

Tetravinylallene

and

Other π -Bond Rich Hydrocarbons

A thesis submitted in fulfillment for the degree of
Doctor of Philosophy
of the Australian National University



Cecile Elgindy

Research School of Chemistry
The Australian National University

October 2019

Declaration

Except where specific acknowledgements of others are made, the work described in this thesis was carried out by the author during the period of May 2015 to October 2019 in the Research School of Chemistry of the Australian National University, Australia, under the supervision of Professor Mick Sherburn. The material presented has not been submitted for any other degree and is less than 100,000 words in length.

Cecile Elgindy

October 2019

Acknowledgements

Firstly, I must thank my supervisor, Professor Mick Sherburn, for giving me the opportunity to be a member of his group and to work on these interesting molecules. I have certainly learnt a lot over the past four years under your supervision.

I must thank Professor Chris McErlean for introducing me to the world of chemical research during my Honours year at the University of Sydney and for being supportive in my decision to move to Canberra. I am indebted to Dr. Lara Malins for her support and encouragement during my candidature, in particular during the preparation of this thesis. I am also grateful to Professor Chris Easton for his advice and guidance during my candidature.

I must also thank the technical staff of the Research School of Chemistry, especially Anithahini Jeyasingham, Chris Blake, Hideki Onagi, Tony Willis, Jas Ward and Michael Gardiner for helping me to obtain data for these oftentimes capricious compounds. This thesis would have been impossible without you. The Research School of Chemistry has given me the opportunity to interact with many academics. In particular, I must thank Professor Henning Hopf, Professor Anthony Hill, Professor Martin Bennett, Professor Nilay Hazari, Dr. Andrew Gilbert and Dr. Tristan Reekie for their time and insights.

The Sherburn group has been a great learning environment. I must thank Sam Drew, Nicholas Green, Kimberly Roper, Michael Scott, Ross Harvey, Mehmet Saglam and Supanimit Chiampanichayakul for showing me the ropes of hydrocarbon chemistry. To the members of Lab 3.77 Josemon George, Yi-Min Fan, Natalie Shadwell and Eliza Tarcoveanu, you have made it enjoyable to turn up to work every day. In particular, I am grateful to Dr. Imants Kreituss for showing me what I should be aiming for and his continued support after leaving. To Meng-Yao, Samantha Rohe, Thomas Loan, Andy Leach and Kate Landau, thank you for reminding me that there is a world outside of the chemistry building. To the Sydney crew Jonathon Chung, Liam Bromhead, Phil Norcott, Alex Norman and Marlowe Graham thank you for those (probably unnecessarily) long lunches and coffees. It was always enjoyable to have stimulating and encouraging discussions even while on break.

Finally, I must thank my family, Mum, Dad, Tarek, Pearl and Nora. This thesis would have been impossible without your love and support. I couldn't have asked for better. To you I am forever indebted.

Publications

Some of the work in this thesis has previously been published:

C. Elgindy, J. Ward, M. S. Sherburn, Tetravinylallene, *Angew. Chem. Int. Ed.* **2019**, *58*, 14573-1577

Abbreviations

%	percentage yield	dppp	1,3-bis(diphenylphosphino)
Δ	heat		propane
$^{\circ}\text{C}$	degree/s Celsius	EI	electron impact
<i>aq.</i>	aqueous	equiv.	molar equivalent(s)
Ar	aryl or argon	ESI	electrospray ionisation
Ac	acetyl	GC	gas chromatography
BHT	2,6-di- <i>tert</i> -butyl-4- methylphenol	h	hour/s
bp	boiling point	$h\nu$	light/photochemistry
br	broad	HMBC	heteronuclear multiple bond coherence
<i>ca</i>	<i>circa</i> (approximately)	HOMO	highest occupied molecular orbital
CAN	ceric ammonium nitrate	HSQC	heteronuclear single quantum coherence
cm^{-1}	wave number	HPLC	high pressure liquid chromatography
cod	1,5-cyclooctadiene	HRMS	high resolution mass spectrometry
COSY	correlated spectroscopy	HWE	Horner-Wadsworth-Emmons
Cp	cyclopentadiene	Hz	Hertz
m-CPBA	meta-chloroperoxybenzoic acid	IMDA	intramolecular Diels–Alder
δ	chemical shift	<i>i</i> -Pr	isopropyl
d	day/s or doublet/s	IR	infrared
DA	Diels–Alder	<i>J</i>	coupling constant
DABCO	1,4-diazabicyclo[2.2.2]octane	LUMO	lowest unoccupied molecular orbital
dba	dibenzylideneacetone	lit.	literature
DBU	1,8-diazabicyclo[5.4.0] undec-7-ene	M	molar
DEAD	diethyl azodicarboxylate	M^+	molecular ion
DIBAL-H	diisobutylaluminium hydride	Me	methyl
DMAP	4-dimethylaminopyridine	min	minute
DMF	dimethylformamide		
DMSO	dimethylsulfoxide		
dppf	1,1'-bis(diphenylphosphino)- ferrocene		

MHz	megahertz	PTAD	<i>N</i> -phenyltriazolinedione
mol	mole	q	quartet
mp	melting point	rt	room temperature
Ms	methanesulfonyl	sat.	saturated
MS	mass spectroscopy	SM	starting material
<i>m/z</i>	mass to charge ratio	t	time
ν	absorption maxima (IR)	<i>t</i> -Bu	<i>tert</i> -butyl
<i>n</i> -BuLi	<i>n</i> -butyl lithium	TBAF	tetra- <i>n</i> -butylammonium fluoride
NaHMDS	sodium bis(trimethylsilyl) amide	TBS	<i>tert</i> -butyldimethylsilyl
NMM	<i>N</i> -methylmaleimide	TCNE	tetracyanoethylene
NPM	<i>N</i> -phenylmaleimide	temp	temperature
NMR	nuclear magnetic resonance	Tf	trifluoromethanesulfonyl
nOe	nuclear Overhauser effect	TFA	trifluoroacetic acid
NOESY	nuclear Overhauser and exchange spectroscopy	THF	tetrahydrofuran
Ph	phenyl	TIPS	triisopropylsilyl
ppm	parts per million	TLC	thin layer chromatography
		<i>p</i> -TsOH	<i>para</i> -toluenesulfonic acid

Abstract

The synthesis of novel hydrocarbons has often been used to further our understanding of structure-reactivity relationships. Hydrocarbons that are rich in π -bonds have additionally served to explore the concepts of conjugation and aromaticity. While computational studies have often served as a starting point to understand these ideas, the synthesis of molecules serves to provide experimental data with which concepts can either be proven or disproven.

This thesis explores the synthesis and chemistry of novel π -bond rich molecules, in particular the multivinylallenes and the [13]annulene carbocation in one review and four experimental chapters. Chapter 1 describes the impetus for exploring the structural space of conjugated hydrocarbons, Chapter 2 provides an overview of the chemistry of vinylallenes, a class of conjugated allenes. Chapter 3 describes the first preparation of the parent tetravinylallene, as well as the first examples of substituted tetravinylallenes, in publication format. Chapter 4 investigates the first synthesis of the parent trivinylallene and includes a study of the first substituted trivinylallenes. Chapter 5 details an improved synthesis of the divinylallenes and a study of the multivinylallene family of molecules. Chapter 6 describes syntheses towards the [13]annulene carbocation, an annulene proposed to have Möbius topology.

While the synthesis and application of vinylallenes have long been known, they have only been reviewed as examples within the larger allene literature. In Chapter 2 an overview of the literature on vinylallenes is presented. In particular this examines their synthesis, reactivity and synthetic applications.

Tetravinylallene is the highest member of the multivinylallene family that has not previously been reported. In Chapter 3 we describe the first synthesis of the parent tetravinylallene molecule using a cross-coupling reaction to incorporate the final vinyl functionality. The approach was extended to the synthesis of the first substituted tetravinylallenes. The half-lives of these molecules were compared to other known π -bond rich hydrocarbons. The reactivity of tetravinylallenes in pericyclic cascades was also explored, which points to the potential synthetic application of these molecules.

Trivinylallene is another member of the multivinylallene family that has also not been reported. Chapter 4 describes the first synthesis of the parent trivinylallene molecule using a cross-coupling approach similar to that used in the synthesis of tetravinylallene. This method was then applied to the synthesis of the first substituted trivinylallenes, investigating the effects of different substitution patterns as well as stereo-electronic effects. The reactivity of trivinylallene in pericyclic reactions is described, as well as comparison with select substituted trivinylallene analogs. Computational analysis of these molecules was performed to rationalise the observed reactivity.

With access to the higher members of the multivinylallene family for the first time, a study of this family of molecules was sought. Chapter 5 initially describes an improved synthesis of the previously reported divinylallenes. This, in conjunction with data from Chapters 3 and 4, enabled a comparison of the properties of the multivinylallenes using NMR and UV-Visible spectroscopy to identify trends within this family of molecules.

Aromaticity is an important concept in organic chemistry, with an evolving definition. While the idea of Möbius aromaticity has often been theorised, the unambiguous synthesis of a Möbius annulene remains unresolved. Finally, Chapter 6 describes syntheses towards the [13]annulene carbocation, a molecule proposed to have Möbius topology. The synthesis towards this molecule focuses on the use of the irontricarbonyl group protecting group strategy in order to target [13]annulenone, another molecule that is yet to be synthesised, as an advanced intermediate. Two different approaches to this molecule were investigated. The first focused on a symmetric disconnection, while the second approach utilised a non-symmetric disconnection to target the 13-membered ring.

Table of Contents

Declaration	iii
Acknowledgements	v
Publications	vii
Abbreviations	viii
Abstract	x
Chapter 1 Conjugated Hydrocarbons	1
1.1 Introduction	1
1.2 Fundamental hydrocarbons	2
1.3 Conjugated hydrocarbons	2
1.4 New π -bond rich molecules	6
Chapter 2 Vinylallenes	7
2.1 Introduction	7
2.2 Synthesis of vinylallenes	8
2.3 Reactivity of vinylallenes	23
2.4 Natural products and application in total synthesis	30
2.5 Multivinyllallenes	34
2.6 Concluding remarks and future work	39
Chapter 3 Tetravinylallene	41
3.1 Introduction	41
3.2 Tetravinylallene	46
3.3 Concluding remarks and future work	52
Supporting Information	53
Chapter 4 Trivinylallene	163
4.1 Introduction	163
4.2 Synthesis of trivinylallenes	167
4.3 Geometry of trivinylallene	185
4.4 Diels–Alder reactions of the trivinylallenes	193
4.5 Concluding remarks and future work	199

Chapter 5 Multivinylallenes	201
5.1 Introduction	201
5.2 Synthesis of divinylallenes	206
5.3 Diels–Alder reactions of the divinylallenes	208
5.4 NMR studies of multivinylallenes	211
5.5 UV-Visible studies of multivinylallenes	216
5.6 Stability of multivinylallenes	220
5.7 Concluding remarks and future work	222
Chapter 6 [13]annulene cation	223
6.1 Introduction	223
6.2 Studies towards the [13]annulene cation	240
6.3 Concluding remarks and future work	247
Chapter 7 Concluding Remarks	249
Chapter 8 Experimental	251
8.1 General Experimental	251
8.2 Experimental for Chapter 4	254
8.3 Experimental for Chapter 5	299
8.4 Experimental for Chapter 6	308
Chapter 9 Supplementary Information	321
Chapter 10 References	323

1

Conjugated Hydrocarbons

1.1 An Introduction

The relationship between the structure and the observed reactivity of a molecule has continually intrigued organic chemists. While the study of structures in the natural world has led to interesting and important findings, the investigation of unnatural molecules has assisted in furthering our understanding of the chemical bond. The desire to understand the limitations of different bonding arrangements, has resulted in the design and synthesis of novel structures, the development of new reactions and has often sought to challenge the accepted wisdom.

1.2 Fundamental Hydrocarbons

The synthesis of hydrocarbons provides a platform on which the known structural space can be extended and thereby further our understanding of structure-reactivity relationships.^[1] The binary nature of hydrocarbon molecules is somewhat deceptive as combining the sp^3 (**1.1**), sp^2 (**1.2**) and sp -hybridised (**1.3** and **1.4**) hydrocarbon building blocks leads to an expansive set of molecules that can be explored (Figure 1.2.1).^[1]

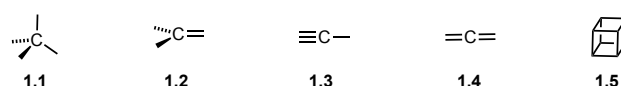


Figure 1.2.1 Hydrocarbon building blocks and the strained cubane molecule

While fundamental and applied synthesis of molecules serve different purposes, they remain co-dependent pursuits in the research of organic chemistry. An archetypal example is cubane (**1.5**), a molecule that was originally considered to be too reactive to synthesise (Figure 1.2.1). The successful synthesis of this strained molecule, despite containing 90° bond angles, demonstrated that it was in fact isolable.^[2] Subsequent derivatives of cubane have since been applied as a bio-isostere in medicinal chemistry.^[3] ^[4] To date, many areas of hydrocarbon chemistry still present synthetic challenges.^[1]

1.3 Conjugated Hydrocarbons

Hydrocarbons rich in π -bonds are a structural space that has been used to explore the carbon-carbon double bond. The five fundamental classes of conjugated hydrocarbons that can be explored by connecting just three carbon-carbon double bond units indicates the variety of molecules that can be investigated in this structural space (Figure 1.3.1).

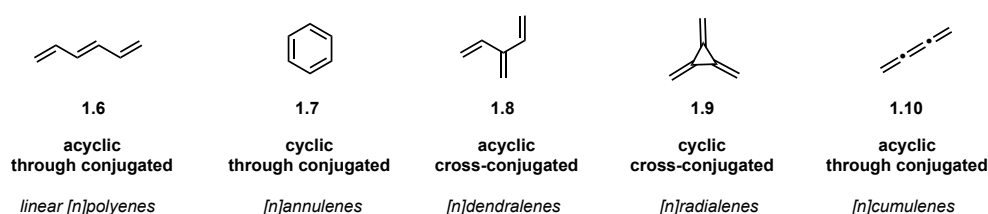


Figure 1.3.1 Fundamental classes of conjugated hydrocarbons

Connecting three double bond units by carbon-carbon single bonds leads to the acyclic through-conjugated hexatriene **1.6**, a member of the linear $[n]$ polyenes (Figure 1.3.1). The all-*E*-linear polyenes (e.g. **1.6**, **1.11** and **1.12**) and related isomers have played an integral role in understanding conjugation and the development of molecular orbital theory (Figure 1.3.2).^{[1] [5]} Extended polyenes also have significant roles in biological settings, such as the function that retinal **1.13** has in enabling vision through *E/Z*-isomerisation (highlighted in red in Figure 1.3.2).^[6]

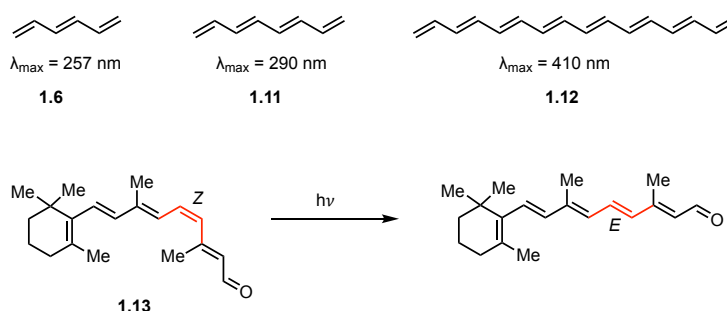


Figure 1.3.2 An example of effect of extended conjugation in the linear $[n]$ polyene family and the role it plays in biological settings

The same connectivity of three double bond units this time in a cyclic arrangement leads to the benzene molecule (**1.7**), the classic example of the annulene family (Figure 1.3.1). The study of this class of conjugated hydrocarbons has led to the development of the concept of aromaticity and the structural implications for the reactivity of these molecules (Figure 1.3.3). The annulenes will be discussed in more detail in Chapter 6.

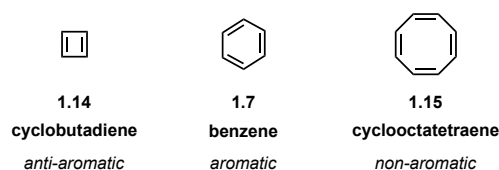


Figure 1.3.3 The first three members of the $[n]$ annulene family demonstrate some of the structure-reactivity relationships observed for this class of molecules

Connecting three double bond units, again by carbon-carbon single bonds, in a cross-conjugated manner gives [3]dendralene (**1.8**), the simplest cross-conjugated member of the $[n]$ dendralene family (Figure 1.3.1). The conjugation of these molecules does not exceed that of 1,3-butadiene (highlighted in green), irrespective of additional cross-conjugated alkenic units (Figure 1.3.4).^[7]

The ability of dendralenes to undergo diene-transmissive Diels–Alder reactions (**1.8** → **1.18** → **1.19**)^[8] leads to a rapid construction of molecular complexity (Figure 1.3.4). This has seen dendralenes applied to natural product synthesis, such as **1.20** in the recent synthesis of amphilectene **1.21** (Figure 1.3.4).^[9] ^[10]

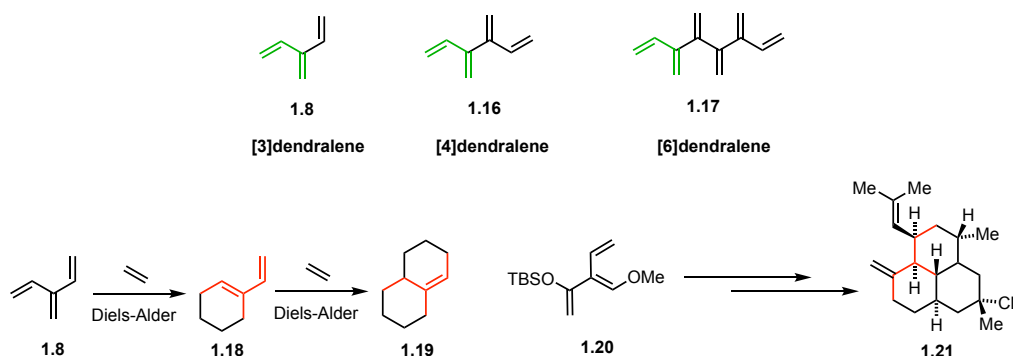


Figure 1.3.4 The [n]dendralene family exhibit the same degree of conjugation as 1,3-butadiene and have been applied in natural product synthesis

Cross-conjugation in a cyclic arrangement furnishes the [n]radialenes of which [3]radialene (**1.9**) is the smallest member (Figure 1.3.1). The reactivity of these molecules has in some cases made it difficult to study these compounds.^[1] The most recent radialene to be reported, [5]radialene (**1.22**), necessitated the use of an irontricarbyl protecting group strategy in order to be synthesised (Figure 1.3.5).^[11]

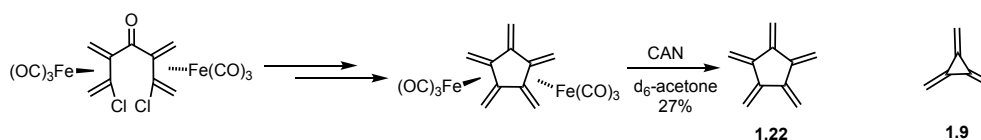


Figure 1.3.5 The smallest member of the radialene family, [3]radialene, and the recently published synthesis of [5]radialene

Three double bond units connected *via* two sp-hybridised carbons gives rise to cumulene (**1.10**), a linear, through-conjugated molecule (Figure 1.3.1). Allene (**1.23**) is the smallest member of this family (Figure 1.3.6) although interest in the higher [n]cumulenes is due to their interesting physical properties, that differ from the linear [n]polyenes and [n]polynes, as well as their potential application in materials chemistry.^[12] ^[13]

More recently, studies of these molecules have revealed that even numbered [n]cumulenes have helical orbitals (**1.24**) while odd numbered [n]cumulenes have perpendicular orbitals (**1.25**) (Figure 1.3.6).^{[14] [15]} While this is not manifested in a difference of stability between even and odd cumulenes, increasing the length of cumulenes results in an observed decrease in stability.
[12] [14]

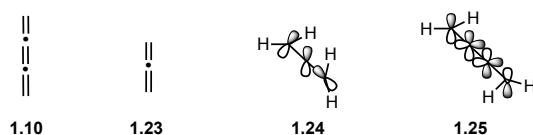


Figure 1.3.6 The smallest of the [n]cumulene molecules, allene, and the different types of orbitals calculated for the even and odd cumulene compounds

Combining the fundamental classes of conjugated molecules further expands the structural space of π -bond rich compounds.^[1] One such example is tetravinylethylene (**1.27**), an acyclic molecule that exhibits both through- and cross-conjugation (Figure 1.3.7).^{[16] [17]} Additionally it has been demonstrated that **1.27** has greater stability than either the hexatriene **1.6** or [3]dendralene (**1.8**) molecules.^[17]

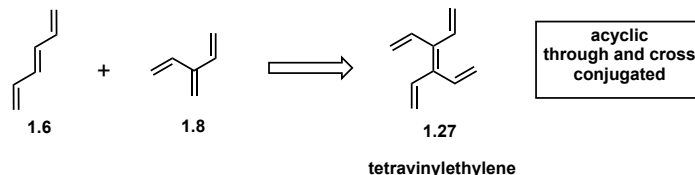


Figure 1.3.7 Tetravinylethylene (**1.27**) is a combination of the linear [n]polyenes and [n]dendralene fundamental classes of conjugated hydrocarbons

The continued study of the fundamental classes of conjugated hydrocarbons, as well as combinations of these classes, is necessary in order to further our understanding of π -bond rich molecules and identify potential applications of these compounds.

1.4 Synthesising new π -bond rich molecules

This thesis aims to contribute to the structural space of π -bond rich molecules by investigating the synthesis of previously unreported compounds and comparing the reactivity and stability of these molecules with known conjugated hydrocarbons.

An overview of vinylallene chemistry is provided in Chapter 2. The work described in Chapters 3, 4 and 5 focuses on the synthesis of the multivinylallenes (**1.28**, **1.29**, **1.30** and **1.31**), a family of conjugated allenes that have not previously been fully explored (Figure 1.4.1).^[18] Detailed in Chapter 6 is syntheses towards the [13]annulene cation (**1.32**), a molecule that has been proposed to have Möbius topology (Figure 1.4.1).^[19]

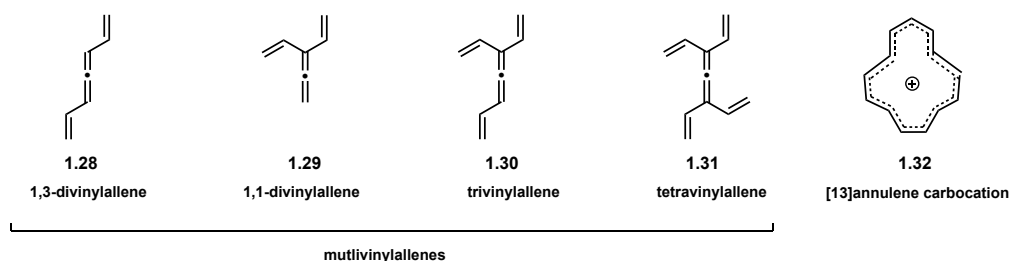


Figure 1.4.1 The multivinylallenes and [13]annulene cation are π -bond rich compounds that were identified as target molecules to be investigated

2

Vinylallenes

2.1 An Introduction

Novel conjugated molecules, as previously mentioned in Chapter 1, can be obtained through the hybridisation of the five fundamental classes; vinylallenes are one such family of molecules. Combining allene (**1.23**), the simplest of the [n]cumulenes, with 1,3-butadiene (**2.1**), the simplest of the linear [n]polyenes, furnishes vinylallene (**2.2**) (Figure 2.1.1).^[18]

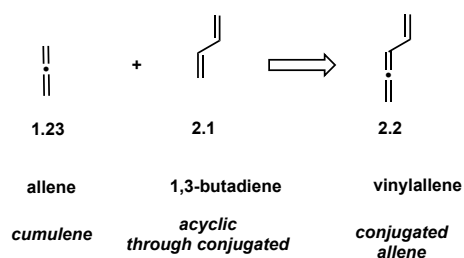


Figure 2.1.1 Vinylallenes can be considered as a combination of different classes of conjugated hydrocarbons

Similarly extending each of the fundamental classes of conjugated hydrocarbons by an sp-hybridised alkenic unit results in a variety of vinylallene structures (Figure 2.1.2). The acyclic through-conjugated and acyclic cross-conjugated vinylallenes (**1.29** and **2.3**) are perhaps the most studied of these structures and exhibit diverse reactivity.^[18]

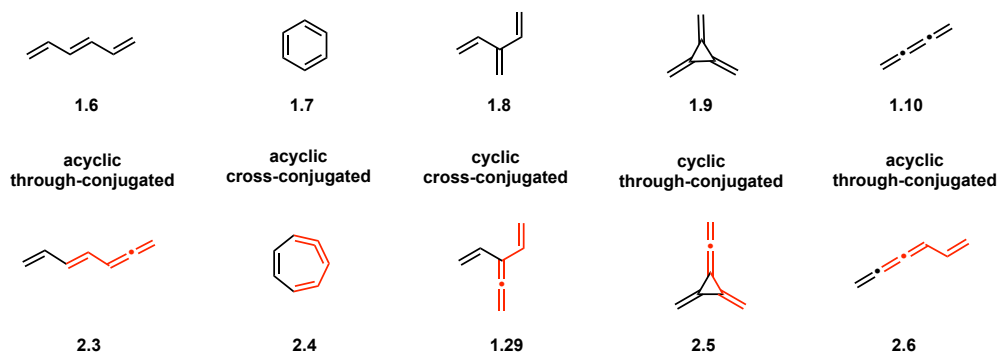


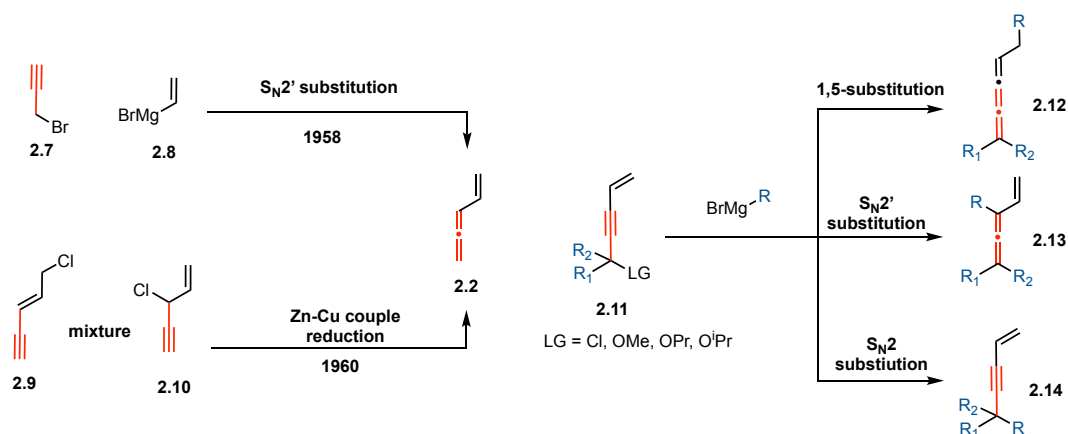
Figure 2.1.2 Vinylallenes as an extension of the fundamental classes of conjugated hydrocarbons

While the synthesis and application of vinylallenes has been reviewed as part of the broader allene literature, information regarding vinylallenes remains scattered.^{[18] [20] [21] [22] [23]} For this reason an overview of the synthesis and reactivity of vinylallenes, in particular of the acyclic structures such as **1.29** and **2.3**, is provided herein.

It should be noted that while this thesis was under examination, a review of recent vinylallene literature was published in October 2019.^[24]

2.2 Synthesis of Vinylallenes

The first reported synthesis of a vinylallene was in 1958 by an S_N2' substitution reaction of propargyl bromide (**2.7**) with vinylmagnesium bromide (**2.8**) (Scheme 2.2.1).^[25] An alternative synthesis was described in 1960 *via* the reduction of chloropentynes (**2.9** and **2.10**) with zinc-copper couple.^[26] Early investigations of vinylallenes, also referred to in the literature as ene-allenes, noted the difficulty in synthesising substituted vinylallenes regioselectively (Scheme 2.2.1).^{[27] [28]} The use of substrates such as **2.11** in substitution reactions often gave mixtures of regioisomers (**2.12**, **2.13** and **2.14**), with product distributions being dependent upon substitution patterns.



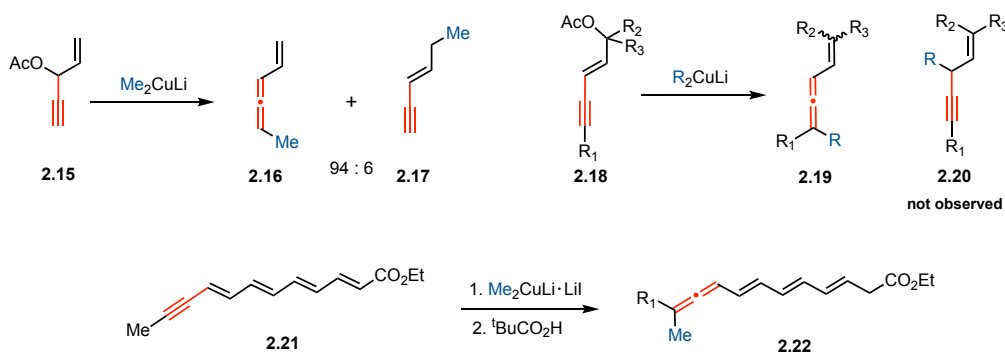
Scheme 2.2.1 Initial reports of vinylallene syntheses and substituted analogs

Since these initial reports, various methods have been developed to obtain both substituted and unsubstituted vinylallenes with the synthesis of chiral vinylallenes also having been reported.

2.2.1 Substitution reactions

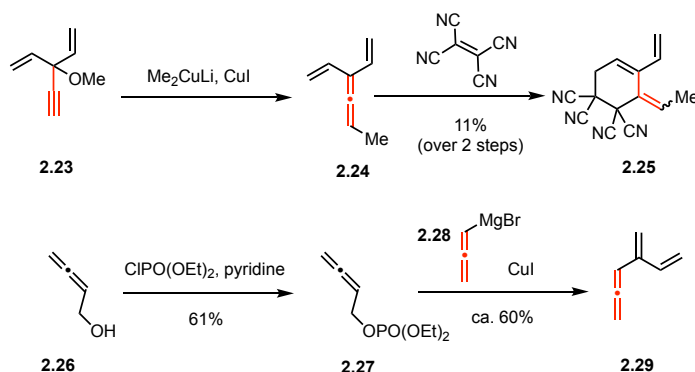
Regioselective syntheses of vinylallenes have been reported when dialkyl-lithium cuprates, rather than Grignard reagents, are used as nucleophilic species in substitution reactions, although careful selection of the starting material is necessary (Scheme 2.2.2). In the case of a 3-substituted pent-1-en-4-yne electrophile (**2.15**), a competing allylic-substitution was observed leading to a mixture of **2.16** and **2.17**.^[29] Ene-yne electrophiles, such as **2.18**, are reported to produce vinylallenes regioselectively, proceeding *via* a 1,5-substitution reaction (also referred to as S_N2'' reactions).^{[30] [31] [32] [33]} The allylic substitution products, such as **2.20**, were not reported for these examples. Organocuprates have also been utilised in 1,6-, 1,8-, 1,10- and 1,12-addition reactions to generate highly conjugated vinylallenes (e.g. **2.21** \rightarrow **2.22**).^[34]

A drawback of vinylallene synthesis using 1,5-substitution reactions is the mixture of *E/Z* isomers that is often observed, such as in the case of **2.19**.^[35] Nevertheless, this method has successfully been applied to the enantioselective synthesis of vinylallenes using chiral precursors in select examples.^[35]



Scheme 2.2.2 Regioselective synthesis of vinylallenes using dialkylcuprate nucleophiles in substitution reactions

Substitution with organocuprates has also been applied to the synthesis of reactive multivinylallenes and allenic dendralenes (Scheme 2.2.3). The first substituted 1,1-divinylallene (**2.24**) was reported in 1987 *via* the S_N2' substitution of **2.23** with dimethylcuprate, although allene **2.24** was obtained as a TCNE Diels–Alder adduct (**2.25**) as **2.24** was found to be too reactive to be isolated (Scheme 2.2.3).^{[36] [37]} Allenic dendralene **2.29** was similarly prepared by the 1,3-substitution of phosphate **2.27** with allenylmagnesium bromide (**2.28**) in the presence of copper(I) iodide (Scheme 2.2.3).^[37]

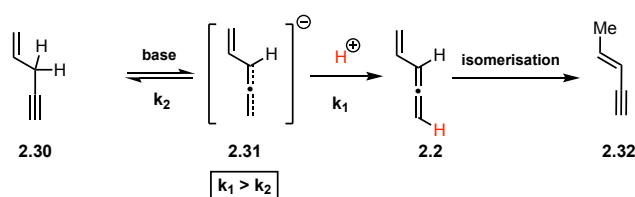


Scheme 2.2.3 Synthesis of vinylallenes **2.24** and **2.29** *via* substitution reactions with organocuprates

While substitution has enabled access to functionalised vinylallenes, this method is primarily limited to the use of dialkylcuprates due to the propensity of divinylcuprates to rapidly undergo reductive elimination. As such, substitution reactions necessitate the use of starting materials such as **2.15** or **2.18** (Scheme 2.2.2) whereby the requisite alkenic component of the vinylallene is already present in the electrophilic precursor. The development of metal-catalysed cross-coupling reactions has overcome this limitation which will be discussed in Section 2.2.8.

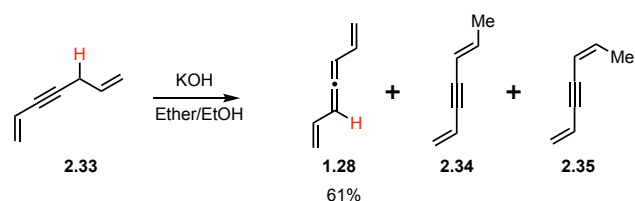
2.2.2 Rearrangement reactions

Another method reported during the initial investigations of vinylallene synthesis was the base mediated rearrangement of enynes such as **2.30** (Scheme 2.2.4). Studies demonstrated that vinylallene (**2.2**) is the kinetically favoured product in these reactions, although continued isomerisation to **2.32** is possible hence, product mixtures have often been reported.^[27] In the case of substituted examples, protonation could occur at either the allenic or alkenic positions, yielding an isomeric mixture *via* parallel reaction pathways. Additionally, substitution at various positions of enyne **2.30** was found to impact upon the rate of the rearrangement. This was attributed to the entropic cost associated with the change in hybridisation.^[27]



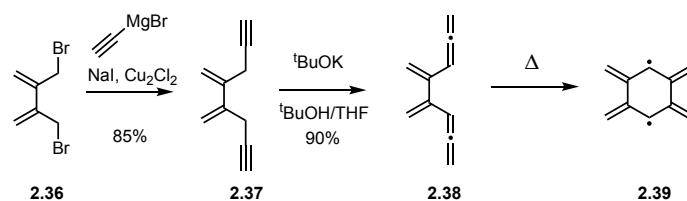
Scheme 2.2.4 Vinylallenes as the kinetically favoured product of base mediated rearrangement reactions from enynes

The first multivinylallene, 1,3-divinylallene (**1.28**), was synthesised using a rearrangement reaction. The base mediated rearrangement of enyne **2.33** gave **1.28** along with a mixture of two other isomers (**2.34** and **2.35**) (Scheme 2.2.5).^[38] Isomers **2.34** and **2.35** are a result of **1.28** undergoing further isomerisation and separation by preparatory gas chromatography was required in order to isolate **1.28**. Similar methods were reported in the synthesis of methyl substituted 1,3-divinylallenes.^[39]



Scheme 2.2.5 Synthesis of 1,3-divinylallene (**1.28**) via rearrangement of **2.33**

A rearrangement reaction was also used to synthesise 2,3-allenyl-1,3-butadiene (**2.38**), a molecule containing two adjoining vinylallene subunits (Scheme 2.2.6).^[40] Compound **2.37** isomerised in the presence of *tert*-BuOK to give **2.38**, which further reacted to form the 1,2,4,5-tetramethylenebenzene diradical (**2.39**) that was subsequently studied.

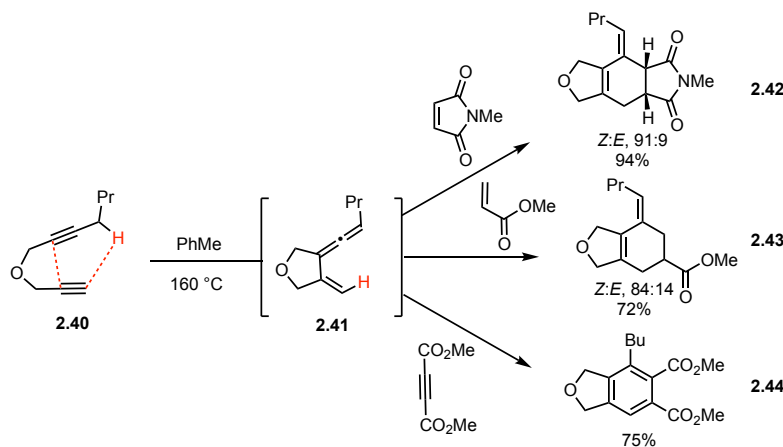


Scheme 2.2.6 Synthesis of 2,3-allenyl-1,3-butadiene (**2.38**) for the study of the 1,2,4,5-tetramethylene benzene diradical (**2.39**)

Currently, no substituted derivatives of **2.38** have been reported in the literature. Although the reason for this is unknown, it may be due to substituted derivatives rearranging to more stable isomers.

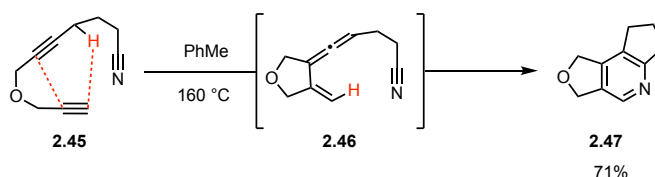
2.2.3 Pericyclic reactions

The intramolecular propargylic ene-type reaction has been used to access exo-cyclic vinylallenes (Scheme 2.2.7). Heating of 1,6-diyne **2.40** yielded vinylallenes with the reactive *s-cis* conformation (**2.41**), which in the presence of a dienophile undergo a subsequent Diels–Alder reaction (Scheme 2.2.7).^[41] This enables the rapid synthesis of multicyclic frameworks (such as **2.42**, **2.43** and **2.44**) that are the result of an overall formal [2+2+2] reaction (Scheme 2.2.7).



Scheme 2.2.7 Formal [2+2+2] using a propargylic ene-Diels–Alder cascade via a reactive vinylallene intermediate

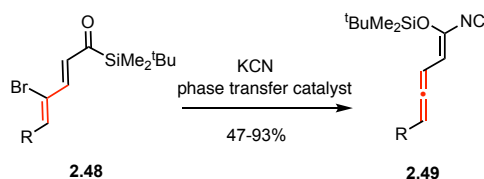
This sequence has been extended to nitrile containing substrates (**2.45**) that undergo an intramolecular aza-Diels–Alder reaction to give access to substituted pyridines (**2.47**) within a multicyclic framework (Scheme 2.2.8).^{[42] [43] [44]}



Scheme 2.2.8 Application of the propargylic ene-Diels–Alder cascade to the synthesis of substituted pyridines

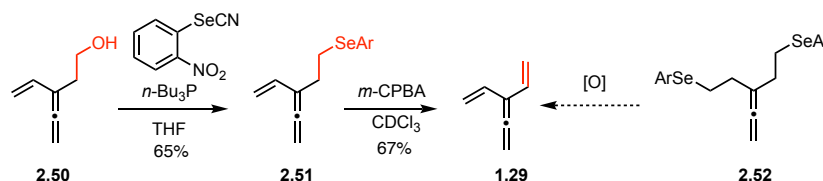
2.2.4 Elimination reactions

The use of elimination reactions to form either the allenic or alkenic portion of vinylallenes have seen limited application. This is perhaps unexpected considering the broad use of elimination reactions in the synthesis of cumulenes.^[1] A Brook-rearrangement-elimination of **2.48** was recently reported to form the allenic component of **2.49**, however, this type of transformation remains an isolated example in vinylallene synthesis (Scheme 2.2.9).^[45]



Scheme 2.2.9 A Brook rearrangement-elimination reaction used to form the allenic portion of select vinylallenes

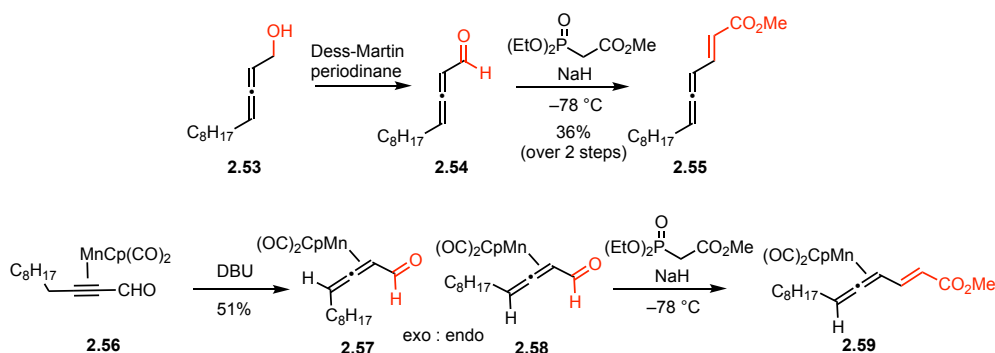
The Grieco–Sharpless reaction was successfully applied to form the final vinyl substituent in the first synthesis of the unsubstituted 1,1-divinylallene **1.29** (Scheme 2.2.10).^[46] Formation of selenide **2.51** from allenol **2.50** with subsequent oxidation and elimination furnished **1.29**. An unsuccessful two-fold oxidation-elimination from diselenide **2.52** had previously been reported in an attempt to synthesise **1.29** (Scheme 2.2.10).^[37] It should be noted that base mediated elimination reactions to form the alkenic portion of vinylallenes, akin to the synthesis of [3]dendralene, have not been reported.^[47]



Scheme 2.2.10 Successful use of the Grieco–Sharpless elimination to form the final alkenic unit of 1,1-divinylallene (**1.29**)

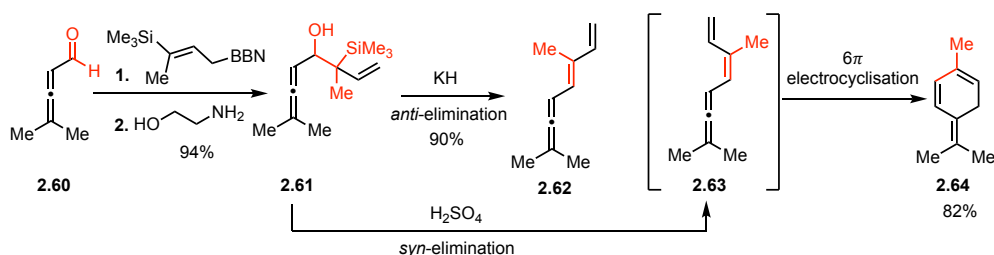
2.2.5 Olefination reactions

Various olefination reactions have been applied to synthesise vinylallenes. Horner-Wadsworth-Emmons (HWE) reactions have been used to obtain ester functionalised vinylallenes from allenic aldehydes (**2.54**) (Scheme 2.2.11).^{[48] [49]} This approach has been applied to multiple syntheses of insect pheromone **2.55**.^{[50] [51] [52]} Manganese complexes have been used to stabilise reactive allenic aldehydes (**2.57** and **2.58**) which react in HWE reactions and have enabled access to chiral vinylallenes (Scheme 2.2.11).^{[53] [54]}



Scheme 2.2.11 Synthesis of ester functionalised vinylallenes via HWE olefination reactions. The formation of manganese complexes gives access to chiral vinylallenes

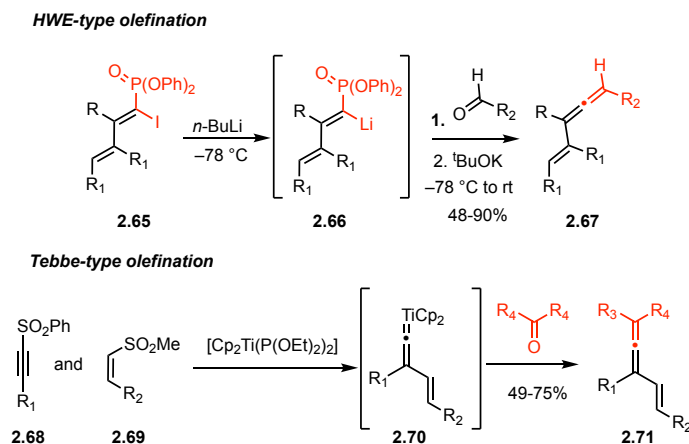
The Peterson olefination has also been employed to form the alkenic portion of vinylallenes with *E/Z* selectivity as in the case of **2.62** and **2.63** (Scheme 2.2.12).^{[55] [56]} This method has not been as widely used as the HWE reaction, presumably due to the longer synthetic sequence and the use of more specialised reagents.



Scheme 2.2.12 Olefination reactions to form the alkenic portion of vinylallenes

Olefination reactions have also been used to synthesise the allenic component of vinylallenes. Lithium-halogen exchange of unsaturated iodophosphonates (**2.65** → **2.66**), followed by a HWE-type olefination with various aldehydes generated functionalised vinylallenes (**2.67**) (Scheme 2.2.13).^[57] A variation of the Tebbe olefination also forms the allenic portion of substituted vinylallenes including substituted 1,3-divinylallenes (Scheme 2.2.13).^[58]

Beginning from *Z*-alkenyl sulfones (**2.69**) and alkynyl sulfones (**2.68**) the reaction is proposed to proceed *via* vinylvinylidene titanium complex **2.70**, which reacts with aldehydes and ketones to form vinylallenes (**2.71**) (Scheme 2.2.13).

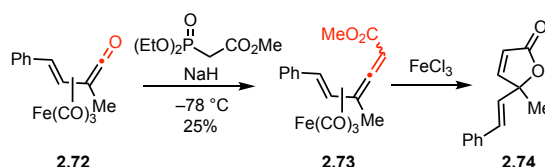


Scheme 2.2.13 Olefination reactions to form allenic component of vinylallenes

It should be noted that although the Zweifel-olefination reaction has recently been reported in the synthesis of allenes, it has not been applied to the synthesis of vinylallenes.^[59]

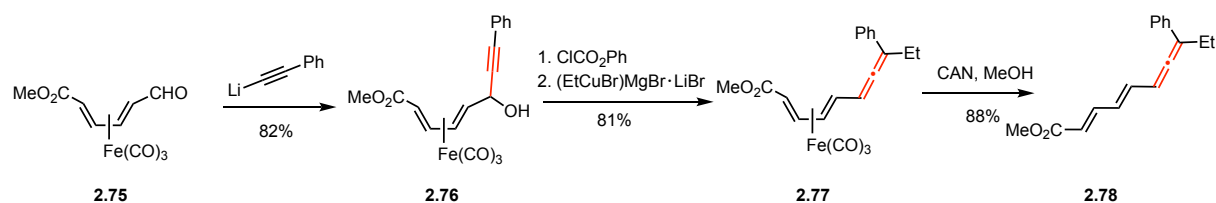
2.2.6 Metal complexes of vinylallenes

Metal complexes of vinylallenes have been synthesised to study their bonding motifs and reactivity. Although vinylallenes do not require the use of metal protecting groups to be synthesised, such an approach towards their synthesis has been reported. The first (vinylallene)irontricarbonyl complexes, such as **2.73**, were reported *via* a HWE reaction from (vinylketene)irontricarbonyl complexes (**2.72**) (Scheme 2.2.14).^{[60] [61] [62]} Attempted decomplexation with FeCl_3 did not result in isolation of the vinylallene, but rather a 5,5-disubstituted 2(5H)-furanone (**2.74**) (Scheme 2.2.14).



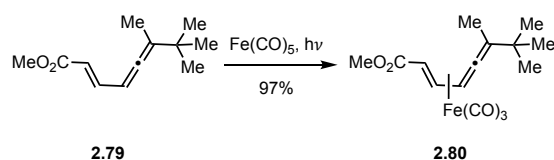
Scheme 2.2.14 Synthesis of vinylallenes as an irontricarbonyl complex *via* HWE olefination

Vinylallenes with extended conjugation, such as **2.78**, have been synthesised from irontricarbonyl complexed butadienes (**2.77**) *via* an S_N2' substitution of propargylic complex **2.76** with alkylcuprates (Scheme 2.2.15).^[63] Decomplexation of the vinylallene complex **2.77** with CAN unveiled the dienyllallene **2.78**.



Scheme 2.2.15 Synthesis of conjugated allenes using an irontricarbonyl protected 1,3-butadiene and alkylcuprate substitution

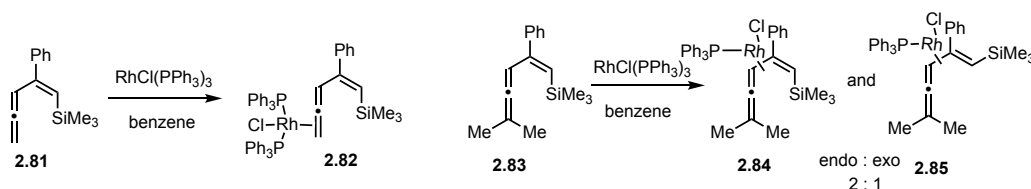
(Vinylallene)irontricarbonyl complexes (**2.80**) have also been synthesised by irradiating vinylallene such as **2.79** in the presence of ironpentacarbonyl. It was noted that the presence of electron-withdrawing substituents, such as esters, resulted in air stable vinylallene complexes (Scheme 2.2.16).^[48] X-ray crystal structures showed that these compounds were π -bound complexes with a σ -interaction between the iron and central sp-hybridised carbon atom.^[48] This resulted in a distorted allene geometry and relatively slow exchange of the iron CO ligands.



Scheme 2.2.16 Synthesis of vinylallene-irontricarbonyl complexes via irradiation

Rhodium vinylallene complexes have also received attention in the literature. Vinylallenes which are unsubstituted at the allenic position (such as **2.81** in Scheme 2.2.17) formed a η^2 -vinylallene rhodium complex (**2.82**)^[64] ^[65], akin to the rhodium-allene complex.^[66]

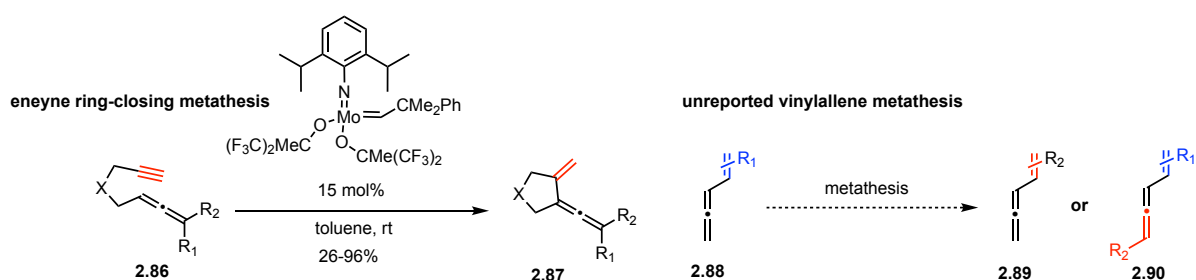
Substitution at the terminal allenic site (such as **2.83** in Figure 2.2.17) resulted in the isolation of a η^4 -vinylallene rhodium complex as a mixture of *endo*- and *exo*-isomers (**2.84** and **2.85**). Similar results were observed with platinum complexes.^[65] The reactivity of vinylallene metal complexes will be discussed in Section 2.3.4.



Scheme 2.2.17 Synthesis of vinylallene-rhodium complexes with different bonding arrangements depending upon the substitution pattern of the vinylallene

2.2.7 Metathesis

The metathesis of allenes is still an underdeveloped area of allene chemistry and the application to vinylallenes is limited.^[67] Exo-cyclic vinylallenes (**2.87**) have been synthesised *via* molybdenum catalysed enyne metathesis using allenynes (**2.86**) (Scheme 2.2.18).^[68] A similar ring-closing reaction was also reported using catalytic $\text{Hg}(\text{OTf})_2$.^[69]

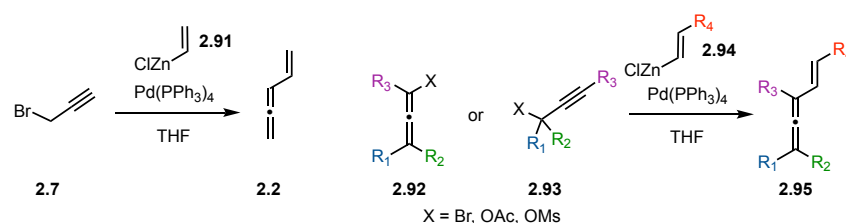


Scheme 2.2.18 Metathesis reactions to synthesise exo-cyclic vinylallenes and metathesis reactions of vinylallene yet to be reported

While metathesis of mono-substituted allenes has been investigated in a single report, it has not been applied to vinylallenes (i.e. **2.88** \rightarrow **2.89** or **2.90**).^[67]

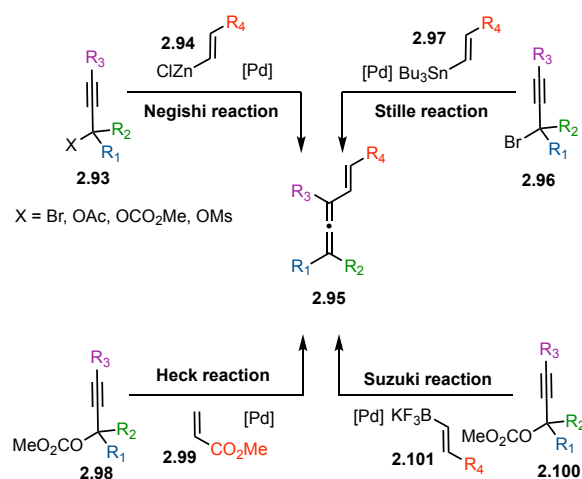
2.2.8 Metal catalysed cross-coupling reactions

Metal-catalysed cross-coupling reactions hold a central position in the repertoire of modern organic chemists so it is not surprising that this method has been applied to the synthesis of vinylallenes. The first report of a palladium(0)-catalysed Negishi cross-coupling reaction between propargylic bromide (**2.7**) and organozinc reagent **2.91** to form vinylallene (**2.2**) was published in 1981 (Scheme 2.2.19).^[70] This method enabled the synthesis of both unsubstituted (**2.2**) and substituted vinylallenes (such as **2.95**) from both propargylic and allenic precursors (**2.92** and **2.93**). It was identified as an attractive method due to the selectivity of the reaction for the allenic product compared to isomerisation reactions.^[71] It should be noted that both propargylic and allenic precursors (**2.92** and **2.93**) are proposed to proceed *via* the same organo-palladium intermediate in the catalytic cycle (**2.110** in Scheme 2.2.22).



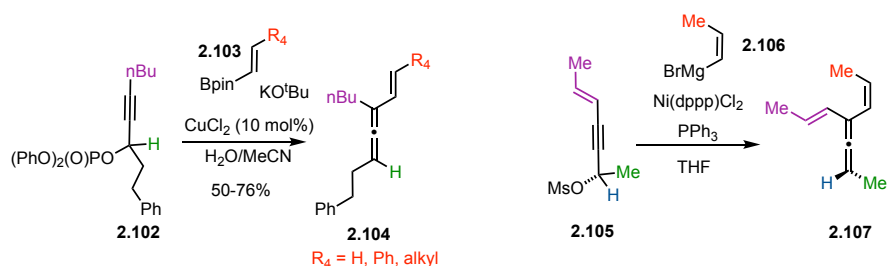
Scheme 2.2.19 First reported syntheses of vinylallene using Negishi cross-coupling reactions and application to the selective synthesis of substituted vinylallenes

Since then, a variety of metal-catalysed cross-coupling reactions have been applied to vinylallene synthesis. Primarily, palladium(0)-catalysed cross-coupling reactions using Negishi^[72] [73] [74] and Suzuki reactions^[75] have been reported (Scheme 2.2.20). Palladium(0)-catalysed Heck^[76], Stille^[77] and carbonylation^[78] reactions have also been reported and applied in natural product synthesis. These cross-coupling reactions frequently make use of a propargylic electrophilic cross-coupling partner and proceed *via* 1,3-transposition to give the vinylallene upon reductive elimination. Reversal of electrophilic-nucleophilic pairing has also been reported in palladium(0)-catalysed cross-coupling reactions between allenylstannanes and alkylhalides.^[79] [80]



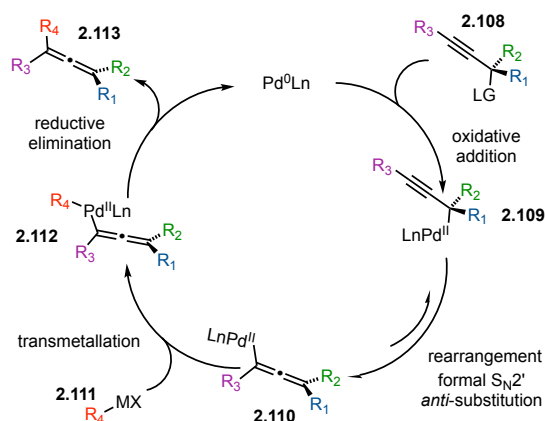
Scheme 2.2.20 Palladium catalysed cross-coupling reactions utilised to synthesise vinylallenes *via* a 1,3-transposition

More recently, copper-catalysed Suzuki conditions have also been reported using functionalised alkenylboronates (**2.103**) to access highly functionalised vinylallenes (**2.104**) (Scheme 2.2.21).^[81] A nickel-catalysed Kumada reaction between mesylate **2.105** and Grignard reagent **2.106** has also been reported in the enantioselective synthesis of substituted 1,1-divinylallene **2.107** (Scheme 2.2.21).^[82] Iron and rhodium catalysed reactions with 1,3-transposition have been reported for allenes, although these reports do not extend to vinylallenes.^{[83] [84]}



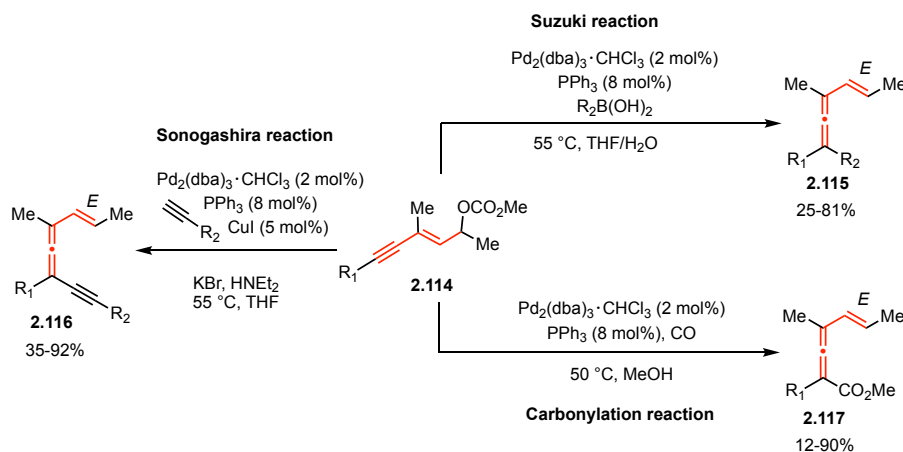
Scheme 2.2.21 Synthesis of vinylallenes using copper-catalysed and nickel-catalysed cross-coupling reactions

With respect to stereochemistry, studies of palladium(0)- and copper(I)-catalysed allene syntheses that proceed *via* 1,3-transposition, indicate that these reactions occur with overall *anti*-substitution resulting in the inversion of stereochemistry (**2.108** \rightarrow **2.113**) (Scheme 2.2.22).^{[85] [86]} A similar mechanism was proposed for the nickel-catalysed Kumada synthesis of **2.107**.^[82]



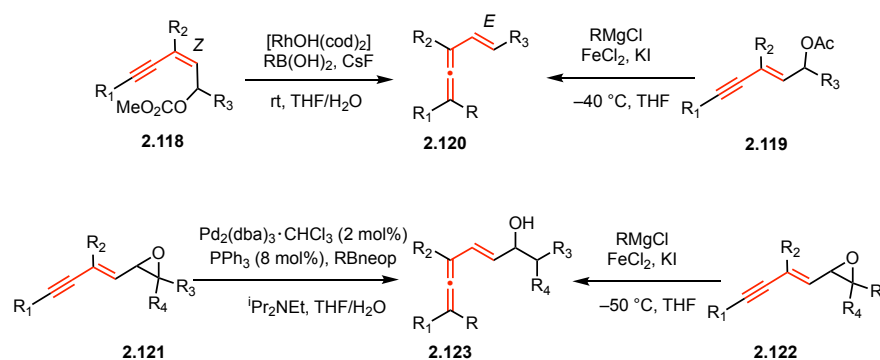
Scheme 2.2.22 Proposed catalytic cycle to justify stereochemical outcome of metal catalysed allene synthesis resulting in overall *anti*-substitution

Vinylallenes have also been synthesised by metal-catalysed cross-coupling reactions that proceed *via* a 1,5-transposition. Palladium(0)-catalysed Suzuki^[87] [88], Sonogashira^[89] and methoxycarbonylation^[90] reactions have been reported to yield vinylallenes from 2-ene-4-yne (such as **2.114** in Scheme 2.2.23) with the resulting vinylallenes (**2.115**, **2.116** and **2.117**) being selectively *E*-configured (Scheme 2.2.23).



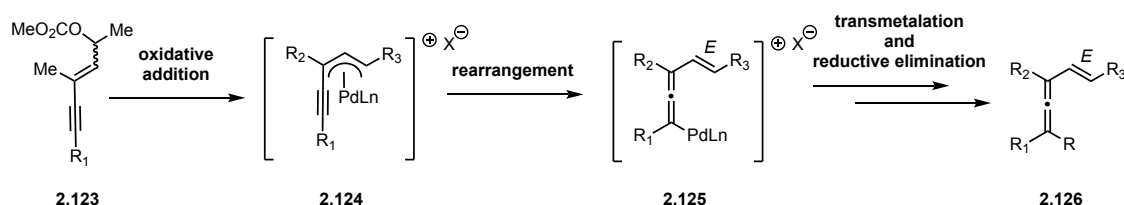
Scheme 2.2.23 Palladium catalysed cross-coupling reaction to synthesise vinylallenes *via* a 1,5-transposition

Rhodium and iron have also been used to catalyse vinylallene syntheses *via* a 1,5-transposition (Scheme 2.2.24).^[91] [92] Rhodium catalysed reactions required a *Z*-configured carbonate (**2.118**) in order to enable oxidative addition and subsequent allene formation. Palladium and iron were also able to catalyse the reaction of enyne oxiranes (**2.121** and **2.122**) to give hydroxy-vinylallene derivatives (**2.123**) (Scheme 2.2.24).



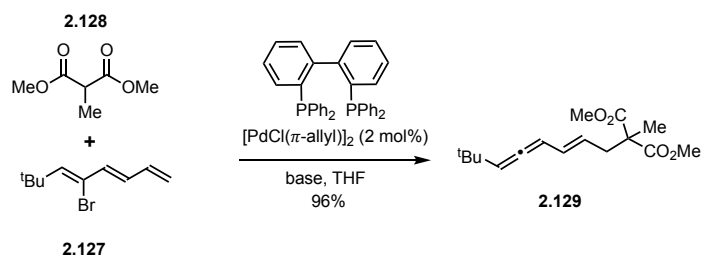
Scheme 2.2.24 Rhodium and iron catalysed synthesis of vinylallenes from carbonates and the synthesis of hydroxy-vinylallenes from oxiranes

Although the mechanism of cross-coupling reactions with 1,5-transposition have not been confirmed, they are proposed to proceed with initial oxidative addition at the allylic site (**2.124**) and rearrange to metal-allene complex **2.125**, which subsequently undergoes transmetalation and reductive elimination (Scheme 2.2.25). Attempts to synthesise chiral allenes from enantioenriched starting materials resulted in the isolation of racemic products. It was proposed that isomerisation of palladium-allyl complex **2.124** was occurring. Studies of chiral ligands in transition metal catalysed cross-coupling syntheses of vinylallenes, and allenes more broadly, from racemic starting materials are yet to be reported. It should be noted that during the review of this thesis enantioselective palladium-catalysed synthesis of allenes was reported from racemic propargylic benzoates.^[93] While these results are of interest, the reaction appears to be limited to a specific substrate scope.



Scheme 2.2.25 Proposed mechanism of metal catalysed vinylallene syntheses that proceed with overall 1,5-transposition

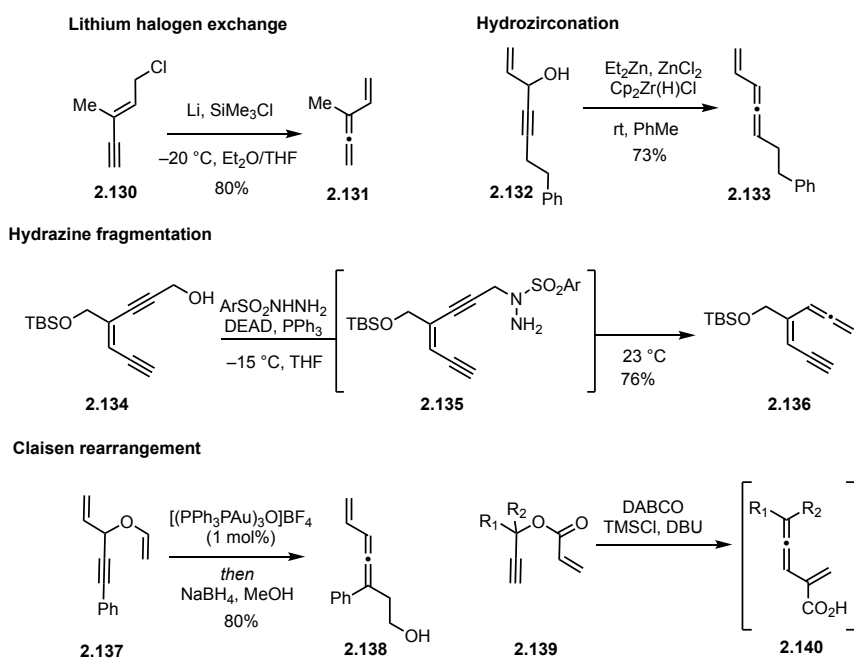
Palladium-catalysed cross-coupling reactions to synthesise vinylallenes have been reported using 2-bromo-1,3,5-triene (**2.127**) precursors (Scheme 2.2.26).^[94] This method was found to give vinylallenes such as **2.129** selectively, however, the use of groups less sterically hindered than the *tert*-butyl functionality, led to mixtures of regioisomers.



Scheme 2.2.26 Synthesis of vinylallenes from 2-bromo-1,3,5-trienes

2.2.9 Other Methods

While the aforementioned methods are commonly applied to the synthesis of vinylallenes other methods have also been reported. This includes lithium-halogen exchange of haloenynes,^[95] hydrazine fragmentation,^[96] hydrozirconation^[97] and Claisen rearrangements^[98] [99] (Scheme 2.2.27). To date, these methods remain as isolated examples within the broader allene literature.



Scheme 2.2.27 Isolated examples of vinylallene synthesis using alternative methods

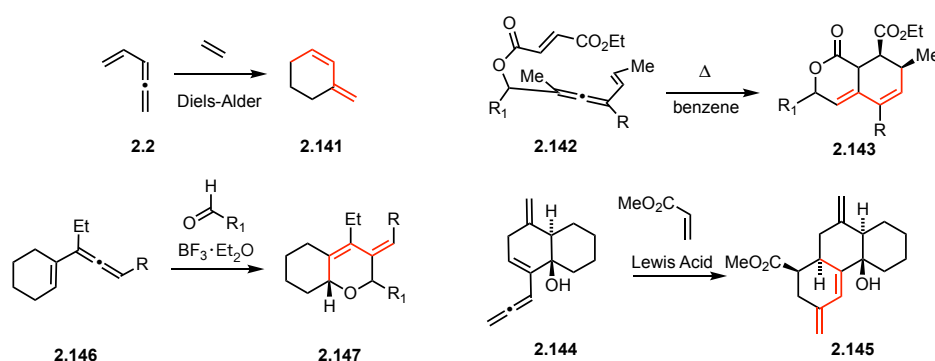
As discussed, vinylallenes can be accessed using a variety of methods. More recently, metal-catalysed cross-coupling reactions have been popularised due to the functional group tolerance of these reactions. Irrespective of the method, access to a variety of vinylallenes has enabled the reactivity of these conjugated allenes to be studied.

2.3 Reactivity of Vinylallenes

Early investigations into the reactivity of vinylallenes focused on cycloaddition and halogenation reactions of these conjugated allenes.^[27] Since then, the known reactivity of vinylallenes has expanded and led to the application of these molecules in natural product synthesis.

2.3.1 Diels–Alder reactions

Cycloaddition reactions of vinylallenes present a useful method to access cyclic frameworks that carry an exo-cyclic alkene (**2.141**) (Scheme 2.3.1).^{[18] [100]} Intramolecular Diels–Alder of vinylallenes, such as **2.142**,^[101] have been reported to construct fused bicyclic structures (Scheme 2.3.1) while intermolecular cycloaddition reactions have been used to construct multicyclic frameworks with exo-cyclic alkenes (**2.145**) (Scheme 2.3.1).^[102] Lewis acid catalysed hetero-Diels–Alder reactions have also been reported to form dihydropyran structures (**2.147**) (Scheme 2.3.1).^{[103] [104]}

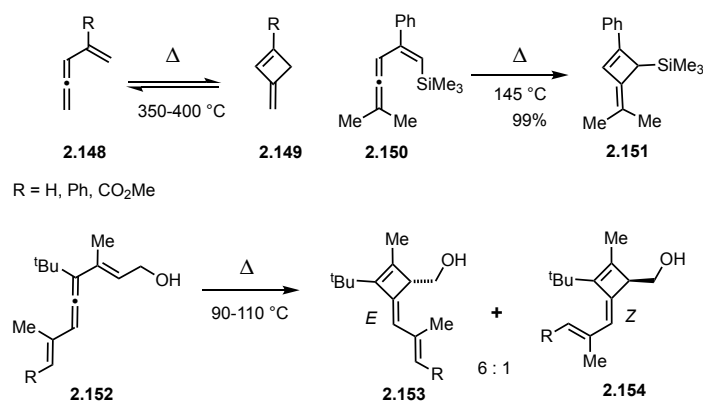


Scheme 2.3.1 Select examples of Diels–Alder reactions with vinylallenes demonstrating rapid access to multicyclic frameworks

Studies of the selectivity of vinylallene cycloadditions indicate that the dienophile approaches from the less sterically encumbered face of the allene while the stereoselectivity of the reaction is dictated by the transition state, whereby reduced 1,3-allylic strain is preferred.^[105] Calculations indicate that an asynchronous transition state is involved, with any radical character being stabilised by the *pseudo*-allylic functionality present in the transition state.^[106]
[107]

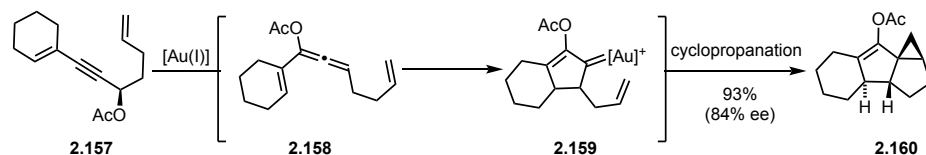
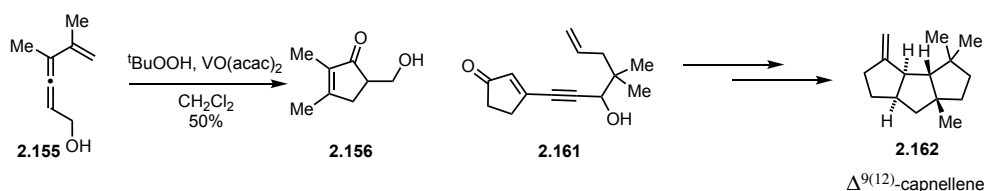
2.3.2 Cyclisation reactions

Intramolecular cyclisations are another type of reaction that have been observed with vinylallenes. Pyrolysis of vinylallenes (**2.148**) or cyclobutenes (**2.149**) were found to result in an equilibrium between the ring closed and ring opened systems. The presence of phenyl and carbonate substituents was found to stabilise the cyclobutene ring (Scheme 2.3.2).^{[108] [109]}



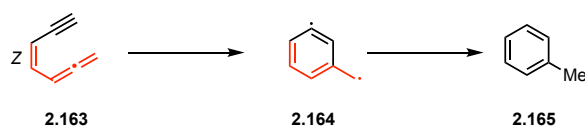
Scheme 2.3.2 Intramolecular conrotatory cyclisation of vinylallenes

Silyl functionality at the terminal alkenic position (**2.150**) was also found to result in a more facile cyclisation than **2.148**, which was attributed to electronic factors.^[110] 1,3-Divinylallenes substituted at the allenic position (**2.152**) underwent an irreversible conrotatory cyclisation at temperatures of 90-110 °C (Scheme 2.3.2).^{[111] [112] [113]} In particular, the presence of a *tert*-butyl substituent resulted in a regioselective and torquoselective cyclisation. The observed selectivity was ascribed to the steric bulk of the *tert*-butyl groups. Nazarov-type cyclisation of vinylallenes occur under either acidic or oxidative conditions to furnish cyclopentenes (such as **2.155** → **2.156**)(Scheme 2.3.3).^[114] Gold-catalysed reactions have also been demonstrated to form linear triquinanes, such as **2.160** from propargylic starting materials (**2.157**) with *in situ* formation of the vinylallene (**2.158**).^[115] Retention of stereochemistry is observed during the cyclisation, making this synthetically useful for synthesis of natural products such as **2.162** from propargylic alcohol **2.161**. Other metal catalysed cyclisations of vinylallenes have been reported with similar reactivity being observed.^{[116] [117] [118]}



Scheme 2.3.3 Nazarov cyclisations using either oxidative conditions or gold(I)-catalysed reactions

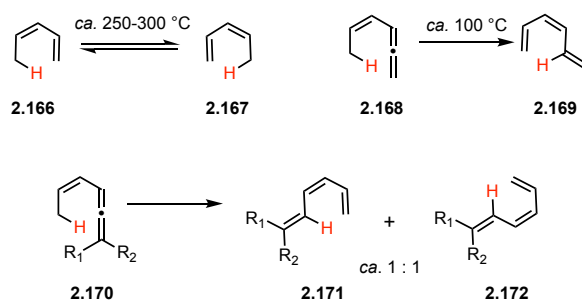
Ene-yne-allenes with a *Z*-configured vinylallene (**2.163**) can form aromatic rings (**2.165**) through the Myers-Saito reaction (Scheme 2.3.4).^{[119] [120] [121]} The reaction is proposed to proceed *via* a biradical intermediate (**2.164**) and proceeds at room temperature, making it more facile than the related Bergman cyclisation. Substitution at various positions has been found to affect the reaction rate.^[122]



Scheme 2.3.4 Myers-Saito reaction of vinylallenes with extended conjugation to form aromatic molecules *via* a biradical intermediate

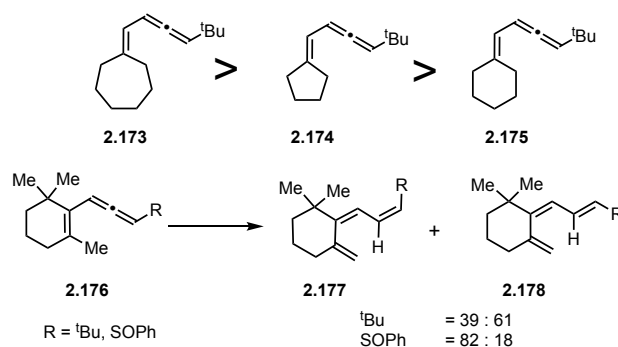
2.3.3 [1,5] Hydrogen Shift

Vinylallenes bearing a *Z*-alkyl substituent (**2.168**) undergo a sigmatropic [1,5] hydrogen shift. This reaction was originally noted for the low activation energies required compared to (*Z*)-1,3-pentadiene (**2.166**) (Scheme 2.3.5).^{[123] [124]} Early reports showed that this facile rearrangement occurred in the case of both acyclic and cyclic vinylallenes^[125] although a lack of *E/Z* selectivity was observed in the 1,3,5-hexatriene products (**2.171** and **2.172**) (Scheme 2.3.5).



Scheme 2.3.5 Early observations regarding the [1,5] hydrogen shift of vinylallenes

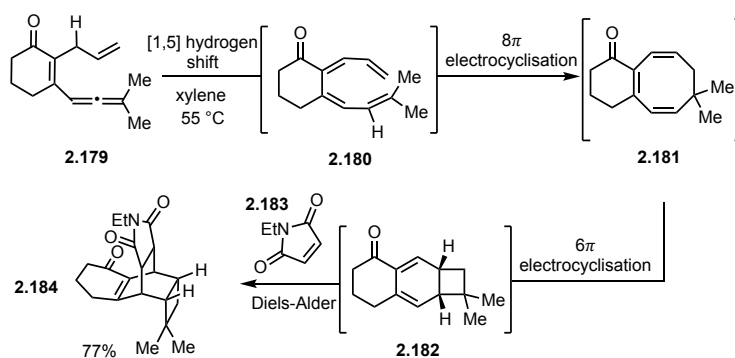
Experimental studies of the [1,5] hydrogen shift of vinylallenes found that both structural and electronic properties of vinylallenes affected the rate of reaction.^{[126] [127]} Proximity of the *Z*-alkyl substituent was found to lead to faster reaction rates (e.g. **2.173** reacts faster than **2.174** and **2.175** in Scheme 2.3.5). The presence of a sulfoxide at the allenic position (**2.176**) had a dramatic rate enhancement relative to alkyl substituents and led to geometric selectivity (**2.177** and **2.178**).^[128] To date, these observations remain poorly understood.^[129] Particular interest in [1,5] hydrogen shift of vinylallenes was due to the application of this reaction to the synthesis of vitamin D derivatives.^{[130] [131]}



Scheme 2.3.6 Examples of the effect of rate enhancement and product ratios due to stereo-electronic effects

Computational studies of the [1,5] hydrogen shift suggested that the lower activation energy required, relative to (*Z*)-1,3-pentadiene, was of both steric and electronic origins.^[132] It was proposed that vinylallenes have a lower steric strain in the transition state geometry and that the biradical character of the transition state is stabilised by the allene, resulting in a more facile migration.

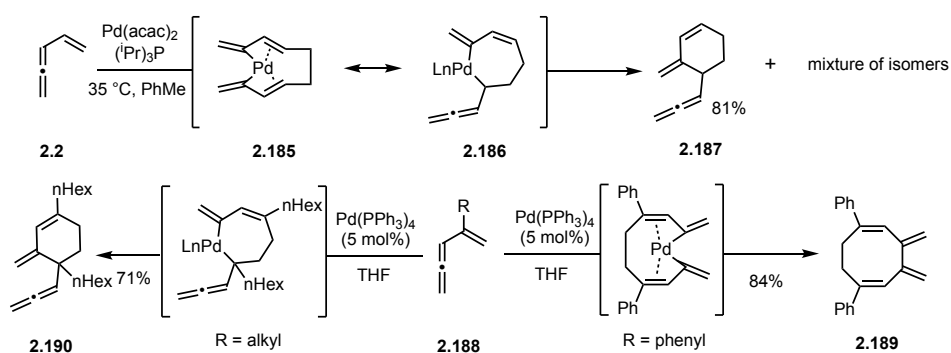
More recently, the [1,5] hydrogen shift has been used in pericyclic cascades to generate structurally complex frameworks.^{[133] [134]} One such example is shown in Scheme 2.3.7. Beginning with a [1,5] hydrogen shift of **2.179**, two subsequent electrocyclisations and trapping of the resulting diene (**2.182**) with dienophile **2.183** led to the rapid construction of a hexacyclic compound (**2.184**).



Scheme 2.3.7 Pericyclic cascade of vinylallene, beginning with a [1,5] hydrogen shift to generate a multicyclic framework

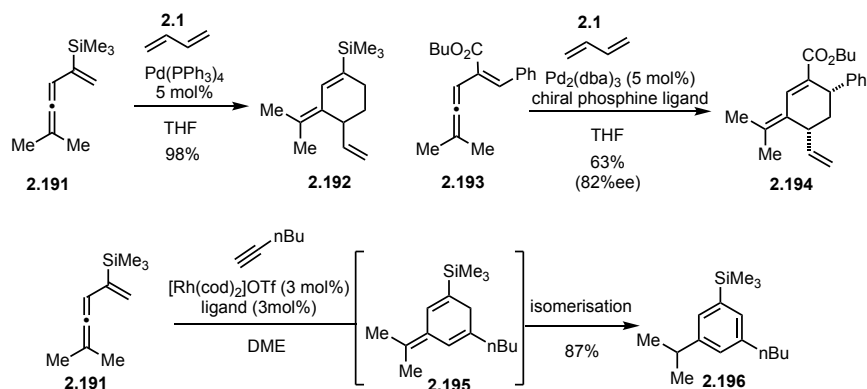
2.3.4 Metal Catalysed Reactions

As previously discussed in section 2.2.6, metals can form a η^4 -vinylallene complex with vinylallenes. In particular, palladium and rhodium catalysed reactions with vinylallenes have been reported to access a variety of compounds. The first reported metal-catalysed reaction of vinylallenes was the palladium-catalysed dimerisation of the vinylallene (**2.2**) (Scheme 2.3.8). The reaction was proposed to proceed *via* palladium complexes **2.185** and **2.186** with the formal [4+2] dimer (**2.187**) being isolated as the major product.^[135] Since then, studies with substituted vinylallenes (**2.188**) have shown that both [4+4] and [4+2] products can be synthesised to obtain eight (**2.189**) or six (**2.190**) membered carbocycles respectively, with product outcomes being determined by substitution at the alkene (Scheme 2.3.8).^{[136] [137]}



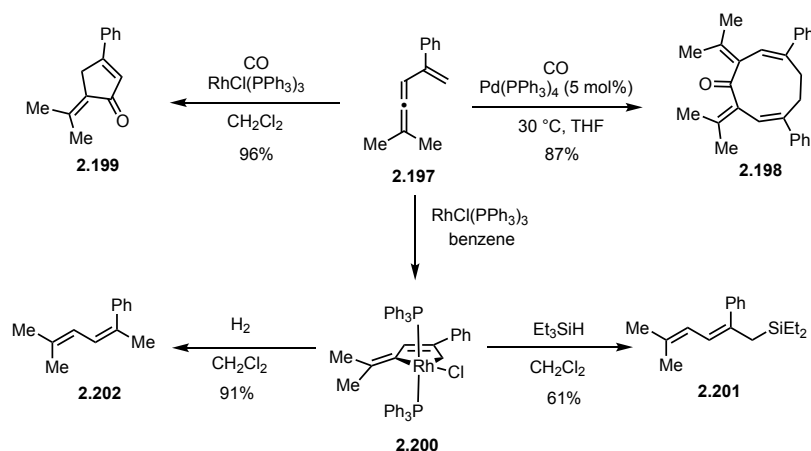
Scheme 2.3.8 Palladium catalysed [4+2] and [4+4] dimerisations of vinylallenes

Substituted vinylallenes, such as **2.191**, have also been shown to undergo palladium catalysed [4+2] reactions with 1,3-butadiene (**2.1**) to form semi-cyclic dienes (**2.192**). Enantioselective reactions could be achieved using chiral ferrocene monophosphate ligands to give chiral semi-cyclic dienes (**2.194**) (Scheme 2.3.9).^[138] ^[139] Rhodium catalysed [4+2] reactions with alkynes yield functionalised benzene structures (**2.196**) upon aromatisation.^[140]



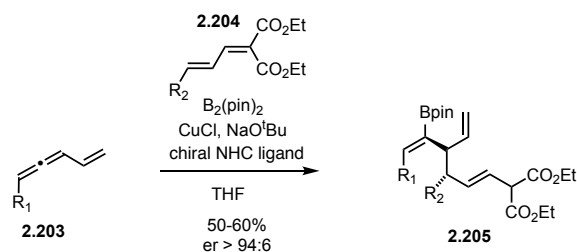
Scheme 2.3.9 Metal catalysed cycloaddition reactions of vinylallenes with dienophiles

Metal-catalysed carbonylation reactions have also been reported in the literature using vinylallenes (Scheme 2.3.10). Palladium-catalysed carbonylation reactions give [4+4+1] products (**2.198**), which initially involves the dimerisation of the vinylallene.^[141] ^[65] ^[137] Alternatively, rhodium catalysed carbonylations yield [4+1] cyclopentenone structures (**2.199**), with the chiral Du-PHOS ligand yielding chiral cyclopentenones.^[142] ^[143] ^[65] Hydrogenation and hydrosilylation reactions have also been reported for rhodium-vinylallene complexes (**2.200**), giving access to substituted butadienes (**2.201** and **2.202** respectively).^[142]



Scheme 2.3.10 Metal catalysed carbonylation reactions of vinylallene **2.197** to give 5- and 9-membered rings and reactivity of the rhodium-allene complex

More recently, vinylallenes (**2.203**) have been used as substrates in a copper(I) catalysed enantioselective 1,6-conjugate addition of unsaturated diester **2.204** (Scheme 2.3.11).^[144] This has enabled access to highly functionalised chiral alkenyl-boronic esters (**2.205**) from achiral vinylallenes.



Scheme 2.3.11 1,6-Conjugate addition to form chiral alkenyl-boronic esters from racemic vinylallenes

As discussed, vinylallenes have the ability to participate in a variety of reactions leading to diverse structures. The recent use of vinylallenes to rapidly access highly functionalised products that may be otherwise difficult to access suggests continued interest in these molecules.

2.4 Natural Products and Application in Total Synthesis

Vinylallenes have been isolated as natural products, proposed as biosynthetic intermediates and applied to the enantioselective total synthesis of natural products.^[21] ^[23] While allenic natural products were first isolated in the late 19th century, it was not until the advent of infrared spectroscopy that allenic structural features could be confirmed.^[21]

2.4.1 Natural Products

Of the three categories of allenic natural products (linear allenes, carotinoids or terpenoids and bromoallenes), vinylallenes have been isolated in the linear and carotinoid classes.^[21] Often the vinylallene is an important structural aspect of the natural products in which they feature. Fungal metabolite mycomycin (**2.206**) is an example of a linear vinylallene natural product that exhibits important antibiotic properties.^[145] ^[146] Another example is the insect pheromone **2.55** of which multiple syntheses have been reported. ^[21] ^[147] Exocyclic vinylallenes **2.207** and **2.208** were more recently isolated from *Pestalotiopsis fici* as fungal metabolites. ^[148] ^[149] ^[150] Compound **2.207** has been proposed as an intermediate in the biosynthesis of the chloropupukeananin ^[150] ^[151] ^[152] ^[153] and pestafalone families of natural products ^[154] ^[155] both of which have been isolated from *Pestalotiopsis fici*.

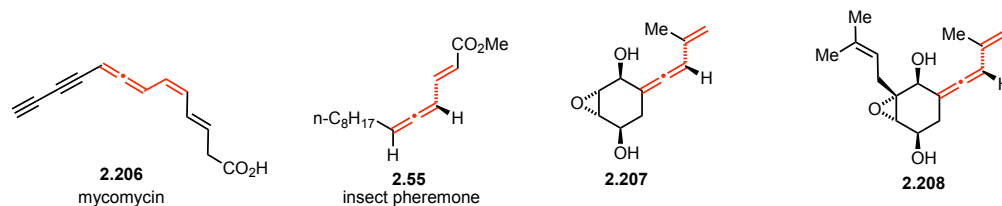


Figure 2.4.1 Linear allene natural products containing a vinylallene portion

Carotinoid vinylallenes have also been elucidated, with numerous compounds having been isolated and synthesised. ^[21] This includes the highly abundant carotinoid, fucoxanthin (**2.209**), as well as the related analogs peridinin (**2.210**) and mimulaxanthin (**2.211**), which contains two vinylallene units.^[21]

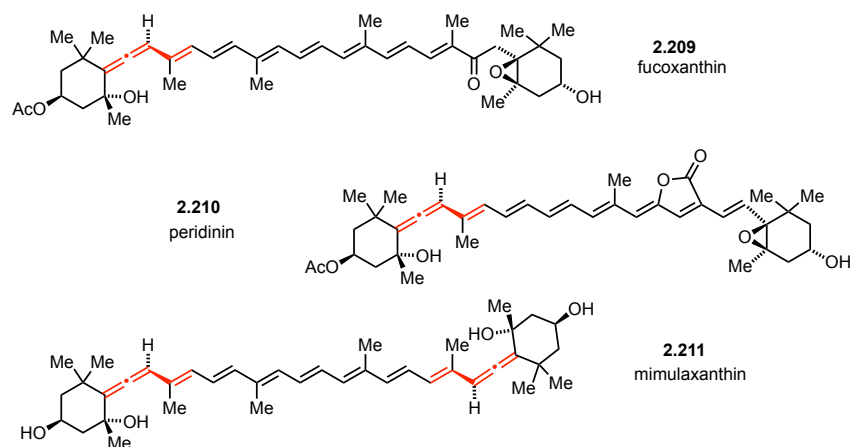
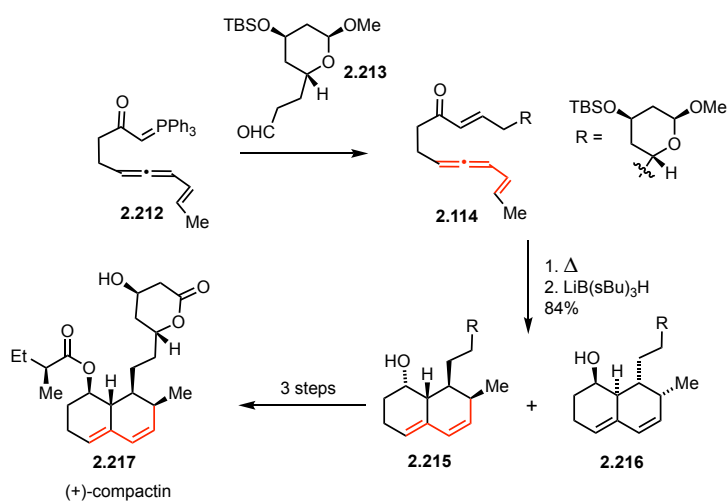


Figure 2.4.2 Carotenoid natural products containing a vinylallene component

2.4.2 Application in Natural Product Synthesis

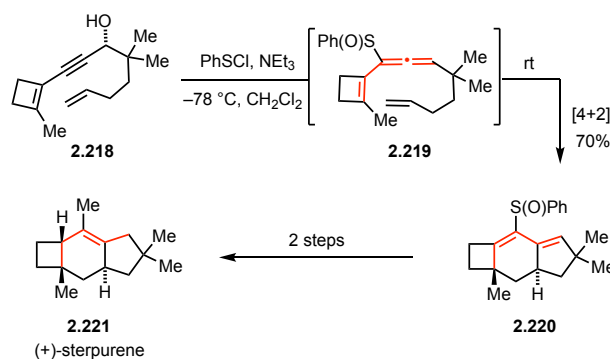
While vinylallenes have the potential to undergo a variety of reactions, their application in natural product synthesis has primarily focused on their ability to rapidly construct multicyclic frameworks *via* an intra- or intermolecular Diels–Alder reaction; a reaction that has demonstrated synthetic utility in natural product synthesis.^[156] Select examples are described to demonstrate the variety of natural products that have been synthesized from a vinylallene building block.

The convergent synthesis of (+)-compactin (**2.217**) used vinylallene **2.212** to form **2.214**, which underwent an intramolecular Diels–Alder reaction to generate the bicyclic core of the molecule (**2.215**).^[157] Separation of diastereomers **2.215** and **2.216** was required to synthesise **2.217** enantioselectively.



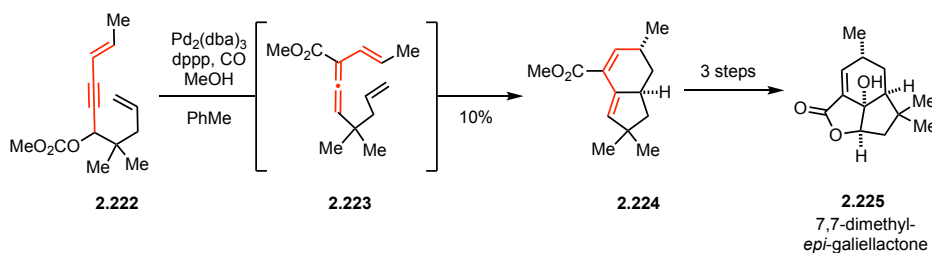
Scheme 2.4.1 Synthesis of (+)-compactin with the key intramolecular Diels–Alder reaction to form the bicyclic core

A similar approach was used in the synthesis of (+)-sterpurene (**2.221**), which contains a tricyclic framework.^[158] Vinylallene **2.219** was synthesized from **2.218** *via* a substitution-[2,3]-sigmatropic shift sequence. The subsequent intramolecular Diels–Alder reaction proceeded to generate the core multicyclic framework (**2.220**). The sulfoxide functionality of **2.219** was used to enable a facile cycloaddition.



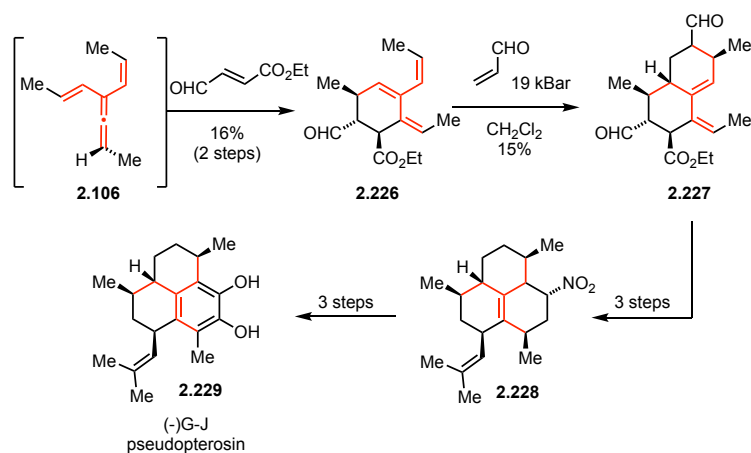
Scheme 2.4.2 Synthesis of (+)-sterpurene using an intramolecular Diels–Alder to form the tricyclic core

Galiellalactone derivatives such as **2.225** have been synthesized *via* a carbonylation-intramolecular Diels–Alder reaction sequence (Scheme 2.4.3).^[159] Vinylallene **2.223** was formed *in situ* from enyne **2.222** to generate bicycle **2.224**. While the low yield of this reaction is undesirable for total synthesis, the approach demonstrates the potential of vinylallenes to rapidly access different multicyclic structures.



Scheme 2.4.3 Synthesis of galiellalactone analog using a vinylallene intermediate

More recently, substituted 1,1-divinylallene **2.106** was used in an enantioselective total synthesis of pseudopterosin (Scheme 2.4.4).^[82] A diene-transmissive Diels–Alder sequence from **2.106** was exploited to construct the tricyclic core (**2.228**) within the first eight steps of the total synthesis. This is currently the shortest synthesis of pseudopterosin (**2.229**).



Scheme 2.4.4 The shortest reported enantioselective synthesis of pseudopterosin via a diene-transmissive Diels–Alder sequence of a 1,1-divinylallene **2.106**

The ability of vinylallenes to rapidly construct multicyclic frameworks enantioselectively has seen their application in a variety of natural product syntheses. The application of the vinylallene building block, is however, underrepresented in natural product synthesis, given their demonstrated success.

2.5 Multivinylallenes

The multivinylallenes are a group of acyclic, unbranched vinylallenes that are related by the sequential incorporation of vinylic units to the allenic core of vinylallene (**2.2**) (Figure 2.5.1). Currently, the parent 1,3-divinylallene (**1.28**) molecule was reported in 1975^[38] and later 1,1-divinylallene (**1.29**) was reported in 2011.^[46] More recently, the first synthesis of tetravinylallene (**1.31**) was disclosed in 2019 (this work is disclosed in Chapter 3). The trivinylallene (**1.30**) structure is yet to be reported in the literature.

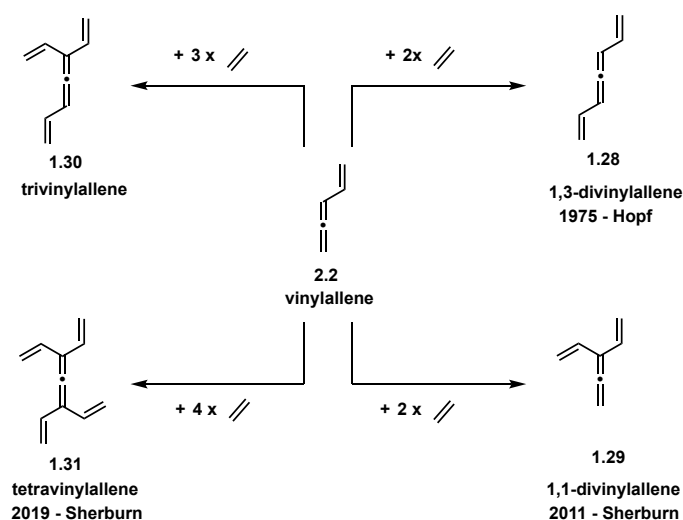


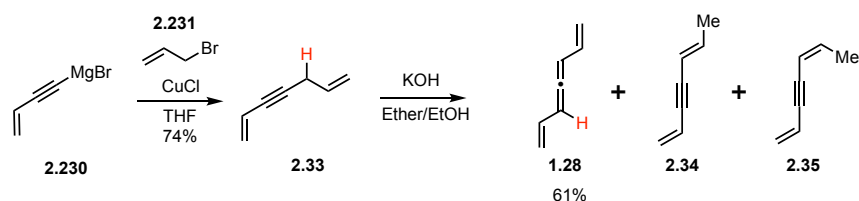
Figure 2.5.1 Construction of the multivinylallenes from the vinylallene core

2.5.1 Syntheses of the divinylallenes

Prior investigations of the multivinylallenes have been limited to the divinylallenes with only **1.28** and **1.29** having been reported. Presumably, the lack of reported syntheses for the higher members of the multivinylallenes family (**1.30** and **1.31**) is due to the assumed instability of these π -bond rich molecules.^[18]

The first reported synthesis of a divinylallene was the parent 1,3-divinylallene (**1.28**) molecule, which was achieved in a two step sequence (Scheme 2.5.1).^[38] Copper(I) catalyzed coupling of 3-buten-1-ynylmagnesium bromide (**2.230**) with allyl bromide (**2.231**) followed by base mediated isomerization afforded **1.28** along with two other isomers (**2.34** and **2.35**) (Scheme 2.5.1).

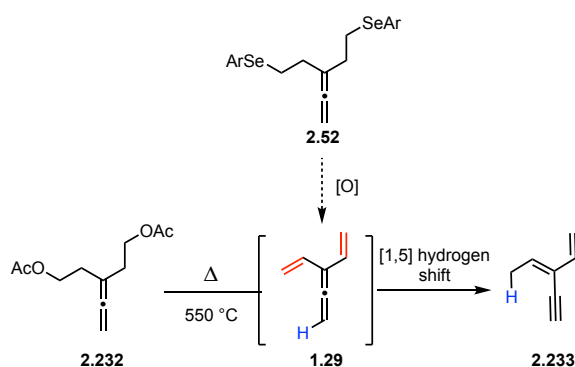
Purification by preparative gas chromatography enabled the isolation of neat 1,3-divinylallene (**1.28**).



Scheme 2.5.1 Synthesis of 1,3-divinylallene (**1.28**) *via* a base mediated isomerisation

1,3-Divinylallene (**1.28**) was observed to be stable enough to be stored under an inert atmosphere at room temperature for several hours, but **1.28** rapidly polymerised upon exposure to air.^[38] Infrared and Raman spectroscopic studies of **1.28** demonstrated that it adopts an *s-trans*, *s-trans* conformation (as shown in Scheme 2.5.1) in the gas, liquid and solid states.^[160] The preference for this conformation is a likely contributing factor to the stability of **1.28** compared to 1,1-divinylallene (**1.29**)

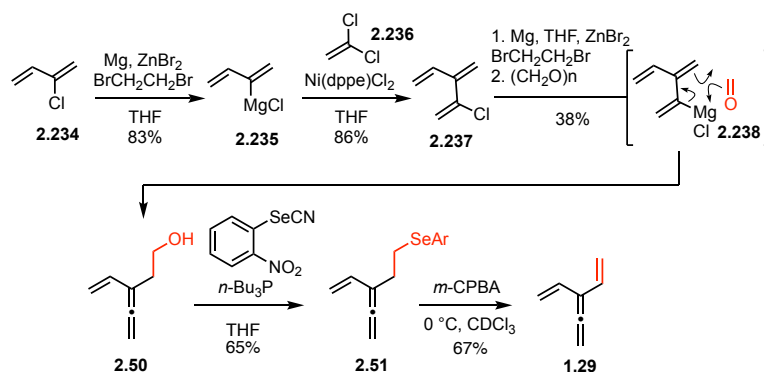
The synthesis of 1,1-divinylallene (**1.29**), the regioisomer of **1.28**, required a different synthetic approach. Attempts to synthesise **1.29** *via* pyrolysis of **2.232** were reported in 1987 however, only compound **2.233** was isolated (Scheme 2.5.2).^[36] It was proposed that this was a result of [1,5] hydrogen shift of **1.29** under these conditions. Efforts to synthesise **1.29** using a two-fold Grieco–Sharpless elimination from **2.52** was also reported to be unsuccessful (Scheme 2.5.2).^[37]



Scheme 2.5.2 Unsuccessful attempts to synthesise 1,1-divinylallene (**1.29**)

The first successful synthesis of 1,1-divinylallene (**1.29**) in 2011 was reported in a five step sequence beginning from chloroprene (**2.234**) (Scheme 2.5.3).^[46] Formation of the Grignard reagent and nickel-catalyzed cross-coupling with 1,1-dichloroethylene (**2.236**) gave 2-chloro-

[3]dendralene (**2.237**). A second Grignard formation step and subsequent addition to formaldehyde (**2.238**) afforded allenol **2.50**. Conversion to the selenide (**2.51**) and Grieco–Sharpless elimination furnished 1,1-divinylallene (**1.29**) as a CDCl₃ solution.



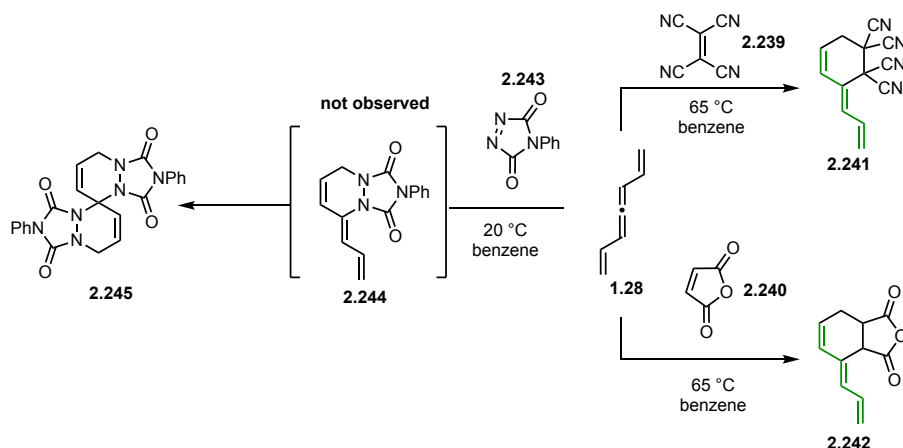
Scheme 2.5.3 First successful synthesis of 1,1-divinylallene (**1.29**) by Sherburn and co-workers

1,1-Divinylallene (**1.29**) was found to be unstable even as a solution and attempts to obtain neat **1.29** were unsuccessful. Currently the decomposition pathway remains unclear, although it is proposed to proceed *via* a Diels–Alder dimerization pathway.^[46] The difference in stability between the divinylallene isomers (**1.28** and **1.29**) encouraged investigations of the unreported multivinylallenes **1.30** and **1.31**.

2.5.2 Reactivity of the divinylallenes

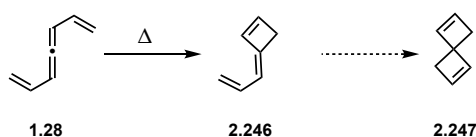
1,3-Divinylallene (**1.28**) was found to undergo a single Diels–Alder reaction in the presence of carbon-based dienophiles TCNE (**2.239**) and maleic anhydride (**2.240**) to form mono-adducts **2.241** and **2.242** respectively (Scheme 2.5.4).^[38] These mono-adducts did not partake in a second cycloaddition with these dienophiles and the lack of reactivity was attributed to the conjugated triene units of **2.241** and **2.242** (highlighted in green in Scheme 2.5.4).

In the presence of a more reactive dienophile, *N*-phenyltriazolinedione (PTAD) (**2.243**), 1,3-divinylallene (**1.28**) underwent a sequence of two Diels–Alder reactions to form bis-adduct **2.245**, which contains a [5.5]spirobicyclic core. In this case, the mono-adduct **2.244** was not observed during the reaction.



Scheme 2.5.4 Study of the Diels-Alder reaction between 1,3-divinylallene (**1.28**) and various dienophiles

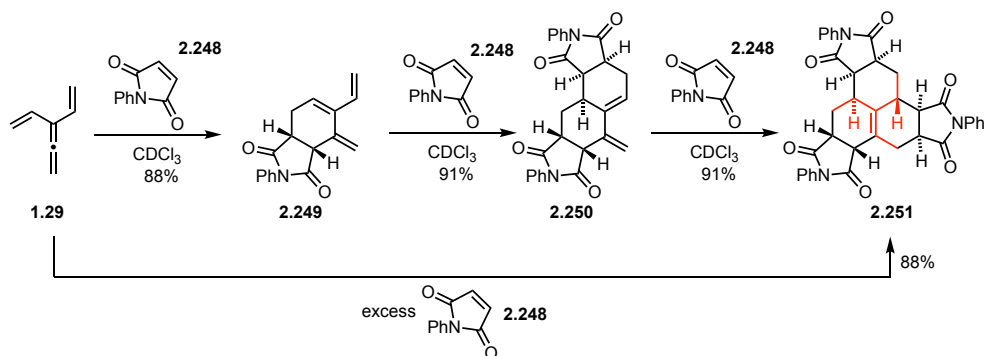
1,3-Divinylallene **1.28** was additionally found to undergo a thermal intramolecular [2+2] cyclisation to form **2.246**, however, further cyclisation to spirobicycle (**2.247**) was not observed (Scheme 2.5.5).^[18] Analogous reactivity was observed for substituted 1,3-divinylallenes (see Section 2.3.2).^{[111] [112] [113]}



Scheme 2.5.5 Intramolecular cyclisation of 1,3-divinylallene to form a conjugated cyclobutene

1,1-Divinylallene (**1.29**) was reported to participate in a diene-transmissive Diels–Alder sequence with the dienophile *N*-phenylmaleimide (NPM) (**2.248**) (Scheme 2.5.6). The cycloaddition cascade could either be performed sequentially *via* **2.249** and **2.250** or as a one-pot reaction to give tris adduct **2.251**.

It should be noted that the first two cycloadditions occurred with *endo*-selectivity, while the third Diels–Alder preferentially formed the *exo*-product as the major diastereomer.



Scheme 2.5.6 Rapid construction of a multicyclic framework *via* a diene-transmissive Diels–Alder sequence from 1,1-divinylallene (**1.29**)

Currently, the multivinylallenes are an incomplete family of molecules of which the known divinylallenes, **1.28** and **1.29**, display the ability to access a variety of structures. The synthesis and study of the divinylallenes encourages investigation of the higher members of the multivinylallene family in order to determine trends of this family of conjugated molecules.

2.6 Concluding Remarks

Vinylallenes are a family of π -bond rich molecules that can be conceived as a combination of the [n]cumulene and linear [n]polyene classes of fundamental conjugated hydrocarbons. This class of conjugated allenes has been identified as a structural motif in a variety of isolated natural products where they play important roles in biological settings. The variety of methods used to synthesise vinylallenes is suggestive of the synthetic utility of these compounds, although a more systematic study regarding the impact of steric and electronic effects on the stability and reactivity of vinylallenes would prove useful for their future application. Such a study could potentially result in the application of these molecules beyond cycloaddition reactions and natural product synthesis. In this regard, research of the multivinylallenes may provide new information about this class of conjugated allenes.

3

Tetravinylallene

3.1 An Introduction

Preamble

As previously mentioned in Chapter 2, tetravinylallene (**1.31**), the highest member of the multivinylallene family, has eluded synthesis with the literature also lacking examples of substituted tetravinylallenes (Figure 3.1.1).^[18] The closely related molecule tetraethynylallene (**3.1**) has also remained absent from the literature despite various attempts to synthesise this molecule.^{[161] [162]} As such, knowledge about allenes that carry four unsaturated substituents directly attached to the central allenic moiety is limited.

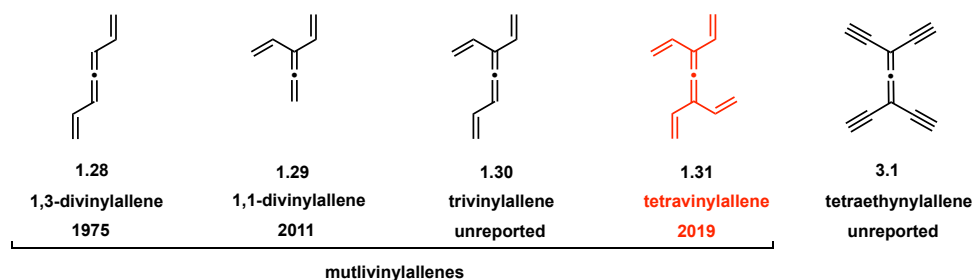


Figure 3.1.1 Tetravinylallene (**1.31**, shown in red) and related conjugated allenes

3.1.1 Tetra-conjugated allenes

Apart from tetravinylallene (**1.31**) and tetraethynylallene (**3.1**), other highly conjugated allenes are also conceivable. Tetracyanoallene (**3.2**) and tetracarboethoxyallene (**3.3**) and tetraphenylallene (**3.4**) are all compounds that bear four unsaturated units attached to the central allene moiety (Figure 3.1.2). Of these related molecules, tetraphenylallene (**3.4**) and tetracarboethoxyallene (**3.3**) are the only ones to have been synthesised and studied.

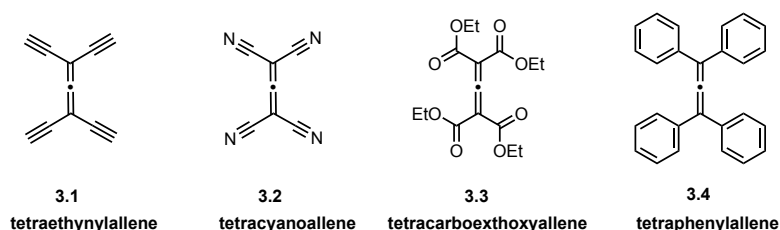
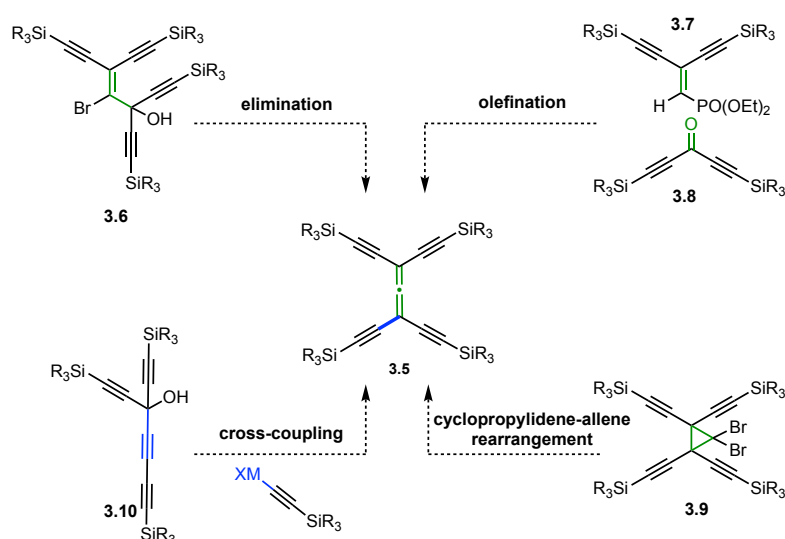


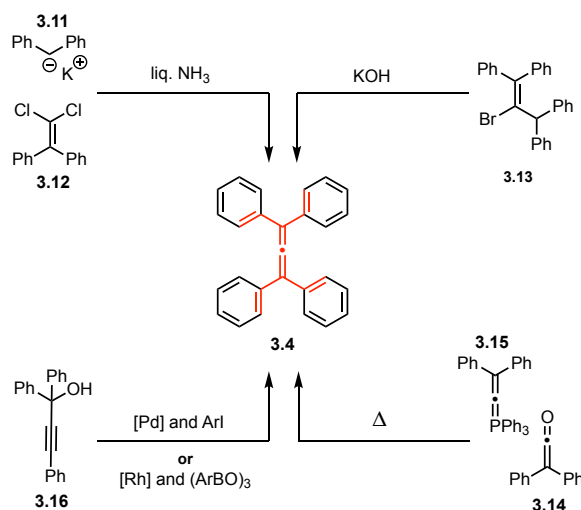
Figure 3.1.2 Conjugated allenes related to the multivinylallene family of molecules

Routes towards tetraethynylallene (**3.1**) have primarily focused on the silyl protected analog **3.5** with disconnections at either the central allene (shown in green) or the C-C bond between the allene and ethynyl groups (shown in blue) (Scheme 3.1.1). Approaches using elimination of **3.6** or olefination reactions between **3.7** and **3.8** were unsuccessful in generating the central allene functionality.^[161] Efforts to use the Doering-LaFlamme rearrangement were undermined by the inability to generate the 1,1-dibromocyclopropane (**3.9**).^[161] Palladium catalysed Sonogashira cross-coupling reactions were also unable to generate tetraethynylallene **3.5**.^[162]



Scheme 3.1.1 Attempted approaches towards the synthesis of tetraethynylallene **3.5**

Tetraphenylallene (**3.4**), which contains an embedded tetravinylallene structure (shown in red) was first synthesised by the reaction of potassium diphenylmethide (**3.11**) with 1,1-dichloro-3,3-diphenylethene (**3.12**) in liquid ammonia (Scheme 3.1.2).^[163] Since then, tetraphenylallene has been synthesised by a variety of methods, including via elimination from **3.13**^[164], Wittig olefination between **3.14** and **3.15**^[165] and metal cross-coupling reactions using **3.16**^[166] ^[167], to access the stable solid.



