Efficient Syntheses of Natural Products and Target Molecules

A thesis submitted in fulfillment of the requirements for admission to the degree of

Doctor of Philosophy

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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 February 2016 to July 2019 in the Research School of Chemistry of the Australian National University, Australia, under the supervision of Professor Michael Sherburn. The material presented has not been submitted for any other degree and is less than 100,000 words in length.

Madison J Sowden

23rd October 2019
Dedicated to my Mum and Dad
Acknowledgements

Firstly, I’d like to thank my supervisor Professor Michael Sherburn. Mick (Bossman), I will never be able to thank you enough for giving me the chance to study with you. Thank you for inspiring me to be a better chemist and a better person. If I can be half the chemist and person you are I will be very happy. I really hope I’ve made you proud over the past 3.5 years and continue to make you proud in the future. I wish that I could work for you forever.

Thanks to the members of the Sherburn group past and present. Nick Magann and Erin Westley aka team lab 3.78 aka team matrine, you two make coming to the lab everyday so easy. Nick, thanks for been my best mate and big brother, working with you has made me a better chemist and person. Thank you for your patience, help and friendship, you are ridiculously talented and I hope one day I can be as clever as you! Erin, you are far smarter and a better chemist than you think you are. Thank you for been an amazing friend and colleague, I am so glad that I have gotten to know you! Natalie Shadwell, thanks for being a wonderful friend during our honours and PhD’s. Thank you for the laughs, support and pep talks, you are amazing! Finally, Dr Nick Green and Dr Chris Newton thanks for teaching me at the start!

Mark Ellison and Alannah McLeod, thank you both so much for been two of the most amazing friends. Mark, I will never be able to thank you enough, but please know that I would not be here without you. Alannah, thank you so much for everything, for the laughs, listening to my ramblings, the coffees, the walks and the lunches. You are truly one of my best friends and I’m so glad I’ve gotten to know you.

“My friends have always been the best of me”

Matt Smith, Doctor Who

To my family and friends, especially Ellen Cliff, Jeremy Nugent, Ellyn Bicknell, Shevaun Ey, Gabriella Leilani Gross, Emily McElligott, Emma Morgan, Kia George and Christen Whisson you are the best of me. Thank you for all of your support over the past 3.5 years, I love you all.

Last and most importantly I’d like to thank my parents, Mum and Dad, Fran and Dave aka Team Sowden. I will never be able to thank you enough for everything you have done and continue to do for me. I love you both more than words. This one’s for you.
Publications and Presentations

This thesis is submitted in publication format.

The following list details the publications and presentations that have resulted from the author’s research during her candidature for the Degree of Doctor of Philosophy:

Publications:


Submitted Publications:


Drafted Publications:


Poster Presentations:

M. J. Sowden and M. S. Sherburn, “2,3-Dialkynyl-1,3-butadienes”, Organic18 Conference, University of Western Australia, Perth, Australia, 2nd-6th December 2018.


*Poster Prize winner.*
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M  molar
M+ molecular ion
Me methyl
min minute
MHz megahertz
mol mole
mp melting point
MS mass spectroscopy
m/z mass to charge ratio
ν absorption maxima (IR)
n-BuLi n-butyl lithium
NMR nuclear magnetic resonance
nOe nuclear Overhauser effect
NOESY nuclear Overhauser and exchange spectroscopy
Ph phenyl
ppm parts per million
q quartet
rt room temperature
sat. saturated
SM starting material
t time
t-Bu tert-butyl
TBS tert-butyldimethylsilyl
temp temperature
THF tetrahydrofuran
TIPS triisopropylsilyl
TLC thin layer chromatography
p-TsOH para-toluenesulfonic acid
In the modern era of organic chemistry, short total syntheses that produce synthetically useful quantities of difficult to access natural products are championed. Natural product total synthesis is strongly supported through: (a) the development of new synthetic methodologies; (b) the exploration of novel chemical structures; and (c) investigation of compound reactivity. This thesis, submitted in publication format, describes the importance associated with the development of practical, short and scalable syntheses of natural products and target molecules. Described herein is the shortest total synthesis of natural product selaginulvin D, the first general synthesis of 2,3-diethynyl-1,3-butadienes, the first synthesis of a family of five novel TEE (tetraethynylethylene)/TVE (tetravinylethylene) hybrids and the first synthesis of a family of dendra-allenes. The importance of development of new synthetic methodology and the ability to access and explore the reactivity associated with fundamental hydrocarbons will be highlighted throughout.

Chapter two describes our four-step total synthesis of the natural product selaginulvin D. Selaginulvin D is isolated from Selaginella pulvinata and is a potent phosphodiesterase-4 inhibitor. Unfortunately, only 8.2 mg of this natural product was isolated from 1 kg of dried plant material. To date our synthesis has furnished >950 mg of this natural product in only 4 steps overall employing a one-pot, 3-fold electrophilic aromatic substitution as the key step. All previous and subsequent syntheses of this natural product are over 9 steps in length, with two of the approaches utilizing an intramolecular dehydro Diels-Alder reaction as the key step.

Chapter three explores the first general method for the synthesis of substituted 2,3-diethynyl-1,3-butadienes. Only five 2,3-diethynyl-1,3-butadienes have previously been reported from 4 separate publications. This chapter describes a versatile method to generate 2,3-diethynyl-1,3-butadienes with all possible substitution patterns. The influence of substitution upon the stability of these compounds is explored. The value of these compounds is also proven in their use in the synthesis of cyclo-octadienes and expanded radialenes and dendralenes.
Chapter four outlines the first synthesis of five novel TEE (tetraethynylethylene)/TVE (tetravinylethylene) hybrids. TVE and TEE have been synthesised previously and have been reported to have vastly different reactivity profiles. TVE is an air/room temperature stable oil while TEE is an unstable crystalline solid at room temperature. The synthesis of the five hybrid compounds was achieved through the use of Sonogashira and Negishi cross-couplings with appropriately functionalised dibromo-olefins. With the hybrids in hand an investigation into the stability and reactivity of these substrates was undertaken. Finally, a more stable series of phenyl substituted compounds was generated to showcase the versatility associated with the designed synthetic routes.

Chapter five summarises the synthesis of a family of dendra-allenes. Nine allenic dendralenes were prepared through the use of either Negishi or Kumada cross coupling reactions with a propargylic carbonate to incorporate the allene. Only one allene is present in each dendra-allene synthesised. With a family of dendra-allene in hand the reactivity trends and stabilities associated with these compounds were explored for the first time.
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Introduction
1 Introduction

1.0 General Introduction

Within organic chemistry, short total syntheses that produce synthetically useful quantities of difficult to access natural products and target molecules are championed. Natural product total synthesis is strongly supported through: (a) the development of new synthetic strategies, tactics and methodologies; (b) the chemical synthesis of fundamentally new chemical structures; and (c) investigations into the reactivities and properties of new chemical structures. Paul Wender described the ideal synthesis as one that can access a high complexity product in a single step from commodity chemicals (Scheme 1). While no ideal synthesis currently exists, the philosophy behind this aspirational goal drives many current research programs, including the research presented in this Thesis.

![Scheme 1: The ideal synthesis](image)

The work presented in this thesis describes short, scalable and efficient syntheses of natural products and unprecedented (or poorly studied) hydrocarbon molecules. Overall, the work aims to move towards the ideal synthesis of selected organic molecules. This introduction is divided into four sections. Each section provides relevant background information for each of the subsequent chapters of the thesis. The first of these sections (Section 1.1) is a review of published work pertaining to the total synthesis of selaginulpavin natural products. This review serves as background for the original research work described in Chapter 2, which discloses the shortest total synthesis of the natural product selaginulpavin D.

A summary of published work on 2,3-diethynyl-1,3-butadienes is provided in Section 1.2. This section is a literature review for the original research described in Chapter 3, which describes a new, efficient method for the synthesis of 2,3-diethynyl-1,3-butadienes. This Chapter also describes the first examples of their use in the synthesis of unprecedented carbon-rich macrocycles.
The third section (Section 1.3) describes previously published work on tetraethynylethylene (TEE) and tetravinylethylene (TVE) and chemical substances with hybrid structures and substituted derivatives. This section serves as a literature review of the relevant prior work pertaining to the original research described in Chapter 4, which describes the first chemical synthesis of five unprecedented fundamental hydrocarbons, namely $C_{10}$ TEE-TVE hybrid structures.

The last section of this introduction (Section 1.4) is a literature review of published work on dendralenes and related, allene-containing structures. This section brings together the relevant literature for Chapter 5, which describes original research focusing on the preparation of a new family of fundamental hydrocarbons, the dendra-allenes, and exploratory studies into their properties and reactivities.

1.1 Introduction to Selaginulpingvlin D

Chapter 2 details the shortest reported total synthesis of the natural product selaginulpingvlin D. The selaginulpingvlin family is a group of 1-arylethynyl-9,9-diarylfuorene 1 natural products that are likely responsible for the anti-inflammatory properties of Selaginella pulvinate maxim. (Selaginellaceae), a plant used widely in traditional Chinese medicine (Figure 1). To date, over 20 members of the selaginulpingvlin family have been isolated. Members of the selaginulpingvlin family differ in substitution at the position $\alpha$- to the alkyne moiety on the fluorene core (i.e. the $R$ group in Figure 1).

![Selaginella pulvinate maxim.](image)

**Figure 1:** Selaginella pulvinate maxim. and the general structure of members of the selaginulpingvlin family of natural products
Selaginpulvin D 17 (Scheme 2) is the simplest member of the family, having no substituent at this site (i.e. Figure 1, 1, \( R = H \)). It has been found to be a potent phosphodiesterase-4 inhibitor. Only limited quantities of selaginpulvin D are isolable from the natural source, with one kilogram of dried whole plant material furnishing only 8.2 mg of natural product. In order to access meaningful quantities of this compound, one must turn to total synthesis.

The first total synthesis of selaginpulvin D was reported by Karmakar and Lee in 2017. This elegant 11 step total synthesis (Scheme 2) showcases a reductive intramolecular hexahydro Diels–Alder reaction to assemble the fluorenone core of the natural product. Karmakar and Lee require 8 steps to access their key intermediate 13, which can then undergo the aforementioned Diels-Alder reaction. A further 3 steps are then required to elaborate this compound into the natural product, producing only 4.2 mg at 4% overall yield for their 11 step synthesis.

Scheme 2: Karmarkar and Lee’s 11 step total synthesis of selaginpulvin D
In 2017, we reported a 4 step total synthesis of selaginpulvin D 17 (Scheme 3). A Suzuki-Miyuara cross-coupling between commercially-available carboxylic acid 18 and boronic acid 19 gave biaryl compound 20. Upon warming biaryl 20 in methanesulfonic acid, an intramolecular SeAr reaction gave the fluorenone, which could then be converted in situ into 1-bromo-9,9-diarylfluorene 22 by adding anisole 21 to the reaction mixture. As such, we were able to generate 3 new carbon-carbon bonds, required for the natural product target structure, in one synthetic step. A challenging Sonogashira cross-coupling between 1-bromo-9,9-diarylfluorene 22 and 4-ethynylanisole 5 was achieved through the use of Buchwald cross-coupling conditions to give the protected natural product 23. Finally, the unconventional use of neat methylmagnesium iodide at elevated temperatures resulted in the formation of selaginpulvilin D 17 in 4 steps and 17% overall yield. To date, over 950 mg of selaginpulvin D 17 has been synthesised via our four-step route.

Scheme 3: Our 2017, 4 step total synthesis of selaginpulvin D

A further two total syntheses of selaginpulvin D 17 have appeared since the publication of our work, with both of these approaches over 9 steps in length (Scheme 4). Thus, later in 2017, Chinta and Baire employed a similar approach to Karmakar and Lee in their formal 9 step synthesis of selaginpulvin D 17 using an enyne-alkyne dehydro-Diels-Alder reaction as the key step (27 → 28). This synthesis yielded 34 mg of the natural product with a 7.5% overall yield. Shortly thereafter, Yin and co-workers published a 13 step synthesis of selaginpulvin D 17 utilising aspects of both our synthesis and Karmakar
and Lee’s approach, to first generate selaginvin C $31$, which was then elaborated into selaginvin D $17$. The work of Yin and co-workers demonstrated that other members of the selaginvin family can be accessed from selaginvin C $31$, and suggested that this is likely what happens in nature. Yin and co-workers were only able to prepare 20 mg of the natural product in a 3% overall yield.\(^3\)

![Scheme 4]

**Scheme 4:** A further two syntheses of selaginvin D$^{3,6}$

Our four-step total synthesis of selaginvin D $17$ is not only the shortest total synthesis of this natural product to date but also the highest overall yielding, also furnishing the largest amount of material. Our synthesis highlights the power of step economy in efficient synthesis, the power of retrosynthetic analysis, and the improvements in step economy gained from the judicious application of multi-bond forming processes.\(^7\) This theme of efficiency and rapid construction of molecular frameworks is carried into the subsequent three chapters of work in this thesis, which focus on structurally distinct groups of fundamental hydrocarbon targets.

### 1.2 **Introduction to 2,3-Diethynyl-1,3-Butadienes**

The remainder of this thesis focuses on the efficient synthesis of $\pi$-bond rich acyclic branched hydrocarbons comprised exclusively of $sp^2$- and $sp$-carbons. There is a widespread misconception that compounds of this type are both difficult to handle and challenging to synthesise. Through the synthesis of such compounds, our group works to
dispel such notions. With the emergence of each new hydrocarbon family, our knowledge and understanding of hydrocarbons expands. These studies help to redefine what can be made, and identify new possibilities for efficient chemical synthesis generally, through the use of these novel hydrocarbons in multi-bond forming processes.

2,3-Diethynyl-1,3-butadiene 32 is a structure comprising only four $sp^2$-carbons and four $sp$-carbons. Little is known about this compound or its substituted analogues, since no general method for the synthesis of substituted 2,3-dialkynyl-1,3-butadienes has been reported. The parent 2,3-dialkynyl-1,3-butadiene 32 can be thought of as a dehydroversion of [4]dendralene 33. As was the case with [4]dendralene 33, predictions/descriptions of 2,3-diethynyl-1,3-butadienes in the literature are of reactive/unstable/unmanageable compounds (Figure 2).8 We have since shown that [4]dendralene is a bench-stable substance that is no less prone to polymerisation than isoprene (which is sold commercially on industrial scale as a neat liquid).28 We strongly suspected that 2,3-diethynyl-1,3-butadiene and its substituted analogues would be similarly manageable. We therefore sought to dispel notions of difficulties associated with 2,3-diethynyl-1,3-butadienes by developing the first simple, general method for their synthesis, and also demonstrate that they are synthetically useful building blocks.

Figure 2: 2,3-Diethynyl-1,3-butadiene 32, [4]dendralene 33, and published statements regarding the assumed instability/reactivity of these compounds.

Five substituted 2,3-diethynyl-1,3-butadienes have been described in the literature (Figure 3): one each from the groups of Larock, Gleiter, and Grigg, and two from Hopf.9,10,11,12 The first synthesis of a 2,3-dialkynyl-1,3-butadiene was reported by Larock in 1975,9 who oxidatively homocoupled an alkenyl mercury compound 34 to generate tetramethylated analogue 35.9 Almost 20 years later, Gleiter and co-workers employed a two-fold nucleophilic substitution reaction on a propargylic dichloride 36 to afford hexa-
substituted 2,3-dialkynyl-1,3-butadiene 38. In 1996, Hopf and co-workers synthesised two substituted 2,3-dialkynyl-1,3-butadienes, 41, through a twofold Negishi cross-coupling reaction with 2,3-dichlorobutadiene 39. Finally, in 1999, Grigg and co-workers utilised a twofold Stille cross-coupling between a propargylic di-carbonate 42 and an alkynyl stannane 43 to afford tetra-substituted 2,3-dialkynyl-1,3-butadiene 44.

**Scheme 5:** Previously synthesised 2,3-diethynyl-1,3-butadienes\(^9,10,11,12\)

Hopf and co-workers’ synthesis of 2,3-diethynyl-1,3-butadienes 41 was the closest to a general approach for substituted 2,3-diethynyl-1,3-butadiene synthesis.\(^11\) The use of unstable 2,3-dichlorobutadiene 39, along with the inability to synthesise/purchase substituted 2,3-dichlorobutadienes limits the number of substituted variants that can be made using this strategy (Scheme 5). However, through a series of two allylic-type transpositions, 2,3-dichlorobutadiene 39 can be – on paper – translated into 1,4-dichlorobut-2-yne 47, which we proposed would react in the same way but would not be prone to polymerization. As a replacement for substituted 1,4-dichlorobut-2-ynes, which in general lack good synthetic procedures, we turned to substituted bis-carbonates 52, which can be synthesised from commodity chemicals in short order.\(^13\)
Scheme 6: Origins of our synthetic strategy to access 2,3-diethynyl-1,3-butadienes.

These easily synthesised bis-carbonates 52 could then be employed in two-fold Sonogashira cross-coupling reactions with functionalised terminal alkynes, to generate a library of highly functionalised 2,3-diethynyl-1,3-butadienes 54 for the first time (Scheme 6). As described in Chapter 3, using this approach we were able to synthesise over 25 symmetric and unsymmetrically-substituted 2,3-diethynyl-1,3-butadienes 54. This synthesis is tolerant of an array of substitution types and patterns.

Scheme 7: Synthetic method to generate 2,3-diethynyl-1,3-butadienes

With a library of 2,3-diethynyl-1,3-butadienes 54 in hand, investigations into the stability and reactivity of these compounds commenced. Hopf and co-workers had previously reported Diels-Alder reactions of their compounds with dienophiles to prepare cyclic Z-enediynes, and the formation of 1,4-cyclooctadienes through thermal [4+4]cycloaddition-dimerisation.11 We were able to expand upon the findings and investigations of Hopf and co-workers, establishing the first half-lives of a large number of substrates and identifying the effects of different substituents on the stability of these compounds. As predicted, in the majority of cases, these substances are easily handled and stored. Furthermore, the value of 2,3-diethynyl-1,3-butadienes as building blocks for the preparation of unprecedented carbon-rich materials was showcased, through their use in the synthesis of expanded radialenes 56 and 57 (Scheme 7) and expanded dendralenes.
1.3 Introduction to TEE/TVE Hybrids

Chapter 4 continues the theme of unsaturated acyclic hydrocarbon chemistry but with a group of molecules that are structurally distinct to the 2,3-diethynyl-1,3-butadienes from Chapter 4. In this Chapter, we focus on five unprecedented structures that can be thought of as hybrids of tetraethynylethylene (TEE) 63 and tetravinylethylene (TVE) 67.

Tetraethynylethylene (TEE) 63 and tetravinylethylene (TVE) 67 are amongst the smallest compounds that contain both through-conjugated and cross-conjugated segments. The Diederich group disclosed the first synthesis of TEE in 1991 via a 5 step route (Scheme 8).

**Scheme 8:** Use of tetramethyl 2,3-diethynyl-1,3-butadiene 55 in the synthesis of expanded radialenes 56 and 57.

A two-fold nucleophilic addition of lithiated TMS acetylene 2 to ethyl acetate 58 yielded secondary alcohol 59, which was oxidised to ketone 60. A Ramirez dibromo-olefination
yielded dibromo-olefin 61, which underwent a two-fold Sonogashira cross-coupling with TMS acetylene 2 followed by global deprotection to generate TEE 63 as an unstable crystalline solid. More recently Low and co-workers disclosed a single step synthesis of TMS protected TEE via a fourfold Sonogashira cross-coupling between tetrachloroethene and TMS acetylene.32

**Scheme 10:** Low and co-workers’ synthesis of protected TEE.32

TVE 67 was first synthesised in the 1960s by Skattebøl and co-workers in four steps from 1,5-cyclo-octadiene 65, and more recently by Sherburn and co-workers in a single step from tetrachloroethylene 68 on multigram scale (Scheme 9).15,16 In contrast to TEE, TVE was found to be a bench stable oil.16

**Scheme 11:** Reported syntheses of TVE14,15

The significant difference in both physical and chemical properties between TEE and TVE, and the value of both compounds as building blocks in carbon-rich materials and chemical synthesis, respectively, prompted us to design and synthesise a series of five TEE/TVE hybrid compounds. The goals of this work were to explore the disparity in stability between TVE and TEE, and provide compounds that might be useful in both materials and molecular synthesis. The five hybrid compounds targeted (Figure 4) were triethynylvinylethylene (TEVE) 74; Z-divinylidiethynylethylene (Z-DVDEE) 71, E-divinylidiethynylethylene (E-DVDEE) 71, gem-divinylidiethynylethylene (gem-DVDEE) 71 and trvinylethynylethylene (TVEE) 70.
None of these five C\textsubscript{10} compounds have been previously reported. Nonetheless, syntheses of substituted analogues of four of the five compounds have been previously reported, and these will be discussed here in turn.

Two substituted examples containing the TVEE core are present in the literature (Scheme 11). The first, pentasubstituted TVEE 80 was reported by Diederich and co-workers\textsuperscript{17}. Propargyl alchol 75 was oxidised to the corresponding aldehyde using PCC with this compound then undergoing dibromo-olefination to give dibromo-ene 76. A two-fold Sonogashira cross-coupling gave triyne 78. Nucleophilic addition of deprotonated triyne 78 to DMF yielded aldehyde 79 which was elaborated into substituted TVEE 80 through condensation with malononitrile. The second example was prepared by Barluenga and co-workers in 3 steps and contained both aryl and alkyl substituents 70.\textsuperscript{18} Barluenga and co-workers synthesised TVEE 85 through demetallation-dimerisation of metal carbenoid 81.

**Figure 3:** Five TEE/TVE hybrid structures
A total of eleven examples substituted E-DVDEE compounds have been previously reported in three publications (Scheme 12). Diedrich and co-workers synthesised three examples of E-DVDEE sub-type 90, containing two 1,1-dibromo-olefins as the alkene components of the compound, in 4 steps from commercial precursors. Diedrich and co-workers commenced their synthesis from diester 86 and employed a two-fold Stille cross-coupling to generate diester 88. Treatment of this ester with DIBAL followed by oxidation with PCC gave dialdehyde 89 which underwent a two-fold dibromo-olefination to give substituted DVDEE 90. Yamamoto and co-workers were able to prepare seven examples of tetra-substituted E-DVDEE 92 with a range of substituents on the termini of the alkenes and alkynes, in only 2-3 steps. This was achieved through the use of a Pd(0)-catalysed dimerization of functionalised propargylic dialkynes 91. Finally, Andersson and co-workers generated an interesting *bis*-1,3-dithiole-4,5-dicarboxylate-substituted *E*-diethynyldivinyl ethylene 95 in 3 steps utilising a highly similar approach to that of Diedrich and co-workers. It is worthy of note that only symmetrically-
substituted systems (i.e. the same groups being present on each of the two alkyne termini, likewise for the two alkenes) have been reported in the literature.

**Scheme 12:** Previously synthesised substituted $E$-diethynyldivinyl ethylenes$^{19, 20, 21}$

Only two examples each of substituted $Z$-divinyldiethynyl ethylenes and $gem$-divinyldiethynyl ethylenes (cf. Figure 4) have been previously reported, as shown in **Scheme 13**. Diedrich and co-workers generated two $Z$-divinyldiethynyl ethylene compounds 104, containing two dibromo-olefins, in 7 steps, using chemistry that is similar to that described above.$^{22}$ Hopf and co-workers made two examples of $gem$-divinyldiethynyl ethylenes 110 in 4 steps starting from 3-buten-2-one 105 and utilising a dibromo-olefination followed by Sonogashira cross-coupling as the key step.$^{23}$
Introduction

Scheme 13: Previously synthesised substituted Z-divinyl diethynyl ethylenes and gem-divinyl diethynyl ethylenes

It is worthy of note that Hopf and co-workers’ examples of gem-divinyl diethynyl ethylenes 110 are cyclohexa-1,4-dienes. Thus, no acyclic gem-DVDEEs have been reported.

It is no coincidence that most of the published examples of substituted TEE-TVE hybrids from the Diederich group contain 1,1-dibromoalkenes. These compounds were prepared as intermediates in Corey-Fuchs reactions: Diederich was aiming to prepare substituted TEE derivatives, and the hybrid compounds were prepared as a means to this end, hence were not studied further.

While substituted examples of Z-DVDEEs, E-DVDEEs, gem-DVDEEs and TVEEs are present in the literature, there are no substituted examples of TEVEs. Furthermore, no syntheses of the unsubstituted parent hybrid compounds 70-74 (Figure 3) have been reported. As such, we developed new synthetic methods and strategies to access both the unsubstituted parent compounds and their substituted analogues. In Chapter 4, a submitted manuscript shows that we were able to synthesise all five hybrid TEE-TVE compounds through the use of cross-couplings of appropriately functionalised dibromoolefins. The two most challenging compounds to synthesise were the Z- and E-DVDEEs.
71 and 72. Recent work published by Sherburn and co-workers provided the most insight in how best to proceed with the synthesis of these two compounds Scheme 14. Sherburn and co-workers synthesised a range of dibromo-olefins from aldehydes 111 and were able to perform $E$-selective mono Negishi cross-coupling reactions on these to generate substituted mono-bromides 113 which could then undergo either stereoinvertive or stereoretentive cross-couplings to give substituted [3]dendralenes 115 or 116.

**Scheme 14:** Previous work with dibromo-olefins by Sherburn and co-workers

While there was literature precedent for stepwise regio- and stereoselective cross-couplings on dibromo-olefins derived from aldehydes, it was not known if this would work on a system like ours, derived from a ketone (Scheme 15).

**Scheme 15:** Syntheses of $Z$- and $E$-DVDEEs mandated the development of unprecedented cross-couplings

As described in detail in Chapter 4, dibromo-olefin 118 underwent a $Z$-selective Negishi cross-coupling to give bromo-triene 119, which could then be elaborated into either the $Z$ or $E$ DVDEE stereoisomers through either stereo-retentive or stereo-invertive cross-couplings (Scheme 16).
The short syntheses of the five hybrid compounds provided access to sufficient quantities of material for further investigations. A series of standardised stability tests involving the exposure of these substrates to acid, air and heat were developed and conducted. In general, these compounds were found to be sufficiently stable to be manipulated using standard laboratory methods.

In order to prove the generality of our new synthetic pathways, a series of tetrphenyl substituted hybrid compounds (Figure 4) were prepared using the same approaches. These compounds were found to be significantly more stable than the parent compounds.

In summary, Chapter 4 provides a blueprint for the synthesis of all five TEE-TVE hybrid structures, and shows that these previously inaccessible compounds are sufficiently stable to be handled in the laboratory. This work paves the way for further developments by the synthetic and materials chemistry communities.

In the last section of this Introduction, we move on to a third sub-class of acyclic, \( \pi \)-bond-rich hydrocarbons, namely the dendra-allenes. Consistent with the work described in Chapters 3 and 4, we focused on developing an efficient and general approach to the synthesis of this unprecedented family of target molecules.
1.4 Introduction to Dendra-Allenes

The dendralenes are a family of acyclic branched hydrocarbon structures comprising exclusively \( sp^2 \)-carbons. Until the year 2000, only [3] and [4]dendralenes were known.\(^{24,25}\) Recently, Sherburn and co-workers have developed practical syntheses for all members of the dendralene family up to [12]dendralene (Figure 5).\(^{26}\) Sherburn and co-workers utilise a ‘lynch-pin’ type approach to the synthesis of the dendralenes which involves the use of two-fold cross-couplings as the key step (Scheme 17). For example, [5]dendralene \(^{127}\) is synthesised via a two-fold Kumada cross-coupling between 1,1-dichloroethylene \(^{126}\) and chloroprene Grignard reagent \(^{125}\).\(^{26}\)

![Scheme 17: [5]Dendralene synthesis](image)

Investigations into the behaviours of the dendralenes unearthed some interesting trends. Sherburn and co-workers observed experimentally that a dendralene with odd numbers of C=C units (red, Figure 5) is less stable than those with even numbers of C=C units (black, Figure 5). Similar alternating behaviour was observed in both the spectroscopic data and chemical reactivity of the compounds.\(^{26}\)

![Figure 5: The [n]dendralenes](image)

The successful syntheses of [3]dendralene through [12]dendralene has opened up previously inaccessible structural possibilities for synthesis. Many variations can be imagined. In this project, attention is focussed on maximising unsaturation in acyclic \( \pi \)-
bond-rich hydrocarbons, which should allow, through multiple addition reactions, even more \( \sigma \)-bond-based structural complexity.

Hopf and co-workers proposed the replacement of one or more C=C unit(s) in [3]dendralene with allenic motifs to generate “dendra-allenes” (Scheme 18).\textsuperscript{27} The Hopf group reported syntheses of the first dendra-allenes, where only one alkene is replaced by an allene, specifically [3]dendra-1-allene \textsuperscript{140} and methyl substituted [3]dendra-2-allene \textsuperscript{137}.\textsuperscript{27} The synthesis of [3]dendra-1-allene was achieved through the use of a copper mediated nucleophilic substitution reaction between phosphate \textsuperscript{138} and allenyl Grignard reagent \textsuperscript{139} as the key step. The synthesis of methyl substituted [3]dendra-2-allene \textsuperscript{137} was also achieved through the use of a nucleophilic substitution reaction as the key step. Shortly after this report, Sherburn and co-workers disclosed the synthesis of unsubstituted [3]dendra-2-allene \textsuperscript{142}, a compound that is more commonly referred to as 1,1-divinylallene.\textsuperscript{28} Sherburn and co-workers utilised a Grieco-Sharpless elimination reaction involving oxidation of organo selenium compound \textsuperscript{141} with m-CPBA, as the key step to give [3]dendra-2-allene \textsuperscript{142}.

The value of allenic dendralenes in total synthesis was subsequently demonstrated, through the use of a chiral, substituted [3]dendra-2-allene \textsuperscript{152} (1,1-divinylallene) in the shortest total synthesis of pseudopterosin G-J aglycone \textsuperscript{164} (Scheme 13).\textsuperscript{29} This chiral substituted [3]dendra-2-allene \textsuperscript{152} could be synthesised via two different routes. An enantioselective synthesis commences with aldehyde \textsuperscript{143}, which was converted in alkyne
in situ, which was deprotonated and reacted with a Weinreb amide to generate ketone in a single step. This ketone was then reduced enantioselectively to secondary alcohol, which was converted into the corresponding mesylate. A Kumada cross-coupling reaction between mesylate and functionalised alkenyl Grignard reagent yielded chiral substituted [3]dendra-2-allene. Secondary alcohol could also be synthesised via a chiral pool based approach in a single step from commercially available (S)-but-3-yn-2-ol. Substituted [3]dendra-2-allene was then utilised in a series of three diene-transmissive Diels-Alder reactions to generate pseudopterosin (-)-G-J glycone in a further 8 steps.


With the importance of allenic dendralenes in total synthesis already proven, it is perhaps surprising that there have been no other reported investigations into the synthesis of higher order members of the family. On the other hand, this fact is most likely due to the
aforementioned (false) assumption that polyenic compounds like these are likely to be unmanageable compounds, being prone to decomposition through several mechanistically distinct (pericyclic, radical, ionic) pathways.

Chapter 5 describes the results of ongoing investigations that aim to synthesise all possible isomers of the [4]allenic dendralenes, the [5]allenic dendralenes, and the [6]allenic dendralenes, along with some representative higher order compounds (Figure 6).

![Figure 6: Family of dendra-allenes](image)

Access to these compounds would allow us to answer the following three questions: (1) Are allenic dendralenes generally more or less stable than their dendralene counterparts? (2) Will we see an alternation in reactivity within this family of compounds as we do the dendralenes (odd members more reactive/unstable than even members)? (3) Does the position of the allene in the dendra-allene structure have a significant effect upon the behaviour of the compounds?

When planning our synthetic strategy, we decided to utilise propargylic carbonates (Figure 7) in either Kumada or Negishi cross-coupling reactions. This is a similar approach to that utilised to make the substituted dendra-allene 152 used in the total synthesis of pseudopterosin (-)-G-J glycone 164, however instead of utilising a mesylate as the leaving group we used a carbonate. These appropriately functionalised carbonates undergo cross-couplings under either Negishi or Kumada conditions to give different dendra-allenes (Figure 7). As described in detail in Chapter 5, this approach has allowed
access to nine allenic dendralenes. The synthesis of the appropriately functionalised carbonates, while challenging, proved crucial to the success of the project.

**Figure 7:** Family of propargylic carbonates used to prepare dendra-allenes

The synthetic work described throughout this Thesis focuses on the development of efficient syntheses of both natural products and target molecules. Furthermore, this work aims to provide new insights into the reactivity of previously unexplored structural space and demonstrate the power of efficiency and strategy in synthesis.
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Chapter Two:

Four-Step Total Synthesis of Selaginpulvilin D
2 Four-Step Total Synthesis of Selaginpulvin D

Prelude

The manuscript was published in Organic Letters on 17 January, 2017. Reprinted (adapted) with permission (Sowden, M. J.; Sherburn, M. S. Org. Lett. 2017, 19, 636). Copyright (2017) American Chemical Society. The other author is my supervisor Professor Michael S. Sherburn. As of 29 July 2019, the paper has been cited 9 times including been highlighted in an “Editorial” in the Journal of American Chemical Society (by Baran, P. S. “Natural Product Total Synthesis: As Exciting as Ever” J. Am. Chem. Soc. 2018. 140. 4751). The project was conceived, designed, evolved and drafted in collaboration with Professor Michael S. Sherburn. The synthetic experiments were carried out by myself.

Selaginpulvin D is a potent phosphodiesterase-4 inhibitory natural product, isolated from Selaginella pulvinata, with only 8.2 mg isolated from 1 kg of dried plant material (Liu, X.; Luo, H.; Huang, Y.; Bao, J.; Tang, G.; Chen, Y.; Wang, J.; Yin, S. Org. Lett. 2014, 16, 282-285). This chapter describes our published four-step total synthesis of the natural product selaginpulvin D. Our approach more than halves the previous step count and allows access to useful quantities of material for the first time. Our synthesis features a one-pot, 3-fold electrophilic aromatic substitution as the key step allowing us to rapidly access the core of the molecule. See Chapter 1 for an analysis of this synthesis.

Karmaker and Lee previously published an eleven step total synthesis of this natural product utilising an intramolecular hexadehydro Diels-Alder reaction as their key step, furnishing 4.2 mg of the natural product (Lee, D.; Karmakar, R. Org. Lett., 2016, 18, 6105-6107). See Chapter 1 for an analysis of this synthesis.
Two syntheses of selaginulvin D have been published since our publication with both of these syntheses been over 9 steps in length (J. S. Zhang, X. Liu, J. Weng, Y. Q. Guo, Q. J. Li, A. Ahmed, G.-H. Tang and S. Yin, *Org. Chem. Front.*, 2017, 16, 283). B. Chinta and B. Baire (*Org. Biomol. Chem.*, 2017, 15, 5908). See **Chapter 1** for an analysis of these syntheses. Our four-step total synthesis of selaginulvin D remains to date the shortest synthesis of this natural product and is unlikely to be surpassed in the foreseeable future.

Through the use of cross-coupling chemistry and novel multi-C-C bond forming event (one-pot, 3-fold electrophilic aromatic substitution) we were able to efficiently synthesise Selaginulvin D in synthetically useful quantities for the first time. Our versatile synthesis could also be amenable to the generation of substituted analogues in short order.
Four-Step Total Synthesis of Selaginulpilin D

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Supporting Information

ABSTRACT: An extremely concise total synthesis of a potent phosphodiesterase-4 inhibitory natural product, selaginulpilin D, is reported. The synthesis features a one-pot, 3-fold electrophilic aromatic substitution sequence to assemble a 9,9-diafluorocore. The approach allows access to useful quantities of a selaginulpilin natural product for the first time.

The selaginulpilin family is a small group of 1-arylthyl-9,9-diafluorocore natural products that are likely responsible for the anti-inflammatory properties of Selaginella paoniana (Hook. et Grev.) Maxim. (Selaginellaceae), a plant used widely in traditional Chinese medicine. One kilogram of dried whole plant material furnished 8.2 mg of selaginulpilin D (1). Karmakar and Lee very recently reported an elegant, 11-step total synthesis of 1 (summarized in Scheme 1), detailed in their supporting information.

Scheme 1. Summary of Karmakar and Lee’s 11-Step Total Synthesis of Selaginulpilin D (1)\(^\text{1,2}^\)

Our synthesis (Scheme 2) commences with a Suzuki–Miyaura coupling of 4-methoxysulfonphenylboronic acid 2 with 2-bromom-6-iodobenzoic acid 3 in an aqueous medium\(^1\) to generate disubstituted 2-phenylbenzoic acid 4. A selective single cross-coupling necessitated the use of the bromomiodozone, since the corresponding disubstituted underwent selective 2-fold couplings.

Received: December 20, 2016
Published: January 17, 2017
On warming in methanesulfonic acid, intramolecular $S_N2$ reaction gave the fluorenone, which could be isolated (see the SI) but was, more conveniently, converted in situ into the 1- bromo-9,9-diarylfluorene 5 simply by addition of anisole. Intramolecular $S_N2$ reaction of 2-arylcinnamic acids to fluorenes are well established, as are 2-fold intramolecular $S_N2$ sequences to convert fluorenes into 9,9-diarylfluor- enes. Nonetheless, the telescoping of these two classical transformations into a one-flask operation is unprecedented. The third step of the synthesis was a challenging Sonogashira coupling to install the 1-ethylthioyl fragment through reaction of stercally encumbered bromide 5 with 4-(methylsulfanyl)- acrylonitrile. Only Buchwald’s second-generation XPhos pre- catalyst 13155 was fruitful, and even then only with a high concentration of the terminal alkyne cross-coupling partner. At lower concentrations, the desired Sonogashira coupling product 6 was generated as a mixture with intramolecular Mizoroki–Heck15 product 7; in the absence of alkyne coupling partner, fused pentacycle 7 was formed exclusively. The natural product 1 was accessed by 4-fold demethylation of the Sonogashira coupling product 6 by heating with neat methylmagnesium iodide at 100 °C. More conventional protocols [BiBr3, RSH/AICl3] gave mixtures of products resulting from additions to the alkyne.

In summary, an uncommonly short total synthesis of the natural product selaginpubin D has been completed. In comparison with the recently reported approach, the present synthesis boasts a dramatic reduction in step count, a significant increase in overall percent yield (6.4% to 17%) and access to a much larger amount of the natural product. The provision of useful quantities of selaginpubin D through chemical synthesis prevents the need for large-scale harvesting of $S$. pulvinata (some 117 kg of dry plant would be needed to produce the same amount of material prepared so far). This synthetic route should be amenable not only to much larger quantities of the natural product but also to the preparation of the remaining members of the selaginpubin family, along with many analogues and derivatives.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free on the ACS Publications website at DOI: 10.1021/acs.orglet.6b03793.

Experimental procedures, product characterizations, $^1H$ and $^{13}C$ and NMR spectra of new compounds, spectroscopic comparisons of the isolated and synthesised natural product, and a detailed synthetic scheme for the previously published total synthesis (PDF)

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Notes

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

This work was supported by the Australian Research Council.
Supporting information

For

Four Step Total Synthesis of Selaginpulvilin D

Madison J. Sowden and Michael S. Sherburn*
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Karmaker and Lee’s total synthesis of selaginulpin D:

![Synthesis Scheme](image)

Selaginulpin D

4.2 mg synthesized
General Methods

NMR Spectroscopy

$^1$H NMR spectra were recorded at 800, 500, 400 or 300 MHz using a Bruker AVANCE 400, AVANCE 800, Varian 400-MR or Mercury 500 MHz spectrometer, as indicated. Residual solvent peaks were used as an internal reference for $^1$H NMR spectra (CDCl$_3$ $\delta$ 7.26 ppm or CD$_2$OD $\delta$ 3.31 ppm). Coupling constants ($J$) are quoted to the nearest 0.5 Hz. The assignment of proton signals was assisted by COSY, HSQC and HMBC experiments. $^{13}$C NMR spectra were recorded at 100 MHz using a Bruker AVANCE 400 or Varian 400-MR spectrometer. Solvent peaks were used as an internal reference for $^{13}$C NMR spectra (CDCl$_3$ $\delta$ 77.0 ppm or CD$_2$OD $\delta$ 49.1 ppm). Assignment of carbon signals was assisted by HSQC and HMBC experiments. The following abbreviations (or combinations thereof) were used to denote $^1$H NMR multiplicities: $s$ = singlet, $d$ = doublet, dd = doublet of doublets, t = triplet, m = multiplet

Infrared Spectroscopy

IR spectra were recorded on a Perkin–Elmer UATR Two spectrometer as a thin film or solid.

Mass Spectrometry

Low-resolution EI mass spectra were recorded on a Finnigan Polaris Q ion trap mass spectrometer using electron impact (EI+) ionization mode at 40 or 70 eV. High-resolution EI mass spectra were recorded on a VG Autospec mass spectrometer operating at 70 eV.

Melting Points

Melting points were measured on a Stanford Research Systems Optimelt Automated Melting Point System and are uncorrected.

Ultraviolet-Visible Spectroscopy

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

Experimental Procedures, Reagents, Chromatography and Glassware

Reactions were conducted under a positive pressure of dry nitrogen in heat gun-dried glassware and at room temperature, unless specified otherwise. Anhydrous solvents were either obtained from commercial sources or dried according to the procedure outlined by
Grubbs and co-workers. Commercially available chemicals were used as purchased, or where specified, purified by standard techniques. Analytical thin-layer chromatography was conducted with aluminum-backed silica gel 60 F254 (0.2 mm) plates supplied by Merck, and visualized using UV fluorescence ($\lambda_{\text{max}} = 254$ nm), or developed using KMnO$_4$ or p-anisaldehyde, followed by heating. Flash chromatography employed Merck Kieselgel 60 silica gel (230–400 mesh). Solvent compositions are given in (v/v). PS 40–60 °C refers to petroleum spirits, boiling point fraction 40–60 °C. PS 60–80 °C refers to petroleum spirits, boiling point fraction 60–80 °C
While commercially available, alkyne S3 was synthesized in house in 2 steps starting from 4-iodoanisole according to a modified version of the published procedure.³

**((4-methoxyphenyl)ethynyl)trimethylsilane:**
4-iodoanisole (6.00 g, 25 mmol, 1.0 mol equiv), trimethylsilyl acetylene (3.76 g, 38 mmol, 1.5 mol equiv), bis(triphenylphosphine) palladium(II) dichloride (200 mg, 0.30 mmol, 1.2 mol %) and copper iodide (114 mg, 0.62 mmol 2.5 mol %), were dissolved in triethylamine (90 mL). The solution was stirred at room temperature for 17 hours. 1M aqueous HCl (20 mL) was added to the reaction mixture and extracted with diethyl ether (3 x 20 mL). The organic extracts were combined, washed with brine, dried over MgSO₄, filtered and the solvent removed under reduced pressure. The crude product was then purified by flash column chromatography (20 % diethyl ether in in PS 40–60 °C), to give the title compound as a brown oil (5.20 g, 99%).³

**1-Ethynyl-4-methoxybenzene:**
4-Methoxyphenyl ethynyl trimethylsilane (5.20 g, 25 mmol, 1.0 mol equiv), and potassium carbonate (5.28 g, 38 mmol, 1.5 mol equiv), were dissolved in methanol (47 mL), and dichloromethane (47 mL) and the solution was stirred at room temperature for 13 h. The solution was run through a pad of silica, eluting with a 1:1 mix of PS 40–60 °C and diethyl ether. The solvent was removed under reduced pressure to give the title compound as a golden brown oil (1.42 g, 84%).³

**3-Bromo-4'methoxy-[1,1'-biphenyl]-2-carboxylic acid**

2-Bromo-6-iodobenzoic acid 3 (3.10 g, 9.5 mmol, 1.0 mol equiv) was dispersed in water (200 mL) and heated to reflux for 1 hour. Pd(OAc)₂ (215 mg, 0.95 mmol, 10 mol %), (4-
methoxyphenyl)boronic acid 2 (2.12 g, 14 mmol, 1.5 mol equiv) and KOH (1.72 g, 31 mmol, 3.0 mol equiv) were added and the reaction mixture was heated under reflux for a further 16 hours. The reaction mixture was cooled to room temperature and acidified to pH 1 with 1M aqueous HCl and extracted with ethyl acetate (3 x 350 mL). The organic extracts were combined, dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude material was dissolved in ethyl acetate (200 mL) and aqueous KOH (10%) was added until a pH of 11 was reached. The aqueous phase was washed twice with ethyl acetate (200 mL), then acidified to pH 1 with 1M aqueous HCl, then extracted with ethyl acetate (3 x 300 mL). The organic extracts were combined, washed with sodium thiosulphate (300 mL), dried over MgSO₄, filtered through a pad of silica and concentrated under reduced pressure, to give the title compound 4 as an off white solid (1.74 g, 60%).

\[ R_f = 0.20 \text{ (20\% ethyl acetate in PS 40–60 °C)} \]

\[ m.p. = 133.7 – 134.8 \text{ °C (recrystallized from dichloromethane)} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 7.53 – 7.48 \text{ (m, 1H), 7.31 -7.23 (m, 4H), 6.87 (d, } J = 8.5 \text{ Hz, 2H), 3.77 (s, 3H) ppm} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 172.7, 159.6, 141.4, 134.3, 131.5, 131.1, 130.7, 129.6, 128.9, 119.2, 114.1, 55.3 \text{ ppm} \]

\[ \text{IR (thin film): } v_{\text{max}} = 3484, 2942, 2836, 1721 \text{ cm}^{-1} \]


\[ \text{HRMS (El): calcd for C}_{14}

\[ \text{H}_{11}\text{O}_{2}{^\text{79}}\text{Br} [M]^{+}: 307.9870; \text{ found: 307.9871;} \text{ calcd for C}_{14}

\[ \text{H}_{11}\text{O}_{2}{^\text{79}}\text{Br [M]^{+}: 305.9892; found 305.9893} \]

1-Bromo-7-methoxy-9,9-bis(4-methoxyphenyl)-9H-fluorene

\[ \begin{align*}
\text{MeO} & \quad \text{COH} \\
\text{Br} & \quad \text{MeO} \\
\text{4} & \quad \text{OMe} \\
\text{MeOH, CH}_2\text{Cl}_2 & \quad \text{MeOH} \\
\text{then add anisole} & \quad \text{then add anisole} \\
60 \text{ °C, 6 h} & \quad 60 \text{ °C, 6 h} \\
then 25 \text{ °C, 12 h} & \quad then 25 \text{ °C, 12 h} \\
65\% & \quad 65\% \\
\end{align*} \]

3-Bromo-4’-methoxy-[1,1’-biphenyl]-2-carboxylic acid 4 (3.30 g, 11 mmol, 1.0 mol equiv) was dissolved in dichloromethane (10 mL) and added to methanesulphonic acid (30 mL) and the solution was heated in an oil bath set to 60 °C (oil bath temperature). After 3 hours anisole (5.9 mL, 55 mmol, 5.0 mol equiv) was added and the reaction mixture was stirred at 60 °C
for a further 3 hours. The reaction mixture was cooled to room temperature and stirred for a further 12 hours before being placed in an ice bath and quenched slowly with water (150 mL) and extracted with dichloromethane (3 x 200 mL). The organic extracts were combined, dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude product was subjected to purification via column chromatography (50% dichloromethane in PS 40–60 °C → 80% dichloromethane in PS 40–60 °C) to give the title compound 5 as a yellow solid (3.4 g, 65%).

\[ R_f = 0.50 \text{ (50% dichloromethane in PS 40–60 °C)} \]
\[ m.p. = 163.5 - 166.0 \text{ °C (recrystallized from dichloromethane)} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 7.65 \text{ (d, } J = 7.5 \text{ Hz, 1H), 7.60 \text{ (d, } J = 8.0 \text{ Hz, 1H), 7.33 \text{ (d, } J = 8.0 \text{ Hz, 1H), 7.25 - 7.18 \text{ (m, 5H), 6.86 \text{ (dd, } J = 8.5, 2.5 \text{ Hz, 1H), 6.82 - 6.71 \text{ (m, 5H), 3.77 \text{ (s, 6H), 3.73 \text{ (s, 3H) ppm}}}} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 160.5, 158.3, 156.2, 148.7, 143.4, 132.9, 131.4, 131.3, 130.5, 129.3, 121.8, 120.8, 118.5, 113.5, 113.1, 110.8, 65.8, 55.4, 55.2 \text{ ppm} \]

\[ \text{IR: } \nu_{\text{max}} = 2951, 2906, 2835, 1605 \text{ cm}^{-1} \]

\[ \text{MS (70 eV, El): } m/z (\%) = 489 ([M^{81}\text{Br}]^\bullet, 100), 487 ([M^{79}\text{Br}]^\bullet, 99), 407 ([M^{80}\text{Br}]^\bullet, 65) \]

\[ \text{HRMS (El): calcd for } C_{28}H_{23}O_3^{81}\text{Br [M]^\bullet: 488.0810, found: 488.0811; calcd for } C_{28}H_{23}O_3^{79}\text{Br [M]^\bullet: 486.0831, found: 486.0829} \]

\[ \text{UV (MeCN) } \lambda_{\text{max}} (\log \epsilon): 235 (4.5), 279 (4.3), 320 (3.7) \text{ nm} \]

1-Bromo-7-methoxy-9H-fluoren-9-one

This reaction can be stopped after the initial cyclisation before the addition of anisole to give the fluorenone intermediate, which can be isolated.

