Department of Chemistry

Towards the Synthesis of Isocoronene

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This thesis is presented for the Degree of
Doctor of Philosophy
of
Curtin University

April 2018

Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgement has been made. This thesis contains no material which has been accepted for the award of any other degree or diploma in any other university.

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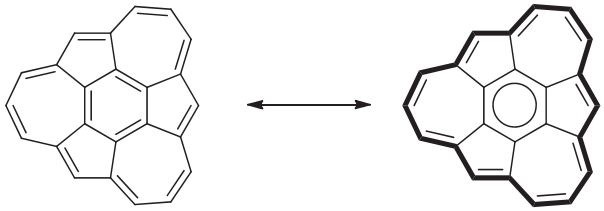
Abstract

The concept of aromaticity and its implications are fundamentally important to a wide range of applied sciences involving organic molecules. Aromaticity arises from the delocalisation of electrons through a cyclic conjugated system known as a conjugated circuit. Monocyclic aromatic compounds possess a single conjugated circuit while polycyclic aromatic hydrocarbons (PAHs) may have numerous potential conjugated circuits. The aromaticity of PAHs is complicated by the presence of multiple conjugated circuits which may have varying contribution to the overall properties depending on several factors such as geometry and topology.

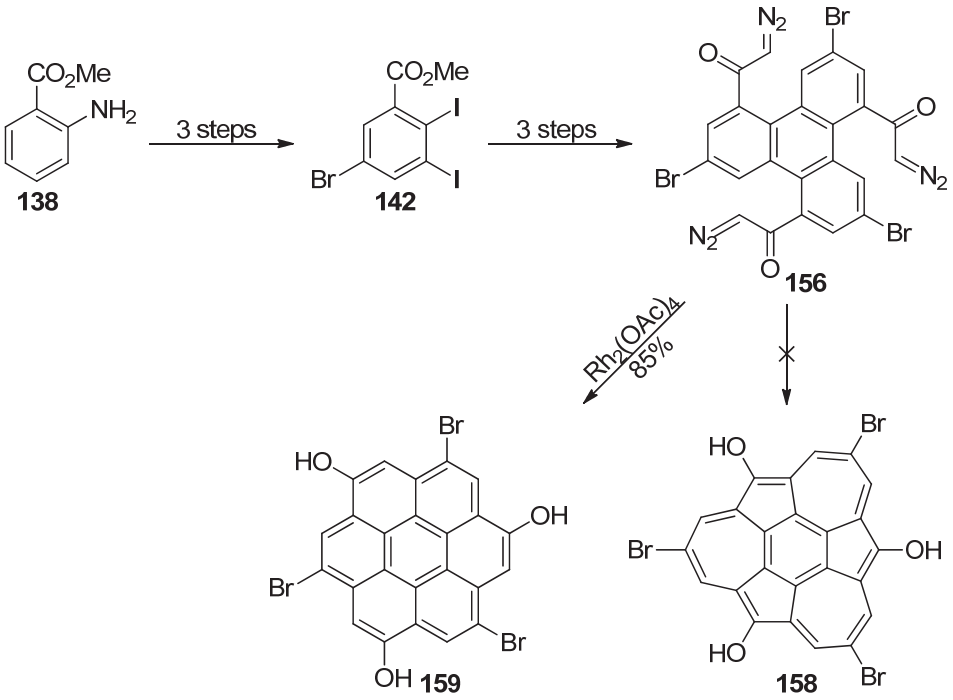
Isocoronene **105** is one example of a PAH classified as a non-benzenoid corannulene. Isocoronene is unique among corannulenes since the conjugated circuits are restricted to the peripheral and central rings only. Isocoronene has been used as a model compound for computational studies into aromaticity and may provide the first example of a superaromatic molecule. The synthesis of novel aromatic structures such as isocoronene is essential in providing unambiguous empirical data which can be used to verify and develop computational methods. In addition, the development of new synthetic methodologies towards PAHs is important in the field of organic electronics. The following thesis describes synthetic strategies and experimental work towards the synthesis of isocoronene.



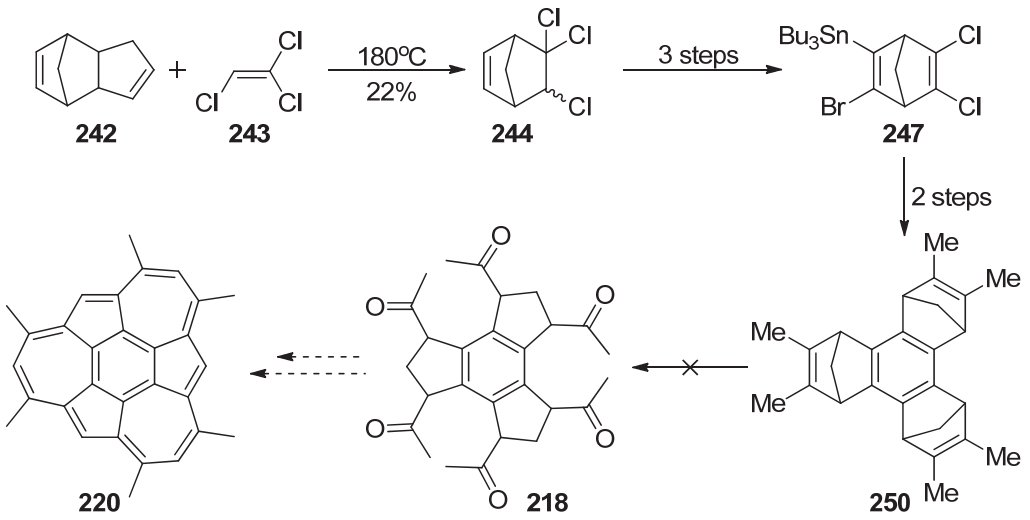
105a **105b**

The initial strategy for the synthesis of isocoronene was through a threefold intramolecular Buchner reaction. The key intermediate triphenylene diazoketone **156** was synthesised from methyl anthranilate **138** in six steps. Rhodium catalysed decomposition of the diazoketone gave coronene **159** in high yield as a single major product with no detectable amount of the desired isocoronene derivative. The formation of coronene was attributed to an intramolecular C-H insertion reaction. The desired Buchner ring expansion may be disfavoured due to the electron

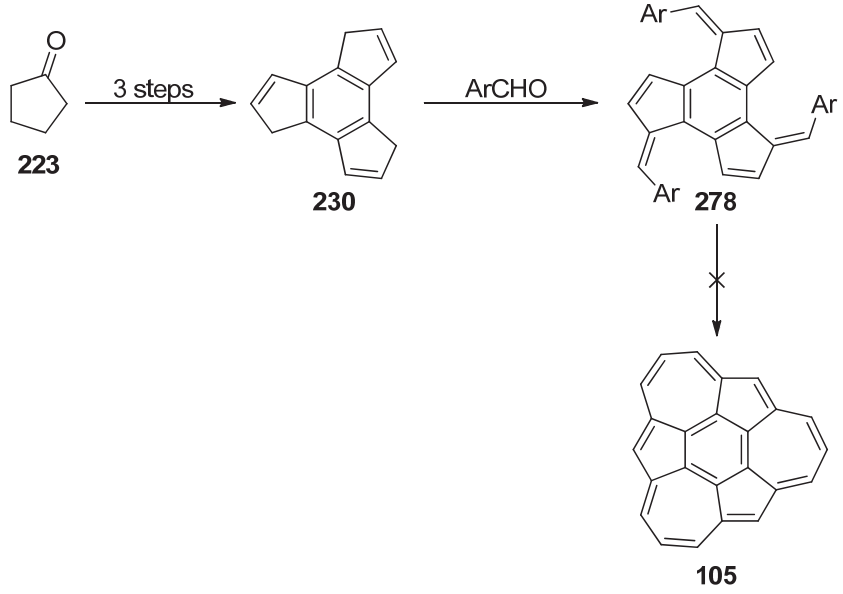
withdrawing carbonyl groups of **156**. The synthesis of coronene **159** through intramolecular C-H insertion has not previously been reported in the literature. This method could be applied to the synthesis of coronene derivatives with substitution patterns and functional groups that are not accessible through known methods.



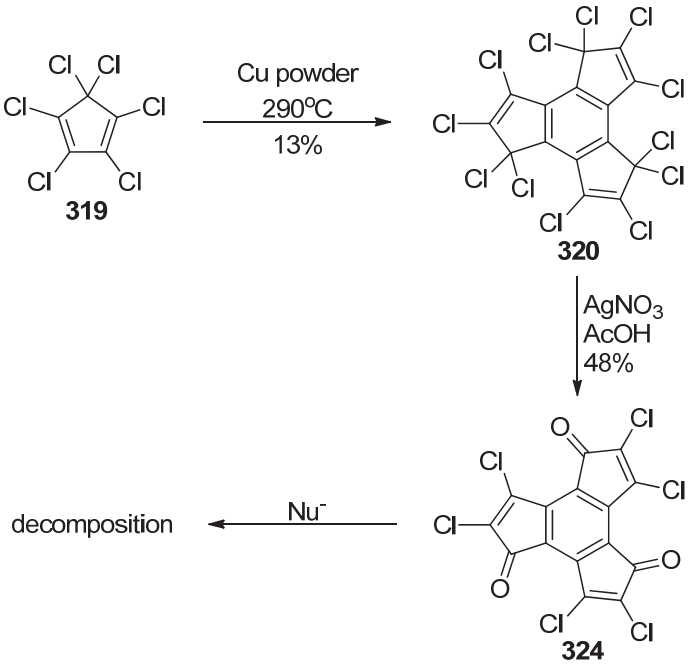
The second approach towards isocoronene involved an intramolecular aldol condensation of trindane derivative **218**. To this end, the norbornadiene cyclotrimer **250** was synthesised in 6 steps from dicyclopentadiene **242** and trichloroethylene **243**. Several attempts were made at the oxidative ring opening of **250** resulting in a product that could not be characterised by NMR.



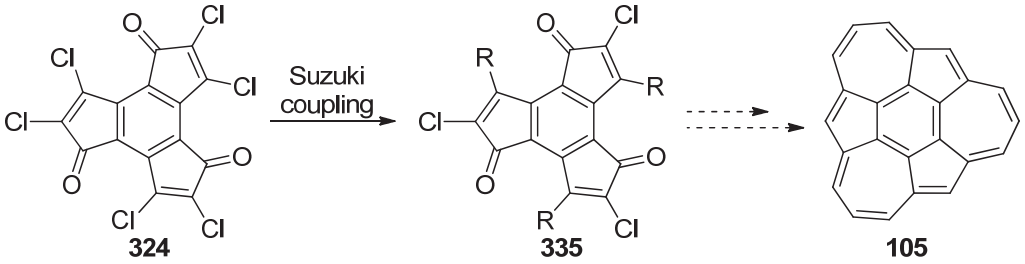
The final synthetic strategy towards isocoronene utilised the trindene ring structure as a key intermediate. The reactivity of trindene **230** towards electrophiles was investigated with the aim of introducing benzylic linking groups for the construction of the isocoronene framework. Trindene was found to react with aromatic aldehydes to give the symmetrical trifulvene product **278**, however no reaction was observed with aliphatic aldehydes. The aryl substituents of **278** are not suitable as linking groups and attempts at introducing linking groups to the aryl trifulvene were not successful. The synthesis of trifulvene is the first reported bond forming reaction with trindene and represents a new class of fulvene structures.



An alternative approach to trindene derivatives was explored through the use of perchlorotrindene **320**. Perchlorotrindene was synthesised in a single step through the cyclotrimerisation reaction of perchlorocyclopentadiene **319**. The geminal dichloro groups of perchlorotrindene were then hydrolysed with silver nitrate to give perchlorotrindenone **324**. The reactivity of perchlorotrindenone towards carbon nucleophiles was subsequently investigated with the objective of introducing substituents at the benzylic positions. Perchlorotrindenone was found to undergo rapid decomposition in the presence of hard and soft carbon nucleophiles. It was concluded that perchlorotrindenone is unstable under basic reaction conditions and so alternative bond forming reactions were considered.



The use of metal catalysed cross coupling reactions was subsequently examined as a method of introducing linking groups to perchlorotrindenone **324**. The cross coupling reaction was expected to occur selectively at the benzylic vinyl chloride positions due to the electron withdrawing effect of the carbonyl. The reactivity of perchlorotrindenone towards the Suzuki coupling reaction was initially investigated using phenylboronic acid. Under standard reaction conditions, perchlorotrindenone reacted with phenylboronic acid to yield the desired triphenyl-trindenone **335** (R = phenyl). This demonstrates the feasibility of introducing the desired carbon chain to perchlorotrindenone through the use of a linear coupling partner. The use of a suitably functionalised coupling partner would open the possibility for an intramolecular ring closing reaction to access the isocoronene ring system.



Acknowledgements

I would like to thank my supervisor Dr Alan Payne for his advice and guidance throughout my studies. It was Alan's enthusiasm and knowledge which inspired me to pursue a doctoral degree in organic chemistry. I would also like to thank my cosupervisor Associate Professor Mauro Mocerino for providing valuable feedback during the writing process. In addition, I am grateful for the funding provided through the Australian Postgraduate Award program which has been essential during my PhD studies. Finally, I would like to thank my friends and family for their support and understanding throughout the entire process.

Contents

List of abbreviations

$[M+H]^+$	Mass of protonated molecular ion
Ac	Acetyl
AcOH	Acetic acid
Ar	Aryl
ASE	Aromatic stabilisation energy
ATR IR	Attenuated total reflectance infrared
br	broad
Bu	Butyl
conc.	concentrated
CuTC	copper(I) thiophenecarboxylate
d	doublet
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DEPT	Distortionless enhancement by polarization transfer
DIBAL	Diisobutylaluminum hydride
DMAD	Dimethyl acetylenedicarboxylate
DMF	*N,N*-Dimethylformamide
DMSO	Dimethylsulfoxide
dppe	1,3-Bis(diphenylphosphino)ethane
eq	Equivalents
ESI	Electron spray ionisation
Et	Ethyl
Et_2O	Diethyl ether
Et_3N	Triethylamine
EtOAc	Ethyl acetate
EtOH	Ethanol
hfacac	Hexafluoroacetylacetonate
HRMS	High resolution mass spectrometry
hrs	hours
HSAB	Hard-soft acid base theory

HWE reaction	Horner–Wadsworth–Emmons reaction
hυ	Photochemical reaction
IBX	2-Iodoxybenzoic
IR	Infrared
J	Coupling constant
LDA	Lithium diisopropylamide
LG	Leaving group
m	Multiplet
m/z	Mass divided by charge
Me	Methyl
MeCN	Acetonitrile
MeOH	Methanol
Ms	Methanesulfonyl
N.R	No reaction observed
NBS	*N*-Bromosuccinimide
n-BuLi	*n*-Butyllithium
NMP	*N*-Methylpyrolidinone
NMR	Nuclear magnetic resonance
Nu^-	Nucleophile
o	*Ortho*
OTf	Trifluoromethanesulfonate
p	*para*
PAH	Polycyclic aromatic hydrocarbon
Ph	Phenyl
ppm	Parts per million
RSE	Resonance stabilisation energy
r.t	Room temperature
R_F	Retardation factor
s	Singlet
t-	Tertiary
t	Triplet
TBAF	Tetrabutylammonium fluoride
t-BuOK	Potassium *tert*-butoxide
TFA	Trifluoroacetic acid

TFAA	Trifluoroacetic anhydride
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
Ts/tosyl	*p*-Toluenesulfonyl
TsO/tosylate	*p* -Toluenesulfonate
TsOH	*p* -Toluenesulfonic acid
w.r.t	With respect to
δ	Chemical shift in ppm
Δ	Heating

Chapter 1

Introduction

Aromaticity is a key element in organic chemistry since it is one of the most powerful thermodynamic driving forces for chemical reactions. After 150 years, many aspects of aromaticity have become well understood however the study of aromaticity continues to be an active area of research. Current research into aromaticity has applications in new materials such as graphene and organic electronics which is highlighted in the recent issue of Chemical Reviews dedicated to 'Challenges in Aromaticity'.[1]

1.1 History of aromaticity

The study of aromaticity was initiated by the discovery of benzene in 1825 by Michael Faraday.[2] Faraday determined the empirical formula of benzene as two equivalents of carbon for every one equivalent of diatomic hydrogen gas. The low molar ratio of hydrogen indicated a high degree of unsaturation in the structure of benzene however the compound was found to have reactivity unlike other known unsaturated compounds. Following the discovery of benzene, several attempts were made at solving the molecular structure based on the known molecular formula of C_6H_6. In 1872 August Kekulé published a structural formula of the benzene ring which conformed to the known properties of the molecule.[3] The proposed structure consisted of a six membered carbon ring with the carbons joined by alternating single and double bonds.

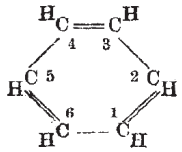


Figure 1.01: Kekulé structure of benzene[3] and the first sample of benzene, isolated by Faraday.[1]

The Kekulé structure may be represented as two isomers in which the double bonds have shifted position (Figure 1.02). An *ortho* disubstituted benzene ring (**1a** and **1b**) would allow for two isomers however this type of isomerism was never observed. Kekulé accounted for this observation by proposing that the two isomers were in equilibrium. Kekulé's benzene ring was crucial for the development of aromatic chemistry however it failed to provide an explanation for the stability of aromatic compounds.

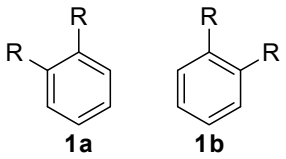


Figure 1.02: Regioisomers of Kekulé's benzene.

A theory for the aromatic stabilisation of the benzene ring was first introduced by Robinson in 1922.[4,5] Robinson proposed that aromatic compounds were stabilised by the cyclic conjugation of six electrons within a ring. This stabilised configuration was termed the aromatic sextet, represented in the structural formula **2a** as a circle drawn within the aromatic ring. The depiction of the π electrons as a continuous circle represents the symmetrical distribution of electrons within the ring resulting in equalisation of all ring forming bonds and atoms.

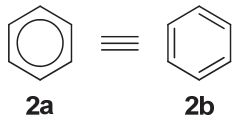


Figure 1.03: Robinson's aromatic sextet.

Robinson discussed the potential for aromaticity in ring systems other than benzene. These included five membered heterocycles and polycyclic aromatic hydrocarbons (PAHs). Robinson applied the sextet notation to naphthalene **3a** and anthracene by using a circle within each of the six membered rings. The use of the sextet in this way is misleading since two sextets would signify a total of 12 π electrons while naphthalene has a total of 10 π electrons. The correct representation of naphthalene using the Robinson notation is shown as **3c**, consisting of one aromatic sextet and two additional π bonds in the adjacent ring.

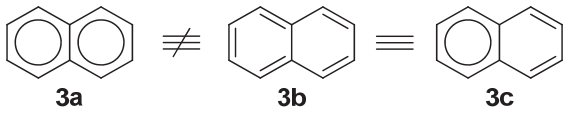


Figure 1.04: Aromatic sextet of naphthalene.

The length of a bond is primarily determined by the bond order with a single bond being the longest. The bond order in the Robinson model of the sextet is intermediate between a single and double bond due to the equal distribution of electrons in the *p*-orbitals. The development of X-ray crystallography allowed the relative positions of atoms to be measured within a crystal structure. The first crystal structure of a benzene ring was determined by Lonsdale in 1929 using hexamethylbenzene.[6] The structure confirmed the predicted planar geometry and equalised bonding within the benzene ring. The six C-C bonds of the benzene ring were found to have an equal length of 1.42 Å. This is an intermediate length between the average of measured values for single and double bonds (Table 1.01). Since the equalisation of bond lengths is the result of electron delocalisation, this can be used as a qualitative indication of aromaticity.

Hybridisation	Bond type	Average length/ Å
Csp^2-Csp^2	σ bond, unconjugated	1.478
Csp^2=Csp^2	π bond, unconjugated	1.316
Csp^2≃Csp^2	aromatic	1.380

Table 1.01: Average of measured bond lengths.[7]

The Robinson model of the aromatic sextet provided a suitable definition of aromaticity based on empirical evidence however it lacked theoretical reasoning. The introduction of quantum mechanics provided a mathematical solution to aromaticity which was developed by Erich Hückel in a series of publications.[8, 9, 10] Hückel's extensive mathematical analysis of the benzene ring was further developed into Hückel's rule which defines the electronic and geometric constraints for aromaticity. The first rule defines the electronic structure of an aromatic compound as a conjugated system of $4n+2$ π electrons where n is any integer. The remaining rules define the geometric requirements for aromaticity. An aromatic compound must have a cyclic configuration of atoms with each possessing a *p*-orbital capable of conjugation. Cyclic conjugation requires overlap of *p*-orbitals which can only occur in a planar conformation, therefore an aromatic ring must be planar. Hückel's rule provides a simple method for the identification of potentially aromatic ring systems.

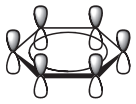


Figure 1.05: Conjugated *p*-orbitals of benzene.

1.2 Aromaticity of non-benzenoid compounds

Hückel's rule expands the definition of aromaticity to conjugated systems other than the aromatic sextet. The smallest aromatic system consists of two electrons in cyclic conjugation ($n = 0$). One example of a two electron aromatic ring is the cyclopropene cation **4** which has been isolated as a stable salt.[11] The cationic position of **4** is sp^2 hybridised with an empty *p*-orbital in conjugation with the π bond. The aromatic

resonance of **4** is supported by the ^{1}H NMR spectrum which shows one singlet at 11.20 ppm for all three protons. The equivalence of all three protons in **4** indicates the π bonds are fully delocalised. The protons are strongly deshielded at 11.20 ppm which can be attributed to the anisotropic effect of the aromatic ring current. In addition, some deshielding may also be attributed to the electron withdrawing effect of the carbocation. Another example of the aromatic cyclopropene system is cyclopropenone **5** where the cyclopropene cation exists as a resonance structure of the carbonyl group. In addition to cyclopropene, two-electron aromaticity may occur in a cyclobutene ring such as the dication **6**. This structure has been isolated in solution as the tetraphenyl derivative.[12]

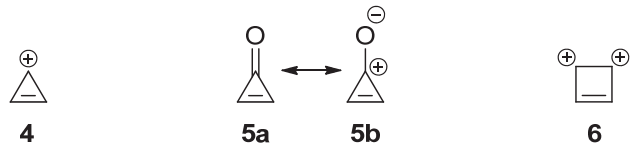


Figure 1.06: Two-electron aromaticity.

The aromatic sextet (n = 1) is the most common electronic configuration and is usually found in five or six membered rings however some seven membered rings are known. The aromatic sextet of a five membered ring consists of two π bonds and one non-bonding pair of electrons in a conjugated *p*-orbital. Common examples of this aromatic structure are the cyclopentadienyl anion **8** and the heterocycles **9**. Cyclopentadiene **7** has a relatively high acidity due to aromatic stabilisation of the conjugate base **8**. Other examples include the expansive range of five membered heterocycles with multiple heteroatoms.

Figure 1.07: Aromaticity in five membered rings.

The aromatic sextet may occur in a seven membered ring such as the tropylium cation **10**. This cation is comparable to the cyclopropene cation **4** where the

carbocation is stabilised by aromaticity. Likewise, the ketone **11** is partially aromatic due to the carbonyl resonance structure **11b**.

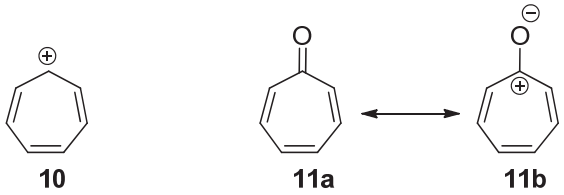


Figure 1.08: Aromaticity in seven membered rings.

The potential for aromaticity in monocyclic systems of ten electrons (n = 2) is hindered by geometric constraints. The ten membered conjugated carbocycle **12** meets the electronic requirement for an aromatic compound with a total of ten π electrons however the lack of a planar geometry prevents cyclic conjugation. The *cis*-isomer **12a** is unable to adopt a planar geometry since the large bond angles (144°) would be highly strained. The geometric isomer **12b** has unstrained bond angles of 120° however steric repulsion of the inward facing hydrogen atoms prevent the required planar geometry for aromaticity. Some nine membered rings are known to have ten electron aromaticity such as the anion **13** and nitrogen heterocycle **14**.[13, 14] These compounds have a high bond angle strain (~140°) which is overcome by the gain in aromatic stabilisation energy resulting in a thermodynamically favourable planar geometry.

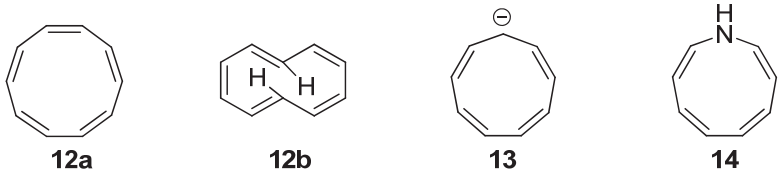
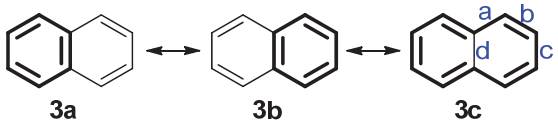


Figure 1.09: Ten electron aromaticity.

1.3 Aromaticity of polycyclic aromatic hydrocarbons

Hückel's rule applies to isolated cyclic systems and therefore does not satisfactorily explain the aromaticity of polycyclic aromatic hydrocarbons (PAHs) such as

naphthalene **3**. In most PAHs there are multiple cyclic pathways that π electrons can follow. Naphthalene has three possible conjugated circuits (Figure 1.9) each of which may contribute to the overall properties and aromaticity of the molecule. Two of the conjugated circuits **3a** and **3b** each consist of a complete aromatic sextet in addition to two localised π bonds. The third conjugated circuit **3c** follows the perimeter of the molecule with 10 π electrons. All of these circuits satisfy Hückel's rule however the π bonds of naphthalene are not equivalent to the benzene ring. This can be demonstrated using the bond lengths of naphthalene which have been calculated from the x-ray crystallographic data.[15] The bond lengths show significant alternation (1.37 – 1.41 Å) which indicates a reduced delocalisation in comparison to the equivalent bond lengths of the benzene ring (1.30 Å). To understand the aromaticity and reactivity of PAHs, the foundation of Hückel's rule and the aromatic sextet must be further developed.



Bond	Length/ Å
a	1.425
b	1.378
c	1.421
d	1.426

Figure 1.10: Conjugated circuits of naphthalene.

1.4 Clar's rule

A system for determining the aromaticity of PAHs was first developed by Clar who presented his findings in the book 'The Aromatic Sextet'.[16] Clar's rule applies the concept of the aromatic sextet to PAHs to determine the relative aromaticity of each conjugated π bond. This allows for the aromaticity and reactivity of PAHs to be predicted. Clar represented the molecules as a series of resonance forms consisting of discreet aromatic sextets separated by localised π bonds. He demonstrated that resonance structures having the greatest number of complete sextets were the primary contributors to the resonance hybrid. Clar's rule is exemplified with phenanthrene **15** which can be represented using two Clar structures. Structure **15a**

has the greatest number of complete sextets and so contributes most to the resonance hybrid. Structure **15b** has a single complete sextet and therefore does not contribute significantly to the properties of phenanthrene. Structure **15a** can be described as a biphenylene structure which is linked with an ethylene bridge. The ethylene bridge does not participate in the aromatic stabilisation and can be regarded as a localised, non-aromatic π bond.

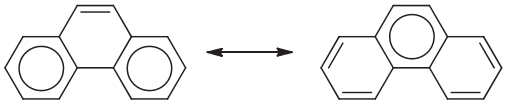
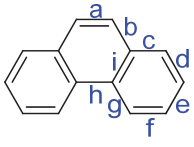


Figure 1.11: Clar structures of phenanthrene.

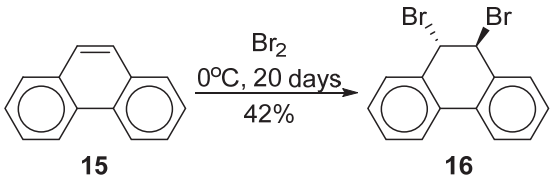
The partial localisation of a π bond is reflected in the geometry and reactivity of phenanthrene. The bond lengths of phenanthrene have been determined using x-ray crystallography (Figure 1.12).[17] The lengths of bonds a, b and h are all close to the lengths of non-aromatic unconjugated bonds. The absence of conjugation is concordant with Clar's prediction of a weak central ring current. The remaining bonds participate in aromatic resonance and therefore show some degree of equalisation.



Bond	Length/ Å
a	1.341
b	1.450
c	1.428
d	1.374
e	1.386
f	1.399
g	1.412
h	1.464
i	1.416

Figure 1.12: Bond lengths of phenanthrene.

The reactivity of phenanthrene is similar to an alkene since the localised π bond is not stabilised by aromaticity. The addition of bromine to phenanthrene yields the dibromide **16** through halogen addition.[18] The dibromide has two complete sextets which are equivalent to the major Clar structure of phenanthrene. As a result there is no significant loss of aromaticity and the reaction is energetically favourable.



Scheme 1.01: Bromination of phenanthrene.

Anthracene **17** is a PAH from the polyacene series of compounds which consist of a linear fused ring system. The linear configuration anthracene results in properties that are different to the regioisomer phenanthrene. Anthracene has three Clar structures **17a-c** with one complete sextet in each of the three rings. These structures alone would indicate equal aromaticity across the entire molecule however this does not explain the observed reactivity of anthracene.

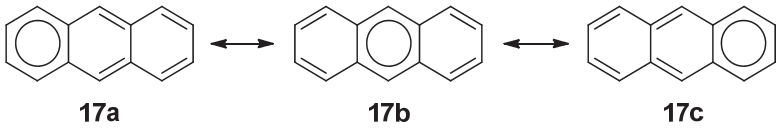
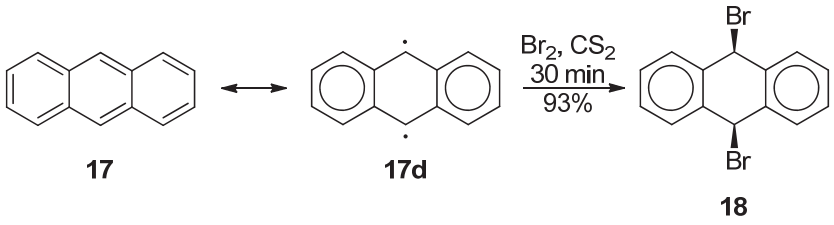


Figure 1.13: Clar structures of anthracene.

The reactivity of anthracene may be explained by an extension of Clar's rule to include a resonance structure with unpaired electrons.[19,20] The extension of Clar's rule allows a fourth Clar structure **17d** to be considered. This structure consists of two complete sextets with two unpaired electrons localised on the central ring. The biradical resonance structure is not generally considered since the unpaired electrons are higher in energy relative to a bonding orbital. In the case of anthracene, the

biradical is a significant resonance contributor due to formation of an additional aromatic sextet. The biradical structure may be used to explain the increased reactivity at the central ring of anthracene. The reactivity of anthracene is exemplified by the reaction with bromine to generate 9,10-dibromo-9,10-dihydroanthracene **18** exclusively as the *syn* stereoisomer (Scheme 1.02).[21,22]



Scheme 1.02: Bromination of anthracene.

1.5 Aromaticity of corannulenes

Corannulenes are a group of PAHs which consist of a central ring that is fully enclosed by a larger perimeter ring. The smallest alternant corannulene is coronene **19**. Coronene has a maximum of three complete sextets which can be represented as two equivalent Clar structures **19a** and **19b**. Clar used the cyclic migration of sextets to represent the overall structure of coronene as shown in structure **19a**. He proposed that a cyclic delocalisation of aromatic sextets would generate a strong peripheral ring current shown as **19c**, leading to an enhanced aromaticity termed superaromaticity.

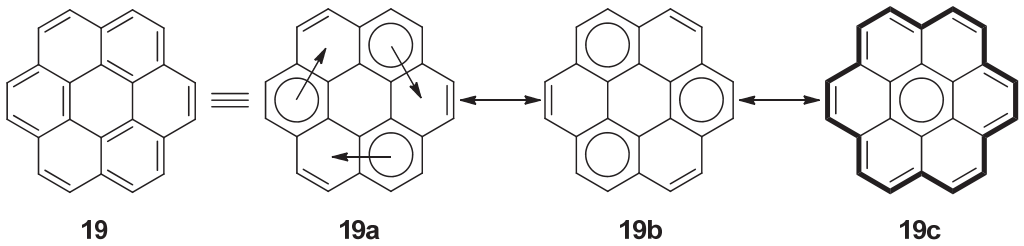
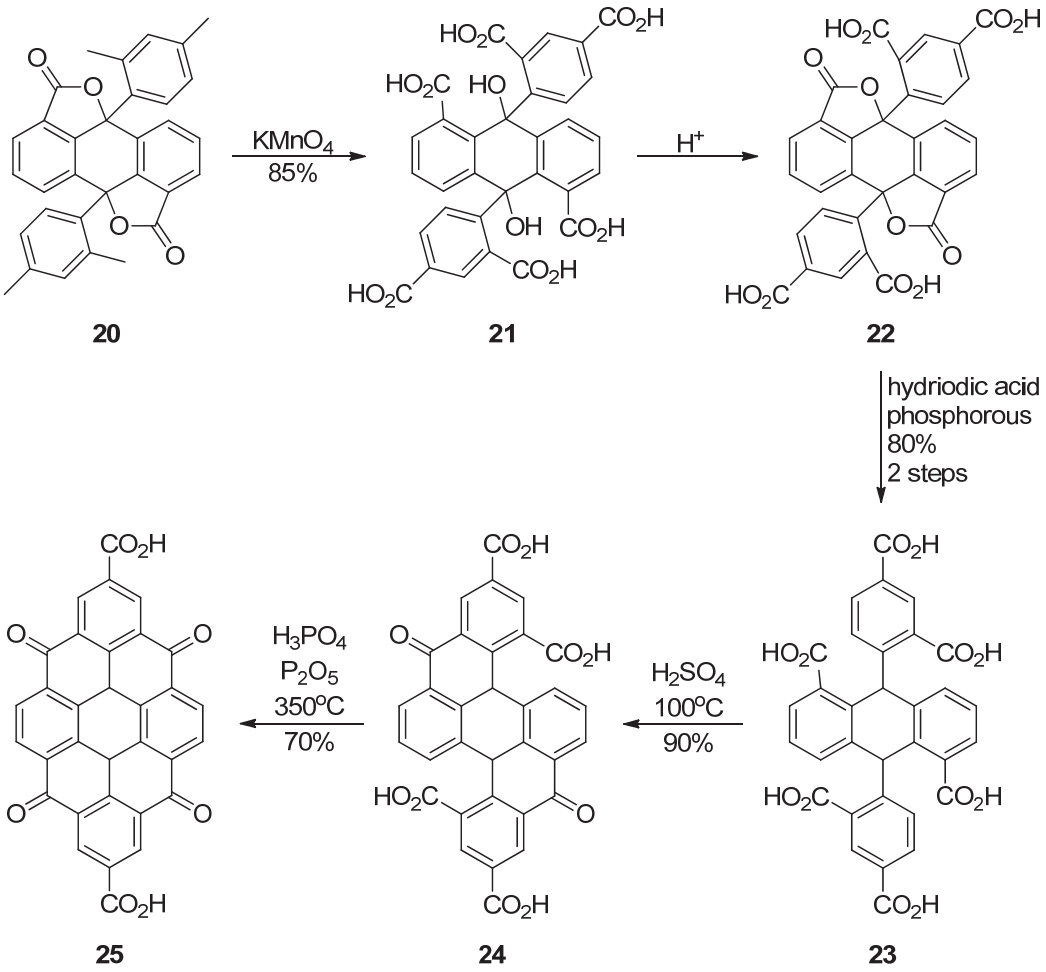


Figure 1.14: Clar structures of coronene **19**.

1.6 Scholl and Meyer synthesis of coronene

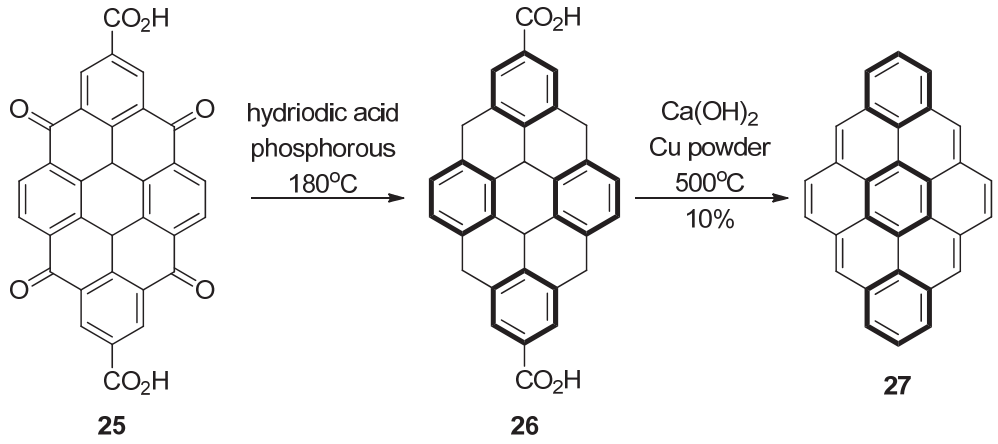
The first synthesis of coronene was published by Scholl and Meyer in 1932 as a culmination of 20 years work.[23] The synthesis was completed in 10 steps starting from the dilactone **20**. Benzylic oxidation of **20** under basic conditions gave the hexacarboxylic acid **21** isolated as the salt. Acidification resulted in rapid lactonisation to yield the tetraacid **22**. The lactone was reduced using red phosphorous and hydroiodic acid resulting in hydrolysis of the lactones followed by deoxygenation of the benzylic alcohol groups to yield the hexa-acid **23** in good yield. The coronene ring system was then formed through a sequence of intramolecular Friedel-Crafts acylation reactions. The hexa-acid **23** was heated with sulfuric acid which resulted in acylation of both phenyl substituents by the adjacent carboxylic acid groups to yield **24**. The second acylation step required more forceful conditions using P_2O_5 at 350 °C. This resulted in intramolecular acylation of the central dihydroanthracene ring system to yield the diacid **25** in good yield. With the coronene ring system formed, the subsequent transformations required aromatisation of the central ring, deoxygenation of the ketone groups and removal of the two additional fused aromatic rings.



Scheme 1.03: Synthesis of intermediate **25**.

