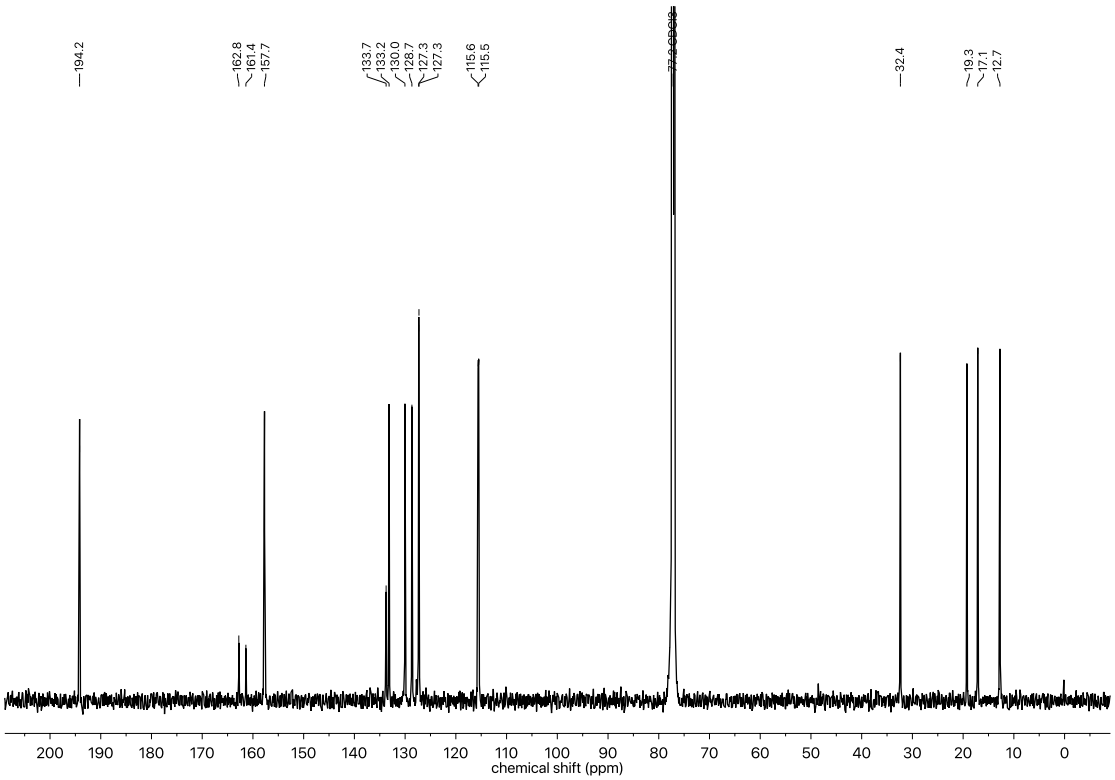


(*E*)-4-(-2-((*E*)-4-Fluorostyryl)cyclopropyl)but-2-enal (109i)

^{1}H NMR:

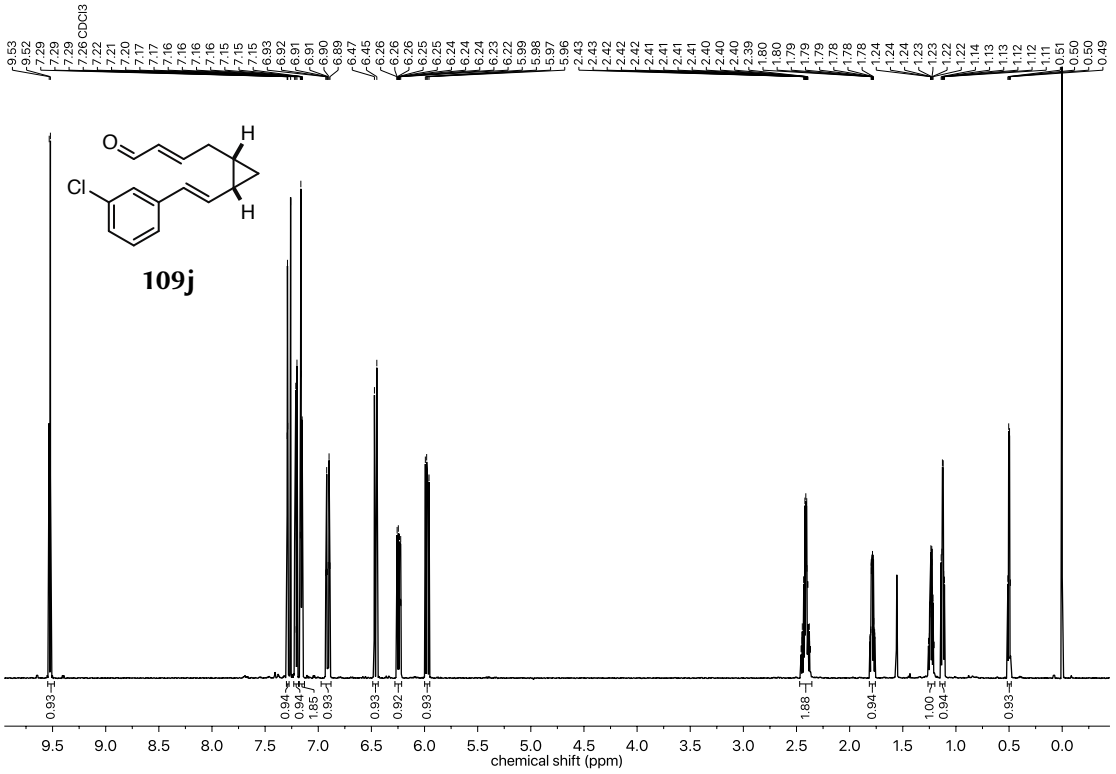


^{13}C NMR:

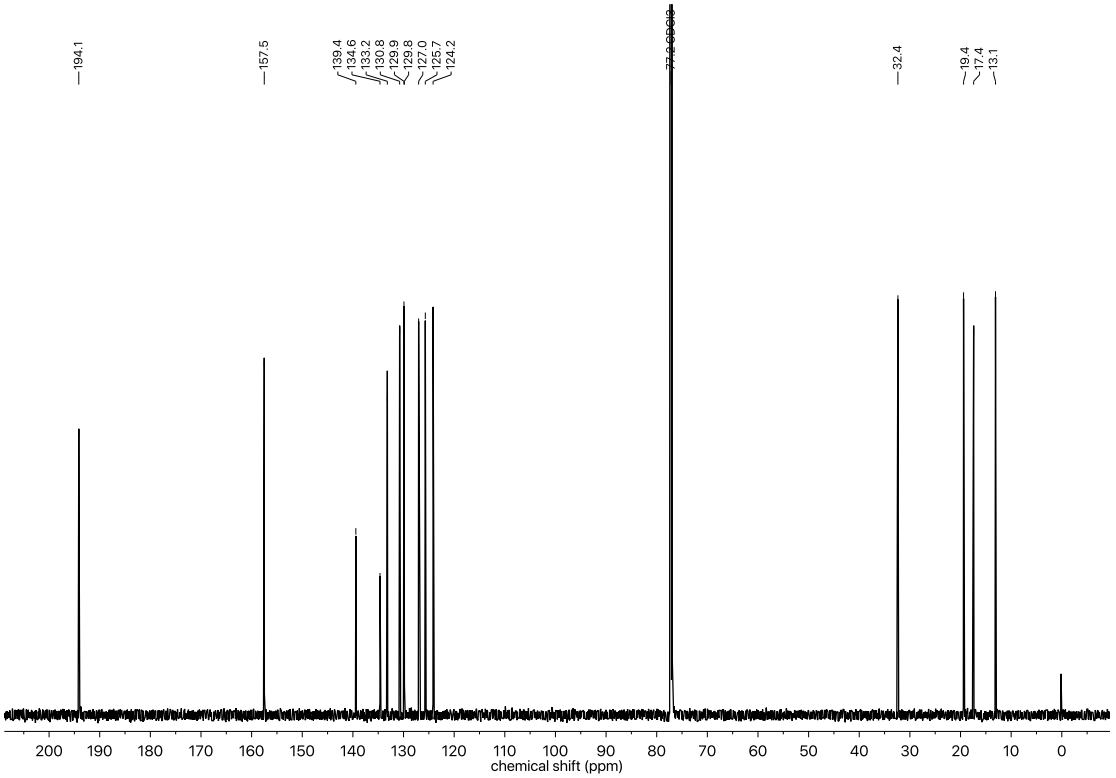


(*E*)-4-(2-((*E*)-3-Chlorostyryl)cyclopropyl)but-2-enal (109j)

^{1}H NMR:

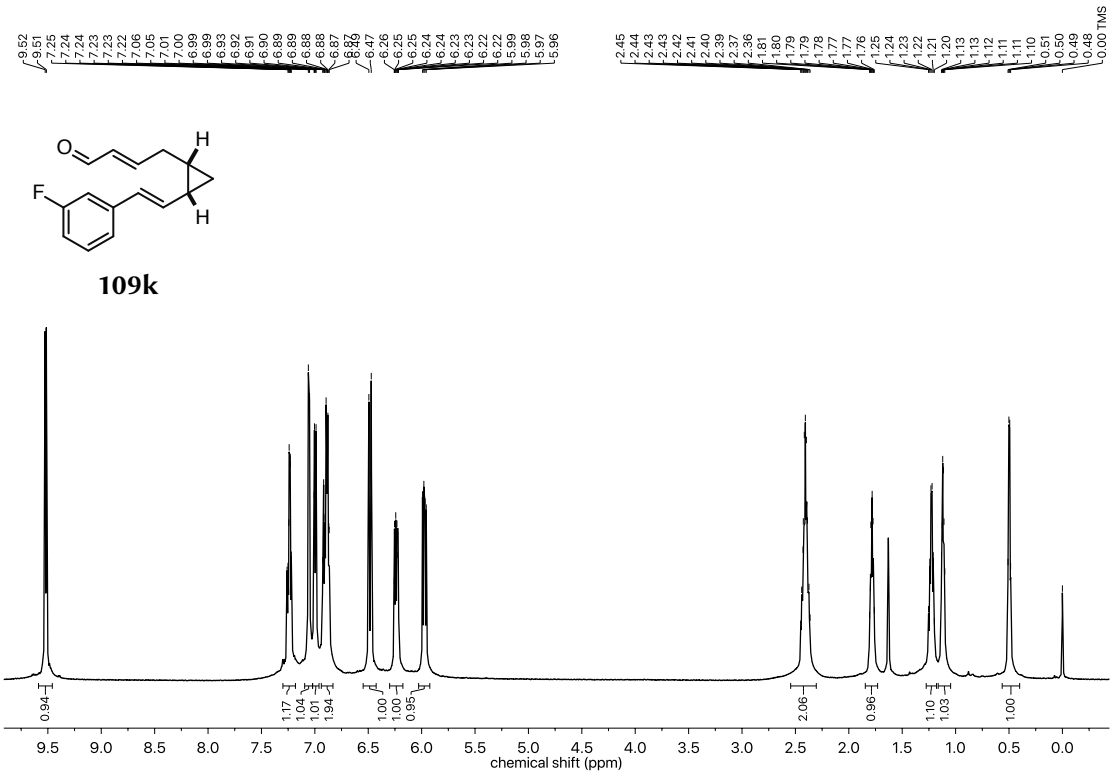


^{13}C NMR:

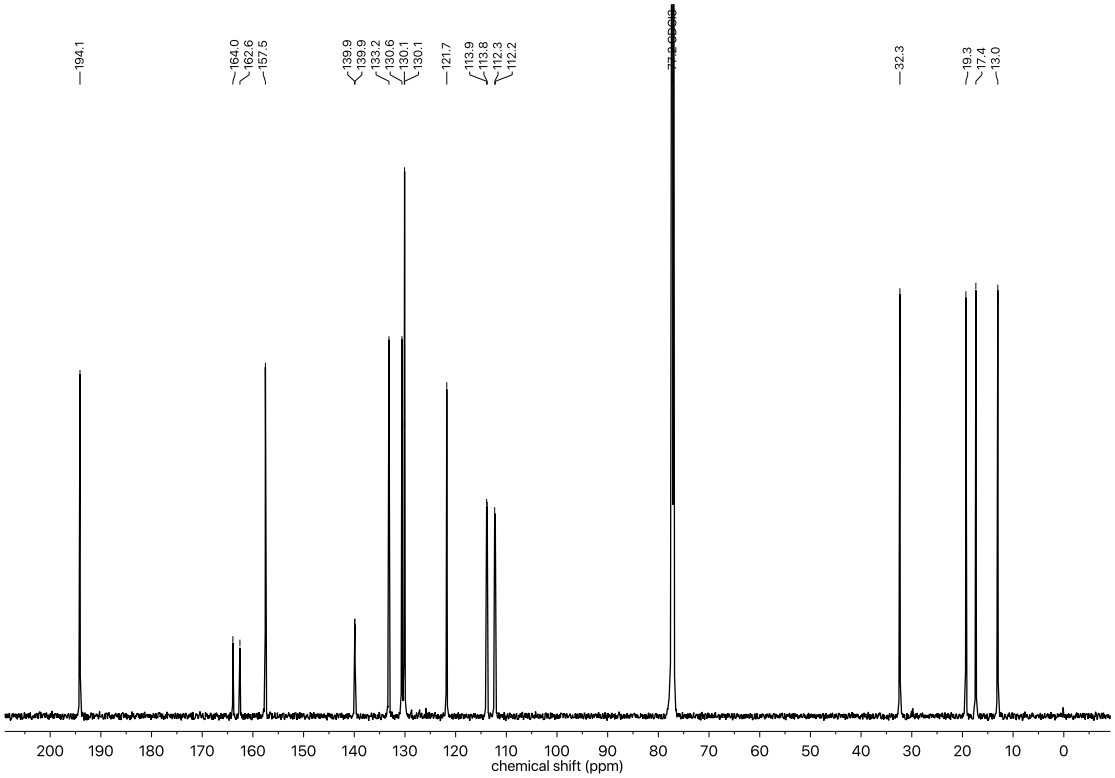


(*E*)-4-(2-((*E*)-3-Fluorostyryl)cyclopropyl)but-2-enal (109k)

^{1}H NMR:

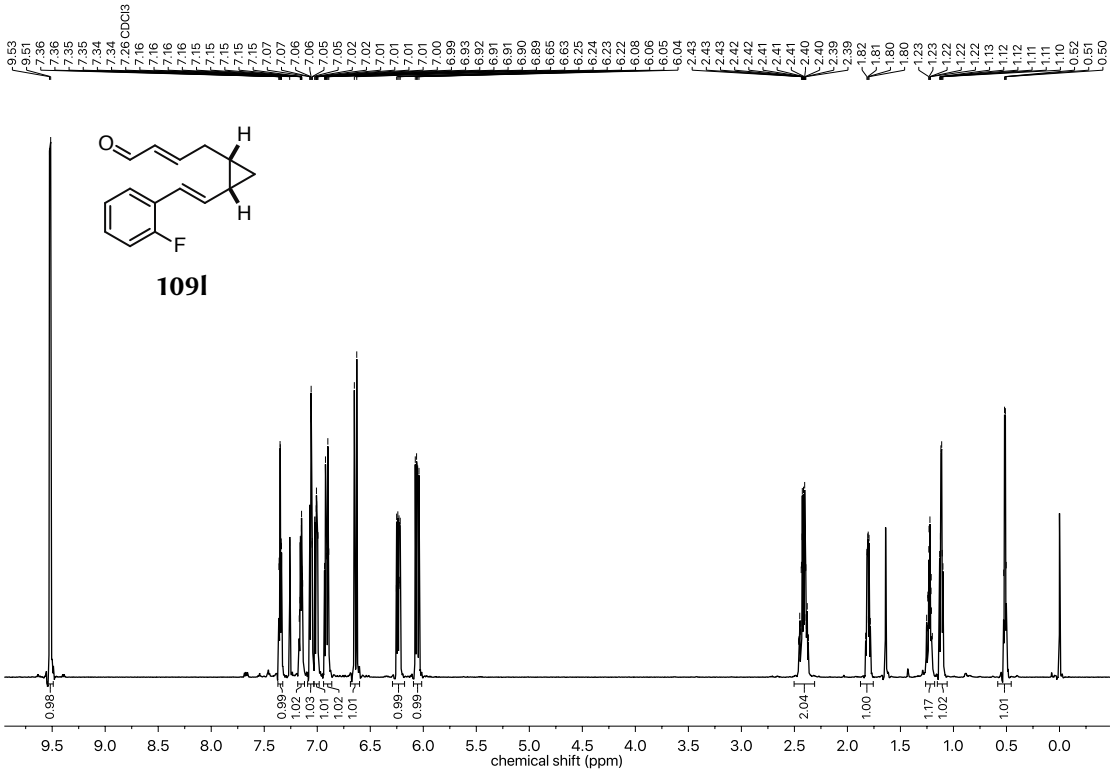


^{13}C NMR:

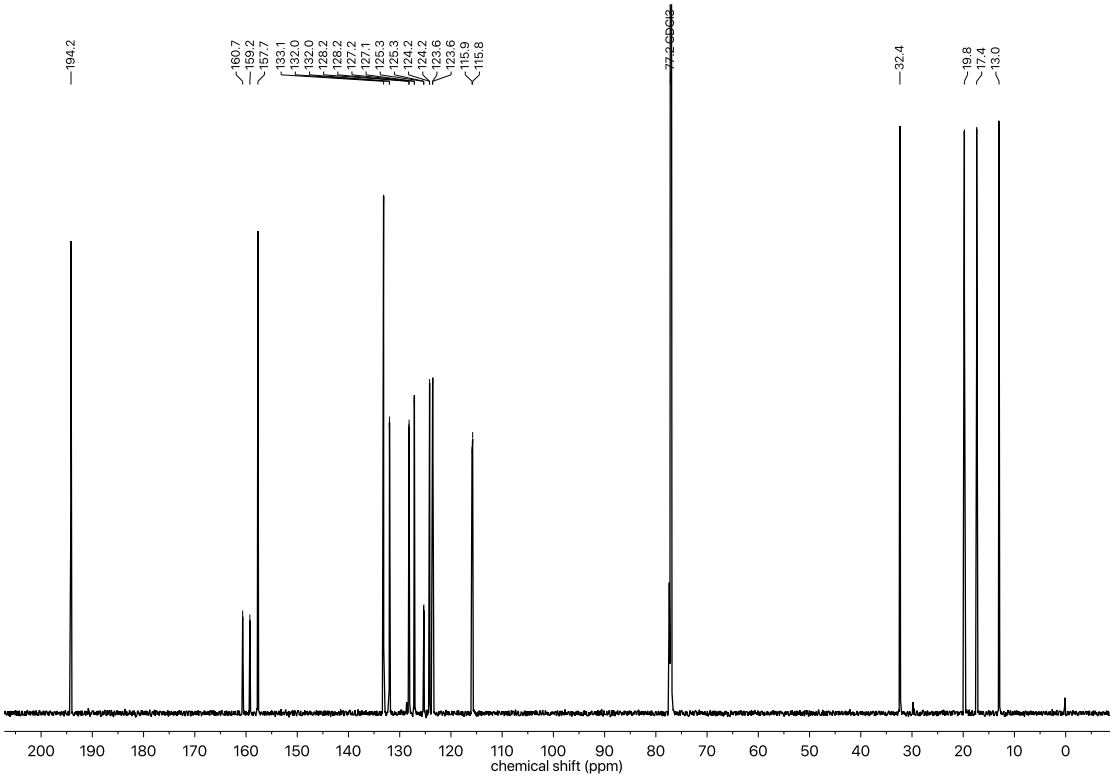


(*E*)-4-(2-((*E*)-2-Fluorostyryl)cyclopropyl)but-2-enal (109l)

^{1}H NMR:

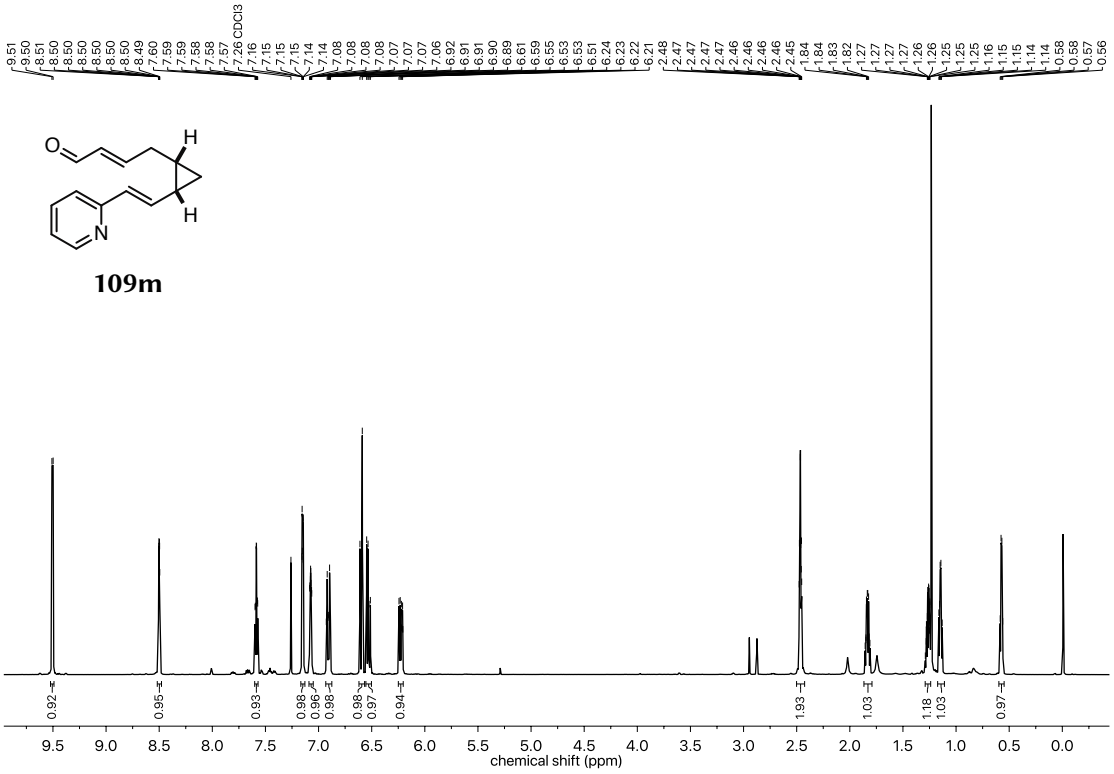


^{13}C NMR:

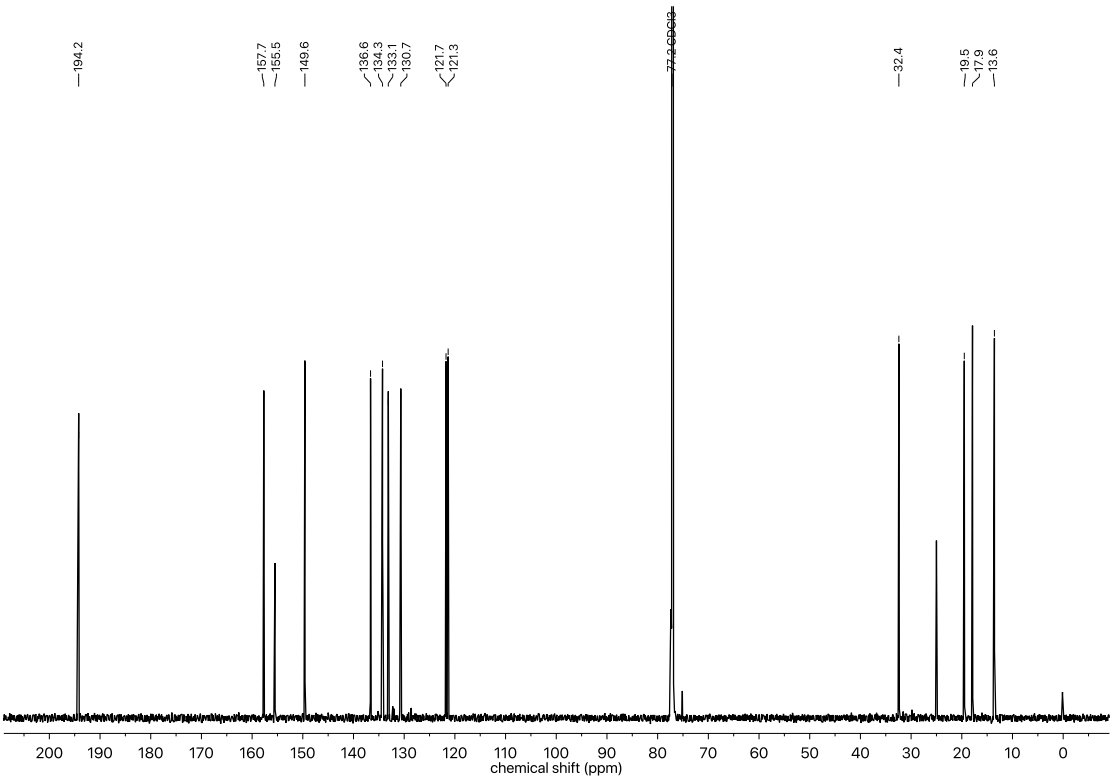


(*E*)-4-(2-((*E*)-2-(Pyridin-2-yl)vinyl)cyclopropyl)but-2-enal (109m)

^{1}H NMR:

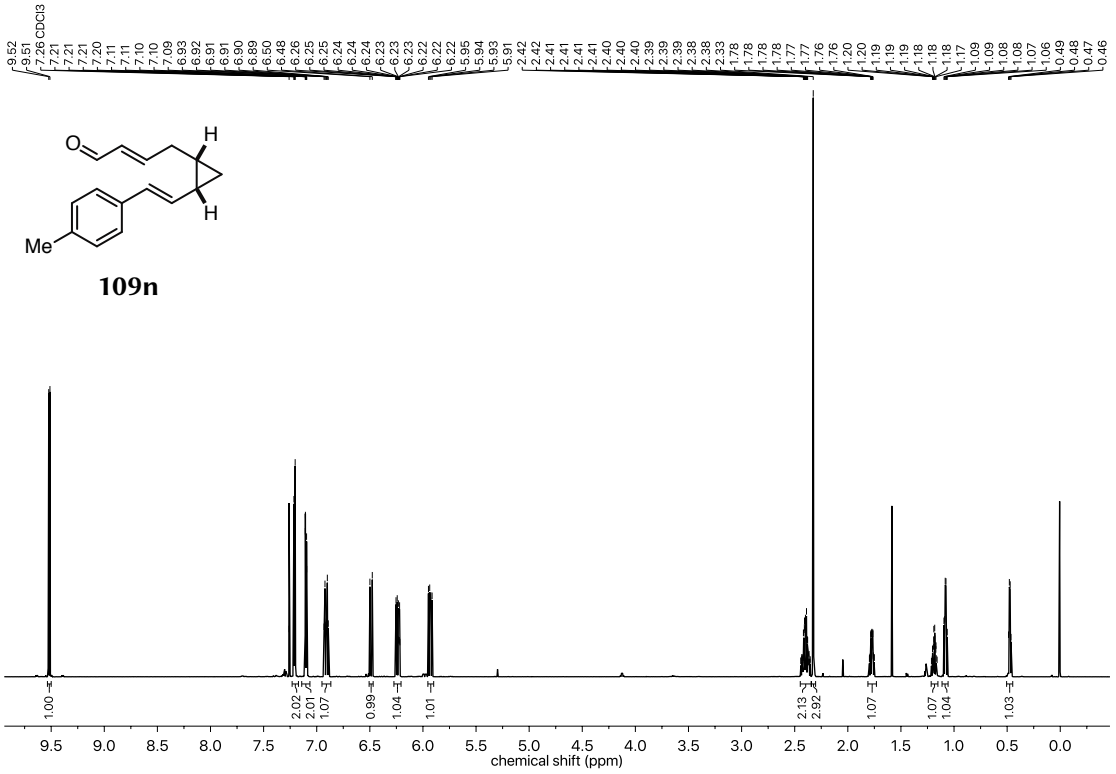


^{13}C NMR:

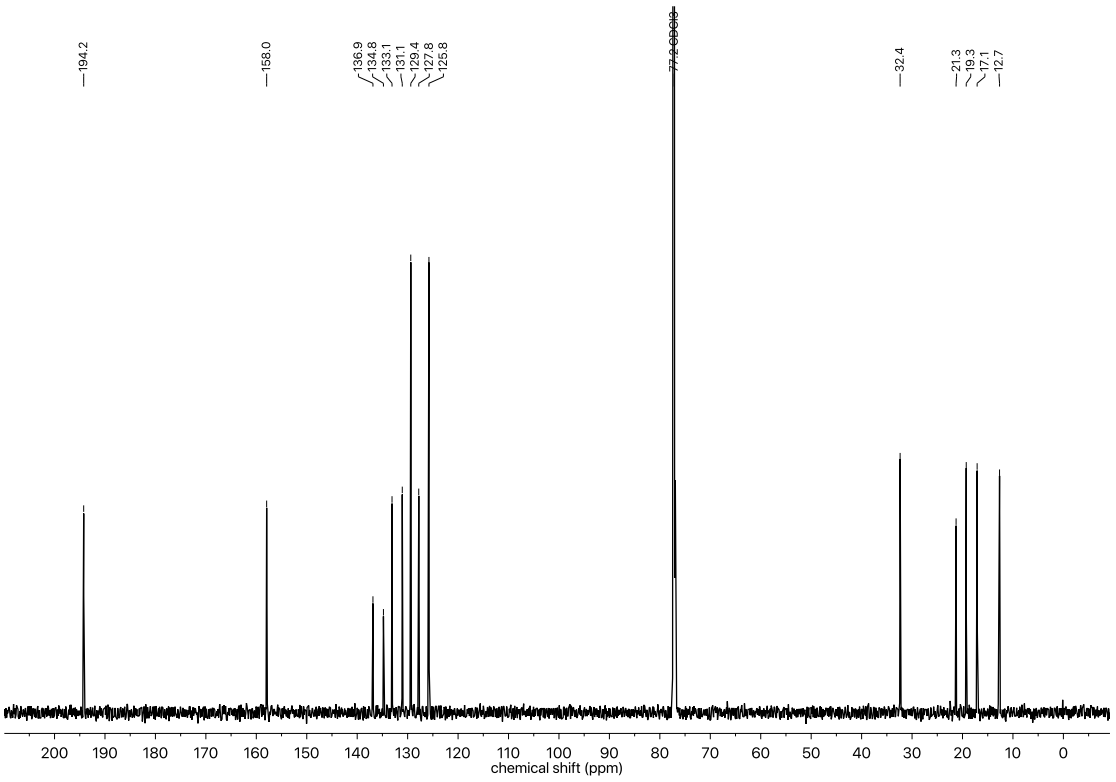


(*E*)-4-(2-((*E*)-4-Methylstyryl)cyclopropyl)but-2-enal (109n)

^{1}H NMR:

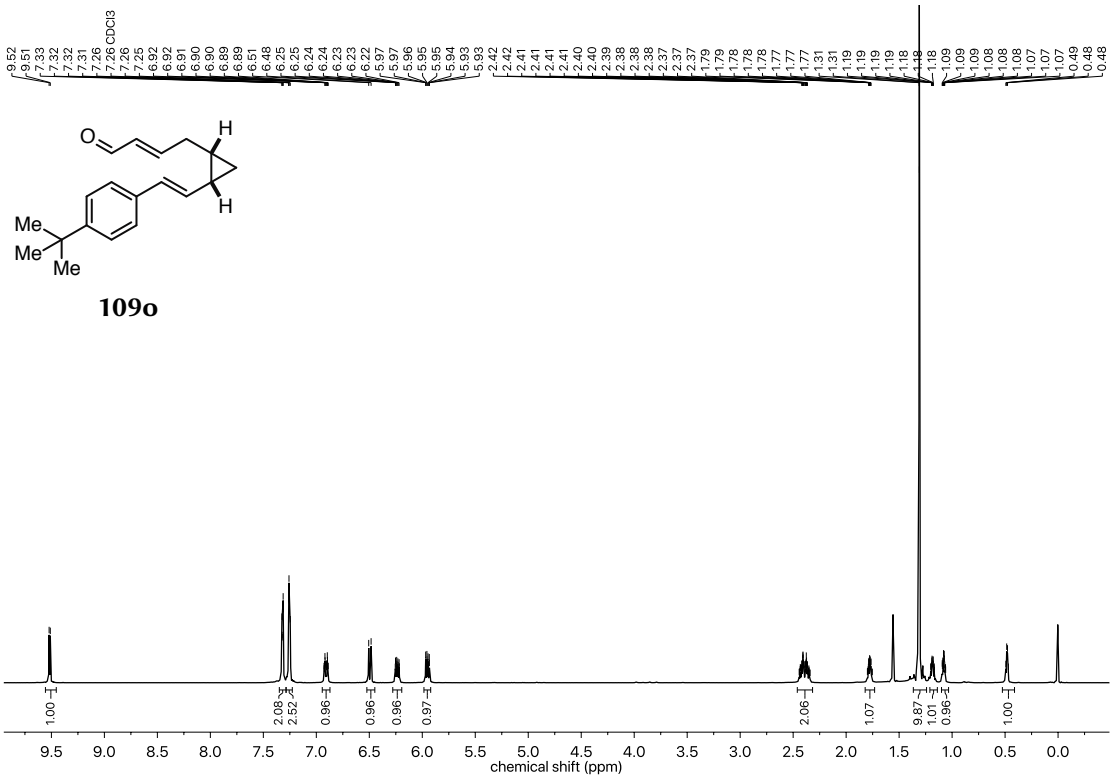


^{13}C NMR:



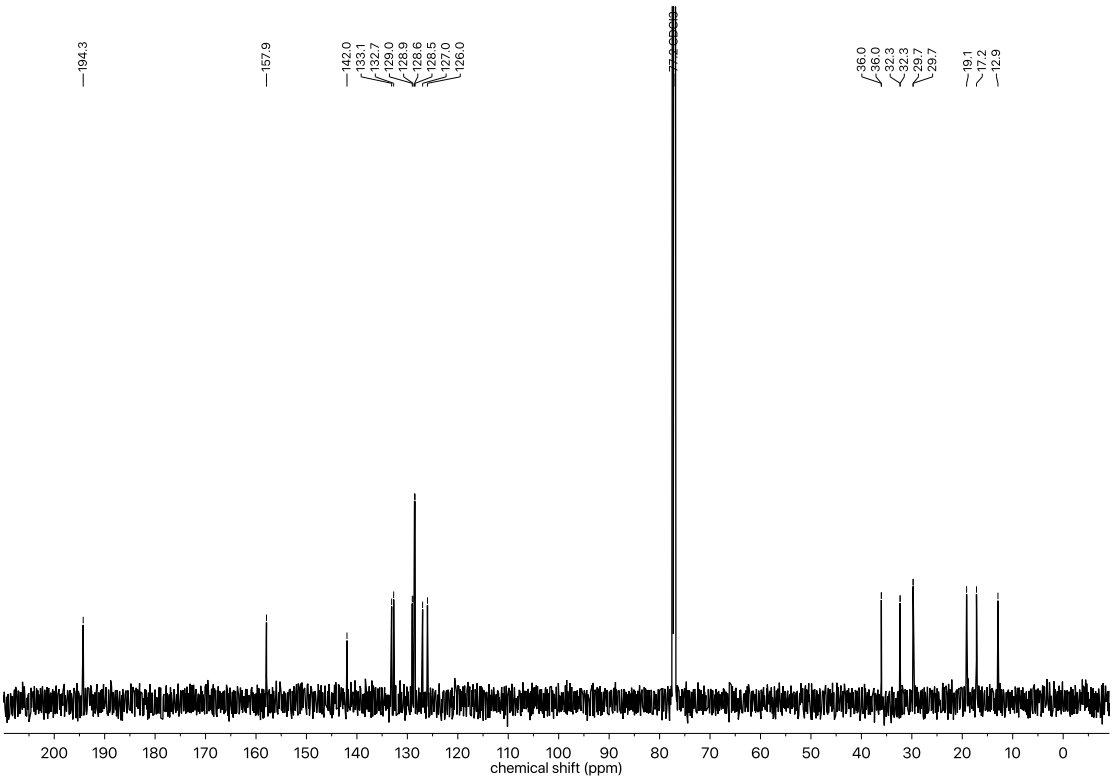
(*E*)-4-(2-((*E*)-4-(*tert*-Butyl)styryl)cyclopropyl)but-2-enal (109o)

^{1}H NMR:



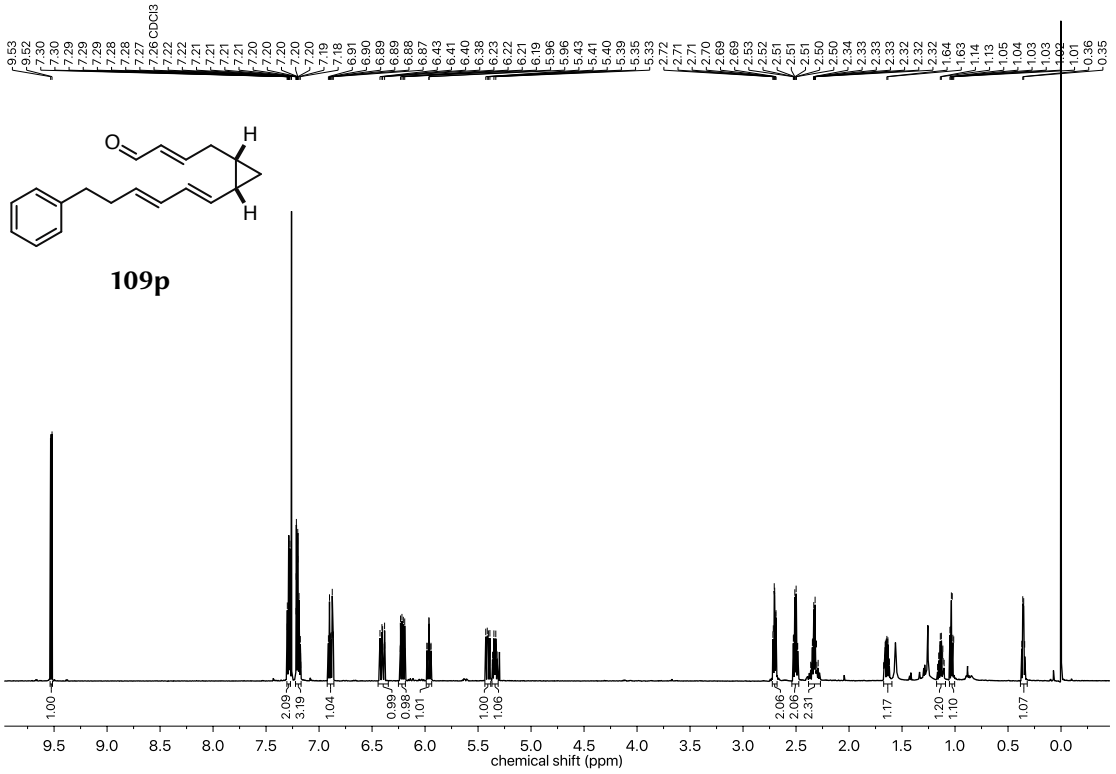
109o

^{13}C NMR:

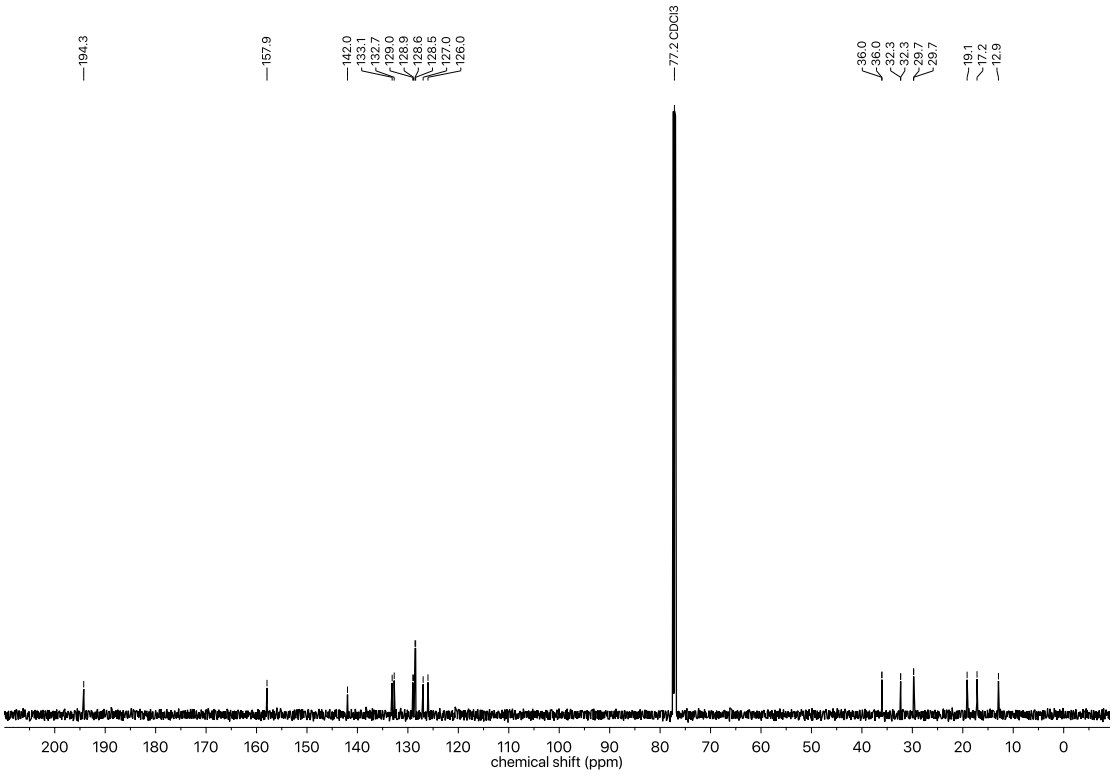


(*E*)-4-(2-((1*E*,3*E*)-6-Phenylhexa-1,3-dien-1-yl)cyclopropyl)but-2-enal (109p)

^{1}H NMR:

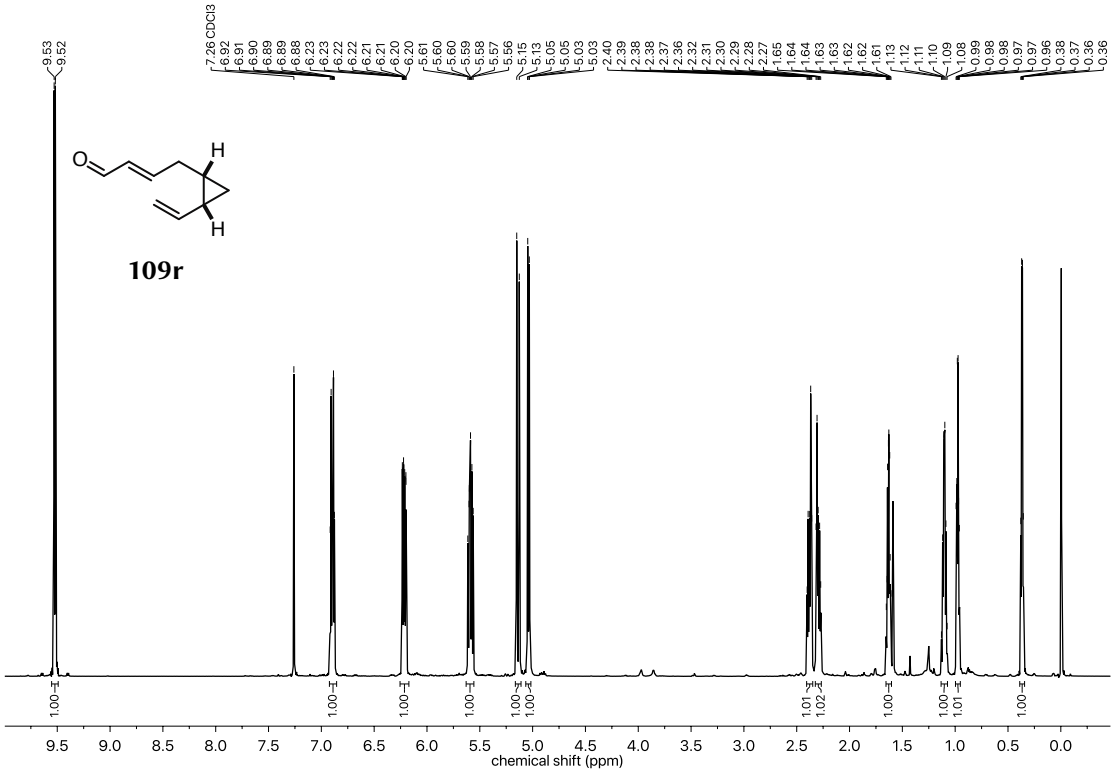


^{13}C NMR:

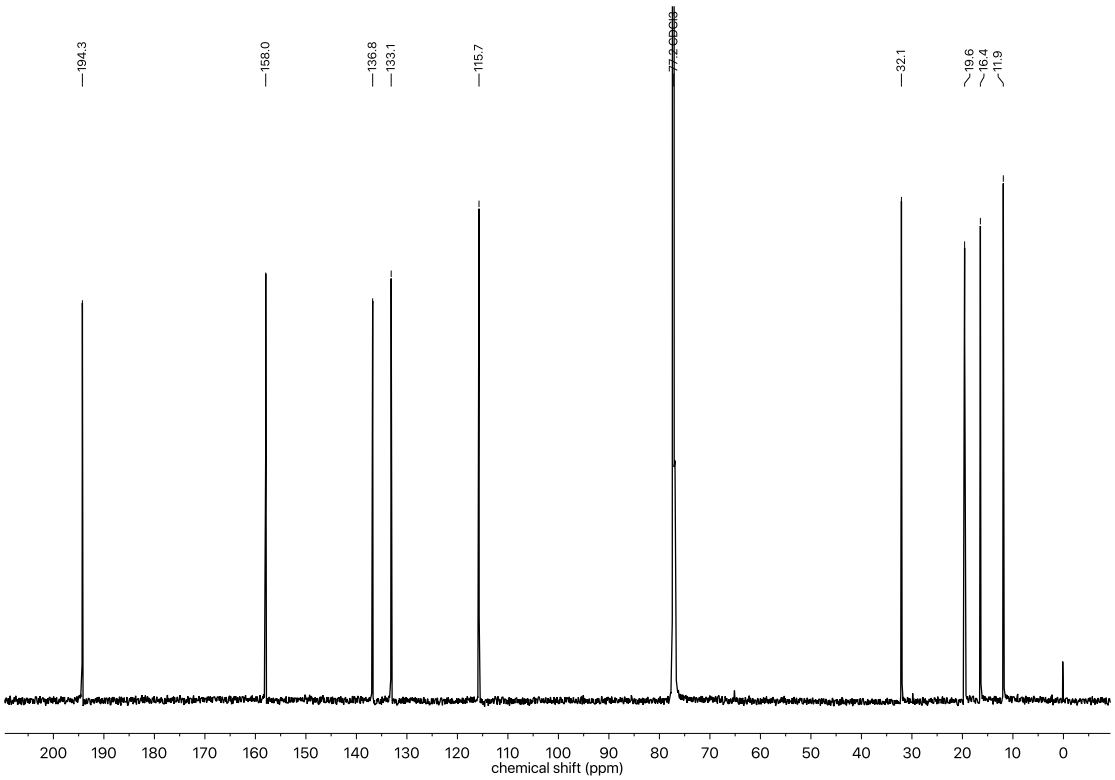


(*E*)-4-(2-Vinylcyclopropyl)but-2-enal (109r)

^{1}H NMR:

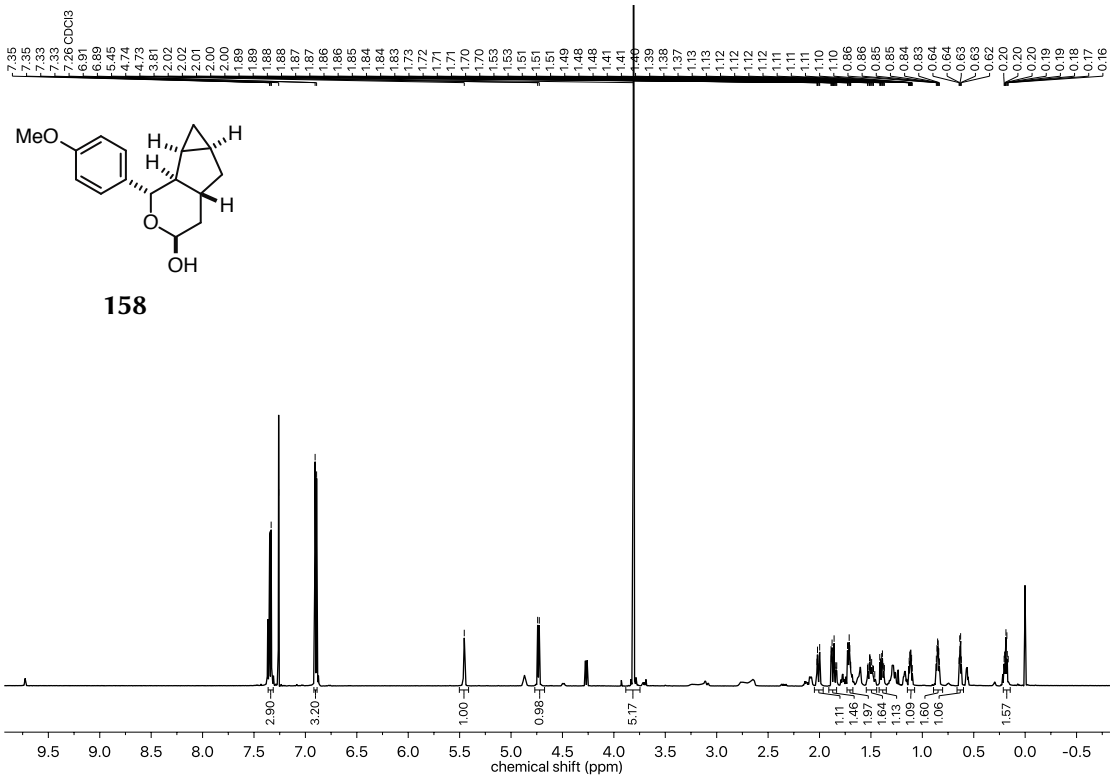


^{13}C NMR:

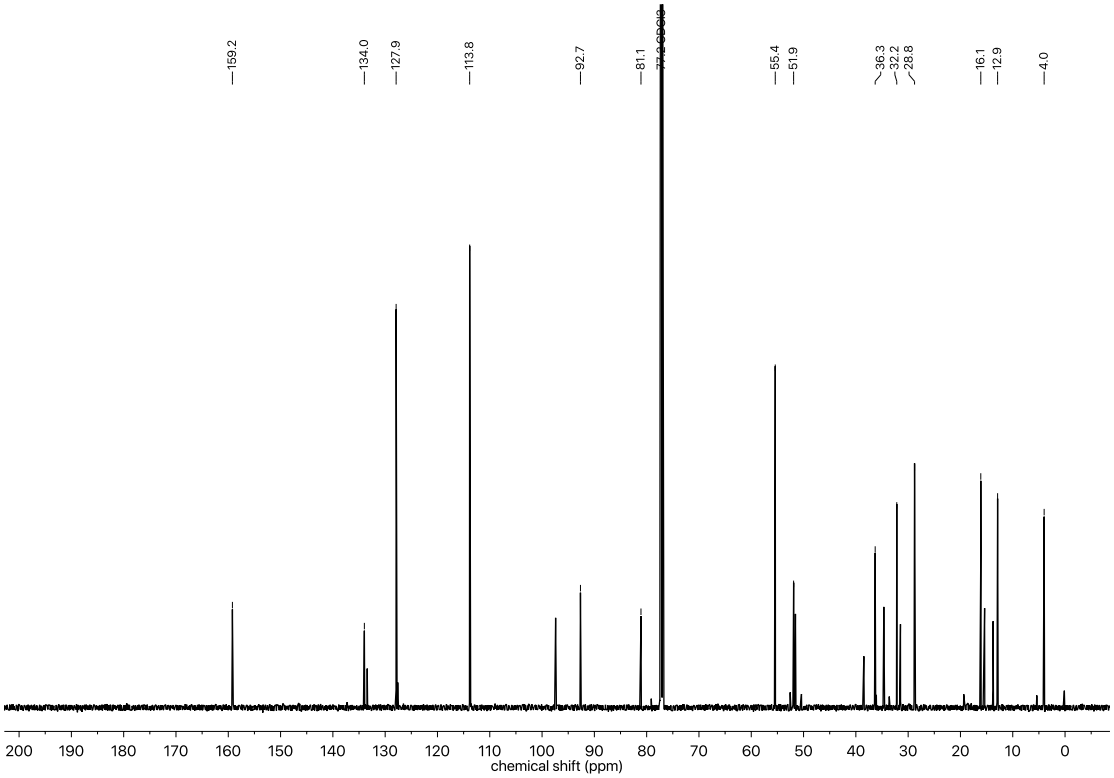


1-(4-Methoxyphenyl)octahydro-1*H*-cyclopropa[4,5]cyclopenta[1,2-*c*]pyran-3-ol (158)

^{1}H NMR:

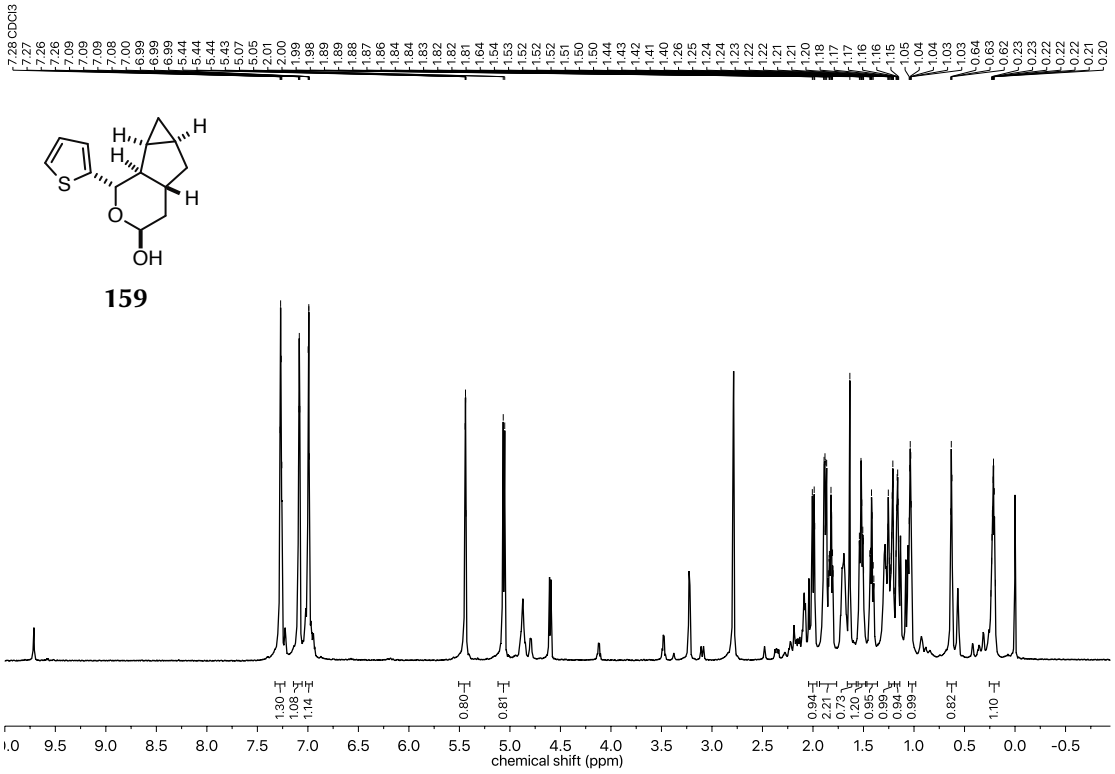


^{13}C NMR:

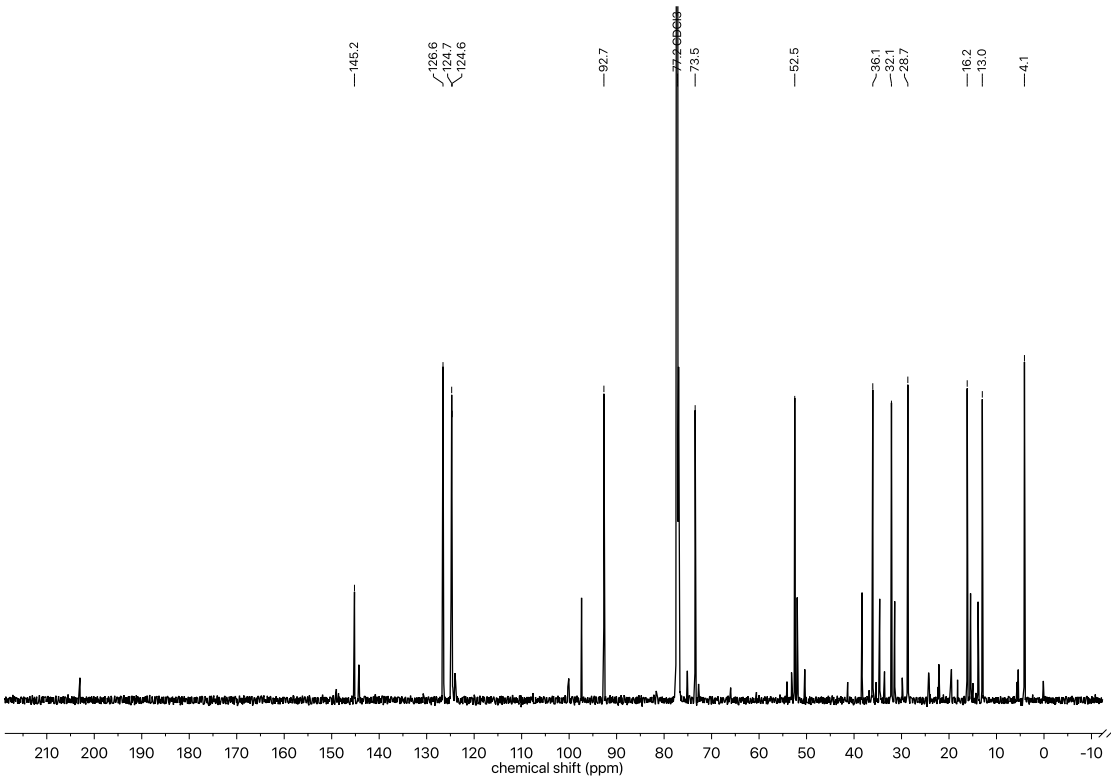


1-(Thiophen-2-yl)octahydro-1*H*-cyclopropa-[4,5]cyclopenta[1,2-*c*]pyran-3-ol (159)

^{1}H NMR:

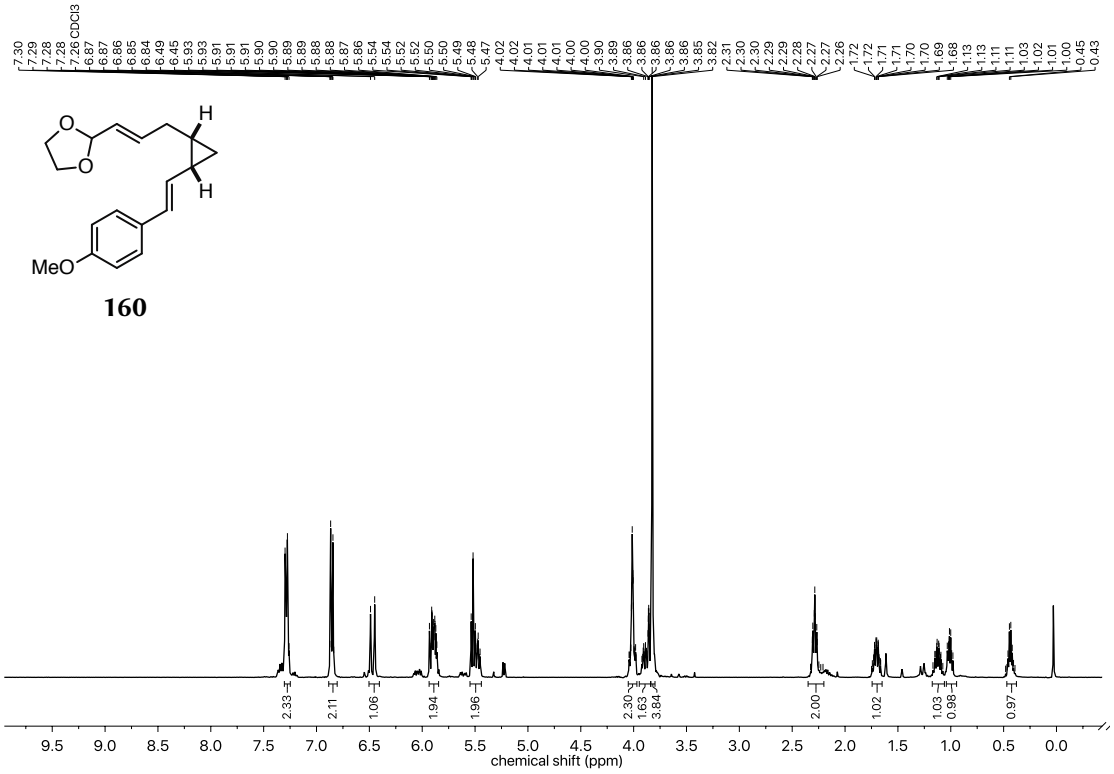


^{13}C NMR:



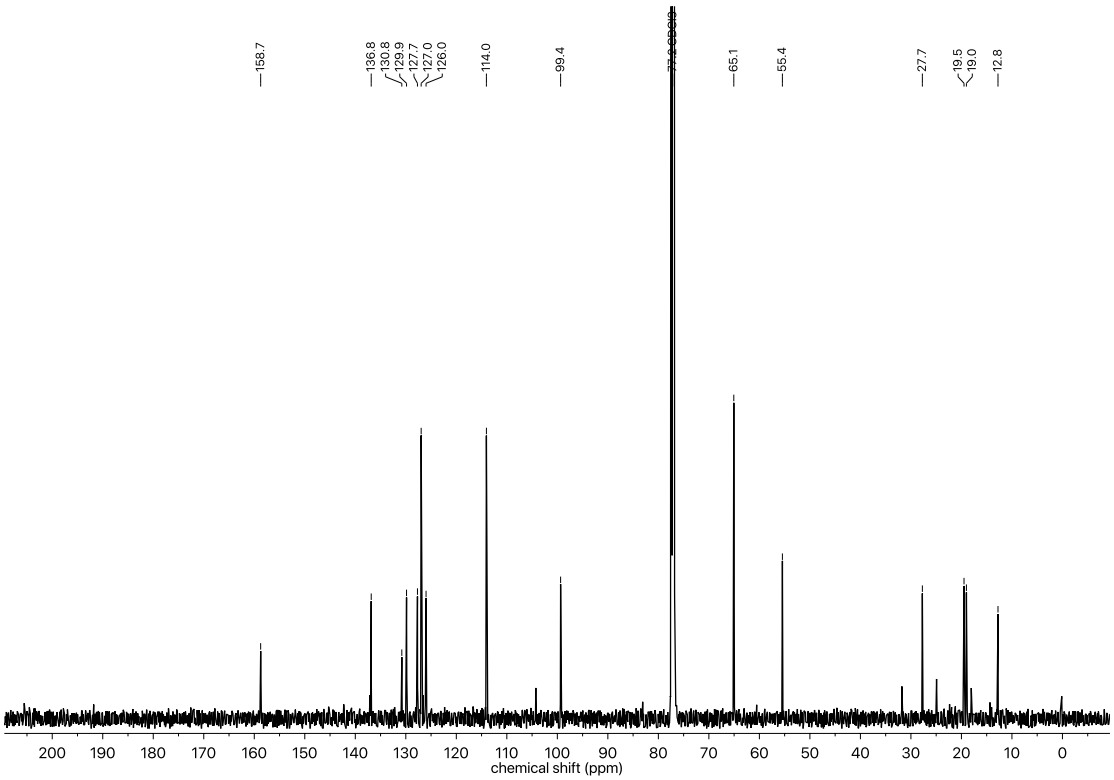
2-((*E*)-3-(2-((*E*)-4-Methoxystyryl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (160)

^{1}H NMR:



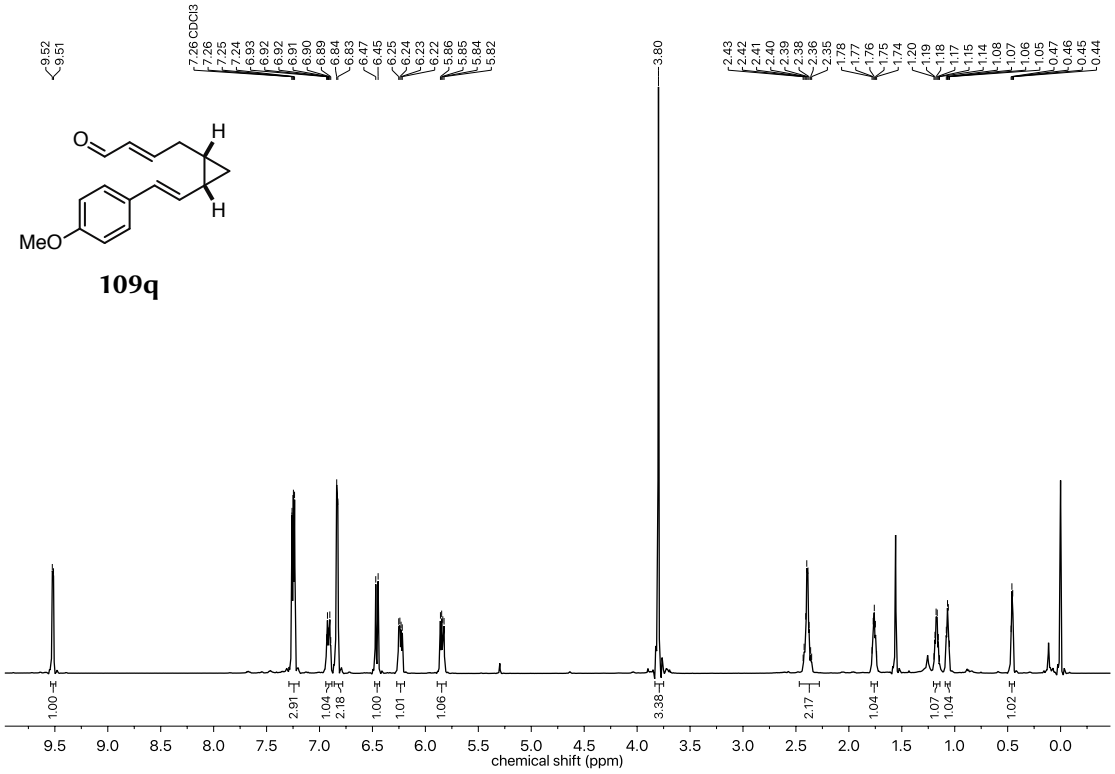
160

^{13}C NMR:



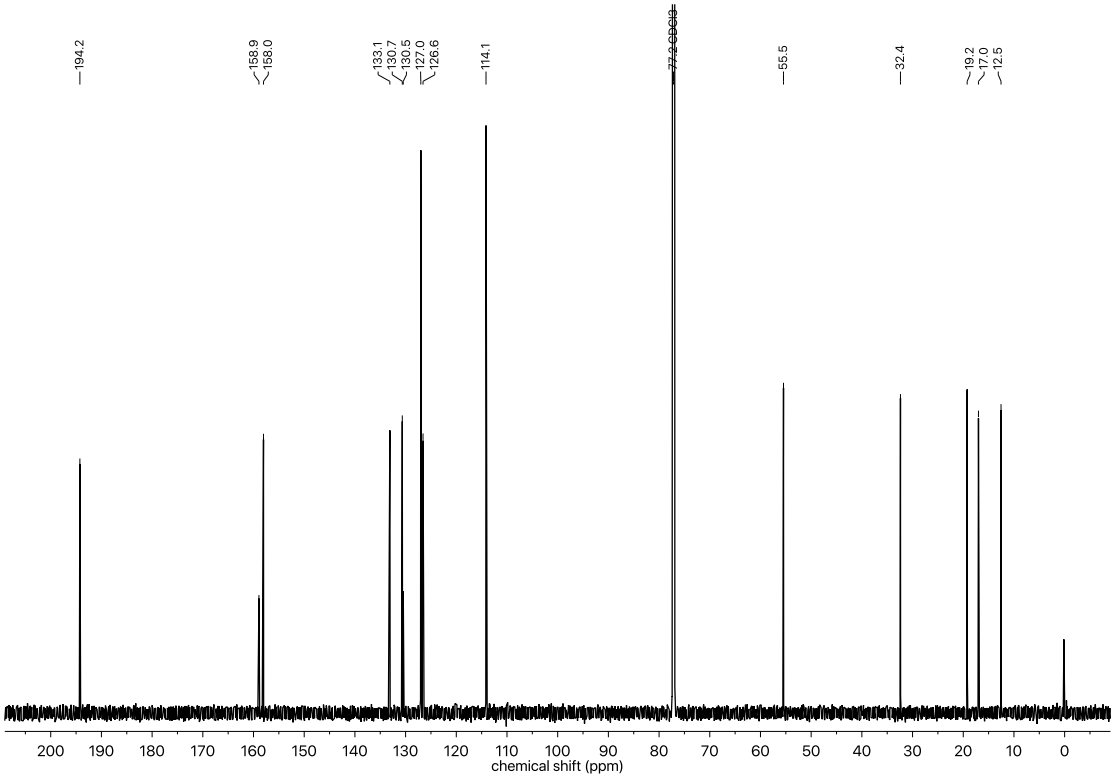
(*E*)-4-(2-((*E*)-4-Methoxystyryl)cyclopropyl)but-2-enal (109q)

^{1}H NMR:



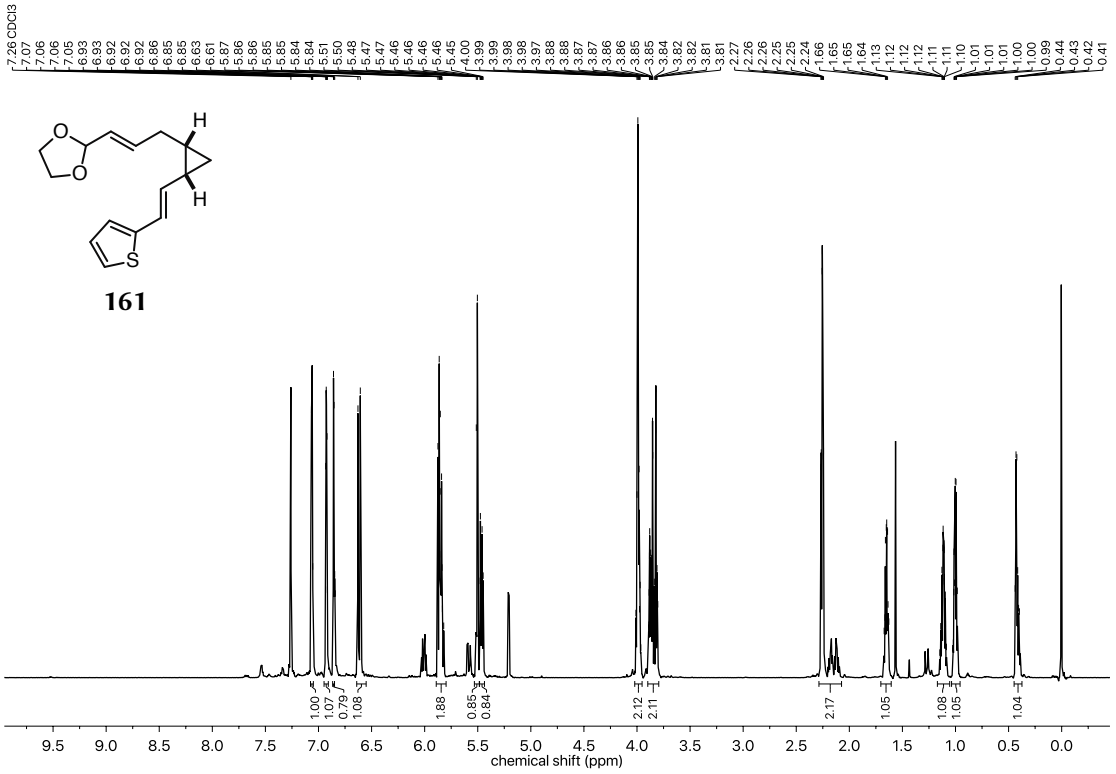
109q

^{13}C NMR:



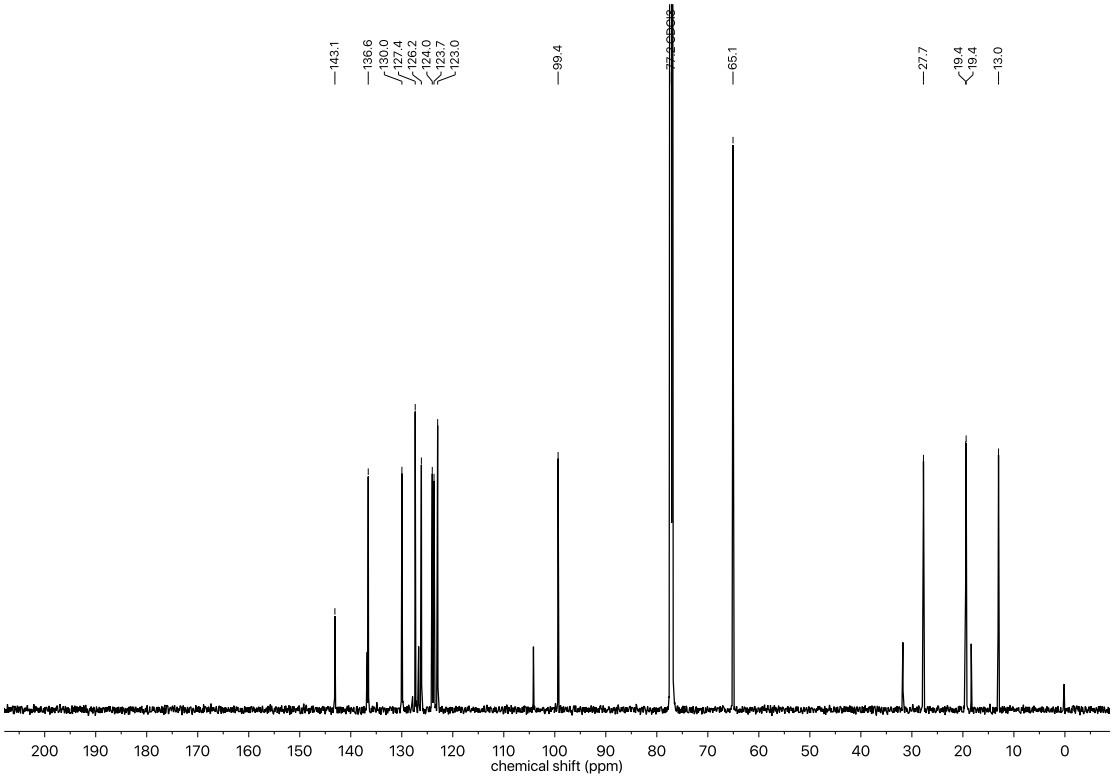
2-((*E*)-3-(2-((*E*)-2-(Thiophen-2-yl)vinyl)cyclopropyl)prop-1-en-1-yl)-1,3-dioxolane (161)

^{1}H NMR:



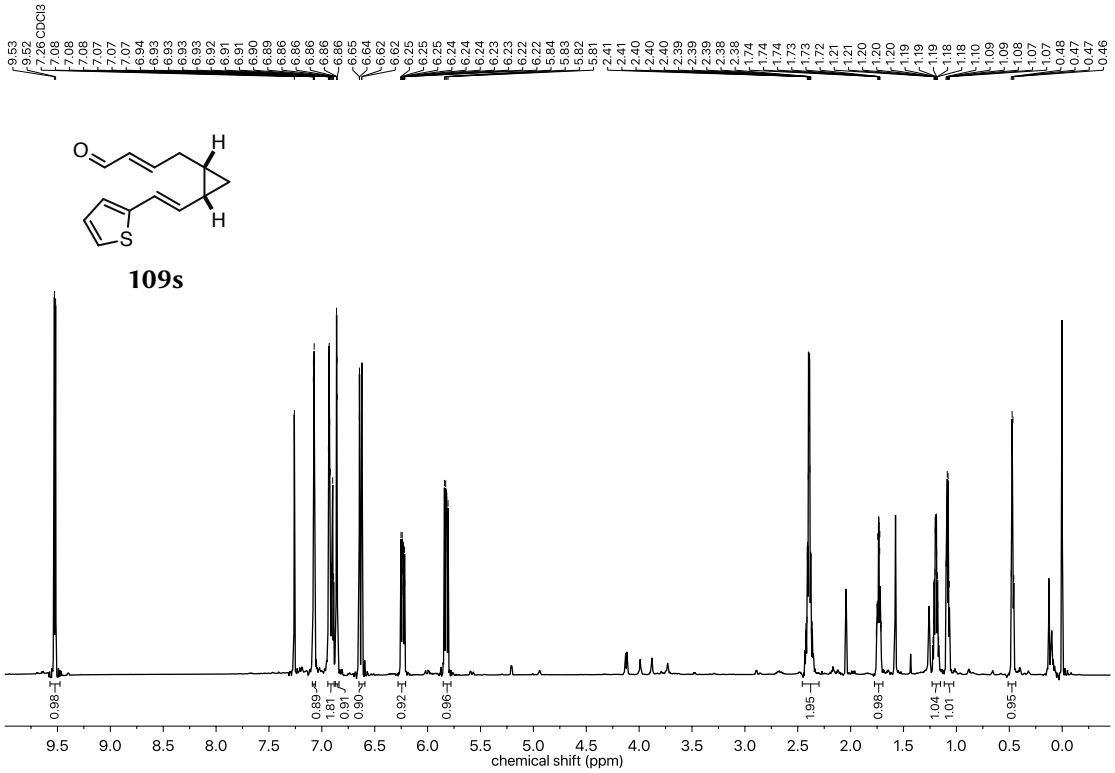
161

^{13}C NMR:

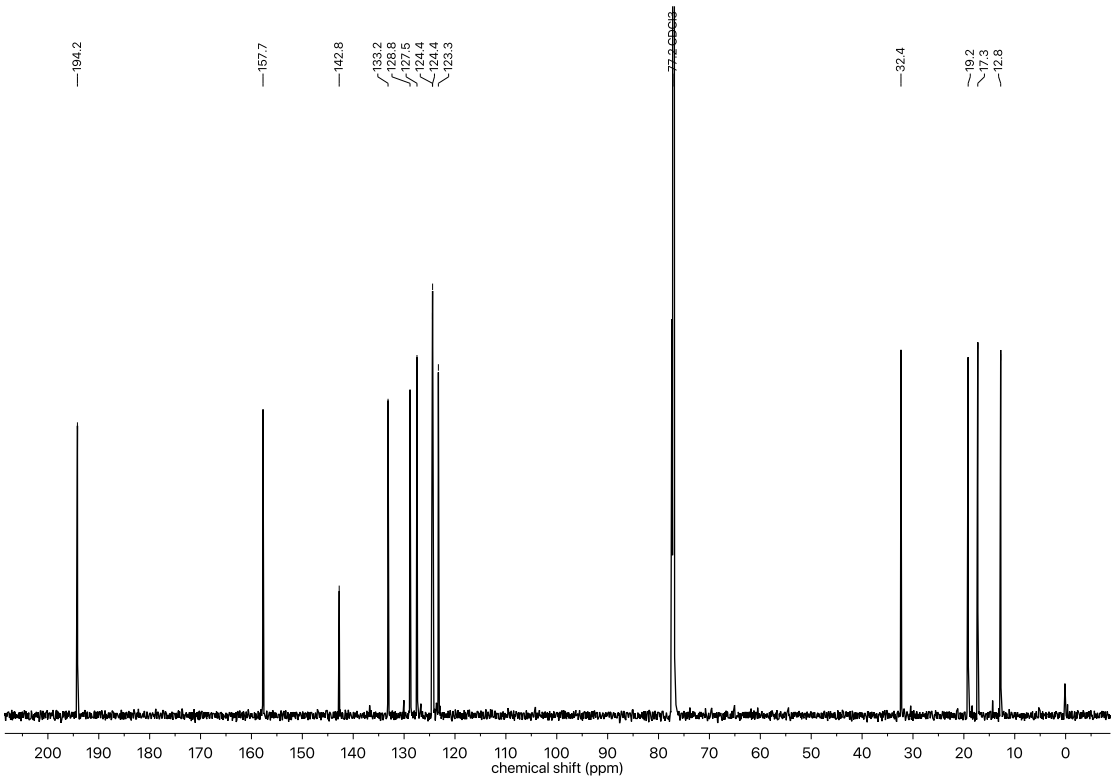


2-(*E*)-4-(2-((*E*)-2-(Thiophen-2-yl)vinyl)cyclopropyl)but-2-enal (109s)

^{1}H NMR:

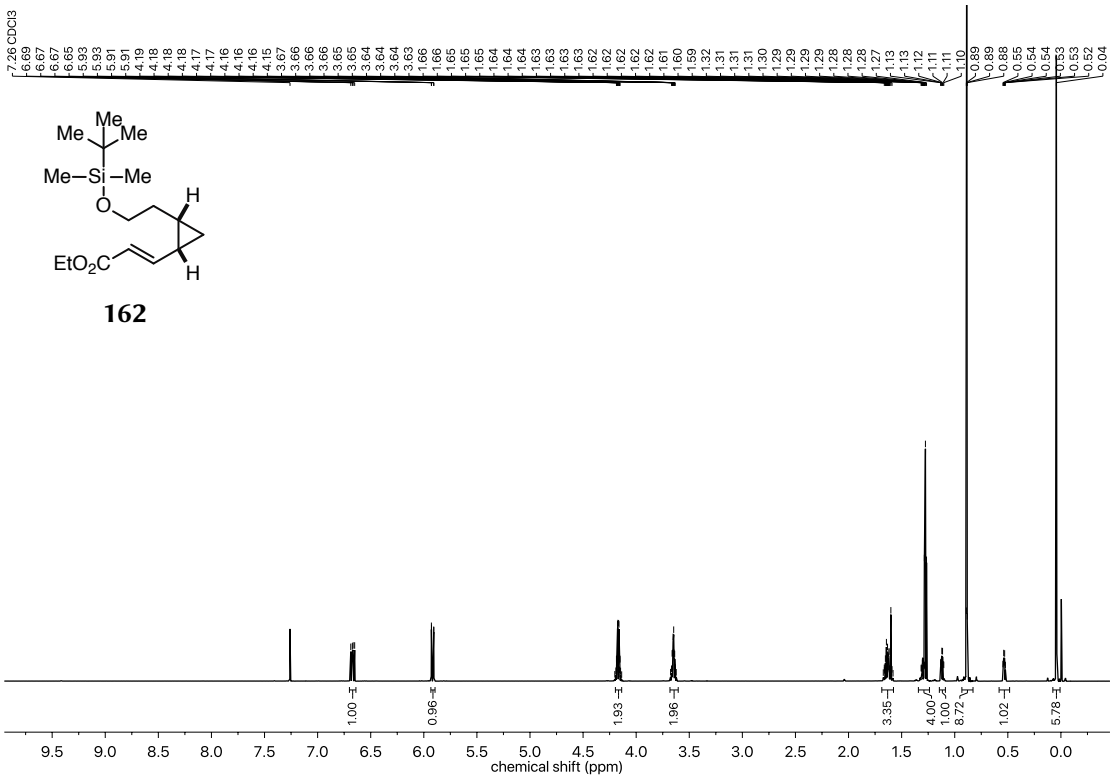


^{13}C NMR:



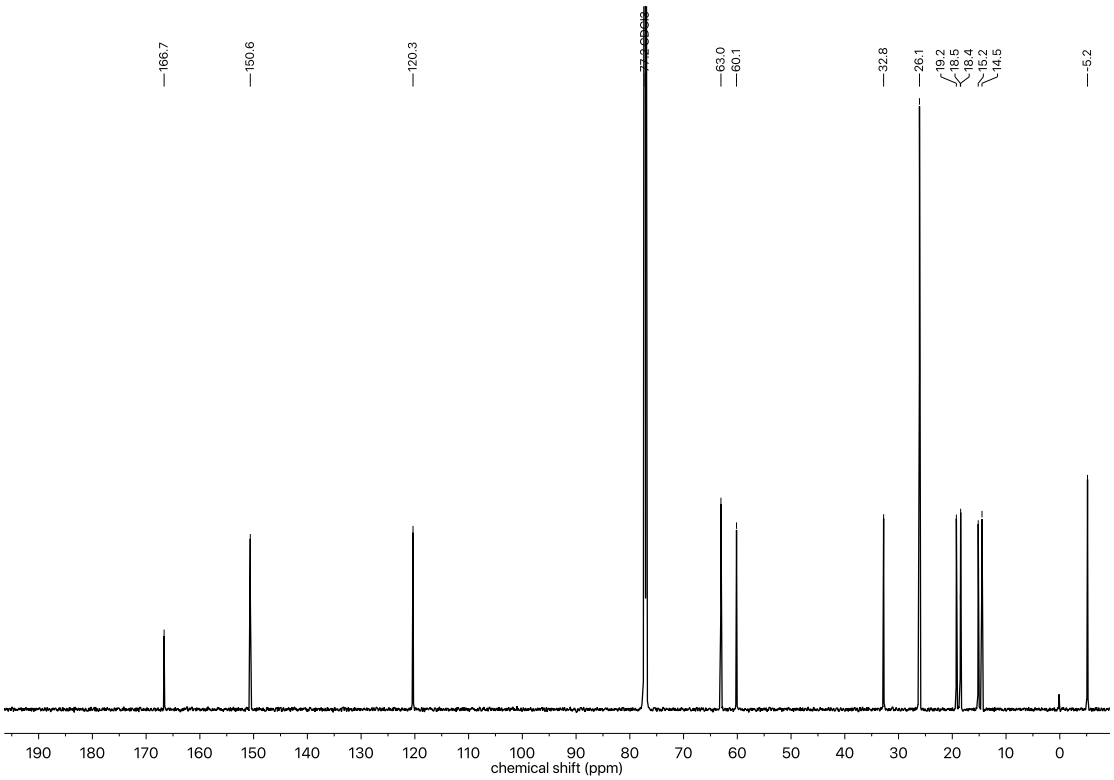
Ethyl (*E*)-3-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)acrylate (162)

^{1}H NMR:



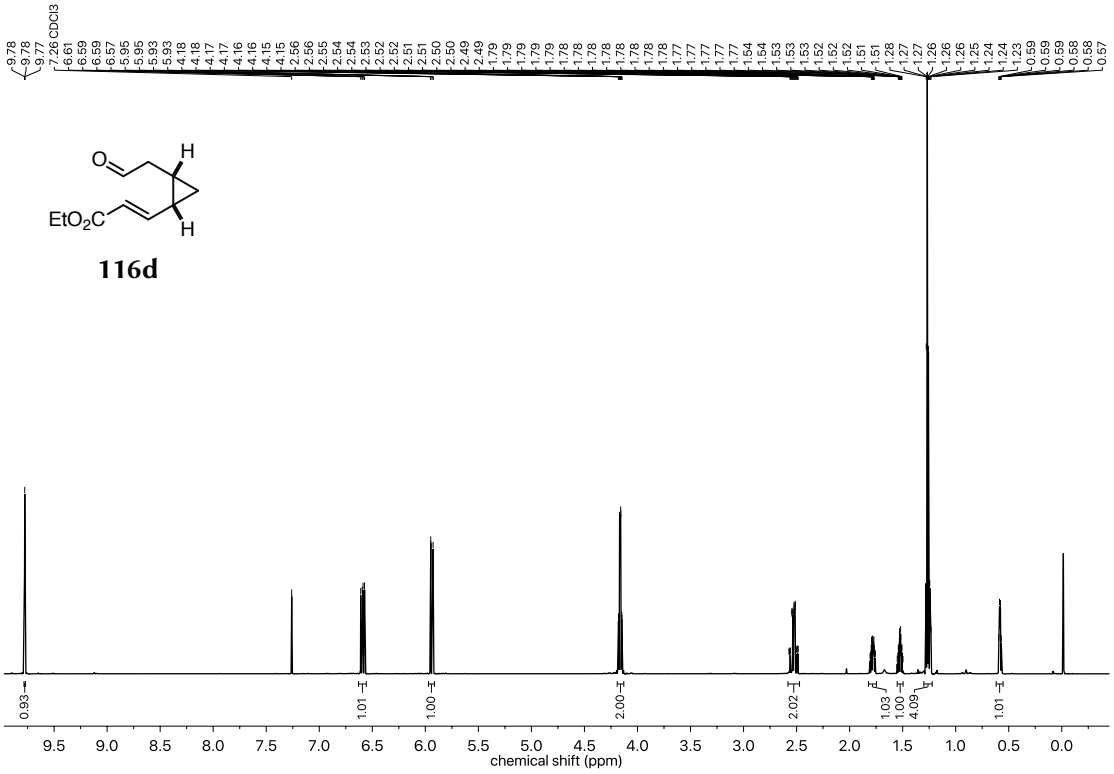
162

^{13}C NMR:

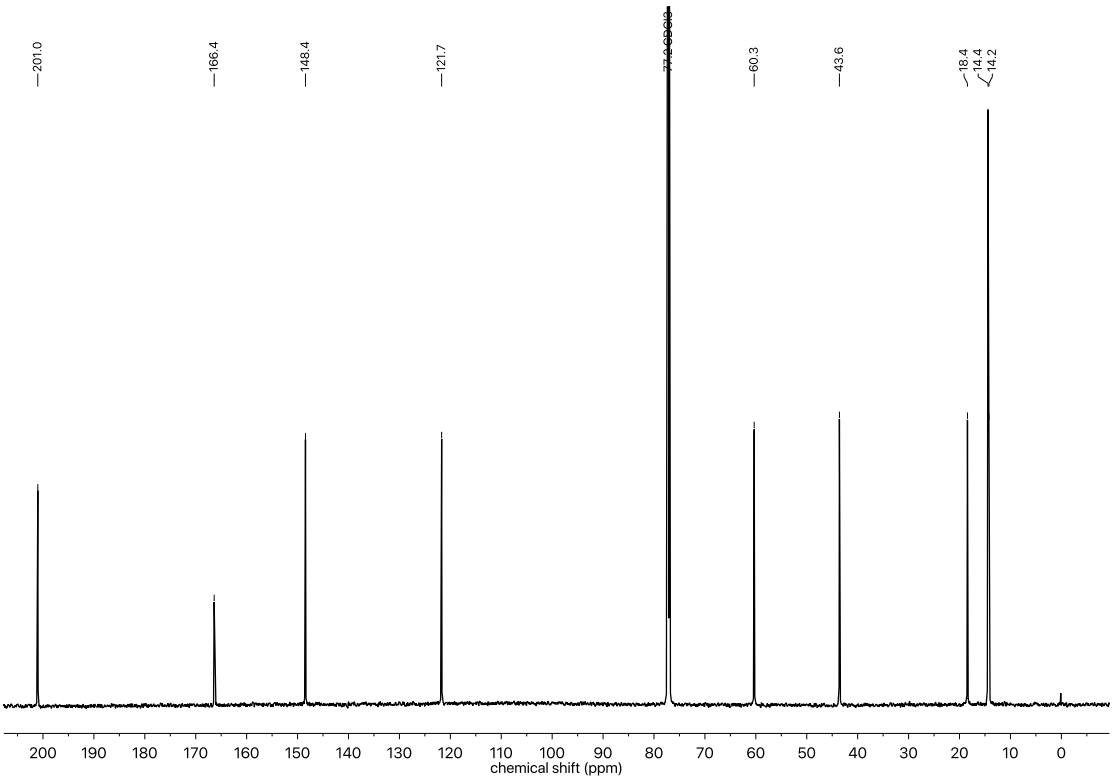


Ethyl (*E*)-3-(2-(2-Oxoethyl)cyclopropyl)acrylate (116d)

^{1}H NMR:

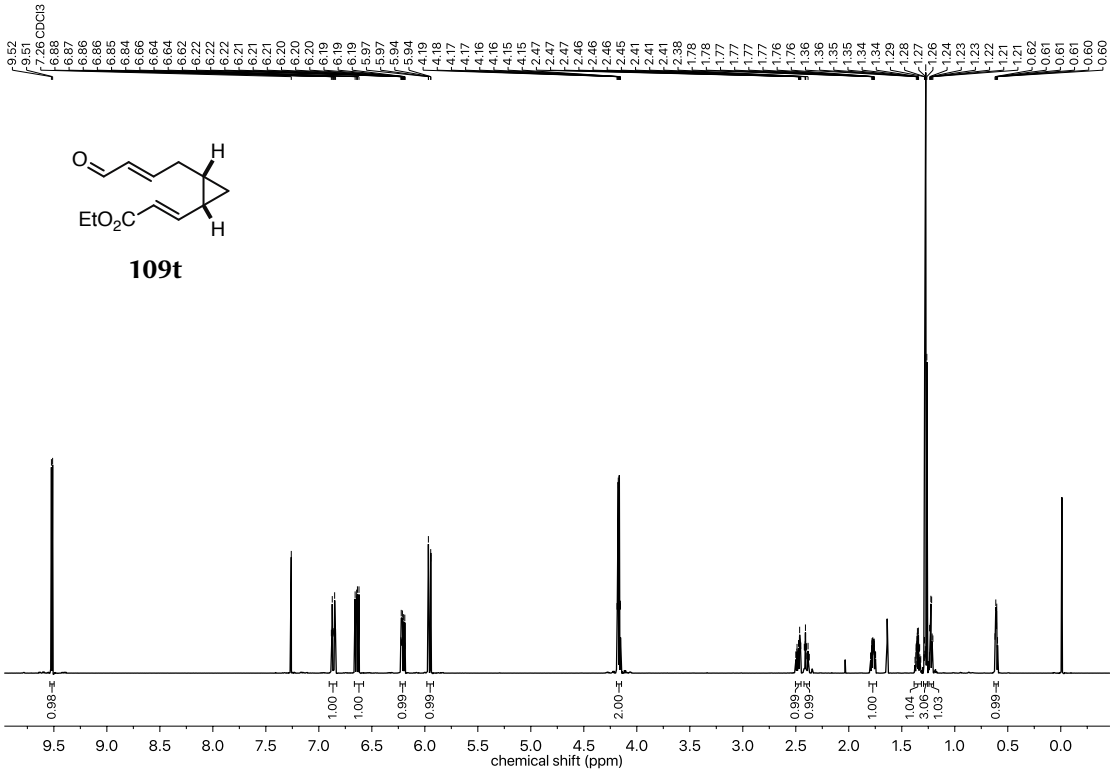


^{13}C NMR:



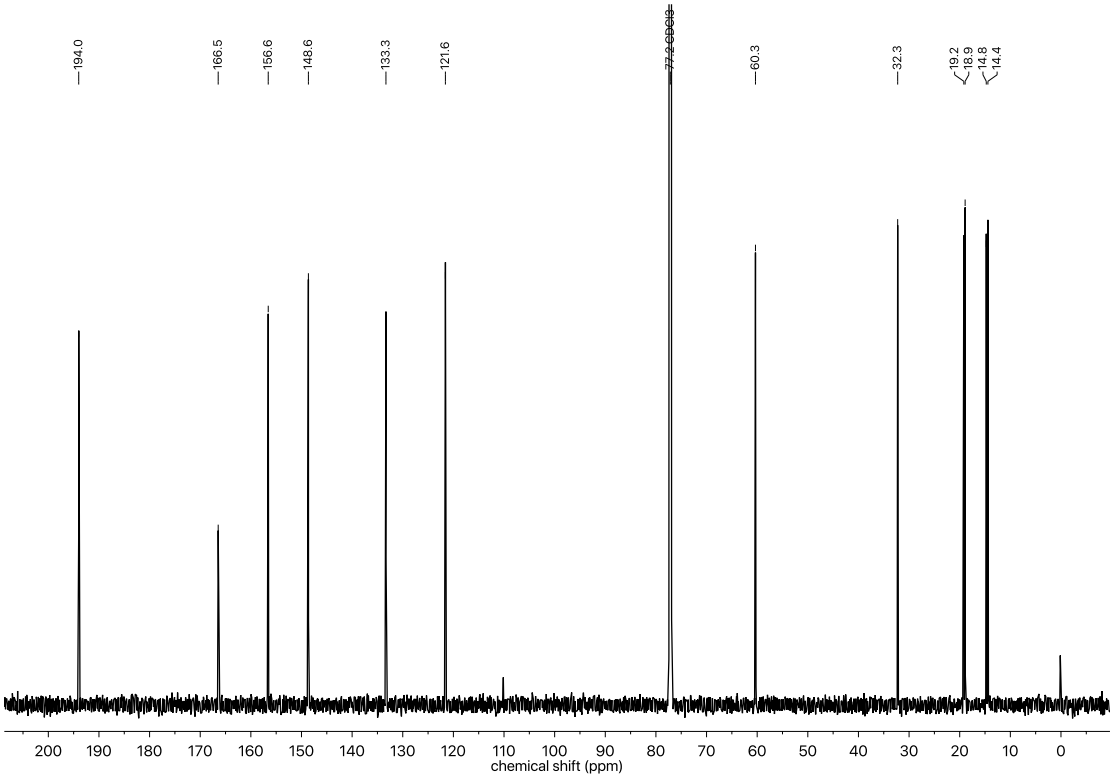
Ethyl (*E*)-3-(2-((*E*)-4-Oxobut-2-en-1-yl)cyclopropyl)acrylate (109t)

^{1}H NMR:



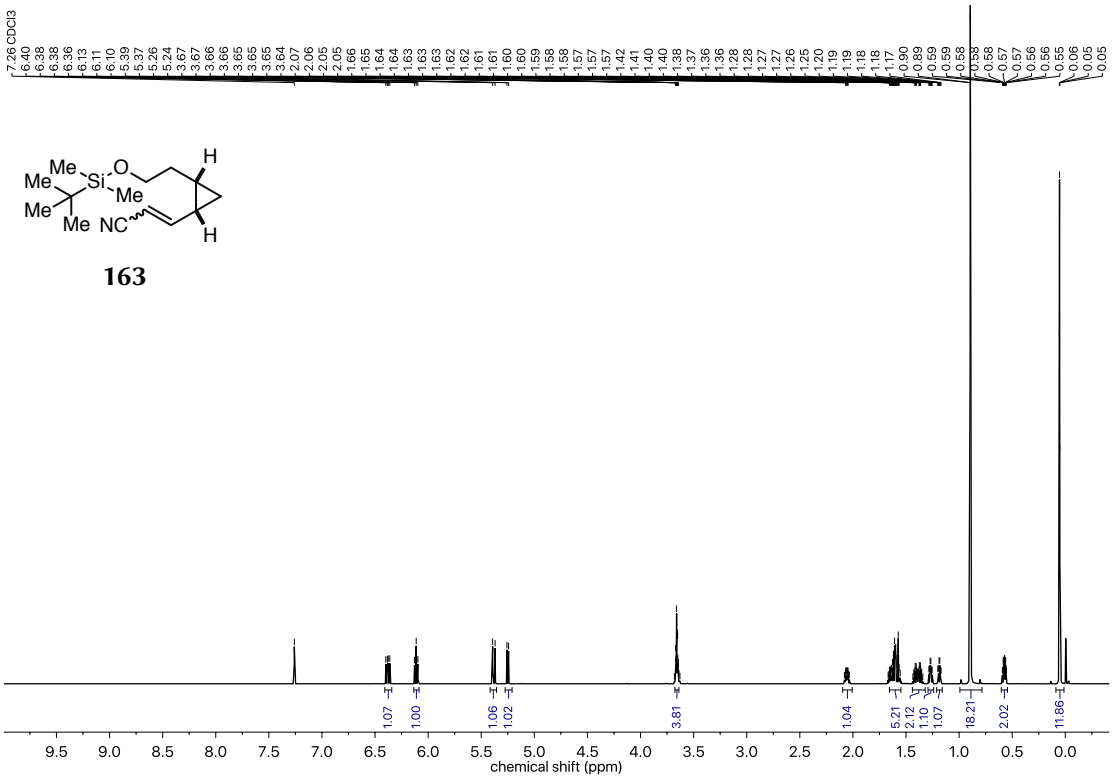
109t

^{13}C NMR:

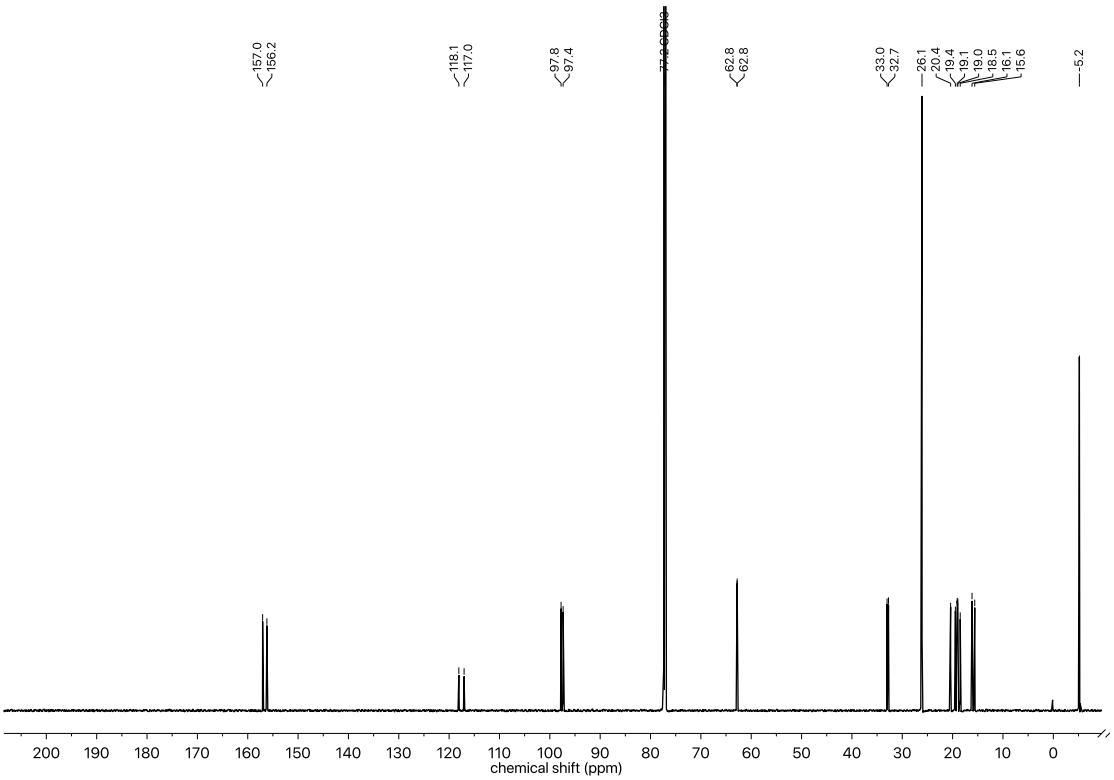


3-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)acrylonitrile (163)

^{1}H NMR:

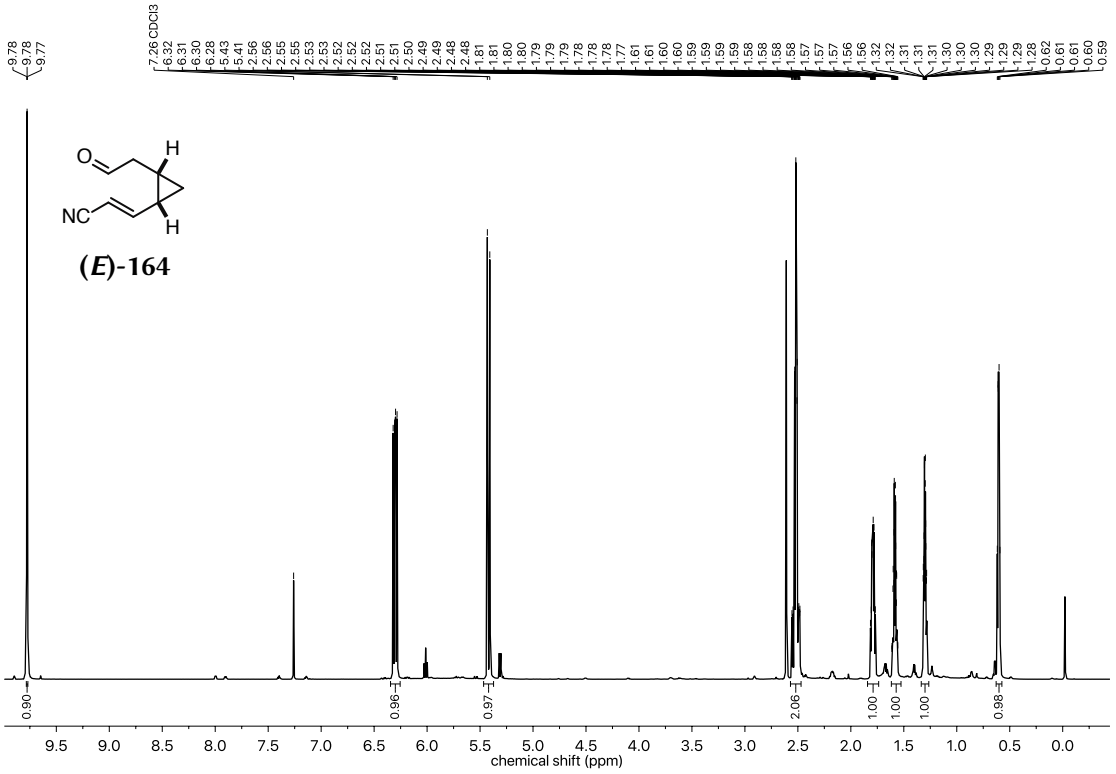


^{13}C NMR:

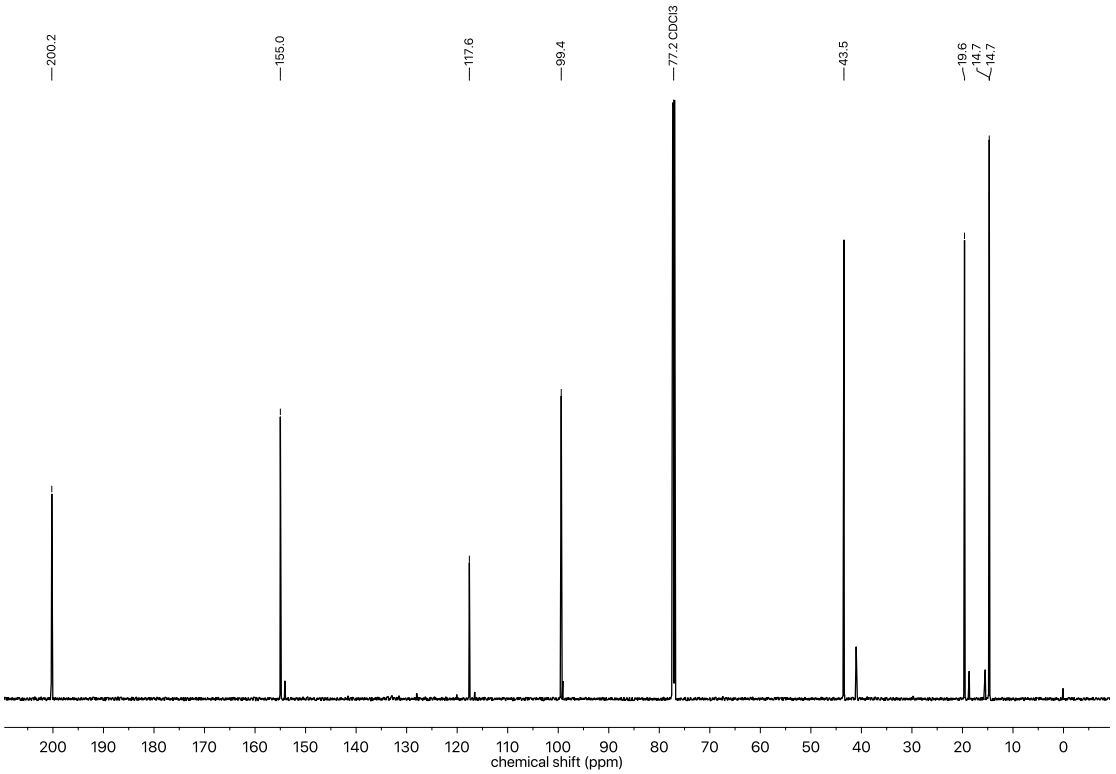


(*E*)-3-(2-(2-Oxoethyl)cyclopropyl)acrylonitrile ((*E*)-164)

^{1}H NMR:

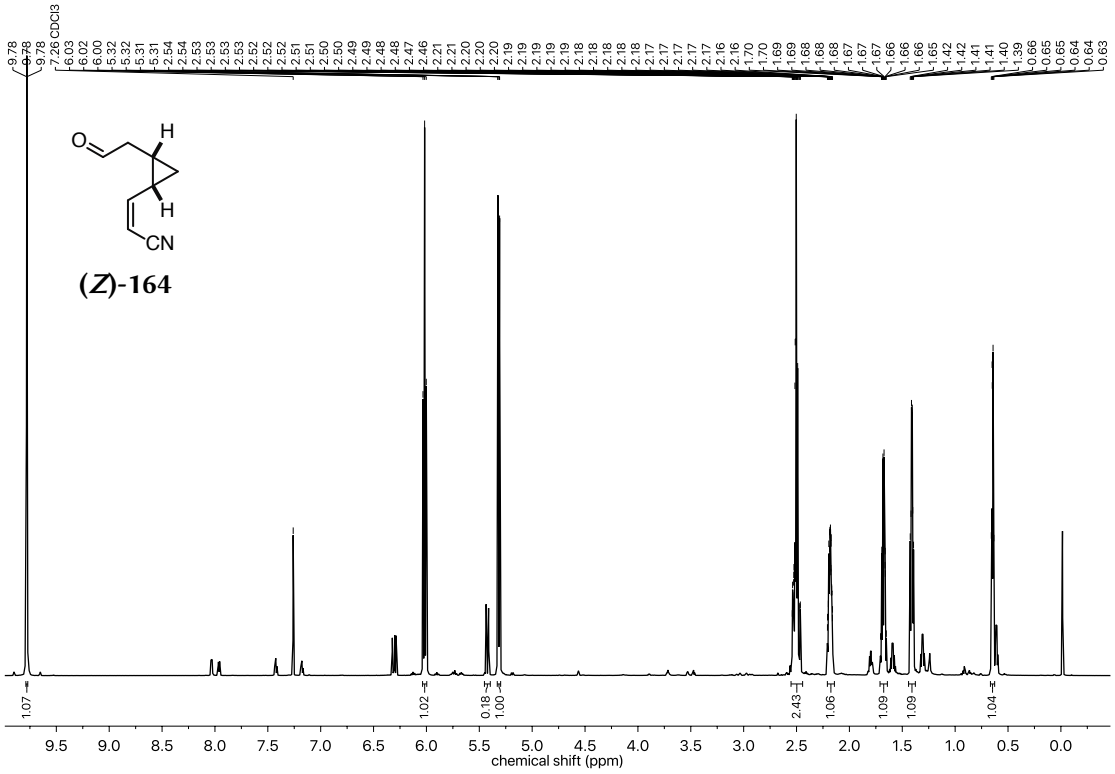


^{13}C NMR:

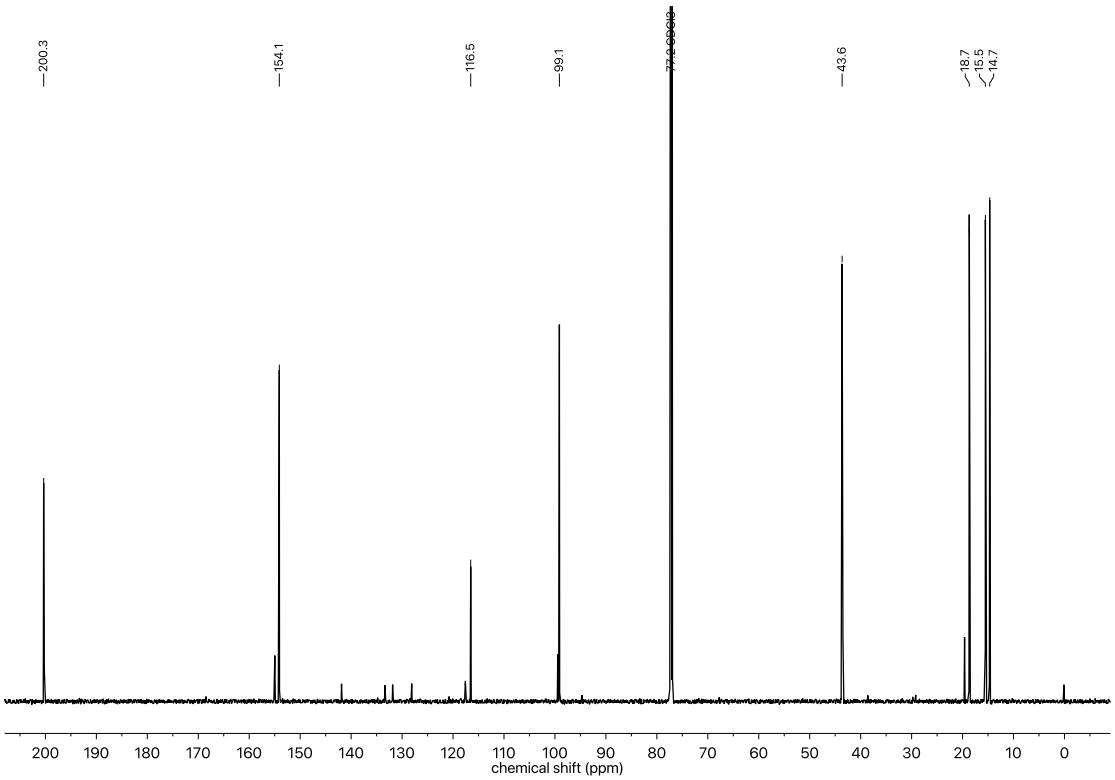


(*Z*)-3-(2-(2-Oxoethyl)cyclopropyl)acrylonitrile ((*Z*)-164)

^{1}H NMR:

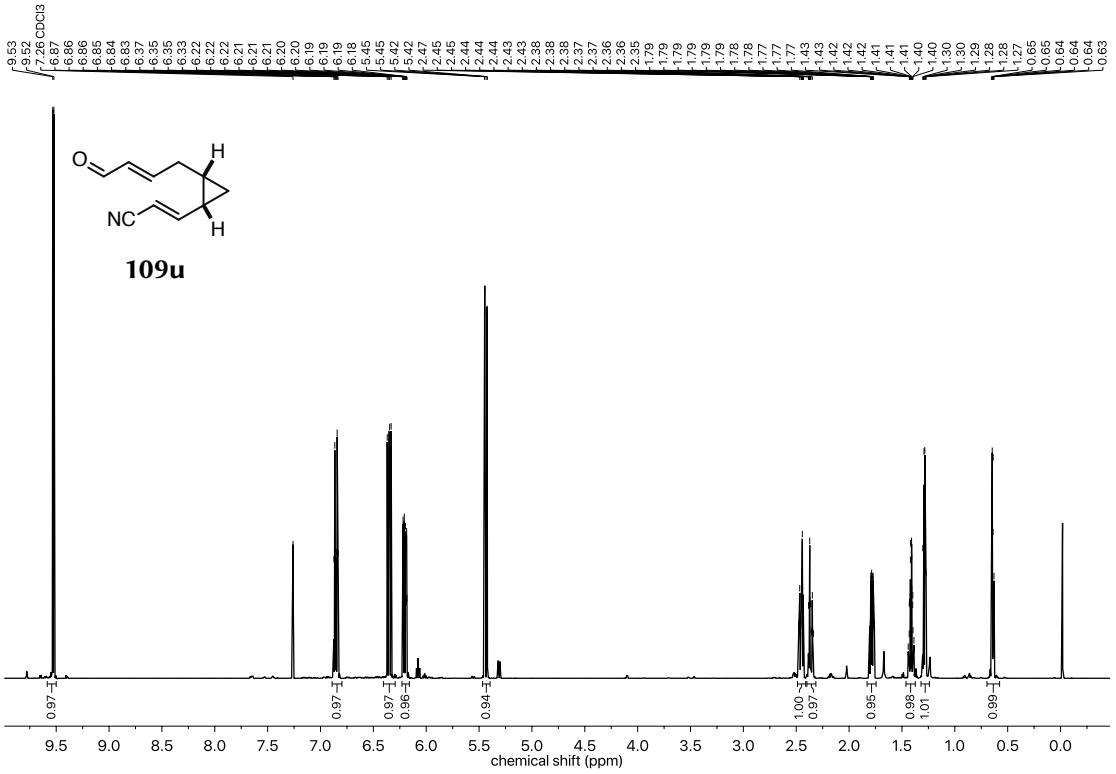


^{13}C NMR:

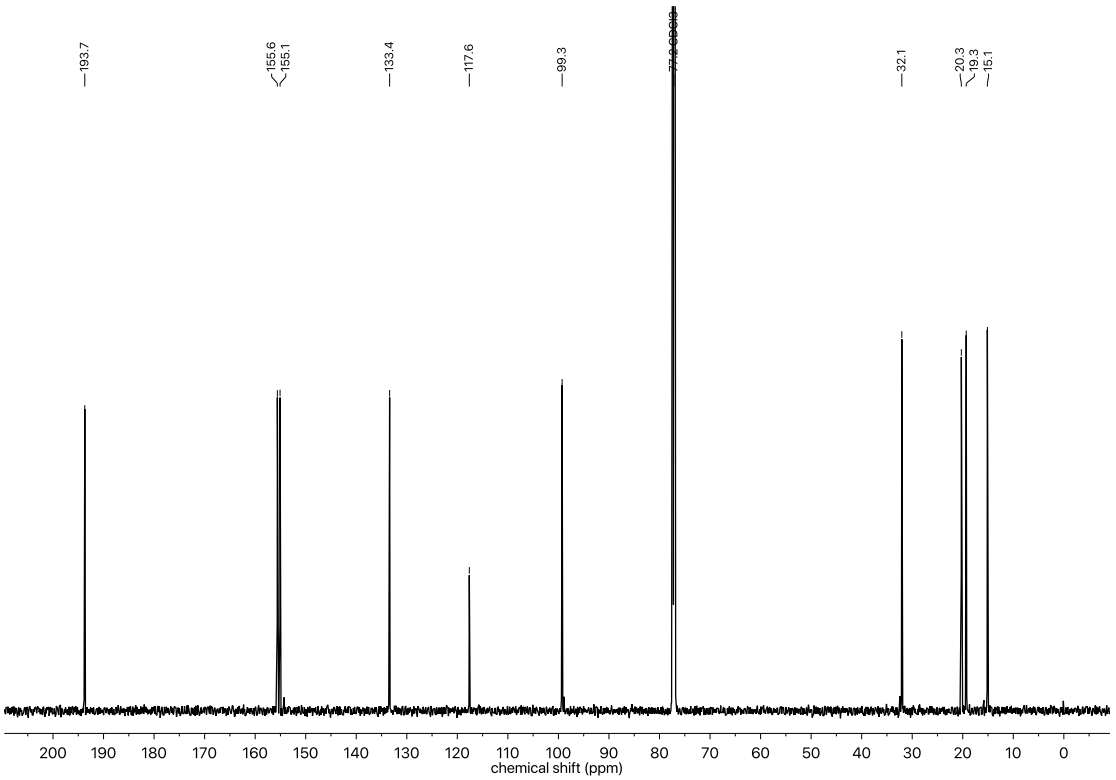


(*E*)-3-(2-((*E*)-4-Oxobut-2-en-1-yl)cyclopropyl)acrylonitrile (109u)

^{1}H NMR:

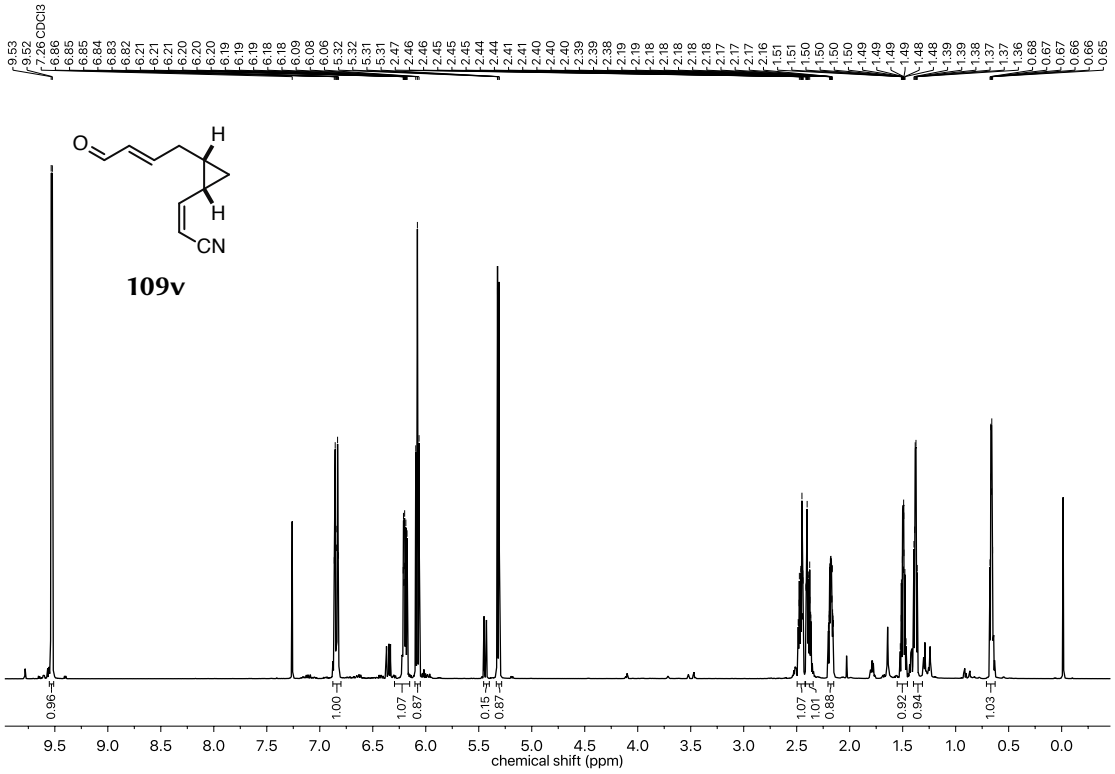


^{13}C NMR:

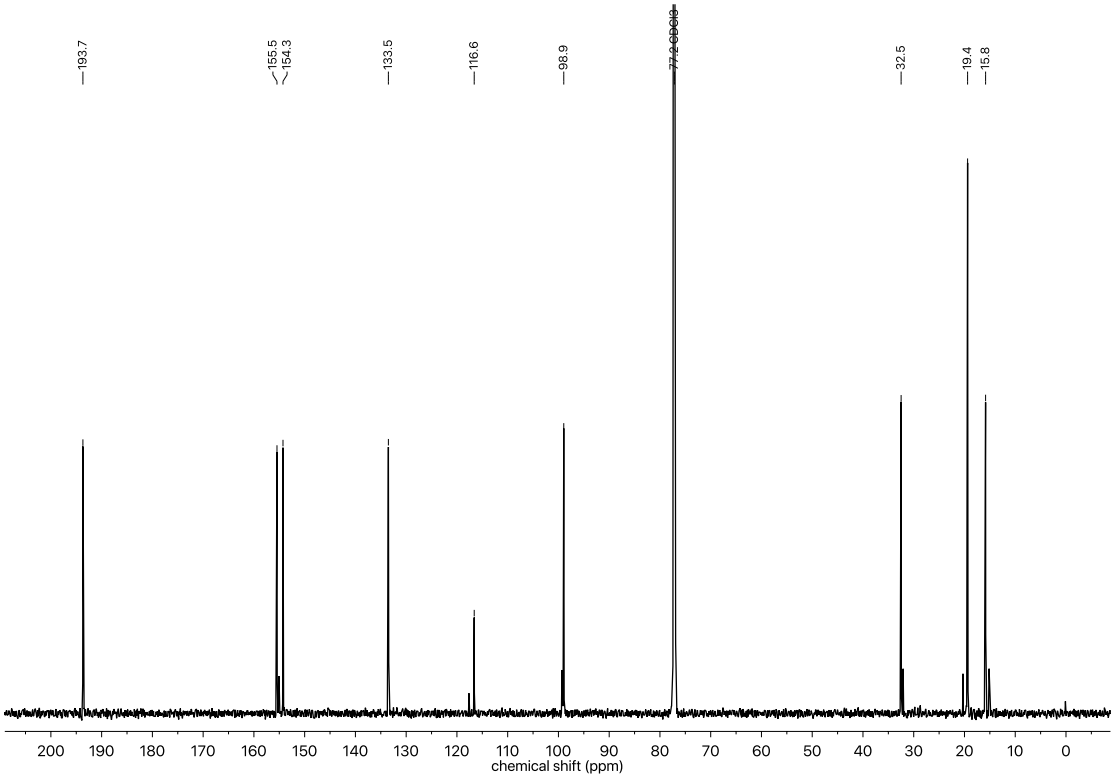


(*Z*)-3-(2-((*E*)-4-Oxobut-2-en-1-yl)cyclopropyl)acrylonitrile (109v)

^{1}H NMR:

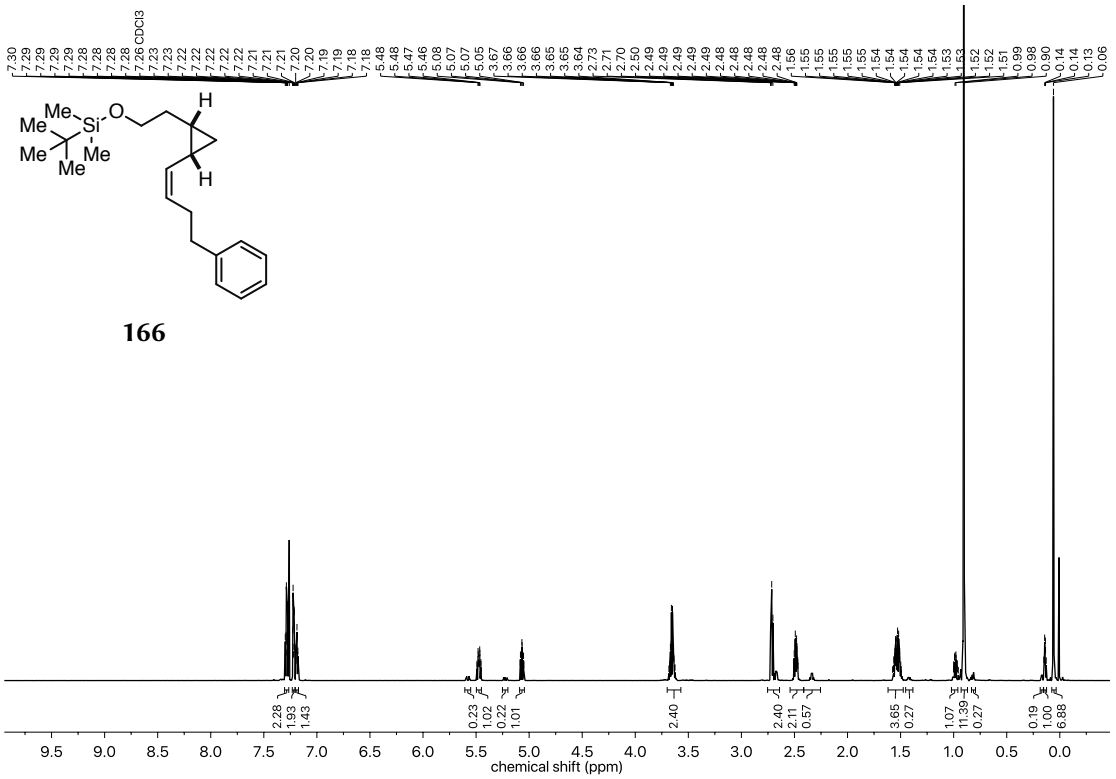


^{13}C NMR:



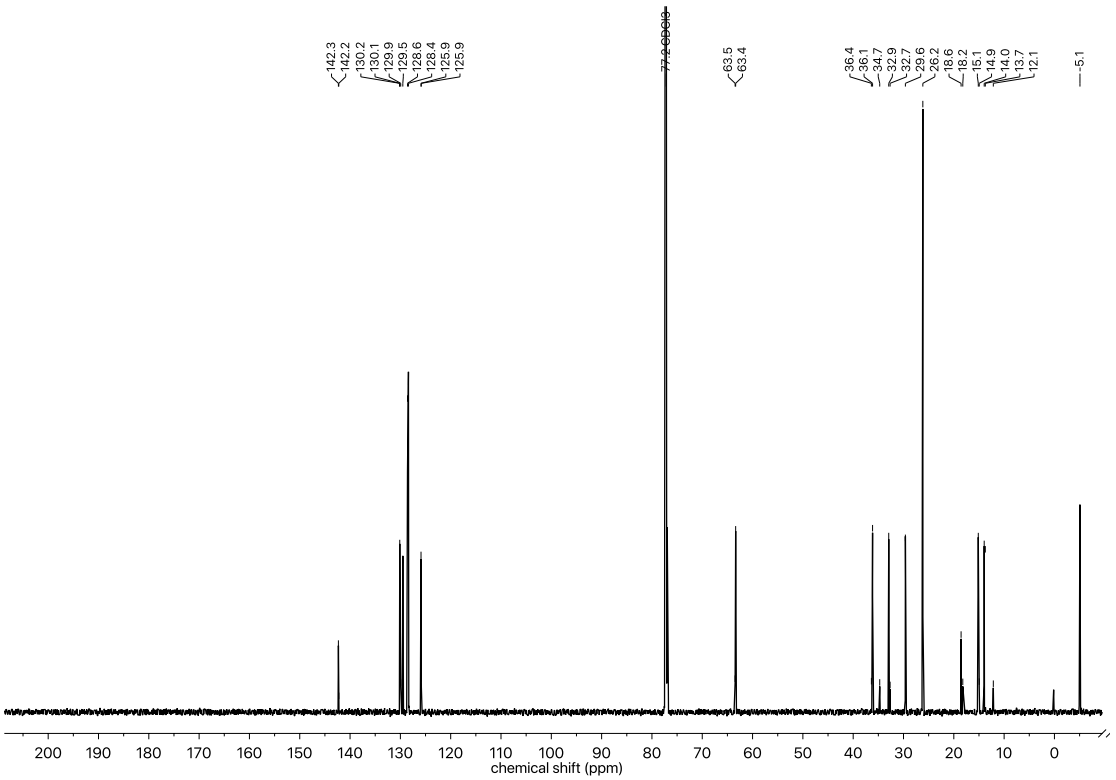
tert-Butyldimethyl(2-(2-(4-phenylbut-1-en-1-yl)cyclopropyl)ethoxy)silane (166)

^{1}H NMR:



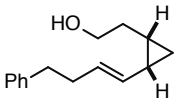
166

^{13}C NMR:

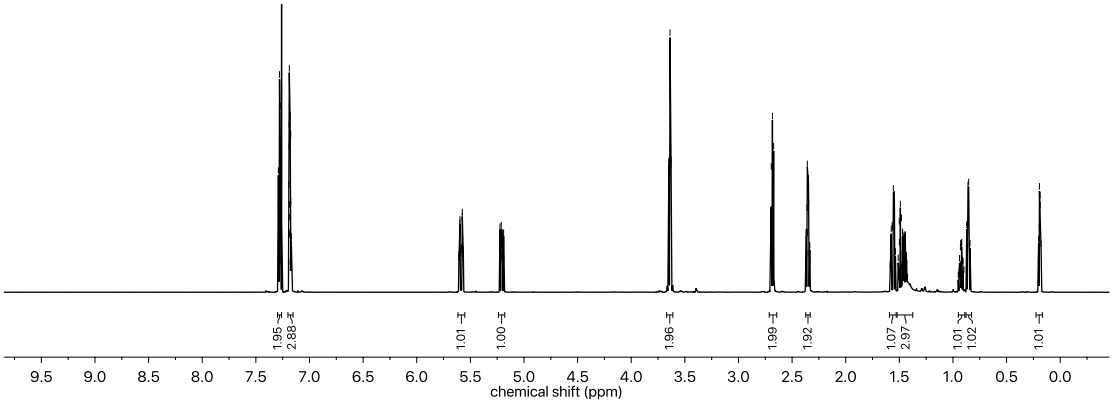


2-(2-((*E*)-4-Phenylbut-1-en-1-yl)cyclopropyl)ethan-1-ol (169)

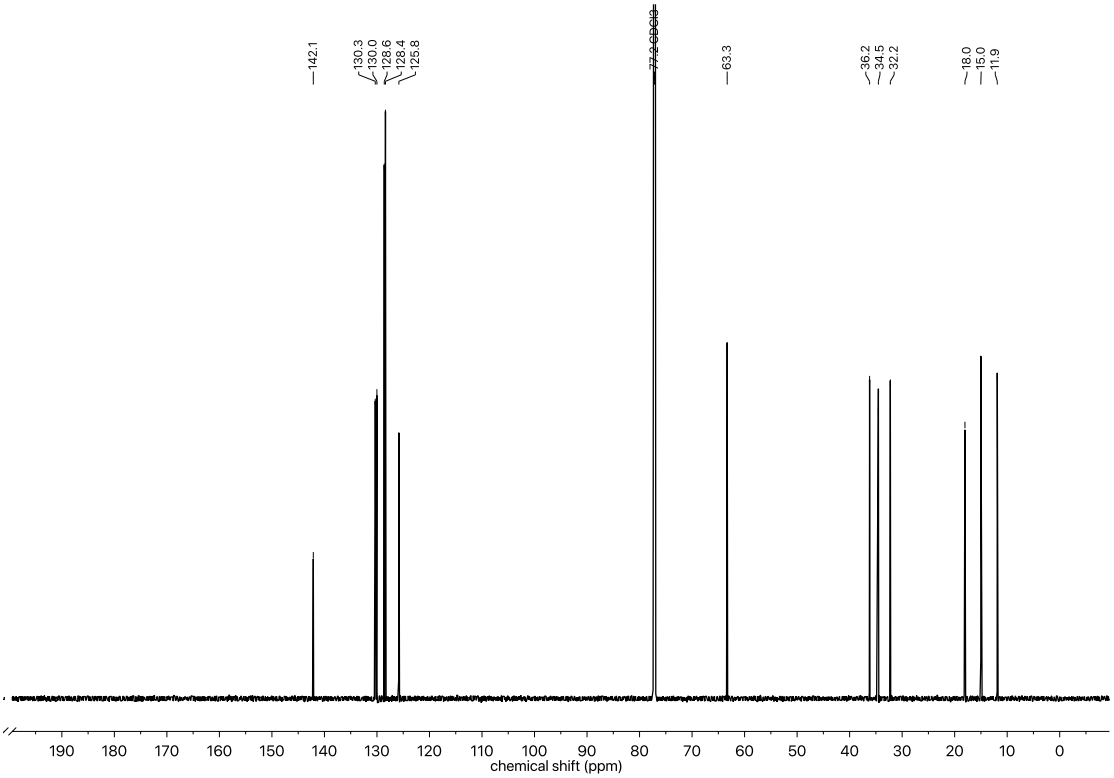
^{1}H NMR:



169

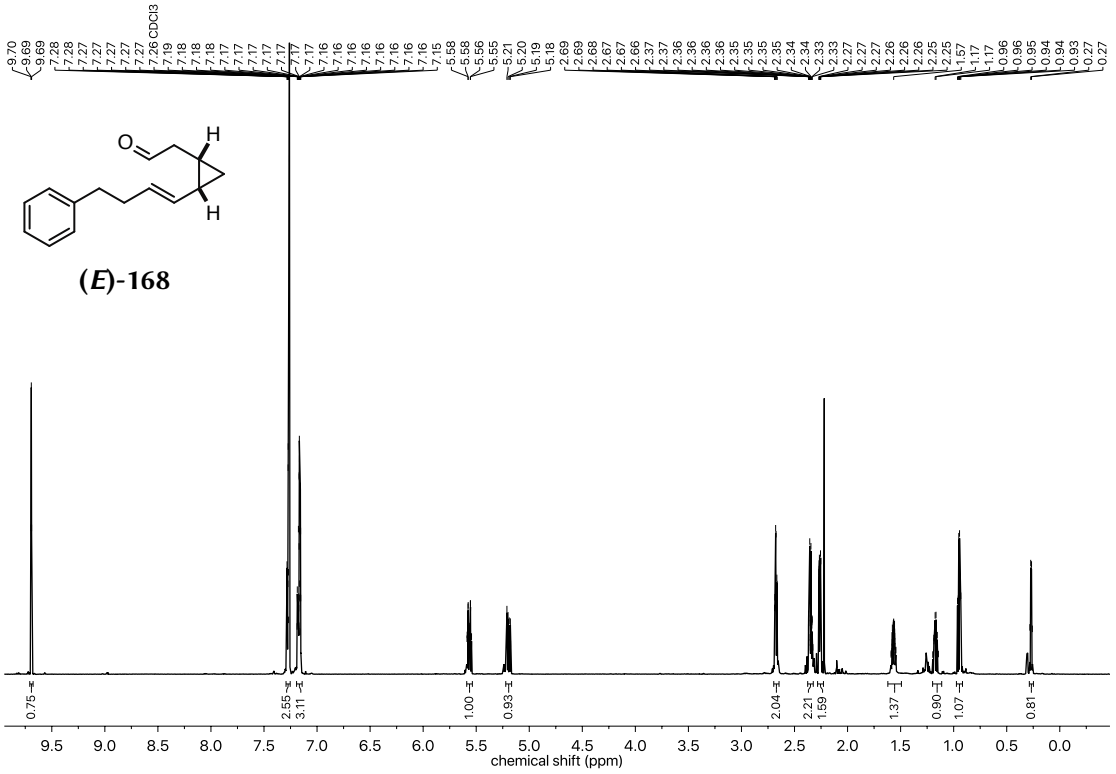


^{13}C NMR:

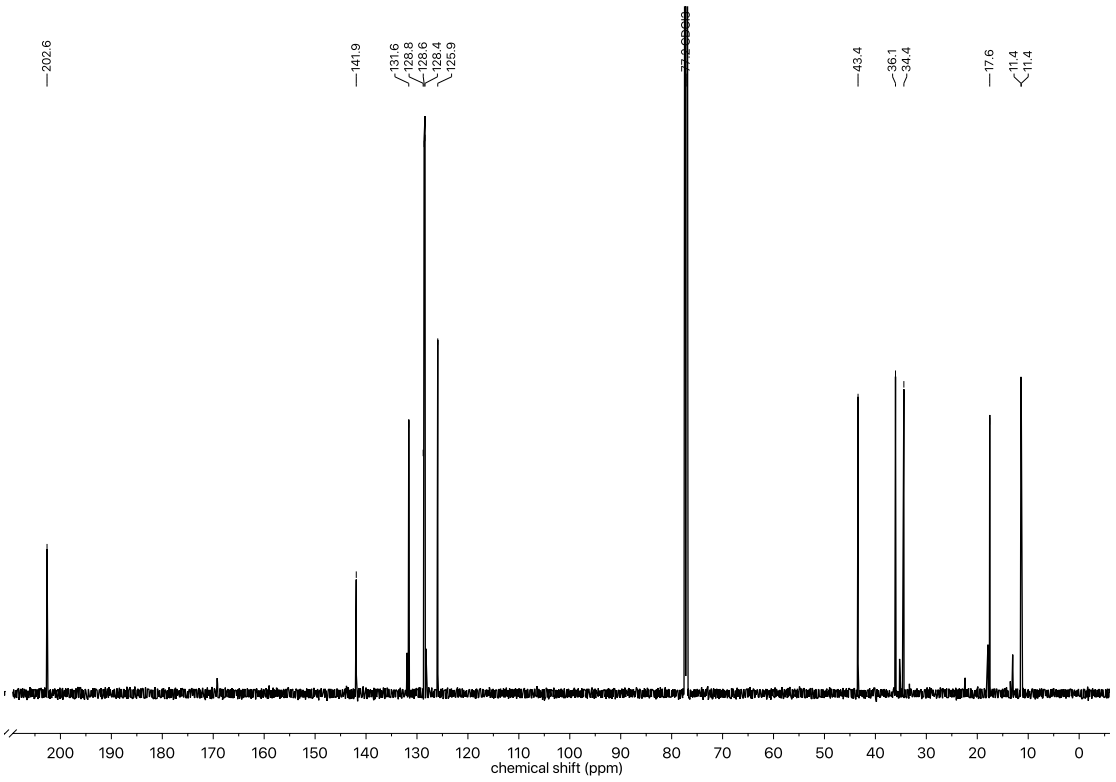


2-(2-((*E*)-4-Phenylbut-1-en-1-yl)cyclopropyl)acetaldehyde ((*E*)-168)

^{1}H NMR:

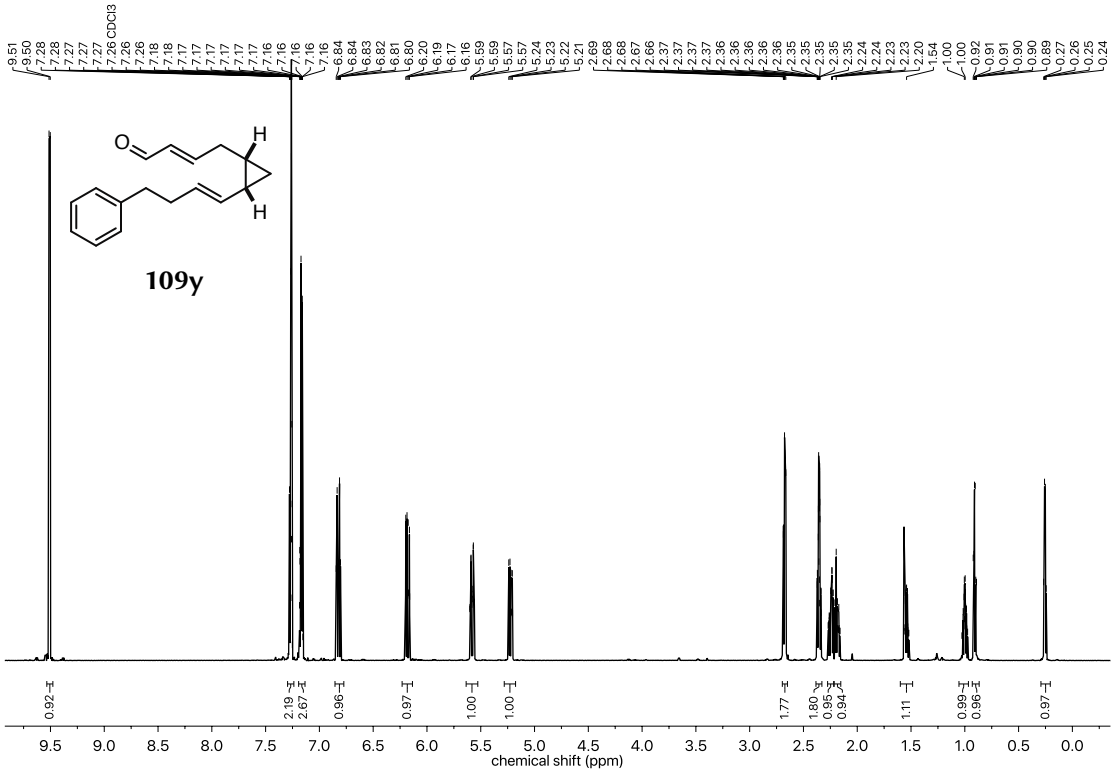


^{13}C NMR:

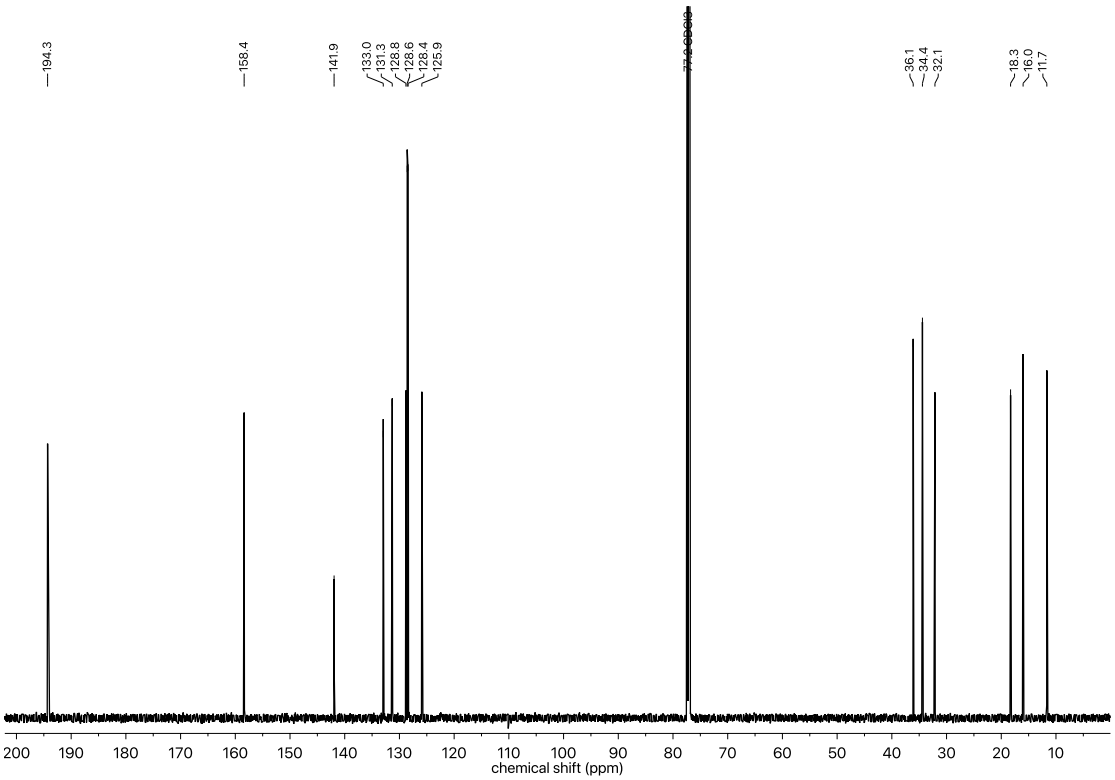


(*E*)-4-(2-((*E*)-4-Phenylbut-1-en-1-yl)cyclopropyl)but-2-enal (109y)

^{1}H NMR:

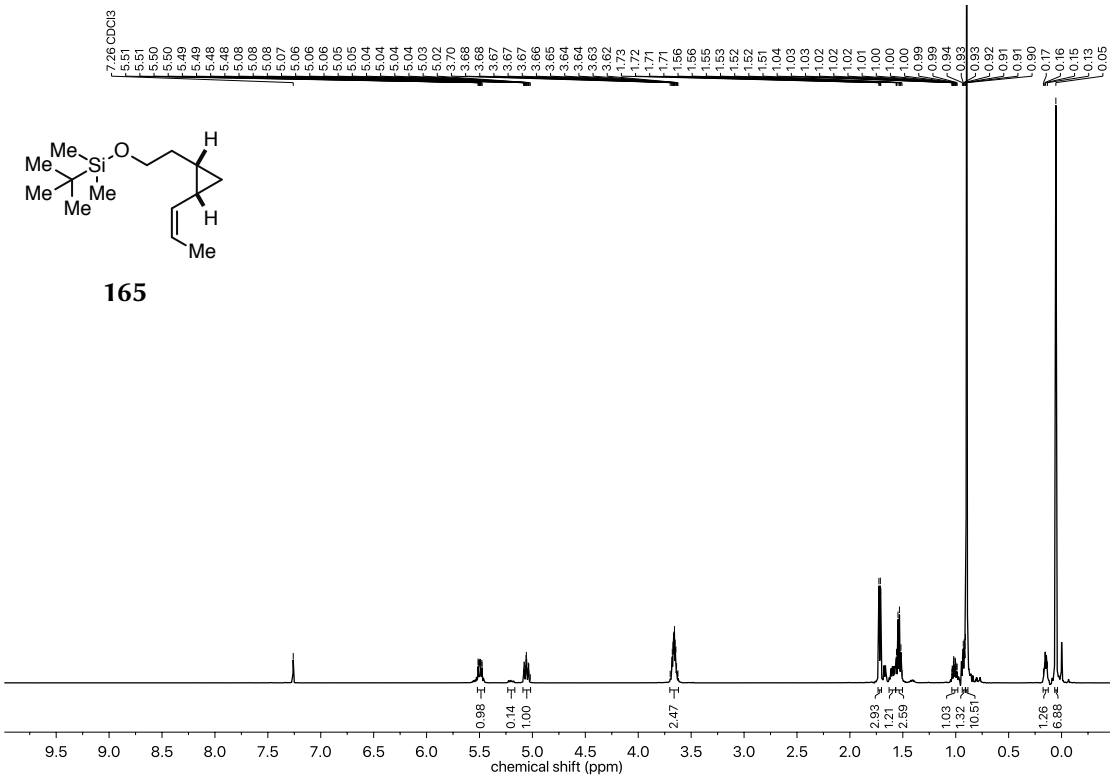


^{13}C NMR:



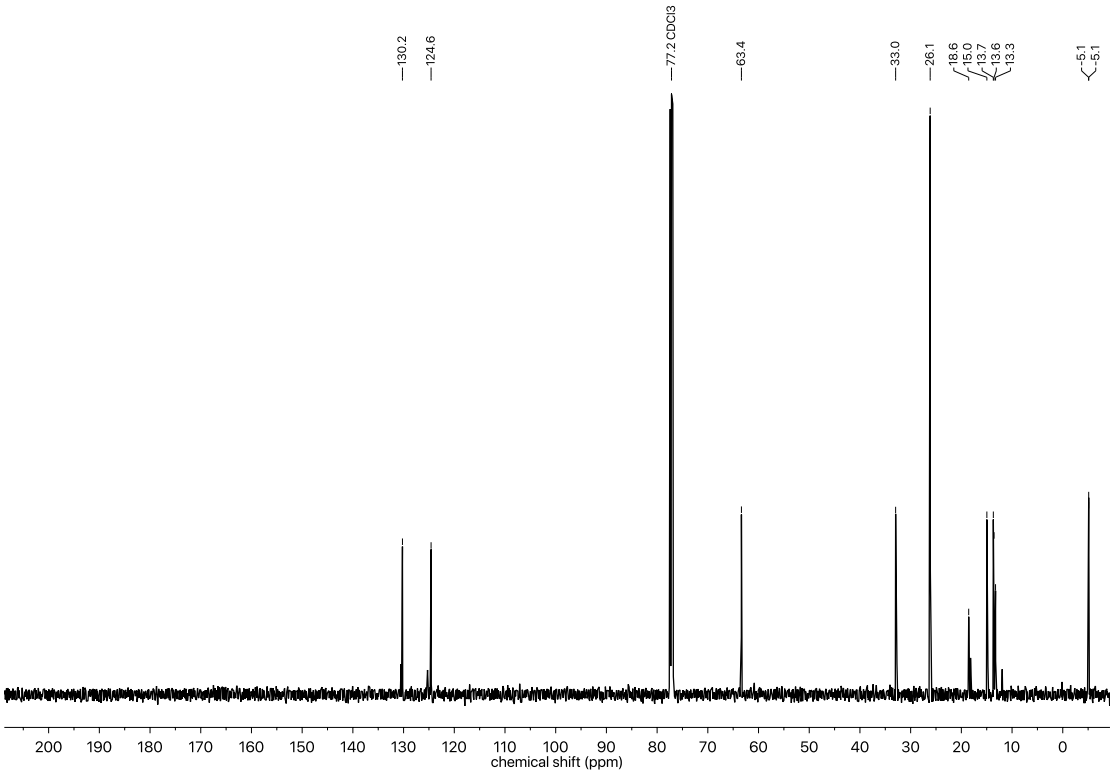
tert-Butyldimethyl(2-(2-((*Z*)-prop-1-en-1-yl)cyclopropyl)ethoxy)silane (165)

^{1}H NMR:



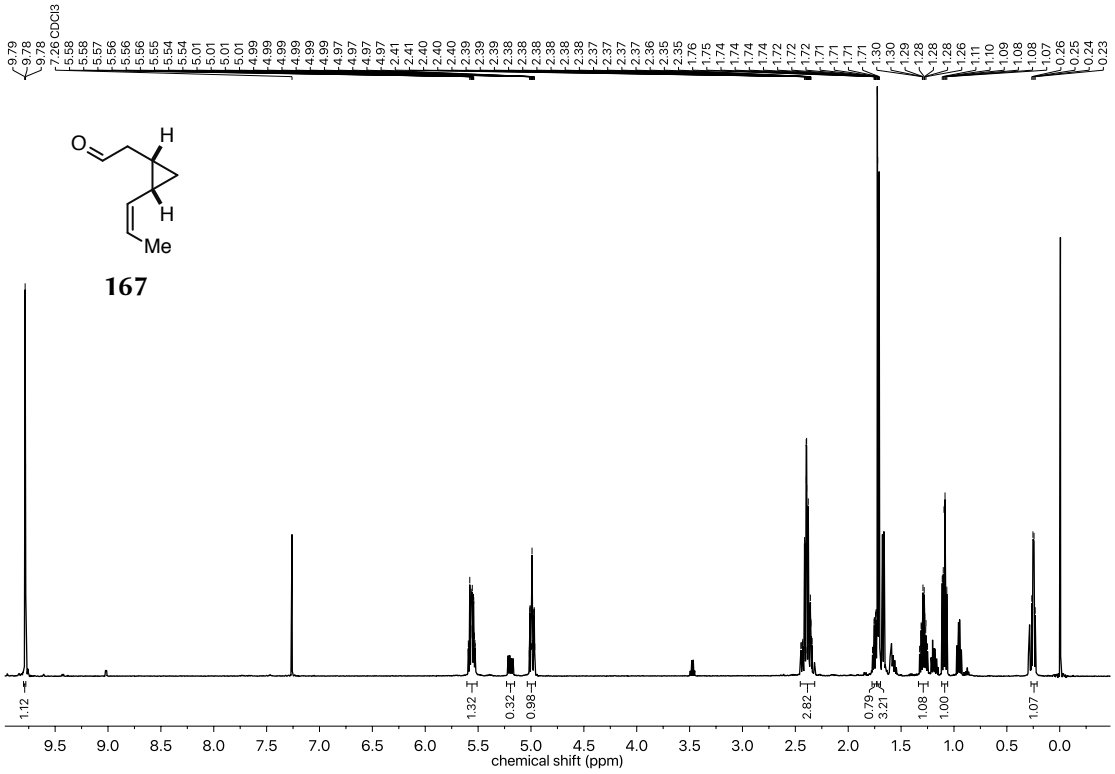
165

^{13}C NMR:

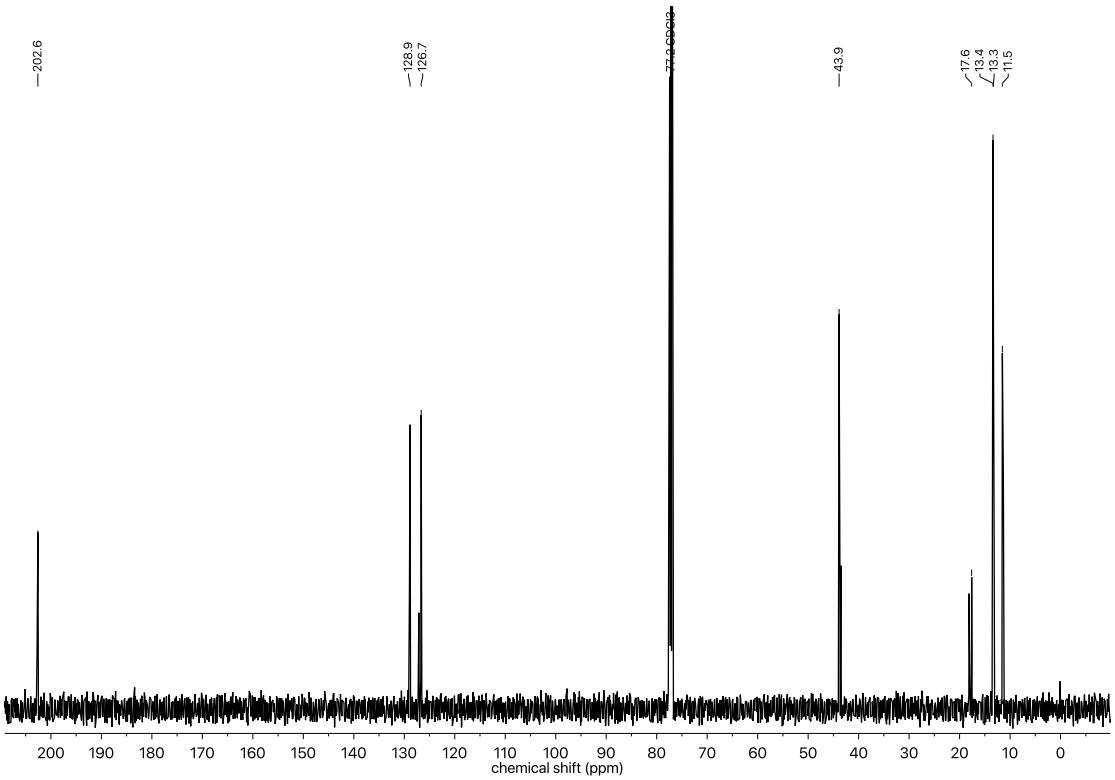


2-(2-((*Z*)-Prop-1-en-1-yl)cyclopropyl)acetaldehyde (167)

^{1}H NMR:

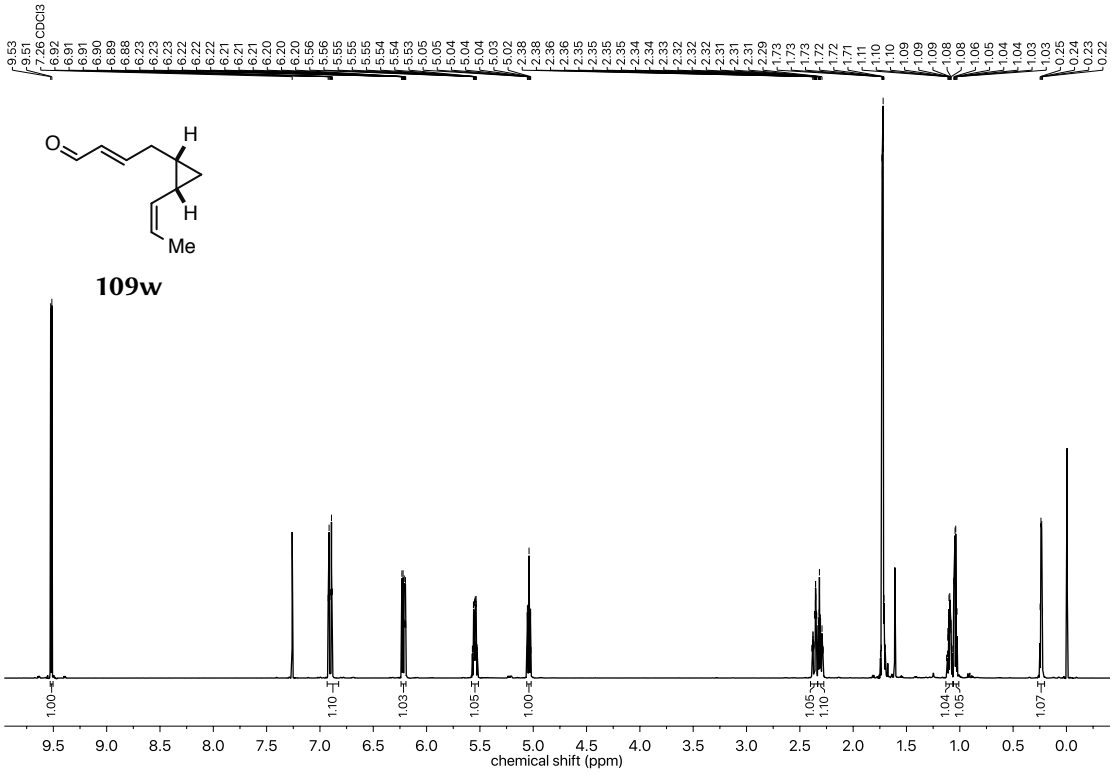


^{13}C NMR:

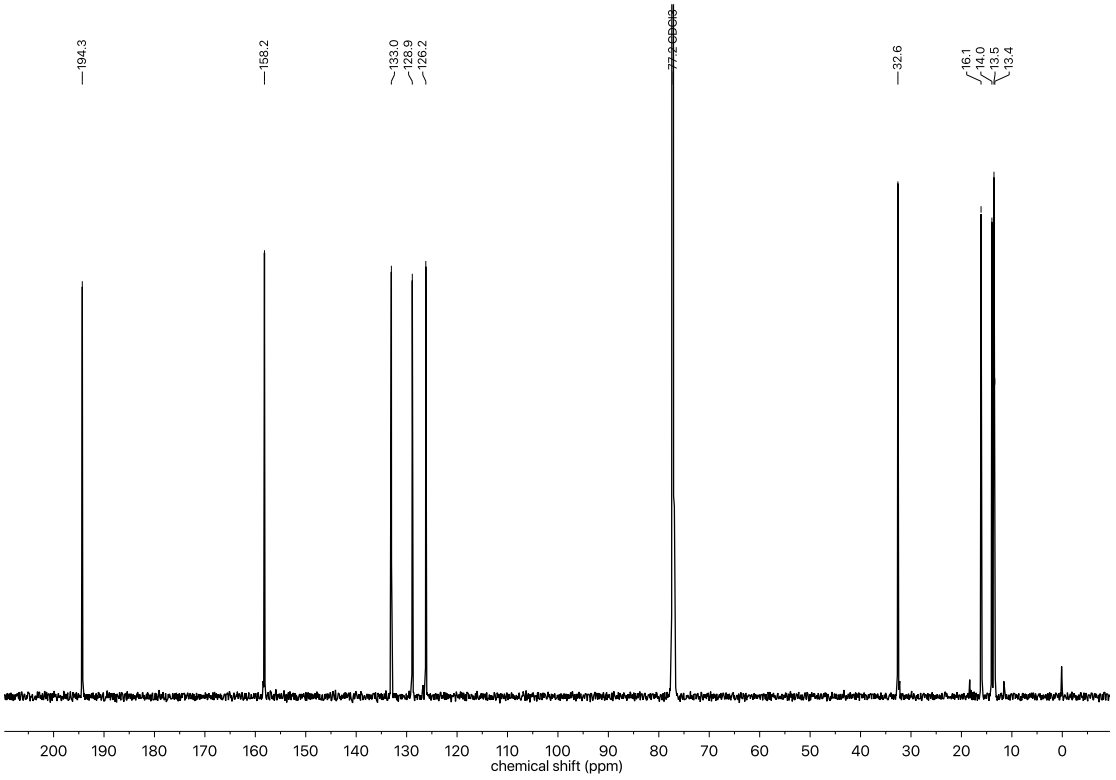


(*E*)-4-(2-((*Z*)-Prop-1-en-1-yl)cyclopropyl)but-2-enal (109w)

^{1}H NMR:

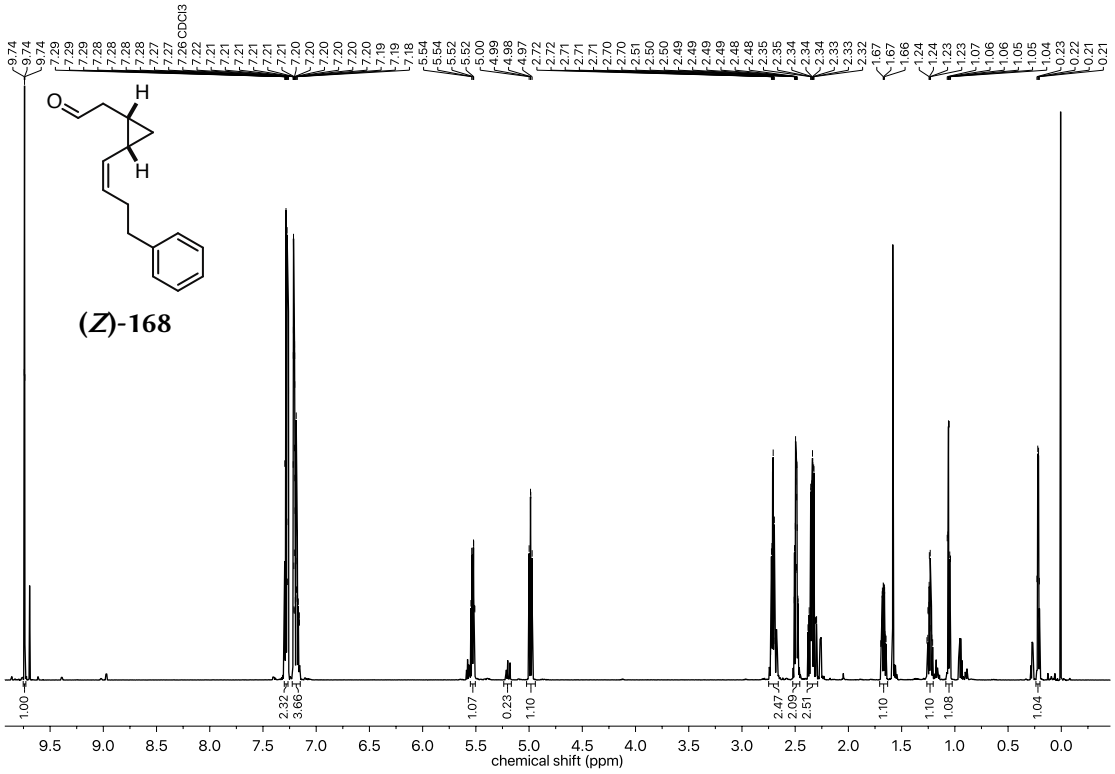


^{13}C NMR:

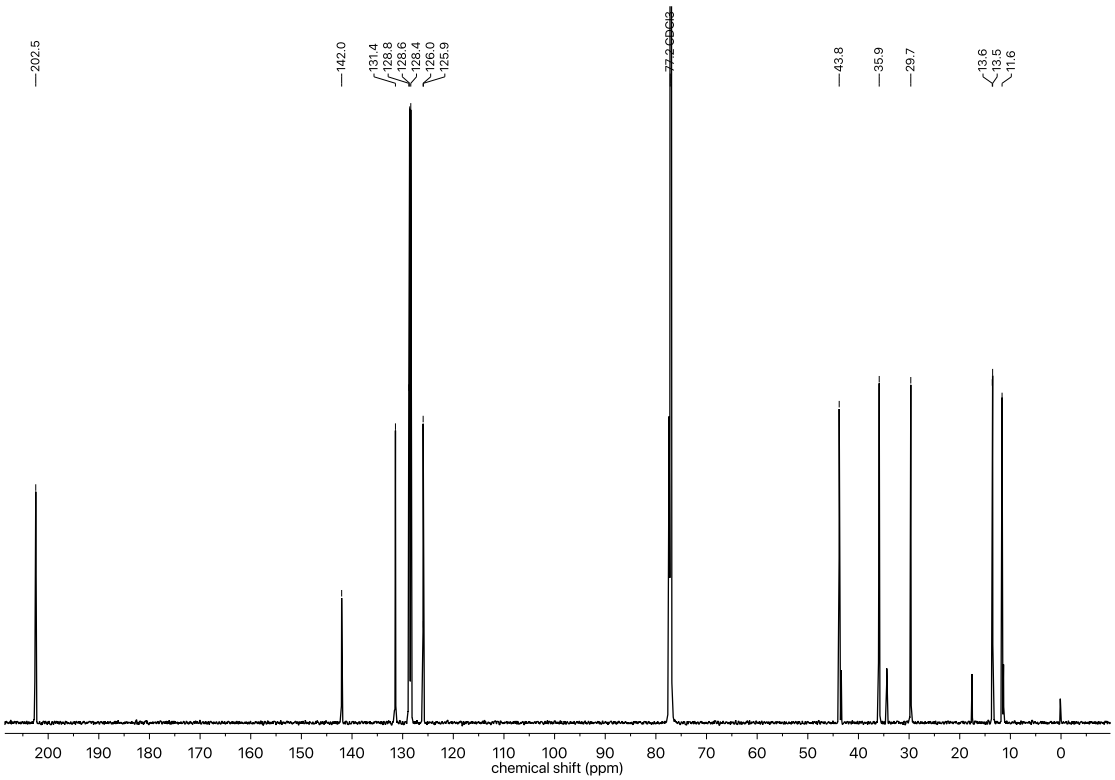


2-(2-((*Z*)-4-Phenylbut-1-en-1-yl)cyclopropyl)acetaldehyde ((*Z*)-168)

^{1}H NMR:

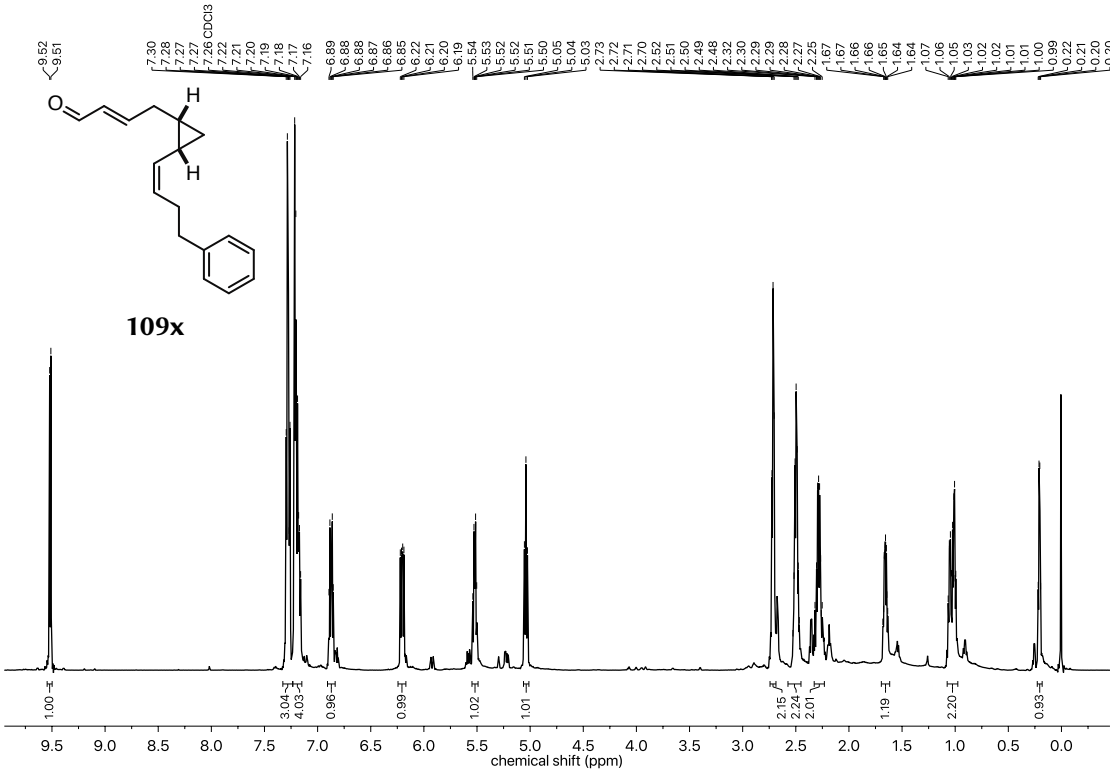


^{13}C NMR:

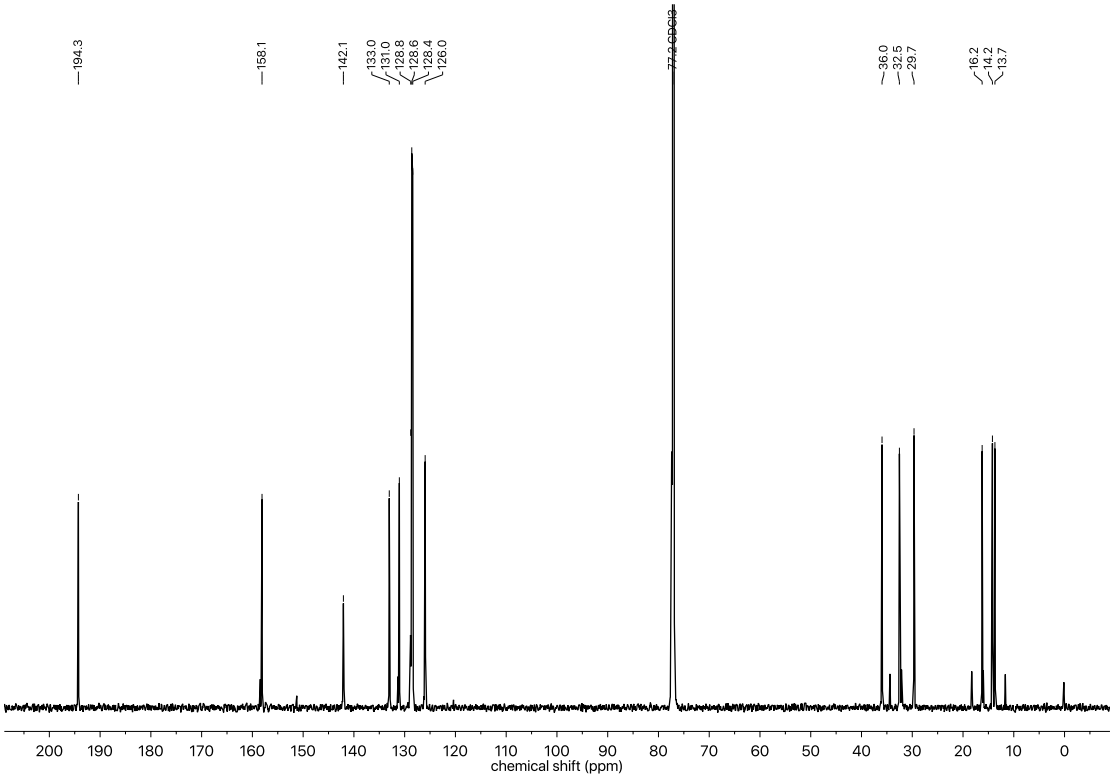


(*E*)-4-(2-((*Z*)-4-Phenylbut-1-en-1-yl)cyclopropyl)but-2-enal (109x)

^{1}H NMR:

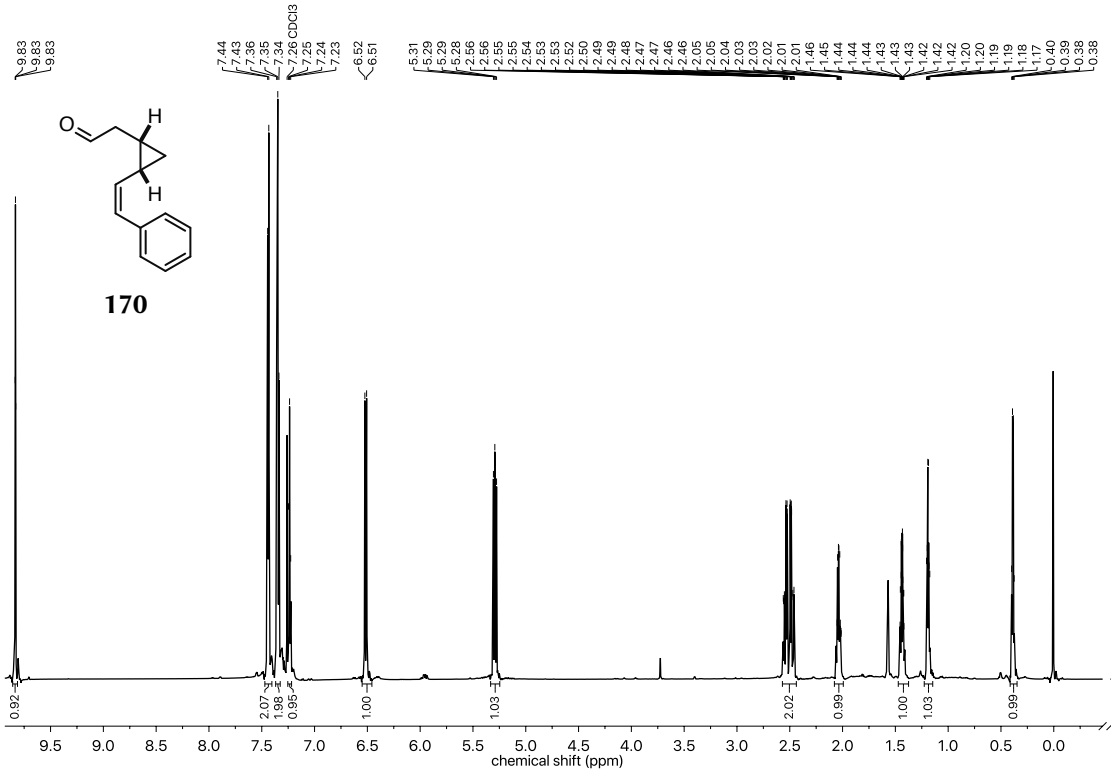


^{13}C NMR:

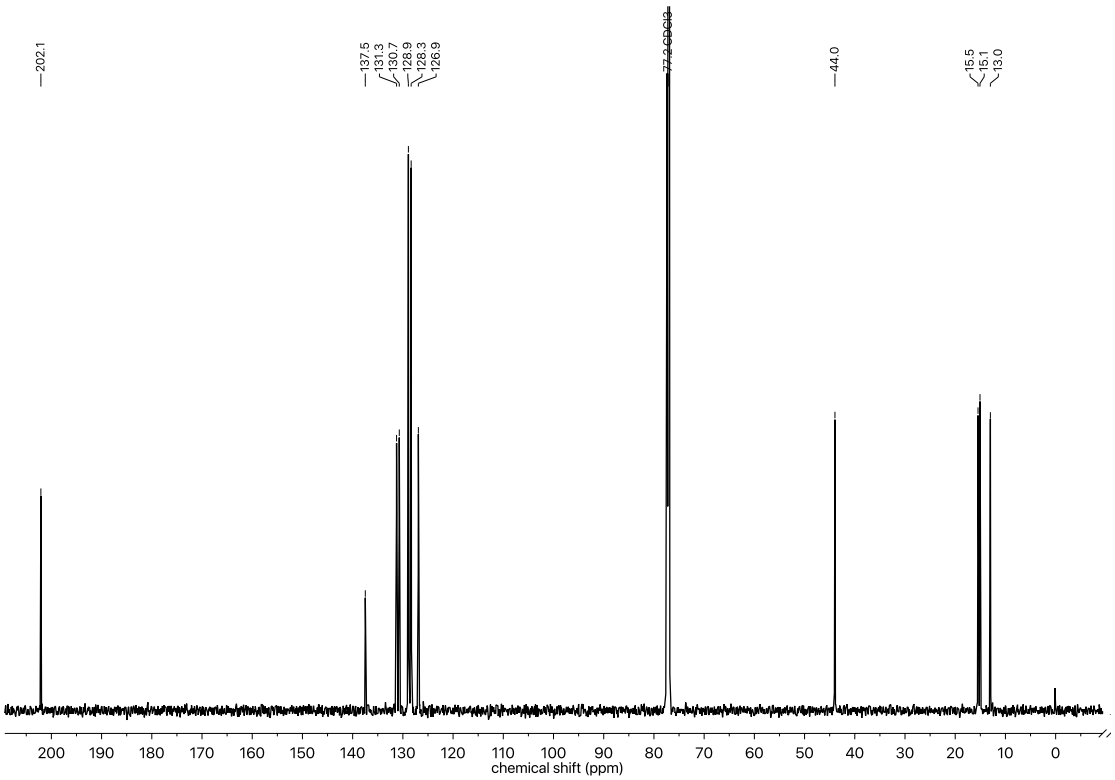


2-(2-((*Z*)-Styryl)cyclopropyl)acetaldehyde (170)

^{1}H NMR:

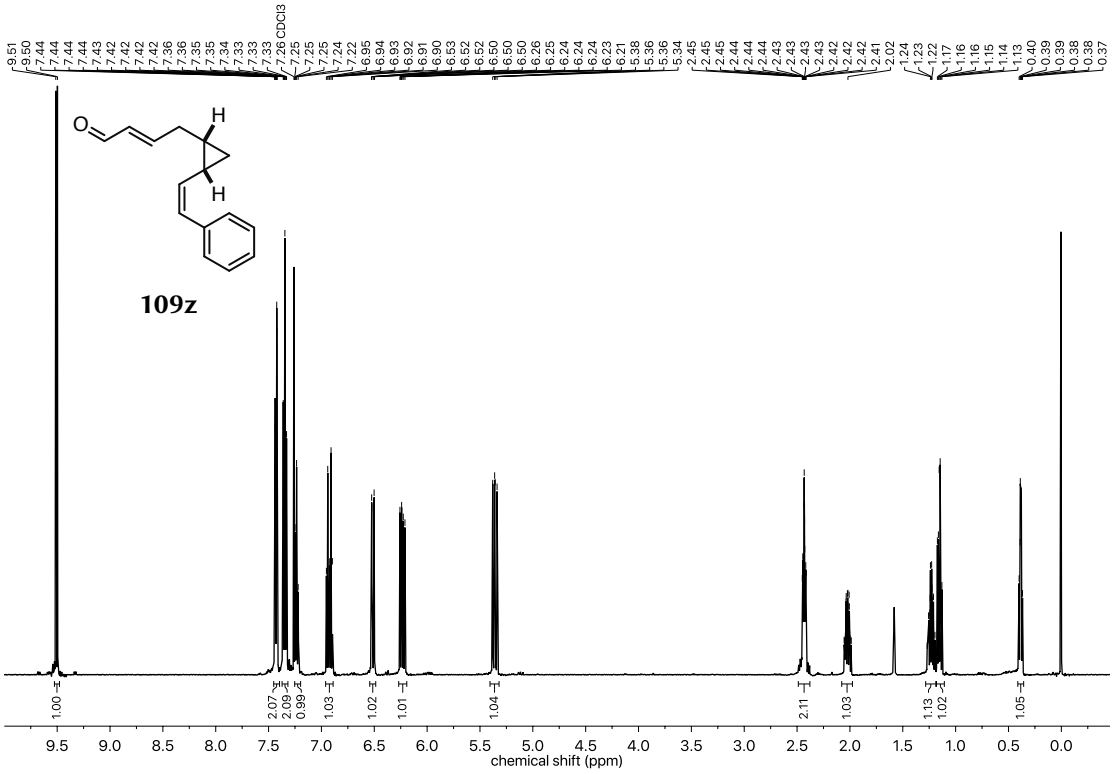


^{13}C NMR:

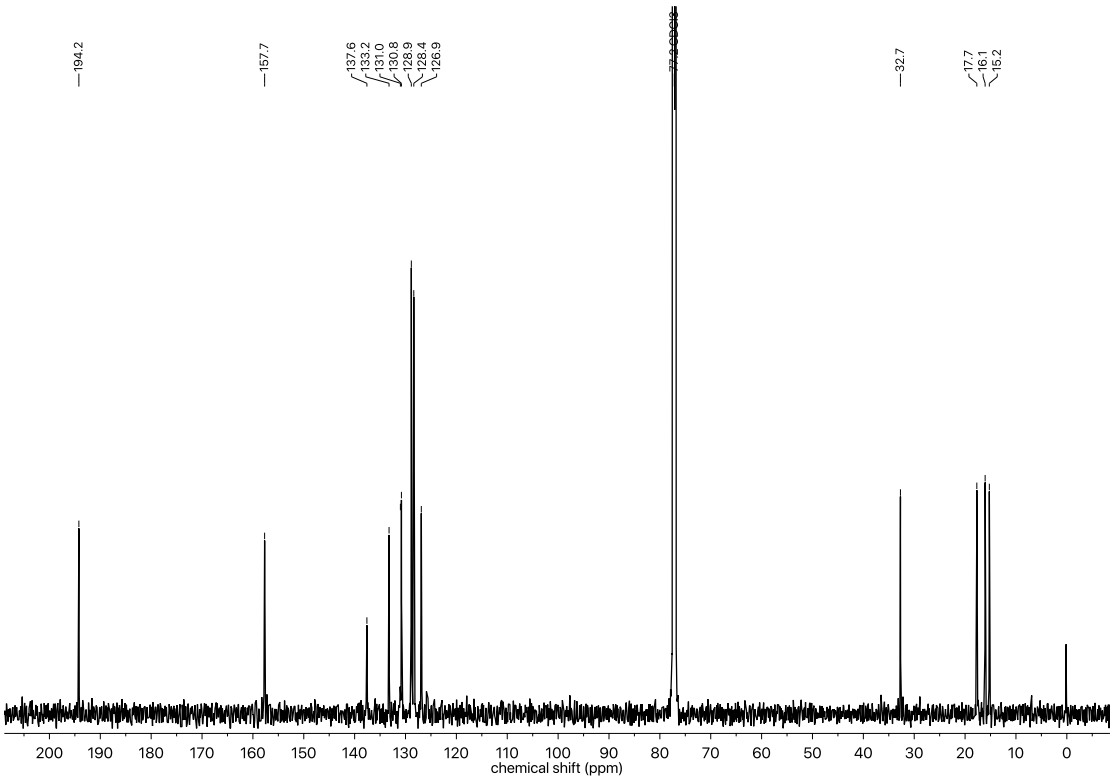


(*E*)-4-(2-((*Z*)-Styryl)cyclopropyl)but-2-enal (109z)

^{1}H NMR:

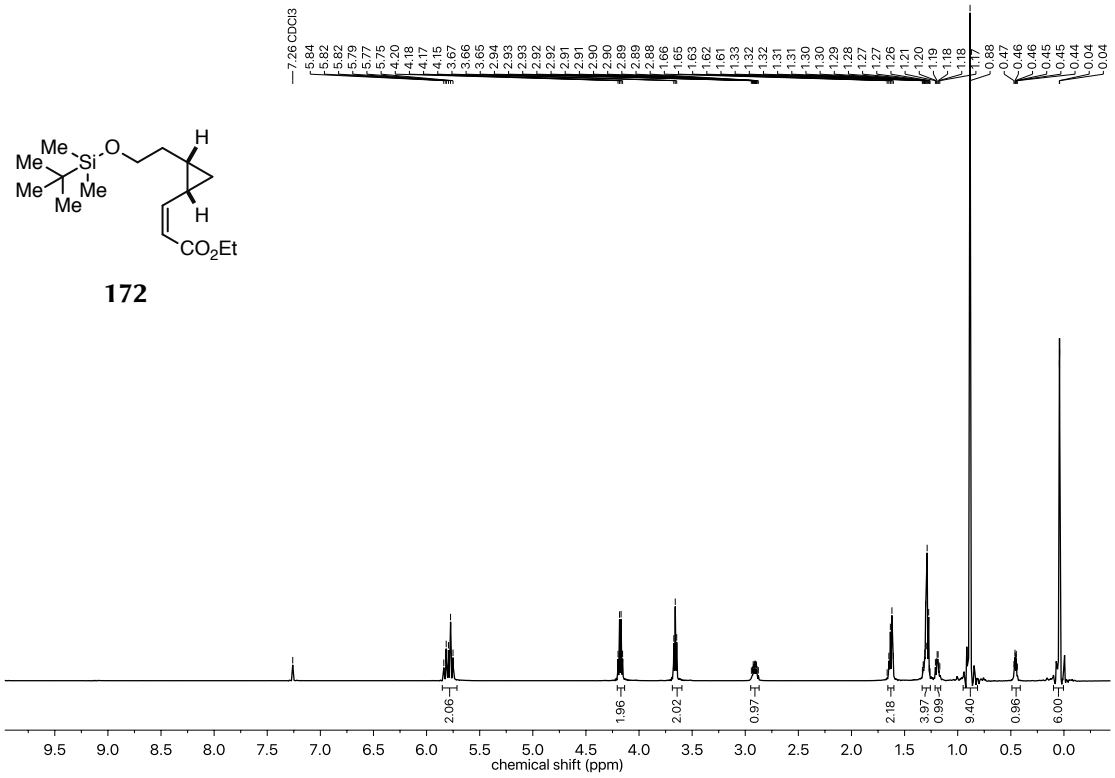


^{13}C NMR:



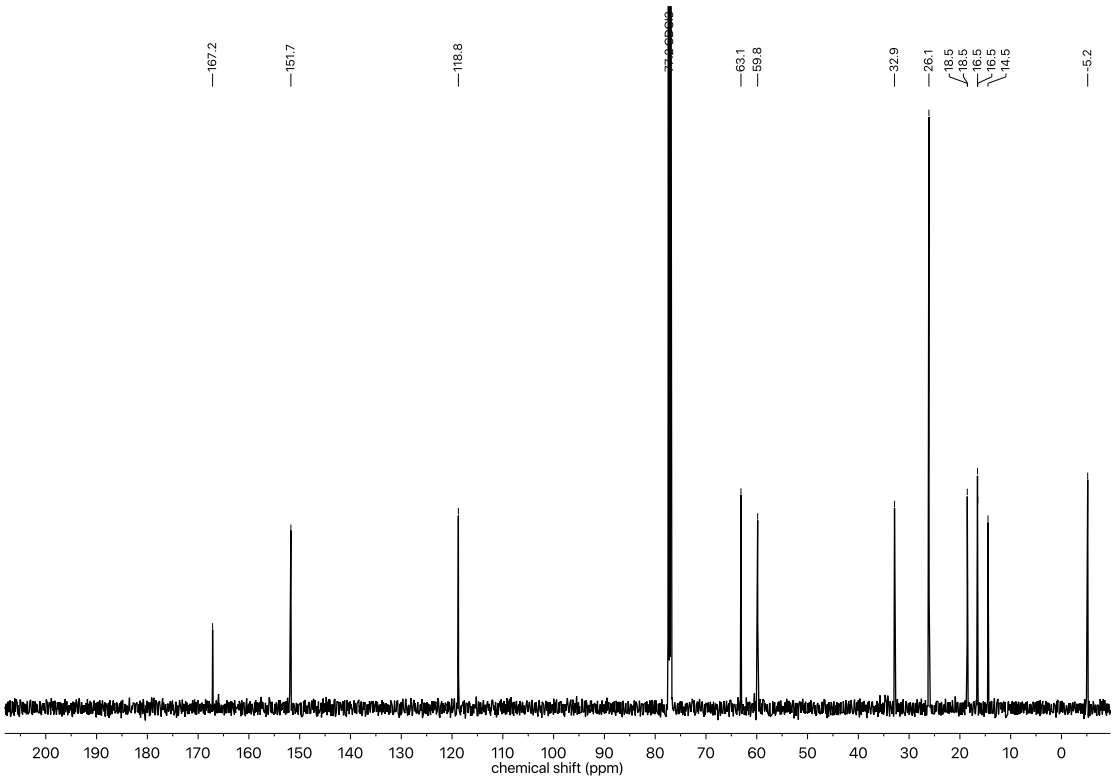
Ethyl (*Z*)-3-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)cyclopropyl)acrylate (172)

^{1}H NMR:



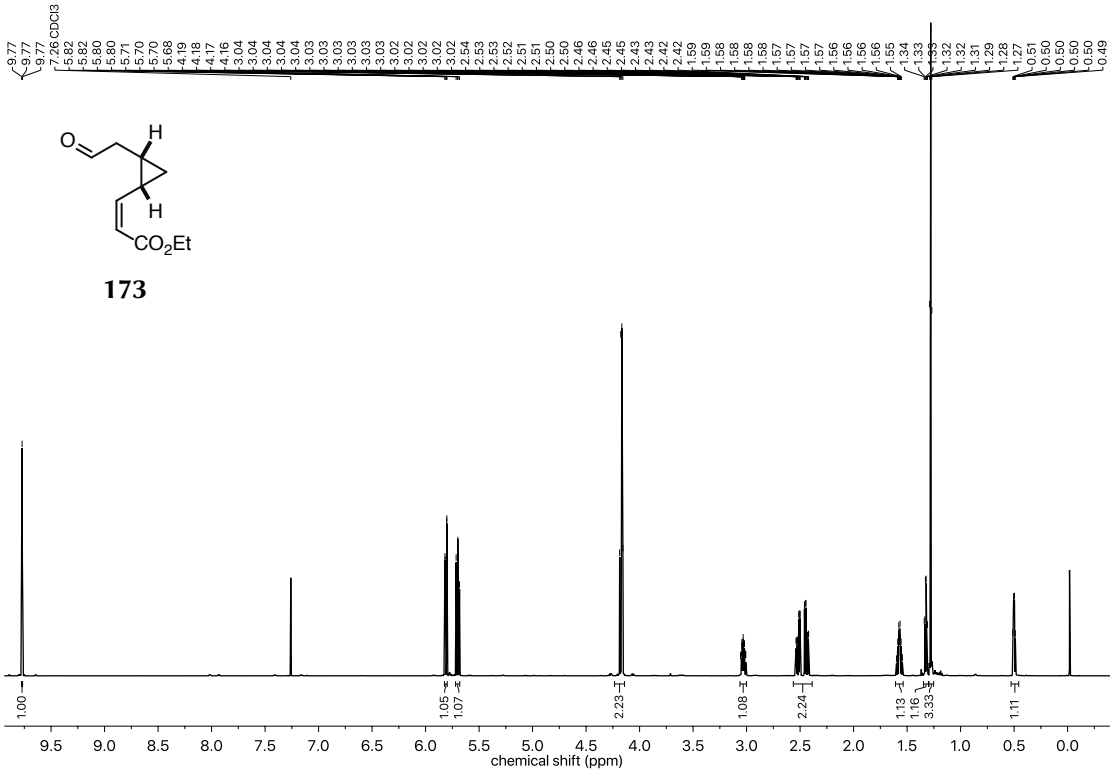
172

^{13}C NMR:



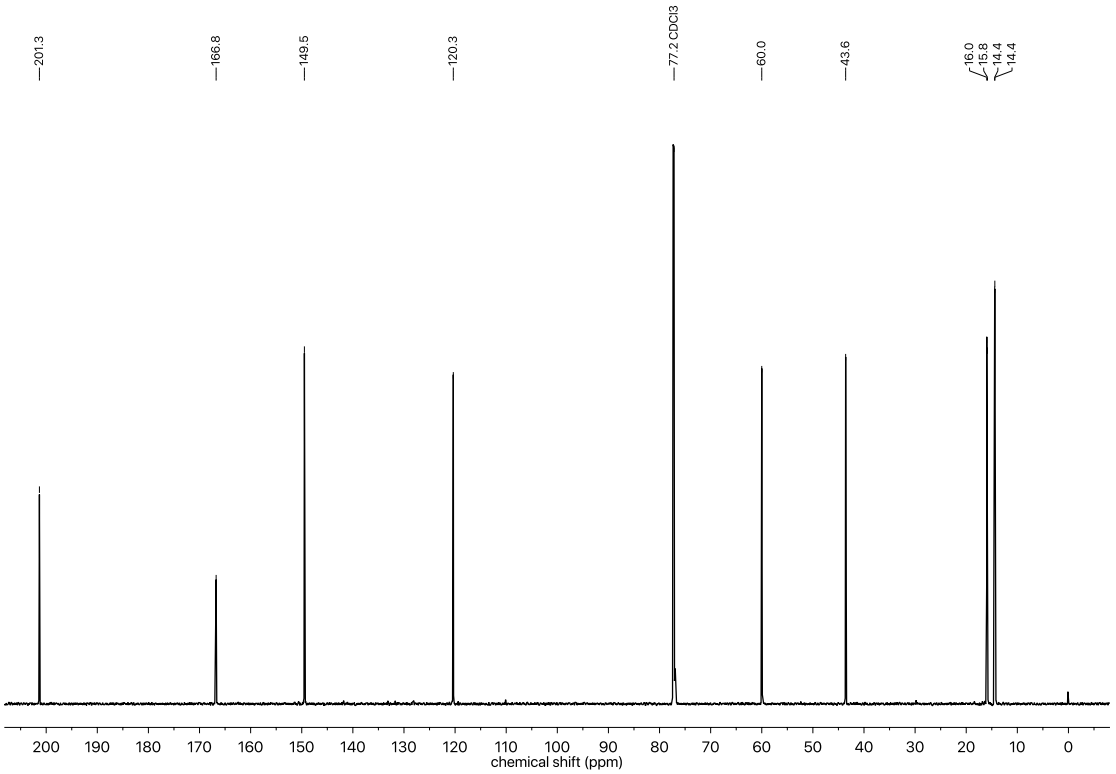
Ethyl (*Z*)-3-(2-(2-Oxoethyl)cyclopropyl)acrylate (173)

^{1}H NMR:



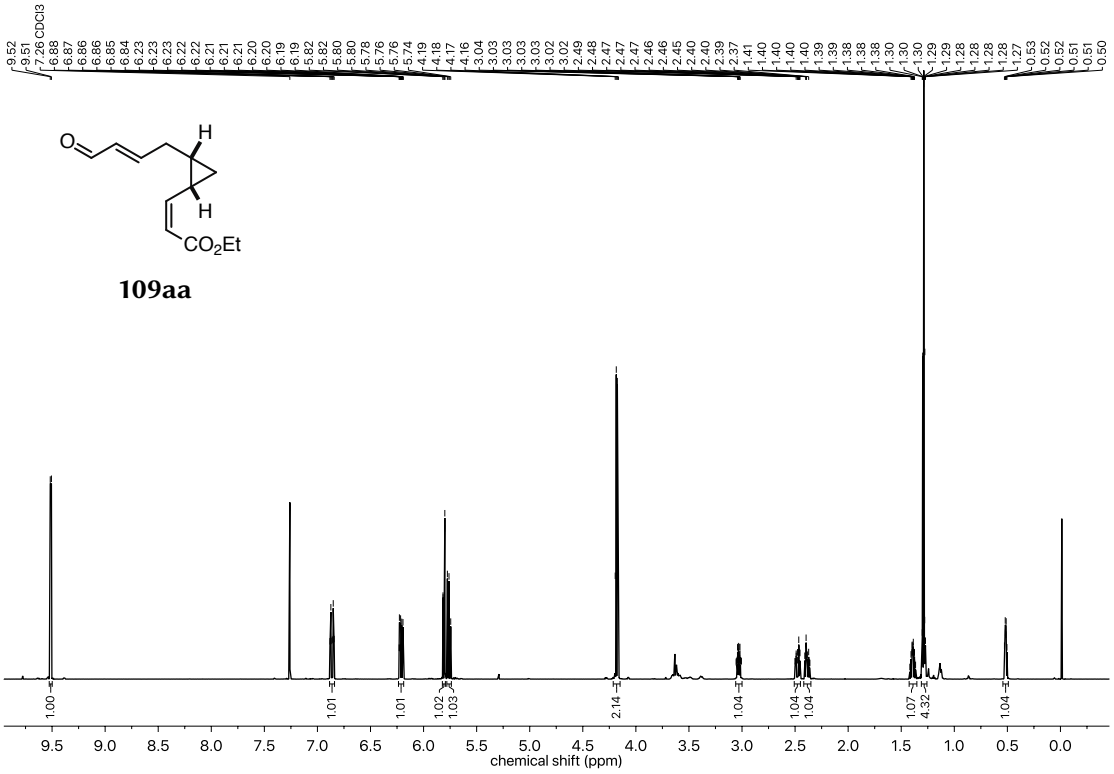
173

^{13}C NMR:



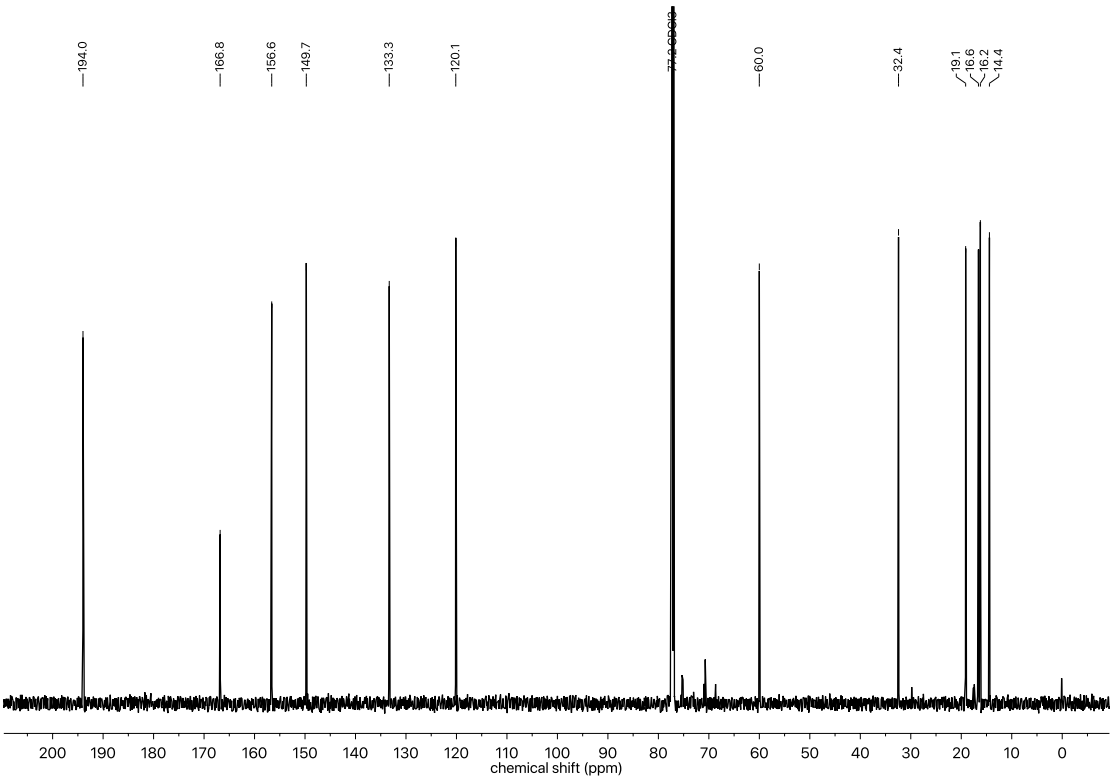
Ethyl (*Z*)-3-(2-((*E*)-4-Oxo-but-2-en-1-yl)-cyclo-propyl)-acrylate (109aa)

^{1}H NMR:



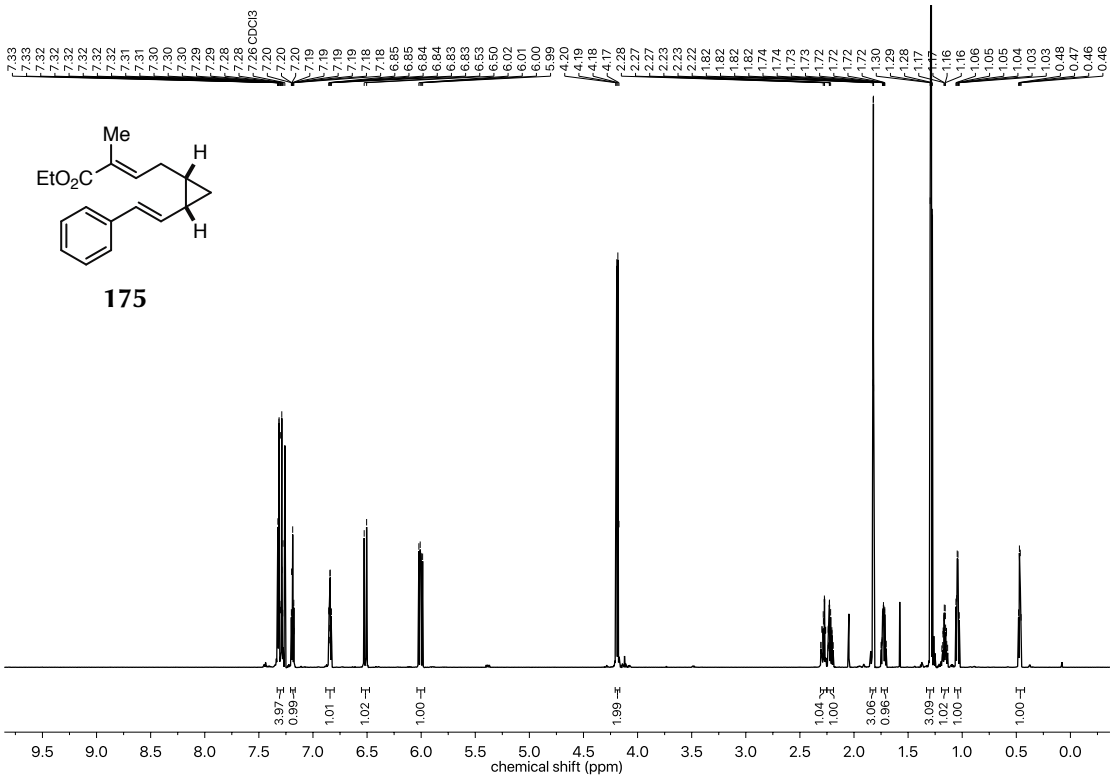
109aa

^{13}C NMR:

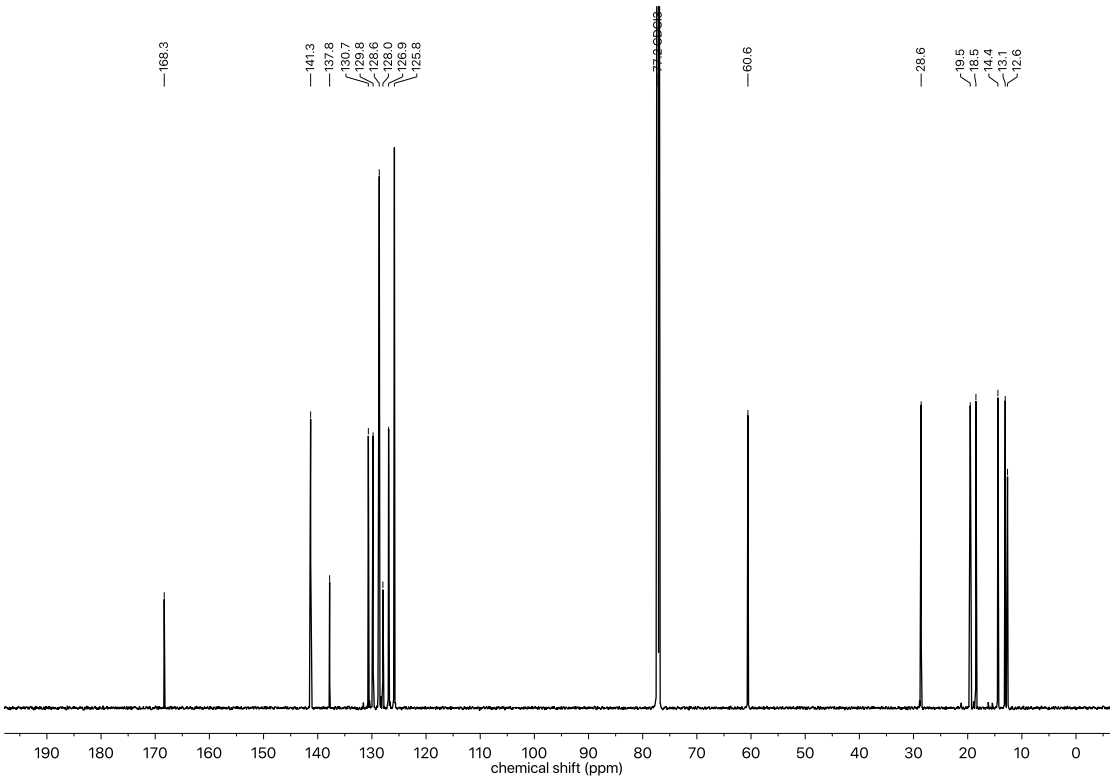


Ethyl (*E*)-2-Methyl-4-(2-((*E*)-styryl)cyclopropyl)but-2-enoate (175)

^{1}H NMR:

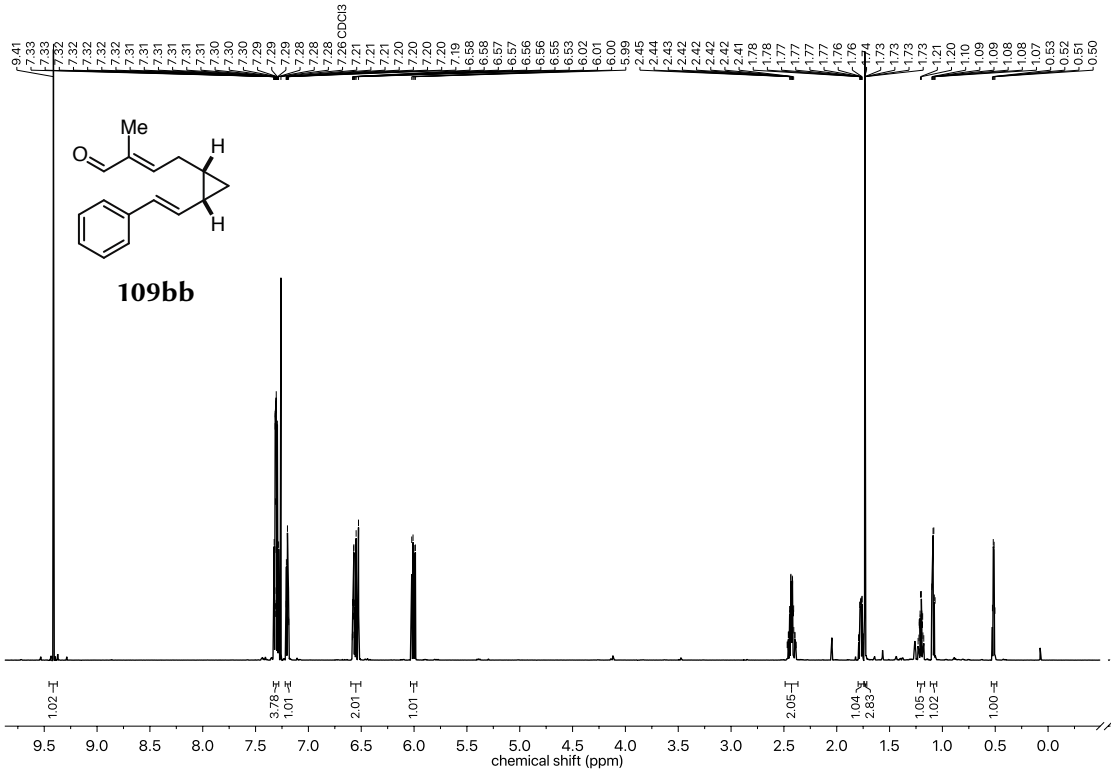


^{13}C NMR:

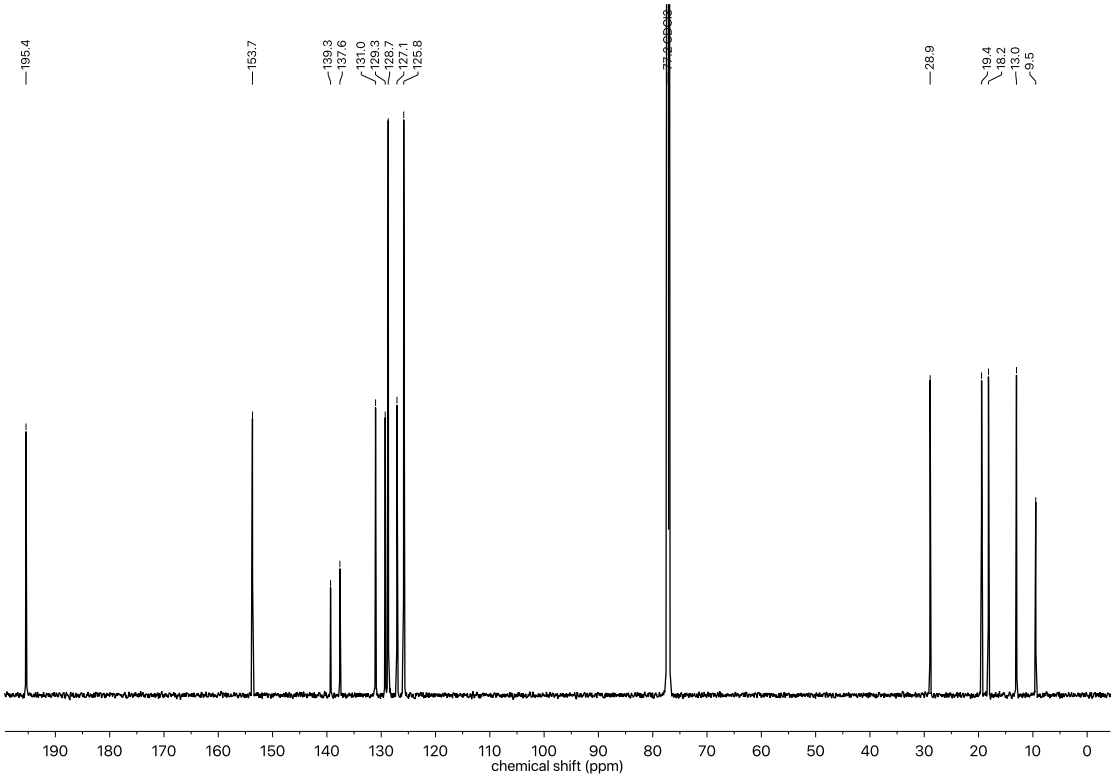


(*E*)-2-Methyl-4-(2-((*E*)-styryl)cyclopropyl)but-2-enal (109bb)