3-Bromo-4’methoxy-[1,1’-biphenyl]-2-carboxylic acid 4 (1.7 g, 5.6 mmol, 1.0 mol equiv) was dissolved in dichloromethane (15 mL) and added to methanesulphonic acid (15 mL). The solution was warmed to 40 °C and stirred for 16 hours. The solution was then cooled to
room temperature before being placed in an ice bath and quenched carefully with H₂O, then extracted with dichloromethane (3 x 150 mL). The organic extracts were combined, dried over MgSO₄ and the solvent removed under reduced pressure. The crude was then subjected to purification via column chromatography (80% dichloromethane in PS 40-60 °C) to give the title compound S1 as a yellow solid (1.2 g, 76%).

\[ R_f = 0.60 \text{ (50% dichloromethane in PS 40–60 °C)} \]
\[ \text{m.p.} = 124.8 \text{ to } 126.9 °C \text{ (recrystallized from dichloromethane)} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{:} \delta = 7.41 \text{ (d, } J = 8.0 \text{ Hz, } 1\text{H), 7.36 (dd, } J = 7.0, 1.0 \text{ Hz, } 1\text{H), 7.32 (dd, } J = 8.0, 1.0 \text{ Hz, } 1\text{H), 7.29 - 7.25 \text{ (m, } 1\text{H), 7.22 (d, } J = 2.5 \text{ Hz, } 1\text{H), 7.01 (dd, } J = 8.0, 2.5 \text{ Hz, } 1\text{H), 3.87 (s, 3H) ppm}} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3\text{:} \delta = 191.0, 161.3, 147.4, 135.7, 135.4, 134.9, 132.9, 131.4, 121.4, 120.6, 120.4, 118.5, 109.3, 55.8 \text{ ppm}} \]

\[ \text{IR: } \nu_{\text{max}} = 3059, 2918, 2836, 1714 \text{ cm}^{-1} \]

\[ \text{MS (70 eV, El): m/z (%): 289 ([M(^{79}\text{Br})]^\bullet, 100), 287 ([M(^{79}\text{Br})]^\bullet, 99), 274 ([M(^{81}\text{Br})]^\bullet - Me, 45), 272 ([M(^{79}\text{Br})]^\bullet - Me, 45)} \]

\[ \text{HRMS (El): calcd for } C_{20}H_{36}O_2^{^{79}\text{Br}} [M]^\bullet : 289.9765, \text{ found: 289.9762;} \text{ calcd for } C_{20}H_{36}O_2^{^{81}\text{Br}} [M]^\bullet : 287.9786, \text{ found: 287.9785} \]

\[ \text{UV (MeOH) } \lambda_{\text{max}} (\text{log } e): 234 (4.1), 269 (4.7) \text{ nm} \]

**7-Methoxy-9,9-bis(4-methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-9H-fluorene**

![Chemical diagram of 7-Methoxy-9,9-bis(4-methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-9H-fluorene](image)

1-Bromo-7-methoxy-9,9-bis(4-methoxyphenyl)-9H-fluorene 5 (1.50 g, 3.1 mmol, 1.0 mol equiv), 1-ethynyl-4-methoxybenzene (6.5 g, 23 mmol, 7.6 mol equiv), XPhos generation 2 precatalyst (150 mg, 0.20 mmol, 6 mol %), XPhos (90 mg, 0.20 mmol, 6 mol %), Cs₂CO₃ (3.30 g, 10 mmol,
3.3 mol equiv) and acetonitrile (1.5 mL) were placed in a 100 mL thick walled glass pressure tube. The tube was sealed and the solution was stirred at 100 °C for 19 hours (Caution: perform behind a blast shield). The solution was cooled to room temperature, diluted with water (200 mL) and extracted with ethyl acetate (4 x 150 mL). The organic extracts were combined, dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude product was subjected to purification via column chromatography (50% dichloromethane in PS 60-80 °C) to give the title compound 6 as an orange solid (1.08 g, 65%).

\[ R_f = 0.30 \] (50% dichloromethane in PS 40–60 °C)
\[ m.p. = 168.0 - 174.1 \, ^\circ{\text{C}} \, \text{(recrystallized from dichloromethane)} \]

\[ ^1H \, \text{NMR} \, (400 \, \text{MHz, CDCl}_3): \delta = 7.59 - 7.56 \, (m, \, 2H), \, 7.26 - 7.2 \, (m, \, 2H), \, 7.17 \, (d, \, J = 9.0 \, Hz, \, 4H), \, 6.92 \, (d, \, J = 9.0 \, Hz, \, 2H), \, 6.81 \, (dd, \, J = 8.0, \, 2.5 \, Hz, \, 1H), \, 6.77 \, (d, \, J = 2.5 \, Hz, \, 1H), \, 6.72 \, (d, \, J = 9.0 \, Hz, \, 2H), \, 6.65 \, (d, \, J = 9.0 \, Hz, \, 4H), \, 3.74 \, (s, \, 3H), \, 3.68 \, (s, \, 3H), \, 3.66 \, (s, \, 6H) \, \text{ppm} \]

\[ ^{13}C \, \text{NMR} \, (100 \, \text{MHz, CDCl}_3): \delta = 160.4, \, 159.6, \, 158.3, \, 155.6, \, 151.9, \, 140.9, \, 135.0, \, 132.8, \, 132.2, \, 130.9, \, 130.3, \, 127.7, \, 121.2, \, 120.8, \, 119.3, \, 115.7, \, 114.0, \, 113.5, \, 113.2, \, 111.2, \, 96.0, \, 87.7, \, 65.1, \, 55.6, \, 55.4, \, 55.3 \, \text{ppm} \]

\[ \text{IR: } v_{\max} = 3000, \, 2955, \, 2933, \, 2835, \, 1605 \, \text{cm}^{-1} \]

\[ \text{MS (70 eV, Ei): } m/z \%: \, 538 \, ([M]^* \cdot, \, 100), \, 507 \, ([M]^* \cdot - \text{OMe}) \cdot, \, 20 \]

\[ \text{HRMS (El): } \text{calcfd for C}_{37}H_{30}O_4 \, [M]^*: \, 538.2144, \, \text{found: } 538.2143 \]

\[ \text{UV (MeCN) } \lambda_{\text{max}} \, (\log \varepsilon): \, 284 \, (4.6), \, 297 \, (4.6), \, 316 \, (4.4) \, \text{nm} \]

**5,9-Dimethoxy-7b-(4-methoxyphenyl)-7bH-indeno[1,2,3-kj]fluorene**

![Chemical Structure](attachment:image.png)

1-Bromo-7-methoxy-9,9-bis(4-methoxyphenyl)-9H-fluorene 5 (100 mg, 0.21 mmol, 1.0 mol equiv), XPhos (16 mg, 0.03 mmol, 15 mol%), XPhos generation 2 pre-catalyst (26 mg, 0.03 mmol, 15 mol%), C₆H₅CO₂H (175 mg, 0.53 mmol, 2.6 mol equiv) and acetonitrile (2 mL) were placed in a 20 mL thick walled glass pressure tube. The tube was sealed and the solution
the solution was stirred at 100 °C for 48 hours (Caution: perform behind a blast shield). The solution was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The crude was subjected to purification via column chromatography (50% dichloromethane in PS 40–60 °C) to give the title compound as a colourless oil (51 mg, 60%).

Rf = 0.45 (50% dichloromethane in PS 40–60 °C)

1H NMR (400 MHz, CDCl₃): δ = 7.61 (d, J =8.5 Hz, 1H), 7.44 (d, J = 8.5 Hz, 1H), 7.27 – 7.19 (m, 4H), 7.08 (d, J = 2.5 Hz, 1H), 7.01 (d, J = 9.0 Hz, 2H), 6.78 (dd, J = 8.5, 2.5 Hz, 1H), 6.70 (dd, J = 8.5, 2.5 Hz, 1H), 6.55 (d, J = 9.0 Hz, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 3.58 (s, 3H) ppm

13C NMR (100 MHz, CDCl₃): δ = 167.2, 159.8, 158.6, 158.1, 153.9, 145.9, 143.9, 139.8, 139.5, 137.1, 136.6, 130.6, 127.4, 126.2, 122.3, 118.7, 118.2, 113.6, 113.1, 112.3, 111.6, 107.8, 65.2, 55.6, 55.5, 55.14 ppm

IR: νmax = 3059, 2954, 2939, 2834, 1603, 1572 cm⁻¹

MS (70 eV, EI): m/z (%): 406 ([M]+•, 100), 391([M]+• - Me, 40), 375 ([M]+• - OMe, 50), 298 ([M]+• - 2OMe, 70), 283 ([M]+• - 3OMe, 60), 268 ([M]+• - 4OMe, 50), 253 ([M]+• - 5OMe, 40), 238 ([M]+• - 6OMe, 30), 223 ([M]+• - 7OMe, 20), 208 ([M]+• - 8OMe, 10), 193 ([M]+• - 9OMe, 5), 178 ([M]+• - 10OMe, 3), 163 ([M]+• - 11OMe, 1), 148 ([M]+• - 12OMe, 1), 133 ([M]+• - 13OMe, 1), 118 ([M]+• - 14OMe, 1), 103 ([M]+• - 15OMe, 1), 88 ([M]+• - 16OMe, 1), 73 ([M]+• - 17OMe, 1), 58 ([M]+• - 18OMe, 1), 43 ([M]+• - 19OMe, 1), 28 ([M]+• - 20OMe, 1), 13 ([M]+• - 21OMe, 1)


4,4’-(7-Hydroxy-1-(4-hydroxyphenyl)ethynyl)-9H-fluorene-9,9-diyl)diphenol (Selaginulpilin D)

7-Methoxy-9,9-bis(4-methoxyphenyl)-1-((4-methoxyphenyl)ethynyl)-9H-fluorene 6 (1.3 g, 2.4 mmol, 1.0 mol equiv) was added to MeMgl (3M in diethyl ether) (16 mL, 48 mmol, 20 mol equiv). The reaction mixture was placed in a 25 °C bath and the diethyl ether was removed under vacuum, to give a solid residue (Caution: we performed this reaction behind a blast shield). The residue was then heated to 160 °C for 45 minutes after which it was cooled to room temperature and placed in an ice bath. The mixture was then dissolved in a 1:1 ethyl acetate : diethyl ether mixture (50 mL). Water was then added drop wise (Caution:
initial vigorous gas evolution) to the reaction mixture (50 mL water was added in total) and the resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent removed under reduced pressure. The crude product was subjected to purification via column chromatography (50% ethyl acetate in PS 40–60 °C) to give the title compound 1 as an off-white solid (765 mg, 67%).

\[ R_f = 0.40 \] (50% ethyl acetate in PS 40–60 °C)

\[ m.p. = 162.7 - 166.0 \degree C \] (recrystallized from diethyl ether)

\[ ^1\text{H NMR} \] (400 MHz, CDCl₃): \[ \delta = 7.61 \] (dd, \( J = 7.5, 1.0 \) Hz, 1H), 7.56 (d, \( J = 8.2 \) Hz, 1H), 7.22-7.20 (m, 1H), 7.17 (dd, \( J = 7.5, 1.0 \) Hz, 1H), 7.07 (d, \( J = 9.0 \) Hz, 4H), 6.84 (d, \( J = 8.5 \) Hz, 2H), 6.74 (dd, \( J = 8.0, 2.5 \) Hz, 1H), 6.68 (d, \( J = 2.5 \) Hz, 1H), 6.65 (d, \( J = 8.5 \) Hz, 2H), 6.56 (d, \( J = 9.0 \) Hz, 4H) ppm

\[ ^{13}\text{C NMR} \] (100 MHz, CDCl₃): \[ \delta = 159.0, 158.9, 157.2, 156.8, 153.2, 142.4, 135.4, 133.7, 132.3, 131.3, 131.0, 128.5, 122.4, 121.7, 119.7, 116.3, 115.7, 115.6, 115.2, 113.4, 97.1, 88.2, 66.1 \] ppm

\[ \text{IR: } \nu_{\text{max}} = 3338, 3294, 1607 \text{ cm}^{-1} \]

\[ \text{MS (70 eV, El): } m/z (%):482 \text{ [(IM)]•}, 100, 389 \text{ [(IM)]• } - \text{ C₆H₆O}, 40 \]

\[ \text{HRMS (El): } \text{calc for } \text{C₃₃H₃₂O₄} \text{ [M]+: } 482.1518 \text{ found: } 482.1513 \]

\[ \text{UV (MeOH) } \lambda_{\text{max}} \text{ (log } e) \text{ 287 (4.6), 298 (4.6), 314 (4.4) nm} \]
References


HMBC Spectrum of 7 in CDCl₃
Selaginpulvinin D
3 spectrum stack plots of $^1$H and $^{13}$C NMR spectra of the natural product as reported by (a) Yin$^4$, (b) Lee$^5$ and (c) ourselves are provided for comparison purposes on the following two pages. That the same compound has been isolated and prepared is abundantly clear. Karmaker and Lee report only $^1$H NMR, $^{13}$C NMR and HRMS data for the natural product and describe the natural product as a solid but do not report an m.p.$^5$ Yin and co-workers report 1 as a colourless oil and provide full characterization data, including UV absorptions and extinction coefficients.$^4$

Our synthesis sample was an off-white solid with m.p. 163 °C -166 °C with UV-vis wavelengths of absorptions that matched those reported by Yin et al.$^4$ Our extinctions coefficients were different, which we attribute to the small quantities of natural product isolated from the plant.
Chapter Three:

2,3-Diethynyl-1,3-butadienes
3 2,3-Diethynyl-1,3-butadienes

Prelude

The manuscript is in draft format and is been prepared to be submitted to the journal Angew. Chem. Int. Ed. The other authors are Jas S. Ward (crystallographer) and my supervisor Professor Michael S. Sherburn. This project was conceived, designed, evolved and drafted in collaboration with Professor Michael S. Sherburn. The synthetic experiments were carried out by myself.

To date there has been no general method for the synthesis of 2,3-diethynyl-1,3-butadienes. Only four syntheses of 2,3-diethynyl-1,3-butadienes have been previously reported with only five of these compounds synthesised to date. One each from Larock (Larock, R. C., J. Org. Chem. 1976, 41, 2241), Gleiter (Gleiter, R., Rockel, H., Irmgartinger, H., Oeser, T. Angew. Chem. Int. Ed. 1994. 33, 1270), Grigg (Boomer, J., Grigg, R. Tetrahedron. 1999. 55, 13463) and two from Hopf (Hopf, H., Theurig, M., Jones, P., Bubenitschek, P. Liebigs Ann. 1996, 1301). The details of these syntheses can be found in Chapter 1.

When discussing 2,3-diethynyl-1,3-butadienes Hopf, H and co-workers stated the following: Although structurally simple, these compounds present a considerable challenge to synthesis. On the one hand, this is connected with the very high propensity of the products – and often also of the substrates and intermediates - to undergo unspecific reactions such as “polymerisation” or “oxidation” (Hopf, H., Theurig, M., Jones, P., Bubenitschek, P. Liebigs Ann. 1996, 1301). It was clear to us that there was an assumption that these compounds would be unstable, making them difficult to synthesise and handle. We sought to dispel these notions and develop a general method for the
synthesis of these compounds based on the use of easily synthesisable di-carbonates in two-fold Sonogashira cross-coupling reactions with terminal alkynes.

This chapter describes a versatile method to generate all possible substitution patterns of 2,3-diethynyl-1,3-butadienes via a two-fold Sonogashira cross-coupling of easily synthesisable carbonate derivatives of 2-butyne-1,4-diols and readily available terminal alkynes.

\[
\begin{align*}
\text{MeO}_2\text{CO} & \xrightarrow{\text{Pd(PPh}_3)_4, \text{CuI, diisopropylamine}} \quad \text{OCO}_2\text{Me} \\
\text{R}_2 & \quad \text{R}_2 \\
\end{align*}
\]

The first coupling proceeds via a propargylic transposition and the second coupling with allylic transposition. The proposed mechanism for the twofold Sonogashira cross-coupling to generate 2,3-dialkynyl-1,3-butadienes commences with oxidative insertion of Pd into the carbonate-carbon (the carbonate acts as a pseudo halogen) bond of but-2-yne-1,4-diyl dimethyl bis(carbonate) which results in the formation of an allene. Transmetallation followed by reductive elimination of Pd gives alkyne substituted allene. A second oxidative insertion of Pd into the remaining carbonate-carbon gives rise to a butadiene which following a second transmetallation step and reductive elimination produces the 2,3-dialkynyl-1,3-butadiene product.
Both symmetrically-substituted and unsymmetrically-substituted compounds were accessible through this method. Investigations into the stability and reactivity associated with these compounds were also undertaken for the first time. Furthermore, the value of these compounds are demonstrated in the synthesis of cyclo-octadienes and expanded radialenes and dendralenes.
| 68 | 3 | 2,3-Diethynyl-1,3-butadienes |
2,3-Diethynyl-1,3-Butadienes

Madison J. Sowden, Jas S. Ward and Michael S. Sherburn*

Dedicated to Professor Henning Hopf

Abstract: The first general preparative access to compounds of the 2,3-diethynyl-1,3-butadiene (DEBD) class is reported. The successful synthesis involves a one pot, twofold Sonogashira-type, Pd(0)-catalyzed union of terminal alkynes and a carbonate derivative of a 2-butenyl-1,4-diol. The synthesis is broad in scope, as evidenced by the preparation of 27 diversely-substituted DEBDS. Members of this structural family are sufficiently stable to be handled using standard laboratory techniques at ambient temperature. They decompose primarily through heat-promoted cycloaddition. Alkyl substitution is shown to slow the rate of decomposition whereas extended conjugation through aryl or alkynyl substitution accelerates it. DEBDS undergo Eiplington-type cyclo-oligomerization to form a new class of expanded radialeses. An iterative sequence of Sonogashira-type couplings generates a new type of expanded dendrite.

In recent times, practical syntheses of sp² and sp-C based acyclic architectures have challenged the widely-held, yet false perception that such compounds are unmanageable. These studies are opening up new regions of poorly chartered structural space, which in turn is fueling unprecedented developments. New directions and applications of acyclic sp² and sp-C rich molecules are in carbon-rich materials and transform-driven step-economic total synthesis of natural products. Broad-spectrum, operationally simple and safe synthetic methods, coupled with a knowledge of stability and structure-reactivity relationships are needed in order to underpin these downstream developments.

This work focusses on the m-bond rich acyclic branched hydrocarbon 2,3-diethynyl-1,3-butadiene (DEBD 1) (Scheme 1), a structure comprising only four sp²-carbons and four sp-carbons. It contains two terminal 1,3-ene units and a central 1,3-butadiene, hence two branch points of cross-conjugation. Relatively little is known about this compound or its substituted analogs since no general method for the synthesis of substituted 2,3-diakynyl-1,3-butadienes has been reported and no structure-reactivity/stability reports have appeared. Five specific substituted DEBDS have been described in the literature: one each from the groups of Larock,1 Green0 and Grupp1 and two from Hopf,1 who also reported the parent hydrocarbon. This last contribution not only uncovered almost everything that is known about DEBDS: it also foretells most of what follows. Thus, Hopf and co-workers reported the Diels-Alder reaction of their compounds with dienophiles to prepare cyclic 2-endynes, which have applications in Bergman cyclonaddiations. They also reported the formation of 1,4-cyclooctadienes, through thermal [4+4]cycloaddition-dimerization of DEBDS. This remarkable transformation represents a formally disallowed process according to Woodward-Hoffman rules. Finally, they proposed (but did not investigate) that DEBDS might serve as precursors to expanded radialeses.

We supplement this already sizeable list of demonstrated and predicted uses of DEBDS by noting their untapped potential as building blocks for polymers, and as ligands in organometallic chemistry. It comes, therefore, as a surprise to learn that these molecules have not been pursued since the most recent of these reports, some 20 years ago. We suspect that a contributing factor relates to the aforementioned reputation of highly unsaturated acyclic compounds for instability. We unequivocally establish here that such concerns are unwarranted. Across 30 different categories of substituents and patterns of substitution, these well behaved compounds can be stored neat in a −20 °C freezer for extended periods without decomposition. In addition to reporting the first general synthesis of DEBDS (Scheme 1), we elucidate the influence of substitution upon reactivity, we show that Hopf's prediction regarding the potential of DEBDS in the synthesis of expanded radialeses is correct—and we identify the specific DEBD substitution pattern required in order to achieve it.

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Supporting information and the ORCID identification numbers for the authors of this article can be found under: https://doi.org/10.1002/anie.20xx.xxx

Scheme 1. 2,3-Diethynyl-1,3-butadienes, DEBD 1, reported substituted analogs, and a summary of the synthesis reported herein.
In terms of atom connectivity perception, the simplest way to visualize the synthesis of a DEBD 4 (or any other 2,3-disubstituted-1,3-butadiene) is by twofold cross-couplings of a 2,3-dihalo-1,3-butadiene 6, which can be accessed from a propargyl diol 8 by twofold substitution with 1,3-transposition (Scheme 2). The reaction proceeds by way of mono-coupled intermediate 7. This is the approach taken by Hopf for the preparation of DEBDs, and one that we have used for 1,3-butadiene, dendracline and radalenine synthesis, and others have used for substituted 1,3-butadiene synthesis. Two challenges with this approach are: (a) 2,3-dihalo-1,3-butadienes are prone to polymerization, and (b) if mono-coupled intermediate 7 is less reactive towards cross-coupling than its precursor, then non-productive pathways (i.e. decomposition) might ensue.

We recently showed that tetra-substituted 2-buten-1,4-diol 2 R=R#H undergoes twofold Pd(0)-catalyzed couplings with aryl (and some alkényl) boronic acids, without the need to pre-activate the hydroxy functionality through covalent derivatization, to form densely-substituted 1,3-butadienes. The twofold cross-coupling proceeds with 1,3-transposition at each C-D or C=C bond change (cf. 2→8→4, Scheme 2). We wanted to devise a synthesis of DEBDs 4 that would permit any substitution pattern; hence the restriction of this earlier method to highly substituted products precluded its application to cases.

 Gratifyingly, there are examples of twofold, 1,3-transposing 2-buten-1,4-diol activated derivatives in the literature, although none of these are Sonogashira-type couplings. We were attracted to this process alicylic, unlike dendraclines and carbonate precursors 2 are robust and not prone to polymerization. Moreover, mono-coupled intermediates 8 were anticipated to be more prone to oxidative decomposition of Pd(0) than precursor 7, which would facilitate (twofold coupling).

Table 1 lists the synthesis of 13 substituted DEBDs carrying substituents at the alkyne terminal. Standard Sonogashira coupling conditions were effective for the reaction between known 2-buten-1,4-diol carboxylate 10 and terminal alkynes 9 throughout, with [Pd(PPh₃)₄] and CuI as co-catalysts and diisopropylamine as base. Alkyne substituents tolerated include alkyl, alkenyl, trityl, aryli, heterocyclic, and hydroxalkyl (from propargyl alcohol precursors) groups.

Isolated yields are generally good, the exceptions generally being due to difficulties faced during separation of the alkyne homocoupling product. While there are several reported methods to address this issue, none were completely effective in our hands. The anomalously low yield of bis-cyclohexyl DEBD 11d is due to its heightened sensitivity to autoxidation.

The 12 new DEBD structures listed in Table 2 show that all conceivable substitutions (mono-, both possible di-, tri-, and tetra-...
3 2,3-Diethynyl-1,3-butadienes

So far, the method has been shown to grant access to DEBDs with a wide variety of terminal alkyn substituents, and variation in the number and type of alkyn substituents. The preparation of the first DABDs with different substituents on the two alkyn termini would require a sequence of couplings with two different alkynes (cf. 2–6–4, Scheme 2), which would be challenging since the second coupling in all cases shown in Tables 1 and 2 are invariably faster than the first. We considered a stepwise synthesis, in which the second cross-coupling could not proceed, for example by using a mono-carbonate derivative of the 2-butyne-1,4-diol, but we were discouraged by the necessity of several additional steps to perform the synthesis, and instead opted for a one flask method in which two alkynes and the dis-carbonate were simultaneously present. Thus, slow addition of the faster reacting acetylene, namely TMS-acetylene 13 to a mixture of the other reaction components delivered the best outcome, with a product ratio approximating to the best case statistical ratio of the three products (i.e. 50:20:25) being obtained (Scheme 3). While the yields are modest, the very short step count (only 2 steps from inexpensive, commercial precursors) and operational simplicity renders this approach challenging to beat.

With 27 new DEBDs in hand, representing a very wide diversity of structural possibilities, we were in a position to examine the influence of substitution upon stability. In general, substituted DEBDs are robust compounds. While we advocate long term storage of pure materials under Ar in a –20 °C freezer, representative neat samples exposed to ambient laboratory light, ambient temperature and air for up to an hour showed no sign of decomposition.

Figure 1 depicts the results of “forced” decomposition by heating variously substituted DEBDs at the same temperature with the same starting concentration solution. The more concentrated the solution of a DEBD, the faster the rate of its decomposition. As mentioned in the introduction, the Hopf laboratory reported the [4+4] cyclodimerization of 11b in 34% yield from an initial 1.0 M concentration solution, with no sign of the [4+2] cyclodimer.1 In our hands, heating concentrated solutions of DEBDs led to substantial polymerization and low yields of dimers, both in the presence or absence of acid- and radical scavengers. Moreover, we observe the formation of a ca. 2:3 mixture of the formal Diels-Alder cyclodimer 18, 19 and the [4+4] cyclodimer 16, 17 in these cases (Scheme 4).
We propose a single stepwise, biradical mechanism to explain these observations instead of two separate, concerted pericyclic cycloadditions in competition. Computational investigations on these and related reactions are underway.

![Scheme 4](image)

As is clear from the results summarized in Figure 1, both the location and nature of substituents upon a DEBD core have a pronounced influence on its stability. The most reactive DEBDs are those carrying a conjugating substituent on either the alkene or alkene termini. Thus, di-phenyl-DEBD 11j and di-1-Hexenyl-DEBD 11i are even more prone to react on heating than is the parent DEBD 1 (prepared by dimerization of 11h). Allyl and trialkyl-substituted DEBD 12k, for example, are inert under the standard conditions. Combustions of stabilizing and destabilizing substituents appear to be somewhat additive, as can be seen from the series of compounds 11 – 12c – 12d.

The most reactive compound prepared was di-(4-cyano-phenyl)-DEBD, 20, which underwent spontaneous cycloaddition at ambient temperature so rapidly that the monomer could not be isolated. Nonetheless, inclusion of four methyl groups at the 1,3-butadiene termini furnished a compound 21 that was readily isolable, (Figure 2).

![Scheme 5](image)

We now return to test the Hopf's prediction of the potential value of DEBD compounds in the synthesis of "expanded" systems.1 Expanded dendralenes and their acyclic variants, expanded dendralenes, are designed molecules in which oligoalkyne "spacers" have been inserted into single bonds connecting two sp²-carbons. Thus far, the established acyclic expanded dendralene structures are the iso-polydiolefinylbenzines (iso-PDAs) and the iso-polytriacetylenes (iso-PTAs), both of which contain a repeating unit comprising a single 1,1-di substituted C=C bond, connected by either a C=C or a –CH=–CH=–C(sp²)– spacer. Thus, iso-PDAs are 2,4-diols (1-en-3-ynes), whereas iso-PTAs are 2,6-diols (1-en-3,5-dienes). To our knowledge, there are no reports of expanded dendralenes comprising 1,3-butadiene units. The synthesis of the first such molecule, an expanded [8]dendralene comprising three 1,3-butadiene units by the method described earlier, is depicted in Scheme 5, in a process that is an iterative approach of the methodology described earlier.
On first inspection, the successful outcome of this reaction is surprising, in light of the fact that both precursors, 22 (generated by desilylation of 12k) and 10, are symmetric bifunctional building blocks. That a polymer is not the product of this reaction is the result of a substantially faster rate of the second C-C cross-coupling relative to the first (cf. 2-8-14, Scheme 2). Evidently, the 38% yield for this reaction is an indication that some of the product 23 reacts with bis-electrophile 10, leading to higher oligomers, which become increasingly unstable. Tripe DEBD product 23 lacks stabilizing alkyl substitution at the central 1,3-buta diene and carries conjugating groups at its alkylene termini, hence it is amongst the least stable of the isolable compounds reported herein, and higher oligomers with the same repeating unit are anticipated to be less stable still.

Finally, we investigated the cyclo-oligomerization of DEBDs to generate expanded radiales. There are many reported expanded radiales comprising, as a repeating unit, a single 1,1-disubstituted C=C bond, connected by either a --C=C-- or a --C=C--C=C-- spacer, i.e. cyclo-oct-FDAs and cyclo-oct-PTAs. To our knowledge, there are no expanded radiales comprising cross-conjugated 1,3-buta diene units. The first such compounds are depicted in Scheme 6, which are prepared by Eglington-type oxidative cyclo-oligomerization of tetramethyl-DEBD monomer 22.

Scheme 6. Eglington-type cyclo-oligomerization of tetramethyl-DEBD 22 gives chiral, carbon-rich cyclodimer 24 and cyclotrimer 25. No cyclo-oligomers were isolated from reactions of the parent DEBD 1 and E,E-dimethyl DEBD 26. It atoms are omitted from the X-ray crystal structures for clarity.

Slow addition of DEBD precursor 22 to the reaction mixture gave cyclodimer 24 (an expanded [6]radialene) as major product, with even slower addition giving rise to mixtures richer in the cyclotrimer 25 (an expanded [8]radialene). Single crystal X-ray analysis was performed on samples of both compounds, which revealed chiral conformations in the crystals, which result from the non-planarity of the 1,3-buta diene units. Significant bending is clearly visible around the diene units of cyclodimer 24, whereas the cyclotrimer appears to be relatively strain-free. Both enantiomeric forms are present in the crystal, and also in solution, with the barrier towards stereomutation found to be higher than 70 °C, by VT NMR analysis.

In stark contrast to the successful cyclo-oligomerization of tetramethyl-DEBD 22, the parent 1, and E,E-dimethyl analog 26 did not furnish isolable monodispers products. We ascribe these results in part to the stability of the precursors and targeted products in these cases, which, according to our improved knowledge of substitution-stability relationships (Figure 1) would be anticipated to be significantly less stable. There is, however, another contributing factor to the lack of success in cyclo-oligomerization of these less-substituted precursors. DFT studies reveal a dramatically different conformational preference for tetramethyl-DEBD 22 to that of the parent DEBD 1 and E,E-dimethyl analog 26. Whereas the former prefers a conformation in which the two ethynyl-groups are arranged roughly orthogonally, the lowest energy conformations of the latter place the two ethynyl-groups in an anti-disposition. Molecular structures found from single crystal X-ray analyses of DEBDs 22 and 26 agree with these calculations. No local energy minimum conformations within 30 kJ/mmol of the preferred conformations could be located. Evidently, for cyclo-oligomerization of 1 or 26 to occur, each individual DEBD unit in the immediate cyclo-oligomer precursor would suffer a substantial energetic penalty.

In summary, 2,3-dialkynyl-1,3-buta dienes (DEBDs) are now readily available, through a short and operationally simple 2-4 step synthesis from commodity chemicals. All possible arrangements of substituents and substitution patterns are accessible from this broad-spectrum approach. In the vast majority of cases DEBDs can be stored neat for extended periods of time in a −20 °C freezer. Heat causes these compounds to decompose, through a mechanism that most likely involves radical dimerization and polymerization. Both the type and number of substituents determine the rate of decomposition of DEBDs, and systems have been designed to both accelerate and impede this process. The first tentative steps towards applying DEBDs in novel materials have been taken, with unprecedented expanded dendralene and radiale units being prepared, which exhibit chiral conformations through restricted rotation. The preparation of expanded dendralene 23 (Scheme 5) and radialenes 24 and 25 (Scheme 6) represent a proof-of-principle.

Evidently, many variations on these themes can be envisaged, including the incorporation of phenylene, heterocyclic, and metal atom spacers, with potential applications of these new materials in optics and electronics.

Acknowledgements
This work was supported by the Australian Research Council. The authors thank Mr Nicholas Magann for useful discussions.
3 2,3-Diethynyl-1,3-butenadienes

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Keywords: hydrocarbons • 1,3-butenadienes • cross-coupling •
cycloadditions • carbon-rich materials

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Alkynes of dienes. The first general synthesis of 2,3-diakynyl-1,3-butadienes (DABDs) uses commodity chemical precursors (acetylene, two terminal alkynes, and two aldehydes/ketones) and involves, as a key step, an unprecedented twofold Sonogashira-type cross-coupling of a 2-butyn-1,4-diol derivative. The process is of extremely wide scope, with 30 structurally diverse examples reported. The value of DABDs in the rapid synthesis of novel expanded dendralenes and expanded radialeines is demonstrated.
Supporting Information

For

2,3-Diethynyl-1,3-butadienes

Madison J. Sowden, Jas S. Ward
and Michael S. Sherburn*
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NMR Spectroscopy

^1H NMR spectra were recorded at 400 MHz using a Bruker AVANCE 400 spectrometer. Residual proto-solvent peaks were used as an internal reference for ^1H NMR spectra (CDCl₃ δ 7.26 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 spectra were recorded at 101 MHz using a Bruker AVANCE 400 spectrometer. Solvent peaks were used as an internal reference for ^13C NMR spectra (CDCl₃ δ 77.0 ppm). Assignment of carbon signals was assisted by HSQC and HMBC experiments. The following abbreviations (or combinations thereof) are used to denote ^1H NMR multiplicities: s = singlet, bs = broad singlet, d = doublet, dd = doublet of doublets, t = triplet, m = multiplet.

Infrared Spectroscopy

IR spectra were recorded on a Perkin–Elmer UATR Two spectrometer as a thin film or solid.

Mass Spectrometry

Low-resolution EI mass spectra were recorded on a Finnigan Polaris Q ion trap mass spectrometer using electron impact (EI+) ionization mode at 40 or 70 eV. High-resolution EI mass spectra were recorded on a VG Autospec mass spectrometer operating at 70 eV. Low-resolution ESI mass spectra were recorded on a Micromass ZMD spectrometer using electrospray (ESI+) ionization mode. High resolution ESI mass spectra were recorded on a Waters LCT Premier time-of-flight (TOF) spectrometer using electrospray ionization (ESI+).

Melting Points

Melting points were measured on a Stanford Research Systems Optimelt Automated Melting Point System and are uncorrected.

Experimental Procedures, Reagents, and Glassware

Reactions were conducted under a positive pressure of dry nitrogen in heat-gunned-dried glassware and at room temperature, unless specified otherwise. Anhydrous solvents were either obtained from commercial sources or dried according to the procedure outlined by Grubbs and co-workers.¹ Commercially available chemicals were used as purchased, or where specified, purified by standard techniques.²
Chromatography
Analytical thin-layer chromatography was conducted with aluminum-backed silica gel 60 F254 (0.2 mm) plates supplied by Merck, and visualized using UV fluorescence (λ<sub>max</sub> = 254 nm), or developed using KMnO<sub>4</sub> or p-anisaldehyde, followed by heating.
Flash chromatography employed Merck Kiesegel 60 silica gel (230–400 mesh). Solvent compositions are given in v/v. PS 40–60 °C refers to petroleum spirits, boiling point fraction 40–60 °C. PS 30–40 °C refers to petroleum spirits, boiling point fraction 30–40 °C.
Preparative thin layer chromatography employed Merck TLC silica gel 60 F<sub>254</sub> glass plates.

Optical Rotation
Optical rotation data was collected on a Rudolph Research Analytical Autopol 1 Automatic Polarimeter using a 14J cell.

X-ray Crystallography
Single crystal X-ray data was collected on a SuperNova (Dual Source) diffractometer using a SuperNova (Cu or Mo) X-ray radiation source or on the MX1 beamline at the Australian Synchrotron. Crystallographic Structures were solved using CrysAlis PRO.

Ultraviolet-Visible Spectroscopy
UV-Vis spectra were recorded using a Shimadzu UV-Visible 2450 spectrometer.
Synthesis of Substituted Alkynes

\((1R,5S)-3-(2,2\text{-Dibromovinyl})-6,6\text{-dimethylbicyclo}[3.1.1]hept-2-ene (S2)\)

A mixture of CBr₄ (44.0 g, 133 mmol) in CH₂Cl₂ (200 mL) was cooled in a 0 °C ice bath. PPh₃ (69.8 g, 266 mmol) was added to the reaction mixture portion wise (CAUTION: exotherm). The reaction mixture was then stirred in the 0 °C bath for a further 20 minutes. \((1R,5S)-6,6\text{-Dimethylbicyclo}[3.1.1]hept-2-ene-3\text{-carbaldehyde} (10.0 g, 66.6 mmol) was added drop wise to the reaction mixture. The solution was warmed to 23 °C and stirred for 2 hours, then poured onto a stirring solution of PS 40-60 °C (1.0 L) and stirred for a further 20 minutes. The mixture was then filtered through a short pad of silica eluting with PS 40-60 °C and the solvent was removed under reduced pressure. This was repeated twice more to remove residual triphenyl phosphine oxide and to give the title compound S2 as a colourless oil (19.0 g, 93%).

\( R_f = 0.73 \) (PS 40-60, 100%)

\(^1\text{H NMR} \) (400 MHz, CDCl₃): \( \delta = 6.87 \) (s, 1H), 5.92 (d, \( J = 1.6 \) Hz, 1H), 2.62 (td, \( J = 5.6, 1.5 \) Hz, 1H), 2.42 (dt, \( J = 8.8, 5.7 \) Hz, 1H), 2.37-2.25 (m, 2H), 2.11 (m, 2.13 - 2.00, 1H), 1.31 (s, 3H), 1.20 (d, \( J = 9.0 \) Hz, 1H), 0.88 (s, 3H) ppm

\(^{13}\text{C NMR} \) (101 MHz, CDCl₃): \( \delta = 143.8, 137.4, 127.6, 86.0, 44.5, 40.3, 37.9, 32.3, 31.7, 26.2, 21.3 \) ppm

\( \text{IR (thin film): } \nu_{\text{max}} = 2984, 2916, 2882, 2825, 1568 \text{ cm}^{-1} \)

\( \text{EIMS (70 ev, EI): } m/z(\%) = 307 \ [(M^6\text{Br}_2)^{+}, 98], 305 \ [(M^6\text{Br}^{79}\text{Br})^{+}, 100], 303 \ [(M^{79}\text{Br}_2)^{+}, 100], 292 \ [(M^{61}\text{Br}_2\text{-CH}_3)^{+}, 15], 290 \ [(M^{61}\text{Br}^{79}\text{Br}\text{-CH}_3)^{+}, 30], 288 \ [(M^{79}\text{Br}_2\text{-CH}_3)^{+}, 17] \)

\( \text{HRMS (EI): calc for } C_{19}H_{14}^{6\text{Br}_2}\text{ [M]^{+}: 307.9421}, \text{ found: 307.9417, calc for } C_{19}H_{14}^{79}\text{Br}\text{ [M]^{+}: 305.9442}, \text{ found: 305.9431, calc for } C_{19}H_{14}^{79}\text{Br}^{79}\text{Br}[M]^{+}: 303.9462, \text{ found: 303.9463} \)
(1R,5S)-3-Ethynyl-6,6-dimethylbicyclo[3.1.1]hept-2-ene (S3)

A mixture of dibromo olefin (S2) (10.0 g, 32.7 mmol) in THF (40 mL) was cooled in a -78 °C bath (dry ice, acetone). n-BuLi ([1.22M in hexane], 67.0 mL, 81.7 mmol) was added drop wise to the reaction mixture so as the internal temperature did not exceed -60 °C. The solution was then warmed to 23 °C and stirred for a further 2 hours. The reaction mixture was quenched with sat. aq. ammonium chloride solution (100 mL) and extracted with PS 30-40 °C (3 x 100 mL), the organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (PS 30-40 °C, 100%), to give the title compound S3 as a colourless oil (1.60 g, 34%).

R_f = 0.63 (PS 40-60, 100%)

1H NMR (400 MHz, CDCl₃): δ = 6.08 – 6.06 (m, 1H), 2.97 (s, 1H), 2.41 (dt, J = 6.9, 5.6 Hz, 1H), 2.34 (dt, J = 10.7, 3.3 Hz, 2H), 2.27 (td, J = 5.7, 1.4 Hz, 1H), 2.17 – 2.07 (m, 1H), 1.29 (s, 3H), 1.24 (d, J = 9.0 Hz, 1H), 0.89 (s, 3H) ppm

13C NMR (101 MHz, CDCl₃): δ = 132.9, 129.4, 84.7, 77.0, 47.1, 40.4, 38.2, 32.3, 31.6, 26.3, 21.2 ppm

IR (thin film): νmax = 3310, 2950, 2920, 2889, 2093 cm⁻¹

MS (70 eV, EI): m/z (%): 146 ([M]⁺, 80), 131 ([M-CH₃]⁺, 100),

HRMS (EI): calcd for C₁₁H₁₄ [M]⁺: 146.1096, found: 146.1095

Optical Rotation: [α]_D^21 = -6.20 (c 1.0, CHCl₃)
(S)-1-Ethynyl-4-(prop-1-en-2-yl)cyclohex-1-ene (S6)

A mixture of CBr₃ (4.40 g, 13.3 mmol) in CH₂Cl₂ (10 mL) was cooled in a 0 °C ice bath. PPh₃ (7.00 g, 26.6 mmol) was added to the reaction mixture portion wise (CAUTION: exotherm). The reaction mixture was then stirred in the 0 °C bath for a further 20 minutes. (S)-4-(Prop-1-en-2-yl)cyclohex-1-ene-1-carbaldehyde (1.00 g, 6.66 mmol) was then added drop wise to the reaction mixture. The solution was warmed to 23 °C and stirred 2 hours then poured onto a stirring solution of PS 40-60 °C (200 mL) and stirred for a further 20 minutes. The resulting suspension was then filtered through a short pad of silica eluting with PS 40-60 °C and the solvent was removed under reduced pressure to give (S)-1-(2,2-dibromovinyl)-4-(prop-1-en-2-yl)cyclohex-1-ene, which was subjected to the next step without further purification.

A mixture of dibromo olefin (2.02 g, 6.66 mmol) in THF (10 mL) was cooled in a –78 °C bath. n-BuLi ([1.45M], 11.4 mL, 16.5 mmol) was added drop wise to the reaction mixture so that the internal temperature did not exceed –60 °C. The solution was warmed to 23 °C and stirred for a further 2 hours. The reaction mixture was quenched with sat. aq. ammonium chloride solution (40 mL) and extracted with PS 40-60 °C (3 x 40 mL), the organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (PS 40-60 °C, 100%), to give the title compound S6 as a colourless oil (477 mg, 50% over 2 steps).

Rᵣ = 0.65 (PS 40-60, 100%)

¹H NMR (400 MHz, CDCl₃): δ = 6.22-6.20 (m, 1H), 4.73 (d, J = 14.0 Hz, 2H), 2.81 (s, 1H), 2.31-2.09 (m, 4H), 2.08 – 1.98 (m, 1H), 1.85 – 1.80 (m, 1H), 1.73 (s, 3H), 0.93 – 0.85 (m, 1H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 149.1, 135.8, 119.1, 109.1 85.3, 74.7, 40.0, 31.0, 29.5, 27.2, 20.7 ppm

IR (thin film): ʋmax = 3311, 3297, 2925, 2858, 2094, 1645 cm⁻¹
**MS** (70 ev, El): m/z (%): 146 ([M]^+), 60, 131 ([M-CH₃]^+), 100,

**HRMS** (El): calc d for C₁₁H₈ [M]^+: 146.1096, found: 146.1095

**Optical Rotation**: [α]₀^2₀ = −21.50 (c 0.4, CHCl₃)
2,3-Dialkynyl-1,3-butadienes from substituted alkynes and but-2-yne-1,4-diyldimethylcarbonate (Table 1)

![Chemical Reaction Diagram]

**Standard Procedure A**
A flask charged with but-2-yne-1,4-diyl dimethyl bis(carbonate) (200 mg, 1.00 mmol), Pd(PPh₃)₄ (57.0 mg, 0.05 mmol, 5 mol %) and Cul (19.0 mg, 0.10 mmol, 10 mol %) was evacuated and backfilled with N₂ twice. THF (2 mL) and diisopropylamine (1 mL) (degassed by N₂ sparging) were then added to the flask followed by alkyne (2.1 – 5.0 mol equiv). The reaction mixture was warmed to 30 °C and stirred for 1 – 3 hours until complete by ¹H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with PS 30-40 °C (3 x 20 mL), the organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar, due to volatility associated with some compounds). The crude product was then purified by flash column chromatography.

**Standard Procedure B**
A flask charged with but-2-yne-1,4-diyl dimethyl bis(carbonate) (200 mg, 1.00 mmol), Pd(PPh₃)₄ (57 mg, 0.05 mmol, 5 mol %) and Cul (19 mg, 0.10 mmol, 10 mol %) was evacuated and filled with N₂ twice. THF (2 mL) and diisopropylamine (1 mL) were freeze-pump-thaw degassed then added to the flask followed by alkyne (2.1 – 4.0 mol equiv). The reaction mixture was warmed to 30 °C and stirred for 1 – 3 hours until complete by ¹H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with diethyl ether (3 x 20 mL), the organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar, due to volatility associated with some compounds). The crude product was then purified by flash column chromatography.
7,8-Dimethylenetetradeca-5,9-diyne (11a)

Prepared according to Standard Procedure A as a colourless oil (130 mg, 61%) from 1-hexyne (246 mg, 3.00 mmol).

**Purification:** Flash chromatography (PS 30-40 °C, 100%).

$R_f = 0.54$ (PS 30-40, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 5.93$ (s, 2H), 5.57 (s, 2H), 2.37 (t, $J = 7.0$ Hz, 4H), 1.59-1.50 (m, 4H), 1.49-1.41 (m, 4H), 0.94-0.91 (m, $J = 7.5$ Hz, 6H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 129.4, 122.7, 93.3, 77.5, 30.5, 21.8, 18.8, 13.4$ ppm

IR (thin film): $\nu_{\text{max}} = 2957, 2930, 2872, 2861, 2224$ cm$^{-1}$

EIMS (70 ev, El): $m/z$ (%): 214 ([M]**+, 100), 199 ([M-Me]**+, 13)

HRMS (El): calcd for C$_{18}$H$_{32}$ [M]**+: 214.1722, found: 214.1721

11,12-Dimethylenedocos-9,13-diyne (11b)

Prepared according to Standard Procedure A as a colourless oil (256 mg, 79%) from 1-decyne (348 mg, 2.50 mmol).