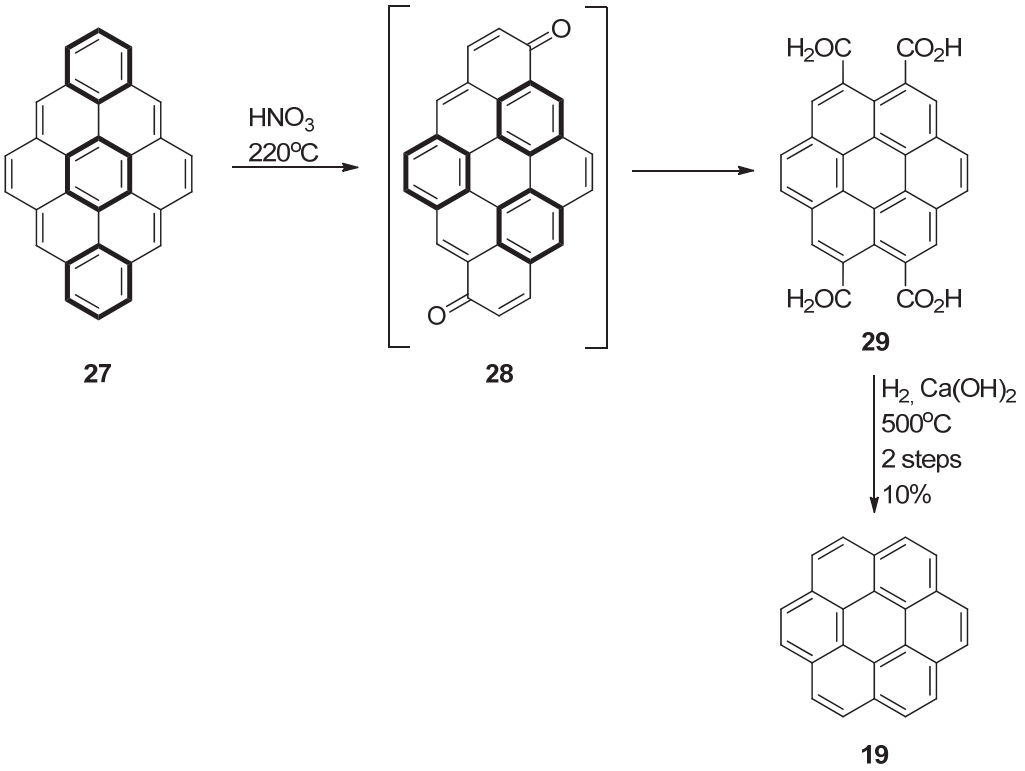
Deoxygenation of the ketone groups of **25** was then achieved by reduction using hydroiodic acid and phosphorous to yield **26**. The diacid **26** contains six sp^3 carbon positions which must be dehydrogenated to form the unsaturated coronene ring system. The dehydrogenation was conducted with concurrent decarboxylation using copper powder at 500 °C to form dibenzoperopyrene **27** in 10% yield. The extremely high temperature and low yield for this transformation could be explained by aromaticity of the starting diacid **26** and peropyrene **27**. At first glance it could be assumed that the fully conjugated sp^2 ring system of peropyrene **27** would have greater aromaticity than the partially saturated diacid **26** due to the greater number of potential aromatic rings. Analysis of peropyrene shows a single Clar structure which possesses the maximum of three complete sextets. All other resonance forms are minor contributors since they have fewer than three complete sextets. In comparison,

the starting diacid **27** has a Clar structure with four complete sextets. The reduced number of complete sextets in the product indicates the formation of peropyrene is energetically unfavourable which explains the high temperature required.



Scheme 1.04: Synthesis of dibenzoperopyrene **27**.

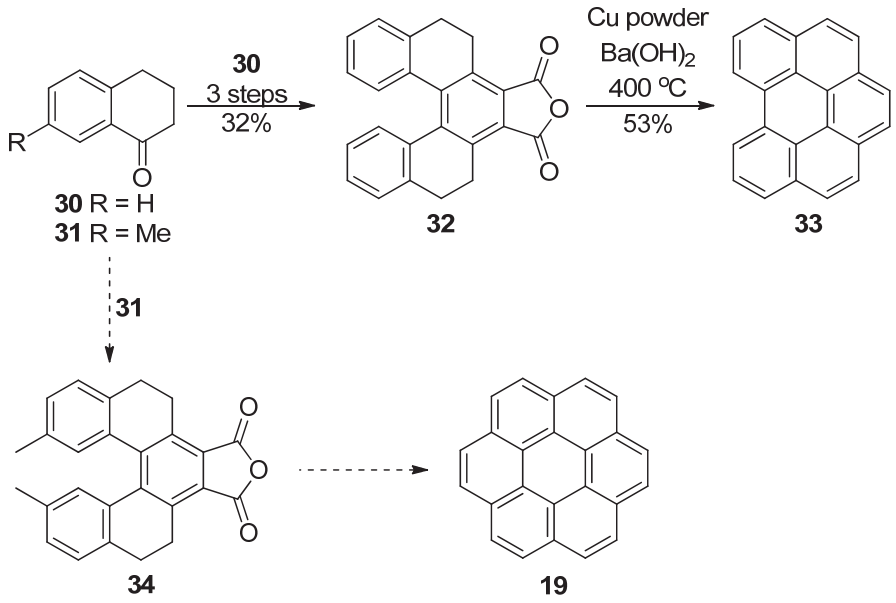
The final reaction sequence for the synthesis was directed towards the removal of the benzene ring fused to the central coronene ring system. In the first step peropyrene **27** was oxidised to the quinone **28** followed by oxidative ring cleavage to yield the tetraacid **29**. The authors reported that quinone **28** may be formed by the addition of sulfuric acid to peropyrene however the quinone was difficult to purify and so the ring cleavage was conducted in a single step. The relatively mild conditions required for the oxidation of peropyrene to the quinone may be explained by aromatic stabilisation. Peropyrene has one major Clar structure with a total of three sextets and six localised π bonds. Excluding radical resonance structures, the remaining Clar structures are minor contributors. In contrast, quinone **28** has two significant Clar structures, each with three complete sextets. The two quinone rings are the only positions which do not have significant aromatic stabilisation. Comparison of the Clar structures of the starting material and product indicate a strong thermodynamic driving force for the oxidation due to increased aromatic stabilisation of the product. The quinone was further oxidised resulting in ring cleavage to yield the tetraacid **29**. The carboxylate groups of **29** were removed by decarboxylative hydrogenolysis at high temperature to yield coronene **19** in low yield.



Scheme 1.05: Synthesis of coronene **19**.

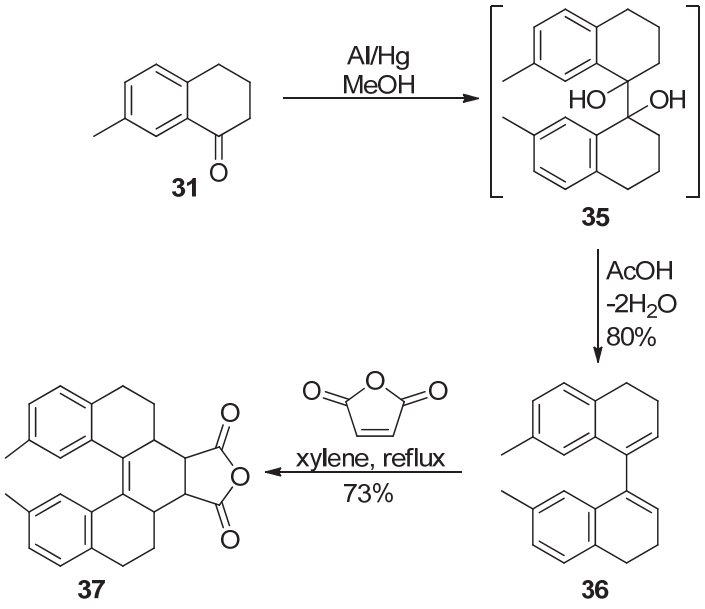
1.7 Newman synthesis of coronene

A alternative synthesis of coronene was reported by Newman who shortened the synthesis to six steps starting from methyltetralone **31**.[24] The authors initially planned to follow the method of Weidlich who reported the synthesis of benzoperylene **33** from tetralone **30**.[25] The key transformation in the synthesis of **33** involves the cyclisation of **32** with concurrent oxidative aromatization and decarboxylation. Newman proposed a similar transformation of **34** with additional cyclisation of the methyl substituents to give coronene **19**.



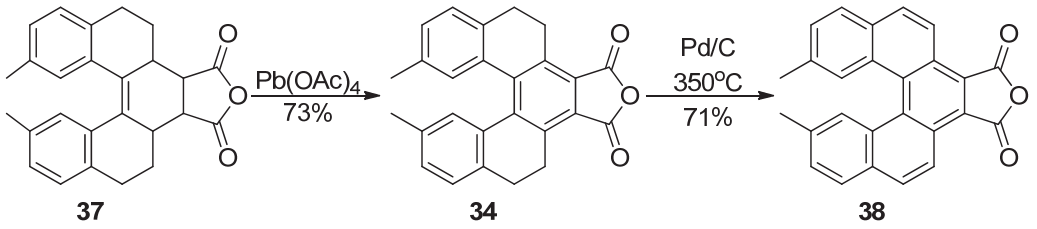
Scheme 1.06: Proposed synthesis of coronene **19**.

The Newmann synthesis of coronene begins with the reductive homocoupling of tetralone **31** to afford the diol dimer **35**. The diol was subsequently dehydrated to provide the diene **36** in high yield. The annulation of **36** was achieved by Diels-Alder reaction with maleic anhydride to yield the adduct **37** as a mixture of two unspecified isomeric forms. The formation of two distinct isomers of **37** is most likely due to axial chirality of the non-planar ring system.



Scheme 1.07: Synthesis of anhydride **37**.

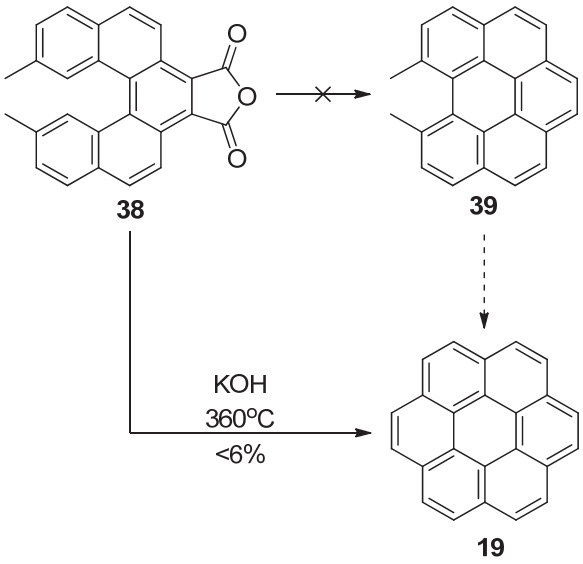
The oxidative aromatisation of **37** was then achieved in two steps. The cyclohexene ring was first aromatised using lead acetate to give intermediate **34** in good yield. The remaining methylene positions were then oxidised using palladium at high temperature to yield the fully aromatised intermediate **38**.



Scheme 1.08: Synthesis of anhydride **38**.

The authors originally planned to synthesise coronene in two steps from the anhydride **38**. Decarboxylation and dehydrogenative coupling of **38** would yield intermediate **39** which could be further oxidised to coronene. After several unsuccessful attempts at decarboxylation, the authors found that coronene could be prepared directly from anhydride **38** by fusion with potassium hydroxide at 360 °C.

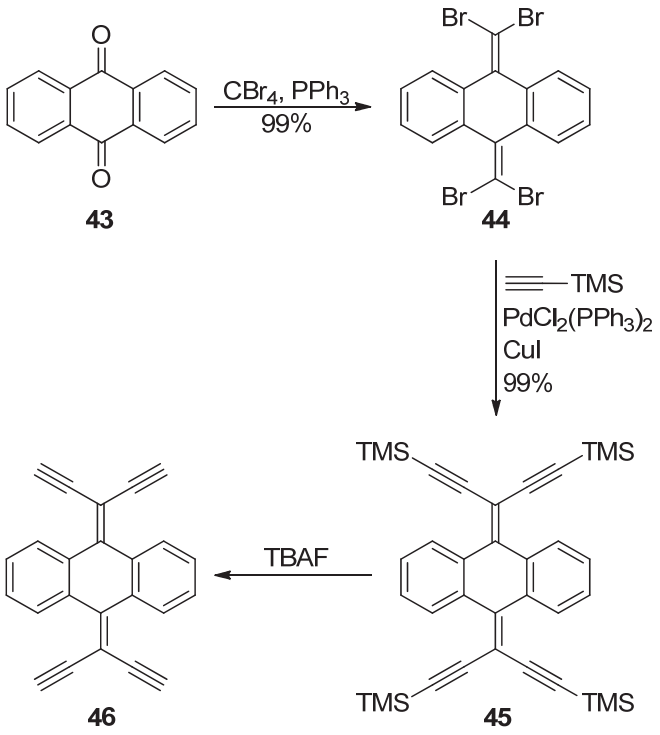
This method gave a highly variable yield of coronene with the yield recorded as 5.5%.



Scheme 1.09: Synthesis of coronene **19**.

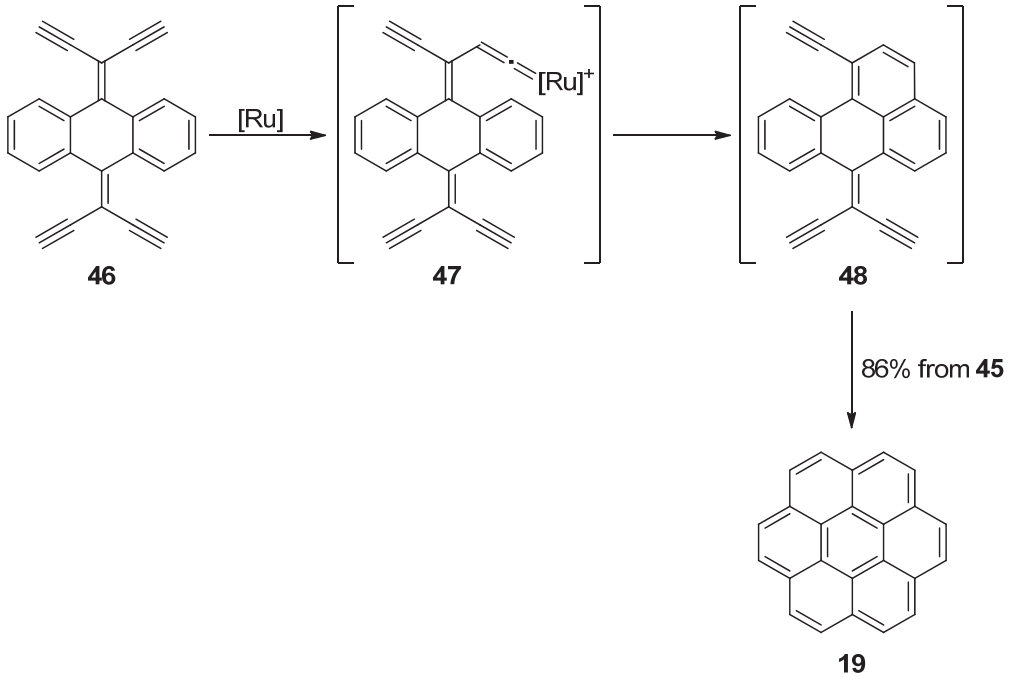
1.8 Scott synthesis of coronene

A highly efficient synthesis of coronene was reported by Scott in 2004, requiring four steps from anthraquinone **43**.[26] The synthesis begins with a Corey-Fuchs olefination of anthraquinone to form the tetrabromide **44** in quantitative yield. Sonogashira coupling at each of the four vinyl bromide positions then introduced four TMS protected acetylene groups leading to **45** in quantitative yield. The removal of the TMS groups was achieved using TBAF to give **46** which was used without purification due to low stability.



Scheme 1.10: Synthesis of alkyne **46**.

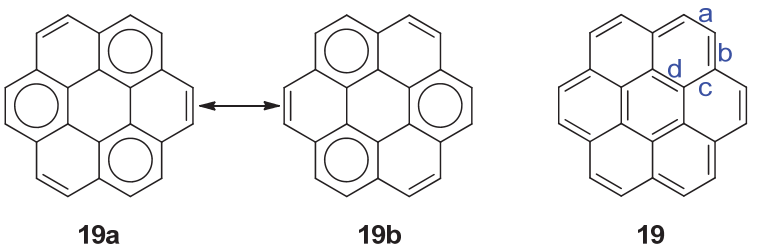
The final step involved the cyclisation of **46** in the presence of a ruthenium catalyst $RuPPh_3(cymene)Cl_2$. The terminal alkyne first forms a ruthenium vinylidene intermediate **47** followed by cyclisation with the adjacent benzene ring to give intermediate **48**. This sequence is repeated four times to yield coronene **19**. The synthesis reported by Scott gave a low yield of 15% from **45** however this was greatly improved by Liu *et al*. with the use of a modified ruthenium catalyst $TpRuPPh_3(CH_3CN)_2PF_6$ resulting in an 86% yield of coronene from **45**.[27]



Scheme 1.11: Synthesis of coronene **19**.

1.9 Aromaticity of coronene

There have been numerous attempts to find evidence of superaromaticity since the concept was introduced by Clar.[28, 29] Computational studies of coronene have been used to estimate the extent of peripheral delocalisation of π electrons which would lead to superaromaticity.[30] Modern computational methods have led to a consensus that coronene has a weak peripheral ring current in contrast to Clar's original prediction. The weak peripheral ring current results in marginally enhanced aromaticity therefore coronene is not a truly superaromatic molecule.[31] The properties of coronene are more accurately represented by the sextet notation of **19a-b**. Coronene may be described as having three fused benzene rings linked by partially localised ethylene bridges. This is reflected in the bond lengths of coronene where the localised π bonds are significantly shorter (1.346 Å) in comparison to the remaining bonds (1.415-1.433 Å).[32]

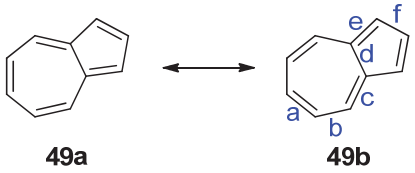


Bond	Length/ Å
a	1.346
b	1.415
c	1.433
d	1.425

Figure 1.15: Bond lengths of coronene.

1.10 Aromaticity of azulene

Benzenoid PAHs in general have been shown to possess a weak peripheral ring current which limits the potential for superaromatic stabilisation. The weak peripheral ring current is due to the predominance of internal ring currents which disrupts delocalisation at the perimeter. A superaromatic PAH would therefore require the ring current to be restricted to the perimeter of the molecule without interference from internal conjugation circuits. Agranat *et al.* made the observation that fused bicyclic PAHs consisting of odd number ring sizes (non-alternant) always have a conjugated circuit that is restricted to the perimeter.[33] One well known example is azulene **49,** a non-alternant isomer of naphthalene **15.** Azulene has two neutral resonance structure (Figure 1.16) both of which have a central single bond (d). Azulene can therefore be described by a 10 π conjugated perimeter with a formal single bond at the centre. This is in contrast to naphthalene **15** whose delocalisation occurs primarily within each of the benzene rings. The delocalised bonding of azulene is reflected in the bond lengths measured from the X-ray crystal structure.[34] The peripheral bonds show significant equalisation close to the ideal aromatic bond 涩梵喜gth with the central bond (d) equivalent in length to a formal single bond (see Table 1.01). This supports a strong peripheral ring current with no significant conjugation through the central bond.



Bond	Length/ Å
a	1.385
b	1.401
c	1.383
d	1.483
e	1.413
f	1.391

Figure 1.16: Bond lengths of azulene.

In contrast to alternant PAHs, azulene is known to have a strong dipole moment, measured as 0.8 D using microwave spectroscopy.[35] Dipole moments arise from an uneven distribution of charge within the molecular structure. The dipole moment of azulene may be explained by the contribution of charge separated resonance structures such as **49c**. Resonance structures which introduce a separation of charge are usually considered too high in energy to contribute to the resonance hybrid. The separation of charge in azulene is stabilised by the formation of an aromatic sextet in either of the two rings (**49d-e**) and so these resonance structures are significant contributors.

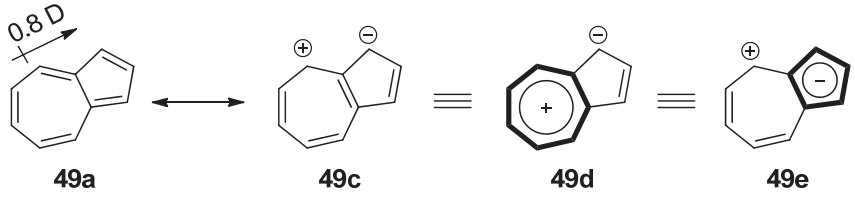
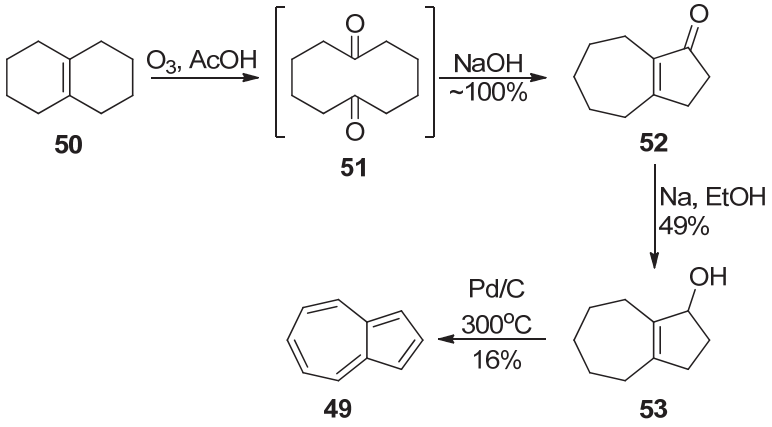


Figure 1.17: Clar structures of azulene.

1.11 Plattner synthesis of azulene

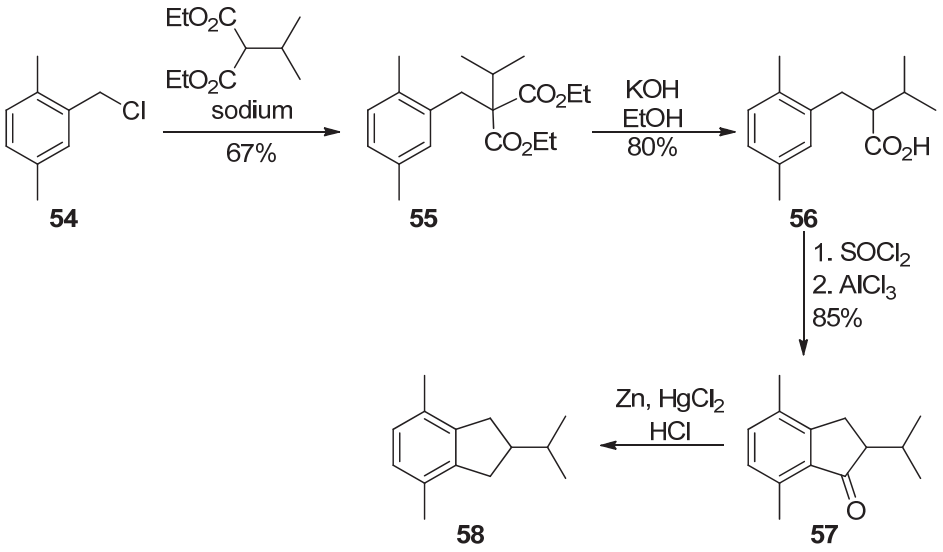
The synthesis of azulene was first reported by St. Pfau and Plattner in 1937.[36] The synthesis utilised the previously reported ketone **52**.[37] The ketone **52** was prepared in quantitative yield by ozonolysis of octalin **50** followed by intramolecular aldol

condensation. The ketone **52** was reduced using sodium metal to afford the alcohol **53** in moderate yield. Deoxygenation and dehydrogenation of the alcohol was achieved using palladium on carbon at 300 °C to produce azulene **49** in low yield.



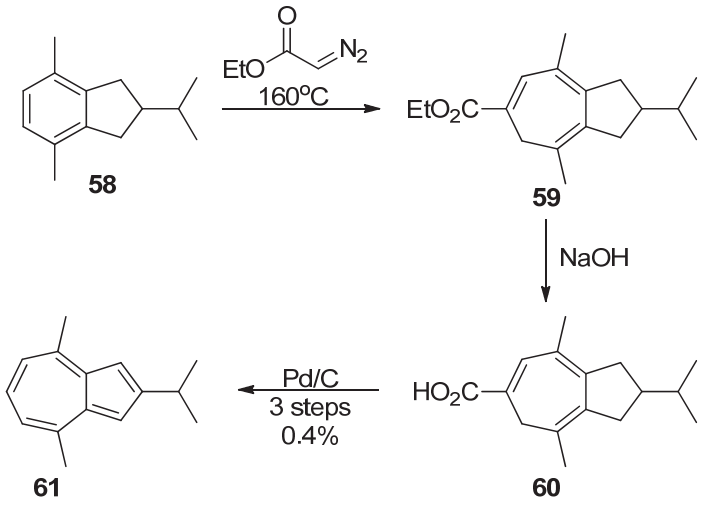
Scheme 1.12: Plattner synthesis of azulene **49**.

An alternative synthesis of the azulene ring system was reported by Plattner in the synthesis of the natural product vetivazulene **61**.[38] The synthesis begins with the alkylation of benzyl chloride **54** yielding the tetra-substituted malonic ester **55** in good yield. Hydrolysis and decarboxylation of the malonic ester produced carboxylic acid **56** in high yield. An intramolecular acylation of the carboxylic acid **56** then introduced the five membered ring of ketone **57**. Clemmensen reduction of the ketone then afforded hydrocarbon **58**.



Scheme 1.13: Synthesis of intermediate **58**.

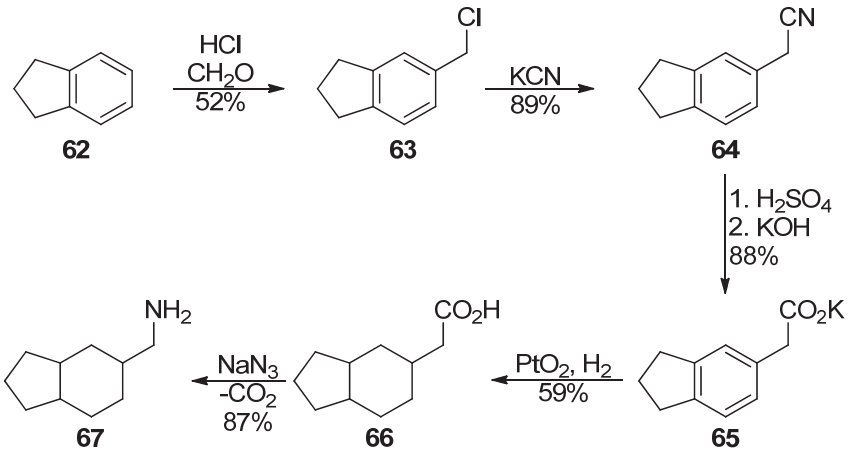
The final steps towards the synthesis of vetivazulene required the benzene ring expansion of hydrocarbon **58** followed by aromatisation. The Büchner ring expansion of **58** afforded the ring expansion product **59** which was later shown to consist of a mixture of regioisomers.[39] The ester **59** was then hydrolysed and treated with palladium to effect the decarboxylative dehydrogenation. After extensive purification vetivazulene **61** was obtained in low yield.



Scheme 1.14: Plattner synthesis of vetivazulene.

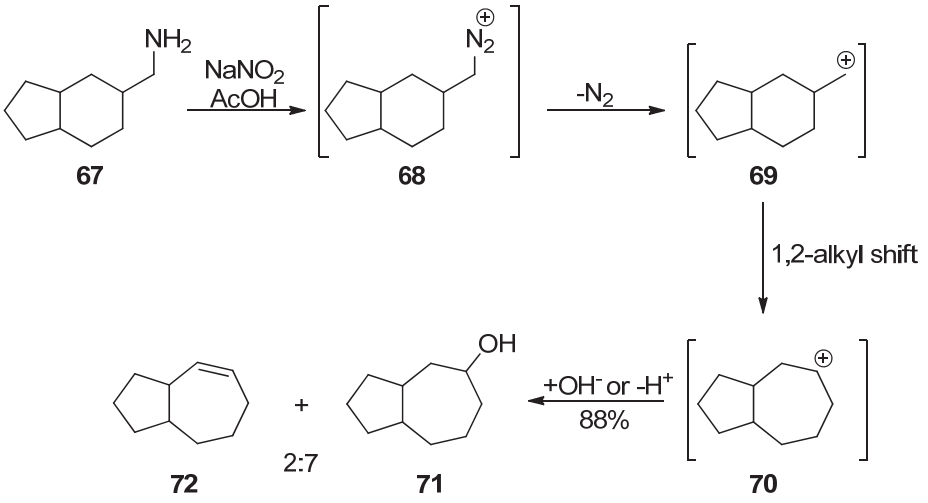
1.12 Arnold synthesis of azulene

Soon after the Plattner synthesis of azulene, an alternative method was reported by Arnold in the synthesis of 5-methylazulene.[40] Comparable to the Plattner synthesis, the azulene ring system was formed through the ring expansion of indane however Arnold's method circumvents the low yielding Büchner ring expansion. In the first step of the synthesis, the Blanc chloromethylation of indane produced benzyl chloride **63** in moderate yield. Nucleophilic substitution of the chloride with cyanide gave the nitrile **64** which was hydrolysed to the acid **65** with high yields reported for both reactions. The benzene ring of **65** was then hydrogenated using Pt_2O to form the fully saturated ring system of carboxylic acid **66** in moderate yield. The carboxylic acid was then converted to the primary amine **67** in high yield through the Curtius rearrangement of the acyl azide intermediate followed by hydrolysis of the isocyanate and decarboxylation of the carbamic acid.



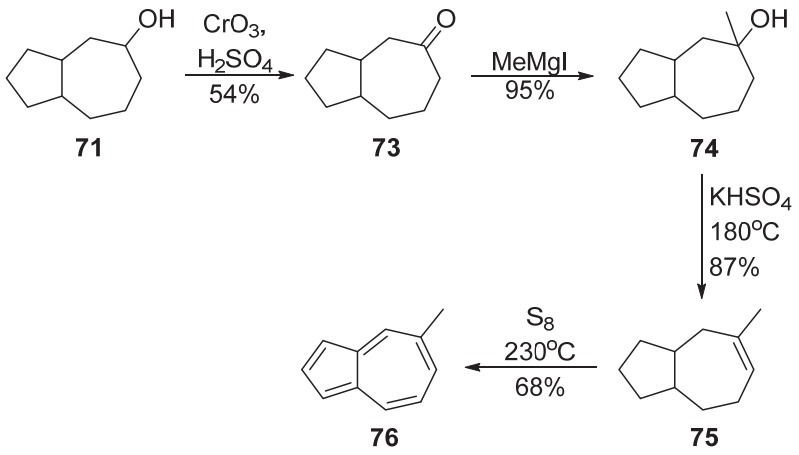
Scheme 1.15: Synthesis of amine **67**.

The next stage of the synthesis involved the ring expansion of the cyclohexane ring of **67** to yield the saturated azulene ring system. Diazotisation of the primary amine gave the unstable alkyl diazonium **68** which rapidly eliminates nitrogen to form the carbocation intermediate **69**. The primary carbocation undergoes a 1,2-alkyl shift to the ring expansion product **70**. This rearrangement is energetically favourable due to stabilisation of the product as a secondary carbocation. The alkyl shift may occur in two possible directions to give two regioisomers however only one isomer is shown for clarity. The carbocation may be quenched by the nucleophilic addition of water to yield the alcohol **71** or through elimination of a proton to yield the alkene **72**. This ring expansion method formed the azulene ring system in high yield with the products isolated in a ratio of 2:7 favouring the desired alcohol **71**.



Scheme 1.16: Synthesis of alcohol **71**.

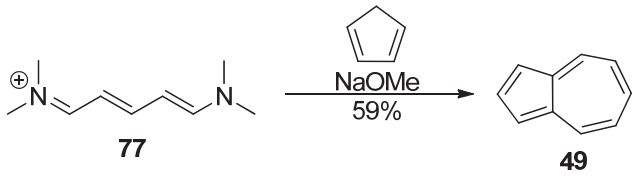
The synthesis of 5-methylazulene from **71** required the regioselective introduction of a methyl group. This was achieved from ketone **73** which was prepared by oxidation of alcohol **71** using Jones' reagent. The methyl group was then introduced by nucleophilic addition of a Gignard reagent to the ketone **73**, providing the alcohol **74** in high yield. Elimination of the alcohol under acidic conditions provided the alkene **75** in high yield. The ring system was then dehydrogenated using sulfur at high temperature to produce 5-methylazulene **76** in good yield.



Scheme 1.17: Arnold synthesis of 5-methylazulene.

1.13 Ziegler-Hafner synthesis of azulene

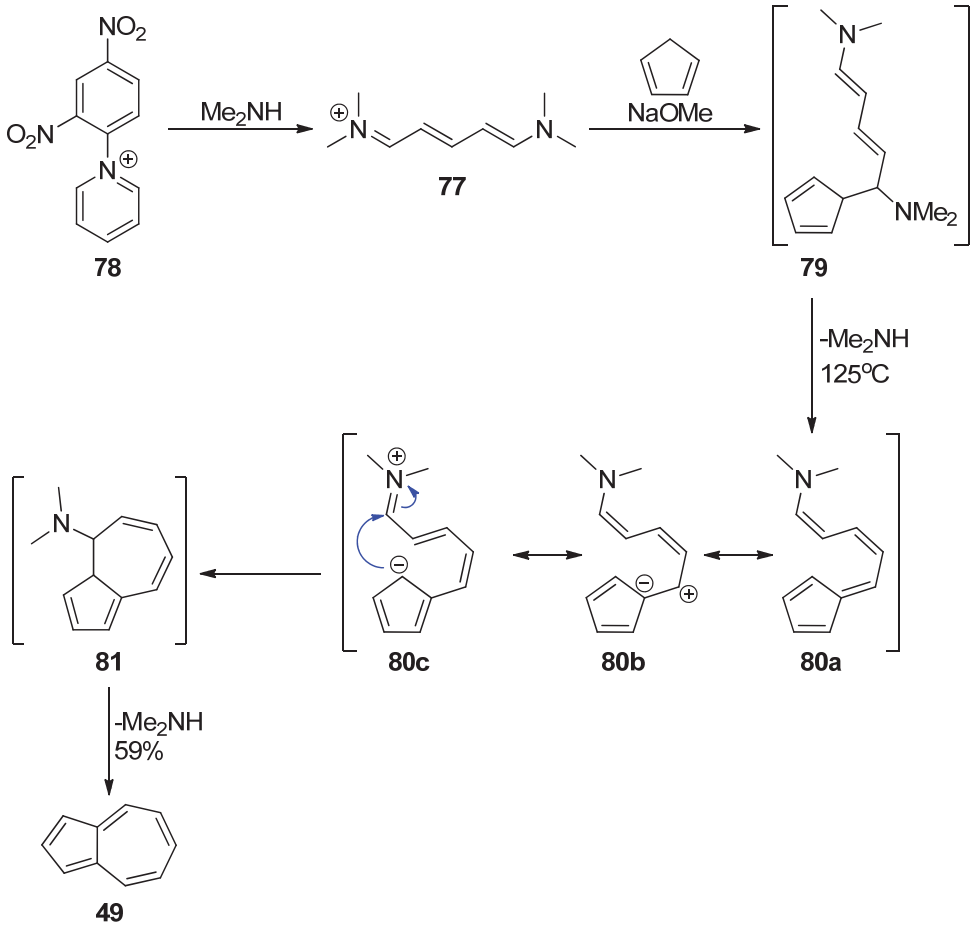
An efficient method for the synthesis of azulene was reported by Ziegler and Hafner in 1955.[41,42,43] The synthesis was completed in a single step from cyclopentadiene with greatly improved yield compared to previous methods. The synthesis involves the annulation of cyclopentadiene with the conjugated iminium salt **77** to form azulene **49** in good yield.



77 **49**

Scheme 1.18: Synthesis of azulene **49**.

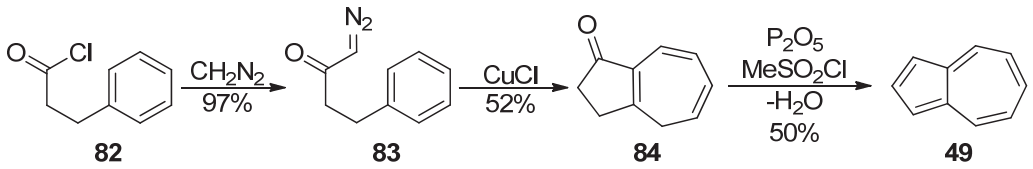
The iminium salt **77** was first prepared from the ring opening reaction of Zincke salt **78**. Addition of cyclopentadiene under strongly basic conditions generated the cyclopentadienyl anion which reacts with the iminium salt **77** to form the adduct **79**. Elimination of Me_2NH then yields the fulvene intermediate **80**. Under thermal conditions, the fulvene undergoes an electrocyclic ring closing reaction to generate the bicyclic intermediate **81**. A second elimination of Me_2NH then leads to azulene **49** in good yield. This procedure is currently the method of choice for the lab scale preparation of azulene since it does not require isolation of intermediates and is amenable to the synthesis of substituted azulenes.



Scheme 1.19: Synthesis of azulene **49**.

1.14 Scott synthesis of azulene

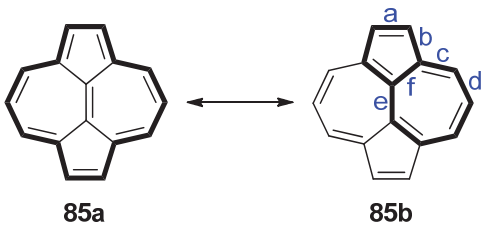
The Plattner synthesis of azulene was later developed into an intramolecular variation by Scott.[44, 45] The method allows the annulation step and Bucher ring expansion to be combined in a single step which greatly shortens the reaction sequence. The first step is the synthesis of diazoketone **83** by the reaction of diazomethane with acid chloride **82**. The cycloheptatriene **84** was obtained in good yield through the intramolecular Büchner ring expansion of the diazoketone **83**. The ketone **84** was then converted to azulene **49** in a single step through condensation and hydride shift.



Scheme 1.20: Scott synthesis of azulene.