Scheme 3.1.2 Various approaches used to synthesise tetraphenylallene

Tetracarboethoxyallene (**3.3**) has been synthesised *via* Wittig olefination akin to the synthesis of tetraphenylallene (**3.4**), although the reduced analog, tetraformylallene, is yet to be reported.^[168] ^[169] Although tetraphenylallene (**3.4**) is ostensibly similar to tetravinylallene (**1.31**), we did not believe that it would be predictive of tetravinylallene (**1.31**). Nevertheless, the comparison of **1.31** and **3.4** would be of interest in understanding conjugated allenes.

3.1.2 Aims: Synthesis and study

Numerous reactions have been developed to synthesise vinylallenes (see Chapter 2 for details), although access to tetra-substituted allenes is more limited.^[170] In the case of tetravinylallene, the need to incorporate unsubstituted vinyl groups prompted the entertainment of three possible disconnections; (1) disconnection of the vinyl group (shown in blue) (2) disconnection of the allene (shown in green) and (3) disconnection at the C-C bond between the allene and vinyl group (shown in red) (Figure 3.1.3).

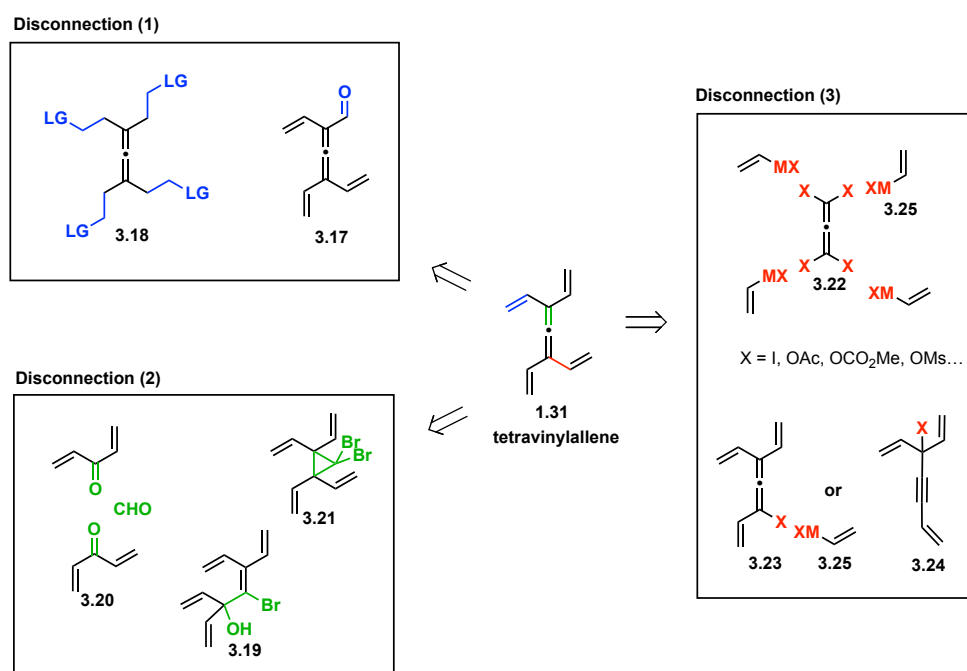
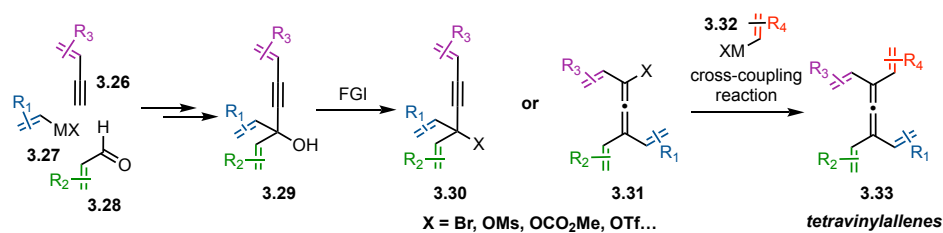


Figure 3.1.3 Retrosynthetic analysis of tetravinylallene unveiled three distinct disconnections

Disconnection of the vinyl group could lead back to an aldehyde functionality (such as **3.17**), which could undergo an olefination reaction (disconnection (1) Figure 3.1.3). Alternatively, an alkyl group substituted with an appropriate leaving group (**3.18**) could be utilised to obtain the final alkene. As these precursors were likely to be unstable, as well as reports of an unsuccessful two-fold elimination to synthesise 1,1-divinylallene,^{[36] [37]} this route was not considered further. Disconnection of the allene would result in the formation of the central sp-hybridised carbon in the final step (disconnection (2) Figure 3.1.3). Elimination of **3.19** and olefination reactions (using substrates such as **3.20**) as well as the Doering-LaFlamme allene synthesis from **3.21** could be considered as potential routes to tetravinylallene (**1.31**) using this approach.^[171] As advanced substrates would be difficult to obtain and were likely to be challenging to handle, this disconnection was not investigated. The final disconnection of the

C-C bond between the allene and the vinyl group led back to an allenic (**3.22** or **3.23**) or an equivalent propargylic (**3.24**) electrophilic cross-coupling partner as well as a vinyl nucleophile (**3.25**) (disconnection (3) Figure 3.1.3).

Due to the successful application of cross-coupling reactions to synthesise substituted divinylallenes^{[91] [82]} as well as accessible starting materials (such as **3.26**, **3.27** and **3.28**), disconnection 3 was investigated for the synthesis of tetravinylallene (Scheme 3.1.3).



Scheme 3.1.3 Proposed synthesis of tetravinylallenes using a cross-coupling reaction to install the final alkenic group

It was proposed that a cross-coupling strategy would also facilitate the incorporation of substitution at the various alkenic positions, thereby enabling the synthesis of substituted tetravinylallenes (**3.33**) (Scheme. 3.1.3).

3.2 Tetravinylallene

The following manuscript, which was accepted for publication in *Angewandte Chemie International Edition* (ACIE) in August 2019, outlines the first synthesis and pericyclic cascade of tetravinylallene (**1.31**) and compares the stability of this molecule to related π -bond rich hydrocarbons. This publication was chosen as a Hot Paper by the editors of ACIE.

Permission has been granted via RightsLink from John Wiley and Sons for reproduction in this thesis (licence number 4663001484237). All experimental work published in this paper is my own. The other authors are Professor Michael Sherburn and Dr. Jas Ward (X-ray crystallographer). The project was conceived and designed through collaboration with M.S. Sherburn. C. Elgindy wrote the first draft of the manuscript and carried out computational study on the geometry of tetravinylallene in collaboration with M.S. Sherburn. J. Ward solved the single crystal X-ray structure of Diels–Alder adducts **15** and **32** (as numbered in the publication).

Hydrocarbons Hot Paper

International Edition: DOI: 10.1002/anie.201908496
German Edition: DOI: 10.1002/ange.201908496

Tetravinylallene

Cecile Elgindy, Jas S. Ward, and Michael S. Sherburn*

Abstract: The first chemical synthesis of tetravinylallene (3,5-divinylhepta-1,3,4,6-tetraene) is reported. The final, key step of the synthesis involves a palladium-catalyzed, Negishi-type cross-coupling involving 1,5-transposition of a penta-2-en-4-yn-1-ol methanesulfonate. The unprecedented fundamental hydrocarbon is sufficiently stable to be purified by flash chromatography. A similar synthetic pathway grants access to the first substituted tetravinylallenes, which provide insights into the influence of substitution upon stability and reactivity. Tetravinylallenes are shown to break new ground in swift structural complexity creation, with three novel sequences reported.

With a structure comprising ten sp^2 -carbons and one sp -carbon, the previously unknown tetravinylallene (TVA) **1** is one of the most C=C-bond-rich acyclic hydrocarbons (Figure 1). Neither the unsubstituted $C_{11}H_{12}$ hydrocarbon

TVA **1** can also be viewed as a pair of [3]dendralene^[3,4] structures **4** conjoined through a central carbon, or as a “stretched” analog of tetravinylethylene^[5] **5**. In addition to its pure aesthetic appeal, we were intrigued by the potential of TVA to serve as an inception point for extended sequences of σ -bond-forming events, leading to rapid structural complexity generation. Such results would serve as a foundation for applications in total synthesis. A substituted 1,1-divinylallene precursor recently delivered the shortest step count total synthesis of pseudopterosin natural products (Figure 1).^[6] The brevity of the synthesis is all the more surprising, since more C–C bonds, rings and stereocenters are forged than other syntheses.^[7]

The origin of the synthetic power of branched, C=C-bond-rich structures is their ability to perform as multi-1,3-butadienes in sequences of [4+2] cycloadditions.^[4,8] Evidently, with more π -bonds than 1,1-divinylallene, TVA **1** could potentially undergo extended addition reaction sequences, thus generating more σ -bonds and greater structural complexity than before. 1,1-Divinylallene **3** readily decomposes,^[2] thereby presenting challenges with its handling. Given its close structural relationship but 50% greater C=C bond content, we were concerned that TVA **1** might be unmanageable. Even if TVA **1** could be accessed, we were unconvinced that its domino cycloaddition sequences would be selective.

Various synthetic approaches to TVA **1** were considered, including elimination reactions (akin to those used for the synthesis of 1,1-divinylallene^[2] **3** and [3]dendralene^[3] **4**), fourfold sp^2 – sp^2 cross-coupling (as employed in a synthesis of tetravinylethylene^[5b] **5**), and base-catalyzed propargyl to allenyl isomerization (deployed in the synthesis of 1,3-divinylallene^[1] **3**). The ultimately successful approach involved a Pd^0 -catalyzed Negishi-type cross-coupling with 1,5-transposition (i.e. **9**→**1**). Such processes are well established with alkyl and aryl nucleophiles^[9] but only two previous reports describe alkenyl nucleophiles.^[10]

The synthesis of the parent hydrocarbon, TVA **1**, commenced with the union of acrolein, ethynyl magnesium bromide and vinyl bromide, to generate dienynol **6**^[11] in 62% yield over 2 steps (Scheme 1). Oxidation with the Dess–Martin periodinane gave dienynone **7**, which underwent 1,2-addition of vinyl lithium to form trienynol **8**.

Attempts to prepare TVA **1** by cross-couplings between the carbonate derivative of tertiary alcohol **8** and vinyl nucleophiles were indeed successful, but the process was not consistently reproducible. While there is significant precedent for vinylallene synthesis through propargyl to allenyl 1,3-transposition,^[12] the desired transformation is demanding for three reasons. Firstly, derivatives of alcohol **8** and its transposed congeners (such as mesylate **9**) were found to be unstable, precluding isolation. Secondly, TVA **1** was found to

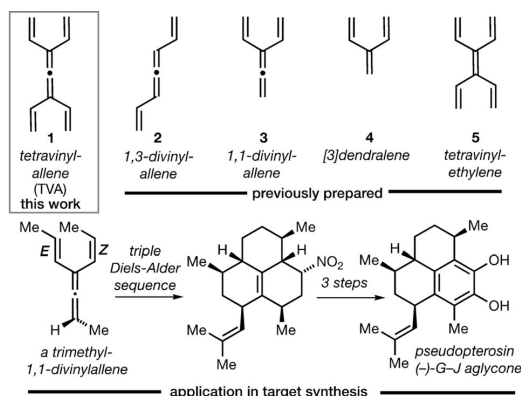
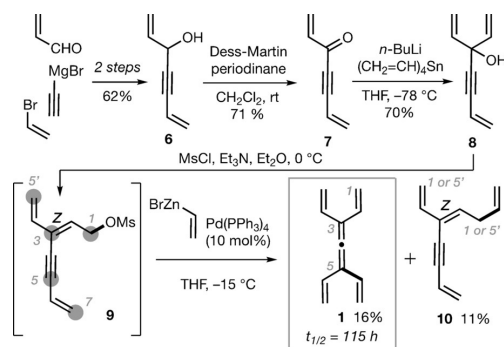


Figure 1. Tetravinylallene **1**, its most closely-related known compounds, and their value in step economic total synthesis.

1 nor substituted derivatives have been reported. The two most closely-related known hydrocarbons are 1,3- and 1,1-divinylallenes, **2** and **3** respectively. Whereas 1,3-divinylallene **3** was reported by the Hopf group in 1975,^[1] the considerably less stable 1,1-divinylallene **3** premiered in 2011.^[2]

[*] C. Elgindy, Dr. J. S. Ward, Prof. M. S. Sherburn
Research School of Chemistry, Australian National University
Canberra, ACT 2601 (Australia)
E-mail: michael.sherburn@anu.edu.au

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under <https://doi.org/10.1002/anie.201908496>.



Scheme 1. The first synthesis of tetravinylallene **1**. The five possible reaction sites of mesylate **9** are highlighted; TVA **1** results from 1,5-transposition through the enyne. $t_{1/2}$ = first half-life of a [0.041 M]_{initial} benzene solution of TVA **1** at 25 °C. Ms = methanesulfonyl.

decompose in the presence of Pd⁰ catalysts, so short reaction times and lower reaction temperatures were mandated. Thirdly, a challenging regioselectivity issue exists, since derivatives of alcohol **8** and transposed mesylate **9** have five potential sites for C–C bond formation (shown as shaded circles in Scheme 1).

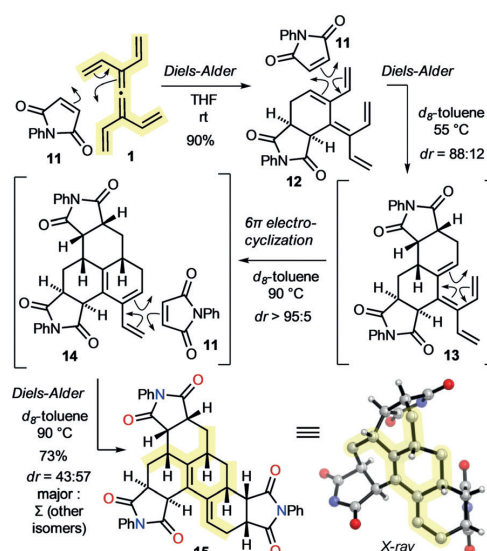
After extensive experimentation (see SI for details), reproducibility came in the form of a Negishi-type coupling of mesylate **9** with vinylzinc bromide, which gave TVA **1** consistently, albeit in modest yield. TVA **1** is the product of sp²–sp² coupling (substitution with 1,5-transposition through the enyne), with side product **10** being the result of sp²–sp³ coupling at two sites (either direct substitution or 1,5-transposition through the pentadiene). Products resulting from 1,3- and 1,7-transpositions were not detected.

TVA **1** was isolated as a colorless oil following purification by flash chromatography. Storage as a neat liquid invariably led to decomposition, which was accelerated significantly by exposure to air, leading to an insoluble white solid which we presume to be polymeric. In solution, TVA **1** was significantly more persistent: a 0.041 M solution in [D₆]benzene held at 25 °C exhibited a first half-life of 115 h, which places its stability greater than 1,1-divinylallene **3**^[2] but lower than [3]dendralene **4**^[3b,c] and tetravinylethylene **5**^[5b] (see SI for details). The first half-life of TVA **1** was ca. 50 % longer in the presence of BHT, suggesting an autoxidative decomposition mechanism but other pathways are, undoubtedly, also involved.^[13]

An MP2/cc-pVTZ computational study (see SI for details) reveals that the lowest energy conformation of TVA **1** is chiral and C₂ symmetric, related to that of 1,1-divinylallene **3**^[2] and [3]dendralene **4**,^[3b] and close to the recently reported B3LYP/6-31G(d) geometry.^[14]

The ability of TVA **1** to serve as a precursor to structurally complex molecules is depicted in Scheme 2.

In the presence of one molar equivalent of the dienophile *N*-phenylmaleimide (NPM) **11**, TVA **1** underwent Diels–Alder cycloaddition at ambient temperature to form pentene **12**. This compound contains an unprecedented 2,4-divinyl-1,3,5-hexatriene π-system.^[15]

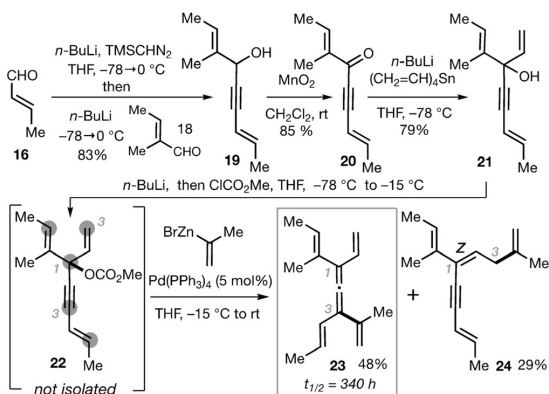


Scheme 2. Tetravinylallene **1** reacts as a triple diene, undergoing a sequence involving three [4+2] cycloadditions and a 6π electrocycloaddition to generate heptacycle **15**, containing seven new C–C bonds and nine new stereocenters. Only stereocenter hydrogens are shown in the X-ray crystal structure.

Bicyclic penta-ene **12** was converted into heptacyclic diene **15** in a one flask operation involving three selective pericyclic reactions. Firstly, warming to 55 °C with NPM brought about a Diels–Alder reaction at the semi-cyclic diene site of **12**, generating *endo*, *anti*-diastereomer **13** as the major product. Increasing the temperature to 90 °C triggered a torquoselective^[16] 6π electrocycloaddition to 2-vinyl-1,3-cyclohexadiene **14**, which underwent a third Diels–Alder reaction at the semi-cyclic diene site to give heptacyclic diene **15** as the major diastereomeric product. Each subsequent step of this series of four pericyclic reactions involves a newly transmitted C=C bond.^[17] Overall, in only two simple synthetic operations, acyclic and achiral TVA **1** was transformed into heptacycle **15**, in the process generating four carbocycles, seven C–C bonds and nine stereocenters. This swift assembly of structural complexity hints at the potential of this new hydrocarbon in target synthesis.

Encouraged by the successful synthesis of the parent TVA **1**, attention shifted to substituted analogs. We targeted two analogs, each carrying four different alkenyl groups branching from a central, tetra-substituted allene core. The aim was to identify substitution patterns that would provide either an enhancement or deterioration of stability relative to the parent compound.

The synthesis of the first target, tetramethyl-TVA **23** (Scheme 3) began with Colvin–Hamill alkylation^[18] of crotonaldehyde **16**, in situ deprotonation and 1,2-addition to tiglic aldehyde **18**, furnishing 1,6-dien-4-yn-3-ol **19**. Oxidation with MnO₂ afforded the corresponding dienyone **20**, which underwent 1,2-addition of vinyl lithium to generate tertiary alcohol **21**, which was converted into carbonate derivative **22**.



Scheme 3. Preparation of the first substituted tetravinyllene **23**. The five possible reaction sites of carbonate **22** are highlighted; substituted TVA **23** results from 1,3-propargyl to allenyl transposition. $t_{1/2}$ = first half-life of a $[0.040 \text{ M}]_{\text{initial}}$ benzene solution of TVA **23** at 25 °C. TMS = trimethylsilyl.

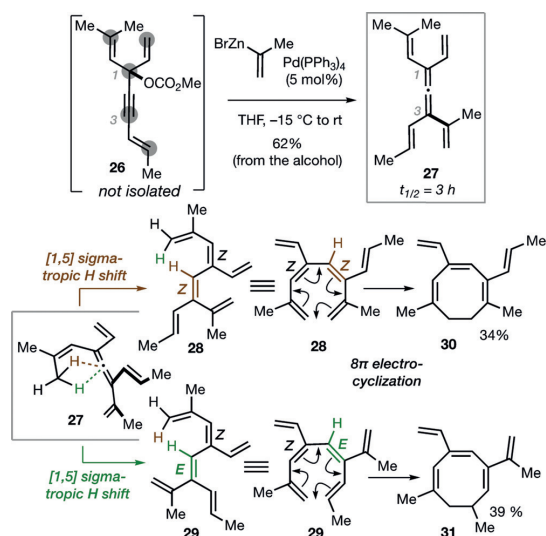
Negishi-type cross-coupling with 2-propenyl zinc bromide proceeded with 1,3-propargyl to allenyl transposition^[12] to deliver the first substituted TVA **23** in 48% yield as a colorless oil. Tetraene **24**, the product of C–C coupling at the unsubstituted terminus through allyl 1,3-transposition, was also isolated in 29% yield.

Internal and terminal *E*-methyl substituents have an overall stabilizing influence. Tetra-methyl TVA **23** was significantly more persistent than the parent molecule **1**, exhibiting a first half-life that was three times longer (see SI for details). Once again, there were no identifiable decomposition products.

The synthesis of the second substituted TVA **27** (Scheme 4), a *gem*-dimethyl analog, followed the same pathway as that of its regioisomer **23** (see SI for details). The Pd⁰-catalyzed cross-coupling reaction between 2-propenyl zinc bromide and carbonate **26** (generated from the corresponding alcohol) delivered TVA **27** in 61% isolated yield, with no regioisomeric products detected. The site selectivity of this process is striking, with reaction at the one desired site (accompanied by propargyl to allenyl 1,3-transposition) from five distinct possibilities.

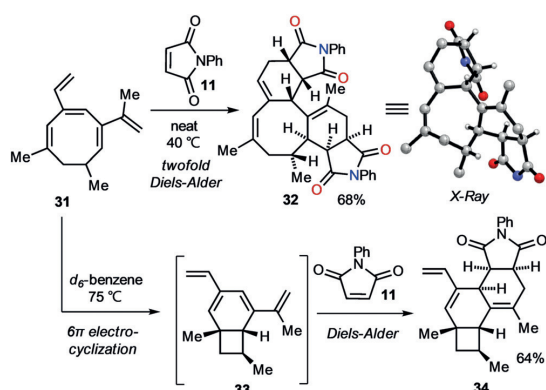
Unexpectedly, substituted analog **27** proved to be the shortest lived of the three TVA compounds, exhibiting a half-life that was one thirtieth of the value of the parent TVA **1**, and cleanly forming isomeric cyclooctatrienes **30** and **31** in a ca. 1:1 ratio (Scheme 4). The short-lived nature of substituted TVA **27** can be traced to the presence of a *Z*-methyl substituent within its structure. We propose a rapid suprafacial sigmatropic [1,5]-H shift to generate the *Z*- and *E*-tetraenes **28** and **29** at ambient temperature, which undergo even faster 8π electrocyclization to the observed products.^[19] This sequence has been seen previously with vinylallenes, but only upon heating with un-activated systems.^[20]

An unanticipated facet of the rapid complexity-building chemistry of TVAs is the ability to form diverse structural types. The five C=C π -system contained in 2,4-di(alkenyl)-



Scheme 4. Synthesis and unimolecular decomposition of substituted TVA **27** at ambient temperature. Carbonate **26** was generated from the corresponding alcohol. $t_{1/2}$ = half-life of a $[0.050 \text{ M}]_{\text{initial}}$ benzene solution of TVA **27** at 25 °C.

1,3,5-cyclo-octatrienes **30** and **31** (Scheme 4) is the same as that of TVA Diels–Alder mono-adduct **12** (Scheme 2). Nevertheless, the two differing settings for the penta-ene stimulate divergent pericyclic domino sequences. Moreover, cyclo-octatriene **31** exhibits additional divergent behavior, as evidenced by the results depicted in Scheme 5. Thus, the same reaction partners (**31** and **11**) furnished either pentacycle **32** or tetracycle **34**, depending upon the reaction temperature and mode of dienophile addition. At lower temperatures without solvent, successive Diels–Alder additions of NPM **11** to the two semi-cyclic diene units of cyclo-octatriene **31** led, stereoselectively, to fused 6-8-6 tricyclic system **32** with seven new stereocenters. On the other hand, stronger heating



Scheme 5. Divergent, rapid structural complexity generation with cyclo-octatriene **31**. Only stereocenter hydrogens are shown in the X-ray crystal structure and phenyl groups are omitted for clarity.

induced a disrotatory, torquoselective transannular 6π electrocyclicization to bicyclo-octadiene **33**,^[21] which underwent selective Diels–Alder addition of NPM **11** at the semi-cyclic diene site more distant from the ring junction methyl substituent to form fused 6-6-4 tricyclic system **34**. Cyclo-octatriene **30** (Scheme 4) undergoes a similar transformation (see SI for details).

In summary, the first syntheses of the parent tetravinylallene **1** and substituted analogs were achieved through the development of Negishi-type Pd⁰-catalyzed cross-coupling processes that proceed with either 1,3-transposition or 1,5-transposition. In principle, these couplings could generate up to five distinct regioisomeric products. The desired allenic regioisomer is the major isolated product in every case. In solution, the parent, unsubstituted TVA **1** is more stable than 1,1-divinylallene **3** but less stable than both [3]dendralene **4** and tetravinylethylene **5**. Surprisingly, the parent unsubstituted TVA is more stable than a substituted analog, with a Z-methyl substituent triggering decomposition by way of a pericyclic reaction cascade, initiated by a sigmatropic [1,5]-H shift. It would appear that Z-substituents carrying an allylic hydrogen should be avoided if more stable TVAs are required. Finally, this work shows that TVAs have an unequalled ability to build diverse multi-ring systems, in the process forging many C–C bonds and creating numerous stereocenters. In this respect, TVAs outshine their [3]dendralene and 1,1-divinylallene relatives: compounds with a proven track record for delivering the most step economic total syntheses.^[6,22]

Acknowledgements

This work was supported by the Australian Research Council (DP160104322). We thank Dr. Hideki Onagi and Chris Blake (Australian National University) for assistance with HPLC separations and NMR experiments, respectively.

Conflict of interest

The authors declare no conflict of interest.

Keywords: allenes · cross-coupling · domino reactions · hydrocarbons · polyenes

How to cite: *Angew. Chem. Int. Ed.* **2019**, *58*, 14573–14577
Angew. Chem. **2019**, *131*, 14715–14719

- [1] U. Mödlhammer, H. Hopf, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 501–502; *Angew. Chem.* **1975**, *87*, 492–493.
[2] K. M. Cergol, C. G. Newton, A. L. Lawrence, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2011**, *50*, 10425–10428; *Angew. Chem.* **2011**, *123*, 10609–10612.
[3] a) First synthesis: A. T. Blomquist, J. A. Verdol, *J. Am. Chem. Soc.* **1955**, *77*, 81–83; b) practical synthesis and half-life measurement in neat form: T. A. Bradford, A. D. Payne, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *J. Org. Chem.* **2010**, *75*, 491–494; c) M. F. Saglam, T. Fallon, M. N. Paddon-Row, M. S. Sherburn, *J. Am. Chem. Soc.* **2016**, *138*, 1022–1032;

- d) half-life measurement in solution: H. Toombs-Ruane, E. L. Pearson, M. N. Paddon-Row, M. S. Sherburn, *J. Chem. Soc. Chem. Commun.* **2012**, *48*, 6639–6641.
[4] For a review on dendralenes, see: H. Hopf, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2012**, *51*, 2298–2338; *Angew. Chem.* **2012**, *124*, 2346–2389.
[5] a) First synthesis: L. Skattebøl, J. L. Charlton, P. deMayo, *Tetrahedron Lett.* **1966**, *7*, 2257–2260; b) practical synthesis and half-life measurement: E. J. Lindeboom, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2014**, *53*, 5440–5443; *Angew. Chem.* **2014**, *126*, 5544–5547.
[6] C. G. Newton, S. L. Drew, A. L. Lawrence, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Nat. Chem.* **2015**, *7*, 82–86.
[7] C. G. Newton, M. S. Sherburn, *Nat. Prod. Rep.* **2015**, *32*, 865–876.
[8] C. G. Newton, M. S. Sherburn in *Cross Conjugation: Modern Dendralene, Radialene and Fulvene Chemistry* (Eds.: H. Hopf, M. S. Sherburn), Wiley-VCH, Weinheim, **2016**, pp. 413–443.
[9] a) M. Purpura, N. Krause, *Eur. J. Org. Chem.* **1999**, 267–275, and references therein. First report: b) J. Gore, J. P. Dulcere, *Chem. Commun.* **1972**, 866–867.
[10] a) M. Üçüncü, E. Karakus, M. Kus, G. E. Akpınar, O. Aksin-Artok, N. Krause, S. Karaca, N. Elmali, L. Artok, *J. Org. Chem.* **2011**, *76*, 5959–5971; b) F. Ziyank, M. Kus, L. Alkan-Karadeniz, L. Artok, *Tetrahedron* **2018**, *74*, 3652–3662; For an example with an alkynyl nucleophile, see c) D. Taç, L. Artok, *Tetrahedron Lett.* **2018**, *59*, 895–898.
[11] I. N. Nazarov, L. B. Fisher, *Zh. Obshch. Khim.* **1950**, *20*, 1107–1113.
[12] For (vinyl)allene synthesis through Pd⁰-catalyzed C–C coupling involving 1,3-propargyl to allenyl transposition, see: a) K. Ruitenberg, H. Kleijn, C. J. Elsevier, J. Meijer, P. Vermeer, *Tetrahedron Lett.* **1981**, *22*, 1451–1452; b) K. Ruitenberg, H. Kleijn, H. Westmijze, J. Meijer, P. Vermeer, *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 405–408; c) E. Keinan, E. Bosch, *J. Org. Chem.* **1986**, *51*, 4006–4016; d) T. Mandai, M. Ogawa, H. Yamoaki, T. Nakata, H. Murayama, M. Kawada, J. Tjusi, *Tetrahedron Lett.* **1991**, *32*, 3397–3398; e) S. Ma, A. Zhang, *J. Org. Chem.* **2002**, *67*, 2287–2294; f) S. Ma, G. Wang, *Angew. Chem. Int. Ed.* **2003**, *42*, 4215–4217; *Angew. Chem.* **2003**, *115*, 4347–4349; g) G. A. Molander, E. M. Sommers, S. R. Baker, *J. Org. Chem.* **2006**, *71*, 1563–1568; h) J. A. Souto, M. Pérez, C. S. López, R. Álvarez, A. Torrado, A. R. de Lera, *J. Org. Chem.* **2010**, *75*, 4453–4462; for Cu^I-catalyzed reactions, see i) M. Yang, N. Yokokawa, H. Ohmiya, M. Sawamura, *Org. Lett.* **2012**, *14*, 816–819.
[13] This experimental half-life was essentially the same in both C₆D₆ and CDCl₃ at the same starting concentration. Increased starting concentrations led to faster decomposition rates and decreased starting concentrations led to slower decomposition rates.
[14] N. Radić, Z. B. Maksić, *J. Org. Chem.* **2019**, *84*, 2425–2438.
[15] C=C-based systems with both through- and cross-conjugation are poorly represented in the literature: see *Cross Conjugation: Modern Dendralene, Radialene and Fulvene Chemistry* (Eds.: H. Hopf, M. S. Sherburn), Wiley-VCH, Weinheim, **2016**.
[16] For recent examples of torquoselective thermal 6π electrocyclicizations through remote stereocontrol, see: a) S. Dongbang, B. Pedersen, J. A. Ellman, *Chem. Sci.* **2019**, *10*, 535–541; b) E. M. Phillips, T. Mesganaw, S. Duttwyler, B. Q. Mercado, J. A. Ellman, A. Patel, K. N. Houk, *Angew. Chem. Int. Ed.* **2015**, *54*, 12044–12048; *Angew. Chem.* **2015**, *127*, 12212–12216; c) Z.-X. Ma, A. Patel, K. N. Houk, R. P. Hsung, *Org. Lett.* **2015**, *17*, 2138–2141; d) A. Patel, G. A. Barcan, O. Kwon, K. N. Houk, *J. Am. Chem. Soc.* **2013**, *135*, 4878–4883; e) G. A. Barcan, A. Patel, K. N. Houk, O. Kwon, *Org. Lett.* **2012**, *14*, 5388–5391.

- [17] Twofold Diels–Alder sequences of [3]dendralenes are *diene-transmissive*, a term introduced by O. Tsuge, E. Wada, S. Kanemasa, *Chem. Lett.* **1983**, *12*, 239–242.
- [18] a) E. W. Colvin, B. J. Hamill, *J. Chem. Soc. Chem. Commun.* **1973**, 151–152; b) E. W. Colvin, B. J. Hamill, *J. Chem. Soc. Perkin Trans. 1* **1977**, 869–874; c) E. C. Hansen, D. Lee, *Org. Lett.* **2004**, *6*, 2035–2038.
- [19] Proposed intermediates **18** and **19** were not observed during the monitoring of this transformation by ^1H NMR spectroscopy.
- [20] For related 1,5-H shifts, see a) K. J. Crowley, *J. Proc. Chem. Soc. London* **1964**, 17; b) K. L. Mikolajczak, M. O. Bagdy, R. B. Bates, I. A. Wolff, *J. Org. Chem.* **1965**, *30*, 2983–2988; c) L. Skattebøl, *Tetrahedron* **1969**, *25*, 4933–4938; d) D. E. Minter, G. J. Fonken, F. T. Cook, *Tetrahedron Lett.* **1979**, *20*, 711–714; e) C. G. Knudsen, R. A. S. Chandraratna, L. P. Walkeapää, Y. S. Chauhan, S. C. Carey, T. M. Cooper, R. R. Birge, W. H. Okamura, *J. Am. Chem. Soc.* **1983**, *105*, 1626–1631; f) G. Shen, A. R. de Lera, T. C. Norman, A. Haces, W. H. Okamura, *Tetrahedron Lett.* **1987**, *28*, 2917–2920; g) G. Shen, T. Tapia, W. H. Okamura, *J. Am. Chem. Soc.* **1987**, *109*, 7499–7507; h) K. Wu, M. M. Midland, W. H. Okamura, *J. Org. Chem.* **1990**, *55*, 4381–4392; i) F. Jensen, *J. Am. Chem. Soc.* **1995**, *117*, 7487–7492; j) Z. Gu, S. Ma, *Chem. Eur. J.* **2008**, *14*, 2453–2464.
- [21] The slow 6π electrocyclicization of these cyclo-octatrienes is unusual but not unprecedented. See, for example, C. Hulot, S. Amiri, G. Blond, P. R. Schreiner, J. Suffert, *J. Am. Chem. Soc.* **2009**, *131*, 13387–13398.
- [22] a) S. V. Pronin, R. A. Shenvi, *J. Am. Chem. Soc.* **2012**, *134*, 19604–19606; b) H.-H. Lu, S. V. Pronin, Y. Antonova-Koch, S. Meister, E. A. Winzeler, R. A. Shenvi, *J. Am. Chem. Soc.* **2016**, *138*, 7268–7271.
- [23] CCDC 1889275 and 1889276 contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.
- [24] Molecular structures from single crystal X-ray analyses were visualized using CYLview 1.0b; C. Y. Legault, Université de Sherbrooke, **2009** (<http://www.cylview.org>).

Manuscript received: July 9, 2019

Accepted manuscript online: August 16, 2019

Version of record online: August 30, 2019

3.3 Concluding Remarks and Future Work

Reported in this chapter is the first synthesis of the parent tetravinylallene molecule (**1.31**) utilising a palladium(0)-catalysed Negishi-type cross-coupling reaction involving a 1,5-transposition. A similar approach was applied to the first synthesis of substituted tetravinylallenes. The presence of a *Z*-alkyl substituent was found to result in a facile [1,5]-H shift followed by an 8π -electrocyclisation to give two cyclooctatrienes, which could react in additional pericyclic cascades. Analysis of the geometry of tetravinylallene (**1.31**) found the lowest energy conformers to be C_2 symmetric and resemble the lowest energy conformers of 1,1-divinylallene (**1.29**) and [3]dendralene (**1.8**). Tetravinylallene (**1.31**) demonstrated stability greater than 1,1-divinylallene (**1.29**), but was less stable than [3]dendralene (**1.8**), tetravinylethylene (**1.27**) and tetraphenylallene (**3.4**).

With access to tetravinylallene (**1.31**) for the first time, this π -bond rich molecule was found to undergo a pericyclic cascade to form a heptacycle, generating seven new bonds and nine new stereocentres in a two step sequence. Each reaction in the sequence proceeded with diastereoselectivity.

Future work will expand the scope of substituted tetravinylallenes to gain an understanding of how stereo-electronic effects alter the stability and reactivity of this molecule. Investigation of this structure within extended frameworks may potential lead to the application of this structure to materials chemistry.

Supporting Information

Tetravinylallene

*Cecile Elgindy, Jas S. Ward, and Michael S. Sherburn**

anie_201908496_sm_miscellaneous_information.pdf

Contents of Supporting Information

Optimisation of tetravinylallene 1 synthesis	S3
Half-life study of tetravinylallene 1	S5
Half-life study of substituted tetravinylallene 22	S7
Synthesis of substituted tetravinylallene 25	S8
Half-life study of substituted tetravinylallene 25	S9
Half-life comparison with other π-bond rich hydrocarbons	S11
Pericyclic reactivity of cyclo-octatriene 28	S12
General Experimental Methods	S13
Experimental Procedures and Characterisation Data	S15
1-Penten-4-yn-3-ol SI-1	S15
1,6-Heptadien-4-yn-3-ol 6	S16
1,6-Heptadien-4-yn-3-one 7	S17
3-Vinylhepta-1-,6-dien-4-yn-3-ol 8	S18
Two-step synthesis of tetravinylallene 1	S19
4-(penta-1,4-dien-3-ylidene)-2-phenyl-5-vinyl-3a,4,7,7a-tetrahydro-1H-isoindole -1,3(2H)-dione 12	S22
Heptacycle 15	S23
3-Methylnona-2,7-dien-5-yn-4-ol 18	S25
3-Methylnona-2,7-dien-5-yn-4-one 19	S26
3-Methyl-4-vinylnona-2,7-dien-5-yn-4-ol 20	S27
3-Methyl-6-(prop-1-en-2-yl)-4-vinylnona-2,4,5,7-tetraene 22	S28
2-Methylnona-2,7-dien-5-yn-4-ol SI-2	S31
2-Methylnona-2,7-dien-5-yn-4-one SI-3	S32
2-Methyl-4-vinylnona-2,7-dien-5-yn-4-ol SI-4	S33
2-Methyl-6-(prop-1-en-2-yl)-4-vinylnona-2,4,5,7-tetraene 25	S34
Cyclo-octatrienes 28 and 29	S35
Synthesis of pentacycle 30	S37
Synthesis of tetracycle 32	S38
Synthesis of tetracycles SI-6 and SI-7	S40
¹H NMR and ¹³C NMR spectra	S44
X-Ray Crystallography Data	S97
UV-visible spectra	S99
Tetravinylallene conformational analysis	S100
References	S110

S2

Optimisation of Tetravinylallene Synthesis

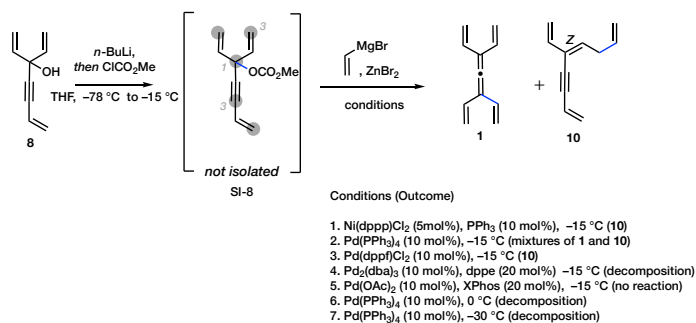
Initial attempts at the cross-coupling reaction were made using the direct carbonate derivative of **8** as the cross-coupling electrophile (**SI-8**, **Scheme S1**) with a variety of metal-catalyzed cross-coupling reactions being attempted.

The nickel catalyzed Kumada reaction was found to produce **10** as a result of C–C coupling through allyl 1,3-transposition. Tetravinylallene was only observed in trace amounts.

The palladium catalyzed Negishi reaction, using Pd(PPh₃)₄, was found to produce both **1** and **10**, with poor selectivity for C–C coupling through allenic or allylic 1,3-transposition being observed. The use of alternative palladium ligands, such as XPhos, dppe or dppf were found to result in either no reaction, starting material decomposition or C–C coupling through allyl 1,3-transposition to give **10**. As such Pd(PPh₃)₄ was used as the preferred catalyst.

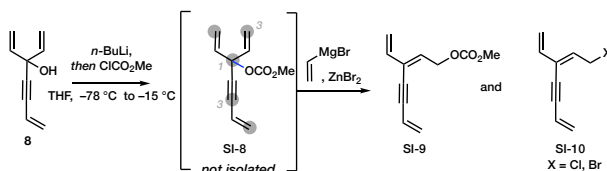
Conditions such as temperature and order of addition were also found to affect the outcome of the reaction. Temperatures above -10 °C were found to cause decomposition of the desired allene **1**, while temperatures below -20 °C were found to result preferentially in the formation of **10**.

The synthesis of tetravinylallene **1** was improved by ensuring that the Grignard reagent was the final reagent added to the reaction mixture containing the carbonate.



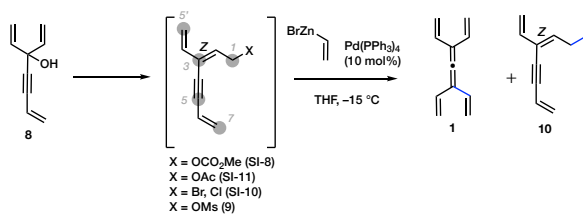
Scheme S1. Initial attempts to synthesise tetravinylallene **1**

Further scrutiny of the Negishi reaction showed that carbonate derivative **SI-8** was undergoing an allyl 1,3-transposition in the presence of the mixture of ZnBr₂ and Grignard reagent (**Scheme S2**) to give **SI-9**. The bromide and chloride derivatives (**SI-10**) were also formed, although they were produced in variable ratios. As such, efforts were focused on the synthesis of the rearranged precursor (**SI-9**) as the cross-coupling electrophile in the synthesis of tetravinylallene **1**.



Scheme S2. Rearrangement of **SI-8**

The rearranged product **SI-9** could be accessed in a single step from alcohol **8**, although it decomposed upon storage (**Scheme S3**). As such, it was synthesized and used directly in the subsequent cross-coupling reaction. The carbonate (**SI-9**) and acetate (**SI-11**) derivatives gave poor selectivity between tetravinylallene **1** and regioisomer **10**. The chloride and bromide derivatives (**SI-9**) gave improved selectivity, however, yields were variable and their use often resulted in the formation of large amounts of an as yet undetermined side-product being observed. The mesylate was found to produce a cleaner reaction with reproducible, albeit lower, yields of tetravinylallene **1**.



Scheme S3. Synthesis of tetravinylallene using rearranged intermediate

Suzuki and Stille reactions were also attempted with tetravinylallene **1** precursors (either **SI-8** or **SI-9**). Heating of these reactions was required (otherwise no reaction was observed), which ultimately resulting in the decomposition of starting material. In the case of the Stille reaction, tetravinylallene **1** was observed in the reaction mixture, however, the extended reaction times resulted in decomposition of tetravinylallene.

Half-life of tetravinylallene

In a C_6D_6 solution of tetravinylallene **1** at an initial concentration of 0.041 M, containing durene as the internal standard was held at 25 °C in a constant temperature bath and 1H NMR spectra were recorded regularly to measure the rate of decomposition and derive a half-life. The 1H NMR data was processed to give the following graph:

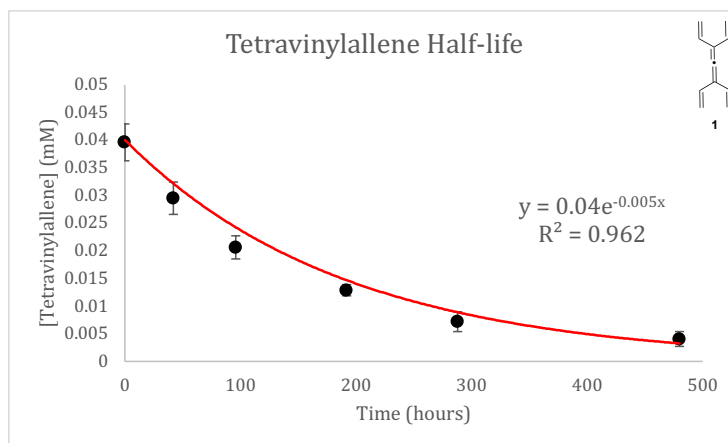


Figure S1. Half-life of tetravinylallene (**1**)

Through analysis of these results tetravinylallene **1** was found to have a first half-life of 115 hours.

The half-life study of tetravinylallene did not result in an identifiable decomposition pathway. In an attempt to determine the mode of decomposition, samples were made of different concentration, with another solvent or with an additive and the half-life experiment was repeated.

Table S1. Half-life of tetravinylallene (**1**) using different conditions

Solvent	Concentration	Additive	First Half-life (hr)
C ₆ D ₆	0.2 M	-	241
C ₆ D ₆	0.4 M	-	115
C ₆ D ₆	0.8 M	-	76
CDCl ₃	0.4 M	-	99
C ₆ D ₆	0.4 M	K ₂ CO ₃	136
C ₆ D ₆	0.4 M	BHT (10 mol%)	171

The decomposition is not significantly altered by the choice of solvent however, the concentration of tetravinylallene (**1**) was found impact the rate of decomposition. We conclude that the decomposition pathway is not acid-catalysed but likely involves autoxidative processes.

Half-life study of allene 22

To determine the effect of substitution on the stability of tetravinylallenes, a solution of allene **22** was subjected to the same conditions. At an initial concentration of 0.040 M in C₆D₆ at 25 °C, allene **22** was found to decompose by 20% over the course of one half-life of the parent tetravinylallene (**1**) and have a half-life of 340 hours (three times that of tetravinylallene **1**) (Figure S2).

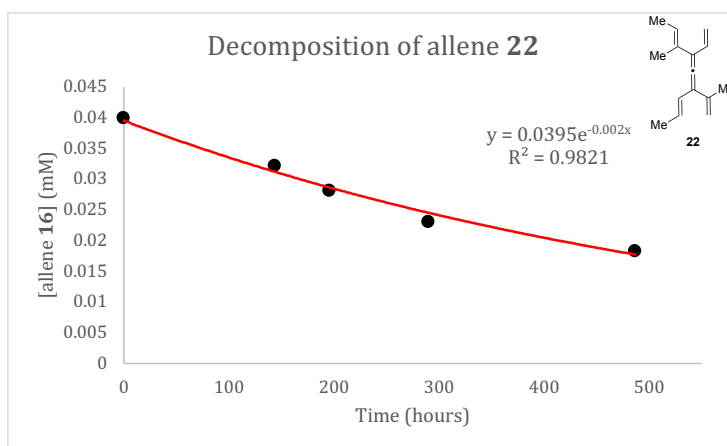
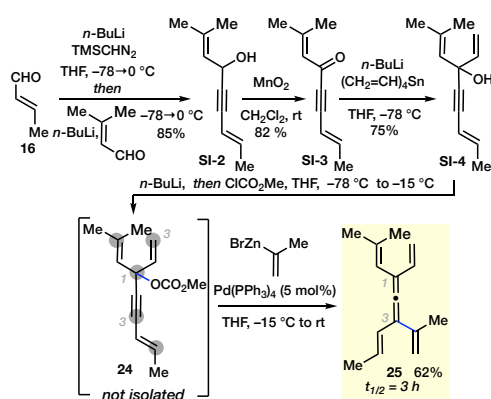


Figure S2. Decomposition study of allene 22

Synthesis of substituted tetravinylallene 25

The synthesis began with Colvin-Hamill alkylation of crotonaldehyde, *in situ* deprotonation and 1,2-addition to 3-methyl-2-butenal to furnish dienynol **SI-2** (Scheme S3). Oxidation with MnO₂ afforded dienyne **SI-3**, which underwent 1,2-addition of vinyl lithium to generate tertiary alcohol **SI-4**. Conversion to the carbonate derivative **24** was performed *in situ* and Negishi-type cross-coupling with 2-propenyl zinc bromide proceeded with 1,3-propargyl to allenyl transposition to yield substituted TVA **25** in 62%.



Scheme S3. Synthesis of substituted tetravinylallene **25**

Half-Life Study of substituted allene **25**

The substituted tetravinylallene **25** was found to undergo a [1,5] hydrogen shift and electrocyclicise to form two cyclooctatrienes (**28** and **29**). A solution of allene **25** at an initial concentration of 0.050 M in C₆D₆, containing durene as the internal standard, was held at 25 °C inside an NMR probe and ¹H NMR spectra were recorded every 1 hour. The ¹H NMR data was processed to give the following graph:

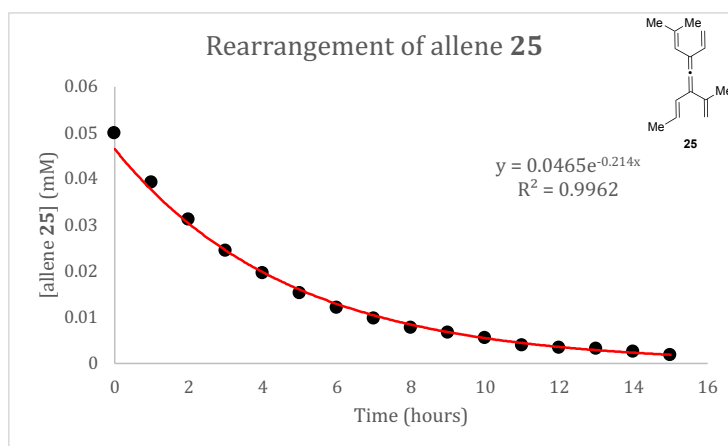
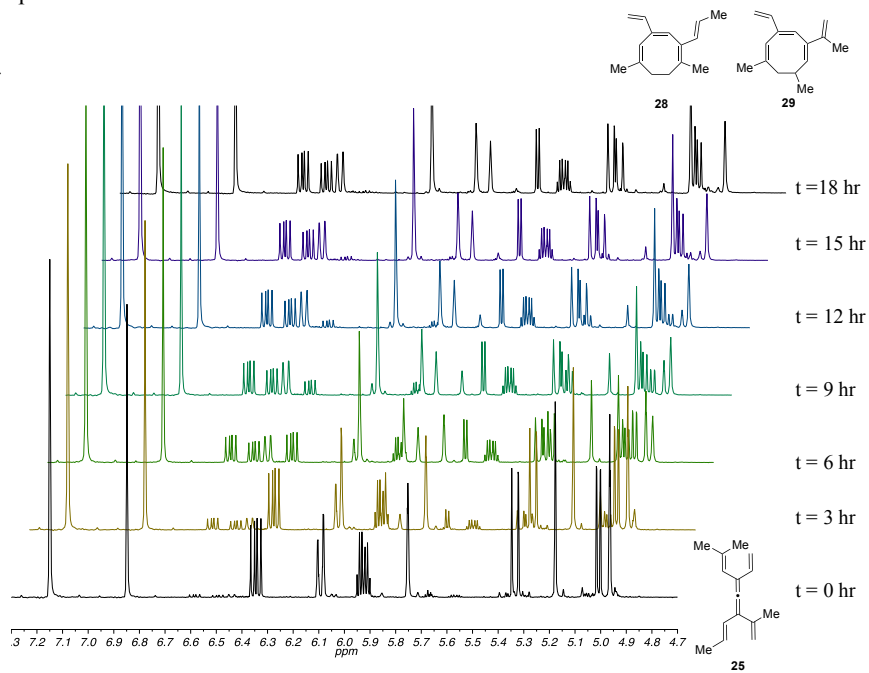


Figure S3. Rearrangement of substituted tetravinylallene **25**

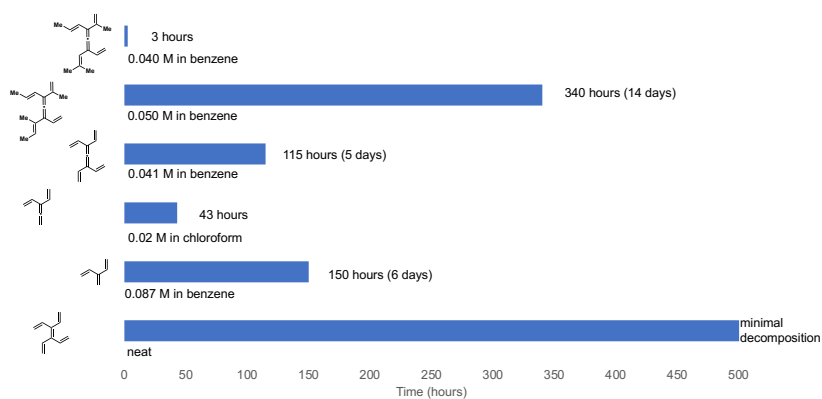
Through analysis of these results substituted tetravinylallene **25** was found to have a half-life of 3 hours arising through a first order process. The rate of reaction at 25 °C was found to be: $r = 0.214[\text{allene}]$. A summary of the data used to generate this graph is presented below.



S10

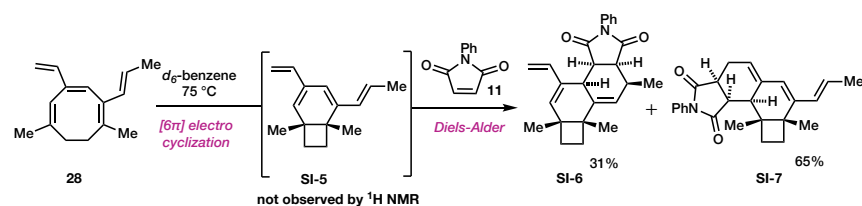
Half-life comparison with other related π -bond rich hydrocarbons

- **[3]Dendralene**: $t_{1/2}$ of 150 hours at an initial concentration of 0.087 M in CDCl_3 at 25 °C. Clean Diels-Alder dimerization was observed.
- **Tetravinylethylene**: stable for weeks when stored neat at room temperature, in light and in air without appreciable decomposition.
- **1,1,-Divinylallene**: $t_{1/2}$ of 43 hours at an initial concentration of 0.02M in CDCl_3 at 25 °C resulting in a complex mixture.



Pericyclic Reactivity of Cyclooctatriene **28**

Cyclo-octatriene **28** was found to undergo a similar pericyclic cascade to that of cyclo-octatriene **29** (Scheme S4). Heating of cyclo-octatriene **28** at 75 °C in the presence of NPM **11**, resulted in a transannular [6 π] electrocyclization (**SI-5**), followed by a Diels-Alder reaction to yield regioisomers **SI-6** and **SI-7** in a ratio of 1:2. The product of the [6 π] electrocyclisation **SI-5** was not observed. Diels-Alder adducts of cyclo-octatriene **28** were also not observed.



General Experimental

NMR spectra

¹H NMR spectra were recorded at 298K, unless specified otherwise, using a Bruker AVANCE 700, Bruker AVANCE 600 or Bruker AVANCE 400 as indicated. Residual solvent peaks were used as an internal reference for ¹H NMR spectra (CDCl₃ δ 7.26 ppm, d₆-benzene δ 7.16 ppm). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. The assignment of proton signals was assisted by COSY, HSQC and HMBC experiments where necessary. ¹³C NMR were recorded at 298K, unless specified otherwise, using a Bruker AVANCE 700, Bruker AVANCE 600 or Bruker AVANCE 400 as indicated. Residual solvent peaks were used as an internal reference for ¹³C NMR spectra (CDCl₃ δ 77.16 ppm, C₆D₆ δ 128.06 ppm). The assignment of carbon signals was assisted by COSY, HSQC and HMBC experiments where necessary. The following abbreviations (or combinations thereof) are used to describe ¹H NMR multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad.

IR spectra

IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer as thin films.

Mass spectrometry

Low-resolution EI mass spectra were recorded on an Agilent HP 6890 series gas GC/MS with a 7683 injector or on a Waters AutoSpec Premier spectrometer magnetic sector instrument. High-resolution EI mass-spectra were recorded on a Waters AutoSpec Premier spectrometer magnetic sector instrument, operating at 70 eV.

Melting points

Melting points were measured on a Stanford Research Systems Optimelt MPA100 and are uncorrected.

Ultraviolet-Visible spectroscopy

UV-visible spectra were recorded using a Shimadzu UV-Visible 2450 spectrometer.

X-ray Crystallography

Single crystal X-ray data was collected on a Supernova (Dual Source) diffractometer using a SuperNova (Cu $K\alpha$ radiation, $\lambda = 1.54184 \text{ \AA}$) X-ray radiation source. Crystallographic structures were solved using CrysAlis PRO package.¹ Structure solution was by ShelXT,² and the structures were refined using ShelXL³ in the OLEX2 program package.⁴

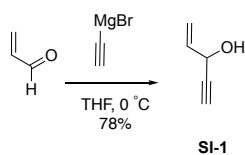
Chromatography

Analytical TLC was performed on Merck silica gel plates, pre-coated with silica gel 60 F₂₅₄ (0.2 mm). Visualisation was effected by quenching of UV fluorescence ($\lambda_{\text{max}} = 254 \text{ nm}$) and by staining with *p*-anisaldehyde, followed by heating. Flash chromatography employed Merck Kieselgel 60 (230-400 mesh) silica gel. Analytical and preparative HPLC were conducted using a Waters 600 Controller with a Waters 717 plus Autosampler and a Waters 2996 Photodiode Array Detector running with Empower Pro Empower 2 software.

Experimental procedures, reagents and glassware

Reactions were conducted under a positive pressure of dry nitrogen in oven-dried glassware and at ambient temperature, unless otherwise specified. Anhydrous solvents were either obtained from commercial sources or dried according to the procedure outlined by Grubbs and co-workers.⁵ Commercially available chemicals were used as purchased, or where specified, purified by standard techniques.⁶ Solvent compositions are given in (v/v). Solutions of *n*-BuLi were titrated against menthol with 2,2'-bipyridine as indicator according to the method of Lin and Paquette.⁷ Grignard reagents were titrated using salicylaldehyde phenylhydrazone according to the procedure of Love and Jones.⁸

1-Penten-4-yn-3-ol SI-1



This compound was prepared according to a modified literature procedure.⁹ A solution of ethynylmagnesium bromide (0.35 M in THF, 300 mL, 0.11 mmol, 1.1 mol. equiv.) was cooled to 0 °C and a solution of acrolein (6.5 mL, 0.10 mmol) in THF (50 mL) was added dropwise over 30 minutes. The resulting yellow-orange solution was warmed to room temperature and stirred for a further 1 hour. The reaction mixture was cooled to 0 °C and quenched with saturated aqueous NH₄Cl (250 mL) and diluted with Et₂O (250 mL). The aqueous layer was separated and extracted with Et₂O (2 x 250 mL). The organic layers were combined, washed with brine (250 mL), dried over anhydrous Na₂SO₄, filtered and concentrated at 100 mbar at 25 °C. Purification by distillation (20 mmHg, 42 °C) afforded propargylic alcohol **SI-1** as a clear colourless oil (6.4 g, 0.78 mmol, 78%). ¹H and ¹³C NMR spectra matched those previously reported.⁹

R_f: 0.19 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 5.99 (ddd, *J* = 17.1, 10.2, 5.2 Hz, 2H), 5.60-5.43 (m, 1H), 5.26 (d, *J* = 10.2 Hz, 1H), 4.94-4.82 (m, 1H), 2.58 (d, *J* = 2.2 Hz, 1H) ppm

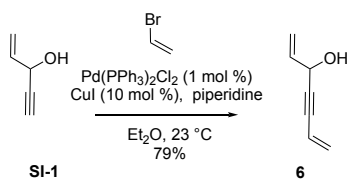
¹³C NMR (100 MHz, CDCl₃): δ 136.6 (CH), 117.0 (CH), 82.7 (C_q), 74.6 (CH), 63.1 (CH) ppm

IR (thin film): ν_{max} = 3377 (br), 3294, 3091, 3023, 2987, 2119, 1687, 1644 cm⁻¹

LRMS (EI): *m/z* (%) = 81 ([M-H]⁺, 71), 63 (31), 53 (100), 39 (94)

HRMS (EI): calculated for C₅H₅O [M-H]⁺ 81.0340; found 81.0337

1,6-Heptadien-4-yn-3-ol **6**



A solution of vinyl bromide (8.0 mL, 110 mmol, 3.6 mol. equiv.) in Et₂O (120 mL) was cooled to 0 °C. Propargylic alcohol **SI-1** (3.00 g, 32.0 mmol), Pd(PPh₃)₂Cl₂ (0.26 g, 0.37 mmol, 1 mol%) and piperidine (7.2 mL, 73 mmol, 2.3 mol. equiv.) were added. CuI (0.68 g, 3.6 mmol, 10 mol%) was added in a single portion and the reaction mixture was stirred at room temperature for 1.5 hours. A solution of saturated aqueous NH₄Cl (200 mL) was added and the aqueous layer was separated and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with 0.2 M HCl (50 mL), saturated aqueous NaHCO₃ (50 mL), water (2 x 50 mL), dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether:Et₂O 40-60, 90:10) afforded propargylic alcohol **6** as a yellow oil (3.1 g, 29 mmol, 79%).

R_f: 0.21 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 5.99 (ddd, *J* = 17.0, 10.2, 4.9 Hz, 2H), 5.84 (ddd, *J* = 17.6, 11.4, 1.7 Hz, 1H), 5.69-5.66 (m, 1H), 5.52 (dd, *J* = 11.3, 2.0 Hz, 1H), 5.47 (dt, *J* = 16.9, 1.4 Hz, 1H), 5.24 (dt, *J* = 10.1, 1.3 Hz, 1H), 5.0 (s, 1H), 1.91 (s, 1H) ppm

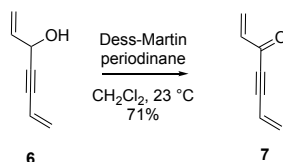
¹³C NMR (175 MHz, CDCl₃): δ 137.0 (CH), 127.9 (CH), 116.7 (CH), 116.6 (CH), 88.43 (C_q), 85.1 (C_q), 63.7 (CH) ppm

IR (thin film): ν_{\max} = 3383(br), 3296, 3092, 2876, 2118, 1644 cm⁻¹

LRMS (EI): *m/z* (%) = 107 ([M-H]⁺, 14), 79 (100), 65 (14), 53 (19)

HRMS (EI): calculated for C₇H₇O [M-H]⁺ 107.0497; found 107.0495

1,6-Heptadien-4-yn-3-one 7



To a solution of propargylic alcohol **6** (2.50 g, 23 mmol) in CH_2Cl_2 (120 mL) was added the Dess-Martin periodinane (14.7 g, 34.7 mmol, 1.5 mol. equiv.) in a single portion. The reaction mixture was stirred at room temperature for 2 hours then diluted with a 1:1 mixture of saturated aqueous solutions of $\text{Na}_2\text{S}_2\text{O}_3$ and NaHCO_3 (200 mL) and stirred for a further 30 minutes. The aqueous layer was separated and extracted with CH_2Cl_2 (3 x 20 mL). The organic layers were combined, dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , petroleum ether 40-60:Et₂O, 60:10) afforded ketone **7** as a yellow oil (1.75 g, 16.5 mmol, 71%).

R_f: 0.26 (90:10, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl_3): δ 6.56 (dd, $J = 17.4, 1.7$ Hz, 1H), 6.42 (dd, $J = 17.4, 10.1$ Hz, 1H), 6.19 (dd, $J = 10.1, 1.1$ Hz, 2H), 6.03-5.94 (m, 2H), 5.83 (dd, $J = 8.5, 4.7$ Hz, 1H) ppm

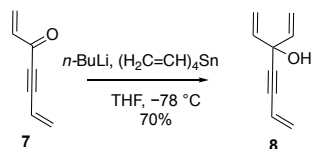
¹³C NMR (100 MHz, CDCl_3): δ 178.9 (C_q), 138.0 (CH), 133.7 (CH), 133.2 (CH), 115.2 (CH), 90.3 (C_q), 86.1 (C_q), ppm

IR (thin film): $\nu_{\text{max}} = 3281, 3103, 3019, 2197, 1643, 1610$ cm^{-1}

LRMS (EI): m/z (%) = 106 ($[\text{M}]^+$, 33), 79 (100), 51 (39)

HRMS (EI): calculated for $\text{C}_7\text{H}_6\text{O}$ $[\text{M}]^+$ 106.0419; found 106.0423

3-Vinylhepta-1,6-dien-4-yn-3-ol **8**



Tetravinyltin (1.7 g, 30 mmol, 1.0 mol. equiv.) was dissolved in THF (15 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 23 mL, 30 mmol, 4.0 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 30 minutes. The mixture was cooled to -78 °C and a solution of ketone **7** (0.80 g, 7.5 mmol) in THF (65 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour. The reaction mixture was then diluted with Et₂O (150 mL) and quenched with a saturated aqueous NH₄Cl (200 mL). The aqueous layer was separated and extracted with Et₂O (2 x 150 mL). The organic layers were combined, washed with brine (100 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **8** as a yellow oil (0.70 g, 5.2 mmol, 70%).

R_f: 0.16 (85:15, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 5.99-5.82 (m, 2H), 5.70 (dd, *J* = 17.5, 2.1 Hz, 1H), 5.63-5.45 (m, 2H), 5.21 (d, *J* = 10.2 Hz, 1H), 2.16 (m, 1H) ppm

¹³C NMR (100 MHz, CDCl₃): δ 139.8 (CH), 128.0 (CH), 116.6 (CH), 115.0 (CH), 88.9 (C_q), 85.9 (C_q), 72.1 (C_q) ppm

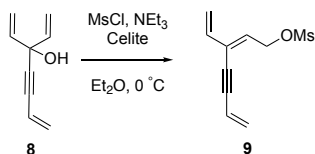
IR (thin film): ν_{max} = 3383(br), 3097, 3020, 2189, 1635, 1604 cm⁻¹

LRMS (EI): *m/z* (%) = 133 ([M-H]⁺, 14), 115(18), 107 (31), 91 (100), 55 (54)

HRMS (EI): calculated for C₉H₉O [M-H]⁺ 133.0653; found 133.0649

Two-step synthesis of tetravinylallene 1

Part 1: 3-Vinylhepta-2,6-dien-4-yn-1-yl methanesulfonate 9



Propargylic alcohol **8** (100 mg, 0.75 mmol) was dissolved in Et₂O (2 mL) and cooled to 0 °C. Celite (300 mg), NEt₃ (1.2 mL, 0.90 mmol, 1.2 mol. equiv.) and methanesulfonyl chloride (70 μL, 0.90 mmol, 1.2 mol. equiv.) were added and the reaction mixture was stirred at 0 °C for 30 minutes, warmed to room temperature and anhydrous MgSO₄ (1.4 g) was added. The reaction mixture was filtered through a pad of Celite, eluting with Et₂O, and concentrated under reduced pressure at 0 °C to provide the allylic mesylate **9** as a yellow oil, which was immediately subjected to the next reaction.

Note: In our hands, mesylate **9** decomposed at room temperature both neat and as a solution. Diluting the crude mesylate in anhydrous THF immediately after preparation, and submitting it to the subsequent reaction without delay minimised this decomposition.

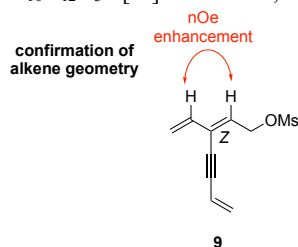
¹H NMR (700 MHz, CDCl₃): δ 6.35 (dd, *J* = 16.9, 10.1 Hz, 1H), 6.05-5.97 (m, 2H), 5.78 (dd, 17.6, 1.9 Hz, 1H), 5.74 (d, *J* = 16.9 Hz, 1H), 5.62 (dd, *J* = 11.2, 1.8 Hz, 1H), 5.36 (d, *J* = 10.2 Hz, 1H), 5.05 (d, *J* = 7.1 Hz, 2H), 3.04 (s, 3H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 135.1 (CH), 129.8 (CH), 128.9 (C_q), 128.8 (CH₂), 119.8 (CH₂), 116.5 (CH), 97.4 (C_q), 82.4 (C_q), 67.8 (CH₂), 38.1 (CH₃) ppm

IR (thin film): ν_{max} = 3099, 3017, 2940, 2206, 1596, 1351 cm⁻¹

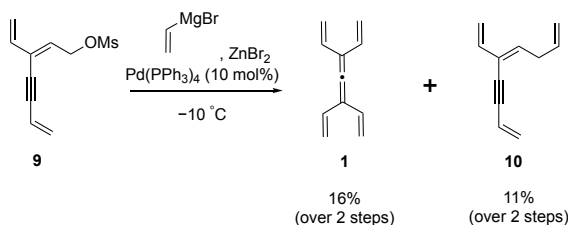
LRMS (EI): *m/z* (%) 212 ([M]⁺, 6), 191(4), 133(12), 115(100), 103(31), 91(29), 79(39)

HRMS (EI): calculated for C₁₀H₁₂O₃S [M]⁺ 212.0507; found 212.0504



Two-step synthesis of tetravinylallene **1**

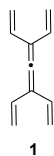
Part 2: Tetravinylallene (3,5-divinylhepta-1,3,4,6-tetraene) **1** and 5-vinylnona-1,5,8-trien-3-yne **10**



A solution of zinc bromide (0.98 M in THF, 1.2 mL, 1.2 mmol, 1.6 mol. equiv.) was cooled to $0\text{ }^\circ\text{C}$ and a solution of vinylmagnesium bromide in THF (0.75 M, 1.6 mL, 1.2 mmol, 1.6 mol. equiv.) was added dropwise. The mixture was stirred for 20 min at $0\text{ }^\circ\text{C}$ then cooled to $-10\text{ }^\circ\text{C}$ and $\text{Pd}(\text{PPh}_3)_4$ (86 mg, 0.074 mmol, 10 mol%) was added in a single portion. A solution of mesylate **9** (from the previous experiment) in THF (2 mL) was added at a rate ensuring the internal temperature reached $-5\text{ }^\circ\text{C}$. On completion of addition the reaction was stirred for a further 40 min at $-10\text{ }^\circ\text{C}$, after which it was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH_4Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 10 mL). The organic layers were combined and washed with water (10 mL) and brine (10 mL), dried over anhydrous MgSO_4 , filtered and concentrated at 370 mbar at $15\text{ }^\circ\text{C}$ until ~6 mL of solvent remained. Analysis of the crude product mixture by ^1H NMR spectroscopy with 1,2,3,5-tetramethylbenzene as an internal standard gave estimated yields of tetravinylallene in 16% yield from alcohol **8** and allylic coupled product **10** in 11% yield from alcohol **8**.

An analytically pure sample of tetravinylallene **1** was obtained for the purposes of characterization *via* flash chromatography on silica gel eluting with pentane to yield tetravinylallene **1** as a colourless oil.

Tetravinylallene **1**



R_f : 0.45 (*n*-pentane)

¹H NMR (700 MHz, CDCl₃): δ 6.30 (dd, *J* = 17.4, 10.6 Hz, 4H), 5.39 (dd, *J* = 17.4, 1.2 Hz, 4H), 5.20 (dd, *J* = 10.6, 1.2 Hz, 4H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 212.5 (C_q), 130.9 (CH), 116.2 (CH₂), 108.4 (C_q) ppm

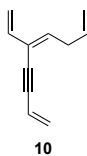
IR (thin film): ν_{max} = 3089, 3052, 3014, 2957, 2926, 2856, 1904, 1610 cm⁻¹

LRMS (EI): *m/z* (%) = 143 ([M-H]⁺, 13), 128 (100), 115 (61), 91 (26), 63 (18)

HRMS (EI): calculated for C₁₁H₁₂ [M]⁺ 144.0939; found 144.0939

UV-VIS: λ_{max} = 206 nm (ε = 95 000), 234 nm (ε = 89 000)

5-Vinylnona-1,5,8-trien-3-yne **10**



R_f : 0.40 (*n*-pentane)

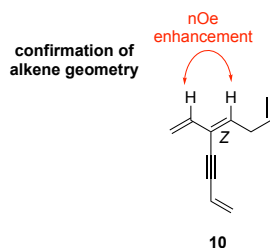
¹H NMR (400 MHz, CDCl₃): δ 6.32 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.02 (dd, *J* = 17.6, 11.1 Hz, 1H), 5.93 (t, *J* = 7.6 Hz, 1H), 5.88-5.76 (m, 1H), 5.70 (dd, *J* = 17.5, 2.1 Hz, 1H), 5.60-5.46 (m, 2H), 5.20-4.94 (m, 3H), 3.16-3.12 (m, 2H) ppm

¹³C NMR (100 MHz, CDCl₃): δ 138.7 (CH), 136.4 (CH), 135.5 (CH), 127.0 (CH₂), 124.3 (C_q), 117.3 (CH), 115.9 (CH₂), 115.6 (CH₂), 95.0 (C_q), 84.5 (C_q), 35.1 (CH₂) ppm

IR (thin film): ν_{max} = 3081, 3011, 2980, 2931, 2196, 1679, 1640 cm⁻¹

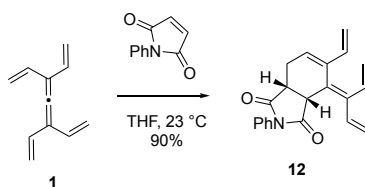
LRMS (EI): *m/z* (%) = 143 ([M-H]⁺, 53), 129 (100), 115 (100), 103 (26), 91 (69), 77 (39), 63 (56)

HRMS (EI): calculated for C₁₁H₁₂ [M]⁺ 144.0939; found 144.0934



S21

4-(penta-1,4-dien-3-ylidene)-2-phenyl-5-vinyl-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione **12**



N-Phenylmaleimide (30 mg, 0.17 mmol, 1.6 equiv.) was added to a solution of tetra-1,3-diene (16 mg, 0.11 mmol) in THF (2 mL). The reaction mixture was stirred for 1 hour at room temperature then concentrated under reduced pressure and purified by flash chromatography (SiO₂, petroleum ether 40-60:EtOAc, 90:10) to afford monoadduct **12** as a yellow oil (30 mg, 0.095 mmol, 90%).

R_f: 0.29 (80:20, petroleum ether 40-60:EtOAc)

¹H NMR (400 MHz, CDCl₃): δ 7.45-7.39 (m, 2H), 7.38-7.32 (m, 1H), 7.20-7.01 (m, 2H), 6.57-6.26 (m, 3H), 6.08 (dd, *J* = 7.4, 3.9 Hz, 1H), 5.96 (dd, *J* = 17.6, 2.2 Hz, 1H), 5.60 (dd, *J* = 11.2, 2.2 Hz, 1H), 5.29 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.23-5.06 (m, 3H), 4.66 (d, *J* = 8.7 Hz, 1H), 3.35 (ddd, *J* = 8.7, 6.9, 1.7 Hz, 1H), 2.85 (ddd, *J* = 15.1, 7.3, 1.7 Hz, 1H), 2.38-2.08 (m, 1H) ppm

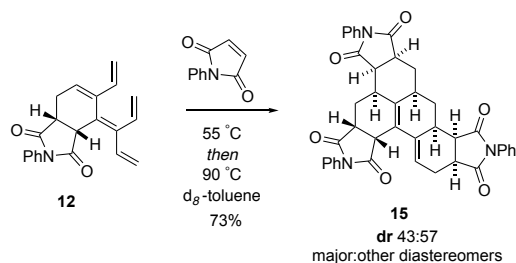
¹³C NMR (100 MHz, CDCl₃): δ 178.9 (C_q), 176.6 (C_q), 141.3 (C_q), 138.8 (C_q), 136.4 (CH), 135.2 (CH), 132.7 (CH), 132.2 (C_q), 129.2 (CH), 128.7 (CH), 128.5 (CH), 127.2 (C_q), 126.6 (CH), 123.1 (CH₂), 117.0 (CH₂), 116.9 (CH₂), 46.5 (CH), 42.2 (CH), 25.3 (CH₂) ppm

IR (thin film): ν_{\max} = 3088, 3002, 2961, 2902, 2854, 1780, 1711, 1597, 1499 cm⁻¹

LRMS (EI): *m/z* (%) = 317 ([M]⁺⁺, 29), 289 (8), 197 (12), 170 (65), 155 (100), 142 (67), 128 (63), 115 (43), 91 (29)

HRMS (EI): calculated for C₂₁H₁₉NO₂ [M]⁺⁺ 317.1416; found 317.1412

Heptacycle 15



N-Phenylmaleimide (90 mg, 0.17 mmol, 2.2 mol. equiv.) and BHT (2.0 mg, 0.0091 mmol, 0.1 mol. equiv.) was added to a solution of monoadduct **12** (29 mg, 0.095 mmol) in d_8 -toluene (1 mL). The reaction mixture was stirred at 55 °C for 48 hours then diluted with d_8 -toluene (5 mL) and heated at 90 °C for a further 12 hours. Concentration under reduced pressure and purification by flash chromatography (SiO₂, CH₂Cl₂:iPrOH, 100:0→96:4) afforded heptacycle **15** as a mixture of diastereomers (dr 43:57, major:other diastereomers) as a pale yellow solid (46 mg, 0.069 mmol, 73%). An analytically pure sample of the major diastereomer **15** was obtained for characterization purposes *via* reverse phase preparative HPLC (Waters SymmetryPrep 7 μ m C18 (150x19mm), 50:50 acetonitrile:H₂O). A crystal of the major diastereomer was obtained from the diastereomeric mixture by recrystallisation from MeOH/CDCl₃. The relative stereochemistry of the major diastereomer was determined by single crystal X-ray analysis.

R_f: 0.31 (96:4, CH₂Cl₂:iPrOH)

m.p.: 193-220 °C (decomp.)

¹H NMR (600 MHz, CDCl₃): δ 7.45 (m, 2H), 7.42-7.35 (m, 4H), 7.28-7.26 (m, 4H), 7.25-7.21 (m, 1H), 7.17-7.08 (m, 4H), 6.34 (dt, J = 6.9, 3.1 Hz, 1H), 3.72 (dd, J = 7.2, 1.8 Hz, 1H), 3.57 (ddd, J = 11.3, 7.2, 5.9 Hz, 1H), 3.38 (dd, J = 10.1, 6.8 Hz, 1H), 3.35-3.32 (m, 1H), 3.31-3.24 (m, 2H), 3.04-3.00 (m, 1H), 2.95 (ddd, J = 15.9, 7.4, 1.5 Hz, 1H), 2.83-2.79 (m, 1H), 2.71-2.67 (m, 2H), 2.51-2.35 (m, 2H), 2.29 (dt, J = 14.9, 2.8 Hz, 1H), 2.08-1.96 (m, 2H) ppm

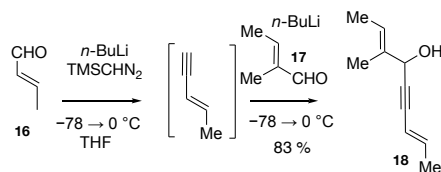
¹³C NMR (150 MHz, CDCl₃): δ 178.7 (C_q), 178.4 (C_q), 178.1 (C_q), 177.1 (C_q), 176.3 (C_q), 175.6 (C_q), 138.1 (2 x C_q), 132.0 (C_q), 132.0 (C_q), 131.6 (C_q), 129.4 (CH), 129.4 (CH), 129.3 (2 x CH), 129.1 (2 x CH), 128.9 (2 x CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 126.9 (2 x CH), 126.5 (2 x CH), 126.4 (2 x CH), 124.7 (C_q), 122.8 (CH), 44.5 (CH), 43.2 (CH), 42.8 (CH), 41.1 (CH), 39.2 (CH), 37.8 (CH), 36.2 (CH), 34.9 (CH), 33.0 (CH), 31.9 (CH₂), 28.1 (CH₂), 26.4 (CH₂), 25.4 (CH₂) ppm

IR (thin film): ν_{\max} = 3066, 2929, 2852, 1778, 1702, 1598, 1498, 1377 cm⁻¹

LRMS (EI): m/z (%) = 663([M]⁺), 92), 488(19), 474(19), 188(27), 174(44), 155(100), 120(82), 117(90)

HRMS (EI): calculated for C₄₁H₃₃N₃O₆ [M]⁺ 663.2369; found 663.2356

3-Methylnona-2,7-dien-5-yn-4-ol **18**



In a round-bottomed flask equipped with a dry ice condenser and pressure equalizing addition funnel, a solution of trimethylsilyldiazomethane (1.8 M in hexanes, 8.7 mL, 16 mmol, 1.1 equiv.) in THF (20 mL) cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 11.0 mL, 16 mmol, 1.1 equiv.) was added dropwise. The resulting orange-yellow solution was stirred for 10 min at $-78\text{ }^{\circ}\text{C}$ then a solution of crotonaldehyde (**16**) (1.0 g, 14.0 mmol) in THF (10 mL) was added. Stirring was continued at $-78\text{ }^{\circ}\text{C}$ for a further 10 min at $0\text{ }^{\circ}\text{C}$ for 15 min before being cooled back to $-78\text{ }^{\circ}\text{C}$. A solution of *n*-BuLi (1.4 M in hexanes, 16 mL, 22 mmol, 1.5 equiv) was added dropwise and the reaction mixture was stirred for 15 min at $-78\text{ }^{\circ}\text{C}$. A solution of tiglic aldehyde (**17**) (2.0 mL, 22 mmol, 1.5 equiv.) in THF (10 mL) was added dropwise and the reaction mixture was warmed to room temperature and stirred for a further 1 hr. Water (50 mL) and Et₂O (50 mL) were added to the reaction mixture and the aqueous layer was separated and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Purification flash chromatography (SiO₂, petroleum ether 40-60: Et₂O:NEt₃, 80:20:1) afforded alcohol **18** as a yellow oil (1.8 g, 12 mmol, 83%).

R_f: 0.27 (80:20 petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 6.16 (dq, $J = 16.1, 6.8\text{ Hz}$, 1H), 5.71-5.68 (m, 1H), 5.52 (dt, $J = 15.8, 1.9\text{ Hz}$, 1H), 4.85 (d, $J = 4.7\text{ Hz}$, 1H), 1.78 (dd, $J = 6.8, 1.8\text{ Hz}$, 3H), 1.75 (s, 3H), 1.64 (d, $J = 6.8\text{ Hz}$, 3H) ppm

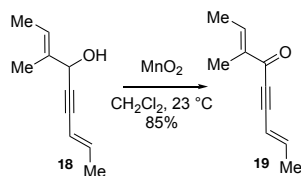
¹³C NMR (100 MHz, CDCl₃): δ 140.4 (CH), 135.2 (C_q), 122.7 (CH), 110.2 (CH), 86.7 (C_q), 84.8 (C_q), 68.7 (CH), 18.8 (CH₃), 13.4 (CH₃), 12.1 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3340(\text{br}), 3029, 2962, 2917, 2861, 2216, 1674\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 150 ([M]⁺, 30), 135 (100), 115 (33), 107 (53), 91 (92), 79 (42), 77 (40), 65 (28)

HRMS (EI): calculated for C₁₀H₁₄O [M]⁺ 150.1045; found 150.1045

3-Methylnona-2,7-dien-5-yn-4-one **19**



To a solution of propargylic alcohol **18** (1.0 g, 6.7 mmol) in CH₂Cl₂ (50 mL) was added manganese dioxide (5.7 g, 67 mmol, 10 equiv.) in a single portion. The reaction mixture was stirred at room temperature for 1 hour then filtered through a pad of silica, flushed with Et₂O (100 mL) and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O, 90:10) afforded ketone **19** as a yellow oil (0.84 g, 5.7 mmol, 85%).

R_f: 0.27 (10:90 Et₂O:petroleum ether 40-60)

¹H NMR (700 MHz, CDCl₃): δ 7.19 (dddt, *J* = 18.4, 7.1, 5.7, 1.3 Hz, 1H), 6.48 (dddd, *J* = 13.8, 10.1, 6.9, 5.3 Hz, 1H), 5.65 (ddd, *J* = 15.8, 3.0, 1.7 Hz, 1H), 1.92 (dt, *J* = 7.1, 1.1 Hz, 3H), 1.87 (dt, *J* = 6.8, 1.5 Hz, 3H), 1.80 (d, *J* = 1.2 Hz, 3H) ppm

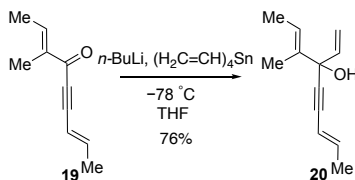
¹³C NMR (175 MHz, CDCl₃): δ 180.5 (C_q), 146.2 (CH), 144.8 (CH), 139.5 (C_q), 109.3 (CH), 90.5 (C_q), 85.1 (C_q), 19.3 (CH₃), 15.2 (CH₃), 10.4 (CH₃) ppm

IR (thin film): ν_{max} = 3042, 3010, 2970, 2916, 2858, 2184, 1622 cm⁻¹

LRMS (EI): *m/z* (%) = 148 ([M]⁺, 49), 133 (81), 120 (18), 105 (100), 93 (95), 79 (37), 65 (49)

HRMS (EI): calculated for C₁₀H₁₂O [M]⁺ 148.0888; found 148.0898

3-Methyl-4-vinylnona-2,7-dien-5-yn-4-ol **20**



A solution of tetravinyltin (0.80 mL, 4.4 mmol, 1.0 mol. equiv.) in THF (20 mL) was cooled to $0\text{ }^\circ\text{C}$ and a solution of $n\text{-BuLi}$ (1.5 M in hexanes, 12 mL, 18.0 mmol, 4.3 mol. equiv.) was added dropwise. The mixture was stirred at $0\text{ }^\circ\text{C}$ for 30 minutes then cooled to $-78\text{ }^\circ\text{C}$. A solution of ketone **19** (0.63 g, 4.2 mmol) in THF (20 mL) was added dropwise and the reaction mixture was stirred for a further 1 hour, diluted with Et_2O (50 mL) and quenched with a saturated aqueous NH_4Cl (50 mL). The aqueous layer was separated and extracted with Et_2O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , petroleum ether 40-60: Et_2O : NEt_3 , 85:15:2) afforded propargylic alcohol **20** as a yellow oil (0.56 g, 3.2 mmol, 76%).

R_f: 0.15 (90:10 petroleum ether 40-60: Et_2O)

¹H NMR (400 MHz, CDCl_3): δ 6.19 (dq, $J = 15.8, 6.8$ Hz, 1H), 5.93 (qd, $J = 6.8, 1.4$ Hz, 1H), 5.86 (dd, $J = 17.0, 10.2$ Hz, 1H), 5.58-5.50 (m, 2H), 5.19 (dd, $J = 10.2, 1.2$ Hz, 1H), 2.06 (OH, s, 1H) 1.79 (dd, $J = 6.8, 1.8$ Hz, 3H), 1.68 (m, 3H), 1.65 (dd, $J = 6.8, 1.2$ Hz, 3H) ppm

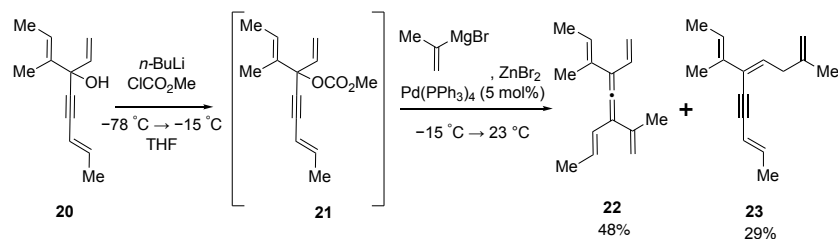
¹³C NMR (100 MHz, CDCl_3): δ 140.4 (CH), 140.4 (CH), 136.4 (C_q), 120.8 (CH), 114.5 (CH_2), 110.3 (CH), 87.8 (C_q), 85.7 (C_q), 75.2 (C_q), 18.8 (CH_3), 13.6 (CH_3), 12.2 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3430(\text{br}), 3230, 3028, 2967, 2917, 2861, 2221, 1640\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 175 ($[\text{M}-\text{H}]^+$, 10), 161 (100), 143 (40), 133 (56), 128 (77), 115 (53), 105 (77), 91 (93), 77 (56)

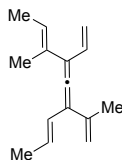
HRMS (EI): calculated for $\text{C}_{12}\text{H}_{15}\text{O}$ $[\text{M}-\text{H}]^+$ 175.1123; found 175.1118

3-Methyl-6-(prop-1-en-2-yl)-4-vinylnona-2,4,5,7-tetraene **22 and
5-(but-2-en-2-yl)-2-methyldeca-1,4,8-trien-6-yne **23****



A solution of propargylic alcohol **20** (100 mg, 0.57 mmol) in THF (4 mL) was cooled to $-78\text{ }^\circ\text{C}$ and a solution of $n\text{-BuLi}$ (1.5 M in hexanes, 0.45 mL, 0.68 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 5 minutes. Freshly distilled methyl chloroformate (0.1 mL, 1.3 mmol, 2.3 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^\circ\text{C}$ for 45 min. A solution of zinc bromide (1.2 M in THF, 0.70 mL, 0.86 mmol, 1.5 mol. equiv.) and $\text{Pd(PPh}_3\text{)}_4$ (32 mg, 0.028 mmol, 5 mol%) were added in a single portion. Subsequently, a solution of isopropenylmagnesium bromide in THF (0.80 M, 1.1 mL, 0.88 mmol, 1.6 mol. equiv.) was added dropwise over 5 minutes. On completion of addition the reaction mixture was stirred for a further 5 min at $-15\text{ }^\circ\text{C}$, then brought to room temperature and stirred for a further 20 minutes. The reaction mixture was diluted with $n\text{-pentane}$ (10 mL) and quenched with saturated aqueous NH_4Cl (10 mL). The aqueous layer was separated and extracted with $n\text{-pentane}$ (3 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous K_2CO_3 , filtered and concentrated at 100 mbar at $0\text{ }^\circ\text{C}$. The resulting solution was subjected to purification by flash chromatography on silica gel eluting with pentane to yield allene **22** as a colourless oil (54 mg, 0.27 mmol, 48%). The allyl cross-coupled product **23** was also isolated as a colourless oil (33 mg, 0.17 mmol, 29%)

3-Methyl-6-(prop-1-en-2-yl)-4-vinylnona-2,4,5,7-tetraene 22



22

R_f: 0.43 (*n*-pentane)

¹H NMR (700 MHz, CDCl₃): δ 6.34 (dd, *J* = 17.1, 10.4 Hz, 1H), 6.00 (dq, *J* = 15.3, 1.7 Hz, 1H), 5.83 (dq, *J* = 15.3, 1.7 Hz, 1H), 5.62 (dddd, *J* = 8.0, 6.8, 5.6, 1.3 Hz, 1H), 5.33 (dd, *J* = 17.1, 1.9 Hz, 1H), 5.16 (dd, 10.4, 1.9 Hz, 1H), 5.07-5.06 (m, 1H), 4.96 (t, *J* = 1.4 Hz, 1H), 1.84 (dd, *J* = 1.4, 0.7 Hz, 3H), 1.76 (dd, *J* = 6.6, 1.7 Hz, 3H), 1.76-1.71 (m, 6H) ppm

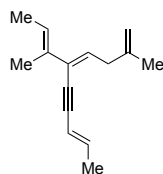
¹³C NMR (175 MHz, CDCl₃): δ 208.5 (C_q), 140.3 (C_q), 132.2 (CH), 131.1 (C_q), 128.4 (CH), 124.7 (CH), 121.9 (CH), 116.5 (CH₂), 112.8 (C_q), 111.8 (CH₂), 110.8 (C_q), 22.2 (CH₃), 18.6 (CH₃), 15.5 (CH₃), 14.3 (CH₃) ppm

IR (thin film): *v*_{max} = 3090, 3020, 2972, 2917, 2858, 1904, 1620 cm⁻¹

LRMS (EI): *m/z* (%) = 200 ([M]⁺, 45), 185 (86), 170 (54), 155 (93), 143 (90), 128 (100), 115 (64), 103 (45), 91 (61), 77 (50)

HRMS (EI): calculated for C₁₅H₂₀ [M]⁺ 200.1565; found 200.1567

5-(but-2-en-2-yl)-2-methyldeca-1,4,8-trien-6-yne 23



23

R_f: 0.40 (*n*-pentane)

¹H NMR (700 MHz, CDCl₃): δ 6.25-6.06 (m, 2H), 5.90 (t, *J* = 7.6 Hz, 1H), 5.71 (dd, *J* = 15.7, 1.8 Hz, 1H), 4.73 (t, *J* = 1.1 Hz, 2H), 3.10 (d, *J* = 7.6 Hz, 2H), 1.82 (dd, *J* = 6.8, 1.8 Hz, 3H), 1.81-1.79 (m, 3H), 1.77-1.74 (m, 6H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 144.8 (C_q), 139.1 (CH), 133.3 (C_q), 131.9 (CH), 127.6 (C_q), 124.8 (CH), 111.2 (CH), 110.8 (CH₂), 94.4 (C_q), 84.4 (C_q), 39.6 (CH₂), 22.8

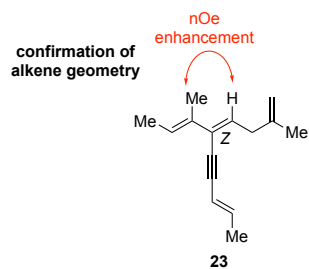
S29

(CH₃), 18.8 (CH₃), 14.2 (CH₃), 13.3 (CH₃) ppm

IR (thin film): ν_{max} = 3076, 3026, 2969, 2935, 2915, 2935, 2915, 2859, 2192, 1650 cm⁻¹

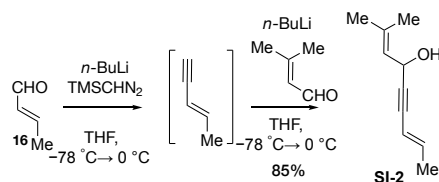
LRMS (EI): m/z (%) = 200 ([M]⁺, 4), 185 (100), 170 (31), 157 (71), 143 (94), 128 (92), 115 (60), 105 (31), 91 (54), 77 (35)

HRMS (EI): calculated for C₁₅H₂₀ [M]⁺ 200.1565; found 200.1567



S30

2-Methylnona-2,7-dien-5-yn-4-ol SI-2



In a round-bottomed flask equipped with a dry ice condenser, a solution of trimethylsilyldiazomethane (1.8 M in hexanes, 8.7 mL, 16 mmol, 1.1 mol. equiv.) in THF (20 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 11.0 mL, 16 mmol, 1.1 mol. equiv.) was added dropwise. The resulting orange-yellow solution was stirred for 10 min at $-78\text{ }^{\circ}\text{C}$ then a solution of crotonaldehyde (1.0 g, 14.0 mmol) in THF (10 mL) was added. Stirring was continued at $-78\text{ }^{\circ}\text{C}$ for a further 10 min, then at $0\text{ }^{\circ}\text{C}$ for 15 min before being cooled back to $-78\text{ }^{\circ}\text{C}$. A solution of *n*-BuLi (1.4 M in hexanes, 16 mL, 22.0 mmol, 1.5 mol. equiv) was added dropwise and the reaction mixture was stirred for 15 minutes at $-78\text{ }^{\circ}\text{C}$. A solution of 3-methyl-2-butenal (2.0 mL, 22.0 mmol, 1.5 mol. equiv.) in THF (10 mL) was added dropwise and the reaction mixture was warmed to room temperature and stirred for a further 1 hr. The reaction was quenched with water (50 mL) and diluted with Et₂O (50 mL). The aqueous layer was separated and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Purification flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 80:20:1) afforded alcohol **SI-2** as a yellow oil (1.80 g, 12.0 mmol, 85%).

R_f: 0.22 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 6.16 (dq, $J = 15.8, 6.8$ Hz, 1H), 5.51 (dt, $J = 15.8, 1.8$ Hz, 1H), 5.37 (dt, $J = 8.7, 1.4$ Hz, 1H), 5.19-5.15 (m, 1H), 1.78 (dd, $J = 6.9, 1.8$ Hz, 3H), 1.74 (dd, $J = 9.7, 1.4$ Hz, 6H) ppm

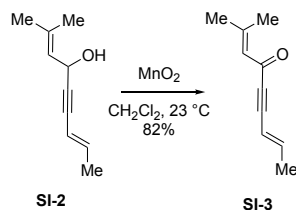
¹³C NMR (100 MHz, CDCl₃): δ 140.4 (CH), 137.0 (C_q), 125.0 (CH), 110.3 (CH), 88.0 (C_q), 83.5 (C_q), 59.7 (C_q), 25.8 (CH₃), 18.8 (CH₃), 18.3 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3349(\text{br}), 3029, 2970, 2915, 2733, 2210, 1673\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 135 ([M-CH₃]⁺, 100), 117 (25), 107 (31), 91 (84), 77 (41), 65 (27). 39 (25)

HRMS (EI): calculated for C₁₀H₁₄O [M]⁺ 150.1045; found 150.1051

2-Methylnona-2,7-dien-5-yn-4-one SI-3



To a solution of propargylic alcohol **SI-2** (1.0 g, 6.7 mmol) in CH_2Cl_2 (50 mL) was added manganese dioxide (5.70 g, 67.0 mmol, 10 mol. equiv.) in a single portion. The reaction mixture was stirred at room temperature for 1 hour then filtered through a pad of silica, flushed with Et_2O (100 mL) and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , petroleum ether 40-60: Et_2O , 90:10) afforded ketone **SI-3** as a yellow oil (0.81 g, 5.5 mmol, 82%).

R_f: 0.39 (80:20, petroleum ether 40-60: Et_2O)

¹H NMR (400 MHz, CDCl_3): δ 6.47 (dq, $J = 15.8, 6.9$ Hz, 1H), 6.26-6.07 (m, 1H), 5.64 (dd, $J = 15.8, 1.8$ Hz, 1H), 2.22 (d, $J = 1.2$ Hz, 3H), 1.93 (d, $J = 1.3$ Hz, 3H), 1.87 (dd, $J = 6.9, 1.8$ Hz, 3H) ppm

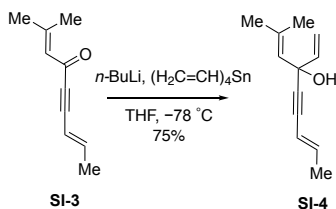
¹³C NMR (100 MHz, CDCl_3): δ 176.9 (C_q), 157.5 (C_q), 146.7 (CH), 126.3 (CH), 109.4 (CH), 89.5 (C_q), 88.8 (C_q), 28.0 (CH_3), 21.2 (CH_3), 19.3 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3037, 2976, 2914, 2856, 2180, 1649, 1628, 1601\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 147 ($[\text{M}]^{+\bullet}$, 10), 133 (100), 119 (8), 105 (90), 91 (48), 77 (38), 65 (25), 53 (18), 39 (43)

HRMS (EI): calculated for $\text{C}_{10}\text{H}_{14}\text{O}$ $[\text{M}]^{+\bullet}$ 147.0810; found 147.080

2-Methyl-4-vinylnona-2,7-dien-5-yn-4-ol SI-4



A solution of tetravinyltin (0.80 mL, 4.4 mmol, 1.0 mol. equiv.) was in THF (20 mL) was cooled to $0\text{ }^\circ\text{C}$ and a solution of $n\text{-BuLi}$ (1.5 M in hexanes, 12 mL, 18.0 mmol, 4.0 mol. equiv.) was added dropwise. The mixture was stirred at $0\text{ }^\circ\text{C}$ for 30 minutes then cooled to $-78\text{ }^\circ\text{C}$. A solution of ketone **SI-3** (0.67 g, 4.6 mmol) in THF (20 mL) was added dropwise and the reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for a further 1 hour then diluted with Et_2O (50 mL) and quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was separated and extracted with Et_2O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , petroleum ether 40-60: Et_2O : NEt_3 , 85:15:2) afforded alcohol **SI-4** as a yellow oil (0.60 g, 3.4 mmol, 75%).

R_f: 0.17 (80:20, petroleum ether 40-60: Et_2O)

¹H NMR (700 MHz, CDCl_3): δ 6.17 (dq, $J = 15.8, 6.8$ Hz, 1H), 5.99 (dd, $J = 17.0, 10.1$ Hz, 1H), 5.60-5.47 (m, 2H), 5.43-5.37 (m, 1H), 5.14 (dd, $J = 10.1, 1.1$ Hz, 1H), 2.05 (-OH, s, 1H) 1.84 (d, $J = 1.4$ Hz, 3H), 1.79 (dd, $J = 6.8, 1.8$ Hz, 3H), 1.74 (d, $J = 1.5$ Hz, 3H) ppm

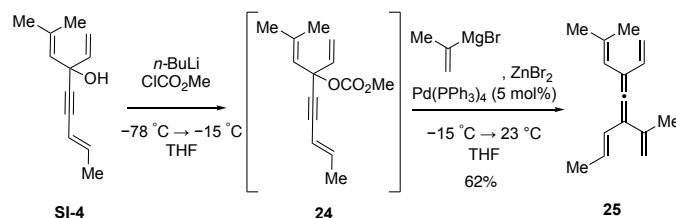
¹³C NMR (175 MHz, CDCl_3): δ 141.0 (CH), 140.2 (CH), 137.5 (C_q), 127.4 (CH), 113.4 (CH_2), 110.4 (CH), 88.4 (C_q), 84.6 (C_q), 70.1 (C_q), 26.9 (CH_3), 19.1 (CH_3), 18.8 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3404(\text{br}), 3078, 2970, 2914, 2855, 2215, 1666, 1635\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 161 ($[\text{M}-\text{CH}_3]^+$, 91), 143 (32), 133 (60), 128 (100), 115 (95), 105 (99), 91 (97), 79 (41)

HRMS (EI): calculated for $\text{C}_{12}\text{H}_{16}\text{O}$ $[\text{M}]^+$ 176.1201; found 176.1201

2-Methyl-6-(prop-1-en-2-yl)-4-vinylnona-2,4,5,7-tetraene 25



A solution of alcohol **SI-4** (150 mg, 0.85 mmol) in THF (5 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (0.90 M in hexanes, 1.10 mL, 1.00 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.30 mmol, 1.5 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.2 M in THF, 1.10 mL, 1.4 mmol, 1.6 mol. equiv.) and Pd(PPh₃)₄ (50 mg, 0.043 mmol, 5 mol%) were added in a single portion. Subsequently, a solution of isopropenylmagnesium bromide in THF (0.75 M, 2.6 mL, 1.3 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. On completion of addition the reaction mixture was stirred for a further 5 min at $-15\text{ }^{\circ}\text{C}$, then brought to room temperature and stirred for a further 20 minutes. The reaction was diluted with *n*-pentane (20 mL) and quenched with saturated aqueous NH₄Cl (20 mL). The aqueous layer was separated and extracted with *n*-pentane (3 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous K₂CO₃, filtered and concentrated at 100 mbar at $0\text{ }^{\circ}\text{C}$. The resulting solution was subjected to purification by flash chromatography on silica gel eluting with pentane to yield allene **25** as a colourless oil (110 mg, 0.53 mmol, 62%).

R_f: 0.48 (*n*-pentane)

¹H NMR (700 MHz, CDCl₃, measured at 253 K): δ 6.26 (dd, $J = 17.4, 10.5$ Hz, 1H), 5.99 (dd, $J = 15.3, 1.7$ Hz, 1H), 5.82 (dq, $J = 15.3, 1.7$ Hz, 1H), 5.62 (s, 1H), 5.23 (dd, $J = 17.4, 1.2$ Hz, 1H), 5.05 (dd, $J = 10.5, 1.2$ Hz, 1H), 5.04 (s, 1H), 4.95 (t, $J = 1.4$, 1H), 1.82 (m, 6H), 1.79 (dd, $J = 6.6, 1.7$ Hz, 3H), 1.66 (m, 3H) ppm

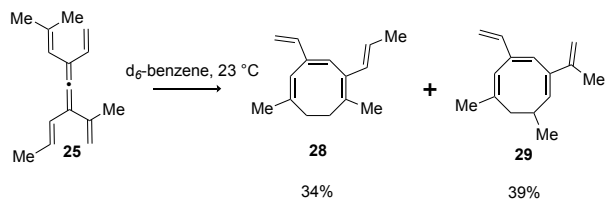
¹³C NMR (175 MHz, CDCl₃, measured at 253 K): δ 211.1 (C_q), 140.1 (C_q), 138.3 (C_q), 135.0 (CH), 129.2 (CH), 124.5 (CH), 116.2 (CH), 113.7 (CH₂), 112.0 (CH₂), 108.4 (C_q), 106.2 (C_q), 26.6 (CH₃), 22.4 (CH₃), 20.2 (CH₃), 18.7 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3091, 3018, 2970, 2915, 2879, 2729, 1905, 1653, 1612\text{ cm}^{-1}$

HRMS (EI): calculated for C₁₅H₂₀ [M]⁺ 200.1565; found 200.1567

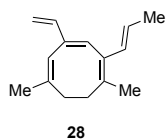
S34

(1Z,3Z,5Z)-1,6-Dimethyl-2-(prop-1-en-1-yl)-4-vinylcycloocta-1,3,5-triene **28 and
(1Z,3Z,5E)-1,7-dimethyl-5-(prop-1-en-2-yl)-3-vinylcycloocta-1,3,5-triene **29****



A solution of allene **25** (114 mg, 0.57 mmol) in C_6D_6 (3 mL) with BHT (2 mg, 9.10 μmol , 0.016 mol. equiv.) was stirred at room temperature for 20 hours after which ^1H NMR spectroscopic analysis indicated a 1:1 ratio of cyclooctatrienes **28** and **29**. The reaction was then concentrated under reduced pressure and subjected to purification by flash chromatography on silica gel eluting with *n*-pentane to yield cyclooctatriene **28** (39 mg, 0.12 mmol, 34%) and cyclooctatriene **29** (44 mg, 0.22 mmol, 39%) as colourless oils.

(1Z,3Z,5Z)-1,6-Dimethyl-2-(prop-1-en-1-yl)-4-vinylcycloocta-1,3,5-triene **28**



R_f: 0.45 (*n*-pentane)

^1H NMR (700 MHz, CDCl_3): δ 6.51 (dd, $J = 17.3, 10.6$ Hz, 1H), 6.40 (dd, $J = 15.5, 1.7$ Hz, 1H), 5.93 (s, 1H), 5.54 (dq, $J = 15.5, 6.6$ Hz, 1H), 5.22 (dd, $J = 17.3, 1.3$ Hz, 1H), 5.03 (dt, $J = 10.6, 0.9$ Hz, 1H), 2.31 (m, 4 H), 1.88 (d, $J = 1.3$ Hz, 3 H), 1.80 (d, $J = 1.3$ Hz, 3 H), 1.79 (dd, $J = 6.6, 1.6$ Hz, 3H) ppm

^{13}C NMR (175 MHz, CDCl_3): δ 141.4 (CH), 139.6 (C_q), 138.5 (C_q), 137.3 (C_q), 131.3 (C_q), 129.2 (CH), 128.8 (CH), 126.6 (CH), 119.9 (CH), 112.9 (CH_2), 33.7 (CH_2), 33.6 (CH_2), 27.9 (CH_3), 18.8 (CH_3), 18.7 (CH_3) ppm

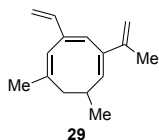
IR (thin film): $\nu_{\text{max}} = 3088, 3006, 2965, 2925, 2868, 2823, 1655, 1619, 1602\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 200 ($[\text{M}]^+$, 78), 185 (45), 172 (76), 157 (100), 143 (85), 129 (70), 115 (84), 105 (24), 91 (39), 77 (27)

HRMS (EI): calculated for $\text{C}_{15}\text{H}_{20}$ $[\text{M}]^+$ 200.1565; found 200.1565

S35

(1Z,3Z,5E)-1,7-Dimethyl-5-(prop-1-en-2-yl)-3-vinylcycloocta-1,3,5-triene 29



R_f: 0.34 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 6.49 (dd, *J* = 17.3, 10.5 Hz, 1H), 5.97 (s, 1H), 5.72 (d, *J* = 1.6 Hz, 1H), 5.67 (d, *J* = 8.0 Hz, 1H), 5.22 (dd, *J* = 17.5, 1.4 Hz, 1H), 5.11-5.01 (m, 1H), 4.90 (dd, *J* = 11.8, 1.8 Hz, 2H), 3.04-2.96 (m, 1H), 2.30-2.24 (m, 1H), 2.08-2.00 (m, 1H), 1.92-1.91 (m, 3H), 1.80 (s, 3H), 1.03 (d, *J* = 6.6 Hz, 3H) ppm

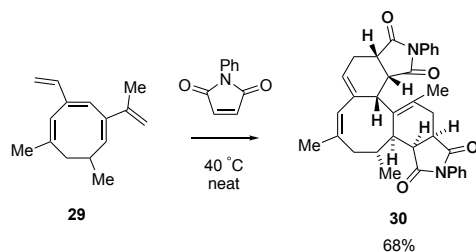
¹³C NMR (100 MHz, CDCl₃): δ 142.9 (C_q), 140.8 (CH), 140.3 (C_q), 138.4 (C_q), 137.8 (CH), 137.6 (C_q), 128.7 (CH), 120.2 (CH), 113.6 (2 x CH₂), 43.3 (CH₂), 32.4 (CH), 27.4 (CH₃), 22.2 (CH₃), 20.8 (CH₃) ppm

IR (thin film): ν_{max} = 3087, 3031, 3005, 2965, 2913, 2873, 2831, 1656, 1617 cm⁻¹

LRMS (EI): *m/z* (%) = 200 ([M]⁺, 17), 185 (13), 158 (100), 143 (425), 128 (38), 115 (23), 91 (12)

HRMS (EI): calculated for C₁₅H₂₀ [M]⁺ 200.1565; found 200.1564

Synthesis of pentacycle **30**



To a solution of cyclo-octatriene **29** (21 mg, 0.107 mmol) in C_2D_2 (1 mL), containing 1,2,3,5-tetramethylbenzene (11 mg, 0.082 mmol) as an internal standard, was added *N*-phenylmaleimide (101 mg, 0.58 mmol, 5.4 mol. equiv.). The reaction mixture was concentrated under reduced pressure and heated at 40 °C for 1 hour. The reaction mixture was then subjected to purification by flash chromatography (SiO₂, petroleum ether 40-60:EtOAc, 90:10 → 50:50) to afford bisadduct **30** (40 mg, 0.073 mmol, 68%) as a colourless solid. A crystal of bisadduct **30** was obtained by recrystallisation from toluene. The relative stereochemistry was determined by single crystal X-ray analysis.

R_f : 0.26 (50:50, petroleum ether 40-60:EtOAc)

m.p. = 121 °C (decomp.)

¹H NMR (600 MHz, CDCl₃): δ 7.46-7.43 (m, 4H), 7.37-7.32 (m, 4H), 7.26-7.14 (m, 2H), 6.10 (s, 1H), 5.80 (dt, *J* = 6.7, 3.1 Hz, 1H), 4.05 (dd, *J* = 10.5, 5.4 Hz, 1H), 3.88 (s, 1H), 3.40 (dd, *J* = 10.9, 5.5 Hz, 1H), 3.33 (td, *J* = 8.8, 1.5 Hz, 1H), 3.27-3.22 (m, 2H), 2.87 (ddd, *J* = 15.9, 7.2, 1.6 Hz, 1H), 2.81-2.69 (m, 1H), 2.60 (dd, *J* = 16.6, 9.7 Hz, 1H), 2.47 (dd, *J* = 13.3, 3.6 Hz, 1H), 2.38-2.32 (m, 1H), 2.06-2.01 (m, 1H), 1.97 (s, 3H), 1.80 (s, 3H), 1.67 (dd, *J* = 13.2, 3.9 Hz, 1H), 0.97 (d, *J* = 6.8 Hz, 3H) ppm

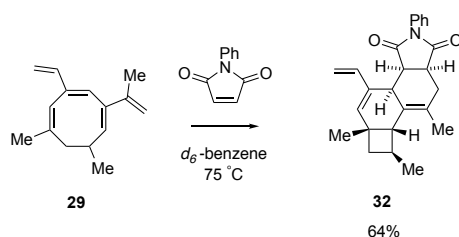
¹³C NMR (150 MHz, CDCl₃): δ 179.9 (C_q), 178.7 (C_q), 178.2 (C_q), 176.9 (C_q), 141.5 (C_q), 139.0 (C_q), 132.4 (C_q), 132.2 (C_q), 131.9 (C_q), 129.2 (CH), 129.2 (CH), 128.7 (CH), 128.4 (CH), 128.3 (CH), 126.7 (CH), 126.5 (CH), 126.3 (CH), 48.9 (CH), 43.9 (CH), 40.4 (CH), 40.1 (CH), 40.0 (CH₂), 32.1 (CH), 29.6 (CH₂), 29.1 (CH₃), 25.7 (CH₂), 20.7 (CH₃), 20.6 (CH₃) ppm

IR (thin film): ν_{max} = 3068, 2967, 2938, 2867, 1777, 1708, 1598, 1499 cm⁻¹

LRMS (EI): *m/z* (%) = 564 ([M]⁺, 100), 531 (23), 372 (17), 358 (18), 306 (35), 174 (85), 119 (60)

HRMS (EI): calculated for C₃₅H₃₄N₂O₄ [M]⁺ 546.2519; found 546.2520

Synthesis of Tetracycle **32**



A solution containing cyclo-octatriene **29** (12 mg, 0.060 mmol) in C₆D₆ (1 mL), containing 1,2,3,5-tetramethylbenzene (14 mg, 0.10 mmol) as an internal standard, was heated to 75 °C for 4 hours. *N*-Phenylmaleimide (20 mg, 0.12 mmol, 2 mol. equiv.) was added and the reaction mixture was heated for a further 6 hours at 75 °C. The reaction mixture was concentrated under reduced pressure and purified by flash chromatography (SiO₂, petroleum ether 40-60:EtOAc, 90:10) to yield monoadduct **32** (14 mg, 0.038 mmol, 64%) as a yellow oil. An analytically pure sample of monoadduct **32** was obtained for characterization purposes *via* reverse phase preparative HPLC (Waters SymmetryPrep 7 μ m C18 (150x19mm), 90:10 acetonitrile:H₂O).