**Purification:** Flash chromatography (PS 30-40 °C).

$R_f = 0.55$ (PS 30-40, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 5.94$ (s, 2H), 5.57 (s, 2H), 2.36 (t, $J = 7.1$ Hz, 4H), 1.56 (p, $J = 7.1$ Hz, 4H), 1.44 – 1.37 (m, 4H), 1.35 – 1.21 (m, 16H), 0.93 – 0.84 (m, 6H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 129.8, 122.8, 93.5, 77.2, 31.9, 29.2, 29.1, 29.0, 28.7, 22.7, 19.3, 14.1$ ppm

IR (thin film): $\nu_{\text{max}} = 2954, 2924, 2854, 2226$ cm$^{-1}$

EIMS (70 ev, El): $m/z$ (%): 326 ([M]**+, 100)
\textbf{HRMS (EI):} calcd for C_{24}H_{38}[M]^{+}: 326.2974 found: 326.2984

(5,6-Dimethylene-deca-3,7-diyn-1,10-diyldibenzene (11c)

Prepared according to \textbf{Standard Procedure A} as colourless oil (181 mg, 58\%) from but-3-yn-1-yldibenzenne (390 mg, 3.00 mmol).

\textbf{Purification:} Flash chromatography (2\% dichloromethane in PS 30-40 °C)

\( R_f = 0.33 \) (PS 30-40, 100\%)

\textbf{\( ^1H \) NMR (400 MHz, CDCl\textsubscript{3}):} \( \delta = 7.34 - 7.28 \) (m, 4H), 7.27 - 7.20 (m, 6H), 5.81 (s, 2H), 5.52 (s, 2H), 2.90 (t, \( J = 7.5 \) Hz, 4H), 2.68 (t, \( J = 7.5 \) Hz, 4H) ppm

\textbf{\( ^{13}C \) NMR (100 MHz, CDCl\textsubscript{3}):} \( \delta = 140.5, 129.2, 128.5, 128.4, 126.3, 123.3, 92.5, 77.9, 35.0, 21.5 \) ppm

\textbf{IR (thin film):} \( \nu_{\text{max}} = 3085, 3062, 3026, 2925, 2859, 2224 \text{ cm}^{-1} \)

\textbf{EIMS (70 ev, El):} \( m/z \) (%): 310 ([M]\textsuperscript{+}, 50), 309 ([M-H]\textsuperscript{-}, 100), 308 ([M-H\textsubscript{2}]\textsuperscript{+}, 90)

\textbf{HRMS (EI):} calcd for C_{24}H_{32} [M]^{+}: 310.1722, found: 310.1723

(3,4-Dimethylenhexa-1,5-diyn-1,6-diyl)dicyclohexane (11d)

Prepared according to \textbf{Standard Procedure A} as white solid (42 mg, 16\%) from ethynylcyclohexane (270 mg, 2.50 mmol).

\textbf{Purification:} Flash chromatography (PS 30-40 °C).

\( R_f = 0.26 \) (PS 30-40, 100\%)

\textbf{\( ^1H \) NMR (400 MHz, CDCl\textsubscript{3}):} \( \delta = 5.94 \) (s, 2H), 5.57 (s, 2H), 2.55 (tt, \( J = 8.8, 3.8 \) Hz, 2H), 1.87 - 1.80 (m, 4H), 1.78 - 1.68 (m, 4H), 1.56 - 1.45 (m, 6H), 1.38 - 1.28 (m, 6H) ppm
$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 129.5$, 122.8, 97.6, 77.2, 32.6, 29.6, 25.9, 24.8 ppm

IR (thin film): $\nu_{\text{max}} = 2932$, 2854, 2226 cm$^{-1}$

EIMS (70 ev, El): $m/z$ (%): 266 ([M]$^{+}$, 100)

HRMS (El): calcd for C$_{20}$H$_{30}$ [M]$^{+}$: 266.2035, found: 266.2039

M.P.: 81.9 – 83.2 °C

$1,1'$-(3,4-Dimethylenehexa-1,5-diyne-1,6-diyl)dicyclohex-1-ene (11e)

![Chemical Structure](image)

Prepared according to Standard Procedure A as a white solid (136 mg, 52%) from 1-ethynylcyclohex-1-ene (316 mg, 3.00 mmol).

**Purification:** Flash chromatography (PS 30-40 °C).

$R_v = 0.44$ (PS 30-40, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.18-6.16$ (m, 2H), 5.97 (s, 2H), 5.62 (s, 2H), 2.23-2.01 (m, 8H), 1.72-1.54 (m, 8H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 135.4$, 129.1, 123.3, 120.5, 94.3, 83.4, 29.1, 25.7, 22.3, 21.5 ppm

IR (thin film): $\nu_{\text{max}} = 2930$, 2858, 2195 cm$^{-1}$

EIMS (70 ev, El): $m/z$ (%): 262 ([M]$^{+}$, 100), 261 ([M-H]$^{+}$, 10)

HRMS (El): calcd for C$_{20}$H$_{22}$ [M]$^{+}$: 262.1722, found: 262.1719

M.P.: 123.4 – 124.6 °C

UV (Acetonitrile) $\lambda_{\text{max}}$ (log $\varepsilon$): 247 (4.2), 273 (4.1)

$(4S,4'S)$-1,1’-(3,4-Dimethylenehexa-1,5-diyne-1,6-diyl)bis(4-(prop-1-en-2-yl)cyclohex-1-ene) (11f)
Prepared according to **Standard Procedure A** as white solid (143 mg, 42%) from (S)-1-ethynyl-4-(prop-1-en-2-yl)cyclohex-1-ene (365 mg, 2.50 mmol).

**Purification:** Flash chromatography (PS 30-40 °C).

$R_f = 0.43$ (ps 30-40, 100%)

$^1H$ NMR (400 MHz, CDCl$_3$): $\delta = 6.19$ (s, 2H), 5.80 (s, 2H), 5.46 (s, 2H), 4.56 (d, $J = 11.9$ Hz, 4H), 2.15 – 1.94 (m, 8H), 1.92 – 1.83 (m, 2H), 1.69 – 1.64 (m, 2H), 1.56 (s, 6H) 1.38 – 1.28 (m, 2H) ppm

$^{13}C$ NMR (101 MHz, CDCl$_3$): $\delta = 149.2, 134.8, 129.0, 123.4, 120.2, 109.1, 94.0, 83.8, 40.1, 31.2, 29.6, 27.2, 20.8$ ppm

IR (thin film): $v_{max} = 3071, 3023, 2964, 2918, 2856, 2201$ cm$^{-1}$

EIMS (70 ev, El): $m/z$ (%): 342 ([M]$,^+$, 100)

HRMS (El): calcg for C$_{20}$H$_{30}$ [M]$^+$: 342.2348, found: 342.2341

**Optical Rotation:** $[\alpha]_D^{22} = -39.00$ (c 1.0, CHCl$_3$)

M.P.: 132.8 – 133.5 °C

UV (Acetonitrile) $\lambda_{max}$ (log $\varepsilon$): 214 (3.7), 248 (3.8), 274 (3.6)

(1$R$,1$R$,5$R$,5$S$)-3$R$-(3,4-Dimethylenehexa-1,5-diyne-1,6-diy1)bis(6,6-dimethylbicyclo[3.1.1]hept-2-ene) (11g)
Prepared according to **Standard Procedure A** as a yellow solid (163 mg, 49%) from (1R,5S)-3-ethynyl-6,6-dimethylbicyclo[3.1.1]hept-2-ene (377 mg, 2.50 mmol).

**Purification:** Flash chromatography (PS 30-40 °C).

**R_f** = 0.60 (PS 30-40, 100%)

**^1H NMR** (400 MHz, CDCl₃): δ = 6.05 – 6.03 (m, 2H), 5.95 (s, 2H), 5.63 (s, 2H), 2.43 (dt, J = 9.0, 5.7 Hz, 2H), 2.37 (dt, J = 10.6, 3.2 Hz, 2H), 2.31 (td, J = 5.6, 1.4 Hz, 2H), 2.14 – 2.09 (m, 2H), 1.32 – 1.24 (m, 10H), 0.91 (s, 6H) ppm

**^13C NMR** (100 MHz, CDCl₃): δ = 131.5, 129.7, 129.0, 123.3, 93.1, 85.7, 47.0, 40.1, 38.0, 32.2, 31.4, 26.0, 21.0 ppm

**IR** (thin film): ν max = 2988, 2953, 2920, 2886, 2827, 2161 cm⁻¹

**EI MS** (70 ev, El): m/z (%): 342 ([M]**, 100)

**HR MS** (El): calcd for C₂₀H₂₈O[M]**: 342.2348, found: 342.2349

**Optical Rotation:** [α]D²¹ = + 24.00 (c 1.0, CHCl₃)

**M.P.:** 125.1 – 128.9 °C

**UV** (Acetonitrile) λ max (log e): 227 (3.7)

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(3,4-Dimethylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (11h)

![Structure](image)

Prepared according to **Standard Procedure A** as a white solid (160 mg, 66%) from TMS acetylene (294 mg, 3.00 mmol).

**Purification:** Flash chromatography (PS 30-40 °C, 100%).

^1H NMR and ^13C NMR spectra matched those reported.

**^1H NMR** (400 MHz, CDCl₃): δ = 6.02 (s, 2H), 5.72 (s, 2H), 0.22 (s, 18H) ppm

**^13C NMR** (101 MHz, CDCl₃): δ = 128.6, 125.1, 101.3, 97.9, 0.2 ppm

(3,4-Dimethylenehexa-1,5-diyne-1,6-diyl)bis(triisopropylsilane) (11i)

![Structure](image)

**Purification:** Flash chromatography (PS 30-40 °C, 100%).

**^1H NMR** (400 MHz, CDCl₃): δ = 6.02 (s, 2H), 5.72 (s, 2H), 0.22 (s, 18H) ppm

**^13C NMR** (101 MHz, CDCl₃): δ = 128.6, 125.1, 101.3, 97.9, 0.2 ppm

S-12
Prepared according to Standard Procedure A as a white solid, (378 mg, 92%) from TIPS acetylene (401 mg, 2.20 mmol).

**Purification:** Flash chromatography (PS 30-40 °C).

\( R_f = 0.87 \) (PS 30-40, 100%)

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \( \delta = 6.10 \) (s, 2H), 5.73 (s, 2H), 1.10 (s, 42H) ppm

\(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)): \( \delta = 129.0, 125.1, 103.2, 94.2, 18.6, 11.3 \) ppm

IR (thin film): \( \nu_{max} = 2942, 2890, 2061, 1461 \text{ cm}^{-1} \)

EIMS (70 ev, El): \( m/z\) (%): 414 ([M]**, 100), 399 ([M-Me]**, 10)

HRMS (El): calcd for C\(_{20}\)H\(_{30}\)Siz [M]**: 414.3138, found: 414.3135

M.P.: 90.9 – 92.3 °C

(3,4-Dimethylenehexa-1,5-diyne-1,6-diyldibenzene (11j))

Prepared according to Standard Procedure A as a white solid (160 mg, 63%) from phenyl acetylene (510 mg, 5.00 mmol).

**Purification:** Flash chromatography (PS 30-40 °C, 100%).

\( R_f = 0.42 \) (PS 30-40, 100%)

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \( \delta = 7.54 – 7.51 \) (m, 4H), 7.37 – 7.35 (m, 6H), 6.21 (s, 2H), 5.85 (s, 2H) ppm

\(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)): \( \delta = 131.9, 129.1, 128.8, 128.6, 124.7, 123.1, 92.8, 86.2 \) ppm

IR (thin film): \( \nu_{max} = 3052, 3032, 2211, 1672 \text{ cm}^{-1} \)

EIMS (70 ev, El): \( m/z\) (%): 254 ([M]**, 100)

HRMS (El): calcd for C\(_{20}\)H\(_{15}\) [M]**: 254.1096, found: 254.1096

M.P.: 151.4 – 154.5 °C

UV (Acetonitrile) \( \lambda_{max}\) (log \( \epsilon\)): 268 (5.1), 281(5.0)
2,2’-(3,4-Dimethylenehexa-1,5-dyne-1,6-diyl)dipyridine (11k)

Prepared according to Standard Procedure B as an orange solid (100 mg, 39%) from 2-ethynylpyridine (412 mg, 4.00 mmol).

**Purification:** Flash chromatography (Et₂O, 100%).

Rₜ = 0.26 (Et₂O, 100%)

1H NMR (400 MHz, CDCl₃): δ = 8.62 (d, J = 4.8 Hz, 2H), 7.68 (td, J = 7.8, 1.8 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 7.28 - 7.21 (m, 2H), 6.30 (s, 2H), 5.96 (s, 2H) ppm

13C NMR (100 MHz, CDCl₃): δ = 150.1, 143.0, 136.2, 127.7, 127.2, 126.5, 123.1, 91.6, 85.4 ppm

IR (thin film): νₘₐₓ = 3057, 3011, 2965, 2924, 2854, 2217 1582 cm⁻¹

EIMS (70 ev, EI): m/z (%): 256 ([M]+**, 100)

HRMS (EI): calcd for C₁₉H₁₂N₂ [M]+*: 256.1000, found: 256.0996

M.P.: 88.0 – 89.7 °C

UV (Acetonitrile) λₘₐₓ (log e): 245 (4.3), 286 (4.4), 326 (3.6)

5,6-Bis([17-hydroxy-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)ethynyl]-2-methyl-3a,4,7,7a-tetrahydro-1H-isocindole-1,3(2H)-dione (S8)
A flask charged with but-2-yn-1,4-diyl dimethyl bis(carbonate) (50.0 mg, 0.25 mmol), Pd(PPh$_3$)$_4$ (15.0 mg, 0.013 mmol, 5 mol %) and Cul (5.0 mg, 0.025 mmol, 10 mol %) was evacuated and filled with N$_2$ twice. THF (1 mL) and diisopropylamine (0.5 mL) (degassed by bubbling N$_2$ through) were then added to the reaction mixture. Ethynylene S7 (273 mg, 0.88 mmol) was added to the reaction mixture which was warmed to 30 °C and stirred for 5 hours until complete by $^1$H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with diethyl ether (3 x 20 mL). The organic extracts were combined, dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was re-dissolved in Et$_2$O and filtered through a short pad of silica and the solvent was removed under reduced pressure (0 °C, 60 mbar). The solid residue was dissolved in CH$_2$Cl$_2$ (2 mL) and N-methyl maleimide (55.0 mg, 0.50 mmol) was added. The solution was stirred at 23 °C for 14 hours until complete by $^1$H NMR spectroscopic analysis. Solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (20% Et$_2$O in PS 30-40 °C to 100% Et$_2$O to 100% MeOH) to yield S8 (70 mg, 36%) as a yellow solid.

$R_f$ = 0.40 (100% EtOAc)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 5.70 (s, 2H), 3.07 (t, $J$ = 3.7 Hz, 2H), 2.94 (s, 3H), 2.65 – 2.17 (m, 16H), 2.30 – 1.91 (m, 4H), 1.86 – 1.49 (m, 14H), 1.45 – 1.30 (m, 6H), 1.17 (s, 6H), 1.11 – 0.91 (m, 4H), 0.86 (s, 6H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 199.6, 178.6, 178.5, 171.2, 171.2, 132.1, 132.0, 132.0, 131.9, 128.6, 128.5, 123.9, 123.8, 99.5, 99.4, 85.3, 85.2, 80.2, 80.2, 53.2, 50.2, 50.2, 47.1, 39.1, 39.1, 38.8, 38.8, 38.6, 36.2, 35.6, 33.9, 32.9, 32.8, 32.7, 31.4, 31.4, 29.4, 25.3, 23.2, 20.7, 17.4, 12.9 ppm

IR (thin film): $\nu_{max}$ = 3415, 2944, 2874, 1701, 1663 cm$^{-1}$

ESIMS (70 ev, ESI): $m/z$ (%): 808 ([M+Na]$^{+}$, 100), 786 ([M]$^{+}$, 35)

HRMS (ESI): calcd for C$_{35}$H$_{50}$O$_4$N [M]$^{+}$: 816.4728, found: 816.4735

M.P.: 117.4 – 119.6 °C
4,5-Dimethyleneocta-2,6-diyne-1,8-diol (11m)

Prepared according to Standard Procedure B as white solid (60 mg, 37%) from propargyl alcohol (123 mg, 2.20 mmol).

**Purification:** Flash chromatography (10% Et₂O in PS 30-40 °C -> 30% -> 50% -> 100%).

\[ R_f = 0.52 \text{ (Et}_2\text{O, 100%) } \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 6.01 \text{ (s, 2H), 5.69 (s, 2H), 4.45 (d, } J = 5.5 \text{ Hz, 4H), 2.02-1.94 (m, 2H) ppm} \]

\[ ^13C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 128.0, 125.0, 90.5, 82.0, 51.4 \text{ ppm} \]

\[ \text{IR (thin film): } \nu_{max} = 3285, 2925, 2853, 2161 \text{ cm}^{-1} \]

\[ \text{EIMS (70 eV, El): } m/z (\%): 162 ([M]^+, 40), 145 ([M-OH]^+, 55), 128 ([M-O_2H]^+, 100) \]

\[ \text{HRMS (El): calcd for C}_{10}\text{H}_{10}\text{O}_2 [M]^+: 162.0681, \text{ found: 162.0679} \]

**M.P.:** 118.7 – 121.1 °C
Synthesis of Substituted but-2-yne-1,4-diyldimethyl carbonates

**Standard Procedure C:**
A 0.1 molar solution of diol (1.0 mol equiv) in THF was cooled in an ice/acetone bath (−20 °C). n-BuLi (2.20 mol equiv) was added dropwise to the reaction mixture, which was stirred for 20 minutes. Methyl chloroformate (2.20 mol equiv) was added and the reaction mixture was warmed to 23 °C and stirred for 1 – 8 h until complete by ¹H NMR spectroscopic analysis. The reaction mixture was then quenched with sat. aq. ammonium chloride (20 mL) and extracted with dichloromethane (3 x 40 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

**Standard Procedure D:**
A 0.2 molar solution of diol (1.0 mol equiv) in CH₂Cl₂ was cooled in an ice bath (0 °C). DMAP (0.02 mol equiv) and i-Pr₂NEt (2.20 mol equiv) were added to the reaction mixture followed by drop wise addition of methyl chloroformate (2.20 mol equiv). The reaction mixture was then warmed to 23 °C and stirred for 12 – 16 h until complete by ¹H NMR spectroscopic analysis. The solvent was removed under reduced pressure and the solid residue was re-dissolved in Et₂O, washed with 1M aq. HCl (50 mL), water (2 x 100 mL) and brine (50 mL). The organic extract was then dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography.

**But-2-yne-1,4-diyldimethyl bis(carbonate) (10)**
Prepared according to **Standard Procedure D** as a colourless oil (6.80 g, 60%), from but-2-yne-1,4-diol.

**Purification:** short silica plug (100% CH$_2$Cl$_2$)

$^1$H NMR and $^{13}$C NMR spectra matched those reported.$^4$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 4.73$ (s, 4H), 3.77 (s, 6H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 155.3$, 81.1, 55.5, 55.4 ppm

**Dimethyl pent-2-yne-1,4-diyi bis(carbonate) (2a)**

\[ \text{MeO}_2\text{CO} \rightleftharpoons \text{OCO}_2\text{Me} \]

Prepared according to **Standard Procedure C** as an orange oil (280 mg, 33%) from known pent-2-yne-1,4-diol$^4$ (400 mg, 4.00 mmol).

**Purification:** Flash chromatography (20% Et$_2$O in PS 40 – 60 °C)

$R_f = 0.23$ (10% Et$_2$O in PS 40 – 60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 5.37$-5.31 (m, 1H), 4.75 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 1.53 (d, $J = 6.7$ Hz, 3H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 155.0$, 154.7, 85.0, 79.0, 64.0, 55.4, 55.2, 54.9, 21.0 ppm

IR (thin film): $\nu_{\text{max}} = 2994$, 2960, 1747 cm$^{-1}$

ESIMS (70 ev, ESI): $m/z$ (%): 239 ([M+Na]$^{+}$, 100)

HRMS (ESI): calcd for C$_9$H$_{12}$O$_3$Na [M]$^{+}$: 239.0526, found: 239.0519

**Dimethyl (1-phenylbut-2-yne-1,4-diyi) bis(carbonate) (2b)**

\[ \text{MeO}_2\text{CO} \rightleftharpoons \text{Ph} \rightarrow \text{OCO}_2\text{Me} \]

Prepared according to **Standard Procedure D** as an orange oil (1.66 g, 43%) from known 1-phenylbut-2-yne-1,4-diol$^4$ (2.27 g, 14.0 mmol).
**Purification:** Flash chromatography (20% EtO in PS 40 – 60 °C)

$R_f = 0.19$ (10% EtOAc in PS 40 - 60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): δ = 7.68 – 7.47 (m, 2H), 7.45 – 7.38 (m, 3H), 6.36 (s, 1H), 4.85 (d, $J = 1.7$ Hz, 2H), 3.84 (d, $J = 2.7$ Hz, 6H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 155.4, 155.0, 136.0, 129.6, 129.0, 128.0, 83.6, 81.8, 69.7, 55.7, 55.4 ppm

IR (thin film): $\nu_{\text{max}}$ = 3007, 2958, 2854, 1748 cm$^{-1}$

ESIMS (70 ev, EI): $m/z$ (%): 301 (M+Na)$^{++}$, 100

HRMS (ESI): calcd for C$_{14}$H$_{13}$O$_{12}$Na [M]$^{++}$: 301.0688, found: 301.0686

3-(9-((Methoxycarbonyl)oxy)-9H-fluoren-9-yl)prop-2-yn-1-yl methyl carbonate (2c)

Prepared according to **Standard Procedure C** as an orange oil (594 mg, 100%) from known 9-((3-hydroxyprop-1-yn-1-yl)-9H-fluoren-9-ol (400 mg, 1.69 mmol).

**Purification:** Flash chromatography (20% EtO in PS 40-60 °C)

$R_f = 0.45$ (10% EtO in PS 40 – 60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): δ = 7.83 (d, $J = 7.6$ Hz, 2H), 7.63 (d, $J = 7.5$ Hz, 2H), 7.43 (t, $J = 7.5$ Hz, 2H), 7.34 (t, $J = 7.5$ Hz, 2H), 4.79 (s, 2H), 3.78 (s, 3H), 3.71 (s, 3H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 154.9, 153.2, 142.7, 139.9, 130.3, 128.4, 125.6, 120.1, 83.8, 80.2, 79.0, 55.5, 55.1, 54.7 ppm

IR (thin film): $\nu_{\text{max}}$ = 3008, 2957, 2848, 1750 cm$^{-1}$

ESIMS (70 ev, ESI): $m/z$ (%): 375 (M+Na)$^{++}$, 100

HRMS (ESI): calcd for C$_{29}$H$_{24}$O$_{12}$Na [M]$^{++}$: 375.0839, found: 375.0830

3-(1-((Methoxycarbonyl)oxy)cyclohexyl)prop-2-yn-1-yl methyl carbonate (2d)
3 2,3-Diethynyl-1,3-butadienes

![Diagram of 2,3-Diethynyl-1,3-butadiene]

Prepared according to **Standard Procedure C** as an orange oil (200 mg, 28%) from known 1-(3-hydroxyprop-1-yn-1-yl)cyclohexan-1-ol\(^6\) (400 mg, 2.60 mmol).

**Purification:** Flash chromatography (20% Et\(_2\)O in PS 40-60 °C)

\( R_f = 0.09 \) (10% Et\(_2\)O in PS 40 – 60 °C)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 4.80 \) (s, 2H), 3.80 (s, 3H), 3.75 (s, 3H), 2.16 – 2.10 (m, 2H), 1.88 – 1.82 (m, 2H), 1.69 – 1.48 (m, 5H), 1.37 – 1.26 (m, 1H) ppm

\(^13\)C NMR (101 MHz, CDCl\(_3\)): \( \delta = 155.1, 153.3, 86.8, 80.1, 55.7, 55.1, 54.3, 36.7 \) (2 x C), 24.9, 22.5 ppm

**IR** (thin film): \( \nu_{\text{max}} = 2940, 2868, 1753 \) cm\(^{-1}\)

**ESIMS** (70 ev, El): m/z (%): 293 ([M+Na]\(^{+}\), 100)

**HRMS** (El): calcld for C\(_{18}\)H\(_{38}\)O\(_3\)Na [M]\(^{+}\): 293.1001, found: 293.1006

**Dimethyl (4-methylpent-2-yn-1,4-diyi) bis(carbonate) (2e)**

![Diagram of Dimethyl (4-methylpent-2-yn-1,4-diyi) bis(carbonate)]

Prepared according to **Standard Procedure C** as an orange oil (300 mg, 37%) from known 4-methylpent-2-yn-1,4-dioli\(^6\) (400 mg, 3.50 mmol).

**Purification:** Flash chromatography (20% Et\(_2\)O in PS 40 – 60 °C)

\(^1\)H NMR and \(^13\)C NMR spectra matched those reported\(^{10}\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 4.73, 3.76, 3.71, 1.64 \) ppm

\(^13\)C NMR (101 MHz, CDCl\(_3\)): \( \delta = 155.0, 153.3, 87.6, 77.9, 73.7, 55.5, 55.0, 54.22, 28.4 \) ppm

**meso-Hex-3-yn-2,5-diyl dimethyl bis(carbonate) (2f)**

S-20
3, 2,3-Diethynyl-1,3-butadienes

Prepared according to **Standard Procedure D** as a colourless oil (3.22 g, 80%), from commercially available (2R,5S)-hex-3-yne-2,5-diol (2.00 g, 17.5 mmol).

**Purification:** Flash chromatography (10% EtO in PS 40-60 °C)

\( R_f = 0.27 \) (10% EtO in PS 40 – 60 °C)

\(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)): \( \delta = 5.36 \) (q, \( J = 6.9 \) Hz, 2H), 3.80 (s, 6H), 1.53 (d, \( J = 6.7 \) Hz, 6H) ppm

\(^{13}\text{C} \text{NMR} \) (101 MHz, CDCl\(_3\)): \( \delta = 154.5, 83.0, 63.9, 54.7, 21.0 \) ppm

**IR** (thin film): \( \nu_{\text{max}} = 2993, 2960, 1746 \) cm\(^{-1}\)

**ESIMS** (70 ev, El): \( m/z \) (%): 253 ([M+Na]**, 100)

**HRMS** (ESI): calcd for C\(_{10}\)H\(_{18}\)O\(_2\)Na [M]**: 253.0663, found: 253.0676

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**Dimethyl (2-methylhex-3-yne-2,5-diyl) bis(carbonate) (2g)**

Prepared according to **Standard Procedure C** as an orange oil (151 mg mg, 20%) from known 2-methylhex-3-yne-2,5-diol\(^6\) (400 mg, 3.13 mmol).

**Purification:** Flash chromatography (20% EtO in PS 40 – 60 °C)

\( R_f = 0.17 \) (10% EtO in PS 40 – 60 °C)

\(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)): \( \delta = 5.37 \) (q, \( J = 6.7 \) Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 1.68 (s, 6H), 1.53 (d, \( J = 6.5 \) Hz, 3H) ppm

\(^{13}\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)): \( \delta = 154.7, 153.3, 85.9, 82.2, 73.9, 64.3, 54.8, 54.3, 28.6, 21.2 \) ppm

**IR** (thin film): \( \nu_{\text{max}} = 2993, 2958, 1748 \) cm\(^{-1}\)

**ESIMS** (70 ev, El): \( m/z \) (%): 267 ([M+Na]**, 100)
HRMS (ESI): calcd for C_{11}H_{16}O_{4}Na [M]^{+}: 267.0845, found: 267.0846

**Dimethyl (4-methyl-1-phenylpent-2-yne-1,4-diyI) bis(carbonate) (2h)**

![Diagram of 2h](image)s

Prepared according to **Standard Procedure C** as a colourless oil (440 mg, 68%) from known 4-methyl-1-phenylpent-2-yne-1,4-diol\(^4\) (400 mg, 2.10 mmol).

**Purification:** Flash chromatography (20% Et\(_2\)O in PS 40-60 °C)

\(R_f = 0.41\) (10% Et\(_2\)O in PS 40 – 60 °C)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.58 – 7.51\) (m, 2H), 7.40 -7.36 (m, 3H), 6.36 (s, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 1.72 (s, 6H) ppm

\(^1^3\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 154.8, 153.2, 136.1, 129.2, 128.6, 127.9, 88.5, 80.4, 73.9, 69.5, 55.0, 54.4, 28.6\) ppm

IR (thin film): \(v_{max} = 2992, 2957, 1747\) cm\(^{-1}\)

ESIMS (70 ev, ESI): \(m/z\) (%): 329 ([M+Na]^{+}, 100)


**2,5-Dimethylhex-3-yne-2,5-diyI dimethyl bis(carbonate) (2i)**

![Diagram of 2i](image)s

Prepared according to **Standard Procedure C** as a colourless oil (3.50 g, 97%), from commercially available 2,5-dimethylhex-3-yne-2,5-diol (2.00 g, 14.0 mmol).

**Purification:** Flash chromatography (10% Et\(_2\)O in PS 40-60 °C)

S-22
$R_f = 0.62$ (10% EtOAc in PS)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.75$ (s, 6H), 1.68 (s, 12H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 153.2, 84.9, 74.1, 54.1, 28.5$ ppm

IR (thin film): $\nu_{\text{max}} = 2992, 2957, 1750$ cm$^{-1}$

ESIMS (70 ev, ESI): $m/z$ (%): 277 ([M]$^+$, 70), 262 ([M-Me]$^+$, 100)

HRMS (ESI): calcd for C$_{12}$H$_{18}$O$_6$ [M]$^+$: 266.1001, found: 266.1001

4-(1-((Methoxycarbonyl)oxy)cyclohexyl)-2-methylbut-3-yn-2-yl methyl carbonate (2))

\[ \text{MeO}_2\text{CO} \]
\[ \text{Me} \]
\[ \text{Me} \]

Prepared according to **Standard Procedure C** as a colourless oil (503 mg, 65%) from known 1-(3-hydroxy-3-methylbut-1-yn-1-yl)cyclohexan-1-ol$^+$ (400 mg, 2.59 mmol).

**Purification:** Flash chromatography (20% Et$_2$O in PS 40-60 °C)

$R_f = 0.50$ (10% Et$_2$O in PS 40 – 60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.66$ (s, 6H), 2.11 – 2.05 (m, 2H), 1.73 – 1.66 (m, 2H), 1.60 (s, 6H), 1.58 – 1.45 (m, 5H), 1.23 – 1.15 (m, 1H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 153.3, 153.1, 87.4, 83.9, 77.7, 74.2, 54.3, 54.2, 36.8, 28.7, 25.1, 22.7$ ppm

IR (thin film): $\nu_{\text{max}} = 2939, 2862, 1750$ cm$^{-1}$

ESIMS (70 ev, ESI): $m/z$ (%): 321 ([M+Na]$^+$, 100)

2,3-Dialkynyl-1,3-butadienes from TMS acetylene and substituted but-2-yne-1,4-diylidimethyl carbonates (Table 2)

\[
\begin{align*}
\text{MeO}_2\text{CO} & \quad \text{R}_1 \quad \text{R}_2 \quad \text{R} \quad 10 \\
\text{COO}_2\text{Me} & \quad \text{R}_3 \quad 2\alpha \text{a}-\text{R}_4 \\
\text{Pd}(\text{PPh}_3)_2 (5 \text{ mol\%}) & \quad \text{CuI} (10 \text{ mol\%}) \\
\text{i-Pr}_2\text{NH/THF (1:2)} & \quad 30 ^{\circ}\text{C} \\
& \quad \text{R}_1 \quad \text{R}_2 \quad \text{R} \quad 12\text{a}-\text{l} \quad \text{R}_3 \quad \text{R}_4 \\
& \quad \text{R}_3 \quad \text{R}_4 \\
\end{align*}
\]

Standard Procedure E:

A flask charged with but-2-yne-1,4-diyl dimethyl bis(carbonate) (1.00 mol equiv Pd(PPh3)_2 (5 mol %) and CuI (10 mol %) was evacuated and backfilled with N₂ twice. THF (2 mL) and diisopropylamine (1 mL) (degassed by bubbling N₂ through) were then added to the flask followed by acetylene (3 mol equiv). The reaction mixture was warmed to 30 °C and stirred for 1 – 3 hours until complete by ¹H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with PS 30-40 °C (3 x 20 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified by flash column chromatography.

\((E)-(3\text{-Ethylidene}-4\text{-methylenehexa}-1,5\text{-diyne}-1,6\text{-diyl})\text{bis(trimethylsilane)} (12\text{a}),\)  
\((Z)-(3\text{-Ethylidene}-4\text{-methylenehexa}-1,5\text{-diyne}-1,6\text{-diyl})\text{bis(trimethylsilane)} (12\text{a})\)

\[
\begin{align*}
\text{Me}_3\text{Si} & \quad \equiv \quad \equiv \quad \text{SiMe}_3 \\
\text{Me} & \quad \equiv \quad \equiv \quad \text{SiMe}_3
\end{align*}
\]

12a(E:Z = 2:3), 43%
Prepared according to Standard Procedure E as a 1:1 mixture of isomers E and Z, (112 mg, 43%), from dimethyl pent-2-yne-1,4-diyl bis(carbonate) 2a (200 mg, 0.93 mmol) and TMS acetylene.

**Purification:** Flash chromatography (PS 30-40 °C).

**Isomer Determination:** The Z and E isomers were determined by reaction with N-methyl maleimide: the E compound reacted to form the Diels-Alder adduct while the Z compound did not.

**(E)-(3-Ethylidene-4-methylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12a)**

**Appearance:** colourless oil

1H NMR (400 MHz, CDCl₃): δ = 6.62 (q, J = 7.1 Hz, 1H), 5.93 (s, 1H), 5.60 (s, 1H), 2.01 (d, J = 7.1 Hz, 3H), 0.23 (s, 9H), 0.22 (s, 9H) ppm

13C NMR (101 MHz, CDCl₃): δ = 137.8, 128.6, 123.0, 122.8, 102.6, 102.0, 99.4, 97.3, 16.7, 0.0, -0.1 ppm

IR (thin film): ν_max = 2963, 2901, 2160, 1250 cm⁻¹

EIMS (70 eV, El): m/z (%): 260 ([M]⁺, 100), 245 ([M-CH₃]⁺, 95)


**(Z)-(3-Ethylidene-4-methylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12a)**

**Appearance:** white solid

1H NMR (400 MHz, CDCl₃): δ = 6.20 (q, J = 7.5 Hz, 1H), 5.75 (s, 1H), 5.74 (s, 1H) 1.98 (d, J = 7.5 Hz, 3H), 0.19 (s, 9H), 0.18 (s, 9H) ppm

13C NMR (101 MHz, CDCl₃): δ = 137.5, 127.6, 126.8, 121.8, 105.1, 104.0, 96.0, 92.1, 15.5, 0.0, -0.3 ppm

IR (thin film): ν_max = 2959, 2898, 2145, 1249 cm⁻¹

EIMS (70 eV, El): m/z (%): 260 ([M]⁺, 100), 245 ([M-CH₃]⁺, 100)


M.P.: 33.2 – 34.0 °C

**(E)-(3-benzylidene-4-methylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12b)**
3 2,3-Diethynyl-1,3-butadienes

 Prepared according to **Standard Procedure E** as a colourless oil, (201 mg, 89%) from dimethyl (1-phenylbut-2-yne-1,4-diyI) bis(carbonate) 2b (200 mg, 0.72 mmol) and TMS acetylene.

**Isomer Determination:** The E isomer in this mono phenyl series was determined by comparing \(^1\text{H} \text{NMR shifts and coupling constants with those in the mono-methyl series (12a)}\)

**Purification:** Flash chromatography (PS 30-40 °C)

\(R_f = 0.40\) (PS 30 – 40 °C, 100%)

\(^1\text{H} \text{NMR (400 MHz, CDCl}_3\text{): } \delta = 7.36-7.34 \text{ (m, 2H), 7.31 – 7.24 (m, 3H), 7.02 (s, 1H), 5.91 (s, 1H), 5.77 (s, 1H), 0.23 (s, 9H), -0.04 (s, 9H) ppm}\)

\(^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\text{): } \delta = 138.9, 136.0, 130.1, 129.0, 128.3, 128.2, 128.0, 121.6, 106.2, 103, 96.8, 95.1, 0.3, -0.1 \text{ ppm}\)

IR (thin film): \(\nu_{\text{max}} = 3024, 2959, 2898, 2141, 1248 \text{ cm}^{-1}\)

EIMS (70 ev, EI): \(m/z \text{ (%): 322 ([M]^{+}, 100), 307 ([M-CH}_3\text{]^{+}, 40)}\)

HRMS (EI): calcld for C\(_{20}\)H\(_{20}\)Si\(_2\) [M]^{+}: 322.1573, found, 322.1574

\((E)-(3\text{-methylene-2-(phenylethynyl)pent-1-en-4-yne-1,5-diyI})\text{dibenzene (5c)}\)

Prepared according to **Standard Procedure E** as a colourless oil, (70 mg, 40%) from dimethyl (1-phenylbut-2-yne-1,4-diyI) bis(carbonate) 2b (200 mg, 0.72 mmol) and phenyl acetylene.

**Isomer Determination:** The E isomer in this mono phenyl series was determined by comparing \(^1\text{H} \text{NMR shifts and coupling constants with those in the mono-methyl series (12a)}\)
**Purification:** Flash chromatography (10% CH₂Cl₂ in PS 30 – 40 °C)

R<sub>f</sub> = 0.28 (PS 30 – 40 °C, 100%)

**¹H NMR** (400 MHz, CDCl₃): δ = 7.54 – 7.45 (m, 4H), 7.37 – 7.29 (m, 5H), 7.26 – 7.17 (m, 4H), 7.13 (s, 1H), 7.09 – 7.01 (m, 2H), 6.02 (s, 1H), 5.86 (s, 1H) ppm

**¹³C NMR** (100 MHz, CDCl₃): δ = 138.0, 136.2, 131.9, 131.8, 130.1, 128.6, 128.6, 128.5, 128.3, 128.3, 128.1, 127.9, 123.6, 123.2, 122.0, 91.8, 90.9, 90.4, 88.2, 77.5 ppm

**IR** (thin film): ν<sub>max</sub> = 3058, 3029, 2923, 2205 cm⁻¹

**EIMS** (70 ev, EI): m/z (%):(%): 330 ([M]⁺, 100), 315 ([M-CH₃]⁺, 30)

**HRMS** (EI): calcld for C<sub>26</sub>H₁₈ [M]⁺: 330.1409, found, 330.1410

(E)-(2-(hex-1-yn-1-yl)-3-methylenenon-1-en-4-yn-1-yl)benzene (12d)

```
C₆H₅
      \__________\___E___\___C₆H₅
      \__________\_____/__________
            \__________\_____/__________
                  Ph            Ph
```

Prepared according to **Standard Procedure E** as a colourless oil, (144 mg, 70%) from dimethyl (1-phenylbut-2-yn-1,4-diyi) bis(carbonate) 2b (200mg, 0.72 mmol) and hexyne.

**Isomer Determination:** The E isomer in this mono phenyl series was determined by comparing **¹H NMR shifts and coupling constants** with those in the mono-methyl series (12a)

**Purification:** Flash chromatography (PS 30-40 °C)

R<sub>f</sub> = 0.60 (PS 30 – 40 °C, 100%)

**¹H NMR** (400 MHz, CDCl₃): δ = 7.44 (d, J = 7.5 Hz, 2H), 6.92 (s, 1H), 5.76 (s, 1H), 5.64 (s, 1H), 2.47 (t, J = 7.0 Hz, 2H), 1.71-1.60 (m, 2H), 1.60-1.51 (m, 2H), 1.36-1.28 (m, 3H), 1.02 (t, J = 7.3 Hz, 3H), 0.93-0.88 (m, 3H) ppm

**¹³C NMR** (100 MHz, CDCl₃): δ = 136.5, 136.2, 129.8, 129.2, 127.9, 127.7, 125.8, 123.3, 92.7, 91.4, 82.1, 79.5, 31.1, 30.7, 22.3, 22.1, 19.5, 19.2, 14.0, 13.9 ppm

**IR** (thin film): ν<sub>max</sub> = 3022, 2957, 2931, 2872, 2861, 2218 cm⁻¹

**EIMS** (70 ev, EI): m/z (%):(%): 290 ([M]⁺, 100)
HRMS (EI): calcd for C_{22}H_{30}[M]^+: 290.2935, found, 290.2041

(3-(9H-Fluoren-9-ylidene)-4-methylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12e)

Prepared according to Standard Procedure E as a colourless oil (194 mg, 49%) from 3-(9-((methoxycarbonyl)oxy)-9H-fluoren-9-yl)prop-2-yn-1-yl methyl carbonate 2c (200 mg, 0.57 mmol) and TMS acetylene.

Purification: Flash chromatography (PS 30-40 °C).

R_{f} = 0.33 (PS 30 – 40 °C, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.77 (d, $J$ = 7.8 Hz, 1H), 8.06 (d, $J$ = 7.9 Hz, 1H), 7.66 (t, $J$ = 7.9 Hz, 2H), 7.41 – 7.26 (m, 3H), 7.23 – 7.17 (m, 1H), 5.94 (d, $J$ = 1.3 Hz, 1H), 5.83 (d, $J$ = 1.3 Hz, 1H), 0.34 (s, 9H), 0.14 (s, 9H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 140.8, 140.4, 137.9, 136.9, 129.5, 129.1, 128.8, 128.1, 127.2, 127.1, 126.7, 125.3, 119.3, 119.3, 119.2, 107.8, 105.2, 102.6, 96.5, 0.25 (2xC) ppm

IR (thin film): $\nu_{max}$ = 3060, 2957, 2898, 2148, 2129, 1445, 1248 cm$^{-1}$

EIMS (70 eV, EI): m/z (%): 396 ([M]$^+$, 100), 381 ([M-CH$_3$]$^+$, 21), 322 ([M-C$_2$H$_5$Si]$^+$, 39)

HRMS (EI): calcd for C$_{22}$H$_{30}$Si$_2$ [M]$^+$: 396.1730, found: 396.1713

(3-Cyclohexylidene-4-methylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12f)

IR (thin film): $\nu_{max}$ = 3060, 2957, 2898, 2148, 2129, 1445, 1248 cm$^{-1}$

EIMS (70 eV, EI): m/z (%): 396 ([M]$^+$, 100), 381 ([M-CH$_3$]$^+$, 21), 322 ([M-C$_2$H$_5$Si]$^+$, 39)

HRMS (EI): calcd for C$_{22}$H$_{30}$Si$_2$ [M]$^+$: 396.1730, found: 396.1713
Prepared according to **Standard Procedure E** as a colourless oil (107 mg, 34%) from 3-(1-((methoxycarbonyl)oxy)cyclohexyl)prop-2-yn-1-yl methyl carbonate **2d** (200 mg, 0.74 mmol) and TMS acetylene.

**Purification:** Flash chromatography (PS 30-40 °C).

\[ R_f = 0.53 \text{ (PS 30 – 40 °C, 100%)} \]

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \(\delta = 5.69\) (d, \(J = 1.8\) Hz, 1H), 5.57 (d, \(J = 1.8\) Hz, 1H), 2.57-2.38 (m, 4H), 1.75-1.40 (m, 6H), 0.18 (bs, 18 H) ppm

\(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)): \(\delta = 153.7, 128.5, 127.2, 114.1, 104.9, 104.0, 97.4, 94.9, 34.7, 31.8, 28.1\) (2 x C), 26.7, 0.4, 0.2 ppm

IR (thin film): \(v_{max} = 2958, 2828, 2855, 2139\) cm\(^{-1}\)

\(\textbf{EIMS}\) (70 eV, EI): \(m/z\) (%): 314 ([M]++, 53), 299 ([M-Me]++, 100)

\(\textbf{HRMS}\) (EI): calcd for C\(_{16}\)H\(_{20}\)Si\(_2\) [M]++: 314.1886, found: 314.1890

\((3\text{-Methylene-4-(propan-2-ylidene)hexa-1,5-diyne-1,6-diyl)bis(trimethylsilane)}\) (12g)

![Image of chemical structure]

Prepared according to **Standard Procedure E** as a colourless oil (140 mg, 51%) from dimethyl (4-methylpent-2-yn-1,4-diyl) bis(carbonate) **2e** (200 mg, 0.87 mmol) and TMS acetylene.

**Purification:** Flash chromatography (PS 30-40 °C).

\[ R_f = 0.72 \text{ (PS 30 – 40 °C, 100%)} \]

\(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \(\delta = 5.70\) (s, 1H), 5.58 (s, 1H), 2.04 (s, 3H), 1.96 (s, 3H), 0.19 (d, \(J = 1.9\) Hz, 18H) ppm

\(^{13}\text{C NMR}\) (101 MHz, CDCl\(_3\)): \(\delta = 146.4, 128.7, 127.2, 117.1, 104.6, 104.2, 97.5, 95.4, 24.9, 21.9, 0.4, 0.2\) ppm

IR (thin film): \(v_{max} = 2959, 2900, 2141, 1248\) cm\(^{-1}\)

\(\textbf{EIMS}\) (70 eV, EI): \(m/z\) (%): 274 ([M]++, 82), 381 ([M-Me]++, 100)

\(\textbf{HRMS}\) (EI): calcd for C\(_{16}\)H\(_{20}\)Si\(_2\) [M]++: 274.1573, found: 274.1585
((3E,4E)-3,4-Diethyldenedehexa-1,5-diyne-1,6-diyld)bis(trimethylsilane) (12h),
((3Z,4E)-3,4-Diethyldenedehexa-1,5-diyne-1,6-diyld)bis(trimethylsilane) (12h),
((3Z,4Z)-3,4-Diethyldenedehexa-1,5-diyne-1,6-diyld)bis(trimethylsilane) (12h)

Prepared according to Standard Procedure E as a 1:1:1 mixture of three isomers (EE, ZE, ZZ), (173 mg, 63%), from 3-{9-(2R,5S)-hex-3-ynyl-2,5-diyldimethyl bis(carbonate) 2f (200 mg, 0.87 mmol) and TMS acetylene.

**Purification:** Flash chromatography (PS 30-40 °C).

**Isomer Determination:** The E/Z diastereomer was easily identified from its more complex 
$^1$H and $^{13}$C NMR spectra. The ZZ and EE isomers were identified by their reaction (or lack of reaction) with N-methyl maleimide. The EE compound reacted to form the Diels-Alder adduct while the ZZ compound did not.