1.15 Aromaticity of azupyrene

Azupyrene **85** is a non-alternant isomer of pyrene consisting of two fused azulene ring systems. Azupyrene was first synthesised by Anderson *et al.* in order to evaluate geometry and aromaticity.[46, 47] Anderson proposed that azupyrene may consist of a delocalised perimeter separated from the central double bond by formal single bonds. The bond lengths of azupyrene were measured by X-ray crystallography which showed that the four bonds connecting the peripheral ring to the centre (bond f) are close to the idealised single bond length (1.478 Å, Table 1.01).[48] This is consistent with delocalisation of the π bonds being restricted to the perimeter. The bond at position b is significantly lengthened in comparison to the remaining peripheral bonds. This could be explained by geometric constraints where the lengthening of bond b reduces the angle strain at the junction of bonds b and f (106°). The magnetic properties of azupyrene indicated a strong ring current consistent with aromaticity however the measured value was lower than expected compared to theory.[47] This led Anderson to conclude that the central bond must participate in conjugation to some degree. This is supported by the resonance structure **85b** of azupyrene which shows a conjugated circuit passing through the central bond.

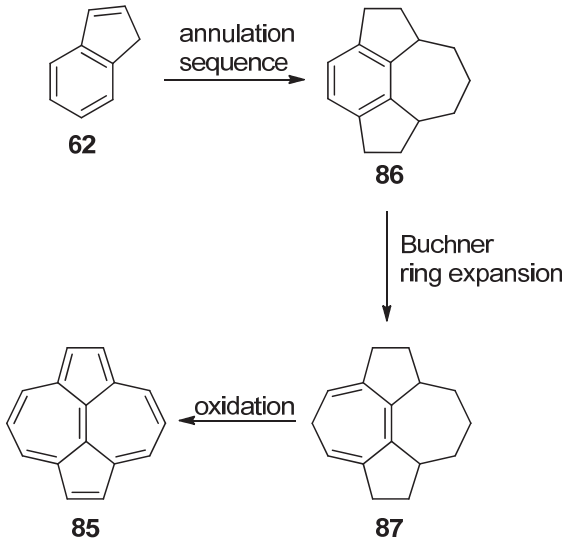


Bond	Length/ Å
a	1.365
b	1.431
c	1.367
d	1.372
e	1.333
f	1.488

Figure 1.18: Conjugated circuits of azupyrene **85**.

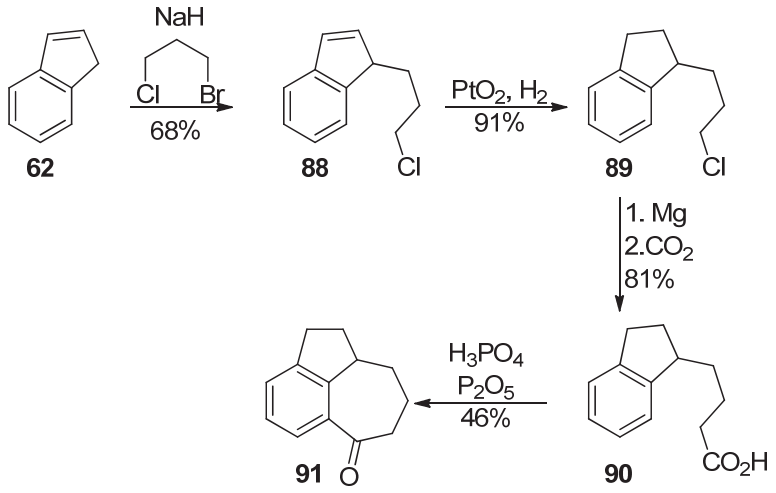
1.16 Anderson synthesis of azupyrene

The Anderson synthesis of azupyrene uses a similar ring forming strategy as the Plattner synthesis of azulene (Scheme 1.14).[46,47] Both syntheses can be summarised in three separate stages, an annulation sequence, followed by a Büchner ring expansion, and finally oxidative aromatisation. The Anderson synthesis begins with indene **62** which undergoes an annulation sequence to introduce two of the required rings. Büchner ring expansion of the benzene ring then forms the final seven membered ring. This gives the partially saturated azupyrene ring system **87** which is aromatised under oxidative conditions to yield azupyrene **85**.



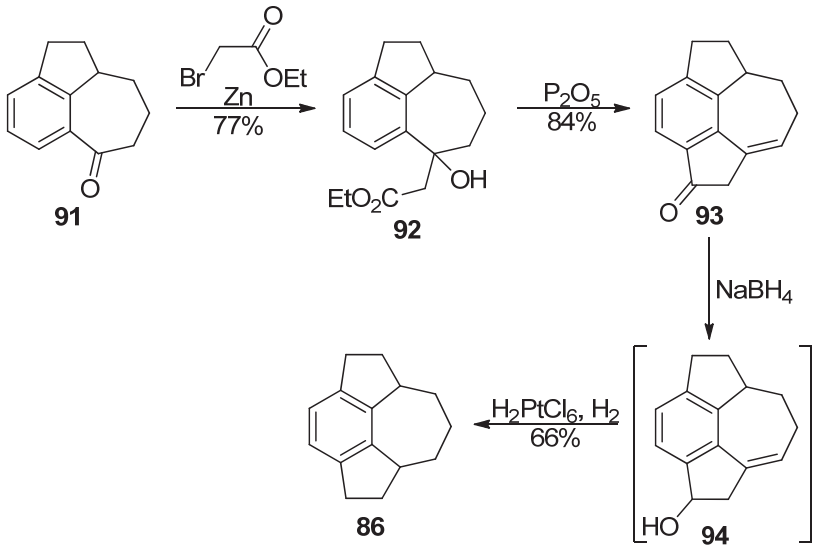
Scheme 1.21: Synthetic strategy towards azupyrene **85**.

Indene **62** was used as the starting material since the active methylene could be used to begin the annulation sequence. Deprotonation of indene followed by nucleophilic halide substitution gave the alkylated indene **88**. Indene was then reduced to indane **89** to prevent undesired reactions in subsequent steps. The alkyl chloride **89** was converted to the Grignard reagent followed by reaction with carbon dioxide to give the carboxylic acid **90**. Intramolecular Friedel-Crafts acylation of **90** then formed the seven membered ring of **91**.



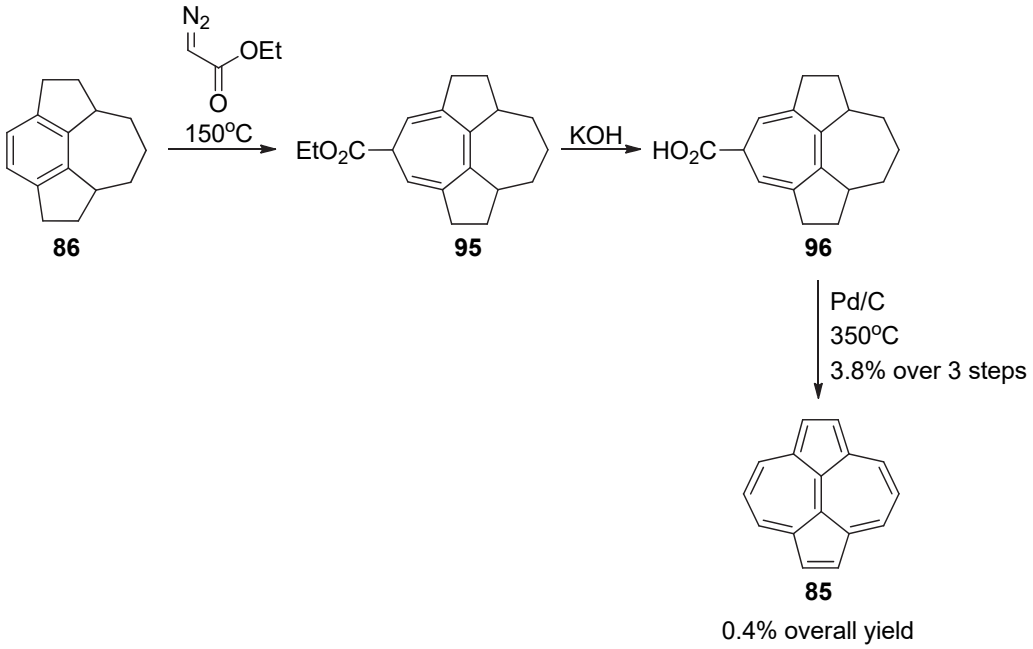
Scheme 1.22: Synthesis of ketone **91**.

The next side chain was introduced to the ketone **91** by a Reformatsky reaction with ethyl bromoacetate to give the hydroxy ester **92**. The dehydration and intramolecular Friedel-Crafts acylation of **92** was achieved in a single step by reaction with P_2O_5 to give **93**. The enone **93** was then reduced to the alcohol **94** using sodium borohydride. Subsequent hydrogenolysis of **94** then provided the hydrocarbon **86** through reduction of the alkene and hydrogenolysis of the benzylic alcohol.



Scheme 1.23: Synthesis of intermediate **86**.

The final ring structure was introduced by the thermally induced Büchner ring expansion to yield the cycloheptatriene **95** as a mixture of regioisomers. The impure mixture was then hydrolysed to give the carboxylic acid **96**. Heating **96** to 350°C in the presence of a palladium catalyst resulted in decarboxylative dehydrogenation to produce the target azupyrene **85** in low yield.

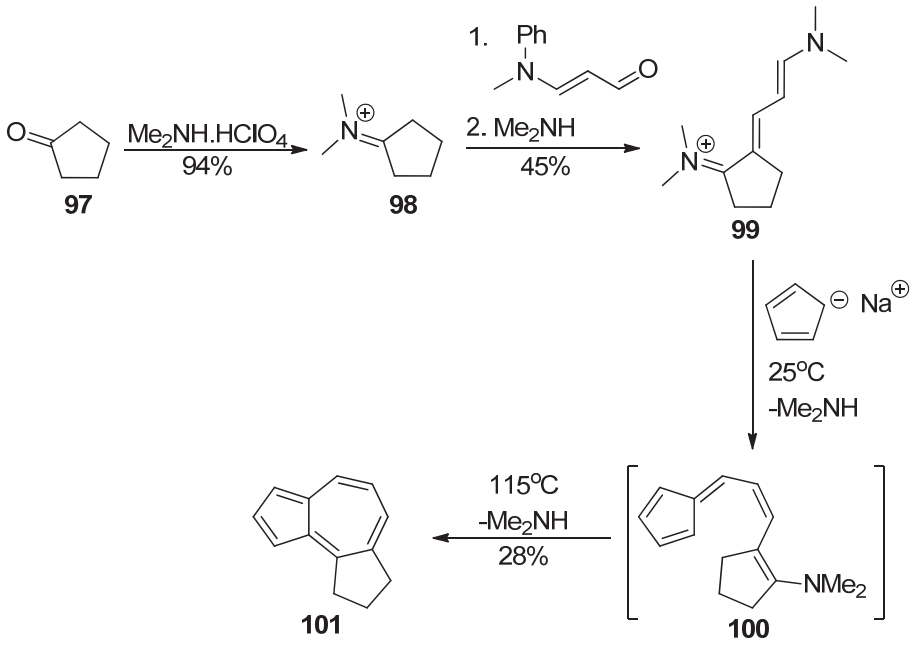


Scheme 1.24: Synthesis of azupyrene **85**.

1.17 Jutz synthesis of azupyrene

Soon after the first synthesis of azupyrene by Anderson, an improved procedure was reported by Jutz with further refinement by Anderson.[49,50] The synthetic approach of the Jutz synthesis of azupyrene is comparable to the synthesis of azulene reported by Ziegler and Hafner (Scheme 1.19) with both methods giving a higher yield in fewer steps compared to the previous methods. The first step of the synthesis is preparation of the annulated azulene **101** using the Ziegler-Hafner method.[41] Condensation of dimethylammonium perchlorate with cyclopentanone provided the iminium salt **98** in very high yield. Aldol condensation of the iminium salt with aminoacrolein followed

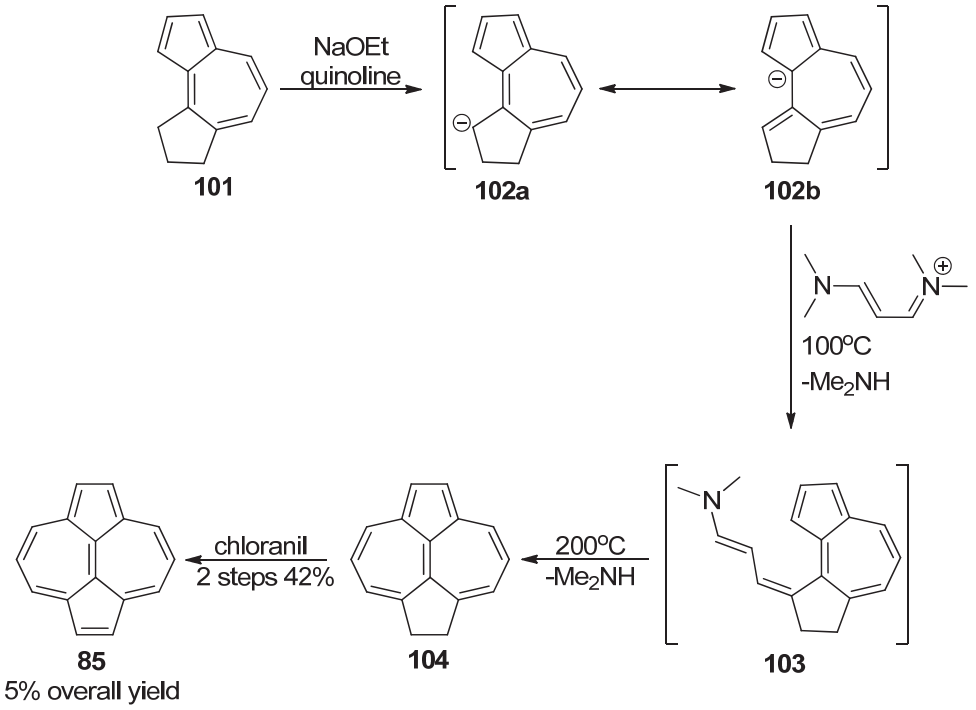
by transamination with dimethylamine provided intermediate **99** in moderate yield. The condensation of sodium cyclopentadienide with the iminium salt produced the fulvene intermediate **100** which was not isolated. The reaction mixture was heated to 115 °C resulting in cyclisation of the fulvene intermediate with elimination of dimethylamine to yield the tricyclic hydrocarbon **101** in moderate yield. The cyclisation is analogous to the Ziegler-Hafner synthesis of azulene (Scheme 1.19).



Scheme 1.25: Synthesis of intermediate **101**.

The azupyrene ring structure could be completed from intermediate **101** through a second annulation reaction using a three carbon linking group. The tricyclic hydrocarbon **101** may be deprotonated using sodium ethoxide since the carbanion is stabilised as the aromatic cyclopentadienide resonance structure **102b**. Condensation of **102** with the iminium salt introduced the three carbon linking chain. The intermediate **103** was not isolated and the reaction mixture was heated to 200°C resulting in electrocyclic ring closure followed by elimination of dimethylamine. The reaction conditions resulted in partial dehydrogenation to yield a mixture of azupyrene **85** and intermediate **104**. The mixture was oxidised using chloranil to yield azupyrene in 42% yield from tricyclic intermediate **101**. The Jutz synthesis of

azupyrene is a significant improvement over the Anderson method in terms of steps (5 vs. 12) and overall yield (5% vs. 0.4%). The improved synthesis was made possible through the use of conjugated iminium salts to effect each annulation reaction in a single step.



Scheme 1.26: Synthesis of azupyrene **85**.

1.18 Aromaticity of isocoronene

Following Agranat,[33] the theory of conjugation in non-alternant corannulenes was further developed by Randić and Vogler.[51, 52, 53] Vogler proposed that the peripheral conjugation of a corannulene would be enhanced if the perimeter was separated from the internal ring by formal single bonds. This type of structure is classified as a conjugation deficient corannulenes due to the reduced number of conjugated circuits compared to the equivalent benzenoid isomer. A conjugation deficient corannulene is achieved by replacing the angular fused benzene rings of an alternant corannulene with odd number rings. This may be demonstrated using the alternant corannulene,

coronene **19**. By replacing the outer benzene rings with alternating five and seven membered rings, a new non-benzenoid structure **105** (isocoronene) is generated.

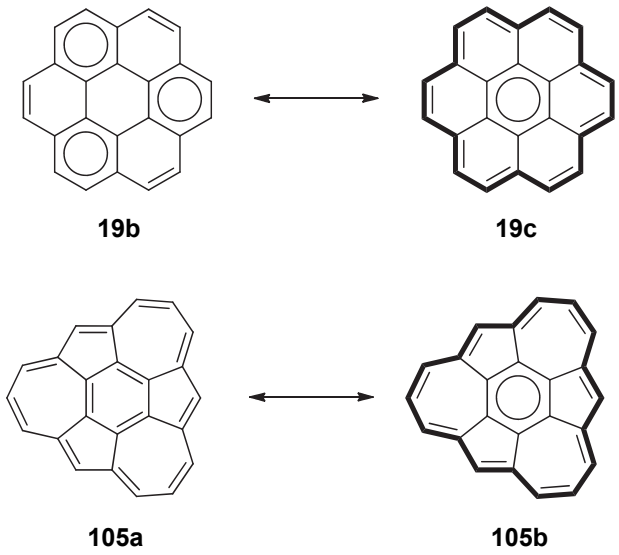


Figure 1.19: Resonance structures of coronene **19** and isocoronene **105**.

The structure of isocoronene **105** was used by Vogler as a model compound to study the properties of conjugation deficient corannulenes.[53] The separation of the peripheral conjugated circuit from the central ring of isocoronene can be demonstrated with resonance structures (Figure 1.20). Ring currents due to zwitterionic resonance structures (e.g. **105d**) are energetically unfavourable due to loss of aromaticity within the central benzene ring. These properties make isocoronene an ideal structure for assessing superaromatic stabilisation according to the definition given by Clar.[16] Vogler used computational methods to calculate the peripheral bond lengths of **105** and found significant alternation.[53] The assumption was made that the calculated bond lengths would be accurate enough to allow for a reliable assessment of electronic structure. The calculated bond lengths were not provided however Vogler concluded that the degree of alternation demonstrated a weak peripheral conjugation of **105**. No reasoning was given for the conclusion even though it is in contrast to the prediction based on resonance structures.

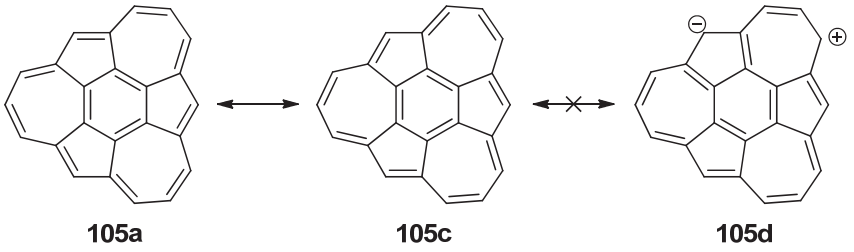
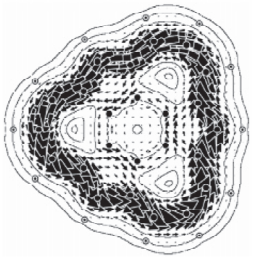
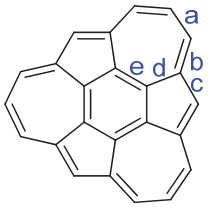


Figure 1.20: Resonance structures of isocoronene **105**.

Interest in isocoronene **105** was recently renewed following a report from Ciesielski *et al.* in 2006.[54] The computational study of **105** indicated an intense peripheral ring current which is consistent with resonance structures. The ring current was calculated from the current density map (Figure 1.21) which displays the direction and magnitude of the ring current. The calculated bond lengths of isocoronene indicated the perimeter was delocalised with minimal bond length alternation (1.416 - 1.403 Å) in contrast to the earlier work by Vogler.[53] The aromaticity of isocoronene was evaluated from the calculated aromatic stabilisation energy (ASE). Unexpectedly, it was found that the ASE of isocoronene was substantially lower than coronene. The authors conclude that predicted ring current of isocoronene supports superaromaticity although the low ASE value gave no indication of enhanced aromaticity. These conflicting results require further investigation before definitive answer to the question of superaromaticity can be reached.





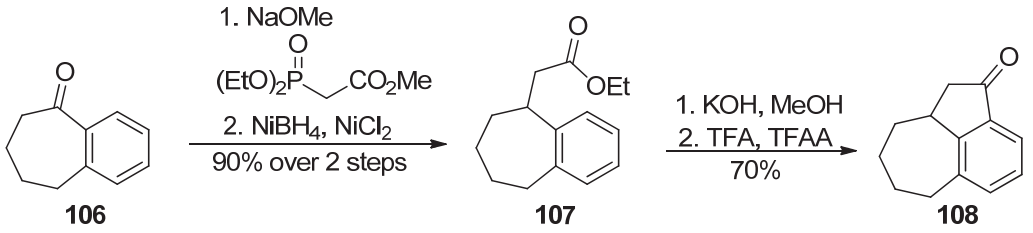
Bond	Length/ Å
a	1.412
b	1.403
c	1.416
d	1.459
e	1.399

Figure 1.21: Calculated bond lengths of isocoronene and current density map.[54]
Arrows indicate the direction and magnitude of ring currents.

1.19 Attempted synthesis of isocoronene

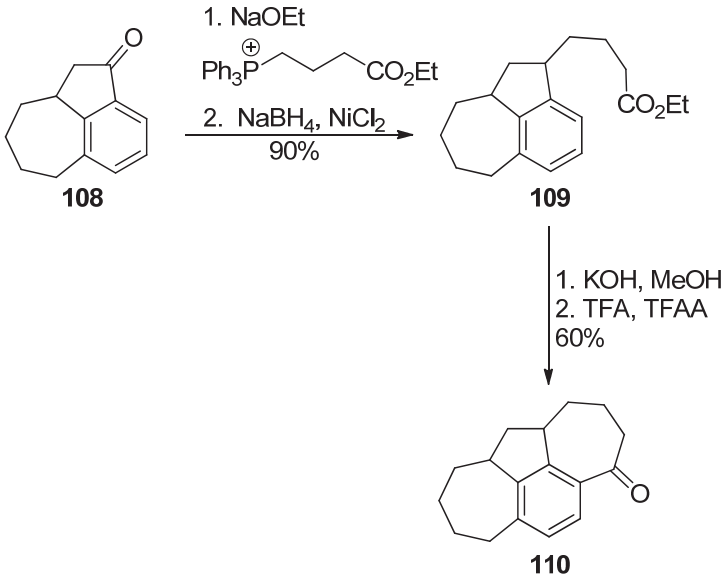
The non-alternant outer ring structure of isocoronene presents a challenging synthetic target. The structure of isocoronene has previously attracted the interest of Hellwinkel during early work on corannulenes.[55] This led to an attempt on the synthesis of isocoronene which was later published.[56] The attempted synthesis by Hellwinkel is the only reported synthetic work towards isocoronene in the literature. The strategy used in the attempted synthesis involved a sequence of intramolecular Friedel-Crafts acylation reactions to form the outer rings. A benzylic ketone is introduced with each annulation which allows the introduction of a linking carbon chain through the Horner-Wadsworth-Emmons (HWE) or Wittig reaction. After complete annulation of the central benzene ring a final oxidative dehydrogenation was planned to form the final outer ring. Aromatisation of the outer perimeter would then yield isocoronene.

The synthesis starts with benzosuberone **106** which provides the central benzene ring of isocoronene fused to a seven membered ring. The annulation sequence is initiated by Wittig reaction at the benzylic ketone of **106**. The formation of a five member ring would require a two carbon linking chain with a terminal acyl group. The carbon chain was introduced through an HWE reaction with the benzylic ketone to yield an intermediate alkene as a mixture of regioisomers. The isomeric mixture was reduced to a single product **107** in high yield using a combination of $NaBH_4$ and $NiCl_2$. The intramolecular Friedel-Crafts acylation of **107** was investigated using a range of conditions. The optimal conditions required hydrolysis of the ester to the carboxylic acid followed by activation of the acid as a mixed anhydride using trifluoroacetic anhydride (TFAA). The optimised conditions provided tricyclic ketone **108** in good yield. In addition to forming a new ring, the annulation sequence introduces a new benzylic ketone which allows for the annulation sequence to be repeated.



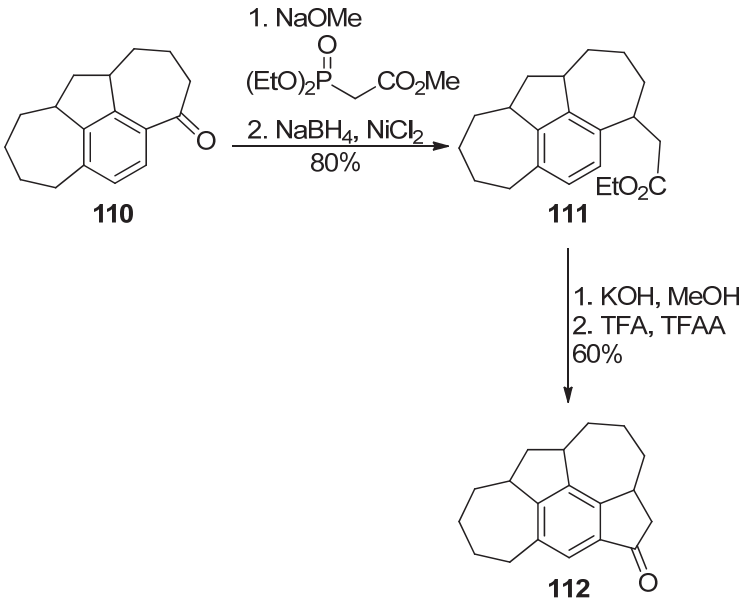
Scheme 1.27: Synthesis of ketone **108**.

The second annulation required formation of a seven membered ring to construct the isocoronene ring structure. This could be achieved by linking the benzylic ketone to the benzene ring using a four carbon linking chain. The carbon chain was introduced to ketone **108** through Wittig reaction. Reduction of the alkene intermediate using $NaBH_4$ and $NiCl_2$ then formed the ethyl ester **109** in high yield. The annulation reaction was performed as before by hydrolysis of the ester followed by intramolecular acylation to yield the tetracyclic ketone **110** in moderate yield.



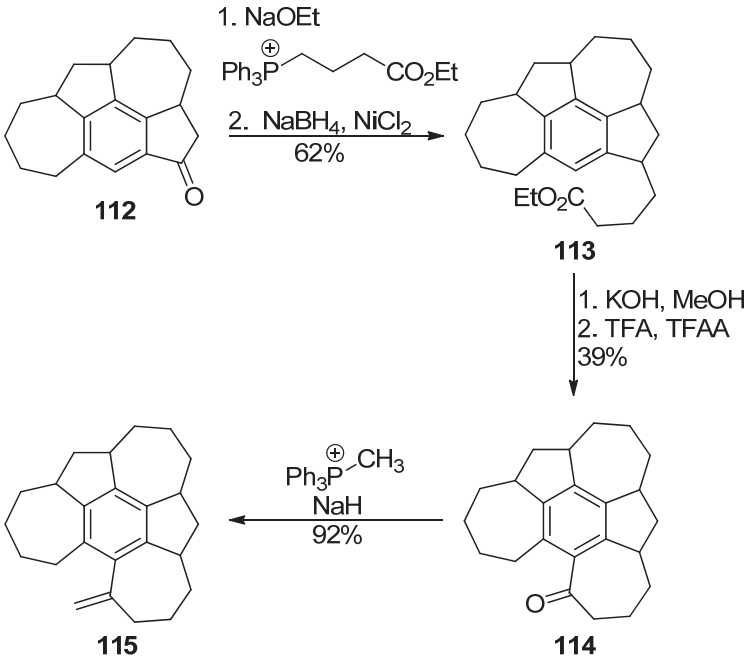
Scheme 1.28: Synthesis of ketone **110**.

With the introduction of a new benzylic ketone, the annulation sequence continued as before. A two carbon linking group was introduced to **110** through HWE reaction followed by reduction of the alkene to produce ethyl ester **111** in high yield. The ester was hydrolysed and then subjected to the standard acylation conditions to form the pentacyclic ketone **112** in moderate yield.



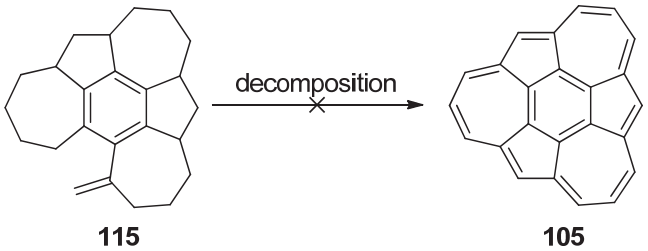
Scheme 1.29: Synthesis of ketone **112**.

The fourth annulation followed the previously reaction sequence to introduce a seven membered ring. The alkyl chain was introduced to ketone **112** by Wittig reaction followed by reduction of the alkene to give the ester **113** in moderate yield. Hydrolysis of the ester followed by acylation using TFAA produced the hexacyclic ketone **114** in low yield. The trend of reduced yield for each successive annulation step could be explained by restricted movement of the ring forming carbon chain due to the increasingly rigid structure. This could reduce the rate of acylation by restricting the interaction between the bond forming positions. The final annulation step would require linking of the benzylic ketone with the adjacent benzylic position using a single carbon linker. The linking group was introduced using a Wittig reaction to yield the alkene **115** in high yield.



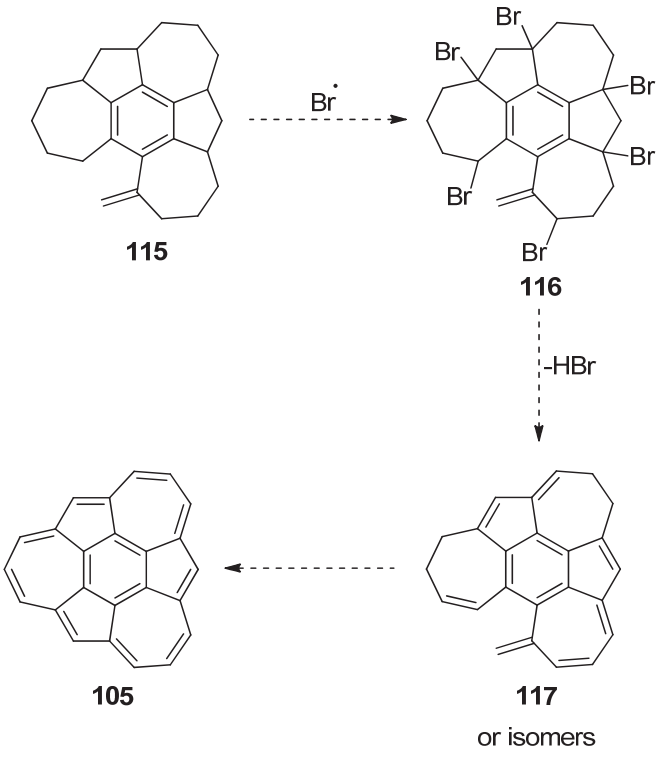
Scheme 1.30: Synthesis of intermediate **115**.

The final annulation step required the formation of a bond between the exocyclic alkene and the adjacent benzylic position. The authors had planned to close the final ring through a dehydrogenation reaction which could subsequently aromatise the perimeter to yield isocoronene. Numerous reaction conditions were investigated using a range of temperatures from 120-400 °C and reagents including Pd/C, sulfur, selenium and DDQ. All attempts at dehydrogenation yielded black tar or coal-like material. Analysis of the reaction products by mass spectrometry gave no indication of isocoronene or partially unsaturated intermediates.



Scheme 1.31: Attempted synthesis of isocoronene **105**.

The authors conclude that global dehydrogenation of **115** is unlikely to succeed since the high reaction temperature resulted in polymerisation of the strained ring system. It was suggested that benzylic radical bromination followed by dehydrobromination may provide an unsaturated intermediate such as **117**. No further work towards isocoronene was published which suggests this approach was not successful.



Scheme 1.32: Proposed synthesis of isocoronene from intermediate **115**.

1.20 Project aims

The theory of aromaticity has been thoroughly investigated for alternant PAHs however there are unanswered questions regarding non alternant structures. The concept of superaromaticity in particular has continued to inspire new research since its inception.[16] The study by Ciesielski *et al.* raises the question of enhanced aromaticity in the delocalised peripheral ring of isocoronene.[54] The conflicting results of a strong ring current with relatively low stabilisation reported by Ciesielski merits

further investigation. Computational studies have failed to give conclusive evidence for the electronic structure and aromaticity of isocoronene. The total synthesis of isocoronene would allow unambiguous determination of physical and chemical properties as evidence regarding the aromaticity of isocoronene. This may provide the first example of superaromaticity which has eluded chemists for over 40 years. The project aims are the total synthesis of isocoronene followed by characterisation and evaluation of aromatic stabilisation.

The previously published work towards the synthesis of isocoronene has made considerable progress towards the final structure with the introduction of all but one of the required rings.[56] This approach was ultimately unsuccessful due to the lack of suitable functionality for the final ring forming reaction. Another disadvantage to the published synthesis is the stepwise approach which required 13 steps to reach the final compound. A more efficient approach towards the synthesis of isocoronene would take advantage of the 3-fold rotational (C_3) symmetry (Figure 1.22). By forming the outer rings of isocoronene in a symmetrical fashion, the number of steps could be reduced.

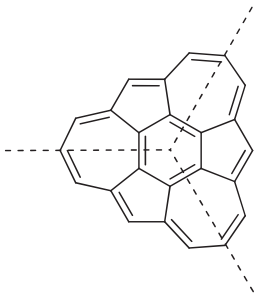
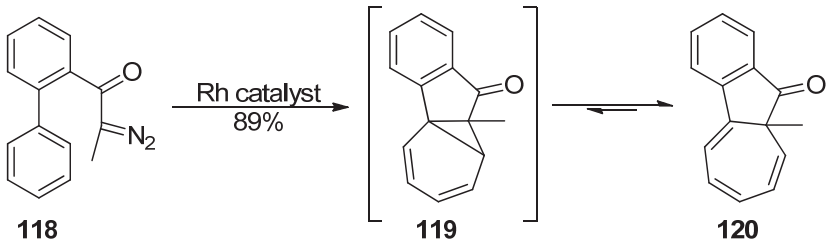


Figure 1.22: Symmetry elements of isocoronene.

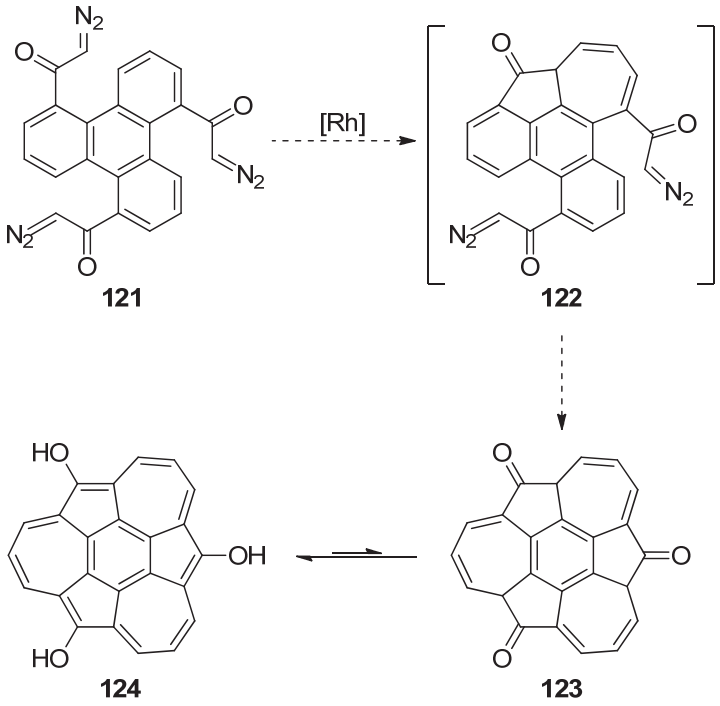
The structure of isocoronene consists of three azulene ring systems which are fused to a central benzene ring. The synthesis of benzo-fused azulenes has previously been achieved through the intramolecular Büchner ring expansion reaction of diazoketone **118**.[57] The reaction proceeds through rhodium catalysed cyclopropanation of the benzene ring to give norcaradiene **119** which undergoes rearrangement to the

cycloheptatriene **120**. This is an efficient method for the synthesis of a benzoazulene ring system and could be applied to the synthesis of isocoronene.



Scheme 1.33: Intramolecular Büchner ring expansion of biphenyl **118**.

The intramolecular Büchner ring expansion could be employed in the synthesis of isocoronene from diazoketone **121**. The Büchner reaction of triphenylene diazoketone **121** would introduce a five membered ring with expansion of the adjacent benzene ring to give the intermediate **122**. Two subsequent ring expansions would then form the ketone **123**. The ketone would be in equilibrium with isocoronene **124** with aromatic stabilisation favouring the enol form.

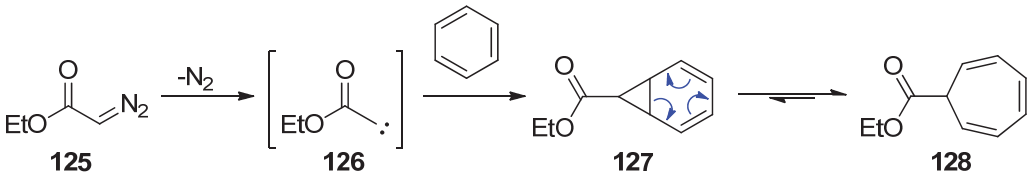


Scheme 1.34: Proposed synthesis of isocoronene from diazoketone **121**.

Chapter 2

Büchner ring expansion approach

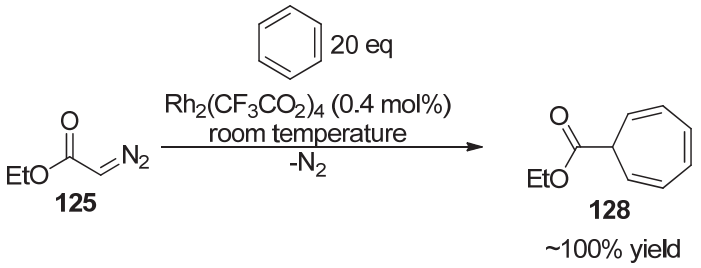
The Büchner ring expansion reaction describes the reaction of a carbene with a benzene ring to yield a cycloheptatriene **128**.[56, 57] The first step of the reaction mechanism is the decomposition of an α-diazo carbonyl compound such as **125** to form a carbene. The carbene is a highly reactive intermediate since it has an incomplete valence shell with only six electrons. The carbene intermediate then reacts with an aromatic π bond through a [2+1] cycloaddition reaction to yield the norcaradiene structure **127**. The norcaradiene is in equilibrium with the seven membered cycloheptatriene ring **128** through a 6π electrocyclic reaction. The equilibrium usually favours the cycloheptatriene isomer however this is influenced by steric and electronic factors.[58]



Scheme 2.01: The Büchner ring expansion.