R_f: 0.12 (90:10, petroleum ether 40-60:EtOAc)

¹H NMR (700 MHz, CDCl₃): δ 7.42-7.38 (m, 2H), 7.35-7.32 (m, 1H), 7.12-7.09 (m, 2H), 6.50 (dd, J = 17.8, 11.1 Hz, 1H), 5.90 (s, 1H), 5.24 (d, J = 17.8 Hz, 1H), 5.12 (d, J = 11.1 Hz, 1H), 3.68 (ddd, J = 8.7, 5.8, 1.3 Hz, 1H), 3.32-3.29 (m, 1H), 3.26-3.24 (m, 1H), 2.76 (d, J = 14.7 Hz, 1H), 2.61 (d, J = 8.0 Hz, 1H), 2.43 (dd, J = 14.7, 6.5 Hz, 1H), 1.90-1.84 (m, 5H), 1.42-1.36 (m, 1H), 1.07 (d, J = 6.2 Hz, 3H), 0.97 (d, J = 1.3 Hz, 3H) ppm

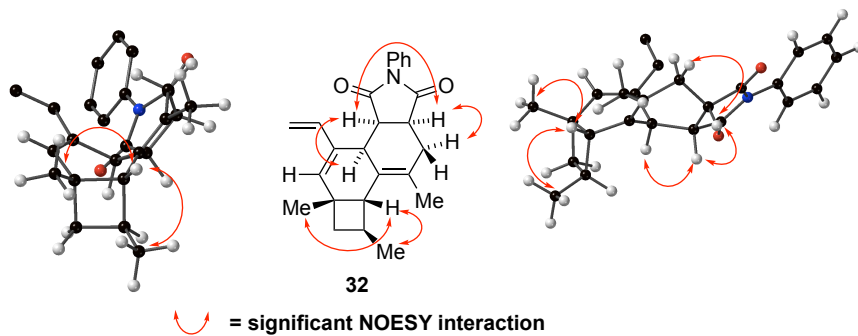
¹³C NMR (175 MHz, CDCl₃): δ 179.0 (C_q), 175.6 (C_q), 139.6 (CH), 139.0 (CH), 132.3 (C_q), 131.2 (C_q), 129.1 (2 x CH), 128.9 (C_q), 128.5 (C_q), 126.6 (CH), 110.8 (CH₂), 48.4 (CH), 42.4 (CH), 41.2 (CH), 41.2 (CH₂), 36.7 (C_q), 34.2 (CH), 34.0 (CH), 31.5 (CH₂), 28.2 (CH₃), 21.1 (CH₃), 19.6 (CH₃) ppm

IR (thin film): ν_{max} = 3085, 3068, 2948, 2922, 2859, 1709, 1599 cm⁻¹

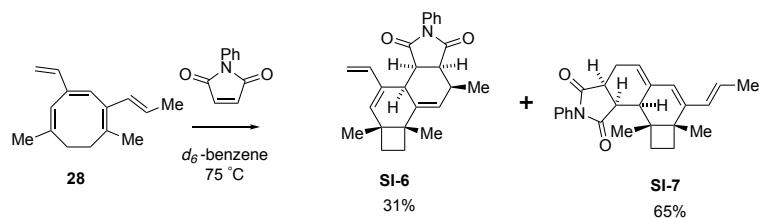
LRMS (EI): m/z (%) = 373 ([M]⁺, 48), 332 (51), 318 (45), 269 (21), 210 (47), 191 (56), 183 (74), 174 (83), 159 (90), 143 (93), 129 (90), 115 (86), 105 (94), 91 (93), 77 (100)

HRMS (EI): calculated for C₂₅H₂₇NO₂ [M]⁺ 373.2042; found 373.2042

Confirmation of stereochemistry
(energy minimized molecular models generated using MMFF94 in iQmol)

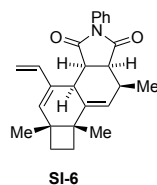


Synthesis of tetracycles SI-6 and SI-7



To a solution of cyclooctatriene **28** (65 mg, 0.32 mmol) in C_6D_6 (1 mL), containing 1,2,3,5-tetramethylbenzene (17 mg, 0.13 mmol) as an internal standard, was added *N*-phenylmaleimide (75 mg, 0.43 mmol, 1.3 mol. equiv.). The reaction mixture was heated at 75 °C for 12 hours, after which time a further portion of *N*-phenylmaleimide (55 mg, 0.32 mmol, 1.0 mol. equiv.) was added. The reaction mixture was heated for a further 6 hours after which, 1H NMR indicated the reaction had gone to completion to afford compounds **SI-6** (0.099 mmol, 31%, by 1H NMR) and **SI-7** (0.21 mmol, 65%, by 1H NMR). Analytically pure samples of **SI-6** and **SI-7** were obtained for characterization purposes *via* flash chromatography purification (SiO_2 , petroleum ether 40-60:EtOAc, 90:10) followed by reverse phase preparative HPLC (Waters SymmetryPrep 7 μ m C18 (150x19mm), 90:10 acetonitrile:H $_2$ O).

Tetracycle SI-6



R_f: 0.23 (80:20, petroleum ether 40-60:EtOAc)

1H NMR (700 MHz, $CDCl_3$): δ 7.40-7.38 (m, 2H), 7.33-7.30 (m, 1H), 7.11-7.08 (m, 2H), 6.51 (dd, J = 17.8, 11.1, 1H), 5.90 (s, 1H), 5.61 (m, 1H), 5.24 (d, J = 17.8 Hz, 1H), 5.13 (d, J = 11.1 Hz, 1H), 3.70 (dd, J = 8.6, 5.5 Hz, 1H), 3.33 (d, J = 5.7 Hz, 1H), 3.17 (dd, J = 8.6, 6.7 Hz, 1H), 2.62-2.57 (m, 1H), 1.97-1.91 (m, 2H), 1.57-1.55 (m, 1H), 1.52 (d, J = 7.3 Hz, 3H), 1.46-1.44 (m, 1H), 1.29 (s, 3H), 0.92 (s, 3H) ppm

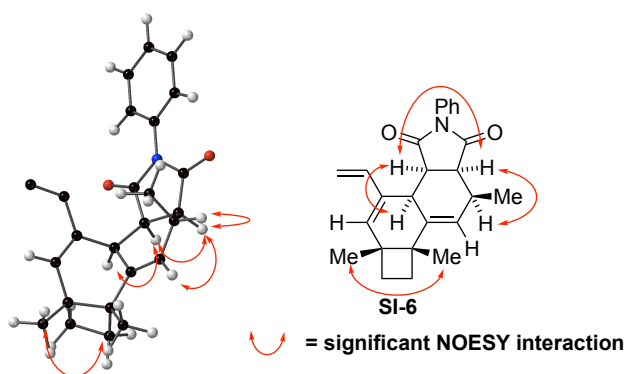
^{13}C NMR (175 MHz, CDCl_3): δ 156.7 (C_q), 175.2 (C_q), 145.1 (C_q), 140.5 (CH), 138.9 (CH), 132.2 (C_q), 129.8 (C_q), 129.1 (CH), 128.4 (CH), 126.6 (CH), 125.3 (CH), 110.8 (CH_2), 45.6 (CH), 43.3 (CH), 41.9 (C_q), 41.0 (C_q), 34.0 (CH), 32.4 (CH_2), 31.8 (CH_2), 31.6 (CH), 22.3 (CH_3), 20.2 (CH_3), 17.2 (CH_3) ppm

IR (thin film): ν_{max} = 3040, 2966, 2932, 2864, 1708, 1598 cm^{-1}

LRMS (EI): m/z (%) = 373 ($[\text{M}]^+$, 95), 358 (65), 345 (48), 330 (17), 200 (33), 185 (36), 172 (100), 157 (63), 142 (46), 129 (36), 115 (24), 91 (26), 77 (17)

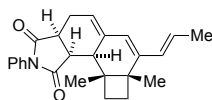
HRMS (EI): calculated for $\text{C}_{25}\text{H}_{27}\text{NO}_2$ $[\text{M}]^+$ 373.2042; found 373.2034

Confirmation of stereochemistry
(energy minimized molecular models generated using MMFF94 in iQmol)



S41

Tetracycle SI-7



SI-7

R_f: 0.19 (80:20, petroleum ether 40-60:EtOAc)

¹H NMR (700 MHz, CDCl₃): δ 7.39 (t, *J* = 7.8 Hz, 2H), 7.3507.29 (m, 1H), 7.14-7.00 (m, 2H), 6.24 (s, 1H), 5.92-5.83 (m, 2H), 5.79 (ddd, *J* = 7.0, 4.3, 2.3 Hz, 1H), 3.47 (dd, *J* = 8.6, 4.6 Hz, 1H), 3.29 (ddd, *J* = 8.6, 7.4, 1.4 Hz, 1H), 2.84 (ddd, *J* = 15.2, 7.3, 1.4 Hz, 1H), 2.36 (ddd, *J* = 15.3, 7.4, 4.5 Hz, 1H), 2.17 (m, 1H), 2.00-1.95 (m, 1H), 1.87-1.81 (m, 2H), 1.78 (d, *J* = 6.4 Hz, 3H), 1.54 (s, 3H), 1.51-1.48 (m, 1H), 1.30 (s, 3H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 179.1 (C_q), 176.7 (C_q), 142.3 (C_q), 138.8 (C_q), 132.2 (C_q), 131.2 (CH), 129.2 (CH), 128.5 (CH), 126.7 (CH), 126.5 (CH), 122.2 (CH), 121.5 (CH), 48.3 (CH), 43.6 (C_q), 43.2 (CH), 42.2 (CH), 40.4 (C_q), 33.3 (CH₂), 30.3 (CH₂), 26.0 (CH₂), 21.7 (CH₃), 21.7 (CH₃), 18.9 (CH₃) ppm

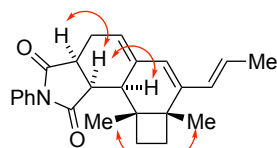
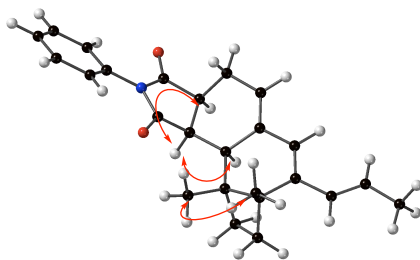
IR (thin film): ν_{max} = 2962, 2931, 2870, 1709, 1599 cm⁻¹

LRMS (EI): *m/z* (%) = 373 ([M]⁺, 100), 360 (45), 345 (65), 330 (32), 197 (36), 183 (48), 172 (96), 160 (55), 129 (61), 91 (50), 77 (40)

HRMS (EI): calculated for C₂₅H₂₇NO₂ [M]⁺ 373.2042; found 373.2043

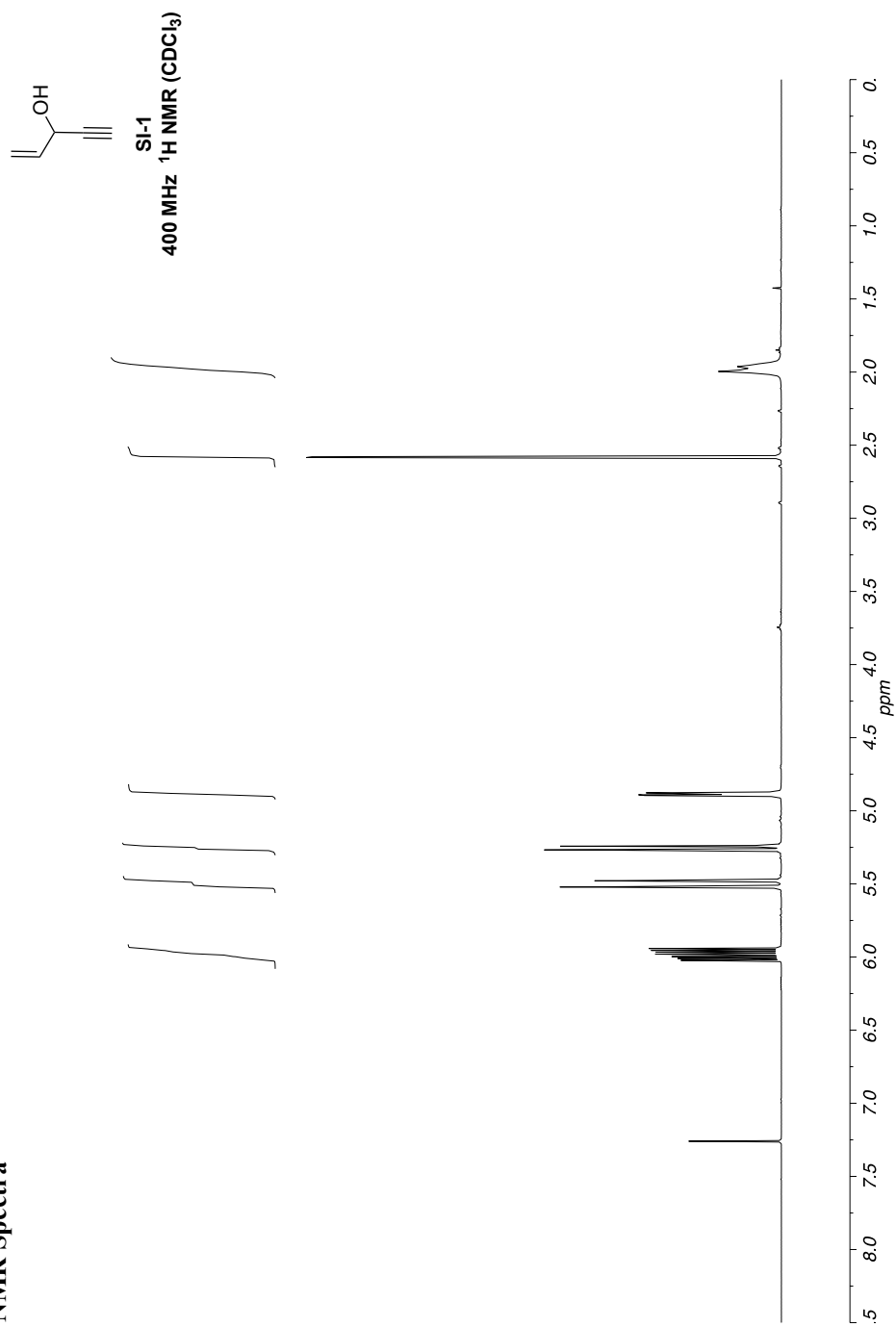
Confirmation of stereochemistry

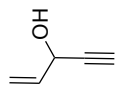
(energy minimized molecular models generated using MMFF94 in iQmol)



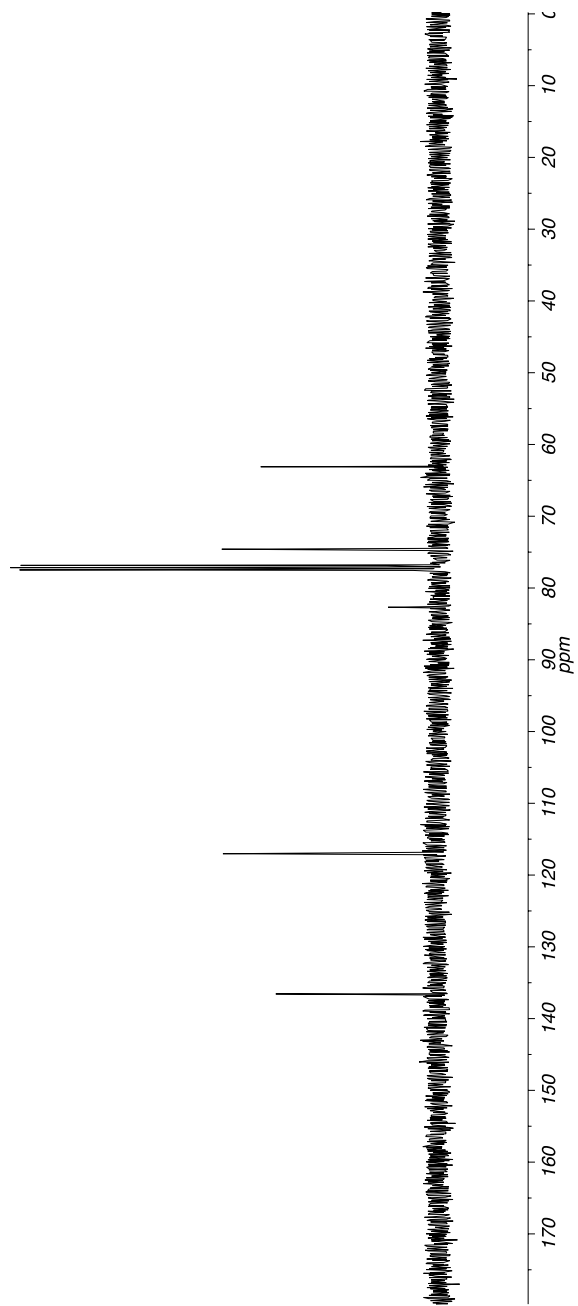
SI-7

= significant NOESY interaction

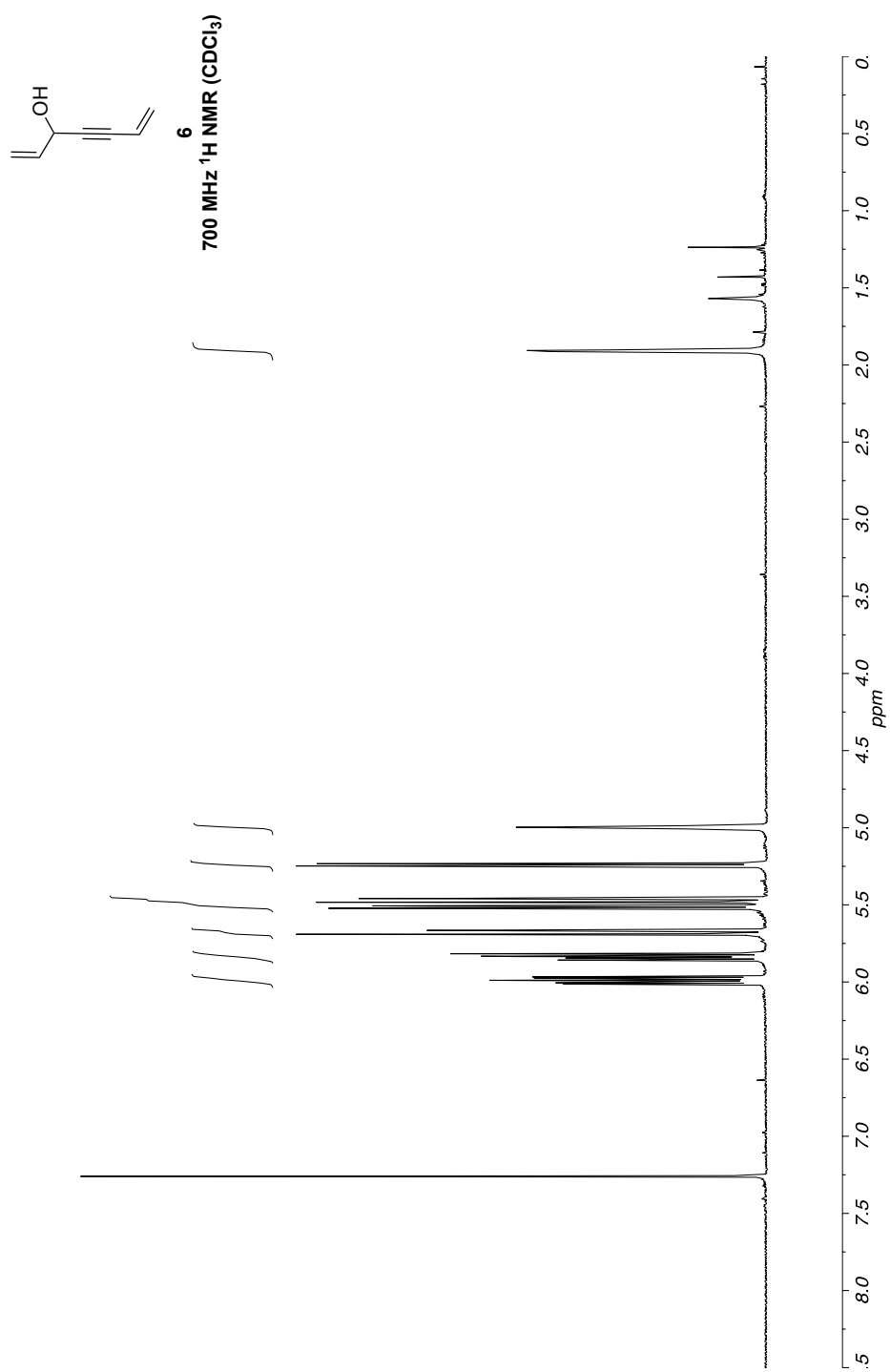
¹H and ¹³C NMR Spectra

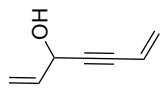


SI-1
100 MHz ^{13}C NMR (CDCl_3)



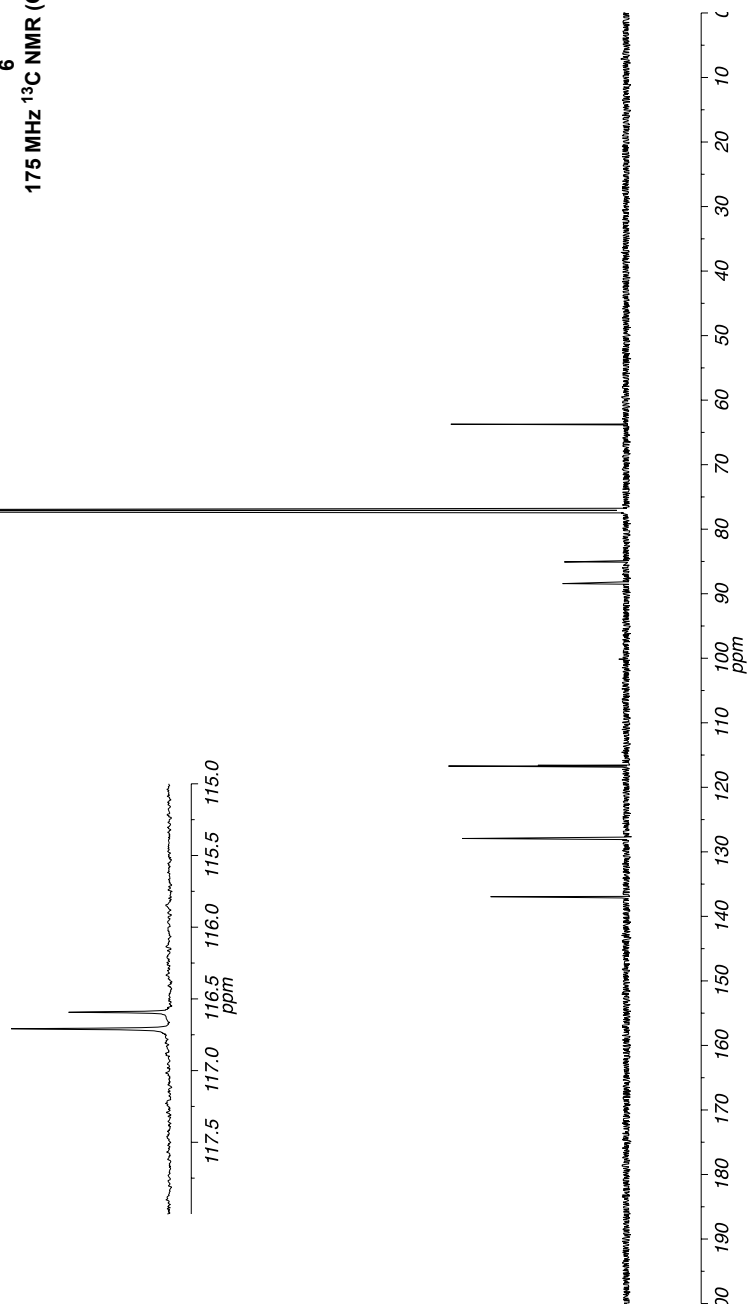
S44



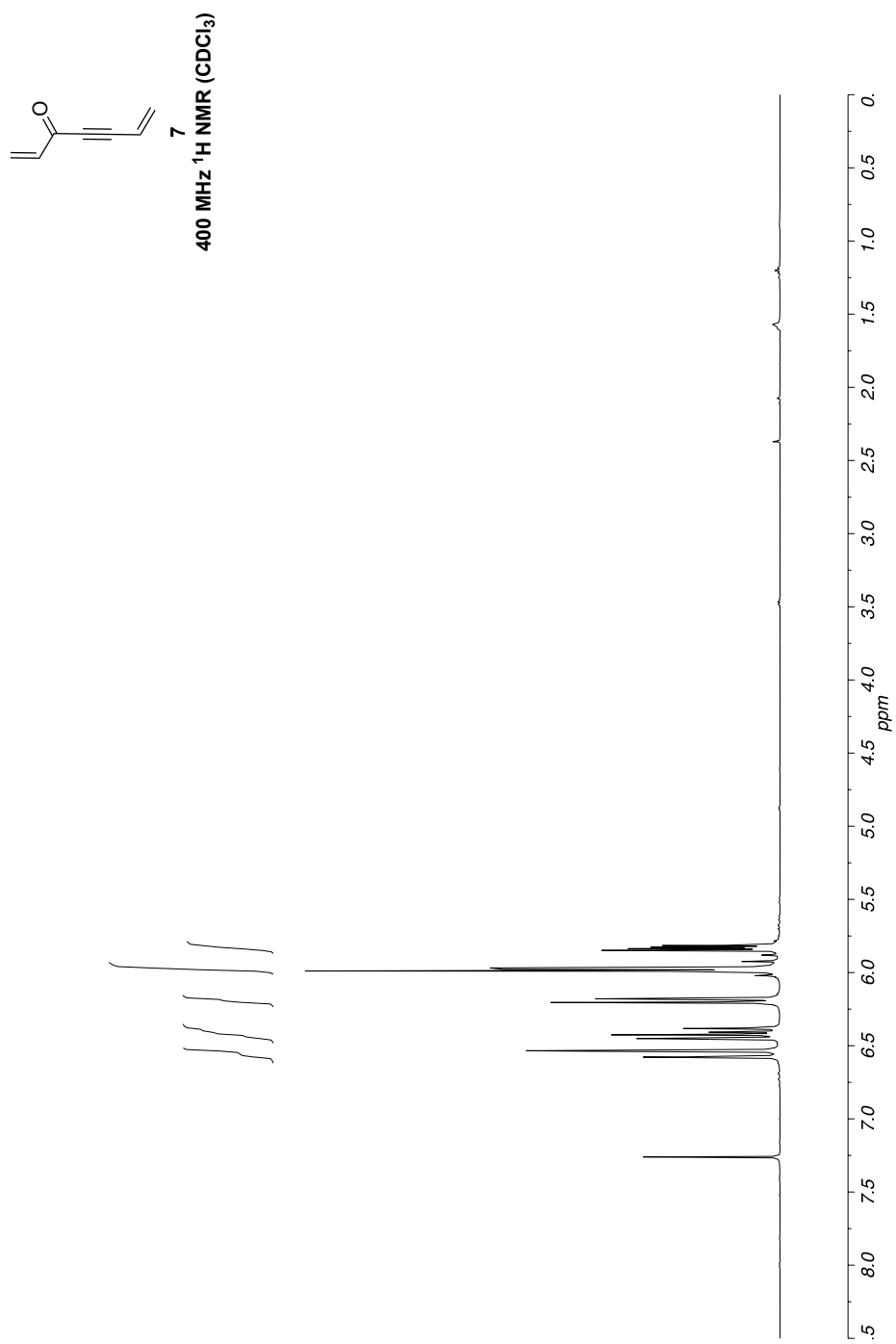


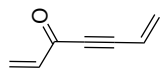
6

175 MHz ^{13}C NMR (CDCl_3)



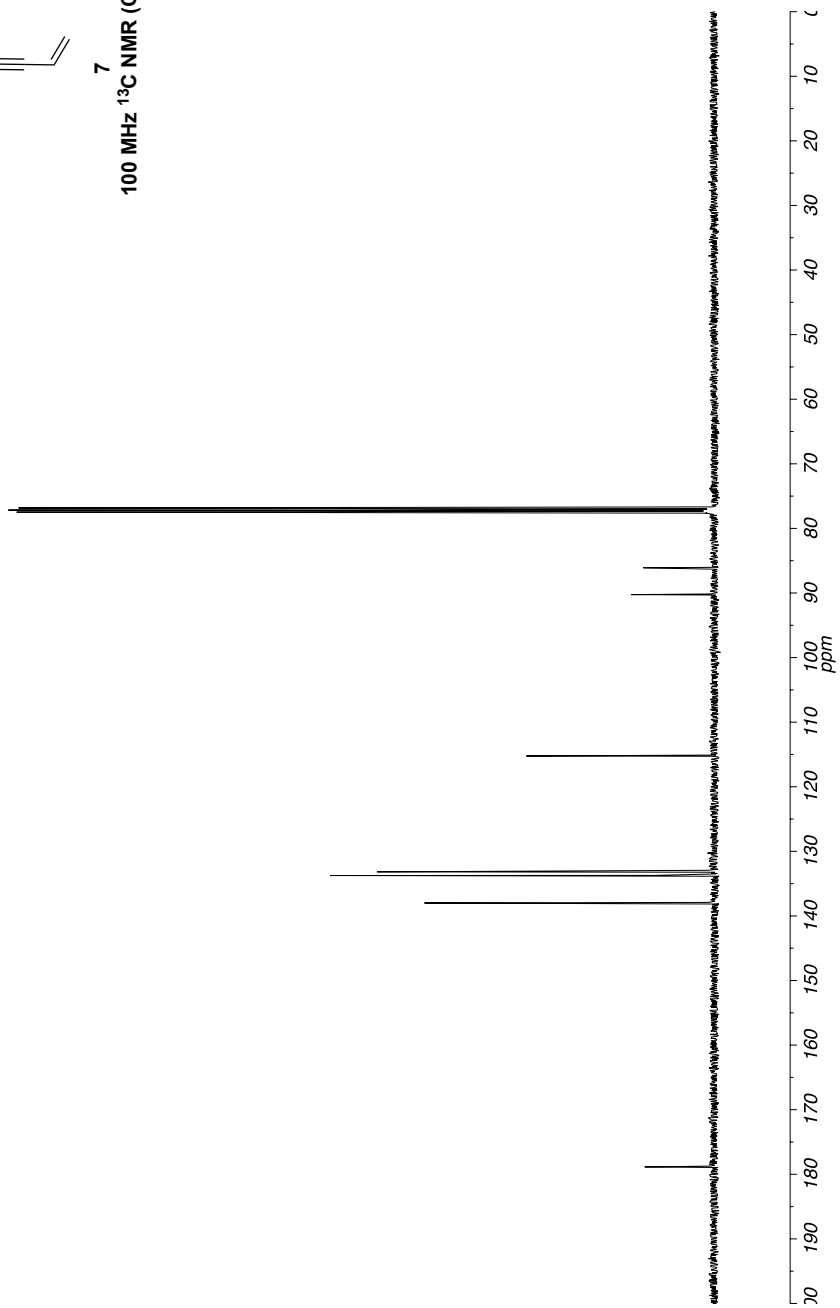
S46



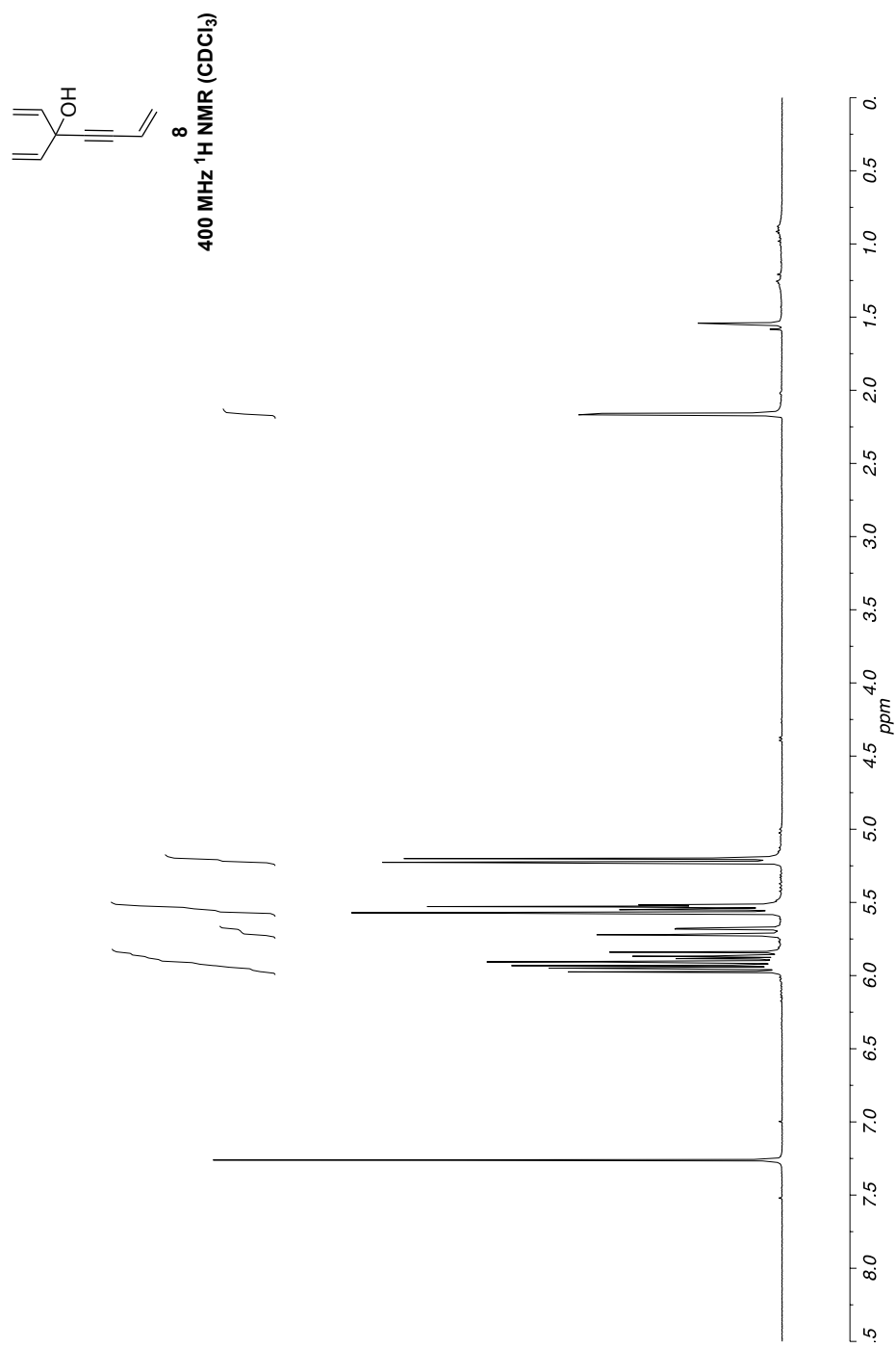


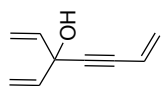
7

100 MHz ^{13}C NMR (CDCl_3)



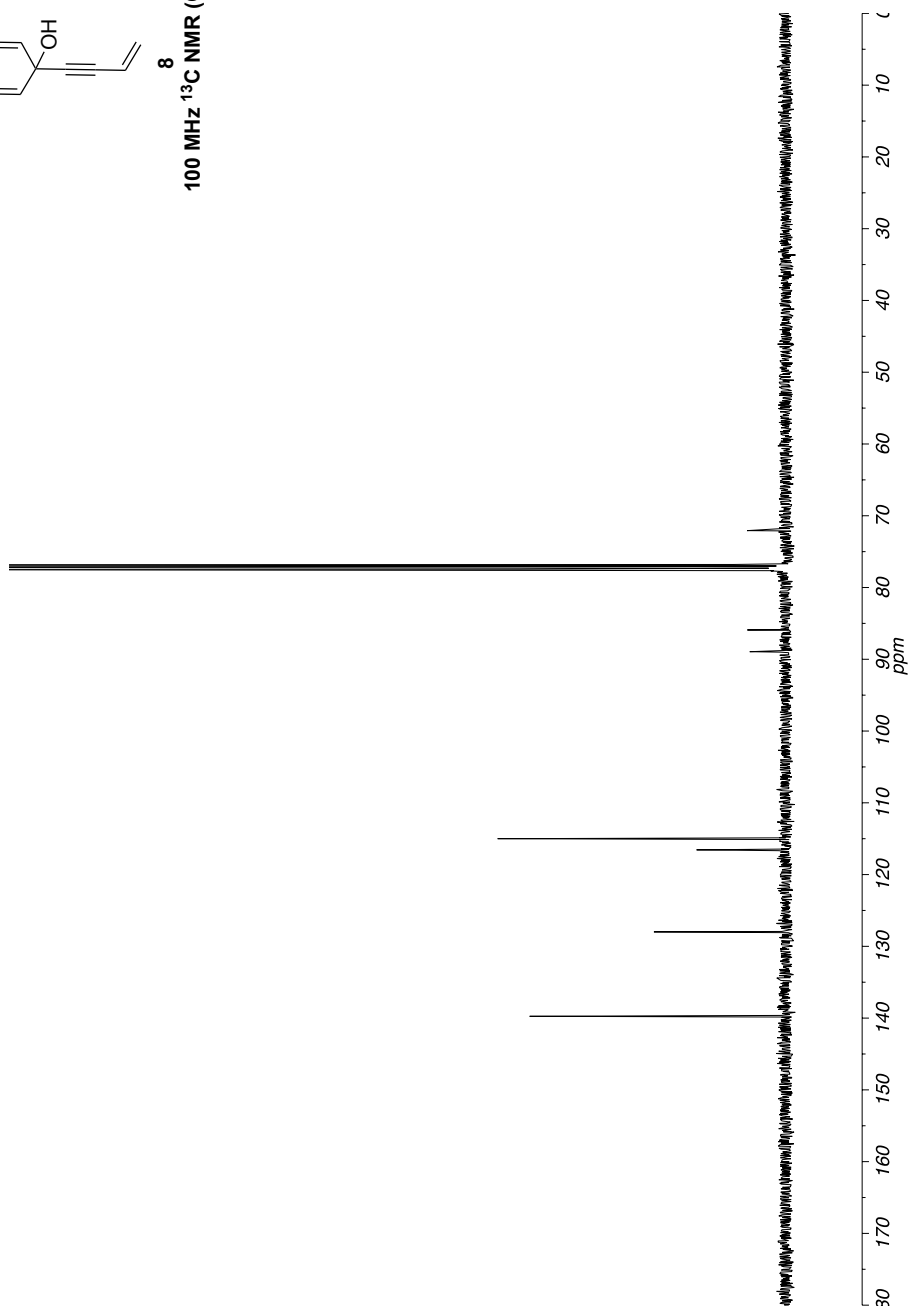
S48



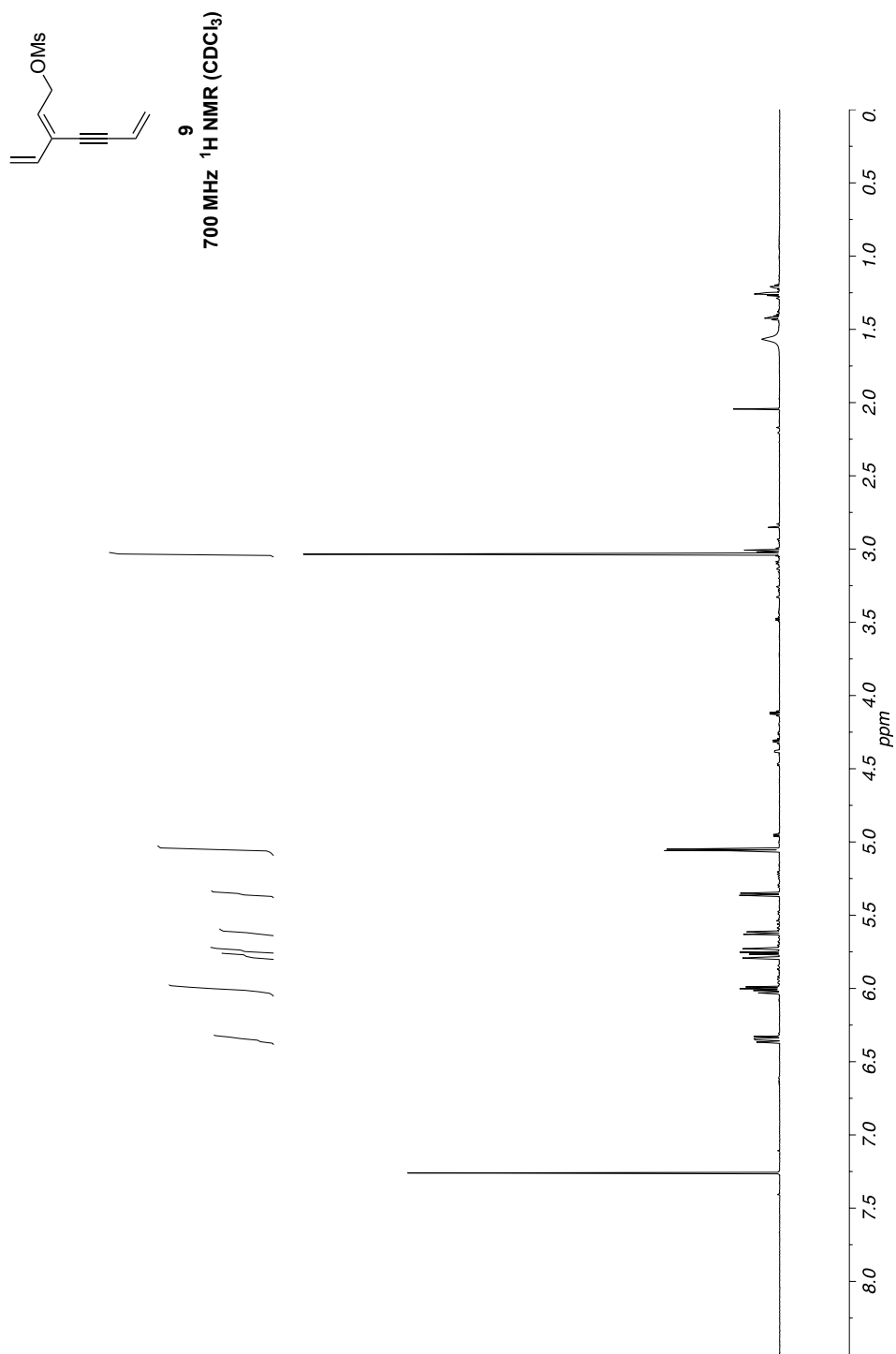


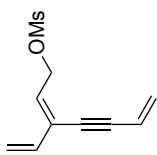
8

100 MHz ^{13}C NMR (CDCl_3)



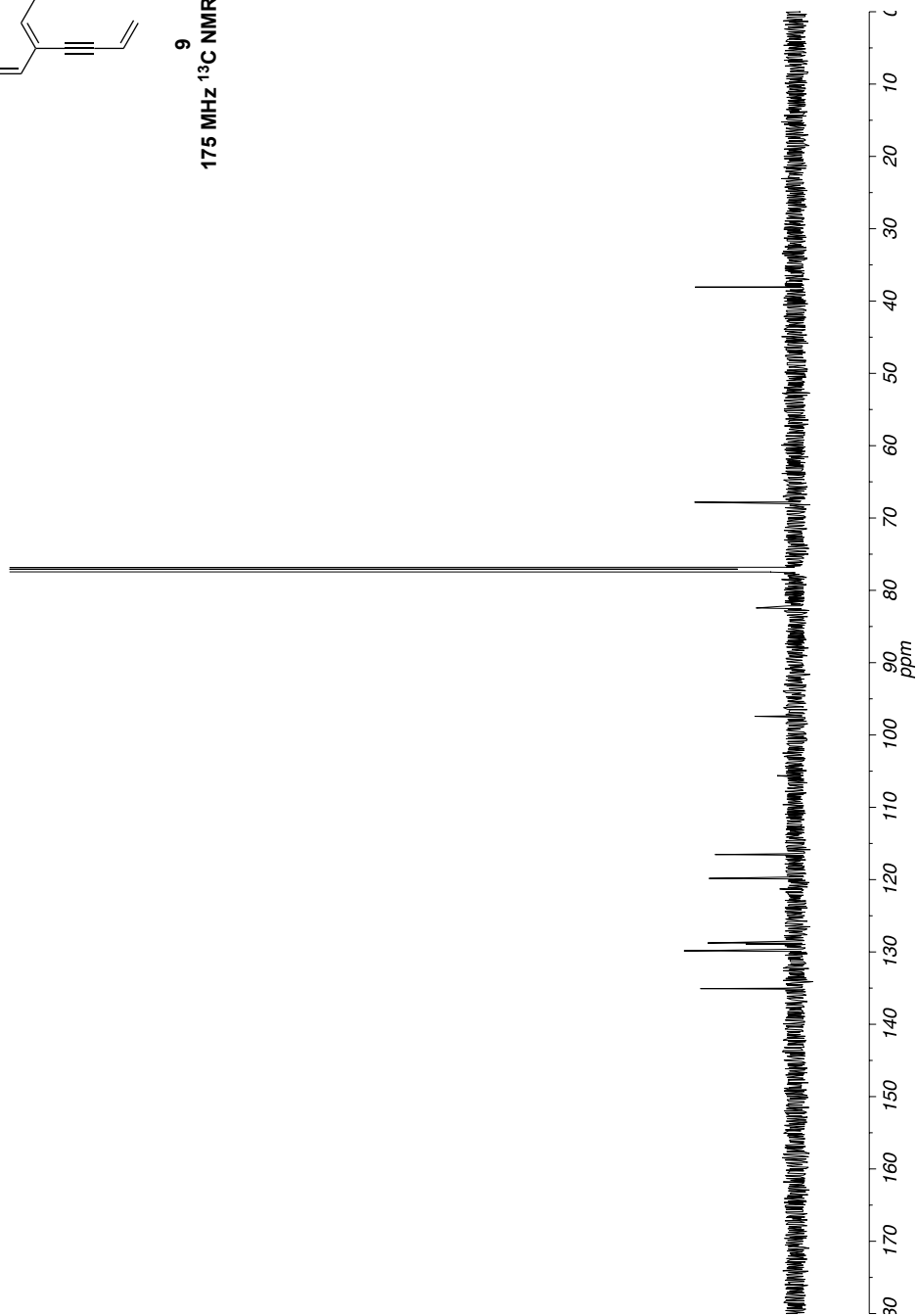
S50



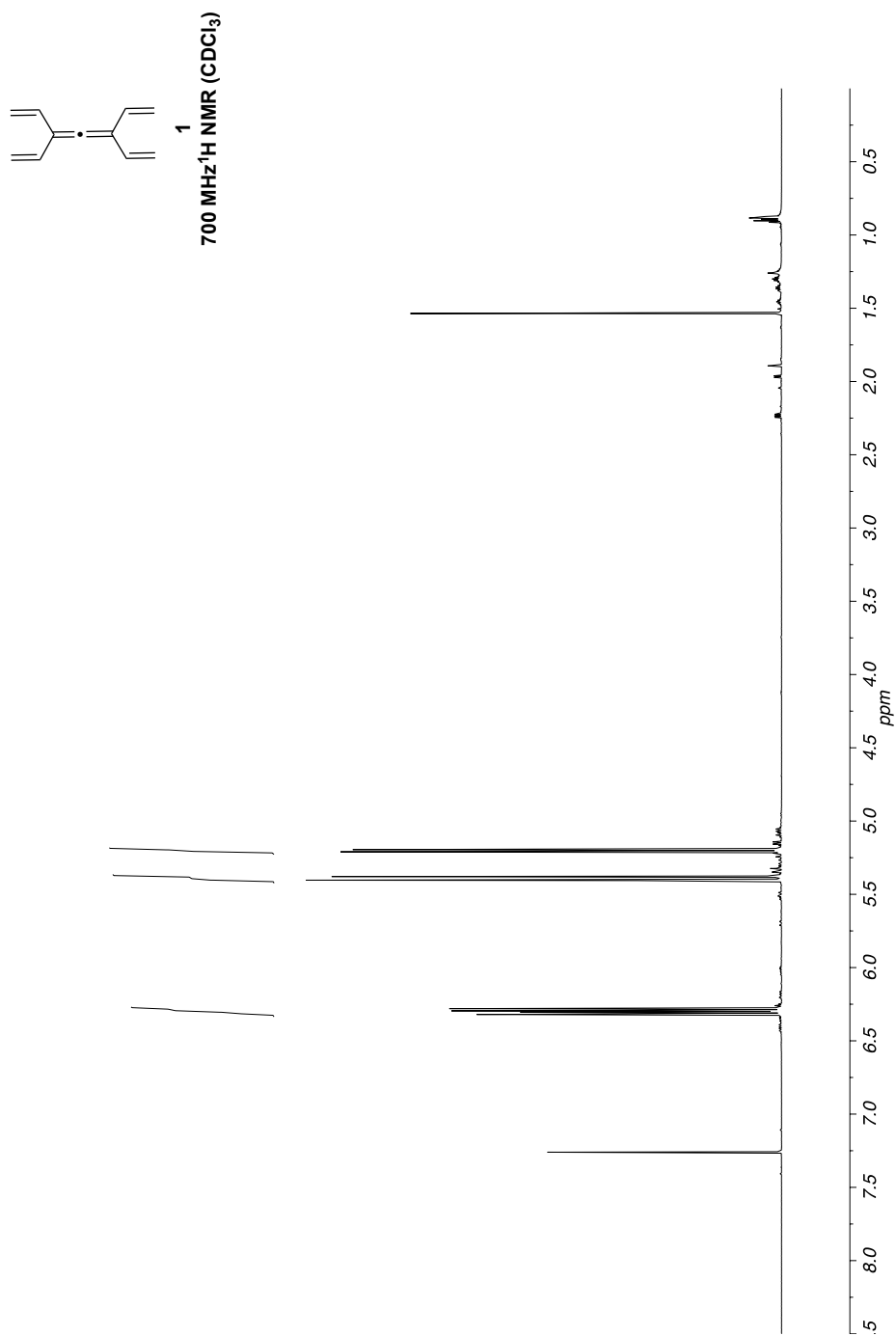


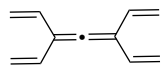
9

175 MHz ^{13}C NMR (CDCl_3)



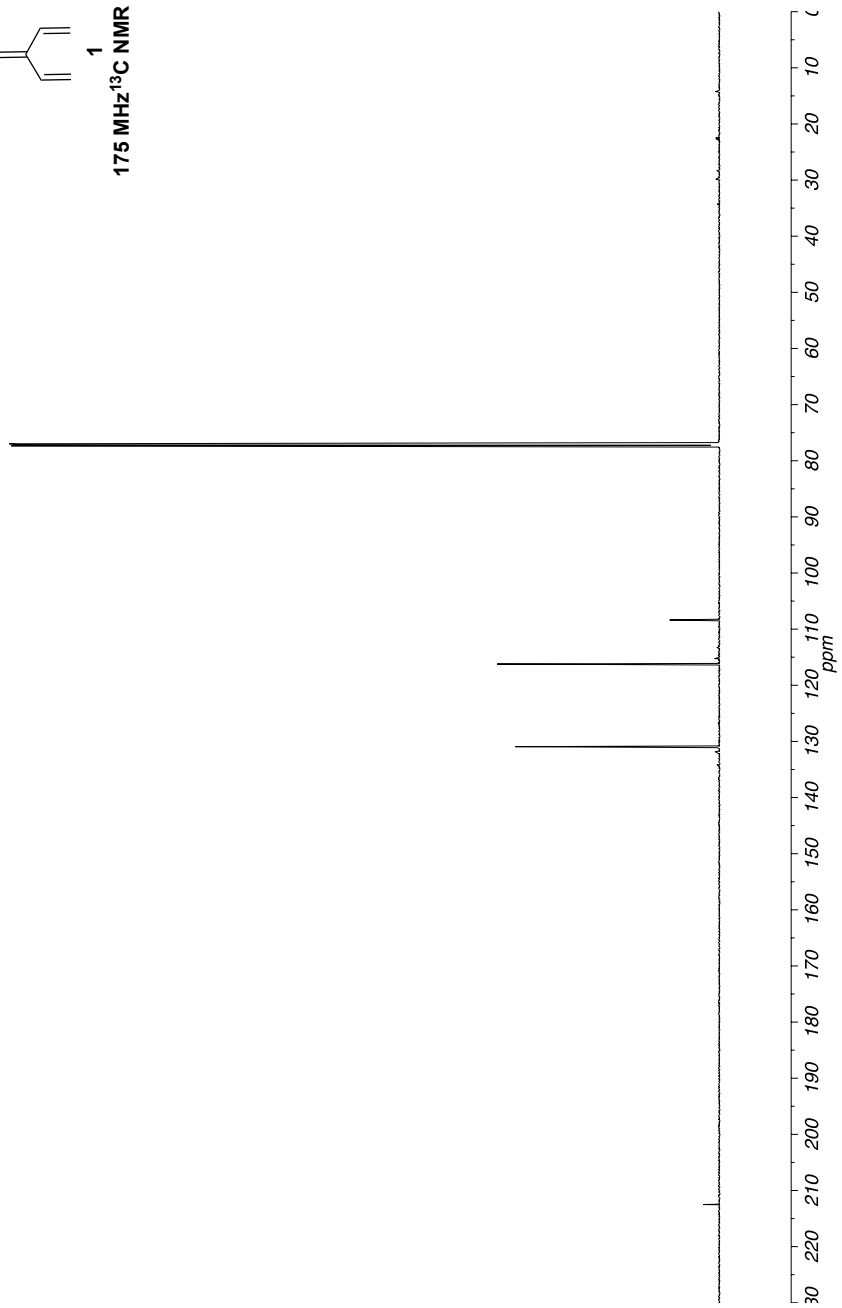
S52



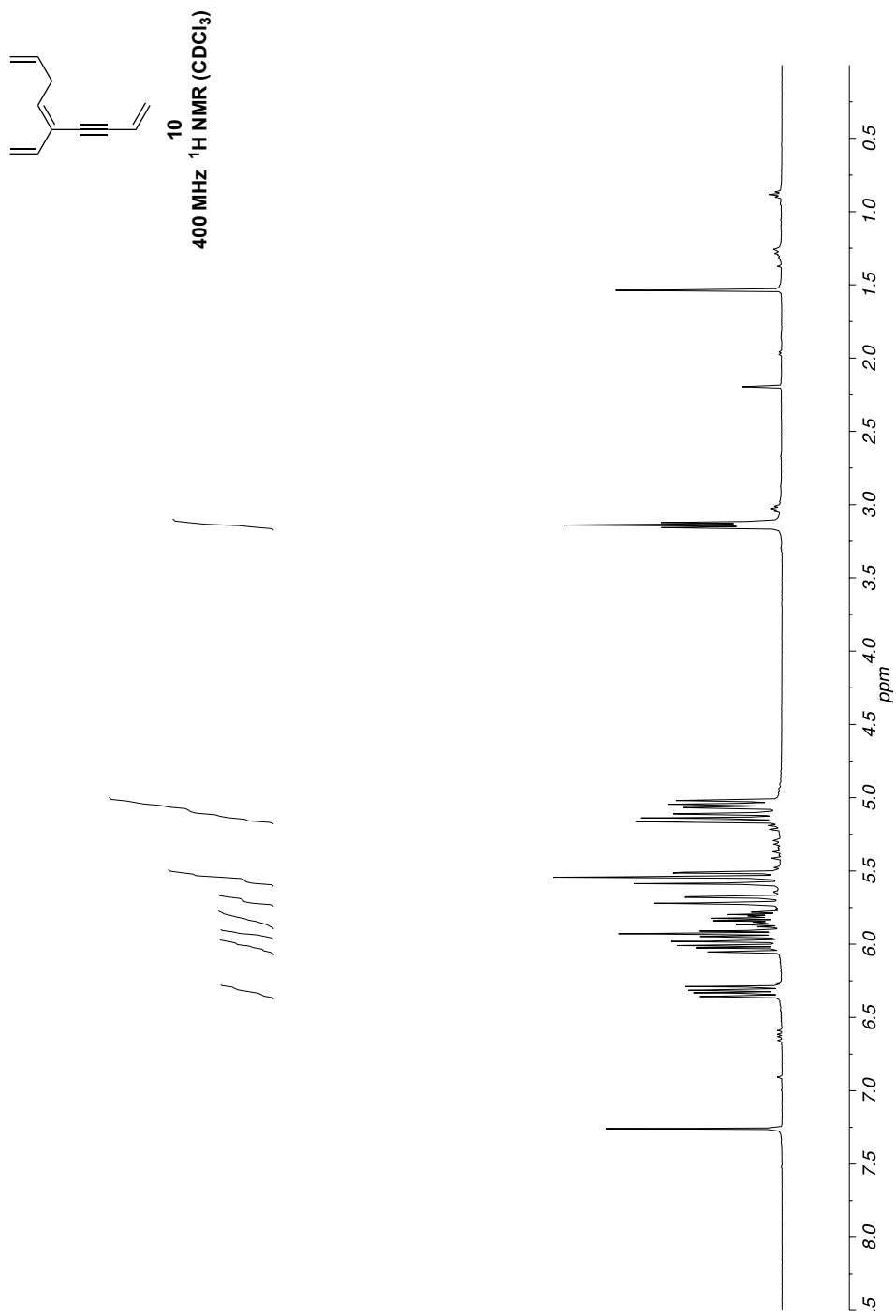


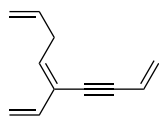
1

175 MHz ¹³C NMR (CDCl₃)

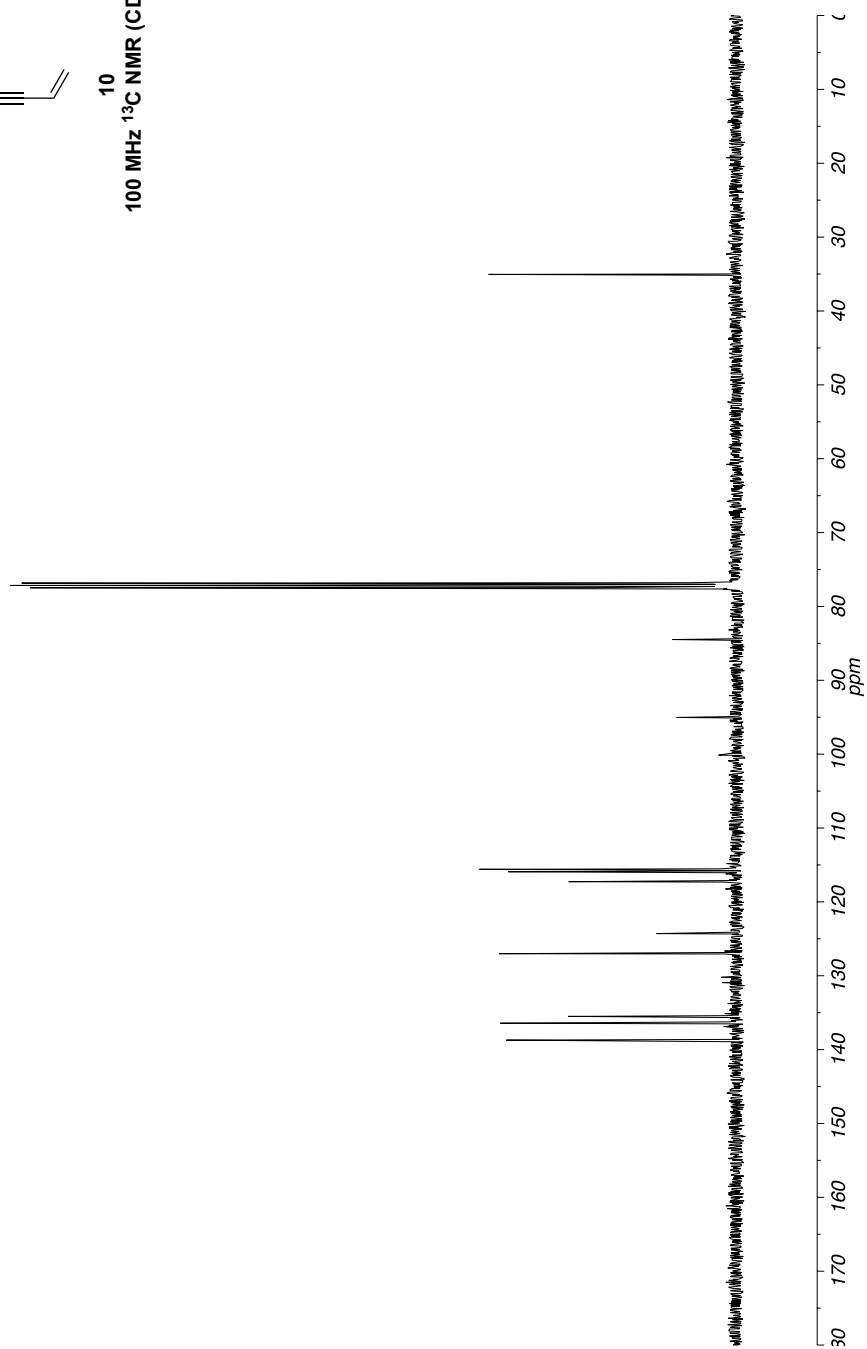


S54

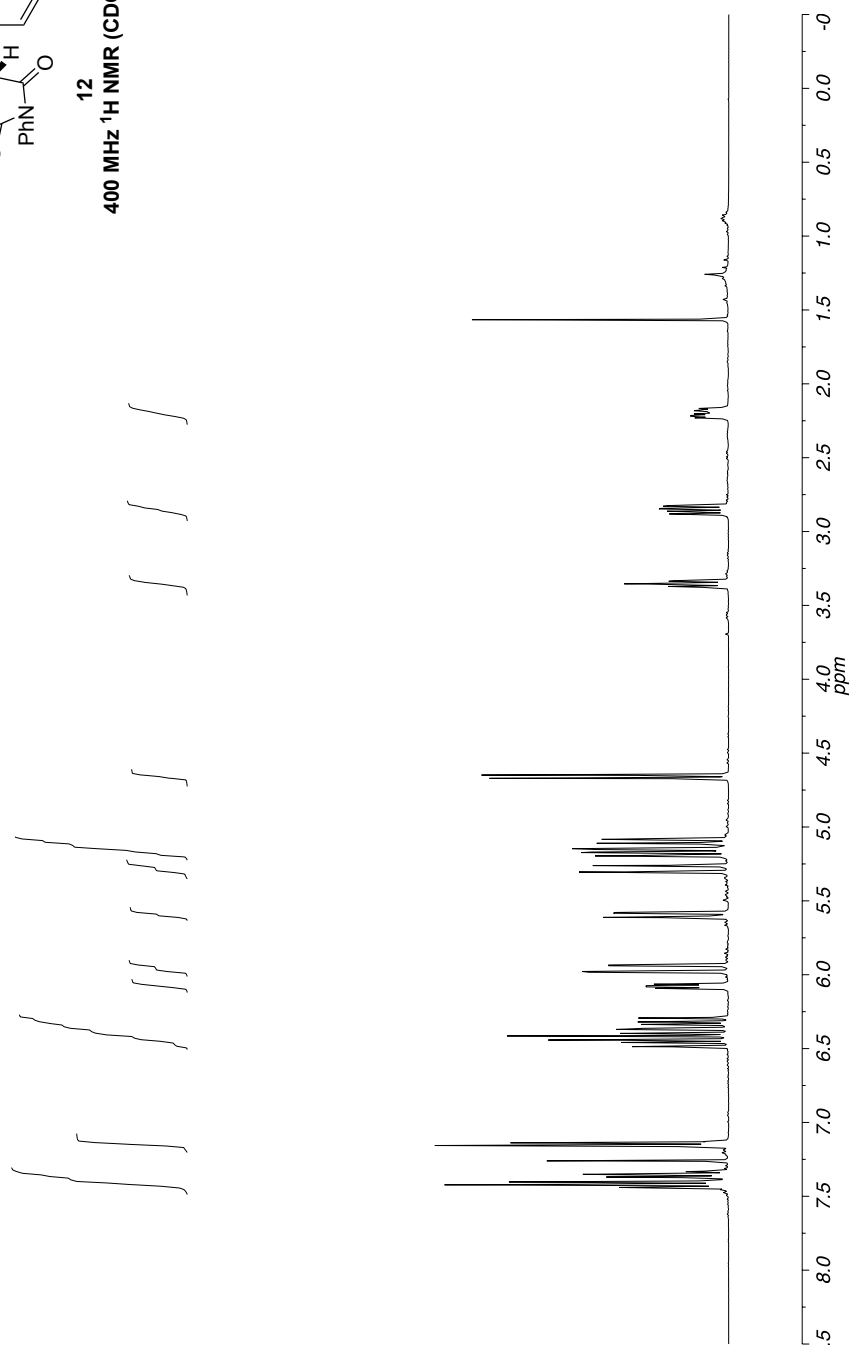
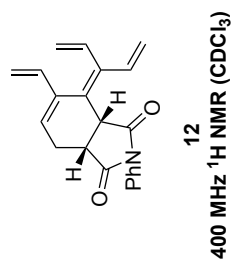


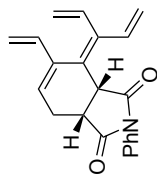


10
100 MHz ^{13}C NMR (CDCl₃)



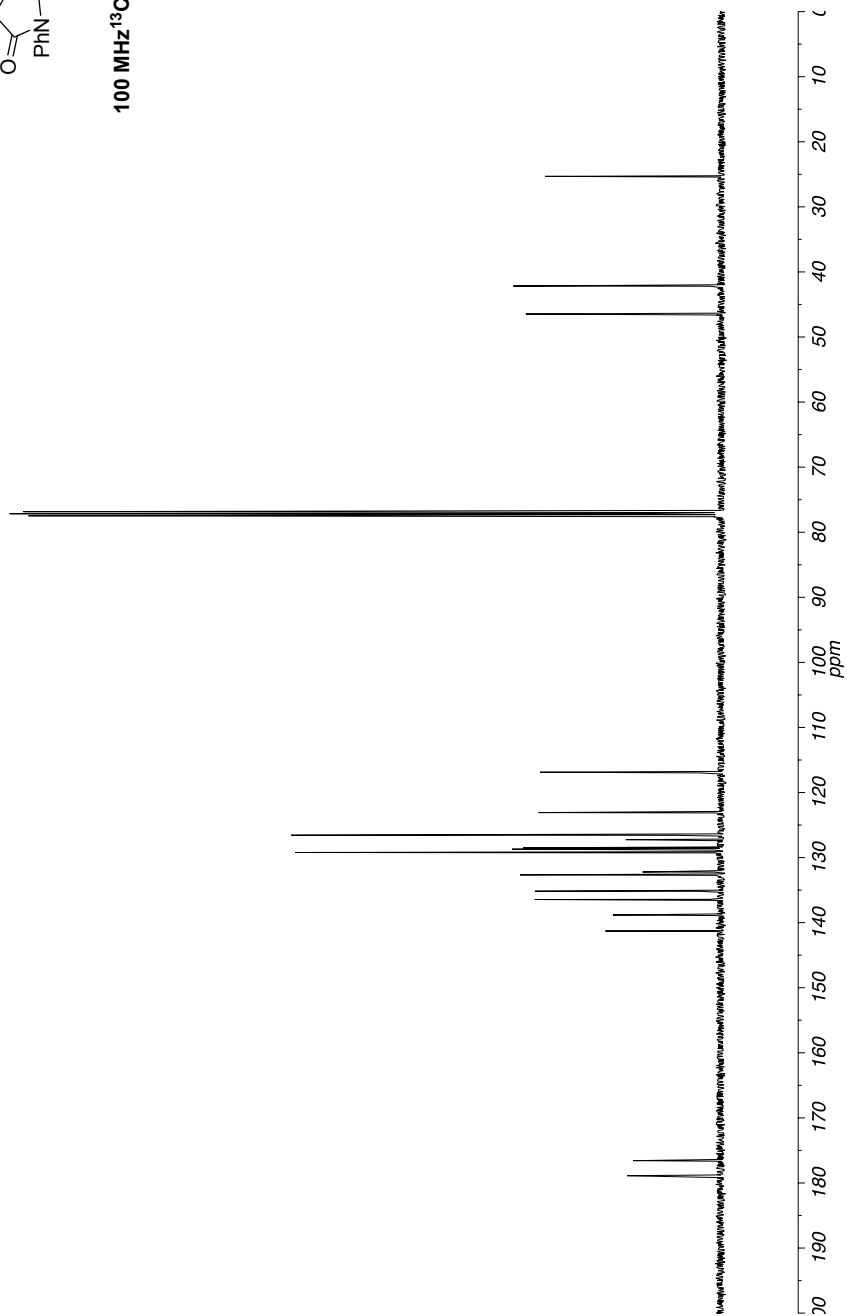
S56



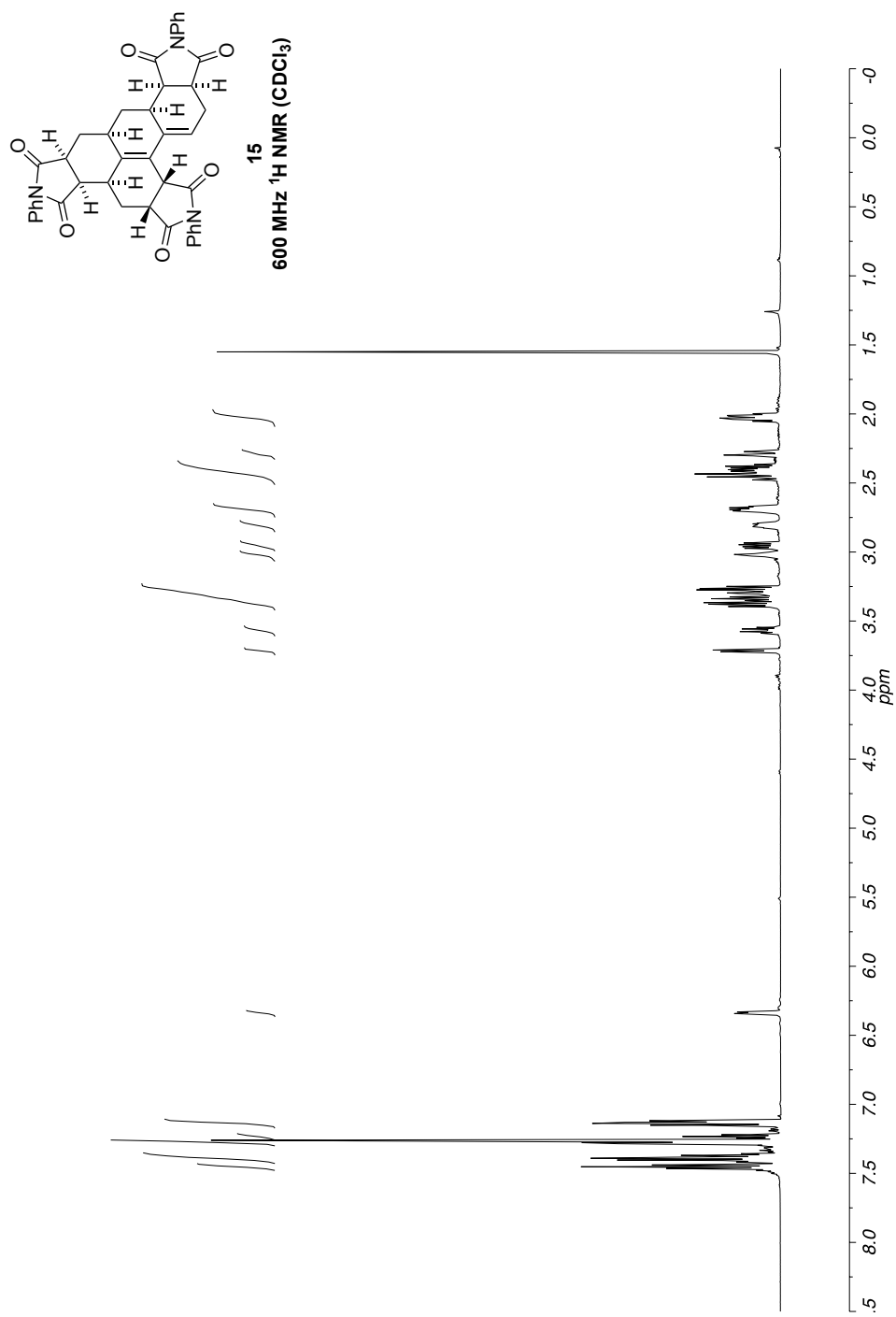


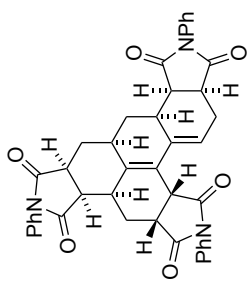
12

100 MHz ^{13}C NMR (CDCl₃)

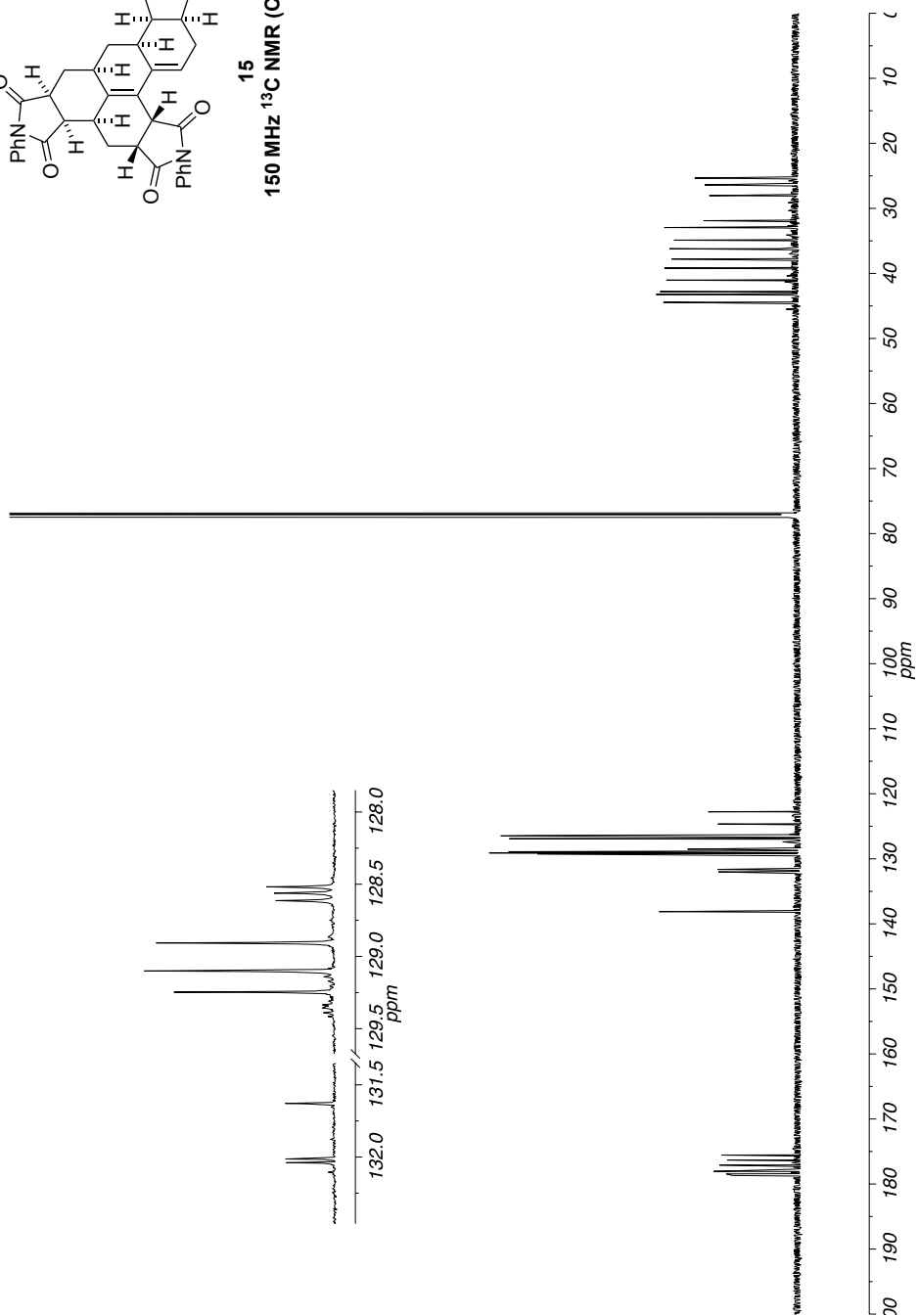


S58

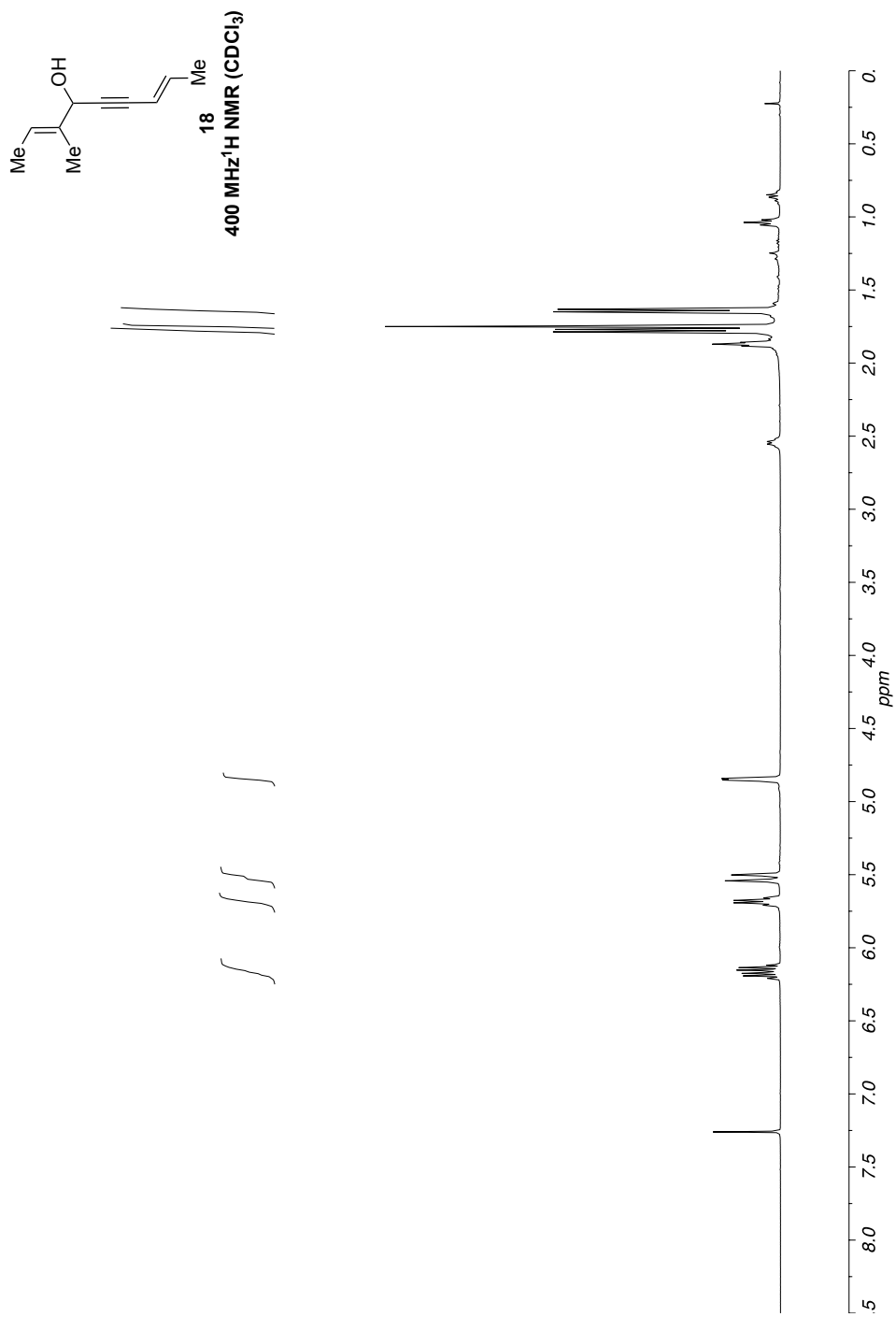


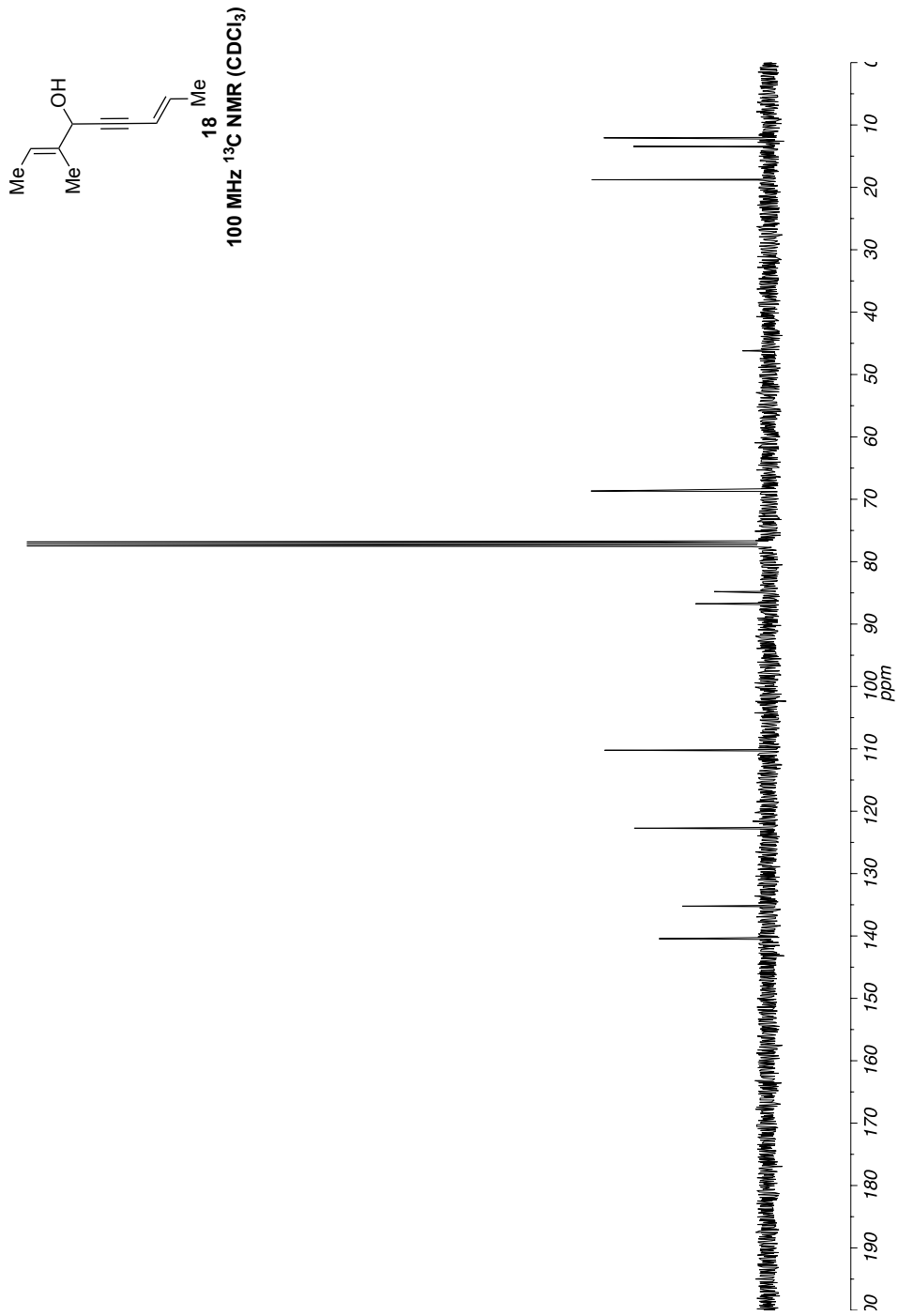


150 MHz ^{13}C NMR (CDCl_3)

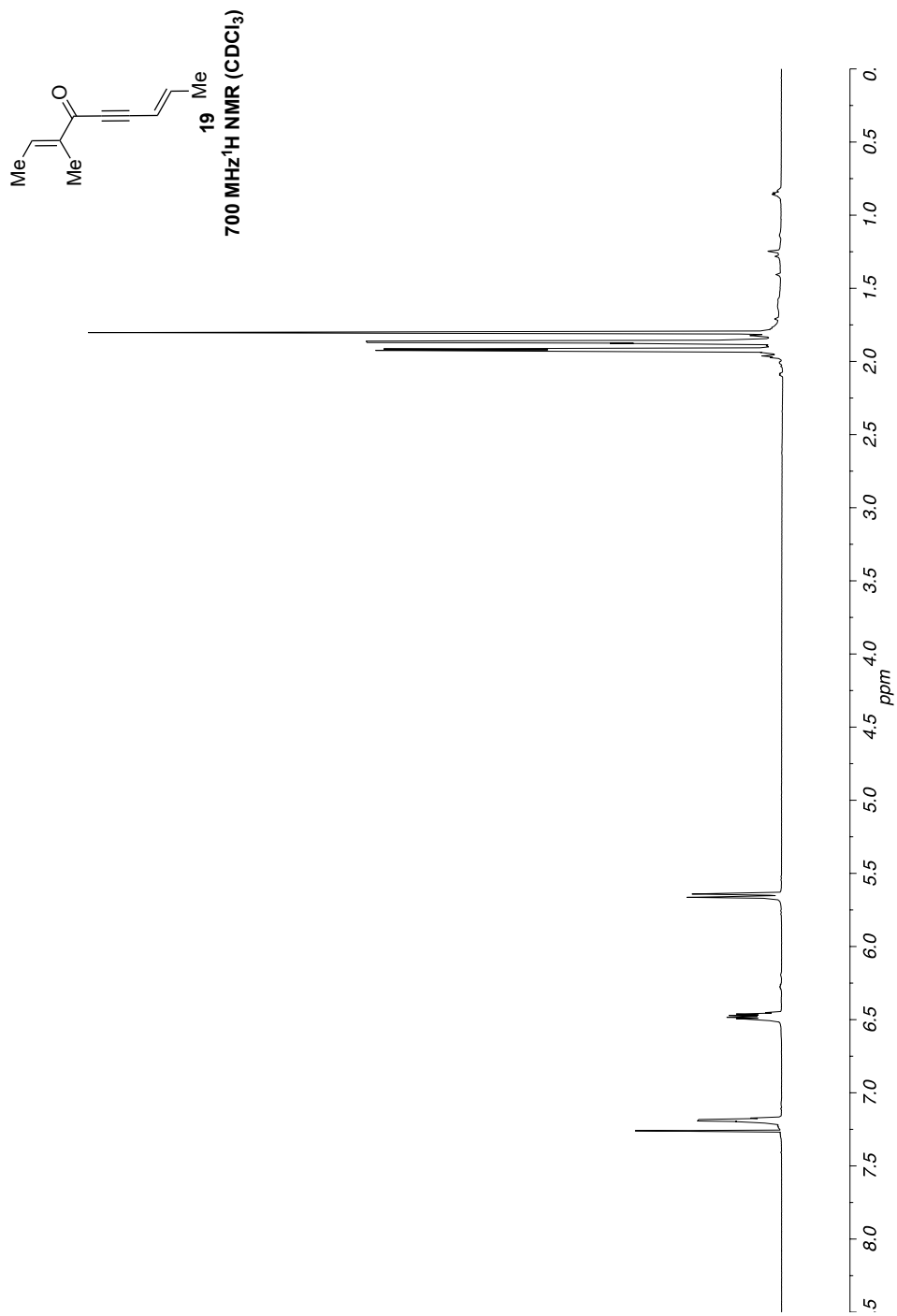


S60

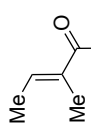




S62

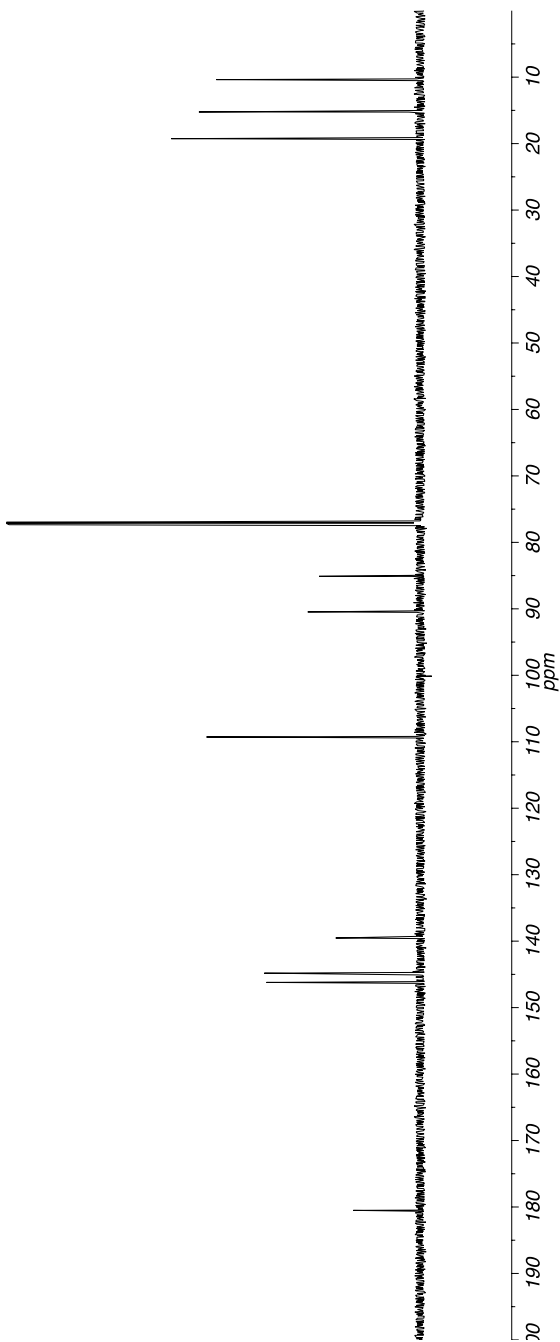


S63

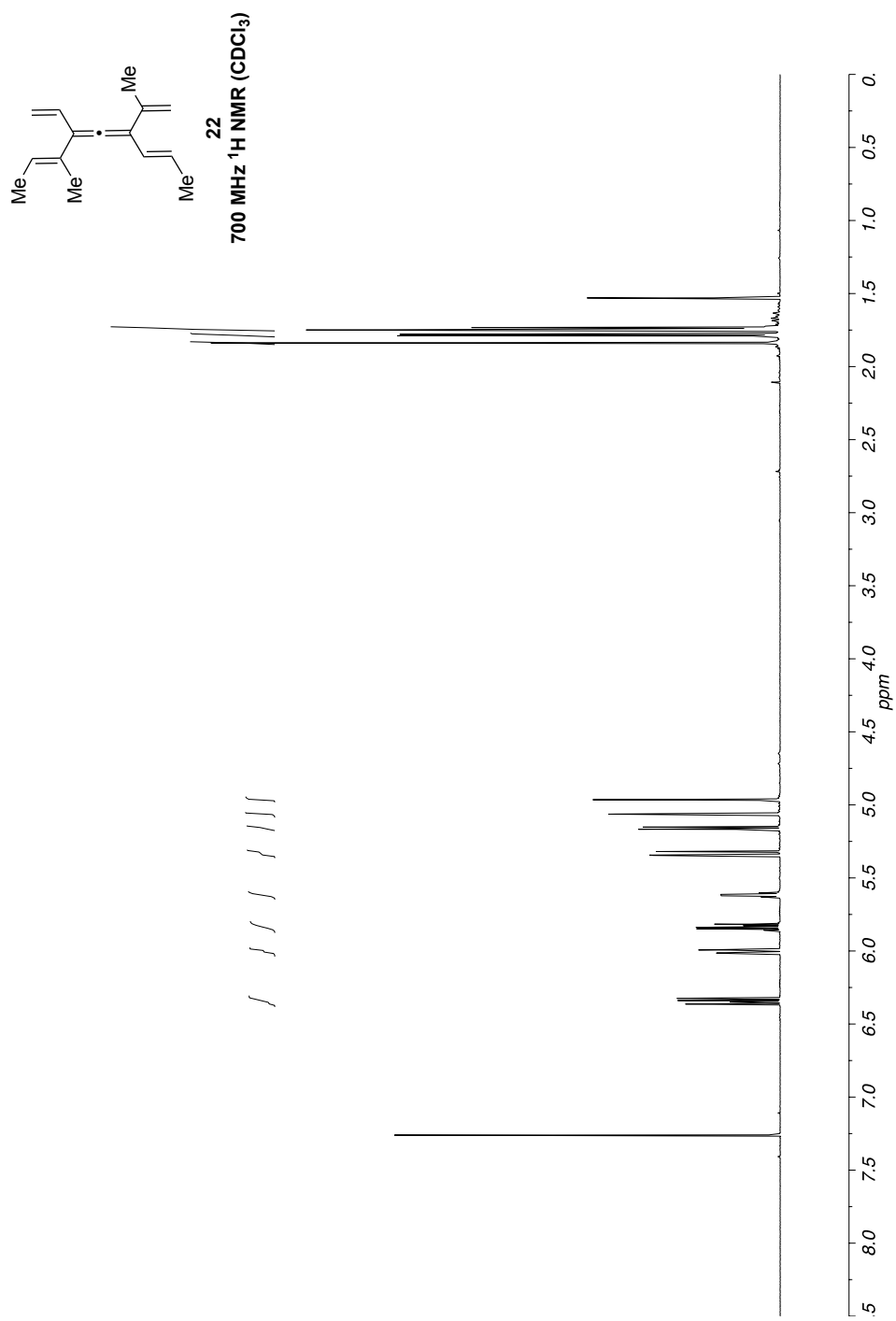


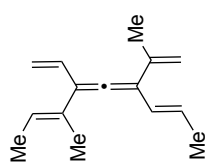
19 Me

175 MHz ¹³C NMR (CDCl₃)

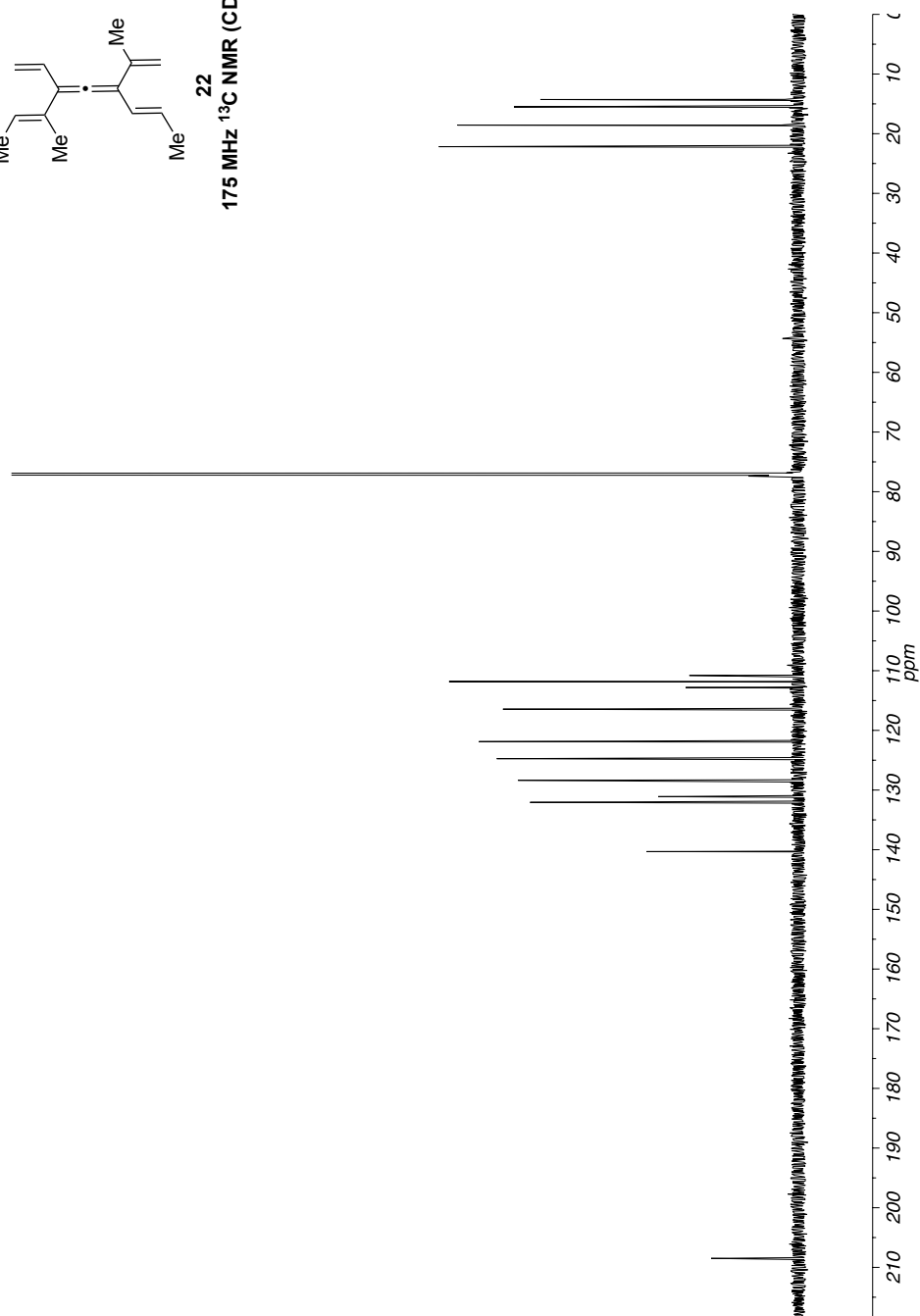


S64

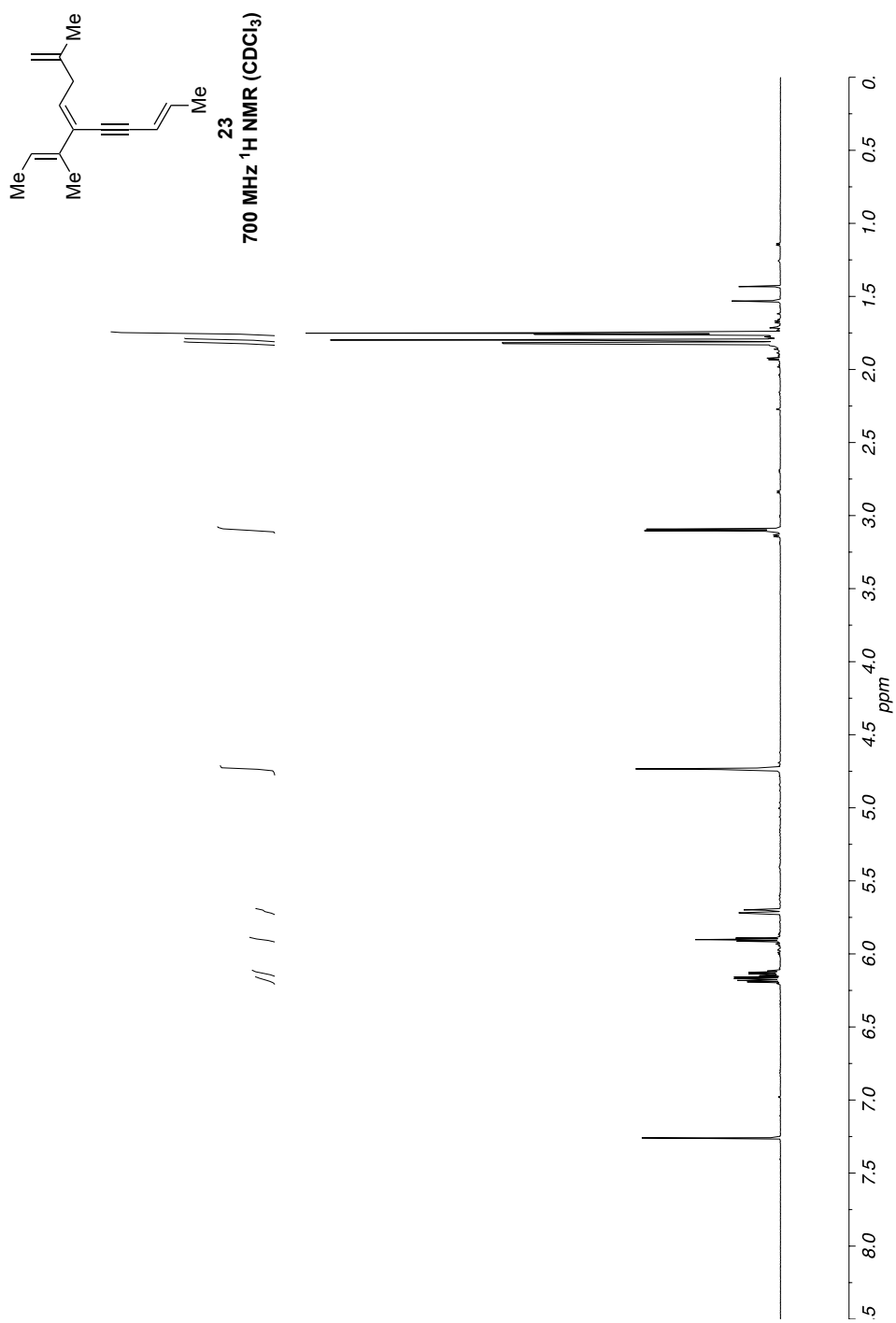


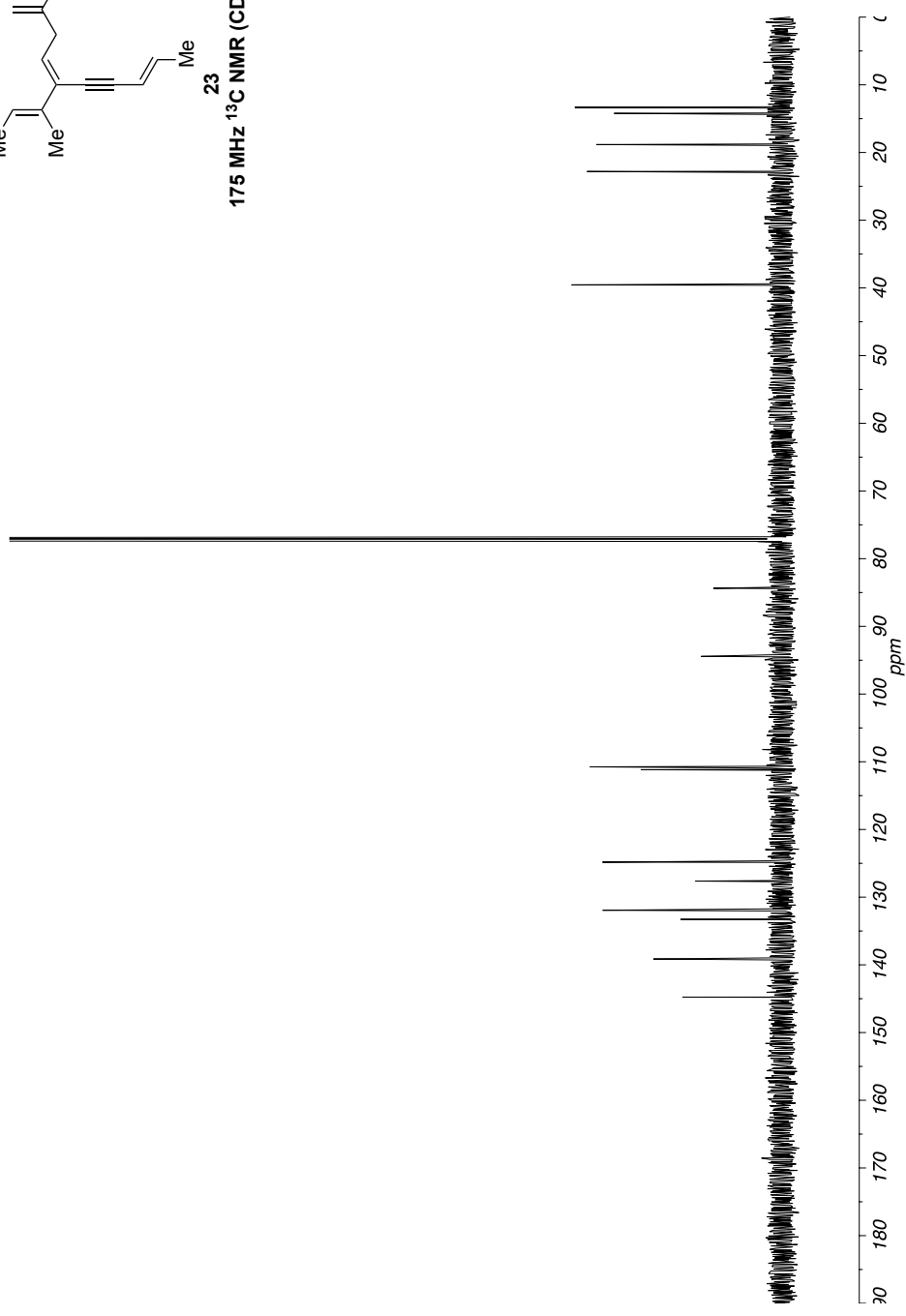
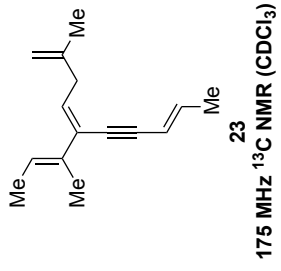


22
175 MHz ^{13}C NMR (CDCl_3)