((3E,4E)-3,4-Diethyldenedehexa-1,5-diyne-1,6-diyld)bis(trimethylsilane) (12h)

**Appearance:** white solid

$R_f = 0.88$ (PS 30 – 40 °C, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.53$ (q, $J = 7.1$ Hz, 2H), 1.98 (d, $J = 6.6$ Hz, 6H), 0.23 (s, 18H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 135.3, 123.0, 102.1, 100.2, 16.5, 0.1$ ppm

IR (thin film): $\nu_{max} = 2957, 2910, 2154, 1248$ cm$^{-1}$

**MS (70 ev, EI):** $m/z$ (%): 274 ([M]+, 100), 259 ([M-H]+, 33)

**HRMS (EI):** calcd for C$_{18}$H$_{20}$Si$_2$: [M]+: 274.1573, found: 274.1570

M.P.: 26.1 – 27.9 °C
((3Z,4E)-3,4-Diethylidenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12h)

Appearance: colourless oil

$R_f = 0.75$ (PS 30 – 40 °C, 100%)

$^1H$ NMR (400 MHz, CDCl₃): $\delta = 6.32$ (q, $J = 7.0$ Hz, 1H), 6.13 (q, $J = 7.5$ Hz, 1H), 1.97 (d, $J = 7.0$ Hz, 3H), 1.94 (d, $J = 7.5$ Hz, 3H), 0.20 (s, 9 H), 0.18 (s, 9H) ppm

$^{13}C$ NMR (101 MHz, CDCl₃): $\delta = 139.6$, 136.0, 122.0, 120.5, 105.7, 101.8, 100.8, 91.5, 16.3, 15.5, 0.0, -0.1 ppm

IR (thin film): $\nu_{\text{max}} = 2959, 2900, 2147, 1248$ cm⁻¹

EIMS (70 eV, EI): $m/z$ (%): 274 ([M⁺], 100), 259 ([M-CH₃]⁺, 40)

HRMS (EI): calcd for C₁₀H₂₀Si₂ [M⁺]: 274.1573, found: 274.1566

((3Z,4Z)-3,4-Diethylidenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12h)

Appearance: white solid

$R_f = 0.67$ (PS 30 – 40 °C, 100%)

$^1H$ NMR (400 MHz, CDCl₃): $\delta = 6.17$ (q, $J = 7.2$ Hz, 2H), 1.70 (d, $J = 7.2$ Hz, 6H), 0.17 (s, 18H) ppm

$^{13}C$ NMR (101 MHz, CDCl₃): $\delta = 137.6$, 119.8, 104.7, 91.8, 15.4, 0.0 ppm

IR (thin film): $\nu_{\text{max}} = 2959, 2899, 2141, 1248$ cm⁻¹

EIMS (70 eV, EI): $m/z$ (%): 274 ([M⁺], 100), 259 ([M-CH₃]⁺, 60)

HRMS (EI): calcd for C₁₀H₂₀Si₂ [M⁺]: 274.1573, found: 274.1578

M.P.: 36.1 – 38.2 °C

(E)-(3-Ethylidene-4-(propan-2-ylidene)hexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12i),

(Z)-(3-Ethylidene-4-(propan-2-ylidene)hexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) (12i)

12i [E:Z = 1:1], 31%
Prepared according to **Standard Procedure E** as a 1:1 mixture of two isomers (Z and E), (70 mg, 31%), from dimethyl (2-methylhex-3-yne-2,5-diyli) bis(carbonate) 2g (150 mg, 0.61 mmol) and TMS acetylene.

**Purification:** Flash chromatography (PS 30–40 °C).

**Isomer Determination:** The Z and E isomers in this trimethyl series were determined by comparing ¹H NMR coupling constants with those in the mono-methyl series (12a).

**(E)-(3-Ethylidene-4-(propan-2-ylidene)hexa-1,5-diyne-1,6-diyli)bis(trimethylsilane)**

(12I)

**Appearance:** colourless oil

Rf = 0.73 (PS 30 – 40 °C, 100%)

¹H NMR (400 MHz, CDCl₃): δ = 6.10 (q, J = 6.9 Hz, 1H), 2.02 (s, 3H), 1.95 (d, J = 7.0 Hz, 3H), 1.89 (s, 3H), 0.20 (s, 9H), 0.19 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 144.9, 138.7, 121.7, 116.9, 104.5, 102.1, 99.6, 96.5, 24.3, 21.5, 16.4, 0.1, 0.0 ppm

IR (thin film): νmax = 2959, 2909, 2853, 2143, 1248 cm⁻¹

EIMS (70 eV, EI): m/z (%): 288 ([M⁺], 100), 273 ([M-CH₃]⁺, 35)

HRMS (EI): calcd for C₃₇H₃₀Si₂ [M⁺]: 288.1730, found: 288.1721

**(Z)-(3-Ethylidene-4-(propan-2-ylidene)hexa-1,5-diyne-1,6-diyli)bis(trimethylsilane)**

(12I)

**Appearance:** white solid

Rf = 0.65 (PS 30 – 40 °C, 100%)

¹H NMR (400 MHz, CDCl₃): δ = 6.13 (q, J = 7.0 Hz, 1H), 2.03 (s, 3H), 1.75 (s, 3H), 1.67 (d, J = 7.1 Hz, 3H), 0.18 (s, 9H), 0.17 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 146.0, 137.1, 121.3, 113.9, 105.1, 103.4, 96.3, 91.1, 23.1, 21.0, 15.2, 0.0, -0.1 ppm

IR (thin film): νmax = 2959, 2908, 2857, 2139, 1248 cm⁻¹

EIMS (70 eV, EI): m/z (%): 288 ([M⁺], 100), 273 ([M-CH₃]⁺, 40)

HRMS (EI): calcd for C₃₇H₃₀Si₂ [M⁺]: 288.1730, found: 288.1723

M.P.: 34.1 – 36.5 °C
(E)-(3-Benzylidene-4-(propan-2-yldiene)hexa-1,5-diyne-1,6-diyi)bis(trimethylsilane) (12j)

Prepared according to **Standard Procedure E** as a colourless oil, (203 mg, 58%) from dimethyl (4-methyl-1-phenylpent-2-yn-1,4-diyi) bis(carbonate) 2h (200mg, 0.65 mmol) and TMS acetylene.

**Isomer Determination**: It was determined that this was the E isomer by comparing ¹H NMR coupling constants with the other compounds previously isolated.

**Purification**: Flash chromatography (PS 30-40 °C).

<table>
<thead>
<tr>
<th>Substance</th>
<th>Rf</th>
<th>Method</th>
<th>Conditions</th>
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<tr>
<td></td>
<td>0.65</td>
<td>Flash chromatography</td>
<td>PS 30 – 40 °C, 100%</td>
</tr>
</tbody>
</table>

¹H NMR (400 MHz, CDCl₃): \( \delta = 7.36 \) (d, \( J = 7.4 \) Hz, 2H), 7.31 – 7.25 (m, 2H), 7.24 – 7.18 (m, 1H), 6.89 (s, 1H), 1.99 (s, 3H), 1.63 (s, 3H), 0.22 (s, 9H), 0.12 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): \( \delta = 146.4, 139.0, 136.5, 129.3, 128.4, 128.1, 121.1, 115.1, 106.4, 103.6, 97.0, 94.4, 23.7, 21.5, 0.4, 0.4 \) ppm

IR (thin film): \( \nu_{max} = 2957, 2926, 2852, 2138, 1248 \) cm⁻¹

EIMS (70 eV, EI): \( m/z \) (%): 350 ([M⁺], 100), 335 ([M-CH₃⁺], 95)

HRMS (EI): calcld for C₂₂H₃₀Si₂ [M⁺]: 350.1886, found: 350.1887

(3,4-Di(propan-2-yldiene)hexa-1,5-diyne-1,6-diyi)bis(trimethylsilane) (12k)

S-33
Prepared according to **Standard Procedure E** as a white solid (210 mg, 70%) from 2,5-dimethylhex-3-yne-2,5-diy diethyl bis(carbonate) 2i (200 mg, 0.78 mmol) and TMS acetylene.

**Purification:** Flash chromatography (PS 30–40 °C).

$R_f = 0.93$ (PS 30 – 40 °C, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 2.01$ (s, 6H), 1.71 (s, 6H), 0.18 (s, 18H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 145.7$, 115.7, 104.08, 96.0, 23.1, 21.1, 0.2 ppm

IR (thin film): $\nu_{\text{max}} = 2963, 2903, 2067, 1248 \text{ cm}^{-1}$

EIMS (70 eV, EI): $m/z$ (%): 302 ([M]$^+$, 100), 287 ([M-Me]$^+$, 30)

HRMS (EI): calcd for C$_{18}$H$_{30}$Si$_2$: [M]$^+$: 302.1886, found: 302.1879

M.P.: 66.5 – 67.5 °C

(3-Cyclohexylidene-4-(propan-2-ylidene)hexa-1,5-diyne-1,6-diy)bis(trimethylsilane)

(121)

Prepared according to **Standard Procedure E** as a colourless oil (62 mg, 18%) from 4-((methoxycarbonyloxy)cyclohexyl)-2-methylbut-3-yn-2-yl methyl carbonate 2j (200mg, 0.67 mmol) and TMS acetylene.

**Purification:** Flash chromatography (ps 30-40 °C).

$R_f = 0.40$ (PS 30-40 °C, 100%)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 2.51 – 2.48$ (m, 2H), 2.18 – 2.13 (m, 2H), 2.00 (s, 3H), 1.73 (s, 3H), 1.66 – 1.61 (m, 2H), 1.57 1.50 (m, 4H), 0.17 (s, 18H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 152.6$, 145.6, 115.4, 112.6, 104.6, 103.8, 95.9, 95.6, 33.1, 31.3, 27.6, 27.3, 26.4, 23.2, 21.1, 0.2, 0.2 ppm

IR (thin film): $\nu_{\text{max}} = 2958, 2928, 2855, 2137, 1248 \text{ cm}^{-1}$

EIMS (70 eV, EI): $m/z$ (%): 342 ([M]$^+$, 100), 327 ([M-CH$_3$]$^+$, 23), 269 ([M- C$_3$H$_7$Si]$^+$, 96)

HRMS (EI): calcd for C$_{20}$H$_{32}$Si$_2$: [M]$^+$: 342.2199, found: 342.2197
(3,4-Dimethylenedeca-1,5-diyn-1-yl)trimethylsilane (14)

A flask charged with but-2-ynyl-1,4-diyln dimethyl bis(carbonate) (200 mg, 1.00 mmol), Pd(PPh₃)₄ (57 mg, 0.05 mmol, 5 mol %) and Cul (19 mg, 0.10 mmol, 10 mol %) was evacuated and filled with N₂ twice. THF (2 mL) and diisopropylamine (1 mL) (degassed by bubbling N₂ through) were then added to the flask followed by hex-1-yn (164 mg, 2.00 mmol). The reaction mixture was warmed to 30 °C and TMS acetylene (196 mg, 2.00 mmol) was then drop wise to the reaction mixture over 1 hour. The reaction mixture was then stirred for a further 3 hours, until complete by ¹H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with PS 30-40 °C (3 x 20 mL), the organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified by prep TLC (100% PS 30-40 °C) to afford compound 14 as a colourless oil (34 mg, 15%).

R<sub>f</sub> = 0.60 (PS 30-40, 100%)

¹H NMR (400 MHz, CDCl₃): δ = 6.02 (s, 1H), 5.94 (s, 1H), 5.69 (s, 1H), 5.59 (s, 1H), 2.37 (t, J = 7.0 Hz, 2H), 1.60 – 1.51 (m, 2H), 1.50 – 1.39 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H), 0.22 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 129.4, 129.0, 125.0, 123.4, 101.7, 97.7, 94.0, 77.0, 30.9, 22.1, 19.2, 13.7, 0.0 ppm

IR (thin film): ν<sub>max</sub> = 2959, 2933, 2873, 2162, 2141, 1250 cm⁻¹

MS (70 ev, El): m/z (%): 230 ([M⁺], 100), 215 ([M-CH₃]⁺, 52),

HRMS (El): calcd for C₁₃H₂₂Si [M⁺]: 230.1491, found: 230.1490

Note: this reaction also gives the symmetric products accounting for the 34% yield.
2-Methyl-5,6-dimethylene-8-(trimethylsilyl)octa-3,7-diyn-2-ol (15)

A flask charged with but-2-yne-1,4-diyl dimethyl bis(carbonate) (200 mg, 1.00 mmol), Pd(PPh₃)₄ (57 mg, 0.05 mmol, 5 mol %) and Cul (19 mg, 0.10 mmol, 10 mol %) was evacuated and filled with N₂ twice. THF (2 mL) and diisopropylamine (1 mL) (degassed by bubbling N₂ through) were then added to the flask followed by 2-methylbut-3-yn-2-ol (168 mg, 2.00 mmol). The reaction mixture was warmed to 30 °C and TMS acetylene (196 mg, 2.00 mmol) was added drop wise to the reaction mixture over 30 minutes. The reaction mixture was then stirred for a further 1.5 hours, until complete by ¹H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with diethyl ether (3 x 20 mL), the organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified by flash column chromatography, (10% diethyl ether in PS 30-40 °C) to yield compound 15 as a white solid (60 mg, 26%).

Rfrog = 0.82 (10% Et₂O in PS 30 – 40 °C)

¹H NMR (400 MHz, CDCl₃): δ = 6.01 (s, 1H), 5.96 (s, 1H), 5.70 (s, 1H), 5.66 (s, 1H), 1.58 (s, 6H), 0.22 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 128.9, 128.1, 125.0, 124.8, 101.4, 98.0, 97.3, 78.8, 65.7, 31.5, 0.0 ppm

IR (thin film): νmax = 3275, 2984, 2958, 2157, 1564, 1250 cm⁻¹

MS (70 ev, El): m/z (%): 232 ([M⁺]²⁺, 85), 217 ([M-CH₃]²⁺, 100)

HRMS (El): calcd for C₂₁H₂₀O₃Si [M⁺]: 323.1283, found: 323.1281

M.P.: 129.8 – 131.1 °C

Note: this reaction also gives the symmetric products accounting for the 26% yield.
Decomposition Studies and Dimerisations:

Decomposition Study Procedure:

1.00 molar solutions of each compound in C₆D₆ were generated and dispensed into small vials. The vials were capped and heated to 70 °C behind a blast shield. Every 5 minutes a vial was diluted with a known quantity (500 µL) of C₆D₆ and an ¹H NMR spectrum was obtained until an approximate half life was reached.

\[
((4\text{-Phenylbut-1-en-3-yn-2-yl})\text{cyclohex-1-ene-1,2,4-trilyl})\text{tris(ethyne-2,1-diyll)tribenzene (18)}
\]

and \((12,52)-1,2,5,6\text{-Tetrakis(phenylethynyl)cycloocta-1,5-diene (16)}\)
A solution of (3,4-dimethylenehexa-1,5-diyne-1,6-diyldibenzene (290 mg, 1.14 mmol) in benzene (1.00 mL) was placed in a vial. The vial was capped and heated to 70 °C (Caution: blast shield) for 6.5 hours. The solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (20% CH2Cl2 in PS 40 – 60 °C) to yield compound 18 as a colourless oil (35 mg, 12% isolated yield, 16% internal standard yield) and compound 16 as a white solid (81 mg, 28% isolated yield, 29% internal standard yield).

((4-(4-Phenylbut-1-en-3-yn-2-yl)cyclohex-1-ene-1,2,4-triyld)tris(ethyne-2,1-diyld))tribenzene (18)

**Appearance:** yellow oil

Rf = 0.95 (50% CH2Cl2 in PS 30 – 40 °C)

1H NMR (400 MHz, CDCl3): δ = 7.59-7.41 (m, 8H), 7.37-7.27 (m, 12H), 6.08 (d, J = 1.3Hz, 1H), 5.71 (d, J = 1.3Hz, 1H), 3.15-3.04 (m, 1H), 2.95-2.81 (m, 1H), 2.74 (d, J = 17.9Hz, 1H), 2.65-2.52 (m, 1H), 2.32-2.19 (m, 1H), 2.06-1.96 (m, 1H) ppm

13C NMR (101 MHz, CDCl3): δ = 135.3, 132.1, 132.0, 131.9, 128.7, 128.7, 128.6, 128.6, 128.5, 128.33, 125.9, 124.4, 123.8, 123.8, 123.6, 123.2, 122.5, 94.7, 94.4, 92.0, 90.9, 90.3, 90.2, 87.4, 85.9, 41.1, 40.9, 32.4, 28.8 ppm

IR (thin film): νmax = 3084, 3055, 3036, 2949, 2929, 2901, 2194, 2148 cm⁻¹

MS (70 eV, EI): m/z (%): 508 ([M⁺], 60)

HRMS (EI): calcd for C92H82 [M⁺]: 508.2191, found: 508.2196

(1Z,5Z)-1,2,5,6-Tetrakis(phenylethynyl)cycloocta-1,5-diene (16)

**Appearance:** yellow solid

Rf = 0.90 (50% CH2Cl2 in PS 30 – 40 °C)

1H NMR (400 MHz, CDCl3): δ = 7.50 – 7.46 (m, 8H), 7.31 – 7.27 (m, 12H), 2.90 (s, 8H) ppm

13C NMR (101 MHz, CDCl3): δ = 131.5, 128.2, 128.1, 128.0, 123.6, 93.9, 91.9, 32.8 ppm

IR (thin film): νmax = 3078, 3029, 2955, 2927, 2187, 1596 cm⁻¹

EIMS (70 eV, EI): m/z (%): 508 ([M⁺], 20), 277 ([M-C2OH2]⁺, 100),

HRMS (EI): calcd for C92H82 [M⁺]: 508.2199, found: 508.2196

M.P.: 90.8 – 91.7 °C

UV (Acetonitrile) λmax (log ε): 224 (4.0), 262 (4.1), 322 (3.9)

XRAY: recrystallized from CHCl3 via slow evaporation
((4-(4-(Trimethylsilyl)but-1-en-3-yn-2-yl)cyclohex-1-ene-1,2,4-triy)tris(ethyne-2,1-diy))tris(trimethylsilane) (19)
and (1Z,5Z)-1,2,5,6-Tetrakis((trimethylsilyl)ethynyl)cycloocta-1,5-diene (17)

A solution of (3,4-dimethylenehexa-1,5-diyne-1,6-diy)bis(trimethylsilane) (170 mg, 0.69 mmol, 1.00 mol equiv) in benzene (690 µL) was placed in a vial. The vial was capped and heated to 70 °C (Caution: blast shield) for 6.5 hours. The solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (20% CH2Cl2 in PS 40 – 60 °C) to yield compound 19 as a colourless oil (17 mg, 10% isolated yield, 12% internal standard yield) and compound 17 as a white solid (23 mg, 14% isolated yield, 18% internal standard yield).

((4-(4-(Trimethylsilyl)but-1-en-3-yn-2-yl)cyclohex-1-ene-1,2,4-triy)tris(ethyne-2,1-diy))tris(trimethylsilane) (19)

Appearance: colourless oil

Rf = 0.71 (20% CH2Cl2 in PS 30 – 40 °C)

1H NMR (400 MHz, CDCl3): δ = 5.89 (s, 1H), 5.56 (s, 1H), 2.73 (ddd, J = 17.9, 3.7, 2.0 Hz, 1H), 2.63 – 2.43 (m, 1H), 2.39 – 2.14 (m, 2H), 1.94 (ddd, J = 13.0, 10.9, 5.1 Hz, 1H), 1.76 – 1/60 (m, 1H), 0.28 – 0.10 (m, 36H) ppm

13C NMR (101 MHz, CDCl3): δ = 134.9, 126.6, 125.2, 123.5, 123.5, 107.7, 105.2, 105.0, 102.7, 99.3, 99.0, 97.1, 90.0, 40.5, 40.4, 32.0, 28.4, 0.4, 0.4, 0.4, 0.2 ppm

IR (thin film): vmax = 2959, 2906, 2170, 2143, 1248 cm⁻¹

ESIMS (70 ev, ESI): m/z (%): 492 ([M]+, 100), 477 ([M-CH3]+, 40), 476 ([M-CH3]+, 40), 464 ([M-CH3]+, 40)

(1Z,5Z)-1,2,5,6-Tetrakis[(trimethylsilyl)ethynyl)cycloocta-1,5-diene (17)

Appearance: white solid

$^1$H NMR and $^{13}$C NMR spectra matched those reported.$^8$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 2.64$ (s, 8H), 0.20 (s, 36H)

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 127.0$, 107.0, 98.9, 33.0, 0.4 ppm

4,4′-(3,4-Di(propan-2-ylidene)hexa-1,5-diyne-1,6-diyl)dibenzonitrile (21)

A flask charged with but-2-yne-1,4-diyi dimethyl bis(carbonate) (200 mg, 0.78 mmol), Pd(PPh$_3$)$_4$ (45 mg, 0.04 mmol, 5 mol %) and CuI (15 mg, 0.08 mmol, 10 mol %) was evacuated and backfilled with N$_2$ twice. THF (2 mL) and diisopropylamine (1 mL) (degassed by bubbling N$_2$ through) were then added to the flask followed by 4-ethylbenzonitrile (344 mg, 2.71 mmol). The reaction mixture was warmed to 30 °C and stirred for 5 hours, upon which it was deemed complete by $^1$H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with CH$_2$Cl$_2$ (3 x 20 mL). The organic extracts were combined, dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified by flash column chromatography (20% CH$_2$Cl$_2$ in PS 30-40 °C) to yield compound 21 as a white solid (120 mg, 33%).

$R_F = 0.18$ (20% CH$_2$Cl$_2$ in PS 30-40 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.57$ (d, $J = 8.4$ Hz, 4H), 7.49 (d, $J = 8.2$ Hz, 4H), 2.12 (s, 6H), 1.84 (s, 6H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 147.3$, 131.9, 131.8, 129.0, 118.7, 114.9, 110.9, 93.2, 90.4, 23.2, 21.3 ppm

IR (thin film): $\nu_{max} = 2924, 2849, 2227, 2169, 1596$ cm$^{-1}$

MS (70 ev, El): m/z (%): 360 ([M]+, 100), 345 ([M-C$_2$H$_5$]+, 45), 330 ([M-C$_2$H$_4$]+, 25)

HRMS (El): calcd for C$_{26}$H$_{20}$N$_2$: [M]+: 360.1626, found: 360.1629

M.P.: 87.1 – 87.8 °C
**UV** (Acetonitrile) $\lambda_{\text{max}}$ (log $\varepsilon$): 222 (4.4), 282 (4.5), 300 (4.5), 319 (4.5)

### 3,4-Diethynyl-2,5-dimethylhexa-2,4-diene (22)

(3,4-Di(propan-2-ylidene)hexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) **12k** (730 mg, 2.41 mmol) was dissolved in a 1:1 mixture of CH$_2$Cl$_2$ and methanol (200 mL). K$_2$CO$_3$ (5.00 g, 36.0 mmol) was added and the solution was stirred at 23 °C for 14 hours then diluted with H$_2$O (100 mL) and extracted with PS 30-40 °C (3 x 50 mL). The organic extracts were combined, dried over MgSO$_4$, filtered and the solvent was removed under vacuum (0 °C, 60 mbar). The crude product was then filtered through a short plug of silica eluting with PS 30-40 °C to yield compound **22** as a colourless solid (380 mg, 99%).

- **R$_f$** = 0.23 (PS 30-40, 100%)
- **$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 3.09 (s, 2H), 2.00 (s, 6H), 1.71 (s, 6H) ppm
- **$^{13}$C NMR** (101 MHz, CDCl$_3$): $\delta$ = 145.8, 114.3, 82.2, 79.2, 22.6, 20.6 ppm
- **IR** (thin film): $\nu_{\text{max}}$ = 3267, 2937, 2911, 2852, 2077 cm$^{-1}$
- **MS** (70 ev, EI): m/z (%): 158 ([M]**, 85), 143 ([M-CH$_3$]**, 50), 128 ([M-C$_2$H$_5$]**, 100),
- **HRMS** (EI): calcld for C$_{12}$H$_{14}$ [M]**: 158.1096, found: 158.1090
- **M.P.**: 54.2 – 55.3 °C
- **XRAY**: recrystallized from PS 30-40 °C via slow evaporation
3,12-Diethynyl-2,13-dimethyl-7,8-dimethylene-4,11-di(propan-2-ylidene)tetradeca-2,12-dien-5,9-diyne (23)

A flask charged with but-2-yne-1,4-diyl dimethyl bis(carbonate) (100 mg, 0.50 mmol), Pd(PPh₃)₄ (22 mg, 0.00 mmol, 5 mol %) and CuI (7.0 mg, 0.08 mmol, 10 mol %) was evacuated and backfilled with N₂ twice. THF (1 mL) and diisopropylamine (0.5 mL) (degassed by bubbling N₂ through) were then added to the flask followed by 3,4-diethynyl-2,5-dimethylhexa-2,4-diene (300 mg, 3.0 mmol). The reaction mixture was warmed to 30 °C and stirred for 1 hour, upon which it was deemed complete by ¹H NMR spectroscopic analysis. The reaction mixture was diluted with water (20 mL) and extracted with CH₂Cl₂ (3 x 20 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified by flash column chromatography (20% CH₂Cl₂ in PS 30-40 °C) to yield compound 23 as yellow oil (71 mg, 38%).

Rₛ = 0.38 (20% CH₂Cl₂ in PS 30 – 40 °C)

¹H NMR (400 MHz, CDCl₃): δ = 5.94 (s, 2H), 5.56 (s, 2H), 3.03 (s, 2H), 1.96 (s, 6H), 1.95 (s, 6H), 1.68 (s, 6H), 1.67 (s, 6H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 145.8, 144.7, 129.5, 123.3, 115.4, 114.8, 100.0, 91.4, 88.6, 82.8, 79.3, 23.0, 22.8, 20.9, 20.9 ppm

IR (thin film): νₓmax = 3291, 2981, 2907, 2850, 2193, 2087 cm⁻¹

MS (70 ev, El): m/z (%): 366 ([M]⁺, 10), 351 ([M-C₃H₆]⁺, 40), 321 ([M-C₆H₅]⁺, 100),

3,4-Dimethylenehexa-1,5-diyne (1)

(3,4-Dimethylenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) 12h (420 mg, 1.70 mmol) was dissolved in a 1:1 mixture of CH₂Cl₂ and methanol (60 mL). K₂CO₃ (2.50 g, 18.0 mmol) was added and the solution was stirred at 23 °C for 4 hours then diluted with H₂O (60 mL) and extracted with PS 30-40 °C (3 x 30 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then filtered through a short plug of silica eluting with PS 30-40 °C to yield compound 1 as a colourless oil (133 mg, 77%).

¹H NMR and ¹³C NMR spectra matched those reported.⁸

¹H NMR (400 MHz, CDCl₃): δ = 6.11 (s, 2H), 5.79 (s, 2H), 3.12 (s, 2H)

(2E,4E)-3,4-diethynyhexa-2,4-diene (26)

((3Z,4Z)-3,4-Diethylidenehexa-1,5-diyne-1,6-diyl)bis(trimethylsilane) 5h(EE) (280 mg, 1.02 mmol) was dissolved in a 1:1 mixture of CH₂Cl₂ and methanol (60 mL). K₂CO₃ (2.50 g, 18.0 mmol) was added and the solution was stirred at 23 °C for 10 hours then diluted with H₂O (100 mL) and extracted with PS 30-40 °C (3 x 50 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then filtered through a short plug of silica eluting with PS 30-40 °C to yield compound 26(EE) as a colourless solid (126 mg, 95%).
R_t = 0.62 (PS 30-40, 100%)

^1H NMR (400 MHz, CDCl3): δ = 6.62 (q, J = 7.3 Hz, 2H), 3.35 (s, 2H), 2.00 (d, J = 6.7 Hz, 6H) ppm

^13C NMR (101 MHz, CDCl3): δ = 135.9, 122.0, 84.8, 78.7, 16.3 ppm

IR (thin film): ν_max = 3268, 2936, 2914, 2849, 2103 cm^-1

MS (70 ev, El): m/z (%): 130 ([M]^+; 100), 115 ([M-CH3]^+; 48)

HRMS (El): calcd for C_{19}H_{10} [M]^+: 130.0783, found: 130.0783

M.P.: 37.6 – 37.9 °C

XRAY: recrystallized from PS 30-40 via slow evaporation

(2Z,4Z)-3,4-Diethynylhexa-2,4-diene (26)

\[ \text{Me}_2\text{Si} \quad \begin{array}{c} \text{Z} \\ \text{Me} \\ 12\text{h (ZZ)} \end{array} \quad \text{Me}\text{Si} \quad \begin{array}{c} \text{Z} \\ \text{Me} \end{array} \quad \text{K}_2\text{CO}_3 \quad \text{CH}_2\text{Cl}_2, \text{MeOH} \quad 23 \degree \text{C} \quad 100\% \quad \begin{array}{c} \text{ZZ} \\ \text{Me} \end{array} \quad 26 \text{(ZZ)} \]

((3E,4E)-3,4-Diethylidenehexa-1,5-diyne-1,6-diy)/bis(trimethylsilane) 5h(ZZ) (720 mg, 2.62 mmol) was dissolved in a 1:1 mixture of CH2Cl2 and methanol (200 mL). K2CO3 (7.00g, 50.7 mmol) was added and the solution was stirred at 23 °C for 14 hours then diluted with H2O (100 mL) and extracted with PS 30-40 °C (3 x 50 mL). The organic extracts we combined, dried over MgSO4, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then filtered through a short plug of silica eluting with PS 30-40 °C to yield compound 26(ZZ) as a colourless oil (340 mg, quantitative).

R_t = 0.58 (PS 30-40, 100%)

^1H NMR (400 MHz, CDCl3): δ = 6.24 (q, J = 7.1 Hz, 2H), 2.86 (s, 2H), 1.72 (d, J = 7.1 Hz, 6H ppm)

^13C NMR (101 MHz, CDCl3): δ = 138.4, 118.8, 83.4, 75.4, 15.4 ppm

IR (thin film): ν_max = 3288, 2913, 2853, 2093 cm^-1

MS (70 ev, El): m/z (%): 130 ([M]^+; 100), 115 ([M-CH3]^+; 48)

HRMS (El): calcd for C_{19}H_{10} [M]^+: 130.0783 found: 130.0784
Cyclic and Acyclic Oligomers:

5,6,11,12-Tetra(propan-2-ylidene)cyclododeca-1,3,7,9-tetrayne (24)
5,6,11,12,17,18-Hexa(propan-2-ylidene)cyclooctadeca-1,3,7,9,13,15-hexayne (25)

CuCl (187 mg, 1.89 mmol) and Cu(OAc)$_2$·H$_2$O (377 mg, 1.89 mmol) were dissolved in pyridine (15 mL) and the solution was heated to 60 °C. 3,4-Diethynyl-2,5-dimethylhexa-2,4-diene (100 mg, 0.63 mmol) dissolved in pyridine (5 mL) was added drop wise over either 5 or 16 hours. The reaction mixture was diluted with CH$_2$Cl$_2$ (60 mL), washed with 1M aq. HCl (2 x 100 mL) and water (3 x 100 mL). The organic extract was then dried over MgSO$_4$, filtered through a short pad of silica (eluting with CH$_2$Cl$_2$) and the solvent was removed under reduced pressure. The crude product was then purified by preparative TLC (10% CH$_2$Cl$_2$ in PS 30-40 °C).

5 hours: dimer 24 (2 mg, 2%), trimer 25 (20 mg, 20%)
16 hours: dimer 24 (18 mg, 18%), trimer 25 (13 mg, 13%)

5,6,11,12-Tetra(propan-2-ylidene)cyclododeca-1,3,7,9-tetrayne (24)

Appearance: yellow solid

$R_f = 0.51$ (20% CH$_2$Cl$_2$ in ps 40-60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 2.01$ (s, 12H), 1.67 (s, 12H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 144.0$, 118.3, 92.4, 81.9, 25.0, 22.2 ppm

IR (thin film): $\nu_{max} = 2929$, 2905, 2846, 2175, 2103, 1607 cm$^{-1}$

MS (70 ev, EI): $m/z$ (%): 312 ([M$^+$], 100), 282 ([M-C$_2$H$_4$]$^+$, 22)

HRMS (EI): calc'd for C$_{26}$H$_{36}$ [M$^+$]: 312.1878, found: 312.1878

M.P.: 127.7 – 129.6 °C

XRAY: recrystallized from CHCl$_3$ via slow evaporation

S-45
5,6,11,12,17,18-Hexa(propan-2-ylidene)cyclooctadeca-1,3,7,9,13,15-hexayne (25)

Appearance: yellow solid

R_f = 0.26 (20% CH_2Cl_2 in ps 40-60 °C)

^1H NMR (400 MHz, CDCl_3): δ = 2.04 – 1.99 (m, 18 H), 1.70 – 1.62 (m, 18H) ppm

^13C NMR (100 MHz, CDCl_3): δ = 147.1, 147.0 (2 x C), 146.7, 146.2, 116.1, 115.8, 115.8 (2 x C), 85.4, 81.5, 81.4, 81.4, 81.3 (2 x C), 78.0, 77.9, 77.9, 77.7 (2 x C), 77.5, 23.7, 23.6, 23.6, 23.5 (2 x C), 21.8, 21.7 (2 x C), 21.7 (2 x C), 21.6 ppm

IR (thin film): ν_max = 2990, 2907, 2849, 2122, 1610 cm⁻¹

ESIMS (70 ev, ESI): m/z (%): 491 ([M+Na]^+, 100)

HRMS (ESI): calcd for C_{36}H_{56}Na [M]^+: 491.2715, found: 491.2700

M.P.: 120.8 – 122.1 °C

XRAY: recrystallized from CHCl_3 via slow evaporation
X-Ray Crystallographic Data

All cif files can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif) using the reference numbers given below.

**Compound 16 – code MJS_I_132_octadiene**

Anisotropic displacement ellipsoid plot of molecule one of C_{60}H_{28} (16) with labelling of selected atoms. Ellipsoids show 30% probability levels. H atoms are shown as spheres of arbitrary radius. CCDC
Compound 26(EE) – code MJS_J_141

Anisotropic displacement ellipsoid plot of molecule one of C_{10}H_{10} (25 EE) with labelling of selected atoms. Ellipsoids show 30% probability levels. H atoms are shown as spheres of arbitrary radius. CCDC
Compound 22 – code MSL5_104

Anisotropic displacement ellipsoid plot of molecule one of C_{12}H_{14} (22) with labelling of selected atoms. Ellipsoids show 30% probability levels. H atoms are shown as spheres of arbitrary radius. CCDC
Compound 24 – code MJS_J_191

Anisotropic displacement ellipsoid plot of molecule one of C_{24}H_{34} (23) with labelling of selected atoms. Ellipsoids show 30% probability levels. H atoms are shown as spheres or arbitrary radius. CCDC
Compound 25 – code MJS_J_154_2

Anisotropic displacement ellipsoid plot of molecule one of C_{36}H_{56} (24) with labelling of selected atoms. Ellipsoids show 30% probability levels. H atoms are shown as spheres or arbitrary radius. CCDC

Acknowledgement: This research was undertaken on the MX1 beamline at the Australian Synchrotron, part of ANSTO.
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2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2-Diehydroyl-1,3-butadienes

S6

400 MHz, CDCl₃
2,3-Diethynyl-1,3-butadienes
3,3-Diethyl-1,3-butadienes
3 2,3-Diethynyl-1,3-butadienes

\[ \begin{align*}
\delta_{13} & = 1.38 \\
\delta_{19} & = 2.26 \\
\delta_{60} & = 3.21 \\
\end{align*} \]

\[ \text{1H NMR, CDCl}_3 \]

\[ 101 \text{ MHz} \]
3,2-Diethyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3
2,3-Diethyl-1,3-butadienes
3,2-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadienes
Diethynyl-1,3-butadiene

11h
400 MHz, CDCl₃
3,2-Diethyl-1,3-butadienes

$\text{Me}_3\text{Si}$

11h

101 MHz, CDCl$_3$
3,2,3-Diethynyl-1,3-butadienes

11i
400 MHz, CDCl₃
2,3-Diethynyl-1,3-butadienes
3, Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes

101 MHz, CDCl₃

Diagram of a molecular structure.
3, Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethyl-1,3-butadienes
3,2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2,3-Diethyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2-Diethynyl-1,3-butadienes
2e
400 MHz, CDCl₃

[Chemical structure image]
2f
400 MHz, CDCl₃
2f
101 MHz, CDCl₃

3
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2g, 101 MHz, CDCl₃
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadiene

$2i$

$400 \text{ MHz, CDCl}_3$
2,3-Diethynyl-1,3-butadienes
2j
101 MHz, CDCl₃
3,3-Diethynyl-1,3-butadienes

12a (E)
400 MHz, CDCl₃
3 2,3-Diethynyl-1,3-butadienes
12a (Z)
400 MHz, CDCl₃
3
2,3-Diethyl-1,3-butadienes
12b (E)
400 MHz, CDCl₃
2,3-Diethynyl-1,3-butadienes
3,2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2,3-Diethylyl-1,3-butadienes
12h (EZ)  
400 MHz, CDCl₃
2,3-Diethynyl-1,3-butadienes
Diethyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes

Diagram with chemical structure and spectroscopic data.
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3
2,3-Diethynyl-1,3-butadienes
Diethynyl-1,3-butadienes
Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,3-Diethynyl-1,3-butadienes

101 MHz, CDCl₃

TMS

17
3
2,3-Diethyl-1,3-butadienes

21
400 MHz, CDCl₃

S-151
3,2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
3,2-Diethynyl-1,3-butadienes

400 MHz, CDCl₃
3 2,3-Diethynyl-1,3-butadienes 233
2,3-Diethynyl-1,3-butadienes
3,2-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
26(ZZ)  
101 MHz, CDCl₃
3,3-Diethynyl-1,3-butadienes
2,3-Diethynyl-1,3-butadienes
Chapter Four:

Unlocking Acyclic $\pi$-Bond Rich Structure Space With Tetraethynylethylene–Tetravinylethylene Hybrids
4 Unlocking Acyclic $\pi$-Bond Rich Structure Space With Tetraethynylethylene–Tetravinylethylene Hybrids

Prelude

The manuscript has been submitted to the journal *J. Am. Chem. Soc.* on 17th August 2019. The other authors are Kelsey L. Horvath, Nicholas L. Magann, Dr Michael Gardiner and my supervisor Professor Michael S. Sherburn. This project was conceived, designed, evolved and drafted in collaboration with Kelsey L. Horvath, Nicholas L. Magann and Professor Michael S. Sherburn. The synthetic experiments were carried out by myself, Kelsey L. Horvath and Nicholas L. Magann. X Ray crystallography and analysis was carried out by Dr Michael Gardiner.

Specific contributions of Madison J. Sowden:
Optimised the five step synthesis of *gem*-DVDEE 6 from ethyl formate.
Optimised the five step syntheses of TVEE 7 and TEVE 3 from acrolein.
Developed the six step syntheses of Z-DVDEE 4 and E-DVDEE 5 from acrolein.
Optimised the two step synthesis of TEE 1 and successfully generated a crystal for X-Ray analysis with Nicholas L. Magann and Michael Gardiner (X-Ray crystallographer).
Synthesised phenyl substituted compounds 32, 33, 34, 35, 36, 37 and 38.
Conducted the air stability, acid stability, heat stability, neat stability, UV vis analysis and DSC experiments on the parent compounds (1, 2, 3, 4, 5, 6, 7) with Nicholas L. Magann.
Wrote and formatted the Supporting Information.

This chapter outlines the first synthesis of five novel TEE (tetraethynylethylene)/TVE (tetravinylethylene) hybrids. TVE and TEE have been synthesised previously and been reported to have vastly different reactivity profiles (see Chapter 1 for more details). TVE is an air/room temperature stable oil while TEE is an unstable crystalline solid at room temperature. Intrigued by this stark difference in reactivity we set out to synthesise a family of five hybrid TEE/TVE compounds and investigate their associated stability. These compounds are: TVEE, Z-DVDEE, E-DVDEE, *gem*-DVDEE and TEVE.
While the parent unsubstituted compounds have not previously been synthesised a number of substituted variants have. There are two examples of the TEVE framework, three of the E-DVDEE framework and one each of the Z-DVDEE and gem-DVDEE frameworks (for further information see Chapter one). No substituted examples of the TVEE framework have been previously reported.

The five parent hybrid compounds which are the focus of this chapter were synthesised via Sonogashira and Negishi cross-couplings on functionalised dibromo-olefins. The synthesis of both Z-DVDEE and E-DVDEE was non-trivial and was achieved through the development of the first stereoselective, single cross-coupling of a 1,1-dibromoalkene.
followed by the first *stereoselective* cross-coupling of a 3-bromo-4-alkynyl-1,3,5-hexatriene.

With the five hybrid structures in hand along with samples of TEE and TVE, an investigation into the stability and reactivity of these substrates was undertaken. The reactivity/stability of these compounds when exposed to a number of conditions including, air, acid and heat are reported.

Finally, a more stable series of phenyl substituted hybrid compounds was generated to showcase the versatility associated with the designed synthetic routes. These compounds were found to be robust, lasting for days when left neat at ambient temperature and in air.
Unlocking Acyclic π-Bond Rich Structure Space With Tetraethynylethylene–Tetravinylethylene Hybrids

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KEYWORDS: hydrocarbons • polymers • cross-coupling • carbon-rich materials

ABSTRACT: Literature reports describe tetraethynylethylene (TEE) as unstable but tetravinylethylene (TVE) as stable. The stabilities of these two known compounds are re-investigated, along with those of five unprecedented TEE/TVE hybrid compounds. The five new C-C hydrocarbons possess a core, tetrasubstituted C=C bond carrying all possible combinations of vinyl and ethynyl groups. A unified strategy is described for their synthesis, whereupon cross-conjugated ketones are dibromo-olefinated then cross-coupled. Due to an incorrect but nonetheless widely-held belief that acyclic π-bond rich hydrocarbons are inherently unstable, a standardised set of robustness tests is introduced. Whereas only TVE survives storage in neat form, all seven hydrocarbons are remarkably robust in dilute solution, generally surviving exposure to moderate heat, light, air and acid. The first X-ray crystal structure of TEE is reported. Sub-groups of hybrids based upon conformational preferences are identified through electronic absorption spectra and associated computational studies. The first substituted examples of the five TEE-TVE hybrids, which are significantly more robust than their unsubstituted parents, exhibit solid state core conformations that are consistent with computed lowest energy conformations of the unsubstituted TEE-TVE hybrids. These new acyclic π-bond rich systems have extensive, untapped potential for the production of stable, conjugated carbon-rich materials.

INTRODUCTION

Tetraethynylethylene (TEE, 1) and tetravinylethylene (TVE, 2), and their five hybrid structures 3-7 are amongst the smallest compounds that contain both through-conjugated and cross-conjugated segments (Figure 1). The Dedderich group disclosed the first synthesis of TEE 1 in 1994.1 Separate studies2-5 subsequently reported TEE 1 as unstable as a solid at 25 ºC–even in the absence of O2–and caution has been expressed regarding the potential for explosive decomposition of TEE.6 The first synthesis of TVE 2 was reported by Skattebol and co-workers in the 1960s.7 In 2014 we reported a one-step, multigram scale synthesis of TVE 2 involving the fourfold Stille coupling of tetraethylthiophene.8 At the same time, we noted the surprising stability of TVE 2, which is a liquid that survives storage on the bench at ambient temperature and pressure. TEE molecules with substituents at the four terminal alkyne positions are stable compounds.9 In fact, the tetrathienylene analog was the first TEE compound to be prepared in 1967.5 Many substituted analogues of TEE 1 have subsequently been prepared and studied, along with oligomeric TEE-based structures, expanded and cyclic systems, with much interest focused on their enormous potential in optical and electrical properties.10 Recent reports describe Glaser-type couplings of TEE 1 to prepare π-graphyne, a two-dimensional carbon allotrope with predicted applications in energy storage and molecular electronics.11

Interest in designed carbon allotropes and associated (generally hydrocarbon-based) model molecular materials comprising sp² and sp carbons is rapidly expanding.12 These efforts are focused on systems that rival the conducting, no band gap, “wonder material” graphenes,13 or exhibit specific band gaps required for devices such as semiconductors.

Figure 1. TEE 1 and TVE 2, and the five possible hybrid structures 3-7 that define the structural possibilities between them. Key: TEVE = tetraethynylethylene; DVDEE = divinylethylene; TVEE = trivinylethylene.

In contrast to the large, established body of important work focused on molecules carrying a TEE core, TVE 2 chemistry is in its infancy, with the first steps toward general synthetic approaches being published in 2014.4-7 These studies demonstrate that a compound with a tetravinylethylene unit serves as a hub for a sequence of up to four pericyclic reactions, each of which creates greater structural complexity. With a tetra cyclic and two stereocenters generated through this process, TVE compounds have great potential in step- and atom-economic target synthesis.

The reported difference in stability between TEE 1 and TVE 2 is stark, and their projected applications are in divergent fields, name-
ly functional materials and target synthesis. These facts prompted us to consider the structures that span the chasm of structural space between TEE 1 and TVE 2: structures which define the most fundamental combinations of sp^2 and sp carbon, hence serve as the foundations of applications in this field. Figure 1 depicts the five possible hybrids of TEE 1 and TVE 2, which feature both vinyl and ethynyl units attached to a tetrasubstituted central ethylene core. Structure 3 carries three ethynyl groups and one vinyl group, 7 carries three vinyl groups and one ethynyl group, and 4, 5 and 6 are the three constitutional and geometrical isomers carrying two ethynyl and two vinyl groups. Surprisingly, none of these five C_5 hydrocarbons have been previously prepared. We devised a method to access compounds 3-7 for two reasons: firstly, in order to provide critical information about structure-stability/reactivity relationships of fundamental acyclic conjugated hydrocarbons; and secondly, to deliver a significantly greater variety of core C_5 structures to encourage applications of TEE and TVE-based structures in new materials and target synthesis.

Whereas the parent hydrocarbons 3-7 have not been prepared, we were encouraged by reports of stable, substituted derivatives of (a) 3=DVDE 5 prepared by Diederich et al., Nelsen et al. and Yamamoto et al., and TEVE 3 by Hauptmann et al., Diederich et al. and Barenghi et al. and (c) of cyclo substituted analogs of gem-DVDE 6 described by Hoeg. No unsubstituted versions of 3=DVDE 4 or TVE 7 have been reported in the literature.

RESULTS AND DISCUSSION

CAUTION: TEE 1 is explosive when in neat crystalline form (vide infra). We strongly recommend that only small quantities be generated and that the compound is handled in solution to minimise the hazard of this highly reactive compound.

Samples of TEE 1 and TVE 2 were prepared by literature methods, involving one, two, fourfold cross-couplings of tetrabromoethylenes with vinyl and ethynyl nucleophiles, respectively. In principle, stepwise sequential couplings with the same vinyl and ethynyl nucleophiles would permit the synthesis of the new hydrocarbons 3-7. The requisite selective cross-couplings of tetrabromoethylenes, however, continue to prove elusive.

The approach that ultimately proved successful (Scheme 1) involved twofold cross-couplings of 1,1-dibromoalkanes. We were inspired by the pioneering work of the Diederich group, who developed this method to prepare substituted dendrines and TVEs. We have previously used this process for the synthesis of substituted dendrines and TVEs. On face value, therefore, the synthesis appears to be trivial. Closer inspection, however, reveals that unprecedented cross-coupling processes must be pioneered in order to achieve a synthesis of hybrids 3-7 using this approach. Firstly, whereas twofold sp2-sp2 cross-couplings of 1,1-dialkynyl-2,2-dibromoethylenes 8 into TEEs 9 and twofold sp2-sp2 cross-couplings of 1,1-dialkynyl-2,2-dibromoethylenes 10 into TVEs 11 are known, there are no examples of gem-DVDE 12 (Scheme 2) syntheses from 1,1-dialkynyl-2,2-dibromoethylenes 8. Secondly, whereas 1-alkynyl-1-alkynyl-2,2-dibromo-ethylenes 13 are known, these are no examples of cross coupling reactions involving them. Thirdly, whilst we have recently reported the stereoselective synthesis of [3]Hendrines 14, 19 from 1,1-dibromo-1,3-butadienes 16 by way of 3-bromo-1,2-nitroethylenes 17, the conversion of 1-alkynyl-1-alkynyl-2,2-dibromoethylenes 13 into 5- and 6-DVDE 20 and 21 would provide new insights into selective cross-coupling reactions. This approach raised several pertinent questions. Firstly, was mono-coupling of dibromide 13 feasible? If so, would the bromine cis- to the alkynyl substituent or the one cis- to the alkynyl substituent be replaced by a new C-C bond? Finally, if selective mono-coupling could be achieved, would it be possible to steer the outcome of the second coupling to obtain each geometrical isomer, 20 and 21?

With the main strategy defined and potential issues identified, one final tactical decision was made. We identified the TIPS- or TMSc-protected terminal alkynyl derivative of the C_5 hydrocarbon as the primary target, and perform a final stage desilylation to obtain the hybrid molecule 3-7. We adopted this approach since it was presumed that the trialkylsilylated derivatives would be both less volatile and more stable than the corresponding hydrocarbon 3-7. This prediction, which extrapolates information from literature reports of trialkylsilylated TEE derivatives, proved to be correct.

Scheme 1. The new transformations under scrutiny (shaded) and the closest precedent to them (unshaded).