Early examples of the Büchner reaction generated the carbene through thermal or photolytic decomposition of ethyl diazoacetate. This method is typically low yielding and forms a mixture of inseparable regioisomers, for example the Plattner synthesis of azulene (Scheme 1.14) and the Anderson synthesis of azupyrene (Scheme 1.24). The introduction of transition metal catalysis greatly improved the synthetic potential of the Büchner reaction. The catalyst facilitates decomposition of the diazo starting material which allows for significant reduction in reaction temperature, increased reaction rate and improved yield and selectivity. The first metal catalyst reported was copper(I), used in the synthesis of azulene by Scott (Scheme 1.20).[45] Soon afterwards, the use of rhodium(II) carboxylate catalysts was reported leading to unprecedented yields and selectivity.[59,60] The effectiveness of rhodium catalysis was

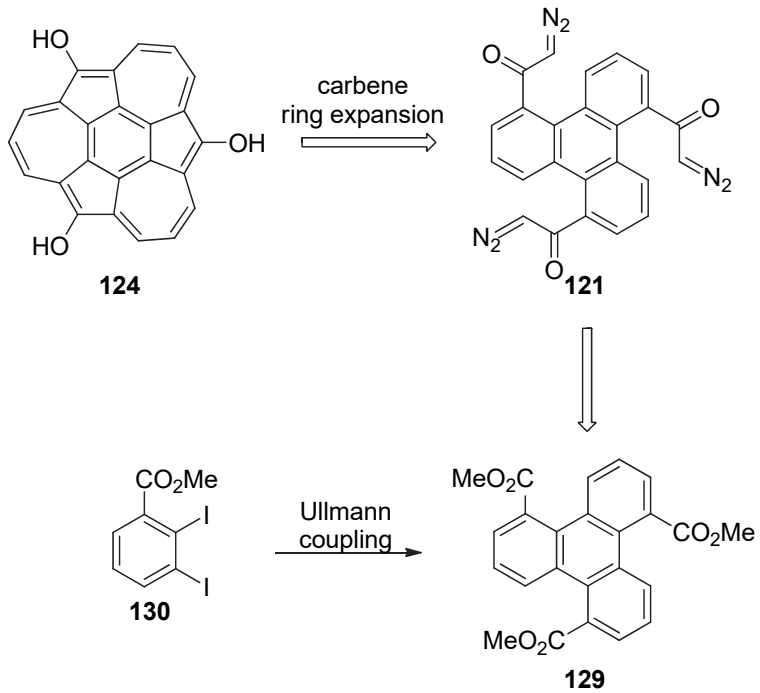
demonstrated by the reaction of ethyl diazoacetate and benzene to produce a quantitative yield of cycloheptatriene as a single regioisomer.



Scheme 2.02: Rhodium catalysed Büchner reaction.

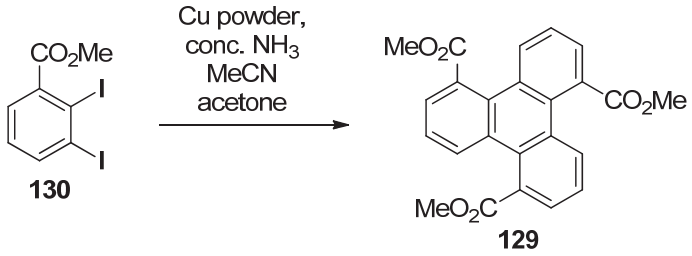
2.1 Proposed synthetic pathway

The proposed retrosynthesis (Scheme 2.03) makes use of the triphenylene ring system. Triphenylene **121** could undergo an intramolecular Büchner ring expansion of the outer rings to form the hydroxy isocoronene **124**. The diazoketone **121** could be prepared from the triphenylene ester **129**. The synthesis of symmetrical triphenylene **129** has previously been reported by Ullmann cyclotrimerisation of the diiodide **130**.[61]



Scheme 2.03: Proposed retrosynthesis of isocoronene.

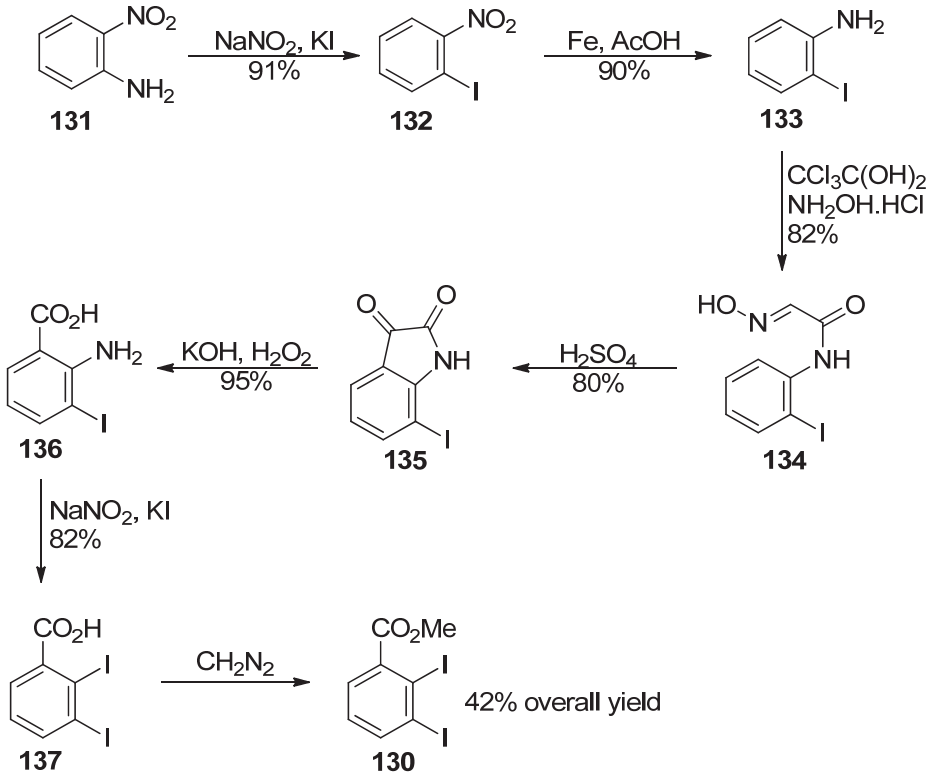
The original Ullmann coupling involved a high temperature reaction of aryl halides in the presence of copper metal to give biphenyl compounds.[62] Further development allowed for lower temperature reaction of aryl halides activated by the presence of an electron withdrawing group in the *ortho* position.[63] More recently a methodology has been developed for the synthesis of substituted triphenylenes by cyclotrimerisation of activated aryl *o*-diiodides using modified Ullmann coupling conditions.[61] The experimental procedure involves the addition of copper powder to a the diiodide in a mixture of solvents. The product was then isolated from the crude reaction mixture by recrystallisation. The reaction yield for the C_3 symmetrical triphenylene triester **129** was not specified.



Scheme 2.04: Synthesis of **129**.

2.2 Synthesis of the diiodide

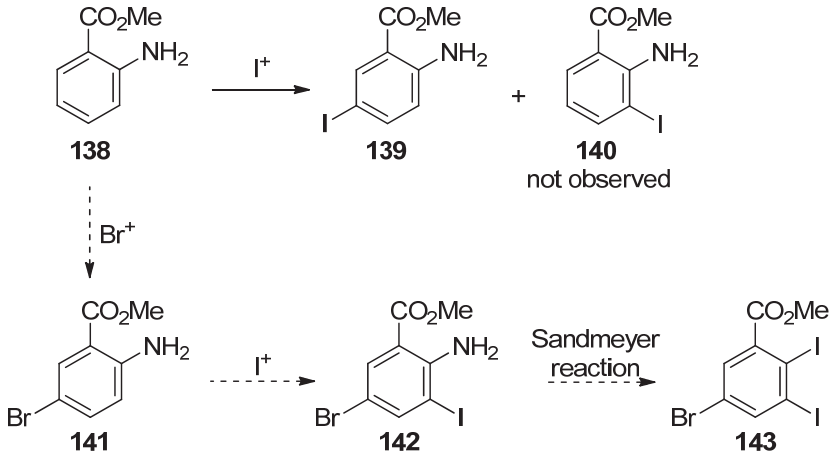
The diiodide used to synthesise the triphenylene ester has been prepared in 7 steps starting from *o*-nitroaniline.[64] Firstly, *o*-nitroaniline was converted to *o*-iodonitrobenzene using a Sandmeyer reaction. Reduction of the nitro group then gave *o*-iodoaniline. Condensation of the aniline with chloral hydrate and hydroxylamine followed by treatment with sulfuric acid then gave 7-iodoisatin **135**. Hydrolysis and oxidation of the isatin using a basic solution of hydrogen peroxide then afforded 3-iodoanthranilic acid. A second Sandmeyer reaction converted the aniline to the diiodide **137** with a final esterification to yielded methyl 2,3-diiodobenzoate **130** in 42% overall yield. The number of steps required for the synthesis of diiodide **130** made it unattractive, therefore an alternative synthesis was devised.



Scheme 2.05: Synthesis of **130**.

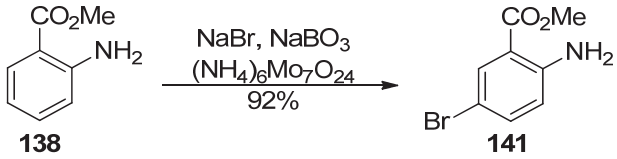
The next step towards the synthesis of the target diiodide would require the introduction of an iodo substituent *ortho* to the amino group of **138**. The iodo substituent could be introduced through an electrophilic aromatic iodination of methyl anthranilate **138** could be used to synthesise the previous intermediate 1**36** which would shorten the synthesis of the diiodide **130** (Scheme 2.05). A review of the literature shows iodination of **138** yields the undesired regioisomer **140** and so an alternative reaction sequence was explored.[65, 66, 67] To overcome the issue of regioselectivity a blocking group strategy was implemented. By first blocking the more reactive position the subsequent iodination would occur at the remaining activated position *ortho* to the aniline. The aryl bromide substituent may be introduced by nucleophilic aromatic substitution and may be removed by catalytic hydrogenation at a later stage.[68] In addition, aryl bromides are relatively unreactive in the Ullmann coupling reaction.[69] Bromination of methyl anthranilate would occur at the more activated less hindered position to give methyl 5-bromoanthranilate **141**. Iodination of **141** would then occur at the remaining activated position to give methyl 5-bromo-3-iodoanthranilate **139**. A Sandmeyer reaction of **142** would then convert

the amine to an iodide yielding methyl 5-bromo-2,3-diiodobenzoate **143**. The proposed synthesis of **143** requires only 3 steps in comparison to the synthesis of **130** requiring 7 steps.



Scheme 2.06: *ortho*-Iodination strategy.

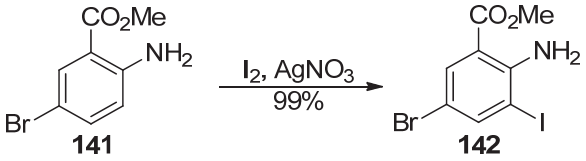
Bromination of methyl anthranilate would occur primarily at the more activated position *para* to the aniline to yield methyl 5-bromoanthranilate **141**. When using molecular bromine the product yield is moderate due to the purification required for removal of the undesired regioisomer.[70] An alternative bromination method using potassium bromide and sodium perborate was chosen since it does not require purification of the crude product.[71] The product was isolated by addition of water and the product was collected by filtration. The ^{1}H NMR spectrum of the product was consistent with literature data for methyl 5-bromoanthranilate.[71] The product yield was calculated as 92% with trace amount of the undesired isomer.



Scheme 2.07: Synthesis of **141**.

After introduction of the bromine blocking group, electrophilic aromatic iodination would occur exclusively at the remaining activated position *ortho* to the aniline. The use of molecular iodine is limited to highly activated substrates due to the poor electrophilicity of iodine. The reactivity can be increased by using a combination of

iodine and silver nitrate to form a highly electrophilic iodine nitrate.[72] Under these conditions **141** reacted rapidly to give a single product. The product was isolated in high yield without the need for further purification. The ^{1}H NMR spectrum showed two aromatic doublets (J = 2.4 Hz) and a singlet at 3.89 ppm with integration of 1:1:3. The singlet was assigned to the methyl ester with the integration of the aromatic signals indicating a tetra substituted aromatic ring. The relative positions of the aromatic protons are confirmed by the coupling constant which indicates *meta* coupling. This is consistent with iodination at the electronically activated position to give the desired product. This compound has been reported previously in the literature however no NMR data was given for comparison.[73]



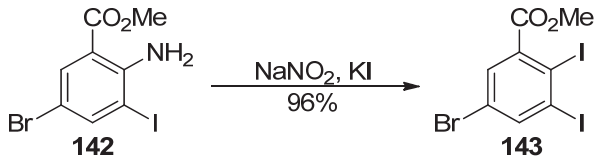
141 **142**

Scheme 2.08: Synthesis of **142**.

The final reaction step for the synthesis of the desired diiodide intermediate **143** is the conversion of the aniline to an iodide through a Sandmeyer reaction. The reaction was initially attempted using the same conditions as previously reported for diiodoanthranilic acid **137**. Sodium nitrite was added to mixture of the aniline and HCl followed by addition of potassium iodide. The ^{1}H NMR spectrum of the crude reaction mixture showed a significant amount of starting material which could not be removed by recrystallisation or using acid/base chemistry. The reason for the lack of reactivity was thought to be due to the low solubility of the starting material in the aqueous reaction mixture.

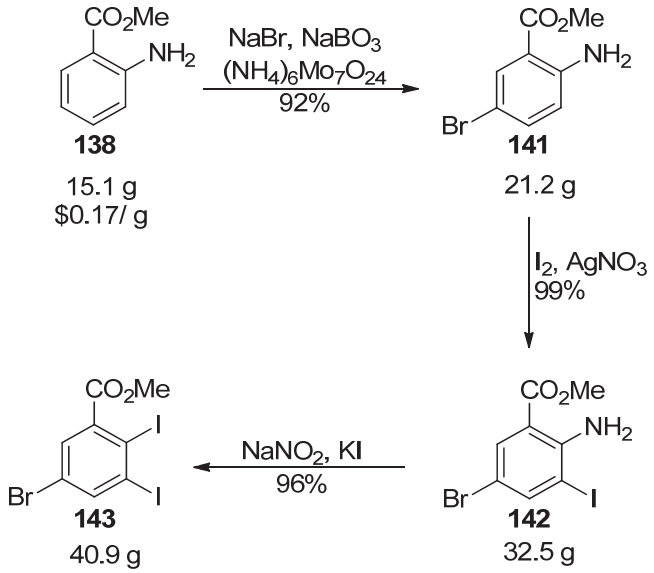
An alternative non-aqueous procedure was used in which the aniline was dissolved in acetic acid followed by addition to a solution of sodium nitrite in concentrated sulfuric acid. This procedure yielded a single product in high yield without the need for further purification. The ^{1}H NMR spectrum of the product showed two aromatic doublets (J = 2.3 Hz), consistent with the substitution pattern of the diiodide **143**. The aromatic signals appeared at a higher chemical shift compared to the starting material which was attributed to the loss of the electron donating amino substituent.

Analysis of the IR spectrum confirmed the loss of amine absorption consistent with the desired product.



Scheme 2.09: Synthesis of **143**.

The reaction sequence was scaled up to a 0.1 mol scale with no loss of yield or purity. Each step of the sequence was operationally simple and did not require any purification. This allowed for the synthesis of 40 g batches of the diiodide from inexpensive starting materials. With synthesis of the diiodide complete the Ullmann coupling was then investigated.

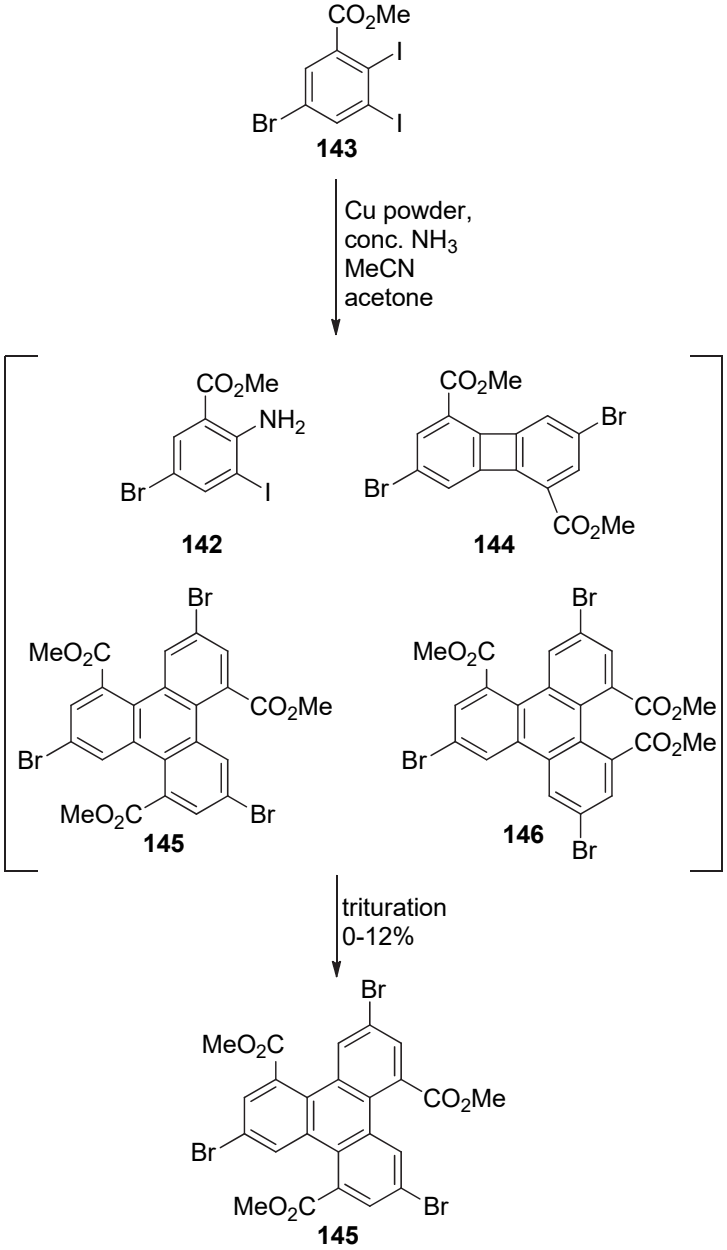


Scheme 2.10: Overall synthesis of **143**.

2.3 Synthesis of triphenylene diazoketone

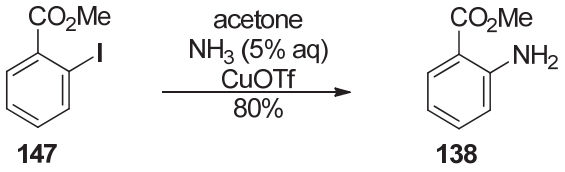
The triphenylene ester **145** could be synthesised by cyclotrimerisation of the diiodide **143** with the coupling procedure described by Abou-Tiem.[61] Copper powder was added to a mixture of the diiodide, acetonitrile, acetone and aqueous ammonia. Trituration of the crude product with boiling ethyl acetate gave a single product as a

white solid. The ^{1}H NMR spectrum showed the same signals and multiplicity as the starting material with a slight change in chemical shift. The symmetrical triphenylene **145** would be expected to have a ^{1}H NMR spectrum similar to the starting diiodide **143** since each aromatic ring is equivalent. Final confirmation of the structure was given by HRMS (calculated for $[M+H]^{+}$ = 636.8497, found 636.8508) corresponding to the correct molecular formula. Repetition of the reaction gave variable yields of 0-12% which prompted optimisation of the reaction conditions.



Scheme 2.11: Synthesis and purification of **145**.

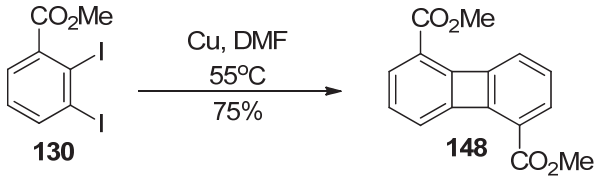
The ^{1}H NMR spectrum of the crude reaction mixture (Scheme 2.11) showed a complex mixture of products. Three of the reaction byproducts were isolated by column chromatography and identified by spectroscopic analysis. The first compound eluted had identical spectra to the previously synthesised aniline **142**. This type of transformation has previously been reported in the Ullmann type coupling of aryl iodide **147** with ammonia (Scheme 2.12).[74]



147 **138**

Scheme 2.12: Ammonia coupling reaction.

The second eluted compound was obtained as a bright yellow solid. The ^{1}H NMR spectrum showed two doublets in the aromatic region and one singlet at 3.85 ppm with integration of 1:1:3. The IR spectrum showed one carbonyl stretch in the ester region. The isolated product was identified as biphenylene **144** which is consistent with the spectral data. The formation of a biphenylene product is supported by previous literature where the Ullmann coupling of the structurally related diiodide **130** gave the biphenylene **148**.[64] The biphenylene structure was confirmed by HRMS (calculated for $[M+H]^{+}$ 424.9024, found 424.9035) however the regiochemistry could not be determined unambiguously.



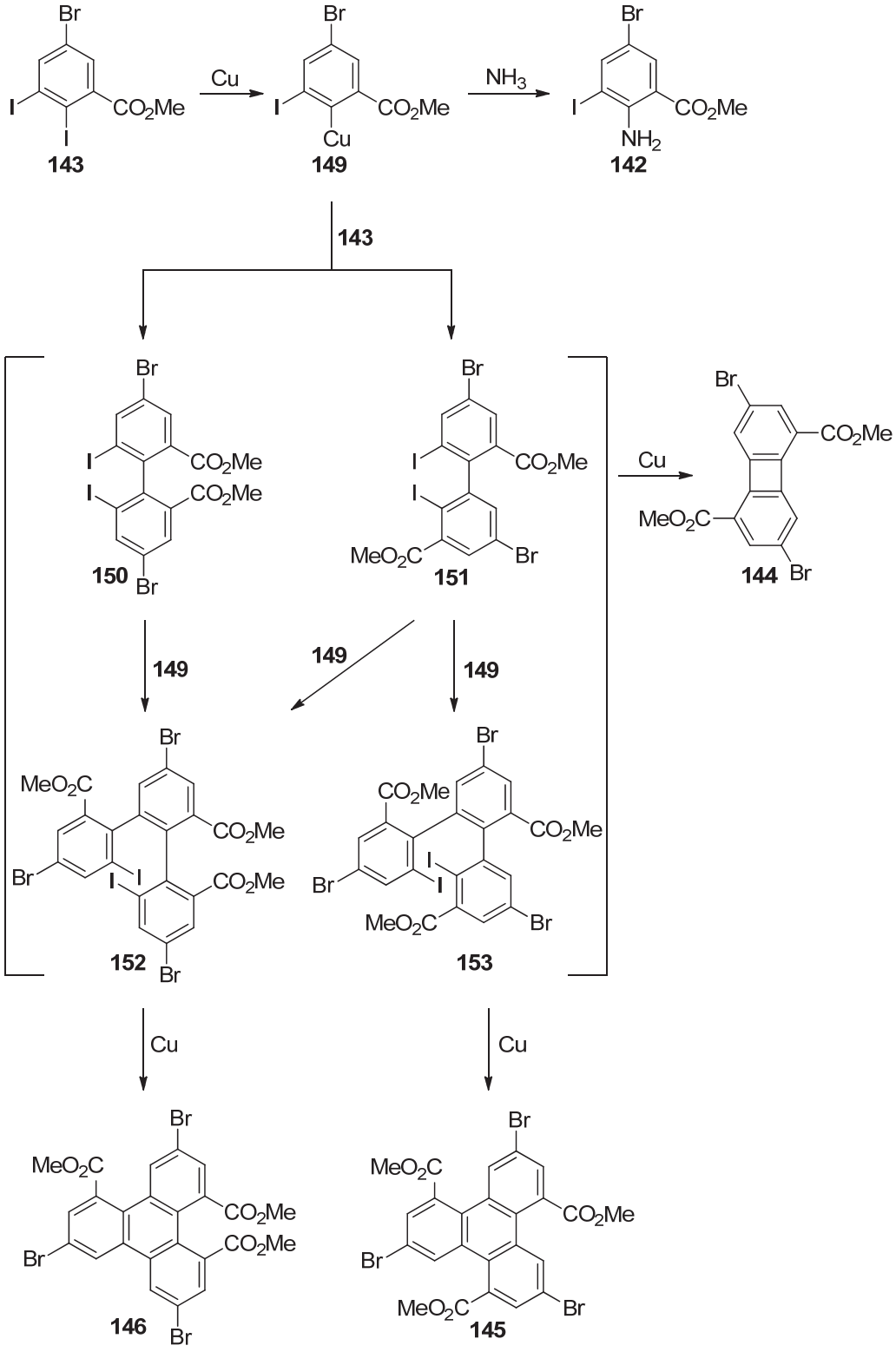
130 **148**

Scheme 2.13: Ullmann coupling of **130**.

The third isolated compound gave an ^{1}H NMR spectrum with 3 singlets near 4 ppm integrating to 3 hydrogens each. In addition, 6 doublets were observed in the aromatic region with integration of 1 each. The ^{13}C NMR spectrum showed 18 aromatic signals in the same region as the symmetrical triphenylene **145**. The compound was therefore assigned as the unsymmetrical triphenylene trimer **146**. The unsymmetrical isomer is the other possible regioisomers which may be formed by

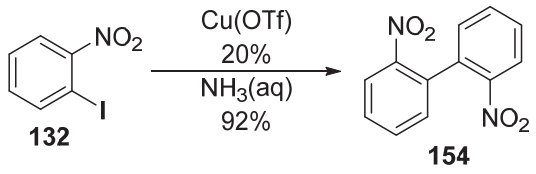
cyclotrimerisation of the diiodide **143**. The triphenylene structure was confirmed by HRMS (calculated for $[M+H]^+$ = 636.8497, found 636.8517).

A plausible reaction pathway to the isolated products is given in the scheme below. The first reaction intermediate **149** is formed by transmetalation at the activated position *ortho* to the carbonyl. This intermediate may react with ammonia to give the aniline **142**. Alternatively, the organocopper intermediate **149** may react with another equivalent of the diiodide **143** to form a dimer. This dimerisation could occur in two different orientations to give two different biphenyl products **150** and **151**. The biphenyl **151** could undergo intramolecular coupling to yield biphenylene **144**. Alternatively, either of the biphenyl intermediates could then react with another equivalent of **149** to yield either of the trimeric intermediates **152** or **153**. The trimers could then undergo copper mediated intramolecular cyclisation to give each of the triphenylene regioisomers **145** and **146**.



Scheme 2.14: Proposed reaction pathways for the Ullmann coupling of **143**.

A review of the relevant literature was undertaken to determine optimal reaction conditions. The use of the acetone/acetonitrile/ammonia system in the Ullmann coupling reaction was first reported by Cohen who found that the coupling of *o*-iodonitrobenzene could be achieved at room temperature in 5 minutes to give the biphenyl **154** in 92% yield.[74, 75, 76] The experimental procedures specified a nitrogen atmosphere was used in all of the coupling reactions.



Scheme 2.15: Ullmann coupling of **132**.

The coupling reaction of diiodide **143** was therefore repeated under nitrogen atmosphere. The use of a nitrogen atmosphere resulted in a noticeable difference in the colour of the reaction mixture. Under atmospheric conditions a green or blue colour was observed however the use of nitrogen atmosphere gave a grey colour reaction mixture. Exposure to the atmosphere during workup resulted in rapid change to a green colour which indicates the reaction mixture is air sensitive. After conducting the reaction under nitrogen atmosphere the ^{1}H NMR spectrum of the crude product was analysed. The major difference in the spectrum was the loss of aromatic signals attributed to the ammonia coupled by-product **142**. This indicates the presence of oxygen in the reaction mixture favours the ammonia coupling reaction pathway.

A second variable that was considered is reaction temperature. It was observed that after an induction period of 3 to 5 minutes the reaction produced a significant exotherm which signified initiation of the reaction. Cooling of the reaction mixture on ice prior to addition of the copper powder resulted in failure of the reaction to initiate. After warming the reaction to room temperature initiation occurred. This could be attributed to a reduced concentration of the halide in the reaction mixture which may not have sufficient solubility at reduced temperature for initiation to occur. An alternative cooling procedure was therefore used in which the reaction was allowed to initiate at room temperature followed by immediate cooling on ice. Following workup, the ^{1}H NMR spectrum of crude product was analysed which

showed the signals attributed to the biphenylene by-product were absent. It was reasoned that a higher reaction temperature caused by the initial exotherm could lead to the kinetically favourable intramolecular coupling of the biphenyl intermediate **151** yielding the strained biphenylene ring system **144**. This is in agreement with literature where biphenylene synthesis from aryl diiodides is conducted at elevated temperature (T > 40 °C, Scheme 2.13).[64]

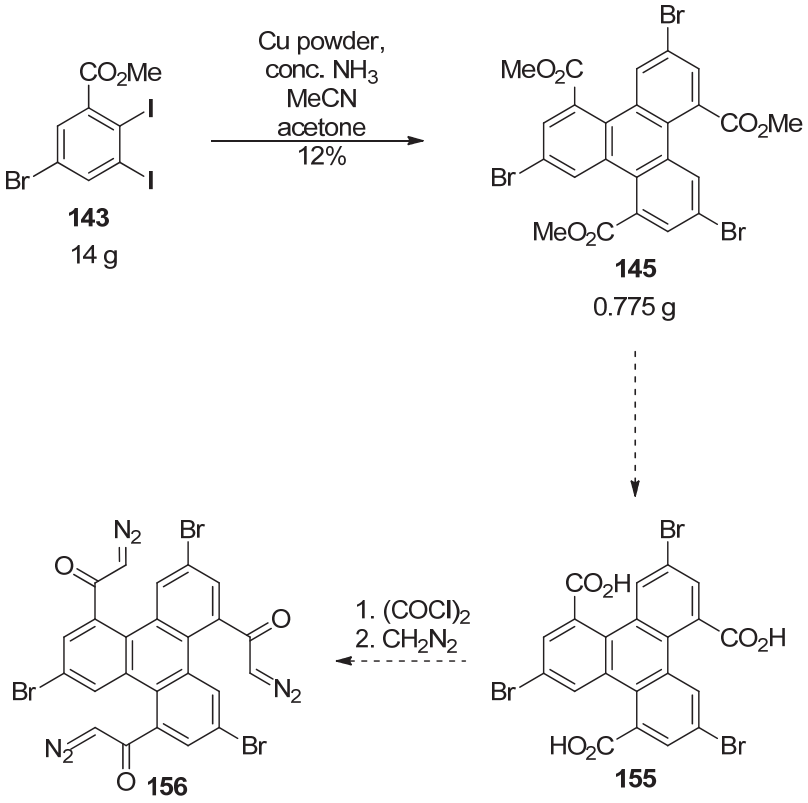
In the process of reaction optimisation, another issue was encountered in which the reaction failed to reach completion or would not reliably initiate. The problem was traced to the source of the copper powder used. Copper powder supplied by Alfa Aesar (cat# A16243) presented no problem however the copper powder supplied by Sigma Aldrich (cat# 207780) was less reactive. Several methods have been used for the preparation of activated copper metal such as reduction of copper salts to form Rieke copper, treatment with a solution of iodine in acetone, or through sonication.[77, 78, 79] Activation by sonication of the copper powder was chosen due to operational simplicity.[79] A mixture of the copper powder and ammonia solution was sonicated for a period of four hours before being added to the reaction mixture. Using this procedure it was found that initiation occurred rapidly and reliably resulting in complete consumption of starting material.

Under all reaction conditions, the two triphenylene regioisomers were formed in a statistical ratio. It was therefore concluded that formation of the undesired unsymmetrical isomer is independent of reaction conditions. The desired symmetrical isomer **145** was readily isolated by trituration to give the desired product in consistent yield and high purity. The remaining mass of the crude product could not be characterised by ^{1}H NMR. This material was presumed to be polymeric and not investigated further. With the reaction conditions optimised attention was focused on the introduction of the diazo groups.

Product distribution (146:145:144:142)				
a) Open to atmosphere, no cooling	30	30	10	30
b) N_2 atmosphere, no cooling	40	40	20	0
c) Cooling, N_2 atmosphere	50	50	0	0
d) Cu activation, N_2, cooling	50	50	0	0

Table 2.01: Product ratio by ^{1}H NMR.

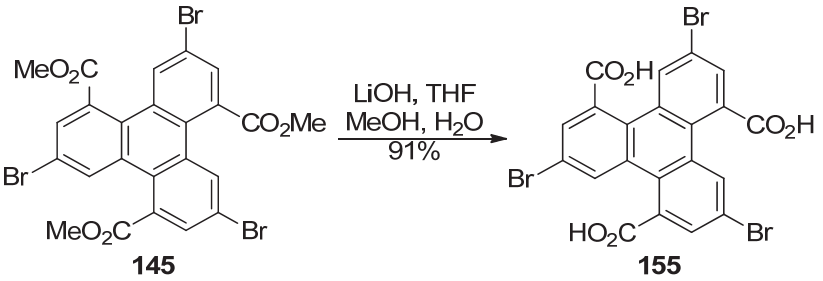
After optimisation of the reaction conditions, the Ullmann coupling of diiodide **143** was scaled up to yield nearly gram scale quantities of triphenylene ester **145** with consistent yields of 12% after purification. The subsequent introduction of the desired diazoketone groups would first require hydrolysis of the ester to yield the triacid **155**. The carboxylic acid could then be converted to the acid chloride followed by reaction with nucleophilic diazomethane to yield the target diazoketone **156**.



Scheme 2.16: Proposed synthesis of **156**.

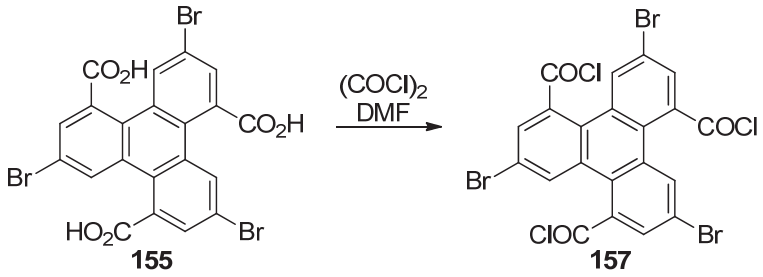
The hydrolysis of ester **145** was conducted under basic conditions using a mixture of solvents to improve solubility of the reaction mixture. A mixture of triphenylene ester **145** and LiOH in THF and aqueous methanol was heated under reflux. The reaction was monitored by TLC showing two intermediate compounds finally forming a single product. After acidic workup, the product was isolated as a single compound. The ^{1}H NMR spectrum of the product showed a loss of the methyl signal consistent with hydrolysis of the triphenylene ester. The ^{13}C NMR and IR spectra

both indicated the presence of a carbonyl which was assigned to the carboxylic acid **155**.



Scheme 2.17: Synthesis of **155**.

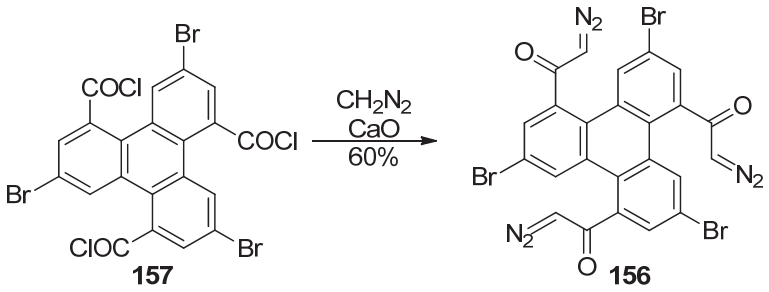
The conversion of a carboxylic acid to a diazoketone may be achieved in two steps via an acid chloride intermediate. The triacid **155** was suspended in DCM and 3.3 equivalents of oxalyl chloride was added followed by a catalytic amount of DMF. The reaction was heated under reflux with completion of the reaction indicated by dissolution of the starting material. The reaction mixture was then concentrated to remove excess oxalyl chloride, yielding **157** as a pale yellow solid.



Scheme 2.18: Synthesis of **157**.

The desired diazoketone functional groups could be introduced to the acid chloride by reaction with diazomethane. The reaction of diazomethane with an acid chloride generates one equivalent of HCl in addition to the desired diazoketone. The diazoketone product is rapidly decomposed by strong acid and so the HCl must be neutralised in the reaction mixture. Several methods have been used for removal of HCl from the reaction mixture such as using an excess of diazomethane, or through the addition of a base such as triethylamine.[80, 81] A more recently published method uses calcium oxide as an acid scavenger which was reported to give higher yields compared to other methods in addition to using stoichiometric diazomethane.[82]

Following this method, dry CaO was added to a solution of diazomethane followed by addition of the acid chloride **157**. Following workup and purification, a yellow solid was obtained. The ^{1}H NMR spectrum of the product showed two broad singlets in the aromatic region and a broad singlet at 5.42 ppm with integration ratios of 1:1:1. The broadening of ^{1}H NMR signals is often seen in diazoketones due to hindered rotation of the C-C bond.[83] The presence of only two aromatic signals indicates the product is a symmetrically substituted triphenylene. The signal at 5.42 ppm was assigned to the diazo group. The presence of a diazoketone substituent was further confirmed by IR showing absorption at 2101 and 1612 cm^{-1} for the diazonium and C=O stretching frequencies respectively. The ^{13}C NMR spectrum showed signals at 189.7(C) and 58.5(CH) ppm assigned to the ketone and diazo groups respectively.



Scheme 2.19: Synthesis of **156**.