^{1}H NMR:

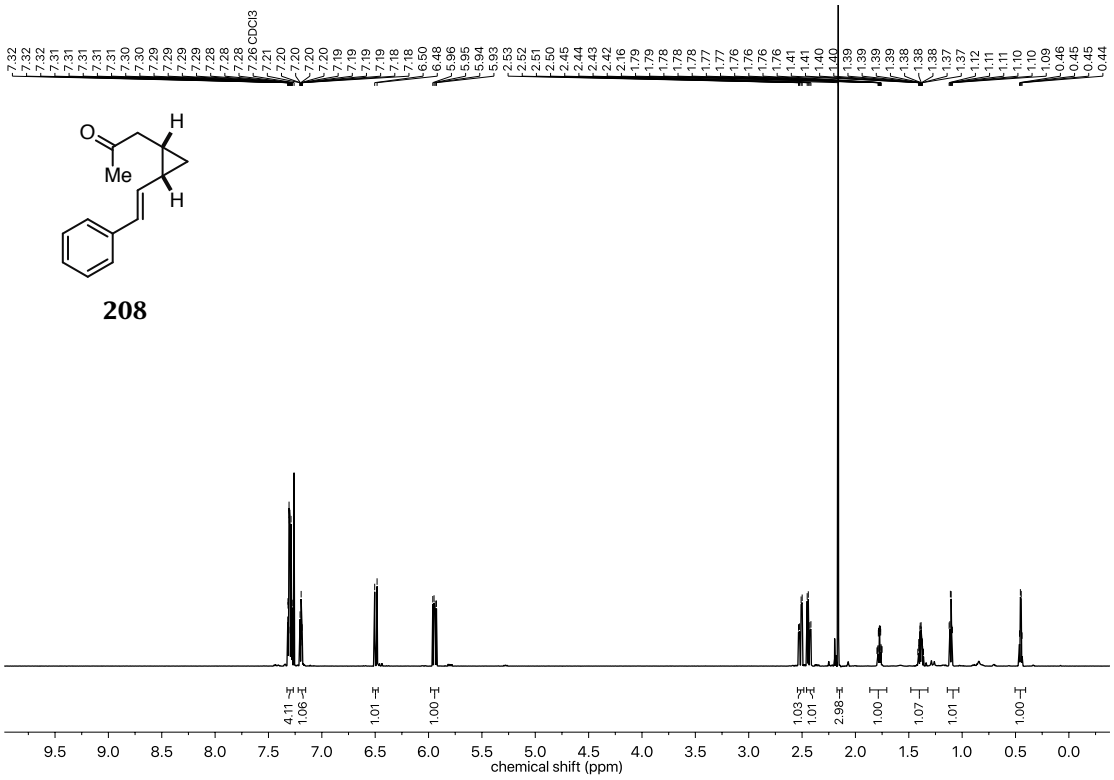


^{13}C NMR:

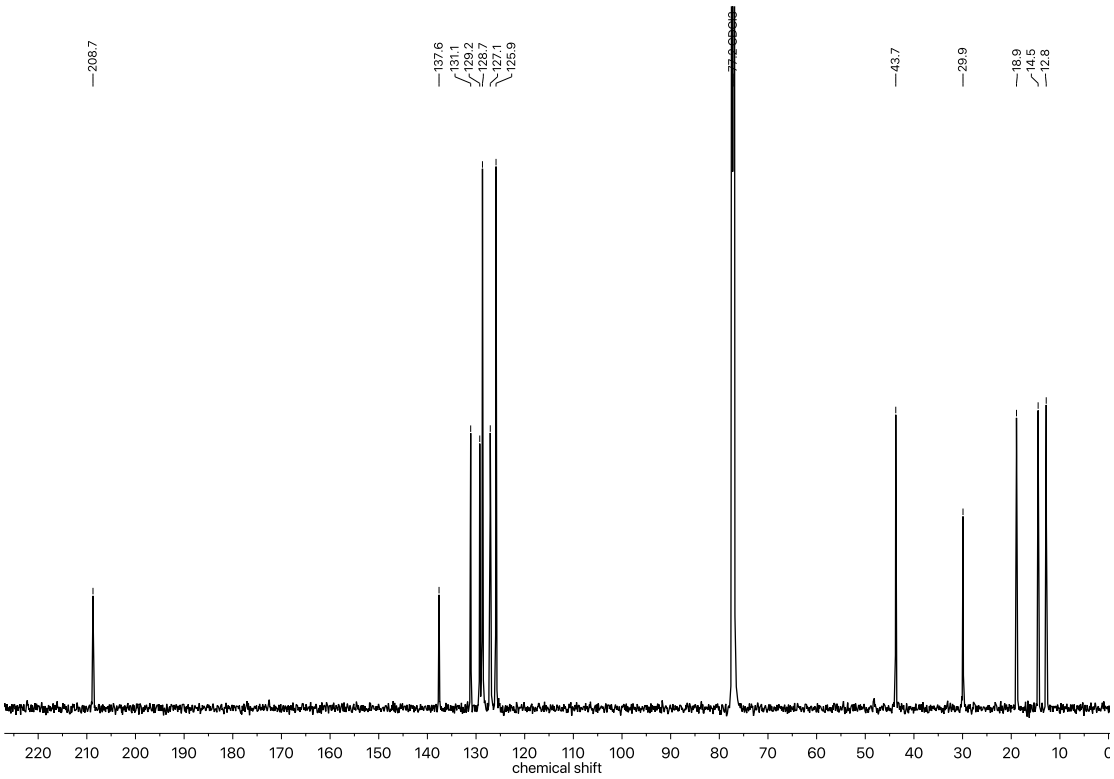


1-(2-((*E*)-Styryl)cyclopropyl)propan-2-one (176)

^{1}H NMR:

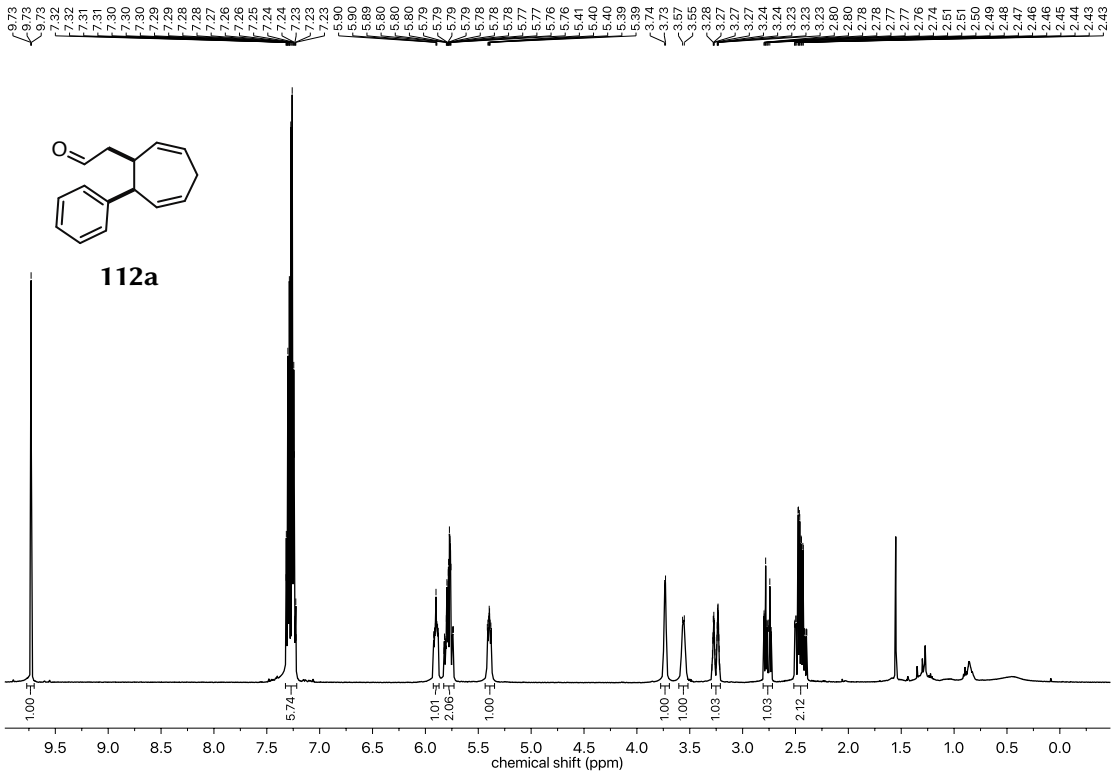


^{13}C NMR:

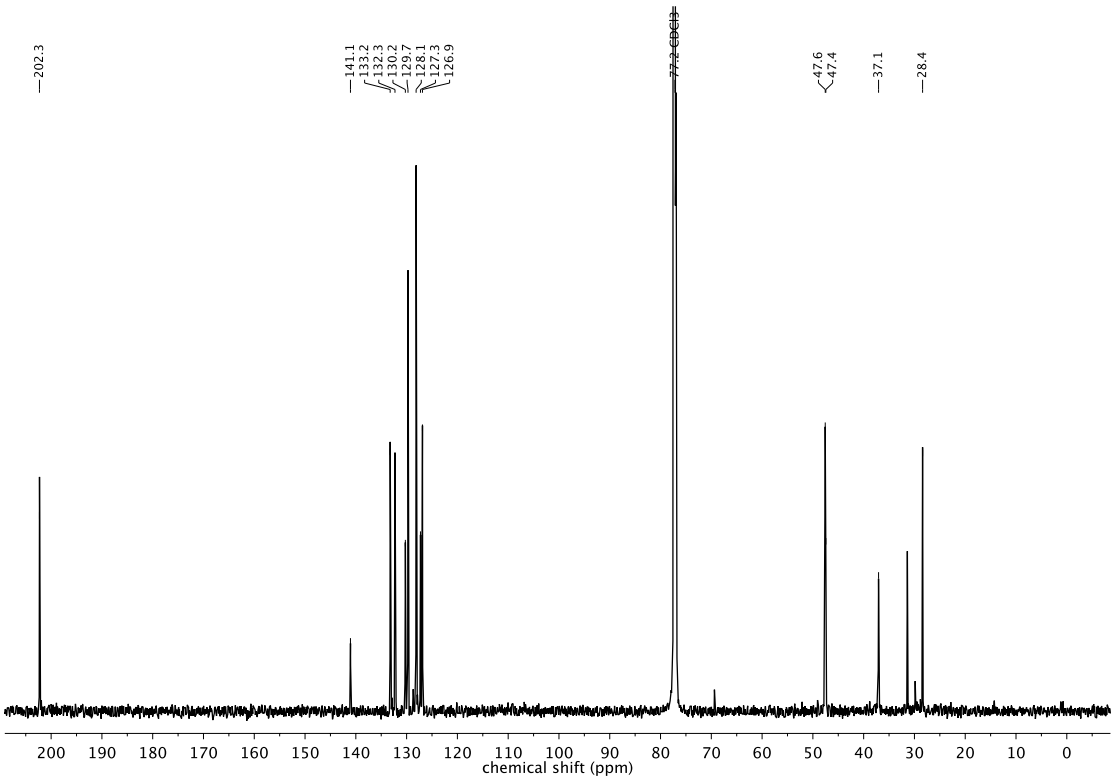


2-((1,7-*cis*)-7-Phenylcyclohepta-2,5-dien-1-yl)acetaldehyde (112a)

^{1}H NMR:

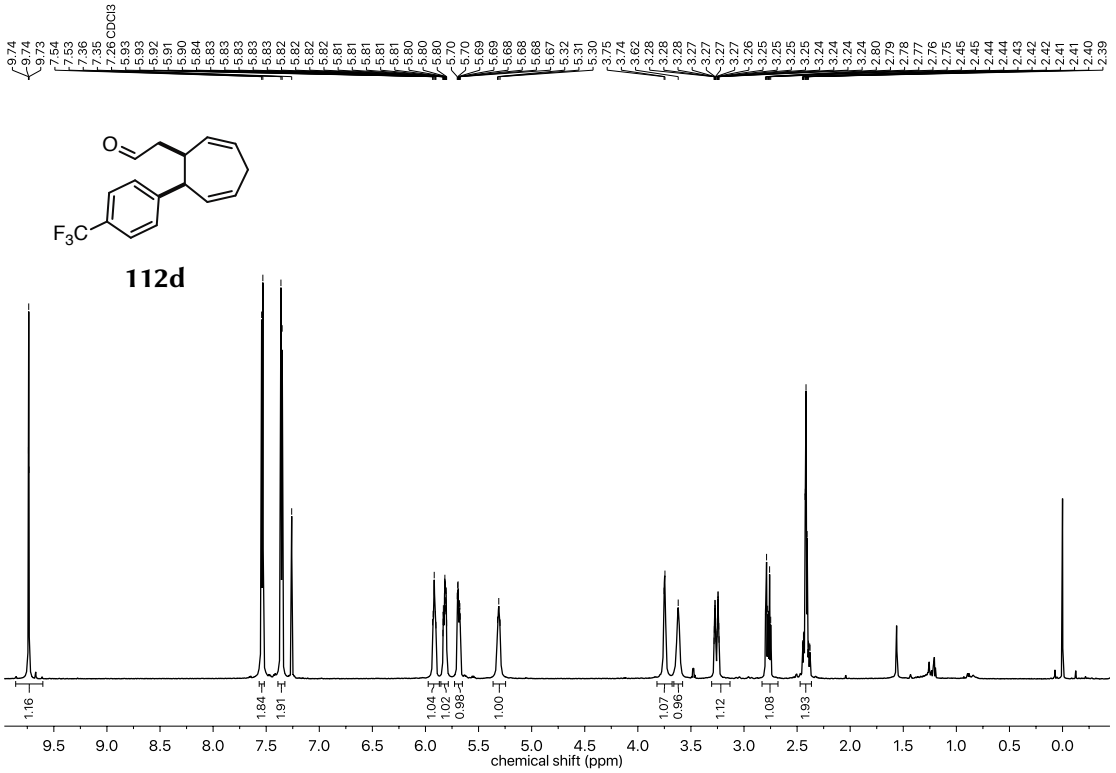


^{13}C NMR:

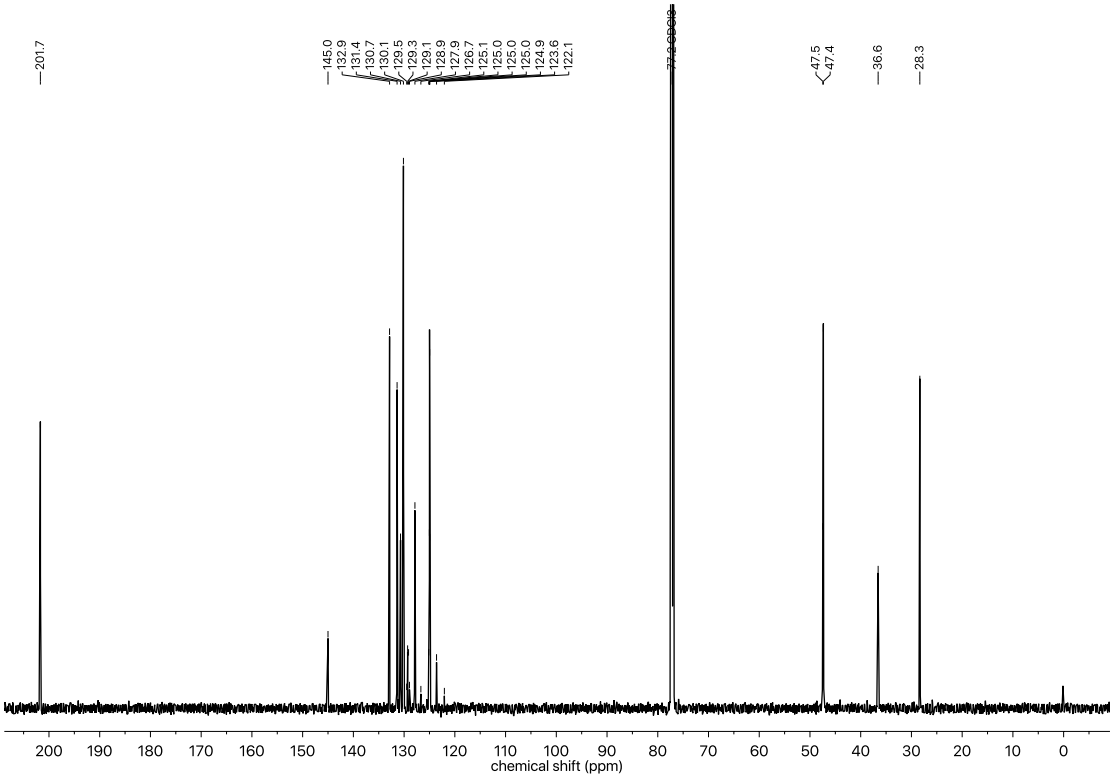


2-((1,7-*cis*)-7-(4-(Trifluoromethyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112d)

^{1}H NMR:

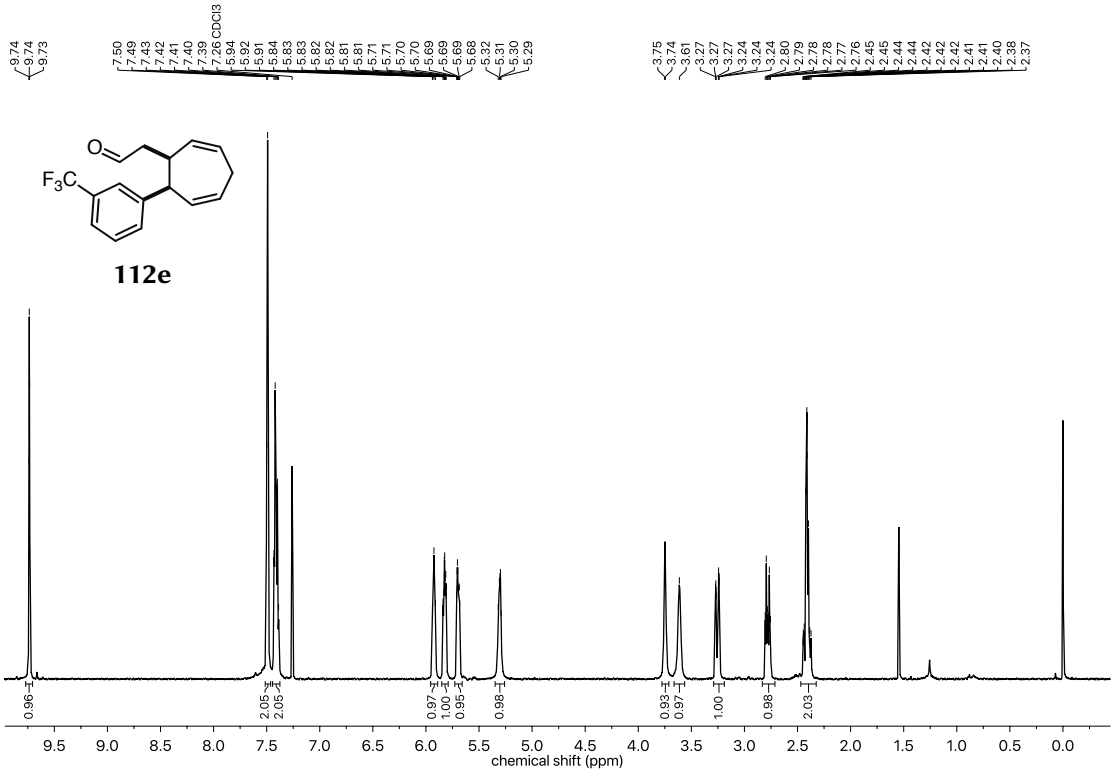


^{13}C NMR:

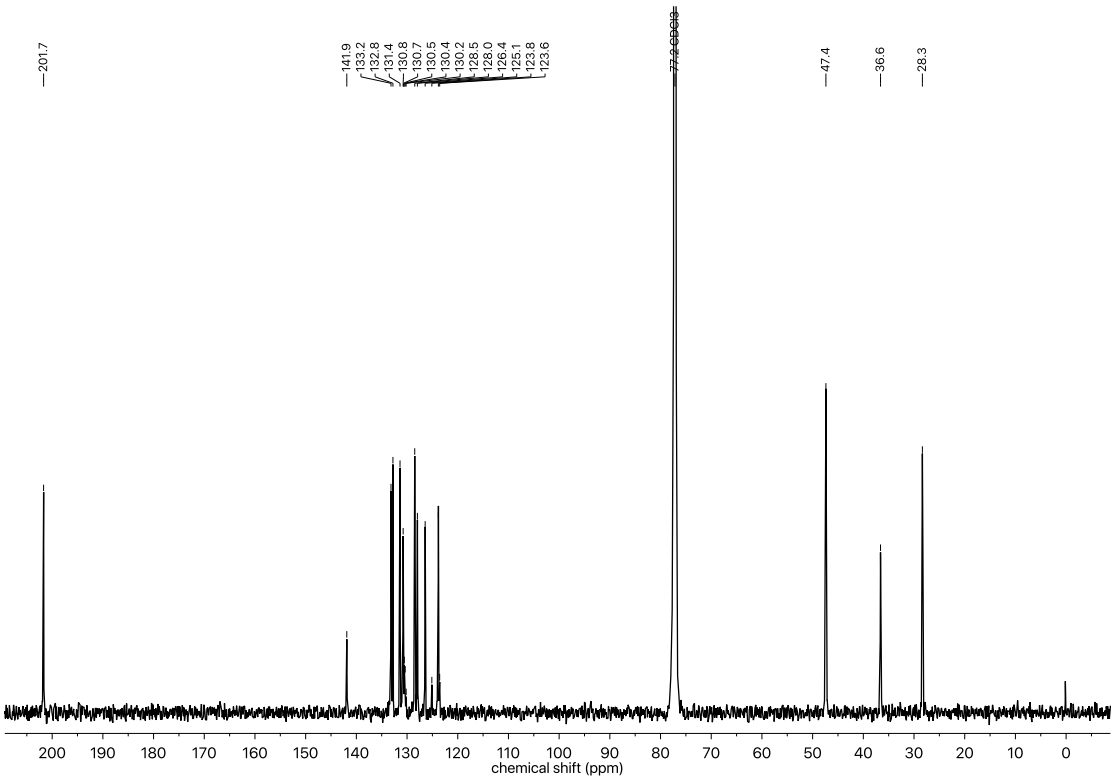


2-((1,7-*cis*)-7-(3-(Trifluoromethyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112e)

^{1}H NMR:

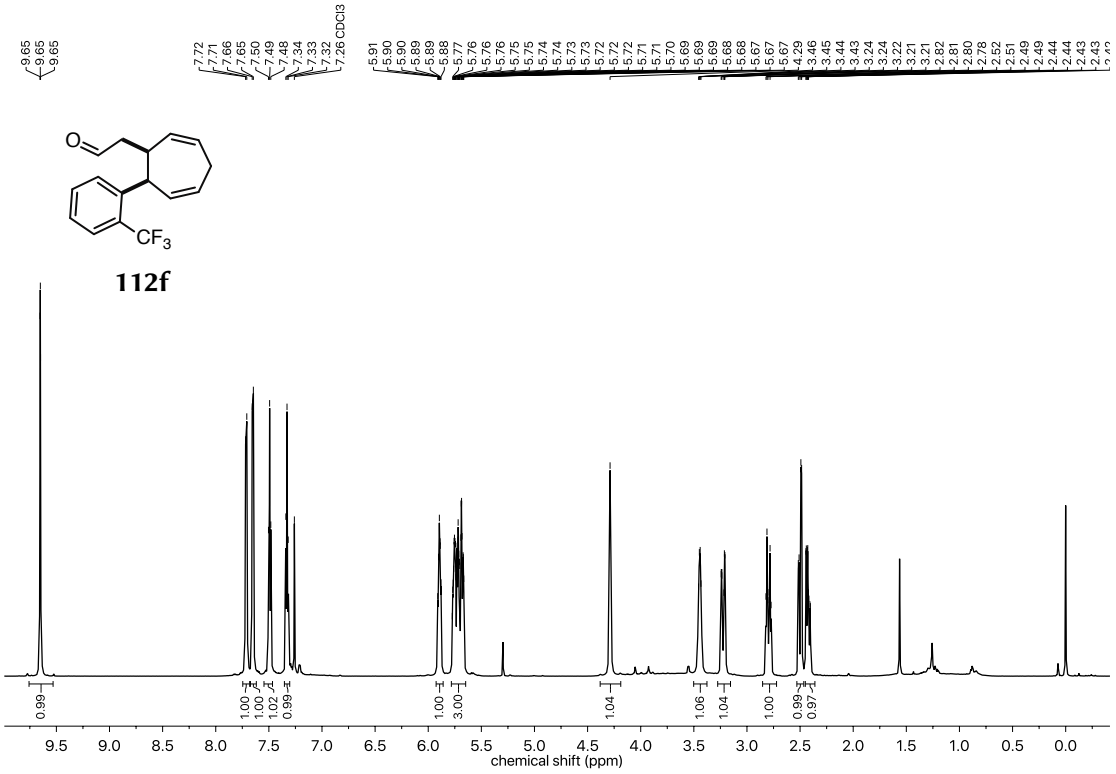


^{13}C NMR:



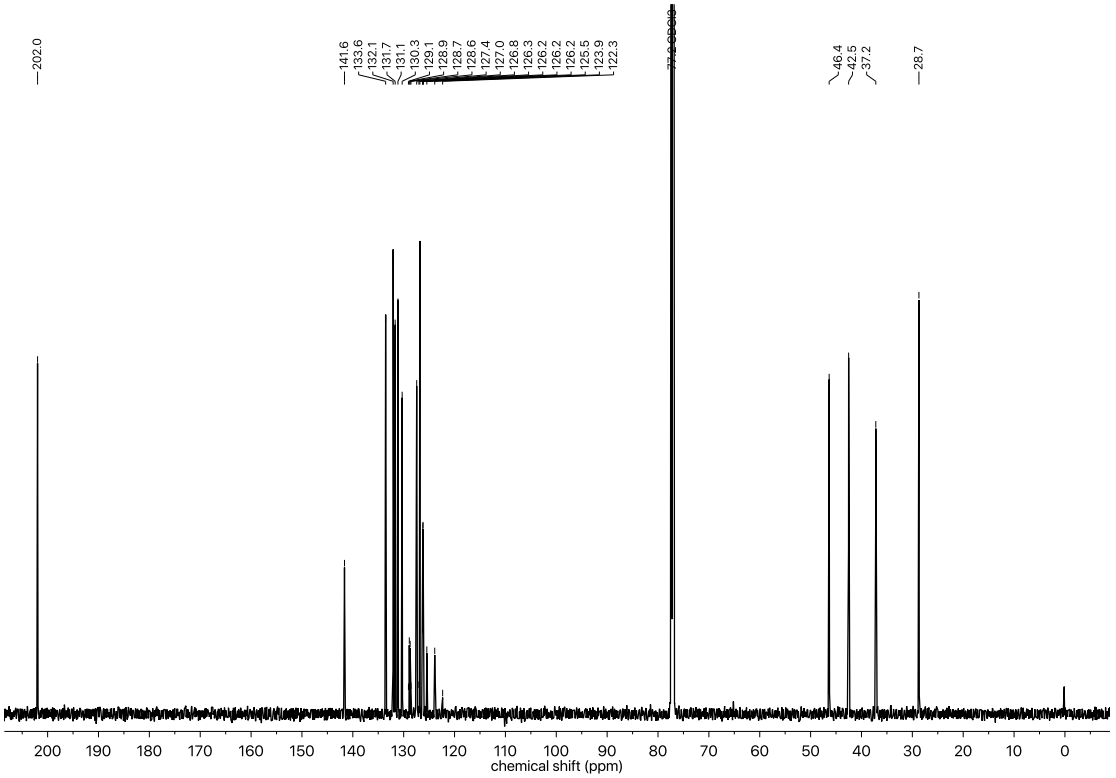
2-((1,7-*cis*)-7-(2-(Trifluoromethyl)phenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112f)

^{1}H NMR:



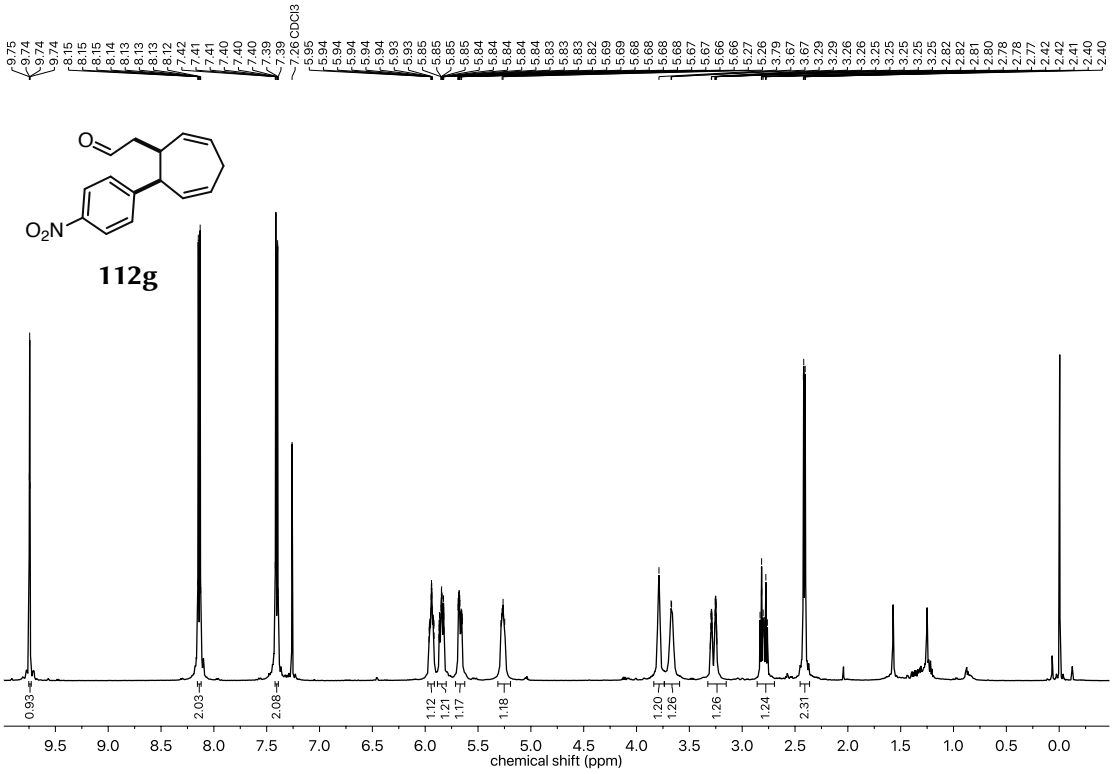
112f

^{13}C NMR:

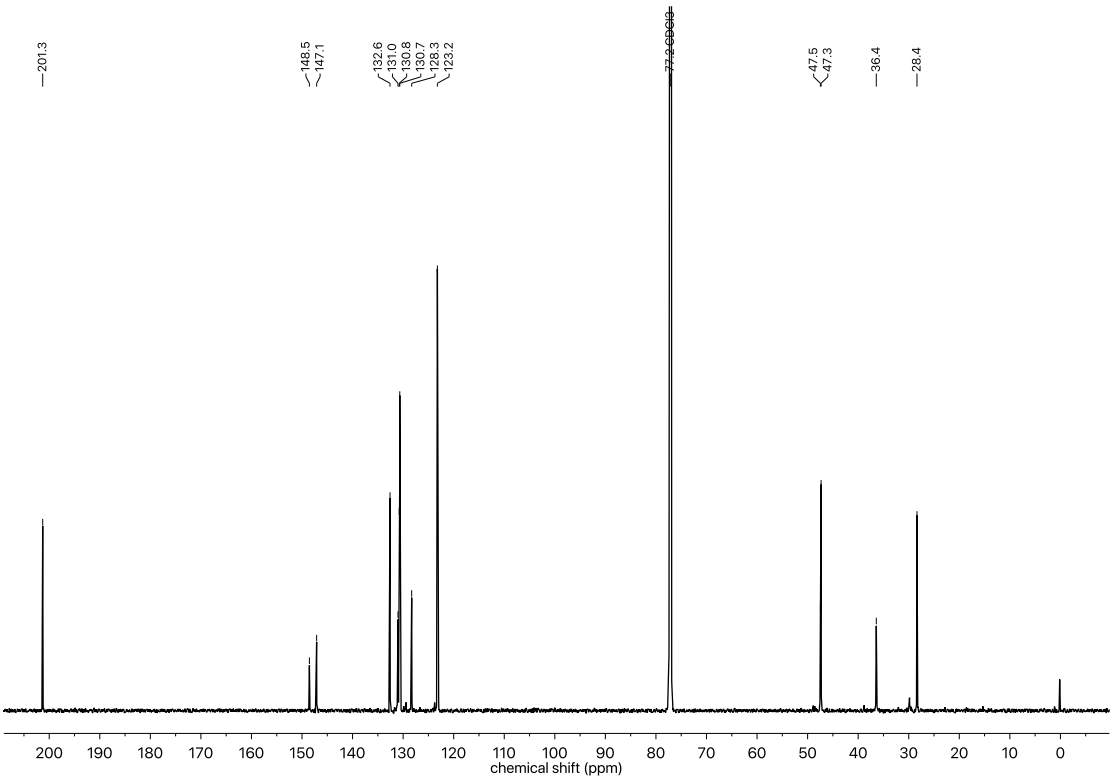


2-((1,7-*cis*)-7-(4-Nitrophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112g)

^{1}H NMR:

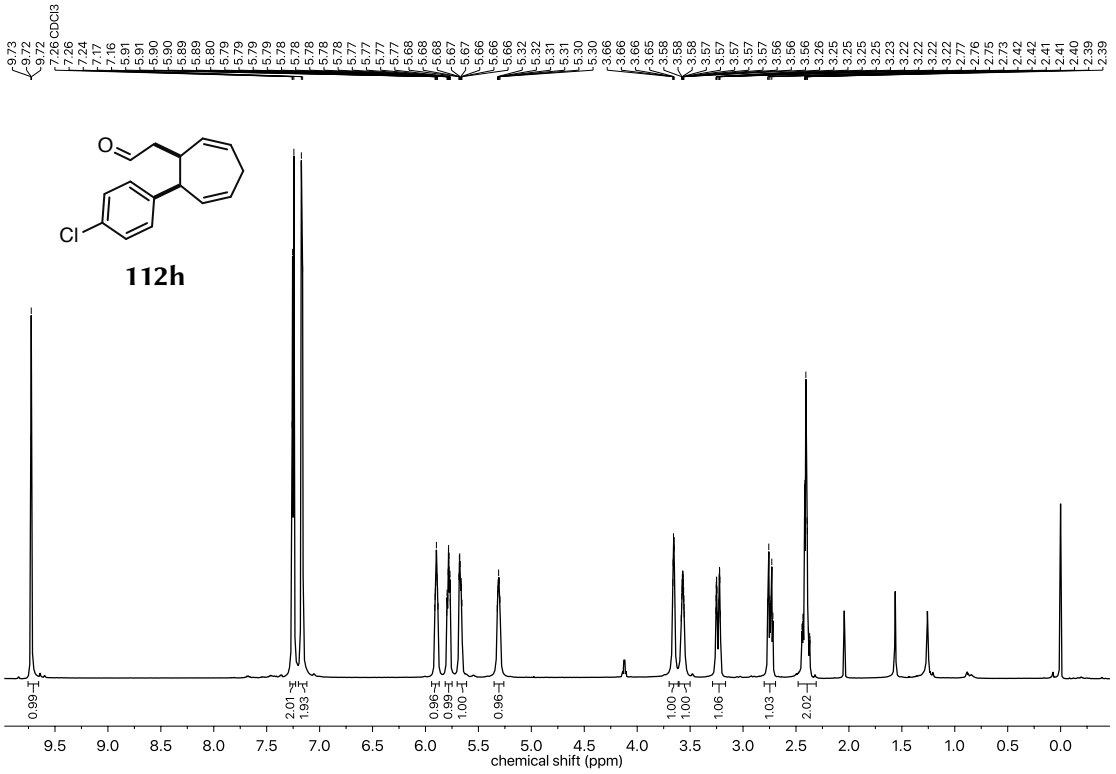


^{13}C NMR:

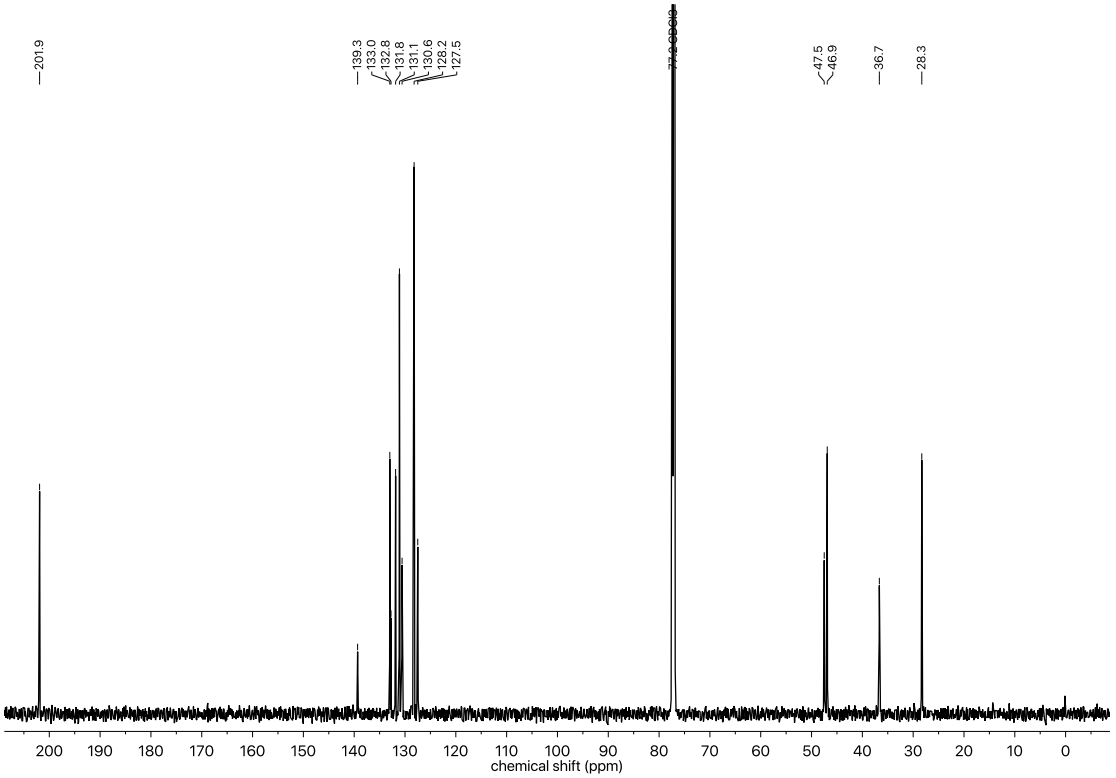


2-((1,7-*cis*)-7-(4-Chlorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112h)

^{1}H NMR:

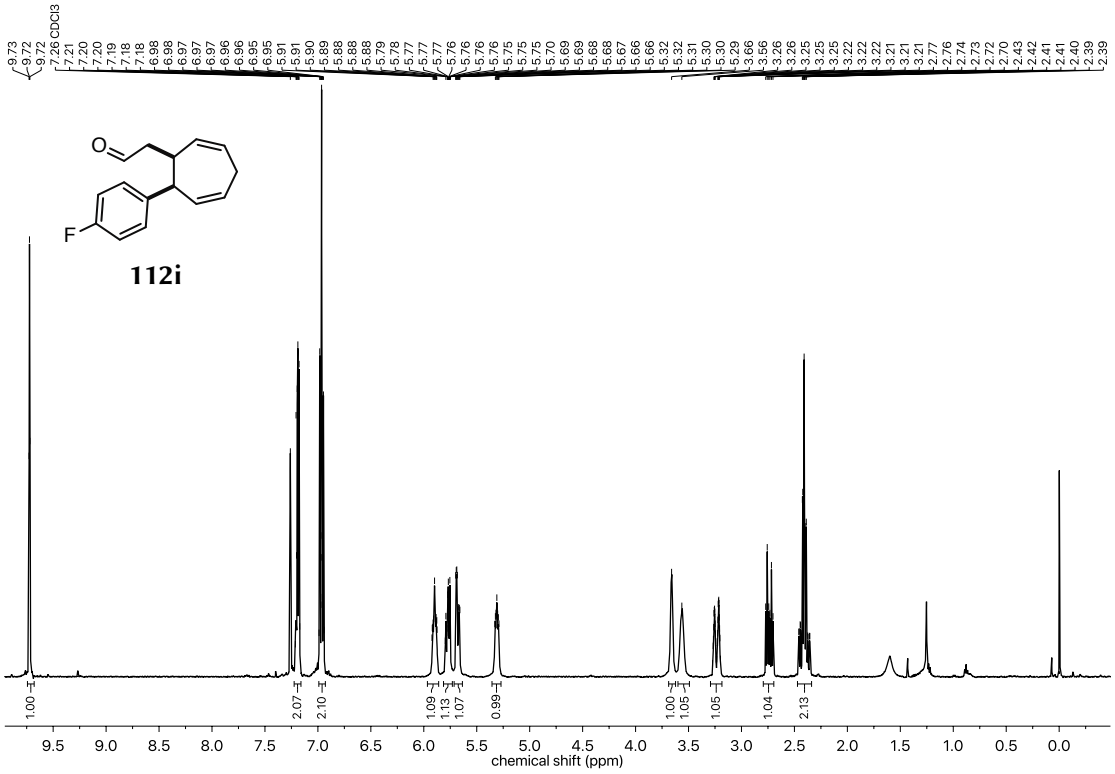


^{13}C NMR:

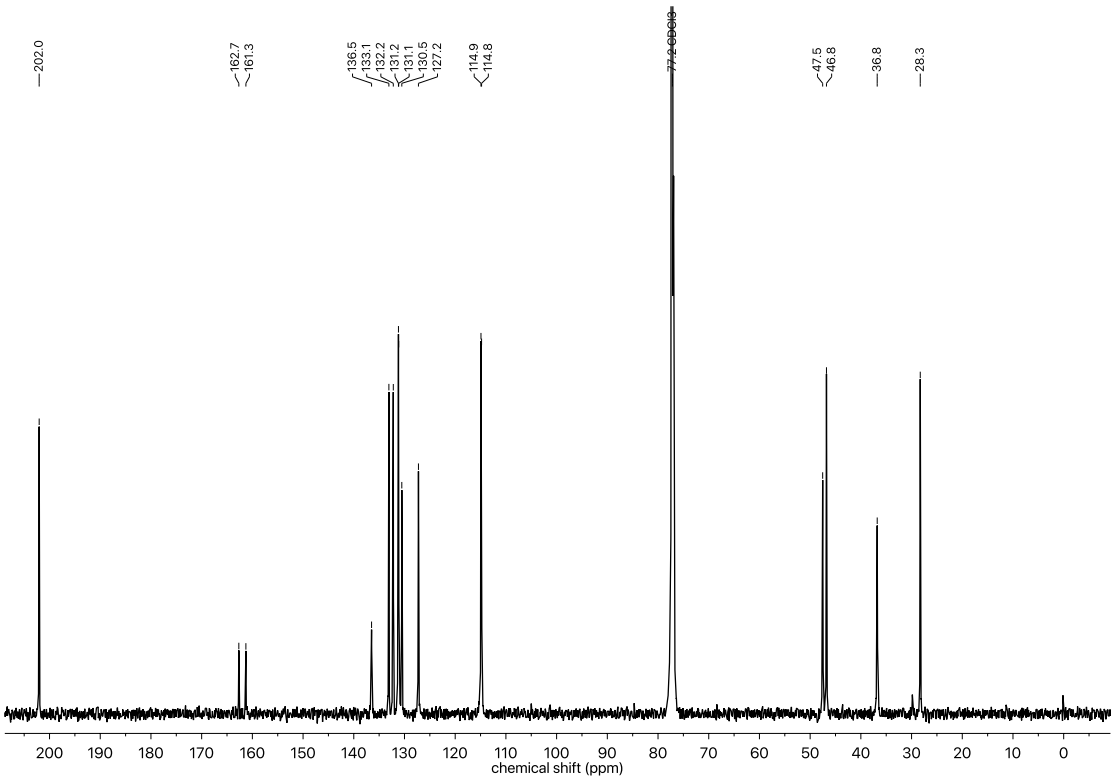


2-((1,7-*cis*)-7-(4-Fluorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112i)

^{1}H NMR:

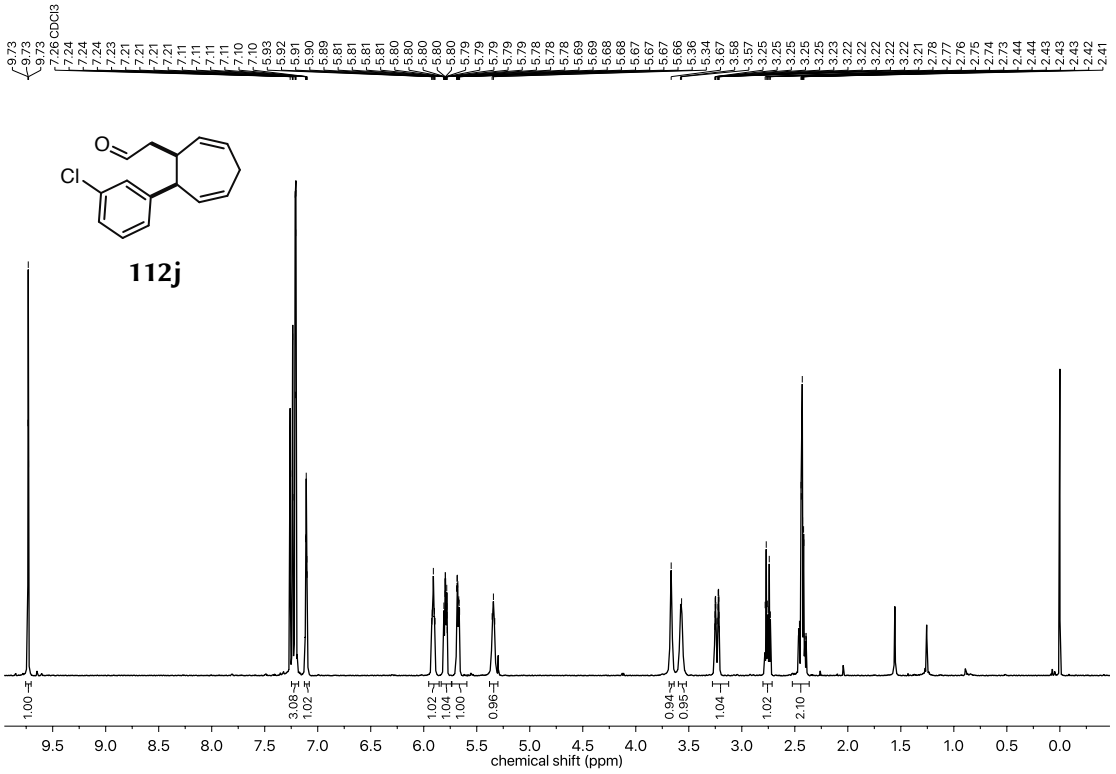


^{13}C NMR:

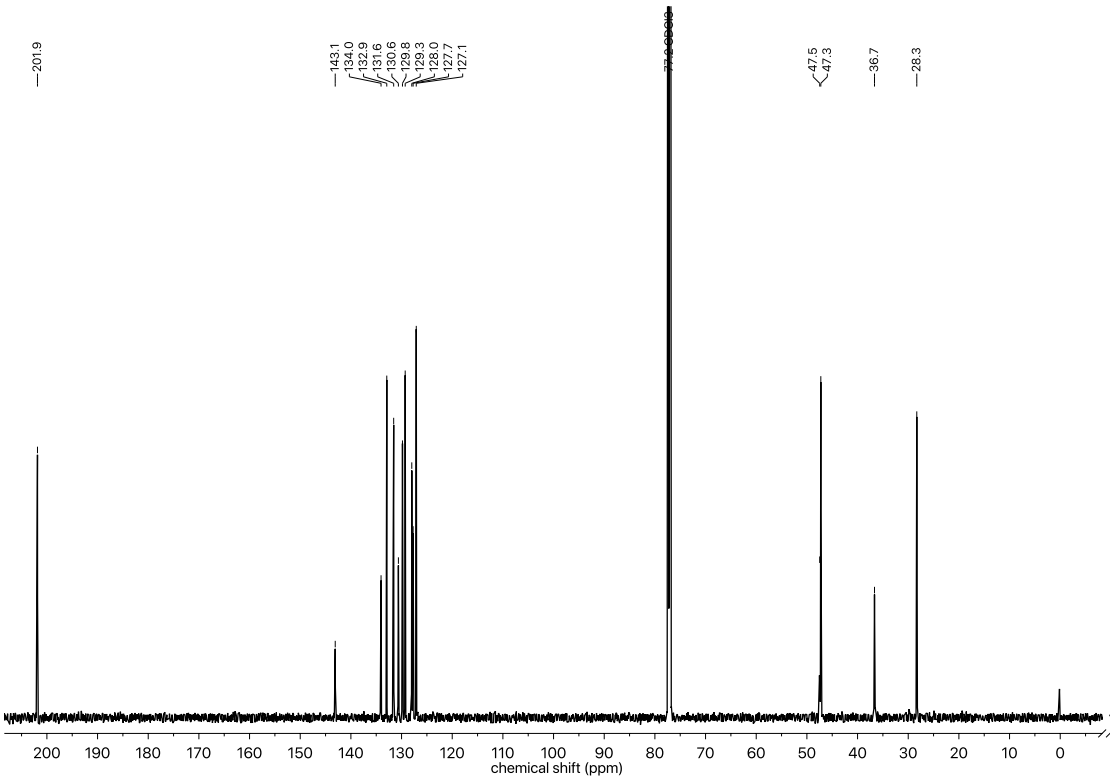


2-((1,7-*cis*)-7-(3-Chlorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112j)

^{1}H NMR:

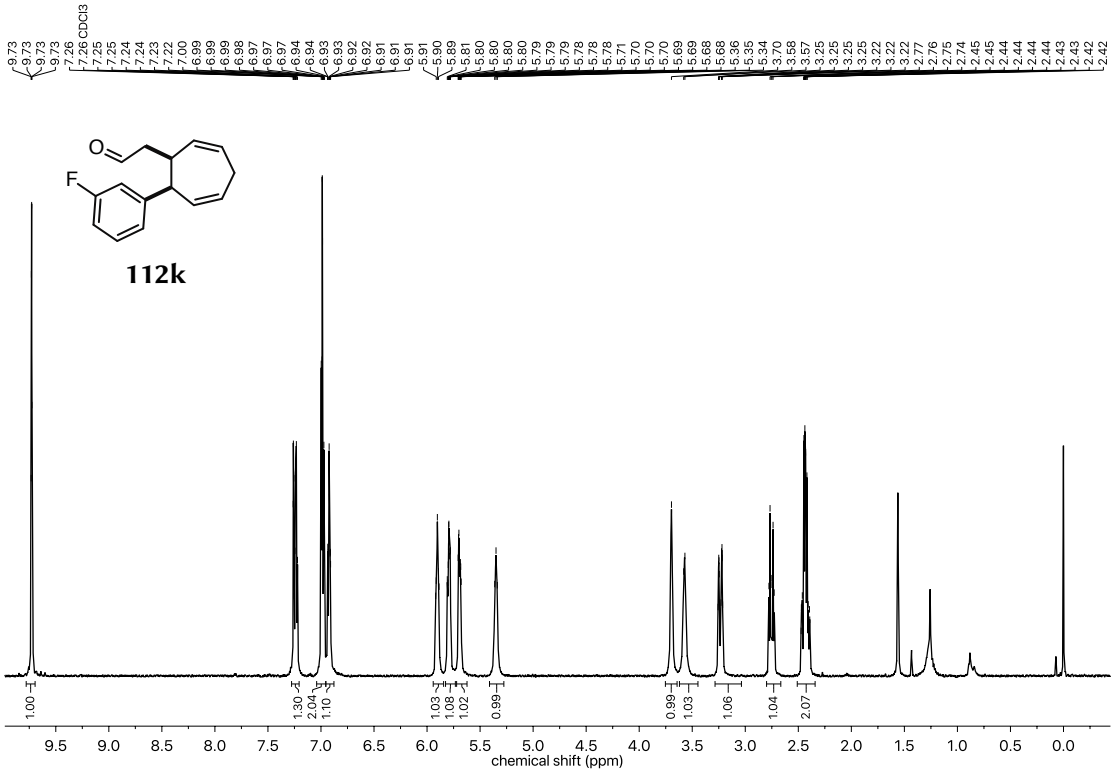


^{13}C NMR:

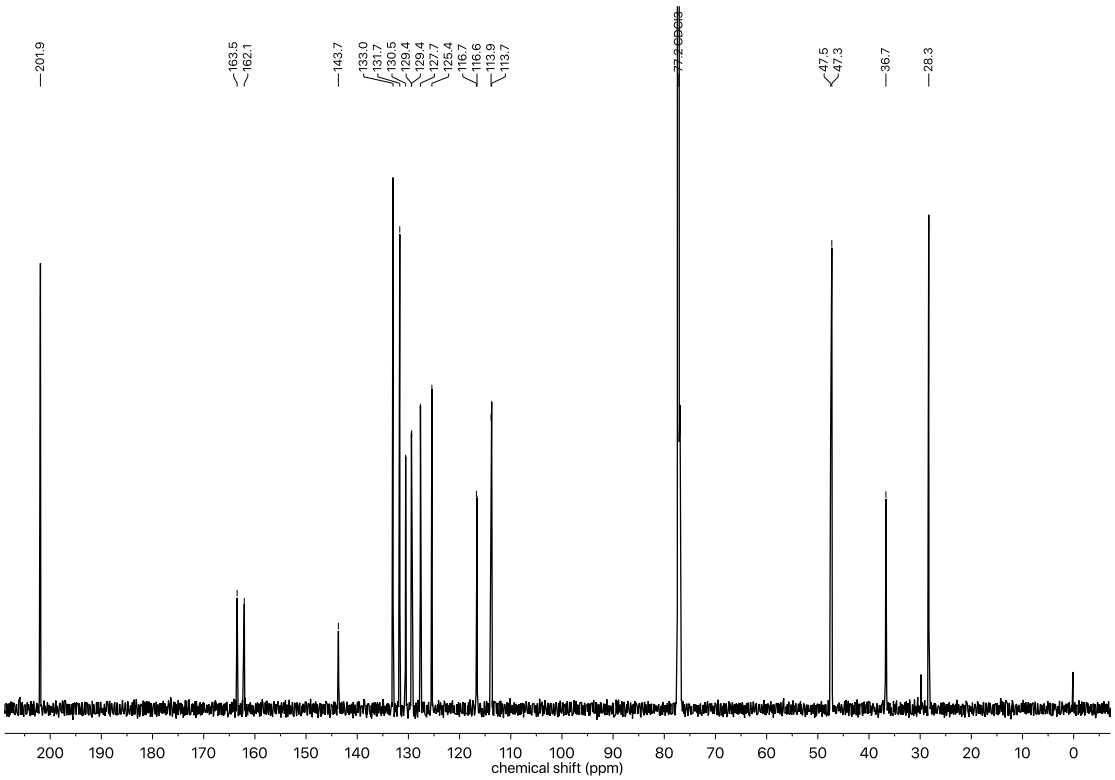


2-((1,7-*cis*)-7-(3-Fluorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112k)

^{1}H NMR:

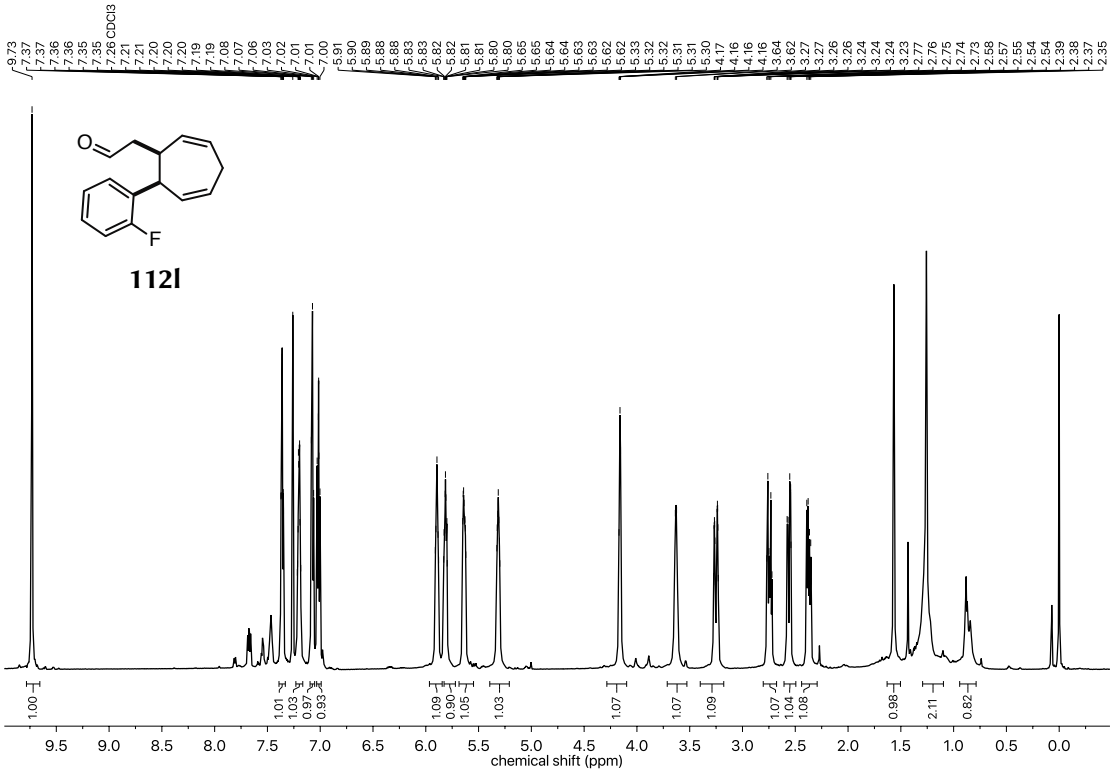


^{13}C NMR:

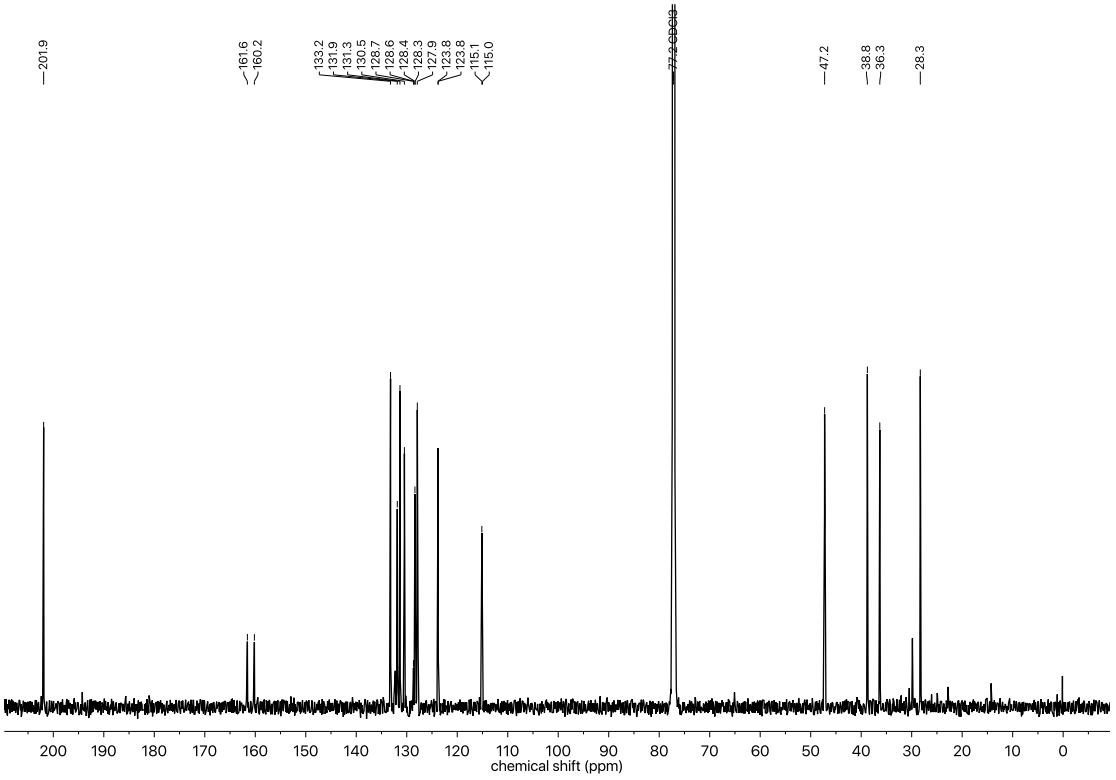


2-((1,7-*cis*)-7-(2-Fluorophenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112l)

^{1}H NMR:

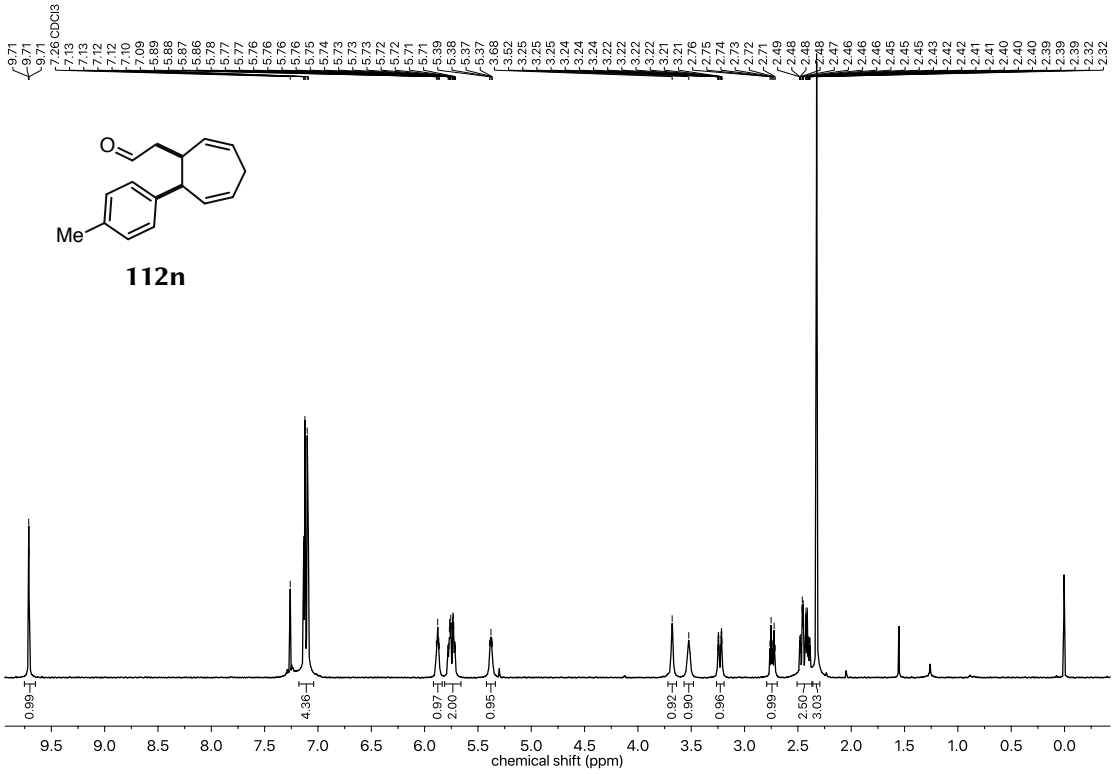


^{13}C NMR:

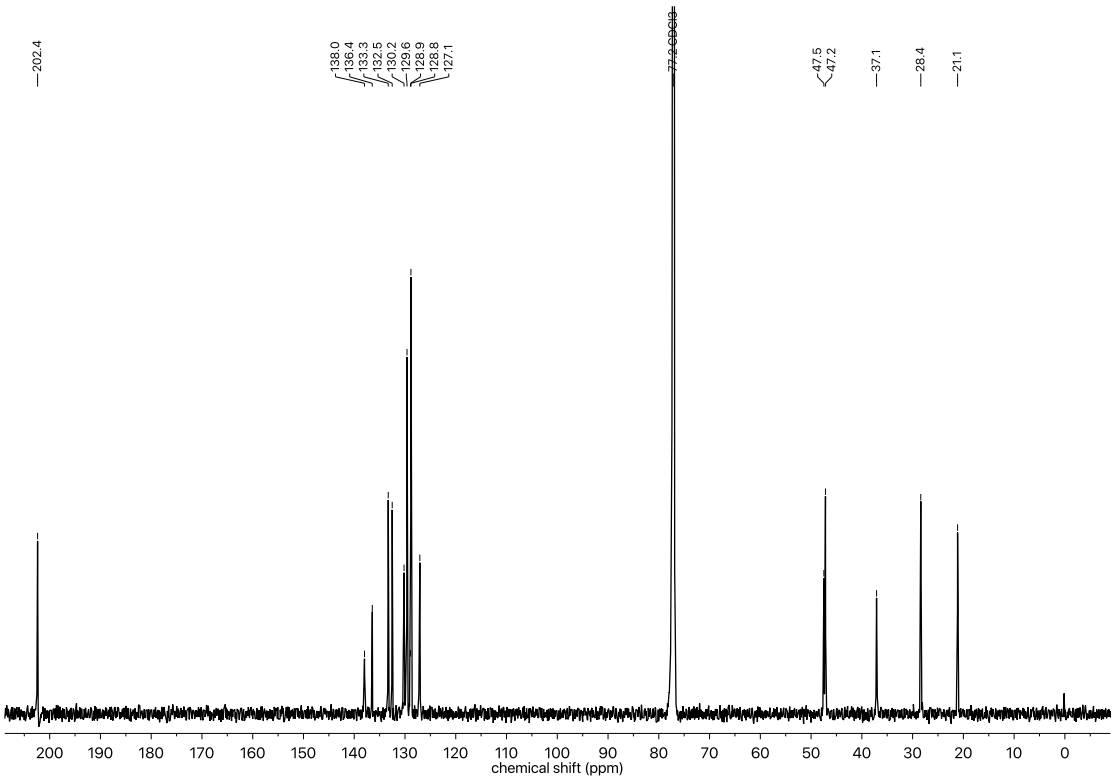


2-((1,7-*cis*)-7-(*p*-Tolyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112n)

^{1}H NMR:

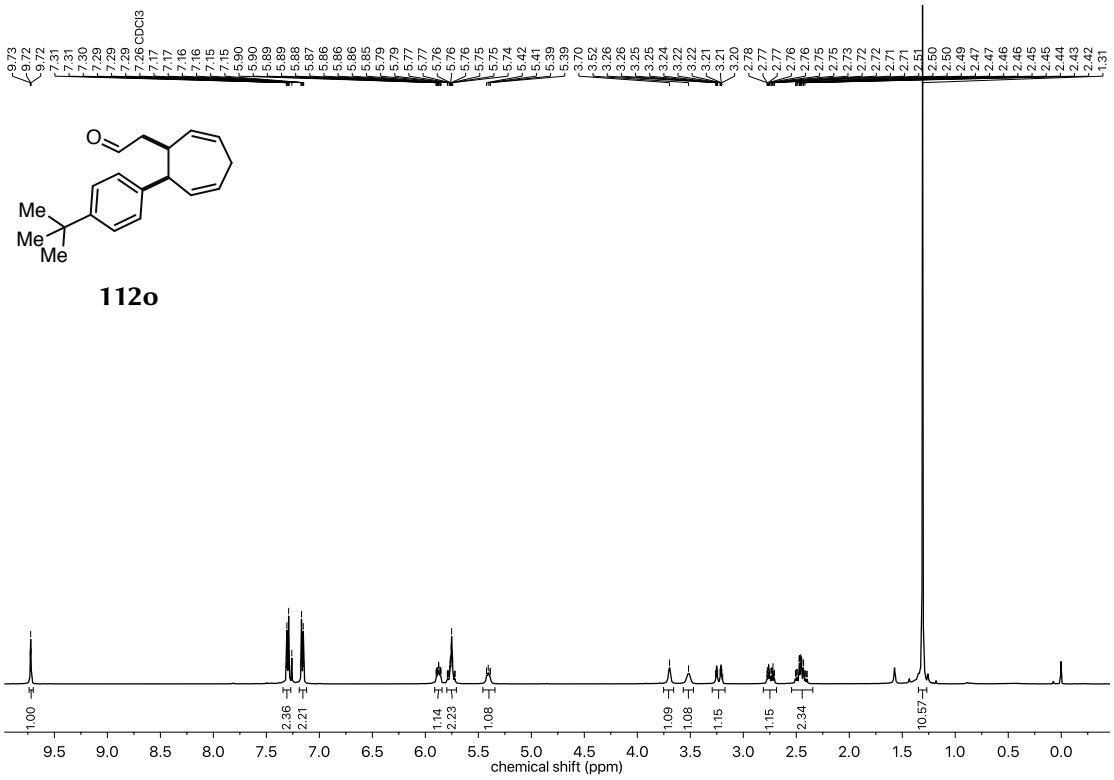


^{13}C NMR:



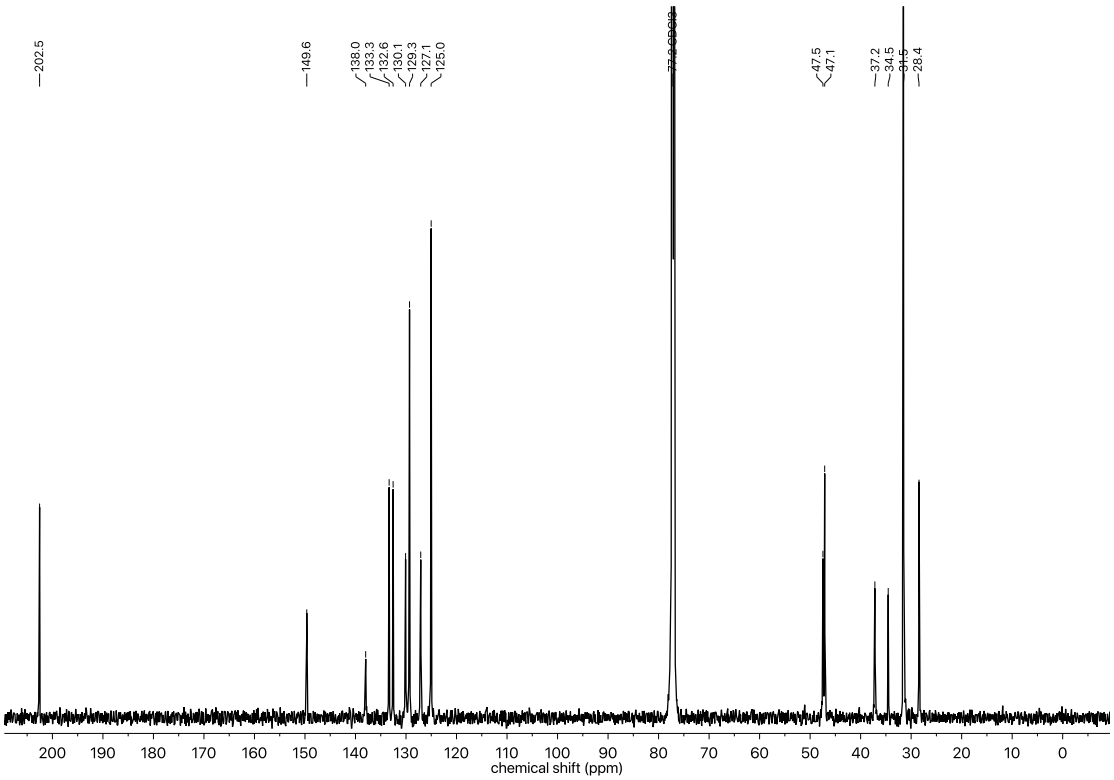
2-((1,7-*cis*)-7-(4-(*tert*-Butyl)-phenyl)-cyclo-hepta-2,5-dien-1-yl)-acet-alde-hyde (112o)

^{1}H NMR:



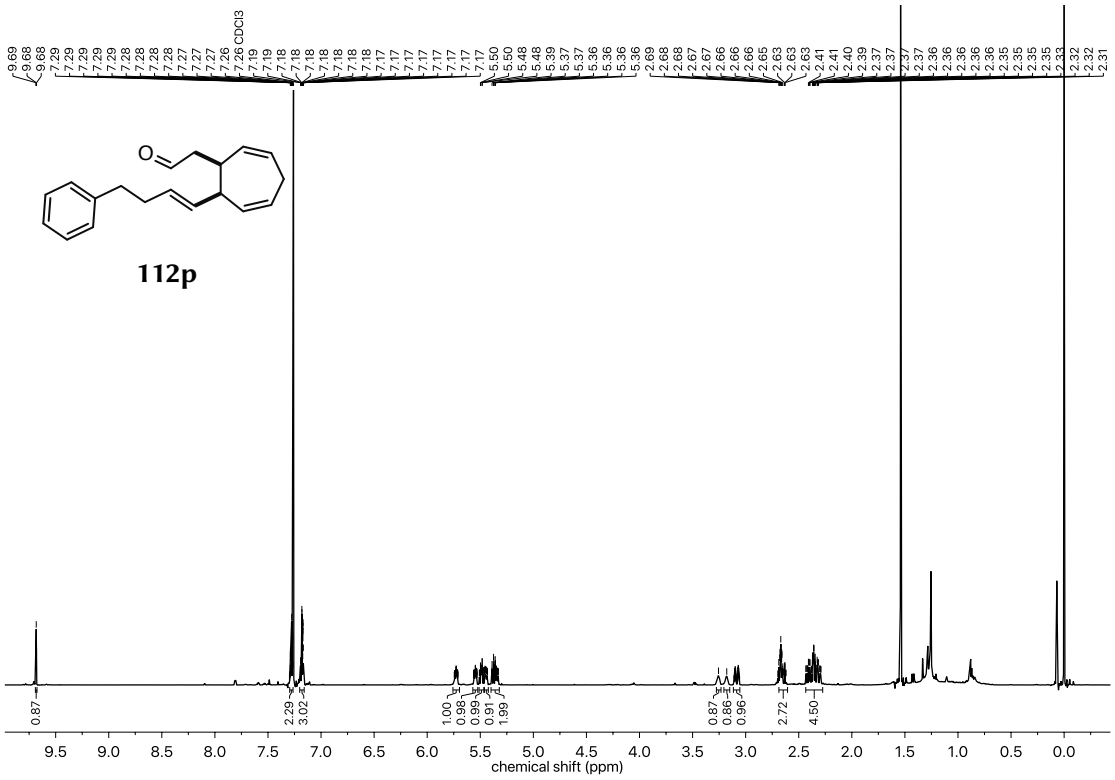
112o

^{13}C NMR:

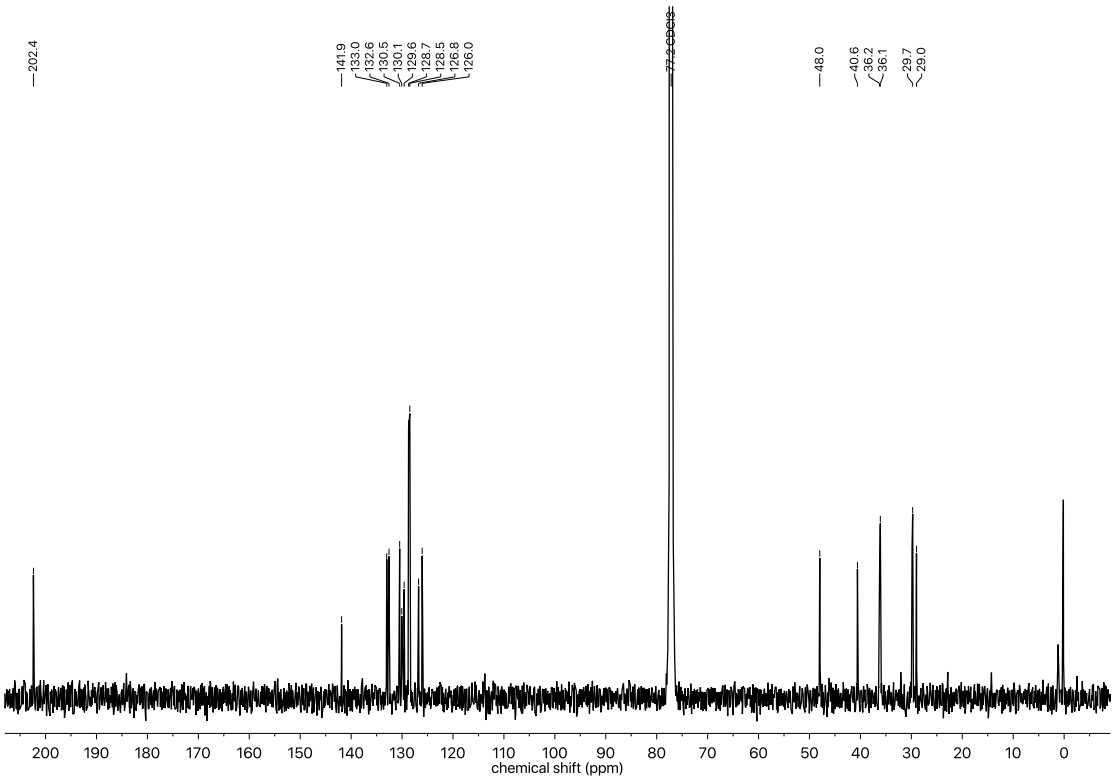


(2-((1,7-*cis*)-7-((*E*)-4-Phenylbut-1-en-1-yl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112p)

^{1}H NMR:

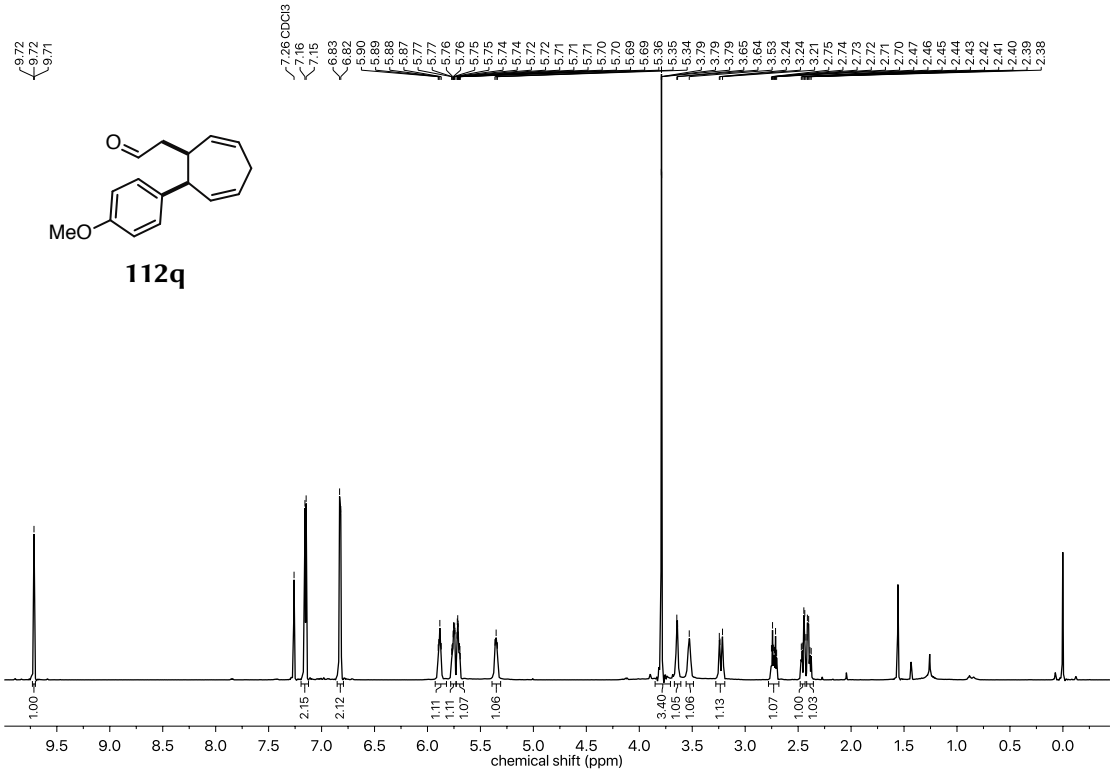


^{13}C NMR:

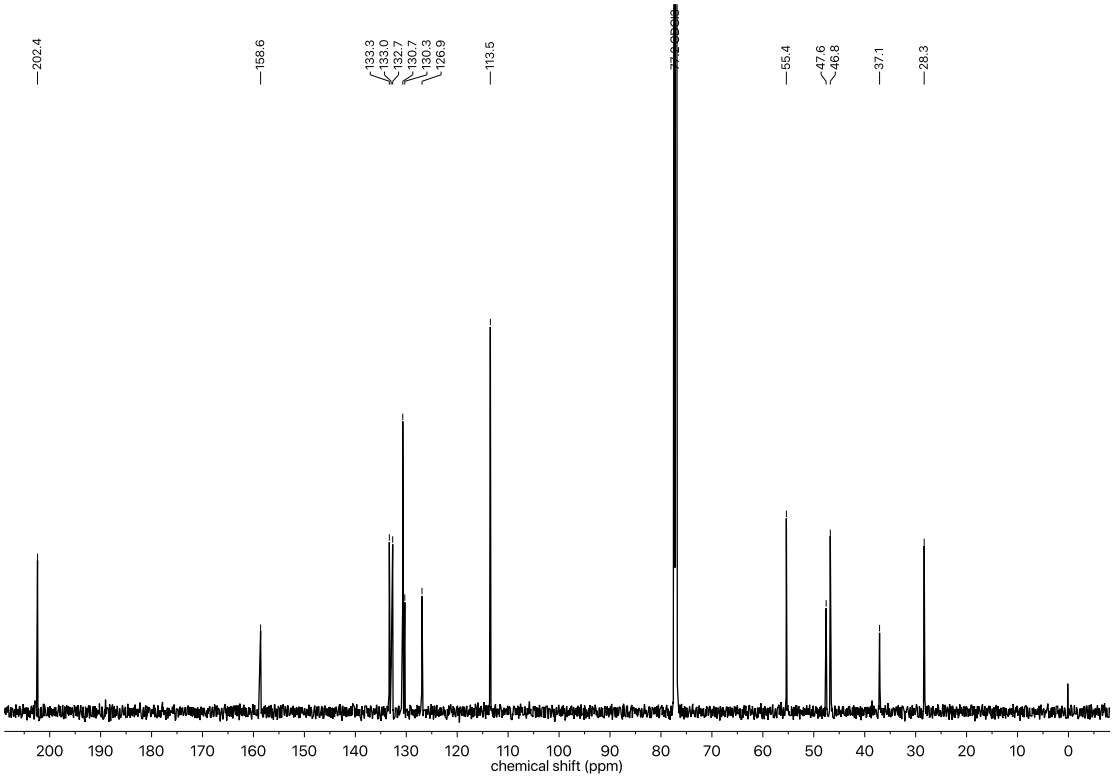


2-((1,7-*cis*)-7-(4-Methoxyphenyl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112q)

^{1}H NMR:

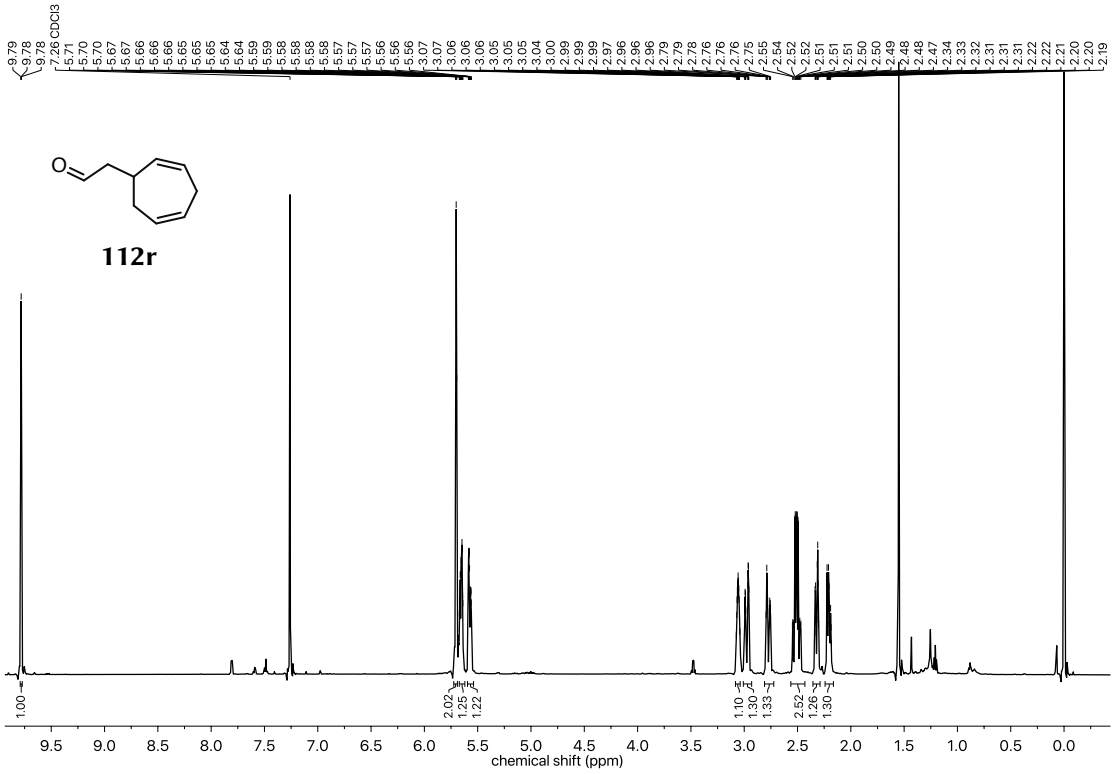


^{13}C NMR:

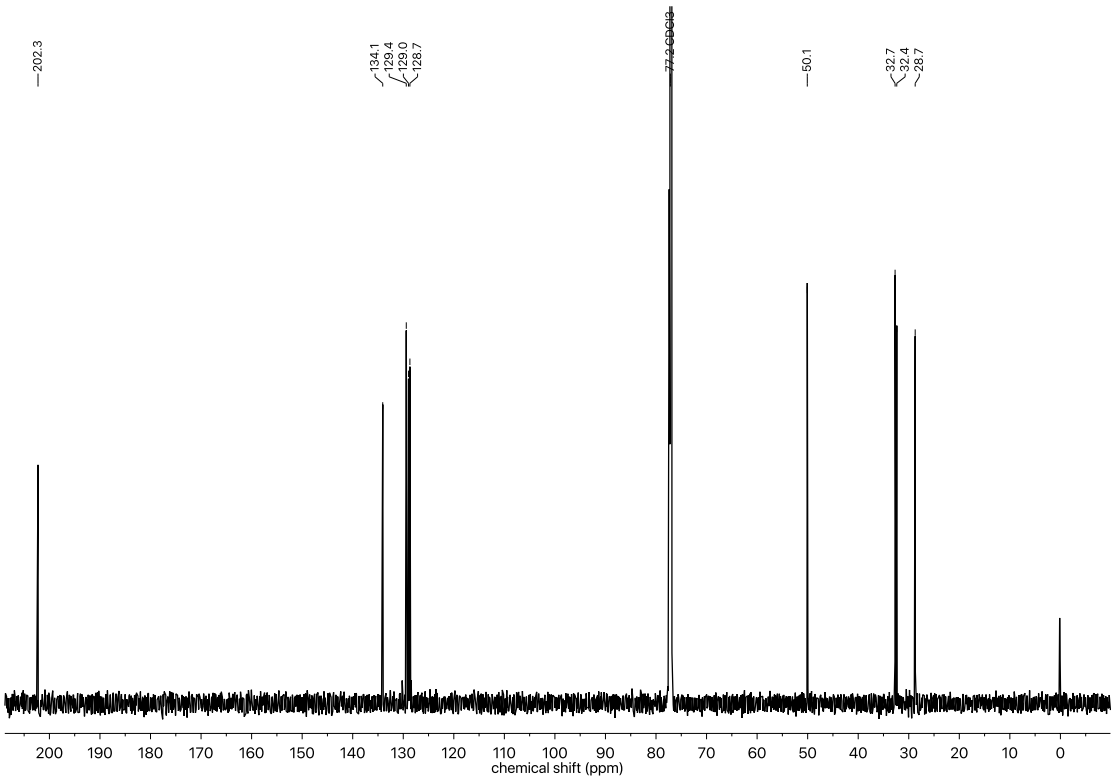


2-(Cyclohepta-2,5-dien-1-yl)acetaldehyde (112r)

^{1}H NMR:

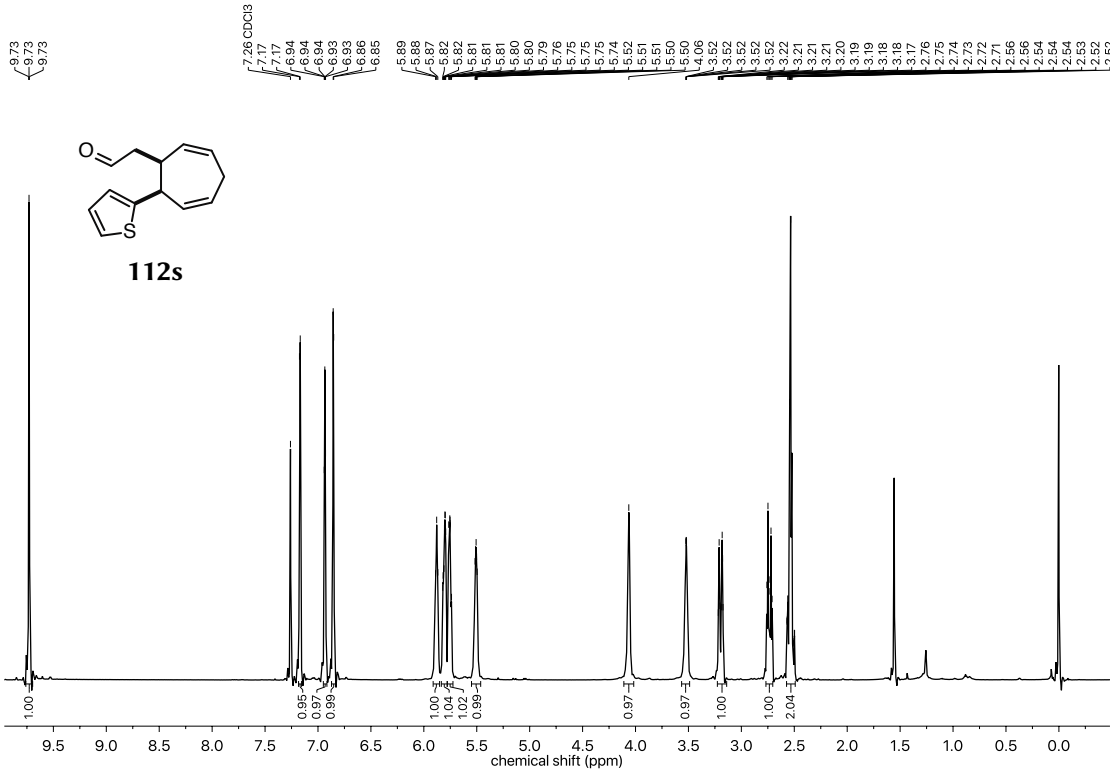


^{13}C NMR:

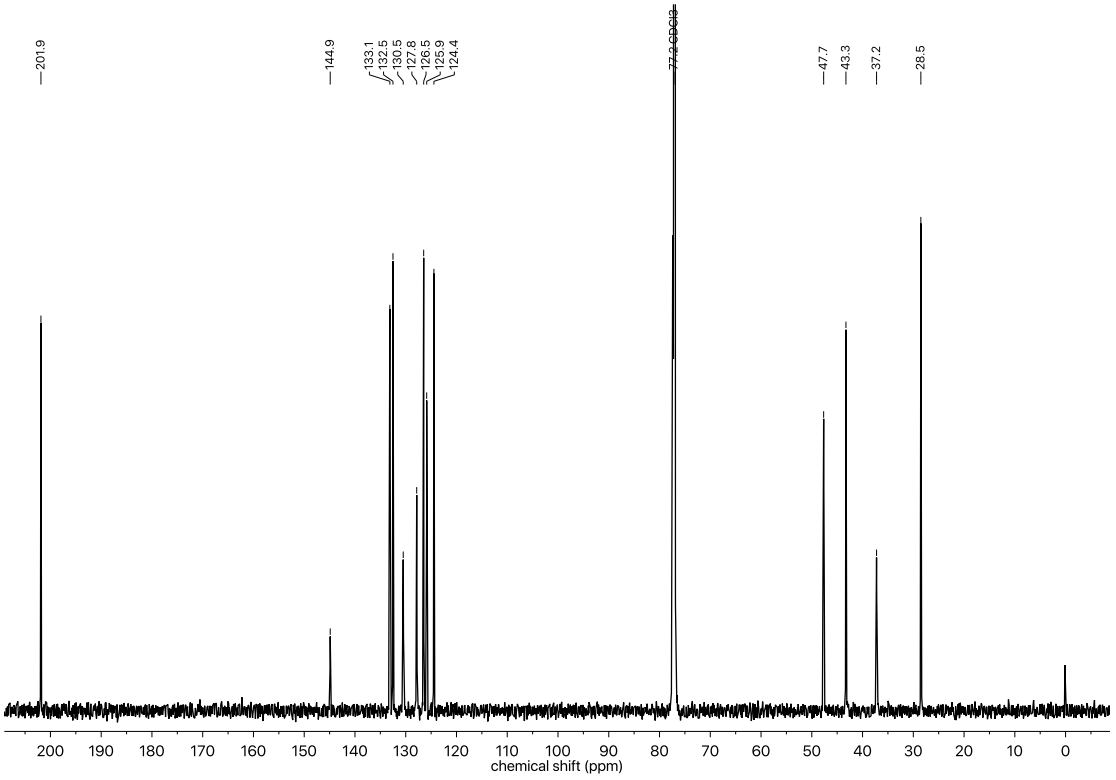


2-((1,7-*cis*)-7-(Thiophen-2-yl)cyclohepta-2,5-dien-1-yl)acetaldehyde (112s)

^{1}H NMR:

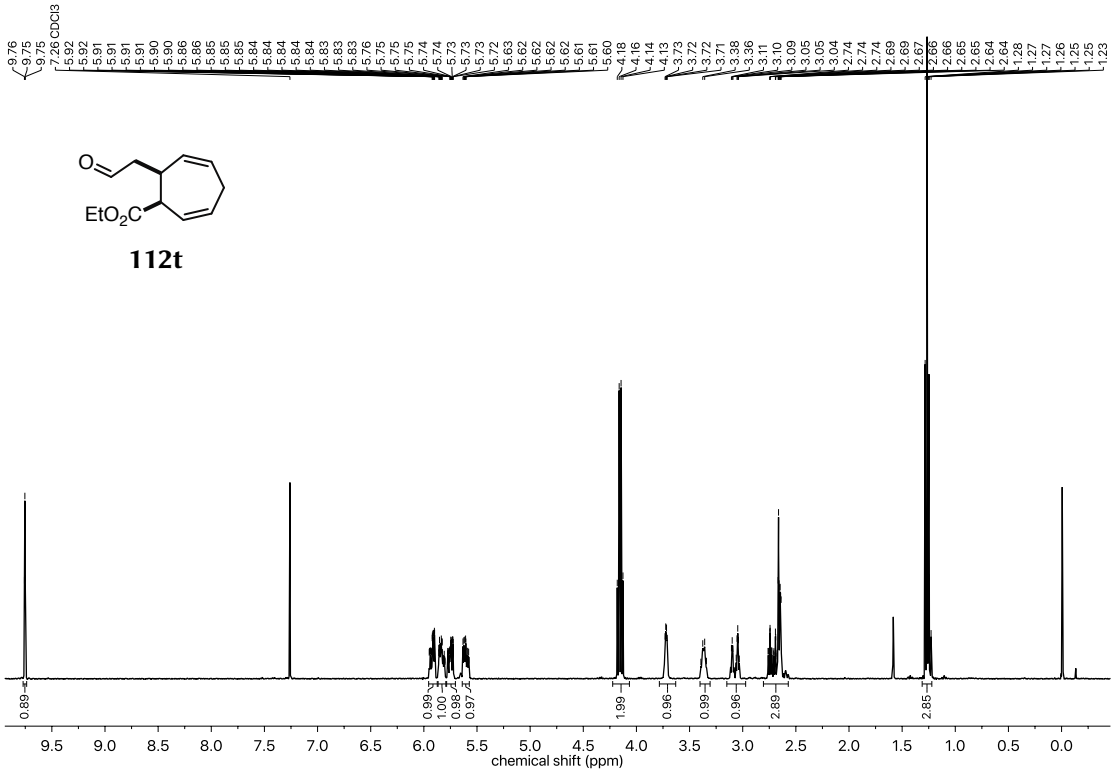


^{13}C NMR:

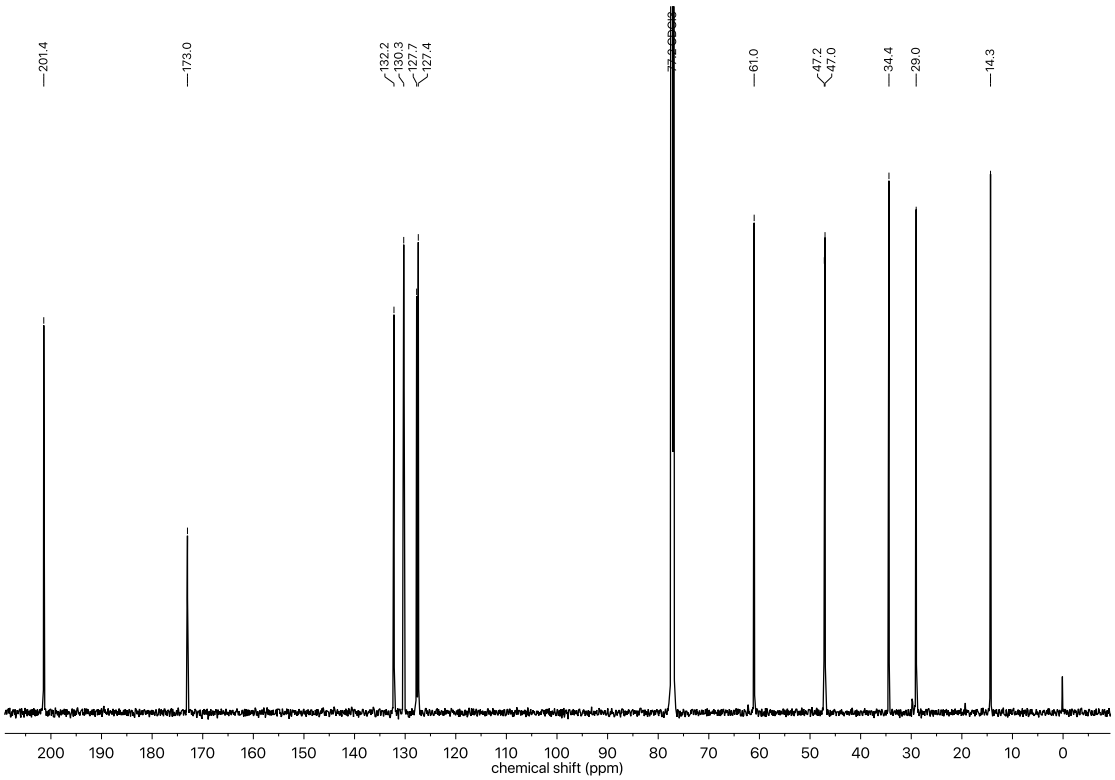


Ethyl (1,7-*cis*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carboxylate (112t)

^{1}H NMR:

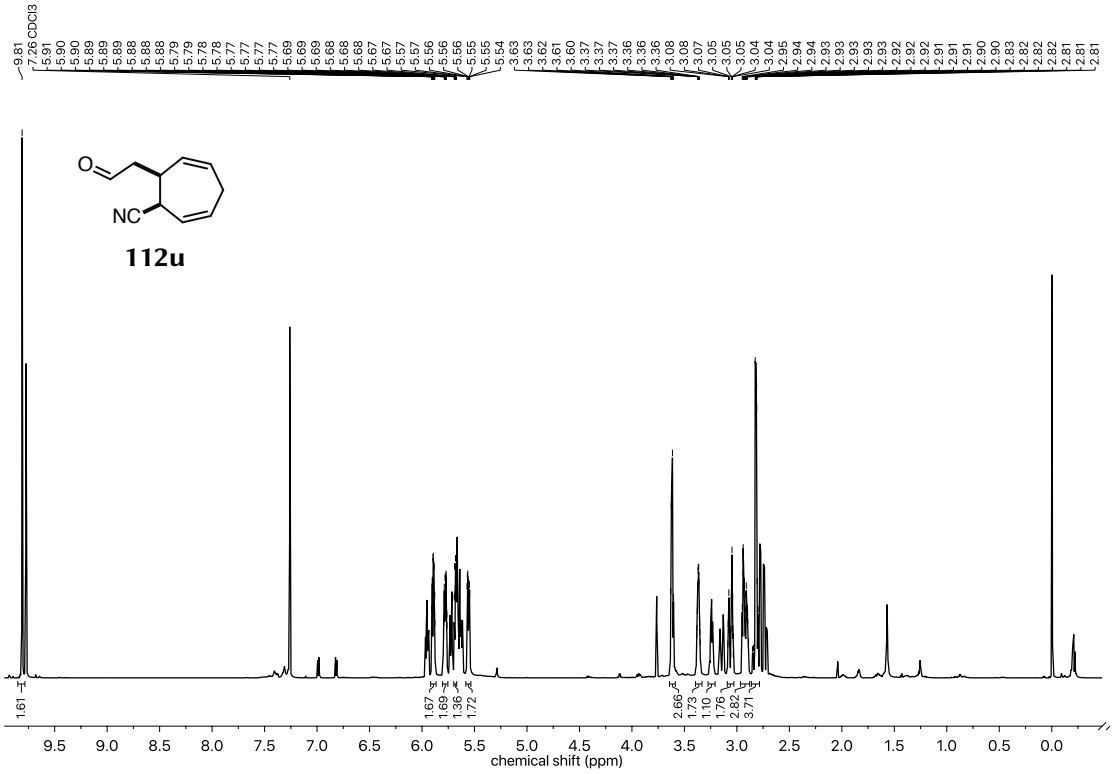


^{13}C NMR:

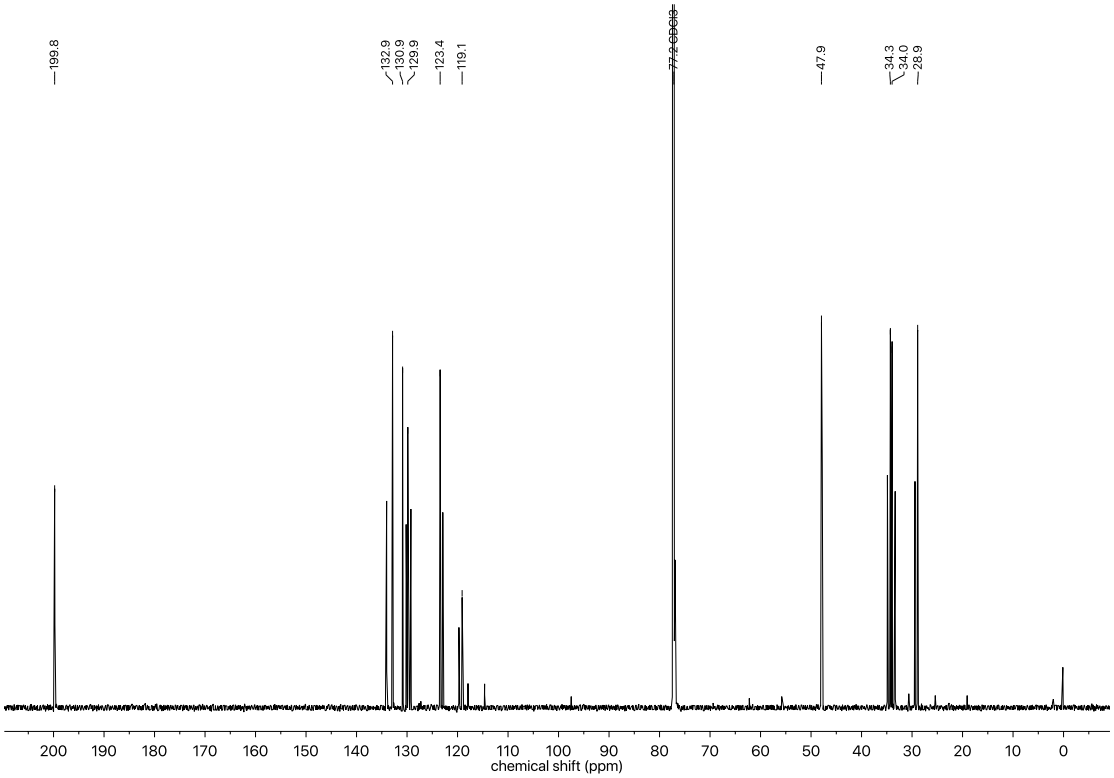


(1,7-*cis*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carbonitrile (112u)