Syntheses of the five new TEE/TVE hybrid hydrocarbons 3-7 are depicted in Scheme 2. gem-DVDE 6 was prepared by a route involving a twofold Negishi cross-coupling of known dibromide 22 with vinylbromide. Dibromides 24 and 25, prepared by Ramirez dibromo-olefination of reported cross-conjugated ketene precursors, were key intermediates en route to the four other
TEE/TVE hybrids 3, 4, 5 and 7. TVEE 7 and TEVE 3 were prepared by the now familiar twofold coupling reaction from TIPS precursors 28, in the former case a Negishi coupling with vinylstannic bromide and in the latter case a Sonogashira process with TMS-acetylene. The final two hybrids, Z/DVDEE 4 and E/DVDEE 5 were the most challenging to prepare and, as detailed above, required the development of the most interesting chemistry. Diiodo 28 underwent a selective cross-coupling with vinylstannic bromide at the bromine cis- to the existing vinyl group, generating bromostannene 28. In a subsequent reaction catalyzed by \( \text{PdCl}_2(\text{dpdf}) \), this compound underwent Negishi coupling with the organostannane derived from TMS-acetylene to form the \( Z \)-configured nitrene-dyne 29, the product of stereoreversion. With \( \text{PdCl}_2(\text{dpdf}) \) as precatalyst, the same precursor 28 underwent a Sonogashira coupling with TMS-acetylene to give 3, the product of stereoreversion. The conversion of chromadiene 25 into bromostannene 28 is unprecedented: there are neither examples of substrates of this type in the literature, nor couplings akin to this. The stereoinvertive Sonogashira coupling of bromostannene 28 into protected \( Z \)-DVDEE 30 is also without precedent.\(^{19}\) In the former case, we propose that a complexation of \( \text{Pd}(0) \) with the adjacent vinyl group promotes oxidative insertion into the cis-disposed C-Br bond. Either recomplexation to the axial C-Br bond of 25 is sterically disfavored by the presence of the TMS group, or the resulting \( \pi \)-complex positions the \( \text{Pd}(0) \) species less optimally for oxidative insertion.

**Scheme 2. Synthesis of TEE 1, TVE 2 and hybrids 3-7.**

![Scheme 2](image)

**Figure 2. X-ray crystal structure of TEE 1 highlighting associations in the solid state through face-face stacking (3.459(3) Å) along the \( b \) axis (a) that is offset due to tilting (26.21(4)°). The stacks, in turn, arrange efficiently (b) viewed down the \( a \) axis) via two distinct types of CH/π interactions (disorder is removed for clarity).**

UV-vis absorption spectra of the seven hydrocarbons 1-7 are depicted in **Figure 3**, which shows three groups of molecules, which are color-coded accordingly: (1) in red, TVE 2; and compounds 6 and 7 which exhibit broad absorptions at 280-300 nm and 220-230 nm; (2) in blue, compounds 3, 4 and 5, which show two distinct, sharper absorption maxima between 300-320 nm and fine structure in their absorptions around 220 nm; and (3) in black, TEE 1, which exhibits a uniquely complex set of absorptions. The longer wavelength absorptions are attributable to the \( \delta \) electron chromophores and the shorter wavelength ones (for compounds 2-7) to \( \pi \) systems.\(^{20}\)
Figure 3. UV-visible absorption spectra of hydrocarbons 1-7 (acetoni-
trile solvent, 43°C).

Computational studies reveal that the group of three compounds which give rise to broad absorption bands (2, 6 and 7, red in Figure 3) are distinct from those that give sharper spectra (3, 4 and 5, blue in Figure 3). The lowest energy conformations of the five new hy-
brid structures were located computationally and are depicted in Figure 4. The reported, non-planar calculated conformations of TVE 2 and the essentially in-plane molecular structure from the X-ray crystal structure analysis of TEE 1 (Figure 2) were replicated computationally. Three of the five hybrid structures, namely TVE 3, 5, DVDEEE 4 and DVDEEE 5 prefer a single, in-plane confor-
mation (Figure 4, top), germ-DVDEEE 6 and TVE 7 prefer non-planar conformation (Figure 4, bottom), with the latter being reminiscent of the calculated lowest energy conformation of TVE 2.

Figure 4. MP2/cc-pVTZ lowest energy conformations of the five new hybrids and TVE. The three above the line are planar; the three below are non-planar.

All 1,3-butadiene residues in the three planar TEE-TVE hybrids 3, 4 and 5 are s-trans. Their preference for the conformations de-
picted in Figure 4 is strong. For example, the second lowest energy conformation of TVE 3 has a skew s-trans 1,3-butadiene (twisted 18° from planarity) and lies a substantial 19.1 kJ/mol higher in energy than that shown in Figure 4 (see the SI for details).

In the preferred, C2 symmetric conformation of germ-DVDEEE 6, the [3]-endodihene (3-methylene-1,4-pentadiene) moiety adopts a skew s-trans-s-trans conformation, with the skew s-trans-gauche conformation only 4.1 kJ/mol higher in energy. Interestingly, the parent [3]-dendohene prefers the skew s-trans-gauche confor-
mation over the skew s-trans-s-trans conformation by 3.7 kJ/mol. To cause this reversal in conformational preference, either the ethynyl substituents in germ-DVDEEE 6 destabilize the skew s-trans-gauche conformation through steric buttressing, or perhaps the skew s-trans-s-trans conformation is stabilized through conjugation.

The lowest energy conformation of TVE 3 is non-planar and C2

TVE 7 prefers a conformation which mimics that of TVE 2, but with a gauche-oriented vinyl group replaced by an ethynyl group. The second lowest energy conformation of TVE 7 (see the SI for details) lies 8.5 kJ/mol higher in energy and has the orientations of the two vinyl groups of the gem-dienyl portion of the molecule reversed.

Thus, in summary, more well-defined UV-vis absorption spectra are generated by the less conformationally flexible molecules 2, 6 and 7, which strongly prefer a single in-plane conformation, whereas the broad absorption bands result from molecules 3, 4 and 5, which have several conformations close in energy to the global minimum, none of which are planar.

As mentioned in the introduction, solid samples of TEE 1 are re-
portedly explosive. Our results confirm these accounts. On one oc-
casion, a ca. 0.5 mg sample in an aluminum cup exploded while being carried in a gloved hand, leaving a charred-like dusting on the glove.8 We assume that solid samples of TEE 1 undergo rapid exothermic intermolecular addition-polymerization, in a similar manner to that proposed for other polyynes.7 TEE 1 is most likely amongst hydrocarbons 1-7 in this regard. We recommend that small quantities of TEE 1 be handled in dilute solution to minimize risk. No such issues were encountered with the remaining hydro-
carbons 2, 7, which presumably is a manifestation of their higher C(sp2)C(sp) ratio, hence greater stability. Differential scanning calorimetry traces for neat samples of compounds 2-7 are included in the Supporting Information. TEVE 3 shows an exothermic peak at the lowest temperature (62°C), EDDVDEEE 5 has the highest (166°C) and the remainder fall in the range 99–110°C.

We recognize that solely providing a synthetic blueprint for new, potentially valuable s-bond-rich acyclic hydrocarbons is unlikely to lead to their immediate use by the community, because there is an incorrect but widely-held assumption that all such compounds are inherently unstable. We propose that the fears of hesitant research-

Evidently, s-bond-rich acyclic hydrocarbons have the potential to react/decompose under a wide variety of conditions. We consid-
er that exposure to light, heat, oxygen and acid are the most signifi-
cant ones in a typical laboratory setting. Thus, we performed a se-
nies of systematic investigations upon these compounds, both as neat samples and as dilute solutions in common solvents, in order to provide quantitative information on their survival. It is important to note that these studies are not focused on identifying the mech-

isms and/or kinetics of specific decomposition processes. In many cases, neither decomposition products nor processes are easily identified. Instead, the primary purpose is to provide empiri-
cal experimental data that establishes conditions required for com-
pound survival. The results of these tests are depicted in Table 1, and are divided into two broad classes: those performed on samples held in dilute solution (columns A-D) and those performed on neat samples (columns E and F). Substrates that decompose in dilute solution will generally (but not always) involve processes that are first order in hydrocarbon, whereas dimerization/oligomerization/polymerization processes will be favored for neat samples.

Table 1. Stability testing on the seven hydrocarbons 1-7 (green = unchanged; red = >90% decomposition; amber = conversion to <80%).

<table>
<thead>
<tr>
<th>Compound</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEE</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
</tr>
<tr>
<td>TVE</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
<td>0.020 M</td>
</tr>
<tr>
<td>1</td>
<td>green</td>
<td>green</td>
<td>green</td>
<td>green</td>
<td>red</td>
<td>red</td>
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<td>red</td>
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<td>5</td>
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<tr>
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<td>green</td>
<td>green</td>
<td>green</td>
<td>red</td>
<td>red</td>
</tr>
</tbody>
</table>

As can be seen from the data in columns E and F, moderate levels of decomposition are observed upon storage of neat samples of hybrids 4-7, and the most alkyne-rich structures 1 and 3 show complete decomposition. Storage at -20 °C slows down the rate of decomposition but generally with insufficient effectiveness to permit long-term storage in this manner.

Since each of the hydrocarbons 1-7 carries, in a Z-disposition about its central tetrasubstituted C=C unit: (a) a pair of C=C(CH) groups and/or (b) a pair of -HC=CH chains; and/or (c) a C=C=CH group and a -HC=CH group, these systems can undergo Bergmann cycloaromatization, [6π]-6π-electrocyclization, and Hopf cycloaromatization, respectively. To our knowledge, these are the first structures to contain the requisite functionality for competition between these three related reactions. The primary decomposition pathway of TVE 2, TVEE 7 and ZDVDEE 4 on heating in dilute solution is 6π-electrocyclization. We have previously noted that the electrocyclization of TVE 2 is more facile than that of substrates lacking additional vinyl groups and this trend is followed with substrates carrying ethynyl groups (thermal 6π-electrocyclizations generally require temperatures of ≥140 °C). We presume that the faster electrocyclization of TVE 2 (complete conversion after 2 h at 120 °C) than Ztrienes 4 and 7 (ca. 25-50% conversion under the same conditions) is due, at least in part, to the presence of two equivalent Z-trienes in TVE 2.

Thermal Hopf-cycloaromatizations of acyclic Z-dienynes usually need temperatures well in excess of 200 °C; hence the stability of ZDVDEE 5 and geno-DVDEE 6 in dilute solution at 120 °C is expected. Bergmann cycloaromatization of acyclic Z-enynes proceeds at temperatures similar to Hopf electrocyclizations. Since the substrate with an internal competition between Bergmann cycloaromatization and 6π-electrocyclization, namely ZDVDEE 4, shows no signs of cycloaromatization, we assume that the mechanism of thermal decomposition of other molecules containing Z-enynes, specifically TEE 1 and TVE 3, does not involve this process.

The aforementioned 6π-electrocyclization products are the only ones identified, with intractable mixtures of (presumably) polymeric products being formed in all other cases. We strongly suspect that these other decomposition pathways are initiated by electrophilic and radical additions to the hydrocarbons, and that these undesired pathways are promoted when samples are more concentrated. Evidence for this proposal comes in the form of exposure of neat samples of TVE 7 to air and TFA. On bubbling air through a neat sample of TVE 7, 66% decomposition of the hydrocarbon was witnessed after 10 minutes, and 90% decomposition was seen on exposure to TFA for 1 h. Negligible decomposition was seen for comparable exposures to dilute solutions of the hydrocarbon (see earlier discussion, and Table 1, columns B and C).

With unsaturated hydrocarbons, it is often found that unsaturated molecules are less persistent than substituted analogs. In the final phase of this study, we investigated if this is true of the TEE-TVE hybrids. Scheme 3 shows the preparation of tetrasubstituted analogues of the five TEE-TVE hybrids in which a phenyl group resides at each of the four alkyne and (Z) alkenic termini. As discussed in the introduction, substituted analogs of some TVE-TVE hybrids have been reported. Nonetheless, all TVE-TVE hybrids depicted in Scheme 3 are novel.
Known 1,1-dibromoalkane 31, and new building block 32, prepared through Ramirez olefination of the known cross-conjugated diphenyl-eneones, underwent twofold Sonogashira couplings with phenylacetylene to deliver tetraphenyl analogs of gem-DVDEE and TVEE, 33 and 34, respectively. Twofold Negishi coupling of dibromide 32 with excess Etsuynol zinc bromide with [PdCl2(dpff)] as precatalyst gave tetraphenyl TVEE 35. Tetraphenyl Z-DVDEE 37 was accessed from dibromide 32 by a two-step sequence that involved firstly, a Z-selective Negishi coupling with the same nucleophile but catalyzed by [Pd(PPh3)4] to afford monobromide 36. This outcome follows the general trend of the first example, with less substituted reagents (Scheme 2, 23-28). A subsequent stereocentred Negishi coupling under Ph conditions with the alkynylzinc reagent derived from phenylacetylene gave Z-DVDEE 37, which was isomerized cleanly into Z-DVDEE 38 with catalytic amounts of molecular iodine.

All five tetraphenyl TEE/TVE hybrids 33, 34, 35, 37, and 38 were solids that proved to be significantly more stable than their unsubstituted parent compounds, surviving storage on the bench in air and ambient light for several days without measurable decomposition. Tetraphenyl TEE 39 and tetraphenyl TVE 40 have been previously reported, as have their X-ray crystal structures. Molecular structures from single crystal X-ray analyses of new hybrids 34 and 33 along with previously reported structures 39 and 40 are depicted in Figure 5, which demonstrates that the new hybrid molecules share conformational traits with their "parent" TEE and TVE structures.

Figure 5. Molecular structures from single crystal X-ray analyses of Ph-
TEE 34 and Ph-gem-DVDEE 33 (right) and those of the known
Ph-TEE 39 and Ph-TVE 40 (left).

Both Ph-TEE 39 and Ph-TVE 34 (this work) have planar acyclic C60 cores, which are fully consistent with, respectively: (a) that from single crystal X-ray analysis of the parent TEE 1 (Figure 2); and (b) the computed minimum energy conformation of the parent TVE 2 (Figure 4). The 8a,8b/TIPS analog of 8a,8b-TMS-β-
DVDEE 30 (Scheme 1) also has a planar C60 core structure (see SI for details of this X-ray structure) with a trans,1,3,5-hexadiene residue, as does a dibenzyl, d-tert-butyl β-DVDEE compound reported earlier by Yamamoto. Once again, the conformations of the C60 cores from these X-ray crystal structures are fully consistent with the computed minimum energy conformation of the parent B-
DVDEE 5 (Figure 4).

Both Ph-TEE 40 and Ph-gem-DVDEE 33 (this work) exhibit non-planar conformations in their C60 cores. The lowest energy conformation of unsubstituted TVE 2 (Figure 4) is not mimicked in the X-ray crystal structure of Ph-TVE 40 but it is nonetheless similar to that of the computed structure exhibits skew anti-gauche conformation at both ends but the X-ray structure of the tetraphenyl analog has one skew anti-gauche end and one skew anti-anti end. The X-ray structure of Ph-gem-DVDEE 33 has a C60 core conformation that is qualitatively the same as the computed lowest energy conformation of the parent molecule, with a skew anti-anti conformation gem-diakene end.

One can envisage scenarios in which either crystal packing forces or substituents would lead to differences in observed computed conformations. Nonetheless, the consistency seen here between theory and experiment across a wide range of structures is conspicuous.

CONCLUSION

In summary, the first chemical syntheses of five related through-
conjugated/cross-conjugated C60 hydrocarbons has been achieved. These structures, along with those of TEE and TVE, represent the fundamental arrangements of sp2 and sp3 carbons in the majority of carbon-based conductors. As such, this work serves as a foundation for applications in this field.

The need to synthesise TVE/TEE hybrids has led to the development of unprecedented synthetic transformations of wider value to the community. Specifically, new regio- and stereoselective cross-coupling variations have been uncovered, which merit de-
ted analysis, optimization and generalization. While studies are ongoing, the methods described herein have been shown to permit the synthesis of both the parent systems and terminally-substituted, tetraphenyl analogs.

The stability of each of the seven unsaturated hydrocarbons has been documented experimentally through the implementation of a series of robustness tests, which will have broader value for those interested in preparing and deploying fundamentally new molecules.

The first X-ray crystal structure of TEE 1 has been obtained, and an explosive decomposition pathway for this molecule has been uncovered. TVE 2 is the only one of the seven hydrocarbons that can be stored as a neat sample at room temperature. Importantly, all seven hydrocarbons can be stored in dilute solution at room temperature in ambient light without fear of decomposition. Each of the five new hybrid hydrocarbons 3-7 are more stable than TEE 1 towards air, and more stable than TVE 3 towards acid. These findings demonstrate the manageable nature of these new substances.

Every substituted TEE, TVE, and hybrid compound carrying a phenyl group at each of the four chain ends is stable as a neat solid at room temperature in air and ambient light.

The conformational behavior of the seven unsubstituted systems has been related to their UV-visible absorption spectra. X-ray crystal structures of the phenyl-substituted systems are broadly consistent with the lowest energy conformations of the unsubstituted congeners. Overall, the structural requirements for in-plane conformations, hence optimal conjugation, has been verified. This fundamental information is essential to the use of these structures in carbon-rich conducting materials.

This study represents the foundations upon which new carbon-rich materials can be designed and constructed, and new acrylic α- bond rich hydrocarbons can be exploited.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: XXXXX.

*Full experimental details, characterisation data, 1H and 13C NMR spectra, X-ray crystallographic and computational studies (PDF).

X-ray crystal structure of substituted DTEVE 2 (CCDC: 1925888) (CIF)
X-ray crystal structure of TEE 5 (CCDC: 1942489) (CIF)
X-ray crystal structure of Phenyle TVE 3 (CCDC: 1942590) (CIF)
X-ray crystal structure of Ph3-TEVE 3 (CCDC: 1942591) (CIF)

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Funding Sources
This work was supported by the Australian Research Council (DP160100322).

Notes
The authors declare no competing financial interest.

ACKNOWLEDGMENT
We warmly thank Dr Kim Roper (ANU) and Mr William Bolokou (ANU) for preliminary experiments and Dr Hidaki Onogi (ANU) for assistance with HPLC separations. Molecular structures from single crystal X-ray analyses and computed structures were visualised using CRYSTALS.16b, C. Y. Legault, Université de Sherbrooke, 2009 (http://www.crystrain.org).

ABBREVIATIONS
TVE, tetraethylethylene; TVE, tetraethylvinylene; TVE, tetra-ethylen(vinyl)ethylene; DVEDE, divinylethylene; TVEVE, tri-(vinyl)ethylene; TIPS, triisopropylsilyl; TMS, trimethylsilyl; DBA, dibenzyldimethylsulfoxide; dppf, 1,1′-bis(diphenylphosphino)ferrocene; TBABF4, tetra-a-butyrammonium fluoride; UV-vis, ultraviolet-visible; rt, room temperature.

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(m) See the Supporting Information for details.


(o) In principle, ene-diyne–sp2-sp2 cross-couplings of 1,1-diaikynyl-2,2-dibromoethanes could also be used here. Challenges with the preparation of the parent 1,1-divinyl-2,2-dibromoethene caused us to focus on this alternative approach.


(s) Stereoretentive and stereo-invertive Negishi coupling of 2-bromo-1,3-butanediols are known: (a) X. Yang, B. Hu, M. Qian, E. Negishi, Clean inversion of configuration in the Pd-catalyzed cross-coupling of 2-bromoo,1,3-dienes, J. Am. Chem. Soc. 2003, 125, 13659-13677; (b) X. Yang, M. Qian, Q. Su, E. Negishi, Highly stereoselective synthesis of (1R)-2-methyl-1,3-dienes by palladium-catalyzed cross-selective –cross-coupling of 1,1-dibromo-1-alkenes with allylic reagents Angew. Chem. Int. Ed. 2004, 43, 2259-2263; (c) reference 23.

(t) Y. Kurosaki, Y. Kazh, Operationally simple and efficient workup procedure for TBAP-mediated desilylation: application to halohydrin synthesis, Org. Lett. 2007, 9, 2569-2572.

(u) The crystals examined deoxo-plate at minimum ambient temperature. They were brought to the microscope cold and selection was done within a minute or so at ambient temperature with partial coloration of the crystals. After ca. 5 mins at ambient
temperature they no longer diffracted. A number of crystals were mounted, screened and stored in liquid nitrogen between screening attempts. This allowed the best crystal to be chosen. The needle-shaped crystals each showed evidence of twinning/not being single which could not be handled with twinning routines. Nevertheless, the diffraction data of the main component yielded good quality metrics, albeit the small crystals diffracted only to moderate resolution with long collection times. See the following section of the main text of the manuscript for further information on the stability of TEE 1.

These UV-vis spectra are consistent with those previously reported. For TVE 2, see reference 6; for TEE 1, see reference 1.

(a) 4- and 2-1,3,5-hexatriene show three absorptions at 245, 250 and 265 nm (J. C. H. Wea, P. L. de Beenuxiti, H. J. Smit, J. Sci. New preparation of 1,3,5-hexatriene and the separation of its geometrical isomers, J. Am. Chem. Soc. 1960, 82, 2537-2540); (b) 4- and 2-hexa-1,5-dien-3-yne show two absorptions at 250 and 262 nm (W. H. Okamara, F. Sontheimer, J. Am. Chem. Soc. 1967, 89, 5991-5992); (c) hexa-1,3,5-dien-5-yne gives a single absorption at 252 nm (F. Sontheimer, D. A. B. Bee-Ehrain, Y. Gassot Unsatyrated mac-
rocyclic compounds. XVIII. The prototropic rearrangement of linear 1,5-diyne to conjugated polyen-yn, J. Am. Chem. Soc. 1961, 73, 1680-1685).


CAUTION: TEE 1 is explosive when in neat crystals form. We strongly recommend that only small quantities be generated and that the compound is handled in solution to minimize the hazard of this highly reactive compound. It’s important to note that only 0.5 mg was once handled at the time of the explosion and the worker was not harmed. We presume that heat from the worker’s hand was involved in the rapid decompensation process. NMR and MS analysis of the residue gave no evidence for the formation of fullerences.


31 Percentage decompositions and detailed methods are provided in the Supporting Information. For an excellent, general review of these and related reactions, see R. K. Mohamed, P. W. Peterson, J. V. Abagian, Concerted reactions that produce diradicals and metastable electronic, steric, conformational, and kinetic control of cycloromanization processes, Chem. Rev. 2013, 113, 7689-7729.

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For another X-ray crystal structure of a substituted TVEE compound, see reference 19.
TEE/TVE Hybrids
Supporting Information for

Unlocking Acyclic $\pi$-Bond Rich Structure Space With Tetraethynylethylene–Tetravinylethylene Hybrids

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General Methods

NMR Spectroscopy

$^1$H NMR spectra were recorded at 400 MHz using a Bruker AVANCE 400 spectrometer or at 600 MHz using a Bruker AVANCE 600 spectrometer. Residual proto-solvent peaks were used as an internal reference for $^1$H NMR spectra (CDCl$_3$ $\delta$ 7.26 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 spectra were recorded at 101 MHz using a Bruker AVANCE 400 spectrometer or at 175 MHz using a Bruker AVANCE 700 spectrometer. Solvent peaks were used as an internal reference for $^{13}$C NMR spectra (CDCl$_3$ $\delta$ 77.0 ppm). Assignment of carbon signals was assisted by HSQC and HMBC experiments. The following abbreviations (or combinations thereof) are used to denote $^1$H NMR multiplicities: s = singlet, bs = broad singlet, d = doublet, dd= doublet of doublets, t = triplet, m = multiplet.

Infrared Spectroscopy

IR spectra were recorded on a Perkin–Elmer UATR Two spectrometer as a thin film or solid.

Mass Spectrometry

Low-resolution EI mass spectra were recorded on an Agilent HP 6890 gas chromatograph/mass spectrometer with a 7683 series injector fitted with a Phenomenex Zebron ZB-1 column (15 m length x 0.25 mm internal diameter x 0.25 µm film thickness) using EI+ ionization mode at 70eV or a Finnigan Polaris Q ion trap mass spectrometer using electron impact (EI+) ionization mode at 40 or 70 eV. High-resolution EI mass spectra were recorded on a VG Autospec mass spectrometer operating at 70 eV. Low-resolution ESI mass spectra were recorded on a Micromass ZMD spectrometer using electrospray (ESI+) ionization mode. High resolution ESI mass spectra were recorded on a Waters LCT Premier time-of-flight (TOF) spectrometer using electrospray ionization (ESI+).

Melting Points

Melting points were measured on a Stanford Research Systems Optimelt Automated Melting Point System and are uncorrected.
Experimental Procedures, Reagents, and Glassware
Reactions were conducted under a positive pressure of dry nitrogen in heat gun-dried glassware and at room temperature, unless specified otherwise. Anhydrous solvents were either obtained from commercial sources or dried according to the procedure outlined by Grubbs and co-workers.1 Commercially available chemicals were used as purchased, or where specified, purified by standard techniques.2

Chromatography
Analytical thin-layer chromatography was conducted with aluminum-backed silica gel 60 F254 (0.2 mm) plates supplied by Merck, and visualized using UV fluorescence (λmax = 254 nm), or developed using KMnO4 or p-anisaldehyde stains, followed by heating. Flash chromatography employed Merck Kieselgel 60 silica gel (230–400 mesh). Solvent compositions are given in %. PS 40–60 °C refers to petroleum spirits, boiling point fraction 40–60 °C. PS 30–40 °C refers to petroleum spirits, boiling point fraction 30–40 °C.

X-ray Crystallography
Single crystal X-ray data was collected on a SuperNova (Dual Source) diffractometer using a SuperNova (Cu or Mo) X-ray radiation source or on the MX1 beamline at the Australian Synchrotron.3 Crystallographic Structures were solved using CrysAlis PRO.

Ultraviolet-Visible Spectroscopy
UV-Vis spectra were recorded using a Shimadzu UV-Visible 2450 spectrometer.

HPLC
Preparative HPLC was performed using a Waters 600E instrument on a Waters XBridge Prep C18 OBD 5 μm, (150 x 19 mm ID) column unless otherwise stated.

Microwave
Reaction conditions invoking microwave irradiation were carried out in a CEM Discover SP microwave synthesis system with an explorer autosampler.

DSC
Decomposition temperatures of the hybrid TEE/TVE compounds were measured at a heating rate of 5 °C/min using a TA Q20 V24.11 Build 124 instrument.
Synthetic Route to 4-Ethynyl-3-vinylhexa-1,3-dien-5-yne (6)

The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

1,5-Bis(triisopropylsilyl)penta-1,4-dyn-3-ol (S2)

Prepared by modification of a procedure by Diederich. A solution of TIPS acetylene (12.7 mL, 56.8 mmol, 2.5 mol equiv) in THF (15 mL) was cooled in a 0 °C ice bath. n-BuLi (1.2M in hexane, 41.2 mL, 49.9 mmol, 2.2 mol equiv) was added dropwise over 10 minutes to the reaction mixture. The reaction mixture was then stirred in the 0 °C bath for a further 30 minutes before being cooled in a −78 °C dry ice/acetone bath. Ethyl formate (22.2 mL, 22.7 mmol) was then added and the reaction mixture was stirred at −78 °C for a further 30 minutes. The solution was then warmed to 0 °C and stirred for 2 hours. The reaction mixture was quenched with sat. aq. ammonium chloride solution (100 mL) and extracted with EtOAc (3 x 100 mL). The organic extracts were combined, dried over MgSO4, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 40-60 °C to 10% EtOAc in PS 40-60 °C) to give the title compound S2 as a pale yellow oil (6.90 g, 77%).

1H NMR and 13C NMR spectra matched those reported.
1H NMR (400 MHz, CDCl3): δ = 5.11 (d, J = 7.9 Hz, 1H), 2.13 (d, J = 7.9 Hz, 1H), 1.17-0.86 (m, 42 H) ppm

13C NMR (101 MHz, CDCl3): δ = 104.6, 86.0, 53.3, 18.8, 11.4 ppm

1,5-Bis(triisopropylsilyl)penta-1,4-diyne-3-one (S3)

![Reaction Scheme]

Prepared by modification of a procedure by Diederich.4
To a solution of alcohol S2 (6.90 g, 17.6 mmol) in CH2Cl2 (150 mL) was added celite (8.00 g) and pyridinium chlorochromate (7.60 g, 35.1 mmol, 2 mol equiv). The solution was stirred at 23 °C for 3 hours. The reaction mixture was filtered through a short pad of silica eluting with CH2Cl2 (200 mL). The solvent was removed under reduced pressure to give the title compound S3 as a bright yellow solid (5.19 g, 75%).

1H NMR and 13C NMR spectra matched those reported.4

1H NMR (400 MHz, CDCl3): δ = 1.11-1.10 (m, 42H) ppm

13C NMR (101 MHz, CDCl3): δ = 160.2, 105.6, 97.9, 18.7, 11.3 ppm

(3-(Dibromomethylene)penta-1,4-diyne-1,5-diyi)bis(triisopropylsilane) (22)

![Reaction Scheme]

Prepared by modification of a procedure by Diederich.4
A solution of CBr4 (8.80 g, 26.6 mmol, 2 mol equiv) in CH2Cl2 (200 mL) was cooled in a 0 °C ice bath. PPh3 (13.9 g, 53.1 mmol, 4 mol equiv) was then added in portions to the reaction mixture over five minutes (CAUTION: Exotherm). The solution was allowed to stir for 30 minutes before ketone S3 (5.19 g, 13.3 mmol) was added. The reaction mixture was warmed to 23 °C and stirred for 1 hour. The reaction mixture was poured onto cold stirring PS 40-60 °C (600 mL) and stirred for 10 minutes. The solution was filtered through a short pad of silica
eluting with PS 40-60 °C. The solvent was removed under reduced pressure to give the title compound 22 as a yellow oil (6.10 g, 84%).

$^1$H NMR and $^{13}$C NMR spectra matched those reported.\(^4\)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.09 (s, 4H ppm)

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 115.3, 109.1, 102.7, 99.7, 18.9, 11.5 ppm

(3-(Penta-1,4-dien-3-ylidene)penta-1,4-diyne-1,5-diyldibis(triisopropylsilane) (23)

A solution of vinylmagnesium bromide (0.60 M in THF, 12.2 mL, 7.33 mmol, 4 mol equiv) in THF (5.00 mL) was cooled in a 0 °C ice bath. ZnBr$_2$ (1.14 M in THF, 8.00 mL, 9.15 mmol, 5 mol equiv) was added dropwise to the reaction mixture over five minutes. The solution was stirred for 30 minutes before the addition of dibromo-olefin 22 (1.00 g, 1.83 mmol) and [PdCl$_2$(dpptf)] (150 mg, 0.09 mmol, 10 mol %). The reaction mixture was warmed to 60 °C and stirred for 4 hours. The reaction mixture was cooled to 23 °C and quenched with sat. aq. ammonium chloride (30 mL) and extracted with PS 30-40 °C (3 x 100 mL). The organic extracts were combined, washed with brine (50 mL), dried over MgSO$_4$, filtered through a pad of silica eluting with PS 30-40 °C and the solvent was removed under reduced pressure to give the title compound 23 (462 mg, 57%) as a yellow oil.

$R_f$ = 0.56 (100% PS 40–60°C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.83 (dd, $J$ = 17.6, 11.3 Hz, 2H), 5.63 (dd, $J$ = 17.7, 1.4 Hz, 2H), 5.40 (d, $J$ = 11.3 Hz, 2H), 1.17-0.89 (m, 42H ppm)

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 148.7, 131.6, 119.8, 103.0, 102.8, 97.0, 17.3, 10.0 ppm

IR (thin film) $\nu$$_{max}$ = 2943, 2892, 2865, 2144, 1463 cm$^{-1}$

ESIMS (ESI$^+$) $m/z$ (%) = 463 ([M + Na]$^+$, 100)

HRMS (EI$^+$) calcd for C$_{23}$H$_{40}$S$_2$ [M]$^+$ 441.3367, found 441.3352.
4-Ethynyl-3-vinylhexa-1,3-dien-5-yne (6)

A solution of diyne 23 (380 mg, 0.863 mmol) in Et₂O (19 mL) was cooled in a 0 °C ice bath. TBAF·xH₂O (1.32 g) was added to the reaction mixture which was stirred at 0 °C for 30 minutes. Dowex® 50WX8 200-400 mesh (2.36 g) and CaCO₃ (760 mg) were then added to the reaction mixture, which was warmed to 23 °C and stirred for 1 hour. The reaction mixture was filtered through a pad of celite eluting with Et₂O (200 mL) and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 6 as a yellow oil (45.0 mg, 41%)

R_f = 0.79 (100% PS 30-40 °C)

^1H NMR (400 MHz, CDCl₃): δ = 6.86 (dd, J = 17.6, 11.2 Hz, 2H), 5.70 (d, J = 17.6 Hz, 2H), 5.52 (d, J = 11.3 Hz, 2H), 3.37 (s, 2H) ppm

^13C NMR (101 MHz, CDCl₃): δ = 153.1, 132.8, 122.6, 101.4, 84.2, 80.7 ppm

GCMS (EI⁺, Ip = 5.113 min) m/z (%): 128 ([M⁺], 80), 127 ([M − H]⁺, 100), 126 ([M − 2H]⁺, 45)

HRMS (EI⁺): calcld for C₂₀H₁₆ [M⁺] 328.08626, found 128.0626

UV Vis (Acetonitrile) λ_max: 296 (28500), 225 (18000)
Synthetic Route to 3-Ethynyl-4-vinylhexa-1,3,5-triene (7) and 3,4-diethynylhexa-1,3-dien-5-yne (3)

The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

5-(Triisopropylsilyl)pent-1-en-4-yn-3-one (S6)

Prepared by modification of a procedure by Hoveyda. A solution of TIPS acetylene (12.0 mL, 53.5 mmol, 1.5 mol equiv) in THF (10 mL) was cooled in a 0 °C ice bath. n-BuLi (1.4M in hexane, 31.0 mL, 42.8 mmol, 1.2 mol equiv) was added dropwise over 10 minutes to the reaction mixture. The reaction mixture was then stirred in
the 0 °C bath for a further 30 minutes before being cooled in a –78 °C dry ice/acetone bath. Acrolein (2.40 mL, 35.7 mmol) was then added and the reaction mixture was stirred at –78 °C for a further 30 minutes. The solution was then warmed to 0 °C and stirred for 2 hours. The reaction mixture was quenched with sat. aq. ammonium chloride solution (100 mL) and extracted with EtOAc (3 x 100 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure to give the crude 5-(triisopropylsilyl)pent-1-en-4-yn-3-ol S5 as a yellow oil. The crude product was subjected to the next reaction without further purification.

A solution of alcohol S5 (8.47 g, 35.7 mmol) in CH₂Cl₂ (300 mL) was cooled in a 0 °C ice bath. Dess-Martin periodinane (DMP) (18.1 g, 42.6 mmol, 1.2 mol equiv) was then added in 2 portions to the reaction mixture over five minutes (CAUTION: Exotherm). The reaction mixture was warmed to 23 °C and stirred for one hour. The solution was then diluted with PS 40-60 °C (700 mL) and filtered through a short pad of silica, eluting with PS 40-60 °C and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 40-60 °C to 100% CH₂Cl₂) to give the title compound S6 as a pale yellow oil (6.67 g, 79% over 2 steps).

¹H NMR and ¹³C NMR spectra matched those reported.⁶

¹H NMR (400 MHz, CDCl₃): δ = 6.62 (d, J = 17.4 Hz, 1H), 6.41 (dd, J = 17.3, 10.2 Hz, 1H), 6.19 (d, J = 10.2 Hz, 1H), 1.22-1.04 (m, 21H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 178.3, 138.2, 133.6, 102.0, 96.4, 18.6, 11.2 ppm

(3-(Dibromomethylene)pent-4-en-1-yn-1-yl)triisopropylsilane (24)

To a solution of ketone S6 (2.50 g, 10.5 mmol) in CH₂Cl₂ (25 mL) was added CBr₄ (5.23 g, 15.8 mmol, 1.5 mol equiv). The reaction mixture was cooled in a –78 °C dry ice/acetone bath and a solution of P(O)Pr₃ (5.70 mL, 23.1 mmol, 2.2 mol equiv) in CH₂Cl₂ (4 mL) was added dropwise over 15 minutes via syringe pump. The reaction was stirred for a further 10 minutes at –78 °C. Sat. aq. sodium bicarbonate (10 mL) was then added to the reaction mixture and the solution was warmed to 23 °C and extracted with CH₂Cl₂ (3 x 20 mL). The
organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 24 as a pale yellow oil (1.13 g, 35%).

$R_T = 0.87$ (100% PS 30-40 °C)

$^1$H NMR (400 MHz, CDCl₃): $\delta = 6.67$ (dd, $J = 16.8$, 10.3 Hz, 1H), 5.91 (d, $J = 16.8$ Hz, 1H), 5.48 (d, $J = 10.4$ Hz, 1H), 1.35-0.97 (m, 21H) ppm

$^{13}$C NMR (101 MHz, CDCl₃): $\delta = 133.1$, 129.7, 121.7, 102.1, 101.6, 101.4, 19.0, 11.5 ppm

IR (thin film): $\nu_{\max} = 2942, 2890, 2864, 1461$ cm$^{-1}$

EIMS (70 eV, El): $m/z$ (%): 394 ([M$^{81}$Br$_2$]$,^+$, 14), 392 ([M$^{81}$Br$^{79}$Br$^{81}$]$,^+$, 26), 390 ([M$^{79}$Br$_2$]$,^+$, 13)

HRMS (El$^+$) calcd for C$_{14}$H$_{18}$Br$_2$Si [M]$^+$ 393.9973, found 393.9960; calcd for C$_{15}$H$_{20}$Br$_2$Si [M]$^+$ 391.9994, found 391.9984; calcd for C$_{15}$H$_{18}$Br$_3$Si [M]$^+$ 390.0014, found 390.0014.

(3,4-Divinylhexa-3,5-dien-1-yn-1-yl)trisopropysilane (26)

To a solution of dibromo olefin 24 (500 mg, 1.27 mmol) in THF (5.00 mL) was added Pd(dppf)Cl$_2$ (105 mg, 0.127 mmol, 10 mol %) and ZnBr$_2$ (1.14 M in THF, 5.60 mL, 6.35 mmol, 5 mol equiv). Vinylmagnesium bromide (0.60 M in THF, 8.50 mL, 5.10 mmol, 4 mol equiv) was then added dropwise over 5 minutes to the reaction mixture. The solution was warmed to reflux and stirred for 1 hour. The reaction mixture was cooled to 23 °C and quenched with sat. aq. ammonium chloride (30 mL) and extracted with PS 30-40 °C (3 x 100 mL). The organic extracts were combined, washed with brine (50 mL), dried over MgSO₄, filtered through a pad of silica eluting with PS 30-40 °C and the solvent was removed under reduced pressure to give the title compound 26 as a yellow oil (152 mg, 42%).

$R_T = 0.74$ (100% PS 30-40 °C)
**1H NMR** (400 MHz, CDCl₃): δ = 7.19 (dd, J = 17.5, 10.8 Hz, 1H), 6.84 (dd, J = 16.9, 10.3 Hz, 1H), 6.47 (dd, J = 17.8, 11.4 Hz, 1H), 5.85 (dd, J = 16.9, 1.8 Hz, 1H), 5.59-5.46 (m, 2H), 5.42-5.24 (m, 3H), 1.14 (s, 21H) ppm

**13C NMR** (101 MHz, CDCl₃): δ = 144.1, 136.5, 133.3, 131.8, 122.4, 121.8, 119.4, 118.6, 103.1, 100.7, 19.0, 11.7 ppm

**IR** (thin film): νmax = 2942, 2925, 2891, 2864, 2135, 1462 cm⁻¹

**EIMS** (70 eV, EI): m/z (%): 286 ([M]⁺, 12), 243 ([M – i-Pr]⁺, 100), 129 ([M – TIPS]⁺, 35)

**HRMS** (EI): calc'd for C₉₈H₁₇₂Si [M]⁺ 286.2117, found 286.2118

3-Ethynyl-4-vinylhexa-1,3,5-triene (7)

![Reaction diagram](attachment:image.png)

A solution of triene 26 (152 mg, 0.531 mmol) in Et₂O (10 mL) was cooled in a 0 °C ice bath. TBAF·xH₂O (5.00 g) was added to the reaction mixture, which was stirred at 0 °C for 1 hour. Dowex® 50WX8 200-400 mesh (9.00 g) and CaCO₃ (5.00 g) were then added to the reaction mixture which was warmed to 23 °C and stirred for 1 hour. The reaction mixture was filtered through a pad of celite eluting with Et₂O (200 mL) and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 7 as a yellow oil (57 mg, 84%)

**Rf** = 0.86 (100% PS 30-40 °C)

**1H NMR** (400 MHz, CDCl₃): δ = 7.13 (dd, J = 17.5, 10.8 Hz, 1H), 6.48 (dd, J = 16.9, 10.4 Hz, 1H), 6.46 (dd, J = 17.7, 11.4 Hz, 1H), 5.80 (dd, J =17.1, 1.7 Hz, 1H), 5.63-5.47 (m, 2H), 5.44-5.24 (m, 3H), 3.47 (s, 1H) ppm

**13C NMR** (101 MHz, CDCl₃): δ = 144.9, 136.2, 133.1, 131.8, 122.7, 120.4, 120.0, 118.6, 86.4, 80.0 ppm

**GCMS** (EI+, tR = 5.128 min) m/z (%): 130 ([M]⁺, 45), 129 ([M – H]⁺, 80), 128 ([M – 2H]⁺, 100)

**HRMS** (EI): calc’d for C₉₂H₁₇₂Si [M]⁺ 130.0783; found 130.0782

**UV vis** (Acetonitrile) λmax: 294 (28600), 224 (21700)
(3-(5-(Triisopropylsilyl)pent-1-en-4-yn-3-ylidene)penta-1,4-diyne-1,5-diyli)bis(trimethylsilane) (27)

To a solution of dibromomolefin 24 (1.00 g, 2.56 mmol) in THF (6.00 mL) and (i-Pr)₂NH (4.00 mL) was added TMS acetylene (1.79 mL, 12.8 mmol, 5 mol equiv). Pd(dppf)Cl₂ (210 mg, 0.256 mmol, 10 mol %) and Cul (48.0 mg, 0.256 mmol, 10 mol %) were then added to the reaction mixture. The solution was stirred at 23 °C for 17 hours. Water (40 mL) was then added to the reaction mixture and extracted with PS 30-40 °C (3 x 40 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 27 (789 mg, 73%) as a pale yellow oil.

R₂ = 0.77 (100% PS 30-40 °C)

¹H NMR (400 MHz, CDCl₃): δ = 6.99 (dd, J = 16.9, 10.2 Hz, 1H), 5.90 (d, J = 16.9 Hz, 1H), 5.43 (d, J = 10.3 Hz, 1H), 1.29-1.01 (m, 21H), 0.36-0.10 (m, 18H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 136.7, 133.7, 121.9, 110.6, 105.5, 105.3, 102.5, 102.1, 102.0, 100.7, 19.1, 11.5, 0.1 x 2C ppm

IR (thin film): νmax = 2958, 2943, 2866, 2895, 2152, 2139 cm⁻¹

EIMS (70 eV, EI): m/z (%): 426 ([M⁺]⁺, 28), 281 ([M – 2 TMS]⁺, 20), 73 (TMS, 100)

HRMS (EI⁺): calcd for C₃₅H₄₂Si₃ [M⁺]⁺ 426.2594, found 426.2592

3,4-Diethynylhexa-1,3-dien-5-yne (3)
A solution of triyne 27 (650 mg, 1.52 mmol) in Et$_2$O (23 mL) was cooled in a 0 °C ice bath. TBAF•xH$_2$O (4.33 g) was added to the reaction mixture which was stirred at 0 °C for 30 minutes. Dowex® 50WX8 200-400 mesh (9.03 g) and CaCO$_3$ (3.61 g) were then added to the reaction mixture, which was warmed to 23 °C and stirred for 1 hour. The reaction mixture was filtered through a pad of celite eluting with Et$_2$O (200 mL) and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 3 as a yellow oil (130 mg, 68%)

R$_f$ = 0.31 (100% PS 30-40 °C)

$^1$H NMR (400 MHz, CDC$_6$): δ = 7.02 (dd, J = 17.0, 10.4 Hz, 1H), 5.93 (d, J = 17.0 Hz, 1H), 5.51 (d, J = 10.3 Hz, 1H), 3.69 (s, 1H), 3.58 (s, 1H), 3.43 (s, 1H) ppm

$^{13}$C NMR (101 MHz, CDC$_6$): δ = 137.7, 132.7, 123.3, 109.4, 90.0, 87.8, 84.3, 81.2, 79.0, 78.7 ppm

GCMS (El$^+$, tR = 5.219 min) m/z (%): 126 ([M]$^+$, 100), 74 ([M-CCH]$^+$, 12

HRMS (El$^+$): calcd for C$_{10}$H$_8$[M]$^+$: 126.0470, found: 126.0471

UV vis(Acetonitrile) $\lambda_{max}$: 313 (26400), 299 (27300), 212 (14200)
**Synthetic Route to (Z)-3,4-Diethynylhexa-1,3,5-triene (4) and (E)-3,4-Diethynylhexa-1,3,5-triene (5)**

The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

**5-(Trimethylsilyl)pent-1-en-4-yn-3-ol (S7)**

Prepared by modification of a procedure by Hoveyda. \(^5\)
A solution of TMS acetylene (11.2 mL, 80.3 mmol, 1.5 mol equiv) in THF (10 mL) was cooled in a 0 °C ice bath. n-BuLi (1.4M in hexane, 45.8 mL, 64.2 mmol, 1.2 mol equiv) was added dropwise over 10 minutes to the reaction mixture. The reaction mixture was then stirred in the 0 °C bath for a further 30 minutes before being cooled in a −78 °C dry ice/acetone bath. Acrolein (3.60 mL, 53.5 mmol) was then added and the reaction mixture was stirred at −78 °C for a further 30 minutes. The solution was then warmed to 23 °C and stirred for 2 hours. The reaction mixture was quenched with sat. aq. ammonium chloride solution (100 mL) and extracted with EtOAc (3 x 150 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure to give the title compound S₇ as a yellow oil (7.50 g, 91%).

¹H NMR and ¹³C NMR spectra matched those reported.⁵

¹H NMR (400 MHz, CDCl₃): δ = 5.94 (ddd, J = 17.4, 10.2, 5.3 Hz, 1H), 5.45 (dd, J = 17.0, 1.7 Hz, 1H), 5.24-5.15 (m, 1H), 4.85 (d, J = 5.3 Hz, 1H), 0.16 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 137.0, 116.8, 104.4, 91.3, 63.7, 0.1 ppm

5-(Trimethylsilyl)pent-1-en-4-yn-3-one (S₈)

\[
\begin{align*}
\text{TMS} & \quad \text{OH} \\
\text{S₇} & \quad \xrightarrow{\text{DMP, CH₂Cl₂ \text{23 °C, 1 h} \text{75%}}} \quad \text{TMS} \\
& \quad \text{S₈}
\end{align*}
\]

Prepared by modification of a procedure by Murakami.⁷

A solution of alcohol S₇ (7.50 g, 48.7 mmol) in CH₂Cl₂ (250 mL) was cooled in a 0 °C ice bath. Dess-Martin periodinane (DMP) (24.7 g, 54.88 mmol, 1.2 mol equiv) was then added in portions to the reaction mixture over 5 minutes (CAUTION: Exotherm). The reaction mixture was warmed to 23 °C and stirred for 1 hour. The solution was then diluted with PS 40-60 °C (700 mL) and filtered through a short pad of silica, eluting with PS 40-60 °C and the solvent was removed under reduced pressure to give the title compound S₈ as a yellow oil (5.53 g, 75%).