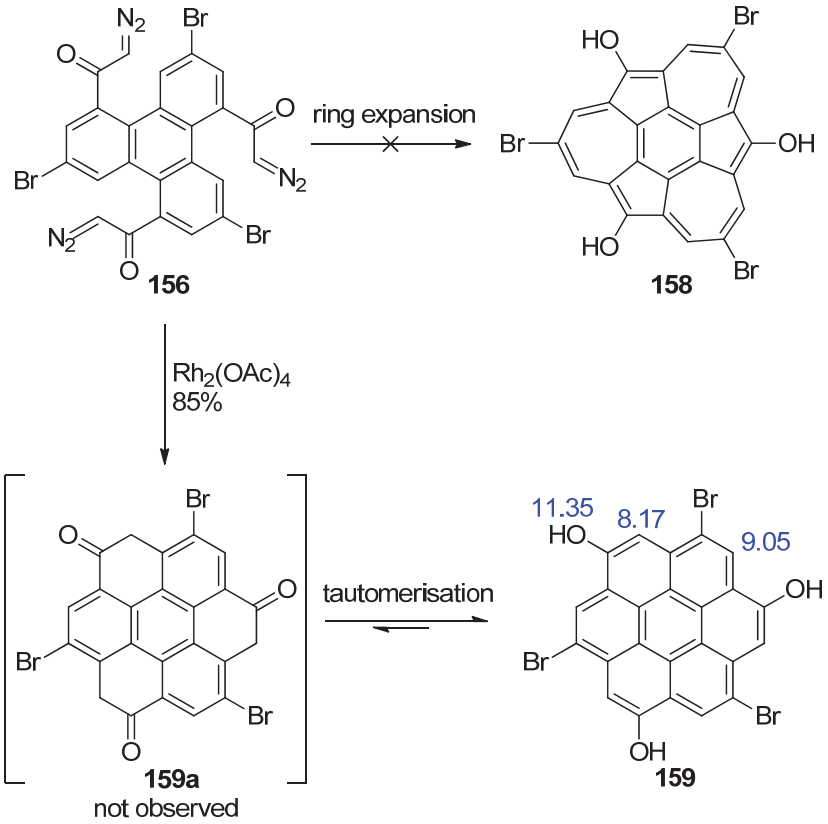
2.4 Büchner ring expansion

With the key diazoketone intermediate **156** synthesised, the final Büchner reaction was investigated. Rhodium(II) carboxylates are most frequently used as catalysts in the Büchner reaction due to their superior reactivity and selectivity over other metals.[57] A solution of triphenylene diazoketone **156** was added dropwise to a catalytic amount of $Rh_2(OAc)_4$ in DCM heated under reflux. During addition of the diazoketone, the formation of an orange coloured precipitate was observed. After addition was complete the reaction mixture was cooled to room temperature and the precipitate was isolated as a dark orange solid in high yield. Concentration of the filtrate gave a trace amount of the same product with minor impurities. The ^{1}H NMR spectrum of the product showed three singlets at 11.35, 9.05 and 8.17 ppm with

integration of 1:1:1. This is not consistent with the expected ^{1}H NMR spectrum of isocoronene **158** since the desired isocoronene would have equivalent protons on each of the seven membered rings due to delocalisation of the outer π bonds. This would give a ^{1}H NMR spectrum consisting of one aromatic singlet and one enolic OH with an integration of 2:1 respectively. An alternative structure was proposed which may form through an intramolecular C-H insertion of the carbene intermediate.[84] This reaction would yield the coronene derivative **159** whose structure is consistent with the observed ^{1}H NMR spectrum. The presence of an exchangeable enolic proton was confirmed by treating the NMR sample with D_2O then collecting the spectrum again. This resulted in suppression of the signal at 11.35 due to deuterium exchange. Therefore the signal at 11.35 was assigned to the OH position with the other signals assigned as the aromatic positions. The lack of signal coupling is consistent with the aromatic signals being located on separate ring systems. In addition, the large increase in chemical shift of the aromatic signals correlates well with the reported ^{1}H NMR spectrum of coronene giving one singlet at 8.89 ppm.[85] The enolic CH position would be strongly shielded and so this was assigned to the signal at 8.17 ppm. The presence of an enol was further confirmed by the IR spectrum which showed strong absorption at 3280 and 1604 cm^{-1} for the O-H and C-O stretches respectively. The loss of the diazo signal at 2101 cm^{-1} confirms decomposition of the diazoketone groups of **156**. Finally, the ^{13}C NMR spectrum showed the carbonyl signal of the starting material had been lost with the signals at 153.0 and 105.1 ppm assigned to the C-O and C-H enol positions respectively. The spectral data supports the assignment of the product as the coronene derivative **159** as a single major product in addition to trace amounts of a complex mixture.

The observed reactivity of a ketocarbene intermediate generated from a diazoketone such as **156** may be rationalised using the HSAB concept. The singlet carbene is a highly reactive Lewis acid since it has an incomplete valence shell of 6 electrons with an unoccupied *p* orbital. Furthermore, the singlet carbene may be classified as a soft Lewis acid since it has no formal charge with the unshared pair of electrons occupying an sp^2 orbital. In addition, the Lewis acidity of the carbene is increased by the presence of an electron withdrawing carbonyl substituent. As a soft Lewis acid, the keto carbene will preferentially react with a soft Lewis base. The π electrons of an aromatic ring may be considered as a soft Lewis base since they are highly

polarisable due to delocalisation. The presence of an electron withdrawing substituent on the aromatic ring has the effect of reducing basicity and increasing hardness of the aromatic π electrons. Therefore, an electron deficient aromatic ring is less reactive towards the Büchner reaction. In this case, the aryl C-H bond may have greater reactivity as a Lewis base leading to the C-H insertion product. The triphenylene diazoketone **156** has strongly electron withdrawing aryl carbonyl groups which may explain the observed selectivity for C-H insertion over the desired Büchner reaction. This is supported by previously reported results where electron deficient arenes were shown to give a lower yield of Büchner ring expansion product with preference to the C-H insertion reaction.[86,87]



Scheme 2.20: Synthesis of **159** with assigned ^{1}H NMR signals (ppm).

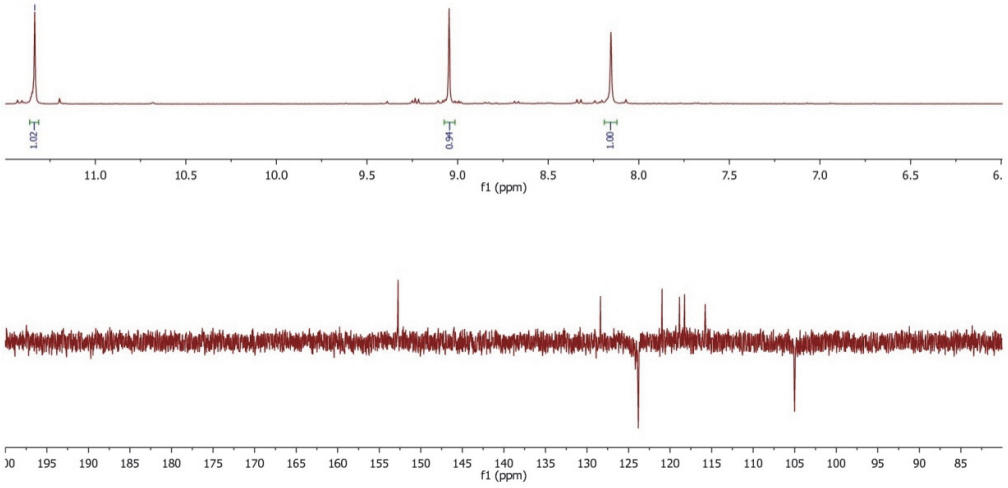
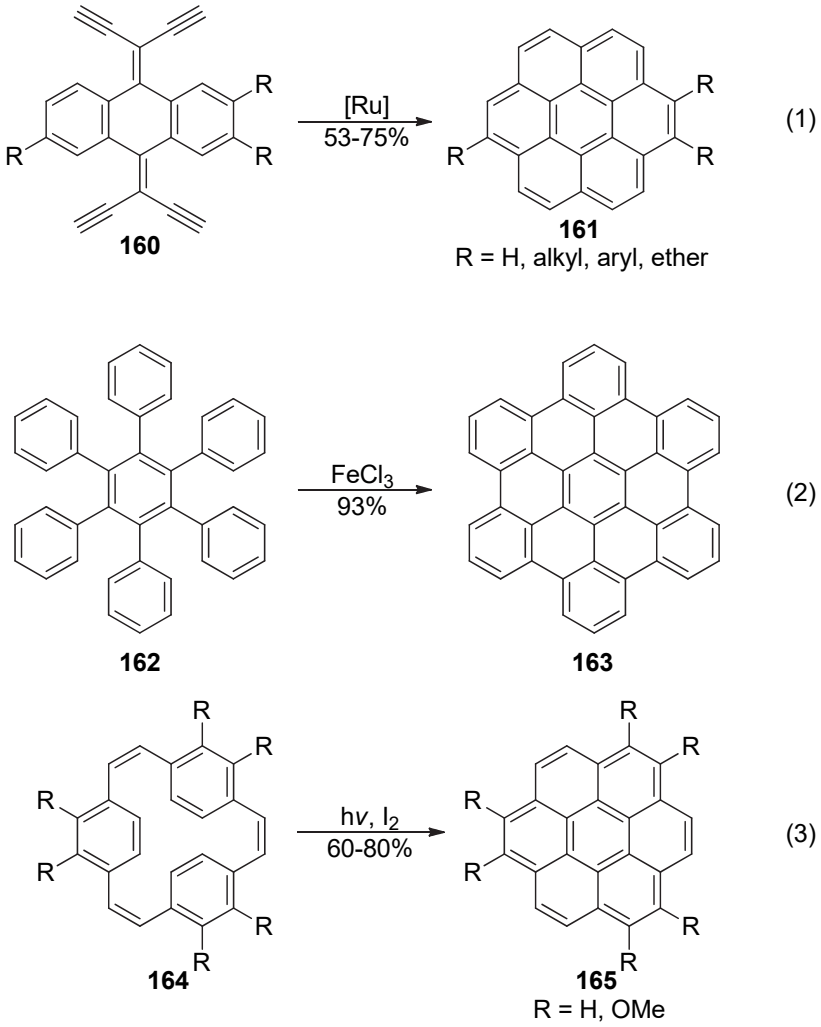


Figure 2.01: ^{1}H NMR and DEPT ^{13}C NMR spectra for **159**.

The synthesis of coronene through intramolecular C-H insertion has not previously been reported in the literature. This method could be applied to the synthesis of coronene derivatives with substitution patterns and functional groups that are not accessible through known methods. Some representative methods for the synthesis of coronene are shown below (Scheme 2.22). There has been one reported synthesis of coronene through a metal carbene intermediate (reaction 1) however this does not proceed through a C-H insertion mechanism. Most reported syntheses of coronene rely on a late stage dehydrogenative cyclisation to form the coronene ring system. This usually requires high temperature under oxidative reaction conditions which results in low yield and poor functional group tolerance. The ring closing reaction using the triphenylene diazoketone **156** was performed under mild conditions which would allow a range of functional groups to be tolerated.



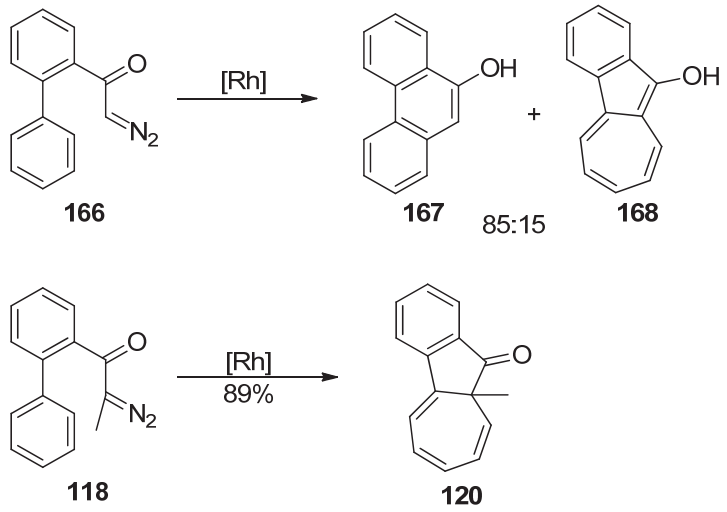
Scheme 2.21: Reported syntheses of coronene derivatives.[27,88,89]

There have been a limited range of coronene derivatives reported despite increased interest in coronene as an example of the smallest unit of graphene.[90] The limiting factor for the synthesis of coronene derivatives is the absence of a general methodology with good yields and functional group tolerance. The synthesis of coronene by intramolecular C-H insertion could provide access to a range of coronene derivatives by using differently substituted triphenylene starting materials.

2.5 Diazoketone derivatives

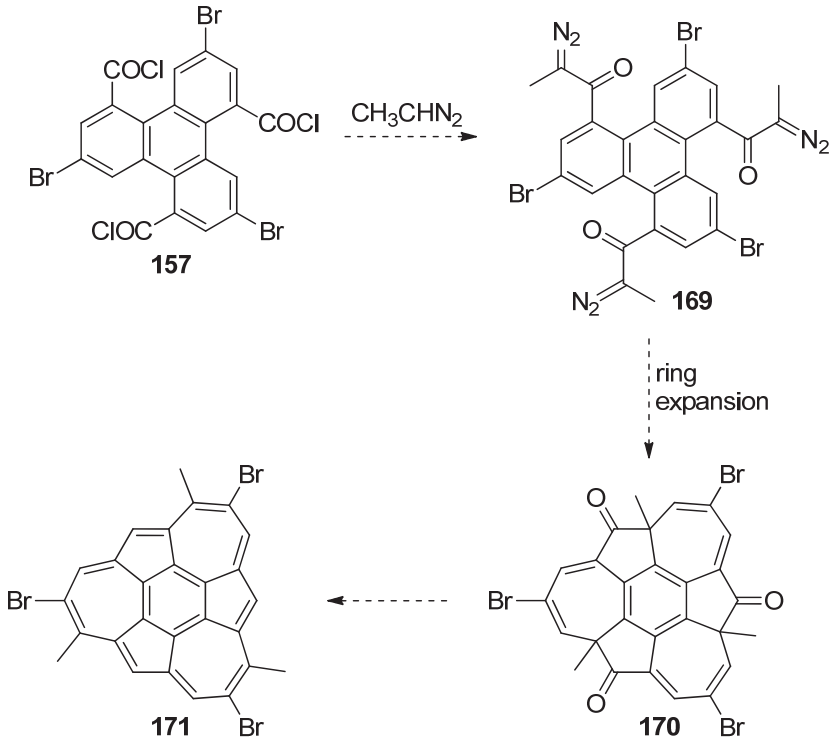
The outcome of the intramolecular Büchner reaction is known to be influenced by substitution at the diazo position of the substrate.[57] The influence of diazo

substitution was demonstrated in the reaction of the biaryl diazoketones **166** and **118** (Scheme 2.22). The unsubstituted diazoketone **166** gave phenanthrene **167** as the main product presumably through a CH insertion reaction. In contrast, the methyl substituted diazoketone **118** gave the ring expansion product **120** in high yield as the sole isolable product.



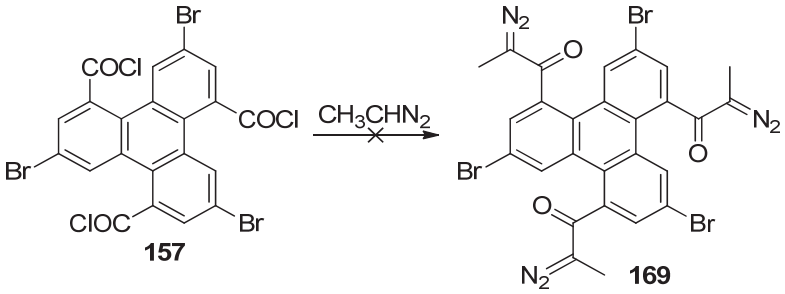
Scheme 2.22: Reactivity of diazoketones.

The methyl substituted diazoketone **169** may favour the desired Büchner ring expansion over the C-H insertion reaction to yield intermediate **170**. From the ring expansion product, a methyl group shift would give the substituted isocoronene **171**. The methyl diazoketone **169** could be synthesised using the same procedure as for diazoketone **156** by substituting diazomethane with diazoethane.



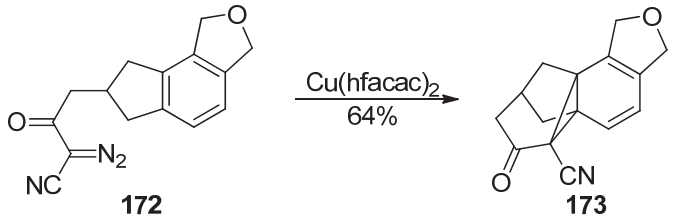
Scheme 2.23: Proposed synthesis of **171**.

The methyl diazoketone **169** may be prepared by reaction of the acid chloride **157** with diazoethane. The triphenylene acid chloride **157** was added to a solution of diazoethane with CaO as an acid scavenger. Following workup a yellow oil was obtained with analysis of the ^{1}H NMR spectrum showing a complex mixture of products. The mixture could not be separated using column chromatography. The formation of a complex mixture of products could be attributed to impurities present in the diazoethane solution. The diazoethane could not be purified or characterised due to low stability and so alternative derivatives were investigated.



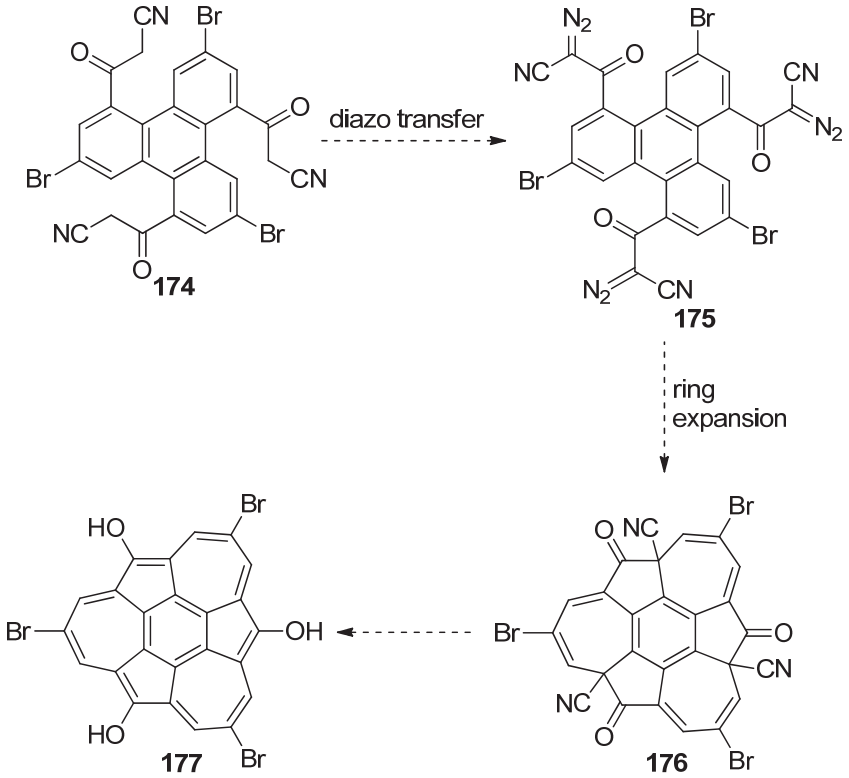
Scheme 2.24: Attempted synthesis of **169**.

An alternative functional group for the Büchner ring expansion reaction is the diazo-ketonitrile. This functional group has the diazo position substituted with a nitrile and has previously been shown to favour intramolecular ring expansion over CH insertion in the synthesis of **173**.[91]



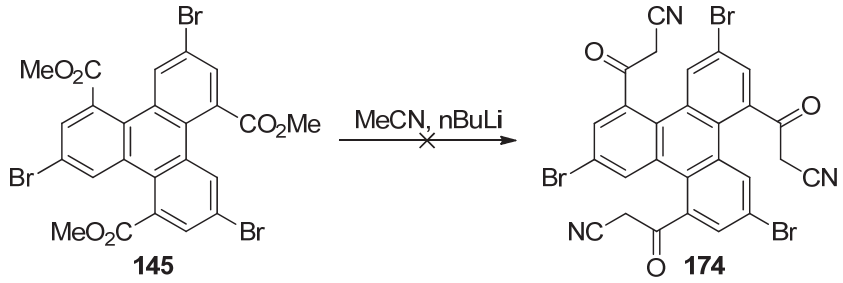
Scheme 2.25: Synthesis of **173**.

The diazo-ketonitrile **175** could be synthesised from ketonitrile **174** through a diazo transfer reaction. The intramolecular ring expansion of diazo-ketonitrile **175** would then yield intermediate **176**. Hydrolysis of the nitrile groups followed by decarboxylation would then yield isocoronene **177**.



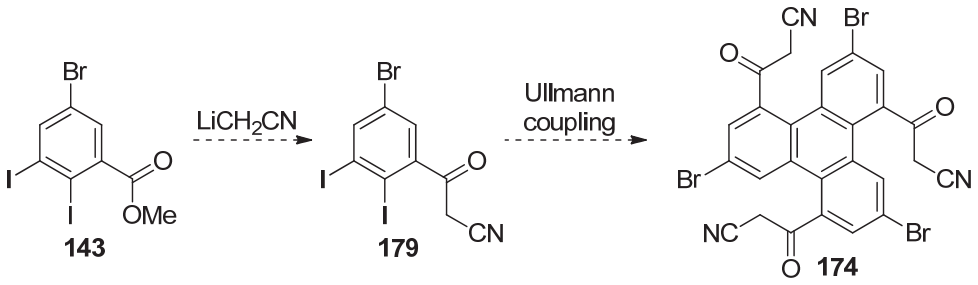
Scheme 2.26: Proposed synthesis of **177**.

The most direct approach to the synthesis of a ketonitrile is the Claisen condensation of an ester with lithiated acetonitrile. Addition of the triphenylene ester **145** to a solution of lithiated acetonitrile resulted in an immediate colour change from colourless to dark red. A pale yellow oil was then obtained after workup. The ^{1}H NMR spectrum showed a complex mixture of products. Two singlets near 4 ppm were assigned to unreacted methyl ester groups indicating incomplete reaction. A large excess of lithiated acetonitrile was used with warming of the reaction mixture to 0 °C however the methyl ester signals were still observed. The incomplete reactivity of **145** towards lithiated acetonitrile could be due to a deactivation of the intermediates after the initial Claisen condensation. Alternative methods for ketonitrile synthesis were subsequently explored.



Scheme 2.27: Attempted synthesis of **174**.

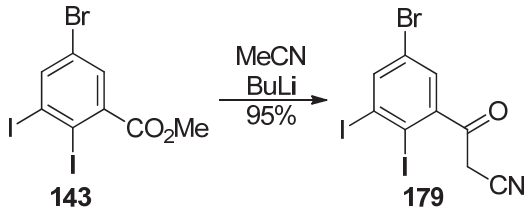
An alternative approach to triphenylene ketonitrile **174** is through the Ullmann cyclotrimerisation of **179**. The ketonitrile **179** may be synthesised by Claisen condensation of **143** with lithiated acetonitrile.



Scheme 2.28: Proposed synthesis of **174**.

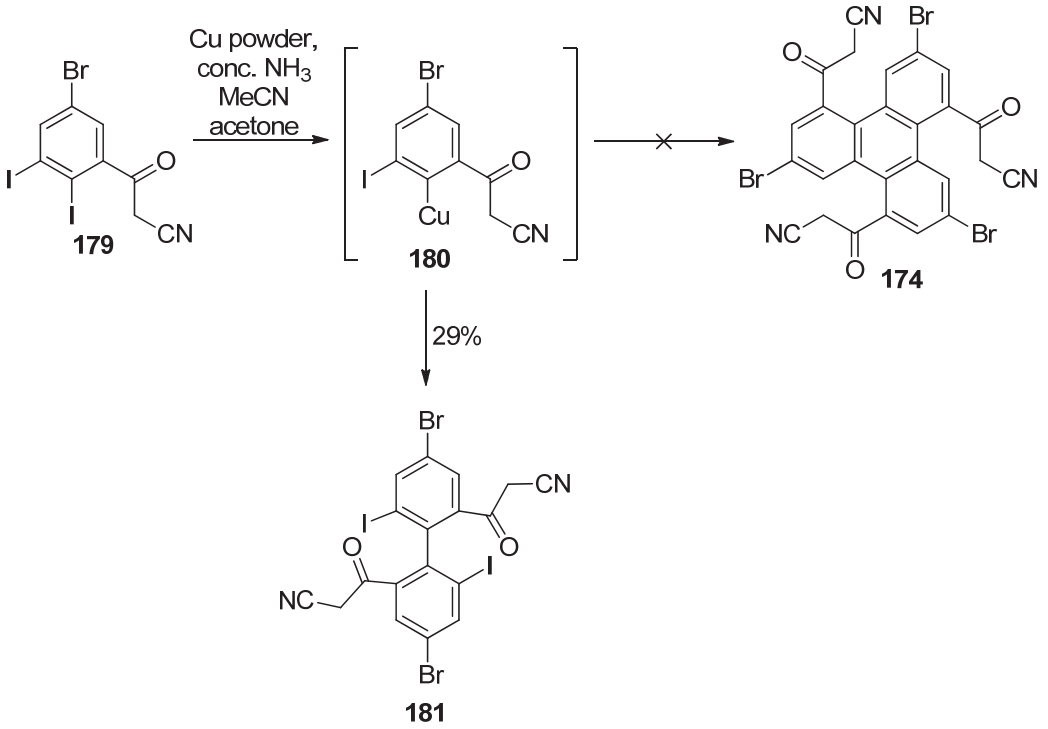
The previously prepared diiodide ester **143** was subject to Claisen condensation with lithiated acetonitrile. Addition of the diiodide ester **143** to a solution of lithiated acetonitrile followed by workup gave a single product in high yield. The ^{1}H NMR

spectrum showed a pair of aromatic doublets and a singlet at 3.99 ppm with integration of 1:1:2 respectively. The singlet at 3.99 ppm has a similar chemical shift to the starting material however the integration has changed to two protons which is consistent with the ketonitrile methylene position of **179**. The ^{13}C NMR spectrum showed a shift of the carbonyl to 193.4 ppm which is typical of a ketone. An additional signal appeared at 113.5 ppm which was assigned to the nitrile.



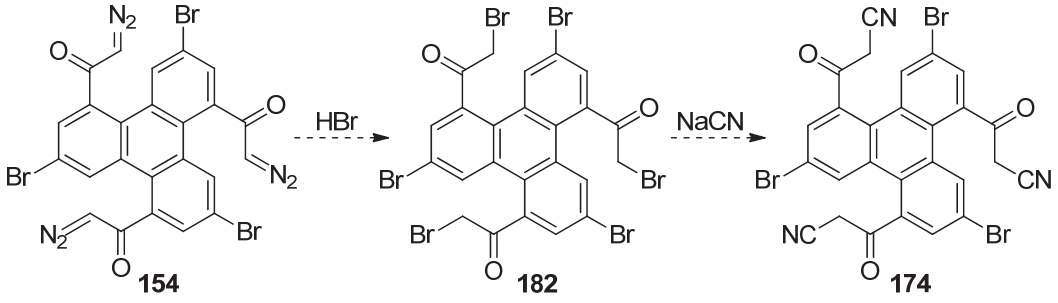
Scheme 2.29: Synthesis of **179**.

The Ullmann coupling cyclotrimerisation of ketonitrile diiodide **179** would lead to the desired triphenylene ketonitrile **174**. Subjecting the diiodide **179** to the previously optimised coupling conditions gave a single major product. The ^{1}H NMR spectrum showed two aromatic doublets and a pair of closely spaced singlets at 4.02 ppm with equivalent integration of each signal. The number of signals and integration indicates the isolated product may be a biphenyl dimer. The ^{13}C-NMR spectrum showed six aromatic signals which is consistent with the symmetrical biphenyl dimer **181**. The splitting of the α-carbonyl signals was attributed to restricted rotation of the biphenyl linking bond The symmetrical biphenyl dimer may be formed through the homocoupling of the activated iodide positions of **179** *ortho* to the aryl carbonyl group. This is in contrast to the reactivity of the diiodide **143** which gave the cyclotrimerisation product with no biphenyl isolated. This difference in reactivity must be attributed to the ketonitrile substituent. Since the ketonitrile group was incompatible with the cyclotrimerisation reaction it would have to be introduced via the triphenylene ester **145**.



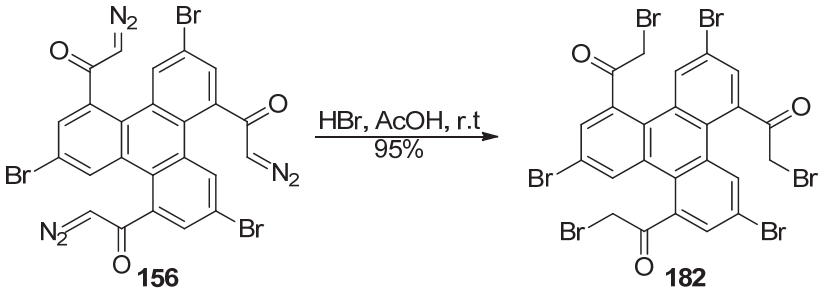
Scheme 2.30: Attempted synthesis of **174**.

An alternative method for the synthesis of the ketonitrile functional group is the nucleophilic substitution reaction of a bromomethyl ketone with cyanide. The bromomethyl ketone **182** may be synthesised from the previously prepared diazoketone **154** by reaction with hydrobromic acid.



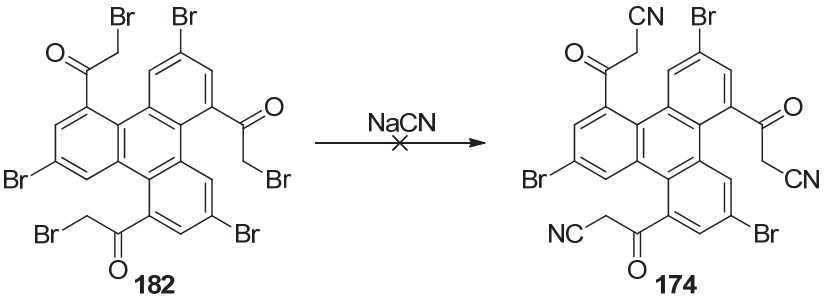
Scheme 2.31: Proposed synthesis of **174**.

Addition of HBr to a solution of the diazoketone **154** in AcOH resulted in visible gas evolution. Following workup, a single product was isolated in high yield. The ^{1}H NMR spectrum showed the loss of the diazo signal at 5.42 ppm with a new signal appearing at 4.17 ppm attributed to the bromomethyl ketone substituent. The aromatic signals and ^{13}C NMR spectrum were consistent with the desired product.



Scheme 2.32: Synthesis of **182**.

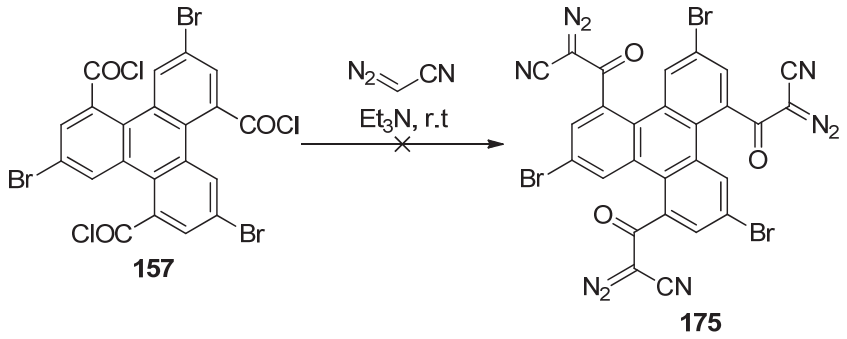
Nucleophilic substitution of bromide with cyanide would then lead to the desired triphenylene ketonitrile **174**. Sodium cyanide was added to a solution of bromomethyl ketone **182** in DMF which resulted in an intense colour change to dark purple followed by red and then black. Aqueous workup of the reaction mixture gave insoluble black material with no organic soluble material isolated. This indicated rapid decomposition under the reaction conditions. The decomposition could be due to the basicity of the cyanide anion which would promote aldol polymerisation of the ketonitrile product. The reaction was repeated at reduced temperature and different solvents however decomposition occurred in each case.



Scheme 2.33: Attempted synthesis of **174**.

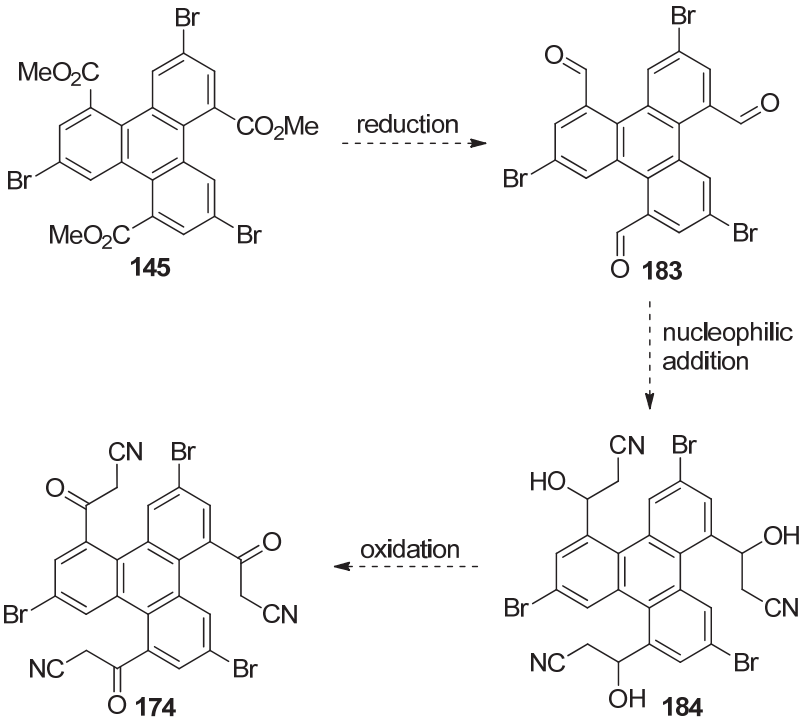
A series of aryl and alky diazoketonitriles have previously been prepared by the acylation of diazoacetonitrile with acyl chlorides.[92] This method could be used in the synthesis of the desired diazoketonitrile intermediate **175**. Diazoacetonitrile was prepared by diazotisation of aminoacetonitrile following a literature method.[93] The triphenylene acyl chloride **157** was added to a solution of diazoacetonitrile and triethylamine. After workup of the reaction mixture a yellow residue was obtained. The ^{1}H NMR spectrum showed a complex mixture of products that could not be

isolated using column chromatography. The formation of the desired diazoketonitrile may have been unsuccessful due to impurities present in the diazoacetonitrile solution. The reagent could not be purified or characterised due to the low stability. Following this result an alternative synthesis was pursued.



Scheme 2.34: Attempted synthesis of **175**.

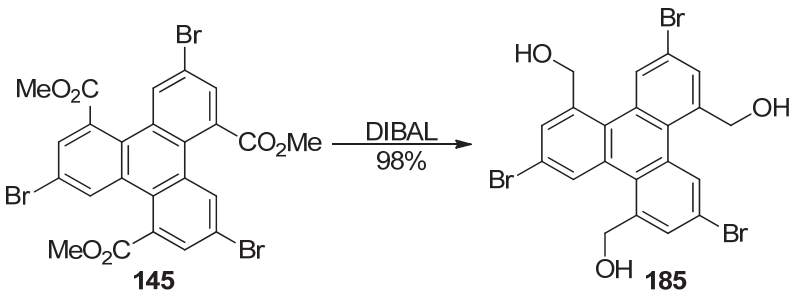
An alternative route to the ketonitrile intermediate **174** is through the oxidation of β-hydroxynitrile **184**. The oxidation could be carried out under mildly acidic conditions which would avoid base catalysed decomposition of the ketonitrile. The hydroxy nitrile could be synthesised by nucleophilic addition of lithiated acetonitrile to the aldehyde **183**. The aldehyde could be prepared by reduction of the previously synthesised ester **145**.



Scheme 2.35: Proposed synthesis of **174**.

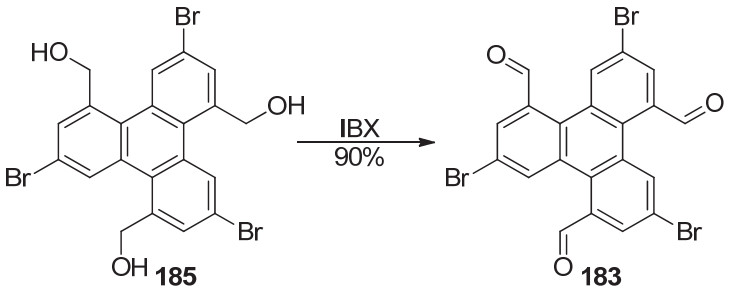
Conversion of the ester to an aldehyde may be achieved by selective reduction using DIBAL however in practice the over reduction to an alcohol often leads to poor yield. The aldehyde **183** could be prepared more easily by reduction of the ester to the alcohol **185** followed by selective oxidation. The ester was added to a suspension of lithium aluminium hydride in THF. After workup, analysis of the ^{1}H NMR spectrum showed several aromatic signals indicating a mixture of products had formed. The signal attributed to the methyl ester of the starting material had been lost which indicates the reduction had occurred. The aromatic region showed several doublets (J = 2.1 Hz) in addition to several apparent triplets (J = 8.2 Hz). The aromatic coupling constants indicate *ortho* coupling was present in some of the reaction products. This was assumed to be the result of partial debromination of the aryl bromide groups. The debromination reaction could be avoided with the use of a more selective reductant such as DIBAL. Addition of excess DIBAL to the triphenylene ester **145** followed by workup gave a single product. The ^{1}H NMR spectrum showed two aromatic doublets (J = 2.1 Hz) in addition to a triplet at 5.96 and a doublet at 4.85 ppm integrating to 1:1:1:2 respectively. This indicated a symmetrical triphenylene with *meta* coupling. The signals at 5.96 and 4.85 ppm were

assigned to the methylene and OH groups respectively. The loss of the carbonyl group was confirmed by the ^{13}C NMR spectrum and the presence of the hydroxy substituent was confirmed by the IR spectrum having a strong absorption at 3282 cm^{-1}.



Scheme 2.36: Synthesis of **185**.