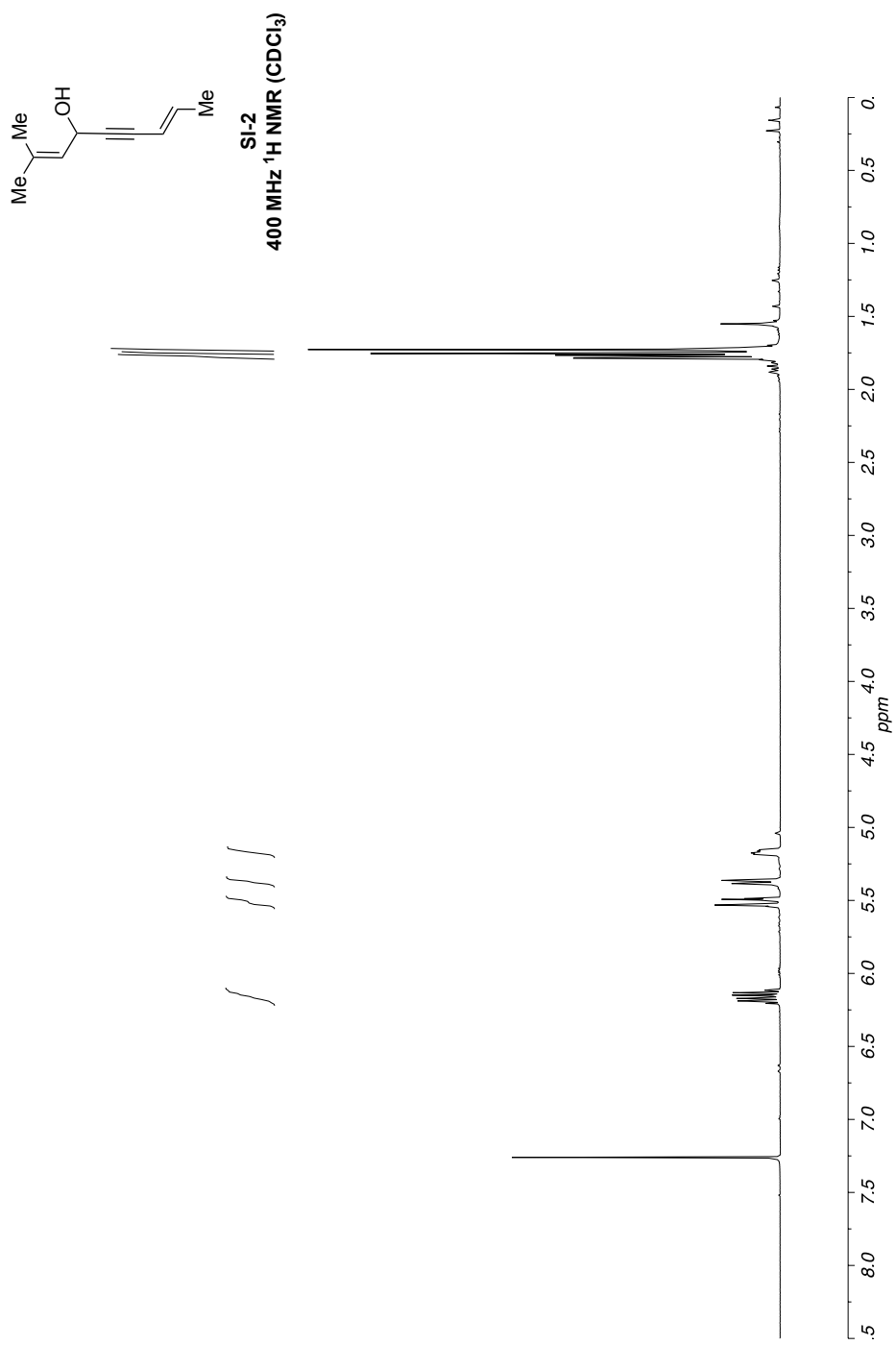


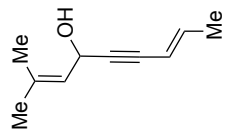
S68



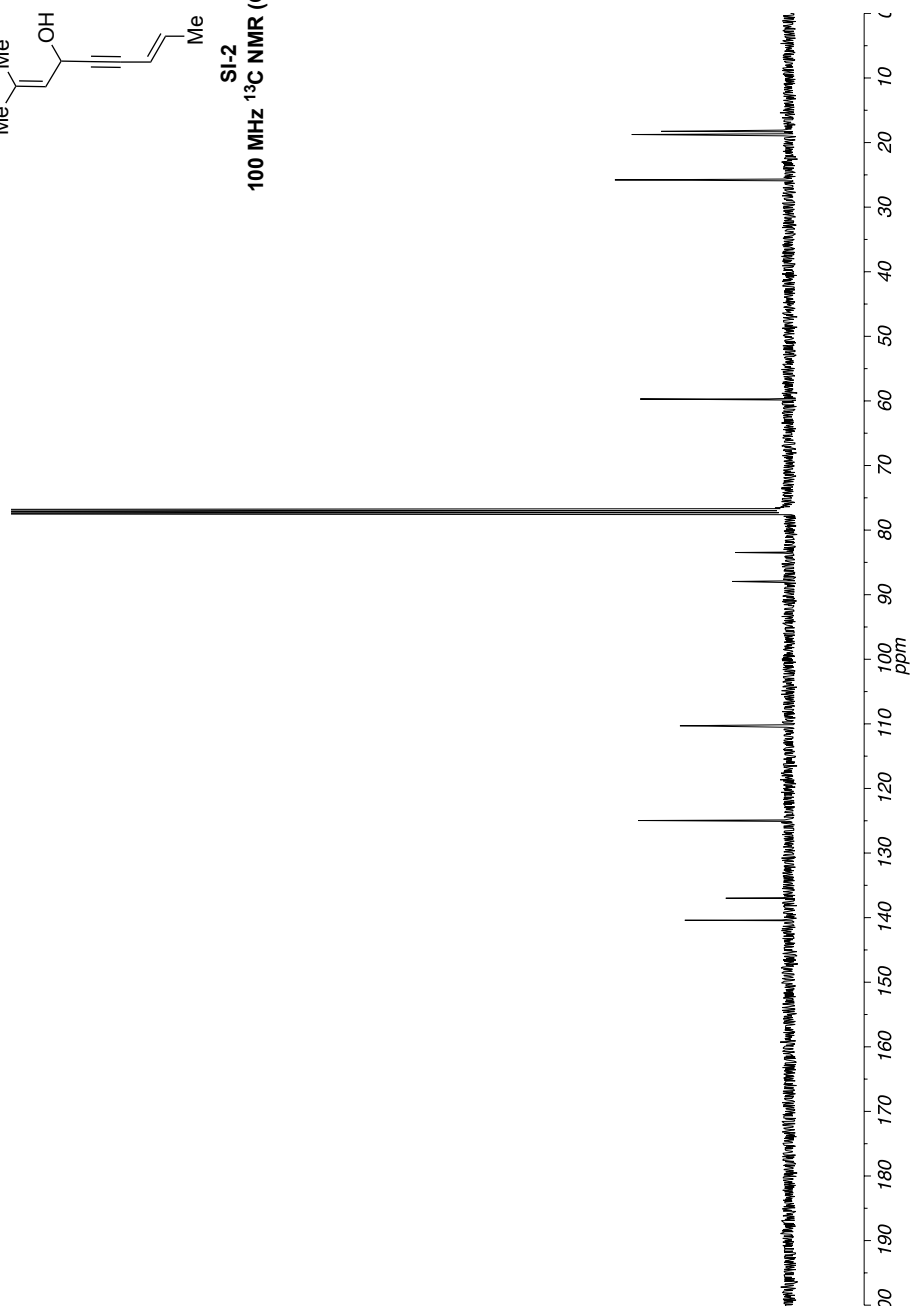


S70

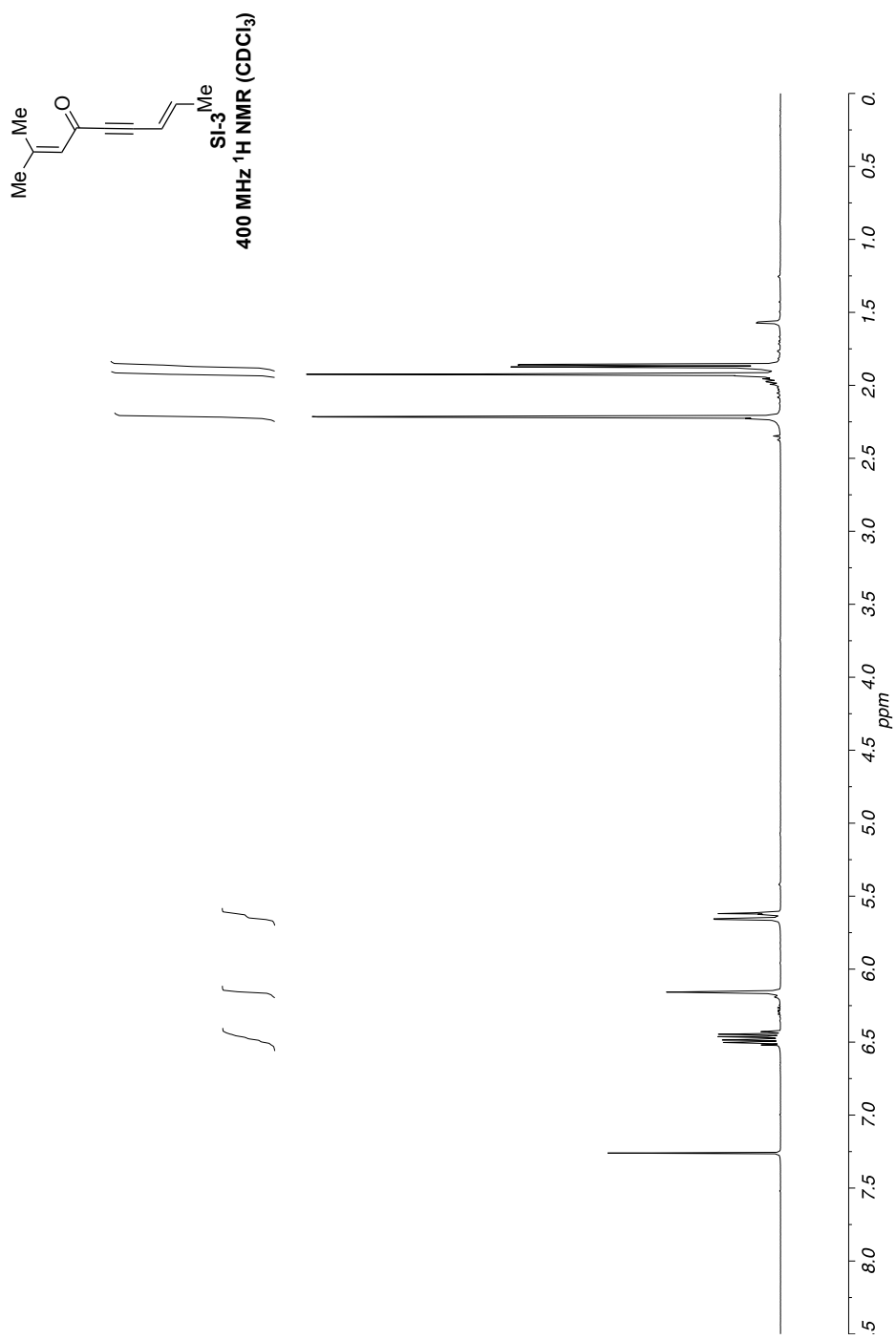


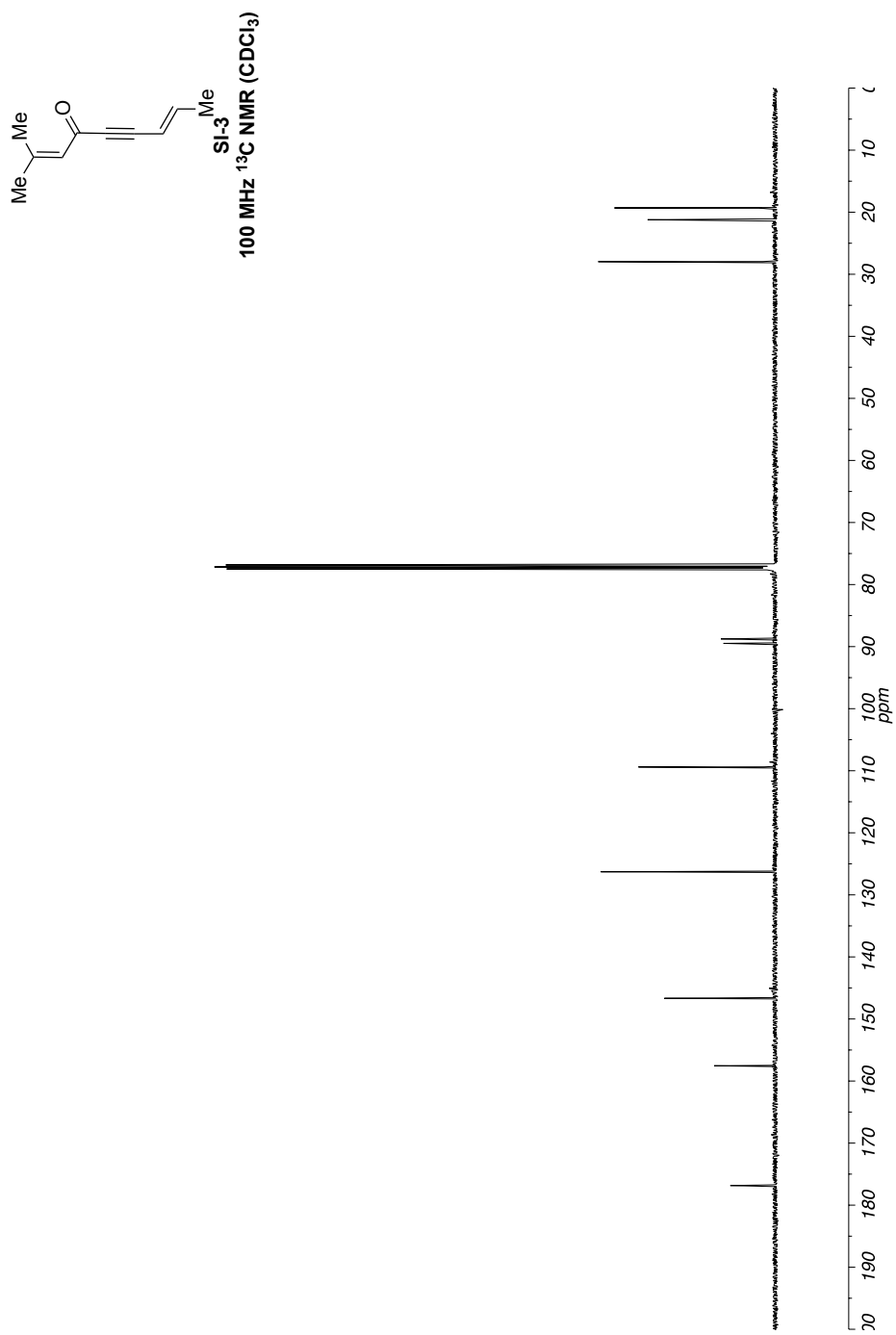


SI-2
100 MHz ^{13}C NMR (CDCl_3)

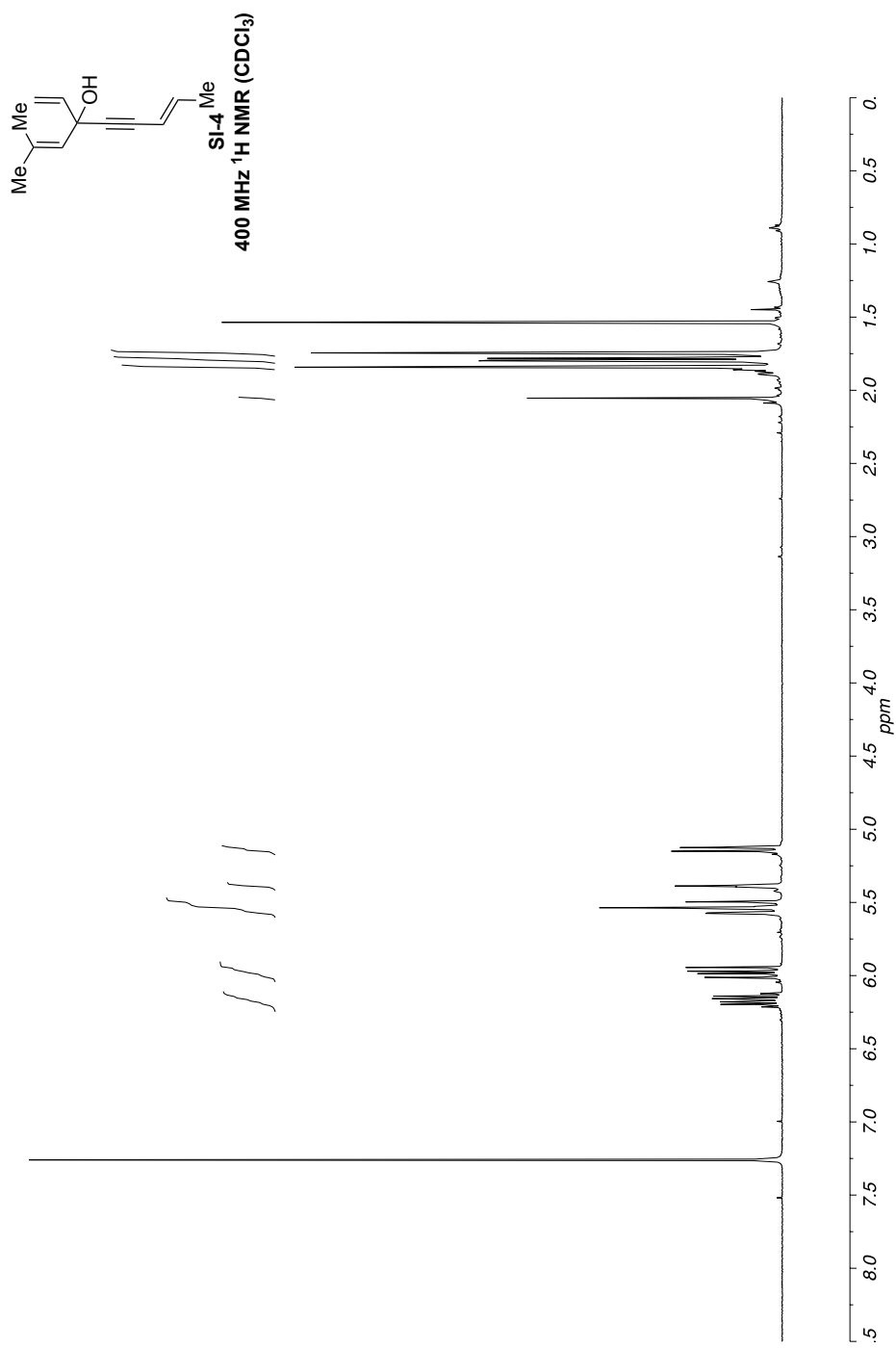


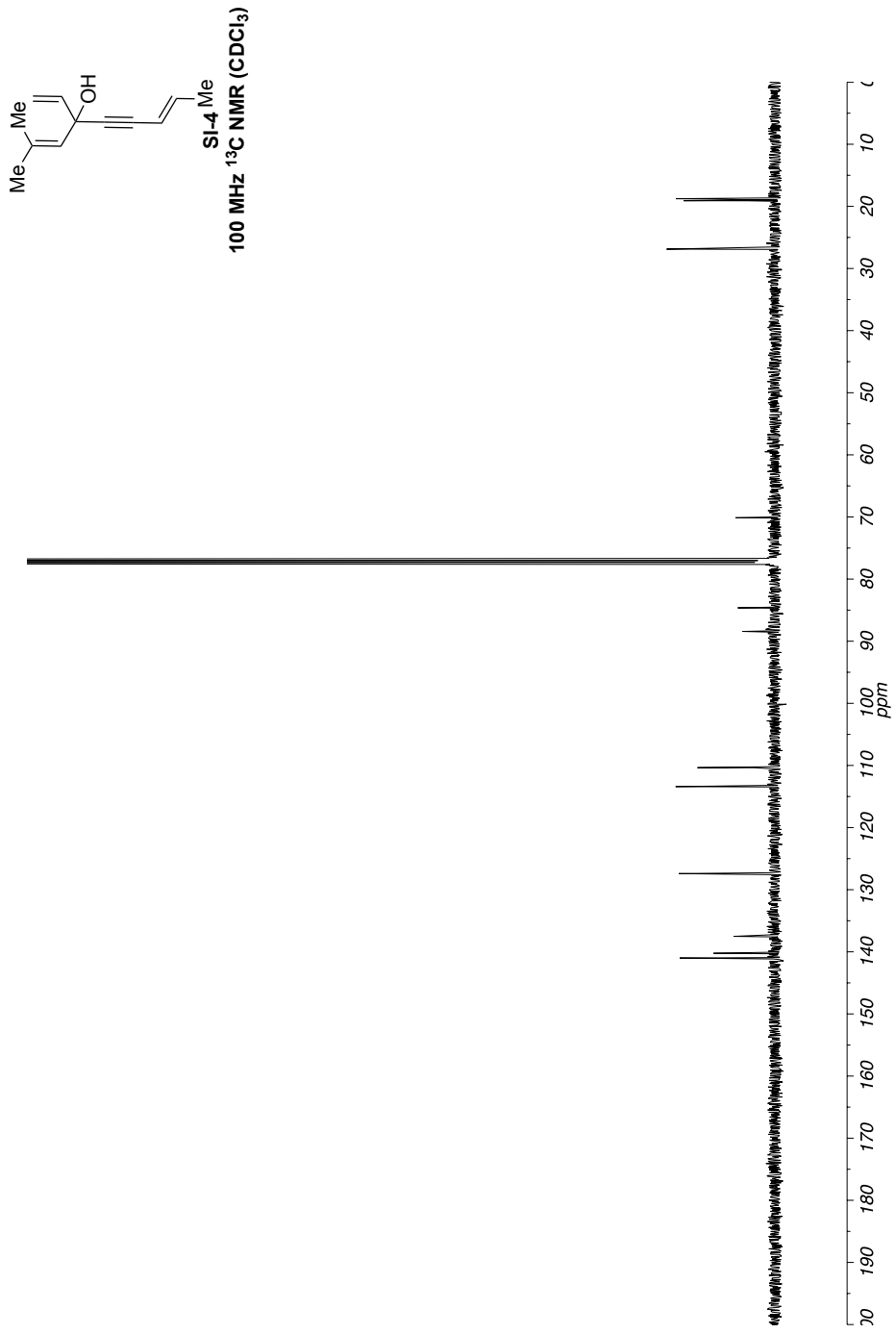
S72



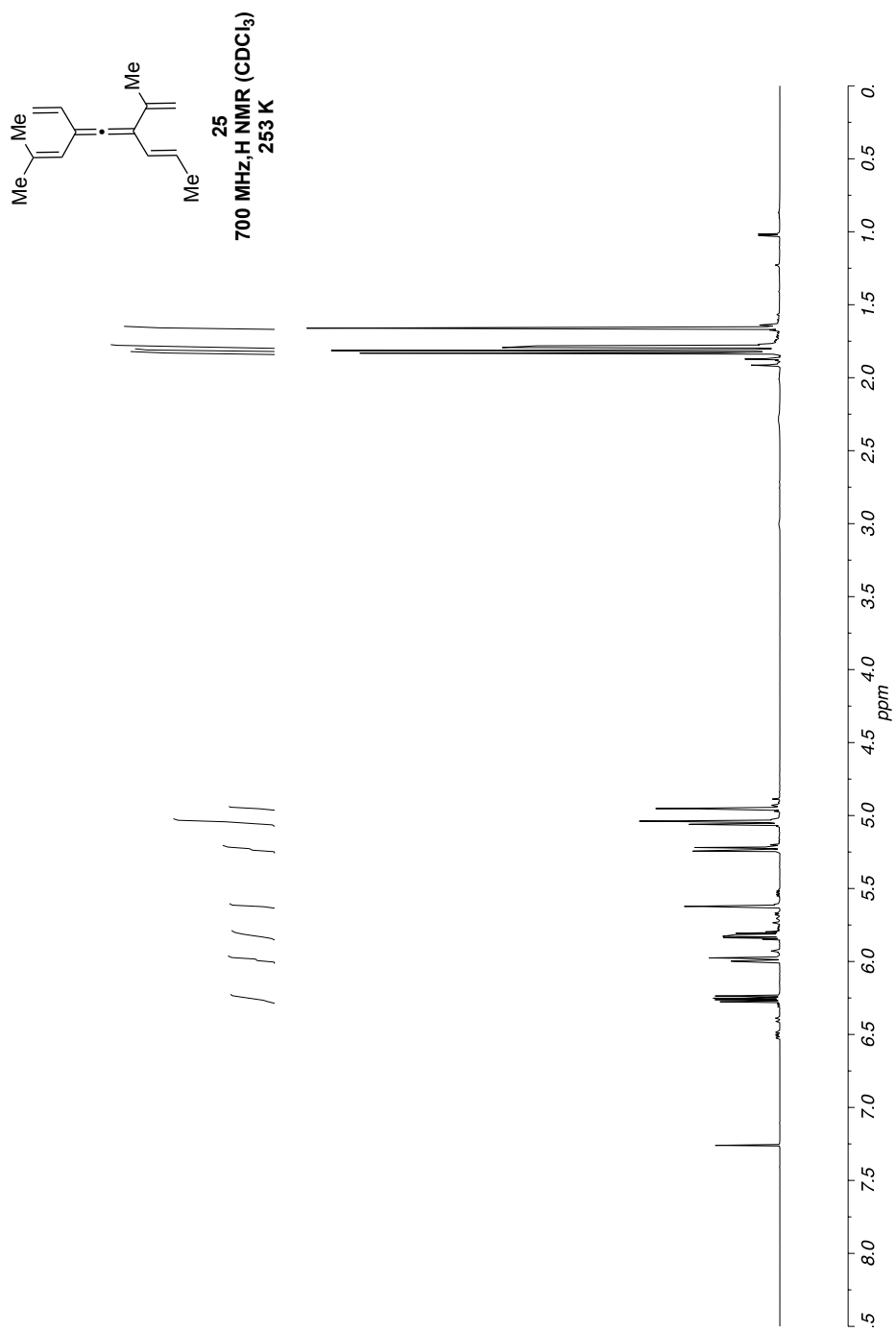


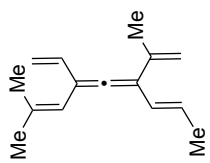
S74



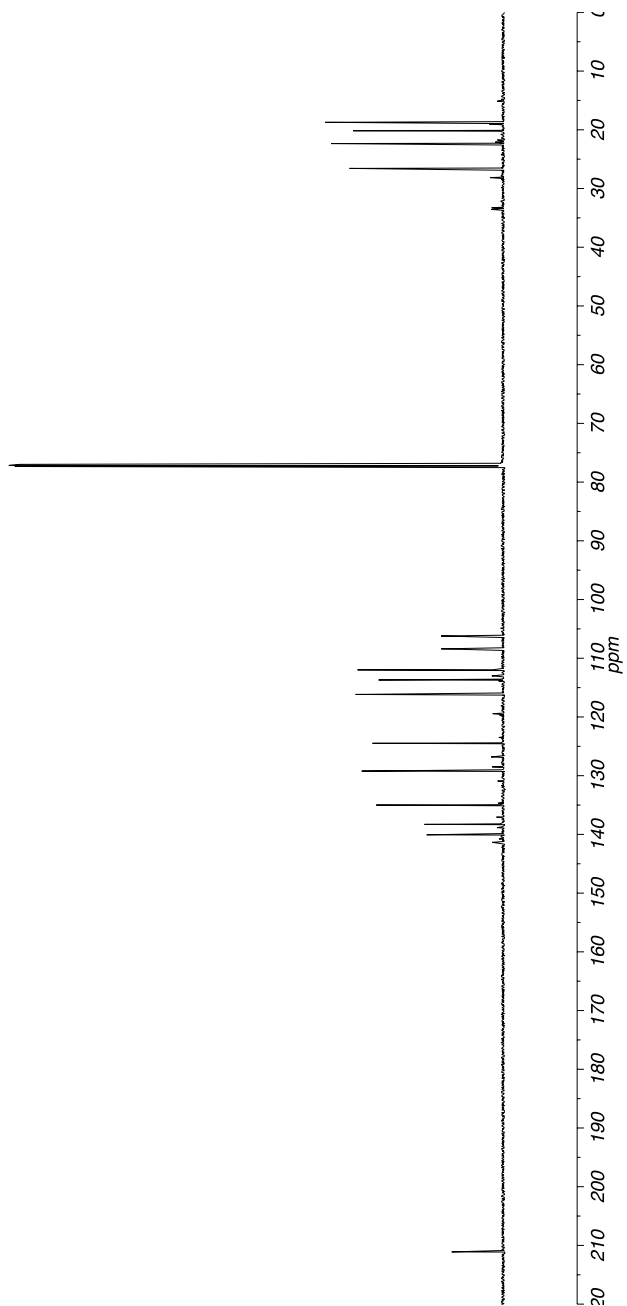


S76

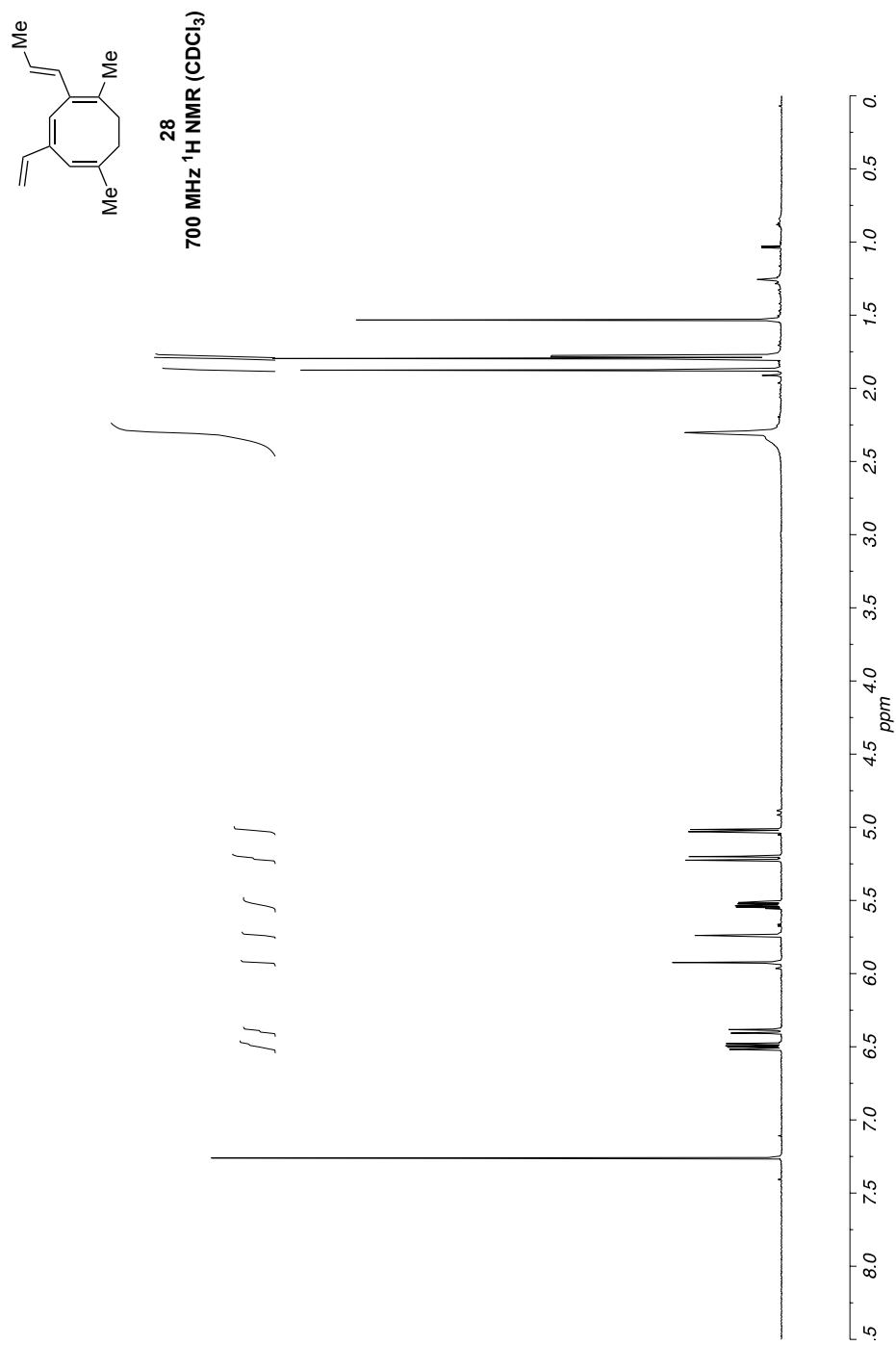


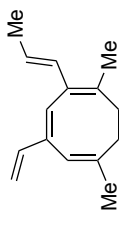


25
175 MHz ¹³C NMR (CDCl₃)
253 K

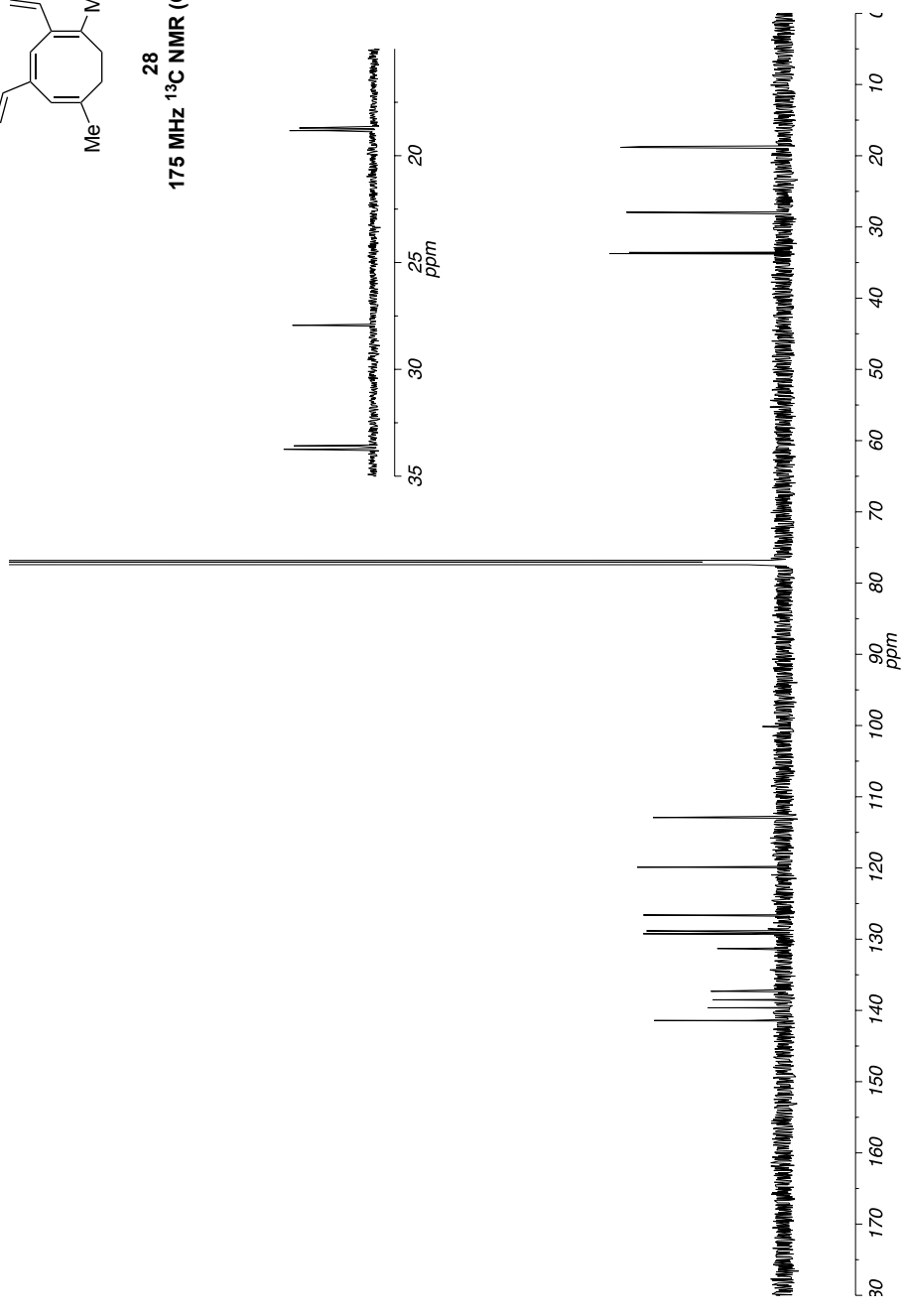


S78

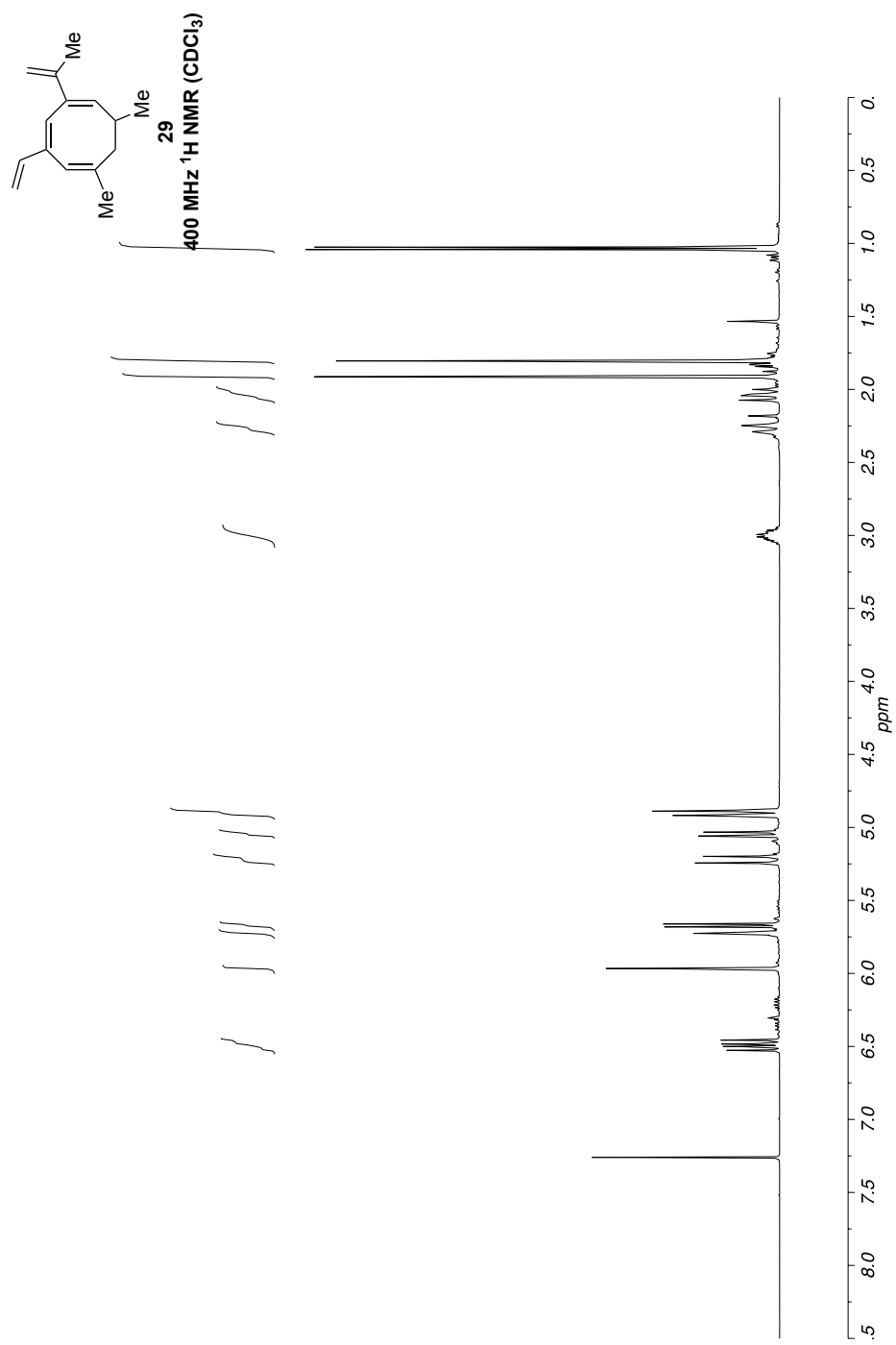


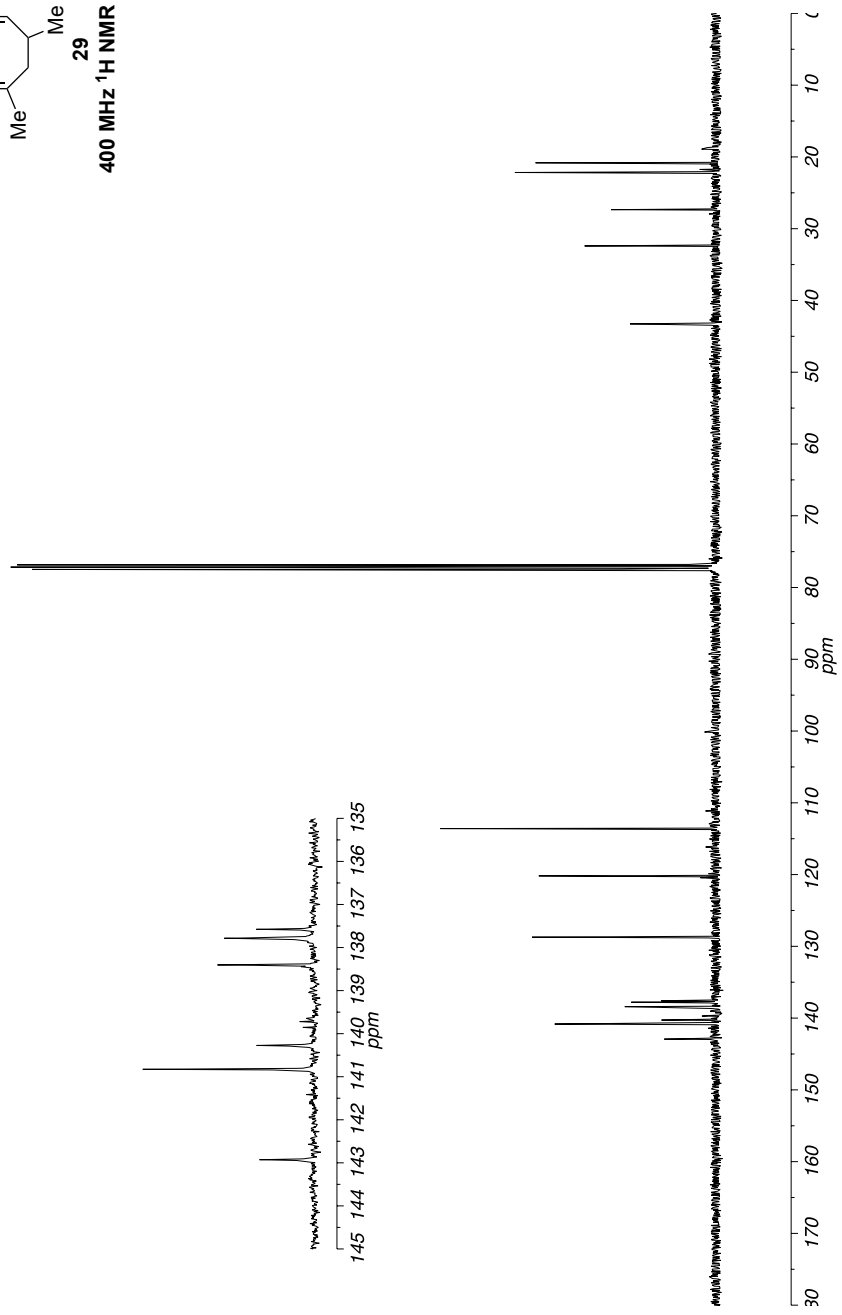
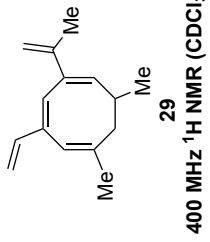


28
175 MHz ¹³C NMR (CDCl₃)

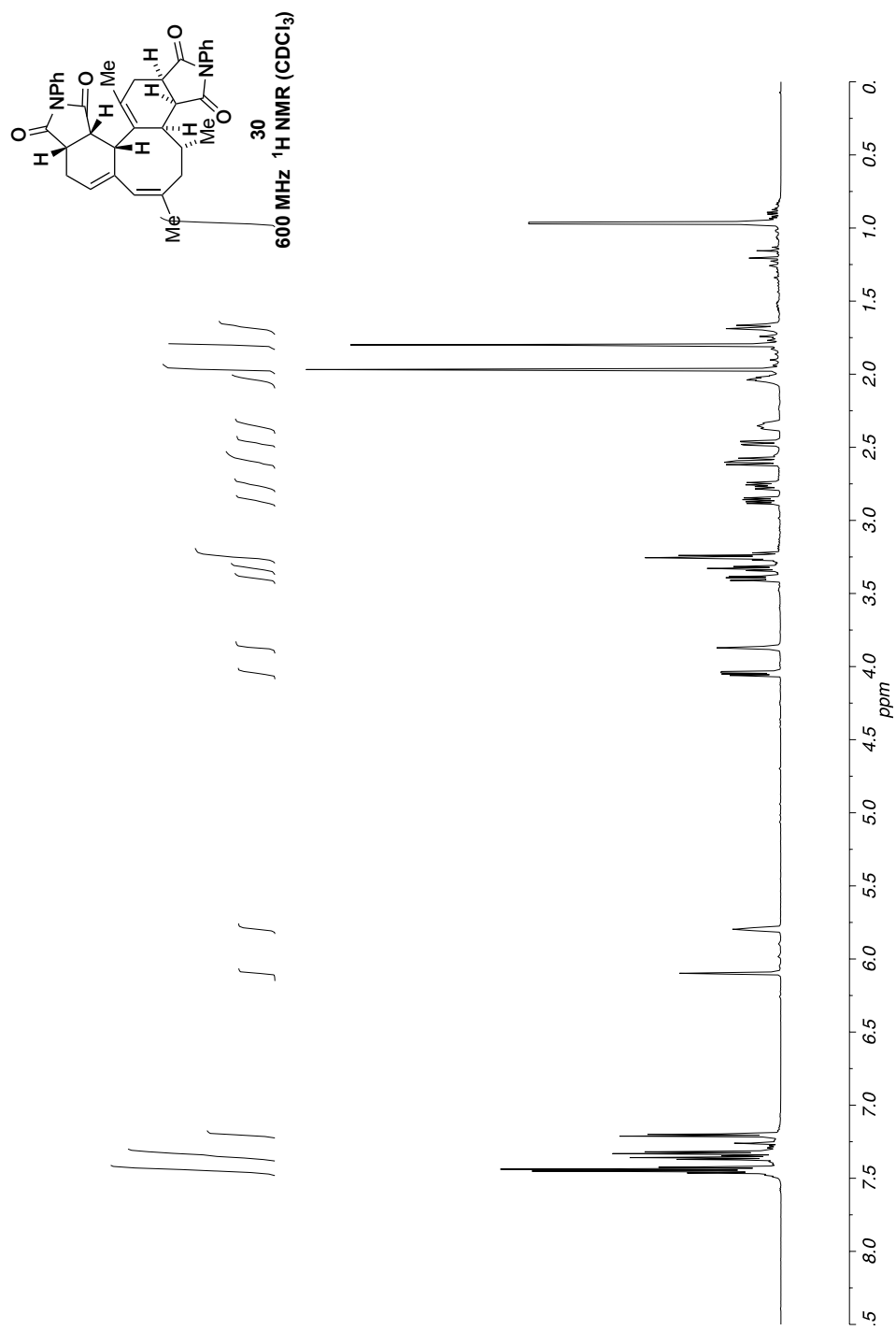


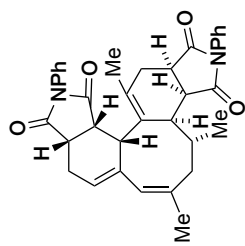
S80



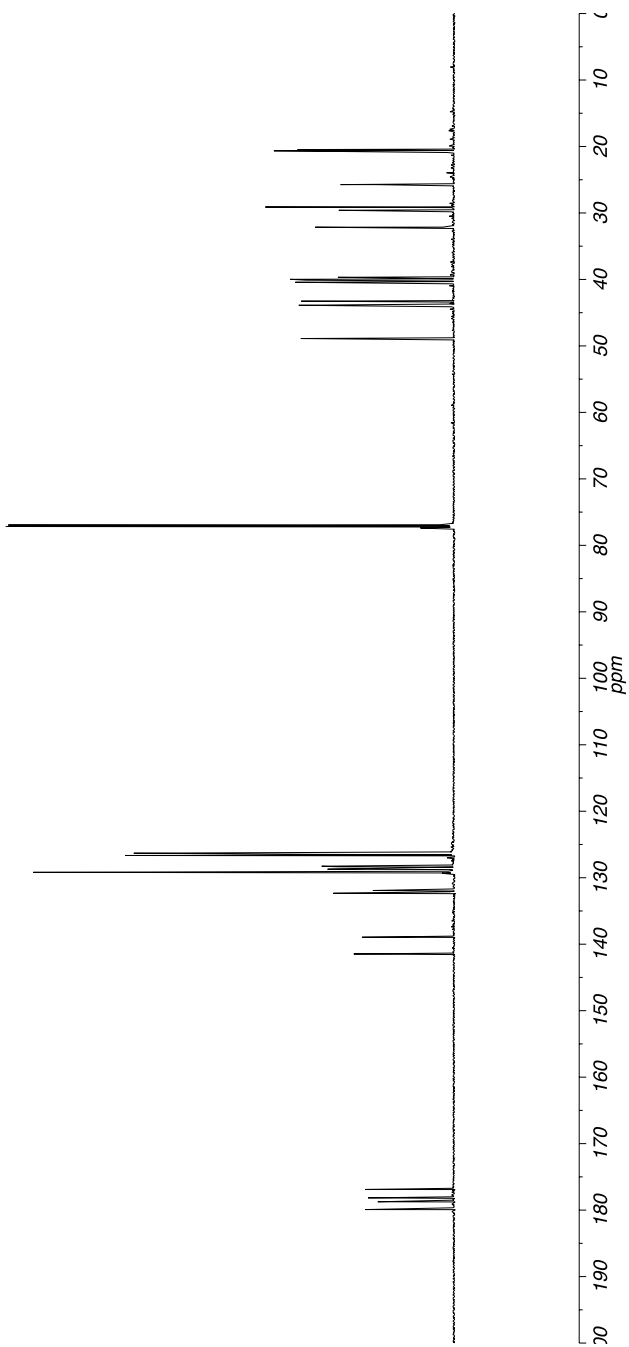


S82

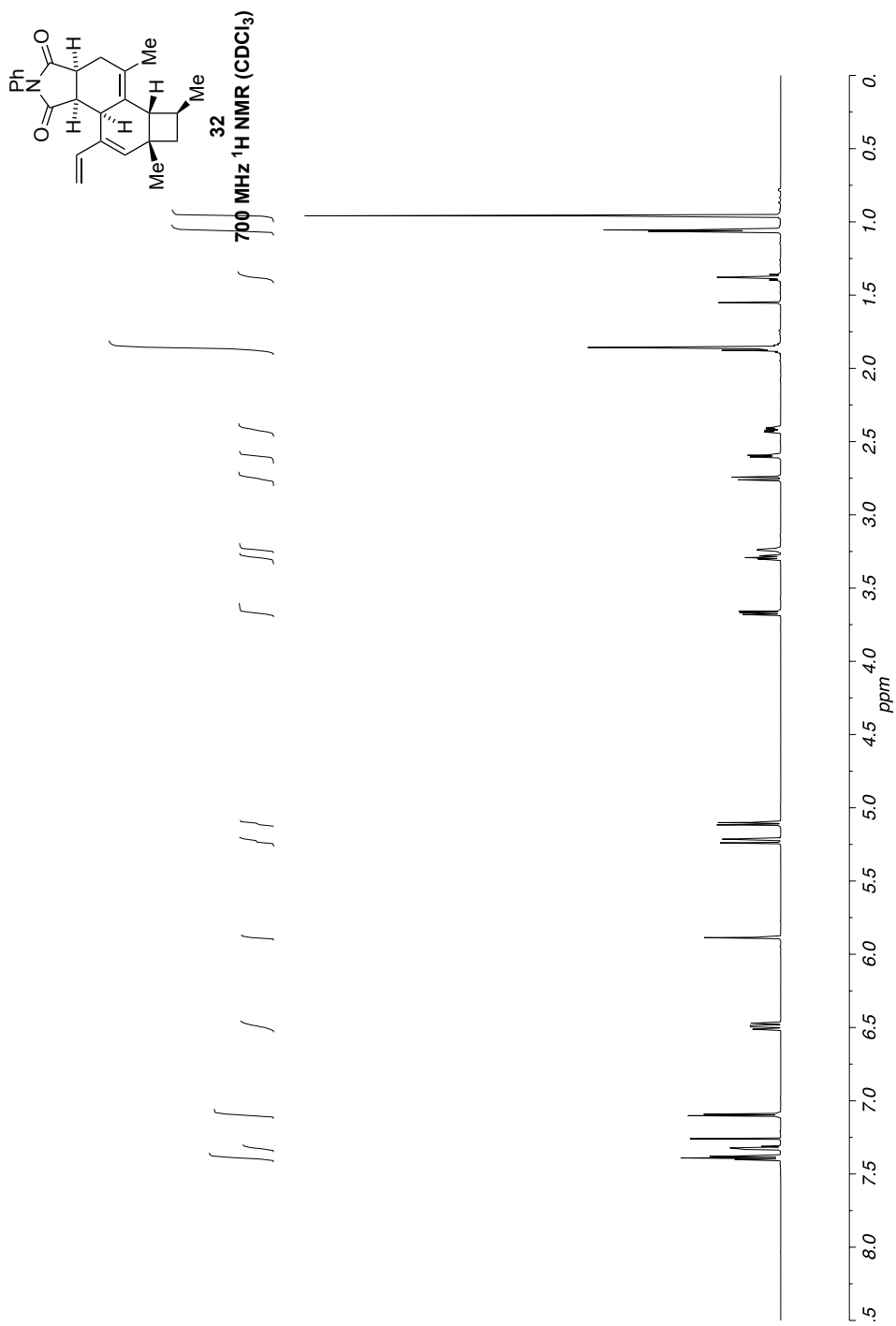


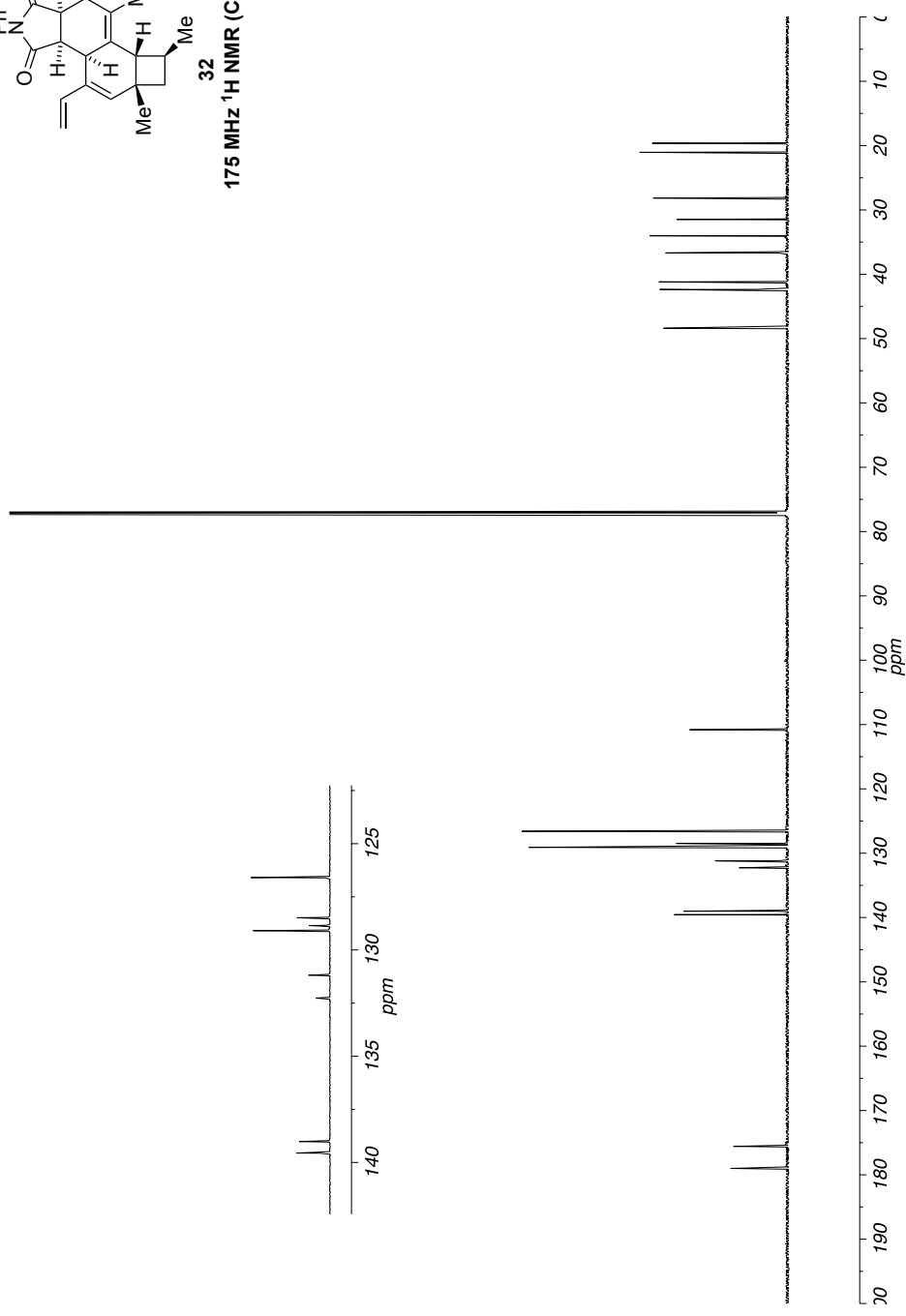
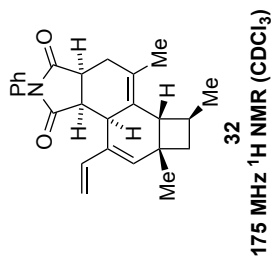


30
150 MHz ^{13}C NMR (CDCl_3)

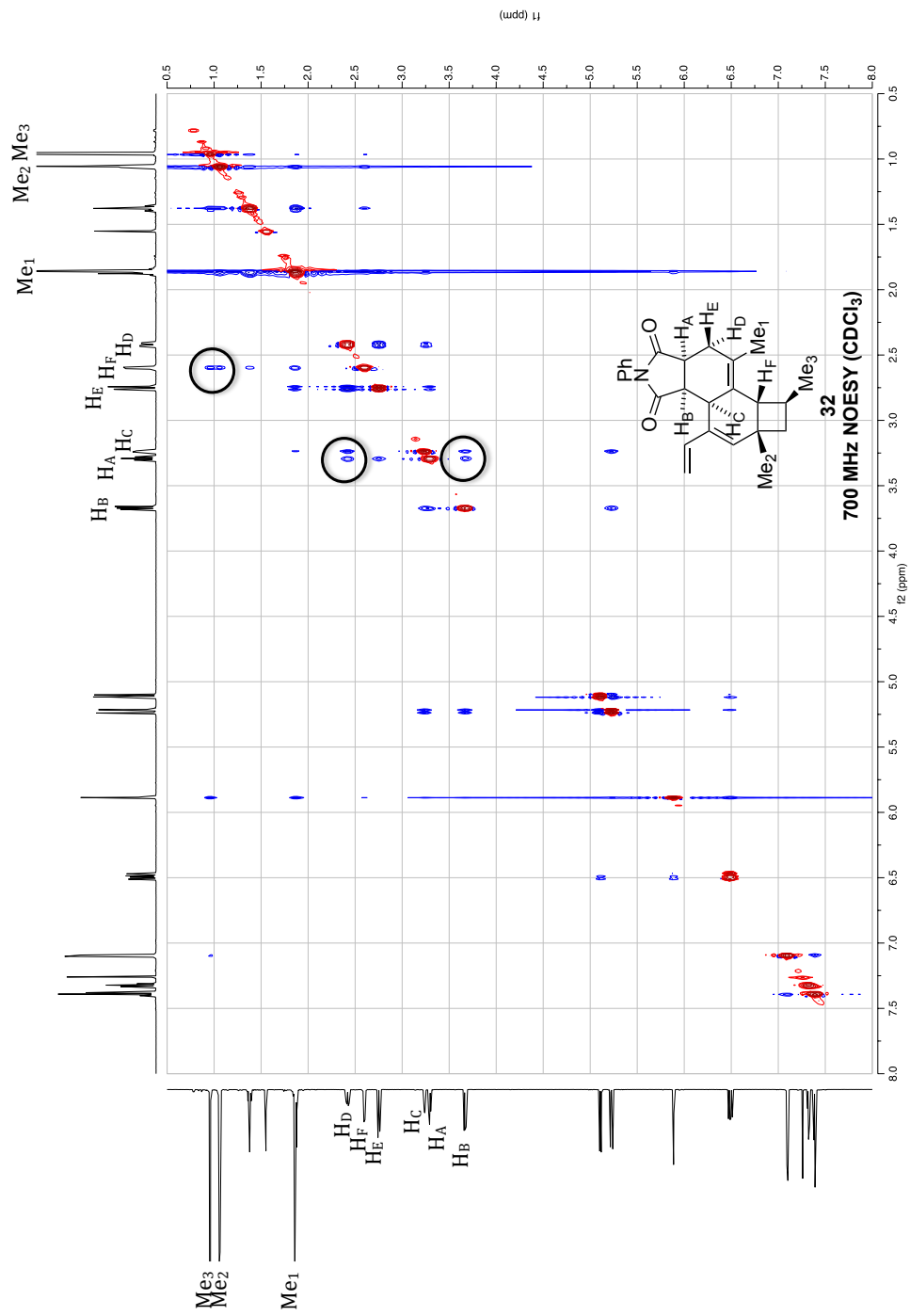


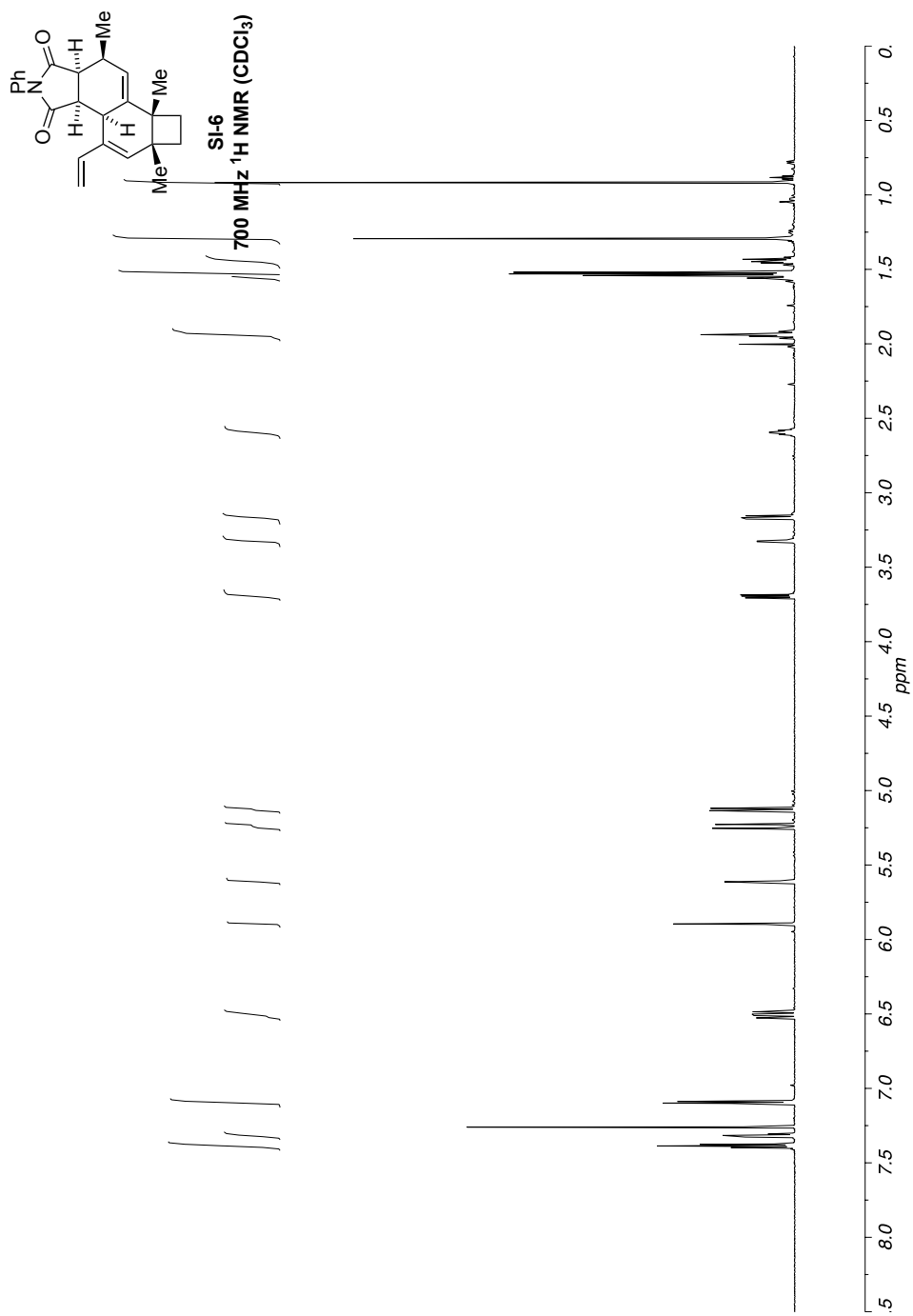
S84



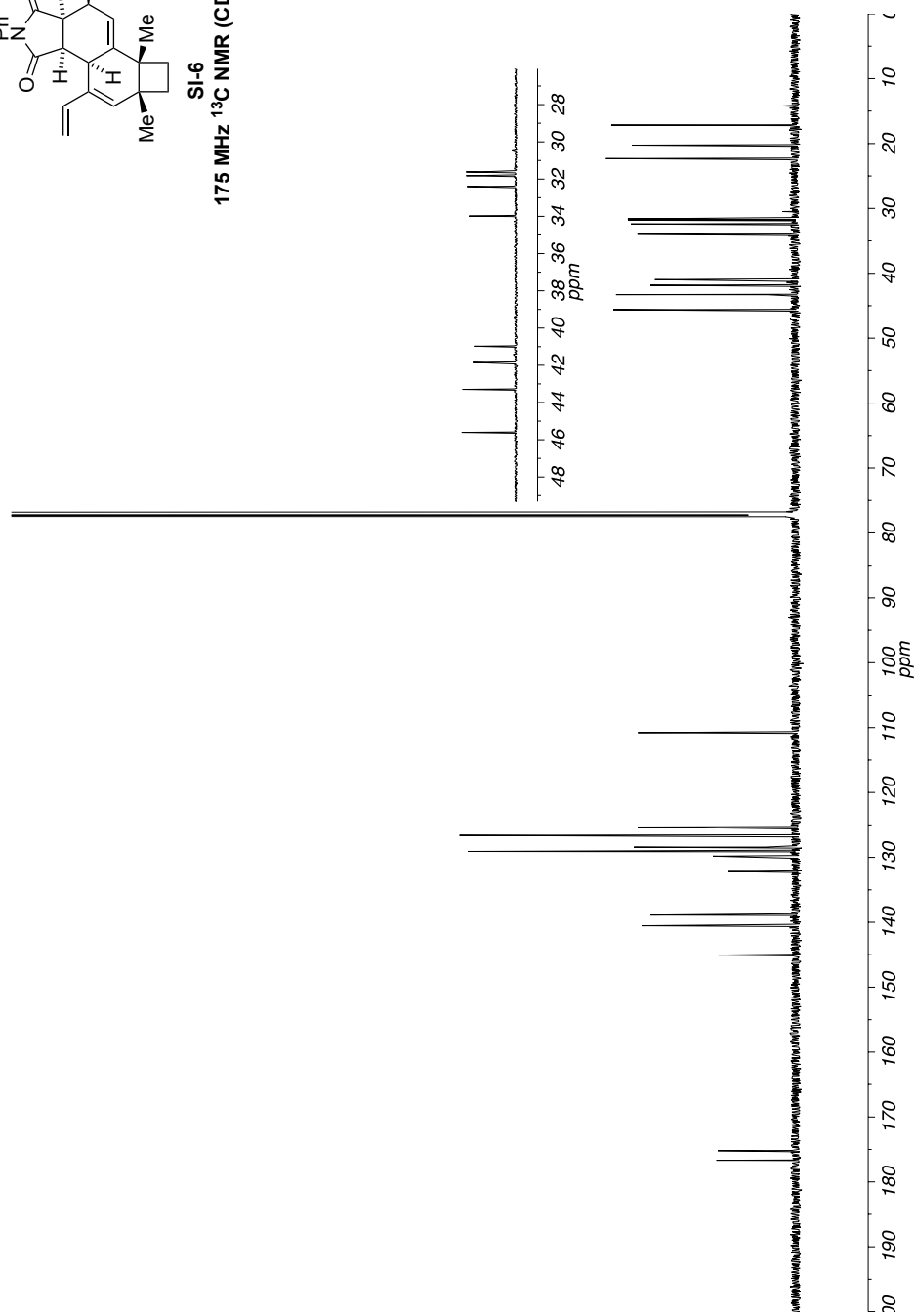
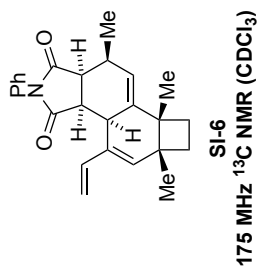


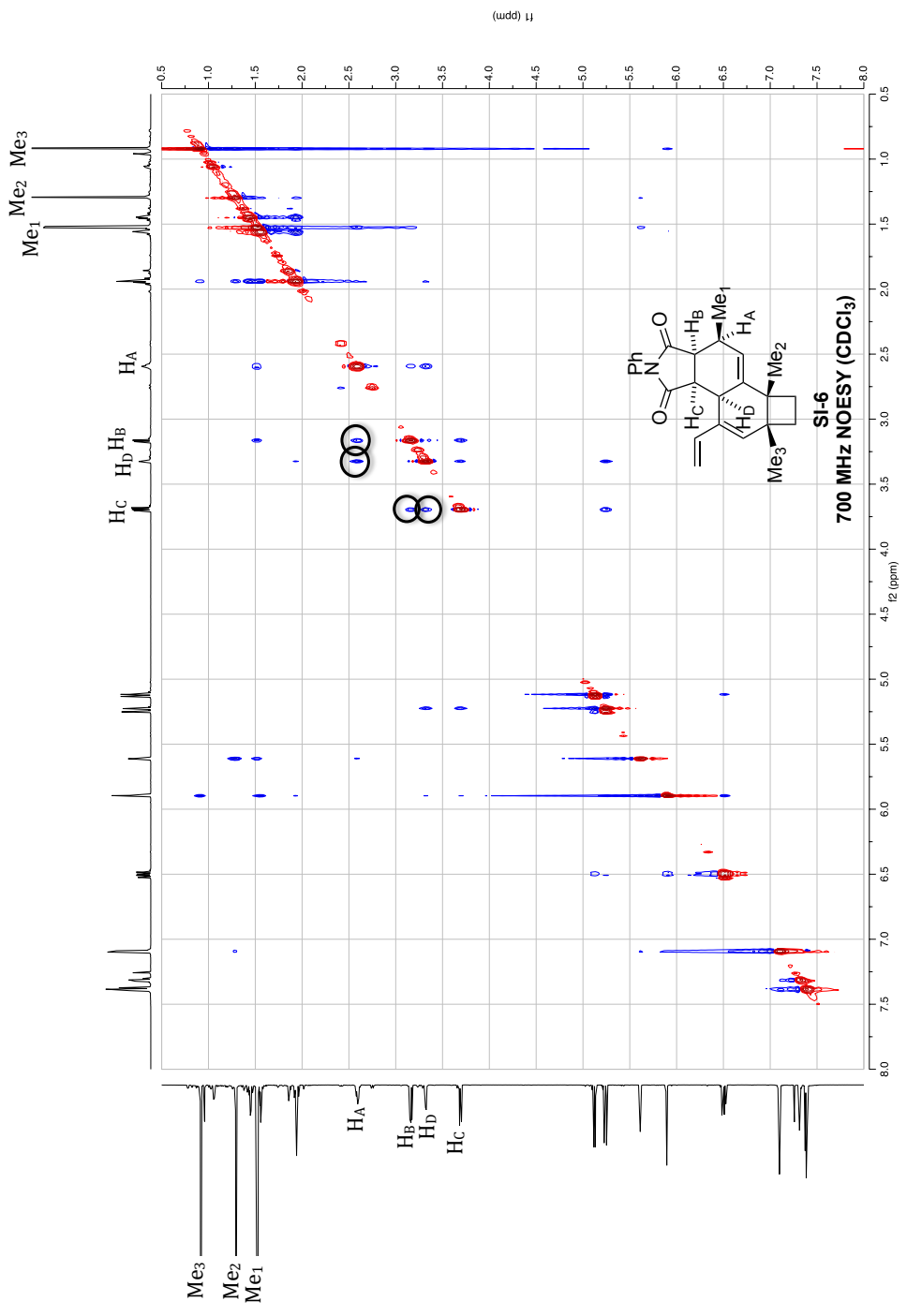
S86

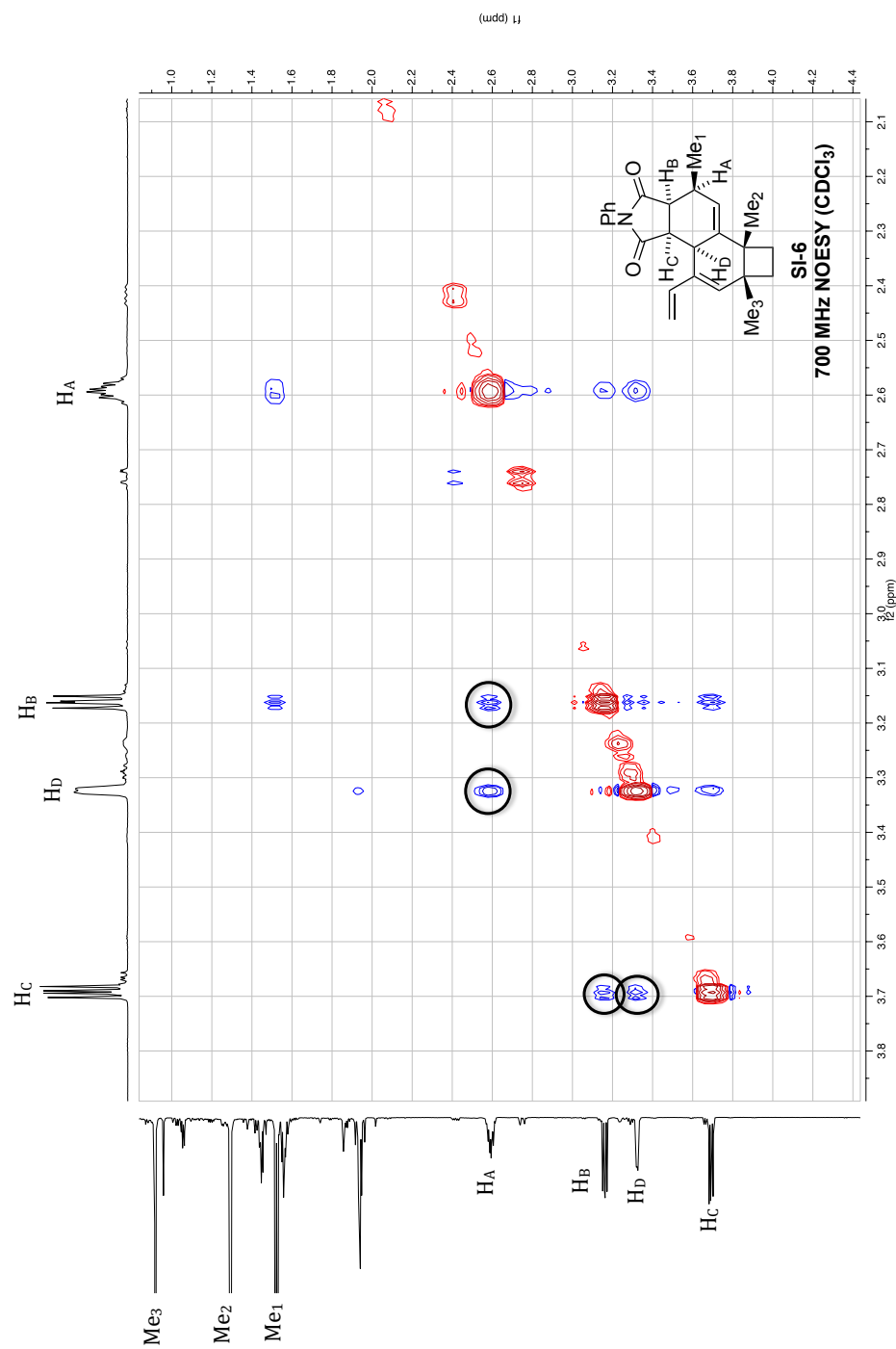


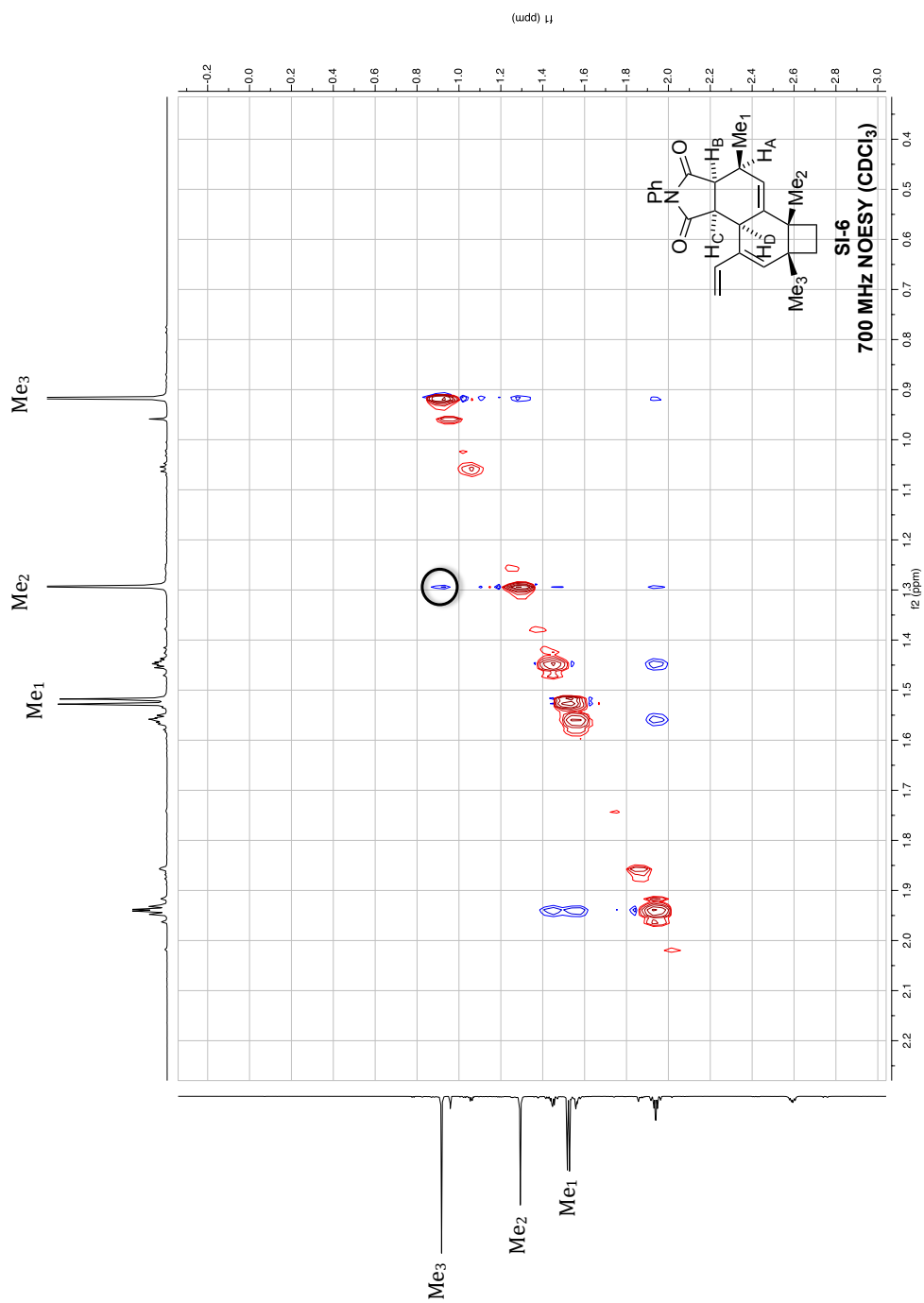


S88

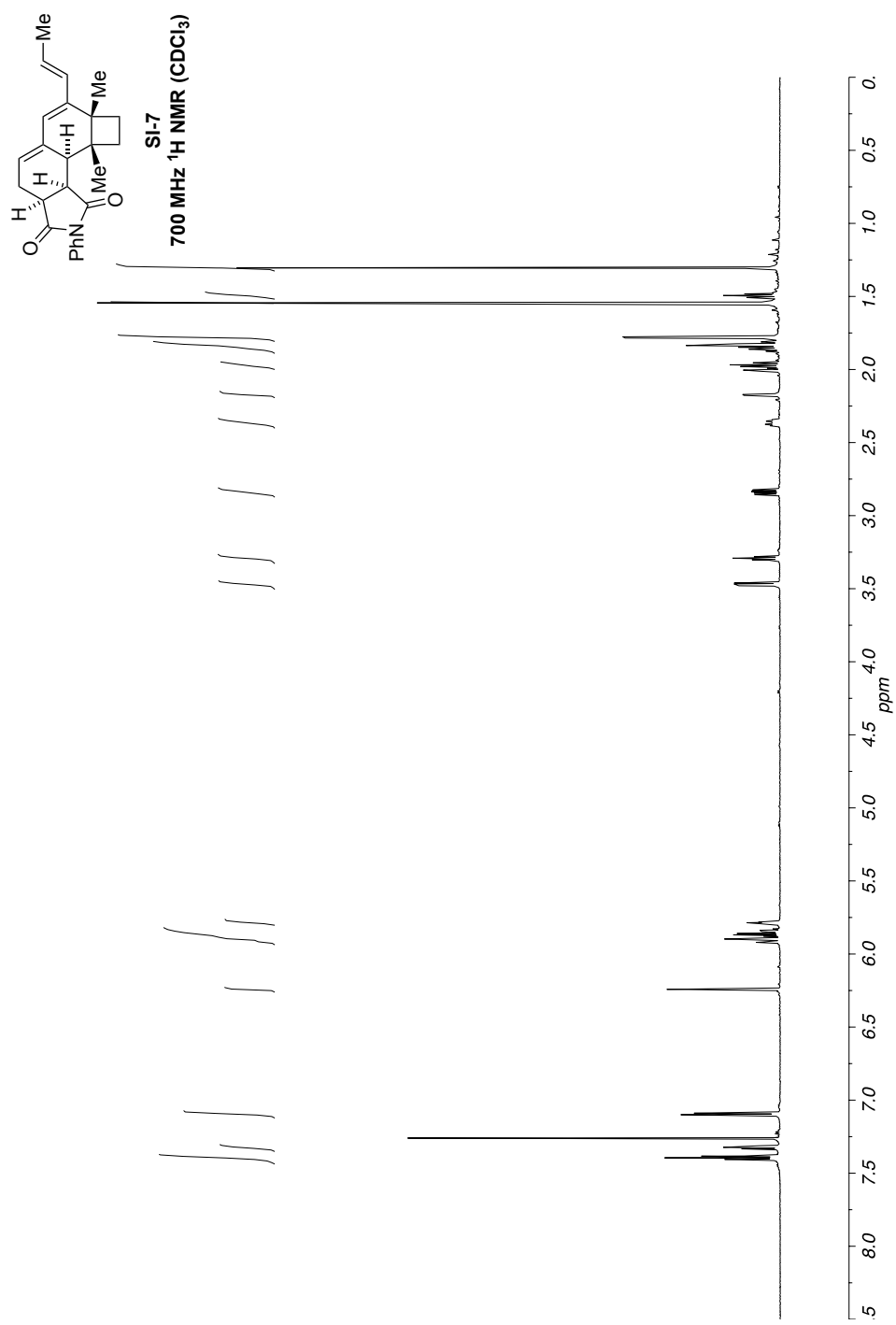


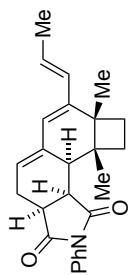




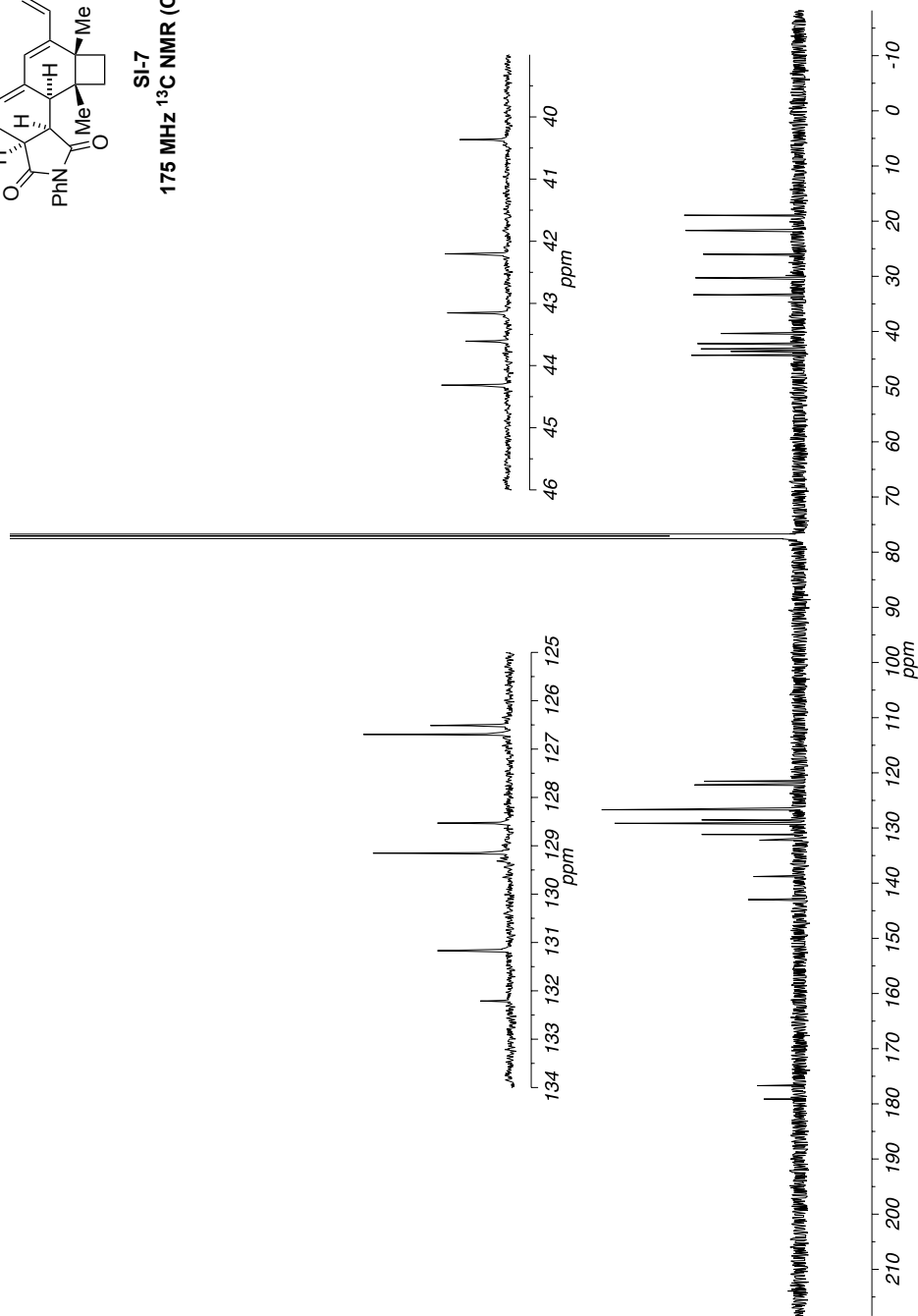


S92

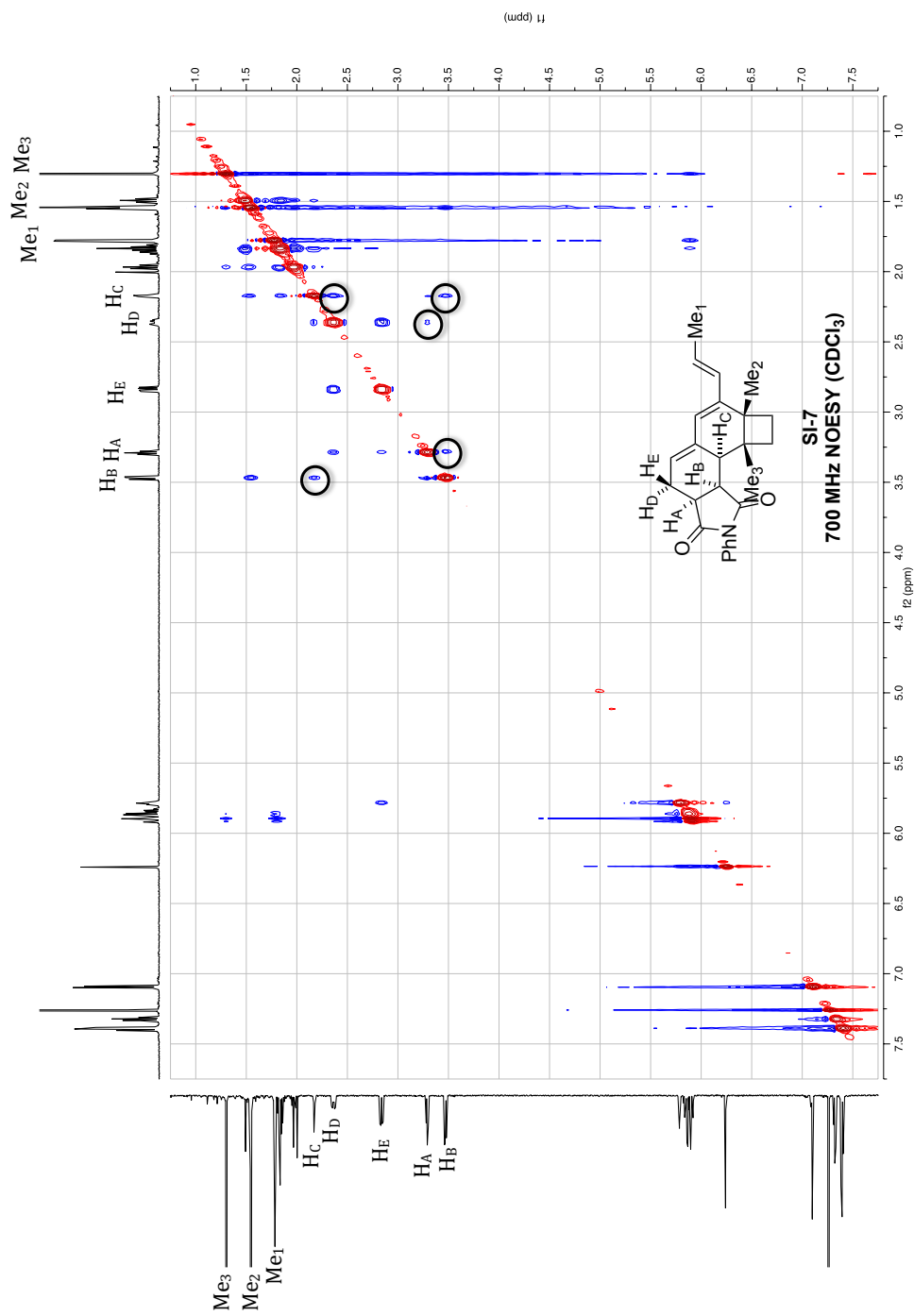


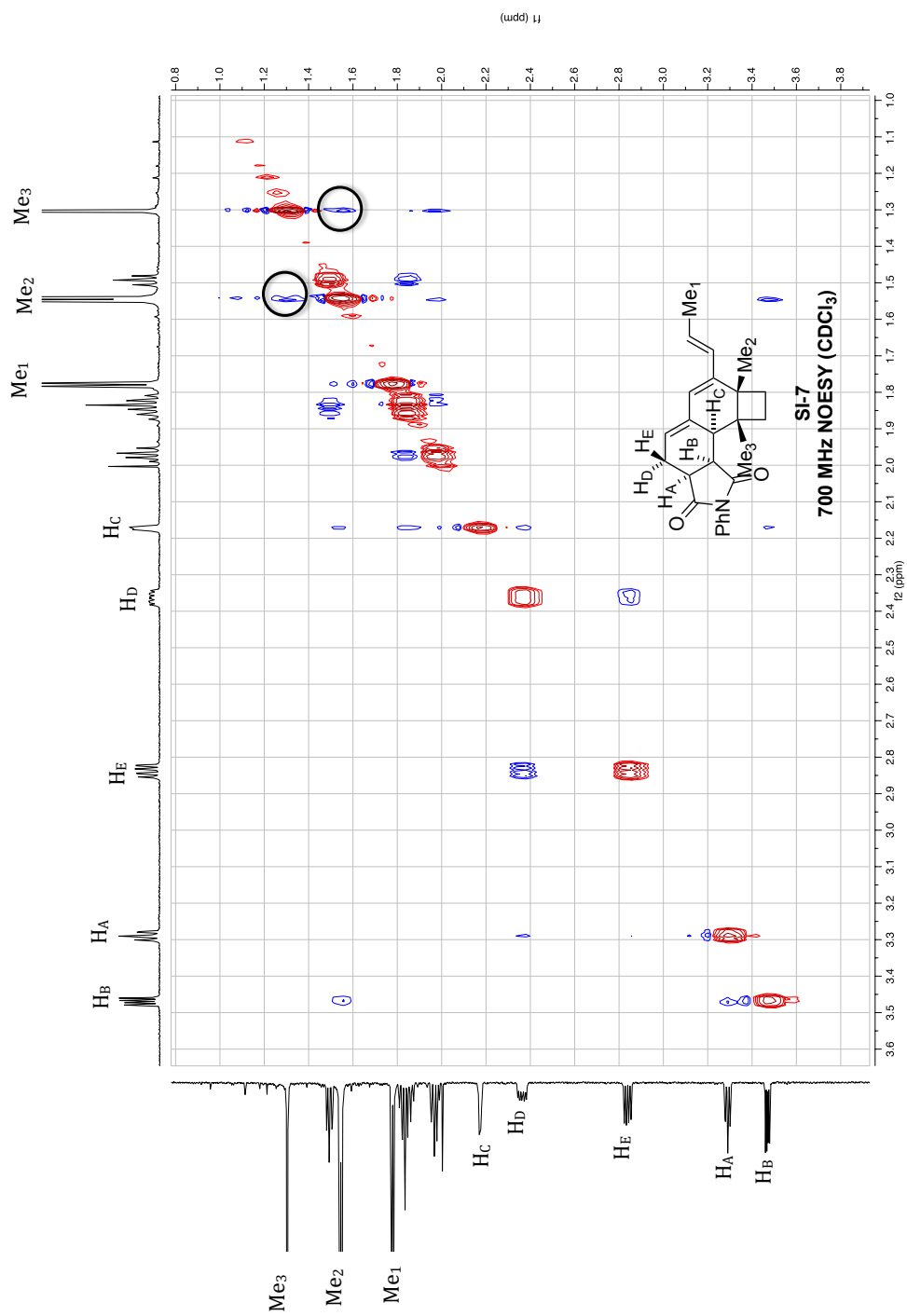


SI-7
 175 MHz ^{13}C NMR (CDCl_3)



S94





X-Ray Crystallographic Data

Note: The crystal structures of Diels-Alder adducts **15** and **37** were obtained from racemic samples.

Compound 15: $C_{41}H_{33}N_3O_6 \cdot CHCl_3 \cdot CH_4O$, $M = 815.11$, $T = 150$ K, triclinic, space group $P-1$ (No. 2), $Z = 2$, $a = 10.7743(5)$, $b = 11.9105(5)$, $c = 15.6870(8)$ Å, $\alpha = 103.916(4)$, $\beta = 100.650(4)$, $\gamma = 94.864(4)^\circ$, $V = 1902.62(16)$ Å³, $D_x = 1.423$ Mg m⁻³, 9342 unique data ($2\theta_{max} = 59.0^\circ$), 5758 with $I > 2\sigma(I)$; $R = 0.088$, $R_w = 0.243$, $S = 1.04$. CCDC 1889276.

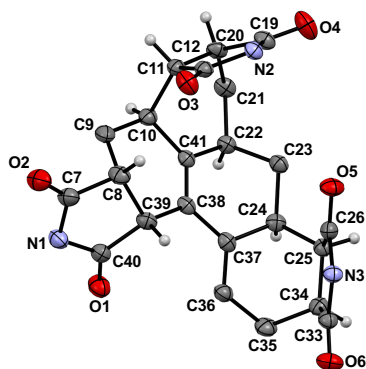


Figure S1. Anisotropic displacement ellipsoid plot of Diels-Alder adduct **15** (CCDC 1889276). Solvent molecules, N-phenyl substituents and selected hydrogen atoms omitted for clarity. Thermal ellipsoids exhibit 30% probability level. Hydrogen atoms drawn as circles with small radii.

Compound 37: $C_{35}H_{34}N_2O_4$, $M = 546.64$, $T = 150$ K, monoclinic, space group $P2_1/n$, $Z = 4$, $a = 15.1661(4)$, $b = 16.9456(4)$, $c = 15.8769(4)$ Å, $\beta = 105.849(3)^\circ$, $V = 3925.23(18)$ Å³, $D_x = 0.925$ Mg m⁻³, 7623 unique data ($2\theta_{\max} = 144.2^\circ$), 6160 with $I > 2\sigma(I)$; $R = 0.063$, $R_w = 0.181$, $S = 1.03$. CCDC 1889275.

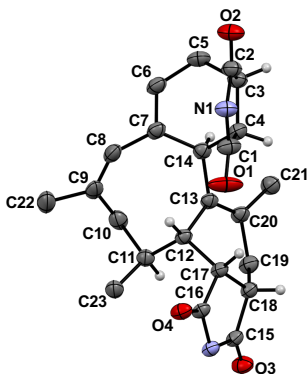


Figure S2. Anisotropic displacement ellipsoid plot of Diels-Alder adduct **37** (CCDC 1889275). Phenyl substituents and selected hydrogen atoms omitted for clarity. Thermal ellipsoids exhibit 30% probability level. Hydrogen atoms drawn as circles with small radii.

UV-Vis comparison

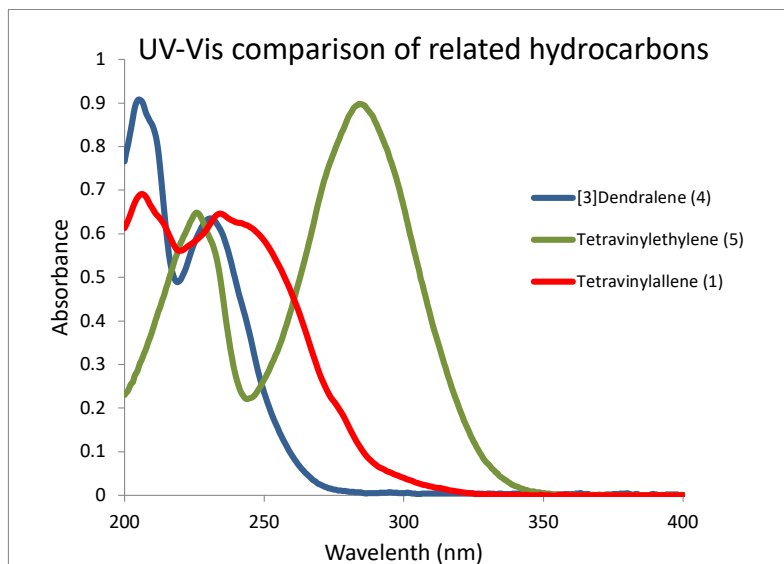


Figure S4. UV-visible comparison of related π -bond rich hydrocarbons

Hydrocarbon	λ_{max} (nm)	ϵ (M ⁻¹ cm ⁻¹)
[3] dendralene (4)	205	20600
	231	14500
Tetravinylethylene (5)	225	10700
	284	14800
Tetravinylallene (1)	206	95000
	234	89000

Table S1. UV-visible spectra of tetravinylallene **1** and related hydrocarbons (hexane, 25 °C)

Tetravinylallene Conformational Analysis

Calculations were carried out on isolated molecules of TVA **1** in the gas phase using the Spartan'18 Parallel Suite package. MP2/cc-pVTZ geometries were located since this level of theory was previously used to study 1,1-divinylallene.^[10] Relative total energy E_{rel} (kJ/mol) refers to 298 K.

An MP2/cc-pVTZ computational study reveals that the lowest energy conformation of TVA **1** is chiral and C_2 symmetric (Figure S5). Each allene terminal C carries one vinyl group in an *anti*-orientation, and another in a *gauche* orientation relative to the conjugating allene C=C bond. The *anti*-dienes are essentially coplanar (dihedral angles = 172°) whereas the *gauche*-dienes are skewed 35° from planarity.^[11] The second lowest energy conformation has the same *anti-gauche* conformation at one side of the central allene but an *anti-anti* arrangement at the other. The third lowest energy conformer again displays the now familiar *anti-gauche* conformation at one side of the molecule but this time with a *syn-syn* conformation at the other.

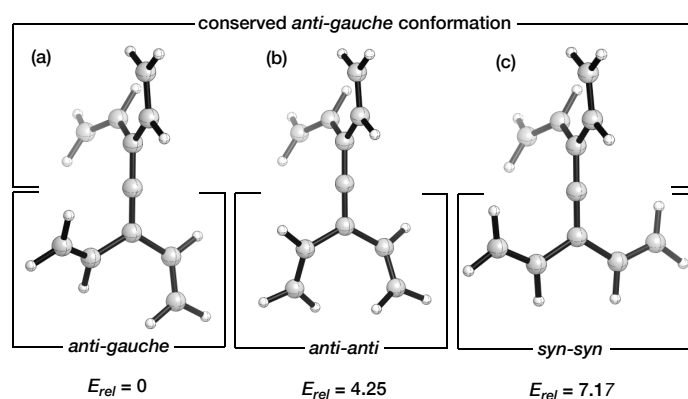


Figure S5. The three MP2/cc-pVTZ lowest energy conformations of TVA **1** (relative energies in kJ/mol, 298 K).

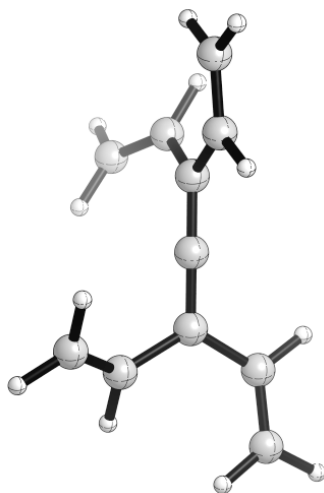
The *anti-gauche* conformation was previously identified as the lowest energy conformation for both 1,1-divinylallene **3**^[10] and [3]dendralene **4**.^[12] Furthermore, the three lowest energy conformations located previously for [3]dendralene **4** are, in increasing energy, *anti-gauche*, *anti-anti* and *syn-syn*,^[12] which match those of TVA **1** very well. Only the lowest energy conformer for 1,1-divinylallene **3** has been reported.^[10] Thus, the preferred conformations of TVA **1** are consistent with those of known, related molecules.

S100

Conformer Relative Energy (E_{rel} , kJ/mol)

CONF1	0
CONF2	4.25
CONF3	7.17
CONF4	7.67
CONF5	8.54
CONF6	11.46
CONF7	11.51
CONF8	13.97

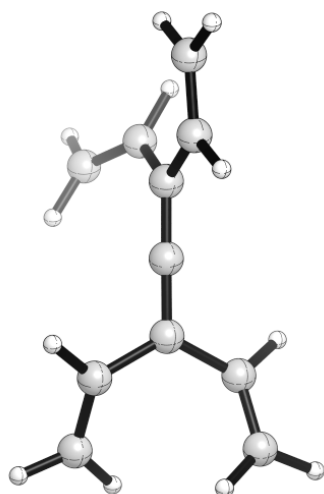
The lowest energy conformer **CONF1** is chiral. Overall, it has C_2 symmetry; the symmetry axis passes through the central *sp*-C and is orthogonal to the C=C=C axis (along the z-axis in the Figure). Each allene terminal C carries one vinyl group in an *anti*-orientation, and another in a *gauche* orientation relative to the conjugating allene C=C bond. In this *double anti-gauche* conformation, each *anti*-diene is essentially coplanar (dihedral angles between the double bonds = 172°) whereas each *gauche* one is skewed 35° out of plane.



CONF1

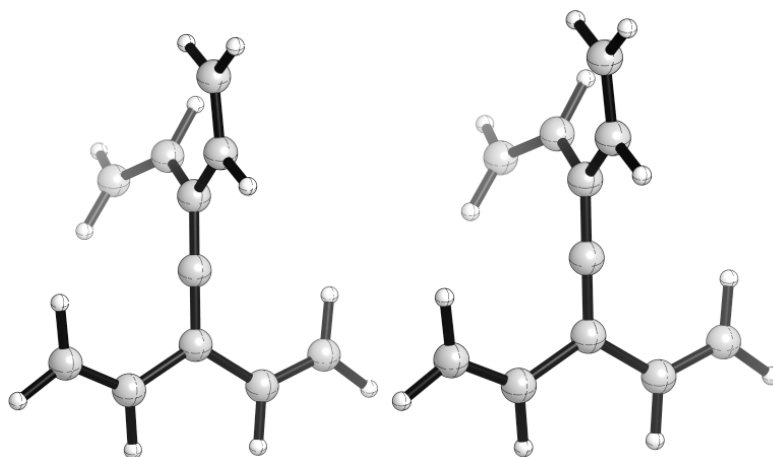
The second lowest energy conformation **CONF2** is also chiral and lies 4.3 kJmol^{-1} higher in energy than **CONF1**. In this structure, one side of the molecule adopts the same *anti-gauche* conformation as in **CONF1** but at the other end, an *anti-anti* arrangement is seen, with the two vinyl groups twisted in opposite directions with respect to the allene C=C bond to which they are conjugated. The twisting from planarity of the butadienes in the *anti-anti* portion of the molecule is 156° .

S101



CONF2

The next higher energy conformers **CONF3** (7.2 kJmol⁻¹ higher than **CONF1**) and **CONF4** (7.7 kJmol⁻¹ higher than **CONF1**) again display the now familiar *anti-gauche* conformation on one side of the molecule but this time with a *syn-syn* conformation on the other. **CONF3** has the two vinyl groups on the *syn-syn* side twisted 19° from planarity, and in opposite directions. The closely-related conformer **CONF4** has the same two vinyl groups rotated only 8° and 4° from planarity.

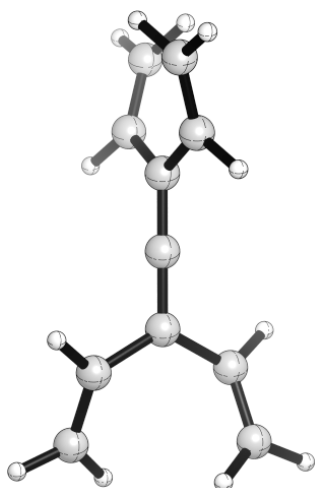


CONF3

CONF4

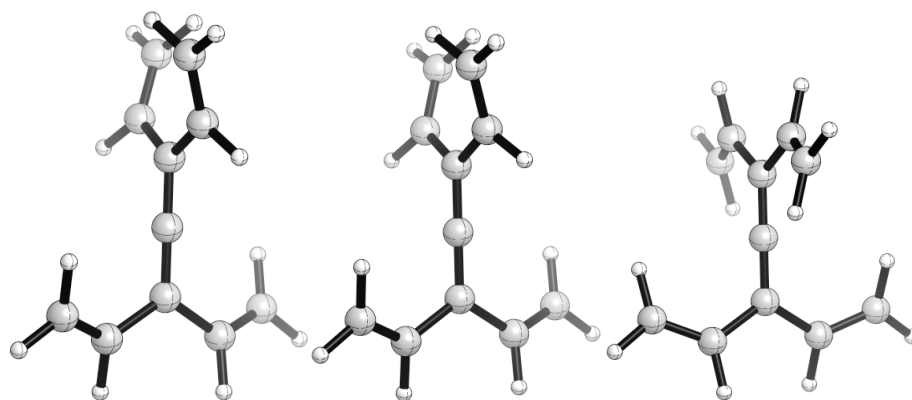
S102

The next higher energy conformer **CONF5** (8.5 kJmol⁻¹ higher than **CONF1**) has *anti-anti* conformations about both allene termini, with dihedral angles between the double bonds of 156°.



CONF5

Next come **CONF6** and **CONF7**, two closely-related conformers with *anti-anti* arrangements at one side and *syn-syn* arrangements at the other (both 11.5 kJmol⁻¹ higher than **CONF1**), and the next highest is a *double syn-syn* conformer **CONF8**, which is 14.0 kJmol⁻¹ higher in energy than **CONF1**.



CONF6

CONF7

CONF8

Focusing on each end of the molecule, it can be seen that the *anti-gauche* conformation is preferred, followed by an *anti-anti* arrangement, which in turn is more stable than a *syn-syn* conformation.

S103

Moreover, the conformations at each end of the molecule are essentially independent, as evidenced by the additive nature of the energetic penalties incurred on changing conformation, i.e.

$$2 \times (\textit{anti-gauche}) E_{\text{rel}} = 0$$

$$1 \times (\textit{anti-gauche}), 1 \times (\textit{anti-anti}) E_{\text{rel}} = 4.25$$

$$1 \times (\textit{anti-gauche}), 1 \times (\textit{syn-syn}) E_{\text{rel}} = 7.2$$

$$2 \times (\textit{anti-anti}) E_{\text{rel}} = 8.5$$

$$1 \times (\textit{anti-anti}), 1 \times (\textit{syn-syn}) E_{\text{rel}} = 11.5$$

$$2 \times (\textit{syn-syn}) E_{\text{rel}} = 14$$

Hence, the energetic penalties are as follows:

$$\textit{anti-gauche} \text{ into } \textit{anti-anti} = 4.25$$

$$\textit{anti-gauche} \text{ into } \textit{syn-syn} = 7.2$$

$$\textit{anti-anti} \text{ into } \textit{syn-syn} = 3$$

The most closely related molecule to TVA that has been analysed computationally and experimentally is [3]dendralene, which has three conformations. ^[12]The lowest energy structure of [3]dendralene is an *anti-gauche* conformer (174° and 41°, respectively), followed by an *anti-anti* conformer (157°; 3.7 kJmol⁻¹ higher in energy) then a *gauche-gauche* conformer (33°; 9.8 kJmol⁻¹ higher in energy than the *anti-gauche* conformer; G4(MP2) values).

Thus, in the broadest terms, the same general conformational preferences are seen in the two portions of the TVA molecule as were previously witnessed in [3]dendralene. There are, however, some interesting differences.

When we compare the *anti-gauche* conformer of [3]dendralene and the same subunit of TVA, we see that the TVA molecule has a slightly less in plane *anti*-butadiene and a lower skew angle in the *gauche* butadiene, which can be accounted for by a slight reduction in the energetic penalty for the skew cisoid diene conformation, due to an absence of a hydrogen at the central allenic carbon.

The *anti-anti* conformers of TVA and [3]dendralene are essentially the same, which suggests that this conformation in [3]dendralene is not influenced significantly by the central methylene protons, and instead reflects a balance between stabilizing π -conjugation and steric strain between the two

S104

terminal methylene *Z*-hydrogens. The calculated energy differences between *anti-gauche* and *anti-anti* conformations for TVA (4.2 kJmol⁻¹) and [3]dendralene (3.7 kJmol⁻¹) are also very similar.

The difference in the conformational preferences between TVA and [3]dendralene is greatest in the third type of structure, a *gauche-gauche* conformer (C=C–C=C dihedral 33°) in [3]dendralene but a *syn-syn* conformer (C=C–C=C dihedral between 4° and 19°) in TVA. Here, the absence of the internal methylene protons in TVA permits each 1,3-butadiene unit to sit in a conformation much closer to an in plane, *cisoid* arrangement. The calculated energy difference between the *anti-gauche* and *syn-syn* conformations for TVA (7.2 kJmol⁻¹) is accordingly lower than the equivalent pair of structures for [3]dendralene (9.8 kJmol⁻¹).

Cartesian coordinates

CONF1

C	1.312948	0.263427	0.073706
C	-0.007664	0.200090	0.118722
C	-1.329546	0.149695	0.139883
C	-2.026770	-0.253357	1.365302
C	-3.344972	-0.483601	1.445857
H	-1.408566	-0.370850	2.247043
H	-3.991669	-0.398556	0.584576
H	-3.794477	-0.776401	2.383133
C	-2.105318	0.506645	-1.064064
C	-1.709706	0.235076	-2.312702
H	-3.043627	1.022265	-0.895875
H	-0.788337	-0.301105	-2.497026
H	-2.300197	0.543989	-3.162714
C	2.000197	1.508803	0.429471
C	3.328566	1.628831	0.566177
H	1.365117	2.370310	0.593876
H	3.993951	0.787905	0.432877
H	3.769222	2.578817	0.829501
C	2.096790	-0.914131	-0.349319
C	1.758005	-2.179368	-0.077442
H	2.994539	-0.710111	-0.921451
H	0.878435	-2.404129	0.511556
H	2.353079	-3.004245	-0.441086

S105

CONF2

C	-0.116398	0.139384	-1.144711
C	-0.047826	0.154177	0.178926
C	0.001584	0.158951	1.500957
C	0.240402	1.414735	2.219564
C	0.450903	1.504822	3.540363
H	0.248351	2.313018	1.614123
H	0.472362	0.631034	4.175427
H	0.618861	2.465092	4.004609
C	-0.196835	-1.094130	2.255820
C	0.217712	-2.294569	1.836906
H	-0.720483	-1.006252	3.201127
H	0.759706	-2.401205	0.906791
H	0.017493	-3.184047	2.416080
C	-1.415491	0.423307	-1.776077
C	-1.602781	0.881033	-3.021949
H	-2.277076	0.286528	-1.133489
H	-0.779302	1.074718	-3.691670
H	-2.601299	1.098104	-3.372054
C	1.111451	-0.162928	-1.898820
C	1.171057	-0.650996	-3.145932
H	2.034948	-0.014111	-1.351745
H	0.283686	-0.857074	-3.723899
H	2.128975	-0.879591	-3.590345

CONF3

C	-0.158806	-0.076647	-1.096533
C	-0.162433	-0.054807	0.226124
C	-0.150556	-0.046484	1.547503
C	-0.401638	-1.273922	2.327419
C	-0.293446	-2.519818	1.851063
H	-0.683564	-1.121328	3.363546
H	0.008711	-2.697566	0.826947
H	-0.505984	-3.373707	2.477024
C	0.121298	1.193507	2.301366
C	0.020252	2.433645	1.807501
H	0.419814	1.055375	3.334560
H	-0.296302	2.600434	0.786290
H	0.253367	3.294299	2.416472
C	1.087136	-0.379040	-1.829096
C	2.303493	-0.009542	-1.413544
H	0.979534	-0.936797	-2.752468
H	2.426456	0.567738	-0.506212
H	3.188080	-0.280090	-1.971859
C	-1.395620	0.190764	-1.838112

S106

C	-1.464565	0.340192	-3.169119
H	-2.297259	0.273328	-1.242469
H	-0.586250	0.287444	-3.795426
H	-2.411716	0.533024	-3.650978

CONF4

C	-0.130732	0.125771	-1.550375
C	-0.064542	0.153155	-0.230353
C	-0.016118	0.161983	1.091333
C	0.314303	1.399531	1.806505
C	0.543579	1.472573	3.125234
H	0.376558	2.295867	1.201760
H	0.514171	0.596840	3.758597
H	0.780540	2.418535	3.589311
C	-0.302476	-1.072739	1.849127
C	0.023588	-2.298163	1.423401
H	-0.812686	-0.949405	2.797600
H	0.553365	-2.437232	0.489813
H	-0.235622	-3.174164	2.000005
C	-1.384753	0.431956	-2.266532
C	-2.565006	0.690958	-1.691835
H	-1.311960	0.437313	-3.348011
H	-2.673137	0.688748	-0.615224
H	-3.435882	0.907882	-2.291900
C	1.048670	-0.220810	-2.368512
C	2.295398	-0.383160	-1.907704
H	0.857480	-0.346314	-3.428674
H	2.523813	-0.253791	-0.857215
H	3.101449	-0.645336	-2.576350

CONF5

C	-0.000186	0.000119	-1.325442
C	-0.000164	0.000165	0.000053
C	0.000149	0.000019	1.325571
C	0.640054	1.129802	2.020132
C	1.126965	1.113725	3.268802
H	0.758920	2.026880	1.424219
H	1.074658	0.235926	3.893674
H	1.618697	1.989275	3.666802
C	-0.639514	-1.129954	2.020139
C	-1.127028	-1.113710	3.268580
H	-0.757694	-2.027314	1.424436
H	-1.075451	-0.235705	3.893191
H	-1.618477	-1.989405	3.666627
C	-1.130224	0.639384	-2.020251
C	-1.113643	1.127126	-3.268643

S107

H	-2.027940	0.756724	-1.424987
H	-0.235230	1.075937	-3.893015
H	-1.989398	1.618061	-3.667117
C	1.129932	-0.639258	-2.020058
C	1.113511	-1.127136	-3.268414
H	2.027551	-0.756532	-1.424659
H	0.235199	-1.076004	-3.892929
H	1.989313	-1.618126	-3.666712

CONF6

C	-0.000025	-0.000015	-1.725707
C	-0.000120	0.000051	-0.404275
C	-0.000134	0.000128	0.920992
C	0.460434	1.214224	1.615270
C	0.950121	1.270544	2.861917
H	0.437258	2.119607	1.020753
H	1.033651	0.393425	3.485575
H	1.303917	2.210286	3.260324
C	-0.460560	-1.213919	1.615437
C	-0.949968	-1.270280	2.862192
H	-0.437414	-2.119242	1.020965
H	-1.033500	-0.393196	3.485762
H	-1.303591	-2.209984	3.260771
C	-1.212889	0.346787	-2.492559
C	-2.460538	0.316990	-2.009020
H	-1.048292	0.634649	-3.524878
H	-2.652870	0.011602	-0.988921
H	-3.301299	0.598197	-2.625376
C	1.212909	-0.346896	-2.492397
C	2.460477	-0.317447	-2.008648
H	1.048446	-0.634498	-3.524796
H	2.652708	-0.012339	-0.988453
H	3.301280	-0.598676	-2.624926

CONF7

C	0.002305	0.000110	-0.918787
C	0.001694	-0.001262	0.406235
C	-0.000075	-0.002076	1.727879
C	-0.090319	-1.259777	2.495184
C	0.135674	-2.483392	2.000773
H	-0.356171	-1.149476	3.540954
H	0.421441	-2.622294	0.965758
H	0.036315	-3.359123	2.624298
C	0.087243	1.255111	2.496418

S108

C	-0.144780	2.477955	2.003301
H	0.355470	1.145086	3.541401
H	-0.433439	2.616028	0.969202
H	-0.047765	3.353718	2.627031
C	1.287853	-0.182744	-1.613513
C	1.450560	-0.646395	-2.860799
H	2.165542	0.042963	-1.020190
H	0.613368	-0.921496	-3.483557
H	2.444694	-0.782313	-3.261264
C	-1.282566	0.186420	-1.614107
C	-1.443215	0.650998	-2.861220
H	-2.161616	-0.032782	-1.020330
H	-0.605295	0.923148	-3.483524
H	-2.436918	0.791594	-3.261146

CONF8

C	-0.000008	0.000000	-1.321503
C	-0.000018	0.000003	-0.000114
C	-0.000003	0.000010	1.321347
C	0.753446	-1.013110	2.086222
C	1.752407	-1.755132	1.592873
H	0.457935	-1.136539	3.122367
H	2.079318	-1.632034	0.568445
H	2.251952	-2.491147	2.204906
C	-0.753433	1.013137	2.086229
C	-1.752429	1.755128	1.592904
H	-0.457876	1.136602	3.122356
H	-2.079387	1.631991	0.568495
H	-2.251956	2.491155	2.204937
C	1.012486	0.753939	-2.086744
C	1.755705	1.751495	-1.592415
H	1.133957	0.460445	-3.123678
H	1.634507	2.076077	-0.567001
H	2.490263	2.252751	-2.204809
C	-1.012485	-0.753941	-2.086764
C	-1.755693	-1.751514	-1.592454
H	-1.133950	-0.460435	-3.123695
H	-1.634500	-2.076107	-0.567043
H	-2.490238	-2.252774	-2.204861

S109

References

- [1] Agilent CrysAlis PRO. Agilent Technologies Ltd, Yarnton, Oxfordshire, England, **2014**.
- [2] G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3–8.
- [3] G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3–8.
- [4] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Cryst.* **2009**, *42*, 339-341.
- [5] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics*, **1996**, *15*, 1518-1520.
- [6] W. L. F. Armarego, C. Chai, *Purification of Laboratory Chemicals* 7th Edn. Butterworth-Heinemann, Oxford, **2012**.
- [7] H. S. Lin, L. A. Paquette, *Synth. Commun.*, **1994**, *24*, 2503-2506.
- [8] B. E. Love, E. G. Jones, *J. Org. Chem.*, **1999**, *64*, 3755-3756.
- [9] A. Czepa, T. Hofmann, *J. Agric. Food. Chem.*, **2004**, *52*, 4508-4514.
- [10] K. M. Cergol, C. G. Newton, A. L. Lawrence, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Angew. Chem. Int. Ed.* **2011**, *50*, 10425-10428.
- [11] This structure is close to the recently reported B3LYP/6-31G(d) geometry: N. Radić, Z. B. Maksić, *J. Org. Chem.* **2019**, *84*, 2425-2438
- [12] M. F. Saglam, T. Fallon, M. N. Paddon-Row, M. S. Sherburn, *J. Am. Chem. Soc.* **2016**, *138*, 1022-1032.