¹H NMR and ¹³C NMR spectra matched those reported.⁷

¹H NMR (400 MHz, CDCl₃): δ = 6.56 (d, J = 17.4 Hz, 1H), 6.37 (dd, J = 17.4, 10.2 Hz, 1H), 6.18 (d, J = 10.3 Hz, 1H), 0.25 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 178.8, 137.9, 134.3, 100.0, 99.6, -0.5 ppm
(3-(Dibromomethylene)pent-4-en-1-yn-1-yl)trimethylsilane (25)

To a solution of ketone S8 (4.30 g, 27.9 mmol) in CH₂Cl₂ (60 mL) was added CBr₄ (13.8 g, 41.9 mmol, 1.5 mol equiv). The reaction mixture was cooled in a –78 °C dry ice/acetone bath and a solution of P(O(Pr)₃ (15.1 mL, 61.4 mmol, 2.2 mol equiv) in CH₂Cl₂ (4.9 mL) was added dropwise over 15 minutes via syringe pump. The reaction was stirred for a further 10 minutes at –78 °C. Sat. aq. sodium bicarbonate (20 mL) was then added to the reaction mixture and the solution was warmed to 23 °C and extracted with CH₂Cl₂ (3 x 50 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then filtered through a short silica plug eluting with PS 30-40 °C and the solvent was removed under reduced pressure to give the title compound 25 as an orange oil (2.64 g, 32%).

Rf = 0.80 (100% PS 30-40 °C)

1H NMR (400 MHz, CDCl₃): δ = 6.65 (ddd, J = 16.8, 10.4, 1.2 Hz, 1H), 5.85 (d, J = 16.9 Hz, 1H), 5.48 (d, J = 10.3 Hz, 1H), 0.25 (s, 9H) ppm

13C NMR (101 MHz, CDCl₃): δ = 132.8, 129.4, 121.8, 105.2, 101.7, 99.7, 0.0 ppm

IR (thin film): νmax = 2956, 2897, 2171, 2144 cm⁻¹

EI-MS (70 eV, EI): m/z (%): 309 (C₇H₁₂Br₂Si, [M]+, 50), 307 (C₇H₁₂Br₂Si, [M]+, 90), 305 (C₇H₁₂Br₂Si, [M]+, 45), 294 (C₇H₁₂Br₂Si, [M-C₆H₆]⁺, 60), 292 (C₇H₁₂Br₂Si, [M-C₆H₆]⁺, 100), 290 (C₇H₁₂Br₂Si, [M-C₆H₆]⁺, 50)

(Z)-(4-Bromo-3-vinylhexa-3,5-dien-1-yn-1-yl)trimethylsilane (25)

To a solution of dibromoolefin 25 (300 mg, 0.97 mmol) in THF (6.00 mL) was added Pd(PPh₃)₄ (56.0 mg, 0.049 mmol, 5 mol %) and ZnBr₂ (1.25 M in THF, 1.54 mL, 1.94 mmol, 2 mol equiv). Vinylmagnesium bromide (0.65 M in THF, 2.25 mL, 1.46 mmol, 1.5 mol equiv) was then added dropwise over 5 minutes to the reaction mixture. The solution was warmed to 35 °C and stirred for 1 hour. The reaction mixture was cooled to 23 °C and quenched with sat. aq. ammonium chloride (10 mL) and extracted with CH₂Cl₂ (3 x 50 mL). The organic extracts were combined diluted with PS 30-40 °C (150 mL), washed with brine (50 mL), dried over MgSO₄, filtered through a pad of silica eluting with dichloromethane/PS 30-40 °C (1:1) and the solvent was removed under reduced pressure (0 °C, 60 mbar) to give the title compound 28 as a yellow oil (120 mg, 51%).

Rf = 0.69 (100% PS 30-40 °C)

¹H NMR (400 MHz, CDCl₃): δ = 6.83 (ddd, J = 37.0, 16.3, 10.5 Hz, 2H), 5.85 (d, J = 16.7 Hz, 1H), 5.79 (d, J = 15.9 Hz, 1H), 5.42 (dd, J = 20.1, 10.5 Hz, 2H), 0.26 (s, 9H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 131.5, 130.5, 130.0, 125.6, 120.5, 105.5, 102.3, 0.2 ppm

IR (thin film): νmax = 2959, 2899, 2148 cm⁻¹

EI-MS (70 eV, EI): m/z (%): 256 (C₁₁H₁₀Br⁺, [M⁺], 100), 254 (C₁₁H₁₀⁺Br⁻, [M⁺⁻H], 98), 241 (C₁₁H₁₀⁺Br⁻, [M−CH₃]⁺, 45), 229 (C₁₁H₁₀⁺Br⁻, [M−CH₃]⁺, 50)

HRMS (EI): calcld for C₁₁H₁₀Si⁺Br⁻ [M⁺] 254.0126, found 254.0128; calcld for C₁₁H₁₀Si⁺⁺Br⁻ [M⁺⁺] 256.0106, found 256.0116
(E)-(3,4-Divinylhexa-3-en-1,5-diyne-1,6-diyl)bis(trimethylsilane) (30)

To a solution of bromide 28 (40 mg, 0.157 mmol) in THF (2 mL) and (i-Pr)_2NH (1 mL) was added TMS acetylene (66.0 µL, 0.470 mmol, 3 mol equiv). [PdCl_2(dppf)] (13 mg, 0.0157 mmol, 10 mol %) and Cul (3.0 mg, 0.0157 mmol, 10 mol %) were then added to the reaction mixture. The solution was stirred at 23 °C for 3 hours. Water (5 mL) was then added to the reaction mixture and extracted with PS 30-40 °C (3 x 10 mL). The organic extracts were combined, dried over MgSO_4, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 30 (16 mg, 38 %) as a pale yellow oil.

R_f = 0.60 (100% PS 30-40 °C)

^1H NMR (400 MHz, CDCl_3): δ = 7.05 (dd, J = 17.0, 10.2 Hz, 2H), 5.84 (dd, J = 17.0, 1.5 Hz, 2H), 5.40 (dd, J = 10.2, 1.5 Hz, 2H), 0.25 (s, 18H) ppm

^13C NMR (101 MHz, CDCl_3): δ = 134.7, 128.8, 120.4, 108.5, 99.7, 0.3 ppm

IR (thin film): ν_max = 2960, 2923, 2902, 2150 cm⁻¹

EI-MS (70 eV, El⁺): m/z (%): 272 ([M⁺], 100), 257 ([M – CH_3⁺], 30)

HRMS (El⁺): calcd for C_{15}H_{26}Si_2 [M⁺] 272.1417, found 272.1415

(E)-3,4-Diethynylhexa-1,3,5-triene (5)

To a solution of triene 16 (16.0 mg, 0.0588 mmol) in MeOH (5.0 mL) was added K_2CO_3 (1.00 g, 7.24 mmol, 123 mol equiv). The reaction mixture was stirred at 23 °C for 3 hours. The reaction mixture was quenched with water (20 mL) and extracted with PS 30-40 °C (3 x 20
mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar) to give the title compound 5 as a yellow oil (5.0 mg, 66%).

Rf = 0.70 (100% pentane)

H NMR (400 MHz, CDCl₃): δ = 7.10 (dd, J = 17.0, 10.3 Hz, 2H), 5.89 (d, J = 17.0 Hz, 2H), 5.44 (d, J = 10.3 Hz, 2H), 3.68 (d, J = 1.7 Hz, 2H) ppm

C NMR (101 MHz, CDCl₃): δ = 134.3, 128.7, 120.9, 90.2, 78.4 ppm

GCMS (EI, tR = 5.212 min) m/z (%): 128 ([M]⁺, 80), 127 ([M - H]⁺, 100), 126 ([M - 2H]⁺, 38)

HRMS (EI⁺): calc'd for C₉H₉ [M]⁺ 128.0626, found 128.0625

UV-vis (Acetonitrile) λmax: 311 (23100), 299 (27400), 286 (21900), 225 (17500), 215 (16000)

(Z)-(3,4-Divinylhexa-3-en-1,5-diyne-1,6-diyli)bis(trimethylsilane) (29)

A solution of TMS acetylene (70 µL, 0.49 mmol, 2 mol equiv) in THF (4 mL) was cooled in a 0 °C ice bath. n-BuLi (1.12 M in hexane, 331 µL, 0.37 mmol, 1.5 mol equiv) was added dropwise over 2 minutes to the reaction mixture. The reaction mixture was then stirred in the 0 °C bath for a further 30 minutes. ZnBr₂ (1.25 M in THF, 434 µL, 0.54 mmol, 2.2 mol equiv) was then added and the reaction mixture was warmed to 23 °C and stirred for 30 minutes. Pd₂dba₃ (13 mg, 0.012 mmol, 5 mol %) and Bu₃P (7 mg, 0.024 mmol, 10 mol %) were then added to the reaction mixture followed by bromide 28 (62 mg, 0.25 mmol). The reaction mixture was warmed to 35 °C and stirred for 30 minutes. The reaction mixture was cooled to 23 °C and quenched with sat. aq. ammonium chloride (10 mL) and extracted with PS 30-40 °C (3 x 10 mL). The organic extracts were combined, washed with brine (20 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified by flash column chromatography (100% PS 30-40 °C) to give the title compound 29 as a yellow oil (25 mg, 37%).
Rf = 0.40 (100% PS 30-40 °C)

1H NMR (400 MHz, CDCl3): δ = 6.84 (dd, J = 16.7, 10.3 Hz, 2H), 5.85 (dd, J = 16.7, 1.5 Hz, 2H), 5.38 (dd, J = 10.3, 1.6 Hz, 2H), 0.25 (s, 18H) ppm

13C NMR (101 MHz, CDCl3): δ = 130.1, 127.6, 121.0, 104.3, 102.3, 0.3 ppm

IR (thin film): \( \nu_{\text{max}} \) = 2959, 2962, 2856, 2143, 1249 cm\(^{-1}\)

EI-MS (70 eV, El): m/z (%): 272 ([M]+, 38), 257 ([M – CH₃]+, 13), 184 ([M – C₃H₇Si]+, 100)

HRMS (EI): calcd for C₁₀H₂₃Si[MHz]⁺: 272.1417, found: 272.1417

(Z)-3,4-Diethynylhexa-1,3,5-triene (4)

To a solution of triene 15 (77 mg, 0.28 mmol) in MeOH (5.00 mL) was added K₂CO₃ (2.00 g, 14.5 mmol, 52 mol equiv). The reaction mixture was stirred at 23 °C for 3 hours. The reaction mixture was quenched with water (10 mL) and extracted with PS 30-40 °C (3 x 20 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure (0 °C, 60 mbar) to give the title compound 4 as a yellow oil (22 mg, 61%).

Rf = 0.35 (100% PS 30-40 °C)

1H NMR (400 MHz, CDCl3): δ = 6.89 (dd, J = 16.7, 10.4 Hz, 2H), 5.89 (d, J = 16.7 Hz, 2H), 5.44 (d, J = 10.4 Hz, 2H), 3.51 (s, 2H) ppm

13C NMR (101 MHz, CDCl3): δ = 130.0, 127.5, 121.5, 86.1, 81.0 ppm

GCMS (EI+, tR = 5.219 min) m/z (%): 128 ([M]+, 80), 127 ([M – H]+, 100), 126 ([M – 2H]+, 50)


UV-vis (Acetonitrile) \( \lambda_{\text{max}} \): 309 (23500), 295 (243000), 285 (18200), 224 (13200), 215 (12800)

Synthesis of TEE (1)
(3-(1,5-Bis(trimethylsilyl)penta-1,4-diyn-3-ylidene)penta-1,4-diyn-1,5-diyldibis(trimethylsilane) (S10)

 Prepared by modification of a procedure by Low.\textsuperscript{9} NE\textsubscript{I3} (70 mL) was subjected to three cycles of freeze-pump-thaw degassing before tetrachloroethylene (375 \( \mu \)L, 3.79 mmol, 1.00 mol equiv) and TMS acetylene (3.00 mL, 22.74 mmol, 6.00 mol equiv) were added. Pd(PPPh\textsubscript{3})\textsubscript{4} (875 mg, 0.758 mmol, 20 mol \%) and Cul (140 mg, 0.758 mmol, 20 mol \%) were then added to the reaction mixture. The solution was heated at reflux for 24 hours. The reaction mixture was then filtered and the filtrate concentrated under reduced pressure. The crude product was then purified by flash column chromatography (100\% PS 30-40 °C) to give the title compound S10 (730 mg, 47\%) as a yellow solid.

\textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectra matched those reported.\textsuperscript{9}

3,4-Diethynylhexa-3-en-1,5-diyn (1)

 Prepared by modification of a procedure by Diederich.\textsuperscript{4} To a solution of protected TEE S10 (380 mg, 0.92 mmol, 1.00 mol equiv) in MeOH (50 mL) was added \( \text{K}_2\text{CO}_3 \) (5.00 g). The solution was stirred at 23 °C for 3 hours. \( \text{H}_2\text{O} \) (50 mL) was added to the reaction mixture and extracted with PS 30-40 °C (3 x 50 mL). The organic extracts were combined, dried over MgSO\textsubscript{4} filtered through a pad of silica eluting with PS 30-40 °C and the solvent was removed under reduced pressure to give the title compound 1 (72 mg, 63\%) as a white crystalline solid.

WE RECOMMEND CAUTION WHEN HANDLING NEAT SAMPLES OF TEE.
$^1$H NMR and $^{13}$C NMR spectra matched that reported.$^4$

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.61$ (s, 4H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 118.9, 87.7, 79.7$ ppm
Alternate Synthesis of (E)-3,4-Diethynylhexa-1,3,5-triene (5)

The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

Dimethyl 2,3-dibromofumarate (S12)

Prepared by modification of a procedure by Ranu. To DMAD S11 (14.2 g, 100 mmol) in AcOH (200 mL) was added NaBr (20.6 g, 200 mmol, 2 mol equiv) and NaBrO₃ (6.03 g, 40.0 mmol, 0.4 mol equiv). The solution was stirred at 23 °C for 24 hours. Sat. aq. sodium bicarbonate was added until pH 7 was reached. The solution was then diluted with sat. aq. sodium thiosulfate (100 mL) and extracted with CH₂Cl₂ (3 x 250 mL). The combined organic extracts were washed with sat. aq. sodium bicarbonate,
dried over MgSO₄, filtered and the solvent was removed under reduced pressure to give the title compound **S12** as a white solid (24.7 g, 82%).

\[ ^1H \text{ NMR and } ^13C \text{ NMR spectra matched those reported} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3): \delta = 3.91 \text{ (s, 6H ppm) } \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3): \delta = 162.8, 112.9, 53.9 \text{ ppm} \]

**Dimethyl 2,3-bis((triisopropylsilyl)ethynyl)fumarate (13)**

Prepared by modification of a procedure by Diederich.⁴

To a solution of ester **S12** (1.00 g, 3.31 mmol) in Et₃N (30.0 mL) was added TIPS acetylene (1.65 mL, 8.28 mmol, 2.5 mol equiv). Pd(PPh₃)₃Cl₂ (116 mg, 0.166 mmol, 5 mol %) and Cul (40.0 mg, 0.210 mmol, 6 mol %) were added to the reaction mixture which was then stirred at 23 °C for 16 hours. The reaction mixture was diluted with Et₂O (100 mL) and washed with brine (2 x 50 mL). The organic extract was dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 40-60 °C to 33% CH₂Cl₂ in PS 40-60 °C) to give the title compound **S13** as a pale yellow solid (1.46 g, 87%).

\[ ^1H \text{ NMR and } ^13C \text{ NMR spectra matched those reported} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3): \delta = 3.81 \text{ (s, 6H), 1.21-0.98 (m, 42H ppm) } \]

\[ ^13C \text{ NMR (101 MHz, CDCl}_3): \delta = 163.2, 127.3, 109.5, 100.4, 52.4, 18.3, 11.1 \text{ ppm} \]
(E)-2-(((Triisopropylsilyl)ethynyl)-3-(((trimethylsilyl)ethynyl)but-2-ene-1,4-diol (S14)

Prepared by modification of a procedure by Diederich. A solution of ester S13 (1.46 g, 2.89 mmol) in CH₂Cl₂ (3.8 mL) was cooled in a 0 °C ice bath. Dibal-H (1.00M in hexane, 14.5 mL, 14.5 mmol, 5 mol equiv) was added dropwise over 15 minutes to the reaction mixture. The reaction mixture was then stirred in the 0 °C bath for a further 5 minutes before being warmed to 23 °C for 30 minutes. The reaction mixture was poured onto a cold solution of brine (100 mL) which was diluted with CH₂Cl₂ (100 mL). The mixture was then filtered through a pad of celite eluting with CH₂Cl₂. To the filtrate was added sat. aq. Rochelle’s salt (100 mL) and brine (100 mL) and extracted with CH₂Cl₂ (3 x 100 mL). The combined organic extracts were dried over MgSO₄, filtered and the solvent was removed under reduced pressure to give the title compound S14 as a white solid (1.20 g, 93%).

¹H NMR and ¹³C NMR spectra matched those reported.

¹H NMR (400 MHz, CDCl₃): δ = 4.42 (s, 4H), 1.18-1.01 (m, 42H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 130.6, 105.8, 102.3, 63.3, 18.6, 11.1 ppm

2,3-Bis((triisopropylsilyl)ethynyl)fumarylaldehyde (S15)

Prepared by modification of a procedure by Diederich. To a solution of diol S14 (1.17 g, 2.60 mmol) in CH₂Cl₂ was added celite (2.00 g) and pyridinium chlorochromate (1.95 g, 8.32 mmol, 5.2 mol equiv). The solution was stirred at 23 °C for 6 hours then filtered through a short pad of silica eluting with CH₂Cl₂ (500 mL).
The solvent was removed under reduced pressure to give the title compound **S15** as a bright yellow solid (1.09 g, 94%).

\(^1\)H NMR and \(^13\)C NMR spectra matched those reported. \(^4\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 10.28\) (s, \(J = 1.1\) Hz, 2H), 1.17-0.93 (m, 42H) ppm

\(^13\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 188.0, 138.0, 115.7, 96.4, 18.4, 11.1\) ppm

\((E)\)-\(\{3,4\)-Divinylhexa-3-en-1,5-diyne-1,6-diyl\}bis(triisopropylsilane) (16)

\[ \text{R} \text{Br} \xrightarrow{\text{MePPH}_{3}} \text{Me} 
\xrightarrow{n-\text{BuLi, THF}} \xrightarrow{23^\circ\text{C, 5 mins}} \text{S15} \]

A solution of methyl triphenyl phosphonium bromide (235 mg, 0.67 mmol, 3 mol equiv) in THF (1.10 mL) was cooled in a 0 °C ice bath. n-BuLi (1.4M in hexane, 360 µL, 0.46 mmol, 2.1 mol equiv) was added and the solution was then warmed to 23 °C and stirred for 5 minutes. The solution was then cooled in a −78 °C dry ice/acetone bath and dialdehyde **S15** (100 mg, 0.22 mmol) in THF (1.00 mL) was added. The reaction mixture was warmed to 23 °C and stirred for 5 minutes. The reaction mixture was quenched with sat. aq. ammonium chloride solution (10 mL) and extracted with CH\(_2\)Cl\(_2\) (3 x 50 mL), the organic extracts were combined, dried over MgSO\(_4\), filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 40-60 °C) to give the title compound **S16** as a yellow oil (67 mg, 69%)

\(R\) 0.90 (100% PS 40–60 °C)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.14\) (dd, \(J = 17.0, 10.3\) Hz, 2H), 5.90 (dd, \(J = 17.0, 1.6\) Hz, 2H), 5.40 (dd, \(J = 10.3, 1.6\) Hz, 2H), 1.12 (s, 42H) ppm

\(^13\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 134.8, 129.0, 120.1, 105.0, 101.5, 18.8, 11.4\) ppm

IR (thin film) \(\nu_{\text{max}} = 2944, 2892, 2866, 2147, 1463\) cm\(^{-1}\)

EIMS (70 eV, EI\(^{+}\)): \(m/z\) (%): 440 ([M]\(^{+}\), 45), 397 ([M–C\(_2\)H\(_4\)]\(^{+}\), 45), 355 ([M–C\(_2\)H\(_6\)]\(^{+}\), 100), 313 ([M–C\(_2\)H\(_6\)]\(^{+}\), 85)

HRMS (EI\(^{+}\)) calcd for C\(_{20}\)H\(_{46}\)Si\(_2\) [M]\(^{+}\) 440.3295, found 440.3286.
(E)-3,4-Diethynylhexa-1,3,5-triene (5)

A solution of diene S16 (56.0 mg, 0.127 mmol, 1.00 mol equiv) in Et₂O (2.5 mL) was cooled in a 0 °C ice bath. TBAF·xH₂O (200 mg) was added to the reaction mixture, which was stirred at 0 °C for 30 minutes. Dowex® 50WX8 200-400 mesh (375 mg) and CaCO₃ (125 mg) were then added to the reaction mixture, which was warmed to 23 °C and stirred for 1 hour. The reaction mixture was filtered through a pad of celite eluting with Et₂O (100 mL) and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% pentane) to give the title compound 5 as a yellow oil (13 mg, 80%)
The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

Synthesis of Z-DVDEE 4 proved to be particularly challenging. We were inspired by the work of Diedrich, in their pursuit of cis-substituted tetraynes, in which the use of a cyclic 1,2-dihaloalkene with the locked in cis-configuration allowed for a twofold Sonogashira cross coupling to introduce the cis-alkynes. However, rather than using a protected cis-butene-1,4-diol we targeted lactol S21, which effectively differentiates the oxidation states at the terminus of the central alkene. This should allow for introduction of both required vinyl groups via sequential methylation, oxidation and methylation events, potentially avoiding the stability and isomerisation issues encountered by Diedrich.
In practice however the chemistry proved challenging to execute. Stability issues under reaction and purification conditions were encountered for many of the compounds in the sequence which severely limited material throughput rendering this route unfeasible. Ultimately, we were able to synthesise small amounts of Z-DVDEE 15 via this route which facilitated our successful approach. Attempts to improve the stability of the compound by carrying through the analogous TIPS protected compounds was unsuccessful.

Issues specific to each compound are discussed at the end of the respective preparation procedures in the section below.

3,4-Dibromo-5-methoxyfuran-2(5H)-one (S18)

Prepared by modification of a procedure by Xu.\textsuperscript{11}
To a solution of dibromide S17 (11.7 g, 45.4 mmol) in MeOH (206 mL) was added BF\textsubscript{3}•Et\textsubscript{2}O (6.71 mL, 54.5 mmol, 1.2 mol equiv) in a single portion. The solution was stirred at 23 °C for 2 days. The solvent was removed under reduced pressure. The crude material was then dissolved in CH\textsubscript{2}Cl\textsubscript{2} (500 mL), washed with sat. aq. sodium bicarbonate (250 mL), dried over MgSO\textsubscript{4}, filtered and the solvent was removed under reduced pressure to give the title compound S18 as an off white solid (11.6 g, 94%).

\textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectra matched those reported.\textsuperscript{11}
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta = 5.77 \) (s, 1H), 3.58, (d, \( J = 1.2 \) Hz, 3H) ppm
\textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}): \( \delta = 163.7, 143.0, 118.6, 103.6, 56.1 \) ppm
5-Methoxy-3,4-bis((trimethylsilyl)ethynyl)furan-2(5H)-one (S19)

To a solution of bromide S18 (2.00 g, 7.35 mmol) in (i-Pr)2NH (10.0 mL) and THF (32.0 mL) was added TMS acetylene (4.11 mL, 29.4 mmol, 4 mol equiv), Pd(PPh3)2Cl2 (516 mg, 0.74 mmol, 10 mol %) and Cul (279 mg, 1.47 mmol, 20 mol %) were added to the reaction mixture which was then subjected to three cycles of freeze/pump/thaw degassing. The reaction was stirred at 23 °C for 1 hour. The reaction mixture was filtered through a pad of silica eluting with Et2O (300 mL), washed with aq. 1M HCl solution (100 mL) then sat. aq. ammonium chloride (100 mL), dried over MgSO4, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 40-60 °C to 5% EtOAc in PS 40-60 °C) to give the title compound S19 as a yellow oil (1.13 g, 50%).

Rf = 0.30 (10% EtOAc in PS 40-60 °C)

1H NMR (400 MHz, CDCl3): δ = 5.76 (s, 1H), 3.54 (s, 3H), 0.28 (s, 9H), 0.26 (s, 9H) ppm

13C NMR (101 MHz, CDCl3): δ = 167.2, 144.4, 123.0, 119.2, 110.9, 102.5, 94.7, 93.1, 56.3, -0.2, -0.3 ppm

IR (thin film): vmax = 2962, 2901, 1783, 1250 cm⁻¹

ESI (70 eV, ESI): m/z (%): 329 ([M+Na]⁺, 100)

HRMS (EI): calcd for C₁₃H₂₂O₃S₂ [M⁺]: 307.1180 found 307.1183

Note: We found that compound S19 was unstable to extended reaction times and during workup. The success of the reaction was highly dependent on the workup and scale on which it was conducted. The procedure reported represents the largest amount of material which could be produced in a single run. Parallelisation of the reaction in 2 g batches alleviated this limitation somewhat but was found to be highly labor intensive and unsuitable for the long sequence that remained to be carried out. We attribute the sensitivity of S19 to the electrophilicity of the enone which has been demonstrated to participate in addition elimination reactions with nucleophiles.
**TMS**

A solution of DIBAL-H (1.00 M in hexane, 17.8 mL, 17.8 mmol, 3.3 mol equiv) in THF (64 mL) was cooled in a 0 °C ice bath. A solution of lactone S19 (1.66 g, 5.40 mmol) in THF (10 mL) was added dropwise over 10 minutes. The reaction mixture was stirred at 0 °C for a further 5 minutes before being warmed to 23 °C and stirred for 14 hours. The reaction mixture was cooled in a 0 °C ice bath and EIOAc (10 mL) was added and the solution warmed to 23 °C over 10 minutes. Sat. aq. Rochelle’s salt (60 mL) was then added and the mixture stirred at 23 °C for a further 1 hour. The reaction mixture was diluted with water (100 mL) and extracted with EIOAc (3 x 100 mL). The combined organic extracts were dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (30% EIOAc in PS 40-60 °C) to give the title compound S20 (1.37 g, 90%) as a pale yellow solid.

<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra matched those reported.<sup>13</sup>

**<sup>1</sup>H NMR (400 MHz, CDCl₃): δ = 4.27 (s, 4H), 2.24 (s, 2H), 0.23 (s, 18H) ppm**

**<sup>13</sup>C NMR (101 MHz, CDCl₃): δ = 131.4, 103.7, 103.6, 61.6, 0.2 ppm**

**Note:** The success of the exhaustive reduction of S19 using DIBAL-H was highly dependent on the cleanliness of the starting S19. Small impurities carried over from the previous reaction promote decomposition of the starting material or product under the reaction conditions resulting in a catastrophic loss in yield (approx. 20% yield is obtained when this happens).
3,4-Bis((trimethylsilyl)ethynyl)-2,5-dihydrofuran-2-ol (S21)

To a solution of IBX (1.75 g, 6.25 mmol, 1.2 mol equiv) in DMSO (13 mL) was added diol S20 (1.46 g, 5.20 mmol) in DMSO (13 mL). The reaction was stirred at 23 °C for 1 hour. The reaction mixture was diluted with water (100 mL) and filtered through a pad of celite eluting with water (100 mL), then CH₂Cl₂ (250 mL). The layers were separated and the organic layer was washed with brine (5 x 100 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure to yield lactol S21 (1.39 g, 96%) as yellow oil.

R_f = 0.25 (10% EtOAc in PS 40-60 °C)

¹H NMR (400 MHz, CDCl₃): δ = 5.96 (s, 1H), 4.77 (dd, J = 14.4, 4.2 Hz, 1H), 4.58 (d, J = 14.4 Hz, 1H), 2.79 (bs, 1H), 0.23 (s, 18H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 131.0, 128.0, 108.4, 106.1, 104.1, 96.3, 95.6, 75.3 x 2C ppm

IR (thin film): ν_max = 3391, 2959, 2900, 2869, 2144, 1249 cm⁻¹

EI-MS (70 eV, El): m/z (%): 278 ([M]+, 10), 260 ([M-OH]+, 50), 126 ([M-CH₂O]+, 100)

HRMS (El): calcd for C₁₄H₂₃O₂Si [M]+ 278.1158, found 278.1153

Note: The product was found to be unstable on silica. It is sufficiently pure after workup to be used in subsequent reactions.
(E)-2,3-Bis(trimethylsilyl)ethynyl)penta-2,4-dien-1-ol (S22)

A solution of methyl triphenyl phosphonium bromide (8.95 g, 25.1 mmol, 5 mol equiv) in THF (25 mL) was cooled in a 0 °C ice bath. n-BuLi (1.4 M in hexane, 14.3 mL, 20.0 mmol, 4 mol equiv) was added to the reaction then warmed to 23 °C and stirred for 30 minutes. The reaction mixture was cooled in a 0 °C ice bath and lactol S21 (1.39 g, 5.01 mmol) in THF (10 mL) was added. The reaction was stirred for 1 hour. The reaction mixture was quenched with sat. aq. ammonium chloride solution (10 mL) and extracted with Et₂O (3 x 100 mL). The combined organic extracts were dried over MgSO₄, filtered and the solvent removed under reduced pressure. The crude product was then purified by flash column chromatography (10% EtOAc in PS 40-60 °C) to give the title compound S22 (250 mg, 18%) as a colorless oil.

R<sub>v</sub> = 0.31 (10% EtOAc in PS 40-60 °C)

¹H NMR (400 MHz, CDCl₃): δ = 6.64 (dd, J = 16.8, 10.3 Hz, 1H), 5.85 (d, J = 16.6 Hz, 1H), 5.40 (d, J = 10.3 Hz, 1H), 4.34 (s, 2H), 0.24 (s, J = 2.0 Hz, 18H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 130.1, 192.4, 128.8, 121.7, 105.7, 104.1, 102.9, 101.1, 60.6, -0.3 ppm

IR (thin film): ν<sub>max</sub> = 3339, 2959, 2899, 2152, 2135, 1248 cm⁻¹

EIMS (70 eV, EI): m/z (%) : 276 ([M]⁺, 100), 216 ([M-CH₃]⁺, 50)

HRMS (EI): calcd for C₁₃H₂₄O₂Si₂ [M]⁺ 276.1366, found 276.1363

Note: Methylation of the lactol S21 under Wittig conditions proved problematic. The reaction was found not to be scalable above 100 mg without incurring a significant loss in yield (18% yield on 1.4 g scale). Attempts to improve the reaction through modifying the number equivalents of the ylide, the use of different bases (KOt-Bu) to form the ylide and modifying the temperature (-78 °C vs 0 °C) at which S21 was added were all detrimental to
the yield of the reaction. We attribute the poor yield to the basicity of the ylide which may promote desialylation of both S21 and S22 resulting in mixtures of mono and bis desialylated compounds.

**(E)-2,3-Bis((trimethylsilyl)ethynyl)penta-2,4-dienal (S23)**

A solution of alcohol S22 (94.0 mg, 0.34 mmol) in CH2Cl2 (4.00 mL) was cooled in a 0 °C ice bath and DMP (173 mg, 0.41 mmol, 1.2 mol equiv) was added in a single portion. The reaction was warmed to 23 °C and stirred for 1 hour. The reaction mixture was filtered through a pad of silica eluting with Et2O and the solvent removed under reduced pressure to give the title compound S23 (32.0 mg, 34%) as a yellow oil.

**Rf** = 0.36 (2% Et2O in PS 40-60 °C)

**^1H NMR** (400 MHz, CDCl3): δ = 9.95 (s, 1H), 7.49 (dd, J = 16.8, 10.3 Hz, 1H), 6.13 (d, J = 16.8 Hz, 1H), 5.68 (d, J = 10.4 Hz, 1H), 0.28 (s, 9H), 0.25 (s, 9H) ppm

**^13C NMR** (101 MHz, CDCl3): δ = 187.8, 139.9, 129.8, 127.4, 125.2, 112.0, 106.8, 101.7, 100.5, 0.1, -0.1 ppm

**IR** (thin film): \( \nu_{\text{max}} = 2960, 2900, 2837, 2153, 1697, 1683, 1249 \text{ cm}^{-1} \)

**EIMS** (70 eV, El): \( m/z \) (%): 274 ([M]+, 100), 259 ([M-CH3]+, 20)

**HRMS** (El): calcd for C19H22O6S2 [M]+ 274.1209, found 274.1209

**Note:** Oxidation under Swern or PCC conditions resulted in complex mixtures of compounds. IBX gives a comparable result in terms of yield to DMP.
(Z)-(3,4-Divinylhexa-3-en-1,5-diyne-1,6-diy)bis(trimethylsilane) (29)

A solution of methyl triphenyl phosphonium bromide (99.3 mg, 0.278 mmol, 2.4 mol equiv) in THF (1 mL) was cooled in a 0 °C ice bath. n-BuLi (1.4 M in hexane, 100 μL, 0.139 mmol, 1.2 mol equiv) was added to the reaction then warmed to 23 °C and stirred for 30 minutes. The reaction mixture was cooled in a 0 °C ice bath and aldehyde 23 (32.0 mg, 0.116 mmol) in THF (1 mL) was added. The reaction was stirred for 1 hour. The reaction mixture was quenched with sat. aq. ammonium chloride solution (5 mL) and extracted with Et₂O (3 x 10 mL). The combined organic extracts were dried over MgSO₄, filtered and the solvent removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 40-60 °C) to give the title compound 29 (12 mg, 38%) as a colorless oil.
Stability Testing:

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<th>dilute solution</th>
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<tr>
<td></td>
<td>ambient temp/light</td>
<td>ambient temp/light and air</td>
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<tr>
<td>1 TEE</td>
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<td>2 TVE</td>
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<td>8 TVE</td>
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Air Stability:

0.025M CDCl₃ solutions of each compound were made. An internal standard (durene) was added to each sample and an initial ¹H NMR spectrum was obtained. Compressed air was then gently bubbled through each sample for 10 minutes. A second ¹H NMR spectrum was then obtained and based on the amount of compound present relative to internal standard it was determined whether any decomposition had occurred.
Acid Stability:

0.025 M CDCl₃ solutions of each compound were made up. An internal standard (durene) was added to each sample. 500 μL of a 0.2M TFA in CDCl₃ solution was then added to 500 μL of each of the solutions to generate an overall 0.1 M TFA solution. An initial ¹H NMR spectrum was obtained. The samples were then left for 1 hour and a second ¹H NMR spectrum was obtained to determine whether any decomposition had occurred.

When compound 6 was placed in a 1M solution of TFA, after 15 minutes, 60% decomposition was seen and after 1 hour the compound had completely decomposed.

Heat Stability:

Dilute solutions of each substrate in deuterated benzene were generated. An internal standard (durene) was added to each sample and an initial ¹H NMR spectrum was obtained. Each sample was then heated to 120 °C for 2 hours in a microwave reactor. After this time another ¹H NMR spectrum was obtained to determine whether any reaction/decomposition had occurred.
TVE 2 has been previously reported to undergo [6π] electrocyclization upon heating at 120 °C for 2 hours in a microwave reactor. It has also been noted that the product of TVE [6π] electrocyclisation is unstable.

Neat Acid and Air Testing of Compound 7

Durene crystals were added to neat samples of the hydrocarbon. The samples were then dissolved in CDCl₃ and ¹H NMR spectra were obtained. Each sample was then concentrated under reduced pressure (0 °C, 60 mbar) and re-dissolved in CDCl₃. A second ¹H NMR was then obtained to ensure no loss of material during the concentration of the sample. Each sample was then concentrated again under reduced pressure (0 °C, 60 mbar).

Acid: to one vial containing a neat sample of compound 7 with durene was added 3 drops of TFA. The vial was capped and left for 1 hour after which time 90% of the sample had decomposed, according to ¹H NMR analysis.

Air: air was bubbled through one vial containing a neat sample of compound 7 with durene for 10 minutes. After 10 minutes, 66% of the sample had decomposed according to ¹H NMR analysis.
Decomposition of Compound 7

We found that the product of [6π] electrocyclization of substrate 7 could not be isolated without decomposition. This product was therefore trapped with N-methyl maleimide to generate S25.

To a microwave vial was added trieneyne 7 (22 mg, 0.16 mmol) in C6D6 (5 mL). N-Methyl maleimide (36 mg, 0.32 mmol, 2.0 mol equiv) was then added, the vial was capped and the solution was sparged with argon for 10 minutes. The vial was then placed in a microwave reactor and heated to 130 °C for 8 hours. The solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (30% EtoAc in PS 40-60 °C) to give the title compound S25 (11 mg, 28%) as a white solid.

Rf = 0.47 (30% EtoAc in PS 40-60 °C)

1H NMR (400 MHz, CDCl3): δ = 6.39-6.31 (m, 1H), 6.29-6.24 (m, 1H), 2.83 (dd, J = 15.5, 7.3 Hz, 1H), 2.67 (s, 1H), 2.56 (s, 3H), 2.52 (dd, J = 12.0, 4.8 Hz, 1H), 2.45 (t, J = 8.3 Hz, 1H), 2.36-2.25 (m, 1H), 2.10-1.96 (m, 1H), 1.96-1.84 (m, 1H), 1.83-1.65 (m, 3H) ppm

13C NMR (101 MHz, CDCl3): δ = 178.7, 177.0, 137.8, 136.5, 122.0, 121.4, 81.1, 78.4, 43.3, 40.5, 34.0, 24.8, 24.5, 24.4, 23.5 ppm

IR (thin film): νmax = 3282, 2926, 2852, 1771, 1694 cm⁻¹

Decomposition of Compound 4

We found that the product of [6π] electrocyclicization of substrate 4 could not be isolated without decomposition. We also found that under thermal conditions, compound 4 underwent inversion of stereochemistry to generate its E-isomer, compound 5.
Neat Stability Testing:

BHT crystals were added to neat samples of each hydrocarbon. The samples were then dissolved in CD$_2$Cl$_2$ and $^1$H NMR spectra were obtained. Each sample was then concentrated under reduced pressure (0 °C, 60 mbar) and re-dissolved in CD$_2$Cl$_2$. A second $^1$H NMR was then obtained to ensure no loss of material during the concentration of the sample. Each sample was then concentrated again under reduced pressure (0 °C, 60 mbar). The vials containing the neat samples were flushed with Ar and sealed. Samples were then either stored at ambient temperature (ca. 23 °C) for 16 hours or at -20°C for 16 hours.

-20 °C neat stability results:

![Diagram showing stability results at -20 °C](image)

Ambient temperature neat stability results:

![Diagram showing stability results at ambient temperature](image)

These results show/demonstrate that the more alkynes present in the molecule the more prone to decomposition the compound is.
All UV visible absorption spectra were recorded in acetonitrile at 23 °C.
TEE Decomposition:

We recommend caution when handling neat samples of TEE.

On one occasion, a ca. 0.5 mg sample in an aluminium cap exploded while being carried in a gloved hand, leaving a charcoal like dusting on the glove (see picture below). We presume that heat from the worker's hand was involved in the rapid decomposition process.
DSC:

Sample: MUS_NM_TVE
Size: 2.0000 mg
Method: Ramp

DSC

File: C:\MUS_NM_TVE.001
Operator: Maddie and Nick
Run Date: 09-May-2016 11:13
Instrument: DSC Q20 V24.11 Build 124

Sample: MUS_NM_tritylene
Size: 1.5000 mg
Method: Ramp

DSC

File: C:\MUS_NM_tritylene.001
Operator: Maddie and Nick
Run Date: 07-May-2016 11:44
Instrument: DSC Q20 V24.11 Build 124
Synthetic Route to (1(E,4E)-3-(1,5-diphenylpenta-1,4-diyn-3-ylidene)penta-1,4-diene-1,5-diyldibenzene (33)

The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

(1(E,4E)-3-(Dibromomethylenepenta-1,4-diene-1,5-diyldibenzene (31)

Prepared by modification of a procedure by Sherburn.\textsuperscript{14}
To a solution of ketone S27 (2.34 g, 10.0 mmol) in PhMe (40 mL) was added CBr\textsubscript{4} (8.29 g, 25.0 mmol, 2.5 mol equiv). The reaction mixture was cooled in a 0 °C ice bath and P(OPr)\textsubscript{3} (12.3 mL, 50.0 mmol, 5 mol equiv) was added dropwise. The reaction was stirred for a further 30 minutes at 0 °C. Sat. aq. sodium bicarbonate (50 mL) was then added to the
reaction mixture and the solution was warmed to 23 °C and extracted with CH₂Cl₂ (3 x 50 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then filtered through a short silica plug eluting with 50% CH₂Cl₂ in PS 40-60 °C and the solvent was removed under reduced pressure to give the title compound 31 as an orange solid (2.17 g, 56%).

¹H NMR and ¹³C NMR spectra matched those reported.¹⁴

¹H NMR (400 MHz, CDCl₃): δ = 7.55-7.45 (m, 4H), 7.41-7.28 (m, 6H), 7.00 (d, J = 16.1 Hz, 2H), 6.83 (d, J = 16.1 Hz, 2H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 141.0, 136.7, 136.0, 129.0, 128.6, 127.0, 126.2, 93.0 ppm

((1E,4E)-3-(1,5-Diphenylpenta-1,4-diyn-3-ylidene)penta-1,4-diene-1,5-diyl)dibenzene (33)

To a solution of dibromoolefins 31 (300 mg, 0.796 mmol) in THF (10.0 mL) and (i-Pr)₂NH (5 mL) was added phenyl acetylene (436 μL, 3.98 mmol, 5 mol equiv. [PdCl₂(dppe)] (65.5 mg, 0.0796 mmol, 10 mol %) and Cul (15.0 mg, 0.0796 mmol, 10 mol %) were then added to the reaction mixture. The solution was stirred at 23 °C for 17 hours. Water (40 mL) was then added to the reaction mixture which was extracted with CH₂Cl₂ (3 x 40 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C → 50% CH₂Cl₂ in PS 30-40 °C) to give the title compound 33 (250 mg, 75%) as an orange solid.

Rf= 0.86 (50% CH₂Cl₂ in PS 30-40 °C)

¹H NMR (400 MHz, CDCl₃): δ = 7.61-7.51 (m, 10H), 7.44-7.28 (m, 12H), 7.18 (d, J = 16.3 Hz, 2H) ppm
$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ = 149.5, 137.4, 136.0, 131.8, 129.1, 128.7, 127.2, 125.9, 123.5, 103.4, 97.1, 88.2 ppm

IR (thin film): $\nu_{\text{max}}$ = 3079, 3057, 3030, 1623, 1595, 1574 cm$^{-1}$

EI-MS (70 eV, EI): $m/z$ (%): 432 ([M]$^+$, 100), 431 ([M-H]$^+$, 30)

HRMS (EI): calcld for C$_{34}$H$_{24}$ [M]$^+$: 432.1878, found 432.1885

MP: 85.2 – 86.0 °C

XRAY: recrystallized from CDCl$_3$
Synthetic Route to (E)-(3-(1,5-diphenylpenta-1,4-diyn-3-ylidene)pent-1-en-4-yn-1,5-diyl)dibenzene (34), ((E)-3,4-di((E)-styryl)hexa-1,3-dien-5-yn-1,6-diyl)dibenzene (35), ((Z)-3,4-di((E)-styryl)hexa-3-en-1,5-diyn-1,6-diyl)dibenzene (37) and ((E)-3,4-di((E)-styryl)hexa-3-en-1,5-diyn-1,6-diyl)dibenzene (38)
The highlighted (grey) reactions/compounds have previously been reported in the literature. The reactions/compounds that are not highlighted are novel.

**(E)-1,5-Diphenylpent-1-en-4-yn-3-one (S29)**

\[
\begin{align*}
\text{Cl} & \quad \text{O} & \quad \text{Ph} \\
\text{S28} & \quad \text{O} & \quad \text{S29}
\end{align*}
\]

Prepared by modification of a procedure by Pacheco.\(^\text{15}\)

To a solution of acyl chloride S28 (3.33 g, 20.0 mmol) in THF (10.0 mL) and Et\(_2\)N (3.50 mL) was added phenyl acetylene (2.63 mL, 24.00 mmol, 1.2 mol equiv). Pd[PPh\(_3\)]\(_2\)Cl\(_2\) (281 mg, 0.80 mmol, 4 mol %) and CuI (152 mg, 0.40 mmol, 2 mol %) were then added to the reaction mixture. The solution was stirred at 35 °C for 1 hour. Water (40 mL) was then added to the reaction mixture which was extracted with Et\(_2\)O (3 x 40 mL). The organic extracts were combined, dried over MgSO\(_4\), filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (20% EtOAc in PS 40-60 °C) to give the title compound S29 (3.82 g, 82%) as an orange solid.

\(^1\)H NMR and \(^13\)C NMR spectra matched those reported.\(^\text{15}\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.92\) (d, \(J = 16.0\) Hz, 1H), 7.70-7.57 (m, 4H), 7.53-7.37 (m, 6H), 6.88 (d, \(J = 16.1\) Hz, 1H) ppm

\(^13\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 178.1, 148.2, 134.0, 132.9, 131.2, 130.6, 129.0, 128.7, 128.6, 128.4, 120.1, 91.5, 86.6\) ppm
(E)-(3-(Dibromomethylene)pent-1-en-4-yne-1,5-diyldibenzene (32)

A solution of CBr₄ (2.86 g, 8.62 mmol, 2 mol equiv) in CH₂Cl₂ (100 mL) was cooled in a 0 °C ice bath. PPh₃ (4.53 g, 17.2 mmol, 4 mol equiv) was then added to portions of the reaction mixture over five minutes (CAUTION: Exotherm). The solution was allowed to stir for 30 minutes before ketone S29 (1.00 g, 4.31 mmol) was added. The reaction mixture was warmed to 23 °C and stirred for 1 hour. The reaction mixture was poured onto cold stirring PS 40-60 °C (500 mL) and stirred for 10 minutes. The solution was filtered through a short pad of silica eluting with 10% CH₂Cl₂ in PS 40-60 °C. The solvent was removed under reduced pressure to give the title compound 32 (900 mg, 54%) as an off white foam.

R₂ = 0.50 (10% CH₂Cl₂ in PS 40-60 °C)

¹H NMR (400 MHz, CDCl₃): δ = 7.62-7.57 (m, 2H), 7.53 (d, J = 6.4 Hz, 2H), 7.43-7.30 (m, 6H), 7.26 (d, J = 15.4 Hz, 1H), 7.13 (d, J = 15.4 Hz, 1H) ppm

¹³C NMR (101 MHz, CDCl₃): δ = 136.5, 136.4, 131.8, 129.3, 129.0, 128.9, 128.9, 128.7, 127.4, 125.0, 122.7, 99.9, 98.6, 85.3 ppm

IR (thin film): v max = 3020, 1616 cm⁻¹

EIMS (70 eV, El): m/z (%): 388 ([M]+, 100)

HRMS (El): calcld for C₁₆H₁₇Br₂ [M]+: 385.9306, found 385.9313

(E)-(3-(1,5-Diphenylpenta-1,4-diyn-3-ylidene)pent-1-en-4-yne-1,5-diyldibenzene (34)
To a solution of dibromolefin 32 (150 mg, 0.39 mmol) in THF (2.0 mL) and (i-Pr)_2NH (1.5 mL) was added phenyl acetylene (185 μL, 1.95 mmol, 5 mol equiv). Pd(PPh_3)_2Cl_2 (13.7 mg, 0.019 mmol, 5 mol %) and Cul (7.4 mg, 0.039 mmol, 10 mol %) were then added to the reaction mixture. The solution was stirred at 30 °C for 22 hours. Water (5 mL) was then added to the reaction mixture which was extracted with CH_2Cl_2 (3 x 5 mL). The organic extracts were combined, dried over MgSO_4, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C ➔ 20% CH_2Cl_2 in PS 30-40 °C) to give the title compound 34 (161 mg, 96%) as an orange solid.