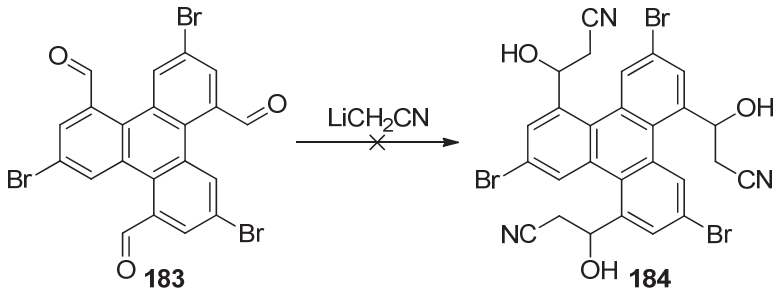
The selective oxidation of a primary alcohol to an aldehyde may be carried out using a number of different oxidants including IBX. Addition of the triphenylene triol **185** to a solution of IBX in DMSO gave a single product after workup. The ^{1}H NMR spectrum showed a singlet at 10.4 ppm and two aromatic doublets with integration of 1:1:1. The signal at 10.4 ppm is characteristic of an aldehyde with the aromatic signals indicating a symmetrical triphenylene. The presence of an aldehyde was confirmed by the ^{13}C NMR spectrum with a CH signal at 189.5 ppm. The product structure was therefore assigned as aldehyde **183**.



Scheme 2.37: Synthesis of **183**.

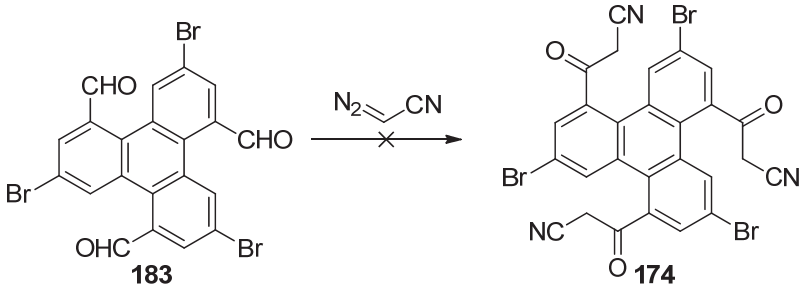
The β-hydroxynitrile could then be synthesised by nucleophilic addition of lithiated acetonitrile to an aldehyde. The triphenylene aldehyde **183** was added to a solution of lithiated acetonitrile followed by acidic workup. The ^{1}H NMR spectrum of the crude product was analysed which showed the starting aldehyde with no other products

observed. This result could be explained by the reversibility of the aldol addition of acetonitrile.[95]



Scheme 2.38: Attempted synthesis of **184**.

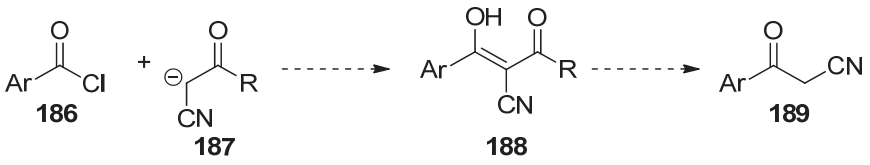
The Roskamp reaction has previously been used to prepare ketonitriles through the reaction of an aldehyde with diazoacetonitrile under mildly acidic conditions.[96] This reaction is irreversible and so avoids any issue with the retro-aldol reaction. Addition of diazoacetonitrile to a mixture of the aldehyde with silver tungstophosphate resulted in gas evolution. After workup, the ^{1}H NMR spectrum of the crude product was analysed which showed unchanged aldehyde **183** with no aromatic products detected. With the aldehyde appearing to be unreactive towards nucleophilic addition, focus was shifted to the more reactive acyl chloride **157**.



Scheme 2.39: Attempted Roskamp reaction of aldehyde **183**.

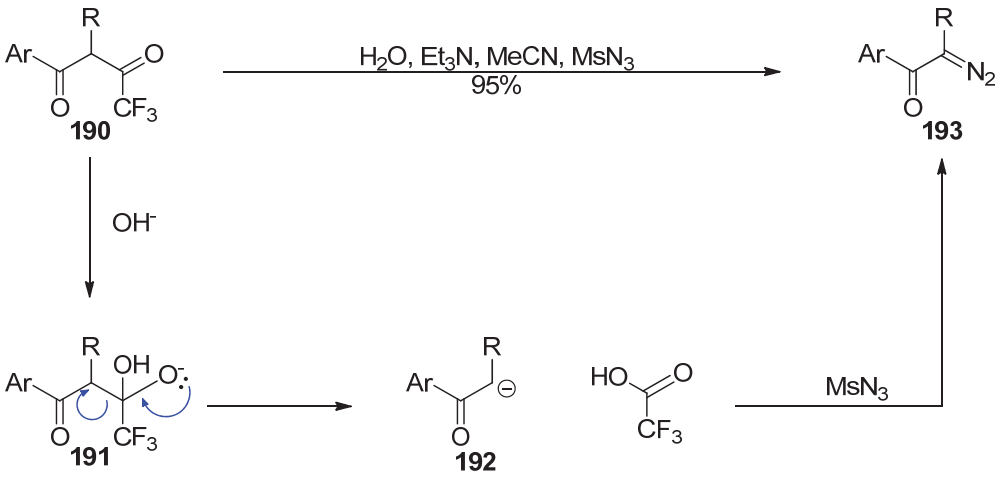
The triphenylene acid chloride was previously shown to be reactive towards diazomethane, a soft carbon nucleophile (Scheme 2.19). The acylated acetonitrile anion **187** could be used as an alternative soft nucleophile which would react with the acid chloride to yield an acylated ketonitrile derivative **188**. The intermediate would favour the enol tautomer which would not undergo decomposition through

self-condensation. The acyl group could then be removed to yield the desired ketonitrile **189**.



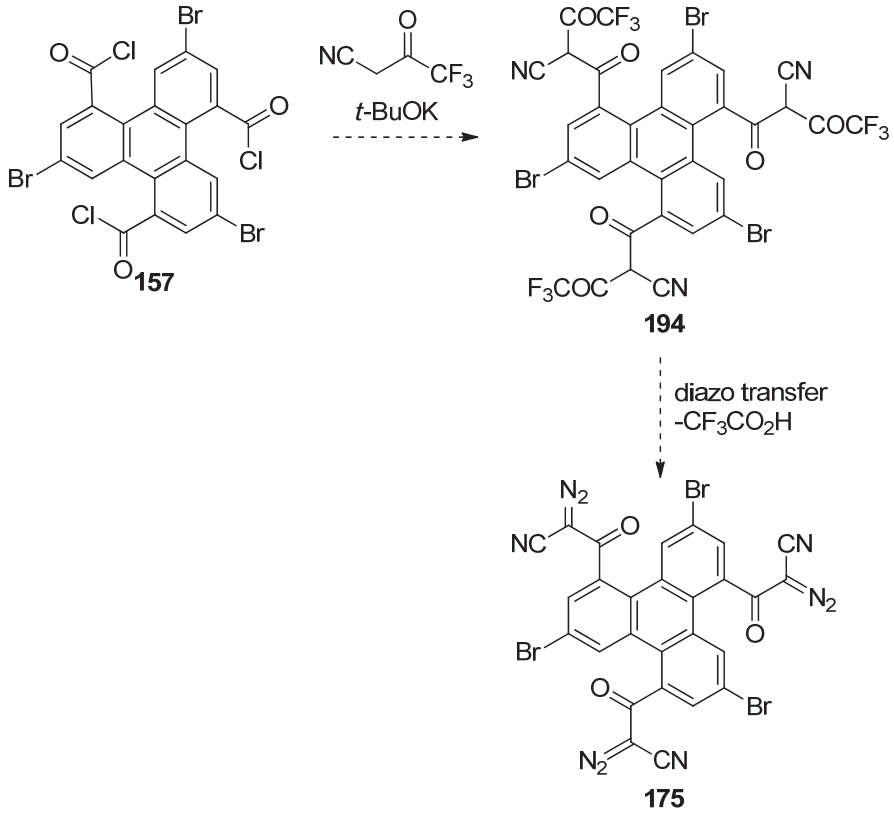
Scheme 2.40: Proposed synthesis of **189**.

The trifluoroacetyl group has previously been used as a labile activating group in the diazo transfer reaction.[97] The trifluoroacetyl group is removed under basic aqueous conditions where the hydrate **191** is formed followed by elimination of trifluoroacetate to generate the enolate **192**. This could be applied to the synthesis of the diazoketonitrile via a trifluoroacetyl derivative.



Scheme 2.41: Synthesis of **193**. [97]

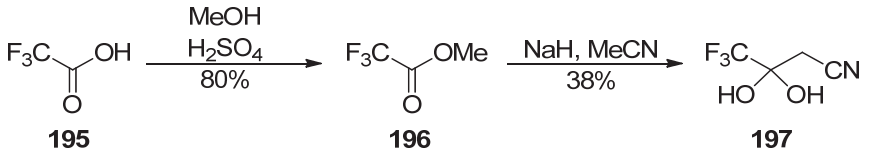
The desired diazoketonitrile **175** could be synthesised from the reaction of trifluoroacetyl acetonitrile with the acyl chloride **157** under basic conditions. Hydrolysis of the trifluoroacyl group followed by introduction of the diazo group would then occur under diazo transfer reaction conditions to yield diazoketonitrile **175**.



Scheme 2.42: Proposed synthesis of **175**.

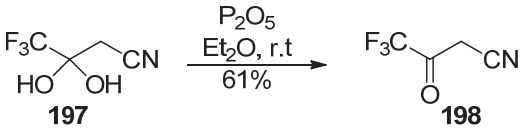
The required trifluoroacetyl acetonitrile has been reported once in the literature prepared by Claisen condensation of acetonitrile with methyl trifluoroacetate.[98] A mixture of acetonitrile, methyl trifluoroacetate and sodium hydride were heated under reflux for 2 hours. After workup the crude product was distilled to yield a colourless oil. Analysis of the ^{1}H NMR spectrum showed a singlet at 2.98 ppm and a broad signal at 7.75 ppm with integration of 1:1. The signal at 2.98 ppm is consistent with the reported data however the signal at 7.75 ppm was not reported. The ^{13}C NMR spectrum showed the absence of the expected carbonyl signal for the desired ketone. The CF_3 group was assigned to 123.1 ppm (J = 289 Hz) on the basis of the C-F coupling magnitude. The α-CF_3 position was identified at 90.7 ppm (J = 32 Hz). The IR spectrum of the product showed a strong O-H absorption with no signal in the carbonyl range. The spectral data indicated the isolated product was the ketone hydrate **197** with the additional ^{1}H NMR signal at 7.75 ppm attributed to the OH groups. This is consistent with the known properties of trifluoromethyl ketones

which have a strong preference for the hydrate due to the electrophilicity of the ketone conferred by the inductive withdrawing effect of the CF_3 group.



Scheme 2.43: Synthesis of **197**.

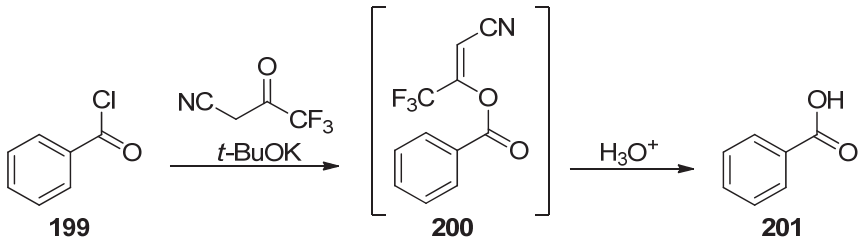
Phosphorous pentoxide has been shown to be effective in the dehydration of trifluoromethylketone hydrate.[99] A solution of the ketone hydrate **197** in Et_2O was vigorously stirred with several portions of P_2O_5 until the indicator showed no further water was removed. The crude product was then distilled to give a pale yellow oil in moderate yield. The ^1H NMR spectrum showed loss of the OH signal from the starting material with one singlet at 3.93 ppm assigned to the methylene group of **198**. The increase in chemical shift of the methylene is consistent with the more strongly electron withdrawing carbonyl group of the desired product. The ^{13}C NMR showed the α-CF_3 carbon to have a chemical shift of 179.6 ppm (J = 39 Hz) which is within the expected range for a ketone.



Scheme 2.44: Synthesis of **198**.

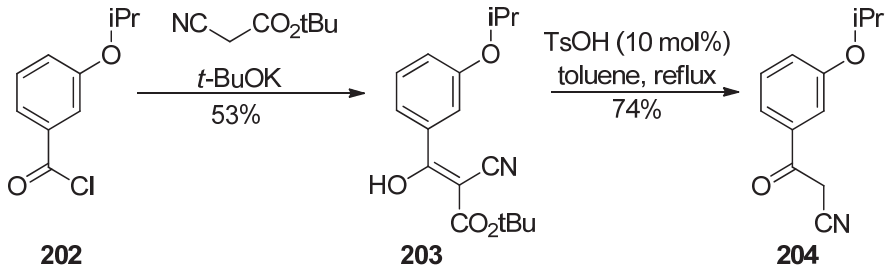
The preparation of the trifluoroacetyl ketonitrile could be achieved by deprotonation of the active methylene of **198** using *t*-BuOK followed by addition of the acyl chloride **157**. Since no literature precedent was available a test reaction was conducted using benzoyl chloride **199**. Trifluoroacetyl acetonitrile was added to a solution of *t*-BuOK and after 30 minutes a solution of benzoyl chloride was added. After 2 hours the reaction was quenched followed by acidic work up to yield a single main product. The analysis of the ^1H NMR and ^{13}C NMR spectra showed the product was benzoic acid **201** with no additional signals that could be attributed to the desired functional group. The formation of benzoic acid could potentially occur through hydrolysis of unreacted benzoyl chloride during workup. This is unlikely as

excess *t*-BuOK would react with benzoyl chloride to form *t*-butyl benzoate which was not observed. After reviewing the literature for trifluoromethyl ketone enolates, it was found that *O*-acylation occurs in preference to the expected *C*-acylation.[100] The resulting enol ester intermediate **200** would be unstable towards hydrolysis during workup resulting in formation of benzoic acid **201**. The unusual reactivity of trifluoroacetyl acetonitrile was attributed to the CF_3 group and so an alternative labile acyl group was investigated.



Scheme 2.45: Reactivity towards test substrate **199**.

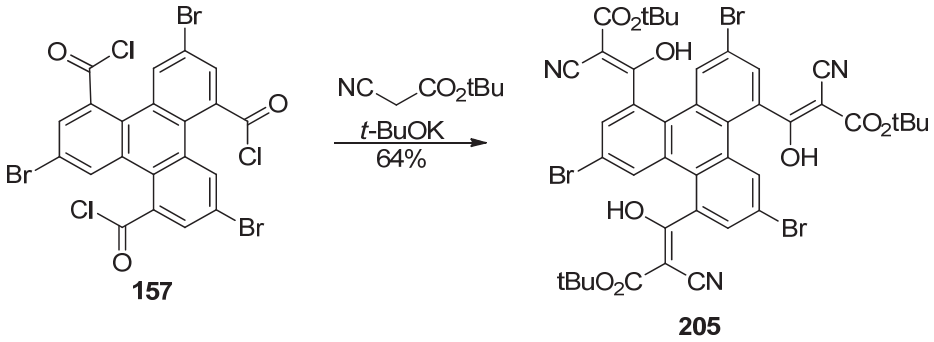
The synthesis of aryl ketonitrile **204** from the acid chloride **202** has previously been reported. [101] The reaction of acid chloride **202** with *t*-butyl cyanoacetate yields the intermediate **203**. The *t*-butylacetate group was then removed by decarboxylation under mild acidic conditions to give the ketonitrile **204** in high yield. This method could be used for the synthesis of the desired ketonitrile **174** from the triphenylene acid chloride **157**.



Scheme 2.46: Synthesis of **204**.

t-Butyl cyanoacetate was added to a solution of *t*-BuOK followed by addition of the acid chloride **157**. The reaction was then quenched and the product isolated. The ^{1}H NMR spectrum showed two aromatic doublets and a singlet at 1.63 ppm with integration of 1:9 respectively. This indicates the product is a symmetrical triphenylene with the signal at 1.63 ppm assigned to the *t*-butyl substituent. The ^{13}C NMR spectrum showed two signals in the carbonyl region at 184.2 and 169.6 ppm

which were attributed to the ester and enol positions respectively. The aromatic region showed seven signals with the signal at 113.9 ppm assigned to the nitrile. Two signals were observed at 86.8 and 84.5 ppm assigned to the quaternary *t*-butyl and the α-enol positions. The structure was confirmed by HRMS which detected a molecular ion at 964.0074 m/z which is in agreement with the calculated value of 964.0002.



Scheme 2.47: Synthesis of **205**.

The triphenylene ketonitrile **174** could be synthesised by decarboxylation of the *t*-butyl ester **205** under thermal conditions. A mixture of **205** in toluene with a catalytic amount of 4-toluenesulfonic acid was heated under reflux. After 18 hours, the product was isolated as a pale yellow solid. The ^{1}H NMR spectrum obtained in DMSO solution showed a complex mixture of products. The signals appeared in three closely spaced groups near 8.8, 8.0 and 5.2 ppm with integration of 1:1:1 respectively. The signal for the *t*-butyl group had disappeared which indicated the decarboxylation was successful. The integration and chemical shift of the signals near 5.2 ppm indicate the presence of an enol. The complexity of the spectrum was attributed to the presence of *E* and *Z* enol isomers. The favoured enol tautomer of the ketonitrile has no intramolecular hydrogen bonding and therefore a mixture of *E* and *Z* configuration are present on the same molecule. The resulting loss of molecular symmetry leads to the complex ^{1}H NMR spectrum observed.

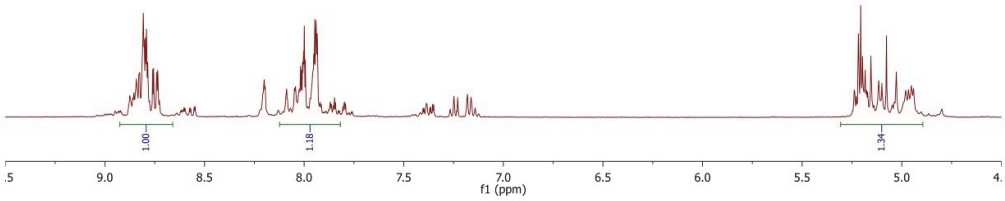


Figure 2.02: ^{1}H NMR spectrum of **174** in d_6-DMSO.

It was possible to obtain a ^{1}H NMR spectrum in $CDCl_3$ although the signal strength was weak due to low solubility. The ^{1}H NMR spectrum in $CDCl_3$ was simplified to a pair of doublets in the aromatic region and a singlet at 3.68 ppm with integration of 1:1:2 respectively. This indicates the molecule is symmetrical which is consistent with the keto form being dominant. This is supported by the loss of the vinyl signal at 5.2 ppm with a new signal at 3.68 ppm assigned to the α-carbonyl position of **174**. The ^{13}C NMR spectrum could not be obtained due to low solubility of **174**.

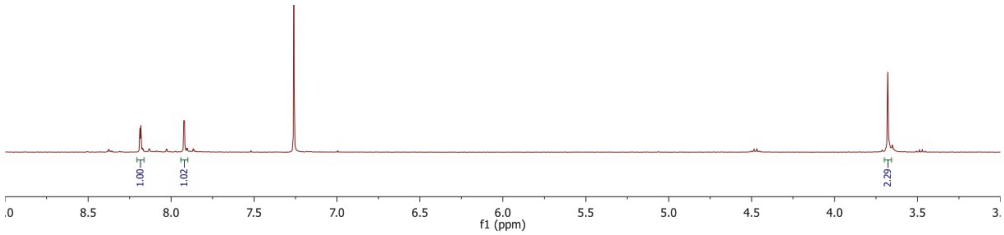
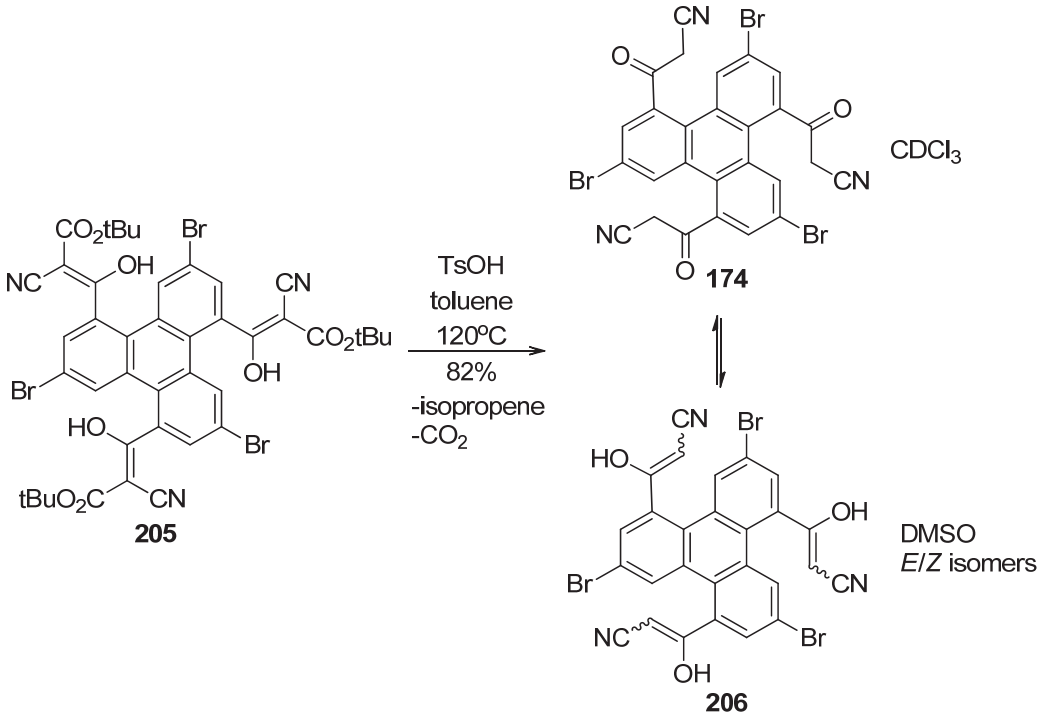


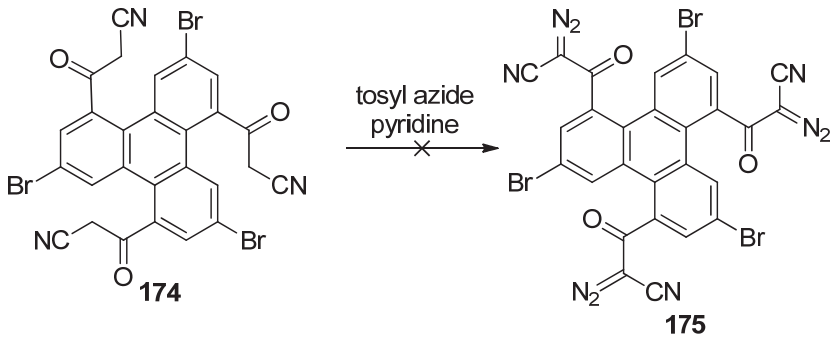
Figure 2.03: ^{1}H NMR spectrum of **174** in $CDCl_3$.

The change in structure of **174** can be rationalised by the effect of solvent polarity on the equilibrium constant of the keto enol tautomerism. $CDCl_3$ is a relatively nonpolar solvent and therefore the keto tautomer is dominant while DMSO is a strongly polar solvent and therefore the enol tautomer is observed. With the desired ketonitrile **174** synthesised, the introduction of the diazo group was investigated.



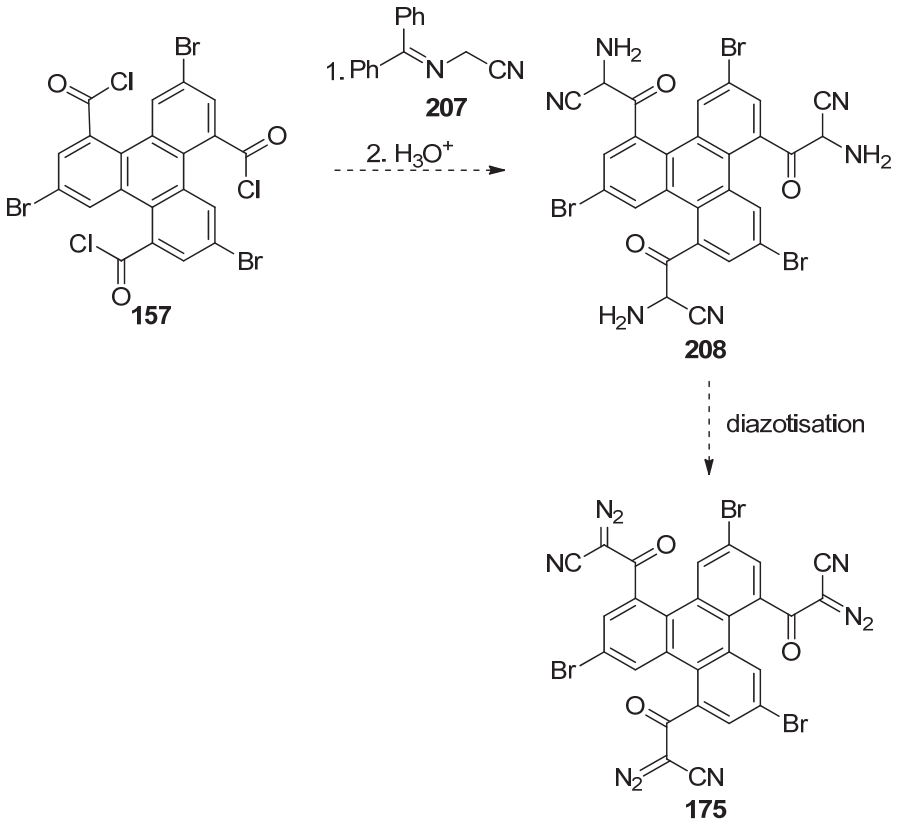
Scheme 2.48: Synthesis and tautomerism of **174**.

The diazo group may be introduced to the activated methylene position of a ketonitrile using a diazo transfer reaction. Standard diazo transfer conditions require a weak organic base to form the enolate which reacts with an electrophilic diazo transfer reagent such a tosyl azide. Addition of pyridine to a solution of tosyl azide and ketonitrile **174** resulted in a colour change from pale yellow to dark red. After removal of the solvent, a dark red residue was obtained. The residue had very low solubility and no product could be isolated from the reaction mixture. The lack of any isolable product could be the result of base catalysed decomposition of the starting material.



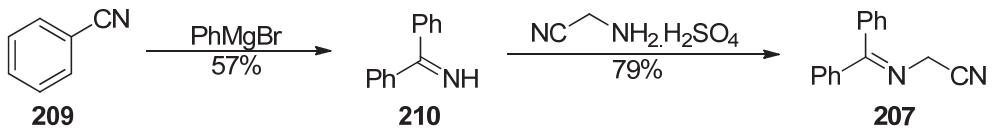
Scheme 2.49: Attempted synthesis of **175**.

An alternative method for the synthesis of a diazoketonitrile involves the diazotisation of an amino ketonitrile.[92] The amino ketonitrile **208** may be prepared by the reaction with an aminoacetonitrile imine **207** derivative followed by acidic workup. The target diazoketonitrile **175** could then be synthesised by diazotisation of **208**.



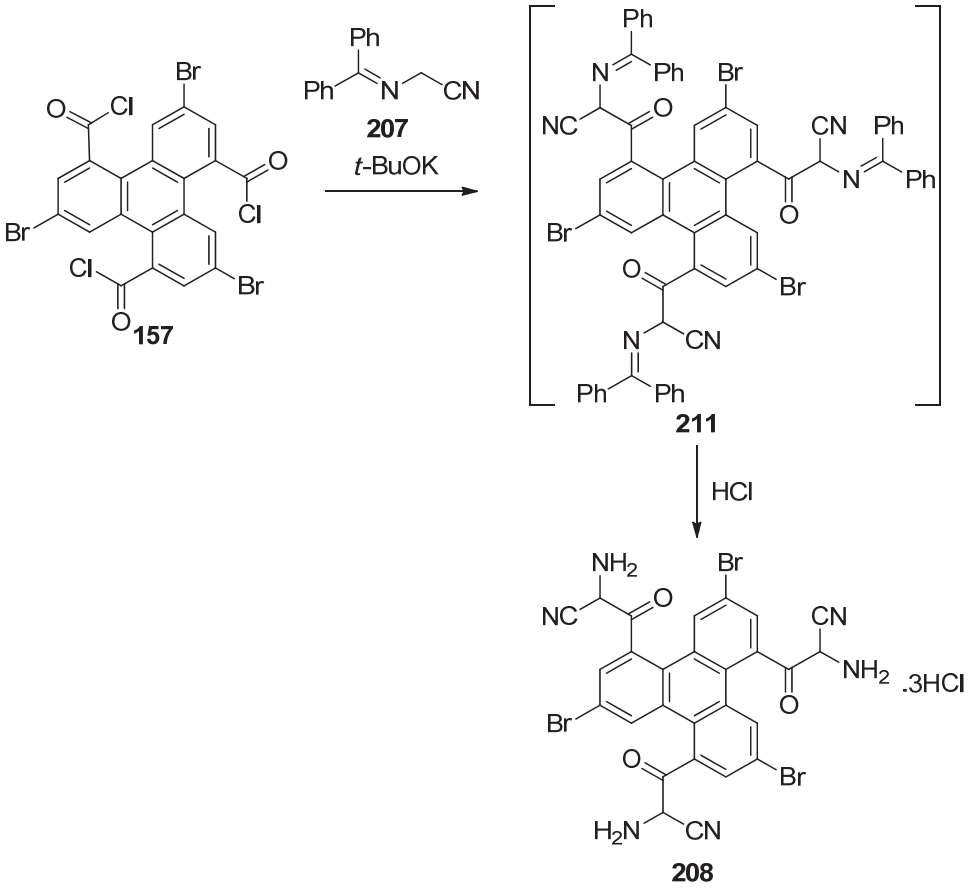
Scheme 2.50: Proposed synthesis of **175**.

The *N*-protected aminoacetonitrile **207** was synthesised according to literature.[102] Diphenylmethylenimine **210** was prepared by addition of phenylmagnesium bromide to benzonitrile. Transamination with aminoacetonitrile gave the aminoacetonitrile imine **207** in good yield with no purification required.



Scheme 2.51: Synthesis of **207**.

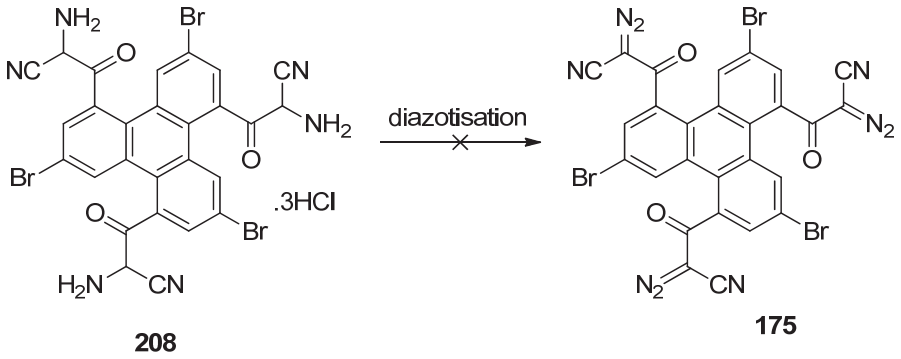
The active methylene of (diphenylmethylene)aminoacetonitrile **207** may be deprotonated with a strong base. The resulting anion can then react with an acyl chloride to yield an α-amino ketonitrile after acidic workup. **207** was added to a solution of *t*-BuOK in THF followed by addition of the triphenylene acyl chloride **157**. The reaction was quenched and the crude product was hydrolysed by addition of aqueous HCl. The aqueous layer was then extracted with ether to remove the benzophenone byproduct. The aqueous layer tested positive using ninhydrin stain which indicated an amine was present. Attempts at neutralising the aqueous layer to isolate the free amine only led to decomposition. It was reasoned that the α-amino ketonitrile **207** was not stable under basic conditions and so an attempt was made to isolate the product as the hydrochloride salt **208**. After acidification and extraction of non-polar byproducts the aqueous layer was concentrated to yield the crude amine hydrochloride in addition to inorganic salt. The organic amine salt was extracted using MeOH, with the inorganic salt removed by filtration. The ^{1}H NMR spectrum of the product in DMSO showed a pair of broad doublets in the aromatic region and a quartet at 3.48 ppm with integration of 1:1:1. The number of aromatic signals indicates the compound is a symmetrical triphenylene with the signal at 3.48 ppm assigned to the α-carbonyl position of **208**. The signal appears as a quartet due to coupling with the $-NH_3^+$ protons. The ^{13}C NMR spectrum showed seven signals in the aromatic region with the signal at 116.6 ppm assigned to the nitrile. The two additional signals appeared at 167.8 and 84.0 ppm which were assigned to the carbonyl and α-carbonyl positions respectively. The IR spectrum showed a strong broad absorption at 2827 cm^{-1} which is typical for an amine salt. The carbonyl absorption appeared at 1707 cm^{-1} however the nitrile signal was not observed. The nitrile signal may not be visible due to overlap from the broad amine signal. With the amino ketonitrile synthesised, diazotisation of the amine would then yield the target diazo ketonitrile.



Scheme 2.52: Synthesis of **208**.

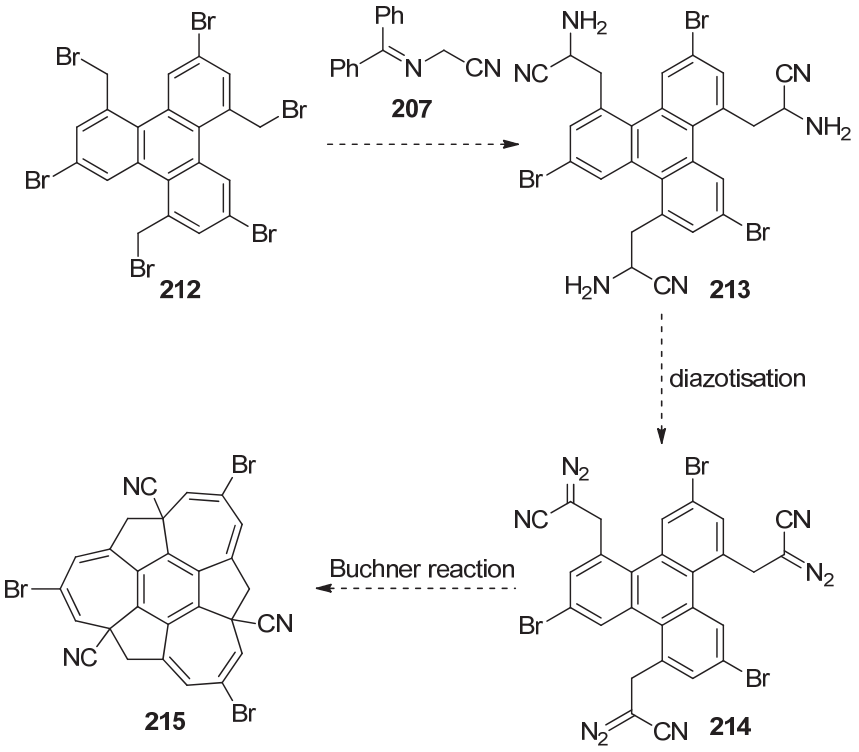
The most commonly used reagent for diazotisation of aminoacetonitrile derivatives is sodium nitrite in aqueous acidic solution.[92] Addition of an acidified solution of sodium nitrite to triphenylene amino ketonitrile **208** gave a rapid colour change from colourless to yellow. This may indicate the formation of the yellow diazo product. After extraction of the reaction mixture with organic solvents the crude product was isolated. Analysis of the ^{1}H NMR spectrum showed numerous signals in the aromatic region which indicated a complex mixture of products. The α-carbonyl signal from the starting material had disappeared and a new signal at 9.50 ppm was observed. The signal at 9.50 ppm indicates the formation of an aldehyde due to hydrolysis of the aminonitrile group. An alternative non-aqueous procedure was then investigated using *t*-butyl nitrite as the diazotisation reagent. Addition of *t*-butyl nitrite to a solution of the amine in acetic acid resulted in a colour change to a yellow solution. After workup, the ^{1}H NMR spectrum of the crude product showed a complex

mixture of products. Following these results further work toward the synthesis of the diazoketonitrile was terminated.



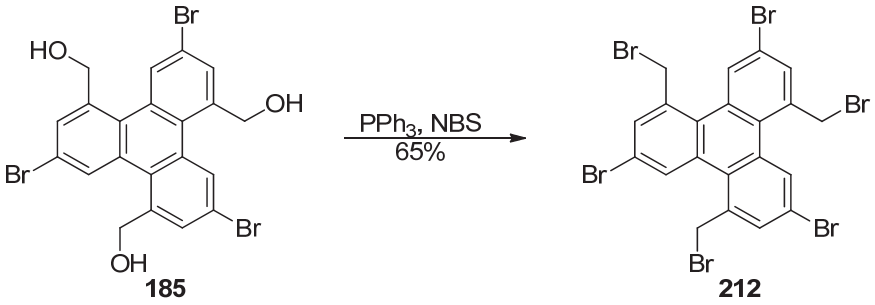
Scheme 2.53: Attempted synthesis of **175**.