^{1}H NMR:

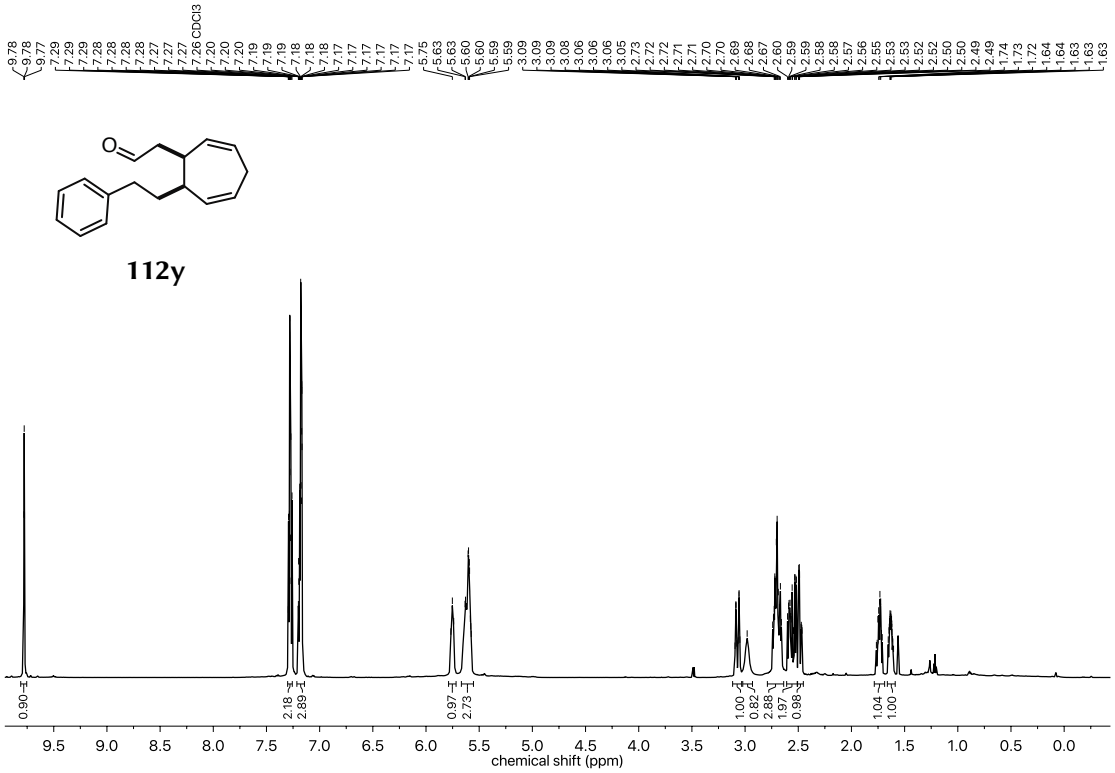


^{13}C NMR:

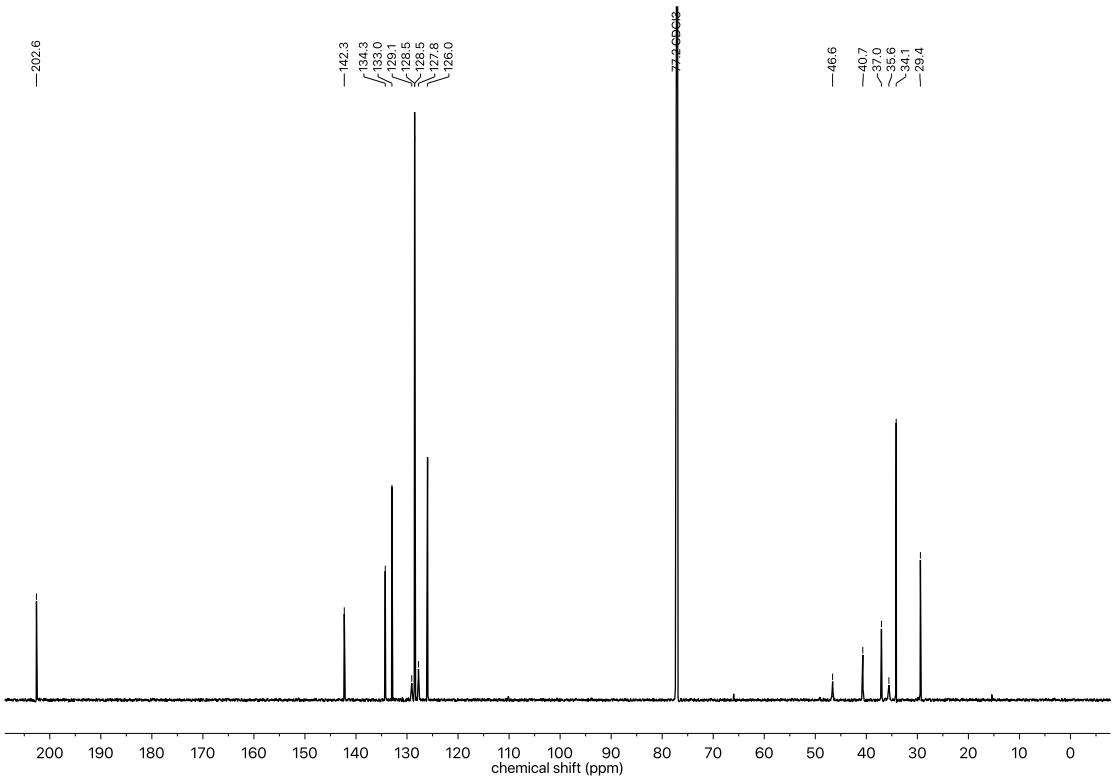


2-((1,7-*cis*)-7-Phenethylcyclohepta-2,5-dien-1-yl)acetaldehyde (112y)

^{1}H NMR:

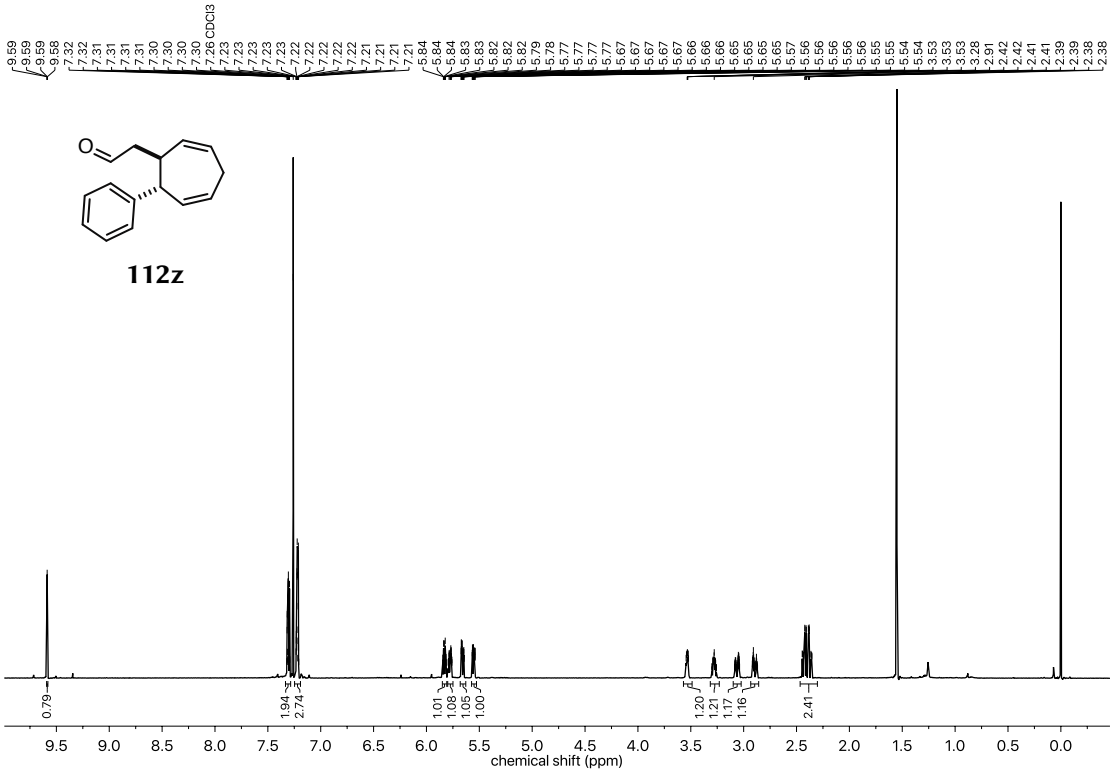


^{13}C NMR:

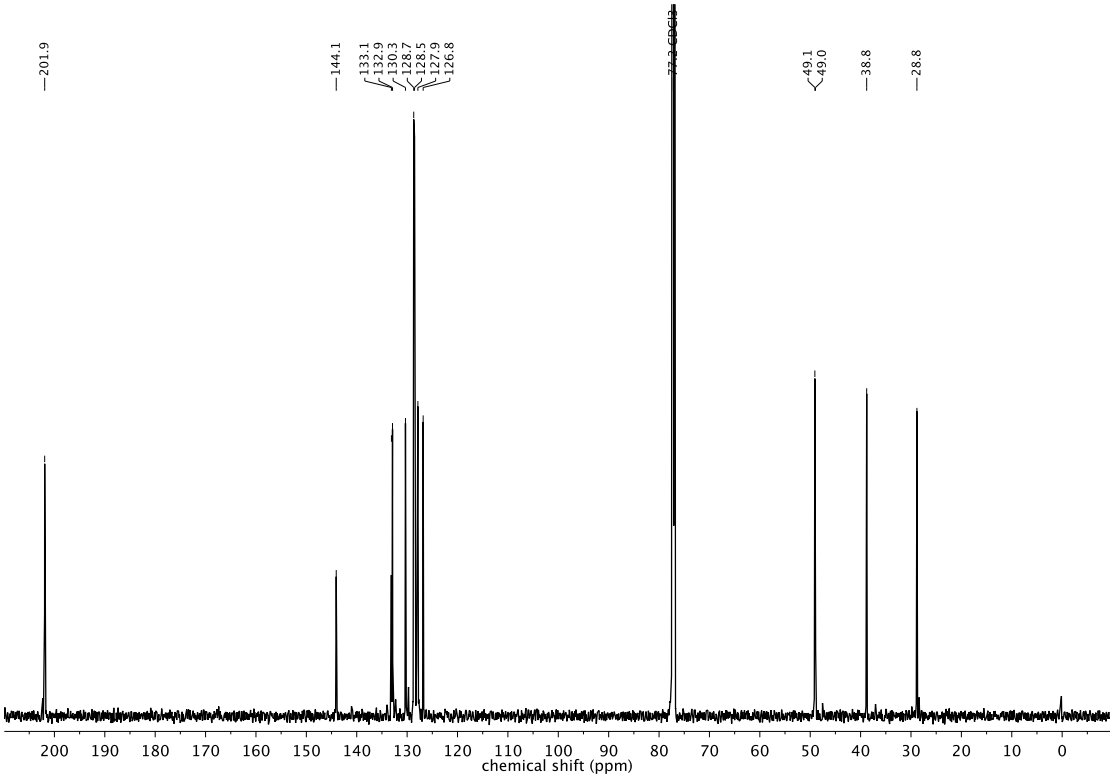


2-((1,7-*trans*)-7-Phenylcyclohepta-2,5-dien-1-yl)acetaldehyde (112z)

^{1}H NMR:

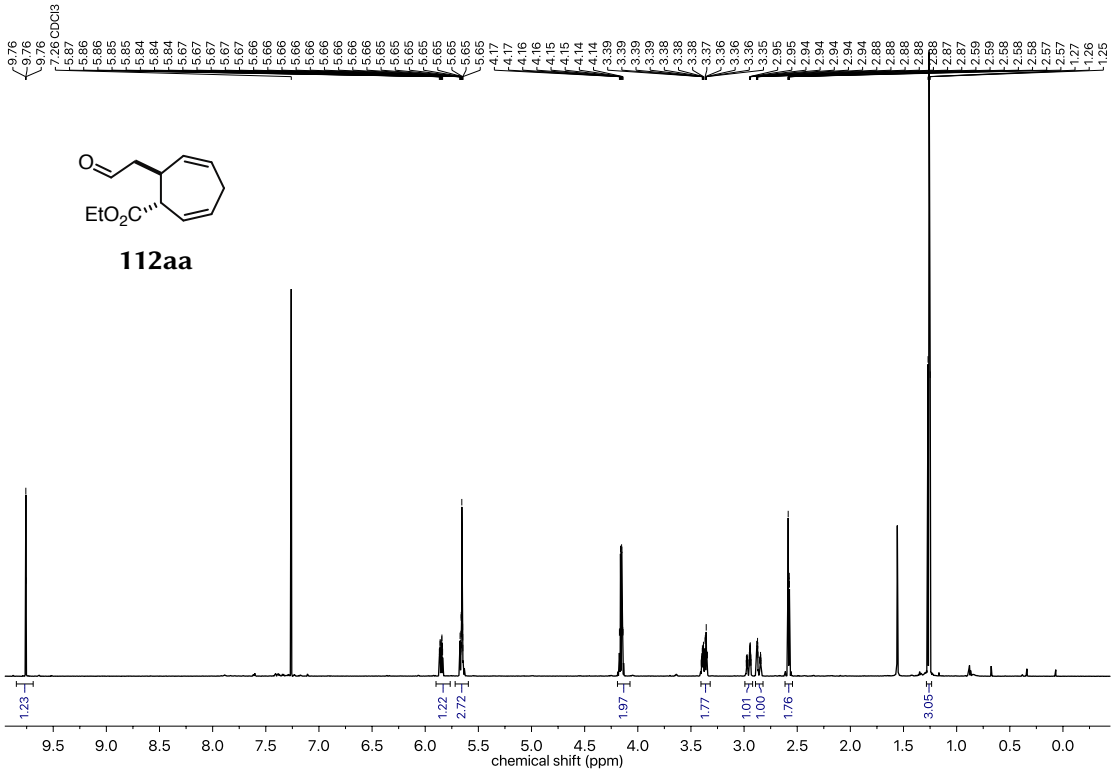


^{13}C NMR:

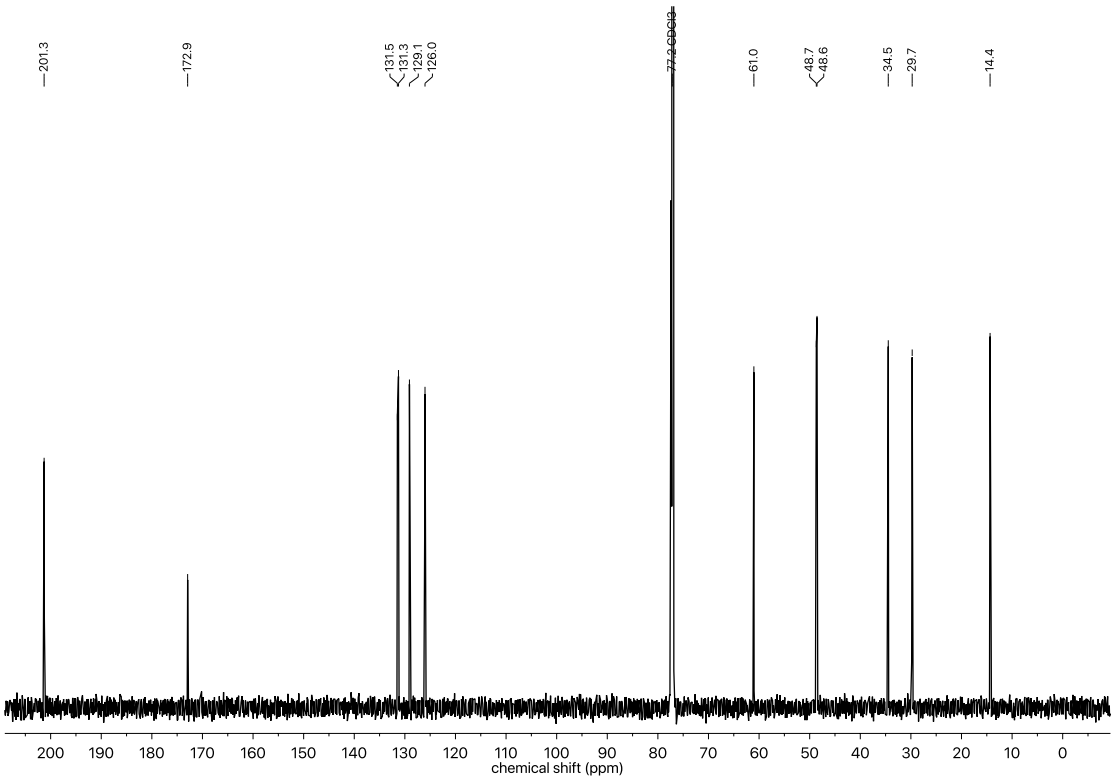


Ethyl (1,7-*trans*)-7-(2-Oxoethyl)cycloheptа-2,5-diene-1-carboxylate (112aa)

^{1}H NMR:

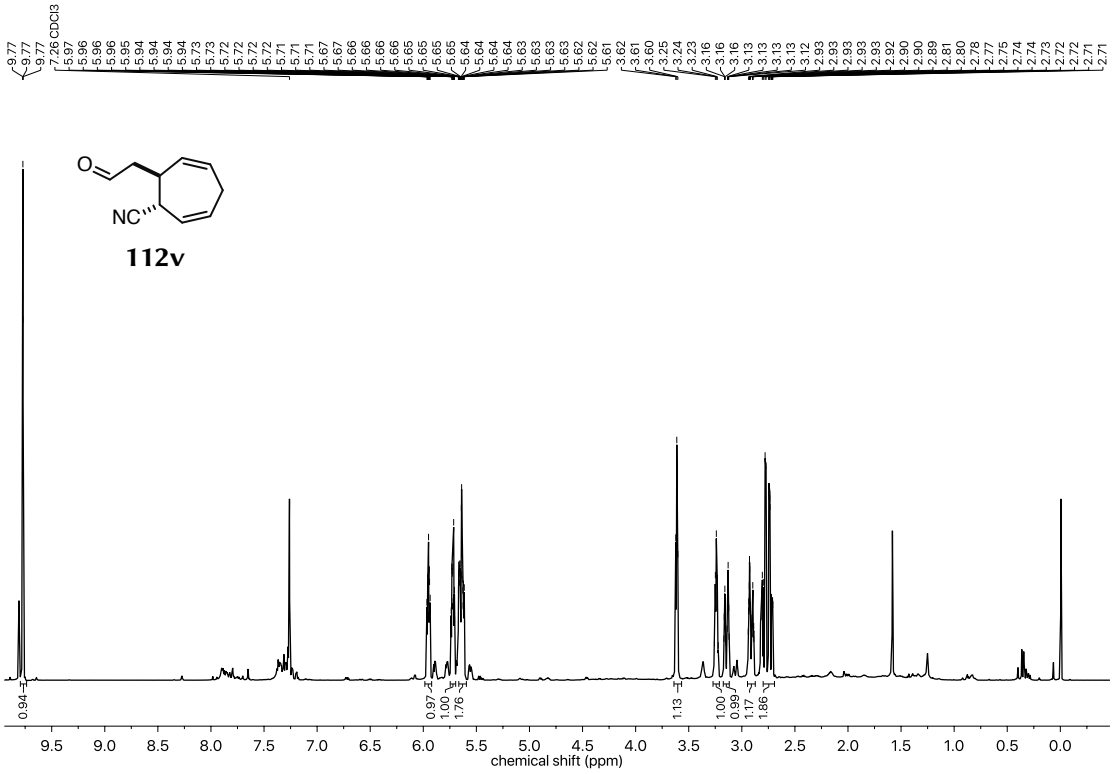


^{13}C NMR:

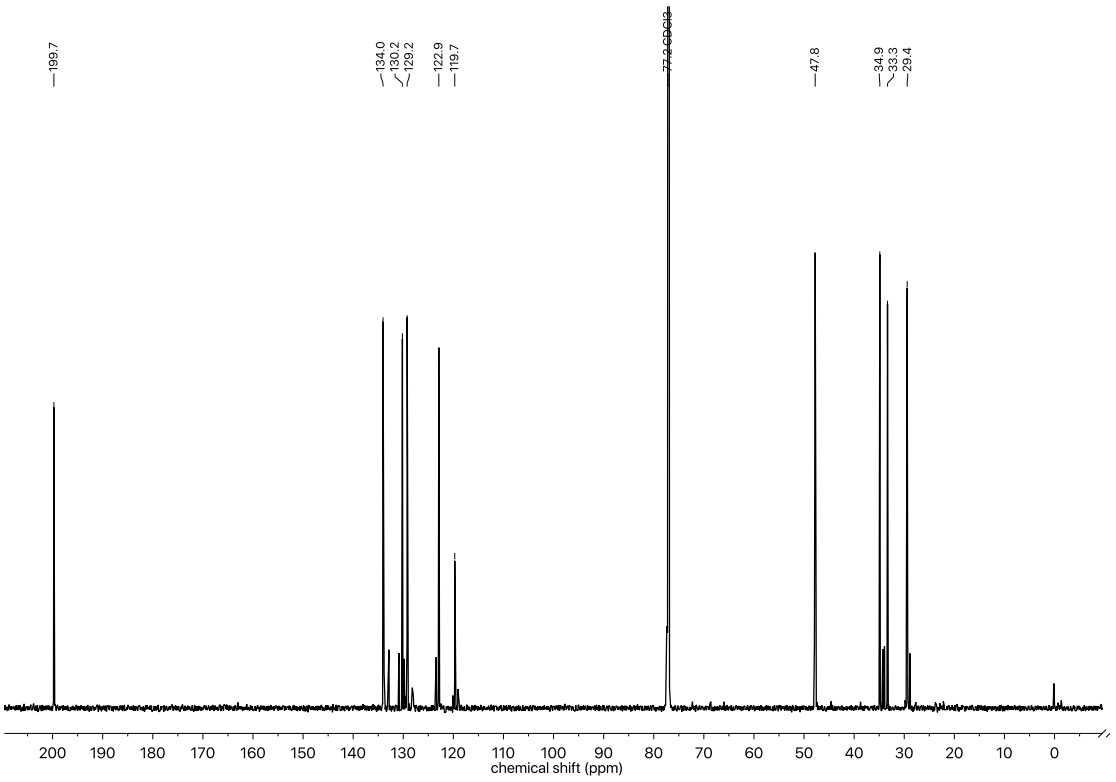


(1,7-*trans*)-7-(2-Oxoethyl)cyclohepta-2,5-diene-1-carbonitrile (112v)

^{1}H NMR:

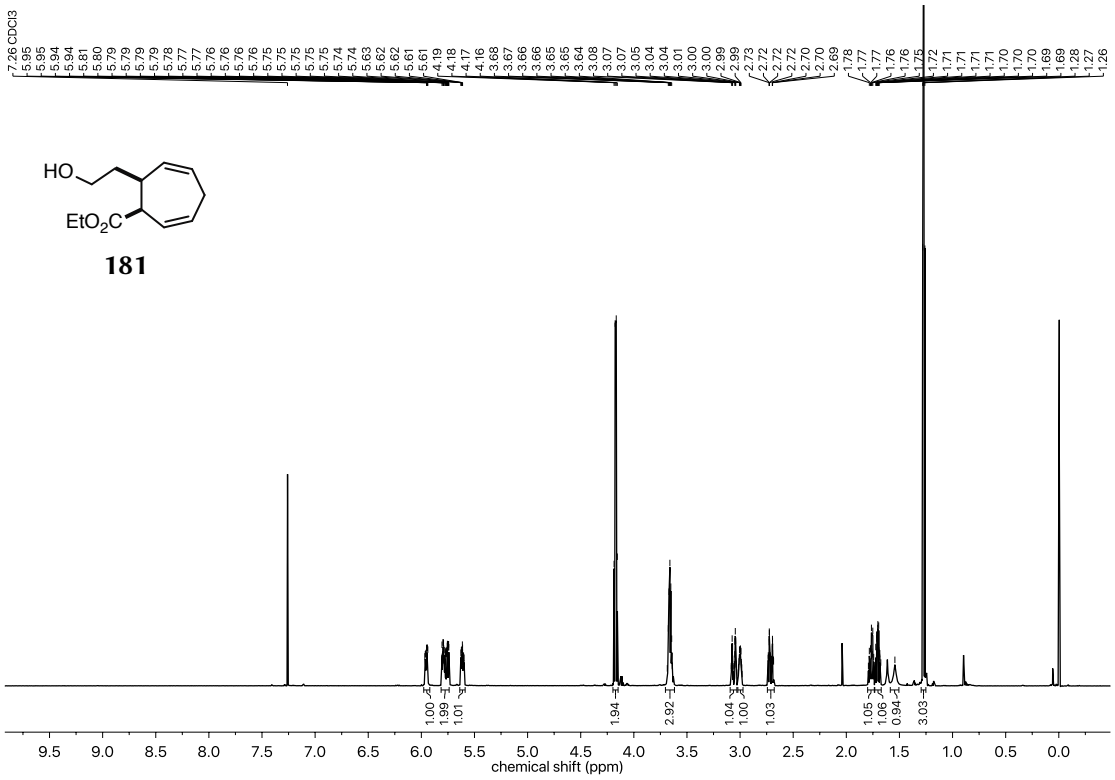


^{13}C NMR:

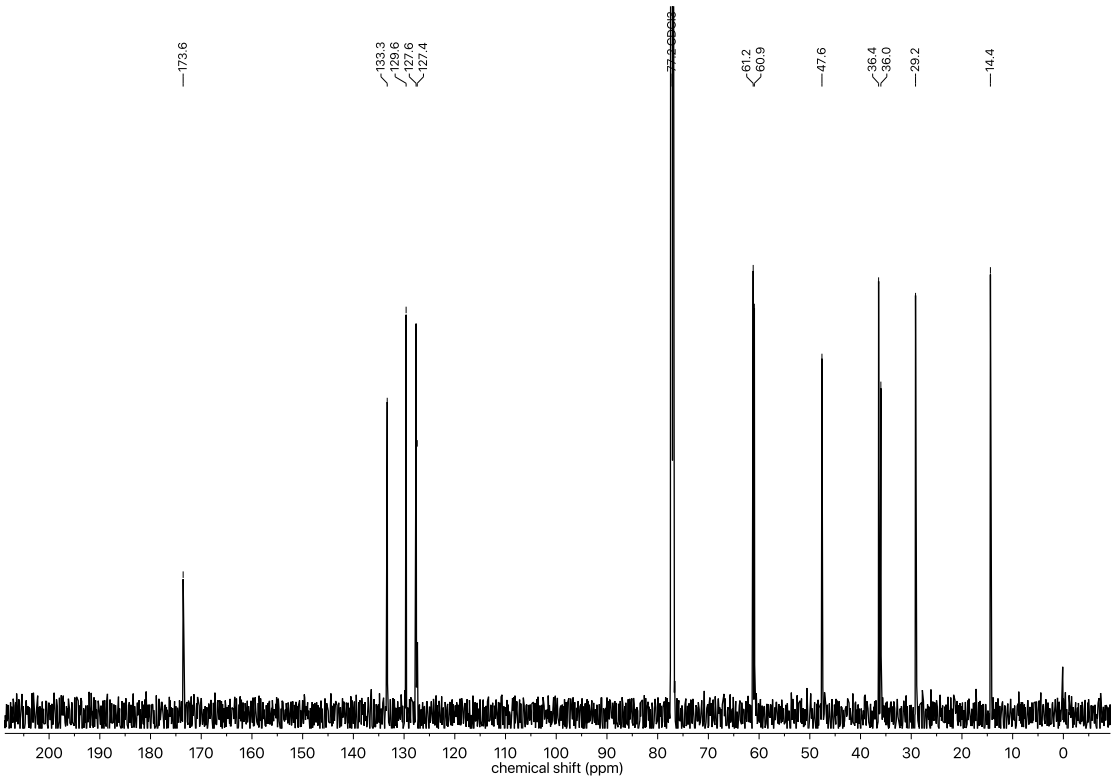


Ethyl (1,7-*cis*)-7-(2-Hydroxyethyl)cyclohepta-2,5-diene-1-carboxylate (181)

^{1}H NMR:

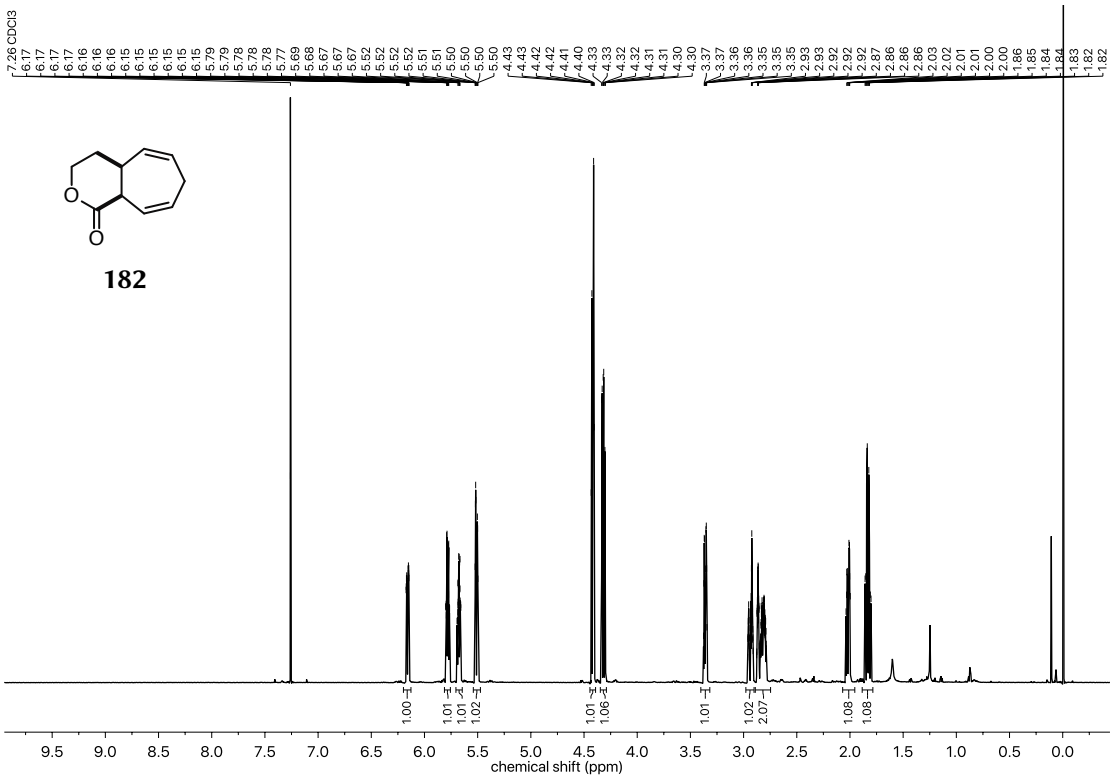


^{13}C NMR:



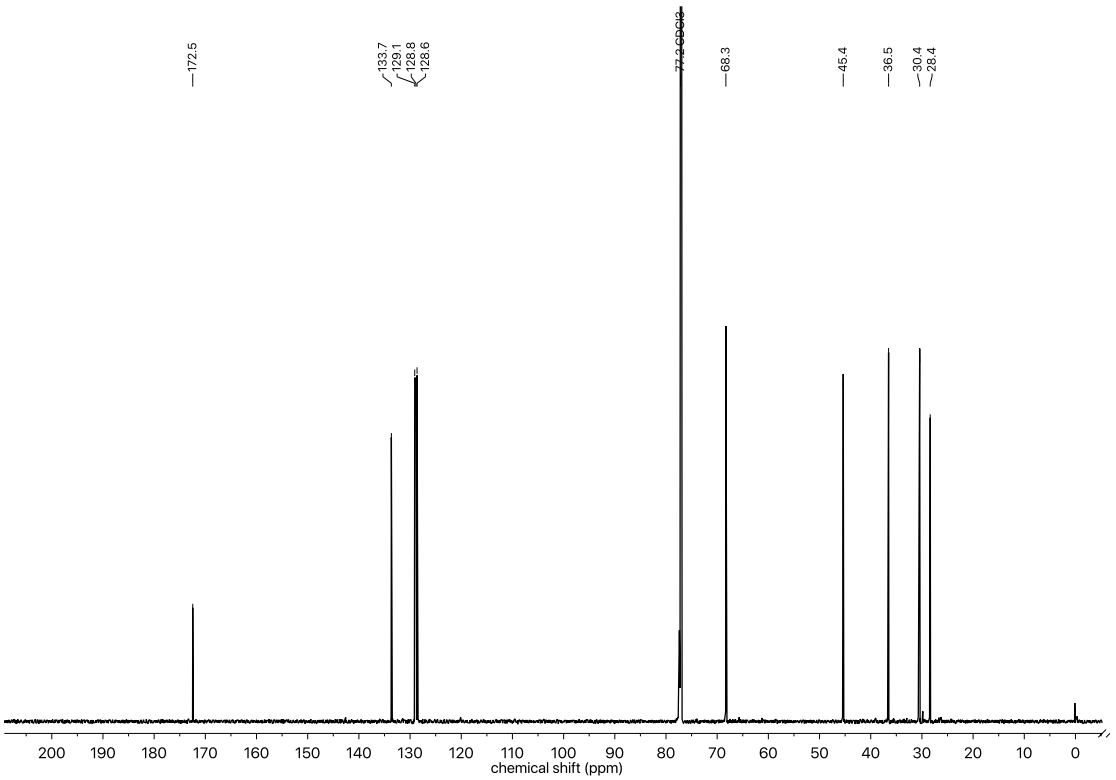
4,4a,7,9a-Tetrahydrocyclohepta[*c*]pyran-1(3*H*)-one (182)

^{1}H NMR:



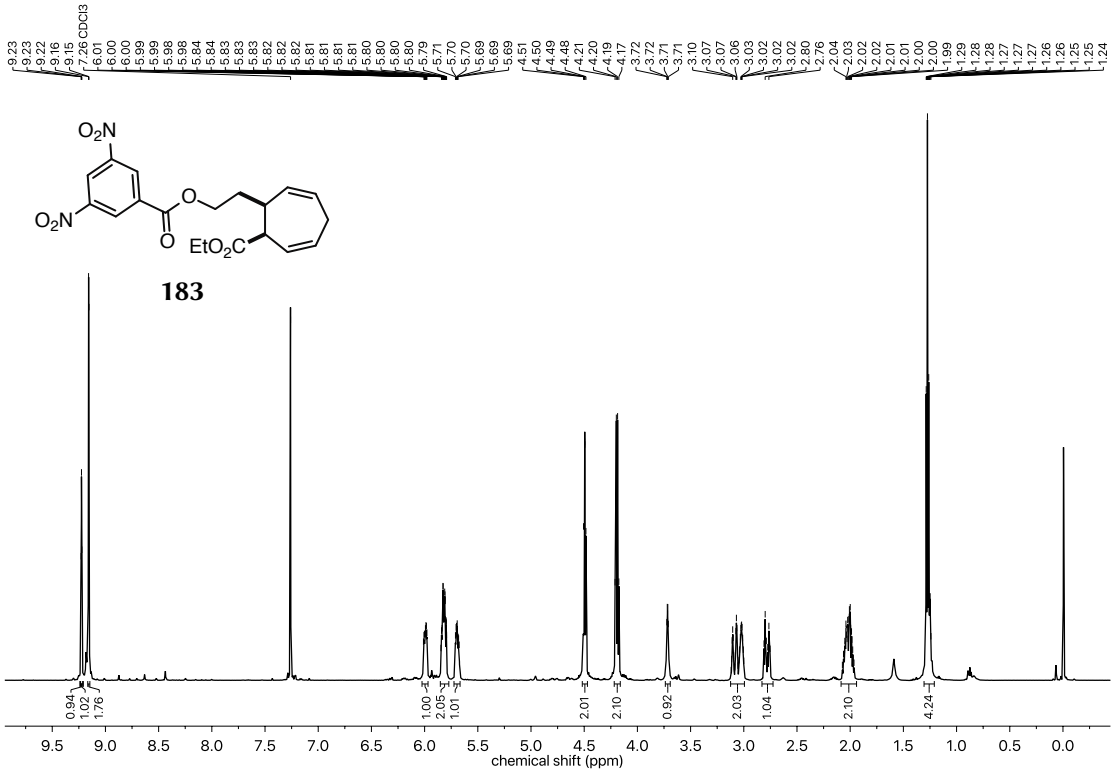
182

^{13}C NMR:

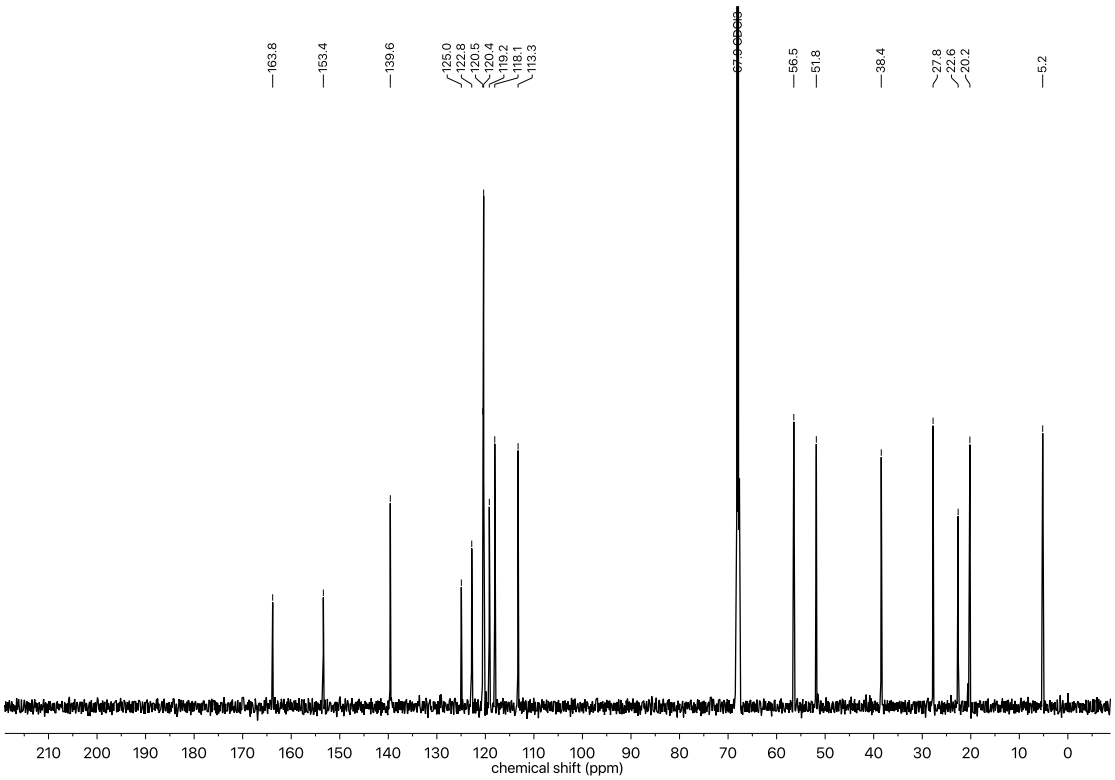


Ethyl 7-(2-((3,5-Dinitrobenzoyl)oxy)ethyl)cyclohepta-2,5-diene-1-carboxylate (183)

^{1}H NMR:

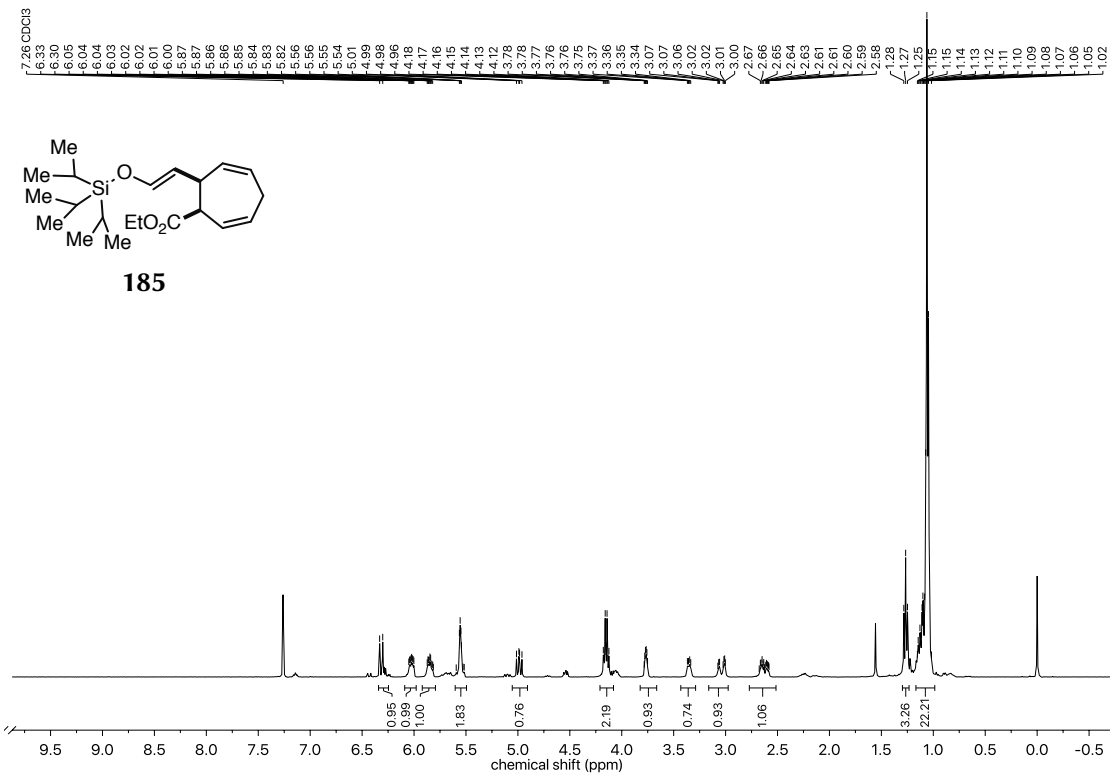


^{13}C NMR:



Ethyl 7-((*E*)-2-((Tri*iso*-propylsilyl)oxy)vinyl)cyclohepta-2,5-diene-1-carboxylate (185)

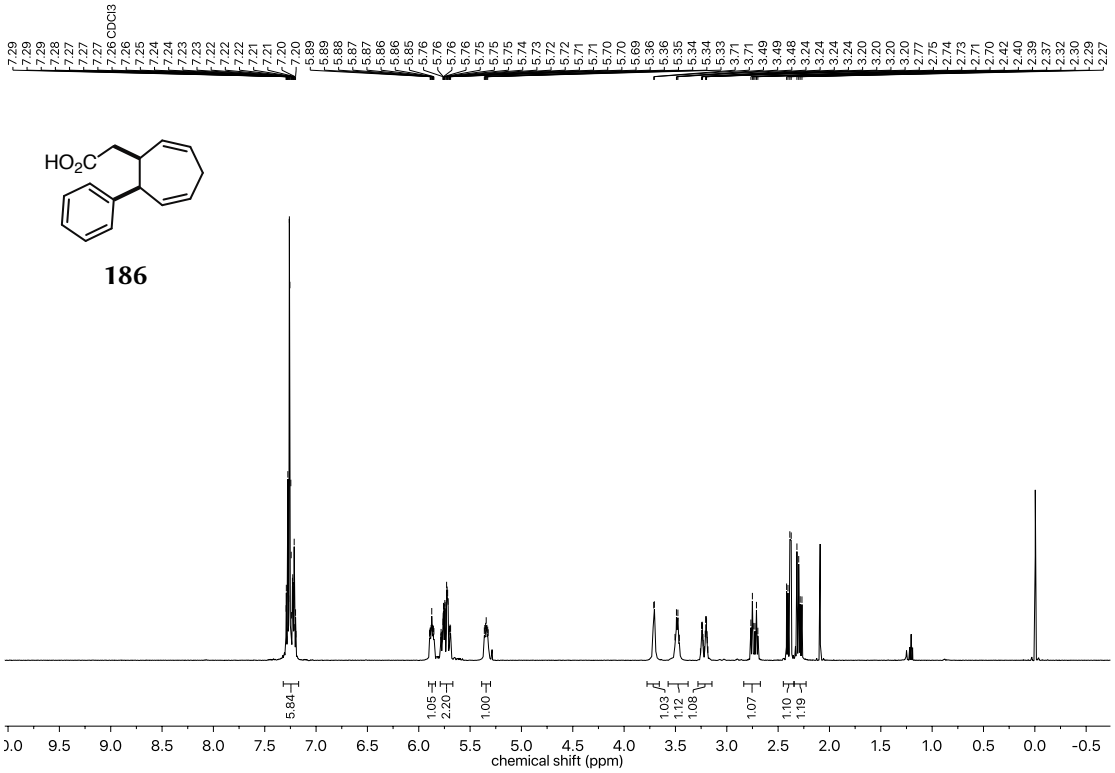
^{1}H NMR:



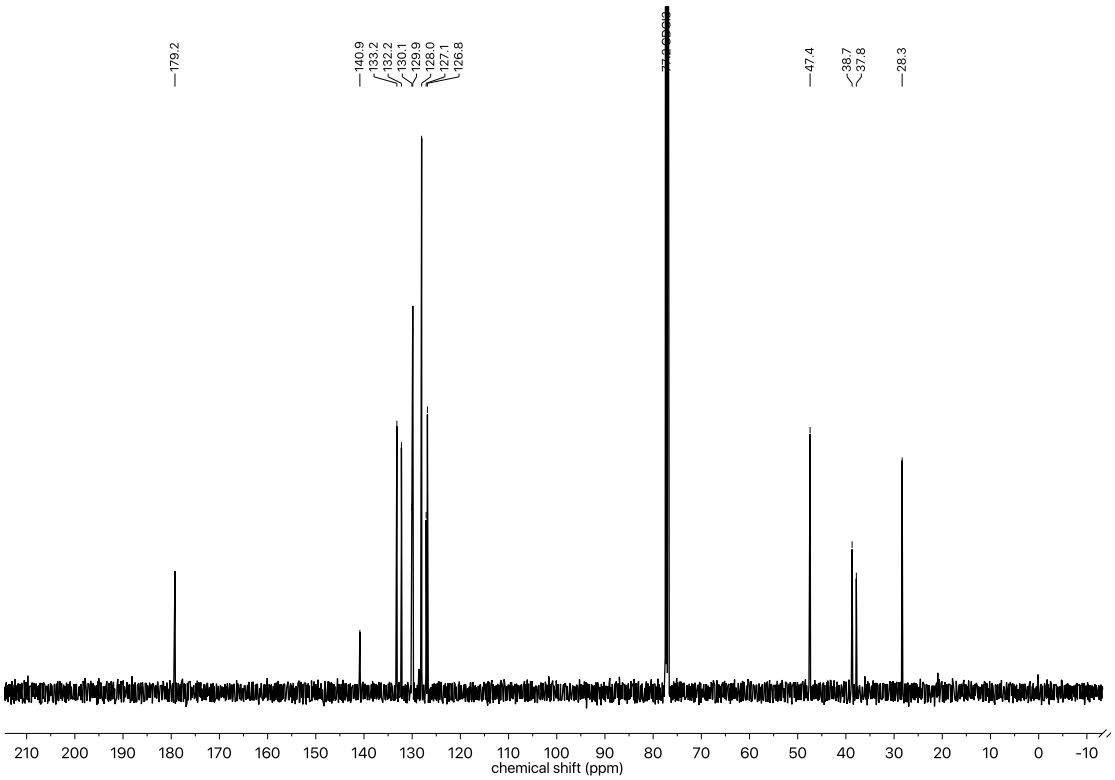
185

2-(7-Phenylcyclohepta-2,5-dien-1-yl)acetic Acid (186)

^{1}H NMR:

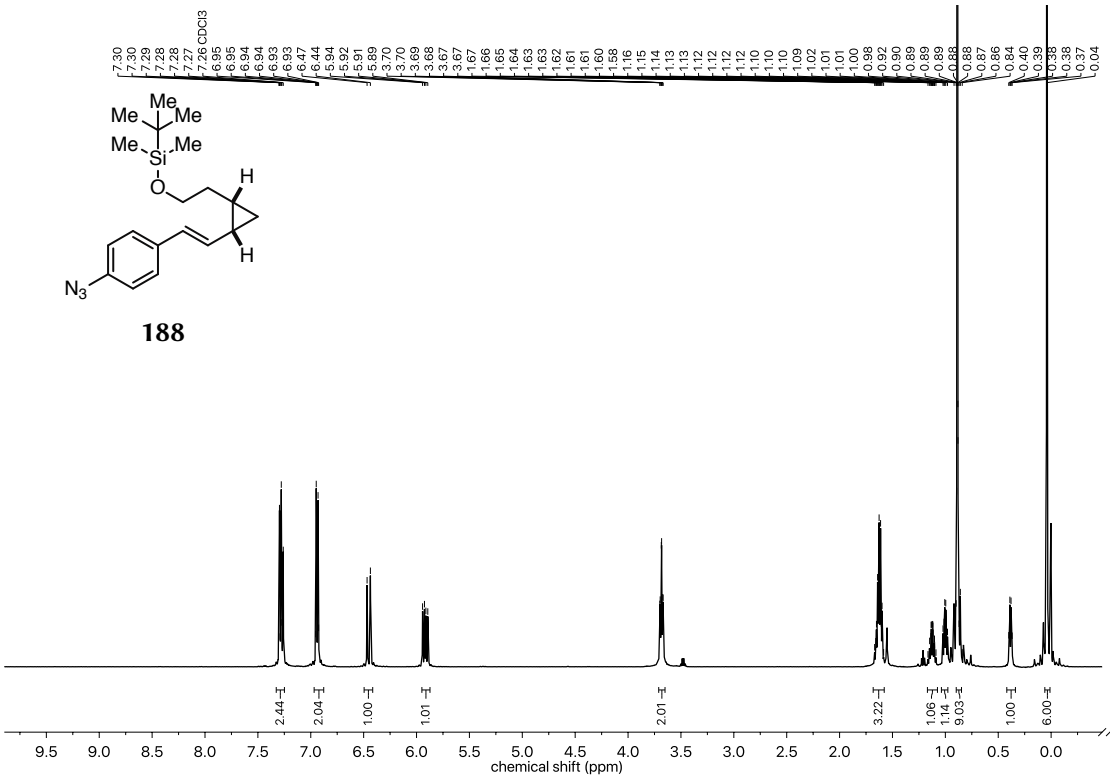


^{13}C NMR:

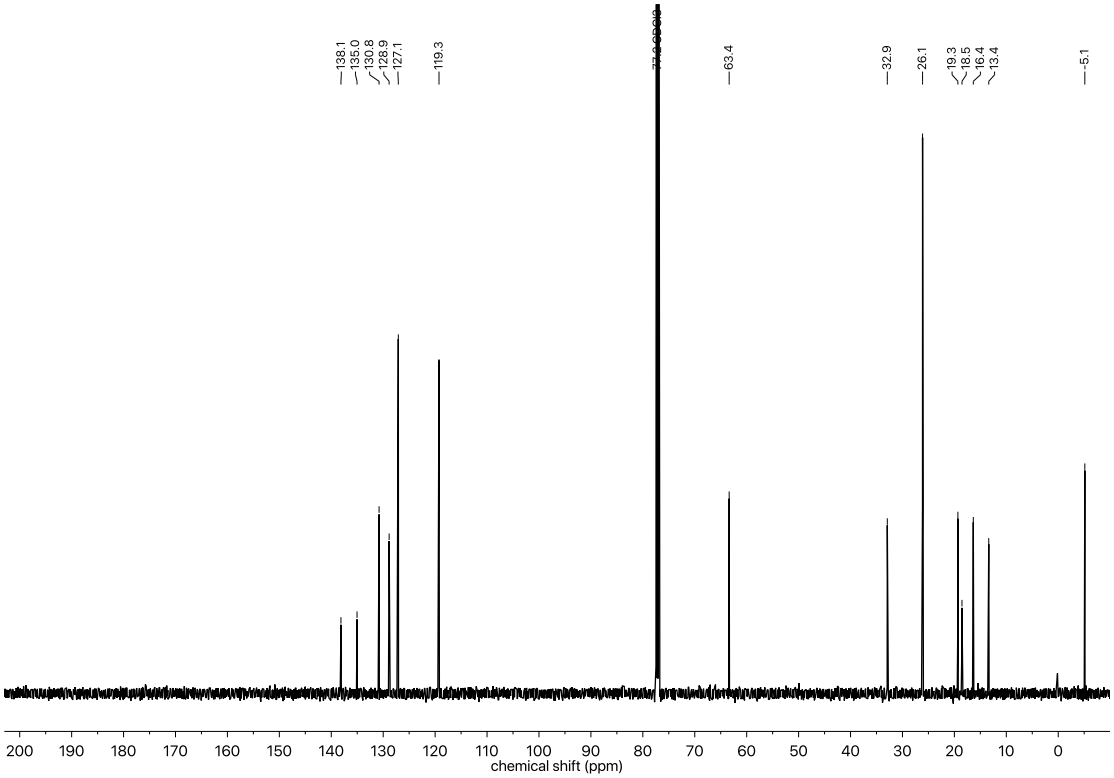


((2-(2-((*E*)-4-Azidostyryl)cyclopropyl)ethoxy)(*tert*-butyl)dimethylsilane (188)