R_f = 0.16 (10% CH_2Cl_2 in PS 40-60 °C)

^1^H NMR (400 MHz, CDCl_3): δ = 7.71-7.54 (m, 9H), 7.45-7.30 (m, 13H) ppm

^1^3^C^ NMR (101 MHz, CDCl_3): δ = 136.9, 136.2, 135.2, 132.0, 132.0, 131.9, 129.2 x 2C, 129.2, 129.1, 129.0, 128.8 x 2C, 128.8, 127.6, 125.8, 123.3, 123.2, 123.0, 109.6, 102.0, 99.7, 96.6, 89.2, 86.5 ppm

IR (thin film): ν_max = 3075, 3064, 3036, 2216, 2186 cm⁻¹

ESIMS (70 eV, ESI): m/z (%): 431 ([M]^+, 100)

HRMS (EI): calc for C_{35}H_{25}Na [M]^+ 453.1619, found 453.1627

MP = 44.0 – 44.5 °C

XRAY: recrystallized from Et_2O

((E)-3,4-Di((E)-styryl)hexa-1,3-dien-5-ynyl-1,6-diyldibenzen (35)

To a solution of dibromolefin 32 (50 mg, 0.129 mmol) in THF (3.00 mL) was added Pd(dppf)Cl_2-tol (10.0 mg, 0.0129 mmol, 10 mol %) and ZnBr_2 (0.82 M in THF, 1.10 mL, 0.90 mmol, 7 mol equiv). 2E-styrenyl magnesium bromide (0.30 M in THF, 2.32 mL, 0.77 mmol, 6 mol equiv) was then added dropwise over 5 minutes to the reaction mixture. The solution
was heated to reflux and stirred for 1 hour. The reaction mixture was cooled to 23 °C and quenched with sat. aq. ammonium chloride (30 mL) and extracted with CH₂Cl₂ (3 x 100 mL). The organic extracts were combined, washed with brine (20 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C → 20% CH₂Cl₂ in PS 30-40 °C → 100% CH₂Cl₂) to give the title compound 35 (37 mg, 67%) as a yellow solid.

Rf = 0.25 (10% CH₂Cl₂ in PS 40-60 °C)

1H NMR (400 MHz, CDCl₃): δ = 7.81 (d, J = 16.1 Hz, 1H), 7.69-7.28 (m, 20H), 7.24-7.13 (m, 3H), 6.96 (d, J = 16.2 Hz, 1H), 6.86 (d, J = 16.4 Hz, 1H) ppm

IR (thin film): νmax = 3078, 3057, 3025, 2964, 2926, 2853 cm⁻¹

EIMS (70 eV, EI): m/z (%): 434 ([M⁺], 100), 432 ([M-2H⁺], 55)

HRMS (EI): calcd for C₃₀H₂₈ 434.2035, found: 434.2037

MP = 75.6 – 76.3 °C

((1E,3Z)-3-((E)-1-Bromo-3-phenylallylidene)pent-1-en-4-yne-1,5-diyl)dibenzene (36)

To a solution of dibromoolefin 32 (100 mg, 0.26 mmol) in THF (3.00 mL) was added Pd(PPh₃)₄ (15.0 mg, 0.026 mmol, 5 mol %) and ZnBr₂ (0.82 M in THF, 634 µL, 0.52 mmol, 2 mol equiv). 2E-styrenylmagnesium bromide (0.30 M in THF, 1.30 mL, 0.39 mmol, 1.5 mol equiv) was then added dropwise over 5 minutes to the reaction mixture. The solution was warmed to 35 °C and stirred for 5 hours. The reaction mixture was cooled to 23 °C and quenched with sat. aq. ammonium chloride (10 mL) and extracted with dichloromethane (3 x 50 mL). The organic extracts were combined, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% PS 30-40 °C → 10% CH₂Cl₂ in PS 30-40 °C) to give the title compound 36 (42 mg, 40%) as a yellow foam.
$R_f = 0.40$ (10% CH$_2$Cl$_2$ in PS 40-60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.68$-7.60 (m, 2H), 7.55 (d, $J = 7.7$ Hz, 4H), 7.51-7.28 (m, 12H), 7.21 (d, $J = 14.5$ Hz, 1H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 137.7$, 136.8, 136.5, 134.8, 131.7, 130.0, 128.9, 128.8, 128.5, 128.4, 127.4, 127.1, 124.7, 123.1, 122.5, 122.3, 99.2, 88.5 ppm

IR (thin film): $\nu_{\text{max}} = 3081, 3058, 3023, 2956, 2922, 2850, 1595, 1573$ cm$^{-1}$

EI MS (70 eV, El): $m/z$ (%): 412 (C$_{20}$H$_{19}$Br, [M]$^+$, 100), 410 (C$_{20}$H$_{19}$Br, [M]$^-$, 98)

HRMS (El): calc for C$_{20}$H$_{19}$Br [M]$^-$ 410.0670, found: 410.0674; C$_{20}$H$_{19}$Br [M]$^+$ 412.0650, found: 412.0645

((Z)-3,4-Di((E)-styryl)hexa-3-en-1,5-diyne-1,6-diyldibenzene (37)

A solution of phenyl acetylene (55 µL, 0.49 mmol, 2 mol equiv) in THF (10 mL) was cooled in a 0 °C ice bath. n-BuLi (1.20M in hexane, 303 µL, 0.36 mmol, 1.5 mol equiv) was added dropwise over 2 minutes to the reaction mixture. The reaction mixture was then stirred in the 0 °C bath for a further 30 minutes. ZnBr$_2$ (0.82 M in THF, 652 µL, 0.54 mmol, 2.2 mol equiv) was then added and the reaction mixture was warmed to 23 °C and stirred for 30 minutes. Pd$_2$(dba)$_3$ (13 mg, 0.012 mmol, 5 mol %) and Bu$_3$P (7 mg, 0.024 mmol, 10 mol %) were then added to the reaction mixture followed by bromide 36 (100 mg, 0.25 mmol). The reaction was stirred at 23 °C for 20 h. The reaction was quenched with sat. aq. ammonium chloride (10 mL) and extracted with CH$_2$Cl$_2$ (3 x 20 mL). The organic extracts were combined, washed with brine (20 mL), dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash preparative HPLC (Waters XBridge Prep C18 OBD column, 5 µm, 150 x 19 mm, eluting with 10% H$_2$O, 20% isopropanol in MeCN) to give the title compound 37 (24 mg, 23%) as a yellow solid.

$R_f = 0.25$ (10% CH$_2$Cl$_2$ in PS 40-60 °C)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.69$-7.54 (m, 7H), 7.50 (d, $J = 15.3$ Hz, 2H), 7.46-7.35 (m, 11H), 7.35-7.27 (m, 4H) ppm

$^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 137.0$, 134.9, 131.7, 128.8, 128.6, 128.4, 128.4, 127.2, 126.5, 123.4, 122.6, 98.7, 88.3 ppm

IR (thin film): $\nu_{\text{max}} = 3081$, 3057, 3023, 2922, 2852, 1753, 1595 cm$^{-1}$

EIMS (70 eV, EI): $m/z$ (%): 432 ([M]$^+$, 100), 431([M-H]$^-$, 25)

HRMS (EI): calcd for C$_{36}$H$_{32}$ [M]$^+$ 432.1878, found: 432.1875

MP = 55.4 – 56.2 °C

$((E)$-3,4-Di((E)-styryl)hexa-3-en-1,5-diyne-1,6-diyldibenzene (38)

To a solution of cis-compound 37 (9 mg, 0.020 mmol) in CDCl$_3$ (1 mL) was added a single crystal of I$_2$. This solution was placed in ambient light for 10 minutes. The reaction was quenched with sat. aq. sodium thiosulphate (5 mL) and extracted with CH$_2$Cl$_2$ (3 x 5 mL). The organic extracts were combined, dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure to give the title compound 38 (9 mg, 100%) as a yellow solid.

$R_f = 0.30$ (10% CH$_2$Cl$_2$ in PS 40-60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.69$ (d, $J = 15.7$ Hz, 2H), 7.61-7.21 (m, 24H) ppm

$^{13}$C NMR (175 MHz, CDCl$_3$): $\delta = 137.4$, 134.6, 131.8, 129.0, 129.0, 128.8, 128.6, 128.4, 127.6, 127.4, 123.3, 102.6, 85.5 ppm

IR (thin film): $\nu_{\text{max}} = 3078$, 3060, 3026, 2953, 2925, 2852 cm$^{-1}$

MP = 58.5 – 59.2 °C

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X-Ray Crystallographic Data

All cif files can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif using the reference numbers given below.

Compound S16 – code NM_F_141

\[ \text{C}_{29}\text{H}_{48}\text{Si}_{12}, \quad M = 440.84. \quad \text{triclinic,} \quad P-1 \text{ (No. 2),} \quad a = 8.1930(6) \text{ Å,} \quad b = 8.2201(8) \text{ Å,} \quad c = 11.2809(11) \text{ Å,} \quad \alpha = 87.909(6)^\circ, \quad \beta = 73.926(8)^\circ, \quad \gamma = 88.488(7)^\circ, \quad V = 729.45(12) \text{ Å}^3, \quad T = 150.00(10) \text{ K,} \quad Z = 1, \quad Z' = 0.5, \quad \mu(\text{MoK}) = 0.133, \quad 8032 \text{ reflections measured,} \quad 3490 \text{ unique} \ (R_{\text{int}} = 0.0392). \]

CCDC: 1942588
Compound 1 – code MJS_M_TEE

C₁₀H₄, Mᵣ = 128.16, orthorhombic, Pnma (No. 62), a = 6.6640(13) Å, b = 3.8545(10) Å, c = 13.965(4) Å, α = β = γ = 90°, V = 358.71(15) Å³, T = 150.00(10) K, Z = 2, Z' = 0.25, μ(CuKα) = 0.504, 957 reflections measured, 223 unique (Rₑₜ = 0.0379)

CCDC: 1942589
Compound 33 – code mjsn44a

C_{25}H_{24}, M_r = 432.53, monoclinic, P2_1/c (No. 14), a = 26.249(5) Å, b = 5.2480(10) Å, c = 17.399(4) Å, β = 93.52(3)°, α = γ = 90°, V = 2392.3(8) Å³, T = 100(2) K, Z = 4, Z’ = 1, μ (Synchrotron) = 0.068, 34356 reflections measured, 6084 unique (R_{exp} = 0.0755)

CCDC: 1942590

Acknowledgement: This research was undertaken on the MX1 beamline at the Australian Synchrotron, part of ANSTO.
Compound 34 – WB-A-3

C_{34}H_{22}. M_r = 430.51, monoclinic, \( \text{i2/a} \) (No. 15), \( a = 16.4126(12) \) Å, \( b = 5.4774(4) \) Å, \( c = 27.182(2) \) Å, \( \beta = 93.495(7)^\circ \), \( \alpha = \gamma = 90^\circ \), \( V = 2439.1(3) \) Å\(^3\), \( T = 150.01(10) \) K, \( Z = 4 \), \( Z' = 0.5 \), \( \mu(\text{MoK}) = 0.066 \), 6037 reflections measured, 2877 unique \( (R_{\text{int}} = 0.0195) \)

CCDC: 1942591
4 TEE/TVE Hybrids
TIPS

23

400 MHz, CDCl$_3$
TEE/TVE Hybrids

400 MHz, CDC$_3$
TEE/TVE Hybrids
27
101 MHz, CDCl₃
400 MHz, CDCl₃

3
3

101 MHz, CDCl₃
TMS-S8, 400 MHz, CDC1\textsubscript{3}
4 TEE/TVE Hybrids

30
101 MHz, CDCl₃
S16
400 MHz, CDCl₃
TEE/TVE Hybrids
TMS

TMS

S19
400 MHz, CDCl₃
all taken on
400 MHz machine in
CDCl₃
all taken on 101 MHz machine in CDCl₃
400 MHz, CDCl₃
TEE/TVE Hybrids
Conformational Analysis: Computational Method, Energies and Cartesian Coordinates

Calculations were carried out on isolated molecules of TEE 1, TVE 2 and TEE-TVE hybrids 3-7 in the gas phase using the Spartan’18 Parallel Suite package. B3LYP/6-31G* geometries within 30 kJ/mol of the minimum energy conformation were located employing a Monte Carlo search, then individual geometries were optimized using the MP2 method with the cc-pVTZ basis set. This level of theory has previously been shown to give reliable results with related structures.\textsuperscript{16} Relative total energy $E_{\text{rel}}$ (kJ/mol) and Boltzmann distributions refer to 298 K.

Names for conformations \textsuperscript{17} refer to the orientation of the vinyl group(s) relative to the central alkene as are as follows:
\textit{s-trans} = in plane conformation; 180° C=C−C=C 1,3-butadiene dihedral angle. 
\textit{s-cis} = in plane conformation; 0° C=C−C=C 1,3-butadiene dihedral angle. 
\textit{gauche} = 60° C=C−C=C 1,3-butadiene dihedral angle.

The measured dihedral angle closest to 0°, 60° or 180° determines the name used for the conformation, with the qualifying descriptor skew used to indicate that there is a twist in the rotatable bond from the ideal angle.

**TEE 1**

enynes = 180°

Energy = $-382.313946$ hartrees

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TEVE 3

Two conformers located. TEVE-A (the *s-trans* butadiene form, \( E_{ad} = 0 \) kJ/mol) and TEVE-B (the *skew s-cis* butadiene form, \( E_{ad} = +19.1 \) kJ/mol). Boltzmann distribution: TEVE-A:TEVE-B = 99.8 : 0.2

**TEVE-A**

*s-trans* 1,3-butadiene = 180°

enynes = 179°, 179°, 180°

Energy = −383.596253 hartrees

\[
\begin{array}{ccc}
C & -0.347144 & 0.075850 & -0.097868 \\
C & 0.983860 & -0.249574 & 0.092655 \\
C & -1.191259 & 0.518180 & 1.012029 \\
H & -0.698006 & 0.565850 & 1.978781 \\
C & -2.485950 & 0.850855 & 0.904431 \\
H & -3.052482 & 1.170259 & 1.773817 \\
H & -3.010335 & 0.816638 & -0.046195 \\
C & 1.606490 & -0.169771 & 1.374937 \\
H & 2.673536 & -0.067241 & 3.384088 \\
C & 2.173148 & -0.115253 & 2.443529 \\
C & 1.816427 & -0.684855 & -0.979606 \\
H & 3.207191 & -1.386850 & -2.639306 \\
C & 2.563166 & -1.058850 & -1.855351 \\
C & -0.917495 & -0.019970 & -1.399386 \\
H & -1.878634 & -0.157489 & -3.458693 \\
C & -1.442515 & -0.087779 & -2.487861
\end{array}
\]

**TEVE-B**
skew s-cis 1,3-butadiene = 18°
enynes = 177°, 178°, 180°
Energy = −383.588978 hartrees

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Z-DVDEE 4

The two lowest energy conformers were located. Z-DVDEE-A (the double s-trans butadiene form, $E_{rel} = 0$ kJ/mol) and Z-DVDEE-B (the skew s-trans–gauche butadiene form, $E_{rel} = +12.2$ kJ/mol). Boltzmann distribution: Z-DVDEE-A : Z-DVDEE-B = 99.3 : 0.7

Z-DVDEE-A
s-trans 1,3-butadienes = 180°
enynes = 177°, 180°
Energy = -384.836286 hartrees

```
C  0.692375 -0.010090  0.048681
C  -0.692375  0.010090  0.048681
C  -1.507002  0.017107 -1.170715
H  -0.976476  0.004238 -2.116874
C  -2.847989  0.035232 -1.198296
H  -3.384165  0.037996 -2.142519
H  -3.440866  0.047897 -0.289349
C  1.507002 -0.017107 -1.170715
H  0.976476 -0.004238 -2.116874
C  2.847989 -0.035232 -1.198296
H  3.384165 -0.037996 -2.142519
H  3.440866 -0.047897 -0.289349
C  -1.390859  0.023452  1.293831
H  -2.554562  0.047345  3.250267
C  -2.024751  0.036903  2.324975
```
Z-DVDEE-B

skew $s$-trans 1,3-butadiene = 172°; skew gauche 1,3-butadiene = 43°;
enynes = 170°, 173°

Energy = $-384.831653$ hartrees
**E-DVDEE 5**

The two lowest energy conformers were located: *E-DVDEE-A* (the *s*-trans butadiene form, \(E_{rel} = 0 \text{ kJ/mol}\)) and *E-DVDEE-B* (the *skew s-cis* butadiene form, \(E_{rel} = +19.2 \text{ kJ/mol}\)). Boltzmann distribution: \(Z\text{-DVDEE-A:Z-DVDEE-B} = 99.8 : 0.2\)

**E-DVDEE-A**

*s*-trans 1,3-butadienes = 180°
enynes = 180°

Energy = \(-384.840529\) hartrees

\[
\begin{array}{cccc}
C & 0.019558 & -0.691521 & 0.000028 \\
C & -0.019558 & 0.691521 & 0.000028 \\
C & -1.283130 & 1.432510 & -0.001129 \\
H & -2.178862 & 0.817765 & -0.004311 \\
C & -1.396304 & 2.769050 & 0.000692 \\
H & -2.372414 & 3.244123 & -0.001213 \\
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C & 1.283129 & -1.432510 & -0.001129 \\
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H & 2.372414 & -3.244123 & -0.001213 \\
H & 0.527304 & -3.420096 & 0.004083 \\
C & -1.192100 & -1.446040 & 0.000114 \\
H & -3.085082 & -2.712728 & 0.001187 \\
C & -2.195294 & -2.124709 & 0.000549 \\
C & 1.192100 & 1.446040 & 0.000114 \\
\end{array}
\]
E-DVDEE-B

$s\text{-}trans$ 1,3-butadiene $= 180^\circ$; $skew$ $s\text{-}cis$ 1,3-butadiene $= 27^\circ$

Enynes $= 175^\circ$, $176^\circ$

Energy $= -384.833234$ hartrees
**gem-DVDEE 6**

The three lowest energy conformers were located: *gem-DVDEE-A* (skew double s-trans conformation, $E_{int} = 0 \text{ kJ/mol}$), *gem-DVDEE-B* (skew s-trans–gauche conformation, $E_{int} = +4.0 \text{ kJ/mol}$) and *gem-DVDEE-C* (skew double s-cis conformation, $E_{int} = +22.6 \text{ kJ/mol}$)

*gem-DVDEE-A* ($E_{int} = 0 \text{ kJ/mol}$)

skew s-trans 1,3-butadienes = 155$^\circ$

enynes = 176$^\circ$

Energy = $-384.831487$ hartrees

\[
\begin{array}{cccc}
C & 0.000053 & 0.000066 & -1.226309 \\
C & -0.000059 & 0.000250 & 0.157654 \\
C & 1.279666 & 0.117846 & 0.864233 \\
H & 2.087060 & 0.553784 & 0.280476 \\
C & 1.553850 & -0.312686 & 2.105085 \\
H & 2.551795 & -0.198264 & 2.518177 \\
H & 0.821650 & -0.814399 & 2.728224 \\
C & -1.279865 & -0.117237 & 0.864121 \\
H & -2.087625 & -0.552498 & 0.279889 \\
C & -1.553751 & 0.312585 & 2.105464 \\
H & -2.551802 & 0.198261 & 2.518392 \\
H & -0.821202 & 0.813587 & 2.729203 \\
C & 1.201781 & 0.097403 & -1.993572 \\
H & 3.070313 & 0.246997 & -3.286576 \\
C & 2.194505 & 0.181259 & -2.681919 \\
C & -1.201524 & -0.097487 & 1.993784 \\
H & -3.069858 & -0.247489 & -3.287007 \\
\end{array}
\]
**TEE/TVE Hybrids**

*gem-DVDEE-B (E$_{\text{rel}}$ = +4.0 kJ/mol)*

- skew s-trans 1,3-butadiene = 172°; skew gauche 1,3-butadiene = 42°
- enyne cis- to skew s-trans 1,3-butadiene = 179°; enyne cis- to skew gauche 1,3-butadiene = 173°

Energy = $-384.829949$ hartrees
**gem-DVDEE-C** ($E_{\text{rel}} = +22.6 \text{ kJ/mol}$)

skew s-cis 1,3-butadienes = 27°, 28°

enynes = 172°, 173°

Energy = $-384.822875$ hartrees

**Chemical Structures**

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The three lowest energy conformers were located. TVEE-A (divinyl end: skew s-trans–gauche; $E_{\text{rel}} = 0 \text{ kJ/mol}$), TVEE-B (skew s-trans–gauche conformation, $E_{\text{rel}} = +8.5 \text{ kJ/mol}$ and TVEE-C (divinyl end: double s-trans; enyne end: skew gauche conformation, $E_{\text{rel}} = +12.5 \text{ kJ/mol}$). Boltzmann distribution: $\text{TVEE-A:TVEE-B:TVEE-C} = 96.2 : 3.1 : 0.6$

TVEE-A ($E_{\text{rel}} = 0 \text{ kJ/mol}$)  
(divinyl end) skew s-trans 1,3-butadiene = 171°; skew gauche 1,3-butadiene = 52°  
(ethynyl, vinyl end) skew s-trans 1,3-butadiene = 173°; enyne = 170°

Energy = −386.072460 hartrees

| C  | 0.039641 | 0.169068 | -0.764101 |
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| C  | 1.445417 | 0.561962 | 1.228010  |
| H  | 2.206317 | 0.943836 | 0.552231  |
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| H  | 2.709668 | 0.750947 | 2.914132  |
| H  | 1.037667 | 0.043060 | 3.258121  |
| C  | -0.947770 | -0.102265 | 1.530746  |
| H  | -1.062760 | 0.600548 | 2.356217  |
| C  | -1.758215 | -1.166387 | 1.481830  |
| H  | -2.540573 | -1.309072 | 2.222459  |
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| C  | -1.236577 | -0.056361 | -1.456055 |
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### TVEE-B ($E_{ew} = +8.5$ kJ/mol)

(divinyl end) skew $s$-trans 1,3-butadiene = 165°; skew gauche 1,3-butadiene = 44°

(ethynyl, vinyl end) skew $s$-trans 1,3-butadiene = 174°; enyne = 168°

Energy = $-386.069223$ hartrees

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**TVEE-C** \((E_{\text{rel}} = +12.5 \text{ kJ/mol})\)

(divinyl end) *skew s-trans* 1,3-butadienes = 149°, 160°

(ethynyl, vinyl end) *skew gauche* 1,3-butadiene = 36°; enyne = 176°

Energy = −386.067706 hartrees

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TVE 2

Conformational analysis of this molecule has been previously reported using the G4(MP2) method. In this earlier work, four conformations within 8 kJ/mol were located. The data from this previous work is reproduced here for ease of visual comparison with the new structures. Please see the original paper for full details. To validate the current method, a conformational analysis of TVE was performed. Three of these four conformers (TVE-A, TVE-B and TVE-D) were located, their geometries and relative energies were in good agreement the previous study. We did not locate in plane hexatriene conformer TVE-C in the present study.

TVE-A ($E_{rel} = 0$ kJ/mol)

TVE-B ($E_{rel} = +6.6$ kJ/mol)

TVE-C ($E_{rel} = +4.9$ kJ/mol)
TVE-D ($E_{rel} = +7.7 \text{ kJ/mol}$)
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(8) Lindebloom, E. J.; Willis, A. C.; Paddon-Row, M. N.; Sherburn, M. S. Angew. Chem. Int. 
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JOC. 2003, 670, 178


2019, 17, 5138


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Chapter Five:

Dendra-allenes


5 Dendra-allenes

Prelude

The manuscript is in draft format and is been prepared for submission to Angew. Chem. Int. Ed. The other author is my supervisor Professor Michael S. Sherburn. This project was conceived, designed, evolved and drafted in collaboration with Professor Michael S. Sherburn. The synthetic experiments were carried out by myself.

Dendra-allenes are defined by Hopf and co-workers in their 2011 paper as been dendralene compounds ‘in which one or more of their ethylene moieties have been replaced by other unsaturated groups in particular by allenic and cumulenic functions” (see below) (Lehrich, F., Hopf, H., Grunenberg, J. Eur. J. Org. Chem. 2011, 2705).

The first reported synthesis of dendra-allenes was by Hopf, H. and co-workers in 2011 (Lehrich, F., Hopf, H., Grunenberg, J. Eur. J. Org. Chem. 2011, 2705). The two dendra-allenes prepared were both [3]allenic dendralenes (see below). 4-Vinylpenta-1,2,4-triene was prepared in four steps while a substituted 1,1-divinylallene was also prepared in four steps. Unfortunately, the parent 1,1-divinylallene evaded synthesis by Hopf and co-workers.

Since the work of the Hopf and Sherburn groups on the allenic dendralenes no further syntheses of members of the allenic dendralene family have been reported. This chapter describes the attempted syntheses of a family of allenic dendralenes (see below).

It is important to note that this work is still currently ongoing and what is presented in this draft manuscript and supporting information represents our achievements to date.
Dendra-allenes
Madison J. Sowden and Michael S. Sherburn*

Abstract: The design, synthesis and emergent behavior of dendra-allenes, a new family of highly unsaturated fundamental hydrocarbons, is described. Previously, only the two smallest members of this family, namely 1,1-divinylallene ([3]dendra-2-allene) and 2-(1,3-butadienyl)-allene ([3]dendra-1-allene), were known. Ten new mono-allenic dendraallenes have been systematically designed, prepared and examined, with molecules prepared comprising up to eight C=C bonds, fourteen sp²-carbons and a single sp-carbon. The successful synthetic approach involves a coupling with 1,3-propargylic to allenic transposition, involving substituted propargylic carbonate electrophiles and (oligo)alkenyl nucleophiles. Remarkably, the majority of the new allenic dendraallenes are found to have comparable stability to their related (non-allenic) dendraallene counterpart, with the alternation in behavior previously witnessed in the dendraallenes being mirrored in their mono-allenic counterparts. Intriguingly, the [1]dendra-2-allene sub-series is shown to have heightened reactivity, which is explained through conformational effects.

The [n]dendra-allenes are a family of acyclic branched hydrocarbon structures comprising exclusively sp²-carbons (Figure 1). The smallest family member, [3]dendra-1-allene, has six carbons, hence three C=C bonds, which are arranged in a cross-conjugated manner. Thus, the two C=C bonds at the ends of the longest chain are not in conjugation with each other, but both are (formally) conjugated to the central C=C bond. Until the turn of this century, of the unsubstituted systems, only [3]- and [4]dendra-allenes were known. Recently, practical methods have been described for the synthesis of every family member up to [12]dendra-allene. With workable quantities of these materials in hand, it was observed experimentally that a dendraallene with odd numbers of C=C units is less stable than the even-parity dendraallenes immediately below and above it. Similar alternating behavior was seen in spectroscopic data and chemical reactivity. [3]Dendraallene and [4]dendraallene are, respectively, the most and least reactive members of the family and the alternation attenuates as the group is ascended. Nonetheless, all [n]dendra-allenes (n=3-12) are manageable in the laboratory without specialized handling techniques. These studies have contributed not only to the discovery of unexpected, emergent behavior; they have also underwritten a resurgence of interest in both the preparation and applications of n-bond-rich acyclic hydrocarbons, which were, prior to this work, thought to be unmanageable.

This paper describes the design, chemical synthesis and study of a family of fundamental hydrocarbon structures that extends each of the [n]dendraallene structures by a single sp-carbon atom. Specifically, it involves the study of [n]dendra-m-allenes (Figure 1), which are a family of structures derived by conceptually inserting a single sp-carbon into any one of the C=C bonds of a dendraallene molecule. Hopf and co-workers completed the synthesis of the first unsubstituted and substituted allenic dendraallenes, [3]dendra-1-allene 3 and methyl-substituted [3]dendra-2-allene in 2011.† We disclosed the synthesis of the parent [3]dendra-2-allene 4 in the same year. The value of allenic dendraallenes in the rapid generation of multicyclic, sp²-carbon-rich architecture has since been demonstrated through the completion of the shortest total synthesis of pseudopteroxin 6.‡ This last paper describes the preparation of only the fourth allenic dendraallene structure that has appeared in the literature, specifically chiral trimethyl analog 5. After testing the ability of the dendra-allenes to extend the [3]dendra-allenes by presenting a synthetic blueprint for the synthesis of all family members, and we reveal new emergent behavior in this fundamental family of hydrocarbons.

Figure 1: Reported dendraallenes and dendra-allenes, their properties and uses, and the focus of the present work.

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Supporting information and the ORCID identification numbers for the authors of this article can be found under: https://doi.org/10.1002/anie.xxxxxx.
The first ten members of the \([n]\)dendra-\(m\)-allenes (\(n=3-6\); \(m=1-3\)) are depicted in Figure 2. Whereas [3]- and [4]dendra-allenes have two possible dendra-allenic counterparts, [5]- and [6]dendra-allenes have three. Every successive pair of \([n]\)dendra-allenes after this will add one more possible monoa-llenic dendraallene structure. Since dendraallenic building blocks are not yet commercially available, the larger the target structure, the more synthetic effort will be required in order to prepare it. Based on our experience in synthesizing the parent \([n]\)dendraallene series up to the dodecaneene, we were confident that allene-containing structures up to this size are feasible. The synthetic effort involved in preparing these higher analogs, however, in addition to the large number of possible structures (six isomers of [11]- and [12]dendra-\(m\)-allene are feasible), coupled with uncertainty regarding their stability, led us to focus initially on the lower members (i.e. \(n=3-6\)). Our approach from the outset was to aim to prepare as many of the conceivable isomers in this structural space as possible, to maximize the chances of observing emergent behavior. Nonetheless, we devised a synthetic plan that would not only permit the preparation of the ten compounds shown in Figure 2. In principle, it would also permit the synthesis of higher “parent” dendra-allenes along with any substituted analogs.

The successful unified synthetic approach builds upon our synthesis of chiral 1,1-divinyllallene 8, where we performed a Kumada-type cross-coupling of an alkynyl nucleophile with a propargyl methanesulfonate. The reaction generates a conjugated vinylallene moiety through a \(sp^2\)-\(sp^2\) coupling, in reaction where the electrophilic partner undergoes a 1,3-propargyl C\(=\)O to alleny C\(=\)C transposition. We decided to use this key coupling reaction as the last step of the synthesis, because of the well-known propensity of allenes to participate in Pd(0)-catalyzed processes. The challenge with the present project was to extend the somewhat simple substrates used previously for this reaction to ones with extended (cross) conjugation. From the many preliminary experiments performed, we ascertained that propargyl carbonate performed well in place of mesityl coupling partners and had the advantage of being more robust, and that Negishi couplings were occasionally more effective than Kumada couplings.

\[\text{Scheme 1}\]

\[\text{figure}\]

\[\text{Scheme 1 shows the appropriately-functionalized propargyl carbonates carrying no substituent (19), a vinyl group (18), a 2-chlorovinyl group (20) and those with [3]- (21), [4]- (22) and [5]dendralenyl-groups (23). These carbonates were paired up with the appropriate vinyl-2-(1,3-butadienyl) and [3]dendralenyl nucleophilic coupling partners, through a systematic series of experiments that examined the effectiveness of Kumada and Negishi-type processes, along with different (pre)catalysts. The best outcomes are shown in Scheme 1, with compounds incompletely characterized at the time of this submission depicted in grey. We are confident that these characterizations can and will be completed in the near future after further optimization.}\]

So far, six dendra-allenes 7-9, 13, 16, 24 have been fully characterized. These compounds are manipulated using standard laboratory techniques and are purified by flash column chromatography or HPLC. Kumada cross-couplings, using [PdCl(\(dppe\))] as precatalyst, were employed for the synthesis of [4]dendra-2-allene 13 and [5]dendra-3-allene 16 and Negishi cross-couplings with [Pd(\(PPH_3\))] were used for the remaining seven reactions.

Figure 2: The first ten members of the series of dendralenic mono-allenes. The eight compounds in the shaded box are reported here for the first time.

Access to these compounds would allow us to answer a number of questions: will these dendra-allenes be more or less stable than their dendralene counterparts? Will we see an alternation in reactivity within this family of compounds as we do the dendralenes (odd members more reactive/unstable than even members)? Could the location of the allene in the chain have a significant effect upon the properties of the molecule?
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Scheme 1: The synthesis of [3]dendra-allenes (n=4-7, m=1-3).

[5]Dendra-1-allene 14, while stable, is challenging to purify due to the presence of [6]dendra-allene, an oxidative homocoupling side product formed in the coupling reaction. The other two greyed structures in Scheme 1 are the most reactive of the allenic dendra-allenes. In fact, challenges arose when attempting to synthesize and isolate three of the dendra-2-allene compounds, namely [5]dendra-2-allene 15, [6]dendra-2-allene 8 and [7]dendra-2-allene 25, with attempts to characterize compounds 15 and 25 still ongoing. [8]Dendra-2-allene 8 was eventually characterized as a solution in pivaldehyde ether to limit its rapid rate of degradation. A similar strategy will be employed to characterize the remaining dendra-2-allene compounds in the near future. It should be noted that, while having [6]dendra-2-allene 8 in solution decreases its decomposition rate, this method is not completely effective; complete decomposition of a ca. 0.01 M solution of 8 was observed at ambient temperature under 24 hours. (As an aside, we note that for synthetic purposes, neat samples of hydrocarbon building blocks are often not needed, so the synthetic value of these compounds is not necessarily compromised by their rapid decomposition.) In contrast to [5]dendra-2-allene 8, a ca. 1 M solution of [5]dendra-3-allene 16 in benzene when heated to 70 °C for 3 hours showed no signs of decomposition. This result shows that this compound is more stable towards self-reaction than the parent [5]dendra-allene.

In all cases of decomposing dendra-allenes, no decomposition products were isolable, which is consistent with our experience with 1,1-divinylallene (3)[dendra-2-allene] 4. In every case, we find that the more concentrated a sample, the faster its rate of decomposition. We therefore ascribe self-reaction as a means of decomposition, although more work is needed to identify whether this involves pericyclic, radical or cationic intermediates.

Based upon experience gained thus far, three general observations regarding the reactivity and stability of the dendra-allenes can be made: (1) In comparison with the parent dendra-allene, an allenic dendra-allene can be either less or more prone to self-reaction/decomposition; (2) If the allene replaces the second allene of a dendra-allene chain, i.e. to make a dendra-2-allene, the compound becomes much less stable than the parent dendra-allene; and (3) the [3]-, [4]-, [5]-, and [6]dendra-2-allenes (4, 13, 15, 8) appear to follow a similar trend in reactivity/stability to the parent dendra-allenes, in that the odd membered compounds are more reactive and difficult to handle than the even compounds. The instability seen in the dendra-2-allene series is not completely surprising with 1,1-divinylallene 4 already reported to show a high propensity towards oligomerization.¹

The origin of the alternation in behavior of the dendra-allenes has been traced to conformational effects. Specifically, the odd dendra-allenes adopt cisoid-conformations of their terminal 1,3-butadiene, which makes them more prone to Diels-Alder dimerization/polymerization.¹ The cause of the high self-reactivity of the dendra-2-allenes is most likely also a manifestation of conformational effects. We presume that the aforementioned cisoid-conformation is even more readily adopted by the terminal vinyl-allene group of a dendra-2-allene, since it lacks one of the two inside hydrogens that sterically
disfavor this conformation, hence leading to an even more rapid decomposition. The observation of the distinct (i.e. alternating low and high) reactivity of odd and even parby dendra-allenes in the dendra-2-allene sub-family is wholly consistent with this preliminary analysis, which awaits supporting computational investigations.

In conclusion we have designed synthetic pathways to successfully access nine dendra-allenes. We have preliminary results regarding the stability of these compounds indicating that the inclusion of an allene in a dendralkene does not necessarily make it more unstable. However, the dendra-2-allene series has been found to be unstable, most likely due to their heightened propensity to undergo Diels-Alder dimerization and oligomerization. Optimization of synthetic routes, half-life studies, and computational studies are ongoing.

Acknowledgements

This work was supported by the Australian Research Council. We warmly thank Dr Erik Lindeboom (ANU), Ms Georgia Howard (ANU) and Ms Cecile Elgindy (ANU) for preliminary experiments and Dr Hideki Onagi (ANU) for assistance with HPLC separations.

Keywords: hydrocarbons • allenes • cross-coupling • carbon-rich materials

Allene and mean family. The ten lowest members of the mono-allenic dendralene family have succumbed to synthesis through a unified strategy. These compounds are generally—but with one notable structural exception—remarkably robust compounds. Alternating behavior related to that seen previously in the dendralenes is observed and explained.
Supporting Information
for
Dendra-allenes

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General Methods

NMR Spectroscopy

$^1$H NMR spectra were recorded at 400 MHz using a Bruker AVANCE 400. Residual protio-solvent peaks were used as an internal reference for $^1$H NMR spectra (CDCl$_3$ $\delta$ 7.26 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. $^{13}$C NMR spectra were recorded at 101 MHz using a Bruker AVANCE 400. Solvent peaks were used as an internal reference for $^{13}$C NMR spectra (CDCl$_3$ $\delta$ 77.0 ppm). Assignment of carbon signals was assisted by HSQC and HMBC experiments. The following abbreviations (or combinations thereof) are used to denote $^1$H NMR multiplicities: s = singlet, bs = broad singlet, d = doublet, dd= doublet of doublets, t = triplet, m = multiplet.

Infrared Spectroscopy

IR spectra were recorded on a Perkin–Elmer UATR Two spectrometer as a thin film or solid.

Mass Spectrometry

Low-resolution EI mass spectra were recorded on a Finnigan Polaris Q ion trap mass spectrometer using electron impact (EI+) ionization mode at 40 or 70 eV. High-resolution EI mass spectra were recorded on a VG Autospec mass spectrometer operating at 70 eV.

Melting Points

Melting points were measured on a Stanford Research Systems Optimelt Automated Melting Point System and are uncorrected.

HPLC

Preparative HPLC was performed using a Waters 600E instrument on a Waters XBridge Prep C18 OBD 5 μm, (150 x 19 mm ID) column unless otherwise stated.

Experimental Procedures, Reagents, Chromatography and Glassware

Reactions were conducted under a positive pressure of dry nitrogen in heat gun-dried glassware and at room temperature, unless specified otherwise. Anhydrous solvents were S5 either obtained from commercial sources or dried according to the procedure outlined by Grubbs and co-workers. Commercially available chemicals were used as purchased, or where specified, purified by standard techniques. Analytical thin-layer chromatography was
conducted with aluminum-backed silica gel 60 F254 (0.2 mm) plates supplied by Merck, and visualized using UV fluorescence (λmax = 254 nm), or developed using KMnO4 or p-anisaldehyde, followed by heating. Flash chromatography employed Merck Kieselgel 60 silica gel (230–400 mesh). Solvent compositions are given in (v/v). PS 40–60 °C refers to petroleum spirits, boiling point fraction 40–60 °C. PS 60–80 °C refers to petroleum spirits, boiling point fraction 60–80 °C.
Syntheses of Required Carbonates:

**Methyl prop-2-yn-1-yl carbonate (19)**

Prepared according to a modified version of the published procedure.³
Propargyl alcohol S1 (3.00 g, 54 mmol), DIPEA (10.3 mL, 59 mmol, 1.1 mol equiv) and DMAP (120 mg, 1.1 mmol, 2 mol %) were dissolved in dichloromethane (100 mL). The reaction mixture was cooled in a 0 °C bath and methyl chloroformate (4.6 mL, 59 mmol, 1.1 mol equiv) was added drop wise to the solution. The solution was stirred at 25 °C for 23 hours. The reaction mixture was diluted with aqueous 1 M HCl (30 mL) and the organic layer was extracted, dried over MgSO₄, filtered through a pad of silica and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (30% ethyl acetate in PS 40- 60 °C), to give the title compound 19 as a yellow oil (4.13 g, 68%).
Spectroscopic data matched those previously reported.³

³¹H NMR (400 MHz, CDCl₃): δ = 4.67 (s, 2H), 3.76 (s, 3H), 2.50 (s, 1H) ppm

³¹C NMR (100 MHz, CDCl₃): δ = 155.3, 77.2, 75.8, 55.4, 55.3 ppm

**Methyl pent-4-en-2-yn-1-yl carbonate (18)**

Prepared according to a modified version of the published procedure.⁴
Vinyl bromide (10.0 g, 94 mmol), propargyl alcohol # (5.76 g, 103 mmol, 1.1 mol equiv), bis(triphenylphosphine) palladium dichloride (655 mg, 0.94 mmol, 1 mol %), copper iodide (710 mg, 3.73 mmol, 4 mol %), diisopropylamine (26.2 mL, 187 mmol, 2.0 mol equiv) were dissolved in THF (150 mL). The solution was stirred at 25 °C for 18 hours. H₂O (100 mL)
was added to the reaction mixture and the resulting mixture was extracted with ethyl acetate (3 x 150 mL). The organic extracts were combined, washed with brine, dried over MgSO₄, filtered through a pad of silica and the solvent was removed under reduced pressure. The crude product S2 was subjected to the next reaction without further purification.

Pent-4-en-2-yn-1-ol (7.67 g, 94 mmol), DIPEA (17 mL, 103 mmol, 1.1 mol equiv) and DMAP (214 mg, 1.9 mmol, 2 mol %) were dissolved in dichloromethane (200 mL). The reaction mixture was cooled in a 0 °C bath and methyl chloroformate (7.6 mL, 103 mmol, 1.1 mol equiv) was added drop wise to the solution. The solution was stirred at 25 °C for 21 hours. The reaction mixture was diluted with aqueous 1 M HCl (100 mL) and the organic layer was extracted, dried over MgSO₄, filtered through a pad of silica and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (10% ethyl acetate in PS 40- 60 °C), to give the title compound 19 as a yellow oil (10.0 g, 76%).

Spectroscopic data matched those previously reported.⁴

¹H NMR (400 MHz, CDCl₃): δ = 5.85-5.72 (m, 1H), 5.66 (dd, J = 17.6, 2.2 Hz, 1H), 5.51 (dd, J = 11.0, 2.2 Hz, 1H), 4.82 (s, 2H), 3.78 (s, 3H) ppm

¹³C NMR (100 MHz, CDCl₃): δ = 155.5, 128.7, 116.4, 86.0, 83.1, 56.3, 55.3 ppm
Route for the Synthesis of 4,5-Dimethylenehept-6-en-2-yn-1-yl methyl carbonate (20):

Prepared according to a modified version of the published procedure. Propargyl alcohol S1 (5.00 g, 89.2 mmol) was dissolved in CH₂Cl₂ (200 mL). The reaction mixture was cooled in a 0 °C bath and triethylamine (13.6 mL, 98.1 mmol, 1.1 mol equiv) and DMAP (217 mg, 1.78 mmol, 0.02 mol equiv) were added to the reaction mixture followed by slow portion-wise addition of TBSCI (14.7 g, 98.1 mmol, 1.1 mol equiv). The solution was stirred at 23 °C for 1 hour. H₂O (200 mL) was added to the reaction mixture and the organic layer was extracted, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then filtered through a pad of silica eluting with 50:50 dichloromethane in PS 40 – 60 °C, to give the title compound S3 as a colourless oil (13.6 g, 90%). Spectroscopic data matched those previously reported.

¹H NMR (400 MHz, CDCl₃): δ = 4.18 (s, 2H), 2.26 (s, 1H), 0.79 (s, 9H), 0.00 (s, 6H) ppm
¹³C NMR (100 MHz, CDCl₃): δ = 82.7, 73.1, 51.8, 26.1, 18.6, -4.9 ppm
Tert-butyl((4-chloropent-4-en-2-yn-1-yl)oxy)dimethylsilane (S4)

\[
\begin{align*}
\text{S3} & \xrightarrow{\text{piperidine, } \text{Et}_2\text{O}} \text{S4} \\
& \text{Cul, Pd(PPh}_3\text{)}_4 \xrightarrow{71\%} \text{OTBS} \text{OTBS}
\end{align*}
\]

Pd(PPh\(_3\))\(_4\) (680 mg, 0.59 mmol, 2.5 mol %) and 1,1-dichloroethylene (27.0 mL, 352 mmol, 15 mol equiv) were dissolved in diethyl ether (200 mL) and allowed to stir at 23 °C for 5 minutes. Copper iodide (112 mg, 0.59 mmol, 2.5 mol %), piperidine (4.60 mL, 47 mmol, 2 mol equiv) and alkyne S3 (4.00 g, 23.5 mmol) were then added to the reaction mixture. The solution was stirred at 23 °C for 22 hours. H\(_2\)O (200 mL) was added to the reaction mixture and the organic layer was extracted, dried over MgSO\(_4\), filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (2% ethyl acetate in PS 40 - 60 °C), to give the title compound S4 as a colourless oil (5.42 g, 71%).

\[R_f = 0.26\text{ (2.5% ethyl acetate in PS 40 - 60 °C)}\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.62\text{ (d, } J = 15.5\text{ Hz, } 2\text{H)}, 4.46\text{ (s, } 2\text{H)}, 0.92\text{ (s, } 9\text{H)}, 0.14\text{ (s, } 6\text{H})\) ppm

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 112\text{.4, 120\text{.3, 89\text{.7, 81\text{.6, 52\text{.2, 26\text{.1, 18\text{.6, -4.9 ppm}}}}}\)]

IR (thin film): \(\nu_{\text{max}} = 2956, 2930, 2865, 1757\text{ cm}^{-1}\)

MS (70 ev, EI): \(m/z\) (%): 232 ([M, \(^{37}\)Cl]\(^{37}\)Cl, 50), 230 ([M, \(^{35}\)Cl]\(^{37}\)Cl, 100)

HRMS (EI): calcd for C\(_{11}\)H\(_{19}\)OSi\(^{35}\)Cl [M]\(^{37}\)Cl: 230.0894; found: 230.0898 calcd for C\(_{11}\)H\(_{19}\)OSi\(^{37}\)Cl [M]\(^{37}\)Cl: 232.0864; found: 232.0865
4-Chloropent-4-en-2-yn-1-yl methyl carbonate (20)

Chloride S4 (1.80 g, 7.79 mmol) was dissolved in THF (100 mL). The reaction mixture was cooled in a 0 °C bath and TBAF (1 M solution in THF, 7.79 mL, 7.79 mmol, 1.0 mol equiv) was added. The solution was stirred at 23 °C for 1.5 hours. H₂O (50 mL) was added to the reaction mixture and the resulting mixture was extracted with diethyl ether (3 x 50 mL). The organic extracts were combined, washed with brine, dried over MgSO₄, filtered through a pad of silica and the solvent was then removed under reduced pressure. The crude product was then used in the following reaction without further purification.

Primary alcohol (903 mg, 7.79 mmol, 1.0 mol equiv), DIPEA (1.63 mL, 9.34 mmol, 1.1 mol equiv) and DMAP (20 mg, 0.16 mmol, 2 mol %) were dissolved in dichloromethane (100 mL). The reaction mixture was cooled in a 0 °C bath and methyl chloroformate (720 μL, 9.34 mmol, 1.1 mol equiv) was added drop wise to the solution. The solution was stirred at 25 °C for 15 hours. The reaction mixture was diluted with saturated aqueous ammonium chloride (50 mL) and the organic layer was extracted, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (5% ethyl acetate in PS 40- 60 °C), to give the title compound 20 as a colourless oil (940 mg, 69% yield over 2 steps).

Rᶠ = 0.32 (10% EtOAc in PS 40 - 60)
¹H NMR (400 MHz, CDCl₃): δ = 5.71 (d, J = 19.9 Hz, 2 H), 4.88 (s, 2 H), 3.83 (s, 3 H) ppm
¹³C NMR (100 MHz, CDCl₃): δ = 155.3, 123.9, 119.6, 84.0, 83.5, 55.7, 55.5 ppm
IR (thin film): νmax = 2959, 1750 cm⁻¹
MS (70 ev, El): m/z (%): 176 ([M, ³⁵Cl]⁺, 50), 174 ([M, ³⁷Cl]⁺, 100)
HRMS (El): calc for C₇H₇O₂Cl [M⁺]: 174.0084, found: 174.0088; calc for C₇H₇O₂³⁵Cl [M⁺]: 176.0054, found: 176.0057
Route for the Synthesis of 4,5-Dimethyleneciclohex-6-en-2-yn-1-yl methyl carbonate (21):

Pd(PPh_3)_4 (700 mg, 0.67 mmol, 2.5 mol %) and 1,1-dichloroethylene (32.0 mL, 401 mmol, 15 mol equiv) were dissolved in diethyl ether (200 mL) and allowed to stir at 23 °C for 5 minutes. Copper iodide (127 mg, 0.67 mmol, 2.5 mol %), piperidine (5.30 mL, 53.5 mmol, 2 mol equiv) and propargyl alcohol (1.50 g, 26.8 mmol) were then added to the reaction mixture. The solution was stirred at 23 °C for 21 hours. H_2O (200 mL) was added to the reaction mixture and the organic layer extracted, dried over MgSO_4, filtered and the solvent was removed under reduced pressure to give the title compound S5 (1.10 g, 35%) as a brown oil.