An alternative method for introducing the aminoacetonitrile group is through nucleophilic substitution of an alkyl bromide. The reaction of bromide **212** with **207** could yield an alkylated aminoacetonitrile **213** which could be diazotised to yield the diazoacetonitrile derivative **214**. This diazo compound could be subjected to the intramolecular Büchner ring expansion reaction to give intermediate **215**. The aromatic ring system on the diazonitrile **214** would have a much greater electron density than diazoketone **156**. The electron rich triphenylene may favour the desired intramolecular Büchner reaction over C-H insertion.[86,87]



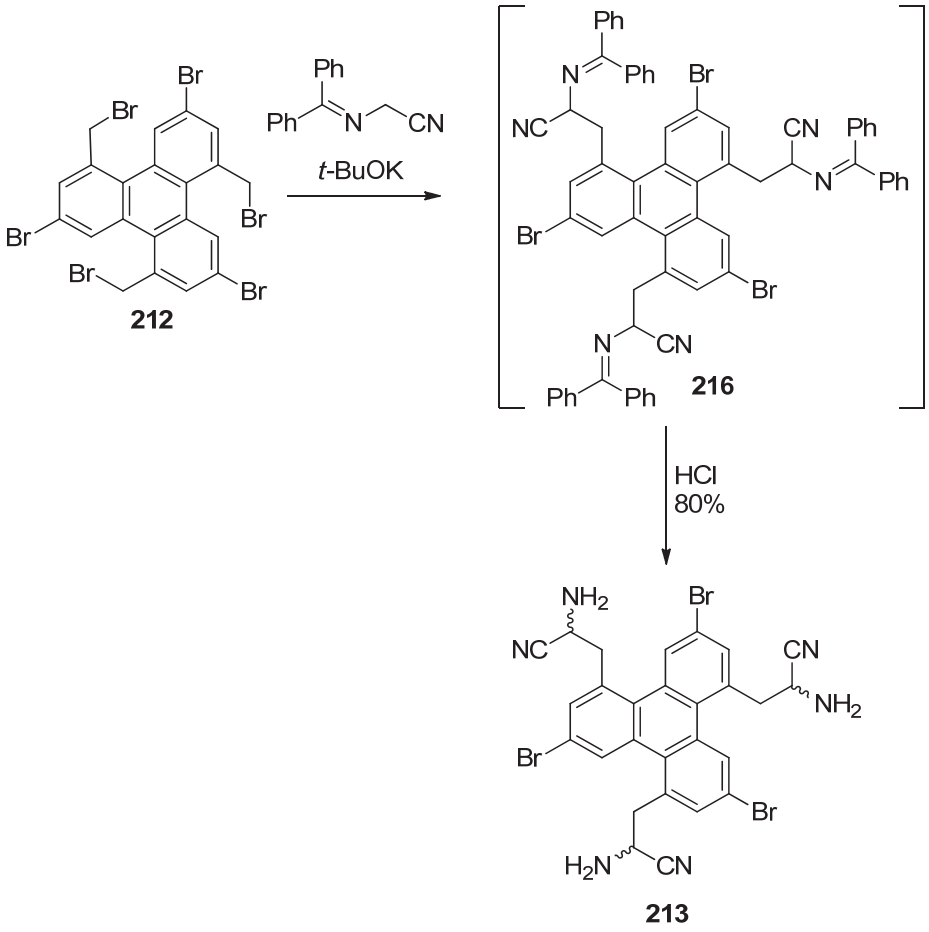
Scheme 2.54: Proposed synthesis of isocoronene ring structure.

The previously prepared triol **185** could be used in the synthesis of bromide **212** through an Appel reaction. NBS was added to a solution of the triol and triphenylphosphine with TLC showing complete conversion of starting material to a single non-polar product. The reaction mixture was filtered through a silica plug and then concentrated to give a white solid in moderate yield. The ^{1}H NMR spectrum showed two aromatic doublets and a singlet at 5.17 ppm with integration of 1:1:2 respectively. The aromatic signals indicate the compound is a symmetrical triphenylene with the signal at 5.17 ppm attributed to the bromomethyl group. The loss of the OH group was confirmed from the IR spectrum which showed no strong absorption around 3000 cm^{-1}. The low yield was attributed to the silica filtration step where some product may be retained as a result of low solubility in the DCM eluent.



Scheme 2.55: Synthesis of **212**.

The nucleophilic substitution of bromide **212** with **207**, followed by acidic workup would provide the aminoacetonitrile derivative **213**. Aminoacetonitrile **207** was added to a solution *t*-BuOK in THF followed by addition of the triphenylene hexabromide **212**. The hexabromide was added as a solid due to the low solubility in THF. After acidic workup, the aqueous solution was neutralised with sodium carbonate then extracted. The organic extract gave a positive test to ninhydrin stain which indicated the presence of an amine. The solvent was removed to give a pale yellow residue in high yield. The ^{1}H NMR spectrum of the product showed two broad aromatic multiplets with two additional broad multiplets at 4.17 and 3.64 ppm with an integration ratio of 1:1:1:2 respectively. The aromatic signals indicate a symmetrical triphenylene structure with the signals 4.17 and 3.64 ppm attributed to the aminoacetonitrile and benzylic position respectively. The broadening and multiplicity of the signals was attributed to overlapping signals from multiple diastereomers due to the formation of three new stereocentres. The presence of multiple stereoisomers is supported by the ^{13}C NMR spectrum which shows closely spaced groups of signals assigned to each of the carbon positions. The ^{13}C NMR spectrum shows 7 groups of signals in the aromatic region with the nitrile assigned to 119.9 ppm. Two signal groups at 44.1 ppm and 40.3 ppm were assigned to the benzylic and α-amino positions respectively. With the structure of the product confirmed, diazotisation of the amine was investigated.



Scheme 2.56: Synthesis of **213**.

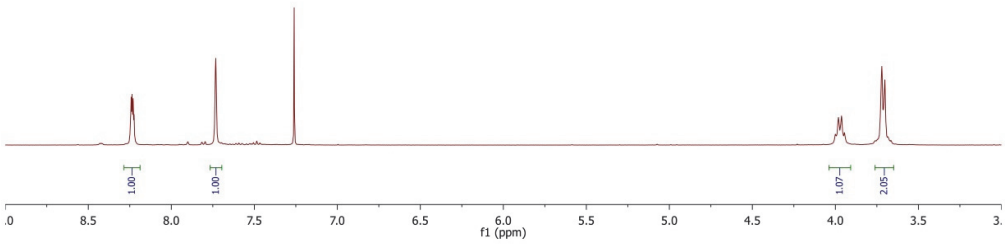


Figure 2.04: ^{1}H NMR spectrum of **213**.

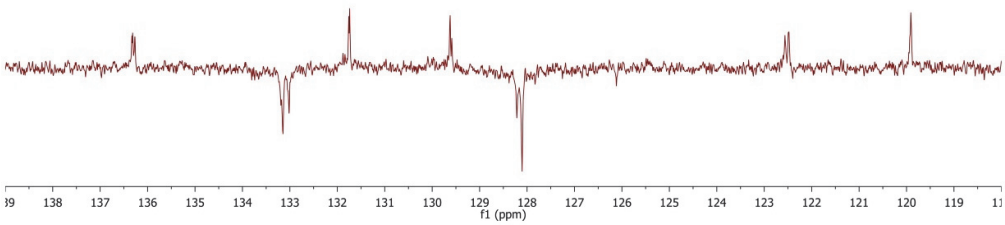
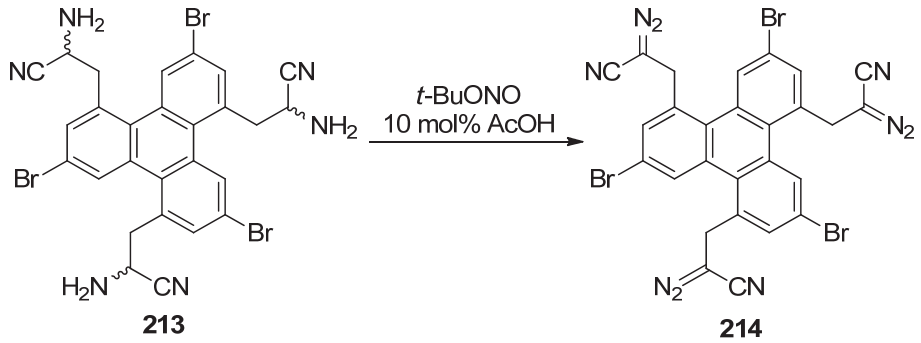


Figure 2.05: DEPT ^{13}C NMR spectrum of **213**.

Diazotisation of aminoacetonitrile has previously been reported in the literature however diazotisation of an alkylated derivative has not been reported.[93] The diazo group of **214** would be partially stabilised by resonance to the nitrile. Therefore **214** would be expected to have similar stability to diazoacetonitrile. Standard diazotisation reactions using sodium nitrite require the use of a strong acid which causes partial decomposition in the preparation of diazoacetonitrile. An alternative diazotisation procedure was investigated using *t*-butyl nitrite in combination with a catalytic amount of weak acid. The use of mild acidic conditions would limit decomposition of the product in the reaction mixture. In addition, the use of *t*-butyl nitrite allows the reaction to be conducted in $CDCl_3$ for the *in situ* analysis of the reaction mixture by ^1H NMR spectroscopy. The triphenylene derivative **213** was dissolved in $CDCl_3$ and *t*-butyl nitrite was added followed by a catalytic amount of acetic acid. After warming the reaction mixture to 50 °C, the ^1H NMR spectrum was recorded. The spectrum showed two aromatic doublets and a singlet at 4.21 ppm with integration ratio of 1:1:2 respectively. The aromatic signals were resolved to a pair of doublets which indicates loss of the stereocentres from the starting material. This is consistent with the conversion of the chiral α-amino positions to the sp^2 diazo group of **214**. The signal at 4.21 ppm was attributed to the benzylic position with the increased chemical shift due to the adjacent diazo group. Attempts at isolating the product were not successful leading only to decomposition. The low stability of the diazonitrile limits its synthetic utility and so the synthesis was not carried forward.



Scheme 2.57: Synthesis of **214**.

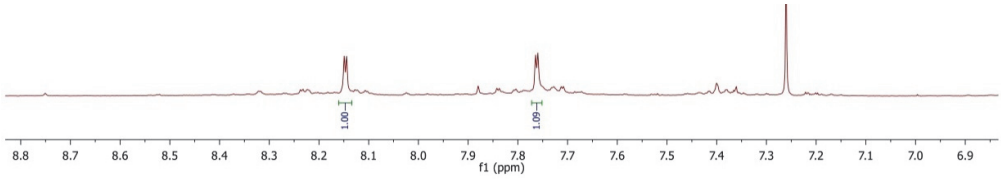
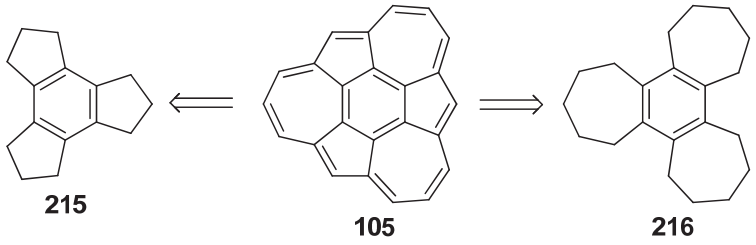


Figure 2.06: ^1H NMR spectrum of reaction mixture containing **214**.

Chapter 3

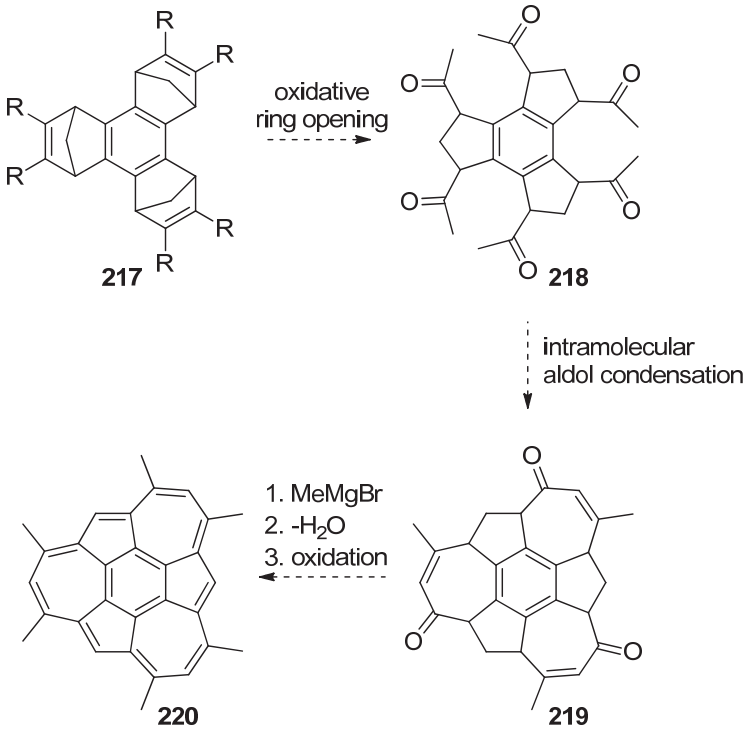
Norbornadiene trimer approach

Following the unsuccessful Buchner ring expansion, alternative approach towards isocoronene was investigated. The trisannulated benzene structures **215** or **216** were considered as intermediates since both structures possess the required central benzene ring and three of the outer rings of the isocoronene ring system. Either intermediate **215** or **216** could lead to the complete isocoronene framework through linking of the adjacent benzylic positions with the appropriate length carbon chain. The ring structure of trindane **215** was chosen since it is prepared in fewer synthetic steps than the triscycloheptenobenzene analogue **216**.[103,104]



Scheme 3.01: Retrosynthesis of isocoronene.

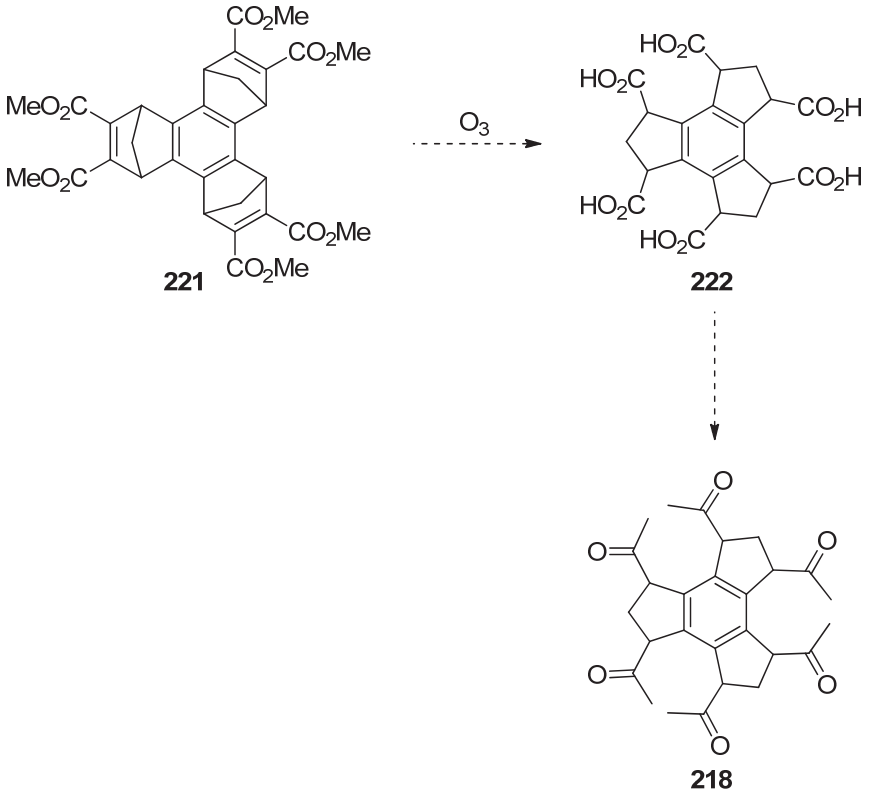
The most direct route for the introduction of linking groups to trindane **215** would involve the alkylation of all six benzylic positions. This approach was not investigated due to potential issues with regioselectivity in C-H activation reactions. An efficient and selective approach to trindane derivatives involves the oxidative ring opening of a norbornadiene cyclotrimer **217**. The oxidative cleavage of the three alkene positions of **217** would yield a trindane derivative with acyl substitution at each of the benzylic positions. The acetyl substituted trindane **218** (R = Me) was chosen as a target intermediate since the acetyl substituents could form the three carbon linking chain through an intramolecular aldol condensation. The intramolecular aldol condensation of **218** would yield **219** as a mixture of two possible regioisomers. The symmetrical isocoronene derivative **220** could then be synthesised through further functional group transformations.



Scheme 3.02: Proposed synthesis of isocoronene **220**.

3.1 Hexabromotrindane

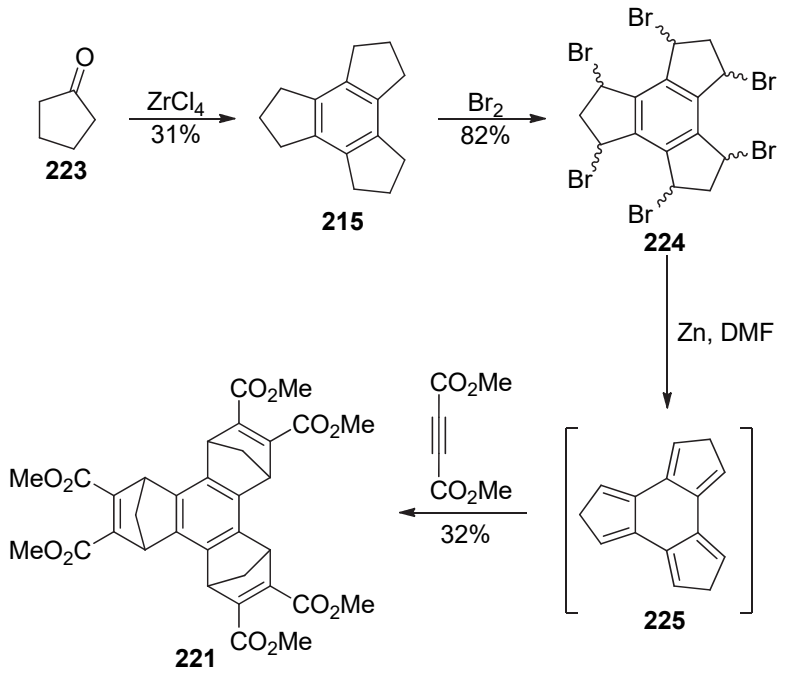
The norbornadiene trimer **221** has previously been reported by Wei *et al.*[104] Ozonolysis of **221** would result in alkene cleavage and oxidative decarboxylation to yield the trindane hexacarboxylic acid **222**. The carboxylic acid groups could then be converted to acetyl groups to yield the target intermediate **218**.



Scheme 3.03: Proposed synthesis of intermediate **218**.

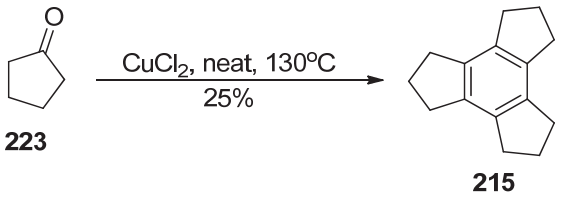
The synthesis of norbornadiene trimer **221** was reported in three steps from cyclopentanone **223** (Scheme 3.04).[104] In the first step, the acid catalysed cyclotrimerisation of cyclopentanone yields trindane **215** in low yield. Radical bromination of trindane then yields the hexabromide **224** as a mixture of stereoisomers. The norbornadiene trimer was then synthesised by reductive dehalogenation of the hexabromide **224** to yield the *o*-quinodimethane intermediate **225**. The quinodimethane undergoes three successive Diels-Alder reactions with dimethyl acetylenedicarboxylate (DMAD) as the dienophile to yield the norbornadiene trimer **221**. The authors propose **225** is formed as an intermediate however this is unlikely due to the highly reactive nature of the quinodimethane. A more plausible reaction pathway would involve stepwise reduction followed by reaction with DMAD. Quinodimethanes are a highly reactive class of dienes due to the driving force of aromatisation of the product.[105] Due to the instability of the quinodimethane **225** the reductive debromination is conducted in the presence of the dienophile without isolation of the intermediate. In addition, a large excess of

DMAD was used to favour the Diels-Alder reaction over other possible reaction pathways.



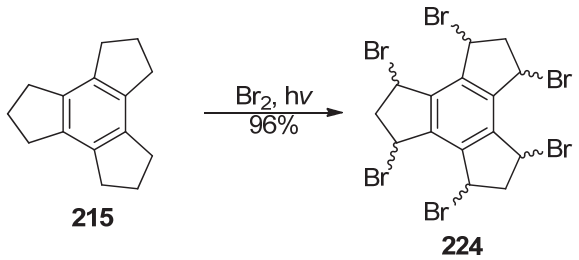
Scheme 3.04: Literature synthesis of trimer **221**.[104]

Trindane **215** may be synthesised from the cyclotrimerisation of cyclopentanone with the use of a Lewis or Brønsted acid catalyst. The reaction proceeds with three successive aldol condensation reactions followed by a final cyclisation.[106] This reaction has been reported using a range of acid catalysts however yields of reactions dropped significantly when scaled up.[107,108,109,110] Anhydrous $CuCl_2$ was chosen as the reaction catalyst since it is easily handled and inexpensive.[110] A mixture of anhydrous copper(II) chloride and neat cyclopentanone was heated under reflux for 18 hours. The organic material was separated and the non-polar material was isolated by silica gel filtration to yield a single compound in low yield. The ^{1}H NMR spectrum showed a triplet at 2.84 ppm assigned to the benzylic positions and a pentet at 2.13 ppm. This was in agreement with the reported literature data.[110] The reaction was scaled up to to provide 8 g batches of trindane in 25% yield. The low yield of trindane was acceptable due to the inexpensive starting materials and simple purification procedure.



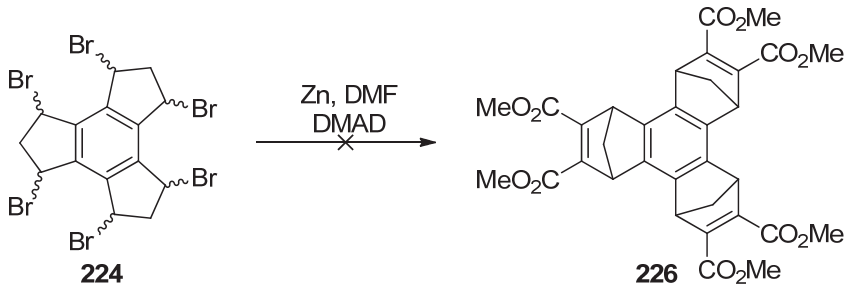
Scheme 3.05: Synthesis of trindane.

The hexabromide **224** may be prepared by radical bromination of trindane **215**.[111] A solution of **215** in chloroform was cooled on ice and bromine was added slowly over 3 hours with the reaction mixture irradiated using a 500 W tungsten halogen lamp. After addition was complete, the reaction mixture was warmed to room temperature. After a further 3 hours, the reaction mixture was worked up and the crude product was isolated as a light brown solid foam. The ^{1}H NMR spectrum was complex consisting of numerous overlapping signals. The signals primarily appeared as two broad groups in the region of 3-4 ppm and 5-6 ppm. The complexity of the ^{1}H NMR spectrum is consistent with the formation of six new asymmetric centres. The loss of signals near 2 ppm is consistent with bromination of the benzylic positions of trindane. Detailed analysis was not possible due to the complexity of the spectrum. The ^{1}H NMR data for the hexabromide **224** has been reported with two groups of signals at 5.47-5.97 and 2.92-3.38 ppm with integration of 5.77 and 6.23 respectively.[111] Comparison of the crude product to the literature data indicates the desired product is present however the purity could not be determined. Additional signals in the crude product appeared as a broad multiplet at 3.5-4.0 ppm and a narrow multiplet at 5.0 ppm. The additional signals were attributed to unidentified impurities formed as reaction byproducts. Attempts at purifying the crude product by trituration or recrystallisation were not successful and so the crude material was used in the subsequent reaction.



Scheme 3.06: Bromination of trindane.

The desired norbornadiene trimer **226** could be synthesised by reductive debromination of the hexabromide **224** in the presence of DMAD. The hexabromide **224** was added to a mixture of zinc powder in DMF with an excess of DMAD. The crude product was isolated and the ^{1}H NMR spectrum analysed. The desired norbornadiene trimer **226** has a characteristic benzylic signal which appears as a doublet at 4.33 ppm. The ^{1}H NMR spectrum of the crude product did not show any significant signal at 4.33 ppm and so it was concluded that the desired product was not formed in any appreciable amount. Multiplets observed near 4.3 ppm were assigned to the bridgehead methine groups of the partially formed norbornadiene structures. The low conversion to the desired product could be attributed to the activity of zinc powder used. The activity of zinc powder has previously been reported as a critical factor in the preparation of *o*-quinodimethane by reductive debromination.[112] It was reported that activation of the zinc powder as a Zn/Ag couple gave reproducible yields of the Diels-Alder adduct. The Zn/Ag couple was prepared according to the reported procedure[112] and used in the reaction of hexabromide **224** with DMAD. The crude ^{1}H NMR spectrum did not show any significant change from the previous reaction conditions and so other variables were considered. Another factor which could affect the reaction outcome is the purity of the hexabromide **224**. The purity of the hexabromide **224** could not be determined by ^{1}H NMR due to the complexity of the spectrum. In addition, the authors did not include experimental or spectral data for the hexabromide **224** and the referenced synthesis was not accessible. The reaction was repeated using different batches of hexabromide however no product was detected.

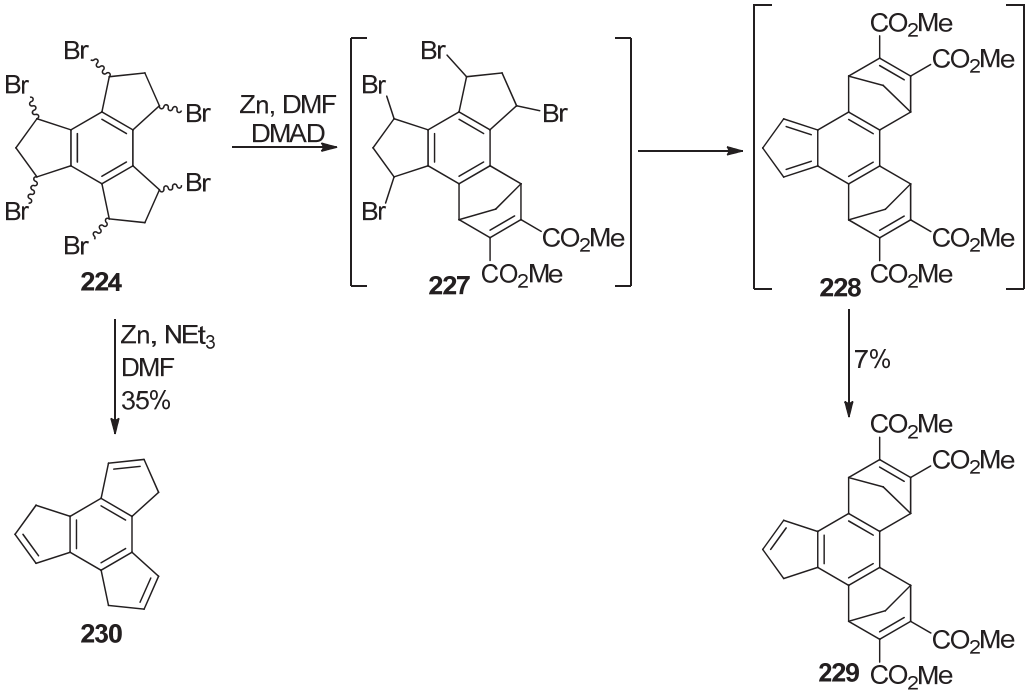


Scheme 3.07: Attempted synthesis of **226**.

The reaction was further investigated by separation of the crude reaction mixture using column chromatography. A single Diels-Alder adduct was isolated in trace

amounts. The ^{1}H NMR spectrum of the isolated product showed three signals in the range of 4.33 to 4.45 ppm with a combined integration of 4 protons. These signals were assigned to the benzylic positions of two non-equivalent norbornadiene ring systems. Two multiplets were observed at 6.52 and 6.95 ppm each integrating to a single proton. These signals were assigned to the vinylic positions of a single indene ring system. The structure was therefore assigned as **229** which is consistent with the remaining signals. The formation of the indene ring system has precedent in literature in which similar reaction conditions with the omission of DMAD gave trindene **230** (Scheme 3.08).[111]

The formation of an indene ring structure may occur through [1,5]-sigmatropic hydride shift of the *o*-quinodimethane intermediate. This type of rearrangement has been reported to occur rapidly at room temperature in the structurally related isoindene.[113] The driving force for the rearrangement is aromatisation of the central ring which is in competition with the Diels-Alder reaction. The desired intermolecular Diels-Alder reaction may be favoured by using a higher concentration of the dienophile. The reaction was therefore repeated using a large excess of DMAD however there was no indication of the desired product. The procedure was abandoned in favour of a more reliable route to the norbornadiene structure.



Scheme 3.08: Formation of byproduct **229**.

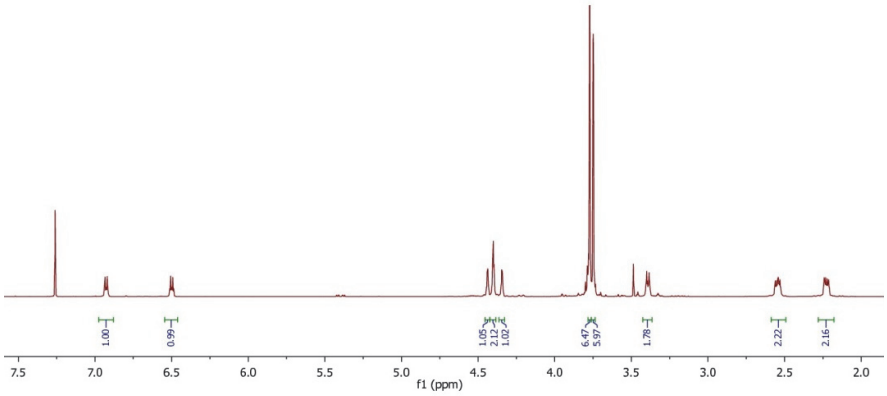
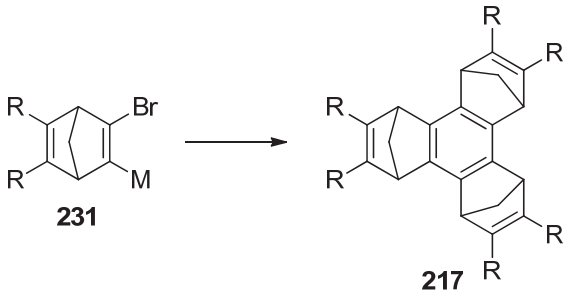


Figure 3.01: ^{1}H NMR spectrum of **229**.

3.2 Ullmann coupling cyclotrimerisation

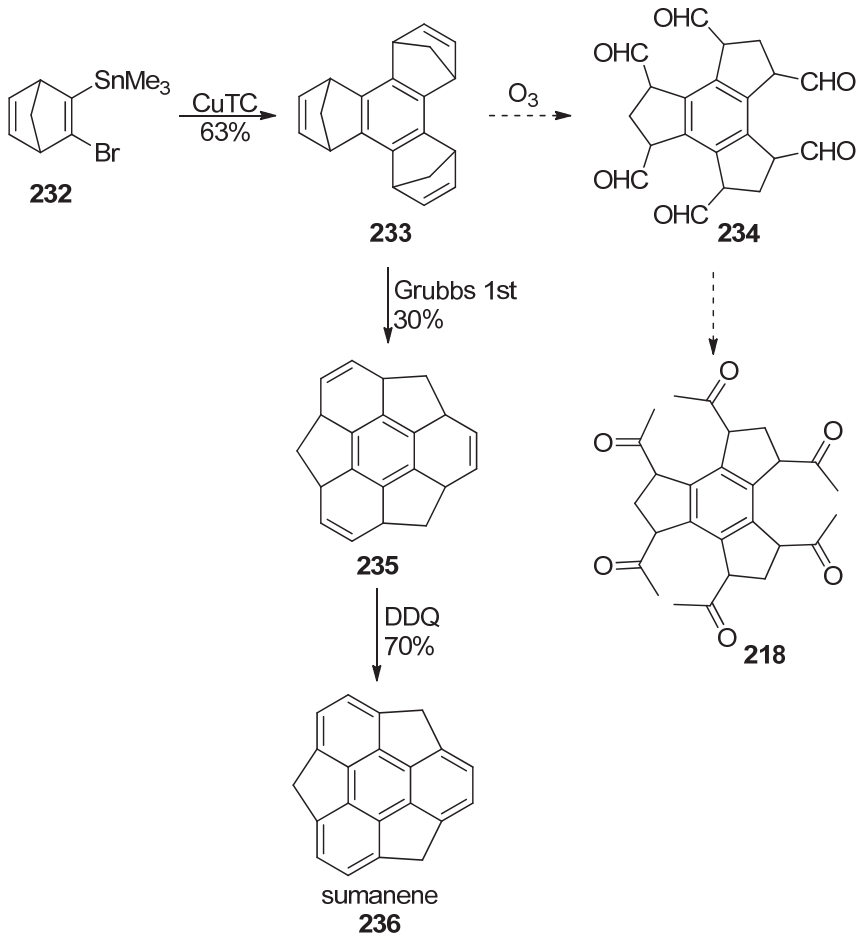
An alternative route to the norbornadiene cyclotrimer involves the cyclotrimerisation of a norbornadiene derivative. The method was first reported by Gassman who used lithiated bromonorbornadiene **231** (R = H, M = Li) in combination with transition metal salts.[114] Further development of the methodology led to the introduction of the Ullmann coupling procedures involving norbornadiene bromostannanes (M = SnR_3).[115] Under optimised conditions the reaction provides the norbornadiene trimer in almost quantitative yield as a mixture of two stereoisomers.[116]



Scheme 3.09: Cyclotrimerisation of **231**.

The unsubstituted norbornadiene trimer **233** has previously been prepared as an intermediate in the synthesis of sumanene **236**.[117] Ullmann coupling of the bromostannane **232** yielded the norbornadiene trimer **233** as a mixture of stereoisomers. The aldehyde **234** could be synthesised by ozonolysis of intermediate

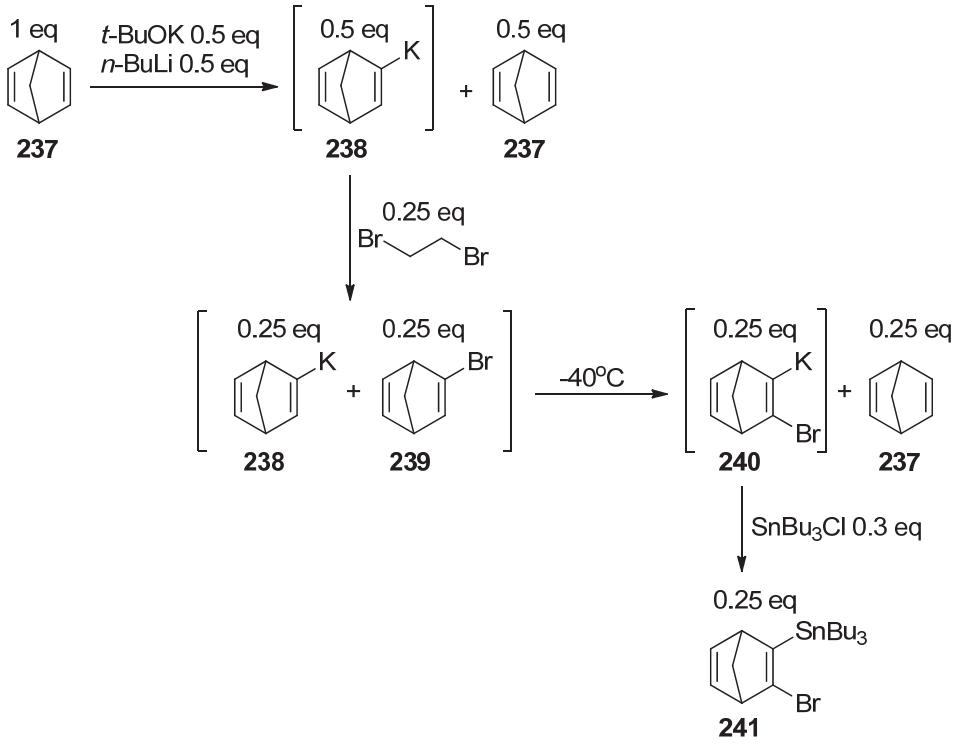
233 followed by reductive workup. Further functionalisation of the aldehyde could then lead to the target trindane derivative **218**.



Scheme 3.10: proposed synthesis of **218**.

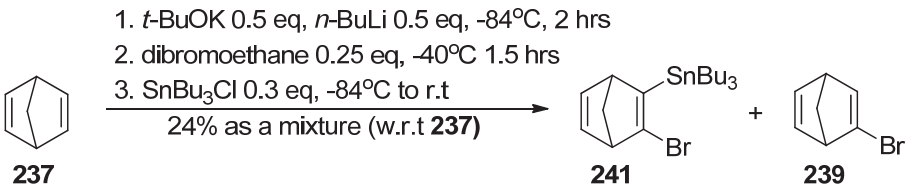
The norbornadiene bromostannane **241** may be synthesised from norbornadiene **237** utilising a multi-step one pot reaction.[117] The first step of the reaction is metallation of the vinylic position of norbornadiene using a combination of *t*-BuOK and *n*-BuLi to give a solution of **238**.[118] An excess of norbornadiene is required to suppress metalation of THF used as the solvent. In the second step of the procedure, 0.5 equivalents of dibromoethane is added relative to the metalated norbornadiene **238**. This converts half of the metalated norbornadiene to bromonorbornadiene **239**. The reaction is then warmed to -40 °C which allows for an acid-base equilibration to occur, forming the metalated bromonorbornadiene **240**. In the final step,

transmetalation of norbornadiene **240** with tributyltin chloride yields the stannane **241**.



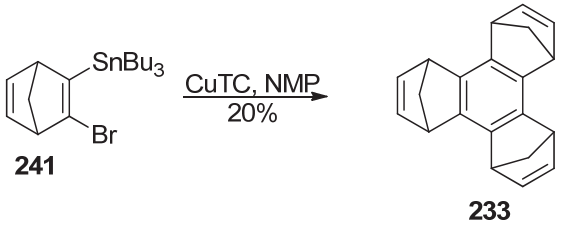
Scheme 3.11: Reaction mechanism for the synthesis of **241**.

Following the reported procedure, BuLi was added to a solution of norbornadiene and *t*-BuOK at -84°C. After 30 minutes, dibromoethane was added to the reaction mixture followed by tributyltin chloride after a further 90 minutes. The ^{1}H NMR spectrum of the crude product indicated the desired product was present in approximately 70% purity with the main impurity identified as 2-bromonorbornadiene **239**.[118] Purification of the product was not possible due to the low polarity of the components. The reaction required precise quantities of reagent and careful control of reaction temperature to obtain a consistent yield.



Scheme 3.12: Synthesis of **241**.

The final step in the synthesis of norbornadiene trimer **233** is the cyclotrimerisation of **241**. The cyclotrimerisation is effected with stoichiometric copper(I) which is introduced in the form of copper(I) thiophene-2-carboxylate (CuTC), a highly active source of copper(I). CuTC was added to a solution of **241** in NMP at -20 °C to provide **233** in low yield as a mixture of diastereomers. The ^{1}H NMR spectrum of the product was in agreement with the reported spectrum for **233**. Trace impurities were observed however purification was not possible due to the low polarity of the product. This route to the norbornadiene trimer was abandoned in favour of an alternative procedure which is less intensive and amenable to scale up.