^{1}H NMR:

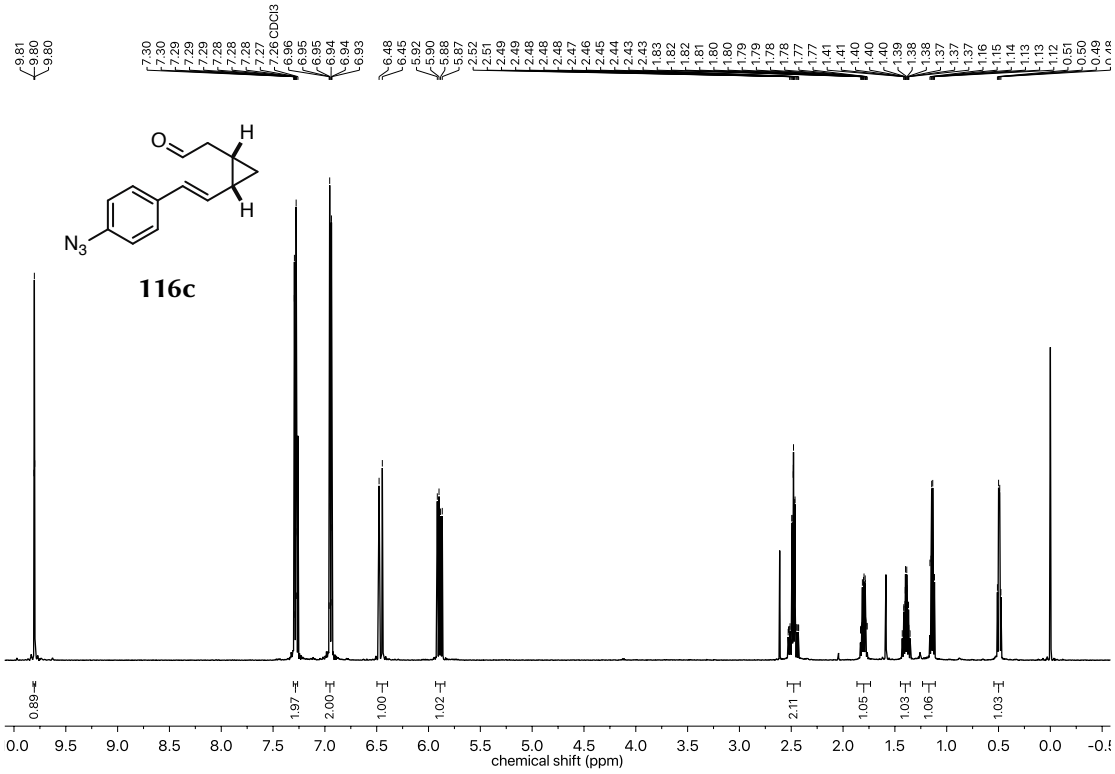


^{13}C NMR:

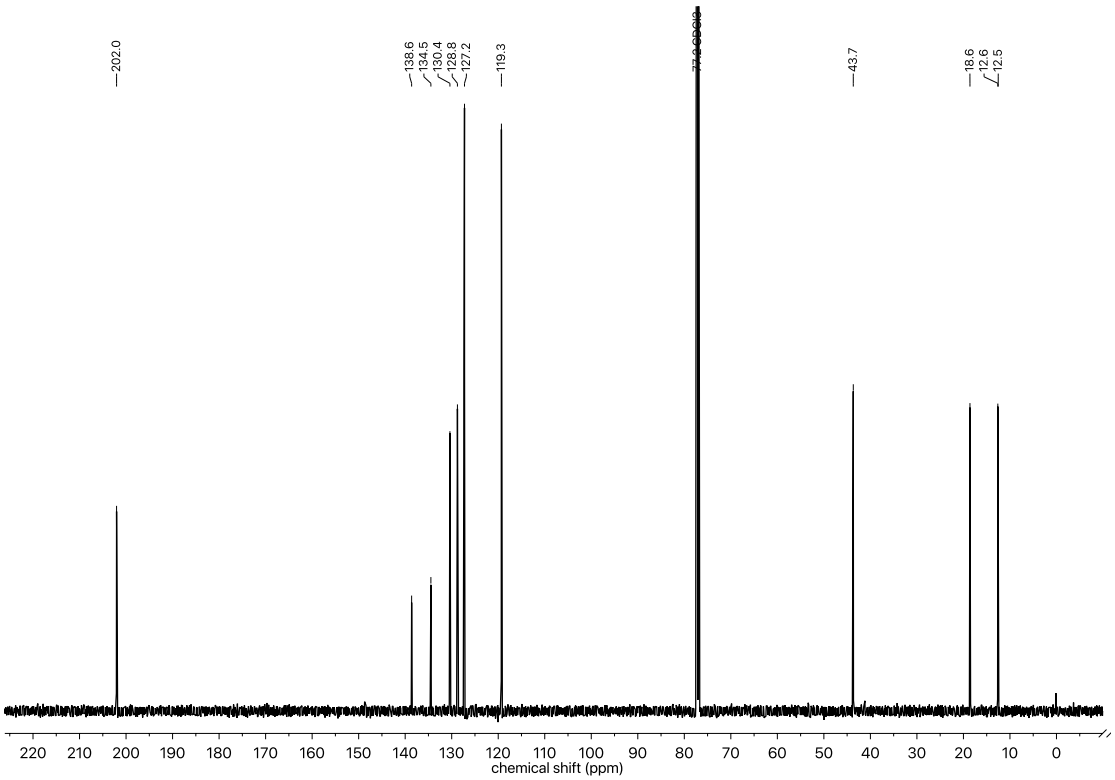


2-(2-((*E*)-4-Azidostyryl)cyclopropyl)acetaldehyde (116c)

^{1}H NMR:

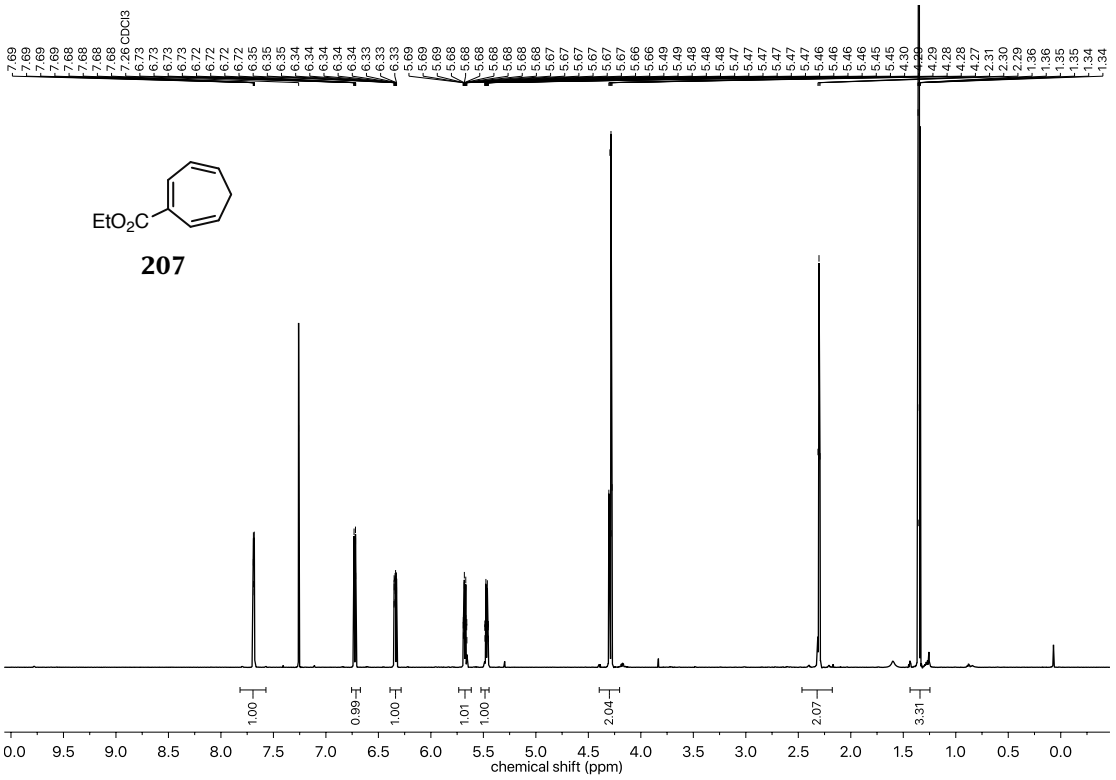


^{13}C NMR:

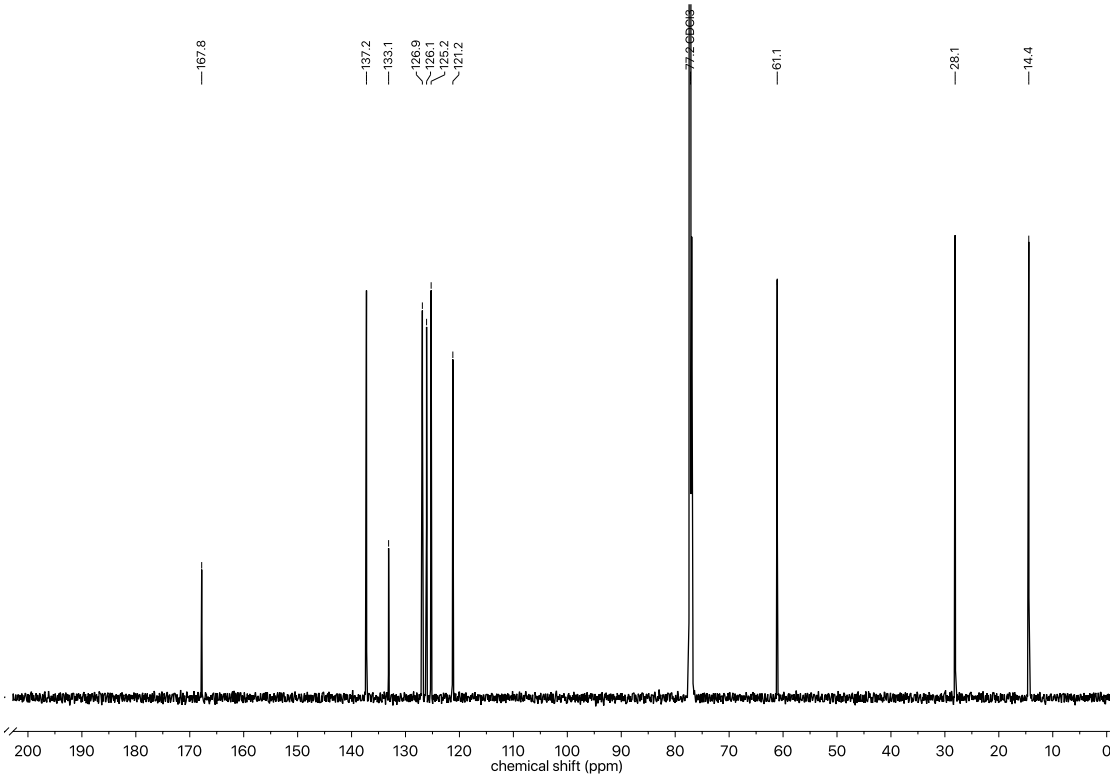


Ethyl Cyclohepta-1,3,6-triene-1-carboxylate (207)

^{1}H NMR:

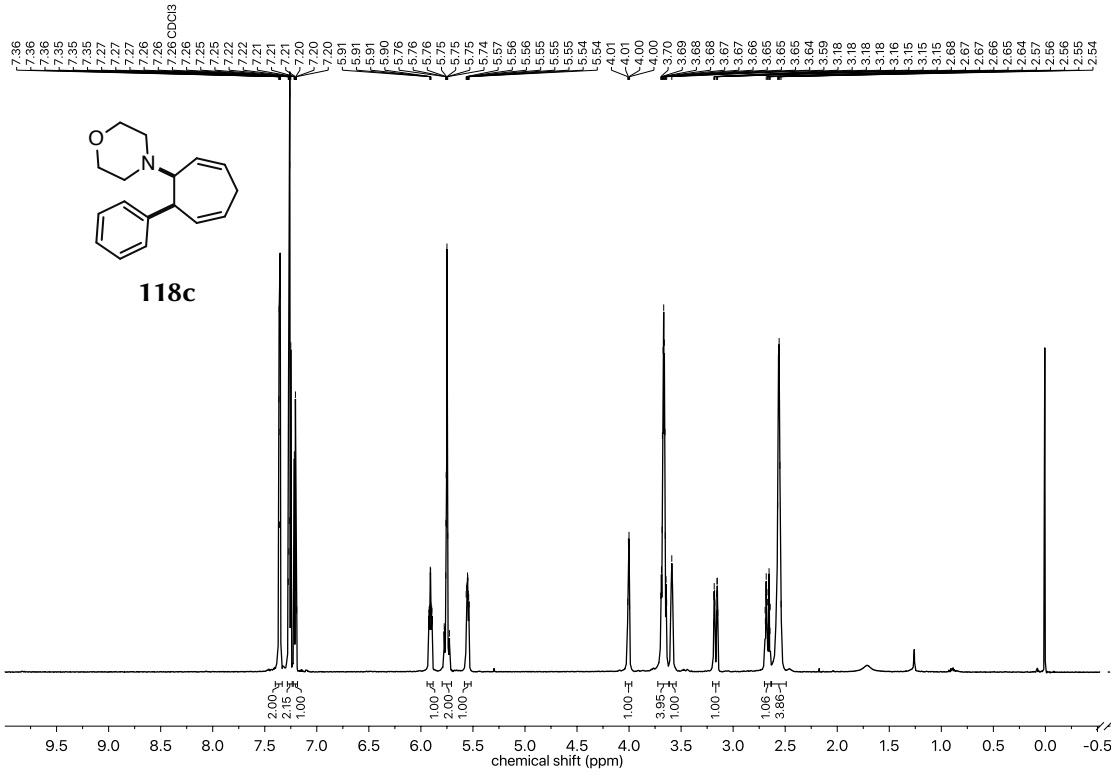


^{13}C NMR:

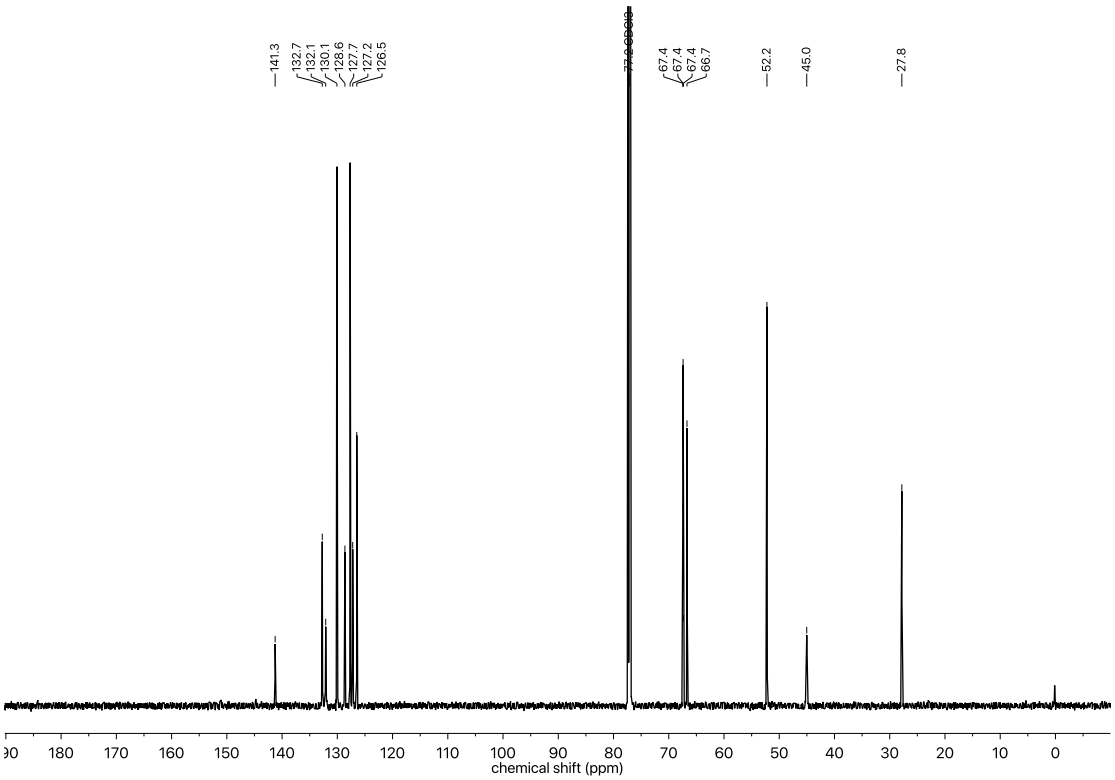


4-(7-Phenylcyclohepta-2,5-dien-1-yl)morpholine (118c)

^{1}H NMR:

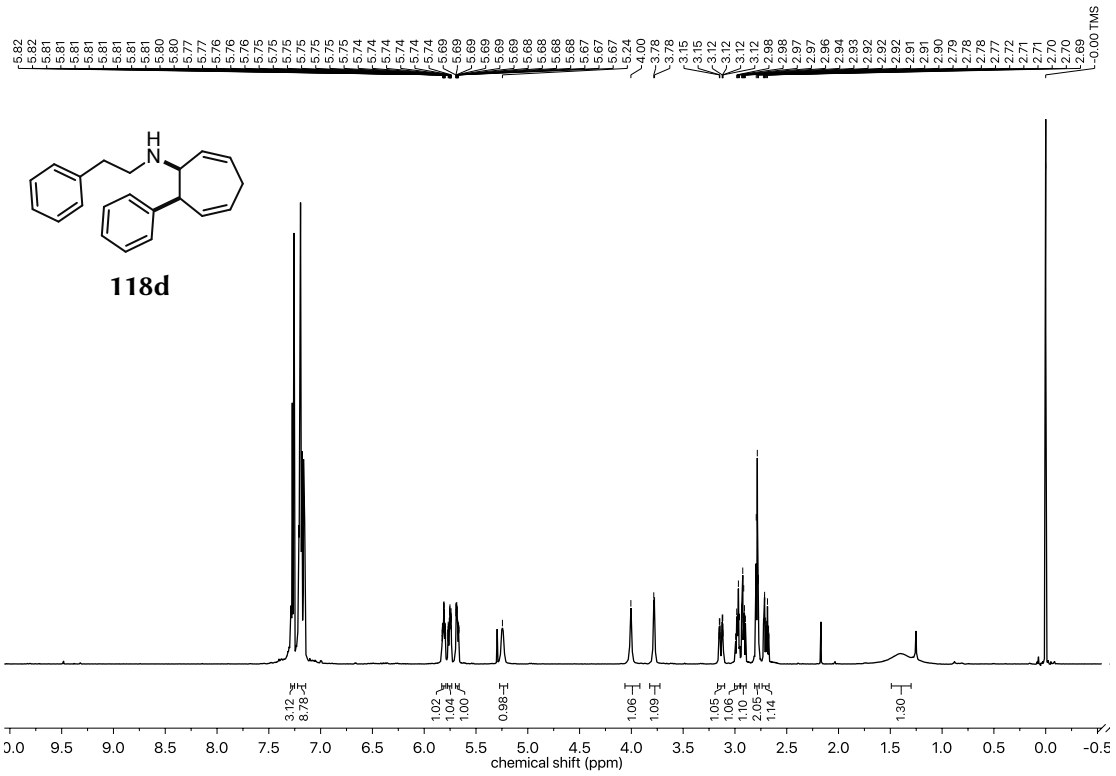


^{13}C NMR:

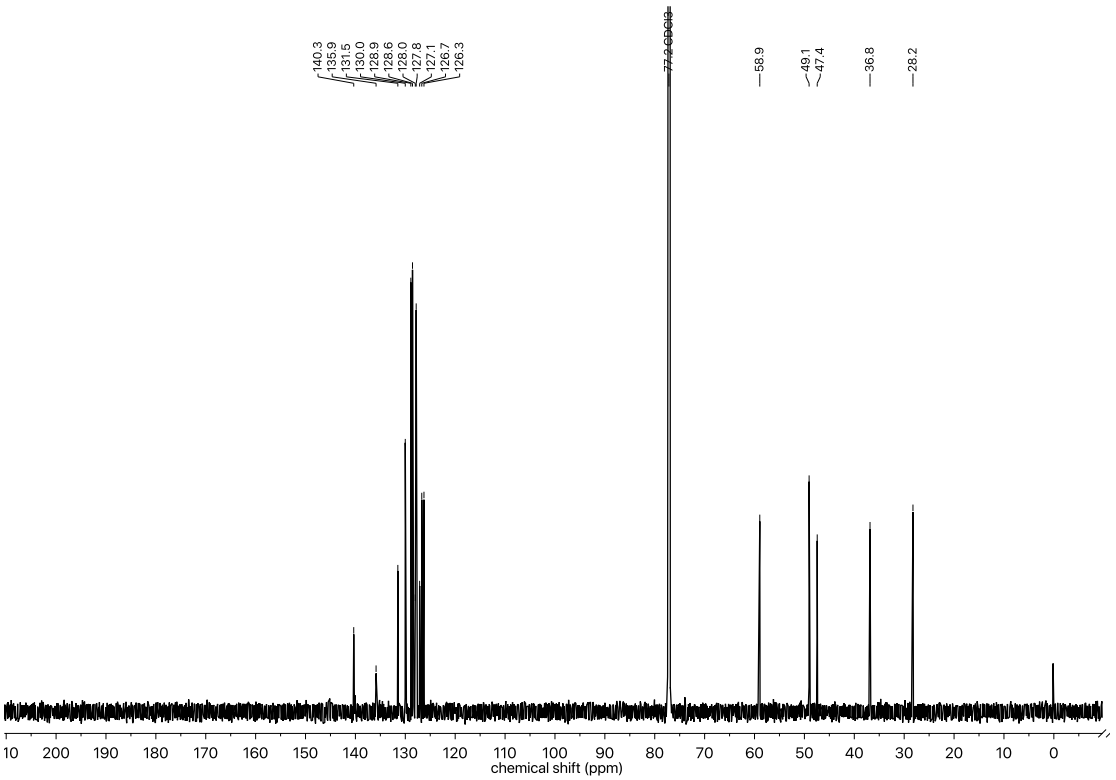


N-Phenethyl-7-phenylcyclohepta-2,5-dien-1-amine (118d)

^{1}H NMR:

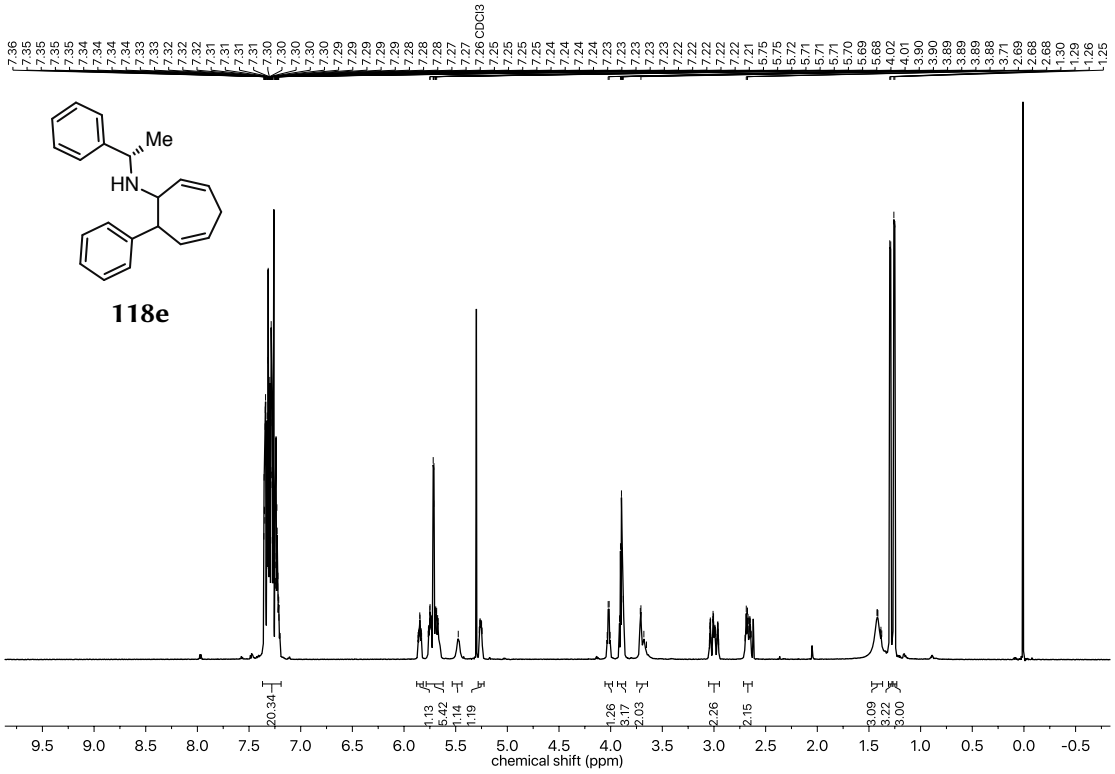


^{13}C NMR:

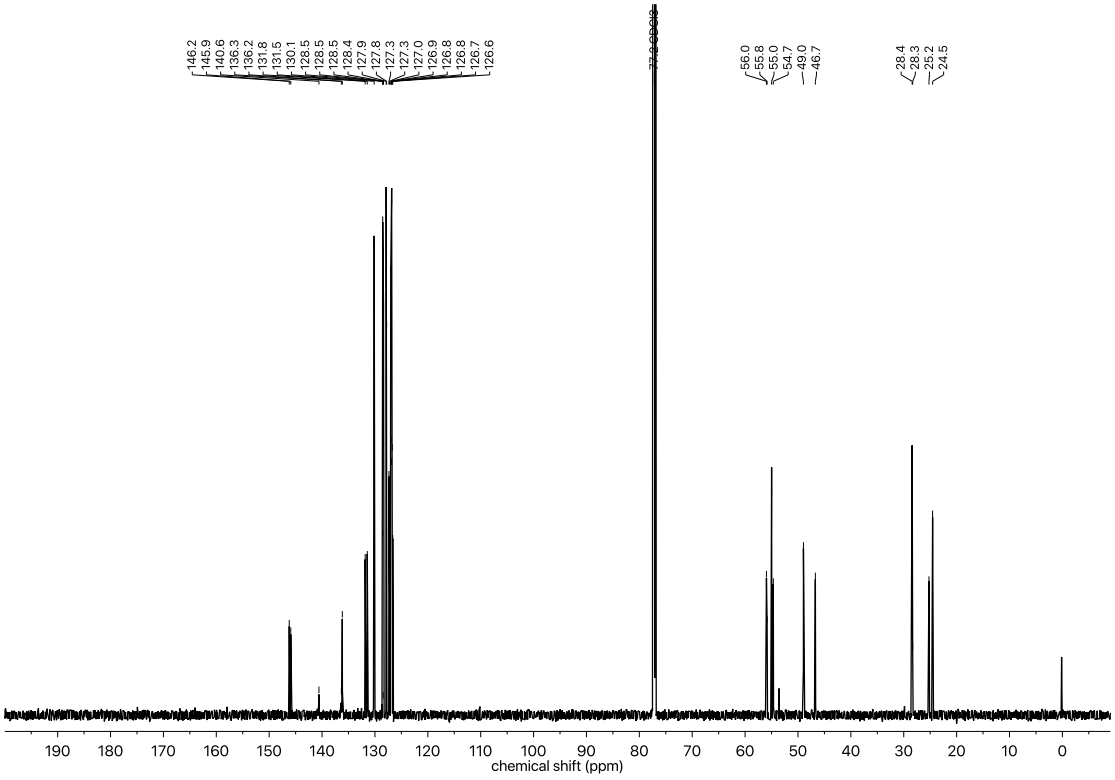


7-Phenyl-*N*-(1-phenylethyl)cyclohepta-2,5-dien-1-amine (118e)

^{1}H NMR:

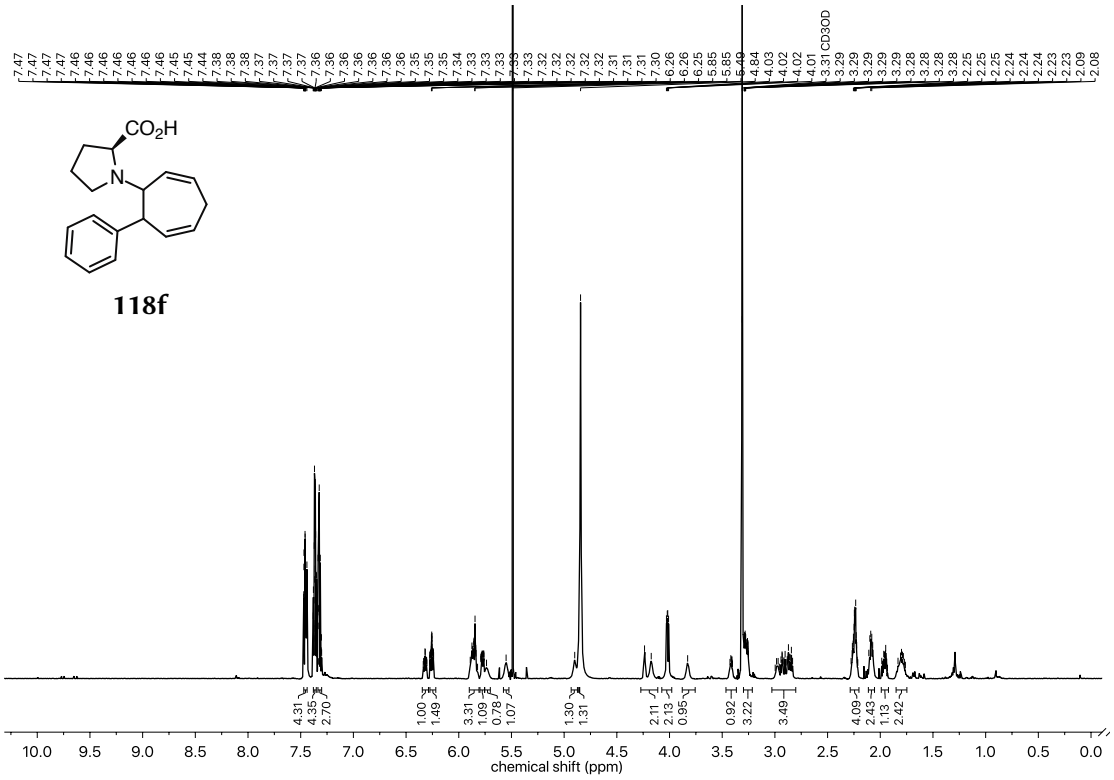


^{13}C NMR:

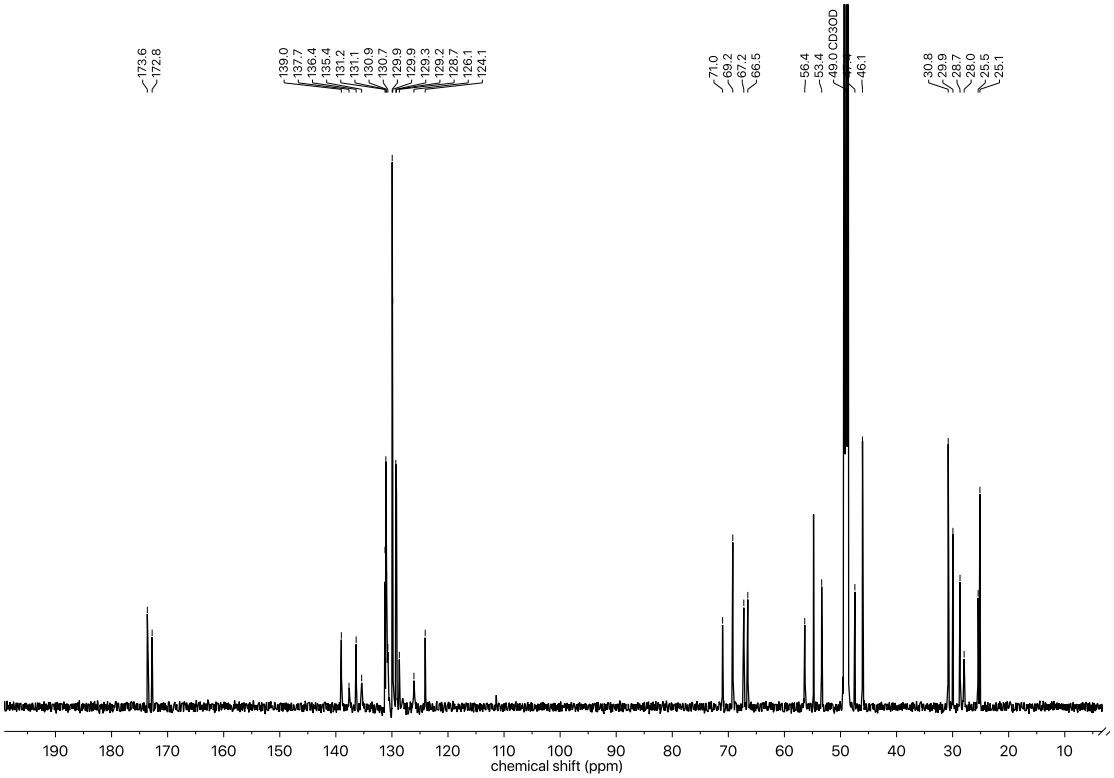


(7-Phenylcyclohepta-2,5-dien-1-yl)-L-proline (118f)

^{1}H NMR:

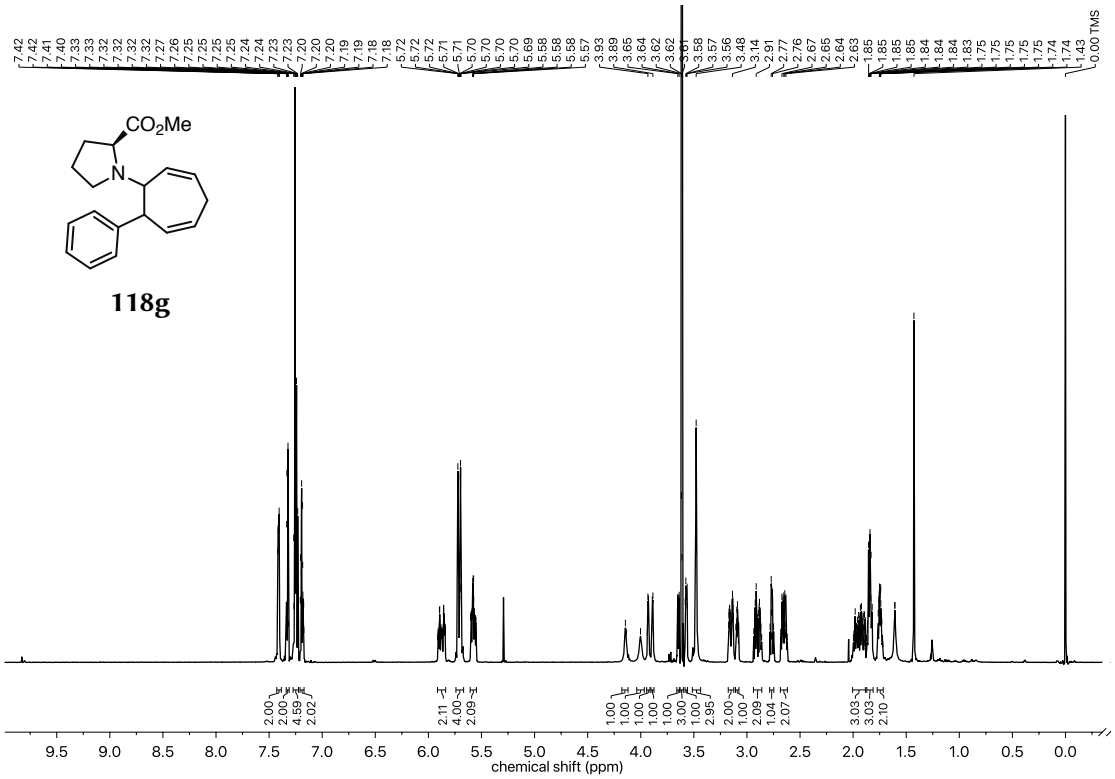


^{13}C NMR:

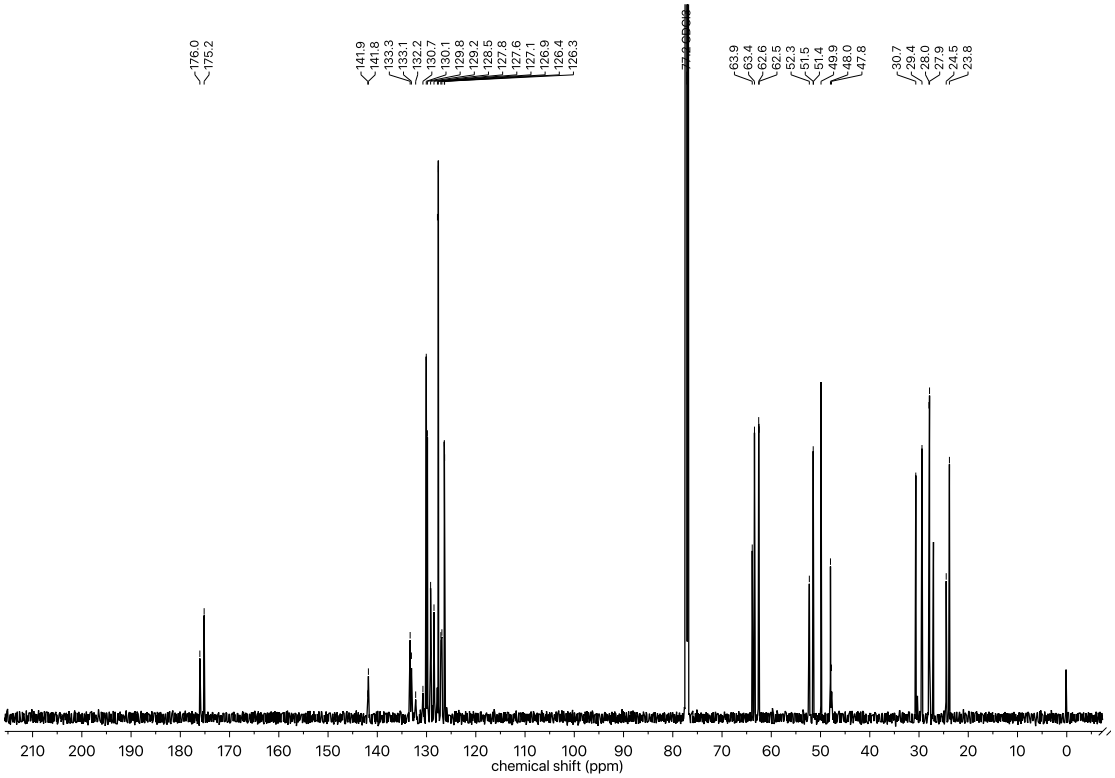


Methyl-(7-phenylcyclohepta-2,5-dien-1-yl)-L-prolinate (118g)

^{1}H NMR:

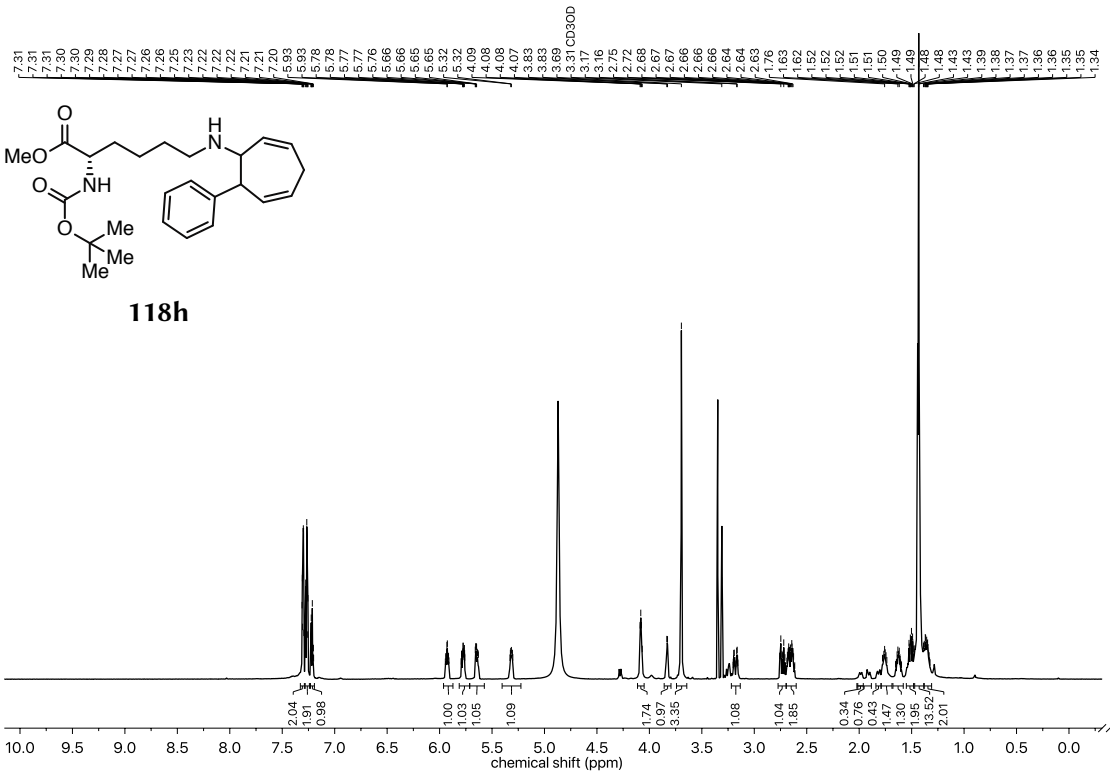


^{13}C NMR:

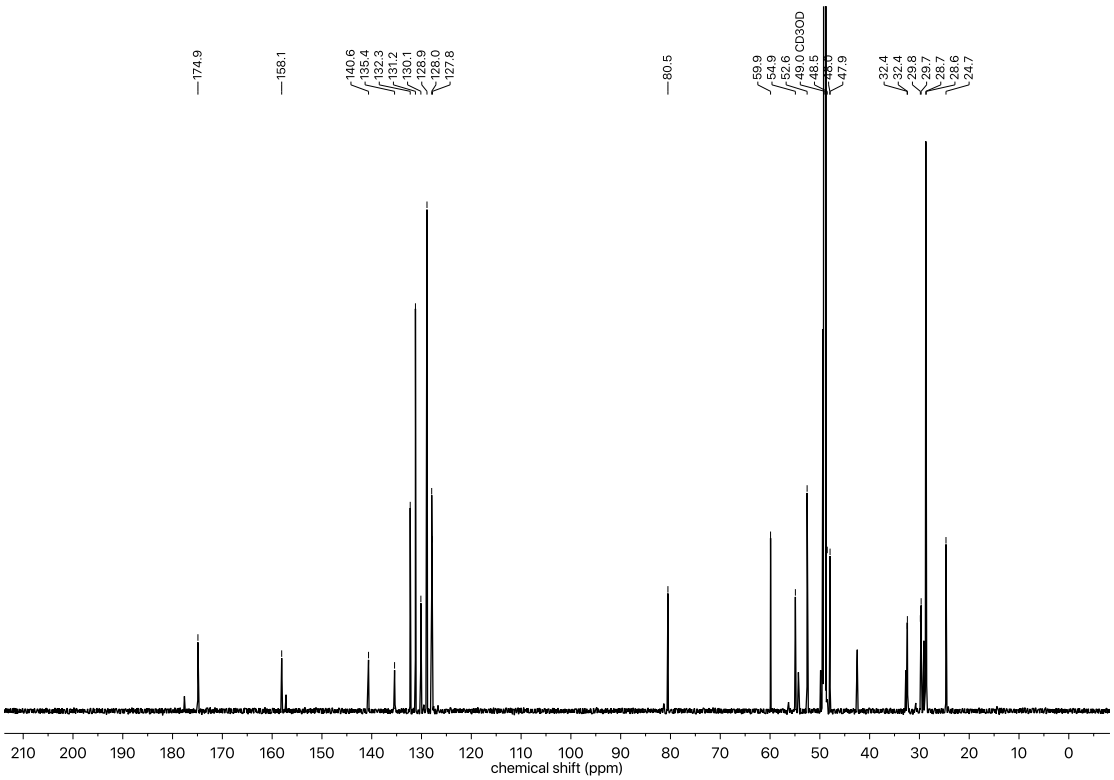


Methyl-N^2-(*tert*-butoxycarbonyl)-N^6-(7-phenylcyclohepta-2,5-dien-1-yl)-L-lysinate (118h)

^{1}H NMR:

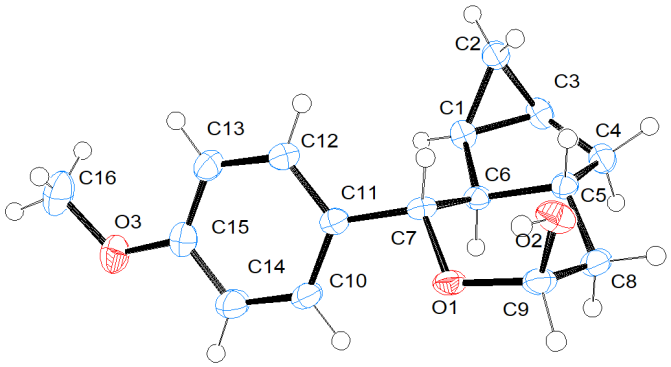


^{13}C NMR:



Crystallographic Data

Lactol 158



Crystal data und structure refinement of lactol **158**.

Empirical Formula	$C_{16}H_{20}O_3$
Formula Weight	260.33
Temperature [K]	100
Wavelength [pm]	154.178
Crystal System	Tetragonal
Space Group	$I4_1/a$
Unit Cell Dimensions	a = 33.3023(9) Å, α = 90° b = 33.3023(9) Å, β = 90° c = 5.2359(2) Å, γ = 90°
Volume [Å^3]	5806.8(4)
Z	44
Calculated Density [g/cm^3]	1.182
Absorption Coefficient [mm^{-1}]	0.651
F(000)	2208
Crystal Size [mm]	0.32 x 0.09 x 0.09
ϑ-Range for Data Collection	3.754–68.333°

Crystal data und structure refinement of lactol **158**.

Limiting Indices	$-37 \leq h \leq 31$, $-38 \leq k \leq 40$, $-6 \leq l \leq 5$
Reflections Collected	6949
Independent Reflections	2648
Completeness to $\vartheta = 67.67$	99.3%
Refinement Method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	1.171
Final R Indices [$I > 2\sigma(I)$]	$R_1 = 0.0656$, $wR_2 = 0.2429$
R Indices (all data)	$R_1 = 0.0790$, $wR_2 = 0.2554$
Extinction Coefficient	0.00074(18)
Largest diff. peak and hole	1.534 and -0.237 $e^-/Å^{-3}$

Bond lengths [Å] of molecule **158**.

O1	C9	1.451(4)
O1	C7	1.452(3)
O2	C9	1.393(4)
O2	H2	0.8400
O3	C15	1.365(4)
O3	C16	1.434(4)
C11	C12	1.375(4)
C11	C10	1.387(4)
C11	C7	1.517(4)
C7	C6	1.520(4)
C7	H7	1.0000
C1	C6	1.506(4)
C1	C2	1.512(4)
C1	C3	1.524(4)
C1	H1	1.0000
C2	C3	1.506(4)
C2	H2A	0.9900
C2	H2B	0.9900

Bond lengths [Å] of molecule **158**.

C6	C5	1.537(4)
C6	H6	1.0000
C12	C13	1.396(5)
C12	H12	0.9500
C4	C3	1.525(4)
C4	C5	1.537(4)
C4	H4A	0.9900
C4	H4B	0.9900
C9	C8	1.526(5)
C9	H9	1.0000
C5	C8	1.515(4)
C5	H5	1.0000
C15	C13	1.385(5)
C15	C14	1.395(5)
C3	H3	1.0000
C13	H13	0.9500
C10	C14	1.373(4)
C10	H10	0.9500
C8	H8A	0.9900
C8	H8B	0.9900
C14	H14	0.9500
C16	H16A	0.9800
C16	H16B	0.9800
C16	H16C	0.9800

Bond angles [°] of molecule **158**.

C9	O1	C7	115.3(2)
C9	O2	H2	109.5
C15	O3	C16	117.5(3)
C12	C11	C10	118.1(3)
C12	C11	C7	119.4(3)
C10	C11	C7	122.4(3)
O1	C7	C11	108.1(2)
O1	C7	C6	107.4(2)
C11	C7	C6	113.6(2)
O1	C7	H7	109.2
C11	C7	H7	109.2
C6	C7	H7	109.2
C6	C1	C2	119.3(2)
C6	C1	C3	106.2(2)
C2	C1	C3	59.49(19)
C6	C1	H1	118.7
C2	C1	H1	118.7
C3	C1	H1	118.7
C3	C2	C1	60.65(19)
C3	C2	H2A	117.7
C1	C2	H2A	117.7
C3	C2	H2B	117.7
C1	C2	H2B	117.7
H2A	C2	H2B	114.8
C1	C6	C7	120.4(2)
C1	C6	C5	104.8(2)
C7	C6	C5	109.5(2)
C1	C6	H6	107.1
C7	C6	H6	107.1
C5	C6	H6	107.1
C11	C12	C13	121.5(3)
C11	C12	H12	119.2

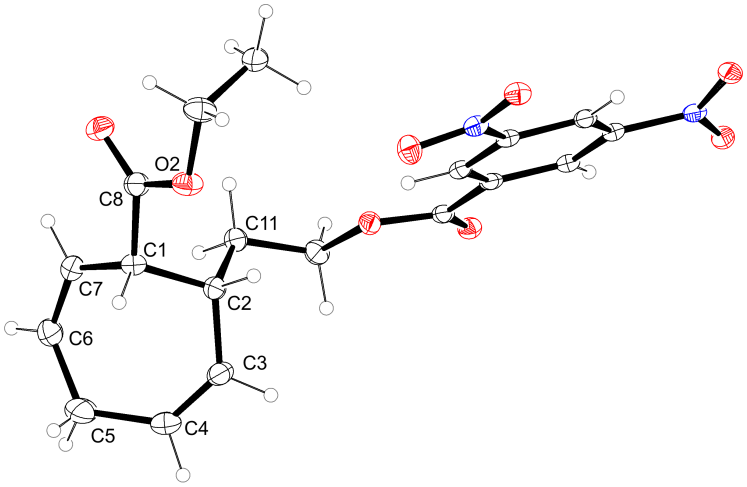
Bond angles [°] of molecule **158**.

C13	C12	H12	119.2
C3	C4	C5	103.6(2)
C3	C4	H4A	111.0
C5	C4	H4A	111.0
C3	C4	H4B	111.0
C5	C4	H4B	111.0
H4A	C4	H4B	109.0
O2	C9	O1	110.9(2)
O2	C9	C8	108.2(2)
O1	C9	C8	112.5(2)
O2	C9	H9	108.4
O1	C9	H9	108.4
C8	C9	H9	108.4
C8	C5	C6	108.9(2)
C8	C5	C4	120.6(3)
C6	C5	C4	103.6(2)
C8	C5	H5	107.7
C6	C5	H5	107.7
C4	C5	H5	107.7
O3	C15	C13	125.1(3)
O3	C15	C14	116.0(3)
C13	C15	C14	118.9(3)
C2	C3	C1	59.85(19)
C2	C3	C4	117.5(3)
C1	C3	C4	108.0(2)
C2	C3	H3	119.0
C1	C3	H3	119.0
C4	C3	H3	119.0
C15	C13	C12	119.6(3)
C15	C13	H13	120.2
C12	C13	H13	120.2
C14	C10	C11	121.4(3)

Bond angles [°] of molecule **158**.

C14	C10	H10	119.3
C11	C10	H10	119.3
C5	C8	C9	108.1(2)
C5	C8	H8A	110.1
C9	C8	H8A	110.1
C5	C8	H8B	110.1
C9	C8	H8B	110.1
H8A	C8	H8B	108.4
C10	C14	C15	120.4(3)
C10	C14	H14	119.8
C15	C14	H14	119.8
O3	C16	H16A	109.5
O3	C16	H16B	109.5
H16A	C16	H16B	109.5
O3	C16	H16C	109.5
H16A	C16	H16C	109.5
H16B	C16	H16C	109.5

Benzoate 183



Formula: $C_{19}H_{20}N_2O_8$

Unit Cell Parameters: monoclinic, $P2_1/c$, $\alpha = 39.309(2)$, $b = 8.9525(5)$, $c = 10.6436(6)$ Å, $\beta = 93.009(2)$°, $V = 3740.4(4)$ Å^3, $Z = 8$, $\mu = 1.04$ mm^{-1}.

Multi-scan absorption correction (TWINABS[386–388]), structure solution using SHELXT[389] and full-matrix least-squares refinement using SHELXL.[390,391] Inspection of the data using cell now indicated a twinned crystal. The refinement converged at $R_1 = 0.063$ [$F_o^2 > 2\sigma(F_o^2)$], $wR_2 = 0.168$ (all reflections) *GOOF* = 1.073 for 6432 observed unique reflections and 7423 unique reflections.

CCDC 1877358 contains the supplementary crystallographic data for this structure. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.