4

Trivinylallene

4.1 An Introduction

Preamble

As previously discussed in Chapters 2 and 3, trivinylallene (**1.30**) is another of the multivinylallenes that has not been reported with substituted analogs also absent from the literature (Figure 4.1.1).^[18] This may be due to the belief that highly conjugated allenes are unstable molecules; such a notion may hold credence given that the closely related molecule triethynylallene (**4.1**) also remains unreported (Figure 4.1.1).

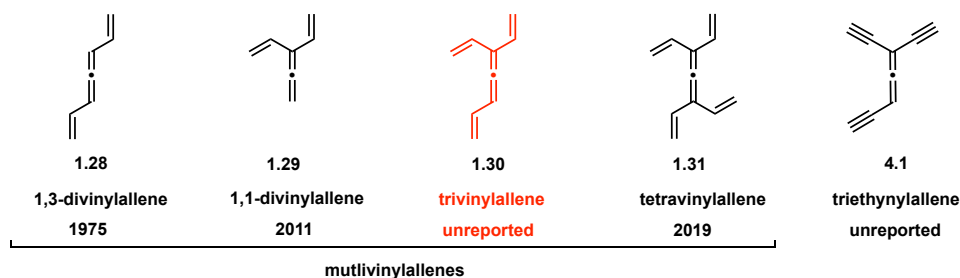


Figure 4.1.1 Trivinylallene (**1.30**, shown in red) and related conjugated allenes

We believed that trivinylallene (**1.30**) could be prepared by adopting the cross-coupling strategy that had successfully been applied to tetravinylallene (**1.31**) and would also enable the synthesis of substituted analogs, thereby permitting the first study of trivinylallenes.

4.1.1 Tri-conjugated allenes

Conjugated allenes related to trivinylallene have primarily remained absent from the literature. Triethynylallene (**4.1**), tricyanoallene (**4.2**), tricarboethoxyallene (**4.3**) and triphenylallene (**4.4**) all have three unsaturated units directly attached to the central allene (Figure 4.1.2). Of these molecules, triphenylallene (**4.4**) is the only one to have been synthesised and studied, though attempted syntheses of triethynylallenes have also been reported.

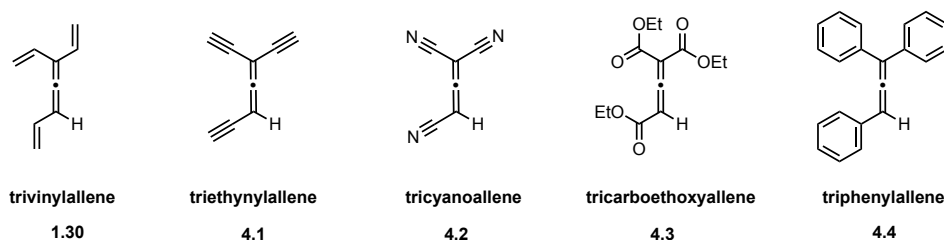
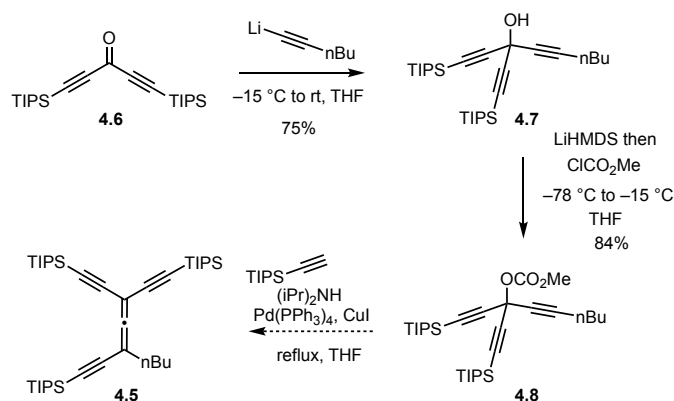


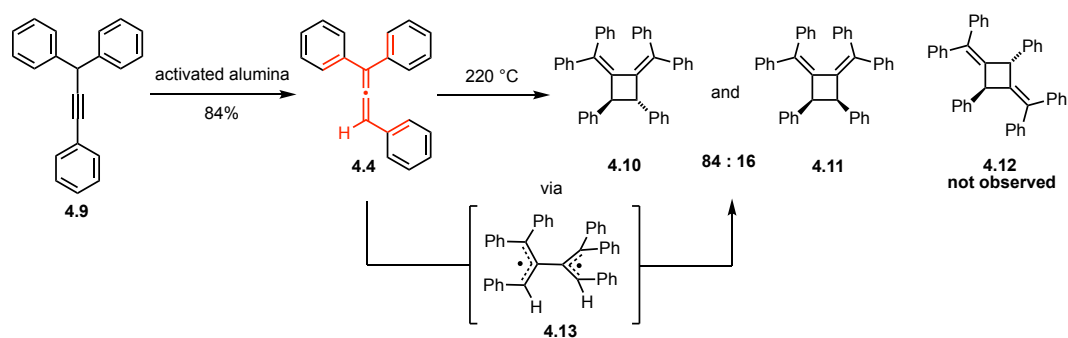
Figure 4.1.2 Conjugated allenes related to trivinylallene (**1.30**)

A single attempted synthesis of the triethynylallene analog **4.5** has been reported, focusing on a cross-coupling approach that had successfully been utilised to access 1,1- and 1,3-diethynylallenes.^[162] The carbonate precursor **4.8** was formed in two steps from ketone **4.6** (Scheme 4.1.1). The cross-coupling reaction gave several products, with the triethynylallene (**4.5**) being tentatively assigned as a product of the reaction by mass spectrometry. It was suggested that **4.5** was rapidly decomposing *via* dimerisation during isolation.^[162]



Scheme 4.1.1 Attempted synthesis of triethynylallene **4.5** *via* a Sonogashira cross-coupling reaction

As with tetravinylallene (**1.31**), the most closely related molecule that has been reported in the literature is triphenylallene (**4.4**), which contains an embedded trivinylallene structure (highlighted in red in Scheme 4.1.2). Triphenylallene (**4.4**), an isolable solid, was first synthesised by the rearrangement of 1,3,3-triphenylalkyne (**4.9**) on activated alumina (Scheme 4.1.2).^[172] Upon heating, triphenylallene (**4.4**) dimerised to give a mixture of cyclobutanes **4.10** and **4.11**, while regioisomer **4.12** was not observed. The dimerization is proposed to proceed *via* a diradical intermediate **4.13**.^[173] [174]



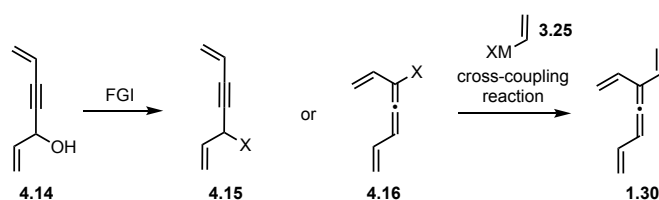
Scheme 4.1.2. Synthesis and dimerization of triphenylallene (**4.4**)

While triphenylallene (**4.4**) is nominally related to trivinylallene (**1.30**), we did not believe that it would be predictive of the stability of trivinylallene (**1.30**). Nevertheless, as with tetravinylallene, it was considered that the comparison of these molecules would be of interest in understanding conjugated allenes.

4.1.2 Aims: Synthesis and study

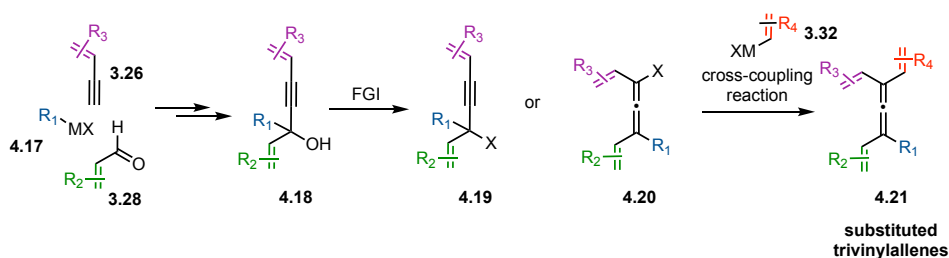
The lack of literature regarding highly conjugated allenes, while perplexing, led us to draw upon our experience with tetravinylallene (**1.31**) to design a synthesis of trivinylallene (**1.30**). Extrapolation from the tetravinylallene synthesis (see Chapter 3 for details) suggested that a cross-coupling approach could also be applied to the synthesis of the unsubstituted trivinylallene molecule (**1.30**) and enable the first study of this compound.

It was envisaged that dienyol **4.14** could be used to access the requisite electrophilic cross-coupling partner (either **4.15** or **4.16**) (Scheme 4.1.3). Subsequent cross-coupling with a vinylic nucleophile (**3.25**) would then furnish the trivinylallene molecule.



Scheme 4.1.3. Proposed synthesis of trivinylallene (**1.30**) using a cross-coupling approach

A successful cross-coupling approach would also permit the study of substituted trivinylallenes (**4.21**). With four potential sites of substitution, it was anticipated that various functional groups (using **3.26**, **3.28** and **4.17**) could be sequentially incorporated into the dienyol (**4.18**) with conversion into the electrophilic cross-coupling partner (**4.19** or **4.20**) (Scheme 4.1.4.). The final, substituted alkenic unit (**3.32**) could subsequently be installed *via* a cross-coupling reaction.



Scheme 4.1.4. Proposed synthesis of substituted trivinylallenes using a cross-coupling approach to incorporate substitution at the four potential sites

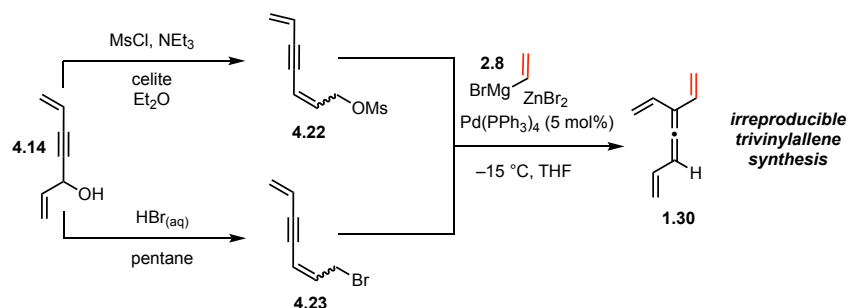
The study of substituted trivinylallenes has a potentially broad scope. Consequently, an initial study of these previously unreported molecules was of interest. As such, these initial investigations aimed to synthesise trivinylallenes substituted at various positions in order to probe steric and electronic effects.

4.2 Synthesis of Trivinylallenes

Investigation of the trivinylallenes began with attempts to synthesise the parent trivinylallene molecule (**1.30**) as our aim was to develop a general synthesis for trivinylallenes unimpeded by any potential steric and electronic effects.

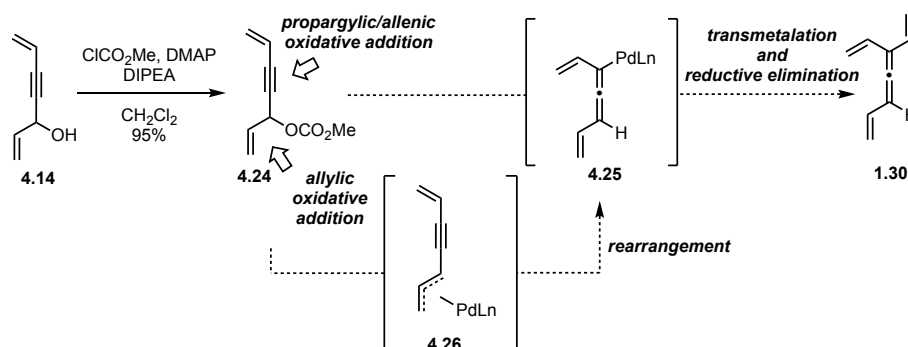
4.2.1 Unsubstituted trivinylallene

The synthesis of the parent trivinylallene began with dienylol **4.14**, an intermediate of the tetravinylallene synthesis (see Chapter 3 for details). Attempts to form a mesylate derivative resulted in rearrangement to form the enyne derivative **4.22** (Scheme 4.2.1). Similar results were observed when dienylol **4.14** was treated with aqueous HBr, resulting in bromide **4.23** being obtained as an inseparable mixture of *E:Z* isomers in a *ca.* 1:1 ratio. While these precursors did yield trivinylallene (**1.30**) when subjected to a palladium(0)-catalysed Negishi cross-coupling reaction with vinylmagnesium bromide (**2.8**), the instability of **4.22** and **4.23** was undesirable and gave irreproducible yields of trivinylallene. As such, a more stable electrophilic cross-coupling partner was sought.



Scheme 4.2.1 Unoptimised initial attempts to synthesise trivinylallene (**1.30**)

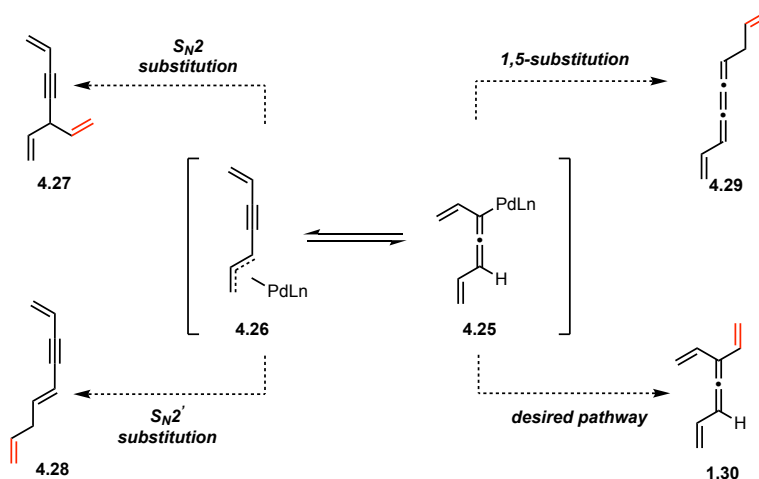
The previous use of carbonates in the synthesis of vinylallenes and ethynylallenes suggested a propargylic carbonate would be a more appropriate precursor to trivinylallene.^{[71] [162]} The carbonate derivative (**4.24**) could be synthesised from dienylol **4.14** to form the electrophilic cross-coupling partner on gram scale (Scheme 4.2.2). Unlike the syntheses of **4.22** and **4.23**, no rearrangement to the enyne was observed with the carbonate derivative. Carbonate **4.24** could also be stored neat for an extended time at -20 °C without noticeable decomposition, making it an ideal trivinylallene precursor. These results contrasted with the unstable carbonate derivative in the tetravinylallene synthesis.



Scheme 4.2.2 Synthesis of **4.24** and cross-coupling reaction to give trivinylallene *via* potential intermediates

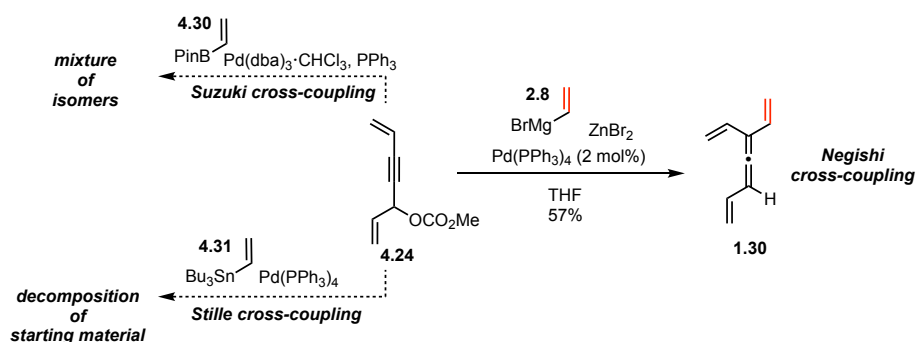
One of the conceivable issues with carbonate **4.24** was the potential for oxidative addition by palladium to occur at the allylic site as well as at the propargylic-allenic site (pointed out in Scheme 4.2.2). We believed that irrespective of the site of oxidative addition, the palladium-allene complex (**4.25**) would be the thermodynamically preferred palladium species (compared to **4.26**),^{[175] [176] [91]} with subsequent transmetalation and reductive elimination furnishing trivinylallene (**1.30**). The terminal ene-yne site is another potential site for oxidative addition, however, it was considered as an unlikely, unproductive pathway.

Nevertheless, various regioisomers could be produced from a cross-coupling reaction (Scheme 4.2.3). Reductive elimination of **4.26**, prior to rearrangement, could result in the formal S_N2 (**4.27**) and S_N2' (**4.28**) substitution products being obtained with cumulene **4.29** another potential product *via* 1,5-substitution of either **4.25** or **4.26**. Although cumulenic products have been observed when vinylallenes were synthesised *via* substitution reactions using Grignard reagents, such products have not been reported in the case of metal catalysed cross-coupling reactions.^[27] As such we did not anticipate this isomer to be a likely reaction outcome.



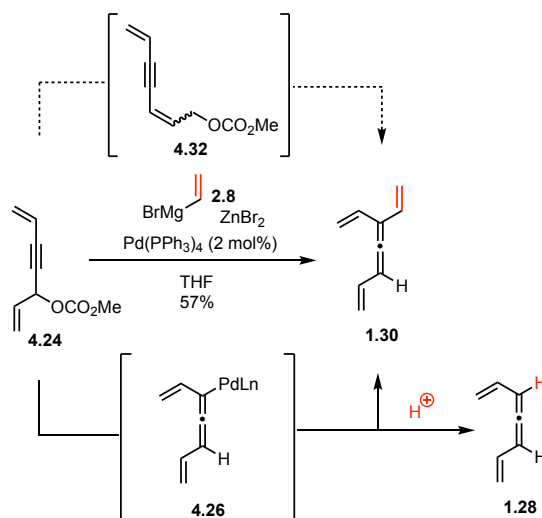
Scheme 4.2.3 Potential isomeric products of the proposed palladium catalysed cross-coupling reaction

A brief investigation of cross-coupling reactions was performed to determine conditions that were amenable to the trivinylallene synthesis (Scheme 4.2.4). Suzuki cross-coupling reactions with **4.30** did not yield a selective synthesis of trivinylallene (**1.30**). Not only were regioisomers observed, but the desired product was found to decompose under the conditions required to carry out the reaction. This was presumed to be due to a palladium(0)-catalysed decomposition pathway that had previously been reported for vinylallene.^[177] Stille cross-coupling reactions failed to yield any trivinylallene (**1.30**) with only consumption of carbonate **4.24** observed. A Pd(PPh₃)₄ catalysed Negishi cross-coupling selectively formed trivinylallene (**1.30**) in 57% yield as a THF solution; the other potential isomers **4.27**, **4.28** and **4.29** were not observed.



Scheme 4.2.4 Investigation of other cross-coupling reactions to synthesise trivinylallene (**1.30**)

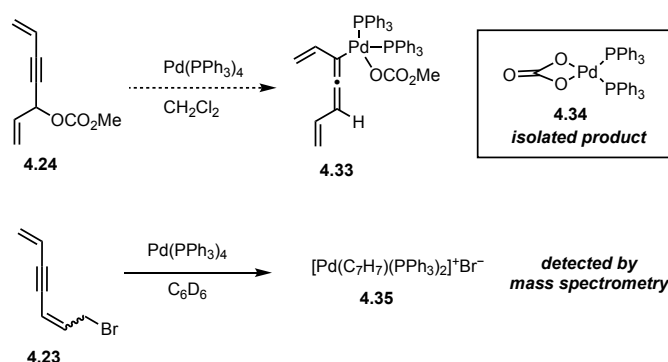
Unlike the synthesis of tetravinylallene (**1.31**), the order of addition of reagents was not found to affect the outcome of the reaction and lower catalyst loadings of 2 mol% could be used. Additionally, carbonate **4.24** was not observed to undergo rearrangement during the reaction, hence it is likely that **4.24** is the species that undergoes oxidative addition rather than species **4.32** (Scheme 4.2.5).



Scheme 4.2.5 Proposed intermediates of cross-coupling reaction

The observation of 1,3-divinylallene (**1.28**) in reaction aliquots, rather than propargylic isomer, suggests the palladium-allene complex (**4.26**) could be the preferred species during the reaction. Although, this does not indicate the site of palladium oxidative addition.

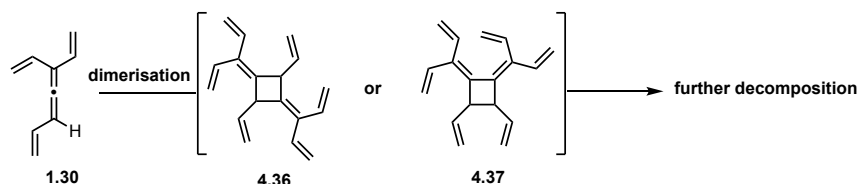
Efforts to observe the palladium-allene complex (**4.33**) were attempted by reacting **4.24** with an equivalent of Pd(PPh₃)₄ as had previously been reported for propargyl bromide (Scheme 4.2.6).^{[175] [176]} While consumption of the carbonate (**4.24**) was observed, only the complex (**4.34**) was isolated, suggesting that palladium-allene complex **4.33** is unstable and was easily hydrolysed. It was proposed that the bromide derivative **4.23** would yield a more stable palladium complex so a similar reaction was attempted using **4.23**. Again, oxidative addition was observed and mass spectrometry analysis indicated the presence of the desired palladium complex (**4.35**), however, the compound was unable to be isolated for characterisation purposes. Further work is required to isolate the palladium-allene complex **4.35** and understand the mechanism of this reaction.



Scheme 4.2.6 Attempted synthesis of palladium-allene complex using carbonate and bromide trivinylallene precursors

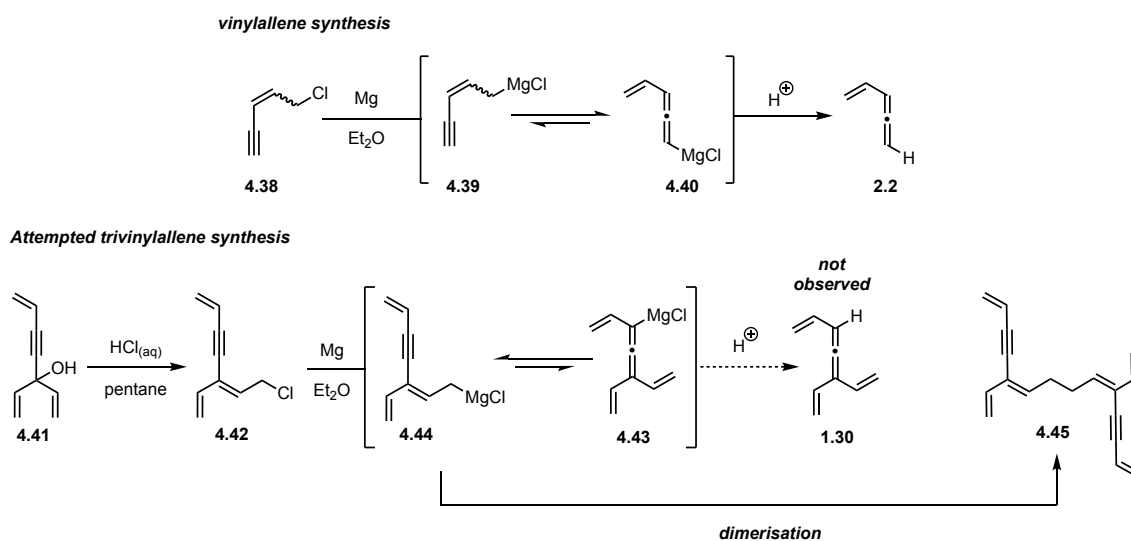
While the site of palladium oxidative addition remains unclear, the Negishi cross-coupling selectively gave trivinylallene (**1.30**) enabling the first synthesis of this molecule and attentions turned to the handling of **1.30**. Efforts to remove THF and obtain a neat sample were unsuccessful with co-distillation of trivinylallene (**1.30**) being problematic. Aqueous extraction of THF from an *n*-pentane solution of trivinylallene (**1.30**) provided a THF-free solution. Subsequent attempts to remove the *n*-pentane and obtain a neat sample of trivinylallene (**1.30**) resulted in decomposition of the allene giving a complex mixture as observed by ¹H NMR and mass spectrometry.

Storage of trivinylallene as an *n*-pentane solution for extended time at $-20\text{ }^{\circ}\text{C}$ also led to decomposition. Significant decomposition was found to occur within a week of storage with the formation of a white polymeric material being observed. Samples of **1.30** in CDCl_3 and d_6 -benzene were found to completely decompose within 48 hours at room temperature, with no identifiable decomposition products being observed. This indicates that trivinylallene is the least stable of the multivinylallenes. Due to difficulties in obtaining solutions of consistent concentration, this synthesis of **1.30** was not found to be amenable towards conducting useful half-life studies required to ascertain the half-life of **1.30** relative to the other multivinylallenes. It is likely that trivinylallene (**1.30**) decomposes *via* a [2+2] dimerisation process to **4.36** or **4.37** although other processes may also be involved (Scheme 4.2.7).^{[162] [178]}



Scheme 4.2.7 Possible decomposition pathway of trivinylallene (**1.30**)

An alternative approach to trivinylallene (**1.30**) was briefly investigated in an attempt to obtain trivinylallene in solvents other than THF. It was envisaged that the allenic Grignard species (**4.43**) could be generated from chloride **4.38** via **4.39** and **4.40** similar to a previously reported synthesis of vinylallene (**2.2**) (Scheme 4.2.8).^[27]



Scheme 4.2.8 Alternate synthesis of trivinylallene (**1.30**) via a Grignard reagent intermediate

When a similar reaction was attempted with chloride **4.42**, derived from alcohol **4.41**, only dimer **4.45** was isolated. The structure of **4.45** was determined by ^1H and ^{13}C NMR spectroscopy and mass spectrometry. Presumably this arises from partial formation of **4.44** which reacts with remaining chloride **4.42**. As a result, this route to trivinylallene (**1.30**) was not further investigated.

While the poor stability of trivinylallene (**1.30**) made storage of the compound difficult, challenges associated with isolating **1.30** resulted in decomposition of trivinylallene. Such results were similar to reported attempts to isolate 1,1-divinylallene (**1.29**), which was proposed to decompose *via* an oligomerisation pathway.^[46] Nevertheless, this indicated the potential of trivinylallene as a reactive dienophile in a diene-transmissive Diels–Alder sequence (see section 4.4 for more details). Furthermore, the instability of the parent trivinylallene (**1.30**) raised questions about the effect of substituents on the stability of this molecule. A study to identify the minimum substitution required for a stable trivinylallene was thus conducted.

4.2.2 Substituted trivinylallenes

As previously mentioned, substituted trivinylallenes have remained absent from the vinylallene literature. With a selective synthesis of the unsubstituted trivinylallene (**1.30**) now in hand, the potential for a similar cross-coupling method to be applied to substituted trivinylallenes was investigated to gain further insight into these molecules.

Mono-substitution

In an effort to determine the minimum level of substitution required to obtain an isolable trivinylallene, mono-substituted trivinylallenes were initially studied. Of the four theoretical sites of substitution, two types were identified; allenic substitution (**4.46**) and alkenic substitution (**4.47**) (Figure 4.2.1).

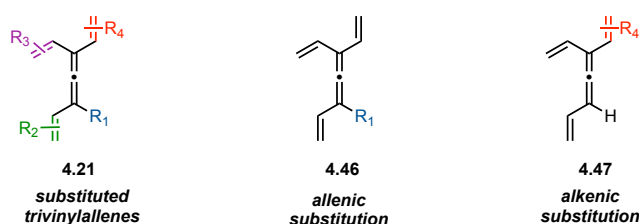
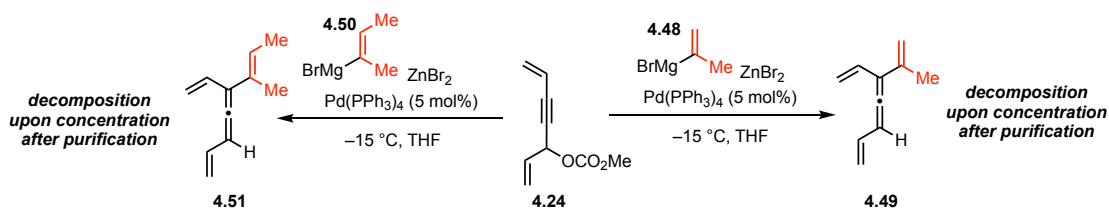


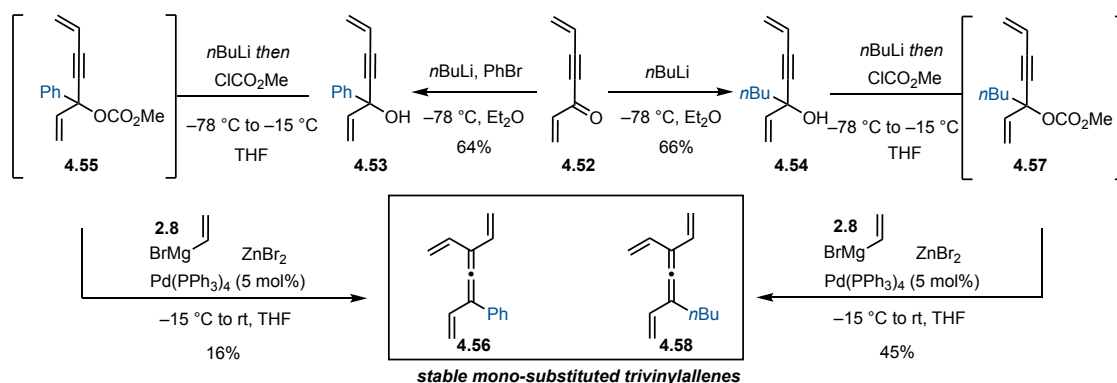
Figure 4.2.1 Potential sites of mono-substitution of trivinylallene

It was envisaged that substitution at the alkenic position (**4.47**) could be readily obtained by utilising a substituted alkenic cross-coupling nucleophile in the Negishi reaction. Attempts to cross-couple carbonate **4.24** with isopropenylmagnesium bromide (**4.48**) were successful, however, concentration of material purified by flash chromatography resulted in decomposition of the desired allene (**4.48**) (Scheme 4.2.9). The use of the more sterically encumbered nucleophile, 1-methyl-1-propenylmagnesium bromide (**4.50**), again did not result in an isolable trivinylallene (**4.51**). While mass spectrometry and ^1H NMR analysis suggested dimerisation and oligomerisation are involved in the decomposition pathway, further studies are required to identify the mechanism of decomposition. These results suggest that while mono-substitution at the alkenic position is attainable, it is insufficient to produce a stable mono-substituted trivinylallene. Such compounds would thus require handling as solutions or treatment as a reactive intermediate in a synthesis.



Scheme 4.2.9 Synthesis of mono-substituted trivinylallenes (**4.49** and **4.51**) at the allenic site

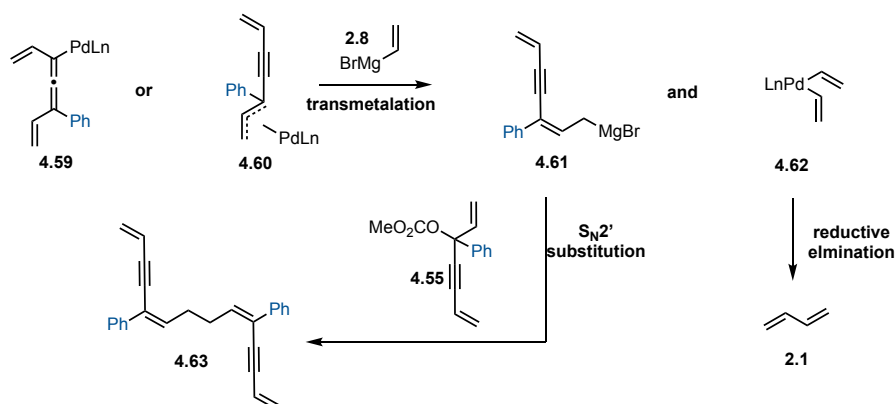
Attentions were thus turned to substitution at the allenic position (**4.46** in Figure 4.2.1). It was envisaged that allenic substitution could be incorporated by addition to ketone **4.52**, another intermediate of the tetravinylallene synthesis. This approach gave access to alcohols **4.53** and **4.54** in 64% and 66% yield respectively (Scheme 4.2.10). The synthesis of the carbonate derivatives (**4.55** and **4.57**) *in situ* and subsequent cross-coupling with vinylmagnesium bromide (**2.8**) yielded the phenyl substituted trivinylallene (**4.56**) in 16% yield and the *n*-butyl substituted trivinylallene (**4.58**) in 45% yield. Both of these trivinylallenes were able to be isolated neat, indicating that substitution at the allenic position is important for overall stability of the trivinylallene molecule.



Scheme 4.2.10 Synthesis of stable mono-substituted trivinylallenes **4.56** and **4.58** functionalised at the allenic site

The syntheses of mono-substituted trivinylallenes **4.56** and **4.58** were found to be regioselective with no isomers being observed, however, the yields may suggest alternative pathways are occurring during the reaction.

The isolation of dimer **4.63** in *ca.* 32% from the synthesis of the phenyl derivative **4.56** may be indicative of the instability of the intermediate palladium complexes **4.59** and **4.60** (Scheme 4.2.11).



Scheme 4.2.11 Possible decomposition pathway of the intermediate palladium-allene complex during the synthesis of allene **4.56**

A possible explanation for the observation of dimer **4.63** could be transmetalation of palladium intermediate **4.59** or **4.60** with vinylmagnesium bromide (**2.8**) (or the organozinc equivalent) to generate **4.61** which substitutes the electrophilic carbonate **4.55** in an S_N2' fashion to give dimer **4.63**. The resulting palladium complex **4.62** could then proceed to reductively eliminate to form 1,3-butadiene (**2.1**), which was observed by ^1H NMR in reaction aliquots.

An equivalent dimer was not observed in the synthesis of the *n*-butyl derivative **4.58**, hence it is likely that other reaction decomposition pathways are present. Nevertheless, the synthesis of mono-substituted trivinylallenes **4.56** and **4.58** have demonstrated that mono-substitution of trivinylallenes at the allenic position is the minimum substitution requirement to obtain isolable trivinylallenes. Interested in whether these trends would extend to higher substitution patterns, our focus turned to di-substituted trivinylallenes.

Di-substitution

Di-substituted trivinylallenes present two possible combinations; substitution at two alkenic positions (**4.64** and **4.65**) or substitution at one alkenic site and the allenic site (**4.66** and **4.67**) (Figure 4.2.2). Each of these possible combinations also have two possible permutations resulting in four possible types of di-substituted trivinylallenes (Figure 4.2.2).

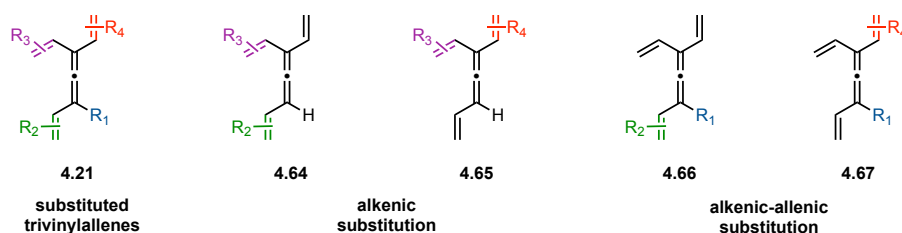
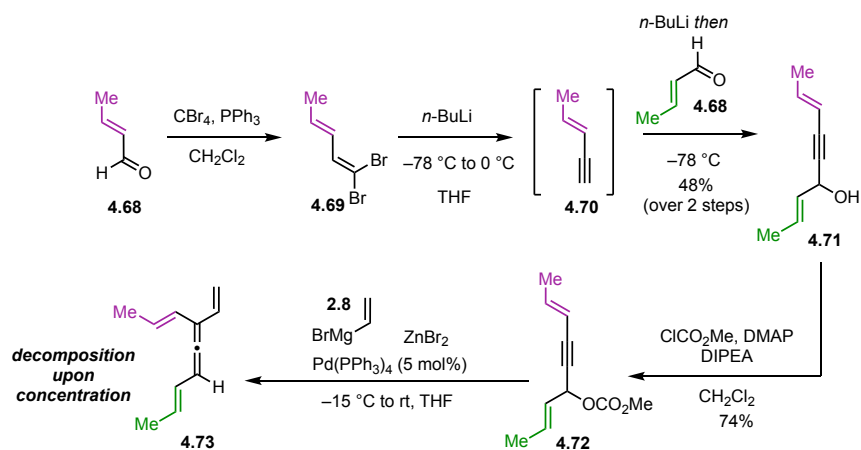


Figure 4.2.2 Possible combinations and permutations of di-substituted trivinylallenes

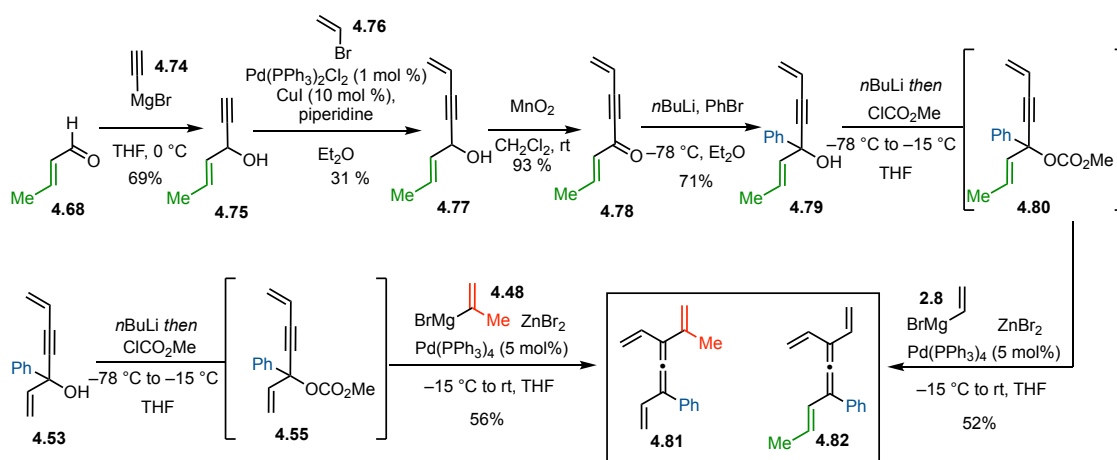
Substitution solely at the alkenic positions was initially investigated focusing on dimethyl substituted trivinylallene **4.73** (Scheme 4.2.12). The carbonate precursor was synthesised in a three step sequence beginning with a Corey-Fuchs reaction of crotonaldehyde (**4.68**) (Scheme 4.2.12). This generated the ene-yne (**4.70**) *in situ* and ensuing addition to a second equivalent of crotonaldehyde (**4.68**) furnished dienylol **4.71**. Subsequent carbonate formation gave the requisite cross-coupling electrophile **4.72**. The following Negishi reaction proceeded to give **4.73**, however, concentration after purification by flash chromatography resulted in decomposition. This result, in conjunction with those of mono-substituted trivinylallenes **4.49** and **4.51**, further indicated the requirement of substitution at the allenic position for the stability of trivinylallenes. As a result, the alternate di-substituted trivinylallenes with allenic functionality (of the type **4.66** and **4.67**) were investigated.



Scheme 4.2.12 Synthesis of a di-substituted trivinylallene functionalised at the alkenic positions

As previously mentioned, two permutations of alkenic-allenic substituted trivinylallenes are possible (Figure 4.2.2). With substitution at the allenic position, a substituted alkene could either be located adjacent to the allenic site (**4.66**), or at the opposite end of the molecule (**4.67**). For the purpose of this study, phenyl substitution at the allenic site was used for ease of handling and analysis with substituted trivinylallenes **4.81** and **4.82** being identified as target molecules (Scheme 4.2.13).

Previously prepared dienyol **4.53** was used as a precursor for substitution pattern **4.81**. The second dienyol (**4.79**) was prepared *via* a four step sequence (Scheme 4.2.13). Addition of ethynylmagnesium bromide (**4.74**) to crotonaldehyde (**4.68**) gave **4.75** and subsequent Sonogashira cross-coupling reaction with vinyl bromide (**4.76**) gave dienyol **4.77**. The aromatic functionality was installed *via* oxidation of **4.77** with manganese dioxide to give ketone **4.78** and addition of phenyl lithium yielded **4.79**. The carbonate derivatives **4.55** and **4.80** were generated *in situ* with the subsequent Negishi-cross-coupling furnishing di-substituted trivinylallenes **4.81** and **4.82** in 56% and 52% yield respectively.



Scheme 4.2.13 Synthesis of stable di-substituted trivinylallenes **4.81** and **4.82**

The successful synthesis and isolation of trivinylallene **4.82** suggests that this substitution pattern of trivinylallenes (**4.66** in Figure 4.2.2) could be stable. Given that **4.82** could be viewed as a substituted 1,1-divinylallene analog (**4.83**) (Figure 4.2.3), this molecule may give insights into the stability of 1,1-divinylallenes, which have been reported to be unstable and difficult to isolate.^{[36] [46] [82]}

The embedded 3'-substituted [3]dendralene (**4.84**) structure within trivinylallene **4.82**, could assist in determining the stability of this substitution pattern of trivinylallenes, given the stability of 3'-substituted [3]dendralenes (**4.84**) (Figure 4.2.3).^[179] Further studies will aid in understanding the broader stability of multivinylallenes and their relationship to other cross-conjugated hydrocarbons.

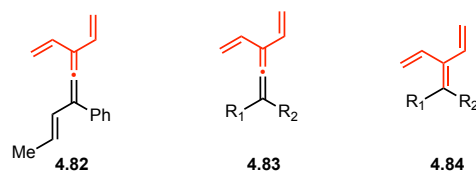


Figure 4.2.3 Structural comparison of trivinylallene **4.82** with closely related hydrocarbon structures with core [3]dendralene structure highlighted in red

The successful synthesis of trivinylallenes **4.81** and **4.82** demonstrated that the cross-coupling approach could be applied to di-substituted trivinylallenes in a selective manner without regioisomers or dimers of electrophilic cross-coupling partners being observed. Again, substitution at the allenic position enabled isolation of these trivinylallenes to be achieved without decomposition. Extension of these trends to tri-substituted trivinylallene was subsequently investigated.

Tri-substitution

Tri-substituted trivinylallenes present two possible combinations; substitution at the three alkenic sites (**4.85**) or substitution at two alkenic sites and the allenic site (**4.86** or **4.87**) (Figure 4.2.4). The second combination also presents two possible permutations, hence three types of tri-substituted trivinylallenes are possible (Figure 4.2.4).

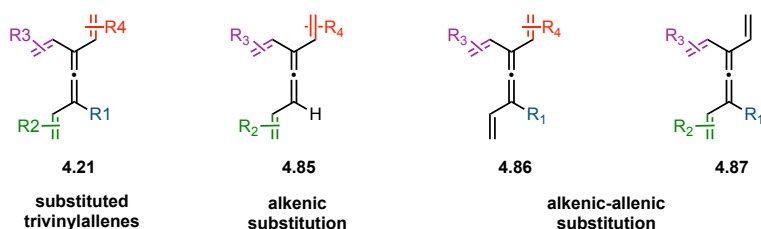
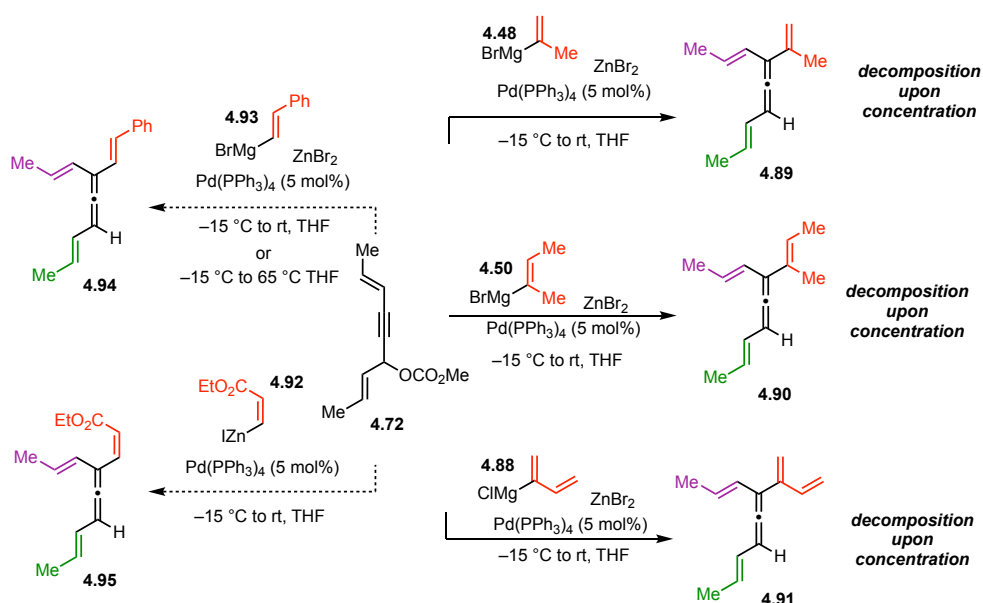


Figure 4.2.4 Possible permutations and combinations of tri-substituted trivinylallene

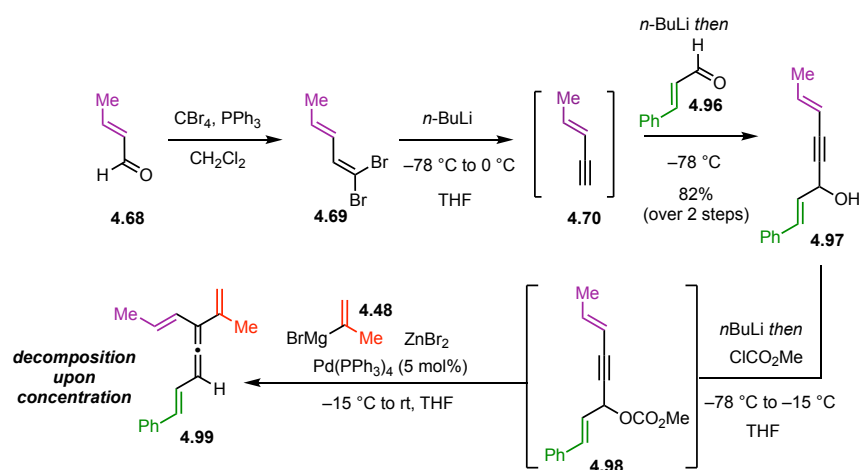
The alkenic substituted trivinylallenes of the type **4.85** were first investigated utilising the precursor carbonate **4.71** and various cross-coupling nucleophiles (Scheme 4.2.14). Methyl substituted alkenic Grignard reagents, isopropenyl- (**4.58**) and 1-methyl-1-propenylmagnesium bromide (**4.50**), as well as the chloroprene Grignard reagent **4.88**^[180] were able to form the desired allenes (**4.89**, **4.90** and **4.91** respectively), however, concentration of material purified by flash chromatography resulted in decomposition (Scheme 4.2.14). Negishi cross-coupling reactions using the esterzinc iodide (**4.92**)^[73] or the styrenyl Grignard reagent (**4.93**)^[181] only resulted in decomposition of the starting carbonate (**4.71**) with trivinylallenes **4.94** and **4.95** not being identified in the reaction mixture or crude material. It has previously been noted that the styrenyl Grignard reagent does not perform well in vinylallene synthesis using the Negishi cross-coupling reaction.^[70]



Scheme 4.2.14 Attempted synthesis of trivinylallenes substituted at the three alkenic positions

Interested to determine if the styrenyl moiety could yield a stable trivinylallene, dienylol **4.97** was synthesised in order to incorporate the styrenyl functionality into the electrophilic cross-coupling partner (**4.98**) (Scheme 4.2.15).

Corey-Fuchs homologation of crotonaldehyde (**4.68**) and addition to *trans*-cinnamaldehyde (**4.96**) gave dienyol **4.97**, which was converted to carbonate **4.98** *in situ*. Subsequent cross-coupling with isopropenylmagnesium bromide (**4.48**) gave the desired allene (**4.99**), however, again decomposition was observed upon concentration of purified material.

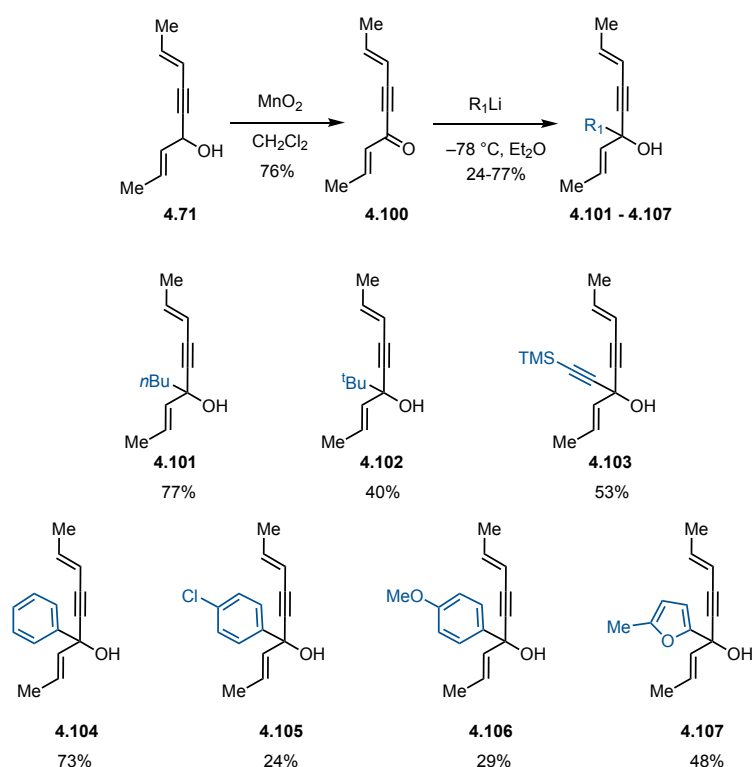


Scheme 4.2.15 Attempted synthesis of tri-substituted trivinylallene functionalised at the three alkenic positions, including a styrenyl group

In conjunction with the previous results of mono- and di-substituted trivinylallenes substituted at the alkenic positions, functionalisation of the allenic position was deemed important for the stability of the trivinylallene molecule. Although a stable tri-alkenic substituted trivinylallene may exist, a poor understanding of the steric and electronic effects that govern trivinylallene stability led us to study alkenic-allenic substituted trivinylallenes (in particular the type **4.87** in Figure 4.2.4) to further comprehend this molecule. Additional studies would be required to identify stable trivinylallenes of the type **4.85** in Figure 4.2.4.

Different functional groups could be incorporated to give various dienyols (**4.101-4.107**) by oxidation of **4.71** with manganese dioxide followed by 1,2-addition of organolithium reagents to ketone **4.100** (Scheme 4.2.16).

We believed that this scope would provide a brief study of tri-substituted trivinylallenes to study the impact of substitution at the allenic position on the synthesis and stability of trivinylallenes. It was considered that methyl substitution at the terminal alkenic position would have minimal impact upon the overall electronics of the trivinylallenes in this brief study.

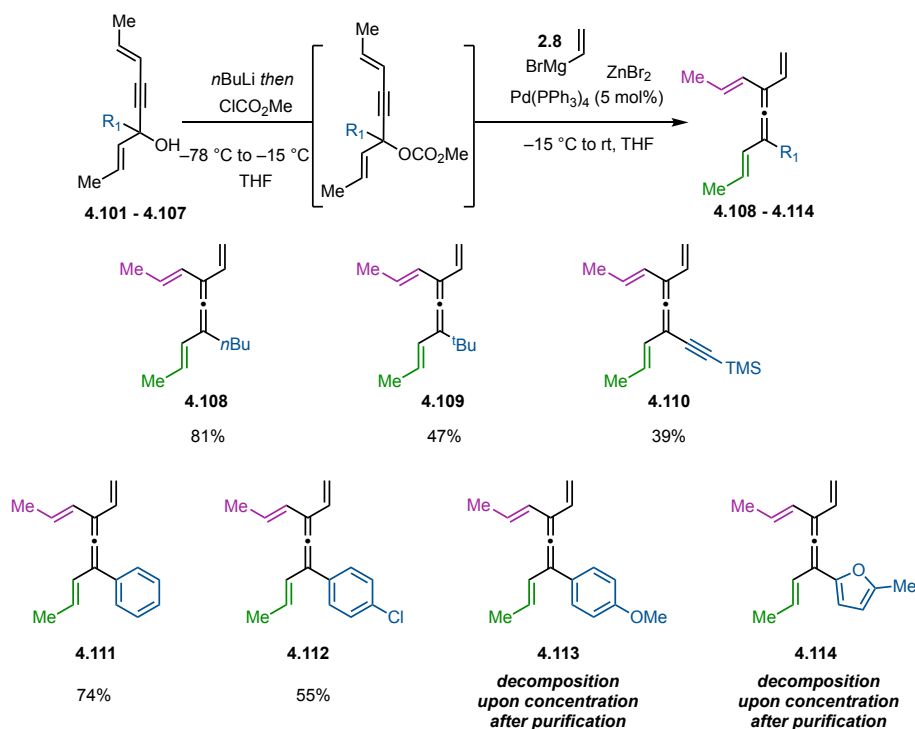


Scheme 4.2.16 Synthesis of tri-substituted trivinylallene dienyol precursors (4.101-4.107)

Carbonate formation *in situ* and subsequent palladium(0)-catalysed Negishi cross-coupling reaction with vinylmagnesium bromide (**2.8**) gave alkenic-allenic tri-substituted trivinylallenes in various yields (**4.109** – **4.114**) (Scheme 4.2.17).

In the case of alkyl substituted trivinylallenes, both the *n*-butyl (**4.108**) and *tert*-butyl (**4.109**) compounds could be synthesised and obtained neat upon purification. The lower yield of **4.109** compared to **4.108** may be attributed to the steric bulk of the *tert*-butyl group destabilising intermediates of the cross-coupling reaction, as **4.109** was observed to be a stable allene.

The TMS-alkyne functionality could also be incorporated into the trivinylallene structure with **4.110** being isolated to give a fully conjugated allenes that could be considered as a dehydro-tetravinylallene. Regioselective cross-coupling syntheses of TMS-alkyne substituted allenes have recently been reported.^[162]



Scheme 4.2.17 Synthesis of tri-substituted trivinylallenes functionalised at two alkenic positions and the allenic site as per **4.87**

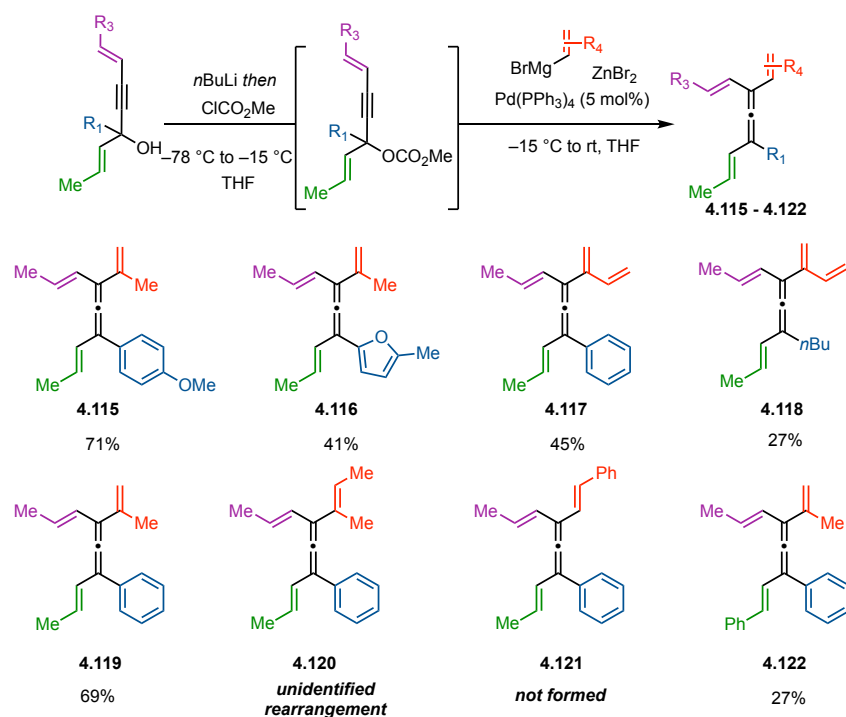
The phenyl analog **4.111** was synthesised in 74% yield, which is higher than was observed for mono- and di-substituted phenyl trivinylallenes (**4.56** in 16%, **4.81** in 56% and **4.82** in 52% yields) (Scheme 4.2.17). This may be due to the terminal methyl groups stabilising the palladium-allene complex, thus preventing alternate pathways in the cross-coupling reaction. To analyse electronic effects on the stability of the trivinylallene molecule, electron-withdrawing and electron-donating substituents were also investigated. The *para*-chlorophenyl (**4.112**) analog could be synthesised although it was found to decompose to a white polymeric material when neat material was exposed to air. The addition of BHT to a solution of **4.112** before concentration of the sample was found to prevent decomposition enabling **4.112** to be isolated in 55% yield, suggestive of an autoxidative decomposition pathway. The electron rich *para*-methoxyphenyl and 2-methylfuran substituted trivinylallenes (**4.113** and **4.114**) could be synthesised, however, these allenes decomposed upon concentration after purification by flash chromatography. In this case, BHT was unable to prevent decomposition indicating a different decomposition pathway to that of **4.112**.

These results demonstrated that stable tri-substituted trivinylallenes, carrying allenic functionality, could be successfully synthesised regioselectively utilising a cross-coupling reaction. Furthermore, it showed that the synthesis and stability of the trivinylallene was affected by the steric bulk of the allenic functionality. With regards to the electron rich derivatives, it was thought that the stability of these molecules could be improved by substituting the third alkenic position. It was conceived that addition increased steric bulk would assist in improving the stability of the electron rich analogs. As such, attentions were turned to tetra-substituted trivinylallenes.

Tetra-substitution

As previously mentioned in Chapter 3, the synthesis of tetra-substituted allenes is limited.^[170] Hence, tetra-substituted trivinylallenes were attractive targets to expand the scope of known tetra-substituted allenes.

The compounds first targeted were the *para*-methoxyphenyl and 2-methylfuran allenes (**4.115** and **4.116**) (Scheme 4.2.18). These compounds could be obtained by formation of the carbonate *in situ* and cross-coupling with isopropenylmagnesium bromide (**4.48**). This yielded **4.115** and **4.116** as isolable trivinylallenes in 71% and 41% yield respectively, although these allenes were found to readily decompose either neat or as solutions at room temperature. The isolation of **4.115** and **4.116** indicates that sterics are likely to play a role in the stability of trivinylallenes carrying electron-donating substituents at the allenic site.



Scheme 4.2.18 Synthesis of tetra-substituted trivinylallenes

The use of different nucleophilic cross-coupling partners was also investigated (Scheme 4.2.18). The chloroprene Grignard reagent (**4.88**) was found to give trivinylallenes **4.117** and **4.118**, which contain an embedded [4]dendralene component. Methyl substituted alkenic Grignard reagents also successfully furnished tetra-substituted trivinylallene **4.119** although **4.120** could be isolated in *ca.* 50% yield, it proceeded to undergo a currently unidentified rearrangement. Efforts to include the styrenyl functionality was again unsuccessful when styrenylmagnesium bromide (**4.93**) was used as the nucleophilic cross-coupling partner, as in the case of **4.121**. Styrenyl functionality could, however, be incorporated into the dienyl precursor and cross-coupling with isopropenylmagnesium bromide (**4.48**) gave allene **4.122** in 27% yield. The synthesis of **4.122** also showcased the ability to synthesise a trivinylallene with four different substituents.

The synthesis of tetra-substituted trivinylallenes concluded our brief study of substituted allenes using a cross-coupling approach. Overall, it was found that a cross-coupling approach was amenable to the incorporation of various functional groups at the allenic site. Although methyl and phenyl substituted alkenes could be integrated into the trivinylallene molecule using this approach, the inclusion of different alkenic functionalities requires further study.

Given the difference in stability of various trivinylallenes geometry calculations of select examples were investigated to gain insight into these observed differences.

4.3 Geometry of Trivinylallenes

Geometry calculations of trivinylallene (**1.30**) were conducted to investigate the lowest energy conformers to enable a comparison with tetravinylallene (**1.31**) and 1,1-divinylallene (**1.29**) and assist in understanding the reactivity of this new molecule. The conformational space of trivinylallene (**1.30**) and select mono-substituted trivinylallenes (**4.56** and **4.58**) were initially explored using the Monte Carlo sampling technique. Geometry optimisation was subsequently performed on conformers within 15 kJ/mol from the lowest energy conformer using MP2/cc-PTVZ. The calculations were conducted with the Spartan 18 software package.

4.3.1 Unsubstituted Trivinylallene

Geometry calculations of the parent trivinylallene molecule (**1.30**) located six types of conformers, each of which fell into one of two categories; the vinyl group adjacent to the allenic hydrogen could adopt either in an *s-trans* conformation or an *s-cis* conformation. The three lowest energy conformations of trivinylallene (**1.30**) belong to the first category of conformers, whereby each has a conserved co-planar (dihedral angle = 180°) *anti*-diene conformation (Figure 4.3.1). The lowest energy conformer of trivinylallene (TRICONF1) has no overall symmetry (i.e. C_1 symmetry) (Figure 4.3.1). At either end of the allene is a vinyl group with an *anti*-orientation, with the third vinyl group in an *gauche*-orientation (Figure 4.3.1). The *anti-gauche* conformation the 1,1-divinylallene portion of TRICONF1 is similar to the lowest energy conformations of 1,1-divinylallene (**1.29**), tetravinylallene (**1.31**) and [3]dendralene (**1.8**) (see Chapter 3 for more details).^{[46] [7]}

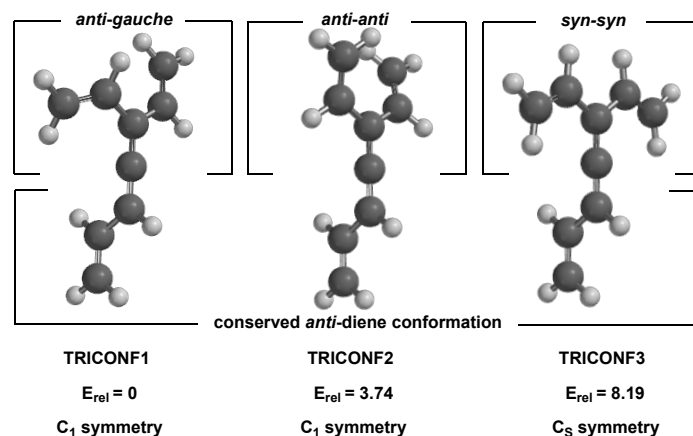


Figure 4.3.1 The three lowest energy conformations of trivinylallene with a conserved *anti*-diene conformation (relative energies in kJ/mol at 298K)

The second lowest energy conformation (TRICONF2) was located 3.74 kJ/mol higher in energy than TRICONF1 (Figure 4.3.1). Here the trivinylallene molecule adopts an *anti-anti* conformation with the two vinyl groups lying on either side of the allenic plane. This resulted in an energetic penalty of *anti-gauche* to *anti-anti* of 3.74 kJ/mol, which is lower than was found for tetravinylallene (4.25 kJ/mol for the same conformational change). This change at the 1,1-divinylallene portion of the molecule did not alter the geometry of the *anti*-diene portion. The third lowest energy conformation (TRICONF3) was located 8.19 kJ/mol higher in energy than TRICONF1 and 4.45 kJ/mol higher than TRICONF2 (Figure 4.3.1). In this case, trivinylallene adopts a *syn-syn* conformation with the two vinyl groups lying essentially in plane (dihedral angle = 0.91°) resulting in C_s symmetry. The energetic penalty of *anti-gauche* to *syn-syn* is 8.19 kJ/mol, which is higher than the case of tetravinylallene (7.20 kJ/mol for the same conformational change). The energetic penalty of *anti-anti* to *syn-syn* of 4.45 kJ/mol, is also higher than the case of tetravinylallene (3.0 kJ/mol for the same conformational change). Again, this change in conformation did not affect the geometry of the *anti*-diene portion of the molecule. The energetic penalties are shown in Table 4.3.1.

The three higher energy conformations of trivinylallene belong to the second category of conformers, whereby each has a conserved *syn*-diene conformation. (Figure 4.3.2). The lowest energy conformation of the *syn*-diene series TRICONF4, has no overall symmetry. At either end of the allene is a vinyl group with an *s-cis* conformation, with the third vinyl group in an *anti*-orientation that lies nearly co-planar (dihedral angle = 173°).

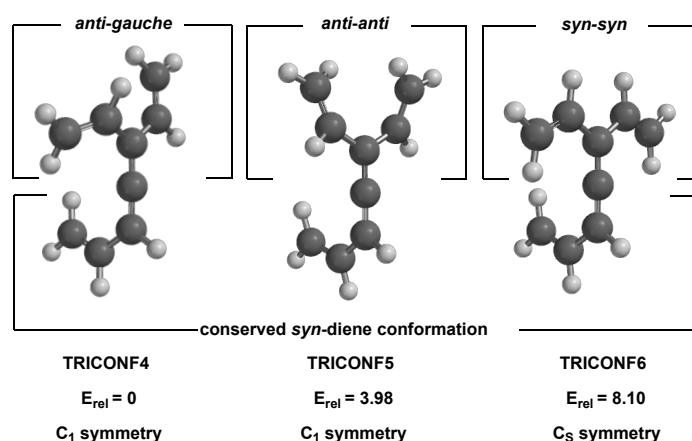


Figure 4.3.2 The three highest energy conformations of trivinylallene with a conserved *gauche*-diene conformation (relative energies in kJ/mol at 298K)

The next highest energy conformation TRICONF5, was located 3.98 kJ/mol higher in energy than TRICONF4 and 13.35 kJ/mol higher than TRICONF1 (Figure 4.3.2). Here the trivinylallene molecule adopts an *anti-anti* conformation with the two vinyl groups lying on either side of the allenic plane. In the case of the conserved *syn*-diene, the resulting energetic penalty of *anti-gauche* to *anti-anti* is 3.98 kJ/mol, which is similar to that observed in the *anti*-diene series (3.74 kJ/mol). This change in conformation did slightly alter the geometry of the *syn*-diene, which is 13° out of plane in TRICONF5. The highest energy conformation TRICONF6 was located 8.10 kJ/mol higher in energy than TRICONF4, 4.12 kJ/mol higher than TRICONF5 and 17.47 kJ/mol higher in energy than TRICONF1 (Figure 4.3.2). In the case of TRICONF6, trivinylallene adopts a *syn-syn* conformation with the two vinyl groups lying essentially in plane (dihedral angle = 2.81°) resulting in C_s symmetry. The energetic penalty of *anti-gauche* to *syn-syn* is 8.10 kJ/mol and of *anti-anti* to *syn-syn* is 4.12 kJ/mol. These values are similar to those of the *anti*-diene series. Again, the change in conformation does alter the geometry of the *syn*-vinyl group which lies in plane (dihedral angle = 0°) in TRICONF6. A comparison of energetic penalties associated with change in conformation is displayed in Table 4.3.1.

Conformational change	<i>anti</i> -diene	<i>syn</i> -diene	tetravinylallene
<i>anti-gauche</i> to <i>anti-anti</i>	3.74	3.98	4.25
<i>anti-gauche</i> to <i>syn-syn</i>	8.19	8.10	7.2
<i>anti-anti</i> to <i>syn-syn</i>	4.45	4.12	3.0

Table 4.3.1 Relative energies between difference between conformations for trivinylallene and compared to tetravinylallene (Relative energies in kJ/mol at 298K)

The two conformations with an *anti-gauche* arrangement (TRICONF1 and TRICONF4) were found to have a relative energy difference of 9.37 kJ/mol with a rotational barrier of 23 kJ/mol calculated using ω B97X-V/6-311G** (Figure 4.3.3).

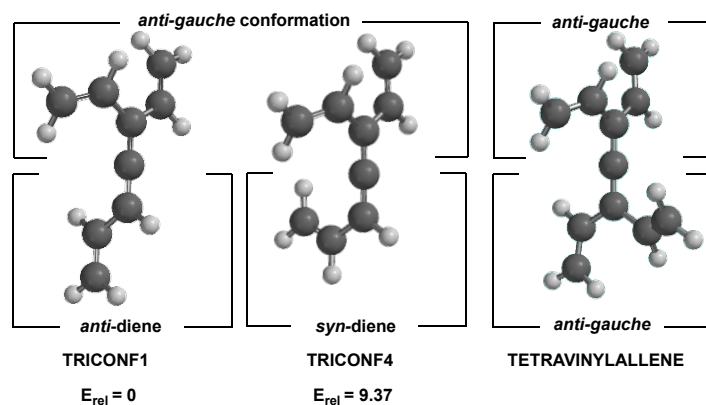


Figure 4.3.3 Comparison of conformations of trivinylallene and tetravinylallene with a conserved *anti-gauche* conformation (relative energies in kJ/mol at 298K)

Both TRICONF1 and TRICONF4 display similar geometry to the *anti-gauche* conformations of tetravinylallene (**1.31**) (see Chapter 3 for details), 1,1-divinylallene (**1.29**) and [3]dendralene (**1.8**).^{[46] [7]} The most noticeable difference in geometry is between TRICONF1 and the lowest energy conformer of tetravinylallene. In the case of TRICONF1, the *anti*-diene is in plane (dihedral angle = 180°) while in the case of tetravinylallene, the equivalent *anti*-diene lies 156° out of plane. This is presumably due to the lack of steric hindrance at the allenic site, which suggests that substitution at the allenic position in trivinylallene may affect the overall conformation of the trivinylallene molecule, in particular the geometry of the adjacent vinyl group. While each of these conformers is accessible at room temperature, these results suggest that a Diels–Alder reaction of trivinylallene (**1.30**) would likely occur at the 1,1-divinylallene portion of the molecule.

4.3.2 Mono-substituted Trivinylallenes

Interest in the geometry of mono-substituted trivinylallenes stemmed from the observed stability of the *n*-butyl and phenyl substituted trivinylallenes (**4.56** and **4.58**). As it was unclear the degree to which allenic substitution would alter the geometry of the trivinylallene molecule, we sought to understand the enhanced stability through geometry calculations of **4.56** and **4.58**. It was also presumed that these calculations would also aid in predicting the reactivity of these molecules in Diels–Alder reactions.

Methyl-trivinylallene (a substitute for n-butyl-trivinylallene)

In order to reduce computational time, the conformational distribution and geometry of *n*-butyl-trivinylallene **4.58** was modelled using a methyl group as the allenic site. Geometry calculations located six potential conformers. Similar to the parent trivinylallene case, each of the conformers fell into either the *s-trans* or *s-cis* conformational categories.

Again, the three lowest energy conformations have a conserved *anti*-diene portion (Figure 4.3.4). These conformations displayed similar relative energies and symmetries as the parent trivinylallene, suggesting that an alkyl substituent has minimal effect upon the geometry of the trivinylallene moiety. It should be noted that a conformer similar to Me-TRICONF1 in which the *anti-gauche* portion is reversed was located at a slightly higher energy.

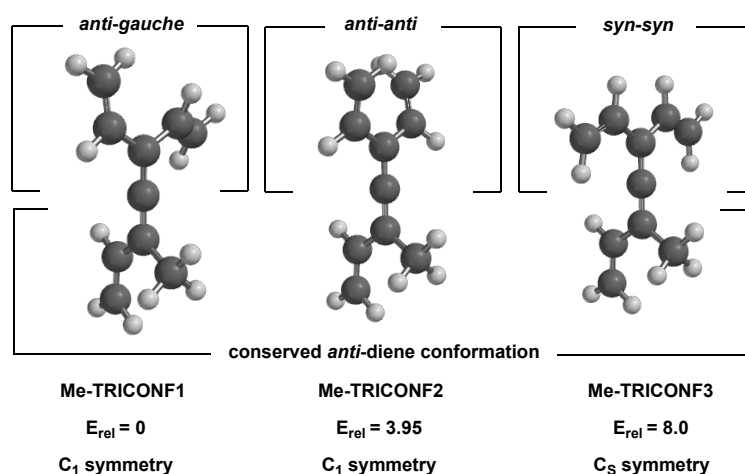


Figure 4.3.4 The three lowest energy conformations of methyl-trivinylallene with a conserved *anti*-diene conformation (relative energies in kJ/mol at 298K)

The three highest energy conformers again contained a conserved *syn*-diene portion and similar relative energies and symmetries were observed compared to trivinylallene. Again, a conformer similar to Me-TRICONF4 was located at a slightly higher energy.

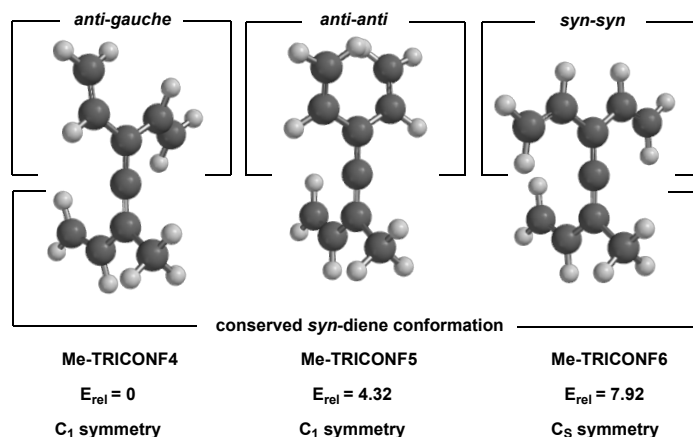


Figure 4.3.5 The three highest energy conformations of the methyl-substituted trivinylallene with a conserved *syn*-diene conformation (relative energies in kJ/mol at 298K)

The two conformations with an *anti-gauche* arrangement (Me-TRICONF1 and Me-TRICONF4) were found to have a relative energy difference of 11.02 kJ/mol, which is higher than what was observed for trivinylallene (Figure 4.3.6). A rotational barrier of 20.67 kJ/mol was calculated using ω B97X-V/6-311G**, which is slightly lower than was calculated for trivinylallene.

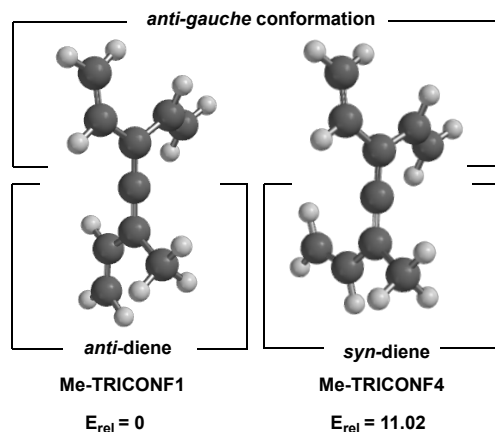


Figure 4.3.6 Comparison of conformations of the methyl-substituted trivinylallene with a conserved *anti-gauche* conformation (relative energies in kJ/mol at 298K)

These results indicated that the presence of an alkyl substituent at the allenic position has minimal impact upon the overall geometry of the trivinylallene portion of the molecule and also did not greatly affect the relative energies of the different conformers. The observed stability of the *n*-butyl substituted trivinylallene (**4.58**) is thus likely due to steric hindrance inhibiting the decomposition pathway, which is proposed to involve dimerization. Hence, it was expected that *n*-butyl trivinylallene (**4.58**) would behave in a similar manner to trivinylallene (**1.30**) in a Diels–Alder reaction.

Phenyl-trivinylallene

In the case of the phenyl-substituted trivinylallene (**4.56**), the three conformers with a conserved *anti*-diene portion were not the lowest energy conformers (Figure 4.3.7). Furthermore, Ph-TRICONF1 and Ph-TRICONF2 had multiple conformational variations with slightly different relative energies. Nevertheless, these conformations displayed similar relative energies as was observed with the parent trivinylallene and methyl-substituted trivinylallene.

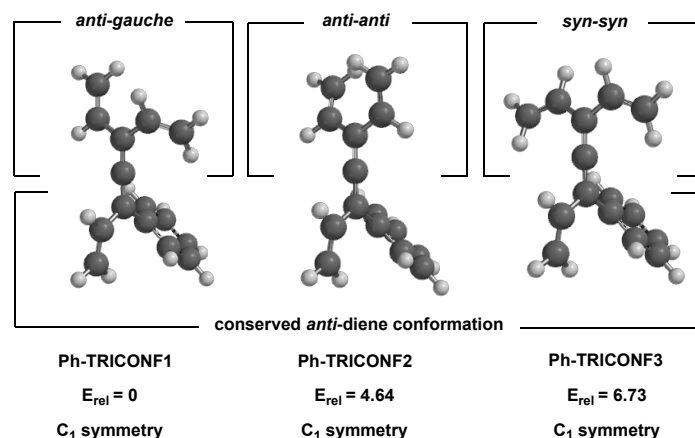


Figure 4.3.7 The three conformations of phenyl-trivinylallene with a conserved *anti*-diene conformation (relative energies in kJ/mol at 298K)

The three conformers with a conserved *syn*-diene portion were also found to have similar relative energies to trivinylallene and the methyl-substituted trivinylallene.

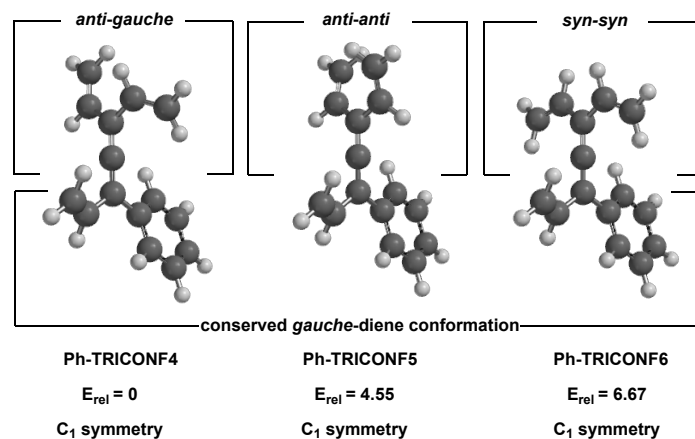


Figure 4.3.8 The three conformations of phenyl-trivinylallene with a conserved *anti*-diene conformation (relative energies in kJ/mol at 298K)

The two conformations with an *anti-gauche* arrangement (Ph-TRICONF1 and Ph-TRICONF4) were found to have a relative energy difference of 2.29 kJ/mol, which is lower than what was observed for the parent trivinylallene and the methyl-substituted trivinylallene (Figure 4.3.9). A rotational barrier of 13.06 kJ/mol was calculated using ω B97X-V/6-311G**, which is lower than calculations for trivinylallene and the methyl-substituted trivinylallene. It is also worth noting that altering between the *anti*-diene and *syn*-diene also resulted in rotation of the phenyl substituent.

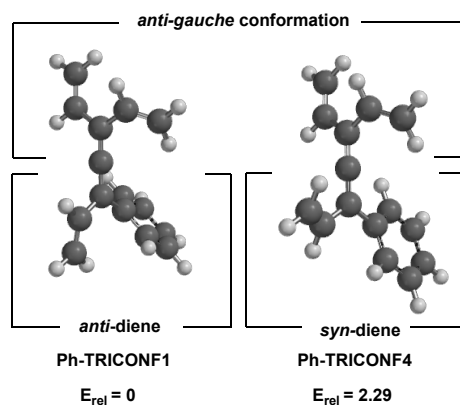


Figure 4.3.9 Comparison of conformations of phenyl-trivinylallene with a conserved *anti-gauche* conformation (relative energies in kJ/mol at 298K)

The presence of a phenyl substituent at the allenic position of trivinylallene was found to decrease the relative energies of the different conformers and did not display the same trends as trivinylallene and the methyl-substituted trivinylallene. The observed stability of the phenyl-substituted trivinylallene (**4.56**) is again likely due to steric factors. In this case, it is unclear whether the phenyl-substituted trivinylallene (**4.56**) would react with similar site selectivity as trivinylallene (**1.30**) in a Diels–Alder reaction.

4.4 Diels–Alder Reactions with the Trivinylallenes

As with the other cross-conjugated hydrocarbons, it is conceivable that trivinylallene (**1.30**) could participate in diene-transmissive Diels–Alder sequence^[182], indicating the potential of **1.30** as a synthetically useful building block for the construction of multicyclic frameworks (Figure 4.4.1).

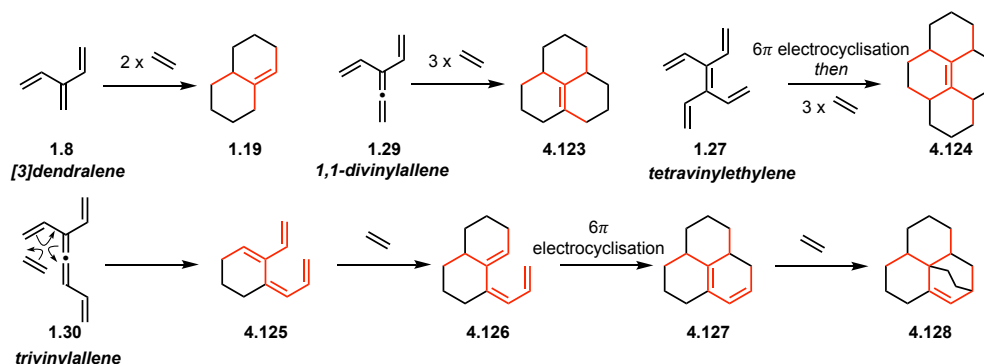
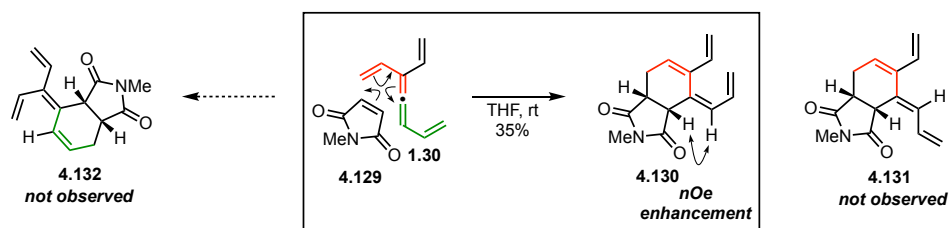


Figure 4.4.1 Rapid construction of molecular complexity using conjugated hydrocarbons in pericyclic cascades using diene-transmissive Diels–Alder reactions

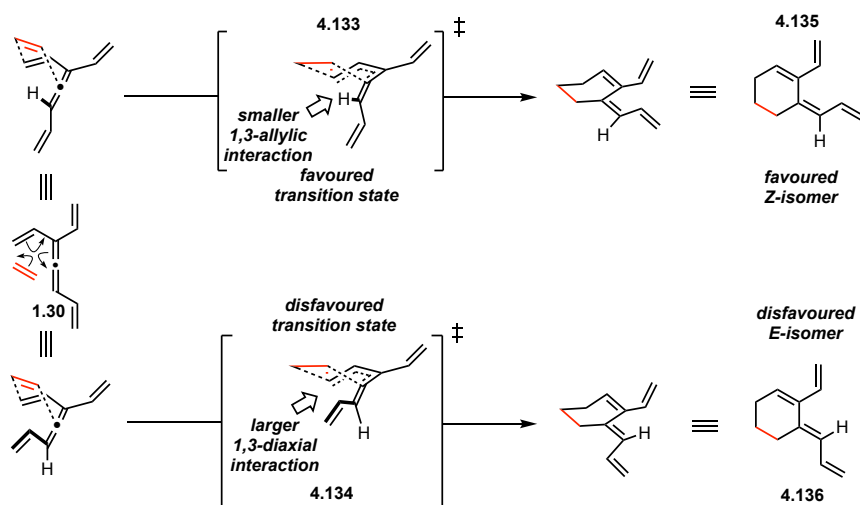
4.4.1 Unsubstituted Trivinylallene

Trivinylallene (**1.30**) was found to rapidly undergo a single Diels–Alder reaction in the presence of a single equivalent of *N*-methylmaleimide (NMM) (**4.129**) at room temperature (Scheme 4.4.1). Unlike the other multivinylallenes, however, trivinylallene (**1.30**) has two non-equivalent dienes that could participate in the first Diels–Alder reaction (highlighted in red and green in Scheme 4.4.1). Bicycle **4.130** was obtained as the sole product of the reaction, containing both a semi-cyclic butadiene and a semi-cyclic triene, and was obtained selectively as the *Z*-isomer, which was determined by NOE. In accordance with the calculated lowest energy conformation of trivinylallene (**1.30**), the requisite *s-cis*-diene conformation is most likely to be at the 1,1-divinylallene portion of the molecule (as shown in Scheme 4.4.1) and thus accounts for the regioselectivity of the Diels–Alder reaction in which the regioisomer **4.132** was not observed.



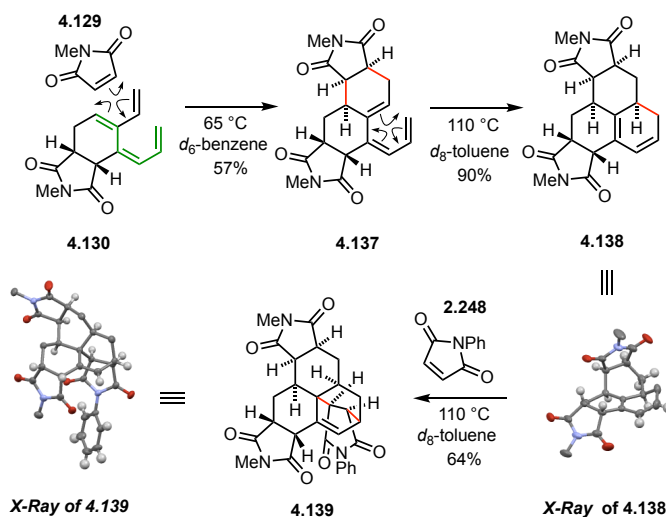
Scheme 4.4.1 Regioselective Diels–Alder reaction of trivinylallene (**1.30**) with NMM (**4.129**). The diene that participates in the Diels–Alder reaction is highlighted in red

The selectivity for the *Z*-isomer can be explained by analysing the transition state of the Diels–Alder reaction (Scheme 4.4.2). As has previously been reported for vinylallenes, the dienophile approaches from the least sterically hindered face of the vinylallene.^[105] In the case of trivinylallene (**1.30**), this occurs in a fashion *anti* to the terminal vinyl group to give transition state **4.133** (rather than **4.134**). The transition state **4.133** results in a *quasi*-allylic functionality whereby the terminal vinyl group is *anti* to the dienophile to reduce undesirable 1,3-allylic interactions, thus leading to the *Z*-isomer **4.135**. Selectivity for *Z*-isomer is important to enable the pericyclic cascade.



Scheme 4.4.2 Rationale for geometric selectivity of Diels–Alder reaction of trivinylallene (**1.30**). The diene component of the Diels–Alder reaction is highlighted in red

The second Diels–Alder reaction with **4.130** occurs at the semi-cyclic diene portion of the molecule, which is presumably governed by this site being the less sterically hindered diene (Scheme 4.4.3). As was observed for tetravinylallene, heating is required for this reaction to proceed, which is likely due to the resulting loss of conjugation of the triene (highlighted in green). The second Diels–Alder proceeds in an essentially selective manner (d.r. 93:7) with the *endo*-, *anti*-diastereomer **4.137** being the major product observed. The bis-adduct (**4.137**) could be synthesised without the 6π -electrocyclisation being observed, which had not been possible in the case of tetravinylallene. This indicates that the *s-trans* conformation of **4.137** is likely to be the preferred.



Scheme 4.4.3 Pericyclic cascade of bicycle **4.130** to form heptacycle **4.139**. X-ray structures of **4.138** and **4.139** are shown with some hydrogens removed for clarity

Subsequent heating of the **4.137** at 110 °C for four hours resulted in a torquoselective 6π -electrocyclisation to give pentacycle **4.138** as a single diastereomer (Scheme 4.4.3). The relative stereochemistry was confirmed by single crystal X-ray analysis. Heating of the cyclohexadiene (**4.138**) in the presence of excess NPM (**2.248**) furnished bridged heptacycle **4.139** as a single *endo*-, *anti*-diastereomer. The relative stereochemistry was determined by single crystal X-ray analysis, demonstrating the ability of trivinylallene (**1.30**) to generate seven new bonds and ten new stereocentres in a four step sequence (the new bonds formed in each reaction are highlighted in Scheme 4.4.3).

Various known amphilectane natural products contain a tricyclic core (**4.140**) and could thus potentially be synthesised using a trivinylallene intermediate (Figure 4.4.2). Examples of natural products include elisabatin A (**4.141**)^[183] and sinulobatin B (**4.142**)^[184], which to date do not have reported total syntheses. It is conceivable that through manipulation of the tricyclic core or its precursor, additional natural products, such as harringtonolide (**4.143**)^[185] [186], could also be targeted.

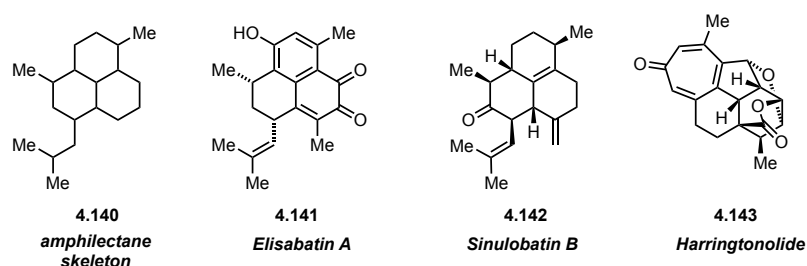


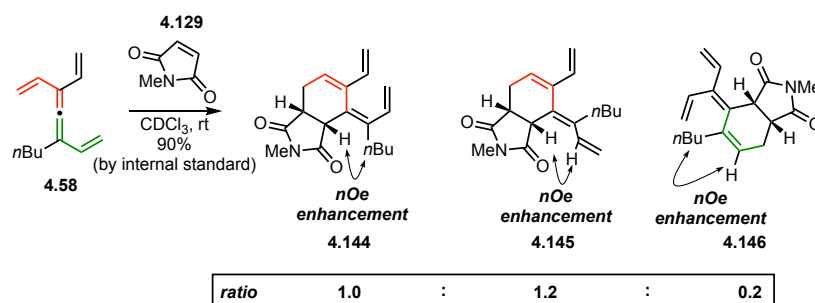
Figure 4.4.2 Natural products that could potentially be synthesised using a trivinylallene

4.4.2 Mono-substituted Trivinylallenes

Vinylallenes carrying di-substitution at the allenic position are known to produce varying mixtures of *E/Z*-isomers (at the newly generated exo-cyclic alkene) when subjected to the Diels–Alder reaction.^{[105] [100]} For this reason, we were interested in studying the selectivity of the Diels–Alder reactivity of trivinylallenes, mono-substituted at the allenic position (**4.56** and **4.58**).

n-Butyl-trivinylallene

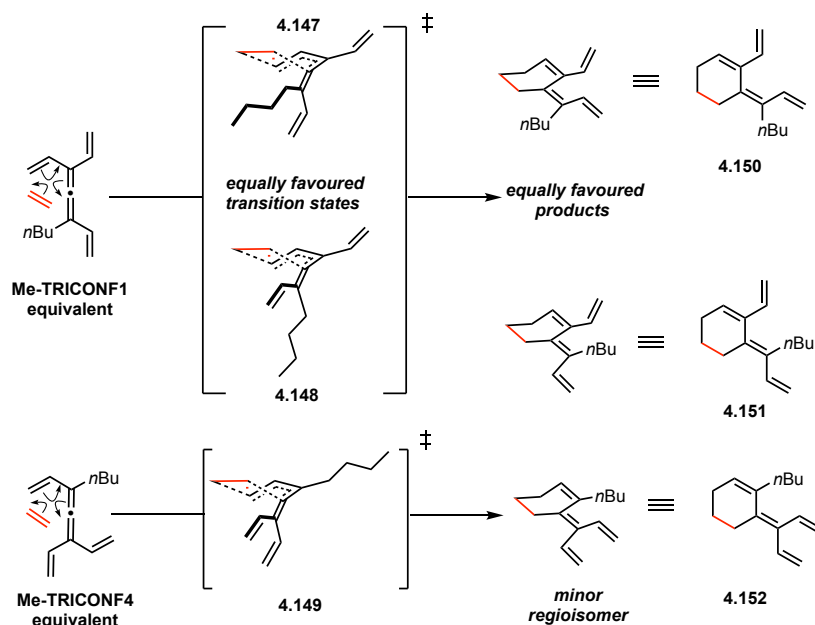
The reaction of *n*-butyl-substituted trivinylallene (**4.58**) with a single equivalent of NMM (**4.129**) gave a mixture of isomers in a ratio of 1.0 : 1.2 : 0.2 with an overall 90% yield determined by internal standard (Scheme 4.4.4). The two major products were identified as a mixture of *E/Z*-isomers (**4.144** and **4.145**) and the minor isomer was identified as regioisomer **4.146** (Scheme 4.4.4). Each of the regioisomers were assigned by NOE.



Scheme 4.4.4 Products isolated from the Diels–Alder reaction of *n*-butyl-trivinylallene (**4.58**) with NMM (**4.129**). The reactive diene portions of **4.58** are highlighted in red and green

The regioselectivity of the reaction correlates with the calculated lowest energy conformation, Me-TRICONF1, whereby the *s-cis* diene is present at the 1,1-divinylallene portion of the molecule (Scheme 4.4.5). The isolation of regioisomer **4.146** (which is depicted as the basic skeleton **4.152** in Scheme 4.4.5) indicates that, notwithstanding lower population, the conformation akin to Me-TRICONF4 is present in solution and suggests that this conformation is highly reactive.

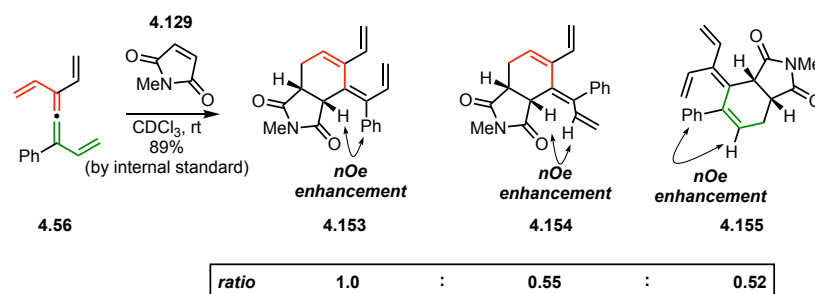
The lack of selectivity between the *E*- and *Z*-isomers **4.144** and **4.145** (depicted by simplified structures **4.150** and **4.151** in Scheme 4.4.5) implies that the difference in energy between the two transition states (**4.147** and **4.148**) is not large, indicating that the *n*-butyl and vinyl groups exert similar 1,3-allylic strain.



Scheme 4.4.5 Rationale for product distribution of the Diels–Alder reaction of allene **4.58** with NMM (**4.129**). The diene component of the Diels–Alder reaction is highlighted in red

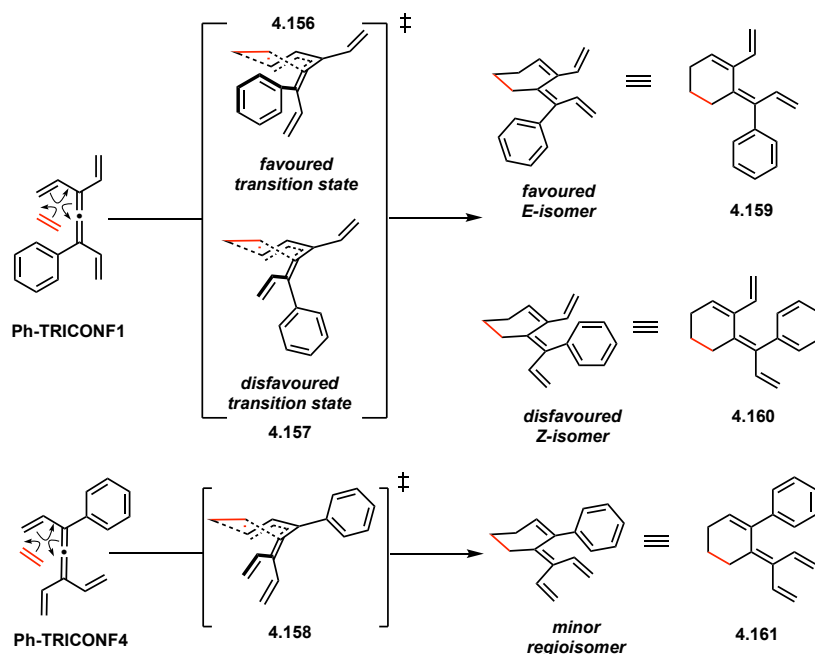
Phenyl-trivinylallene

The reaction of phenyl-substituted trivinylallene (**4.56**) with a single equivalent of NMM (**4.129**) gave a mixture of isomers in a ratio of 1.0 : 0.55 : 0.52, with an overall 89% yield by internal standard (Scheme 4.4.6). The major isomer was identified as the *Z*-isomer **4.153**, with the *E*-isomer **4.154** and regioisomer **4.155** being identified as the minor products of the reaction, all of which were determined by NOE.



Scheme 4.4.6 Diels–Alder reactivity of *n*-phenyl-trivinylallene (**4.56**) with NMM (**4.129**). The reactive diene portions of **4.56** are highlighted in red and green

The observation of **4.153** as the major product of the reaction, correlates with the calculated lowest energy conformation of Ph-TRICONF1 whereby the *s-cis* diene is present at the 1,1-divinylallene portion of the molecule (Scheme 4.4.7). The selectivity for the *E*-isomer (**4.159** in Scheme 4.4.7) implies that there is a difference in energy between the two transition states (**4.156** and **4.157** in Scheme 4.4.7), indicating that the vinyl group is preferentially positioned *anti* to the dienophile in the transition state. Whether this preferred transition state is due to reduced 1,3-allylic strain or a favourable π -interaction, is currently unclear. Similar regioselectivity has recently been reported although an explanation for the observed regioselectivity was not provided.^[88] While favourable π -interactions have previously been used to explain outcomes of the Diels–Alder reaction more generally, they have not been reported in this setting.^[187]

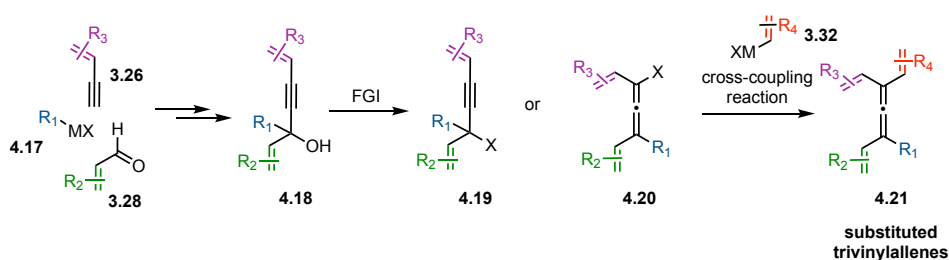


Scheme 4.4.7 Rationale for regioisomer distribution of Diels–Alder reaction. The diene component of the reaction is highlighted in red

Given the small difference in the relative energies of Ph-TRICONF1 and Ph-TRICONF4 (see section 4.3.2) the observation of regioisomer **4.161** as only a minor product of the reaction may indicate that transition state **4.158** is also disfavoured. Nevertheless, these brief studies regarding the Diels–Alder reaction of mono-substituted trivinylallenes **4.56** and **4.58**, show that substitution at the allenic position impacts the product distribution of the reaction. Studies of additional examples, by alteration of the allenic and alkenic substituent, would assist in understanding the influence of steric and electronic effects on the Diels–Alder reaction of substituted trivinylallenes and establish the reason for transition state **4.156** being stabilised.

4.5 Concluding Remarks and Future Work

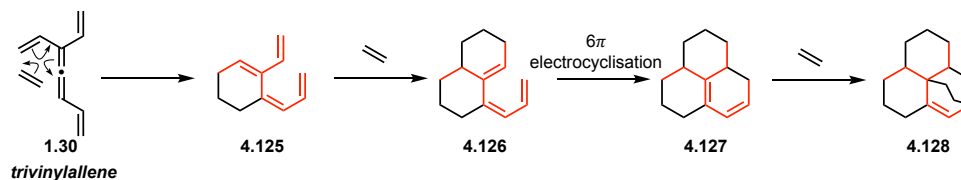
Reported in this chapter is the first synthesis of the parent trivinylallene molecule (**1.30**) utilising a palladium(0)-catalysed Negishi-type cross-coupling approach involving a 1,3-transposition, which resulted in a selective, scalable synthesis. A similar approach was applied to the first synthesis of substituted trivinylallenes, enabling a brief study to be undertaken in order to understand the requirements for stability (Scheme 4.5.1). Substitution at the allenic position was found to be necessary to isolate trivinylallenes, although this does not preclude the use of the less stable trivinylallenes as reactive intermediates in syntheses. Analysis of the geometry of trivinylallene (**1.30**) and select mono-substituted derivatives (**4.56** and **4.58**) found these molecules to have similar lowest energy conformers to that of tetravinylallene (**1.31**) and 1,1-divinylallene (**1.29**).



Scheme 4.5.1 Successful synthesis of trivinylallenes using a palladium catalysed cross-coupling approach

With access to these molecules for the first time, Diels–Alder reactions were conducted to determine the ability of trivinylallenes to participate in pericyclic sequences (Scheme 4.5.2). Trivinylallene (**1.30**) was found to undergo a pericyclic cascade to form a heptacyclic structure containing ten new stereocentres with each reaction in the sequence occurring diastereoselectively (Scheme 4.5.2). Mono-substituted trivinylallenes at the allenic position, were found to form mono-Diels–Alder adducts with lower selectivity than the parent molecule.

The reactivity of trivinylallene (**1.30**) suggests that this molecule is a potentially useful intermediate in natural product synthesis. Use of organocatalysts or Lewis acids may lead to improved regioselectivity in the case of Diels-Alder reactions with substituted trivinylallenes.



Scheme 4.5.2 Observed reactivity of trivinylallene (**1.30**) in a pericyclic cascade. The embedded structure of trivinylallene in each of the compounds is highlighted in red

Future work will probe the stability of trivinylallenes such as **4.162** and **4.163** whereby substituents, different to those presented in this study, are incorporated at the various alkenic positions to further understand the implications of steric and electronic effects on the trivinylallene molecule (Figure 4.5.1 (a)). The synthesis of the *tert*-butyl derivative of trivinylallene (**4.164**), is also of interest as it may display alternative Diels-Alder reactivity to **4.56** and **4.58** given that preliminary calculations suggest that the lowest energy conformation contains the *s-cis* diene at the position adjacent to the allenic *tert*-butyl group (Figure 4.5.1 (b)). The tri-*tert*-butyl-trivinylallene (**4.165**) is also an interesting target molecule to investigate as a potentially stable trivinylallene that does not carry substitution at the allenic position.

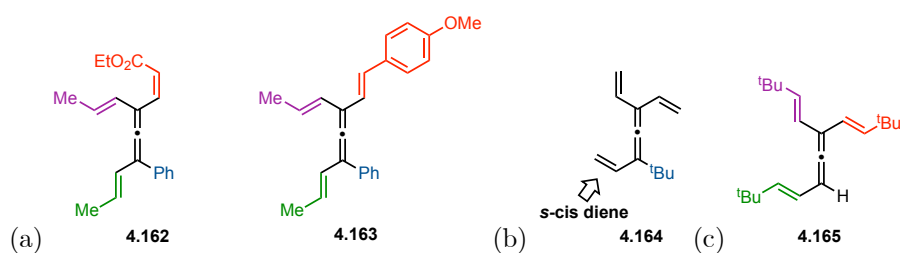


Figure 4.5.1 Substituted trivinylallenes of interest for future work

5

Multivinylallenes

5.1 Introduction

Preamble

While carrying out the research described in Chapter 3 and Chapter 4, it became evident that studies of the divinylallenes (**1.28** and **1.29** in Figure 5.1.1) had primarily focused on the synthesis and Diels–Alder reaction of these molecules, with only brief reports regarding their physical properties.^[38] ^[160] ^[46] The reported syntheses of **1.28** and **1.29** were either lengthy or not regioselective.^[38] ^[46]

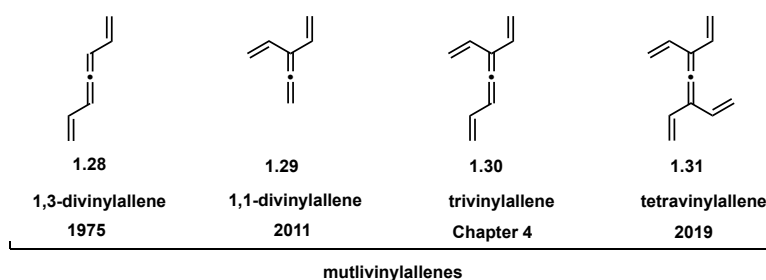


Figure 5.1.1 The family of multivinylallene molecules

We believed that an improved synthesis of the divinylallenes could be achieved using a cross-coupling approach thereby providing a unified synthesis of the multivinylallenes. Additionally, we believed this would permit a direct comparative study of the ^1H and ^{13}C NMR spectra multivinylallenes as well as their UV-Visible properties in order to identify any trends within the series of molecules (Figure 5.1.1).

5.1.1 Di-conjugated allenes

Contrary to the higher members of the multivinylallene family, various di-conjugated allenes have been reported (Figure 5.1.2). In this series of allenes, the two unsaturated units can be attached to the central allene in either a 1,1- or 1,3-substitution pattern.

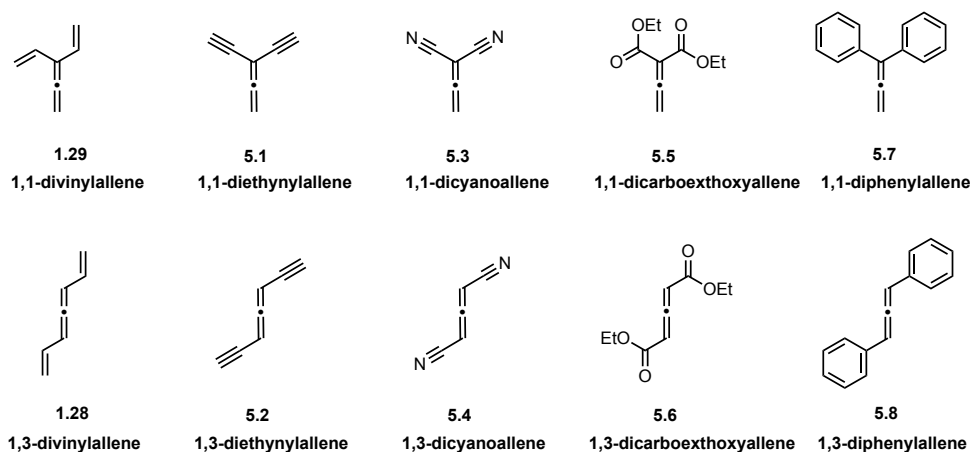
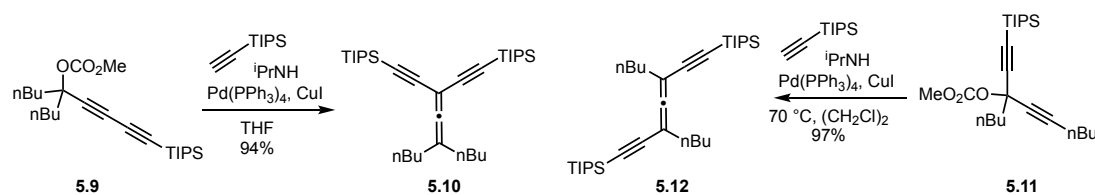


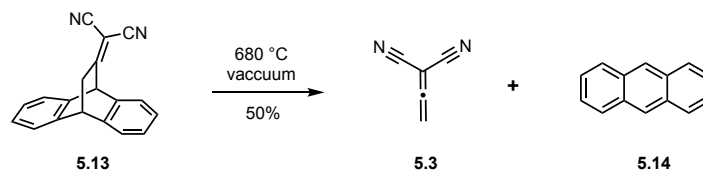
Figure 5.1.2 Di-conjugated allenes with both 1,1- and 1,3-disubstitution patterns

The parent diethynylallene molecules (**5.1** and **5.2**) have not been reported, however, various substituted examples have been studied. Examples of diethynylallenes (**5.10** and **5.12** in Scheme 5.1.1) have been synthesised by Sonogashira cross-coupling reactions (Scheme 5.1.1).^[188] In particular, 1,3-diethynylallenes were investigated for their potential application in materials chemistry.^[188]



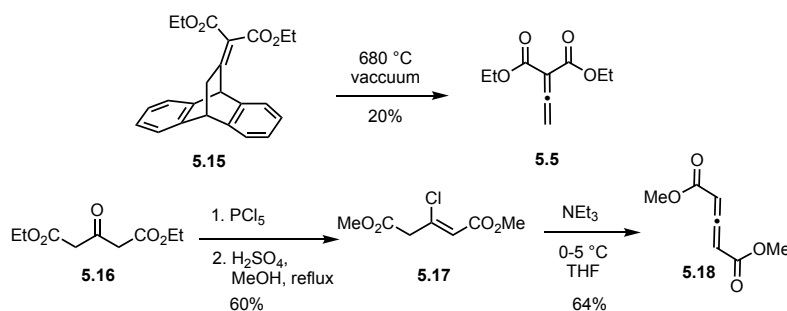
Scheme 5.1.1 Recent syntheses of diethynylallenes using Sonogashira cross-coupling reactions

The synthesis of 1,1-dicyanoallene (**5.3**) was reported *via* a flash-thermolytic retro-Diels–Alder reaction of **5.13** (Scheme 5.1.2).^[189] Upon isolation, **5.3** was found to be an unstable molecule, polymerizing rapidly at 0 °C. Currently, the 1,3-dicyanoallene (**5.4**) is not reported in the literature.