R_f = 0.30 (20%EtOAc in PS 40-60 °C)

^1H NMR (400 MHz, CDCl_3): δ = 5.67 (d, J = 17.0 Hz, 2H), 4.43 (s, 2H), 1.63 (bs, 1H) ppm

^13C NMR (100 MHz, CDCl_3): δ = 122.7, 119.6, 88.7, 81.9, 50.9 ppm

IR (thin film): ν max = 3300, 2919, 2863, 1603 cm^{-1}

MS (70 ev, Ei): m/z (%): 118 ([M, 35Cl]^{+}, 50), 116 ([M, 35Cl]^{2+}, 100)

HRMS (EI): calcd for C_{12}H_{10}O^{35Cl}[M]^{+}: 116.0029; found: 116.0028 calcd for C_{12}H_{10}O^{37Cl}[M]^{2+}: 117.9999; found: 117.9998
4,5-Dimethylenehept-6-en-2-yn-1-yl methyl carbonate (21)

A solution of ZnBr₂ (0.82 M in THF, 27.0 mL, 22.2 mmol, 4 mol equiv) in THF (6.00 mL) was cooled in a 0 °C ice bath and chloroprene Grignard reagent (0.95 M in THF, 17.6 mL, 16.7 mmol, 3 mol equiv) was added drop wise over 5 minutes to the reaction mixture. The solution was stirred for 20 minutes before chloride X (600 mg, 5.56 mmol) and Pd(dppf)Cl₂ (228 mg, 0.28 mmol, 5 mol %) were added to the reaction mixture. The reaction was then warmed to 23 °C and stirred for 3 hours. Water (20 mL) and Et₂O (50 mL) were then added to the reaction mixture, which was stirred for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was then subjected to the following reaction without further purification.

Primary alcohol S₅ (746 mg, 5.56 mmol), DIPEA (1.16 mL, 6.67 mmol, 1.2 mol equiv) and DMAP (14 mg, 0.11 mmol, 2 mol %) were dissolved in dichloromethane (50 mL). The reaction mixture was cooled in a 0 °C bath and methyl chloroformate (602 µL, 7.78 mmol, 1.4 mol equiv) was added drop wise to the solution. The solution was stirred at 23 °C for 21 hours. The reaction mixture was diluted with saturated aqueous ammonium chloride (50 mL) and the organic layer extracted, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (100% CH₂Cl₂), to give the title compound 21 as a colourless oil (300 mg, 28% yield over 2 steps).

**Rₛ = 0.80 (100% CH₂Cl₂)**

**¹H NMR (400 MHz, CDCl₃):** δ = 6.40 (ddd, J = 17.3, 10.8, 1.0 Hz, 1H), 5.65-5.59 (m, 2H), 5.47 (ddd, J = 17.2, 1.5 Hz, 2H), 5.32 (d, J = 1.5 Hz, 1H), 5.20 (dd, J = 10.8, 1.5 Hz, 1H), 4.90 (s, 2H), 3.82 (s, 3H) ppm

**¹³C NMR (100 MHz, CDCl₃):** δ = 155.5, 144.5, 135.0, 129.5, 124.4, 117.7, 117.2, 86.2, 83.6, 56.4, 55.4 ppm
IR (thin film): $v_{\text{max}} = 2958, 2854, 1751 \text{ cm}^{-1}$

MS (70 ev, EI): $m/z$ (%): 192 ([M]*, 100), 177 ([M-CH$_3$]*, 45)

HRMS (EI): calcld for C$_{11}$H$_{12}$O$_3$[M]*: 192.0786, found: 192.0783
Route for the Synthesis of Methyl (4,5,6-trimethyleneoct-7-en-2-yn-1-yl) carbonate (22):

A solution of ((3-bromoprop-2-yn-1-yl)oxy)(tert-butyl)dimethylsilane (200 mg, 0.81 mmol, 1.0 mol equiv) in THF (3 mL) was cooled in a -78 °C (dry ice/acetone) bath. n-BuLi (0.90 M in hexane, 1.0 mL, 0.97 mmol, 1.2 mol equiv) was added dropwise over 5 minutes. The reaction was stirred at -78 °C for a further 20 minutes. ZnBr₂ (0.93 M in THF, 1.7 mL, 1.62 mmol, 2.0 mol equiv) was then added. The reaction was stirred for a further 5 minutes at -78 °C before being warmed to 23 °C and stirred for 20 minutes. Pd(PPh₃)₄ (46 mg, 0.04 mmol, 5 mol %) and 2-bromo-3,4-dimethylenehexa-1,5-diene (150 mg, 0.81 mmol) were then added and stirring was continued for 1 hour. The reaction was quenched with sat. aq. ammonium chloride (10 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was then purified by flash column...
chromatography (100% PS 40-60 °C → 50% CH₂Cl₂ in PS 40-60 °C), to give the title compound S9 as a colourless oil (60 mg, 27%).

Rₓ = 0.77 (50% CH₂Cl₂ in PS 40-60 °C)

¹H NMR (400 MHz, CDCl₃): δ = 6.41 (dd, J = 17.4, 10.5 Hz, 1H), 5.77 (d, J = 1.8 Hz, 1H), 5.53 (s, 1H), 5.45 (s, 1H), 5.26 (d, J = 1.9 Hz, 1H), 5.21-5.06 (m, 4H), 4.51 (s, 2H), 0.93 (s, 9H), 0.15 (s, 6H) ppm

¹³C NMR (100 MHz, CDCl₃): δ = 146.8, 145.8, 137.6, 129.8, 124.1, 118.9, 118.8, 117.1, 89.6, 83.1, 52.4, 26.1, 18.6, -4.8 ppm

IR (thin film): νmax = 2953, 2929, 2894, 2861, 1833, 1573 cm⁻¹

MS (70 ev, El): m/z (%): 274 ([M⁺], 100), 273 ([M-H]⁺, 30), 259 ([M-CH₃]⁺, 25)

HRMS (El): calcld for C₁₇H₂₃OSe [M⁺]: 274.1753, found: 274.1750

Methyl (4,5,6-trimethylenoct-7-en-2-yn-1-yl) carbonate (22)

A solution of tert-butyldimethyl(4,5,6-trimethylenoct-7-en-2-yn-1-yl)oxy)silane (60 mg, 0.22 mmol, 1.0 mol equiv) in THF (3.0 mL) was cooled in a 0 °C ice bath. TBAF (1.0 M in THF, 240 µL, 0.24 mmol, 1.1 mol equiv) was then added dropwise over 5 minutes. The solution was then warmed to 23 °C and stirred for 2 hours. Water (20 mL) was then added and the solution was extracted with diethyl ether (3 x 20 mL). The combined organic fractions were washed with water (100 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure to yield 4,5,6-trimethylenoct-7-en-2-yn-1-ol. The crude compound was subjected to the next step without further purification.

A solution of 4,5,6-trimethylenoct-7-en-2-yn-1-ol (35 mg, 0.22 mmol) in CH₂Cl₂ (5 mL) was cooled in a 0 °C ice bath. DMAP (3.0 mg, 0.022 mmol, 10 mol %) and DIPEA (84 µL, 0.48 mmol, 2.2 mol equiv) were then added to the reaction mixture followed by methyl chloroformate (20 µL, 0.24 mmol, 1.1 mol equiv). The solution was warmed to 23 °C and stirred for 21 hours. The solvent was then removed under reduced pressure and the residue was re-dissolved in CH₂Cl₂ (20 mL), washed with water (3 x 10 mL), dried over MgSO₄,
filtered through a pad of silica (eluting with CH₂Cl₂) and the solvent was removed under reduced pressure to yield the title compound 22 as a yellow oil (46 mg, 96% over two steps)

\[ \text{Rf} = 0.67 \text{ (50% CH₂Cl₂ in PS 40 – 60 °C) } \]

\(^1\text{H NMR} \) (400 MHz, CDCl₃): \( \delta = 6.41 \) (dd, \( J = 17.4, \ 10.4 \) Hz, 1H), 5.75 (d, \( J = 1.7 \) Hz, 1H), 5.59 (s, 1H), 5.50 (s, 1H), 5.30 – 5.06 (m, 5H), 4.93 (s, 2H), 3.83 (s, 3H) ppm

\(^{13}\text{C NMR} \) (100 MHz, CDCl₃): \( \delta = 155.5, \ 146.6, \ 144.8, \ 137.5, \ 129.2, \ 125.3, \ 119.1, \ 119.0, \ 117.2, \ 85.5, \ 84.0, \ 56.4, \ 55.4, \ 53.7 \) ppm

\( \text{IR (thin film): } \nu_{\text{max}} = 3090, \ 3006, \ 2957, \ 2855, \ 1752 \text{ cm}^{-1} \)

\( \text{MS (70 ev, El): } m/z \%: 218 ([M]^{2+}, \ 100), \ 203 ([M-CH₃]^{2+}, \ 52) \)

\( \text{HRMS (El): calcd for C}_{13}H_{14}O₂[M]^{2+}: 218.0943, \text{ found: 218.0948} \)
Route for the Synthesis of Methyl (4,5,6,7-tetramethylenenon-8-en-2-yn-1-yl) carbonate (S11):

Tert-butyldimethyl[(4,5,6,7-tetramethylenenon-8-en-2-yn-1-yl)oxy]silane (S11)

A solution of (3-bromoprop-2-yn-1-yl)oxy)(tert-butyl)dimethylsilylamine (1.37 g, 5.48 mmol, 1.2 mol equiv) in THF (20 mL) was cooled in a -20 °C (ice/acetone) bath. n-BuLi (0.90 M in hexane, 7.10 mL, 6.40 mmol, 1.4 mol equiv) was added drop wise to the reaction mixture over 15 minutes. The reaction was stirred at -20 °C for a further 20 minutes. ZnBr₂ (0.93 M in THF, 8.80 mL, 8.23 mmol, 1.80 mol equiv) was then added. The reaction was stirred for a further 5 minutes at -20 °C before being warmed to 23 °C and stirred for 20 minutes. Pd(PPh₃)₄ (265 mg, 0.33 mmol, 5 mol %) and 2-bromo-3,4,5-trimethylenhepta-1,6-diene (969 mg, 4.57 mmol) were then added and the reaction was stirred for 2 hours. The reaction mixture was quenched with sat. aq. ammonium chloride (20 mL) and extracted with diethyl ether (3 x 100 mL). The combined organic layers were washed with brine (20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was then
purified by flash column chromatography (100% PS 40-60 °C → 10% diethyl ether in PS 40-60 °C), to give the title compound S11 as a colourless oil (317 mg, 24%).

R_v = 0.86 (10% diethyl ether in PS 40-60 °C)

^1H NMR (400 MHz, CDCl_3): δ = 6.43 (dd, J = 17.4, 10.7 Hz, 1H), 5.61 (s, 1H), 5.54 (s, 1H), 5.47 (s, 1H), 5.40 (d, J = 17.4 Hz, 1H), 5.31 (s, 1H), 5.27 (s, 1H), 5.22 (s, 1H), 5.14 (d, J = 11.6 Hz, 1H), 5.08 (s, 1H), 4.48 (s, 2H), 0.92 (s, 9H), 0.14 (s, 6H) ppm

^13C NMR (100 MHz, CDCl_3): δ = 147.1, 146.4, 146.4, 136.9, 130.2, 124.2, 118.6, 117.8, 117.0, 116.8, 89.3, 83.7, 52.4, 26.1, 18.6, -4.8 ppm

IR (thin film): ν_max = 2955, 2928, 2885, 2857, 1820, 1572 cm⁻¹


HRMS (EI): calcld for C_{10}H_{20}O_Si [M]^+^*: 300.1909, found: 300.1908

Methyl (4,5,6,7-tetramethylene-8-en-2-yn-1-yl) carbonate (23)

A solution of tert-butyldimethyl(4,5,6,7-tetramethylene-8-en-2-yn-1-yl)oxy)silane (317 mg, 1.05 mmol) in THF (10 mL) was cooled in a 0 °C ice bath. TBAF (1.0 M in THF, 1.05 mL, 1.05 mmol, 1.0 mol equiv) was then added drop wise over 5 minutes. The solution was then warmed to 23 °C and stirred for 2 hours. Water (10 mL) was then added and the solution was extracted with diethyl ether (3 x 30). The combined organic fractions were washed with water (10), dried over MgSO_4, filtered and the solvent was removed under reduced pressure to yield 4,5,6,7-tetramethylene-8-en-2-yn-1-ol. The crude compound was subjected to the next step without further purification.

A solution of 4,5,6,7-tetramethylene-8-en-2-yn-1-ol (196 mg, 1.05 mmol, 1.0 mol equiv) in CH_2Cl_2 (20 mL) was cooled in a 0°C ice bath. DMAP (13.0 mg, 0.105 mmol, 10 mol %) and DiPEA (403 μL, 2.31 mmol, 2.2 mol equiv) were then added followed by methyl chloroformate (89 μL, 1.16 mmol, 1.1 mol equiv). The solution was warmed to 23 °C and stirred for 21 hours. The solvent was then removed under reduced pressure and the residue was re-dissolved in CH_2Cl_2 (30 mL), washed with water (3 x 20 mL), dried over MgSO_4,
filtered through a pad of silica (eluting with CH$_2$Cl$_2$) and the solvent was removed under reduced pressure to yield the title compound 23 as a yellow oil (92 mg, 36% yield over 2 steps)

$R_f = 0.77$ (50% CH$_2$Cl$_2$ in PS 40-60 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.43$ (dd, $J = 17.3$, 10.7 Hz, 1H), 5.65-5.46 (m, 3H), 5.40 (dd, $J = 17.4$, 1.5 Hz, 1H), 5.32 (s, 1H), 5.29 -5.20 (m, 3H), 5.15 (d, $J = 10.9$, 1H), 5.08 (s, 1H), 4.91 (s, 2H), 3.83 (s, 3H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 155.5$, 146.6, 146.3, 146.2, 136.8, 129.6, 125.4, 118.9, 117.9, 117.1, 116.8, 86.1, 83.7, 56.4, 55.4 ppm

IR (thin film): $\nu_{max} = 3092, 3007, 2956, 2856, 1753$ cm$^{-1}$

MS (70 eV, ESI): m/z (%): 267 ([M+Na]$^+$, 100)

HRMS (ESI): calcd for C$_{13}$H$_{17}$O$_2$ [M$^+$]: 245.1172, found: 245.1168
**Allenic Dendralene Syntheses:**

4,5-Dimethylenehepta-1,2,6-triene (7)

![Diagram of synthesis](image)

To a 3 neck 500 mL rbf equipped with a dry ice condenser and addition funnel was added Mg turnings (614 mg, 25.3 mmol, 2.9 mol equiv) in THF (10.0 mL), 1,2-Dibromoethylene (377.5 µL, 4.36 mmol, 0.5 mol equiv) was then added dropwise, activating the Mg turnings. ZnBr₂ (1.09 M in THF, 400 µL, 0.44 mmol, 5 mol %) was then added. A solution of 2-chloro-[3]dendralene S13 (1.00 g, 8.74 mmol) and 1,2-dibromoethylene (377.5 µL, 4.36 mmol, 0.5 mol equiv) in THF (10 mL) was added via the addition funnel at such a rate that the solution was continuously at reflux. Once the addition was complete the reaction mixture was heated to reflux for a further hour then allowed to cool to 23 °C.

In a separate flask a solution of ZnBr₂ (1.09 M in THF, 12.0 mL, 13.1 mmol, 1.5 mol equiv) in THF (10.00 mL) was cooled in a 0 °C ice bath for 20 minutes. The [3]dendralenyl Grignard reagent S14 was then added over 5 minutes via cannula. The reaction mixture was warmed to 23 °C and stirred for 20 minutes. Pd(PPh₃)₄ (500 mg, 0.44 mmol, 5 mol %) was then added followed by carbonate 19 (1.50 g, 13.1 mmol, 1.5 mol equiv). The reaction mixture was stirred at 23 °C for 14 hours then poured onto a mixture of stirring cold PS 30-40 °C (300 mL) and water (300 mL). 1M aq. HCl (10 mL) was then added to the solution. The organic layer was separated, washed with brine (200 mL), dried over MgSO₄, filtered and concentrated under reduced pressure (0 °C, 60 mbar). The crude product was then purified by flash preparative HPLC (Waters XBridge Prep C18 OBD column, 5 µm, 150 x 19 mm, eluting with 20% H₂O in MeCN) to give the title compound 7 (206 mg, 20%) as a colourless oil.

Rᵣ = 0.88 (100% PS 30-40 °C)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.38$ (dd, $J = 17.4$, 10.6 Hz, 1H), 5.91 (t, $J = 6.7$ Hz, 1H), 5.27 (d, $J = 17.3$ Hz, 1H), 5.19 (d, $J = 14.2$ Hz, 2H), 5.15-5.07 (m, 2H), 4.98 (s, 1H), 4.88 (d, $J = 6.8$ Hz, 2H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 210.9, 147.1, 142.2, 137.5, 117.0, 116.6, 115.7, 95.1, 77.8$ ppm

IR (thin film): $\nu_{max} = 2958, 2922, 2852, 1732$ cm$^{-1}$

HRMS (EI): calcd for C$_9$H$_{10}$ [M]$:^{+}$: 118.0704, found: 118.0702

4-Methylene-3-vinylhexa-1,2,5-triene (13)

\[
\begin{align*}
\text{Ni(dpppe)Cl$_2$ (23 mg, 0.04 mmol, 3 mol %) and triphenylphosphine (23 mg, 0.08 mmol, 6 mol %) was flushed with N$_2$ twice. THF (3 mL) was then added, followed by carbonate 18 (200 mg, 1.43 mmol, 1.0 mol equiv). The reaction mixture was then cooled in a 0 °C ice bath and the chloroprene Grignard reagent (4.0 mL, 0.45 M in THF, 1.86 mmol, 1.3 mol equiv) was added drop wise over five minutes. The reaction was allowed to warm to 23 °C and stirred for 6 hours. H$_2$O (100 mL) was added and the resulting mixture was extracted with PS 30 – 40 °C (50 mL x 3). The combined organic extracts were washed with brine, dried over MgSO$_4$, filtered through a pad of silica, eluting with PS 30-40 °C and the solvent was removed under reduced pressure (0 °C, 50 mbar), to give the title compound 13 as a colourless oil (83 mg, 48%).}

R$_f$ = 0.88 (100% PS 30-40 °C)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.41$ (dd, $J = 17.3$, 10.5 Hz, 1H), 6.27 (dd, $J = 17.3$, 10.5 Hz, 1H), 5.43-5.29 (m, 2H), 5.26-5.06 (m, 4H), 4.99 (d, $J = 1.5$ Hz, 2H) ppm

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 210.3, 141.6, 136.7, 132.8, 117.7, 116.5, 115.5, 105.1, 76.3$ ppm

IR (thin film): $\nu_{max} = 3091, 2975, 2925, 1933$ cm$^{-1}$

MS (70 ev, EI): m/z (%): 235 ([M+C$_9$H$_{10}$]$^{+}$, 20), 118 ([M]$^{+}$, 25), 115 ([M-H$_2$]$^{+}$, 100)
HRMS (El): calcd for C9H10 [M]+: 118.0783, found: 118.0771

3,5-Dimethylene-4-vinylidenehepta-1,6-diene (16)

To a solution of carbonate 20 (200 mg, 1.15 mmol) in THF (5.00 mL) was added Ni(dppe)Cl2 (18.0 mg, 0.035 mmol, 3 mol %) and PPh3 (18.0 mg, 0.069 mmol, 6 mol %). The reaction mixture was cooled in a -10 °C ice/acetone bath. The chloroprene Grignard reagent (0.72 M in THF, 1.75 mL, 1.26 mmol, 1.1 mol equiv) was then added dropwise over 10 minutes. The reaction was warmed to 23 °C and stirred until 1H NMR analysis confirmed that no carbonate x remained. The reaction mixture was then cooled in a -10 °C ice/acetone bath and vinylmagnesium bromide (0.78 M, 4.42 mL, 3.45 mmol, 3 mol equiv) was added dropwise over 10 minutes. The reaction was then warmed to 23 °C and stirred for a further 2 hours. H2O (20 mL x 3) was added and the resulting mixture was extracted with PS 30 – 40 °C (20 mL x 3). The combined organic extracts were washed with brine, dried over MgSO4, filtered through a pad of silica, eluting with PS 30-40 °C and the solvent was removed under reduced pressure (0 °C, 60 mbar). The crude product was then purified via flash chromatography (100% PS 30-40 °C) to give the title compound 16 (40.0 mg, 24%) as a colourless oil.

Rf = 0.68 (100% PS 30-40 °C)

1H NMR (400 MHz, CDCl3): δ = 6.48-6.36 (m, 2H), 5.43 (dd, J = 17.5, 1.3 Hz, 2H), 5.32 - 5.26 (m, 2H), 5.17-5.09 (m, 4H), 4.99 (s, 2H) ppm

13C NMR (100 MHz, CDCl3): δ = 209.1, 142.2, 136.6, 116.9, 116.3, 77.5, 77.1 ppm

IR (thin film): γmax = 2923, 2853, 1935 cm⁻¹

MS (70 ev, El): m/z (%): 144 [M⁺⁺, 15], 129 [M-CH3]⁺⁺, 95, 128 [M-CH2]⁺⁺, 100

3,4,6-Trimethylene-5-vinylideneocta-1,7-diene (9)

A solution of ZnBr₂ (0.82 M in THF, 2.54 mL, 2.08 mmol, 4 mol equiv) was cooled in a 0 °C ice bath. The chloroprene Grignard reagent (0.95 M in THF, 1.64 mL, 1.56 mmol, 3 mol equiv) was then added drop wise over 5 minutes. The solution was stirred for 20 minutes before methyl 4,5-dimethylenepent-6-yn-1-yl methyl carbonate 21 (100 mg, 0.52 mmol) and Pd(PPh₃)₄ (60.0 mg, 0.052 mmol, 10 mol %) were added. The reaction was then warmed to 23 °C and stirred for 3 hours. Water (20 mL) and PS 30-40 °C (20 mL) were then added, and the solution was stirred for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with PS 30-40 °C) and concentrated under reduced pressure (0 °C, 60 mbar). The crude product was then purified via flash chromatography (100% PS 30-40 °C) to give the title compound 9 (88.0 mg, 61%) as a colourless oil.

R_f = 0.69 (100% PS 30-40 °C)

1H NMR (400 MHz, CDCl₃): δ = 6.42 (ddd, J = 17.7, 10.4, 7.7 Hz, 2H), 5.45-5.28 (m, 3H), 5.24-5.08 (m, 7H), 4.89 (s, 2H) ppm

13C NMR (100 MHz, CDCl₃): δ = ppm

IR (thin film): ν_max = 3069, 3007, 2925, 2854, 1935 cm⁻¹

MS (70 ev, El): m/z (%): 170 ([M]+, 25), 169 ([M-H]+, 65), 155 ([M-CH₃]+, 95), 141 ([M-C₂H₅]+, 100), 128 ([M-C₃H₇]+, 100)

4,5,6-Trimethylene-3-vinylocta-1,2,7-triene (8)

A solution of ZnBr₂ (0.82 M in THF, 3.35 mL, 2.75 mmol, 4 mol equiv) in THF (5.00 mL) was cooled in a 0 °C ice bath. Vinyl magnesium bromide (0.63 M in THF, 3.27 mL, 2.06 mmol, 3 mol equiv) was then added drop wise over 5 minutes. The solution was stirred for 20 minutes before methyl (4,5,6-trimethylenoct-7-en-2-yn-1-yl) carbonate 22 (150 mg, 0.69 mmol) and Pd(PPh₃)₄ (79 mg, 0.069 mmol, 10 mol %) were added. The reaction was then warmed to 23 °C and stirred for 2 hours. Water (10 mL) and PS 30-40 °C (10 mL) were then added and stirring was continued for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with PS 30-40 °C) and concentrated under reduced pressure (0 °C, 60 mbar). The crude product was then purified via flash chromatography (100% PS 30-40 °C) to give the title compound 8 (20.0 mg, 17%) as a colourless oil.

**Note:** this compound is unstable and was characterized as a solution in PS 30-40 °C

**R_f** = 0.82 (100% PS 30-40 °C)

**¹H NMR** (400 MHz, CDCl₃): δ = 6.43 (dd, J = 17.3, 10.5 Hz, 1H), 6.28 (dd, J = 17.3, 10.3 Hz, 1H), 5.40-5.18 (m, 6H), 5.15-5.07 (m, 4H), 4.96 (s, 2H) ppm


**HRMS** (El): calcd for C₁₃H₁₄ [M⁺]: 170.1096, found: 170.1094
A solution of ZnBr₂ (0.82 M in THF, 3.35 mL, 2.75 mmol, 4 mol equiv) was cooled in a 0 °C ice bath. The chloroprene Grignard reagent (0.95 M in THF, 2.17 mL, 2.06 mmol, 3 mol equiv) was then added drop wise over 5 minutes. The solution was stirred for 20 minutes before methyl (4,5,6-trimethylenoeoct-7-en-2-yn-1-yl) carbonate 22 (150 mg, 0.69 mmol) and Pd(PPh₃)₄ (79.0 mg, 0.069 mmol, 10 mol %) were added. The reaction was then warmed to 23 °C and stirred for 2 hours. Water (10 mL) and PS 30-40 °C (10 mL) were then added and stirring was continued for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with PS 30-40 °C) and concentrated under reduced pressure (0 °C, 30 mbar). The crude product was then purified via flash chromatography (100% PS 30-40 °C) to give the title compound 24 (55.0 mg, 41%) as a colourless oil.

Rᵥ = 0.73 (100% PS 30-40 °C)

¹H NMR (400 MHz, CDCl₃): δ = 6.45 (ddd, J = 16.4, 10.8, 4.7 Hz, 2H), 5.50 (d, J = 17.3 Hz, 2H), 5.39 – 5.09 (m, 10H), 4.95 (s, 2H) ppm

¹³C NMR (100 MHz, CDCl₃): δ = 209.6, 147.7, 146.8, 143.8, 142.3, 137.8, 136.8, 117.9, 117.8, 117.3, 116.7, 116.2, 106.1, 76.9 ppm

IR (thin film): νmax = 3089, 3013, 2964, 2927, 2859, 1934 cm⁻¹

MS (70 eV, El): m/z (%): 195 ([M]+, 50), 181 ([M-CH₃]+, 40), 167 ([M-C₃H₅]+, 70), 165 ([M-C₃H₇]+, 100)

Synthesised Compounds That Are Presenting Purification/Stability Based Challenges

4,5,6-Trimethyleneocta-1,2,7-triene (14)

A solution of 2-bromo-[4]dendralene S16 (380 mg, 2.05 mmol, 4 mol equiv) in THF (5.00 mL) was cooled in a -78 °C dry ice/acetone bath. n-BuLi (1.50 M in hexane, 1.37 mL, 2.05 mmol, 4 mol equiv) was added dropwise over 10 minutes. The solution was stirred for 30 minutes before ZnBr₂ (0.82 M in THF, 3.17 mL, 2.60 mmol, 5 mol equiv) was added dropwise over 5 minutes. The reaction mixture was stirred at -78 °C for a further 5 minutes before being warmed to 0 °C. The solution was stirred for 40 minutes. Pd(PPh₃)₄ (60 mg, 0.052 mmol, 10 mol %) and carbonate 19 (59 mg, 0.52 mmol) were then added to the reaction mixture which was then warmed to 23 °C and stirred for 3 hours. Water (10 mL) and PS 30-40 °C (10 mL) were then added and stirring was continued for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with PS 30-40 °C) and concentrated under reduced pressure (0 °C, 60 mbar).

*Note:* reaction works well, unfortunately an unidentified byproduct is produced during the reaction and this cannot be separated from the product using flash chromatography. HPLC will be required to purify this compound.
4,5-Dimethylene-3-vinylhepta-1,2,6-triene (15)

A solution of ZnBr₂ (0.82 M in THF, 2.54 mL, 2.08 mmol, 4 mol equiv) in THF (10.0 mL) was cooled in a 0 °C ice bath. Vinylmagnesium bromide (0.65 M in THF, 2.40 mL, 1.56 mmol, 3 mol equiv) was then added drop wise over 5 minutes. The solution was stirred for 20 minutes before carbonate 21 (100 mg, 0.52 mmol) and Pd(PPh₃)₄ (60 mg, 0.052 mmol, 10 mol %) were added. The reaction was then warmed to 23 °C and stirred for 2 hours. Water (10 mL) and PS 30-40 °C (10 mL) were then added to the reaction mixture, which was stirred for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried
over MgSO₄, filtered through a pad of silica (eluting with PS 30-40 °C) and concentrated under reduced pressure (0 °C, 60 mbar) to give the crude product.

**Note:** reaction works well, unfortunately the target material begins to decompose during purification. Furthermore, concentration of the sample results in rapid decomposition of the compound.

![NMR spectrum](image)

**4,5,6,7-Tetramethylene-3-vinylhexa-1,2,8-triene**

\[
\begin{align*}
&\text{MgBr} \\
&\text{ZnBr}_2, \text{Pd}(\text{PPh}_3)_4, \text{THF} \\
&23 \degree \text{C}, 2 \text{ h}
\end{align*}
\]

A solution of ZnBr₂ (0.93 M in THF, 396 µL, 0.369 mmol, 3 mol equiv) in THF (2.0 mL) was cooled in a 0 °C ice bath. Vinylmagnesium bromide (1.18 M in THF, 208 µL, 0.246 mmol, 2
mol equiv) was then added drop wise over 5 minutes. The solution was stirred for 20 minutes before carbonate 23 (30.0 mg, 0.123 mmol) and Pd(PPh3)4 (7.0 mg, 0.006 mmol, 5 mol %) were added. The reaction was then warmed to 23 °C and stirred for 2 hours. Water (50 mL) and PS 30-40 °C (10 mL) were then added to the reaction mixture, which was stirred for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO4, filtered and concentrated under reduced pressure (0 °C, 60 mbar) to give the crude product.

Note: reaction works well, unfortunately the target material decomposed during attempts to purify via flash column chromatography.
Attempted Alternate Approach to 3,5-Dimethylene-4-vinylidenehepta-1,6-diene (16)

Route for the Synthesis of Methyl (4-methylenehex-5-en-2-yn-1-yl) carbonate (22):

3-Bromoprop-2-yn-1-ol (S19)

A solution of propargyl alcohol (2.0 g, 35.7 mmol) in acetone (20 mL) was cooled in a -78 °C bath. N-Bromosuccinimide (7.6 g, 42.8 mmol, 1.2 mol equiv) and silver nitrate (606 mg, 8.92 mmol, 10 mol %) were then added. The reaction mixture was then allowed to warm to 23 °C and stir for 19 hours. The solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (100% PS 40-60 °C → 10% ethyl acetate in PS 40-60 °C → 20% ethyl acetate in PS 40 - 60 °C), to give the title compound S19 as a yellow solid (3.22 g, 67%).

Spectroscopic data matched those previously reported.\(^5\)
((3-Bromoprop-2-yn-1-yl)oxy)(tert-butyl)dimethylsilane (S8)

A solution of bromide S19 (3.07 g, 22.7 mmol), Et3N (3.4 mL, 25.0 mmol, 1.1 mol equiv), DMAP (55 mg, 0.45 mmol, 2 mol %) in dichloromethane (150 mL) was cooled in a 0 °C ice bath. TBSCI (3.76 g, 25.0 mmol, 1.1 mol equiv) was then added and the reaction was allowed to warm to 23 °C and stirred for 2 hours. H2O (100 mL) was added to the reaction mixture and the organic layer was extracted, dried over MgSO4, filtered and the solvent was removed under reduced pressure. The crude product was then filtered through a short pad of silica, eluting with 10% ethyl acetate in PS 40-60 °C to give the title compound S8 as a yellow oil (4.33 g, 77%).

Rf = 0.75 (100% PS 40-60 °C)

1H NMR (400 MHz, CDCl3): δ = 4.31 (s, 2H), 0.89 (s, 9H), 0.10 (s, 6H) ppm

13C NMR (100 MHz, CDCl3): δ = 78.9, 52.8, 44.9, 26.1, 18.5, -4.9 ppm

IR (thin film): νmax = 2954, 2929, 2865, 2857, 2219, 1472, 1463 cm⁻¹

HRMS (EI): calcld for C9H16OSiBr [M⁺]: 247.0154, found: 247.0157; calcld for C9H16OSiBr [M⁺]: 249.0133, found: 249.0131

Tert-butyl(dimethyl)((4-methylenehex-5-en-2-yn-1-yl)oxy)silane (S20)

ZnBr2 (0.9 M in THF, 18.7 mL, 16.8 mmol, 1.4 mol equiv) in THF (30 mL) was cooled in a 0°C ice bath. The chloroprene Grignard reagent (0.58 M in THF, 25.0 mL, 14.4 mmol, 1.2 mol equiv) was then added to the reaction mixture drop wise over 10 minutes. The solution was stirred for 20 minutes before Pd(dpff)Cl2 (495 mg, 0.60 mmol, 5 mol %) and bromide
S8 (3.00 g, 12.0 mmol, 1.0 mol equiv) were added. The reaction was allowed to warm to 23 °C and stirred for 22 hours. H₂O (100 mL) was added to the reaction mixture and the resulting mixture was extracted with diethyl ether (50 mL x 3). The combined organic extracts were washed with brine, dried over MgSO₄, filtered and the solvent removed under reduced pressure. The crude product was then purified by flash column chromatography (10% diethyl ether in PS 40-60 °C), to give the title compound S20 as a colourless oil (1.35 g, 51%).

Rₛ = 0.62 (10% Et₂O in PS 40-60 °C).

¹H NMR (400 MHz, CDCl₃): δ = 6.34 (dd, J = 17.0, 10.2 Hz, 1H), 5.70-5.59 (m, 1H), 5.51 (s, 1H), 5.42 (s, 1H), 5.24 (d, J = 10.3, 1H), 4.50 (s, 2H), 0.92 (s, 9H), 0.14 (s, 6H) ppm

¹³C NMR (100 MHz, CDCl₃): δ = 136.3, 130.1, 124.1, 118.0, 90.5, 81.6, 52.4, 26.1, 18.6, -4.8 ppm

IR (thin film): νmax = 2955, 2929, 2887, 2857, 1571 cm⁻¹

MS (70 ev, El): m/z (%): 222 ([M]+, 100), 207 ([M-CH₃]+, 55)

HRMS (El): calcd for C₁₉H₂₂OSi [M]+: 222.144, found: 222.1443

**Methyl (4-methylenehex-5-en-2-yn-1-yl) carbonate (S22)**

Tert-butylidimethyl[(4-methylenehex-5-en-2-yn-1-yl)oxy]silane S20 (489 mg, 2.20 mmol) in THF (5.0 mL) was cooled in a 0 °C ice bath. TBAF (1.0 M in THF, 2.20 mL, 2.20 mmol, 1.0 mol equiv) was then added drop wise over 5 minutes to the reaction mixture. The solution was then warmed to 23 °C and stirred for 2 hours. Water (50 mL) was then added to the reaction mixture and the solution was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic fractions were washed with water (20 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure to yield 4-methylenehex-5-en-2-yn-1-ol S21. This material was subjected to the next step without further purification.

A solution of crude 4-methylenehex-5-en-2-yn-1-ol S21 (2.20 mmol) in CH₂Cl₂ (20 mL) was cooled in a 0°C ice bath. DMAP (6.0 mg, 0.044 mmol, 10 mol %) and DIPEA (461 µL, 2.64
mmol, 2.2 mol equiv) were then added to the reaction mixture followed by methyl chloroformate (304 µL, 2.64 mmol, 1.1 mol equiv). The solution was warmed to 23 °C and stirred for 21 hours. The solvent was then removed under reduced pressure and the residue was re-dissolved in CH₂Cl₂ (100 mL), washed with water (3 x 10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with CH₂Cl₂) and the solvent was removed under reduced pressure to yield the title compound **S22** as a yellow oil (316 mg, 87% over two steps)

**Rf** = 0.45 (20% Et₂O in PS 40-60 °C)

**¹H NMR** (400 MHz, CDCl₃): δ = 6.34 (dd, J = 17.0, 10.2 Hz, 1H), 5.62 (d, J = 17.1 Hz, 1H), 5.56 (s, 1H), 5.48 (s, 1H), 5.32 – 5.22 (m, 1H), 4.92 (s, 2H), 3.83 (s, 3H) ppm

**¹³C NMR** (100 MHz, CDCl₃): δ = 155.4, 135.7, 129.3, 125.1, 118.3, 84.8, 83.9, 56.2, 55.3 ppm

**IR** (thin film): νmax = 3012, 2958, 1750 cm⁻¹

**MS** (70 ev, EI): m/z (%): 166 ([M⁺], 100)

**HRMS** (EI): calcd for C₉H₁₀O₂ [M⁺]: 166.0630, found: 166.0630

**Gram Scale Sequence with No Purification Between Steps:**

ZnBr₂ (43 mL, 0.9 M in THF, 40 mmol, 2.5 mol equiv) in THF (60 mL) was cooled in a 0 °C ice bath. The chloroprene Grignard reagent (0.58 M in THF, 55 mL, 32 mmol, 2.0 mol equiv) was then added to the reaction mixture drop wise over 10 minutes. The solution was stirred for 20 minutes before Pd(PPh₃)₄ (924 mg, 0.80 mmol, 5.0 mol %) and bromide **S8** (4.00 g, 16.0 mmol, 1.0 mol equiv) were added. The reaction was allowed to warm to 23 °C and stirred for 18 hours. H₂O (100 mL) was added to the reaction mixture and the resulting mixture was extracted with CH₂Cl₂ (100 mL x 3). The combined organic extracts were washed with brine, dried over MgSO₄, filtered and the solvent removed under reduced pressure to give crude tert-butyldimethyl((4-methylenehex-5-en-2-yn-1-yl)oxy)silane **S20**. The crude product was subjected to the next step without further purification.

Crude tert-butyldimethyl((4-methylenehex-5-en-2-yn-1-yl)oxy)silane **S20** (16 mmol) in THF (50 mL) was cooled in a 0 °C ice bath. TBAF (1.0 M in THF, 16 mL, 16 mmol, 1.0 mol equiv) was then added drop wise over 5 minutes to the reaction mixture. The solution was then warmed to 23 °C and stirred for 2 hours. Water (100 mL) was then added to the reaction mixture and the solution was extracted with CH₂Cl₂ (3 x 100 mL). The combined organic
fractions were washed with water (50 mL), dried over MgSO₄, filtered and the solvent was removed under reduced pressure to yield 4-methylenehex-5-en-2-yn-1-ol S21. The crude compound was subjected to the next step without further purification.

A solution of crude 4-methylenehex-5-en-2-yn-1-ol S21 (16 mmol) in CH₂Cl₂ (100 mL) was cooled in a 0 °C ice bath. DMAP (193 mg, 1.6 mmol, 10 mol %) and DIPEA (6.2 mL, 35 mmol, 2.2 mol equiv) were then added to the reaction mixture followed by methyl chloroformate (1.4 mL, 18 mmol, 1.1 mol equiv). The solution was warmed to 23 °C and stirred for 21 hours. The solvent was then removed under reduced pressure and the residue was re-dissolved in CH₂Cl₂ (100 mL), washed with water (3 x 10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with CH₂Cl₂) and the solvent was removed under reduced pressure to yield the title compound S22 as a yellow oil (1.20 g, 45% over three steps).

**3,5-Dimethylene-4-vinylidenehepta-1,6-diene (S16)**

\[
\text{S22} \xrightarrow{\text{ZnBr₂, THF, Pd(dppf)Cl₂}} \xrightarrow{23 °C, 3 h} \text{S22} \xrightarrow{\text{MgCl}} \text{ZnBr₂} \xrightarrow{\text{O}_3\text{Me}} \text{OCCO}_2\text{Me}
\]

A solution of ZnBr₂ (0.82 M in THF, 4.44 mL, 3.64 mmol, 4 mol equiv) in THF (5.0 mL) was cooled in a 0 °C ice bath. The chloroprene Grignard reagent (0.95 M in THF, 2.90 mL, 2.72 mmol, 3 mol equiv) was then added drop wise over 5 minutes. The solution was stirred for 20 minutes before carbonate S22 (150 mg, 0.91 mmol) and Pd(PPh₃)₄ (105 mg, 0.091 mmol, 10 mol %) were added. The reaction was then warmed to 23 °C and stirred for 3 hours. Water (10 mL) and PS 30-40 °C (10 mL) were then added and stirring was continued for a further 5 minutes. The organic layer was then extracted, washed with water (10 mL), dried over MgSO₄, filtered through a pad of silica (eluting with PS 30-40 °C) and concentrated under reduced pressure (0 °C, 60 mbar) to give the crude product.
NOTE: this reaction gave a large number of products including the target material. Unfortunately, only very small quantities of the target material could be attained after purification rendering this route unviable.
References


(3) Kenny, M., Christensen, J., Coles, S. J., Franckevicius, Org. Lett. 2015, 171 53926-3929


21
400 MHz, CDCl₃
22
101 MHz, CDCl₃
400 MHz, CDCl₃
Chapter Six:

Conclusions and Future Work
6 Conclusions and Future Work

The publications included in this thesis highlight the importance of step economic and efficient syntheses of both natural products and target molecules. The importance of synthesizing fundamental hydrocarbons to learn more about structure and reactivity relationships is also highlighted throughout the publications. Chapter One disclosed the shortest synthesis of natural product selaginulpilvin D to date. This four step approach utilized a three-fold one pot electrophilic aromatic substitution sequence as the key step to generate the fluorene core of the molecule, in the process generating three new carbon-carbon bonds (scheme 1). A Sonogashira cross-coupling employing Buchwald’s conditions provided the methylated natural product which underwent a four-fold demethylation using neat MeMgI to generate the natural product in a 17% overall yield (scheme 1).

Scheme 1: Four-step total synthesis of selaginulpilvin D

Our approach is significantly shorter than those previously and subsequently reported and generates synthetically useful quantities of the natural product (ca. 1 g) for the first time. This synthesis highlights the power of step economy in efficient syntheses.
Inspired by our efficient synthesis in Chapter One we moved to Chapter Two and started to apply the same ideology to specific fundamental hydrocarbon target molecules. This chapter explored the development of a new synthetic method to rapidly generate 2,3-diethynyl-1,3-butadienes. Only five 2,3-diethynyl-1,3-butadienes had previously been reported in the literature.

Figure 1: 2,3-Diethynyl-1,3-butadiene synthesis and compounds which can be made from them (extended radialenes and cyclooctadienes).

In 1-2 steps commencing from commodity chemicals, substituted diols are generated which then undergo a two-fold nucleophilic acyl substitution reaction to yield bis-carbonates (figure 1). These bis-carbonates can then be utilized in a two-fold Sonogashira cross-coupling with 2 mol equiv of a functionalized alkyne to give substituted 2,3-diethynyl-1,3-butadienes. We found the scope of this two-fold Sonogashira cross-coupling to be broad with over 25 examples of substituted 2,3-diethynyl-1,3-butadienes prepared. This large library of substrates allowed us to explore the stabilities and reactivities of these compounds in depth for the first time. Furthermore, the synthesis of these compounds facilitated the generation of expanded radialenes, dendralenes and cyclooctadienes (figure 1), the synthesis of which showcases the power of 2,3-diethynyl-1,3-butadienes in further reactions.

Chapter Three was another target synthesis project which involved the development of new chemical reactions to efficiently generate five novel tetravinylethylene (TVE)/tetra
Conclusions and Future Work

Ethynyethylene (TEE) hybrids (figure 2). TVE and TEE had both been synthesised previously with these compounds having vastly different properties. TVE was known to be a bench stable oil while TEE is an unstable crystalline solid.

![Known Compounds and Five Novel Hybrid Compounds](image)

**Figure 2:** Known compounds TVE and TEE; novel compounds TVEE, gem-DVDEE, E-DVDEE, Z-DVDEE and TEVE

We were successfully able to synthesise all five of the hybrid compounds through the use of either two-fold or mono cross-couplings of dibroolefins. The most challenging compounds to synthesise were E-DVDEE and Z-DVDEE. These compounds required the development and use of a series of unprecedented chemical reactions. From the dibromoolefin we were able to generate a Z-triene via a selective Negishi cross-coupling (scheme 2). The Z-triene could then be elaborated into Z-DVDEE via a stereo-retentive Negishi cross-coupling (scheme 2). E-DVDEE was accessed via a novel stereo-invertive Sonogashira cross-coupling of the Z-triene (scheme 2). The development and employment of these novel reactions in the synthesis of these compounds provided us with useful quantities of these new hydrocarbons.

![Scheme 2: Synthesis of Z-DVDEE and E-DVDEE](image)
With these compounds in hand we were able to systematically evaluate what makes these compounds tick through a series of stability tests. Interestingly these compounds were found to be far more robust than anticipated. To showcase the versatility of the synthetic routes devised, we also synthesised a series of phenyl substituted compounds (figure 3). These compounds were found to be more stable than the parent hydrocarbons.

*Figure 3: Phenyl substituted TVE/TEE hybrids*

Investigations into the use of this newly developed chemistry in the generation of other substituted structures are on going in our research group.

In Chapter Four we found ourselves targeting yet another family of unexplored fundamental hydrocarbons. Consistent with our other syntheses we focused on developing an efficient approach to the synthesis of these target molecules. It was our desire to generate a family of dendra-allenes in which an allene replaced one alkene unit of the corresponding dendralene. We wished to target all possible regioisomers of the [3]dendra-allenes, [4]dendra-allenes, [5]dendra-allenes, [6]dendra-allenes and two of the possible four isomers of the [7]dendra-allenes (figure 4).

*Figure 4: Family of dendra-allenes targeted in Chapter 4*
After exploring a number of ways to access the dendra-allenes we decided upon the use of a number of substituted propargylic carbonates (Figure 5). In total seven substituted propargylic carbonates were synthesised to provide us with a variety of options when synthesizing the dendra-allenes. While the strategy to target each allenic dendralene was consistent, we found that each of the desired compounds required slightly differing sets of reaction conditions. Developing this library of carbonates proved crucial in the success of this project.

![Figure 5: Carbonates synthesised en route to a family of dendra-allenes](image)

So far we have successfully synthesised and characterized 6 dendra-allenes (shown in black in Figure 6). We have also been able to synthesise the compounds shown in grey in Figure 6, however problems relating to the stability of these compounds have so far prohibited us from completing the characterisation of these compounds.

![Figure 6: A family of dendra-allenes](image)

Based upon our first hand experience, we can draw three preliminary conclusions regarding the stability and reactivity of these compounds: (1) some dendra-allenes
appear to be at least as stable as the corresponding dendralene; (2) if the allene replaces the second alkene from the end of the chain the compound is less stable than the corresponding dendralene; (3) the compounds with the allene replacing the second alkene seem to be following a similar alternating trend in reactivity to the dendralenes in that the odd compounds are less stable than the even compounds. Further investigations into the reactivity and stability associated with these compounds is currently underway.

The work described in this thesis has focused on the development of efficient syntheses of both natural products and target molecules. We have developed the shortest total synthesis of selaginulpilin D, provided the first general method for the synthesis of 2,3-diethynyl-1,3-butadienes and developed efficient synthetic pathways to access two families of previously unexplored fundamental hydrocarbons. Furthermore, we have provided new insights into the reactivity and stability of these compounds, particularly the fundamental hydrocarbons we have synthesised. With the information we have gained regarding these compounds and their behaviours we have challenged the notion that π-bond-rich hydrocarbons are unmanageable and as such unusable in either total synthesis or the synthesis of other target molecules. This thesis demonstrates the power of efficiency and strategy in synthesis whether that be of natural products or of designed molecules.