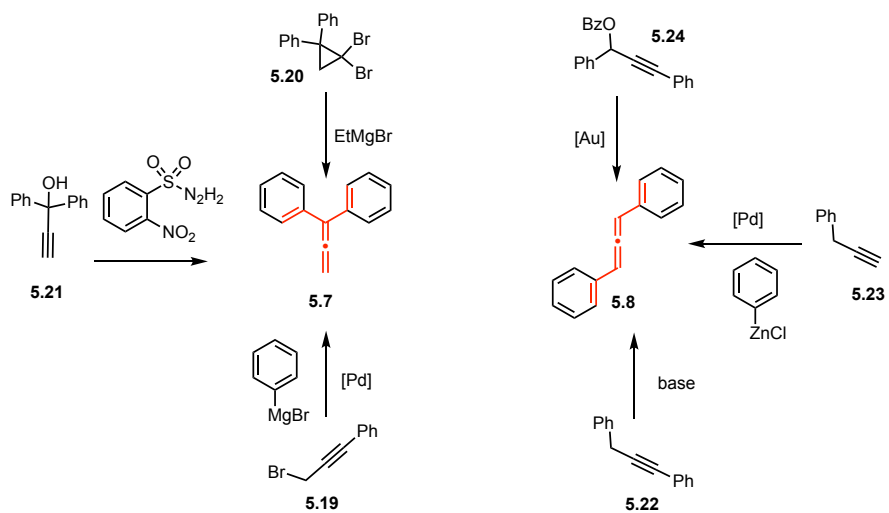
Scheme 5.1.2 Synthesis of 1,1-dicyanoallene *via* a thermolytic retro-Diels–Alder reaction

1,1-Dicarboethoxyallene (**5.5**) has also been synthesized using a thermolytic retro-Diels–Alder reaction, whereby **5.5** was found to be stable for several days at room temperature (Scheme 5.1.3).^[189] The 1,3-dicarbomethoxyallene **5.18** has also been synthesized *via* a three-step sequence from **5.16** and was reportedly less stable than **5.5** (Scheme 5.1.3).^[190]



Scheme 5.1.3 Reported synthesis of **5.5** and **5.18** using thermolytic retro-Diels–Alder and elimination reactions

1,1-Diphenylallene (**5.7**) and 1,3-diphenylallene (**5.8**) both contain an embedded divinylallene structure (highlighted in red in Scheme 5.1.4). The syntheses of **5.7** and **5.8** do not report special handling of the diphenylallenes, indicating that they are likely more stable than the other di-conjugated allenes discussed. 1,1-Diphenylallene (**5.7**) has been synthesized using a variety of reactions including cross-coupling reactions with **5.19**,^[73] a Doering–LaFlamme rearrangement of **5.20**^[191] and reductive deoxyallenylation of **5.21**^[192] (Scheme 5.1.4).

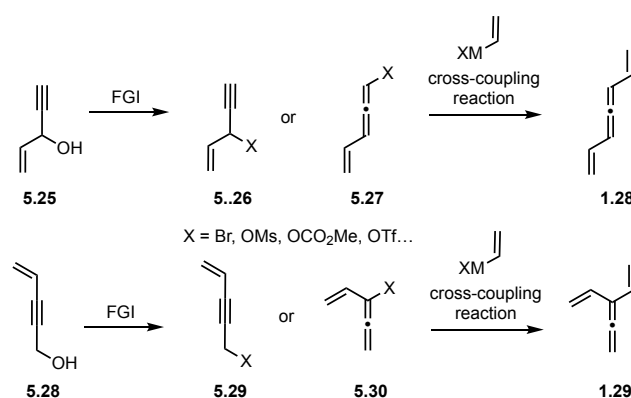


Scheme 5.1.4 Examples of syntheses of 1,1-diphenylallene and 1,3-diphenylallene

1,3-Diphenylallene (**5.8**) has also been synthesized *via* various methods including base-mediated isomerization of **5.22**, ^[193] cross-coupling reactions with **5.23** ^[70] and gold-catalysed rearrangements of **5.24** ^[194] (Scheme 5.1.4).

5.1.2 Aims: Synthesis and study

Conducting a comparative study of the multivinylallenes served as an incentive to identify a unified synthetic approach to this family of molecules. It was envisaged that the cross-coupling approach used to synthesise tri- and tetravinylallene (**1.30** and **1.31** respectively) could also be utilised to synthesise the divinylallenes (**1.28** and **1.29**). The synthesis of 1,3-divinylallene (**1.28**) was proposed using a derivative of enyol **5.25**, such as **5.26** or **5.27**, while 1,1-divinylallene (**1.29**) could be accessed using the enyol regioisomer **5.25** (Scheme 5.1.5). The successful synthesis of trivinylallene using a carbonate electrophilic cross-coupling partner gave confidence regarding the regioselectivity of these reactions to synthesise the divinylallenes selectively.



Scheme 5.1.5. Proposed synthesis of the divinylallenes using a cross-coupling approach

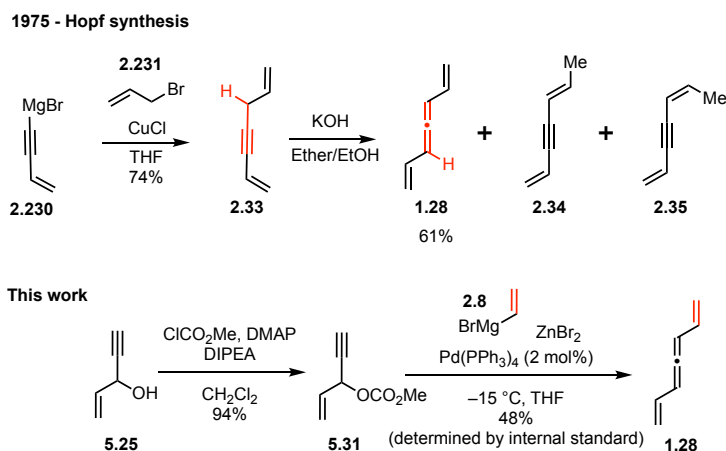
As part of a comparative study, we were interested in determining whether trends, akin to those observed for the dendralene series, would be observed in the multivinylallene series.^[7] In particular, UV-Visible, ¹H NMR and ¹³C NMR spectroscopy and computational studies were of interest as these had previously been used to uncover the diminishing alternation pattern of the dendralene series. ^[7]

5.2 Synthesis of Divinylallenes

As earlier mentioned, both 1,3-divinylallene (**1.28**) and 1,1-divinylallene (**1.29**) have previously been synthesised (see Chapter 2 section 5 for details). Substituted examples have also been reported using various methods (see Chapter 2 for details). Consequently, the following work focused on providing a short and regioselective synthesis of the parent divinylallenes.

5.2.1 1,3-Divinylallene

Prior investigations of the divinylallenes targeted 1,3-divinylallene (**1.28**), whereby the allene functionality was synthesised using the base mediated rearrangement of **2.33** in the final step (Scheme 5.2.1).^[38] Preparatory gas chromatography was required to separate **1.28** from the two additional regioisomers (**2.34** and **2.35**) which also formed during the reaction. We believed a cross-coupling approach using the conditions developed to synthesise trivinylallene, could overcome regioselectivity issues and be applied to the synthesis of 1,3-divinylallene (**1.28**). The synthesis began with the conversion of enol **5.25**, an intermediate of tri- and tetravinylallene syntheses, to carbonate **5.31** (Scheme 5.2.1). Carbonate **5.31** did not rearrange to the enyne structure and could be stored neat for an extended time at $-20\text{ }^{\circ}\text{C}$ without noticeable decomposition. Subsequent palladium(0)-catalysed Negishi cross-coupling reaction with vinylmagnesium bromide (**2.8**) selectively gave 1,3-divinylallene (**1.28**) as a THF solution in 48% with no other regioisomers being observed (compared to the mixture of isomers obtained by the Hopf synthesis as shown in Figure 5.2.1). Aqueous extraction of THF from an *n*-pentane solution of 1,3-divinylallene provided a THF-free solution of **1.28**, although it should be noted that significant loss of material was incurred during this process.

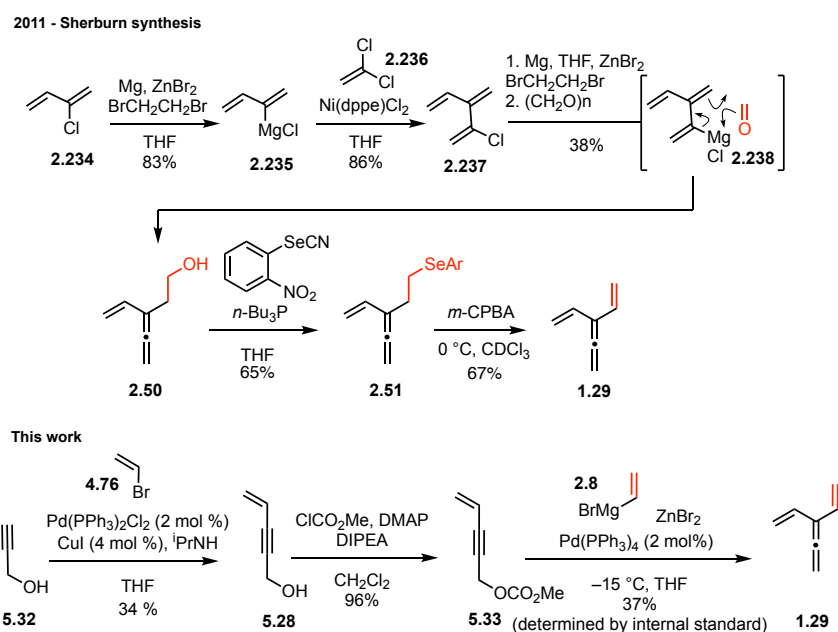


Scheme 5.2.1 Comparison of 1,3-divinylallene (**1.28**) syntheses *via* either an isomerisation reaction or a Negishi cross-coupling reaction. The final bond forming steps are highlighted in red

Comparatively, the 1975 synthesis gave neat 1,3-divinylallene (**1.28**) in 45% yield over two steps, but required purification by gas chromatography, while our cross-coupling approach gave **1.28** in overall 35% yield regioselectively as a THF solution in three steps from acrolein.

5.2.2 1,1-Divinylallene

The first synthesis of 1,1-divinylallene (**1.29**) was reported in 2011 and utilised an oxidative-elimination reaction to furnish **1.29** as a CDCl₃ solution in the final step.^[46] We believed a cross-coupling approach using the conditions developed to synthesise trivinylallene could also be applied to divinylallene **1.29**. The new synthesis of 1,1-divinylallene began with the Sonogashira cross-coupling of propargyl alcohol (**5.32**) and vinylbromide (**4.76**) to give enynol **5.28** (Scheme 5.2.3). The carbonate (**5.33**) was subsequently synthesised and as with **5.31**, could be stored at -20 °C without decomposition. Palladium(0)-catalysed Negishi cross-coupling reaction with vinylmagnesium bromide (**2.8**) gave 1,1-divinylallene as a THF solution in 37%. Again, no other regioisomers were observed and 1,1-divinylallene (**1.29**) was handled as a THF solution. Aqueous extraction provided a THF-free *n*-pentane solution of 1,1-divinylallene.



Scheme 5.2.3 Comparison of the syntheses of 1,1-divinylallene (**1.29**) *via* either an elimination reaction or a Negishi cross-coupling reaction. The final bond forming steps are highlighted in red

Comparatively, the 2011 synthesis gave 1,1-divinylallene (**1.29**) in 12% yield over five steps as a CDCl₃ solution, while our cross-coupling approach also gave **1.29** in 12% yield as a THF solution in three steps from propargyl alcohol (**5.32**).

5.3 Diels–Alder reactions of the Divinylallenes

Diels–Alder reactions of the [n]dendralenes and tetravinylethylene has been used to probe the reactivity of these hydrocarbons.^{[7] [17]} The multivinylallenes can form a variety of multicyclic frameworks via a sequence of pericyclic reactions (Figure 5.3.1). Chapters 3 and 4 described the reactivity of tri- and tetravinylallene (**1.30** and **1.31**) for the first time. These molecules were found to be reactive dienes that generated less reactive mono-adducts. 1,1-Divinylallene (**1.29**) has previously been reported to participate in a diene-transmissive Diels–Alder sequence to form a core tricyclic structure (**4.123**).^[46] A similar Diels–Alder sequence was later applied to the synthesis of pseudopterosin.^[82]

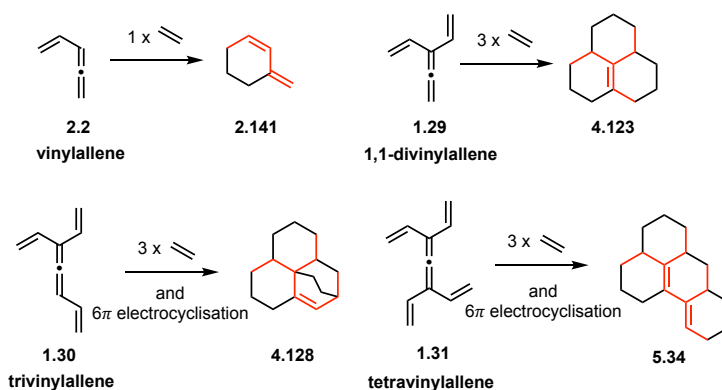
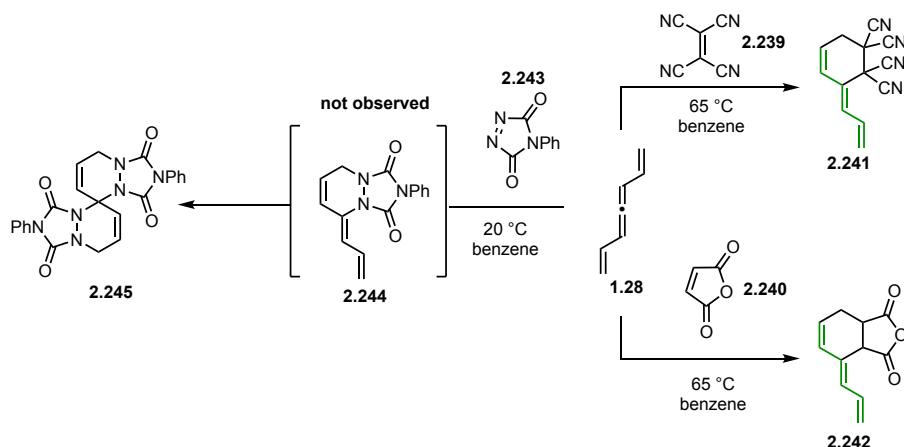


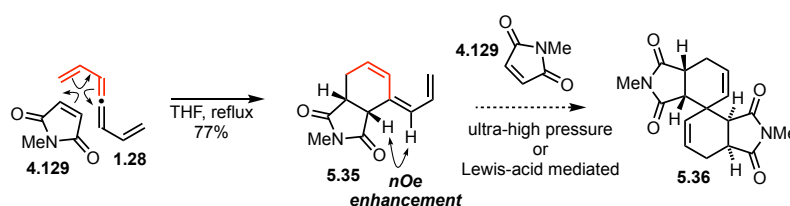
Figure 5.3.1 Vinylallenes have been used to generate a variety of multicyclic frameworks through a sequence of pericyclic reactions. The embedded vinylallene structures are highlighted in red

Previously, Diels–Alder reactions of 1,3-divinylallene (**1.28**) with TCNE (**2.239**) or maleic anhydride (**2.240**) only resulted in isolation of the mono-Diels–Alder adduct (Scheme 5.3.1). A second cycloaddition to form a [5.5]spirobicycle was only possible using the highly reactive dienophile PTAD (**2.243**).^[38] The conjugated triene unit (highlighted in green in Scheme 5.3.1) was cited as the likely reason for the poor reactivity of the monoadducts.



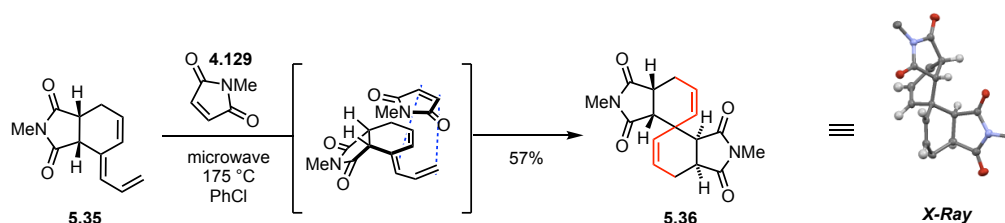
Scheme 5.3.1 Previously reported Diels–Alder reactions of 1,3-divinylallene by Hopf and co-workers [38] intrigued by the lack of reactivity displayed by mono-adducts **2.241** and **2.242**, we sought to reinvestigate the Diels–Alder reactivity of 1,3-divinylallene (**1.28**). A successful two-fold Diels–Alder sequence could have potential applications in the synthesis of spirobicyclic natural products^[195] and drug discovery.^[196]

Heating a 0.050 M solution of 1,3-divinylallene (**1.28**) at reflux in the presence of NMM (**4.129**) proceeded to generate mono-adduct **5.35** as a single isomer (Scheme 5.3.2). The need to heat this reaction for the Diels–Alder to proceed suggests that **1.28** is the least reactive of the multivinylallenes. By comparison, the reaction of trivinylallene (**1.30**) with NMM was complete within an hour at room temperature at a concentration of 0.028 M. A potential reason for the lower reactivity of **1.28** is the preferred *s-trans*, *s-trans* conformer that the molecule adopts, which was previously determined by IR studies.^[160] The reaction of mono-adduct **5.35** in a second Diels–Alder reaction with excess NMM (**4.129**) in an ultra-high-pressure reactor (pressure of 20 kbar at *ca.* 298 K) produced only trace quantities of the desired spirobicycle (**5.36**). Primarily decomposition of the monoadduct (**5.35**) was observed. Lewis-acid catalysed Diels–Alder reactions either resulted in no reaction or decomposition of **5.35**. This indicated that such conditions were not conducive to **5.35** adopting the *s-cis* diene conformation necessary for the Diels–Alder reaction (as shown in Scheme 5.3.2).



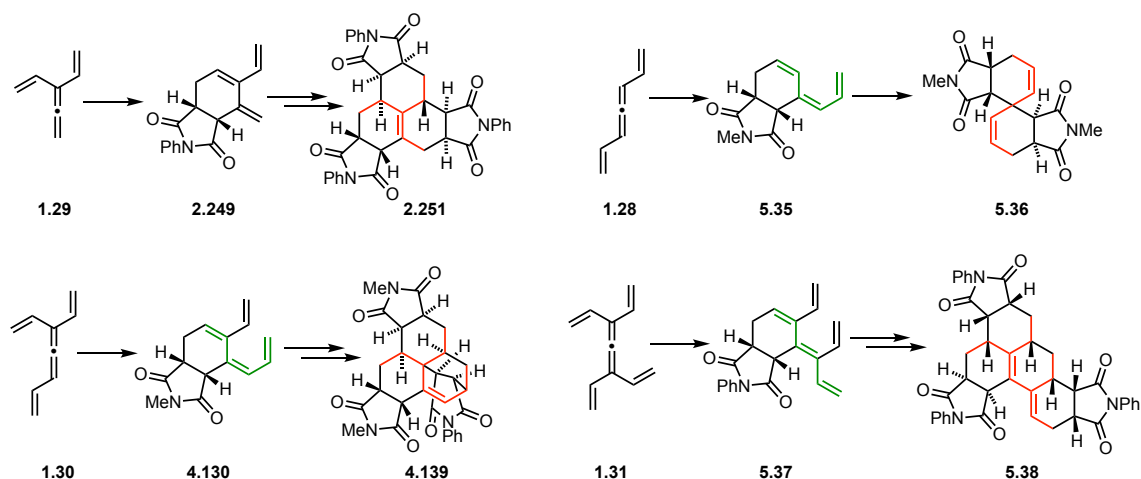
Scheme 5.3.2 Diels–Alder reactivity of 1,3-divinylallene (**1.28**) with NMM (**4.129**) and initial attempts to form the [5.5]spirobicycle (**5.36**). The diene component is highlighted in red

Returning to thermal conditions for the second Diels–Alder reaction, high temperatures and extended reaction times were investigated. Heating mono-adduct **5.35** in the presence excess NMM (**4.129**) at reflux in benzene for 48 hours was found to generate [5.5]spirobicyclic (**5.36**) in yields of *ca.* 5% (Scheme 5.3.3). Neither the addition of BHT (in order to prevent decomposition of **5.35**) nor heating at reflux in toluene were able to improve yields for this reaction. Improved conditions were found in the case of microwave irradiation at 175 °C, which reduced the reaction time to 2.5 hours and gave **5.36** in 57 % yield. The stereochemistry of **5.36** was confirmed by single crystal X-ray analysis (Scheme 5.3.3). The structure implied that the second Diels–Alder occurred in an *endo* fashion with NMM (**4.129**) approaching the diene from the less sterically encumbered face as shown in Scheme 5.3.3.



Scheme 5.3.3 Successful synthesis of [5.5]spirobicyclic **5.36** using microwave reaction conditions. The X-ray structure of **5.36** is shown with some hydrogens omitted for clarity. The embedded structure of 1,3-divinylallene in **5.36** is highlighted in red

These results demonstrate that each of the multivinylallenes reacted selectively in Diels–Alder reactions to form a mono-adduct, which could further react to form various multicyclic frameworks (**2.251**, **5.36**, **4.139** and **5.38**) (Scheme 5.3.4). Where through-conjugation is present in the mono-adduct (highlighted in green for **5.35**, **4.130** and **5.37**), the subsequent Diels–Alder required heating to proceed. The difference in reactivity of 1,3-divinylallene (**1.28**) compared to the other multivinylallenes (**1.29**, **1.30** and **1.31**) suggests that the 1,1-divinyl substitution pattern results in the presence of an *s-cis* diene and thus a more facile Diels–Alder reaction.



Scheme 5.3.4 Summary of the pericyclic cascades conducted with the multivinylallenes. The multivinylallene structures embedded in the multicyclic frameworks are highlighted in red

5.4 NMR Studies of the Multivinylallenes

Previously, NMR studies have been utilised to uncover a diminishing alternation pattern in the dendralene family of molecules, which was also reflected in UV-Visible studies.^[7] Thus, comparison of the multivinylallenes was of interest to determine if any trends regarding the chemical environment of these molecules could be observed. For this study the ^1H NMR and ^{13}C NMR spectra of allene (**1.23**), vinylallene (**2.2**), 1,3-divinylallene (**1.28**), 1,1-divinylallene (**1.29**), trivinylallene (**1.30**) and tetravinylallene (**1.31**) were obtained (Figure 5.4.1).

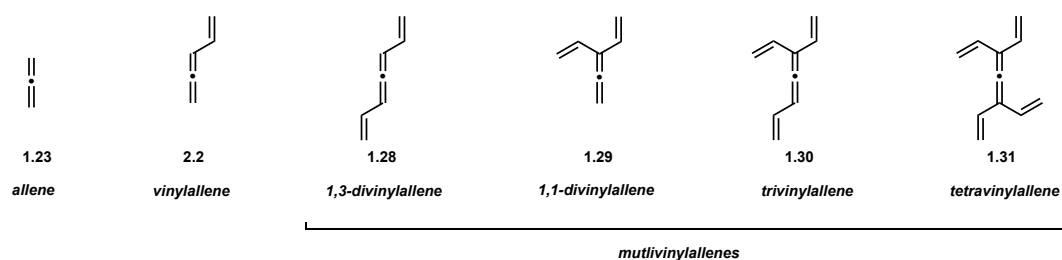


Figure 5.4.1 Allenes studied by ^1H NMR and ^{13}C NMR spectroscopy to determine trends within the multivinylallene family

For the purpose of this study, allene (**1.23**)^[197] and vinylallene (**2.2**)^[70] were synthesised according to literature procedures and CDCl_3 solutions of **1.23** and **2.2** were obtained. In the case of **1.23**, the synthesised allene gas was bubbled through a CDCl_3 solution, while a THF-free isopentane solution of **2.2** was obtained *via* aqueous extraction, with subsequent removal of isopentane from a CDCl_3 solution under reduced pressure.

5.4.1 ^1H NMR Spectra

For the purposes of the following discussion, H_A (red) refers to the allenic methylene protons, H_B (blue) refers to the allenyl/butadienyl methine protons and H_C (green) refers to the vinylic methine protons (Figure 5.4.2).

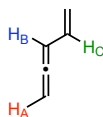


Figure 5.4.2 Assignment of protons for discussion of ^1H NMR spectra

Comparison of the ^1H NMR spectra showed that the incorporation of vinylic groups resulted in a downfield shift of the methylene allenic protons (H_A) (**1.23** \rightarrow **2.2** \rightarrow **1.29** in Figure 5.4.3). This implies that the two halves of the allene are not isolated across the central sp -hybridised carbon. An equivalent trend was observed for the butadienyl methine (H_B) protons, where the incorporation of vinylic groups resulted in a downfield shift (**2.2** \rightarrow **1.28** \rightarrow **1.30** in Figure 5.4.3).

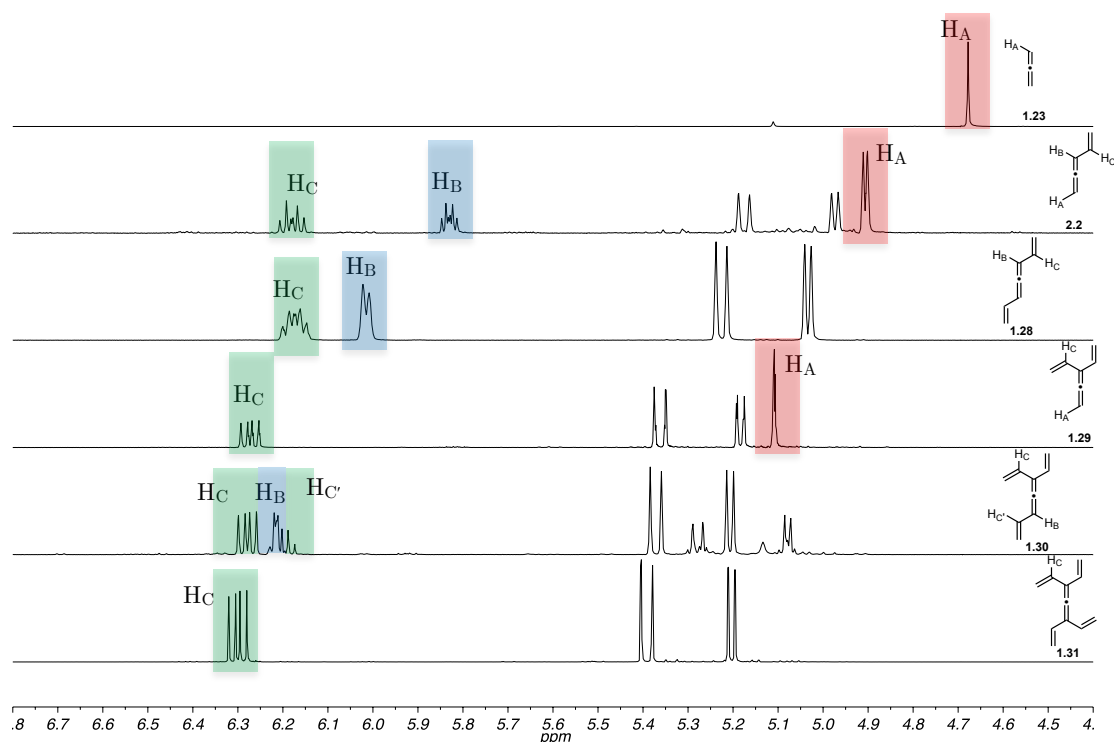


Figure 5.4.3 Comparative ^1H NMR spectra of allene (**1.23**), vinylallene (**2.2**), 1,3-divinylallene (**1.28**), 1,1-divinylallene (**1.29**), trivinylallene (**1.30**) and tetravinylallene (**1.31**) (in order from top to bottom)

The vinylic methine (H_C) protons showed a downfield shift moving from a vinylallene unit (as in **2.2**, **1.28** and **1.30** (H_C') in Figure 5.4.3) to a 1,1-divinylallene unit (as in **1.29**, **1.30** and **1.31** in Figure 5.4.3). A small downfield shift of the H_C protons is observable between the compounds containing a 1,1-divinylallene unit (**1.29** \rightarrow **1.30** \rightarrow **1.31** in Figure 5.4.3). It is also worth noting the complex multiplicity observed in the case of the H_B and H_C protons of 1,3-divinylallene (**1.28**), indicative of magnetic non-equivalence.

Comparison of 1,1-divinylallene (**1.29**) and tetravinylallene (**1.31**) with [3]dendralene (**1.8**) and tetravinylethylene (**1.27**) was of interest in order to understand the impact of the allenic group on a 1,1-divinyl functionality (Table 5.4.1). Minor differences in the chemical shifts between the allenic protons of 1,1-divinylallene (**1.29**) and the alkenic protons of [3]dendralene (**1.8**) were observed (only a 0.05 ppm difference). The vinylic protons of tetravinylethylene (**1.27**) were the most deshielded, followed by [3]dendralene (**1.8**) and then tetravinylallene (**1.31**).





Hydrocarbon	Methylene (H_A type) chemical shift (ppm)	Methine (H_C type) chemical shift (ppm)
[3]dendralene  (1.8)	5.16	6.46
tetravinylethylene  (1.27)	—	6.62
1,1-divinylallene  (1.29)	5.11	6.27
tetravinylallene  (1.31)	—	6.30

Table 5.4.1 1H NMR comparison of related π -bond rich hydrocarbons

5.4.2 ^{13}C NMR Spectra

For the purposes of the following discussion, C_1 refers to the sp -hybridised allenic carbon (red), C_2 refers to sp^2 -hybridised allenic methylene carbon (blue), C_3 refers to the sp^2 -hybridised methine carbon (green) and C_4 refers to the sp^2 -hybridised 1,1-divinyl substituted carbon (purple) (Figure 5.4.4). The comparison of the ^{13}C NMR spectra (Figure 5.4.5) of this set of molecules was of interest to determine if similar patterns could be observed as in the ^1H NMR spectra.

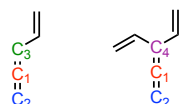


Figure 5.4.4 Assignment of carbons for discussion of ^{13}C NMR spectra

Comparison of the ^{13}C NMR showed that all of the allenes displayed a similar chemical shift for the central sp -hybridised carbons (C_1). Incorporation of vinylic groups led to a downfield shift of the C_2 (**1.23** \rightarrow **1.2** \rightarrow **1.29** in Figure 5.4.5), C_3 (**2.2** \rightarrow **1.28** \rightarrow **1.30** in Figure 5.4.5) and C_4 (**1.29** \rightarrow **1.30** \rightarrow **1.31** in Figure 5.4.5).

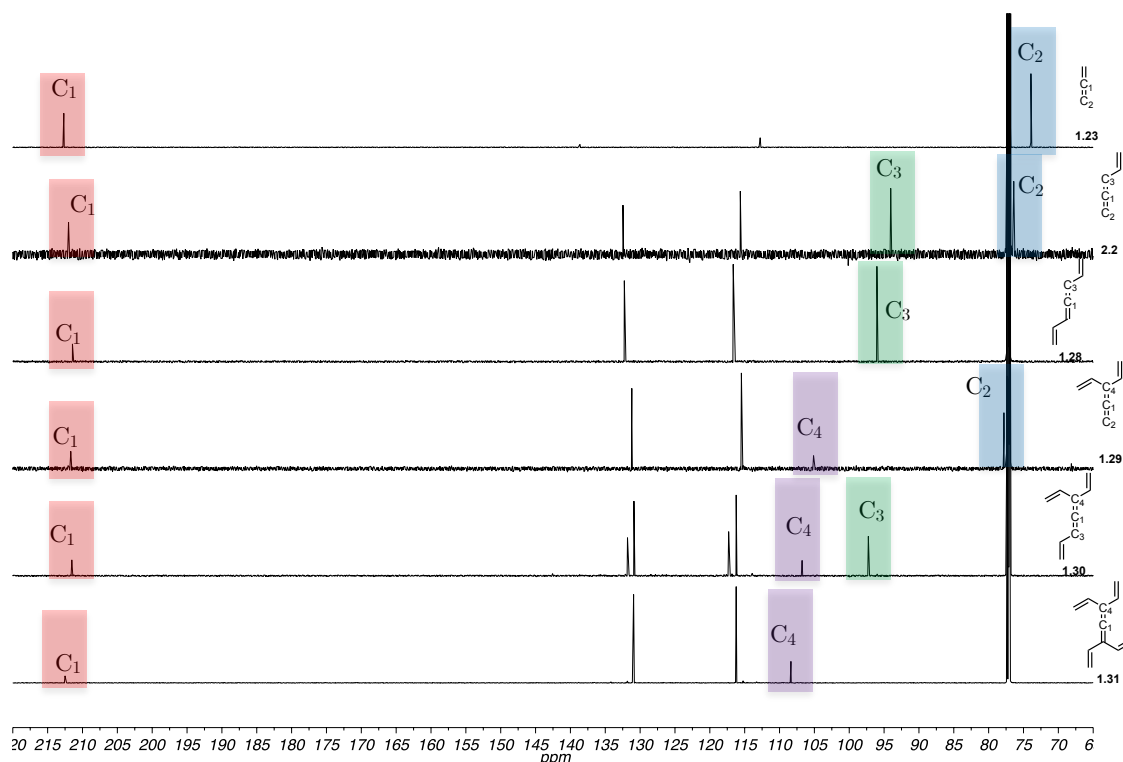


Figure 5.4.5 Comparative ^{13}C NMR spectra of allene (**1.23**), vinylallene (**2.2**), 1,3-divinylallene (**1.28**), 1,1-divinylallene (**1.29**), trivinylallene (**1.30**) and tetravinylallene (**1.31**) (in order from top to bottom)

The ^{13}C NMR spectra showed similar trends to those of the ^1H NMR spectra, whereby sequential incorporation of vinylic groups resulted in a downfield shift for the allenic carbons (i.e. C_2 , C_3 and C_4 carbons). This trend was not reflected in the methylene and methine vinylic carbons (unlabelled peaks for **2.2**, **1.28**, **1.29**, **1.30** and **1.31** in Figure 5.4.5), which did not significantly alter chemical shift with the incorporation of additional vinylic groups. It is also worth noting that the most symmetrically substituted compounds, allene (**1.23**) and tetravinylallene (**1.31**), display the most deshielded sp -hybridised allenic (C_1) carbons.

Comparison with [3]dendralene (**1.8**) and tetravinylethylene (**1.27**) showed little difference in the shift of the vinylic methine carbon (Table 5.4.2). A more noticeable difference between the molecules is observed at the sp^2 -hybridised 1,1-divinyl substituted carbon, located at either an alkenic or allenic position. Tetravinylallene (**1.31**) displayed the most shielded environment with [3]dendralene (**1.8**) being the least shielded of this series.




Hydrocarbon	Vinylic methine carbon (ppm)	1,1-Divinyl-substituted carbon (ppm)
[3]dendralene 	135.9	144.7
tetravinylethylene 	134.7	136.7
tetravinylallene 	130.9	108.4

Table 5.4.2 ^{13}C NMR comparison of π -bond rich hydrocarbons

The NMR studies indicated that the sequential addition of vinylic groups to the central allene resulted in both allenic and vinylic protons becoming increasingly deshielded (Figure 5.4.3). This was similarly observed for certain allenic carbons although the central carbon of the allene became increasingly shielded (Figure 5.4.5). This suggests that with the addition of each vinylic group, the overall electron density shifts towards the central allenic carbon. To elucidate additional trends, attention was turned to UV-Visible studies of the multivinylallenes.

5.5 UV-Visible Studies of the Multivinylallenes

The electronic difference between cross-conjugation and through conjugation is observable using UV-Visible absorption, making it a useful technique to study π -bond rich hydrocarbons. The all-*E*-linear polyene series are a set of through conjugated molecules (see Chapter 1 section 3 for more details), whereby additional conjugation results in absorption at an increasing wavelength. Particularly relevant to this work is 1,3-butadiene (**2.1**), which displays a single absorption maximum of $\lambda_{\text{max}} = 217 \text{ nm}$ (ϵ 21 000) in the *s-trans* conformation.^[198] Lower intensity absorptions are observed for *s-cis*-diene conformations (*ca.* ϵ 10 000).^[198] The [4-12]dendralenes, a family of cross-conjugated molecules, have a single absorption maximum of $\lambda_{\text{max}} = 215 \text{ nm}$ with an overall increase in the extinction coefficient (ϵ 20 600 – 63 600), albeit with an up-down alternation between even and odd membered dendralenes.^[7] As such, the [n]dendralenes do not display conjugation greater than that of 1,3-butadiene (**2.1**). The case of [3]dendralene (**1.8**) is an exception, displaying two absorption maxima of $\lambda_{\text{max}} = 205 \text{ nm}$ (ϵ 20 600) and 231 nm (ϵ 14 500), which have been attributed to the *s-cis*, *s-trans* and *s-cis*, *s-cis* conformations respectively (Figure 5.5.1).^[7] The related molecule tetravinylethylene (**1.27**) has two absorption maxima of $\lambda_{\text{max}} = 225 \text{ nm}$ and 284 nm correlating to the butadiene and hexatriene portions of the molecule (highlighted blue in Figure 5.5.1).^[17]

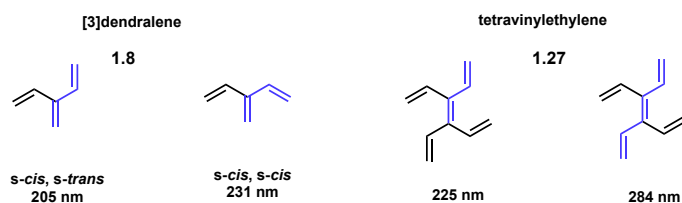


Figure 5.5.1 Conjugation observed in UV-Visible studies of π -bond rich hydrocarbons with the conjugated portion of the molecules highlighted in blue

To probe the UV-Visible properties of the multivinylallenes and how they relate to other π -bond rich hydrocarbons, *n*-hexane solutions of the multivinylallenes, as well as vinylallene, were prepared. The spectra obtained are displayed in Figure 5.5.2 and Table 5.1.1.

Vinylallene (**2.2**) was found to have an absorption maximum of $\lambda_{\text{max}} = 215 \text{ nm}$ (ϵ 21 000) thereby displaying similar absorption to that of *s-trans*-1,3-butadiene (**2.1**). 1,1-Divinylallene (**1.29**) displayed two absorption maxima of $\lambda_{\text{max}} = 206 \text{ nm}$ (ϵ 20 000) and 248 nm (ϵ 8 300), while 1,3-divinylallene (**1.28**) was found to have two distinct absorption maxima of $\lambda_{\text{max}} = 224 \text{ nm}$ (ϵ 69 000) and 230 nm (ϵ 67 000), matching previously reported

values. These results indicate that the two divinylallenes have distinct electronic properties. 1,1-Divinylallene (**1.29**) and vinylallene (**2.2**) display similar spectra indicating comparable electronic properties. The $\lambda_{\text{max}} = 248$ nm of 1,1-divinylallene (**1.29**) has previously been attributed to a higher energy conformation.^[46] Additional peaks in the spectra of **2.2** and **1.29** may suggest other conformers are also present. 1,3-Divinylallene (**1.28**) displays absorption at longer wavelengths than vinylallene (**2.2**) and 1,1-divinylallene (**1.29**), suggesting additional conjugation to that of **2.2** and **1.29** albeit, a departure from the conjugation of extended linear polyenes.^[198] The difference of only 6 nm between the two absorption maxima is unlikely to be due to the presence of multiple conformations as was proposed for [3]dendralene (Figure 5.5.1).^[160] [7]

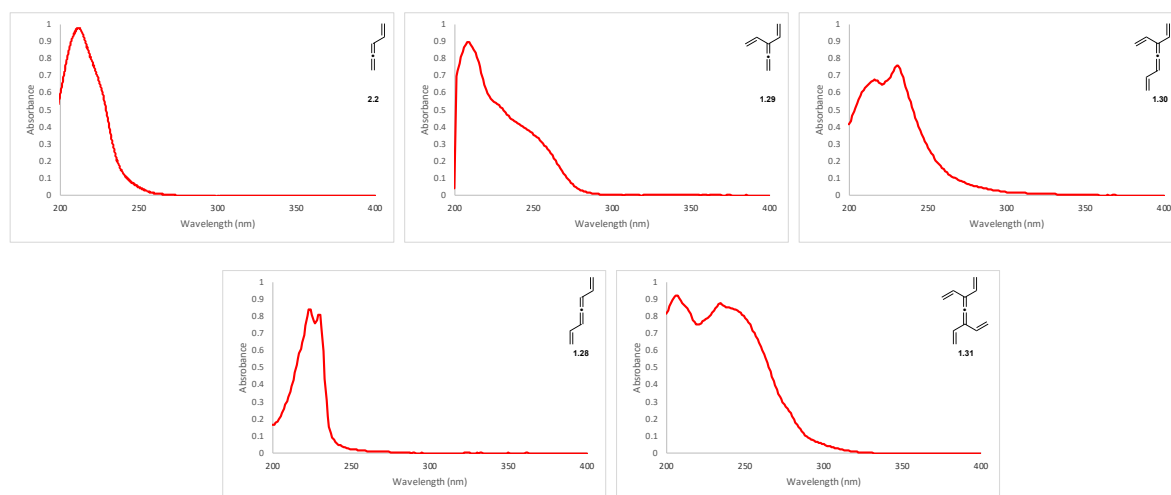


Figure 5.5.2 UV-Visible spectra of the multivinylallene series categorised according to the symmetry of the vinylallene

Trivinylallene (**1.30**) also displays two absorption maxima of $\lambda_{\text{max}} = 216$ nm (ϵ 20 300) and 230 nm (ϵ 22 600), suggesting again that conjugation does not exceed that of *s-trans*-1,3-butadiene. Tetravinylallene (**1.31**) exhibits two absorption maxima of $\lambda_{\text{max}} = 206$ nm (ϵ 95 000) and 234 nm (ϵ 89 000), thus absorbing at approximately the same wavelengths as [3]dendralene (**1.8**) (Table 5.5.1), although it does not appear to display through-conjugation, as per tetravinylethylene (**1.27**) (Table 5.5.1).








Hydrocarbon (in <i>n</i> -hexanes)	λ_{max} (nm)	ϵ ($\text{M}^{-1}\text{cm}^{-1}$)	Symmetry of lowest energy conformer
vinylallene 	211	21 000	C_1
1,1-divinylallene 	206 248	20 000 8 300	C_1
1,3-divinylallene 	224 230	69 000 67 000	C_2
trivinylallene 	216 230	20 300 22 600	C_1
tetravinylallene 	206 234	95 000 89 000	C_2
[3]dendralene 	205 231	20 600 14 500	C_1
tetravinylethylene 	225 284	10 700 14 800	C_2

Table 5.5.1 Comparison of UV-Visible studies of the multivinylallene series

Contrary to the ^1H and ^{13}C NMR spectra, the UV-Visible studies do not indicate a correlation between the number of vinyl substituents and the absorption spectra. Rather, a clear distinction in the intensity of absorption between C_2 symmetric (1,3-divinylallene (**1.28**) and tetravinylallene (**1.31**)) and C_1 symmetric (vinylallene (**2.2**), 1,1-divinylallene (**1.29**) and trivinylallene (**1.30**)) vinylallenes was observed, with higher order symmetry correlating to a larger extinction co-efficient.

As the intensity of absorption cannot not be accounted for simply by the summation of 1,3-butadiene units, it was considered that the C_2 symmetric multivinylallenes exhibit conjugation throughout the molecule leading to stronger absorption. Coarctate orbitals have previously been proposed in cyclic systems to describe Möbius aromaticity.^[199] More recently it was proposed that symmetric linear cumulenic systems have degenerate helical orbitals thereby enabling conjugation throughout the molecule (Figure 5.5.3).^{[14] [200]} The helical orbitals display equal and opposite handedness for the HOMO and HOMO+1 (as well as the LUMO and LUMO+1).^[14] This is different to the traditional representation of allene orbitals (as shown at the top of Figure 5.5.3).

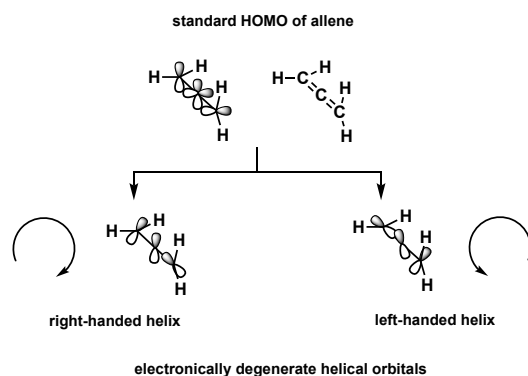


Figure 5.5.3 Helical orbitals of symmetric allenes compared to the standard HOMO of allenes that have a nodal plane at the central sp-hybridised carbon

Preliminary calculations of the multivinylallenes suggest that 1,3-divinylallene (**1.28**) and tetravinylallene (**1.31**) do have degenerate helical orbitals (HOMO, HOMO +1 and LUMO, LUMO +1 in Figure 5.5.4). Comparatively, vinylallene (**2.2**) displays conjugation at the butadiene portion of the molecule and exhibits a nodal plane at the central sp-hybridised carbon (Figure 5.5.4). This is in line with the standard depiction of allenic orbitals (as shown at the top of Figure 5.5.3), which are perpendicular on either side of the central allenic carbon.

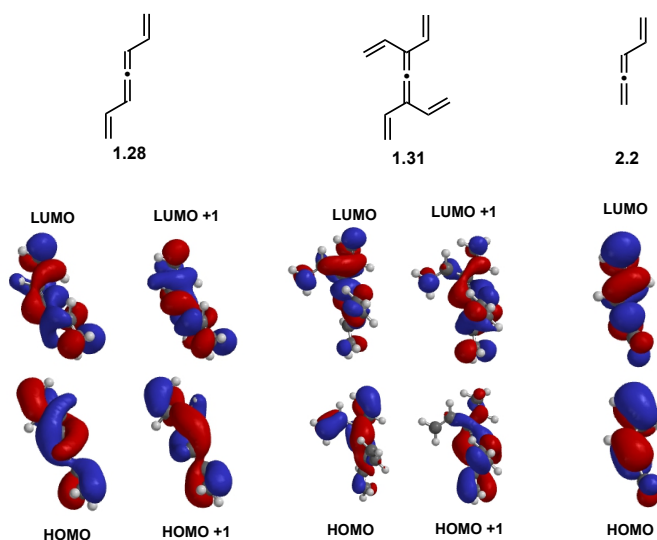


Figure 5.5.4. Preliminary calculations for frontier orbitals of 1,3-divinylallene (**1.28**), tetravinylallene (**1.31**) and vinylallene (**2.2**). TD-DFT calculations were performed with B3LYP/6-311+G** using lowest energy conformations that were geometry optimised with MP2/cc-PTVZ. The calculations were conducted using the Spartan 18 software package

It is likely that the orbital degeneracy is a factor contributing to the high intensity of absorption observed in the UV-Visible studies, however, additional investigations, including higher level calculations, are required to understand the observed electronic properties of **1.28** and **1.31**. This would be of particular interest given that the potential application of molecules with helical orbitals to linear carbon wires has been noted.^[15]

5.6 Stability of the Multivinylallenes

The relative stability of π -bond rich hydrocarbons is of interest as it contributes to understanding the structure-reactivity relationship of this broad family of molecules. Trends obtained from such studies additionally enable predictions regarding the stability of unknown molecules yet to be made.

The half-life of 1,1-divinylallene (**1.29**) has previously been reported and that of tetravinylallene (**1.31**) is disclosed in Chapter 3 (Figure 5.6.1).^[46] The reactivity of 1,3-divinylallene (**1.28**) is alluded to in prior studies, which states that **1.28** can be stored for several hours neat although it readily polymerised when exposed to air, however, a half-life was not reported.^[38] Unfortunately, our syntheses of **1.28**, **1.29** and **1.30** made it difficult to obtain solutions of these compounds in deuterated solvents at comparable concentrations to enable useful studies. Accordingly, the relative stability is provided in Figure 5.6.1 based on observations obtained during the handling of these molecules.

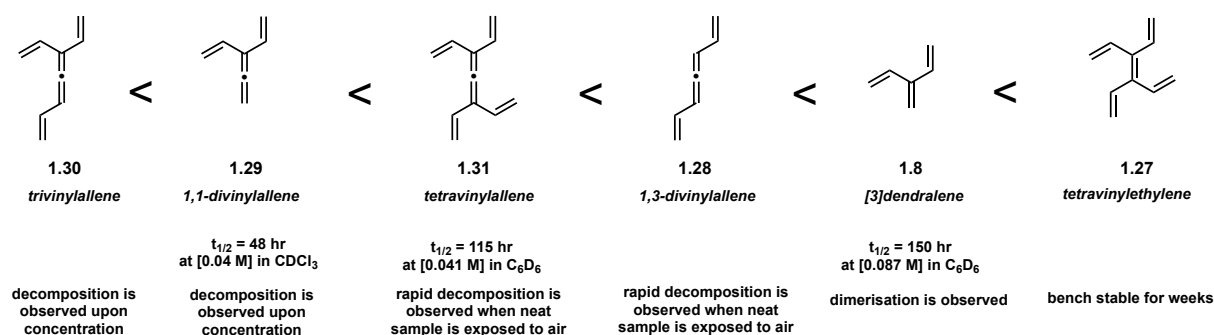
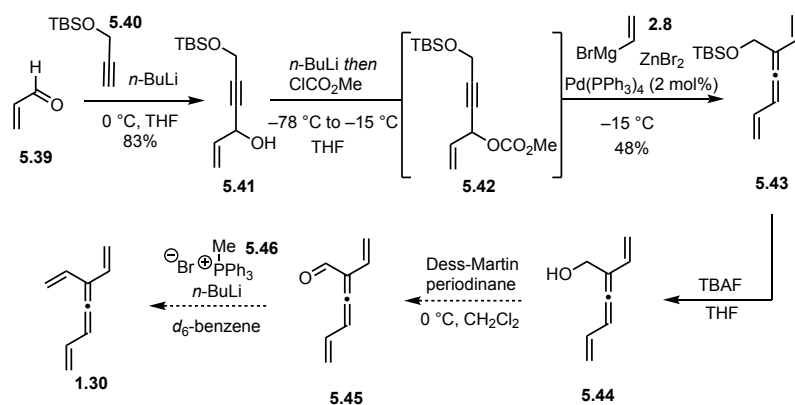


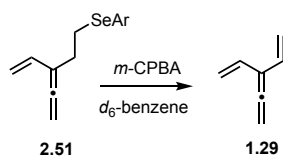
Figure 5.6.1 Relative stability of the multivinylallene family in qualitative terms

An alternative approach to the synthesis of **1.30** was investigated in order to conduct half-life studies. The second generation synthesis focused on a Wittig olefination, conducted in d_6 -benzene, install the final vinyl group (Scheme 5.6.1). Vinylallene **5.43** could be obtained in a two step sequence from acrolein (**5.39**) and subsequent deprotection and oxidation yielded **5.43**. Unfortunately, aldehyde **5.45** was found to be too unstable and additionally did not undergo the requisite olefination with phosphonium salt **5.46** to form divinylallene **1.30**. Rather, decomposition of **5.45** was observed. This is perhaps expected given the reactivity of 2-formyl-1,3-butadiene molecules.^[201]



Scheme 5.6.1 Attempted synthesis of trivinylallene (**1.30**) using a Wittig olefination to install the final vinyl group

The potential to perform the Grieco–Sharpless elimination in d_6 -benzene was identified as a method to obtain **1.28**, **1.29** and **1.30** as d_6 -benzene solutions at the requisite concentrations. This had not previously been attempted in the synthesis of **1.29**.^[46] Using material synthesised by a previous member of the Sherburn group, Chris Newton, the elimination reaction of **2.51** was tested on milligram scale (Scheme 5.6.2).



Scheme 5.6.2 Successful preliminary experiment to obtain a d_6 -benzene solution of 1,1-divinylallene and proposed synthesis of trivinylallene using this approach

The reaction successfully produced **1.29** as a d_6 -benzene solution, indicating that this reaction could be used to synthesise trivinylallene (**1.30**) and 1,3-divinylallene (**1.28**). This would enable comparative half-life studies of multivinylallenes to be conducted.

5.7 Concluding Remarks and Future Work

Reported in this chapter is a unified approach to the synthesis of the multivinylallene family utilising a palladium-catalysed Negishi-type cross-coupling approach. This enabled a regioselective, scalable synthesis of 1,1-divinylallene and 1,3-divinylallene. With all members of this family of conjugated allenes in hand, ^1H and ^{13}C NMR and UV-Visible studies of the multivinylallenes were conducted. Future work will focus on using computational methods to explain the origins of the observed electronic properties of the multivinylallenes.

Re-analysis of the Diels–Alder reactivity of 1,3-divinylallene (**1.28**) found that a two-fold Diels–Alder sequence using carbon-based dienophiles is possible, thereby giving ready access to a [5.5]spirobicyclic structures (Figure 5.7.1). Future application of 1,3-divinylallenes to the synthesis of spirobicyclic natural products, such as majusculone (**5.49**) and aphidicolin (**5.50**) (Figure 5.7.1), could lead to improved syntheses of these compounds.

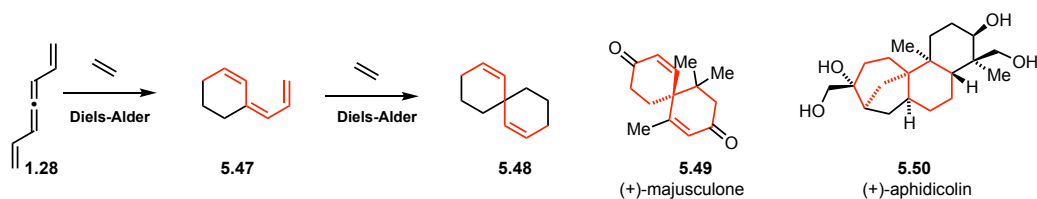
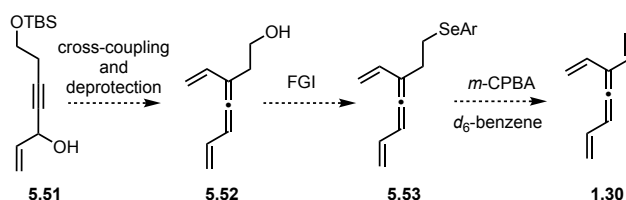


Figure 5.7.1 Two-fold Diels–Alder reaction of 1,3-divinylallene (**1.28**) and potential target molecules for natural product syntheses. The embedded 1,3-divinylallene structure is highlighted in red

While only qualitative results were obtained for stability of the multivinylallene series, an alternative synthesis of trivinylallene (**1.30**) has been identified using a Grieco–Sharpless elimination (Scheme 5.7.1). Future work would focus on conducting this synthesis and applying a similar strategy to the divinylallenes (**1.28** and **1.29**) to obtain quantitative data regarding the stability of the multivinylallenes. Given the stability of 1,3-divinylallenes, such as **5.44**, this is likely to be a viable synthetic route.



Scheme 5.7.1 Proposed final step to synthesis multivinylallenes *via* a Grieco–Sharpless elimination

6

[13]Annulene cation

6.1 Introduction

Preamble

Aromaticity is a fundamental concept that underlies much of modern organic chemistry and has intrigued theoretical and experimental chemists alike.^[202] Originally used to describe the pleasant odour of benzoic acid derivatives, the term *aromatic* is now more broadly used to describe a class of molecules that exhibit greater than expected stability.^[203] Advancements in synthetic and computational methods, as well as instrumentation, have led to the development of this concept beyond the benzene molecule. Current studies of aromaticity aim to improve our understanding of this concept, which to date remains ambiguously defined.^[204]

6.1.1 Aromaticity

The isolation of benzene (**1.2**) by Faraday in 1825 and Kekulé's structural proposition in 1865 played pivotal roles in understanding the nature of the chemical bond and aromatic chemistry (Figure 6.1.1).^{[205] [206]} Subsequent studies have focused on explaining the unexpected stability and reactivity of annulenes and in turn, applying such theories to other molecules.

Annulenes are a class of monocyclic conjugated molecules that historically have been used to study aromaticity (Figure 6.1.1).^{[1] [207]} This class of conjugated hydrocarbons, of which benzene (**1.7**) is the classic example, have captivated chemists for their interesting properties and reactivity, which differ from that of olefinic compounds. Modern usage of the term aromaticity has been broadened to now include other structures, such as heterocycles (e.g. **6.2**), ionic ring systems (e.g. **6.3**), homoaromatic compounds (e.g. **6.4**) and macromolecules (e.g. **6.5**) (Figure 6.1.1).^[208]

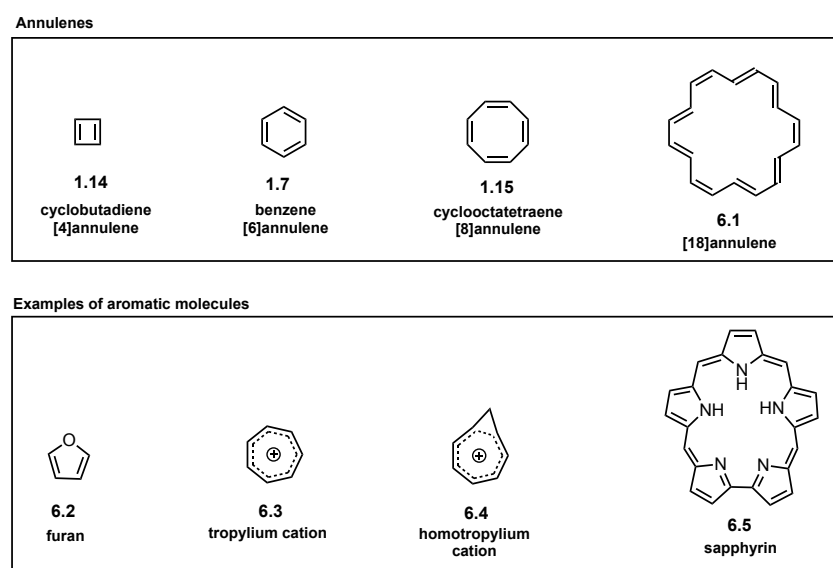


Figure 6.1.1 Annulenes that have been influential in understanding aromaticity and other examples of aromatic molecules

An explanation of the unexpected stability of benzene was proposed in the 1930s by Hückel using molecular orbital methods (Figure 6.1.2).^[209] It was suggested that the cyclic arrangement of six π electrons in a planar ring led to orbital degeneracy and thus the observed stability of the benzene molecule (**1.7**). This explanation became more generally accepted upon the synthesis of the tropylium cation (**6.3**) in 1951 by Doering and co-workers.^[210]

The sextet rule now forms the basis of Hückel's rules of aromaticity, whereby cyclic compounds with continuous conjugation are considered aromatic if they contain $(4n+2)\pi$ electrons (where $n = 0, 1, 2, 3\dots$). While the definition of aromaticity has evolved from this initial set of rules, Hückel's $(4n+2)$ rule is still routinely used to determine the aromaticity of a molecule.

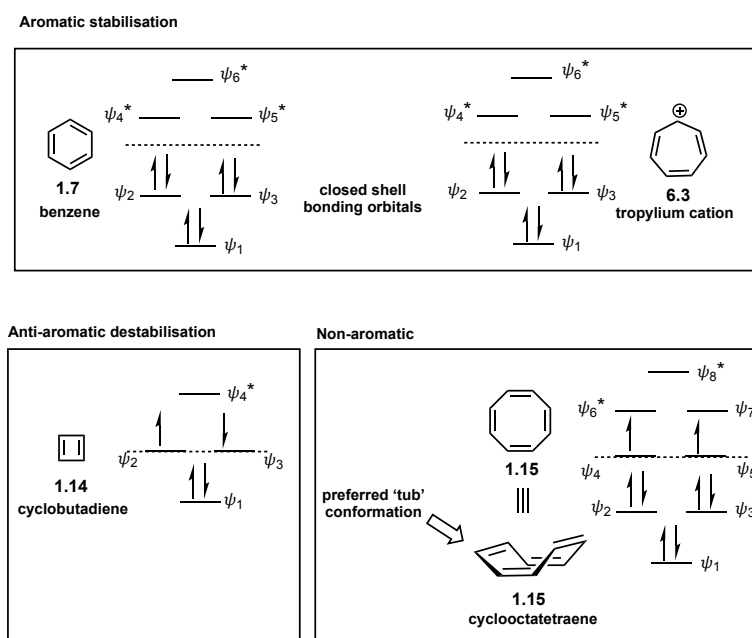


Figure 6.1.2 Hückel molecular orbitals used to justify stabilisation of benzene and reactivity of non-aromatic or anti-aromatic molecules

Planar, cyclic conjugated molecules containing $(4n)\pi$ electrons are deemed *anti-aromatic* due to the destabilisation and increased reactivity that they exhibit (Figure 6.1.2). Cyclobutadiene (**1.14** in Figure 6.1.2) is an example of an anti-aromatic molecule, containing 4π electrons. Due to its high reactivity, **1.14** has only been studied in an argon matrix or as an iron tricarbonyl complex as **1.14** readily dimerises.^[211] Compounds that do not satisfy all of the requirements of Hückel's rules are considered to be *non-aromatic*, exhibiting no additional stabilisation. Cyclooctatetraene (**1.15**), with 8π electrons, was originally theorised to be anti-aromatic (Figure 6.1.2). The non-planarity of **1.15**, however, prevents electron delocalisation, resulting in no additional stabilisation or destabilisation, making this compound an example of non-aromaticity.^{[212] [213] [214] [215]}

While Hückel's rules have successfully been applied to a number of molecules, defining aromaticity is made difficult by the lack of a singular determinant by which to measure aromaticity.^[216] As a result, geometric, electronic and magnetic properties, in conjunction with computational methods, are used to determine the aromaticity of a molecule. Values derived

from benzene (1.7) are often used as a comparison, although standardisation remains an issue.^[202]

Regarding geometry, bond length equalisation is used as a measure of π electron delocalisation in molecules.^[217] X-ray crystal analysis is used, where possible, to analyse bond lengths although they can be calculated using the harmonic oscillator measure of aromaticity (HOMA).^[218] This method analyses bond length alternation and an increase in mean bond length. While planarity is no longer considered a strict requirement for aromaticity, it is still considered as necessary to the extent that delocalisation of the π electrons is possible.^[203]

Magnetic susceptibility is another property of compounds that is measured to determine aromaticity.^[217] NMR spectroscopy is used to analyse the aromatic ring current (often referred to as tropicity) that is observable for aromatic compounds. In the case of ^1H NMR, this results in an observable upfield shift (diatropicity) for endocyclic protons and a downfield shift (paratropicity) for exocyclic protons for aromatic compounds. Nucleus independent chemical shift (NICS) is a computational method that calculates the magnetic shielding at the centre of the ring, with a negative value indicating aromaticity.^[219] This has become a popular method to predict the aromaticity of molecules, although limitations occur when applied to systems that exhibit ring strain.^[216] Infrared and UV-Visible spectroscopy as well as the reactivity of molecules in electrophilic substitution reactions are also used to analyse the aromaticity of molecules. Methods used to measure aromaticity are summarised in Figure 6.1.3.

Geometry		Magnetic Susceptibility	
X-ray	equal bond lengths	^1H NMR	diatropicity
HOMA		NICS	negative value
Reactivity		Spectroscopy	
electrophilic substitution		UV-Visible	high energy
		IR/Raman	symmetry

Figure 6.1.3 Methods used to measure determine aromaticity of molecules and the observed properties of aromatic compounds

While focus has primarily been on compounds that adhere to Hückel aromaticity, other types of aromaticity have also been hypothesised. Möbius topology has been proposed to result in aromatic stabilisation with $(4n)\pi$ electrons (see Section 6.1.2 below), resulting a formal reversal of Hückel aromaticity.^[220] Another reversal of Hückel aromaticity was proposed for molecules in the lowest triplet state with $(4n)\pi$ electrons, referred to as Baird aromaticity.^[221] Recently, this type of aromaticity has been suggested as useful for the development of electronic switches.^[222]

Continued investigations of aromaticity are important to either prove or disprove current theories and thus further our understanding of the chemical bond and its potential applications. Additionally, they serve to highlight limitations in our understanding structure-reactivity relationships and current synthetic methods.

6.1.2 Möbius Aromaticity

In 1964 Heilbröner proposed a type of aromaticity complementary to the Hückel rules: Möbius aromaticity.^[220] This theory predicts that molecules with $(4n)\pi$ electrons arranged along a Möbius topology, whereby there is a 180° twist in the molecule, display additional stabilisation and thus aromatic character (Figure 6.1.4). The proposed stability of these molecules arises from the degenerate closed shell occupancy imposed by the twisted structure (Figure 6.1.4). The stability of these molecules is additionally governed by the physical constraints of ring sizes. Small rings are unable to incorporate the 180° twist to adopt the Möbius topology, while larger rings are often too flexible and interconvert with the planar Hückel anti-aromatic structure.^[223] ^[224] As such, few hydrocarbon Möbius annulenes have been predicted to be more stable than the Hückel variant. While Möbius porphyrin structures have been synthesised and shown to be aromatic, there are limited examples of Möbius annulenes which are described below.^[225] ^[226]

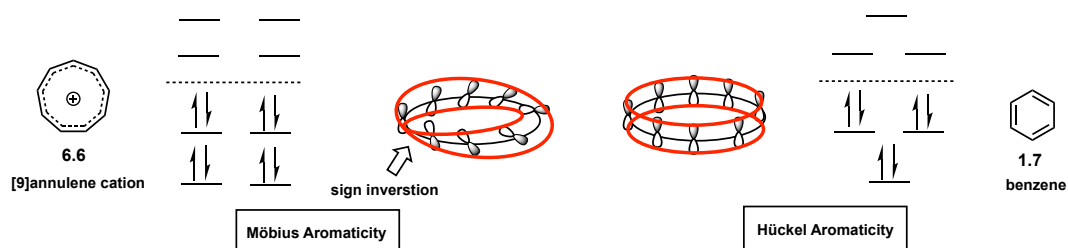
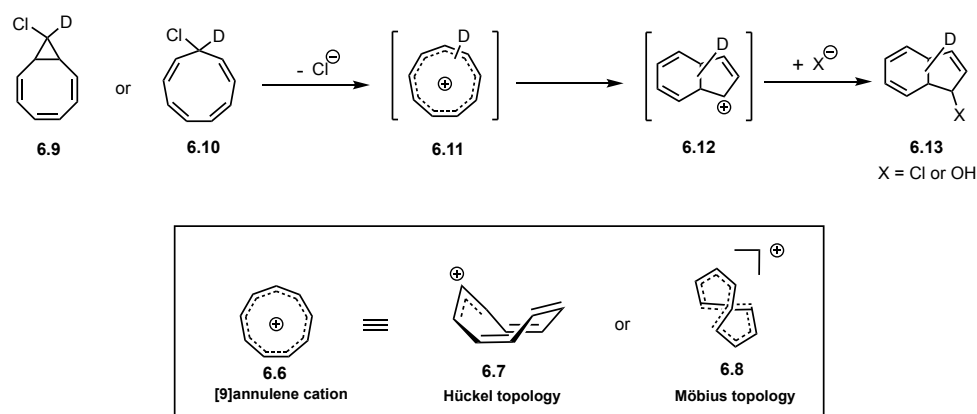


Figure 6.1.4 Degeneracy of Möbius and Hückel aromaticity leading to closed shell structures resulting in stabilisation

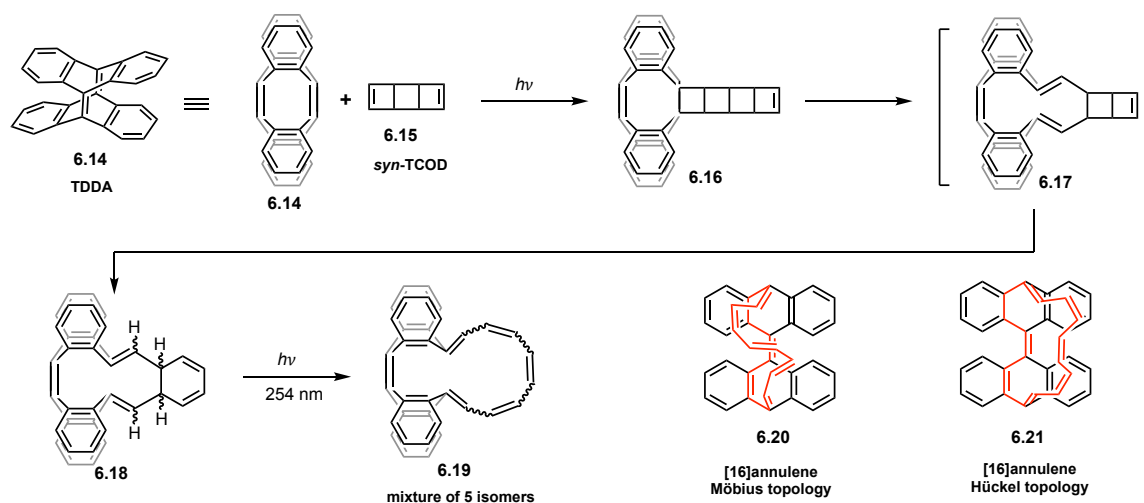
In 1998 it was suggested the cyclononatetraenyl cation (**6.6**) adopted a Möbius topology (**6.8**) as an intermediate in the thermal rearrangement of bicyclo[6.1.0]nonatrienyl chloride (**6.9**) to form dihydroindenyl chloride (**6.13**) (Scheme 6.1.1).^[227] Scrambling observed during deuterium labelling studies, along with the ease of cation formation indicated that an aromatic intermediate was present. The proposed structure was the [9]annulene cation (**6.6**), which could not be isolated or trapped. Computational analysis indicated that the cation adopted a Möbius topology (**6.8**), being lower in energy than the planar Hückel structure (**6.7**).



Scheme 6.1.1 Study of the [9]annulene cation (**6.6**) and proposed topologies

Reanalysis of this work, using more modern computational methods, suggested that the Hückel and Möbius topologies were closer in energy than had previously been calculated.^[228] Additional laser flash photolysis studies indicated that the Hückel structure (**6.7**) is likely to be the preferred conformer.

The synthesis of a neutral Möbius [16]annulene hydrocarbon structure was disclosed in 2003, using a bianthraquinodimethane bridge to stabilise the Hückel anti-aromatic annulene (Scheme 6.1.2).^[229] The synthesis began with irradiation of tetradehydroanthracene (TDDA) (**6.14**) with *syn*-tricyclooctadiene (*syn*-TCOD) (**6.15**). Various compounds were isolated from the reaction, including **6.18** as a mixture of two isomers. Irradiation of **6.18** gave the bridged [16]annulene structure (**6.19**) as a mixture of five isomers. Characterisation of these isomers by NMR and X-ray analysis identified two isomers with Möbius topology and one isomer with Hückel topology. Aromaticity of the C₂ symmetric Möbius isomer (**6.20**) was justified by aromatic stabilisation calculations and bond-length equalisation relative to the Hückel isomer (**6.21**).^[230]



Scheme 6.1.2 Synthesis of a tethered Möbius [16]annulene (**6.21**) by Herges and co-workers

Criticism of this work pointed to the lack of experimental and computational data to support the claims of aromaticity.^[231] It was noted that the geometric criteria (HOMA and bond length equalisation) and magnetic properties of **6.20** (NICS values and magnetic susceptibility) were consistent with bond localisation. It was further contended that there was no energetic stabilisation of the Möbius topology, resulting in the conclusion that the neutral Möbius [16]annulene hydrocarbon was not aromatic.

Currently, an unambiguous synthesis of an aromatic Möbius annulene is yet to be reported. Since these reports, however, further investigations into aromatic Möbius annulenes have identified new structures as potential Möbius molecules.

6.1.3 [13]Annulene carbocation and the related [13]annulenone

Charged annulene compounds have recently been investigated as potential Möbius structures.^[232] Computational analysis of Möbius [9]- (**6.6**), [13]- (**1.32**), [17]- (**6.22**) and [21]annulene (**6.23**) carbocations was reported by Herges and co-workers in 2010 to determine the feasibility of stable cationic structures.^[19] Of the annulene cations studied, the [13]annulene cation (**1.32**) was found to be the most stable, relative to the Hückel topology (Figure 6.1.5).

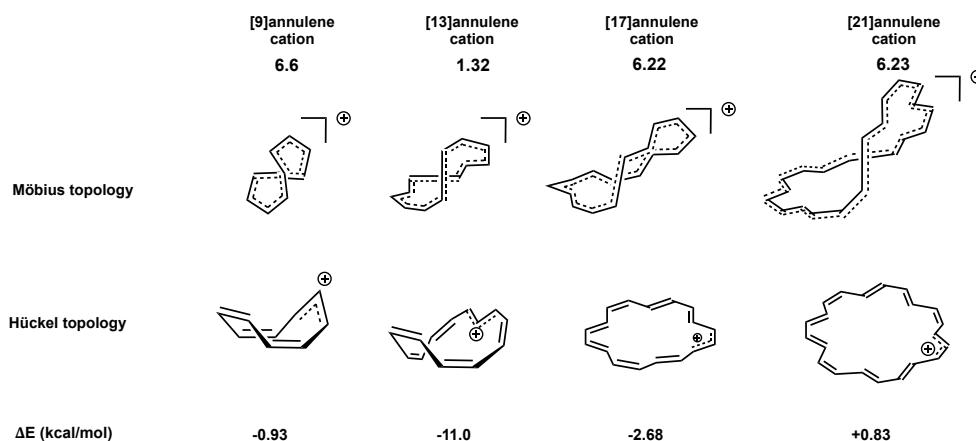
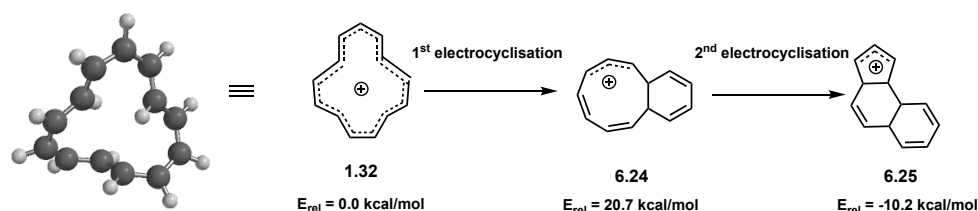


Figure 6.1.5 Stability of Möbius annulene cations relative to the Hückel topology

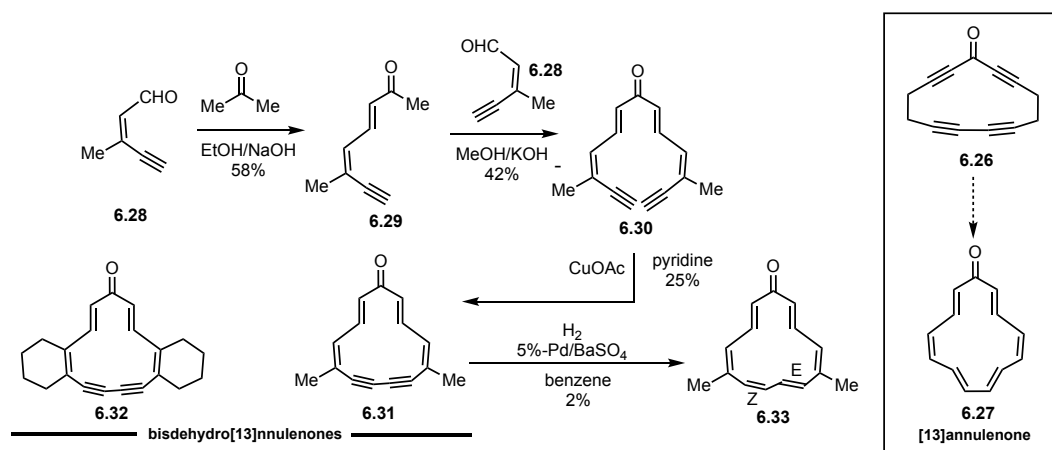
The three lowest energy Möbius conformers of [13]annulene cation (**1.32**) were found to be more stable than the Hückel topologies. The lowest energy structure of [13]annulene cation (**1.32**) is calculated to be C_2 symmetric (Scheme 6.1.3). This structure was proposed to be stable enough to isolate and characterise at low temperatures, with electrocyclization of the cation (**1.32** \rightarrow **6.24** \rightarrow **6.25**) calculated to be an unfavourable pathway.



Scheme 6.1.3 Lowest energy conformer of [13]annulene (**1.32**) as calculated by Herges and co-workers and a potential decomposition pathway

A molecule related to the [13]annulene carbocation (**1.32**) is [13]annulenone (**6.27**), another molecule that has eluded synthesis (Scheme 6.1.4). Sondheimer and co-workers focused on using **6.26** as a precursor to **6.27**, however, **6.26** was unable to be converted into the desired compound.^[233] ^[234] The [13]annulenone (**6.27**) was not expected to be stable and dimerization was proposed as a likely decomposition pathway.^[234] Successful syntheses of

bisdehydro[13]annulenones, such as **6.31** and **6.32**, were reported *via* a sequence of condensation reactions with oxidative coupling forming the 13-membered ring (Scheme 6.1.4).^{[235] [236]} The endocyclic protons of the bisdehydro[13]annulenones were found to be weakly paratropic, indicating anti-aromatic properties. Hydrogenation of **6.31** gave **6.33** with an *s-trans*, *s-cis* diene geometry, which was found to be atropic using ¹H NMR studies, indicating that the alkenic geometry is important for electron delocalisation.^[184]



Scheme 6.1.4 Synthesis and reduction of bisdehydro[13]annulenones and unsuccessful approach to [13]annulenone

Given the previously reported results, it was proposed that a protecting group strategy would be required to synthesise the [13]annulene cation or the potential precursor [13]annulenone.^[180] Irontricarboxyl protection of a 1,3-butadiene building block was thus considered in order to stabilise intermediates and obtain the requisite geometry of the *E,E*-butadiene portion of the annulene.^[180]

6.1.4 Protection of reactive polyenes as irontricarboxyl complexes

Coordination of irontricarboxyl to 1,3-butadienes has served as a useful method to alter the reactivity of dienes. Since the irontricarboxyl complex of 1,3-butadiene was first reported in 1930,^[237] it has been used as a diene protecting group (i.e. a method to stabilise reactive dienes) (Figure 6.1.6 (a)) and as a chiral auxiliary (Figure 6.1.6 (b)).^[238] Furthermore, it has been used to facilitate nucleophilic addition on otherwise unreactive dienes (Figure 6.1.6 (d)) and has been applied to natural product synthesis (Figure 6.1.6 (c)). Examples of this synthetic utility are shown in Figure 6.1.6.

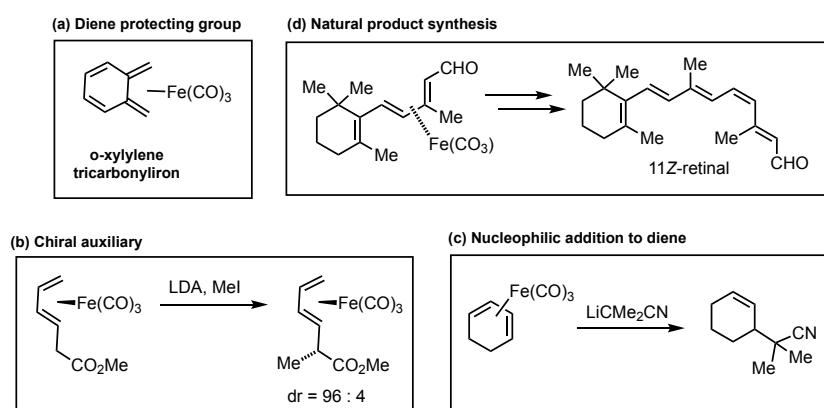


Figure 6.1.6 Synthetic application of irontricarbonyl [239] [240] [241] as a diene protecting group, a chiral auxiliary^[242], in natural product synthesis^[243] and nucleophilic addition to dienes.^{[244] [245]}

As is desirable with protecting groups, irontricarbonyl complexes are useful due to the ease and relatively mild conditions with which the complexes can be formed and decomplexation can occur. Ironpentacarbonyl ($\text{Fe}(\text{CO})_5$) (**6.35**) was initially used as the source of irontricarbonyl, requiring high temperatures and pressures,^{[237] [246]} however, other eighteen electron carbonyliron clusters, nonacarbonyldiiron ($\text{Fe}_2(\text{CO})_9$) (**6.36**) and dodecacarbonyltriiron ($\text{Fe}_3(\text{CO})_{12}$) (**6.37**), require lower temperatures of 60–80 °C (Figure 6.1.7).^{[247] [248]} More recently, organic transfer reagents such as tricarbonyl(benzylideneacetone)iron (**6.38**)^[249] or the reactive yet capricious Grevels' reagent (**6.39**)^[250] are amongst a variety of reagents developed to enable facile complexation.^[251]

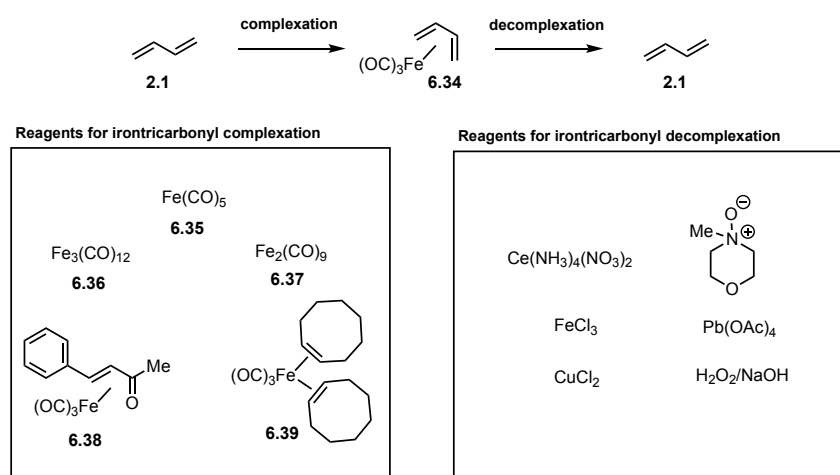


Figure 6.1.7 Protection and deprotection methods for the use of irontricarbonyl protection of 1,3-butadiene

Removal of the irontricarbonyl group can be performed using a variety of methods (Figure 6.1.7).^[238] Single electron oxidants, such as ceric ammonium nitrate ^[252] ^[253], and two electron oxidants such as *N*-methylmorpholine *N*-oxide ^[254] are just some of the methods that provide mild conditions for decomplexation.

An additional benefit of the irontricarbonyl complex is inertness to a variety of reaction conditions.^[238] It is stable in the presence of Grignard and organozinc reagents, enabling functionalisation of otherwise difficult conjugated aldehydes. Wittig reactions, osmium catalysed dihydroxylations and Pd/C hydrogenation are just some of the reactions that have been demonstrated to be compatible with the irontricarbonyl functionality.^[238]

In particular relation to hydrocarbon synthesis, the irontricarbonyl moiety has been used to access a variety of compounds that would otherwise be difficult to synthesise and study. (Figure 6.1.8) Anti-aromatic compounds, such as cyclobutadiene (**6.40**),^[211] ^[255] and Diels–Alder dimerising molecules, such as cyclopentadienone (**6.41**),^[256] ^[257] ^[258] can be stabilised. Irontricarbonyl has also been used to stabilise compounds prone to isomerisation, such as homopentalene (**6.42**) ^[259] and *Z,Z,Z,Z*-cyclononatetraene (**6.43**) ^[260].

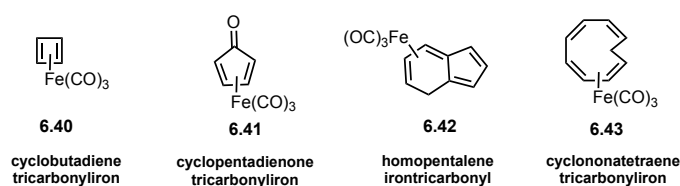
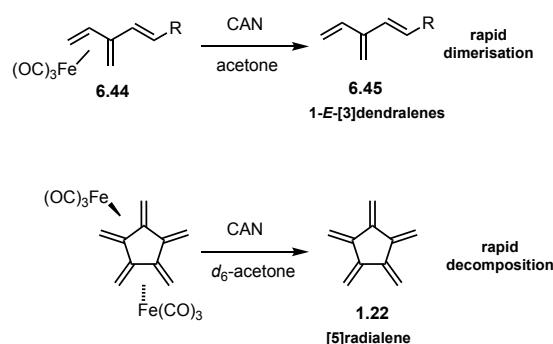


Figure 6.1.8 Unstable polyenes stabilised as irontricarbonyl complexes

More recently, the irontricarbonyl moiety has been used in the synthesis of the 1-*E*-[3]dendralenes (**6.45** from **6.44**),^[261] which otherwise undergo rapid dimerization, and also enabled the synthesis of the unstable [5]radialene (**1.22**) molecule for the first time (Scheme 6.1.5).^[11]



Scheme 6.1.5 Recent application of irontricarbonyl protection to synthesise unstable polyenes

The demonstrated ability of the irontricarboxyl group to enable the synthesis of otherwise unstable hydrocarbons suggested it would be useful in the synthesis of the [13]annulene cation (**1.32**).^[180] This protecting group strategy was therefore considered necessary as the synthesis was likely to proceed *via* unstable intermediates.

6.1.5 Previous Syntheses

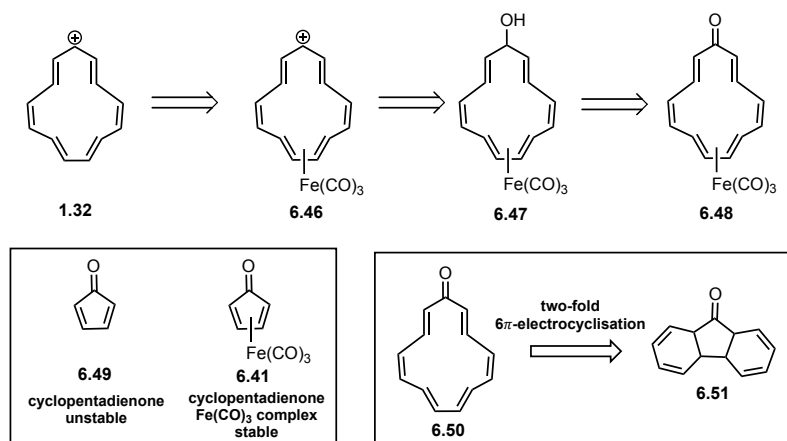
To date, there are no reported syntheses or attempted syntheses of the [13]annulene carbocation (**1.32**) in the literature, or of any cationic annulene other than the [9]annulene carbocation (**6.6**). Synthetically, the [13]annulene cation presents a number of challenges:

1. 13-membered rings are a difficult ring size to construct
2. The correct *E/Z* geometry should be incorporated to readily access the proposed lowest energy conformation of the [13]annulene cation and prevent electrocyclisations
3. The later stage of the synthesis may involve the handling of anti-aromatic compounds
4. The synthesis of annulenes with Möbius topology is not well defined

Within the Sherburn group, efforts have been made to synthesise the [13]annulene cation, although none so far have been unsuccessful. The next section will outline work conducted within the Sherburn group to synthesise **1.32** using a cross-coupling approach.

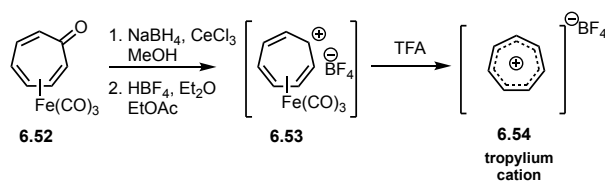
6.1.6 First Generation approach to the [13]annulene cation

Previous work within the Sherburn group focused on synthesising the [13]annulene cation (**1.32**) using an irontricarboxyl protecting group strategy to target annulenone **6.48**, an otherwise anti-aromatic compound (**6.50**) (Scheme 6.1.6).^[262] ^[263] It was considered that the annulenone (**6.48**) would enable access to **1.32** *via* a reduction, carbocation formation sequence (Scheme 6.1.6). Deprotection of the irontricarboxyl would then furnish the [13]annulene cation (**1.32**). Protection of the diene as an irontricarboxyl complex was identified as necessary to prevent a potential two-fold 6π -electrocyclisation (**6.50** \rightarrow **6.51**), similar to how irontricarboxyl complexation of cyclopentadienone stabilises this anti-aromatic compound (**6.49** and **6.41**).^[256] ^[257] ^[258] The more successful aspects of this work are discussed below.



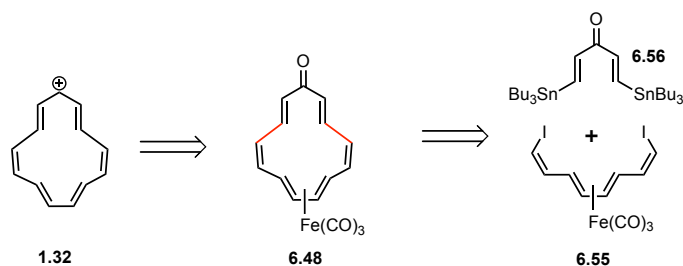
Scheme 6.1.6 Retrosynthesis of [13]annulene (**1.32**) to irontricarbonyl protected [13]annulenone (**6.48**)

This reaction sequence had been successfully modelled with irontricarbonyl tropone complex (**6.52**) to generate the tropylium carbocation as a tetrafluoroborate salt (**6.54**) (Scheme 6.1.7). Luche conditions gave selective reduction of the carbonyl, which was converted into the cationic species (**6.53**) using HBF_4 . Rapid and complete decomplexation was achieved using TFA to give the tropylium carbocation (**6.54**) as the fluoroborate salt.



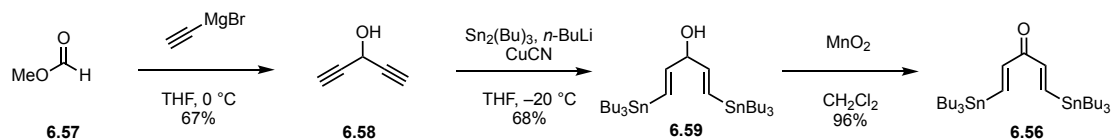
Scheme 6.1.7 Modelling of the proposed endgame using the tropylium cation

With the endgame of the [13]annulene cation (**1.32**) synthesis successfully modelled, focus turned to the synthesis of the 13-membered ring. Retrosynthetic analysis of the irontricarbonyl protected annulenone (**6.48**) identified the single bonds between the *E* and *Z* alkenes as potential sites for disconnection (highlighted in red in Scheme 6.1.8). The proposed forward synthesis involved a two-fold Stille cross-coupling reaction between di-iodide **6.55** and bis-stannane **6.56**. This symmetric route was proposed to enable rapid synthesis of advanced intermediates as well as the symmetric [13]annulenone (**6.48**).



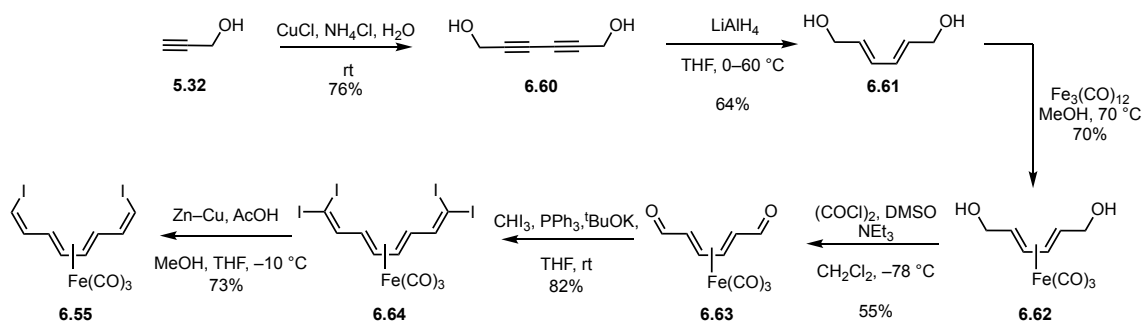
Scheme 6.1.8 Proposed retrosynthesis of [13]annulene using a two-fold Stille cross-coupling

The bis-stannane (**6.56**) was synthesised in a three-step sequence from methyl formate (**6.57**) (Scheme 6.1.9). Two-fold addition of ethynylmagnesium bromide gave diynol (**6.58**), with subsequent hydrostannylation to give **6.59** and oxidation giving the desired bis-stannane (**6.56**).



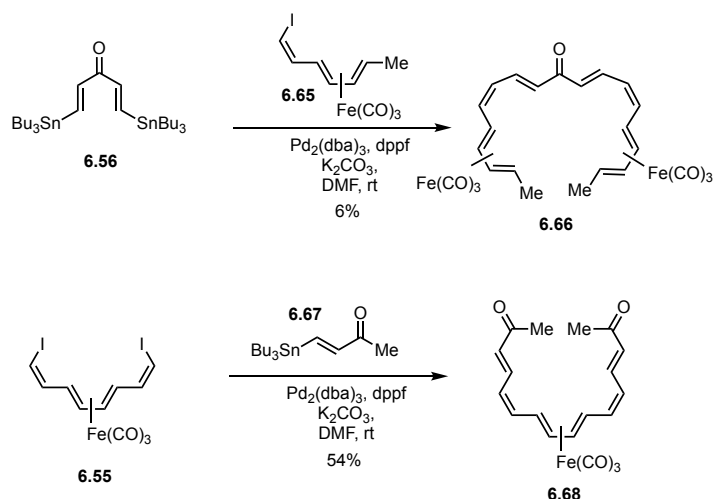
Scheme 6.1.9 Synthesis of bis-stannane **6.56** from methylformate

The *Z,Z*-diiodide complex (**6.55**) was synthesised by di-iodination of di-aldehyde complex **6.63** followed by a *Z*-selective reduction using Zn-Cu couple (Scheme 6.1.10). Dialdehyde complex (**6.63**) was obtained via a four-step sequence from propargyl alcohol (**5.32**).



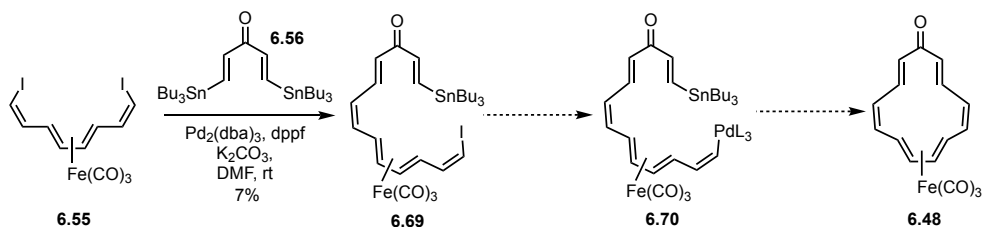
Scheme 6.1.10 Synthesis of di-iodide irontricarbonyl complex **6.55**

Reactivity of the bis-stannane (**6.56**) was initially modelled using mono-iodide **6.65** in a two-fold Stille cross-coupling reaction using Pd(dppf). While the yield for this reaction was only 11%, it demonstrated the ability of **6.56** to undergo the two-fold cross-coupling reaction. The reactivity of the di-iodide (**6.55**) was modelled in another two-fold Stille cross-coupling reaction using stannane **6.67** (Scheme 6.1.11). The ability of the **6.55** to undergo a two-fold cross-coupling reaction while conserving the geometry of the *Z*-alkenes indicated the potential of this proposed synthetic route.



Scheme 6.1.11 Model studies of Stille cross-coupling reactions using cross-coupling partners **6.55** and **6.56**

Attempts to form the 13-membered ring *via* the cross-coupling of diiodide **6.55** and bis-stannane **6.56**, however, were unsuccessful (Scheme 6.2.12). While the singly cross-coupled intermediate (**6.69**) could be obtained, all attempts at macrocyclization failed and palladium migration was cited as a potential decomposition pathway. It is also likely that the formation of the 14-membered palladacycle is not favoured, thereby preventing reductive elimination and formation of **6.48**.



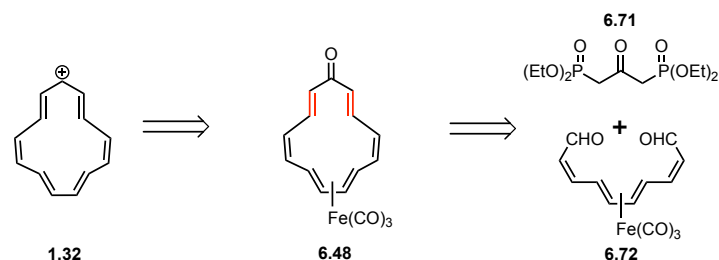
Scheme 6.1.12 Attempted ring closure *via* Stille cross-coupling reaction

These results indicated that this disconnection was unlikely to facilitate the formation of the [13]annulenone complex (**6.48**). As a result, alternative synthetic routes were considered for future investigations.

6.1.7 Aims: Synthesis of the [13]annulene cation

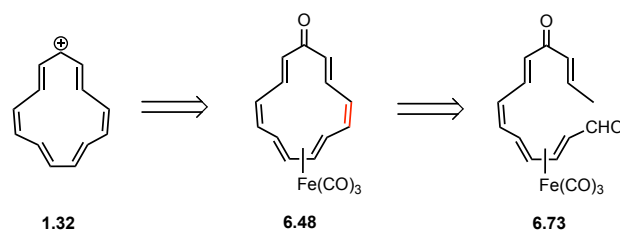
The inability to synthesise [13]annulene cation (**1.32**) or **6.48** using a cross-coupling approach indicated that an alternate route should be investigated. As such, the [13]annulene cation still presents a synthetic challenge and the study of this molecule would assist in our understanding of Möbius annulenes, as well as aromaticity more broadly. The previous investigations suggested that a step-wise approach towards ring closure could potentially be more likely to result in ring-closure. Additionally, the irontricarbonyl protecting group, which ensures an *s-cis*, *s-cis* conformation of the *E,E*-diene, could make it difficult to access **6.48**, which is likely to have a preferred *s-trans*, *s-trans* conformation, perhaps indicating decomplexation at a different stage of the synthesis might be necessary. With this in mind, alternative syntheses were considered.

A synthetic route proposed by a former member of the Sherburn group, Sam Drew, suggested that disconnection of the α,β -unsaturated *E*-olefins could be achieved using a two-fold Horner-Wadsworth-Emmons (HWE) olefination (highlighted in red in Scheme 6.1.13). It was anticipated that this could be performed using bis-phosphonate **6.71** and di-aldehyde **6.72**. This would again involve approaching the synthesis from a symmetric standpoint.



Scheme 6.1.13 Proposed retrosynthesis using a two-fold olefination reaction

Alternatively, a non-symmetric approach to the synthesis of this molecule could also be envisaged with formation of the final *Z*-alkene occurring after ring closure from **6.73** (highlighted in red in Scheme 6.1.14). This approach could enable an otherwise difficult ring-closure (see Section 6.6.2 for more details).



Scheme 6.1.14 Proposed retrosynthesis of non-symmetric route using aldol condensation to as the ring closing reaction

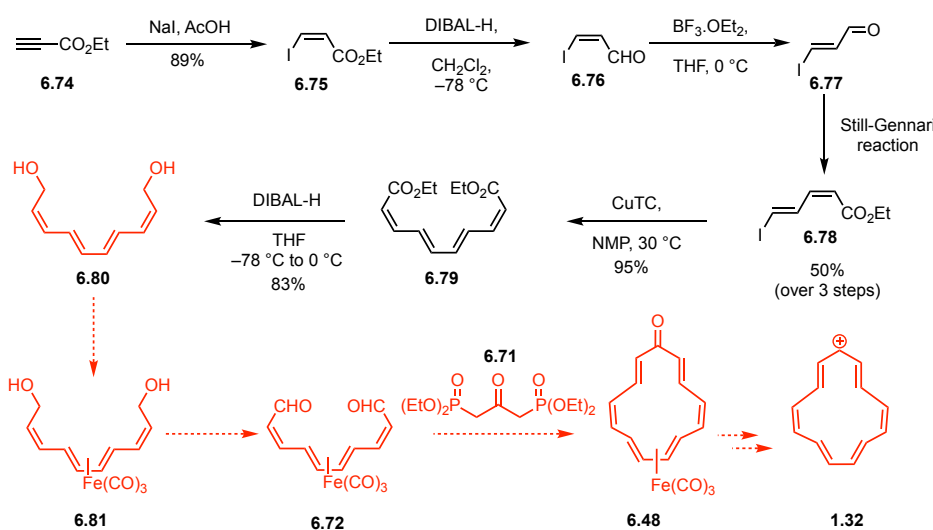
While ultimately the purpose of these efforts was to synthesise the [13]annulene cation (**1.32**), it was envisaged that unproductive routes would contribute to our understanding of the synthesis of the annulene carbocations as well as potential synthetic intermediates.

6.2 Studies towards the [13]annulene cation

The following sections discuss two synthetic approaches towards the [13]annulene cation (**1.32**) were investigated: (1) a symmetric approach and (2) a non-symmetric approach.

6.2.1 Second Generation approach to the [13]annulene cation

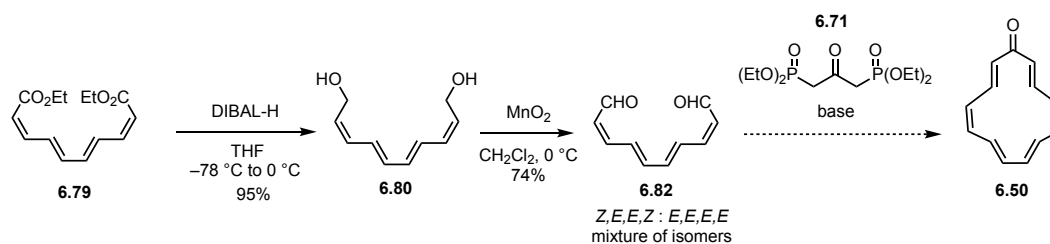
The first route that was investigated was a two-fold olefination approach to perform the ring closure and construct the final *E*-alkenes of the irontricarbonyl protected [13]annulenone (**6.48**) (Scheme 6.2.1). It was proposed that the ring could be formed via the union of dialdehyde **6.72** and bis-phosphonate **6.71**. Access to the *Z,E,E,Z* diester (**6.79**) had already been demonstrated by previous member of the Sherburn group, Sam Drew, *via* a five step sequence (Scheme 6.2.1). Iodination of ethyl propiolate (**6.74**) to form **6.75**, followed by reduction to **6.76**, isomerisation and Still-Gennari olefination gave *E,Z*-ester (**6.78**). Ullmann coupling of **6.78** with CuTC gave **6.79** and reduction using DIBAL-H furnishing diol **6.80**.



Scheme 6.2.1 Proposed forward synthesis via a two-fold olefination approach. The section of the synthesis that remained to be investigated is highlighted in red

While the bis-phosphonate **6.71** has previously been demonstrated to undergo two-fold olefination reactions, it has not been explored for ring formation.^{[264] [265] [266]} The bis-phosphonate was thus synthesised according to literature procedures.

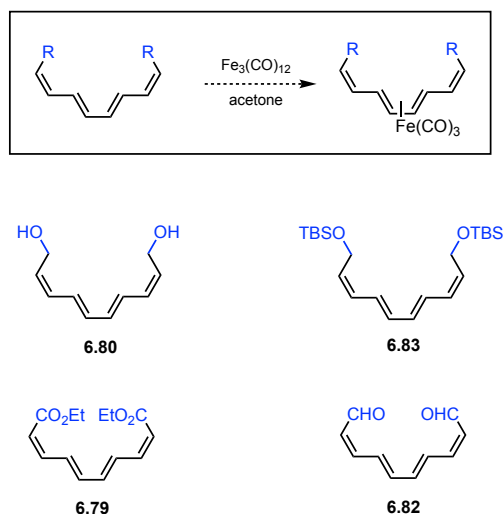
Initially a route without irontricarboxyl protection was investigated (Scheme 6.2.2). Work conducted in Schemes 6.2.2 and 6.2.3 were conducted with undergraduate student Tegan O'Brien. Diester **6.79**, which had been synthesised by Sam Drew, was reduced with DIBAL-H to give the unstable compound **6.80** and oxidation with manganese dioxide gave dialdehyde **6.82** as an irreproducible mixture of isomers. This two-step sequence was found to be necessary as the reduction was unable to form **6.82** selectively. The dialdehyde (**6.82**) was found to be thermally unstable and readily isomerised to the *E,E,E,E*-isomer. Due to the instability of **6.82**, it was immediately subjected to a two-fold HWE reaction.



Scheme 6.2.2 Attempted two-fold olefination without irontricarboxyl protection

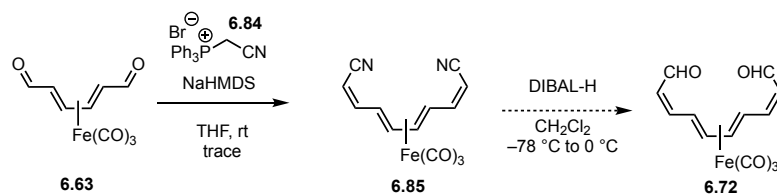
The two-fold HWE reaction between the dialdehyde (**6.82**) and bis-phosphonate (**6.71**) yielded a complex mixture in which the desired [13]annulene (**6.50**) could not be identified by ^1H NMR or mass spectrometry (Scheme 6.2.2). These results indicated that a route with irontricarboxyl protection of the *E,E*-diene might stabilise intermediates and assist in the ring closure by providing conformational restriction.

Complexation of various tetraenes was attempted, however, each reaction resulted in complex mixtures (Scheme 6.2.3). The desired iron complex was unable to be identified, although it is likely that diiron complexes were being formed with coordination being directed to the terminal butadiene sites upon isomerisation.



Scheme 6.2.3 Attempted irontricarboxyl protection of various tetraenes

An alternate route to the irontricarboxyl dialdehyde complex was investigated (Scheme 6.2.4). Using **6.63**, from the first generation approach, a two-fold Wittig reaction with phosphonium salt **6.84** gave the desired dinitrile complex (**6.85**) in only trace quantities, with the major products being a mixture of *E,E,E,E* and *Z,E,E,E* isomers. Reduction of **6.85** did not result in **6.72** being observed, with only the *E,E,E,E*-isomer being identified in the reaction mixture. As such, this route was abandoned.



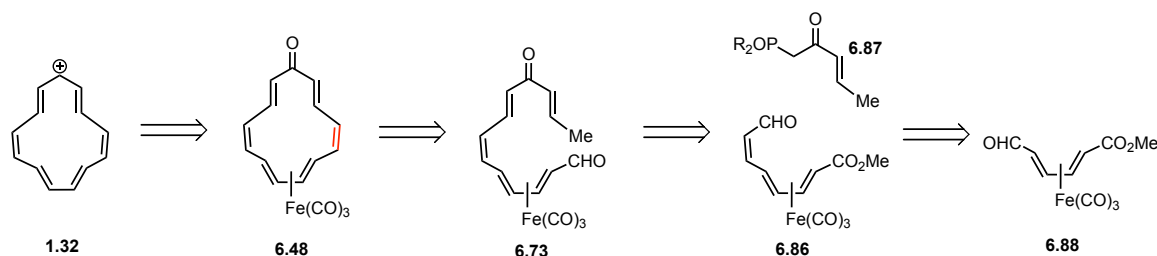
Scheme 6.2.4 Alternate route to dialdehyde complex **6.72**

The difficulty in obtaining the requisite intermediates and their propensity to isomerise suggested that a two-fold olefination reaction of dialdehyde **6.72** was not readily feasible so an alternative route to the [13]annulene cation (**1.32**) was sought.

6.2.2 Third Generation approach to the [13]Annulene cation

The previous two approaches had focused on a symmetric route to form the target [13]annulenone structure (**6.48**). Both of these routes had been unable to form the 13-membered ring using either a two-fold cross-coupling or HWE reaction so a new route was devised to conduct the cyclisation using a single ring closing event (Scheme 6.2.5). It was proposed that a non-symmetric route would enable a more controlled ring closing reaction and would involve intermediates that were less prone to isomerisation.

Disconnection at the final *Z*-olefin (highlighted in red) was identified as a plausible strategy, invoking a vinylogous aldol reaction of **6.73** for the forward synthesis (Scheme 6.2.5). It was envisaged that **6.73** could be synthesised by an olefination reaction between **6.86** and **6.87** starting from complex **6.88**.



Scheme 6.2.5 Retrosynthesis for non-symmetric route to [13]annulene cation

Vinylogous aldol reactions have previously been utilised for ring closing reactions for medium ring sized systems (**6.89**, **6.90** and **6.91**), albeit using less conformationally restricted substrates (Figure 6.2.1).^{[267] [268] [269]} In particular it has been applied to 12- and 14-membered rings, which indicated that this approach could potentially be applied to the desired 13-membered ring system.^[270]

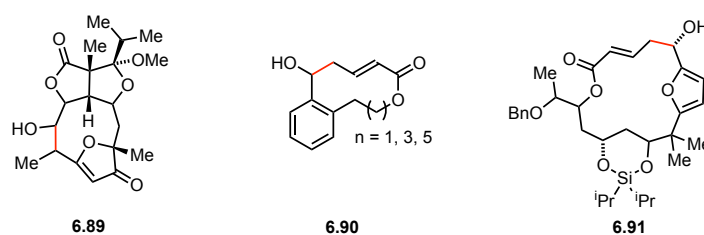
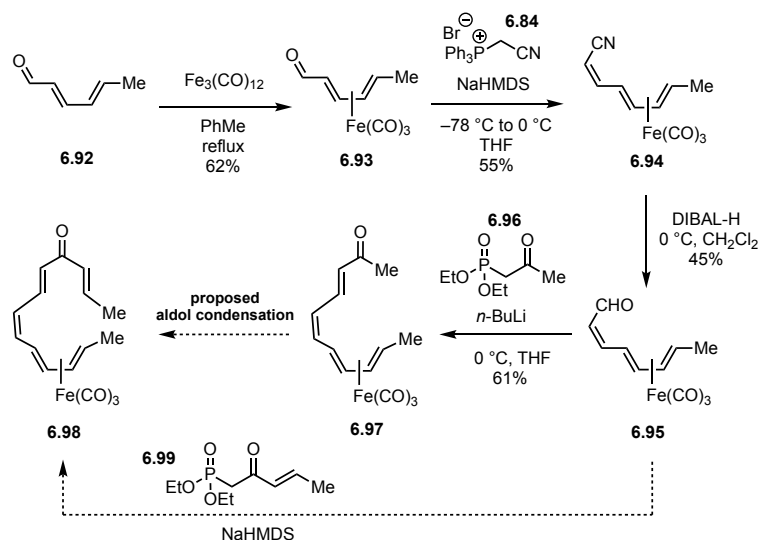


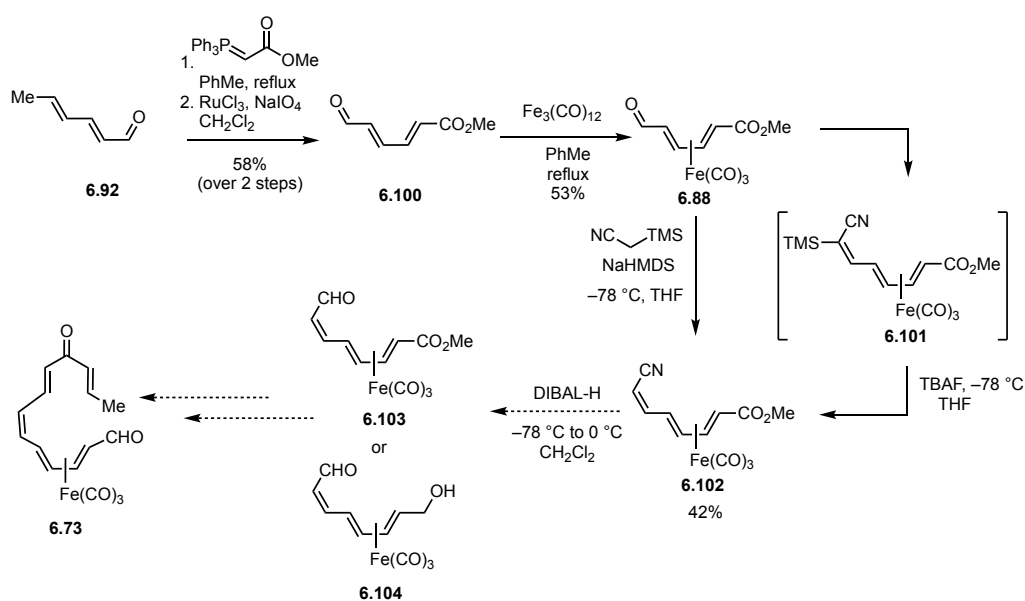
Figure 6.2.1 Examples of compounds made via an intramolecular vinylogous aldol reaction

The synthesis was initially modelled with iron complex **6.93** (Scheme 6.2.6). Olefination using Wittig conditions gave nitrile **6.94** and subsequent reduction of the nitrile with DIBAL-H gave aldehyde **6.95**. The use of methylphosphonate **6.96** in an HWE reaction demonstrated olefination could be performed to obtain the requisite ketone. When the HWE reaction was attempted using the α,β -unsaturated phosphonate **6.99**, the reaction was found to be significantly slower, resulting in decomposition of **6.95** before formation of **6.98** could occur above trace quantities. Despite this, it was envisaged that the methyl ketone could undergo an aldol condensation reaction with acetaldehyde to incorporate the requisite *E*-alkene. Attention was thus turned to the [13]annulene system.



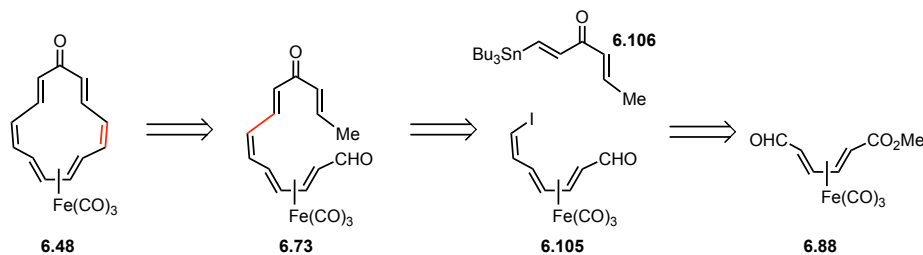
Scheme 6.2.6 Model study of a non-symmetric approach

The synthesis began with formation of ester **6.100** via a two-step olefination-oxidative cleavage sequence from **6.92** (Scheme 6.2.7). Complexation with $\text{Fe}_3(\text{CO})_{12}$ gave **6.88**, although the Wittig reaction was unable to form nitrile **6.102**. Peterson olefination gave mixtures of **6.101** and **6.102**, however, upon treatment with TBAF, **6.101** could be converted into **6.102**. Reduction of **6.102** to **6.103** did not occur selectively, presumably due to activation of the ester by the irontricarbonyl group. Attempts to reduce both the nitrile and ester functionalities to form **6.104** was unsuccessful, which may indicate instability of such irontricarbonyl complexes. A more direct route to ketone **6.73** was investigated in order to minimise manipulation of oxidation states and reduce the step count.



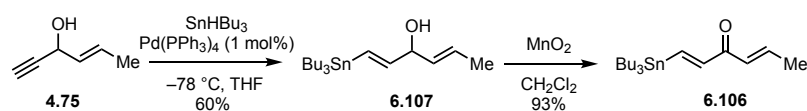
Scheme 6.2.7 Attempted non-symmetric route to access complex **6.73**

An alternative route to ketone **6.73** was devised using a Stille cross-coupling reaction between mono-iodide **6.105** and conjugated stannane **6.106** (Scheme 6.2.8). This proposed route would enable direct access to ketone **6.73** without requiring manipulation of oxidation states.



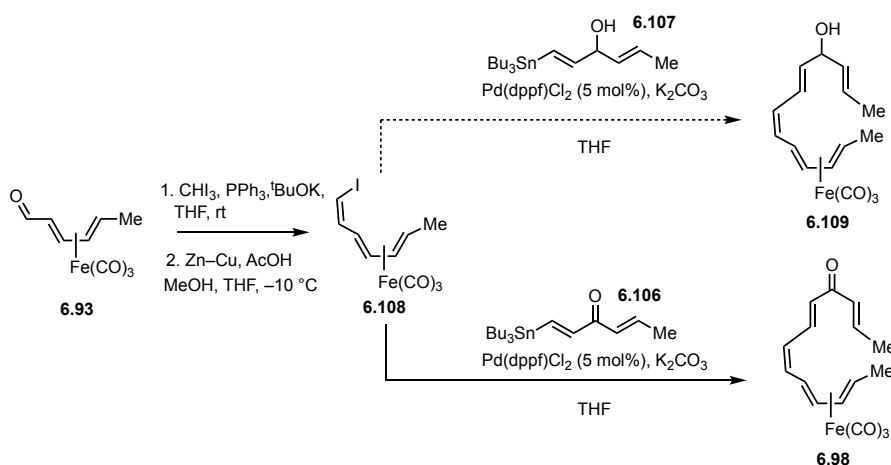
Scheme 6.2.8 Alternative retrosynthesis of annulenone **6.48**

Using a regioselective palladium catalysed hydrostannylation, stannane **6.107** was obtained from enynol **4.75**. Subsequent oxidation with manganese dioxide gave the requisite tributylstannane **6.106** (Scheme 6.2.9).



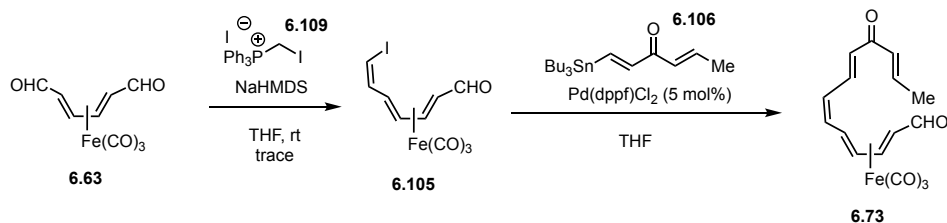
Scheme 6.2.9 Synthesis of Stille cross-coupling partners

The Stille cross-coupling reaction was modelled using the mono-iodide **6.108** that had previously been synthesised from **6.93** by previous member of the Sherburn group, Kimberley Roper (Scheme 6.2.10). Cross-coupling reactions of ketone **6.106** with iodide **6.108** found that **6.98** could be formed with retention of configuration of the *Z*-alkene using Pd(dppf) as a catalyst. Attempts to react stannane **6.107** with **6.108** were unsuccessful with these conditions (Scheme 6.2.10).



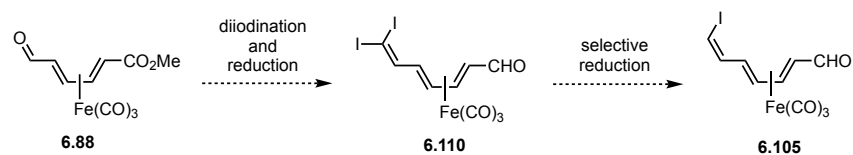
Scheme 6.2.10 Stille cross-coupling model system to access ketone **6.98**

The cross-coupling conditions using stannane **6.106** were subsequently applied to iodoaldehyde **6.105**, a compound previously synthesised from **6.63** by Kimerley Roper using a Stork-Zhao-Wittig reaction with phosphonium iodide **6.109** (Scheme 6.2.11).



Scheme 6.2.11 Stille cross-coupling using iodoaldehyde **6.105** to access ketone **6.73**

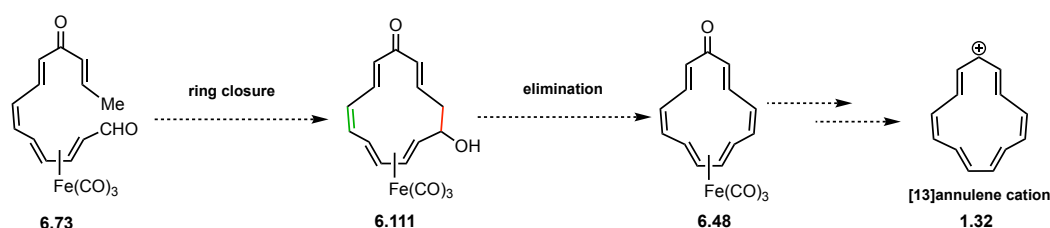
The product of the cross-coupling reaction **6.73**, was assigned by ¹H NMR and mass spectrometry, although the small amounts of impure material available prevented full characterisation. Nevertheless, these results indicated that this route could potentially lead to formation of the cyclisation precursor, although the ring closing reaction still needs to be tested. Unfortunately, the lack of material also meant the ring closing aldol was unable to be tested, hence a scalable synthesis of iodide **6.105** will be required for future studies that attempt this synthetic route (Scheme 6.2.12).



Scheme 6.2.12 Proposed synthesis of **6.110** to enable a larger scale synthesis of **6.74** and study of the ring closure

6.3 Conclusions and Future Work

Reported in this chapter are two different approaches to the synthesis of the [13]annulene cation (**1.32**). The second generation symmetric approach was unable to utilise a two-fold HWE reaction to form the [13]annulenone (**6.48**). The third approach focused on using an aldol reaction to construct the 13-membered ring. A method was successfully developed to obtain the requisite precursor (**6.73**) using a Stille cross-coupling reaction. Unfortunately, due to a lack of material, the ring closing reaction was unable to be attempted.



Scheme 6.3.1 Future work involving cyclisation reaction to form 13-membered ring

As the outcome of the third generation approach remains ambiguous, future work should focus on the cyclisation reaction in order to form the 13-membered ring (**6.111**). Whether a vinylogous aldol can be applied to this conjugated system may require the investigation of various conditions (Scheme 6.3.1). Hydration of the second *Z*-alkene (highlighted in green) may also be necessary to increase conformational flexibility and enable ring closure, which would ultimately require a two-fold elimination to form the [13]annulenone (**6.48**).

Studies towards the [13]annulene cation (**1.32**) indicate that despite the symmetry of **1.32** and the target precursor **6.48**, a non-symmetric (rather than a symmetric) approach is most likely to lead to a successful synthesis. This appears to be particularly relevant to the ring closing reaction, where symmetric routes were shown to lead to unfavourable disconnections.

The iron tricarbonyl protecting group has been demonstrated as necessary for the attempted approaches in order to handle highly conjugated molecules without decomposition and retaining the desired alkene geometry. The restricted flexibility incurred by the iron tricarbonyl group may assist in the ring closing reaction, however, tactical design of the ring closing precursor and strategic removal of the iron tricarbonyl in order to access [13]annulene cation (**1.32**), which has a preferred *s-trans*, *s-trans* conformation.

A successful synthesis of the [13]annulene cation would greatly assist in our understanding of Möbius structures and the study of aromaticity more broadly.

7

Concluding Remarks

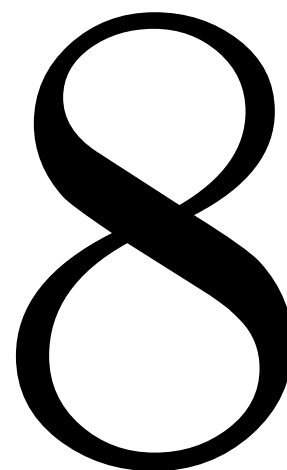
Devising and synthesising novel compounds to expand the known structural space is a never-ending task. This thesis has aimed to contribute to the literature of π -bond rich molecules and further our understanding of these compounds.

Chapters 3, 4 and 5 were dedicated to the synthesis and study of the multivinylallenes, a family of conjugated allenes. Therein was reported the first synthesis of tetravinylallene and trivinylallene, the two highest members of the multivinylallene family which have not previously been reported. The approach of a Negishi cross-coupling reaction to install the final alkenic group was also successfully applied to the synthesis of the first substituted examples of tetra- and trivinylallenes. Additionally, this approach was used to synthesise the divinylallenes in short, scalable and regioselective sequences, albeit as THF solutions. Diels–Alder reactions of the multivinylallenes demonstrated the ability of these simple molecules to rapidly construct

a variety of multicyclic frameworks. Spectroscopic studies highlighted interesting electronic properties of 1,3-divinylallene and tetravinylallene and are worthy of further investigations.

Chapter 6 presented work towards the [13]annulene cation, a molecule that has been calculated to have Möbius topology. Although various routes towards the [13]annulene cation were presented, a non-symmetric route towards the target molecule was identified as a route to be pursued in the future. This work additionally demonstrated the necessity for the use of an irontricarbonyl protecting group in order to handle the highly conjugated intermediates of this synthetic route.

Although the [13]annulene cation remains an unsolved problem, these investigations contribute to developing syntheses of highly conjugated molecules. The successful synthesis of the multivinylallenes has answered the question regarding their synthesis and has opened the door to further inquiries regarding the reactivity and physical properties of π -bond rich molecules.



Experimental

8.1 General Experimental

NMR spectra

^1H NMR spectra were recorded at 298K, unless specified otherwise, using a Bruker AVANCE 800, Bruker AVANCE 700, Bruker AVANCE 600 or Bruker AVANCE 400 as indicated. Residual solvent peaks were used as an internal reference for ^1H NMR spectra (CDCl_3 δ 7.26 ppm, C_6D_6 δ 7.16 ppm, $(\text{CD}_3)_2\text{CO}$ δ 2.05 ppm). Coupling constants (J) are quoted to the nearest 0.1 Hz. The assignment of proton signals was assisted by COSY, HSQC and HMBC experiments where necessary. ^{13}C NMR were recorded at 298K, unless specified otherwise, using a Bruker AVANCE 800, Bruker AVANCE 700, Bruker AVANCE 600 or Bruker AVANCE 400 as indicated. Residual solvent peaks were used as an internal reference for ^{13}C NMR spectra

(CDCl₃ δ 77.16 ppm, C₆D₆ δ 128.06 ppm, (CD₃)₂CO δ 29.84, 206.26 ppm). The assignment of carbon signals was assisted by COSY, HSQC and HMBC experiments where necessary. The following abbreviations (or combinations thereof) are used to describe ¹H NMR multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad.

IR spectra

IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer as thin films.

Mass spectrometry

Low-resolution EI mass spectra were recorded on an Agilent HP 6890 series gas GC/MS with a 7683 injector or on a Waters AutoSpec Premier spectrometer magnetic sector instrument. High-resolution EI mass-spectra were recorded on a Waters AutoSpec Premier spectrometer magnetic sector instrument, operating at 70 eV.

Melting points

Melting points were measured on a Stanford Research Systems Optimelt MPA100 and are uncorrected.

Ultraviolet-Visible spectroscopy

UV-visible spectra were recorded using a Shimadzu UV-Visible 2450 spectrometer at 25 °C.

X-ray Crystallography

Single crystal X-ray data was collected on a Supernova (Dual Source) diffractometer using a SuperNova (Cu $K\alpha$ radiation, $\lambda = 1.54184 \text{ \AA}$) X-ray radiation source. Crystallographic structures were solved using CrysAlis PRO package.^[271] Structure solution was by ShelXT,^[272] and the structures were refined using ShelXL^[273] in the OLEX2 program package.^[274]

Chromatography

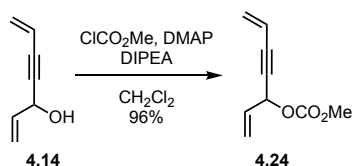
Analytical TLC was performed on Merck silica gel plates, pre-coated with silica gel 60 F₂₅₄ (0.2 mm). Visualisation was effected by quenching of UV fluorescence ($\lambda_{\text{max}} = 254$ nm) and by staining with *p*-anisaldehyde, followed by heating. Flash chromatography employed Merck Kieselgel 60 (230-400 mesh) silica gel. Analytical and preparative HPLC were conducted using a Waters 600 Controller with a Waters 717 plus Autosampler and a Waters 2996 Photodiode Array Detector running with Empower Pro Empower 2 software.

Experimental procedures, reagents and glassware

Reactions were conducted under a positive pressure of dry nitrogen in oven-dried glassware and at ambient temperature, unless otherwise specified. Anhydrous solvents were either obtained from commercial sources or dried according to the procedure outlined by Grubbs and co-workers.^[275] Commercially available chemicals were used as purchased, or where specified, purified by standard techniques.^[276] Solvent compositions are given in (v/v). Solutions of *n*-BuLi were titrated against menthol with 2,2'-bipyridine as indicator according to the method of Lin and Paquette.^[277] Grignard reagents were titrated using salicylaldehyde phenylhydrazone according to the procedure of Love and Jones.^[278]

8.2 Experimental for Chapter 4

Hepta-1,6-dien-4-yn-3-yl methyl carbonate **4.24**



To a solution of dienynol **4.14** (3.0 g, 28 mmol), *N,N*-diisopropylethylamine (6.0 ml, 34 mmol, 1.2 mol. equiv.) and DMAP (76 mg, 0.62 mmol, 0.022 mol. equiv.) in CH₂Cl₂ (60 mL) was cooled to 0 °C and methylchloroformate (3.0 mL, 39 mmol, 1.4 mol. equiv.) was added dropwise. After the addition was complete, the reaction mixture was brought to room temperature and stirred for a further 18 hours. The reaction mixture was then concentrated under reduced pressure and the residue was dissolved in Et₂O (50 mL), washed with aqueous 2M HCl (2 x 50 mL), saturated aqueous NaHCO₃ solution (50 mL) and brine (50 mL), dried over anhydrous MgSO₄ and filtered through a short plug of silica. The solvent was removed under reduced pressure to give **4.24** (4.5 g, 2.7 mmol, 96%) as a pale yellow oil.

R_f : 0.31 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 6.01-5.89 (m, 1H), 5.88-5.76 (m, 2H), 5.75-5.67 (m, 1H), 5.62-5.50 (m, 2H), 5.35 (dd, *J* = 10.1, 1.1 Hz, 1H), 3.81 (s, 3H) ppm

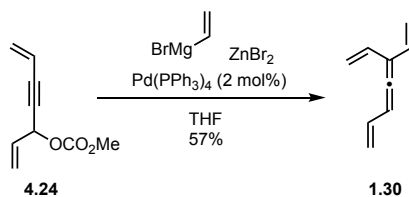
¹³C NMR (100 MHz, CDCl₃): δ 154.9 (C_q), 132.5 (CH), 128.8 (CH₂), 119.7 (CH₂), 116.3 (CH), 86.5 (C_q), 84.3 (C_q), 68.8 (CH), 55.4 (CH₃) ppm

IR (thin film): ν_{max} = 3098, 3015, 2958, 2854, 2233, 1749, 1646, 1600 cm⁻¹

LRMS (EI): *m/z* (%) = 166([M-H]⁺, 4), 151(45), 121(5), 107(34), 91(100)

HRMS (EI): calculated for C₉H₉O [M]⁺ 165.0552; found 165.0548

3-Vinylhepta-1,3,4,6-tetraene **1.30**



A solution of methylcarbonate **4.24** (520 mg, 3.1 mmol) in THF (5 mL) was cooled to $-15\text{ }^\circ\text{C}$ and a solution of zinc bromide (1.0 M in THF, 4.5 mL, 4.5 mmol, 1.5 mol. equiv.) and $\text{Pd(PPh}_3)_4$ (75 mg, 0.064 mmol, 2 mol%) were added in a single portion. Subsequently, a solution of vinylmagnesium bromide in THF (0.70 M, 6.5 mL, 4.5 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. The reaction mixture was then stirred for a further 2 hours at $-15\text{ }^\circ\text{C}$ and was quenched with methanol (0.5 mL). Analysis of the crude product mixture by ^1H NMR spectroscopy with 1,2,3,5-tetramethylbenzene as an internal standard gave estimated yields of trivinylallene in 60% yield from carbonate **4.24**.

An analytically pure sample of trivinylallene **1.30** was obtained for the purposes of characterization by dilution of the crude mixture with *n*-pentane (50 mL) with aqueous wash of the organic layer with water until no THF was observed by ^1H NMR spectroscopy. The organic layer was then washed with brine, dried over anhydrous MgSO_4 and filtered through a short plug of silica. To the *n*-pentane solution was added CDCl_3 (5 mL) and the *n*-pentane was removed 250 mbar at $0\text{ }^\circ\text{C}$ to give **1.30** as a solution in CDCl_3 . If required additional purification by bulb to trap distillation at room temperature of the CDCl_3 solution (with the receiver flask at $-78\text{ }^\circ\text{C}$) could be performed to remove any oligomerization products generated during the removal of *n*-pentane.

R_f : 0.51(*n*-pentane)

^1H NMR (700 MHz, CDCl_3 , measured at 253K): δ 6.28 (ddd, $J = 17.4, 10.6, 1.0$ Hz, 2H), 6.23-6.17 (m, 2H), 5.37 (dt, 17.3, 1.1 Hz, 2H), 5.28 (dd, $J = 16.1, 1.5$ Hz, 1H), 5.21 (dt, $J = 10.6, 1.1$ Hz, 2H), 5.10-5.06 (m, 1H) ppm

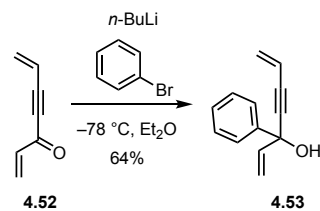
^{13}C NMR (175 MHz, CDCl_3): δ 211.5 (C_q), 131.8 (CH), 130.9 (CH), 117.3 (CH), 116.22 (CH), 106.8 (C_q), 97.3 (CH) ppm

LRMS (EI): m/z (%) = 117 ($[\text{M-H}]^{+\bullet}$, 100), 115 (75), 91(63), 65(42)

HRMS (EI): calculated for C_9H_{10} $[\text{M}]^{+\bullet}$ 118.0783; found 118.0779

UV-VIS: λ_{max} = 216 nm ($\epsilon = 58\ 000$), 230 nm ($\epsilon = 65\ 000$)

3-Phenylhepta-1,6-dien-4-yn-3-ol 4.53



Bromobenzene (1.5 g, 9.6 mmol, 1.7 mol. equiv.) was dissolved in Et₂O (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 6.8 mL, 9.5 mmol, 1.7 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 40 minutes. The mixture was cooled to -78 °C and a solution of ketone **4.52** (0.61 g, 5.7 mmol) in Et₂O (25 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour. The reaction mixture was then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.53** as a yellow oil (0.67 g, 3.6 mmol, 64%).

R_f : 0.31 (petroleum ether 40-60: Et₂O 85:15)

¹H NMR (400 MHz, CDCl₃): δ 7.63 (d, *J* = 7.7 Hz, 2H), 7.39-7.29, m, 2H), 6.09 (dd, *J* = 16.9, 10.2 Hz, 1H), 5.91 (dd, *J* 17.6, 11.1 Hz, 1H), 5.73 (dd, *J* = 17.7, 2.1 Hz, 1H), 5.62-5.54 (m, 2H), 5.21 (d, *J* = 10.1 Hz, 1H), 2.48 (s, 1H, -OH) ppm

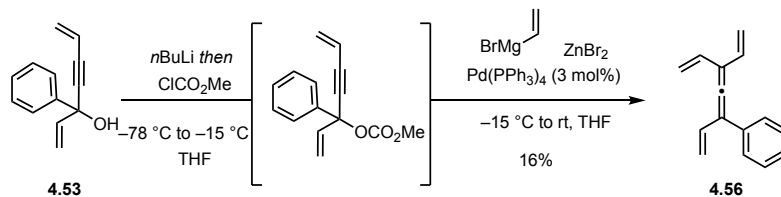
¹³C NMR (100 MHz, CDCl₃): δ 143.1 (C_q), 141.5 (CH), 128.5 (2 x CH), 128.1 (CH), 128.1 (CH₂), 125.9 (2 x CH), 116.6 (CH), 114.1 (CH₂), 90.4 (C_q), 86.1 (C_q), 75.5 (C_q) ppm

IR (thin film): ν_{max} = 3546, 3410 (br), 3091, 3061, 3029, 2986, 2199, 1640, 1599, 1491 cm⁻¹

LRMS (EI): *m/z* (%) = 183 ([M-H]^{+•}, 62), 165 (55), 155 (53), 141 (100), 128 (65), 115 (48), 105 (59), 91 (24), 79 (86)

HRMS (EI): calculated for C₁₃H₁₁O [M-H]^{+•} 183.0810; found 183.0809

(5-vinylhepta-1,3,4,6-tetraen-3-yl)benzene **4.56**



A solution of alcohol **4.53** (150 mg, 0.81 mmol) in THF (4 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.80 mL, 1.1 mmol, 1.4 mol. equiv.) was added dropwise and stirred for 20 minutes. Freshly distilled methyl chloroformate (0.1 mL, 1.3 mmol, 1.6 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 45 min. A solution of zinc bromide (1.0 M in THF, 1.2 mL, 1.2 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (25 mg, 0.022 mmol, 3 mol%) were added in a single portion. Subsequently, a solution of vinylmagnesium bromide in THF (0.70 M, 1.7 mL, 1.2 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. On completion of addition the reaction mixture was brought to room temperature and stirred for a further 40 minutes. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (3 x 10 mL). The organic layers were combined, washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.56** as a colourless oil (27 mg, 0.27 mmol, 16%).

R_f : 0.42 (*n*-pentane)

¹H NMR (700 MHz, CDCl₃): δ 7.39-7.31 (m, 4H), 7.29-7.26 (m, 1H), 6.49 (dd, $J = 17.3, 10.5$ Hz, 1H), 6.36 (dd, $J = 17.3, 10.4$ Hz, 2H), 5.45 (dd, $J = 17.3, 1.2$ Hz, 2H), 5.38 (dd, $J = 17.3, 1.4$ Hz, 1H), 5.29 (dd, $J = 10.5, 1.4$ Hz, 1H), 5.23 (dd, $J = 10.7, 1.2$ Hz, 2H) ppm

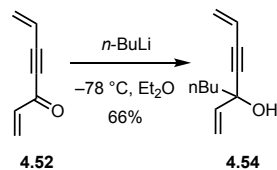
¹³C NMR (175 MHz, CDCl₃): δ 2.115 (C_q), 135.4 (C_q), 132.2 (CH), 131.1 (2 x CH), 128.6 (2 x CH), 127.9 (2 x CH), 127.6 (2 x CH), 117.6 (CH₂), 116.2 (2 x CH₂), 110.7 (C_q), 108.4 (C_q) ppm

IR (thin film): $\nu_{\text{max}} = 3087, 3059, 3019, 2971, 2933, 2855, 1907, 1608, 1598, 1492, 1428, 1408\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 193 ([M-H]⁺, 32), 179(57), 178(100), 165(62), 152(26), 128(11), 115(38), 91(13)

HRMS (EI): calculated for C₁₅H₁₄ [M]⁺ 194.1096; found 194.1091

5-Vinylnon-1-ene-3-yn-5-ol 4.54



A solution of *n*-BuLi (1.4 M in hexanes, 5.3 mL, 7.4 mmol, 1.5 mol. equiv.) was dissolved in Et₂O and cooled to -78 °C. A solution of ketone **4.52** (0.52 g, 4.9 mmol) in Et₂O (25 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour. The reaction mixture was then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.54** as a yellow oil (0.53 g, 3.2 mmol, 66%).

R_f : 0.22 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 5.97-5.80 (m, 2H), 5.66 (d, *J* = 17.6 Hz, 1H), 5.55-5.47 (m, 2H), 5.17 (d, *J* = 10.2 Hz, 1H), 2.013 (s, 1H, -OH), 1.80-1.65 (m, 2H), 1.50-1.29 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm

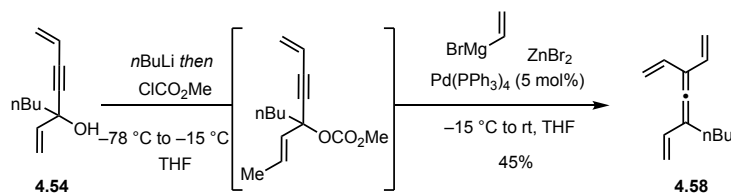
¹³C NMR (100 MHz, CDCl₃): δ 141.3, 127.5, 116.8, 114.6, 90.8 (C_q), 84.6 (C_q), 72.1 (C_q), 42.2, 26.6, 22.9, 14.2(CH₃) ppm

IR (thin film): ν_{max} = 3367 (br), 3089, 3013, 2957, 2934, 2863, 1846, 1610 cm⁻¹

LRMS (EI): *m/z* (%) = 163 ([M-H]⁺•, 10), 137(18), 113(22), 107(100), 77(24), 55(49)

HRMS (EI): calculated for C₁₁H₁₅O [M-H]⁺• 163.1123; found 163.1122

3,5-Divinylanona-1,3,4-triene 4.58



A solution of alcohol **4.54** (200 mg, 1.2 mmol) in THF (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.9 mL, 1.3 mmol, 1.1 mol. equiv.) was added dropwise and stirred for 20 minutes. Methyl chloroformate (0.2 mL, 2.6 mmol, 2.2 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 45 min. A solution of zinc bromide (1.0 M in THF, 1.8 mL, 1.8 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (70 mg, 0.061 mmol, 5 mol%) were added in a single portion. Subsequently, a solution of vinylmagnesium bromide in THF (0.70 M, 2.6 mL, 1.8 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. On completion of addition the reaction mixture was brought to room temperature and stirred for a further 40 minutes. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (3 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.58** as a colourless oil (95 mg, 0.55 mmol, 45%).

R_f : 0.50 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 6.34-6.23 (m, 3H), 5.34 (d, $J = 17.3\text{ Hz}$, 2H), 5.23 (d, $J = 17.5\text{ Hz}$, 1H), 5.15 (d, $J = 10.5\text{ Hz}$, 2H), 5.06 (d, $J = 10.7\text{ Hz}$, 1H), 2.24 (t, $J = 7.5\text{ Hz}$, 2H), 1.50-1.31 (m, 4H), 0.93-0.87 (m, 3H) ppm

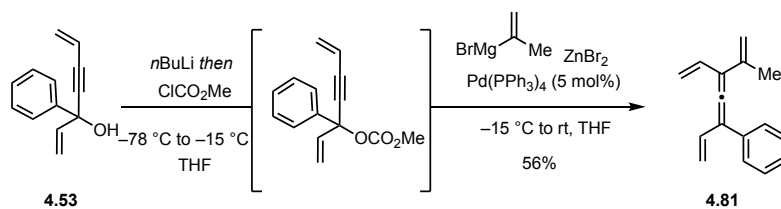
¹³C NMR (100 MHz, CDCl₃): δ 210.8 (C_q), 134.2 (CH), 131.8 (CH x 2), 115.3 (CH₂ x 2), 113.3 (CH₂), 108.1 (C_q), 106.9 (C_q), 29.9 (CH₂), 28.3 (CH₂), 22.7 (CH₂), 14.1 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3091, 3015, 2957, 2927, 2860, 1913, 1804, 1610\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 174 ([M]⁺•, 33), 145(13), 131(59), 117(100), 104(14), 91(48)

HRMS (EI): calculated for C₁₃H₁₈ [M]⁺• 174.1409; found 174.1407

(6-Methyl-5-vinylhepta-1,3,4,6-tetraen-3-yl)benzene **4.81**



A solution of alcohol **4.53** (131 mg, 0.71 mmol) in THF (2 mL) was cooled to $-78\text{ }^\circ\text{C}$ and a solution of $n\text{-BuLi}$ (1.2 M in hexanes, 0.70 mL, 0.84 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 20 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 1.8 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^\circ\text{C}$ for 60 min. A solution of zinc bromide (1.0 M in THF, 1.0 mL, 1.0 mmol, 1.4 mol. equiv.) and $\text{Pd}(\text{PPh}_3)_4$ (40 mg, 0.035 mmol, 5 mol%) were added in a single portion. Subsequently, a solution of isopropenylmagnesium bromide in THF (0.80 M, 1.5 mL, 1.2 mmol, 1.7 mol. equiv.) was added dropwise over 5 minutes. On completion of addition the reaction mixture was brought to room temperature and stirred for a further 15 minutes. The reaction mixture was diluted with $n\text{-pentane}$ (10 mL) and quenched with a solution of saturated aqueous NH_4Cl (10 mL). The aqueous layer was separated and extracted with $n\text{-pentane}$ (3 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO_4 , filtered and concentrated at 100 mbar at $10\text{ }^\circ\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO_2 , $n\text{-pentane}$) afforded allene **4.81** as a colourless oil (83 mg, 0.40 mmol, 56 %).

R_f : 0.40 ($n\text{-pentane}$)

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.39 (m, 5H), 6.51 (dd, $J = 17.3, 10.5$ Hz, 1H), 6.39 (dd, $J = 14.4, 10.4$ Hz, 1H), 5.47 (d, $J = 17.2$ Hz, 1H), 5.37 (d, $J = 17.2$ Hz, 1H), 5.30-5.21 (m, 2H), 5.13 (s, 1H), 5.04 (s, 1H), 1.90 (s, 3H) ppm

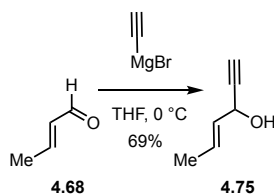
$^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 209.8 (C_q), 139.4 (C_q), 135.7 (C_q), 132.5 (CH), 130.9 (CH), 128.6 (CH), 127.7 (CH), 127.5 (CH), 117.3 (CH_2), 117.3 (CH_2), 112.9 (CH_2), 111.6 (C_q), 111.1 (C_q), 22.1 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3087, 3058, 2972, 2945, 2918, 1907, 1615, 1607, 1598, 1492, 1448\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 193 ($[\text{M}-\text{H}]^{+\bullet}$, 32), 179(57), 178(100), 165(62), 152(26), 128(11), 115(38), 91(13)

HRMS (EI): calculated for $\text{C}_{16}\text{H}_{16}$ $[\text{M}]^{+\bullet}$ 208.1252; found 208.1254

(E)-Hex-4-en-1-yn-3-ol 4.75



A solution of ethynylmagnesium bromide (0.50 M in THF, 300 mL, 150 mmol, 1.1 mol. equiv.) was cooled to 0 °C and a solution of crotonaldehyde (11 mL, 136 mmol) in THF (50 mL) was added dropwise over 30 minutes. The resulting yellow-orange solution was stirred for a further 1 hour at 0 °C. The reaction mixture was quenched with a solution of saturated aqueous NH₄Cl (250 mL) and diluted with Et₂O (250 mL). The aqueous layer was separated and extracted with Et₂O (2 x 150 mL). The organic layers were combined, washed with brine (250 mL), dried over anhydrous MgSO₄, filtered and concentrated. Purification by distillation (20 mmHg, 58-64 °C) afforded alcohol **4.75** as a clear colourless oil (10 g, 104 mmol, 69%).

R_f : 0.40 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 5.94 (dq, *J* = 13.4, 6.6 Hz, 1H), 5.70-5.50 (m, 1H), 4.83 (s, 1H), 2.56 (d, *J* = 2.1 Hz, 1H), 1.74 (dd, *J* = 6.5, 1.5 Hz, 3H) ppm

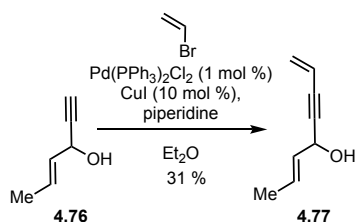
¹³C NMR (100 MHz, CDCl₃): δ 129.8 (CH), 129.2 (CH), 83.5 (C_q), 73.9 (CH), 82.8 (CH), 17.5 (CH₃) ppm

IR (thin film): ν_{max} = 3369 (br), 3292, 3035, 2969, 2942, 2919, 2857, 2121, 1671, 1447 cm⁻¹

LRMS (EI): *m/z* (%) = (96 [M-H]⁺, 92), 95(100), 91(17)

HRMS (EI): calculated for C₆H₈O [M]⁺ 96.0575; found 96.0575

(E)-Octa-2,7-dien-5-yn-4-ol 4.77



A solution of vinyl bromide (8.0 mL, 110 mmol, 3.4 mol. equiv.) in Et₂O (150 mL) was cooled to 0 °C. Propargylic alcohol **4.75** (3.1 g, 32 mmol), Pd(PPh₃)₂Cl₂ (250 mg, 0.36 mmol, 1 mol%) and piperidine (8.0 mL, 81 mmol, 2.5 mol. equiv.) were added. CuI (610 mg, 3.2 mmol, 10 mol%) was added in a single portion and the reaction mixture was stirred at room temperature for 1.5 hours. A solution of saturated aqueous NH₄Cl (200 mL) was added and the aqueous layer was separated and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with aqueous 0.2 M HCl (50 mL), saturated aqueous NaHCO₃ (50 mL), water (2 x 50 mL), dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether:Et₂O 40-60, 90:10) afforded alcohol **4.77** as a yellow oil (1.2 g, 9.8 mmol, 31%).

R_f : 0.10 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 5.95-5.80 (m, 2H), 5.69-5.61 (m, 2H), 5.50 (dd, *J* = 11.1 Hz, 1H), 4.94 (t, *J* = 5.9 Hz, 1H), 1.74 (d, *J* = 6.5 Hz, 3H) ppm

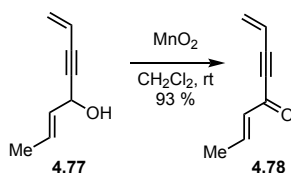
¹³C NMR (100 MHz, CDCl₃): δ 130.2 (CH), 129.2 (CH), 127.7 (CH₂), 116.7 (CH), 89.2 (C_q), 84.7 (C_q), 63.5 (CH), 17.5 (CH₃) ppm

IR (thin film): ν_{max} = 3324 (br), 3105, 3035, 3014, 2969, 2943, 2918, 2856, 1851, 1610, 1447 cm⁻¹

LRMS (EI): *m/z* (%) = 122 ([M]^{+•}, 32), 121(22), 107(59), 105(71), 91(31), 79(100), 77(90)

HRMS (EI): calculated for C₉H₁₀O [M]^{+•} 122.0732; found 122.073

(E)-Octa-2,7-dien-5-yn-4-one 4.78



To a solution of alcohol **4.77** (440 mg, 3.6 mmol) in CH₂Cl₂ (30 mL) was added manganese dioxide (3.2 g, 36 mmol, 10 mol. equiv.) in a single portion. The reaction mixture was stirred at room temperature for 30 min then filtered through a pad of silica, flushed with Et₂O (100 mL) and concentrated under reduced pressure to afford ketone **4.78** as a yellow oil (400 mg, 3.3 mmol, 93%).

R_f : 0.28 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.23-7.12 (m, 1H), 6.19 (dt, *J* = 15.6, 1.8 Hz, 1H), 5.98-5.93 (m, 2H), 5.86-5.70 (m, 1H), 1.99 (d, *J* = 6.9 Hz, 3H) ppm

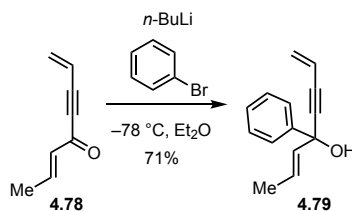
¹³C NMR (100 MHz, CDCl₃): δ 178.4 (C_q), 149.8 (CH), 133.9 (CH), 132.6 (CH₂), 115.4 (CH), 89.4 (C_q), 86.6 (C_q), 18.6 (CH₃) ppm

IR (thin film): ν_{max} = 3107, 3040, 3021, 2981, 2946, 2916, 2849, 2254, 2187, 1644, 1623, 1441 cm⁻¹

LRMS (EI): *m/z* (%) = 120 ([M]^{+•}, 40), 91(99), 79(100), 65(18), 51(38)

HRMS (EI): calculated for C₈H₈O [M]^{+•} 120.0575; found 120.0576

(E)-4-Phenylocta-2,7-dien-5-yn-4-ol 4.79



Bromobenzene (0.6 mL, 5.7 mmol, 1.6 mol. equiv.) was dissolved in Et₂O (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 4.0 mL, 5.6 mmol, 1.6 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 30 minutes. The reaction mixture was cooled to -78 °C and a solution of ketone **4.78** (420 mg, 3.5 mmol) in Et₂O (10 mL) was added dropwise. The reaction mixture was stirred for a further 1 hour at -78 °C then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL) and the aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.79** as a yellow oil (490 g, 2.5 mmol, 71%).

R_f : 0.38 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (700 MHz, CDCl₃): δ 7.62-7.61 (m, 2H), 7.38-7.35 (m, 2H), 7.31-7.28 (m, 1H), 6.03 (dq, *J* = 15.0, 6.7 Hz, 1H), 5.91 (dd, *J* = 17.6, 11.2 Hz, 1H), 5.75-5.71 (m, 2H), 5.54 (dd, *J* = 11.2, 2.0 Hz, 1H), 2.42 (s, 1H, -OH), 1.74 (dd, *J* = 6.7, 1.8 Hz, 3H) ppm

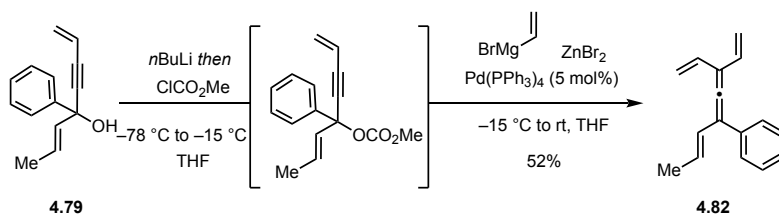
¹³C NMR (175 MHz, CDCl₃): δ 143.9 (C_q), 134.9 (CH), 128.4 (2 x CH), 127.9 (CH₂), 127.8 (CH), 126.2 (CH), 125.8 (2x CH), 116.7 (CH), 91.1 (C_q), 85.8 (C_q), 73.2 (C_q), 17.5 (CH₃) ppm

IR (thin film): ν_{max} = 3549, 3402(br), 3061, 3029, 2966, 2943, 2916, 2881, 2856, 1667, 1599, 1489, 1448 cm⁻¹

LRMS (EI): *m/z* (%) = 197 ([M-H]^{+•}, 25), 183(77), 178(46), 165(83), 155(100), 141(48), 128(54), 115(22), 105(65), 91(44), 77(88)

HRMS (EI): calculated for C₁₄H₁₄O [M]^{+•} 198.1045; found 198.1038

(*E*)-(6-Vinylocta-2,4,5,7-tetraen-4-yl) benzene **4.82**



A solution of alcohol **4.79** (100 mg, 0.50 mmol) in THF (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.50 mL, 0.70 mmol, 1.4 mol. equiv.) was added dropwise and stirred for 20 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.6 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 45 min. A solution of zinc bromide (1.0 M in THF, 0.80 mL, 0.80 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (30 mg, 0.026 mmol, 5 mol%) were added in a single portion. Subsequently, a solution of vinylmagnesium bromide in THF (0.70 M, 0.52 mL, 0.75 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. On completion of addition the reaction mixture was brought to room temperature and stirred for a further 40 minutes. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (3 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous K₂CO₃, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.82** as a colourless oil (55 mg, 0.26 mmol, 52%).

R_f : 0.28 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 7.37-7.25 (m, 5H), 6.36 (dd, $J = 17.3, 10.6\text{ Hz}$, 2H), 6.13 (dd, $J = 15.4, 1.8\text{ Hz}$, 1H), 5.84 (dq, $J = 13.4, 6.7\text{ Hz}$, 1H), 5.44 (d, $J = 17.4\text{ Hz}$, 2H), 5.20 (d, $J = 10.6\text{ Hz}$, 2H), 1.83 (dd, $J = 6.8, 1.5\text{ Hz}$, 3H) ppm

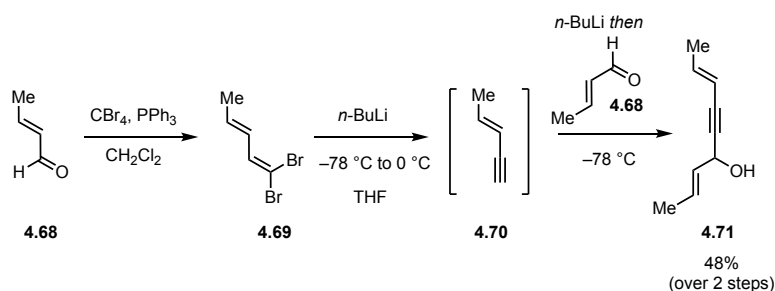
¹³C NMR (100 MHz, CDCl₃): δ 210.9 (C_q), 136.1 (C_q), 131.4 (CH), 129.7 (CH), 128.6 (2 x CH), 127.8 (2 x CH), 127.5 (CH), 125.6 (CH), 115.8 (CH₂), 110.4 (C_q), 108.1 (C_q), 18.6 (CH₃) ppm

IR (thin film): ν_{max} = 3091, 3056, 3016, 2965, 2932, 2913, 2874, 2852, 1905, 1811, 1610, 1597, 1492 cm⁻¹

LRMS (EI): m/z (%) = 208 ([M]⁺,15), 193(67), 178(100), 165(63), 152(25), 128(15), 115(63), 91(19)

HRMS (EI): calculated for C₁₆H₁₆ [M]⁺ 208.1252; found 208.1250

(2*E*, 7*E*)-Nona-2,7-dien-5-yn-4-ol 4.71



A solution of crotonaldehyde (4.1 g, 50 mmol) in CH_2Cl_2 (250 mL) was cooled to $0\text{ }^\circ\text{C}$ and CBr_4 (33 g, 99 mmol, 2.0 mol. equiv.) was added in a single portion. To this mixture was added PPh_3 (52 g, 200 mmol, 4.0 mol. equiv.) over 5 minutes in 5 x 10 g portions. The reaction was stirred at $0\text{ }^\circ\text{C}$ for 30 minutes, then diluted with *n*-pentane (100 mL). The mixture was filtered through a pad of celite and concentrated under reduced pressure (not below 100 mbar at $25\text{ }^\circ\text{C}$). The crude mixture was taken up in *n*-pentane and filtered through a pad of silica. Concentration under reduced pressure afforded dibromoolefin **4.69** as a colourless oil (8.0 g), which was immediately subjected to the next step without further purification. ^1H and ^{13}C NMR matched reported data.^[279] Note: this reaction was carried out in the dark by turning off the fumehood light.

^1H NMR (400 MHz, CDCl_3): δ 6.89 (d, $J = 10.0$ Hz, 1H), 6.20-6.04 (m, 1H), 5.92 (dq, $J = 14.0, 6.7$ Hz, 1H), 1.77 (d, $J = 6.6$ Hz, 3H) ppm

^{13}C NMR (100 MHz, CDCl_3): δ 137.2 (CH), 134.3 (CH), 128.7 (CH), 88.3 (C_q), 18.7 (CH_3) ppm

A solution of the crude dibromoolefin **4.69** in THF (50 mL) was cooled to $-78\text{ }^\circ\text{C}$ and $n\text{-BuLi}$ (1.4 M in hexanes, 50 mL, 71 mmol, 2.0 mol. equiv.) was added dropwise. The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 30 minutes and then at $0\text{ }^\circ\text{C}$ for a further 30 minutes. The reaction mixture was then cooled to $-78\text{ }^\circ\text{C}$ and a solution of crotonaldehyde (3.0 g, 42.0 mmol, 1.2 mol. equiv.) in THF (50 mL) was added dropwise. The reaction was stirred at $-78\text{ }^\circ\text{C}$ for a further 30 minutes and subsequently quenched with a solution of saturated aqueous NH_4Cl (100 mL) and diluted with Et_2O (50 mL). The aqueous layer was separated and extracted with Et_2O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , petroleum ether 40-60: Et_2O , 80:20) afforded alcohol **4.71** as a yellow oil (3.3 g, 24 mmol, 48% over 2 steps).

R_f : 0.11 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 6.18 (dq, *J* = 16.2, 6.7 Hz, 1H), 5.94-5.83 (m, 1H), 5.63 (ddt, *J* = 15.2, 6.2, 1.6 Hz, 1H), 5.56-5.49 (m, 1H), 4.91 (t, *J* = 6.3 Hz, 1H), 1.78 (d, *J* = 6.7 Hz, 3H), 1.73 (d, *J* = 6.6 Hz, 3H) ppm

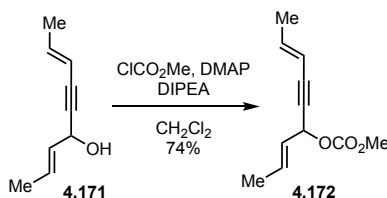
¹³C NMR (100 MHz, CDCl₃): δ 140.6 (CH), 130.5 (CH), 128.9 (CH), 110.2 (CH), 86.8 (C_q), 84.8 (C_q), 63.6 (CH), 18.8 (CH₃), 17.6 (CH₃) ppm

IR (thin film): ν_{max} = 3347, 3029, 2962, 2917, 2855, 2206, 1671, 1436 cm⁻¹

LRMS (EI): *m/z* (%) = 136 (17), 121 (100), 115 (20), 107(24), 91 (98), 77 (98)

HRMS (EI): calculated for C₉H₁₂O [M]⁺• 136.0888; found 136.0889

Methyl ((2*E*,7*E*)-nona-2,7-dien-5-yn-4-yl) carbonate **4.172**



To a solution of dienynol **4.171** (1.0 g, 7.3 mmol), *N,N*-diisopropylethylamine (1.5 ml, 8.8 mmol, 1.2 mol. equiv.) and DMAP (18 mg, 0.15 mmol, 0.02 mol. equiv.) in CH₂Cl₂ (80 mL) was cooled to 0 °C and methylchloroformate (0.70 mL, 8.8 mmol, 1.2 mol. equiv.) was added dropwise. After the addition was complete, the reaction mixture was brought to room temperature and stirred for a further 18 hours. The reaction mixture was then concentrated under reduced pressure and the residue was dissolved in Et₂O (50 mL), washed with aqueous 2M HCl (2 x 50 mL), saturated aqueous NaHCO₃ solution (50 mL) and brine (50 mL), dried over anhydrous MgSO₄ and filtered through a short plug of silica. The solvent was removed under reduced pressure to give **4.172** (1.1 g, 5.7 mmol, 74%) as a pale yellow oil.

R_f : 0.42 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 6.22 (dq, *J* = 16.1, 6.9 Hz, 1H), 6.09-5.93 (m, 1H), 5.77 (d, *J* = 6.8 Hz, 1H), 5.61 (ddd, *J* = 15.2, 6.9, 1.7 Hz, 1H), 5.56-5.46 (m, 1H), 3.79 (s, 3H), 1.79 (dd, *J* = 6.8, 1.8 Hz, 3H), 1.75 (d, *J* = 6.6 Hz, 3H) ppm

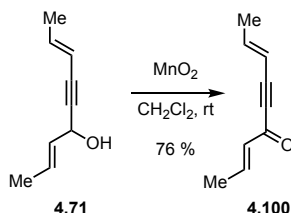
¹³C NMR (100 MHz, CDCl₃): δ 155.0 (C_q), 141.6 (CH), 132.3 (CH), 126.1 (CH), 109.9 (CH), 86.3 (C_q), 82.7 (C_q), 69.2 (CH), 55.0 (CH₃), 18.8 (CH₃), 17.7 (CH₃) ppm

IR (thin film): ν_{max} = 3036, 2958, 2856, 2218, 1747, 1698, 1673 cm⁻¹

LRMS (EI): m/z (%) = 194([M]⁺•, 45), 179(39), 135(76), 119(99), 103(68), 91(100)

HRMS (EI): calculated for C₁₁H₁₄O₃ [M]⁺• 194.0943; found 194.0941

(2*E*, 7*E*)-Nona-2,7-dien-5-yn-4-one 4.100



To a solution of alcohol **4.71** (3.0 g, 22 mmol) in CH₂Cl₂ (150 mL) was added manganese dioxide (20 g, 230 mmol, 11 mol. equiv.) in a single portion and the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was then filtered through a pad of silica, flushed with Et₂O (300 mL) and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60: Et₂O, 90:10) afforded ketone **100** as a yellow oil (2.3 g, 17 mmol, 76%).

R_f : 0.24 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.15 (dq, *J* = 15.8, 6.9 Hz, 1H), 6.51 (dq, *J* = 15.9, 6.9 Hz, 1H), 6.18 (dd, *J* = 15.7, 6.2, 1.7 Hz, 1H), 5.66 (dd, *J* = 15.8, 1.9 Hz, 1H), 1.97 (dd, *J* = 6.9, 1.6 Hz, 3H), 1.88 (dd, *J* = 7.0, 1.8 Hz, 3H) ppm

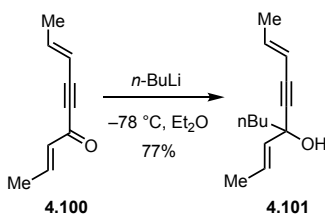
¹³C NMR (100 MHz, CDCl₃): δ 178.7 (C_q), 149.1 (CH), 147.0 (CH), 134.0 (CH), 109.1 (CH), 90.6 (C_q), 85.3 (C_q), 19.3 (CH₃), 18.5 (CH₃) ppm

IR (thin film): ν_{max} = 3040, 2978, 2916, 2192, 1652, 1620, 1440 cm⁻¹

LRMS (EI): m/z (%) = 134 (83), 119 (22), 105 (37), 93 (100), 77 (41), 65 (95)

HRMS (EI): calculated for C₉H₁₀O [M]⁺• 134.0732; found 134.0729

(E)-5-((E)-prop-1-en-1-yl)dec-8-en-6-yn-5-ol 4.101



A solution of *n*-BuLi (1.4 M in hexanes, 4.8 mL, 6.7 mmol, 1.7 mol. equiv.) was dissolved in Et₂O (10 mL) and cooled to -78 °C. A solution of ketone **4.100** (530 mg, 3.9 mmol) in Et₂O (20 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at -78 °C. The reaction mixture was then diluted a solution of saturated aqueous NH₄Cl solution (100 mL) and the aqueous layer was separated and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.101** as a pale yellow oil (570 mg, 3.0 mmol, 77%).

R_f : 0.44 (petroleum ether 40-60:Et₂O, 80:20)

¹H NMR (400 MHz, CDCl₃): δ 6.16 (dq, *J* = 15.9, 6.8 Hz, 1H), 5.97 (dq, *J* = 15.3, 6.6 Hz, 1H), 5.59-5.48 (m, 2H), 1.79 (dd, *J* = 6.8, 1.8 Hz, 3H), 1.75-1.60 (m, 5H), 1.48-1.24 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H) ppm

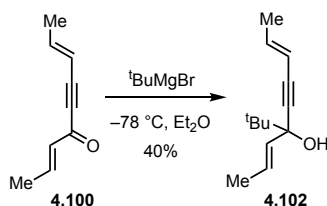
¹³C NMR (100 MHz, CDCl₃): δ 140.1 (CH), 134.7 (CH), 126.3 (CH), 110.4 (CH), 89.1 (C_q), 84.5 (C_q), 71.8 (C_q), 42.7 (CH₂), 26.8 (CH₂), 22.9 (CH₂), 18.7 (CH₃), 17.5 (CH₃), 14.2 (CH₃) ppm

IR (thin film): ν_{max} = 3412 (br), 3028, 2958, 2936, 2861, 2731, 2184, 1666 cm⁻¹

LRMS (EI): *m/z* (%) = 191 ([M-H]⁺, 3), 174(14), 145(14), 135(100), 117(19), 105(14), 91(33)

HRMS (EI): calculated for C₁₃H₂₀O [M]⁺ 192.1514; found 192.1514

(2*E*,7*E*)-4-(*tert*-butyl)nona-2,7-dien-5-yn-4-ol 4.102



A solution of *tert*-butylmagnesium chloride solution (2.0 M in Et_2O , 2.8 mL, 5.6 mmol, 1.5 mol. equiv.) was dissolved in Et_2O (10 mL) and cooled to $-78\text{ }^\circ\text{C}$. A solution of ketone **4.100** (500 mg, 3.7 mmol) in Et_2O (10 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at $-78\text{ }^\circ\text{C}$. The reaction mixture quenched with a solution of saturated aqueous NH_4Cl (100 mL) and the aqueous layer was separated and extracted with Et_2O (3 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , petroleum ether 40-60: Et_2O : NEt_3 , 85:15:2) afforded alcohol **4.102** as a pale yellow oil (430 mg, 2.2 mmol, 40%).

R_f : 0.33 (petroleum ether 40-60: Et_2O , 80:20)

¹H NMR (700 MHz, CDCl_3): δ 6.15 (dq, $J = 15.8, 6.8$ Hz, 1H), 5.97 (dq, $J = 15.3, 6.6$ Hz, 1H), 5.67-5.64(m, 1H), 5.56-5.28 (m, 1H), 1.79 (dd, $J = 6.8, 1.8$ Hz, 3H), 1.74 (dd, $J = 6.5, 1.7$ Hz, 3H), 1.01 (s, 9H) ppm

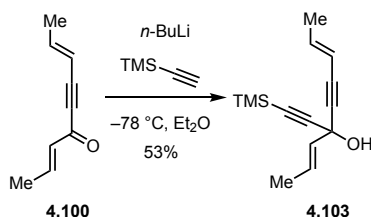
¹³C NMR (175 MHz, CDCl_3): δ 139.7 (CH), 131.7 (CH), 127.2 (CH), 110.5 (CH), 88.9 (C_q), 84.9 (C_q), 77.5 (C_q), 39.0 (C_q), 25.3 (3 x CH_3), 18.7 (CH_3), 17.2 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3469$ (br), 3030, 2964, 2916, 2873, 2184, 1668, 1525, 1447 cm^{-1}

LRMS (EI): m/z (%) = 192 ($[\text{M}]^{+\bullet}$, 3), 177(16), 159(8), 135(100), 115(30), 107(35), 91(70)

HRMS (EI): calculated for $\text{C}_{13}\text{H}_{20}\text{O}$ $[\text{M}]^{+\bullet}$ 192.1514; found 192.1510

(2*E*, 7*E*)-4-((trimethylsilyl)ethynyl)nona-2,7-dien-5-yn-4-ol 4.103



Trimethylsilylacetylene (0.8 mL, 5.6 mmol, 1.5 mol. equiv.) was dissolved in Et₂O (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 4.0 mL, 5.6 mmol, 1.5 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 30 minutes. The mixture was cooled to -78 °C and a solution of ketone **4.100** (500 mg, 3.7 mmol) in Et₂O (15 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at -78 °C. The reaction mixture was then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.103** as a pale yellow oil (450 mg, 1.9 mmol, 53%).

R_f: 0.42 (petroleum ether 40-60:Et₂O, 80:20)

¹H NMR (400 MHz, CDCl₃): δ 6.29-6.10 (m, 2H), 5.69 (dd, *J* = 15.1, 1.7 Hz, 1H), 5.54 (dd, *J* = 15.8, 1.9 Hz, 1H), 1.82-1.73 (m, 6H), 0.20 (s, 9H) ppm

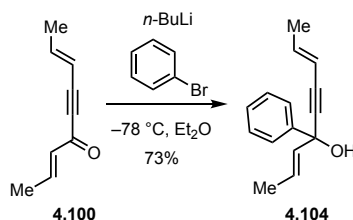
¹³C NMR (100 MHz, CDCl₃): δ 141.4 (CH), 131.6 (CH), 127.9 (CH), 110.0 (CH), 103.9 (C_q), 89.3 (C_q), 86.4 (C_q), 83.4 (C_q), 63.9 (C_q), 18.9 (CH₃), 17.4 (CH₃), -0.07 (3 x CH₃) ppm

IR (thin film): ν_{max} = 3426 (br), 3032, 2963, 2915, 2860, 2218, 2176, 1672 cm⁻¹

LRMS (EI): *m/z* (%) = 231 ([M-H]⁺•, 5), 217(35), 201(22), 189(9), 159(10), 141(18), 115(15), 97(15), 73(100)

HRMS (EI): calculated for C₁₄H₂₀OSi [M]⁺• 232.1283; found 232.1275

(2*E*, 7*E*)-4-Phenylnona-2,7-dien-5-yn-4-ol 4.104



Bromobenzene (1.0 mL, 9.6 mmol, 2.1 mol. equiv.) was dissolved in Et₂O (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 7.0 mL, 9.8 mmol, 2.2 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 30 minutes. The mixture was cooled to -78 °C and a solution of ketone **4.100** (600 mg, 4.5 mmol) in Et₂O (25 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at -78 °C. The reaction mixture was then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.104** as a yellow oil (700 g, 3.3 mmol, 73%).

R_f : 0.25 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.63-7.60 (m, 2H), 7.38-7.34 (m, 2H), 7.30-7.27 (m, 1H), 6.23 (dq, *J* = 15.8, 6.8 Hz, 1H), 6.01 (dq, *J* = 15.2, 6.6 Hz, 1H), 5.73 (dd, *J* = 15.2, 1.6 Hz, 1H), 5.60 (dd, *J* = 15.9, 1.8 Hz, 1H), 2.40-2.39 (m, 1H, -OH), 1.81 (dd, *J* = 6.8, 1.8 Hz, 3H), 1.73 (dd, *J* = 6.6, 1.6 Hz, 3H) ppm

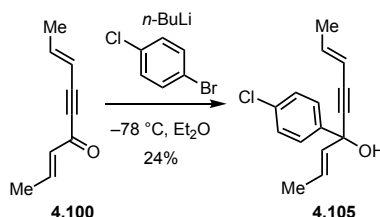
¹³C NMR (100 MHz, CDCl₃): δ 144.2 (C_q), 140.7 (CH), 135.2 (CH), 128.4 (2 x CH), 127.8 (CH), 125.9 (CH), 125.8 (2 x CH), 110.2 (CH), 88.7 (C_q), 85.9 (C_q), 73.2 (C_q), 18.8 (CH₃), 17.5 (CH₃) ppm

IR (thin film): ν_{max} = 3409(br), 3063, 3028, 2964, 2938, 2915, 2858, 2217, 1672, 1597, 1489, 1448 cm⁻¹

LRMS (EI): *m/z* (%) = 211 ([M-H]⁺, 24), 197(94), 179(100), 178(97), 169(81), 165(68), 153(55), 141(52), 128(41), 115(37), 105(42), 91(23), 77(30)

HRMS (EI): calculated for C₁₅H₁₆O [M]⁺ 212.1201; found 212.1200

(2*E*, 7*E*)-4-(4-Chlorophenyl)nona-2,7-dien-5-yn-4-ol 4.105



1-Bromo-4-chlorobenzene (1.5 g, 9.6 mmol, 1.7 mol. equiv.) was dissolved in Et₂O (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 6.8 mL, 9.5 mmol, 1.7 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 40 minutes. The mixture was cooled to -78 °C and a solution of ketone **4.100** (610 mg, 5.7 mmol) in Et₂O (25 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at -78 °C. The reaction mixture was then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.105** as a pale yellow oil (330 mg, 1.3 mmol, 24%).

R_f : 0.36 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.56-7.49 (m, 2H), 7.34-7.29 (m, 2H), 6.23 (dq, *J* = 15.9, 6.8 Hz, 1H), 6.00 (dq, *J* = 15.2, 6.6 Hz), 1H), 5.68 (dd, *J* = 15.2, 1.7 Hz, 1H), 5.58 (dd, *J* = 15.8, 1.9 Hz, 1H), 2.38 (s, 1H, -OH), 1.81 (dd, *J* = 6.9, 1.8 Hz, 3H), 1.73 (dd, *J* = 6.6, 1.6 Hz, 3H) ppm

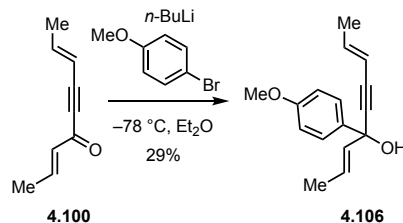
¹³C NMR (100 MHz, CDCl₃): δ 142.7 (C_q), 141.0 (CH), 134.9 (CH), 133.6 (C_q), 128.5 (2 x CH), 127.4 (2 x CH), 126.4 (CH), 110.0 (CH), 88.3 (C_q), 88.2 (C_q), 72.8 (C_q), 18.8 (CH₃), 17.5 (CH₃) ppm

IR (thin film): ν_{max} = 3381 (br), 3033, 2967, 2940, 2915, 2853, 2219, 1669, 1595, 1579, 1488 cm⁻¹

LRMS (EI): *m/z* (%) = 245 ([M-H]⁺, 6), 231(41), 211(33), 193(53), 178(82), 165(53), 152(53), 139(100), 111(45), 93(39), 75(31)

HRMS (EI): calculated for C₁₅H₁₅O³⁵Cl [M]⁺ 246.0811; found 246.0809

(2*E*, 7*E*)-4-(4-Methoxyphenyl)nona-2,7-dien-5-yn-4-ol 4.106



1-Bromo-4-methoxybenzene (0.70 mL, 5.6 mmol, 1.4 mol. equiv.) was dissolved in THF (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 4.0 mL, 5.6 mmol, 1.4 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 40 minutes. The mixture was cooled to -78 °C and a solution of ketone **4.100** (500 mg, 3.7 mmol) in THF (10 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at -78 °C. The reaction mixture was then diluted with Et₂O (100 mL) and quenched with a solution of saturated aqueous NH₄Cl (100 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.106** as an orange oil (270 g, 1.1 mmol, 29%).

R_f : 0.24 (petroleum ether 40-60:Et₂O, 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.53 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.22 (dq, *J* = 16.0, 6.8 Hz, 1H), 5.98 (dq, *J* = 15.4, 6.6 Hz, 1H), 5.72 (dd, *J* = 15.2, 1.8 Hz, 1H), 5.60 (dd, *J* = 15.8, 2.0 Hz, 1H), 3.81 (s, 3H), 2.34-2.33 (m, 1H, -OH), 1.80 (dd, *J* = 6.8, 1.7 Hz, 3H), 1.73 (dd, *J* = 16.5, 1.5 Hz, 3H) ppm

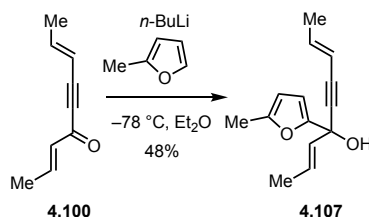
¹³C NMR (100 MHz, CDCl₃): δ 159.3 (C_q), 140.6 (CH), 136.4 (C_q), 135.3 (CH), 127.1 (2 x CH), 125.6 (CH), 113.7 (2 x CH), 110.3 (CH), 88.9 (C_q), 85.8 (C_q), 72.9 (C_q), 55.5 (CH₃), 18.8 (CH₃), 17.5 (CH₃) ppm

IR (thin film): ν_{max} = 3456 (br), 3028, 2999, 2967, 2932, 2916, 2855, 2834, 2214, 1607, 1584, 1508 cm⁻¹

LRMS (EI): *m/z* (%) = 242 ([M]^{+•}, 19), 241(19), 227(60), 209(42), 199(100), 184(51), 165(66), 152(49), 141(32), 128(23), 115(43)

HRMS (EI): calculated for C₁₆H₁₈O [M]^{+•} 242.1307; found 242.1305

(2*E*, 7*E*)-4-(5-methylfuran-2-yl)nona-2,7-dien-5-yn-4-ol 4.107



2-Methylfuran (0.60 mL, 5.6 mmol, 1.4 mol. equiv.) was dissolved in THF (10 mL) and cooled to 0 °C. A solution of *n*-BuLi (1.4 M in hexanes, 4.0 mL, 5.6 mmol, 1.4 mol. equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 40 minutes. The mixture was cooled to -78 °C and a solution of ketone **4.100** (500 mg, 3.7 mmol) in THF (10 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour at -78 °C. The reaction mixture was then diluted with Et₂O (50 mL) and quenched with a solution of saturated aqueous NH₄Cl (50 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O:NEt₃, 85:15:2) afforded alcohol **4.107** as an orange oil (390 g, 1.8 mmol, 48%).

R_f: 0.15 (petroleum ether 40-60: Et₂O, 85:15)

¹H NMR (700 MHz, CDCl₃): δ 6.29-6.18 (m, 2H), 6.09 (dq, *J* = 15.3, 6.5 Hz, 1H), 5.94-5.79 (m, 2H), 5.58 (dd, *J* 15.8, 1.5 Hz, 1H), 2.30 (d, *J* = 1.1 Hz, 3H), 1.80 (dd, *J* = 6.8, 1.4 Hz, 3H), 1.77 (dd, *J* = 6.6, 1.4 Hz, 3H) ppm

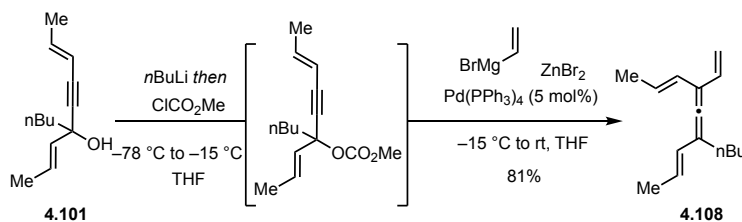
¹³C NMR (175 MHz, CDCl₃): δ 153.5 (C_q), 152.7 (C_q), 141.0 (CH), 131.5 (CH), 127.7 (CH), 110.1 (CH), 107.7 (CH), 106.3 (CH), 85.6 (C_q), 85.0 (C_q), 68.6 (C_q), 18.8 (CH₃), 17.6 (CH₃), 13.9 (CH₃) ppm

IR (thin film): ν_{max} = 3420 (br), 3030, 2968, 2935, 2918, 2879, 2856, 2218, 1695 cm⁻¹

LRMS (EI): *m/z* (%) = 216 ([M]^{+•}, 45), 201(85), 173(100), 159(49), 145(55), 128(36), 115(50), 109(87), 91(65)

HRMS (EI): calculated for C₁₄H₁₆O₂ [M]^{+•} 216.1150; found 216.1154

(*E*)-6-((*E*)-prop-1-en-1-yl)-4-vinyldeca-2,4,5-triene 4.108



A solution of alcohol **4.101** (320 mg, 1.7 mmol) in THF (10 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 1.4 mL, 2.0 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.2 mL, 2.6 mmol, 1.5 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 minutes. A solution of zinc bromide (1.00 M in THF, 2.3 mL, 2.3 mmol, 1.4 mol. equiv.) and Pd(PPh₃)₄ (91 mg, 0.079 mmol, 5 mol%) were added in a single portion. A solution of vinylmagnesium bromide in THF (0.75 M, 3.3 mL, 2.5 mmol, 1.5 mol. equiv.) was added dropwise over 10 minutes. On completion of addition the reaction mixture was stirred for a further 40 minutes at room temperature. The reaction was diluted with *n*-pentane (20 mL) and quenched with a solution of saturated aqueous NH₄Cl (20 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 20 mL). The organic layers were combined and washed with brine (50 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.108** as a colourless oil (280 mg, 1.4 mmol, 81%).

R_f : 0.64 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 6.25 (dd, $J = 17.4, 10.6$ Hz, 1H), 5.95-5.91 (m, 2H), 5.82-5.63 (m, 2H), 5.29 (dd, $J = 17.4, 1.4$ Hz, 1H), 5.05 (dd, $J = 10.6, 1.4$ Hz, 1H), 2.18 (t, $J = 7.4$ Hz, 2H), 1.78 (m, 6H), 1.46-1.27 (m, 4H), 0.89 (t, 7.2Hz, 3H) ppm

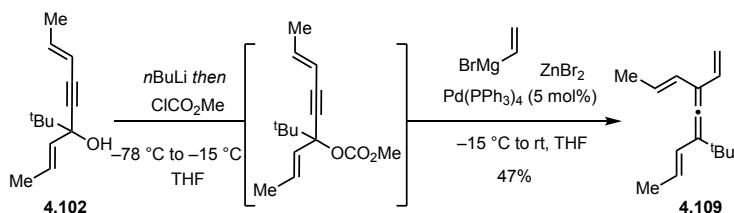
¹³C NMR (100 MHz, CDCl₃): δ 209.4 (C_q), 133.3 (CH), 128.1 (CH), 127.0 (CH), 125.2 (CH), 124.6 (CH), 114.2 (CH₂), 107.3 (C_q), 106.4 (C_q), 95.1 (C_q), 30.0 (CH₂), 29.2 (CH₂), 22.8 (CH₂), 18.6 (CH₃), 18.5 (CH₃), 14.1 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3015, 2958, 2928, 2857, 1914, 1613, 1448\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 202 ([M]^{+•},15), 187(55), 173(17), 160(49), 145(100), 131(96), 117(92),105(81), 91(87), 77(66)

HRMS (EI): calculated for C₁₅H₂₂ [M]^{+•} 202.1722; found 202.1724

(2*E*,7*E*)-4-(*tert*-butyl)-6-vinylnona-2,4,5,7-tetraene 4.109



A solution of alcohol **4.102** (200 mg, 1.0 mmol) in THF (5 mL) was cooled to -78 °C and a solution of *n*-BuLi (1.4 M in hexanes, 1.2 mL, 1.7 mmol, 1.7 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 1.3 mol. equiv.) was added dropwise and the reaction mixture was stirred at -15 °C for 40 minutes. A solution of zinc bromide (1.00 M in THF, 1.5 mL, 1.5 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (62 mg, 0.054 mmol, 5 mol %) were added in a single portion. A solution of vinylmagnesium bromide in THF (0.75 M, 2.5 mL, 1.9 mmol, 1.9 mol. equiv.) was added dropwise over 10 minutes. On completion of addition the reaction mixture was stirred for a further 40 minutes at room temperature. The reaction was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl solution (10 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at 10 °C until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.109** as a colourless oil (110 mg, 53 mmol, 47%).

R_f : 0.48 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 6.28 (dd, *J* = 17.4, 10.6 Hz, 1H), 5.96 (dt, *J* = 15.5, 1.6 Hz, 1H), 5.88-5.66 (m, 3H), 5.31 (dd, *J* = 17.4, 3.1 Hz, 1H), 5.06 (dd, *J* = 10.6, 1.3 Hz, 1H), 1.79 (d, *J* = 6.6 Hz, 3H), 1.75 (d, *J* = 3.79 Hz, 3H), 1.10 (s, 9H) ppm

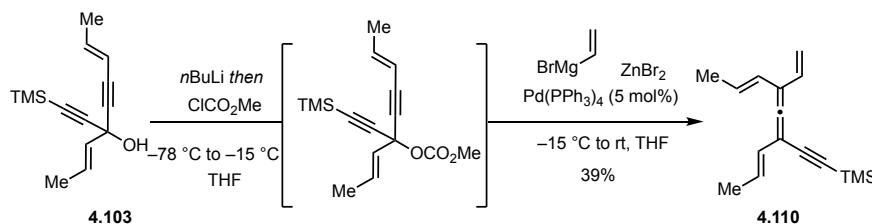
¹³C NMR (100 MHz, CDCl₃): δ 205.2 (C_q), 133.4 (CH), 128.2 (CH), 126.0 (CH), 125.6 (CH), 124.4 (CH), 116.4 (C_q), 113.5 (CH₂), 107.4 (C_q), 34.7 (C_q), 29.6 (CH₃), 18.6 (CH₃), 18.6 (CH₃) ppm

IR (thin film): ν_{max} = 3090, 3018, 2960, 2932, 2872, 1933, 1613, 1464 cm⁻¹

LRMS (EI): *m/z* (%) = 203 ([M]^{+•}, 42), 175(22), 161(25), 147(28), 134(62), 119(100), 105(63), 91(58)

HRMS (EI): calculated for C₁₅H₂₃ [M]^{+•} 203.1800; found 202.1792

Trimethyl(*E*)-3-((*E*)-prop-1-en-1-yl)-5-vinylocta-3,4,6-trien-1-yn-1-yl)silane **4.110**



A solution of alcohol **4.103** (180 mg, 0.77 mmol) in THF (2 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.80 mL, 1.1 mmol, 1.4 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 1.7 mol. equiv.) was added dropwise and the reaction mixture was stirred for 1 hour at $-15\text{ }^{\circ}\text{C}$. A solution of zinc bromide (1.00 M in THF, 1.1 mL, 1.1 mmol, 1.4 mol. equiv.) and Pd(PPh₃)₄ (48 mg, 0.042 mmol, 5 mol %) were added in a single portion. A solution of vinylmagnesium bromide in THF (0.70 M, 1.6 mL, 1.1 mmol, 1.4 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was brought to room temperature and stirred for a further 1 hour. The reaction mixture was diluted with *n*-pentane (20 mL) and quenched with saturated aqueous NH₄Cl (20 mL) and the aqueous layer was separated and extracted with *n*-pentane (2 x 20 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.110** as a yellow oil (73 mg, 0.30 mmol, 39%).

R_f : 0.34 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 6.30-6.09 (m, 2H), 5.98-5.89 (m, 1H), 5.78 (dd, $J = 15.1, 1.6$ Hz, 1H), 5.67 (dd, $J = 15.8, 1.8$ Hz, 1H), 5.27 (dd, $J = 17.5, 1.2$ Hz, 1H), 5.14 (dd, $J = 10.4, 1.2$ Hz, 1H), 1.80 (m, 6H), 0.21 (s, 9H) ppm

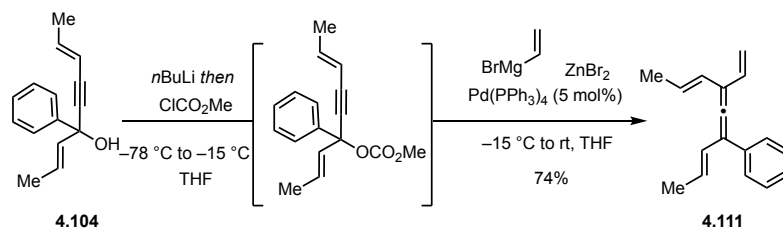
¹³C NMR (100 MHz, CDCl₃): δ 216.5 (C_q), 139.1 (CH), 132.3 (CH), 126.4 (CH), 125.7 (CH), 117.6 (CH), 111.2(CH₂), 102.1 (C_q), 92.3 (C_q), 88.6 (C_q), 80.1 (C_q), 12.8 (CH₃), 12.1 (CH₃), 0.6 (3 x CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3092, 3007, 2958, 2914, 2859, 2145, 1887, 1611, 1447\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 242 ([M-C₂H₄]⁺•, 65) 169(21), 153(26), 115(21), 73 (100)

HRMS (EI): calculated for C₁₇H₁₈ [M]⁺• 242.1491; found 242.1492

((2*E*,7*E*)-6-Vinylnona-2,4,5,7-tetraen-4-yl)benzene 4.111



A solution of alcohol **4.104** (100 mg, 0.47 mmol) in THF (2 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.40 mL, 0.57 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.7 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 minutes. A solution of zinc bromide (1.0 M in THF, 0.71 mL, 0.71 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (27 mg, 0.024 mmol, 5 mol%) were added in a single portion. A solution of vinylmagnesium bromide in THF (0.75 M, 0.95 mL, 0.71 mmol, 1.5 mol. equiv.) was added dropwise over 10 minutes. On completion of addition the reaction mixture was stirred for a further 1 hour at room temperature. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL) and the aqueous layer was separated and extracted with *n*-pentane (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.111** as a pale yellow oil (87 mg, 0.35 mmol, 74%).

R_f : 0.19 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 7.55-7.34 (m, 4H), 7.34-7.24 (m, 1H), 6.40 (dd, $J = 17.4, 10.6$ Hz, 1H), 6.20 (dd, $J = 15.4, 1.7$ Hz, 1H), 6.07 (dd, $J = 15.5, 1.6$ Hz, 1H), 6.04-5.80 (m, 2H), 5.47 (dd, $J = 17.4, 1.3$ Hz, 1H), 5.22 (dd, $J = 10.6, 1.3$ Hz, 3H), 1.87 (m, 6H) ppm

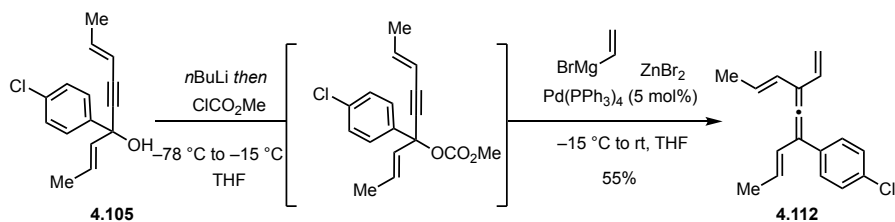
¹³C NMR (100 MHz, CDCl₃): δ 210.6 (C_q), 136.4 (C_q), 132.4 (CH), 129.3 (CH), 128.5 (2 x CH), 127.9 (CH), 127.7 (2 x CH), 127.3 (CH), 126.0 (CH), 124.5 (CH), 115.2 (CH₂), 109.8 (C_q), 107.9 (C_q), 18.6 (CH₃), 18.6 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3087, 3020, 2913, 2855, 1901, 1614, 1597, 1447\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 222 ([M]⁺, 63), 207 (100), 192 (83), 178 (88), 165 (82), 152 (23), 129 (33), 115 (32)

HRMS (EI): calculated for C₁₇H₁₈ [M]⁺ 222.1409; found 222.1405

1-Chloro-4-((2*E*,7*E*)-6-vinylnona-2,4,5,7-tetraen-4-yl)benzene **4.112**



A solution of alcohol **4.105** (100 mg, 0.41 mmol) in THF (2 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.35 mL, 0.49 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.7 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 1 hour. A solution of zinc bromide (1.00 M in THF, 0.61 mL, 0.61 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (23 mg, 0.020 mmol, 5 mol %) were added in a single portion. A solution of vinylmagnesium bromide in THF (0.75 M, 0.81 mL, 0.61 mmol, 1.5 mol. equiv.) was added dropwise over 10 minutes. On completion of addition the reaction mixture was stirred for a further 1 hour at room temperature. The reaction mixture was diluted with Et₂O (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with Et₂O (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) afforded allene **4.112** as a pale yellow oil (64 mg, 0.35 mmol, 55 %).

Note: A crystal of BHT was added to the collected fractions after flash chromatography otherwise decomposition of the allene was observed upon concentration under reduced pressure.

R_f : 0.11 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 7.28 (m, 4H), 6.32 (dd, $J = 17.3, 10.6$ Hz, 1H), 6.09 (dd, $J = 15.4, 1.7$ Hz, 1H), 6.01-5.97 (m, 1H), 5.93-5.76 (m, 2H), 5.40 (dd, $J = 17.4, 1.3$ Hz, 1H), 5.17 (dd, $J = 10.6, 1.3$ Hz, 1H), 1.81 (m, 6H) ppm

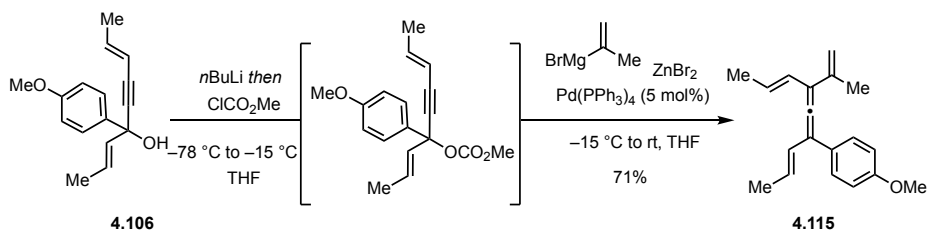
¹³C NMR (100 MHz, CDCl₃): δ 210.5 (C_q), 135.0 (C_q), 133.0 (C_q), 132.1 (CH), 129.6 (CH), 129.0 (2 x CH), 128.7 (2 x CH), 128.3 (CH), 125.6 (CH), 124.3 (CH), 115.6 (CH₂), 108.9 (C_q), 108.2 (C_q), 18.6 (CH₃), 18.6 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3088, 3017, 2960, 2912, 2876, 2852, 1902, 1647, 1614, 1592, 1488\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 256 ([M]⁺•, 100), 241(95), 214(35), 206(97), 191(83), 178(70), 165(65), 129(41)

HRMS (EI): calculated for C₁₇H₁₇³⁵Cl [M]⁺• 256.1019; found 256.1014

1-Methoxy-4-((2*E*,7*E*)-6-(prop-1-en-2-yl)nona-2,4,5,7-tetraen-4-yl)benzene **4.115**



A solution of alcohol **4.106** (160 mg, 0.66 mmol) in THF (5 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.6 mL, 0.84 mmol, 1.3 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.0 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 minutes. A solution of zinc bromide (1.00 M in THF, 1.0 mL, 1.0 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (37 mg, 0.032 mmol, 5 mol %) were added in a single portion. A solution of isopropenylmagnesium bromide in THF (0.80 M, 1.5 mL, 1.2 mmol, 1.8 mol. equiv.) was added dropwise over 10 minutes. On completion of addition the reaction mixture was stirred for a further 40 minutes at room temperature. The reaction mixture was diluted with Et₂O (10 mL) and quenched with a solution of saturated aqueous NH₄Cl solution (10 mL). The aqueous layer was separated and extracted with Et₂O (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at 10 °C until *ca.* 3 mL of solvent remained. Purification by flash column chromatography (SiO₂, *n*-pentane: Et₂O 98:2) yielded allene **4.115** as an orange oil (130 mg, 0.47 mmol, 71%).

R_f : 0.24 (*n*-pentane: Et₂O 98:2)

¹H NMR (700 MHz, CDCl₃): δ 7.30 (d, $J = 8.7$ Hz, 2H), 6.87 (d, $J = 8.7$ Hz, 2H), 6.13 (dd, $J = 15.3, 1.9$ Hz, 1H), 6.03 (dd, $J = 15.4, 1.9$ Hz, 1H), 5.92-5.87 (m, 1H), 5.85-5.79 (m, 1H), 5.10 (s, 1H), 5.03-4.92 (m, 1H), 3.81 (s, 3H), 1.88 (s, 3H), 1.82 (dd, $J = 6.8, 1.7$ Hz, 3H), 1.79 (dd, $J = 6.6, 1.7$ Hz, 3H) ppm

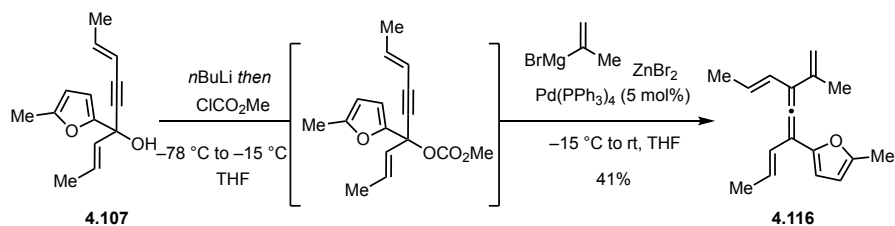
¹³C NMR (175 MHz, CDCl₃): δ 208.8 (C_q), 158.9 (C_q), 140.4 (C_q), 128.9 (C_q), 128.7 (CH), 128.6 (2 x CH), 128.5 (CH), 126.5 (CH), 124.6 (CH), 114.0 (2 x CH), 112.0 (CH₂), 110.6 (C_q), 109.5 (C_q), 55.4 (CH₃), 22.2 (CH₃), 18.6 (CH₃), 18.6 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3092, 3001, 2959, 2933, 2913, 2851, 2838, 1903, 1767, 1607, 1508\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 266 ([M]^{+•}, 25), 251 (18), 238(52), 224(100), 209(25), 165(21), 115(15)

HRMS (EI): calculated for C₁₉H₂₂O [M]^{+•} 266.1671; found 266.1669

2-Methyl-5-((2*E*,7*E*)-6-(prop-1-en-2-yl)nona-2,4,5,7-tetraen-4-yl)furan **4.116**



A solution of alcohol **4.107** (100 mg, 0.46 mmol) in THF (5 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.40 mL, 0.55 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.8 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.00 M in THF, 0.70 mL, 0.70 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (27 mg, 0.023 mmol, 5 mol%) were added in a single portion. A solution of isopropenylmagnesium bromide (0.70 M THF, 1.0 mL, 0.70 mmol, 1.5 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was stirred for a further 40 minutes at room temperature. The reaction was diluted with Et₂O (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with Et₂O (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. The resulting solution was subjected to purification by flash chromatography (SiO₂, *n*-pentane: Et₂O 90:10) yielded allene **4.116** as an orange oil (46 mg, 0.19 mmol, 41%).

R_f : 0.61 (petroleum ether: Et₂O 80:20)

¹H NMR (700 MHz, CDCl₃): δ 6.19 (d, $J = 3.2$ Hz, 1H), 6.09-5.96 (m, 4H), 5.92 (dq, $J = 15.2, 6.6$ Hz, 1H), 5.13-5.12 (m, 1H), 5.05-4.94 (m, 1H), 2.29 (d, $J = 1.0$ Hz, 3H), 1.87 (d, $J = 0.7$ Hz, 3H), 1.84-1.82 (m, 3H) 1.79 (dd, $J = 6.6, 1.7$ Hz, 3H) ppm

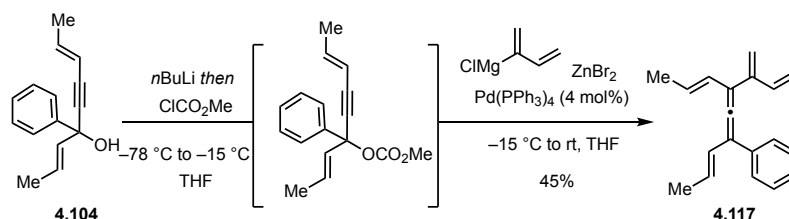
¹³C NMR (175 MHz, CDCl₃): δ 208.5 (C_q), 151.9 (C_q), 147.8 (C_q), 140.4 (C_q), 129.3 (CH), 128.6 (CH), 124.5 (CH), 123.8 (CH), 112.7 (C_q), 112.4 (CH₂), 107.8 (CH), 107.4 (CH), 102.0 (C_q), 22.0 (CH₃), 18.6 (CH₃), 18.6 (CH₃), 13.9 (CH₃) ppm

IR (thin film): ν_{max} = 3092, 3023, 2959, 2916, 2873, 2855, 2731 1912, 1745, 1619 cm⁻¹

LRMS (EI): m/z (%) = 240 ([M]^{+•},95), 225(29), 197(31), 182(27), 167(33), 139(35), 97(100), 69(92)

HRMS (EI): calculated for C₁₇H₂₀O [M]^{+•} 240.1514; found 240.1515

((2*E*,7*E*)-6-(buta-1,3-dien-2-yl)nona-2,4,5,7-tetraen-4-yl)benzene **4.117**



A solution of alcohol **4.104** (100 mg, 0.47 mmol) in THF (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.50 mL, 0.70 mmol, 1.5 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.8 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.00 M in THF, 0.80 mL, 0.80 mmol, 1.7 mol. equiv.) and Pd(PPh₃)₄ (24 mg, 0.021 mmol, 4 mol%) were added in a single portion. A solution of the chloroprene Grignard reagent (0.60 M in THF, 1.5 mL, 0.75 mmol, 1.6 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was stirred for a further 1 hour at $-15\text{ }^{\circ}\text{C}$. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) yielded allene **4.117** as a colourless oil (53 mg, 0.21 mmol, 45%).

R_f : 0.29 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 7.34-7.13(m, 5H), 6.36 (dd, $J = 17.3, 10.5$ Hz, 1H), 6.13-6.02 (m, 1H), 5.98-5.91 (m, 1H), 5.82-5.62 (m, 2H), 5.32 (d, $J = 17.3$ Hz, 1H), 5.25 (s, 1H), 5.15 (s, 1H), 5.06 (d, $J = 10.6$ Hz, 1H), 1.76 (d, $J = 6.7$ Hz, 3H), 1.70 (d, $J = 6.7$ Hz, 3H) ppm

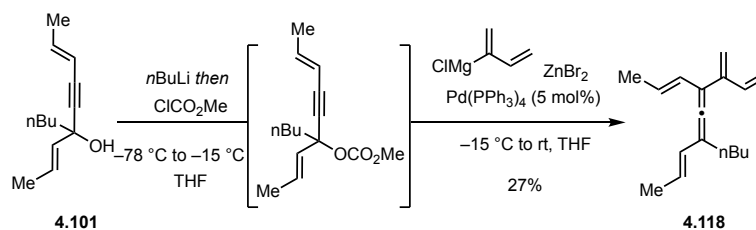
¹³C NMR (100 MHz, CDCl₃): δ 208.2 (C_q), 142.8 (C_q), 137.1 (CH), 136.7 (C_q), 129.2 (CH), 128.5 (2 x CH), 128.0 (CH), 127.8 (2 x CH), 127.2 (CH), 126.4 (CH), 126.3 (CH), 117.0 (CH₂), 116.7 (CH₂), 108.5 (C_q), 107.8 (C_q), 18.6 (CH₃), 18.5 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3087, 3023, 2960, 2932, 2913, 2884, 1852, 1913, 1623, 1587\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 248 ([M]⁺,11), 23), 233(100), 219(61), 203(65), 191(63), 178(55), 165(60), 152(27), 141(29), 128(32), 115(48), 105(25)

HRMS (EI): calculated for C₁₉H₂₀ [M]⁺ 248.1565; found 248.1566

3-Methylene-4,6-di((*E*)-prop-1-en-1-yl)deca-1,4,5-triene 4.118



A solution of alcohol **4.101** (100 mg, 0.52 mmol) in THF (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.50 mL, 0.70 mmol, 1.3 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.5 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.00 M in THF, 0.75 mL, 0.75 mmol, 1.4 mol. equiv.) and Pd(PPh₃)₄ (26 mg, 0.022 mmol, 4 mol%) were added in a single portion. A solution of the chloroprene Grignard reagent (0.60 M in THF, 1.5 mL, 0.75 mmol, 1.5 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was stirred for a further 1 hour at $-15\text{ }^{\circ}\text{C}$. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) yielded allene **4.118** as a colourless oil (32 mg, 0.14 mmol, 27%).

R_f : 0.62 (*n*-pentane)

¹H NMR (700 MHz, CDCl₃): δ 6.47-6.29 (m, 1H), 5.96-5.86 (m, 1H), 5.76-5.51 (m, 2H), 5.38 (dd, $J = 17.0, 1.4$ Hz, 2H), 5.24 (t, $J = 1.3$ Hz, 1H), 5.15-5.00 (m, 2H), 2.15 (dq, $J = 17.6, 7.5$ Hz, 2H), 1.76 (dd, $J = 1.7$ Hz, 3H), 1.74 (dd, $J = 6.7, 1.7$ Hz, 3H), 1.47-1.42 (m, 2H), 1.37-1.30 (m, 2H), 0.89 (t, $J = 7.4$ Hz, 3H) ppm

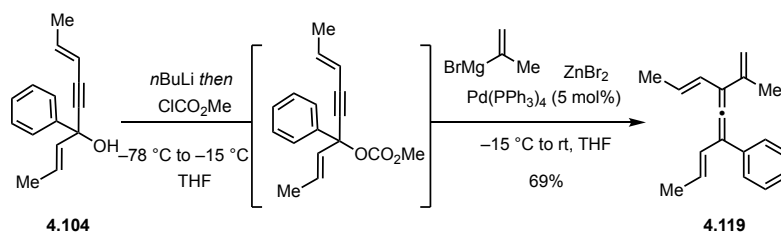
¹³C NMR (175 MHz, CDCl₃): δ 207.5 (C_q), 143.4 (C_q), 137.3 (CH), 128.6 (CH), 127.8 (CH), 126.9 (CH), 124.4 (CH), 116.6 (CH₂), 116.3 (CH₂), 106.5 (C_q), 106.1 (C_q), 30.1 (CH₂), 29.2 (CH₂), 22.7 (CH₂), 18.6 (CH₃), 18.4 (CH₃), 14.2 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3092, 3009, 2957, 2930, 2872, 2858, 2740, 1927, 1588, 1448\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 228 ([M]⁺, 11), 213(25), 199(29), 185(29), 171(57), 157(57), 143(100), 129(90), 115(51), 105(30), 91(51)

HRMS (EI): calculated for C₁₇H₂₄ [M]⁺ 228.1878; found 228.1873

((2*E*,7*E*)-6-(prop-1-en-2-yl)nona-2,4,5,7-tetraen-4-yl)benzene 4.119



A solution of alcohol **4.104** (100 mg, 0.48 mmol) in THF (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.40 mL, 0.58 mmol, 1.2 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 2.7 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.00 M in THF, 0.75 mL, 0.75 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (28 mg, 0.024 mmol, 5 mol%) were added in a single portion. A solution of the isopropenylmagnesium bromide (0.70 M in THF, 1.1 mL, 0.75 mmol, 1.5 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was stirred for a further 1 hour at room temperature. The reaction mixture was diluted with *n*-pentane (10 mL) and quenched with a solution of saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 10 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous MgSO₄, filtered and concentrated at 100 mbar at $10\text{ }^{\circ}\text{C}$ until *ca.* 3 mL of solvent remained. Purification by flash chromatography (SiO₂, *n*-pentane) yielded allene **4.119** as a colourless oil (77 mg, 0.33 mmol, 69%).

R_f : 0.26 (*n*-pentane)

¹H NMR (400 MHz, CDCl₃): δ 7.41-7.30 (m, 4H), 7.27-7.18 (m, 1H), 6.22-6.13 (m, 1H), 6.04 (d, $J = 15.3$ Hz, 1H), 5.96-5.76 (m, 2H), 5.11 (s, 1H), 5.00 (s, 1H), 1.89 (s, 3H), 1.83 (d, $J = 6.5$ Hz, 3H), 1.79 (d, $J = 6.5$ Hz, 3H) ppm

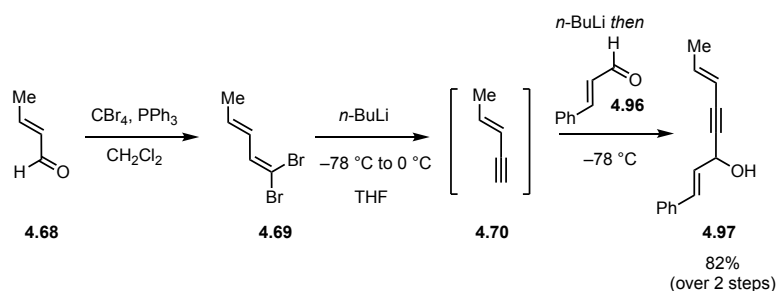
¹³C NMR (100 MHz, CDCl₃): δ 209.2 (C_q), 140.2 (C_q), 136.7 (C_q), 128.9 (CH), 128.7 (CH), 128.5 (2 x CH), 127.5 (2 x CH), 127.1 (CH), 126.2 (CH), 124.5 (CH), 112.2 (CH₂), 110.8 (C_q), 110.0 (C_q), 22.1 (CH₃), 18.6 (CH₃), 18.6 (CH₃) ppm

IR (thin film): ν_{max} = 3087, 3023, 2962, 2935, 2914, 2879, 2853, 1731, 1908, 1619, 1597, 1492, 1447 cm⁻¹

LRMS (EI): m/z (%) = 236 ([M]^{+•}, 11), 221(80), 206(58), 192(70), 179(85), 165(85), 143(51), 129(68), 115(62), 105(27), 91(60)

HRMS (EI): calculated for C₁₈H₂₀ [M]^{+•} 236.1565; found 248.1564

(1*E*,6*E*)-1-Phenylocta-1,6-dien-4-yn-3-ol **4.97**



A solution of crotonaldehyde (4.1 g, 50 mmol) in CH₂Cl₂ (250 mL) was cooled to 0 °C and CBr₄ (32.0 g, 96 mmol, 1.9 mol. equiv.) was added in a single portion. To this mixture was added PPh₃ (52 g, 200 mmol, 4 mol. equiv.) over 5 minutes in 5 x 10 g portions. The reaction was stirred at 0 °C for 30 minutes, then diluted with *n*-pentane (100 mL). The mixture was filtered through a pad of celite and concentrated under reduced pressure (not below 100 mbar at 25 °C). The crude mixture was taken up in pentane and filtered through a pad of silica. Concentration under reduced pressure afforded dibromoolefin **4.69** as a yellow oil (10.4 g), which was immediately subjected to the next step without further purification. ¹H and ¹³C NMR matched reported data.^[279]

¹H NMR (400 MHz, CDCl₃): δ 6.89 (d, *J* = 10.0 Hz, 1H), 6.20-6.04 (m, 1H), 5.92 (dq, *J* = 14.0, 6.7 Hz, 1H), 1.77 (d, *J* = 6.6 Hz, 3H) ppm

¹³C NMR (100 MHz, CDCl₃): δ 137.2 (CH), 134.3 (CH), 128.7 (CH), 18.7 (CH₃) ppm

A solution of dibromoolefin **4.69** in THF (50 mL) was cooled to -78 °C and *n*-BuLi (1.4 M in hexanes, 66 mL, 92.0 mmol, 2.1 mol. equiv.) was added dropwise. The reaction was stirred at -78 °C for 30 minutes and then at 0 °C for a further 30 minutes. The reaction was then cooled to -78 °C and a solution of *trans*-cinnamaldehyde (7.4 g, 56.0 mmol, 1.2 mol. equiv.) in THF (50 mL) was added dropwise. The reaction was stirred at this temperature for a further 30 minutes and subsequently quenched with a solution of saturated aqueous NH₄Cl (100 mL) and diluted with Et₂O (50 mL). The aqueous layer was separated and extracted with Et₂O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, Et₂O: petroleum ether 40-60, 20:80) afforded alcohol **4.97** as a yellow oil (8.0 g, 41 mmol, 82% over 2 steps).

R_f : 0.19 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.40 (d, *J* = 8.1 Hz, 2H), 7.35-7.28 (m, 2H), 7.26 (dd, *J* = 7.4, 1.4 Hz, 1H), 6.75 (d, *J* = 15.8 Hz, 1H), 6.30 (ddd, *J* = 15.8, 6.0, 1.3 Hz, 1H), 6.21 (dq, *J* = 15.8, 7.2 Hz, 1H), 5.55 (dd, *J* = 15.8, 1.9 Hz, 1H), 5.15 (s, 1H), 1.80 (d, *J* = 6.7 Hz, 3H) ppm

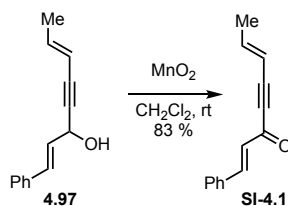
¹³C NMR (100 MHz, CDCl₃): δ 140.9 (CH), 136.3 (C_q), 131.9 (CH), 128.7 (2 x CH), 128.4 (CH), 128.2 (CH), 126.9 (2 x CH), 110.1 (CH), 86.3 (C_q), 85.4 (C_q), 63.6 (CH), 18.8 (CH₃) ppm

IR (thin film): ν_{max} = 3326 (br), 3086, 3059, 3017, 2964, 2940, 2913, 2852, 2214, 1664, 1600, 1581 cm⁻¹

LRMS (EI): *m/z* (%) = 197 ([M-H]⁺•, 47), 183(100), 165(63), 155(63), 141(56), 128(50), 115(50), 105(56), 93(63)

HRMS (EI): calculated for C₁₄H₁₄O [M]⁺• 198.1045; found 198.1039

(1*E*,6*E*)-1-Phenylocta-1,6-dien-4-yn-3-one **SI-4.1**



To a solution of alcohol **4.79** (4.8 g, 24.0 mmol) in CH₂Cl₂ (150 mL) was added manganese dioxide (14.0 g, 155 mmol, 6.5 mol. equiv.) in a single portion. The reaction mixture was stirred at room temperature for 2 hours. The reaction was then filtered through a pad of silica, flushed with Et₂O (300 mL) and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, Et₂O: petroleum ether 40-60, 10:90) afforded ketone **SI-4.1** as an orange oil (3.9 g, 20 mmol, 83%).

R_f : 0.33 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 7.69 (d, *J* = 16.1 Hz, 1H), 7.53-7.42 (m, 2H), 7.35-7.30 (m, 3H), 6.69 (dd, *J* = 16.2, 1.1 Hz, 1H), 6.49 (dq, *J* = 15.6, 6.9 Hz, 1H), 5.64 (d, *J* = 15.8 Hz, 1H), 1.82 (d, *J* = 7.0 Hz, 3H) ppm

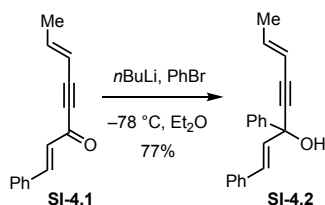
¹³C NMR (100 MHz, CDCl₃): δ 178.5 (C_q), 148.0 (CH), 147.4 (CH), 134.3 (C_q), 131.2 (CH), 129.2 (2 x CH), 128.7 (2 x CH), 128.7 (CH), 109.2 (CH), 91.1 (C_q), 85.7 (C_q), 19.4 (CH₃) ppm

IR (thin film): ν_{max} = 3061, 3029, 2972, 2943, 2912, 2848, 2190, 1677, 1650, 1630, 1612, 1598, 1575 cm⁻¹

LRMS (EI): m/z (%) = 196 ($[M]^{+\bullet}$, 76), 195(85), 181(100), 167(67), 153(84), 141(26), 128(18), 115(36), 102(50), 93(49)

HRMS (EI): calculated for $C_{14}H_{12}O$ $[M]^{+\bullet}$ 196.0888; found 196.0884

(1*E*,6*E*)-1,3-Diphenylocta-1,6-dien-4-yn-3-ol SI-4.2



Bromobenzene (0.70 mL, 6.7 mmol, 1.2 mol. equiv.) was dissolved in Et_2O (10 mL) and cooled to $0\text{ }^\circ\text{C}$. A solution of *n*-BuLi (1.4 M in hexanes, 4.5 mL, 6.3 mmol, 1.1 mol. equiv.) was added dropwise and the reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 45 minutes. The mixture was cooled to $-78\text{ }^\circ\text{C}$ and a solution of ketone **SI-4.1** (1.1 g, 5.5 mmol) in Et_2O (15 mL) was then added dropwise and the reaction mixture was stirred for a further 1 hour. The reaction mixture was then diluted with Et_2O (100 mL) and quenched with a saturated aqueous NH_4Cl (100 mL). The aqueous layer was separated and extracted with Et_2O (2 x 50 mL). The organic layers were combined, washed with brine (100 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO_2 , *n*-pentane: Et_2O : NEt_3 , 85:15:2) afforded alcohol **SI-4.2** as a yellow oil (1.2 g, 4.3 mmol, 77%).

R_f : 0.26 (*n*-pentane: Et_2O 85:15)

¹H NMR (400 MHz, CDCl_3): δ 7.71-7.66 (m, 2H), 7.42-7.35 (m, 4H), 7.33-7.28 (m, 3H), 7.25-7.21 (m, 1H), 6.92 (d, $J = 15.7$ Hz, 1H), 6.39 (d, $J = 15.8$ Hz, 1H), 6.28 (dq, $J = 16.3, 6.8$ Hz, 1H), 5.64 (dt, $J = 16.3, 6.8$ Hz, 1H), 2.54 (s, 1H, -OH), 1.83 (d, $J = 6.9$ Hz, 3H) ppm

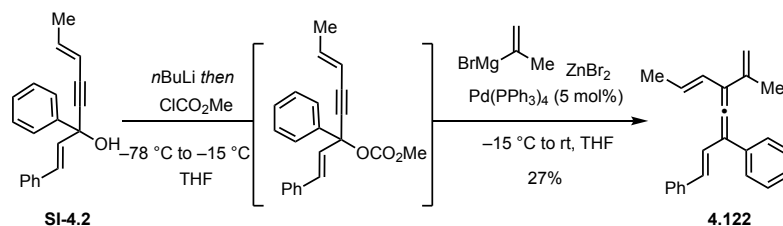
¹³C NMR (100 MHz, CDCl_3): δ 143.7 (C_q), 141.1 (CH), 136.4 (C_q), 133.2 (CH), 129.1 (CH), 128.7 (CH), 128.5 (2 x CH), 128.0 (CH), 127.1 (2 x CH), 126.0 (2 x CH), 110.0 (CH), 88.2 (C_q), 86.5 (C_q), 73.4 (C_q), 18.9 (CH_3) ppm

IR (thin film): ν_{max} = 3544, 3402 (br), 3082, 3059, 3026, 2966, 2937, 2907, 2878, 2848, 2214, 1884, 1809, 1625, 1600 cm^{-1}

LRMS (EI): m/z (%) = 1274 ($[M]^{+\bullet}$, 20), 259(28), 231(13), 215(20), 197(16), 181(30), 169(52), 155(20), 131(25), 115(19), 105(100), 93(35), 77(51)

HRMS (EI): calculated for $\text{C}_{20}\text{H}_{18}\text{O}$ $[M]^{+\bullet}$ 274.1358; found 274.1360

((1*E*,6*E*)-5-(prop-1-en-2-yl)octa-1,3,4,6-tetraene-1,3-diyl)dibenzene **4.122**



A solution of alcohol **SI-4.2** (230 mg, 0.84 mmol) in THF (3 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 0.90 mL, 1.3 mmol, 1.5 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.1 mL, 1.3 mmol, 1.5 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.00 M in THF, 1.3 mL, 1.3 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (49 mg, 0.042 mmol, 5 mol%) were added in a single portion. A solution of the isopropenylmagnesium bromide (0.80 M in THF, 1.6 mL, 1.3 mmol, 1.5 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was stirred for a further 1 hour at $-15\text{ }^{\circ}\text{C}$. The reaction mixture was diluted with *n*-pentane (20 mL) and quenched with saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with *n*-pentane (2 x 20 mL). The organic layers were combined and washed with brine (50 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, *n*-pentane:Et₂O, 99:1) yielded allene **4.122** as a colourless oil (69 mg, 0.23 mmol, 27%).

R_f : 0.16(*n*-pentane:Et₂O, 99:1)

¹H NMR (400 MHz, CDCl₃): δ 7.41-7.30 (m, 4H), 7.27-7.18 (m, 1H), 6.22-6.13 (m, 1H), 6.04 (d, $J = 15.3$ Hz, 1H), 5.96-5.76 (m, 2H), 5.11 (s, 1H), 5.00 (s, 1H), 1.89 (s, 3H), 1.83 (d, $J = 6.5$ Hz, 3H), 1.79 (d, $J = 6.5$ Hz, 3H) ppm

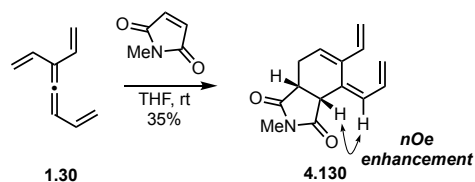
¹³C NMR (100 MHz, CDCl₃): δ 209.2 (C_q), 140.2 (C_q), 136.7 (C_q), 128.9 (CH), 128.7 (CH), 128.5 (2 x CH), 127.5 (2 x CH), 127.1 (CH), 126.2 (CH), 124.5 (CH), 112.2 (CH₂), 110.8 (C_q), 110.0 (C_q), 22.1 (CH₃), 18.6 (CH₃), 18.6 (CH₃) ppm

IR (thin film): $\nu_{\text{max}} = 3081, 3058, 3025, 2965, 2914, 2852, 1900, 1800, 1617, 1597\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 298 ([M]⁺•, 100), 283(40), 254(29), 241(30), 228(17), 215(21), 205(38), 191(32), 165(40), 152(18), 141(12), 129(20), 115(30)

HRMS (EI): calculated for C₂₃H₂₂ [M]⁺• 298.1722; found 298.1725

(Z)-4-Allylidene-2-methyl-5-vinyl-3a,4,7,7a-tetrahydro-1H-isindole-1,3(2H)-dione 4.130



N-Methylmaleimide (70 mg, 63 mmol, 1.5 mol. equiv.) was added to a solution of trivinylallene (**1.30**) (51 mg, 0.43 mmol) in THF (*ca.* 15 mL) with 1,2,4,5-tetramethylbenzene (49 mg, 0.37 mmol) as an internal standard. The reaction mixture was stirred for 1 hour at room temperature then concentrated under reduced pressure and purified by flash chromatography (SiO₂, *n*-pentane:Et₂O, 50:50) to afford monoadduct **4.130** as a yellow oil (35 mg, 0.15 mmol, 35%).

R_f: 0.19 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 6.44 (dt, *J* = 17.0, 10.6 Hz, 1H), 6.31-6.17 (m, 2H), 5.95-5.92 (m, 1H), 5.31-5.19 (m, 2H), 5.14-5.08 (m, 2H), 3.66 (d, *J* = 8.7 Hz, 1H), 3.25-3.20 (m, 1H), 2.93 (s, 3H), 2.74 (ddd, *J* = 15.5, 7.2, 1.9 Hz, 1H), 2.22-2.15 (m, 1H) ppm

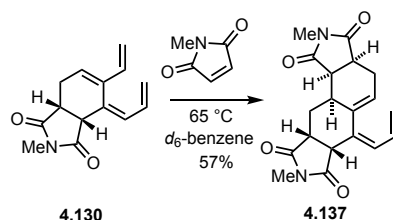
¹³C NMR (175 MHz, CDCl₃): δ 179.6 (C_q), 177.0 (C_q), 139.9 (C_q), 135.1 (CH), 134.3 (CH), 132.1 (CH), 128.8 (C_q), 128.1 (CH), 119.1 (CH₂), 116.7 (CH₂), 50.7 (CH), 41.3 (CH), 25.4 (CH₃), 25.0 (CH₂) ppm

IR (thin film): ν_{max} = 3087, 2952, 2852, 1777, 1702, 1699, 1695, 1433 cm⁻¹

LRMS (EI): *m/z* (%) = 229 ([M]^{+•}, 65), 214 (15), 201(11), 144(80), 129(100), 115(74), 91(35)

HRMS (EI): calculated for C₁₄H₁₅NO₂ [M]^{+•} 229.1103; found 229.1105

Tetracycle 4.137



N-Methylmaleimide (100 mg, 0.90 mmol, 1.5 equiv.) and BHT (13 mg, mmol, 0.1 equiv.) was added to a solution of monoadduct **4.130** (137 mg, 0.60 mmol) in benzene (1 mL). The reaction mixture was stirred for 18 hours at 65 °C then concentrated under reduced pressure and purified by flash chromatography (SiO₂, *n*-pentane:EtOAc, 50:50 → 25:75) to afford bisadduct **4.137** as a colourless foam (116 mg, 0.34 mmol, 57%).

R_f : 0.21 (50:50, *n*-pentane:EtOAc)

¹H NMR (800 MHz, CDCl₃): δ 6.22-6.14 (m, 2H), 5.98-5.86 (m, 1H), 2.32 (d, *J* = 15.8 Hz 1H), 5.11-5.07 (m, 1H), 3.54 (d, *J* = 9.2 Hz, 1H), 3.31-3.25 (m, 1H), 3.15-3.11 (m, 1H), 3.08-3.05 (m, 1H), 2.94 (s, 3H), 2.89-2.82 (m, 4H), 2.44-2.34 (m, 2H), 2.22-2.16 (m, 1H), 2.13-2.07 (m, 1H) ppm

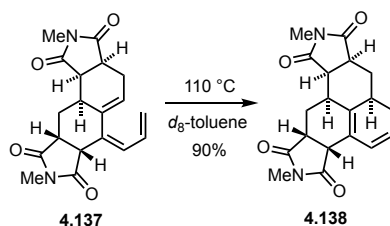
¹³C NMR (200 MHz, CDCl₃): δ 179.4 (C_q), 179.3 (C_q), 177.1 (C_q), 177.1 (C_q), 136.2 (C_q), 133.4 (CH), 132.0 (CH), 130.9 (C_q), 128.7 (CH), 120.5 (CH₂), 49.6 (CH), 42.9 (CH), 40.9 (CH), 40.0 (CH), 33.8 (CH), 25.3 (CH₃), 25.2 (CH₂), 24.9 (CH₃), 23.8 (CH₂) ppm

IR (thin film): ν_{max} = 2937, 2872, 2858, 177.4, 1689, 1434 cm⁻¹

LRMS (EI): *m/z* (%) = 340 ([M]⁺•, 100), 322(18), 284(22), 254(41), 227(18), 214(52)

HRMS (EI): calculated for C₁₉H₂₀N₂O₄ [M]⁺• 340.1423; found 340.1424

Pentacycle 4.138



A solution of bisadduct **4.137** (77 mg, 0.23 mmol) and BHT (78 mg, 0.35 mmol, 1.5 equiv.) in d_8 -toluene (5 mL) was stirred for 4 hours at $110\text{ }^\circ\text{C}$. The reaction mixture then concentrated under reduced pressure and purified by flash chromatography (SiO_2 , n -pentane:EtOAc, 50:50 \rightarrow 0:100) to afford **4.138** as a colourless solid (69 mg, 0.20 mmol, 90%). A crystal of BHT was added to the sample to prevent decomposition. A crystal structure was obtained by recrystallisation from benzene. The relative stereochemistry was obtained by single crystal X-ray analysis.

R_f : 0.43 (EtOAc)

m.p.: 208-216 $^\circ\text{C}$

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ 6.36 (d, $J = 9.8$ Hz, 1H), 5.88 (t, $J = 8.0$ Hz, 1H), 3.45 (q, $J = 7.5$ Hz, 1H), 3.27 (d, $J = 8.2$ Hz, 1H), 3.17 (dd, $J = 9.2, 6.0$ Hz, 1H), 3.09-3.01 (m, 1H), 2.95-2.89 (m, 6H), 2.81-2.71 (m, 2H), 2.62-2.50 (m, 1H), 2.22-2.12 (m, 1H), 2.10-1.98 (m, 2H), 1.67 (t, $J = 18.6$ Hz, 1H) ppm

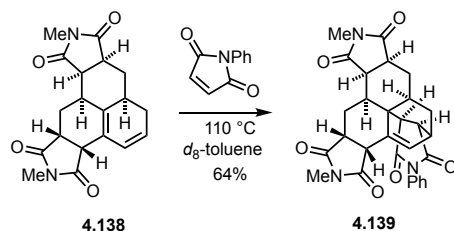
$^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 180.3 (C_q), 179.6 (C_q), 178.1 (C_q), 176.9 (C_q), 131.2 (C_q), 127.6 (CH), 126.0 (CH), 123.7 (C_q), 43.8 (CH), 42.0 (CH), 39.5 (CH), 37.5 (CH), 32.6 (CH), 31.7 (CH), 29.3 (CH_2), 26.1 (CH_2), 25.1 (CH_3), 24.9 (CH_3), 23.8 (CH_2) ppm

IR (thin film): $\nu_{\text{max}} = 3052, 2937, 2871, 2826, 1772, 1698, 1433\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 340 ($[\text{M}]^{+\bullet}$, 77), 322(23), 280(17), 254(27), 214(58), 167(29), 141(52), 127(100), 112(62)

HRMS (EI): calculated for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_4$ $[\text{M}]^{+\bullet}$ 340.1423; found 340.1417

Hetpacycle 4.139



N-Phenylmaleimide (65 mg, 0.38 mmol, 3.5 equiv.) and BHT (5 mg, 0.022 mmol, 0.2 equiv.) was added to a solution of bisadduct **4.138** (39 mg, 0.11 mmol) in toluene (1.5 mL). The reaction mixture was stirred for 72 hours at 110 °C then concentrated under reduced pressure and purified by flash chromatography (SiO₂, *n*-pentane:EtOAc, 50:50 → 0:100) to afford trisadduct **4.139** as a white solid (36 mg, 0.070 mmol, 64 %). A crystal structure was obtained by recrystallisation from ethyl acetate. The relative stereochemistry was determined by single crystal X-ray analysis.

R_f : 0.24 (EtOAc)

m.p.: 328-332 °C (decomposition)

¹H NMR (400 MHz, CDCl₃): δ 7.47-7.32 (m, 3H), 7.23-7.17 (m, 2H), 6.84 (d, *J* = 6.8 Hz, 1H), 3.56 (d, *J* = 9.8 Hz, 1H), 3.47-3.39 (m, 1H), 3.33-3.28 (m, 1H), 3.27-3.22 (m, 1H), 3.15 (q, *J* = 9.5 Hz, 1H), 3.06-2.99 (m, 5H), 2.97-2.92 (m, 1H), 2.45 (s, 3H), 2.17-2.03 (m, 2H), 2.02-1.94 (m, 1H), 1.62 (s, 1H), 1.59-1.49 (m, 1H), 1.43-1.25 (m, 2H), 0.98 (t, *J* = 10.7 Hz, 1H) ppm

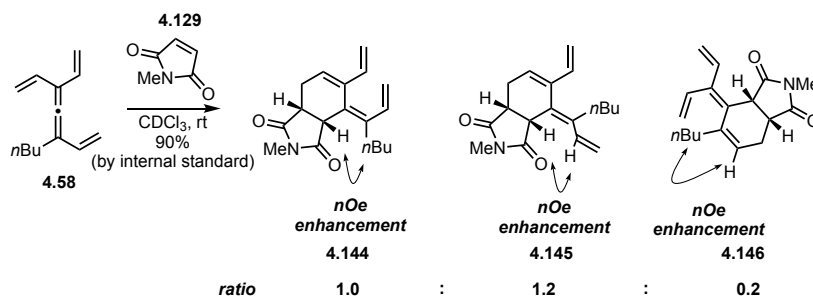
¹³C NMR (100 MHz, CDCl₃): δ 179.0 (C_q), 177.9 (C_q), 177.8 (C_q), 177.0 (C_q), 176.6 (C_q), 176.0 (C_q), 135.0 (CH), 131.5 (CH), 130.8 (C_q), 128.8 (CH x 2), 128.8 (CH), 127.2 (CH x 2), 49.5 (CH), 43.4 (CH), 42.1 (C_q), 41.8 (CH), 41.0 (CH), 40.8 (CH), 39.1 (CH), 36.9 (CH), 34.3 (CH), 33.1 (CH₂), 31.6 (CH), 25.1 (CH₃), 24.8 (CH₃), 24.6 (CH₂), 24.3 (CH₂) ppm

IR (thin film): ν_{max} = 2935, 2869, 1771, 1692, 1598, 1500 cm⁻¹

LRMS (EI): *m/z* (%) = 513 ([M]^{+•}, 11), 495(8), 340(22), 175(9), 84(100)

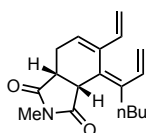
HRMS (EI): calculated for C₂₉H₂₇N₃O₆ [M]^{+•} 513.1900; found 513.1901

Diels–Alder reaction of allene 4.58



N-Methylmaleimide (50 mg, 0.45 mmol, 1.2 equiv.) and BHT (80 mg, 0.36 mmol, 0.97 equiv.) was added to a solution of *n*-butyl trivinylallene (**4.58**) (65 mg, 0.37 mmol) in CDCl₃ (5 mL) containing 1,2,3,5-tetramethylbenzene (10 mg, 0.075 mmol) as an internal standard. The reaction mixture was stirred at room temperature for 18 hours after which, ¹H NMR indicated the reaction had gone to completion to afford compounds **4.144**, **4.145** and **4.146**. Analytically pure samples of **4.144**, **4.145** and **4.146** were obtained for the purposes of characterization *via* flash chromatography purification then concentrated under reduced pressure and purified by flash chromatography (SiO₂, *n*-pentane:Et₂O, 50:50) followed by reverse phase preparative HPLC.

Diels–Alder-adduct 4.144



4.144

R_f : 0.31 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 6.37 (dd, *J* 17.5, 11.0 Hz, 1H), 6.23 (dd, *J* = 17.3, 10.6 Hz, 1H), 5.91 (dd, *J* = 7.4, 4.0 Hz, 1H), 5.28 (dd, *J* = 17.5, 1.1 Hz, 1H), 5.11 (d, *J* = 17.3 Hz, 1H), 5.06 (dd, *J* = 11.0, 1.1 Hz, 1H), 5.03 (d, *J* 10.6 Hz, 1H), 4.19 (d, *J* = 8.5 Hz, 1H), 3.21 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H), 2.90 (s, 3H), 2.71 (ddd, *J* = 15.1, 7.3, 1.6 Hz, 1H), 2.55-2.41 (m, 2H), 2.13-2.02 (m, 1H), 1.69-1.61 (m, 1H), 1.49-1.33 (m, 3H), 0.95 (t, *J* = 7.1 Hz, 3H) ppm

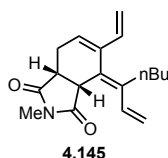
¹³C NMR (175 MHz, CDCl₃): δ 179.9 (C_q), 177.0 (C_q), 141.5 (C_q), 138.7 (C_q), 136.8 (CH), 135.5 (CH), 127.9 (CH), 126.9 (C_q), 116.3 (CH₂), 113.7 (CH₂), 45.3 (CH), 42.1 (CH), 32.6 (CH₂), 27.7 (CH₂), 25.3 (CH₂), 25.2 (CH₃), 23.2 (CH₂), 14.2 (CH₃) ppm

IR (thin film): ν_{max} = 3094, 2956, 2932, 2872, 2858, 17777, 1699, 1627, 1431 cm⁻¹

LRMS (EI): m/z (%) = 285 ($[M]^{+\bullet}$, 28), 256(18), 242(19), 228(41), 215(20), 171(22), 157(42), 143(100), 129(90), 115(60), 91(40)

HRMS (EI): calculated for $C_{18}H_{23}NO_2$ $[M]^{+\bullet}$ 285.1729; found 285.1731

Diels–Alder-adduct 4.145



R_f : 0.23 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 6.68 (dd, $J = 17.3, 1.1$ Hz, 1H), 6.25 (dd, $J = 17.3, 10.6$ Hz, 1H), 5.90 (dd, $J = 7.4, 3.9$ Hz, 1H), 5.58 (dd, $J = 17.3, 1.6$ Hz, 1H), 5.34 (dd, $J = 11.1, 1.6$ Hz, 1H), 5.18 (d, $J = 17.3$ Hz, 1H), 5.02 (d, $J = 10.4$ Hz, 1H), 4.38 (d, $J = 8.5$ Hz, 1H), 3.18 (ddd, $J = 13.7, 10.3, 6.1$ Hz, 1H), 2.90 (s, 3H), 2.71 (ddd, $J = 15.0, 7.3, 1.6$ Hz, 1H), 2.32 (ddd, $J = 13.7, 10.3, 6.1$ Hz, 1H), 2.16 (ddd, $J = 13.7, 9.8, 4.8$ Hz, 1H), 2.09-2.01 (m, 1H), 1.38-1.32 (m, 1H), 1.31-1.13 (m, 3H), 0.83 (t, $J = 7.3$ Hz, 3H) ppm

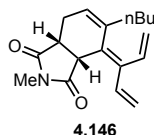
¹³C NMR (175 MHz, CDCl₃): δ 180.0 (C_q), 177.4 (C_q), 142.0 (C_q), 140.4 (C_q), 135.5 (CH), 134.2 (CH), 127.7 (CH), 125.6 (C_q), 118.1 (CH₂), 115.5 (CH₂), 44.9 (CH), 42.3 (CH), 31.7 (CH₂), 31.1 (CH₂), 25.3 (CH₃), 25.0 (CH₂), 22.8 (CH₂), 14.0 (CH₃) ppm

IR (thin film): $\nu_{\max} = 3093, 2957, 2940, 2871, 1777, 1699, 1697, 1433$ cm⁻¹

LRMS (EI): m/z (%) = 285 ($[M]^{+\bullet}$, 78), 256(55), 242(52), 228(88), 215(46), 171(49), 157(73), 143(100), 129(95), 115(72), 91(56)

HRMS (EI): calculated for $C_{18}H_{23}NO_2$ $[M]^{+\bullet}$ 285.1729; found 285.1728

Diels–Alder-adduct 4.146



R_f : 0.35 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 6.50 (dd, $J = 17.5, 11.1$ Hz, 1H), 6.43 (dd, $J = 17.5, 10.7$ Hz, 1H), 5.83 (dd, $J = 17.5, 2.1$ Hz, 1H), 5.75-5.72 (m, 1H), 5.49 (dd, $J = 11.1, 2.1$ Hz, 1H), 5.28 (dd, $J = 17.5, 1.7$ Hz, 1H), 5.23 (dd, $J = 10.7, 1.6$ Hz, 1H), 4.37 (d, $J = 8.5$ Hz, 1H), 3.12 (ddd,

$J = 8.6, 7.0, 1.6$ Hz, 1H), 2.94 (s, 3H), 2.67 (ddd, $J = 15.0, 7.3, 1.6$ Hz, 1H), 2.36-2.27 (m, 1H), 2.16-2.08 (m, 1H), 2.07-1.99 (m, 1H), 1.31-1.20 (m, 1H), 1.19-1.09 (m, 2H), 1.04-0.94 (m, 1H), 0.82 (t, $J 7.3$ Hz, 3H) ppm

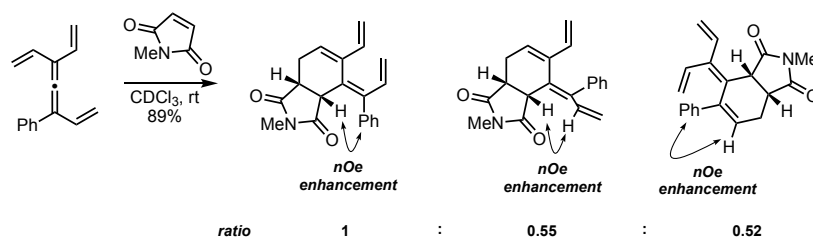
^{13}C NMR (175 MHz, CDCl_3): δ 180.2 (C_q), 178.0 (C_q), 143.5 (C_q), 136.8 (C_q), 135.5 (CH), 133.6 (CH), 130.8 (C_q), 125.4 (CH), 122.0 (CH_2), 118.3 (CH_2), 46.4 (CH), 41.0 (CH), 35.9 (CH_2), 31.1 (CH_2), 25.2 (CH_3), 24.4 (CH_2), 22.3 (CH_2), 14.0 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 2965, 2933, 2857, 1776, 1700, 1629, 1433$ cm^{-1}

LRMS (EI): m/z (%) = 285 ($[\text{M}]^{+\bullet}$, 41), 243(71), 228(40), 157(50), 143(96), 128(100), 115(68), 91(52)

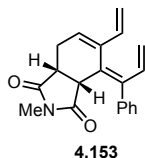
HRMS (EI): calculated for $\text{C}_{18}\text{H}_{23}\text{NO}_2$ $[\text{M}]^{+\bullet}$ 285.1729; found 285.1730

Diels–Alder reaction of allene 4.56



N-Methylmaleimide (20 mg, 0.18 mmol, 1.3 equiv.) and BHT (30 mg, 0.14 mmol, 1.0 equiv.) was added to a solution of phenyl trivinylallene (**4.56**) (28 mg, 0.14 mmol) in CDCl_3 (5 mL) containing 1,2,3,5-tetramethylbenzene (10 mg, 0.075 mmol) as an internal standard. The reaction mixture was stirred at room temperature for 18 hours after which, ^1H NMR indicated the reaction had gone to completion to afford compounds **4.153**, **4.154** and **4.155** in 89%. Analytically pure samples of **4.153**, **4.154** and **4.155** were obtained for the purposes of characterization *via* flash chromatography purification then concentrated under reduced pressure and purified by flash chromatography (SiO_2 , *n*-pentane: Et_2O , 50:50) followed by reverse phase preparative HPLC (Grace Alltima C18 5 μm (250 x 22 mm), 75:25 acetonitrile, H_2O).

Diels–Alder adduct 4.153



R_f : 0.36 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 7.42-7.39 (m, 2H), 7.36-7.33 (m, 1H), 6.65 (dd, *J* = 17.2, 10.6 Hz, 1H), 6.33 (dd, *J* = 17.3, 10.6 Hz, 1H), 6.0 (dd, *J* 7.3, 3.8 Hz, 1H), 5.33 (d, *J* = 17.4 Hz, 1H), 5.18-5.13 (m, 2H), 4.75 (dd, *J* = 17.3, 1.5 Hz, 1H), 3.77 (d, *J* = 8.6 Hz, 1H), 3.04-3.00 (m, 1H), 2.89 (s, 3H), 2.73 (ddd, *J* = 15.2, 7.3, 1.5 Hz, 1H), 2.20-2.14 (m, 1H) ppm

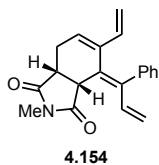
¹³C NMR (175 MHz, CDCl₃): δ 180.2 (C_q), 178.0 (C_q), 143.5 (C_q), 136.8 (C_q), 135.5 (CH), 133.6 (CH), 130.8 (C_q), 125.4 (CH), 122.0 (CH₂), 118.3 (CH₂), 46.4 (CH), 41.0 (CH), 35.9 (CH₂), 31.1 (CH₂), 25.2 (CH₃), 24.4 (CH₂), 22.3 (CH₂), 14.0 (CH₃) ppm

IR (thin film): ν_{max} = 3090, 3054, 3025, 2894, 2857, 1776, 1694 cm⁻¹

LRMS (EI): *m/z* (%) = 305 ([M]^{+•}, 100), 277(52), 219(60), 205(52), 194(52), 178(48), 165(40), 141(22), 129(42), 115(68), 91(50)

HRMS (EI): calculated for C₂₀H₁₉NO₂ [M]^{+•} 305.1416; found 305.1417

Diels–Alder adduct 4.154



R_f : 0.21 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 7.24-7.18 (m, 3H), 7.12-7.00 (m, 3H), 5.91 (dd, *J* = 7.4, 3.8 Hz, 1H), 5.63 (dd, *J* = 17.4, 10.5 Hz, 1H), 5.45 (dd, *J* = 10.8, 1.1 Hz, 1H), 5.34 (dt, *J* = 17.3, 1.1 Hz, 1H), 4.84 (d, *J* = 17.3 Hz, 1H), 4.54-4.48 (m, 2H), 3.34 (t, *J* = 7.9 Hz, 1H), 2.94 (s, 3H), 2.87-2.78 (m, 1H), 2.33 (ddd, *J* = 15.2, 7.1, 3.8 Hz, 1H) ppm

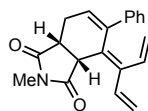
¹³C NMR (175 MHz, CDCl₃): δ 179.9 (C_q), 177.2 (C_q), 142.0 (C_q), 141.3 (C_q), 139.8 (C_q), 135.5 (CH), 133.4 (CH), 130.3 (2 x CH), 127.9 (2 x CH), 127.6 (CH), 127.5 (CH), 127.2 (C_q), 121.8 (CH₂), 115.0 (CH₂), 41.1 (CH), 41.8 (CH), 25.4 (CH₃), 24.9 (CH₂) ppm

IR (thin film): ν_{max} = 3090, 3054, 3023, 2953, 2851, 1775, 1695 cm⁻¹

LRMS (EI): m/z (%) = 305 ($[M]^{+\bullet}$,92), 277(45), 219(66), 205(97), 194(95), 178(69), 165(58), 152(25), 129(47), 115(100), 91(65)

HRMS (EI): calculated for $C_{20}H_{19}NO_2$ $[M]^{+\bullet}$ 305.1416; found 305.1420

Diels–Alder adduct **4.155**



R_f : 0.27 (50:50, *n*-pentane:Et₂O)

¹H NMR (700 MHz, CDCl₃): δ 7.29-7.23 (m, 4H), 7.22-7.19 (m, 1H), 6.50 (dd, $J = 17.6, 11.2$ Hz, 1H), 6.18 (dd, $J = 17.6, 11.2$ Hz, 1H), 6.01 (dd, $J = 17.3, 10.8$ Hz, 1H), 5.90 (d, $J = 17.6$ Hz, 1H), 5.57 (d, $J = 11.2$ Hz, 1H), 5.12 (d, $J = 17.4$ Hz, 1H), 4.86 (d, $J = 10.7$ Hz, 1H), 4.58 (d, $J = 8.7$ Hz, 1H), 3.27 (t, $J = 8.1$ Hz, 1H), 2.91 (s, 3H), 2.88 (dd, $J = 14.9, 7.4$ Hz, 1H), 2.22 (ddd, $J = 14.9, 7.6, 3.7$ Hz, 1H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 180.0 (C_q), 177.9 (C_q), 143.0 (C_q), 140.7 (C_q), 139.2 (C_q), 135.5 (CH), 133.1 (CH), 129.1 (C_q), 128.7 (2 x CH), 127.4 (CH), 126.6 (2 x CH), 126.5 (CH), 122.5 (CH₂), 117.7 (CH₂), 46.5 (CH), 41.7 (CH), 25.5 (CH₃), 25.2, (CH₂) ppm

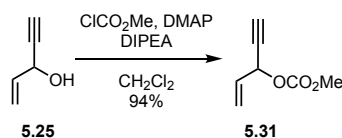
IR (thin film): $\nu_{\max} = 3093, 3056, 3026, 2951, 2929, 2852, 1774, 1695$ cm⁻¹

LRMS (EI): m/z (%) = 305 ($[M]^{+\bullet}$,84), 277(11), 219(55), 205(68), 194(100), 178(65), 165(50), 154(42), 128(25), 115(33), 91(22)

HRMS (EI): calculated for $C_{20}H_{19}NO_2$ $[M]^{+\bullet}$ 305.1416; found 305.1419

8.3 Experimental for Chapter 5

Methyl pent-1-en-4-yn-3-yl carbonate **5.31**



To a solution of enynol **5.25** (1.3 g, 16 mmol), *N,N*-diisopropylethylamine (3.4 ml, 19 mmol, 1.2 mol. equiv.) and DMAP (40 mg, 0.32 mmol, 0.020 mol. equiv.) in CH_2Cl_2 (50 mL) was cooled to 0 °C and methylchloroformate (1.5 mL, 19 mmol, 1.2 mol. equiv.) was added dropwise. After the addition was complete, the reaction mixture was brought to room temperature and stirred for a further 18 hours. The reaction mixture was then concentrated under reduced pressure and the residue was dissolved in Et_2O (50 mL), washed with 2M HCl (2 x 50 mL), saturated aqueous NaHCO_3 solution (50 mL) and brine (50 mL), dried with MgSO_4 and filtered through a short plug of silica. The solvent was removed under reduced pressure to give **5.31** (2.1 g, 15 mmol, 94%) as a pale yellow oil.

R_f : 0.20 (petroleum ether 40-60: Et_2O 80:20)

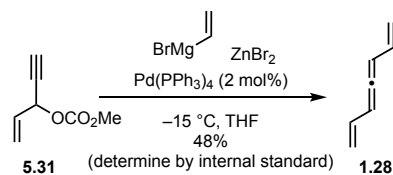
¹H NMR (400 MHz, CDCl_3): δ 5.94 (ddd, $J = 17.1, 10.1, 5.7$ Hz, 1H), 5.76-5.70 (m, 1H), 5.61 (dt, $J = 16.9, 1.1$ Hz, 1H), 5.38 (d, $J = 10.2$ Hz, 1H), 3.83 (s, 3H), 2.64 (d, $J = 2.2$ Hz, 1H) ppm

¹³C NMR (100 MHz, CDCl_3): δ 154.9 (C_q), 132.1 (CH), 120.0 (CH_2), 78.5 (C_q), 76.3 (CH), 68.1 (CH), 55.3 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3294, 3008, 2960, 2856, 2127, 1747, 1694, 1442$ cm^{-1}

HRMS (EI): calculated for $\text{C}_7\text{H}_8\text{O}_3$ $[\text{M}]^+ \bullet$ 140.0473; found 140.0467

Hepta-1,3,4,6-tetraene 1.28



A solution of methylcarbonate **5.31** (520 mg, 3.7 mmol) in THF (3 mL) was cooled to $-15\text{ }^\circ\text{C}$ and a solution of zinc bromide (1.0 M in THF, 5.4 mL, 5.4 mmol, 1.5 mol. equiv.) and $\text{Pd(PPh}_3)_4$ (88 mg, 0.076 mmol, 2mol%) were added in a single portion. Subsequently, a solution of vinylmagnesium bromide in THF (0.70 M, 7.6 mL, 5.4 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. The reaction mixture was then stirred for a further 1 hour at $-15\text{ }^\circ\text{C}$ and was quenched with methanol (0.5 mL). Analysis of the crude product mixture by ^1H NMR spectroscopy with 1,2,3,5-tetramethylbenzene as an internal standard gave estimated yields of trivinylallene in 48% yield from carbonate **5.31**.

An analytically pure sample of trivinylallene **1.28** was obtained for the purposes of characterization by dilution of the crude mixture with *n*-pentane (50 mL) with aqueous wash of the organic layer with water until no THF was observed by ^1H NMR spectroscopy. The organic layer was then washed with brine, dried over anhydrous MgSO_4 and filtered through a short plug of silica. To the *n*-pentane solution was added CDCl_3 (5 mL) and the *n*-pentane was removed 250 mbar at $0\text{ }^\circ\text{C}$ to give **1.28** as a solution in CDCl_3 . If required additional purification by bulb to trap distillation at room temperature of the CDCl_3 solution (with the receiver flask at $-78\text{ }^\circ\text{C}$) could be performed to remove any oligomerization products generated during the removal of *n*-pentane.

R_f: 0.12 (50:50, *n*-pentane:Et₂O)

^1H NMR (700 MHz, CDCl_3): δ 6.21-6.13 (m, 2H), 6.04-5.99 (m, 2H), 5.25-5.20 (m, 2H), 5.03 (dt, $J = 10.0, 1.2\text{ Hz}$, 2H) ppm

^{13}C NMR (175 MHz, CDCl_3): δ 211.4 (C_q), 132.3 (CH), 116.7 (CH), 96.0 (CH) ppm

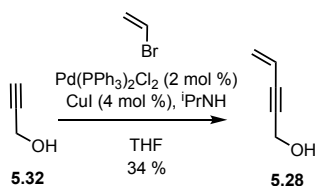
IR (thin film): $\nu_{\text{max}} = 3086, 3012, 2987, 1929, 1612, 1413, 1244, 1146\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 91 ($[\text{M-H}]^{+\bullet}$, 100), 65 (33), 39(13)

HRMS (EI): calculated for C_7H_8 $[\text{M}]^{+\bullet}$ 92.0626; found 92.0630

UV-VIS: $\lambda_{\text{max}} = 224\text{ nm}$ ($\epsilon = 69\text{ 000}$), 230 nm ($\epsilon = 67\text{ 000}$)

Pent-4-en-2-yn-1-ol 5.28



To a solution of vinyl bromide (4.0 mL, 55 mmol, 1.2 mol. equiv.), Pd(PPh₃)₂Cl₂ (0.55 g, 0.78 mmol, 2 mol%), CuI (0.34 g, 1.8 mmol, 4 mol%) and *N,N*-diisopropylethylamine (13 mL, 90 mmol, 2.0 mol. equiv.) in THF (220 mL) was added propargylic alcohol (2.5 g, 45 mmol). The reaction mixture was stirred at room temperature for 22 hours. The reaction mixture was diluted with Et₂O (200 mL) and a solution of saturated aqueous NH₄Cl (200 mL) was added and the aqueous layer was separated and extracted with Et₂O (3 x 50 mL). The organic layers were combined, washed with 0.2 M HCl (100 mL), saturated aqueous NaHCO₃ (100 mL), water (2 x 100 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:Et₂O 40-60, 80:20) afforded enynol **5.28** as a yellow oil (1.3 g, 16 mmol, 34%).

R_f : 0.11 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 5.82 (ddt, *J* = 17.6, 11.0, 1.9 Hz, 1H), 5.66 (dd, *J* = 17.6, 2.2 Hz, 1H), 5.50 (dd, *J* = 11.0, 2.2 Hz, 1H), 4.39 (d, *J* = 1.9 Hz, 2H) ppm

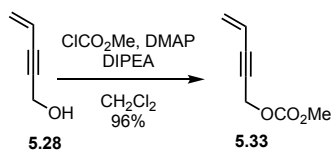
¹³C NMR (100 MHz, CDCl₃): δ 127.7 (CH₂), 116.7 (CH), 88.0 (C_q), 84.6 (C_q), 51.7 (CH₂) ppm

IR (thin film): ν_{max} = 3310(br), 3108, 3013, 2867, 1852, 1600, 1412 cm⁻¹

LRMS (EI): *m/z* (%) = 81 ([M-H]⁺, 100), 63 (34), 53(74)

HRMS (EI): calculated for C₅H₆O [M]⁺ 82.0419; found 82.0422

Methyl pent-4-en-2-yn-1-yl carbonate **5.33**



To a solution of enynol **5.28** (1.7 g, 20 mmol), *N,N*-diisopropylethylamine (4.2 ml, 24 mmol, 1.2 mol. equiv.) and DMAP (50 mg, 0.40 mmol, 0.020 mol. equiv.) in CH_2Cl_2 (100 mL) was cooled to 0 °C and methylchloroformate (1.9 mL, 24 mmol, 1.2 mol. equiv.) was added dropwise. After the addition was complete, the reaction mixture was brought to room temperature and stirred for a further 18 hours. The reaction mixture was then concentrated under reduced pressure and the residue was dissolved in Et_2O (50 mL), washed with 2M HCl (2 x 50 mL), saturated aqueous NaHCO_3 solution (50 mL) and brine (50 mL), dried with MgSO_4 and filtered through a short plug of silica. The solvent was removed under reduced pressure to give **5.33** (2.7 g, 19 mmol, 96%) as a colourless oil.

R_f : 0.20 (petroleum ether 40-60: Et_2O 80:20)

¹H NMR (400 MHz, CDCl_3): δ 5.95-5.76 (m, 1H), 5.70 (dd, $J = 17.6, 2.4$ Hz, 1H), 5.54 (dd, $J = 10.9, 2.3$ Hz, 1H), 4.86 (d, $J = 1.9$ Hz, 2H), 3.82 (s, 3H) ppm

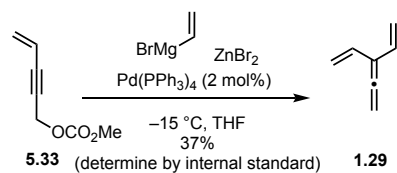
¹³C NMR (100 MHz, CDCl_3): δ 155.4 (C_q), 128.6 (CH), 116.3 (CH_2), 85.9 (C_q), 83.0 (C_q), 56.2 (CH_2), 55.3 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3014, 259, 2858, 2236, 1749, 1602, 1444$ cm^{-1}

LRMS (EI): m/z (%) = 140($[\text{M}-\text{H}]^{+\bullet}$, 20), 125(16), 113(5), 95(5), 81(44), 65(100)

HRMS (EI): calculated for $\text{C}_7\text{H}_8\text{O}_3$ $[\text{M}]^{+\bullet}$ 140.0473; found 140.0472

3-Vinylpenta-1,2,4-triene **1.29**



A solution of methylcarbonate **5.33** (500 mg, 3.6 mmol) in THF (3 mL) was cooled to $-15\text{ }^\circ\text{C}$ and a solution of zinc bromide (1.0 M in THF, 5.4 mL, 5.4 mmol, 1.5 mol. equiv.) and $\text{Pd}(\text{PPh}_3)_4$ (87 mg, 0.075 mmol, 2mol%) were added in a single portion. Subsequently, a solution of vinylmagnesium bromide in THF (0.70 M, 7.6 mL, 5.4 mmol, 1.5 mol. equiv.) was added dropwise over 5 minutes. The reaction mixture was then stirred for a further 1 hour at $-15\text{ }^\circ\text{C}$ and was quenched with methanol (0.5 mL). Analysis of the crude product mixture by ^1H NMR spectroscopy with 1,2,3,5-tetramethylbenzene as an internal standard gave estimated yields of trivinylallene in 37% yield from carbonate **5.35**.

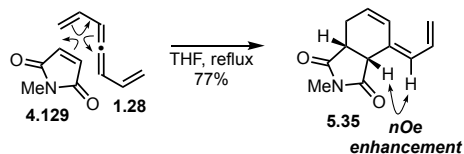
An analytically pure sample of trivinylallene **1.29** was obtained for the purposes of characterization by dilution of the crude mixture with *n*-pentane (50 mL) with aqueous wash of the organic layer with water until no THF was observed by ^1H NMR spectroscopy. The organic layer was then washed with brine, dried over anhydrous MgSO_4 and filtered through a short plug of silica. To the *n*-pentane solution was added CDCl_3 (5 mL) and the *n*-pentane was removed 250 mbar at $0\text{ }^\circ\text{C}$ to give **1.29** as a solution in CDCl_3 . If required additional purification by bulb to trap distillation at room temperature of the CDCl_3 solution (with the receiver flask at $-78\text{ }^\circ\text{C}$) could be performed to remove any oligomerization products generated during the removal of *n*-pentane. ^1H NMR and ^{13}C NMR spectra matched previously reported data.^[46]

^1H NMR (700 MHz, CDCl_3): δ 6.27 (dd, $J = 17.4, 10.7$ Hz, 2H), 5.36 (dd, $J = 17.4, 1.3$ Hz, 2H), 5.18 (dd, $J = 10.8, 1.4$ Hz, 2H), 5.12-5.10 (m, 2H) ppm

^{13}C NMR (175 MHz, CDCl_3): δ 211.7 (C_q), 131.2 (CH), 115.5 (CH_2), 105.1 (C_q), 77.8 (CH_2) ppm

UV-VIS: $\lambda_{\text{max}} = 206\text{ nm}$ ($\epsilon = 20\,000$), 248 nm ($\epsilon = 8\,300$)

(*E*)-4-Allylidene-2-methyl-3a,4,7,7a-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 5.35



N-Methylmaleimide (155 mg, 1.4 mmol, 1.3 mol. equiv.) and BHT (82 mg, 0.37 mmol, 0.36 mol. equiv.) was added to a solution of 1,3-divinylallene (**1.28**) (96 mg, 1.0 mmol) in THF (20 mL). The reaction mixture was stirred for 18 hours at 65 °C then concentrated under reduced pressure and purified by flash chromatography (SiO₂, *n*-pentane:Et₂O, 50:50) to afford monoadduct **5.35** as a pale yellow solid (162 mg, 0.80 mmol, 77%).

R_f : (50:50, *n*-pentane:Et₂O)

m.p.: 75-81 °C

¹H NMR (700 MHz, CDCl₃): δ 6.69 (dt, *J* = 16.7, 10.7 Hz, 1H), 6.63 (d, *J* = 9.4 Hz, 1H), 6.37 (d, *J* = 11.3 Hz, 1H), 5.92-5.83 (m, 1H), 5.36 (d, *J* = 16.7 Hz, 1H), 5.22 (d, *J* = 10.1 Hz, 1H), 3.65 (d, *J* = 8.7 Hz, 1H), 3.18 (td, *J* = 8.3, 2.6 Hz, 1H), 2.98 (s, 3H), 2.74 (ddd, *J* = 17.8, 6.0, 2.7 Hz, 1H), 2.41 (ddd, *J* = 17.7, 7.6, 3.3 Hz, 1H) ppm

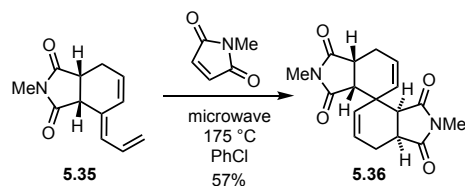
¹³C NMR (125 MHz, CDCl₃): δ 179.4 (C_q) , 177.5 (C_q), 131.5 (CH), 130.4 (CH), 127.3 (CH), 126.1 (C_q), 124.7 (CH), 119.6 (CH₂), 44.6 (CH), 38.7 (CH), 25.5 (CH₃), 22.6 (CH₂) ppm

IR (thin film): ν_{max} = 3089, 3045, 2946, 2899, 2853, 1776, 1692, 1615, 1668, 1432 cm⁻¹

LRMS (EI): *m/z* (%) = 203 ([M]^{+•}, 82), 118(100), 91(70)

HRMS (EI): calculated for C₁₂H₁₃NO₂ [M]^{+•} 203.0946; found 203.0943

Tetracycle 5.36



N-Methylmaleimide (202 mg, 1.82 mmol, 4.8 mol. equiv.) and BHT (2 mg, 0.0091 mmol, 0.02 mol. equiv.) was added to a solution of monoadduct (**5.35**) (78 mg, 0.38 mmol) in chlorobenzene (2 mL) in a 10 mL snap-cap microwave vessel, fitted with a magnetic stirring bar. The reaction mixture was subjected to microwave irradiation (175 °C, 2.5 hours, ramp time 1 min, maximum power 200W), concentrated under reduced pressure and purified by flash chromatography (SiO₂, *n*-pentane:EtOAc, 50:50 → 0:100) to afford **5.36** as a colourless solid (69 mg, 0.22 mmol, 57%).

R_f : 0.25 (50:50, *n*-pentane:EtOAc)

¹H NMR (400 MHz, CDCl₃): δ 6.66 (d, *J* = 9.9 Hz, 1H), 5.96-5.88 (m, 2H), 5.86-5.80 (m, 1H), 4.02 (dd, *J* = 8.6, 1.7 Hz, 1H), 3.37 (td, *J* = 8.4, 3.2 Hz, 1H), 3.17-3.04 (m, 2H), 2.96 (s, 3H), 2.91 (s, 3H), 2.66-2.47 (m, 3H), 2.41-2.29 (m, 1H) ppm

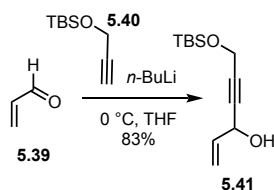
¹³C NMR (100 MHz, CDCl₃): δ 179.9 (C_q), 179.5 (C_q), 178.3 (C_q), 177.8 (C_q), 136.5 (CH), 133.8 (CH), 128.3 (CH), 127.3 (CH), 46.6 (CH), 45.2 (CH), 40.3 (C_q), 39.0 (CH), 38.5 (CH), 25.2 (CH₃), 24.9 (CH₃), 24.3 (CH₂), 23.9 (CH₂) ppm

IR (thin film): ν_{max} = 3043, 2949, 2868, 1772, 1691, 1437 cm⁻¹

LRMS (EI): *m/z* (%) = 314 ([M]^{+•}, 48), 203(22), 118(35), 84 (100)

HRMS (EI): calculated for C₁₇H₁₈N₂O₄ [M]^{+•} 314.1267; found 314.1266

6-((*tert*-butyldimethylsilyl)oxy)hex-1-en-4-yn-3-ol **5.41**



A solution of alkyne **5.40** (600 mg, 3.5 mmol) in THF (5 mL) was cooled to 0 °C and *n*-BuLi (1.4 M in hexanes, 2.5 mL, 3.5 mmol, 1.0 mol. equiv.) was added dropwise. The reaction mixture was stirred for 30 minutes at 0 °C then acrolein (0.30 mL, 4.5 mmol, 1.3 mol. equiv.) was added dropwise. The reaction mixture was stirred for a further 1 hour at 0 °C and then quenched with a saturated aqueous solution of NH₄Cl (10 mL) and diluted with Et₂O (10 mL). The aqueous layer was separated and extracted with Et₂O (3 x 10 mL). The organic layers were combined, washed with brine (10 mL), dried over MgSO₄, filtered and concentrated under reduced vacuum. Purification by flash column chromatography (SiO₂, *n*-pentane:Et₂O, 80:20) gave **5.41** as a yellow oil (650 mg, 2.9 mmol, 83%).

R_f : 0.16 (80:20, *n*-pentane:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 6.01-5.90 (m, 1H), 5.50-5.39 (m, 1H), 5.22 (dt, *J* = 10.2, 1.4 Hz, 1H), 4.97-4.85 (m, 1H), 4.37 (s, 2H), 0.91 (s, 9H), 0.12 (s, 6H) ppm

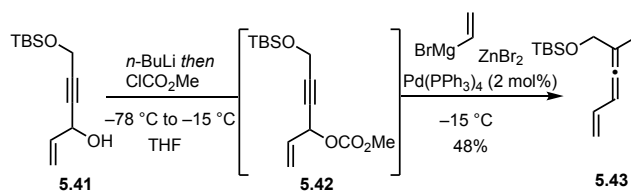
¹³C NMR (100 MHz, CDCl₃): δ 136.9 (CH), 116.6 (CH₂), 85.2 (C_q), 83.6 (C_q), 63.4 (CH), 51.9 (CH₂), 26.0 (3 x CH₃), -5.0 (2 x CH₃) ppm

IR (thin film): ν_{max} = 3361 (br), 2955, 2929, 2885, 2858, 1472, 1464 cm⁻¹

LRMS (ESI): *m/z* (%) = 249 ([M+Na]⁺, 100)

HRMS (ESI): calculated for C₁₂H₂₂O₂NaSi [M+Na]⁺ 249.12813; found 249.12759

tert-Butyldimethyl((2-vinylhexa-2,3,5-trien-1-yl)oxy)silane **5.43**



A solution of alcohol **5.41** (300 mg, 1.3 mmol) in THF (5 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of *n*-BuLi (1.4 M in hexanes, 1.3 mL, 1.8 mmol, 1.4 mol. equiv.) was added dropwise and stirred for 15 minutes. Methyl chloroformate (0.2 mL, 2.6 mmol, 2.0 mol. equiv.) was added dropwise and the reaction mixture was stirred at $-15\text{ }^{\circ}\text{C}$ for 40 min. A solution of zinc bromide (1.00 M in THF, 2.0 mL, 2.0 mmol, 1.5 mol. equiv.) and Pd(PPh₃)₄ (74 mg, 0.064 mmol, 5 mol%) were added in a single portion. A solution of vinylmagnesium bromide in THF (0.70 M, 2.8 mL, 2.0 mmol, 1.5 mol. equiv.) was added dropwise. On completion of addition the reaction mixture was stirred for a further 20 minutes at $-15\text{ }^{\circ}\text{C}$. The reaction was diluted with Et₂O (10 mL) and quenched with saturated aqueous NH₄Cl (10 mL). The aqueous layer was separated and extracted with Et₂O (3 x 10 mL). The organic layers were combined and washed with brine (50 mL), dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The resulting solution was subjected to purification by flash chromatography (SiO₂, *n*-pentane) yielded allene **5.43** as a colourless oil (148 mg, 0.63 mmol, 48%).

R_f : 0.61 (petroleum ether 40-60: Et₂O 80:20)

¹H NMR (400 MHz, CDCl₃): δ 6.10-6.04 (m, 2H), 5.32-5.19 (m, 1H), 5.09 (d, $J = 10.9$ Hz, 1H), 5.03 (d, $J = 9.9$ Hz, 1H), 4.36 (s, 2H), 0.89 (s, 9H), 0.07 (s, 6H) ppm

¹³C NMR (100 MHz, CDCl₃): δ 209.7 (C_q), 132.3 (2 x CH), 132.1 (2 x CH), 116.5 (CH₂), 114.5 (CH₂), 107.1 (C_q), 97.0 (CH₂), 26.0 (3 x CH₃), -5.1 (CH₃), -0.51 (CH₃) ppm

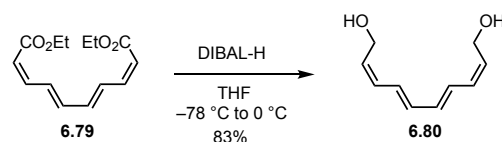
IR (thin film): ν_{max} = 2954, 2929, 2889, 2857, 1930, 1728, 1691, 1613 cm⁻¹

LRMS (EI): m/z (%) = 179 ([M-C₄H₉]⁺, 28), 149(6), 105(16), 89(32), 75 (100)

HRMS (EI): calculated for C₁₄H₂₄OSi [M]⁺ 236.1596; found 236.1591

8.4 Experimental for Chapter 6

(2*Z*,4*E*,6*E*,8*Z*)-deca-2,4,6,8-tetraene-1,10-diol **6.80**



A solution of diester **6.79** (100 mg, 0.40 mmol) in THF (3.0 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of DIBAL-H (1.0 M in hexanes, 1.8 mL, 1.8 mmol, 4.5 mol. equiv.) was added dropwise. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for a further 5 minutes and then at $0\text{ }^{\circ}\text{C}$ for 1.5 hours. The reaction mixture was subsequently cooled to $-78\text{ }^{\circ}\text{C}$ and MeOH (1.0 mL) was added dropwise. The mixture was diluted with EtOAc (20 mL) and saturated aqueous solution of potassium sodium tartrate (20 mL). A crystal of BHT was added to the mixture which was stirred for 10 minutes at room temperature. The layers were separated and the aqueous layer was extracted with EtOAc (30 mL). The organic layers were combined and washed with saturated aqueous potassium sodium tartrate (10 mL), brine (10 mL), dried over MgSO_4 , filtered through a pad of Celite and concentrated under reduced pressure to yield the crude diol **6.80** as a pale yellow solid (63 mg, 0.38 mmol, 95%).

R_f : 0.43 (EtOAc)

¹H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 6.61 (td, $J = 11.2, 3.0$ Hz, 2H), 6.50-6.22 (m, 2H), 6.19-5.97 (m, 2H), 5.59 (dt, $J = 12.2, 6.7$ Hz, 2H), 4.28 (d, $J = 6.6$ Hz, 4H) ppm

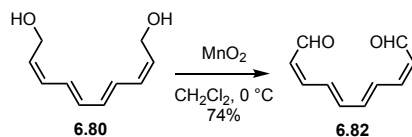
¹³C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 134.6 (2 x CH), 133.2 (2 x CH), 129.7 (2 x CH), 129.4 (2 x CH), 58.8 (2 x CH_2) ppm

IR (thin film): $\nu_{\text{max}} = 3351$ (br), 3266 (br), 3020, 2919, 2866, 1468, 1448 cm^{-1}

LRMS (EI): m/z (%) = 166 ($[\text{M}]^{+\bullet}$, 65), 117(28), 105(25), 91(100), 79(73)

HRMS (EI): calculated for $\text{C}_{10}\text{H}_{14}\text{O}_2$ $[\text{M}]^{+\bullet}$ 166.0994; found 166.0992

(2*Z*,4*E*,6*E*,8*Z*)-deca-2,4,6,8-tetraenedial 6.82



A solution of diol **6.80** (17 mg, 0.10 mmol) was dissolved in CH₂Cl₂ (5.0 mL) and cooled to 0 °C and manganese dioxide (500 mg, 5.8 mmol, 58 mol. equiv.) was added in a single portion and the reaction mixture was stirred for a further 1.5 hours. The reaction mixture was filtered through a pad of celite and concentrated under reduced pressure to yield the crude dialdehyde **6.82** as a yellow solid (12 mg, 0.074 mmol, 74%).

R_f : 0.36 (50:50, pentane:EtOAc)

¹H NMR (600 MHz, (CD₃)₂CO): δ 10.27 (d, *J* = 7.5 Hz, 2H), 7.5-7.53 (m, 2H), 7.16, dd, *J* = 12.1, 11.0 Hz, 2H), 6.99-6.69 (m, 2H), 5.91 (ddd, *J* = 10.9, 7.6, 0.9 Hz, 2H) ppm

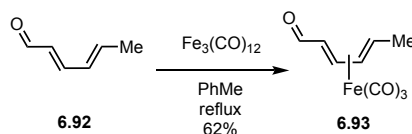
¹³C NMR (150 MHz, (CD₃)₂CO): δ 190.9 (2 x CH), 146.3 (2 x CH), 141.4 (2 x CH), 131.6 (2 x CH), 129.4 (2 x CH) ppm

IR (thin film): ν_{max} = 3300, 3032, 2917, 2848, 1657, 1610 cm⁻¹

LRMS (EI): *m/z* (%) = 162 ([M]^{+•}, 79), 133(31), 115(29), 105(65), 94(100), 77(95)

HRMS (EI): calculated for C₁₀H₁₀O₂ [M]^{+•} 162.0681; found 162.0680

2,4-Hexadienal irontricarbonyl complex 6.93



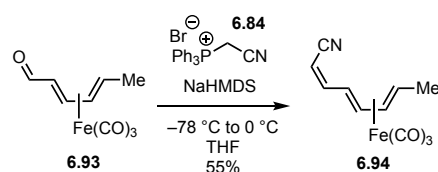
A solution of 2,4-hexadienal (**6.92**) (600 mg, 6.2 mmol) and Fe₃(CO)₁₂ (2.0 g, 4.0 mmol, 0.65 mol. equiv.) in toluene (10 mL) was heated at 80 °C for 2 hours. The reaction mixture was filtered through a pad of Celite, filtered with CH₂Cl₂ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (SiO₂, petroleum ether 40-60:EtOAc, 90:10) to give aldehyde complex **6.93** as an orange oil (0.97 g, 3.9 mmol, 62 %).

¹H NMR and ¹³C NMR spectra matched previously reported data.^{[280] [281]}

¹H NMR (400 MHz, CDCl₃): δ 9.22 (d, *J* = 4.6 Hz, 1H), 5.74 (dd, *J* = 8.3, 4.9 Hz, 1H), 5.27 (dd, *J* = 8.7, 5.1 Hz, 1H), 1.68 (dd, *J* = 8.9, 5.9 Hz, 1H), 1.48 (d, *J* = 6.1 Hz, 3H), 1.24 (dd, *J* = 8.3, 4.4 Hz, 1H) ppm

¹³C NMR (100 MHz, CDCl₃): δ 209.5 (C_q, CO), 196.2 (CH), 89.7 (CH), 81.3 (CH), 60.5 (CH), 54.7 (CH), 19.2 (CH₃) ppm

Irontricarbonyl nitrile complex **6.94**



A suspension of phosphonium bromide (**6.84**) (200 mg, 0.51 mmol, 1.2 mol. equiv.) in THF (1 mL) was cooled to 0 °C and NaHMDS (2.0 M in THF, 0.26 mL, 0.51 mmol, 1.2 mol. equiv.) was added dropwise becoming an orange colour. The reaction mixture was stirred at 0 °C for 10 minutes and then cooled to -78 °C. A solution of complex **6.93** (100 mg, 0.42 mmol) in THF (2.5 mL) was added dropwise and the reaction mixture was then stirred at 0 °C for 20 hours, then quenched with saturated aqueous NH₄Cl solution (30 mL) and diluted with Et₂O (30 mL). The aqueous layer was separated and extracted with Et₂O (3 x 30 mL). The organic layers were combined, washed with brine (30 mL), dried over MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography (SiO₂, petroleum ether 40-60:EtOAc, 90:10) afforded nitrile complex **6.94** as a yellow solid (60 mg, 0.23 mmol, 55%).

R_f: 0.18 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 6.27 (t, *J* = 10.7 Hz, 1H), 5.37-5.28 (m, 1H), 5.15 (dd, *J* = 9.1, 4.9 Hz, 1H), 5.06 (d, *J* = 10.6 Hz, 1H), 2.01-1.88 (m, 1H), 1.84-1.72 (m, 1H), 1.49 (d, *J* = 6.4 Hz, 1H) ppm

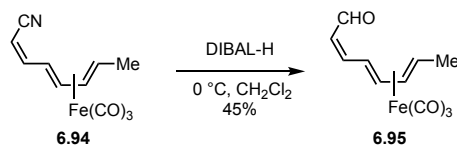
¹³C NMR (100 MHz, CDCl₃): δ 210.6 (C_q, CO), 154.6 (CH), 116.8 (C_q), 94.2 (CH), 87.9 (CH), 82.5 (CH), 59.7 (CH), 53.5 (CH), 19.3 (CH₃) ppm

IR (thin film): ν_{max} = 3079, 2970, 2912, 2862, 2212, 2042, 1964, 1597 cm⁻¹

LRMS (EI): *m/z* (%) = 259 ([M]^{+•},5), 231(20), 203(45), 175(100), 155(40), 148(42)

HRMS (EI): calculated for C₁₁H₉NO₃⁵⁶Fe [M]^{+•} 258.9932; found 258.9929

Irontricarbonyl aldehyde complex **6.95**



A solution of nitrile **6.94** (45 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was cooled to $0\text{ }^\circ\text{C}$ and DIBAL-H was added dropwise (0.8 M in hexanes, 0.33 mL, 0.26 mmol, 1.5 mol. equiv.). The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 1 hour, then filtered through a pad of silica, flushed with Et_2O and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2 , petroleum ether 40-60: Et_2O , 80:20) gave aldehyde complex **6.95** as a yellow solid (20 mg, 0.076 mmol, 45%).

R_f : 0.12 (80:20, petroleum ether 40-60: Et_2O)

¹H NMR (600 MHz, CDCl_3): δ ppm

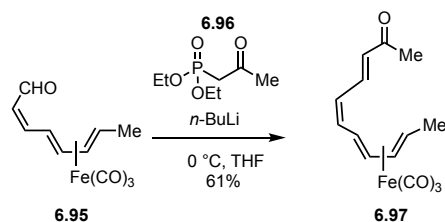
¹³C NMR (150 MHz, CDCl_3): δ 210.8 (C_q , CO), 190.0 (CH), 152.3 (CH), 124.4 (CH), 87.8 (CH), 84.5 (CH), 59.4 (CH), 52.5 (CH), 19.4 (CH_3) ppm

IR (thin film): ν_{max} = 2962, 2924, 2855, 2043, 1968, 1665, 1603, 1572 cm^{-1}

LRMS (EI): m/z (%) = 262 ($[\text{M}]^{+\bullet}$, 11), 234(22), 206(51), 178(49), 148(30), 134(100), 122(18)

HRMS (EI): calculated for $\text{C}_{11}\text{H}_{10}\text{O}_4^{56}\text{Fe}$ $[\text{M}]^{+\bullet}$ 261.9928; found 261.9925

Irontricarbonyl ketone complex **6.97**



A solution of phosphonate **6.98** (52 mg, 0.27 mmol, 1.7 mol.equiv.) of THF (2 mL) was cooled to $0\text{ }^\circ\text{C}$ and $n\text{-BuLi}$ (1.4 M in hexanes, 0.20 mL, 0.28 mmol, 1.8 mol. equiv.) was added dropwise. The reaction mixture was stirred for 30 minutes at $0\text{ }^\circ\text{C}$ then a solution of aldehyde complex **6.95** (45 mg, 0.16 mmol) in THF (3 mL) was added dropwise. The reaction mixture was stirred for a further 2 hours at $0\text{ }^\circ\text{C}$ and then quenched with a saturated aqueous NH_4Cl solution (10 mL) and diluted with Et_2O (10 mL). The aqueous layer was separated and extracted with Et_2O (3 x 10 mL). The organic layers were combined, washed with brine (10 mL), dried over MgSO_4 and concentrated under reduced vacuum. Purification by flash column chromatography (SiO_2 , petroleum ether 40-60: Et_2O , 80:20) gave ketone complex **6.97** as a yellow solid (31 mg, 0.10 mmol, 61%).

R_f : 0.26 (50:50, petroleum ether 40-60: Et_2O)

¹H NMR (400 MHz, CDCl_3): δ 7.47 (t, $J = 13.5$ Hz, 1H), 6.17 (t, $J = 15.4$ Hz, 1H), 6.00 (t, $J = 11.2$ Hz, 1H), 5.78 (t, $J = 10.7$ Hz, 1H), 5.34-5.23 (m, 1H), 5.11 (dd, $J = 8.8, 5.0$ Hz, 1H), 2.29 (s, 3H), 2.06 (t, $J = 9.7$ Hz, 1H), 1.61 (d, $J = 8.1$ Hz, 1H), 1.48 (d, $J = 6.3$ Hz, 3H) ppm

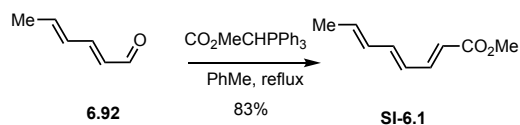
¹³C NMR (100 MHz, CDCl_3): δ 211.6 (C_q , $\underline{\text{C}}\text{O}$), 198.6 (C_q), 142.2 (CH), 137.2 (CH), 1308 (CH), 125.4 (CH), 86.7 (CH), 82.9 (CH), 58.3 (CH), 54.3 (CH), 27.9 (CH_3), 19.4 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3022, 2964, 2918, 2862, 2033, 1950, 1666, 1643, 1608, 1585\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 302 ($[\text{M}]^{+\bullet}, 5$), 246 (28), 218 (100)

HRMS (EI): calculated for $\text{C}_{14}\text{H}_{14}\text{O}_4^{56}\text{Fe}$ $[\text{M}]^{+\bullet}$ 302.0241; found 302.0240

Methyl (2*E*,4*E*,6*E*)-octa-2,4,6-trienoate **SI-6.1**



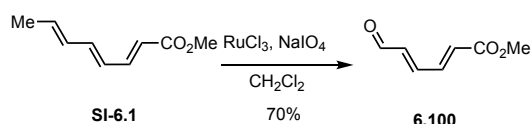
A solution of 2,4-hexadienal (**6.92**) (900 mg, 9.3 mmol) and methyl(triphenylphosphoranylidene)acetate (3.8 g, 11 mmol, 1.2 mol. equiv.) were heated at 60 °C for 12 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (SiO₂, petroleum ether 40-60:Et₂O, 80:20) to yield **SI-6.1** a low melting colourless solid (1.2 g, 7.7 mmol, 83 %). ¹H NMR and ¹³C NMR spectra matched previously reported data.^[282]

¹H NMR (400 MHz, CDCl₃): δ 7.28 (dd, *J* = 15.3, 11.3 Hz, 1H), 6.50 (dd, *J* = 15.0, 10.7 Hz, 1H), 6.23-6.07 (m, 2H), 5.92 (dt, *J* = 14.8, 7.0 Hz, 1H), 5.83 (d, *J* = 15.3 Hz, 1H), 3.71 (s, 3H), 1.80 (d, *J* = 7.1 Hz, 3H) ppm

¹³C NMR (100 MHz, CDCl₃): δ 167.0 (C_q), 144.6 (CH), 140.8 (CH), 134.7 (CH), 131.0 (CH), 127.3 (CH), 119.4 (CH), 50.9 (CH₃), 18.1 (CH₃) ppm

HRMS (EI): calculated for C₉H₁₂O₂ [M]⁺• 152.0837; found 152.0834

Methyl (2*E*,4*E*)-6-oxohexa-2,4-dienoate **6.100**



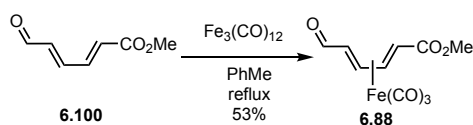
To a solution of triene (**SI-6.1**) (1.1 g, 7.0 mmol) in 9:1 mixture of acetonitrile:water (35 mL) was added ruthenium trichloride hydrate (89 mg, 0.39 mmol., 6 mol%) and sodium periodate (3.1 g, 1.4 mmol, 2.0 mol. equiv.) The reaction mixture was stirred at room temperature for 12 hours, filtered through a pad of Celite and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (SiO₂, petroleum ether 40-60:Et₂O, 80:20) to yield **6.100** a low melting colourless solid (1.1 g, 4.9 mmol, 70 %). ¹H NMR and ¹³C NMR spectra matched previously reported data.^[283]

¹H NMR (700 MHz, CDCl₃): δ 9.64 (d, *J* = 7.7 Hz, 1H), 7.39 (dd, *J* = 15.4, 11.3 Hz, 1H), 7.15 (dd, *J* = 15.4, 11.3 Hz, 1H), 6.39 (dd, *J* = 15.5, 7.7 Hz, 1H), 6.28 (d, *J* = 15.4 Hz, 1H), 3.77 (s, 3H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 192.9 (CH), 165.9 (CH), 147.2 (CH), 140.6 (CH), 137.1 (CH), 129.5 (CH), 52.1 (CH₃) ppm

HRMS (EI): calculated for C₇H₈O₃ [M]⁺• 140.0473; found 140.0473

Irontricarbonyl complex **6.88**



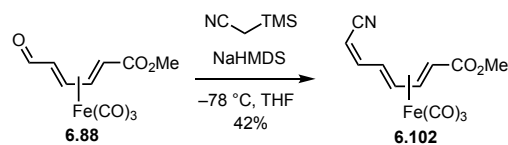
A solution of compound **6.100** (500 mg, 3.6 mmol) and Fe₃(CO)₁₂ (2.0 g, 4.0 mmol, 1.1 mol. equiv.) in toluene (30 mL) was heated at 90 °C 2 hours under an atmosphere of argon. The reaction mixture was filtered through a pad of Celite, filtered with CH₂Cl₂ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (SiO₂, petroleum ether 40-60:Et₂O, 80:20) to give irontricarbonyl complex **6.88** as a yellow solid (530 mg, 1.9 mmol, 53 %). ¹H NMR spectra matched previously reported data.^[284]

¹H NMR (700 MHz, CDCl₃): δ 9.44 (d, *J* = 3.4 Hz, 1H), 6.09-6.03 (m, 1H), 6.0 (ddd, *J* = 8.3, 5.1, 1.1 Hz, 1H), 3.73 (s, 3H), 1.52 (ddd, *J* = 8.3, 3.5, 1.0 Hz, 1H), 1.47 (dd, *J* = 8.2, 1.1 Hz, 1H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 195.6 (C_q), 171.8 (CH), 88.0 (CH), 84.7 (CH), 55.1 (CH), 52.2 (CH), 47.8 (CH₃) ppm Note: CO was not observed in ¹³C NMR

HRMS (EI): calculated for C₁₀H₈O₆⁵⁶Fe [M]⁺• 279.9670; found 279.9665

Irontricarboxyl complex **6.102**



A solution of (trimethylsilyl)acetonitrile (0.30 mL, 2.2 mmol, 1.2 mol. equiv.) in THF (10 mL) was cooled to $-78\text{ }^\circ\text{C}$ and NaHMDS (1.8 M in THF, 1.2 mL, 2.2 mmol, 1.2 mol. equiv.). The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 15 minutes and a solution of irontricarboxyl complex **6.88** (500 mg, 1.8 mmol) in THF (15 mL) was added dropwise. The reaction mixture was stirred for a further 1 hour and a solution of TBAF (1.0 M in THF, 2.5 mL, 2.5 mmol, 1.4 mol. equiv.) was added dropwise. The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 2 hours and was then quenched with a saturated aqueous NH_4Cl solution (mL) and diluted with Et_2O (mL). The aqueous layer was separated and extracted with Et_2O (3 x mL). The organic layers were combined, washed with brine (mL), dried over MgSO_4 , filtered and concentrated under reduced vacuum. Purification by flash column chromatography (SiO_2 , petroleum ether 40-60: Et_2O , 80:20) to give nitrile complex **6.102** as a yellow solid (224 mg, 0.74 mmol, 42%).

R_f : 0.22 (50:50, petroleum ether 40-60: Et_2O)

¹H NMR (400 MHz, CDCl_3): δ 6.33 (t, $J = 10.8$ Hz, 1H), 5.92 (ddd, $J = 8.2, 5.0, 1.1$ Hz, 1H), 5.57 (ddd, $J = 8.5, 5.1, 1.1$ Hz, 1H), 5.20 (dd, $J = 10.7, 0.8$ Hz, 1H), 3.69 (s, 3H), 2.27-2.15 (m, 1H), 1.58 (dd, $J = 8.3, 1.1$ Hz, 1H) ppm

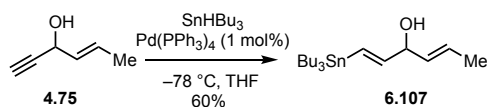
¹³C NMR (100 MHz, CDCl_3): δ 172.1 (C_q), 153.1 (CH), 116.3 (C_q), 96.3 (CH), 86.1 (CH), 86.1 (CH), 54.8 (CH), 52.1 (CH_3), 47.3 (CH) ppm Note: $\underline{\text{C}}\text{O}$ was not observed in ^{13}C NMR

IR (thin film): $\nu_{\text{max}} = 3075, 2954, 2214, 2060, 1986, 1710, 1629, 1599\text{ cm}^{-1}$

LRMS (EI): m/z (%) = 303 ($[\text{M}]^{+\bullet}$, 2), 275(22), 247(78), 219(100), 187(83), 161(55), 134(43), 78(75)

HRMS (EI): calculated for $\text{C}_{12}\text{H}_9\text{NO}_4^{56}\text{Fe}$ $[\text{M}]^{+\bullet}$ 302.9830; found 302.9826

(1*E*,4*E*)-1-(tributylstannyl)hexa-1,4-dien-3-ol **6.107**



A solution of alcohol (**4.75**) (500 mg, 5.2 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (60 mg, 0.052 mmol, 10 mol%) in THF (10 mL) was cooled to -78°C and tributyltinhydride (2.0 mL, 7.4 mmol, 1.4 mol equiv.) was added dropwise. The reaction mixture was stirred at -78°C for 1 hour then concentrated reduced pressure. The resulting residue was purified by flash column chromatography (SiO_2 , *n*-pentane: Et_2O , 90:10) to give stannane **6.107** as a colourless oil (1.2 g, 3.1 mmol, 60 %).

R_f: 0.23 (90:10, *n*-pentane: Et_2O)

¹H NMR (400 MHz, CDCl_3): δ 6.21 (d, $J = 19.2$ Hz, 1H), 6.05 (dd, $J = 19.1, 5.1$ Hz, 1H), 5.72 (dt, $J = 13.3, 6.8$ Hz, 1H), 5.54 (dd, $J = 15.5, 6.7$ Hz, 1H), 4.60-4.50 (m, 1H), 1.74 (d, $J = 6.4$ Hz, 3H), 1.56-1.44 (m, 6H), 1.38-1.28 (m, 6H), 0.97-0.78 (m, 15H) ppm

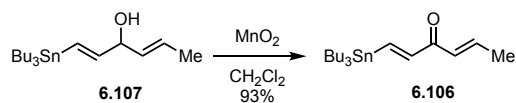
¹³C NMR (100 MHz, CDCl_3): δ 149.3 (CH), 132.7 (CH), 128.2 (CH), 127.5 (CH), 76.2 (CH), 29.2 (CH_2), 27.4 (CH_2), 17.9 (CH_3), 13.9 (CH_2), 9.6 (CH_3) ppm

IR (thin film): $\nu_{\text{max}} = 3321$ (br), 2956, 2925, 2871, 2871, 1667, 1602, 1464 cm^{-1}

LRMS (EI): m/z (%) = 331 ($[\text{M}-\text{C}_4\text{H}_9]^+$, 100), 275(41), 217(18), 177(28), 137(25),

121(20)**HRMS** (EI): calculated for $\text{C}_{14}\text{H}_{27}\text{O}^{120}\text{Sn}$ $[\text{M}-\text{C}_4\text{H}_9]^+$ 331.1084; found 331.1088

(1*E*,4*E*)-1-(tributylstannyl)hexa-1,4-dien-3-one 6.106



To a solution of alcohol (**6.107**) (594 mg, 1.5 mmol) in CH₂Cl₂ (10 mL) was added manganese dioxide (220 mg, 25 mmol, 17 mol. equiv.) in a single portion. The reaction mixture was stirred at room temperature for 1 hour then filtered through a pad of silica, flushed with Et₂O (100 mL) and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, petroleum ether 40-60:Et₂O, 80:20) afforded stannane **6.106** as a colourless oil (532 mg, 1.4 mmol, 93 %).

R_f : 0.49 (80:20, petroleum ether 40-60:Et₂O)

¹H NMR (400 MHz, CDCl₃): δ 7.65 (dd, *J* = 19.6, 1.5 Hz, 1H), 7.02-6.86 (m, 1H), 6.76 (dd, *J* = 19.6, 1.5 Hz, 1H), 6.49 (d, *J* = 15.6 Hz, 1H), 1.94 (d, *J* = 6.7 Hz, 3H), 1.58-1.44 (m, 6H), 1.31 (q, *J* = 7.3 Hz, 6H), 1.05-0.95 (m, 6H), 0.90 (t, *J* = 7.3 Hz, 9H) ppm

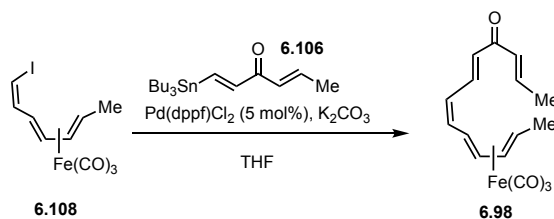
¹³C NMR (100 MHz, CDCl₃): δ 187.9 (C_q), 150.7 (CH), 144.6 (CH), 143.7 (CH), 129.2 (CH), 29.2 (CH₂), 27.4 (CH₂), 18.7 (CH₃), 13.8 (CH₂), 9.9 (CH₃) ppm

IR (thin film): ν_{max} = 2956, 2925, 2872, 2853, 1680, 1667, 1623, 1569 cm⁻¹

LRMS (EI): *m/z* (%) = 329 ([M-C₄H₉]⁺, 100), 273(50), 215(72), 177(22), 137(20), 121(23)

HRMS (EI): calculated for C₁₄H₂₅O¹²⁰Sn [M-C₄H₉]⁺ 329.0927; found 329.0930

Irontricarbonyl complex **6.98**



To a solution of iodide (**6.108**) (115 mg, 0.32 mmol) and stannane **6.106** (170 mg, 0.44 mmol, 1.4 mol. equiv.) in THF (4 mL) were added Pd(dppf)Cl₂ · toluene (23 mg, 0.028 mmol, 9 mol%) and K₂CO₃ (124 mg, 0.90 mmol, 2.8 mol. equiv.) in a single portion. The reaction mixture was stirred at room temperature for 12 hours concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, *n*-pentane:Et₂O, 80:20) afforded ketone **6.98** as a colourless oil (78 mg) containing a tributylstannane impurity.

R_f : 0.12 (80:20, *n*-pentane:Et₂O)

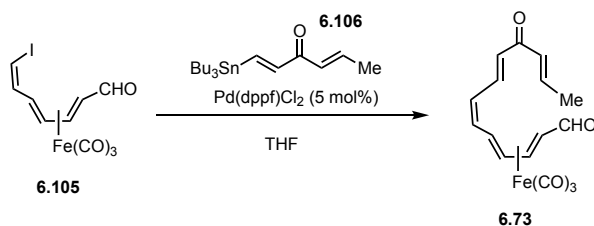
¹H NMR (700 MHz, CDCl₃): δ 7.59 (ddd, *J* = 15.1, 11.9, 1.1 Hz, 1H), 6.93 (dd, *J* = 15.5, 6.9 Hz, 1H), 6.41 (d, *J* = 15.0 Hz, 1H), 6.34 (dt, *J* 16.8, 2.3 Hz, 1H), 6.02 (t, *J* = 10.6 Hz, 1H), 5.76 (t, *J* = 10.8 Hz, 1H), 5.25 (ddd, *J* = 8.4, 4.9, 1.1 Hz, 1H), 5.09 (dd, *J* = 9.0, 4.8 Hz, 1H), 2.14-2.10 (m, 1H), 1.93 (dd, *J* = 6.9, 1.7 Hz, 3H), 1.62-1.57 (m, 1H), 1.46 (d, *J* = 6.2 Hz, 3H) ppm

¹³C NMR (175 MHz, CDCl₃): δ 211.5 (C_q, C=O), 189.3 (C_q), 143.1 (CH), 142.1 (CH), 136.9 (CH), 131.4 (CH), 128.5 (CH), 125.7 (CH), 86.7 (CH), 82.8 (CH), 58.3 (CH), 54.8 (CH), 19.3 (CH₃), 18.6 (CH₃) ppm

IR (thin film): ν_{max} = 3036, 3016, 2957, 2919, 2872, 2856, 2035, 1954, 1659, 1627, 1608, 1579, 1442 cm⁻¹

HRMS (EI): calculated for C₁₆H₁₆O₄⁵⁶Fe [M]⁺• 328.0398; found 328.0399

Irontricarboxyl complex **6.73**



To a solution of iodide (**6.105**) (2 mg, 0.0053 mmol) and stannane **6.106** (4 mg, 0.010 mmol, 1.9 mol. equiv.) in THF (0.5 mL) were added $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{toluene}$ (2 mg, 0.0024 mmol, 45 mol%) in a single portion. The reaction mixture was stirred at room temperature for 12 hours concentrated under reduced pressure. Purification by flash column chromatography (SiO_2 , *n*-pentane: Et_2O , 50:50) afforded complex **6.73**.

R_f: 0.12 (50:50, *n*-pentane: Et_2O)

¹H NMR (400 MHz, CDCl_3): δ 9.43 (d, $J = 3.4$ Hz, 1H), 7.63 (t, $J = 12$ Hz, 1H), 7.06-6.88 (m, 2H), 6.51 (d, $J = 14.9$ Hz, 1H), 6.36 (d, $J = 15.8$ Hz, 1H), 6.19 (t, $J = 11.2$ Hz, 1H), 5.93-5.74 (m, 2H), 5.55 (dd, $J = 8.7, 4.9$ Hz, 1H), 2.71 (t, $J = 9.8$ Hz, 1H), 1.96 (d, $J = 6.9$ Hz, 3H), 1.77 (d, $J = 8.2$ Hz, 1H) ppm

IR (thin film): $\nu_{\text{max}} = 3047, 2963, 2869, 2734, 2057, 1994, 1676, 1659, 1625, 1612, 1580$ cm^{-1}

HRMS (ESI): calculated for $\text{C}_{16}\text{H}_{14}\text{O}_5^{56}\text{FeNa}$ $[\text{M}+\text{Na}]^{+\bullet}$ 365.00829; found 365.00848

9

Supplementary Information

X-Ray Crystallographic Data

X-ray crystallography .cif files for compounds for **4.34**, **4.138**, **4.139** and **5.35** are provided in the uploaded supplementary information file. Single crystal X-ray analyses were performed by Dr. Anthony Willis, Dr. Jas Ward and Dr. Michael Gardiner.

Computational Data

The geometry calculation .xyz files for compounds **1.30**, **4.56** and **4.58** in Chapter 4 and **1.28**, **1.29** and **1.31** in Chapter 5 are provided in the uploaded supplementary file. Calculations were performed by Cecile Elgindy

NMR Spectra

The ^1H and ^{13}C NMR spectra of compounds reported in the Experimental section (Chapter 8) are provided in the uploaded supplementary information file.

10

References

- [1] H. Hopf, *Classics in hydrocarbon chemistry: Syntheses, concepts, perspectives*, Wiley-VCH, Weinheim, **2000**.
- [2] P. E. Eaton, T. W. Cole, *Journal of the American Chemical Society* **1964**, *86*, 3157-3158.
- [3] K. F. Biegasiewicz, J. R. Griffiths, G. P. Savage, J. Tsanaktsidis, R. Priefer, *Chemical Reviews* **2015**, *115*, 6719-6745.
- [4] T. A. Reekie, C. M. Williams, L. M. Rendina, M. Kassiou, *Journal of Medicinal Chemistry* **2019**, *62*, 1078-1095.
- [5] *The Chemistry of Dienes and Polyenes, Vol. 1*, J. Wiley and Sons, Chichester, **1997**.
- [6] R. R. Rando, **1990**, *29*, 461-480.
- [7] M. F. Saglam, T. Fallon, M. N. Paddon-Row, M. S. Sherburn, *Journal of the American Chemical Society* **2016**, *138*, 1022-1032.
- [8] T. Otohiko, W. Eiji, K. Shuji, **1983**, *12*, 239-242.

- [9] C. G. Newton and M. S. Sherburn in *Cross Conjugation*, Wiley- VHC, Weinheim, **2016**, p 413-444.
- [10] S. V. Pronin, R. A. Shenvi, *Journal of the American Chemical Society* **2012**, *134*, 19604-19606.
- [11] E. G. Mackay, C. G. Newton, H. Toombs-Ruane, E. J. Lindeboom, T. Fallon, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Journal of the American Chemical Society* **2015**, *137*, 14653-14659.
- [12] J. A. Januszewski, R. R. Tykwinski, *Chemical Society Reviews* **2014**, *43*, 3184-3203.
- [13] W. Xu, E. Leary, S. Hou, S. Sangtarash, M. T. González, G. Rubio-Bollinger, Q. Wu, H. Sadeghi, L. Tejerina, K. E. Christensen, N. Agraït, S. J. Higgins, C. J. Lambert, R. J. Nichols, H. L. Anderson, **2019**, *58*, 8378-8382.
- [14] C. H. Hendon, D. Tiana, A. T. Murray, D. R. Carbery, A. Walsh, *Chemical Science* **2013**, *4*, 4278-4284.
- [15] M. H. Garner, A. Jensen, L. O. H. Hyllested, G. C. Solomon, *Chemical Science* **2019**, *10*, 4598-4608.
- [16] L. Skattebøl, J. L. Charlton, P. deMayo, *Tetrahedron Letters* **1966**, *7*, 2257-2260.
- [17] E. J. Lindeboom, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, **2014**, *53*, 5440-5443.
- [18] H. Hopf, in *Modern Allene Chemistry* (Ed.: N. K. a. A. S. K. Hashmi), Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, **2004**, pp. 185-241.
- [19] E.-K. Mucke, F. Köhler, R. Herges, *Organic Letters* **2010**, *12*, 1708-1711.
- [20] *Modern Allenes Chemistry, Vol. 1-2*, Wiley-VCH, Germany, **2004**.
- [21] A. Hoffmann-Röder, N. Krause, **2004**, *43*, 1196-1216.
- [22] S. Y. a. S. Ma, *Chemical Communications* **2011**, 5384-5418.
- [23] S. Yu, S. Ma, **2012**, *51*, 3074-3112.
- [24] M. A. María, J. A. Palenzuela*, *Current Organic Chemistry* **2019**, *23*, 3004-3026.
- [25] L. Groizeleau-Miginiac, *R. Acad. Sci.* **1958**, 2156.
- [26] H. H. L. a. M. C. W. E. R. H. Jones, *J. Chem. Soc.* **1960**, 341.
- [27] I. Z. Egenburg, *Russian Chemical Reviews* **1978**, *5*, 900-933.
- [28] M. S. S. Sh. O. Badanyan, *Armenian Journal of Chemistry* **1974**, 651.
- [29] C. Descoins, J. B. Siddall, C. A. Henrick, *Tetrahedron Letters* **1972**, 3777-&.
- [30] J. P. D. J. Gore, *J. Chem. Soc., Chem. Commun.* **1972**, 866-867.

- [31] J. P. D. M. Bertrand, G. Gil, M. L. Roumestant, *Tetrahedron Letters* **1979**, 1845-1846.
- [32] M. Purpura, N. Krause, *European Journal of Organic Chemistry* **1999**, 267-275.
- [33] N. Krause, A. Gerold, *Angewandte Chemie-International Edition in English* **1997**, *36*, 187-204.
- [34] U. Koop, G. Handke, N. Krause, *Liebigs Annalen* **1996**, 1487-1499.
- [35] N. Krause, M. Purpura, *Angewandte Chemie-International Edition* **2000**, *39*, 4355-+.
- [36] H. H. Friedhelm Lehrich, *Tetrahedron Letters* **1987**, *28*, 2697-2700.
- [37] F. Lehrich, H. Hopf, J. Grunenberg, *European Journal of Organic Chemistry* **2011**, 2705-2718.
- [38] U. Modlhammer, H. Hopf, *Angewandte Chemie-International Edition in English* **1975**, *14*, 501-502.
- [39] G. B. O. A. N. Stepanian, Sh. O. Badanian, *Armenian Journal of Chemistry* **1982**, 522-527.
- [40] W. R. Roth, R. Langer, M. Bartmann, B. Stevermann, G. Maier, H. P. Reisenauer, R. Sustmann, W. Muller, *Angewandte Chemie-International Edition in English* **1987**, *26*, 256-258.
- [41] J. M. Robinson, T. Sakai, K. Okano, T. Kitawaki, R. L. Danheiser, *Journal of the American Chemical Society* **2010**, *132*, 11039-11041.
- [42] T. Sakai, R. L. Danheiser, *Journal of the American Chemical Society* **2010**, *132*, 13203-13205.
- [43] P. J. Hamzik, A. S. Goutierre, T. Sakai, R. L. Danheiser, *Journal of Organic Chemistry* **2017**, *82*, 12975-12991.
- [44] M. Sasaki, P. J. Hamzik, H. Ikemoto, S. G. Bartko, R. L. Danheiser, *Organic Letters* **2018**, *20*, 6244-6249.
- [45] M. Ando, M. Sasaki, I. Miyashita, K. Takeda, *Journal of Organic Chemistry* **2015**, *80*, 247-255.
- [46] K. M. Cergol, C. G. Newton, A. L. Lawrence, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Angewandte Chemie-International Edition* **2011**, *50*, 10425-10428.
- [47] T. A. Bradford, A. D. Payne, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *The Journal of Organic Chemistry* **2010**, *75*, 491-494.
- [48] C. E. Kerr, B. E. Eaton, J. A. Kaduk, *Organometallics* **1995**, *14*, 269-273.
- [49] C. Spino, S. Frechette, *Tetrahedron Letters* **2000**, *41*, 8033-8036.

- [50] A. C. Oehlschlager, E. Czyzewska, *Tetrahedron Letters* **1983**, *24*, 5587-5590.
- [51] A. G. B. Ledoussal, A. Le Coq, *Tetrahedron Letters* **1985**, *26*, 51-52.
- [52] D. A. Mundal, K. E. Lutz, R. J. Thomson, *Journal of the American Chemical Society* **2012**, *134*, 5782-5785.
- [53] M. Franck-Neumann, D. Martina, D. Neff, *Tetrahedron-Asymmetry* **1998**, *9*, 697-708.
- [54] A. Roy, B. A. Bhat, S. D. Lepore, *Organic Letters* **2015**, *17*, 900-903.
- [55] Y. W. Andemichael, K. K. Wang, *Journal of Organic Chemistry* **1992**, *57*, 796-798.
- [56] Y. W. Andemichael, Y. Huang, K. K. Wang, *Journal of Organic Chemistry* **1993**, *58*, 1651-1652.
- [57] Z. F. Xi, W. X. Zhang, Z. Y. Song, W. X. Zheng, F. Z. Kong, T. Takahashi, *Journal of Organic Chemistry* **2005**, *70*, 8785-8789.
- [58] A. Ogata, M. Nemoto, K. Kobayashi, A. Tsubouchi, T. Takeda, *Chemistry-a European Journal* **2007**, *13*, 1320-1325.
- [59] R. J. Armstrong, M. Nandakumar, R. M. P. Dias, A. Noble, E. L. Myers, V. K. Aggarwal, *Angewandte Chemie-International Edition* **2018**, *57*, 8203-8208.
- [60] L. Hill, S. P. Saberi, A. M. Z. Slawin, S. E. Thomas, D. J. Williams, *Journal of the Chemical Society-Chemical Communications* **1991**, 1290-1292.
- [61] L. Hill, C. J. Richards, S. P. Saberi, S. E. Thomas, *Pure and Applied Chemistry* **1992**, *64*, 371-377.
- [62] S. P. Saberi, S. E. Thomas, *Journal of the Chemical Society-Perkin Transactions 1* **1992**, 259-265.
- [63] K. Nunn, P. Mosset, R. Gree, R. W. Saalfrank, K. Peters, H. G. Vonschnering, *Angewandte Chemie-International Edition in English* **1992**, *31*, 224-226.
- [64] M. Murakami, K. Itami, Y. Ito, *Angewandte Chemie-International Edition* **1995**, *34*, 2691-2694.
- [65] M. Murakami, K. Itami, Y. Ito, *Organometallics* **1999**, *18*, 1326-1336.
- [66] Kashiwaga, T, N. Yasuoka, N. Kasai, M. Kukudo, *Journal of the Chemical Society D-Chemical Communications* **1969**, 317-&.
- [67] M. Ahmed, T. Arnauld, A. G. M. Barrett, D. C. Braddock, K. Flack, P. A. Procopiu, *Organic Letters* **2000**, *2*, 551-553.
- [68] M. Murakami, S. Kadowaki, T. Matsuda, *Organic Letters* **2005**, *7*, 3953-3956.

- [69] S. H. Sim, S. I. Lee, J. Seo, Y. K. Chung, *Journal of Organic Chemistry* **2007**, *72*, 9818-9821.
- [70] K. Ruitenbergh, H. Kleijn, C. J. Elsevier, J. Meijer, P. Vermeer, *Tetrahedron Letters* **1981**, *22*, 1451-1452.
- [71] K. Ruitenbergh, H. Kleijn, H. Westmijze, J. Meijer, P. Vermeer, *Recueil Des Travaux Chimiques Des Pays-Bas-Journal of the Royal Netherlands Chemical Society* **1982**, *101*, 405-409.
- [72] E. Keinan, E. Bosch, *Journal of Organic Chemistry* **1986**, *51*, 4006-4016.
- [73] S. M. Ma, A. B. Zhang, *Journal of Organic Chemistry* **2002**, *67*, 2287-2294.
- [74] S. M. Ma, G. W. Wang, *Angewandte Chemie-International Edition* **2003**, *42*, 4215-4217.
- [75] G. A. Molander, E. M. Sommers, S. R. Baker, *Journal of Organic Chemistry* **2006**, *71*, 1563-1568.
- [76] T. Mandai, M. Ogawa, H. Yamaoki, T. Nakata, H. Murayama, M. Kawada, J. Tsuji, *Tetrahedron Letters* **1991**, *32*, 3397-3398.
- [77] J. A. Souto, M. Perez, C. S. Lopez, R. Alvarez, A. Torrado, A. R. de Lera, *Journal of Organic Chemistry* **2010**, *75*, 4453-4462.
- [78] T. Mandai, S. Suzuki, A. Ikawa, T. Murakami, M. Kawada, J. Tsuji, *Tetrahedron Letters* **1991**, *32*, 7687-7688.
- [79] R. A. Gibbs, W. H. Okamura, *Tetrahedron Letters* **1987**, *28*, 6021-6024.
- [80] C.-W. Huang, M. Shanmugasundaram, H.-M. Chang, C.-H. Cheng, *Tetrahedron* **2003**, *59*, 3635-3641.
- [81] M. Y. Yang, N. Yokokawa, H. Ohmiya, M. Sawamura, *Organic Letters* **2012**, *14*, 816-819.
- [82] C. G. Newton, S. L. Drew, A. L. Lawrence, A. C. Willis, M. N. Paddon-Row, M. S. Sherburn, *Nature Chemistry* **2015**, *7*, 82-86.
- [83] S. N. Kessler, J. E. Backvall, *Angewandte Chemie-International Edition* **2016**, *55*, 3734-3738.
- [84] J. Ruchti, E. M. Carreira, *Organic Letters* **2016**, *18*, 2174-2176.
- [85] C. J. Elsevier, P. M. Stehouwer, H. Westmijze, P. Vermeer, *Journal of Organic Chemistry* **1983**, *48*, 1103-1105.
- [86] C. J. Elsevier, P. Vermeer, *Journal of Organic Chemistry* **1989**, *54*, 3726-3730.

- [87] F. Ziyanak, M. Kus, L. Alkan-Karadeniz, L. Artok, *Tetrahedron* **2018**, *74*, 3652-3662.
- [88] D. Tac, L. Artok, *Tetrahedron Letters* **2018**, *59*, 895-898.
- [89] G. E. Akpınar, M. Kus, M. Ucuncu, E. Karakus, L. Artok, *Organic Letters* **2011**, *13*, 748-751.
- [90] E. S. Karagoz, M. Kus, G. E. Akpınar, L. Artok, *Journal of Organic Chemistry* **2014**, *79*, 9222-9230.
- [91] M. Ucuncu, E. Karakus, M. Kus, G. E. Akpınar, O. Aksin-Artok, N. Krause, S. Karaca, N. Elmaci, L. Artok, *Journal of Organic Chemistry* **2011**, *76*, 5959-5971.
- [92] D. Tac, I. A. Aytac, A. O. Karatavuk, M. Kus, F. Ziyanak, L. Artok, *Asian Journal of Organic Chemistry* **2017**, *6*, 1415-1420.
- [93] H. Wang, H. Luo, Z.-M. Zhang, W.-F. Zheng, Y. Yin, H. Qian, J. Zhang, S. Ma, *Journal of the American Chemical Society* **2020**.
- [94] M. Ogasawara, L. Y. Fan, Y. H. Ge, T. Takahashi, *Organic Letters* **2006**, *8*, 5409-5412.
- [95] J. P. Dulcere, J. Grimaldi, M. Santelli, *Tetrahedron Letters* **1981**, *22*, 3179-3180.
- [96] A. G. Myers, B. Zheng, *Journal of the American Chemical Society* **1996**, *118*, 4492-4493.
- [97] X. T. Pu, J. M. Ready, *Journal of the American Chemical Society* **2008**, *130*, 10874-+.
- [98] B. D. Sherry, F. D. Toste, *Journal of the American Chemical Society* **2004**, *126*, 15978-15979.
- [99] Y. X. Li, Y. L. Sheng, B. S. Zhang, *Chinese Chemical Letters* **2013**, *24*, 137-139.
- [100] C. Spino, C. Thibault, S. Gingras, *Journal of Organic Chemistry* **1998**, *63*, 5283-5287.
- [101] C. Spino, B. Hill, P. Dubé, S. Gingras, *Canadian Journal of Chemistry* **2003**, *81*, 81-108.
- [102] R. Clément, C. M. Grisé, L. Barriault, *Chemical Communications* **2008**, 3004-3006.
- [103] D. Regás, M. a. M. Afonso, A. Galindo, J. A. Palenzuela, *Tetrahedron Letters* **2000**, *41*, 6781-6784.
- [104] D. Regás, J. M. Ruiz, M. M. Afonso, J. A. Palenzuela, *The Journal of Organic Chemistry* **2006**, *71*, 9153-9164.
- [105] H. J. Reich, E. K. Eisenhart, W. L. Whipple, M. J. Kelly, *Journal of the American Chemical Society* **1988**, *110*, 6432-6442.
- [106] M. L. Ferreiro, J. Rodríguez-Otero, E. M. J. S. C. Cabaleiro-Lago, **2004**, *15*, 323-326.

- [107] J. B. Wright, J. Pranata, *Journal of Molecular Structure: THEOCHEM* **1999**, *460*, 67-78.
- [108] E. Gil-Av, J. Herling, *Tetrahedron Letters* **1967**, *8*, 1-4.
- [109] D. J. Pasto, W. Kong, *The Journal of Organic Chemistry* **1989**, *54*, 4028-4033.
- [110] M. Murakami, H. Amii, K. Itami, Y. Ito, **1995**, *34*, 1476-1477.
- [111] J. G. Rey, J. Rodríguez, A. R. de Lera, *Tetrahedron Letters* **1993**, *34*, 6293-6296.
- [112] S. López, J. García Rey, J. Rodríguez, A. R. de Lera, *Tetrahedron Letters* **1995**, *36*, 4669-4672.
- [113] S. López, J. Rodríguez, J. G. Rey, A. R. de Lera, *Journal of the American Chemical Society* **1996**, *118*, 1881-1891.
- [114] M. A. Tius, *Chemical Society Reviews* **2014**, *43*, 2979-3002.
- [115] G. Lemièrre, V. Gandon, K. Cariou, A. Hours, T. Fukuyama, A.-L. Dhimane, L. Fensterbank, M. Malacria, *Journal of the American Chemical Society* **2009**, *131*, 2993-3006.
- [116] F. Delbecq, J. Goré, *Tetrahedron Letters* **1976**, *17*, 3459-3460.
- [117] R. Baudouy, F. Delbecq, J. Gore, *Tetrahedron* **1980**, *36*, 189-195.
- [118] M. Franck-Neumann, F. Brion, **1979**, *18*, 688-689.
- [119] A. G. Myers, E. Y. Kuo, N. S. Finney, *Journal of the American Chemical Society* **1989**, *111*, 8057-8059.
- [120] A. G. Myers, P. S. Dragovich, *Journal of the American Chemical Society* **1989**, *111*, 9130-9132.
- [121] R. Nagata, H. Yamanaka, E. Okazaki, I. Saito, *Tetrahedron Letters* **1989**, *30*, 4995-4998.
- [122] L. K. Sydnes, *Chemical Reviews* **2003**, *103*, 1133-1150.
- [123] K. J. Crowley, *Proceedings of the Chemical Society of London* **1964**, 17-&.
- [124] Mikolajc.Kl, M. O. Bagby, R. B. Bates, I. A. Wolff, *Journal of Organic Chemistry* **1965**, *30*, 2983-&.
- [125] L. Skattebol, *Tetrahedron* **1969**, *25*, 4933-+.
- [126] G. Y. Shen, R. Tapia, W. H. Okamura, *Journal of the American Chemical Society* **1987**, *109*, 7499-7506.
- [127] K. M. Wu, M. M. Midland, W. H. Okamura, *Journal of Organic Chemistry* **1990**, *55*, 4381-4392.

- [128] W. H. Okamura, G. Y. Shen, R. Tapia, *Journal of the American Chemical Society* **1986**, *108*, 5018-5019.
- [129] O. N. Faza, C. S. Lopez, A. R. de Lera, *Journal of Organic Chemistry* **2007**, *72*, 2617-2624.
- [130] C. G. Knudsen, R. A. S. Chandraratna, L. P. Walkeapaa, Y. S. Chauhan, S. C. Carey, T. M. Cooper, R. R. Birge, W. H. Okamura, *Journal of the American Chemical Society* **1983**, *105*, 1626-1631.
- [131] W. H. Okamura, *Accounts of Chemical Research* **1983**, *16*, 81-88.
- [132] F. Jensen, *Journal of the American Chemical Society* **1996**, *118*, 297-297.
- [133] S. Ma, Z. Gu, *Journal of the American Chemical Society* **2006**, *128*, 4942-4943.
- [134] Z. H. Gu, S. M. Ma, *Chemistry-a European Journal* **2008**, *14*, 2453-2464.
- [135] H. Siegel, H. Hopf, A. Germer, P. Binger, **1978**, *111*, 3112-3118.
- [136] M. Murakami, K. Itami, Y. Ito, *Synlett* **1999**, 951-953.
- [137] P. H. Lee, K. Lee, Y. J. Kang, *Journal of the American Chemical Society* **2006**, *128*, 1139-1146.
- [138] M. Murakami, K. Itami, Y. Ito, *Journal of the American Chemical Society* **1997**, *119*, 7163-7164.
- [139] M. Murakami, R. Minamida, K. Itami, M. Sawamura, Y. Ito, *Chemical Communications* **2000**, 2293-2294.
- [140] M. Murakami, M. Ubukata, K. Itami, Y. Ito, *Angewandte Chemie-International Edition* **1998**, *37*, 2248-2250.
- [141] M. Murakami, K. Itami, Y. Ito, *Angewandte Chemie-International Edition* **1998**, *37*, 3418-3420.
- [142] M. Murakami, K. Itami, Y. Ito, *Journal of the American Chemical Society* **1996**, *118*, 11672-11673.
- [143] M. Murakami, K. Itami, Y. Ito, *Journal of the American Chemical Society* **1997**, *119*, 2950-2951.
- [144] Y. M. Huang, S. Torker, X. H. Li, J. del Pozo, A. H. Hoveyda, *Angewandte Chemie-International Edition* **2019**, *58*, 2685-2691.
- [145] E. A. Johnson, K. L. Burdon, *Journal of Bacteriology* **1947**, *54*, 280-280.
- [146] W. D. Celmer, I. A. Solomons, *Journal of the American Chemical Society* **1952**, *74*, 1870-1871.

- [147] D. F. Horler, *Journal of the Chemical Society C-Organic* **1970**, 859-&.
- [148] J. M. Renaud, G. Tsoupras, H. Stoeckli-evans, R. Tabacchi, *Helvetica Chimica Acta* **1989**, *72*, 1262-1267.
- [149] D. R. Sanson, H. Gracz, M. S. Tempesta, D. S. Fukuda, W. M. Nakatsukasa, T. H. Sands, P. J. Baker, J. S. Mynderse, *Tetrahedron* **1991**, *47*, 3633-3644.
- [150] L. Liu, S. C. Liu, L. H. Jiang, X. L. Chen, L. D. Guo, Y. S. Che, *Organic Letters* **2008**, *10*, 1397-1400.
- [151] T. Suzuki, S. Kobayashi, *Organic Letters* **2010**, *12*, 2920-2923.
- [152] M. Yu, B. B. Snider, *Tetrahedron* **2011**, *67*, 9473-9478.
- [153] T. Suzuki, S. Watanabe, S. Kobayashi, K. Tanino, *Organic Letters* **2017**, *19*, 922-925.
- [154] X.-L. Yang, J.-Z. Zhang, D.-Q. Luo, *Natural Product Reports* **2012**, *29*, 622-641.
- [155] L. Liu, S. Liu, X. Chen, L. Guo, Y. Che, *Bioorganic & Medicinal Chemistry* **2009**, *17*, 606-613.
- [156] K. C. Nicolaou, S. A. Snyder, T. Montagnon, G. Vassilikogiannakis, **2002**, *41*, 1668-1698.
- [157] G. E. Keck, D. F. Kachensky, *Journal of Organic Chemistry* **1986**, *51*, 2487-2493.
- [158] R. A. Gibbs, K. Bartels, R. W. K. Lee, W. H. Okamura, *Journal of the American Chemical Society* **1989**, *111*, 3717-3725.
- [159] R. Gidlof, M. Johansson, O. Sterner, *Organic Letters* **2010**, *12*, 5100-5103.
- [160] A. Phongsatha, P. Klaboe, H. Hopf, B. N. Cyvin, S. J. Cyvin, *Spectrochimica Acta Part a-Molecular and Biomolecular Spectroscopy* **1978**, *34*, 537-540.
- [161] T. Lange, J. D. vanLoon, R. R. Tykwinski, M. Schreiber, F. Diederich, *Synthesis-Stuttgart* **1996**, 537-&.
- [162] R. Livingston, L. R. Cox, S. Odermatt, F. O. Diederich, *Helvetica Chimica Acta* **2002**, *85*, 3052-3077.
- [163] F. B. Kirby, W. G. Kofron, C. R. Hauser, *The Journal of Organic Chemistry* **1963**, *28*, 2176-2179.
- [164] E. Weber, W. Seichter, I. Goldberg, **1990**, *123*, 811-820.
- [165] B. Inés, D. Palomas, S. Holle, S. Steinberg, J. A. Nicasio, M. Alcarazo, **2012**, *51*, 12367-12369.
- [166] L.-M. Wei, L.-L. Wei, W.-B. Pan, M.-J. Wu, *Synlett* **2005**, *2005*, 2219-2223.
- [167] N. Liu, Y. Zhi, J. Yao, J. Xing, T. Lu, X. Dou, **2018**, *360*, 642-646.

- [168] R. Gompper, J. Schelble, C. S. Schneider, *Tetrahedron Letters* **1978**, *19*, 3897-3900.
- [169] D. Palomas, S. Holle, B. Inés, H. Bruns, R. Goddard, M. Alcarazo, *Dalton Transactions* **2012**, *41*, 9073-9082.
- [170] S. Ma, Q. Liu, X. Tang, Y. Cai, **2017**, *6*, 1209-1212.
- [171] W. von E. Doering, P. M. LaFlamme, *Tetrahedron* **1958**, *2*, 75-79.
- [172] T. L. Jacobs, D. Dankner, S. Singer, *Tetrahedron* **1964**, *20*, 2177-&.
- [173] E. V. Dehmlow, G. C. Ezimora, *Tetrahedron Letters* **1972**, 1265-&.
- [174] P. Capdevielle, J. Rigaudy, *Tetrahedron* **1979**, *35*, 2093-2100.
- [175] C. J. Elsevier, H. Kleijn, K. Ruitenbergh, P. Vermeer, *Journal of the Chemical Society-Chemical Communications* **1983**, 1529-1530.
- [176] C. J. Elsevier, H. Kleijn, J. Boersma, P. Vermeer, *Organometallics* **1986**, *5*, 716-720.
- [177] H. Siegel, A. Germer, P. Binger, H. Hopf, *Chem. Ber.-Recl.* **1978**, *111*, 3112-3118.
- [178] S. L. Skraba, R. P. Johnson, *The Journal of Organic Chemistry* **2012**, *77*, 11096-11100.
- [179] J. George, J. S. Ward, M. S. Sherburn, *Chemical Science* **2019**.
- [180] H. Toombs-Ruane, Australian National University **2013**.
- [181] S.-K. Hua, Q.-P. Hu, J. Ren, B.-B. Zeng, *Synthesis* **2013**, *45*, 518-526.
- [182] C. G. Newton, Sheburn, M. S., in *Cross Conjugation*, pp. 413-444.
- [183] A. D. Rodríguez, C. Ramírez, I. I. Rodríguez, *Journal of Natural Products* **1999**, *62*, 997-999.
- [184] H. Higuchi, N. Hiraiwa, S. Kondo, J. Ojima, G. Yamamoto, *Tetrahedron Letters* **1996**, *37*, 2601-2604.
- [185] J. G. Buta, J. L. Flippen, W. R. Lusby, *The Journal of Organic Chemistry* **1978**, *43*, 1002-1003.
- [186] H.-J. Zhang, L. Hu, Z. Ma, R. Li, Z. Zhang, C. Tao, B. Cheng, Y. Li, H. Wang, H. Zhai, **2016**, *55*, 11638-11641.
- [187] R. Gleiter, L. A. Paquette, *Accounts of Chemical Research* **1983**, *16*, 328-334.
- [188] R. Livingston, L. R. Cox, S. Odermatt, F. Diederich, **2002**, *85*, 3052-3077.
- [189] A. Hakiki, Z. Jabry, J.-L. Ripoll, A. Thuillier, *Tetrahedron Letters* **1984**, *25*, 3461-3462.
- [190] T. M. D. T. A. Bryson, *Organic Syntheses* **1977**, *57*, 62.
- [191] M. S. Baird, A. V. Nizovtsev, I. G. Bolesov, *Tetrahedron* **2002**, *58*, 1581-1593.
- [192] Z. Liu, P. Liao, X. Bi, **2014**, *20*, 17277-17281.
- [193] M. Oku, S. Arai, K. Katayama, T. Shioiri, *Synlett* **2000**, *2000*, 493-494.

- [194] B. Bolte, Y. Odabachian, F. Gagosz, *Journal of the American Chemical Society* **2010**, *132*, 7294-7296.
- [195] L. K. Smith, I. R. Baxendale, *Organic & Biomolecular Chemistry* **2015**, *13*, 9907-9933.
- [196] Y. Zheng, C. M. Tice, S. B. Singh, *Bioorganic & Medicinal Chemistry Letters* **2014**, *24*, 3673-3682.
- [197] H. N. Cripps, Kiefer, E. F., *Organic Syntheses* **1962**, *42*, 12.
- [198] I. F. a. D. H. Williams, *Spectroscopic Methods in Organic Chemistry*, Fifth Edition ed., McGraw-Hill, UK, **1995**.
- [199] H. S. Rzepa, *Chemical Reviews* **2005**, *105*, 3697-3715.
- [200] M. H. Garner, R. Hoffmann, S. Rettrup, G. C. Solomon, *ACS Central Science* **2018**, *4*, 688-700.
- [201] M. Franck-Neumann, D. Martina, M.-P. Heitz, *Journal of Organometallic Chemistry* **1986**, *301*, 61-77.
- [202] T. M. Krygowski, M. K. Cyrański, Z. Czarnocki, G. Häfeli, A. R. Katritzky, *Tetrahedron* **2000**, *56*, 1783-1796.
- [203] P. v. R. Schleyer, *Chemical Reviews* **2001**, *101*, 1115-1118.
- [204] R. Hoffmann, *American Scientist* **2015**, *103*, 18.
- [205] M. Faraday, **1825**, *115*, 440-466.
- [206] A. Kekulé, *Bulletin de la Societe Chimique de Paris* **1865**, *2*, 98-110.
- [207] F. Sondheimer, R. Wolovsky, *Journal of the American Chemical Society* **1962**, *84*, 260-269.
- [208] *Chemical Reviews* **2001**, *101*, 1115-1566.
- [209] E. Hückel, *Grundzüge der Theorie Ungesättigter und aromatischer Verbindungen*, VCH, **1938**.
- [210] W. von E. Doering, F. L. Detert, *Journal of the American Chemical Society* **1951**, *73*, 876-877.
- [211] G. F. Emerson, L. Watts, R. Pettit, *Journal of the American Chemical Society* **1965**, *87*, 131-133.
- [212] R. Willstätter, E. Waser, **1911**, *44*, 3423-3445.
- [213] H. S. Kaufman, I. Fankuchen, H. Mark, *Nature* **1948**, *161*, 165-165.
- [214] M. Trætteberg, F. Kaufmann, K. Motzfeldt, D. Williams, E. Bunnenberg, C. Djerassi, R. Records, *Acta Chemica Scandinavica - ACTA CHEM SCAND* **1966**, *20*, 1724-1726.

- [215] R. B. Turner, B. J. Mallon, M. Tichy, W. V. E. Doering, W. R. Roth, G. Schroeder, *Journal of the American Chemical Society* **1973**, *95*, 8605-8610.
- [216] Z. Chen, C. S. Wannere, C. Corminboeuf, R. Puchta, P. v. R. Schleyer, *Chemical Reviews* **2005**, *105*, 3842-3888.
- [217] T. M. Krygowski, M. K. Cyrański, *Chemical Reviews* **2001**, *101*, 1385-1420.
- [218] J. Kruszewski, T. M. Krygowski, *Tetrahedron Letters* **1972**, *13*, 3839-3842.
- [219] P. v. R. Schleyer, C. Maerker, A. Dransfeld, H. Jiao, N. J. R. van Eikema Hommes, *Journal of the American Chemical Society* **1996**, *118*, 6317-6318.
- [220] E. Heilbronner, *Tetrahedron Letters* **1964**, *5*, 1923-1928.
- [221] N. C. Baird, *Journal of the American Chemical Society* **1972**, *94*, 4941-4948.
- [222] W.-Y. Cha, T. Kim, A. Ghosh, Z. Zhang, X.-S. Ke, R. Ali, V. M. Lynch, J. Jung, W. Kim, S. Lee, S. Fukuzumi, J. S. Park, J. L. Sessler, T. K. Chandrashekar, D. Kim, *Nature Chemistry* **2017**, *9*, 1243.
- [223] S. Martín-Santamaría, B. Lavan, H. S. Rzepa, *Journal of the Chemical Society, Perkin Transactions 2* **2000**, 1415-1417.
- [224] C. Castro, C. M. Isborn, W. L. Karney, M. Mauksch, P. v. R. Schleyer, *Organic Letters* **2002**, *4*, 3431-3434.
- [225] M. Stepień, L. Latos-Grażyński, N. Sprutta, P. Chwalisz, L. Szterenber, **2007**, *46*, 7869-7873.
- [226] Z. S. Yoon, A. Osuka, D. Kim, *Nature Chemistry* **2009**, *1*, 113.
- [227] M. Mauksch, V. Gogonea, H. Jiao, P. v. R. Schleyer, **1998**, *37*, 2395-2397.
- [228] G. Bucher, S. Grimme, R. Huenerbein, A. A. Auer, E. Mucke, F. Köhler, J. Siegwarth, R. Herges, **2009**, *48*, 9971-9974.
- [229] D. Ajami, O. Oeckler, A. Simon, R. Herges, *Nature* **2003**, *426*, 819-821.
- [230] C. S. Wannere, D. Moran, N. L. Allinger, B. A. Hess, L. J. Schaad, P. v. R. Schleyer, *Organic Letters* **2003**, *5*, 2983-2986.
- [231] C. Castro, Z. Chen, C. S. Wannere, H. Jiao, W. L. Karney, M. Mauksch, R. Puchta, N. J. R. v. E. Hommes, P. v. R. Schleyer, *Journal of the American Chemical Society* **2005**, *127*, 2425-2432.
- [232] E.-K. Mucke, B. Schönborn, F. Köhler, R. Herges, *The Journal of Organic Chemistry* **2011**, *76*, 35-41.

- [233] G. M. Pilling, F. Sondheimer, *Journal of the American Chemical Society* **1968**, *90*, 5610-5611.
- [234] F. Sondheimer, G. M. Pilling, *Journal of the American Chemical Society* **1971**, *93*, 1977-1984.
- [235] P. D. Howes, E. LeGoff, F. Sondheimer, *Tetrahedron Letters* **1972**, *13*, 3691-3694.
- [236] T. M. Cresp, J. Ojima, F. Sondheimer, *The Journal of Organic Chemistry* **1977**, *42*, 2130-2134.
- [237] H. Reihlen, A. Gruhl, G. v. Heßling, O. Pfrengle, **1930**, *482*, 161-182.
- [238] B. C. G. S. Louis S. Hegedus, *Transition Metals in the Synthesis of Complex Organic Molecules*, Third Edition ed., University Science Books, Sausalito, California, **2010**.
- [239] W. R. Roth, J. D. Meier, *Tetrahedron Letters* **1967**, *8*, 2053-2058.
- [240] Y. Shvo, E. Hazum, *Journal of the Chemical Society, Chemical Communications* **1975**, 829-830.
- [241] R. C. Kerber, E. C. Ribakove, *Organometallics* **1991**, *10*, 2848-2853.
- [242] J. T. Wasicak, R. A. Craig, R. Henry, B. Dasgupta, H. Li, W. A. Donaldson, *Tetrahedron* **1997**, *53*, 4185-4198.
- [243] A. Wada, N. Fujioka, Y. Tanaka, M. Ito, *The Journal of Organic Chemistry* **2000**, *65*, 2438-2443.
- [244] M. F. Semmelhack, J. W. Herndon, J. K. Liu, *Organometallics* **1983**, *2*, 1885-1888.
- [245] M. F. Semmelhack, H. T. M. Le, *Journal of the American Chemical Society* **1985**, *107*, 1455-1457.
- [246] A. J. Birch, P. E. Cross, J. Lewis, D. A. White, S. B. Wild, *Journal of the Chemical Society A: Inorganic, Physical, Theoretical* **1968**, 332-340.
- [247] R. B. King, T. A. Manuel, F. G. A. Stone, *Journal of Inorganic and Nuclear Chemistry* **1961**, *16*, 233-239.
- [248] S. V. Ley, C. M. R. Low, A. D. White, *Journal of Organometallic Chemistry* **1986**, *302*, C13-C16.
- [249] J. A. S. Howell, B. F. G. Johnson, P. L. Josty, J. Lewis, *Journal of Organometallic Chemistry* **1972**, *39*, 329-333.
- [250] H. Fleckner, F. W. Grevels, D. Hess, *Journal of the American Chemical Society* **1984**, *106*, 2027-2032.
- [251] H.-J. Knölker, *Chemical Reviews* **2000**, *100*, 2941-2962.

- [252] J. D. Holmes, R. Pettit, *Journal of the American Chemical Society* **1963**, *85*, 2531-2532.
- [253] L. Watts, J. D. Fitzpatrick, R. Pettit, *Journal of the American Chemical Society* **1965**, *87*, 3253-3254.
- [254] J. D. Rainier, J. E. Imbriglio, *The Journal of Organic Chemistry* **2000**, *65*, 7272-7276.
- [255] R. Pettit, Henery, J., Napierski, J., Breslow, R., *Organic Syntheses* **1970**, *50*, 21.
- [256] E. Weiss, R. G. Merenyi, W. Hubel, *Chemistry & Industry* **1960**, 407-408.
- [257] E. Weiss, R. Merényi, W. Hübel, **1962**, *95*, 1170-1178.
- [258] W. Reppe, H. Vetter, **1953**, *582*, 133-161.
- [259] A. Eisenstadt, *Tetrahedron Letters* **1976**, *17*, 3543-3546.
- [260] E. J. Reardon, M. Brookhart, *Journal of the American Chemical Society* **1973**, *95*, 4311-4316.
- [261] H. Toombs-Ruane, E. L. Pearson, M. N. Paddon-Row, M. S. Sherburn, *Chemical Communications* **2012**, *48*, 6639-6641.
- [262] K. Roper, *Unpublished work*.
- [263] W. Zhang, *Honours Thesis Towards the synthesis of the [13]annulene carbocation*, **2014**.
- [264] A. G. Jarvis, P. E. Sehnal, S. E. Bajwa, A. C. Whitwood, X. Zhang, M. S. Cheung, Z. Lin, I. J. S. Fairlamb, **2013**, *19*, 6034-6043.
- [265] R. Wang, C. Chen, X. Zhang, C. Zhang, Q. Zhong, G. Chen, Q. Zhang, S. Zheng, G. Wang, Q.-H. Chen, *Journal of Medicinal Chemistry* **2015**, *58*, 4713-4726.
- [266] X. Zhang, R. Wang, G. R. Perez, G. Chen, Q. Zhang, S. Zheng, G. Wang, Q.-H. Chen, *Bioorganic & Medicinal Chemistry* **2016**, *24*, 4692-4700.
- [267] G. Casiraghi, F. Zanardi, G. Appendino, G. Rassu, *Chemical Reviews* **2000**, *100*, 1929-1972.
- [268] K.-i. Takao, H. Ochiai, K.-i. Yoshida, T. Hashizuka, H. Koshimura, K.-i. Tadano, S. Ogawa, *The Journal of Organic Chemistry* **1995**, *60*, 8179-8193.
- [269] J. A. Gazaille, J. A. Abramite, T. Sammakia, *Organic Letters* **2012**, *14*, 178-181.
- [270] J. A. Abramite, T. Sammakia, *Organic Letters* **2007**, *9*, 2103-2106.
- [271] A. T. L. Agilent CrysAlis PRO, Yarnton, Oxfordshire, England, **2014**.
- [272] G. Sheldrick, *Acta Crystallographica Section A* **2015**, *71*, 3-8.
- [273] G. Sheldrick, *Acta Crystallographica Section C* **2015**, *71*, 3-8.
- [274] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *Journal of Applied Crystallography* **2009**, *42*, 339-341.

- [275] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518-1520.
- [276] in *Purification of Laboratory Chemicals (Seventh Edition)* (Eds.: W. L. F. Armarego, C. Chai), Butterworth-Heinemann, Boston, **2013**.
- [277] H.-S. Lin, L. A. Paquette, *Synthetic Communications* **1994**, *24*, 2503-2506.
- [278] B. E. Love, E. G. Jones, *The Journal of Organic Chemistry* **1999**, *64*, 3755-3756.
- [279] E. Métay, Q. Hu, E.-i. Negishi, *Organic Letters* **2006**, *8*, 5773-5776.
- [280] K. Aoki, Y. Igarashi, H. Nishimura, I. Morishita, K. Usui, *Tetrahedron Letters* **2012**, *53*, 6000-6003.
- [281] G. F. Docherty, G. R. Knox, P. L. Pauson, *Journal of Organometallic Chemistry* **1998**, *568*, 287-290.
- [282] N. Kobayashi, H. Kuniyoshi, K. Ishigami, H. Watanabe, *Bioscience, Biotechnology, and Biochemistry* **2008**, *72*, 2708-2715.
- [283] Y. Shang, X. Jie, K. Jonnada, S. N. Zafar, W. Su, *Nature Communications* **2017**, *8*, 2273.
- [284] K. Godula, H. Bärmann, W. A. Donaldson, *The Journal of Organic Chemistry* **2001**, *66*, 3590-3592.