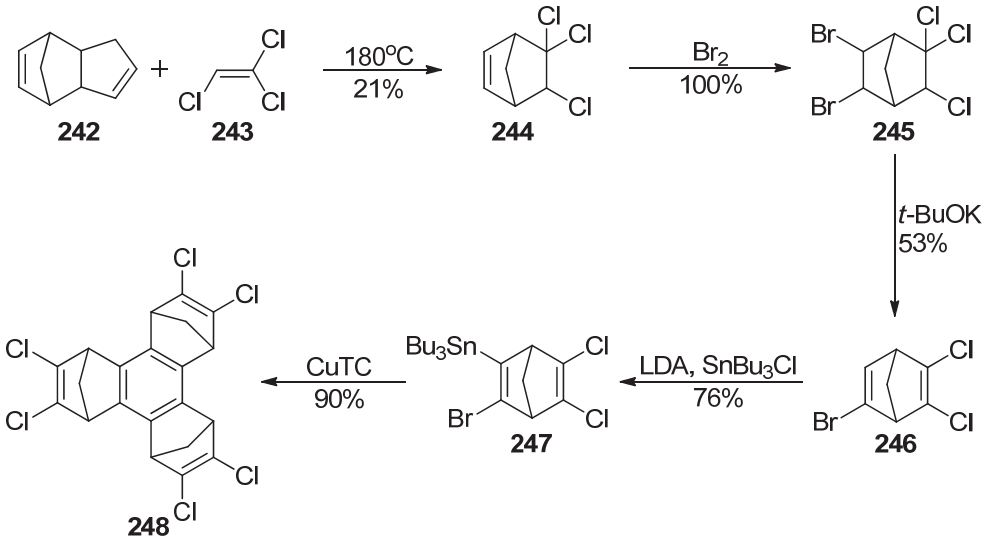


241 **233**

Scheme 3.13: Synthesis of **233**.

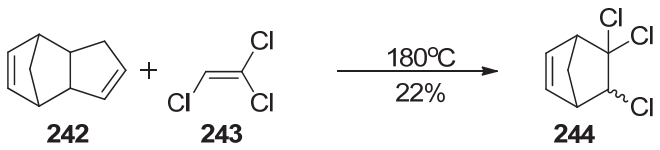
3.3 Alternative approach to the norbornadiene trimer

The chlorinated norbornadiene bromostannane **247** has previously been used in the Ullmann cyclotrimerisation reaction to yield norbornadiene trimer **248**.[119] The synthesis begins with a Diels-Alder reaction between cyclopentadiene and trichloroethylene to give trichloronorbornene **244**. Addition of bromine then yields the halogenated norbornane **245**. Under basic conditions, two successive elimination reactions lead to the norbornadiene **246**. The unsubstituted vinyl position of **246** may be deprotonated with a strong base followed by addition of tributyltin chloride to yield the norbornadiene bromostannane **247**. The Ullmann cyclotrimerisation of **247** then yields the norbornadiene trimer **248**.



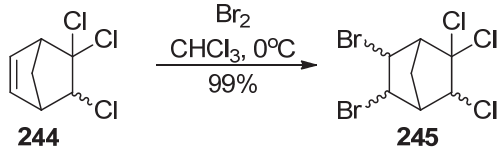
Scheme 3.14: Synthesis of **248**.

In the first step, trichloronorbornene **244** is synthesised by the Diels-Alder reaction between cyclopentadiene and trichloroethylene. At high temperatures, cyclopentadiene is formed *in situ* from the more conveniently available dicyclopentadiene **242**. Following the literature procedure, a mixture of dicyclopentadiene and trichloroethylene was heated to 180 °C for 18 hours in a pressure reactor.[120] The product was then isolated from the reaction mixture by vacuum distillation to give a partially crystalline oil in low yield. The ^{1}H NMR spectrum of the product showed two doublets at 4.77 and 4.19 ppm with nearly equal integration. These signals were assigned to the chlorinated methine position of the two diastereomeric products. A multiplet was observed at 6.31 ppm which was assigned to the vinylic protons. Four multiplets appearing in the range of 3.04 to 3.54 ppm were assigned to the allylic positions of **244**. Multiplets appearing in the range of 1.91 to 2.31 ppm were assigned to the methylene position. The spectrum is consistent with the reported literature data.[120]



Scheme 3.15: Synthesis of **244**.

The second step requires bromination of the double bond of norbornene **244**. Addition of bromine to a solution of **244** at 0 °C resulted in rapid reaction as indicated by loss of the characteristic bromine colour. After the reaction was complete the product was isolated as a pale yellow oil in nearly quantitative yield. The ^{1}H NMR spectrum of the crude product was complex which indicates a mixture of diastereomers. There were no signals observed in the vinylic region, consistent with bromination of the alkene. The crude product was used in the next step without further purification.



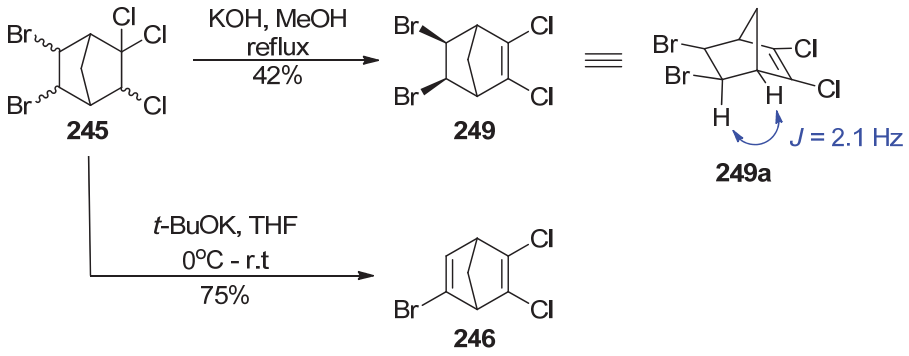
244 **245**

Scheme 3.16: Synthesis of **245**.

The next step in the reaction sequence required two subsequent elimination reactions to introduce the two alkene bonds of norbornadiene **246**. The elimination would be regioselective since the bridgehead alkene regioisomer is unfavourable according to Bredt's rule. A solution of KOH in methanol was added to norbornane **245** and after 18 hours the product was isolated. The ^{1}H NMR spectrum showed four signals at 4.25, 3.19, 2.38 and 2.17 ppm with integration of 2:2:1:1 respectively. The absence of signals in the vinylic region indicated the desired elimination at the vicinal dibromide position did not occur. The signal at 4.25 ppm (J = 2.1 Hz) was assigned to the bromide positions with the bridgehead signal at 3.19 ppm and the methylene signals at 2.38 and 2.17 ppm. The number of signals indicates the molecule is symmetrical and therefore the structure of the product must be assigned as the *syn* dibromide **249**. The unexpected *syn* stereochemistry is presumably due to neighbouring group participation in the bromination reaction however the mechanism is uncertain. The proposed structure was supported by the ^{13}C NMR spectrum which showed a signal at 133.7 ppm attributed to the symmetrical alkene of **249**. The stereochemistry of the product was tentatively assigned based on the observed vicinal coupling constant between the bridgehead and α-bromo positions (J = 2.1 Hz) according to the Karplus equation. The weak coupling indicates the dihedral angle is near 90° and therefore the structure was assigned as **249a**. The

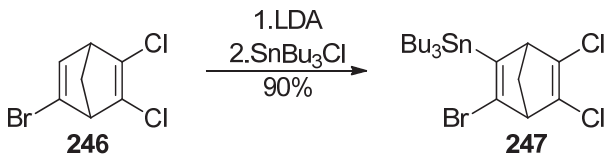
selective elimination of the chloride to yield **249** indicates the bromide substituent is less reactive towards elimination.

The use of a stronger base such as potassium *t*-butoxide could allow for elimination to occur at the less reactive bromide position of norbornane **245**. A solution of *t*-BuOK in THF was added to norbornane **245** at 0 °C followed by warming to room temperature. After consumption of the starting material, the product was isolated by silica gel filtration to give a single product in high yield. The ^{1}H NMR spectrum showed a singlet at 6.84 ppm and two pairs of multiplets at 3.51 and 2.53 ppm with integration of 1:1:1:1:1. The signal at 6.84 ppm was assigned to a vinyl position. The presence of a vinylic proton indicates elimination had occurred at the vicinal dibromide position. The two multiplets near 3.51 ppm were assigned to the non-equivalent bridgehead positions while the two signals at 2.53 ppm were assigned to the two methylene protons.



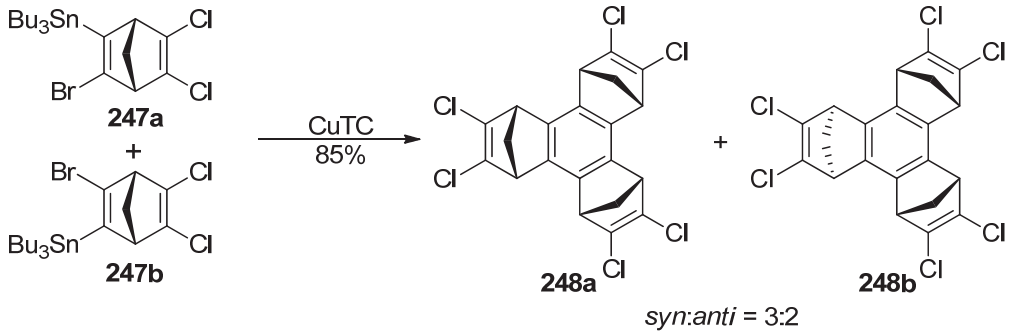
Scheme 3.17: Synthesis of **249**.

The following step in the sequence requires introduction of the organostannane group to the unsubstituted vinylic position of norbornadiene **246**. The vinylic position may be deprotonated using a strong base such as LDA. Subsequent addition of tributyltin chloride would then introduce the stannane group. The norbornadiene **246** was added to a solution of LDA at -84 °C followed by addition of tributyltin chloride. After workup, the product was purified by silica gel filtration to yield a pale yellow oil in high yield. The ^{1}H NMR spectrum showed the loss of the vinylic signal which is consistent with substitution at the vinylic position of **246**. A group of signals were observed in the region of 1.5 to 1.9 ppm attributed to the tributylstannane substituent of **247**. The remaining signals were similar to the starting material with a slight change in chemical shift consistent with the introduction of the stannane substituent.



Scheme 3.18: Synthesis of **247**.

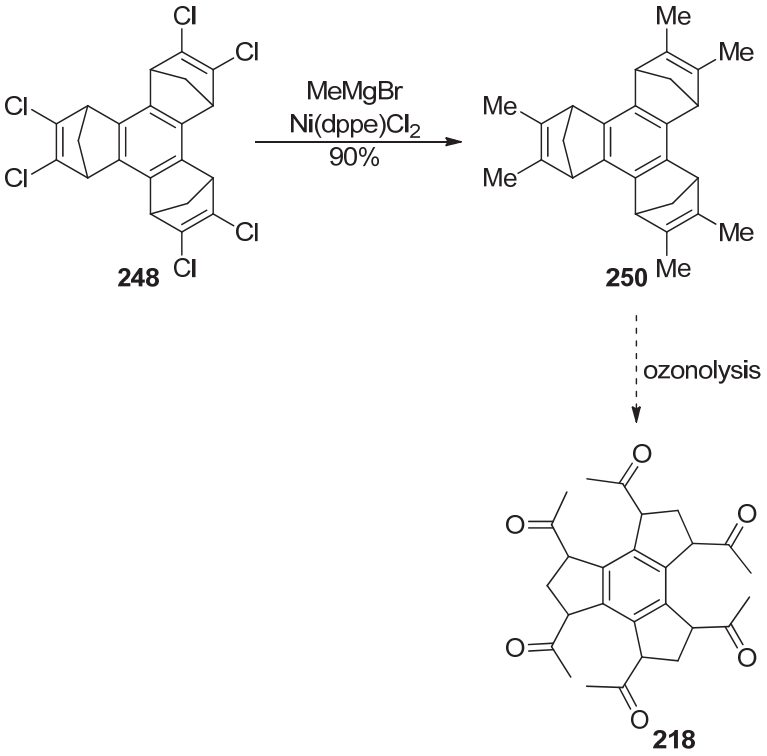
The next step in the proposed synthesis involved the Ullmann coupling cyclotrimerisation of norbornadiene bromostannane **247** to form the norbornadiene trimer **248**. CuTC was added to a solution of **247** in dry degassed NMP at -15 °C. After 3 hours, the product was isolated as a pale brown semi-solid. The solid was triturated with petroleum spirits to give a light brown solid in high yield. Analysis of the ^{1}H NMR spectrum showed three groups of multiplets at 3.89, 2.66 and 2.25 ppm with integration of 2:1:1 respectively. The signals near 3.89 ppm were assigned to the benzylic positions of **248**. Signals at 2.66 and 2.25 ppm were assigned to the methylene positions of **248**. The benzylic signals were observed as a triplet and a closely spaced multiplet. The triplet was assigned to the *syn* isomer **248a** based on rotational symmetry. The ratio of *syn* to *anti* isomers was measured as 3:2 respectively from integration of the benzylic signals. This is in contrast to the reported ratio of 1:2.[119] The formation of the *syn* isomer **248a** occurs through the cyclotrimerisation of a single enantiomer of **247**. In comparison to the previously reported reaction outcome, the trimerisation of a single enantiomer of **247** is strongly favoured over coupling of the two different enantiomers. The difference in the *syn* to *anti* ratio of **248** could not be attributed to the enantiomeric ratio of **247** since it is synthesised as a racemic mixture. In comparison to the reported synthesis of **248** the only significant difference is the trialkyl stannane substituent of **247** since the literature procedure used a trimethyltin analogue. The tributyltin substituent would greatly increase the steric interaction between coupling partners relative to the trimethyltin analogue. The increased steric interaction could lead to a change in the relative reaction rate for the coupling of the two different enantiomers of **247**. A decrease in the relative reaction rate for coupling of the two enantiomers of **247** would result in a greater proportion of the *syn* isomer of **248** being formed which is consistent with the observed product ratio. The synthesis of **248** was amenable to scale up providing a 10 gram batch of the product without decrease in yield.



Scheme 3.19: Cyclotrimerisation of **247**.

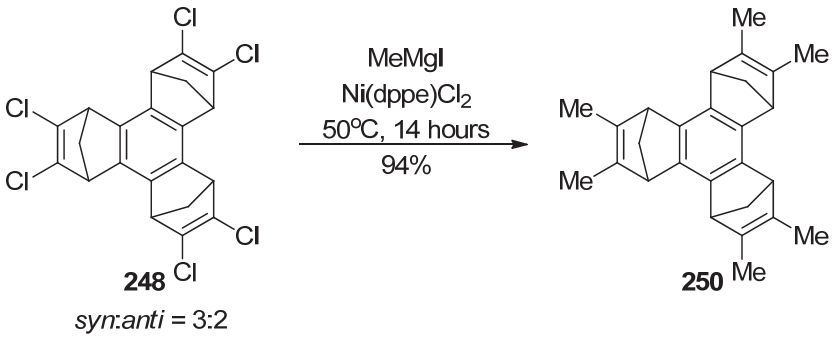
3.4 Ring cleavage of the norbornadiene trimer

With the norbornadiene trimer **248** synthesised in multigram quantities the next step was oxidative cleavage to afford a substituted trindane. The desired acyl substituted trindane **218** could be obtained directly from the ring cleavage of the hexamethyl norbornadiene trimer **250**. The synthesis of the hexamethyl derivative **250** has previously been reported through Kumada coupling of the hexachloride **248**.[119]



Scheme 3.20: Proposed synthesis of **218**.

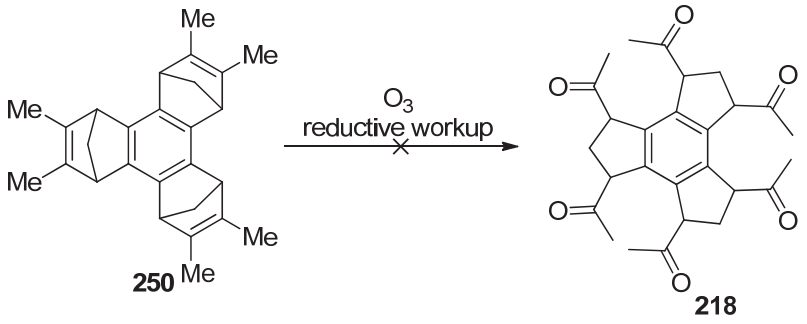
The vinyl chloride **248** was subjected to Kumada coupling conditions using a methyl Grignard reagent. Methylmagnesium iodide was prepared from methyl iodide and magnesium in THF. It was subsequently found that THF is an unsuitable solvent for the preparation of MeMgI due to precipitation of the Grignard reagent. This has been noted previously in the literature with the precipitate identified as $CH_3MgI(THF)_2$.[121] The reaction solvent was changed to diethyl ether which was found to be suitable for the preparation of MeMgI. A solution of MeMgI was added to a suspension of norbornadiene trimer at room temperature followed by a catalytic amount of $Ni(dppe)Cl_2$. After 18 hours, the mixture was quenched and the product was isolated as a light brown residue in high yield. The ^1H NMR spectrum showed predominantly starting material with a trace of a new product. The low conversion could be explained by the low solubility of **248** in diethyl ether. The solubility would be greater at a higher temperature and so the reaction was run again with heating to 80°C in a sealed tube. The ^1H NMR spectrum of the product showed partial conversion to product. During workup it was observed that the characteristic colour of the nickel catalyst was absent. This indicated the catalyst was not stable under the higher temperature reaction conditions. The reaction was then repeated with heating to 50 °C. The product was analysed by ^1H NMR which showed complete consumption of the starting material to give a single product in high yield. The ^1H NMR spectrum of the product showed a group of singlets at 1.66 ppm which were assigned to the newly formed methyl substituents. The observed signals were consistent with the reported literature data.[119]



Scheme 3.21: Synthesis of **250**.

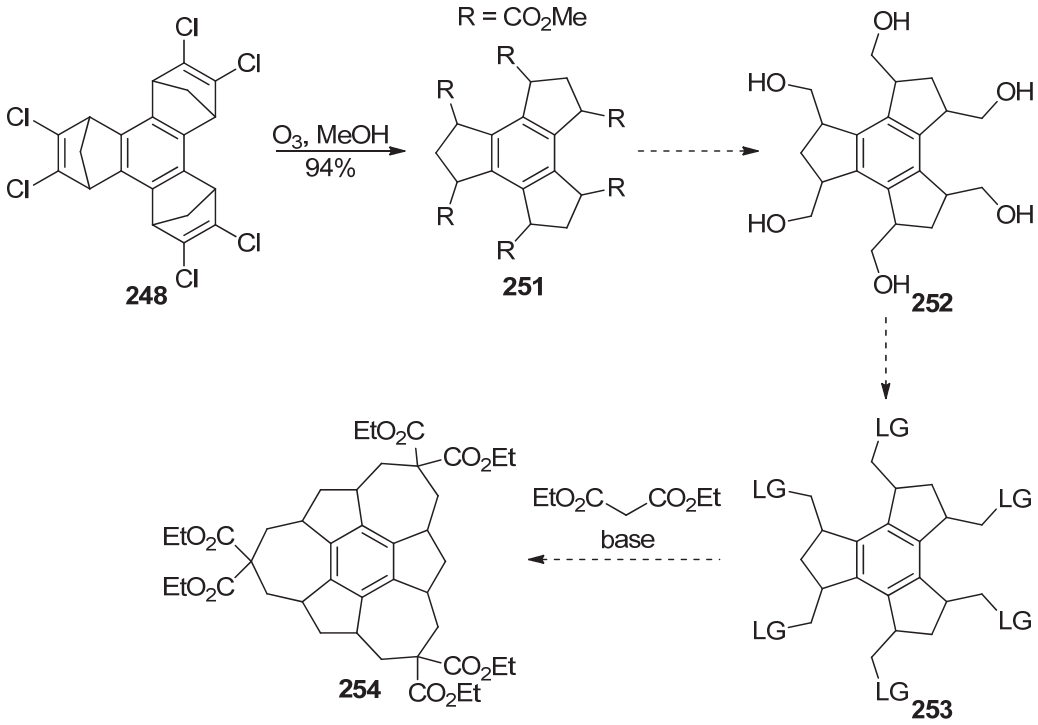
The target trindane derivative **218** could subsequently be synthesised by oxidative ring cleavage of norbornadiene trimer **250**. Ozonolysis of **250** would cleave each of

the six membered rings to form the six acetyl substituents of **218**. Ozonized oxygen was passed through a solution of **250** until a blue colour indicated the presence of excess ozone. After reductive workup using thiourea, the product was isolated as a pale yellow solid. Analysis of the ^{1}H NMR spectrum showed complete consumption of the starting material with new signals appearing as broad multiplets centred at 3.25, 2.2 and 0.7 ppm. The formation of acetyl substituents would give characteristic singlets near 2 ppm however these signals were clearly absent. The absence of any signals attributable to acetyl groups indicates the trindane **218** was not present in the crude product. The extreme signal broadening may indicate the formation of a stable polymeric ozonide. The reaction was therefore repeated using alternative reagents for the reductive workup. Thiourea was replaced with other reductants such as triphenylphosphine and sodium borohydride however the ^{1}H NMR spectra showed no change in the isolated product and so the reaction was abandoned.



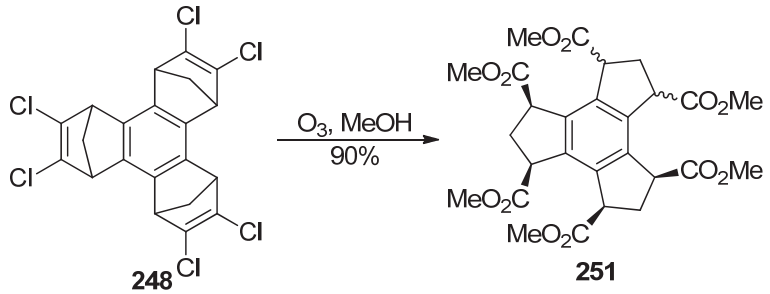
Scheme 3.22: Attempted synthesis of **218**.

Ozonolysis of the hexachloride **248** in methanol has been reported to yield the trindane hexaester **251** in high yield.[122] The difference in reaction outcome from ozonolysis of the hexachloride **248** in comparison to the hexamethyl derivative **250** may be due to differences in the reaction pathway.[123] After synthesis of the trindane **251**, the ester groups could be linked to form the isocoronene ring structure. This could be achieved by reduction to the alcohol **252** followed by conversion to suitable leaving groups **253**. The one carbon linking group could then be introduced through nucleophilic substitution with a malonate ester to give the saturated isocoronene derivative **254**.



Scheme 3.23: Proposed synthesis of isocoronene ring structure.

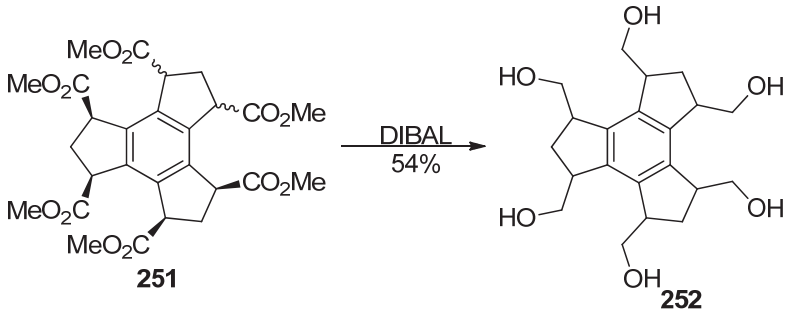
Ozonolysis of the hexachloride **248** in the presence of methanol would yield the trindane hexaester **251** through ring cleavage.[122] Ozonised oxygen was passed through a solution of hexachloride **248** in DCM and methanol until a blue colour persisted. After removal of the excess ozone the reaction mixture was concentrated to yield the product as a pale yellow residue in high yield. The ^{1}H NMR spectrum was consistent with literature data for **251** with the newly formed methyl esters observed as a group of singlets near 3.6 ppm.



Scheme 3.24: Synthesis of **251**.

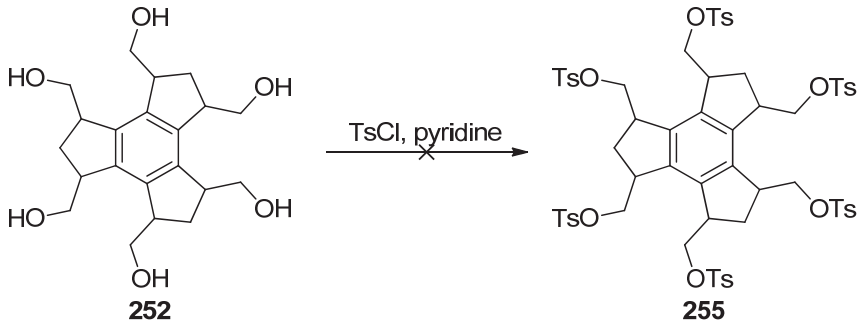
Reduction of all six ester groups of **251** would lead to the hydroxymethyl trindane **252**. An excess of DIBAL was added to a solution of the hexaester **251** followed by

workup to give a colourless residue in moderate yield. The ^{1}H NMR spectrum did not display any resonances in the region of 3.6 ppm which could be attributed to the methyl ester groups of the starting material. The new signals were very broad and appeared primarily in the region of 4.6, 3.5 and 2 ppm. Detailed analysis of the spectrum was not possible due to the absence of distinct signals. The broadening of the signals could be due to intramolecular hydrogen bonding between the hydroxy groups resulting in conformational restriction. A similar broadening of signals has been reported for a structurally related cyclopentane derivative.[124]



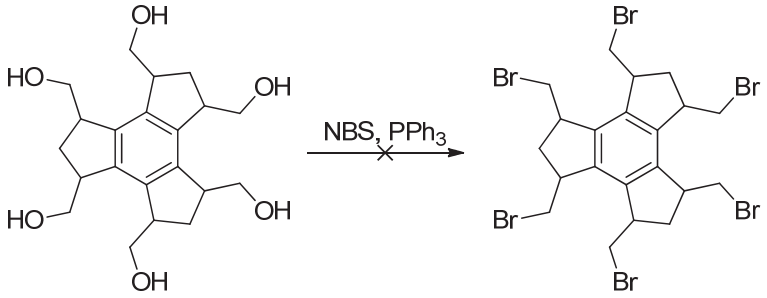
Scheme 3.25: Synthesis of **252**.

The next step of the proposed reaction sequence required conversion of the hydroxy groups of **252** to leaving groups for a nucleophilic substitution. This could be achieved by formation of the tosylate ester **255**. A solution of the alcohol **252** in pyridine chloroform and tosyl chloride was heated under reflux overnight. After workup the product was obtained as a brown oil. Analysis of the ^{1}H NMR spectrum showed the signals attributed to the starting material. An alternative leaving group was then investigated since the starting material appeared unreactive towards tosyl chloride.



Scheme 3.26: Attempted synthesis of **255**.

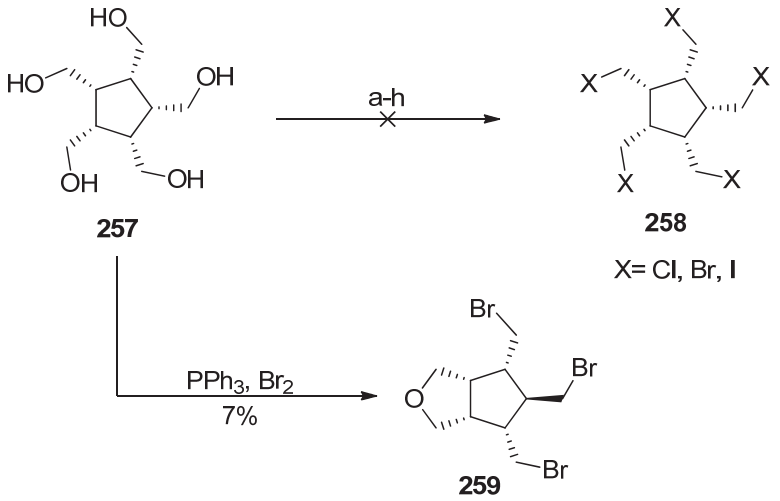
The leaving groups could be introduced as the hexabromide **256** which could be prepared from the alcohol **252** through an Appel reaction. NBS was added to a solution of triphenylphosphine and **252**. After two hours, the product was isolated as a pale yellow residue. The product was analysed by TLC which indicated that triphenylphosphine was the only non-polar compound present. In addition, analysis of the ^{1}H NMR spectrum did not give any distinct signals which could be attributed to the desired product.



252 **256**

Scheme 3.27: Attempted synthesis of **256**.

The difficulties encountered with reactions of **252** may be explained by the close proximity of the hydroxy groups. Similar results have been reported for the structurally related cyclopentane **257**.[125] Numerous conditions were investigated for synthesis of the halide **258** with a complex mixture obtained in each case. The cyclic ether **259** was the only product isolated. The formation of the cyclic ether indicates a competing intramolecular reaction of an intermediate with a nearby alcohol. These results indicate the synthesis of the hexabromide **256** from the indane **252** is not feasible. Alternative methods of synthesising trindane derivatives were then investigated.



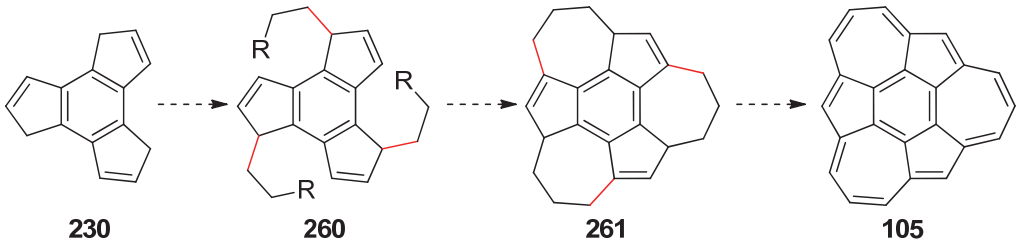
Scheme 3.28: Attempted synthesis of **258**.

a) HBr, H_2SO_4; b) PBr_3; c) $SOBr_2$; d) PPh_3, CBr_4; e) PPh_3, Br_2; f) $SOCl_2$; g) PCl_3; h) red P, I_2

Chapter 4

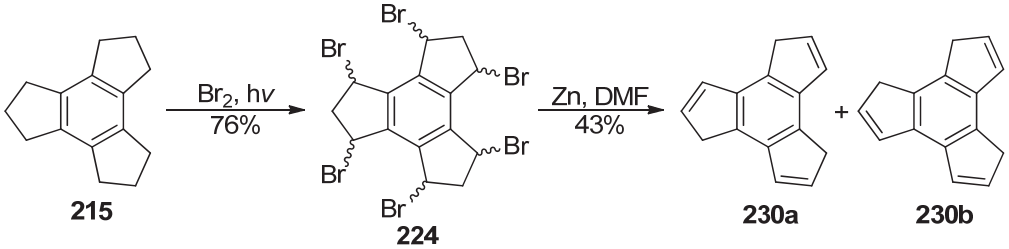
Trindene approach

The synthesis of isocoronene could be accomplished from trindene **230** by linking the benzylic positions with three membered carbon chains. The side chains could be introduced by deprotonating the active methylene positions of trindene **230** followed by reaction with an electrophile to yield **260**. The final ring closing reaction could then be achieved by deprotonation of alkylated trindene **260** with subsequent intramolecular cyclisation. The partially saturated isocoronene **261** could then be aromatised under oxidative conditions to yield isocoronene **105**.



Scheme 4.01: Revised synthesis of isocoronene.

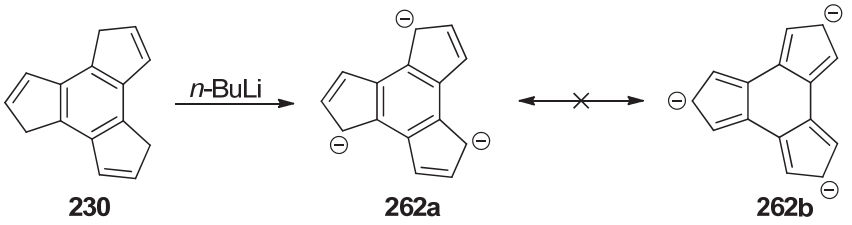
The synthesis of trindene **230** has previously been reported in two steps from trindane **215** by Katz and Slusarek.[111] In the first step, the radical bromination of trindane yields the hexabromide **224** as a mixture of diastereomers. In the second step, zinc powder is used for the reductive debromination of **224** to provide a moderate yield of trindene as a mixture of two regioisomers **230a** and **230b**.



Scheme 4.02: Synthesis of trindene. [111]

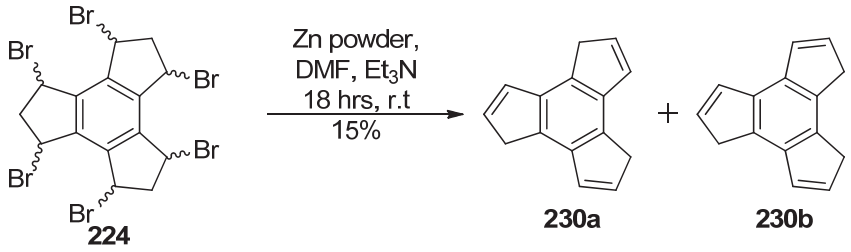
4.1 Trindene trianion

In addition, Katz and Slusarek investigated the deprotonation of trindene using *n*BuLi. By treating trindene with three equivalents of *n*BuLi, the three active methylene groups are deprotonated to yield the trindene trianion **262**. The methylene groups of trindene are relatively acidic since the negative charge of the conjugate base is stabilised by the aromaticity in each of the five membered rings. According to Clar's rule, the negative charge will be localised at the benzylic positions since the alternative resonance forms such as **262b** do not have an aromatic sextet at the central benzene ring.



Scheme 4.03: Formation of the trindene trianion.[111]

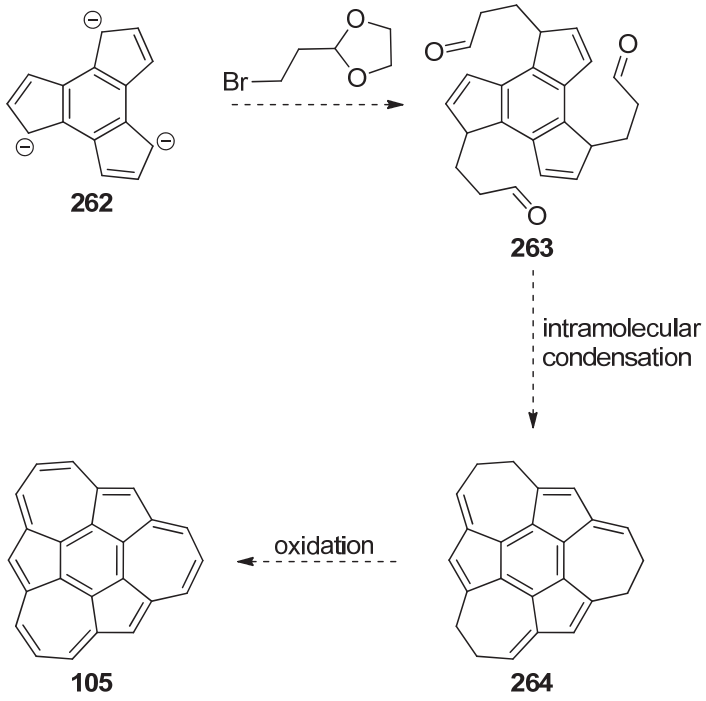
The method of Katz and Slusarek was followed to synthesise trindene **230** by reductive debromination of the previously prepared hexabromotrindane **224**.[111] The hexabromide was added to a mixture of zinc powder and triethylamine in DMF resulting in a dark reaction mixture. After TLC indicated consumption of starting material, the non-polar components of the reaction mixture were isolated by extraction with hexanes. The crude product was then purified by silica gel filtration to yield a colourless white solid in low yield. The ^{1}H NMR spectrum of the product showed two groups of multiplets in the vinylic region and a group of signals at 3.50 ppm with integration of 1:1:2 respectively. This is in accordance with the reported literature data for **230**. The signals were observed as complex multiplets, consistent with the formation of two regioisomers **230a** and **230b** as previously reported. The reaction yield was consistently in the range of 12 to 17% which is significantly lower than the reported yield average of 35%. This may be attributed to impurities present in the starting hexabromide **224** as previously discussed (Chapter 3.1).



Scheme 4.04: Synthesis of trindene.

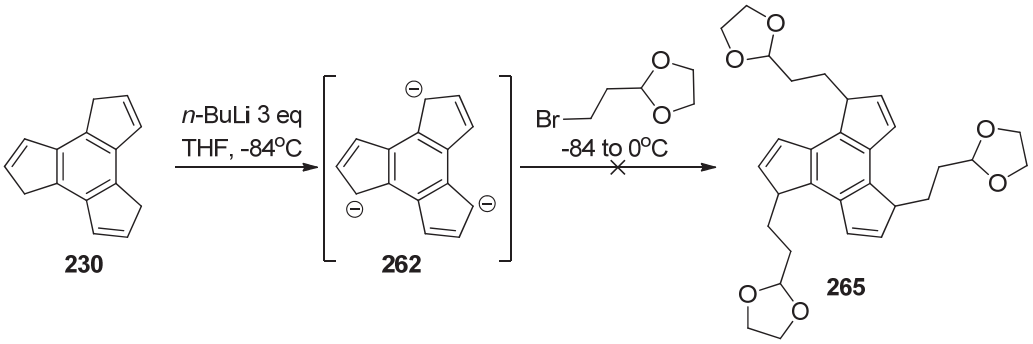
4.2 Alkylation of trindene

The functionalisation of trindene has not been reported in literature to date however alkylation of the structurally related indene anion is well known.[126, 127] The trindene trianion was prepared according to literature by treating trindene with three equivalents of *n*BuLi.[111] Reaction of the trianion with an electrophile would be expected to occur selectively at the benzylic position due to localisation of the negative charge (Scheme 4.03). The regioselective functionalisation of the trindene trianion **262** was previously demonstrated by ^{1}H NMR spectroscopy after quenching with D_2O although no other functionalisation reactions were reported.[111] The required three carbon linking group could be introduced as a side chain by nucleophilic substitution of an alkyl bromide with the trianion **262**. The trindene trialdehyde **263** could be prepared by nucleophilic substitution of 3-bromopropanal acetal with **261** followed by acidic workup. The aldehyde could then be utilised for cyclisation by intramolecular condensation to yield the partially saturated isocoronene **264**. Isocoronene **105** could then be synthesised by oxidative aromatisation.



Scheme 4.05: Proposed synthesis of isocoronene.

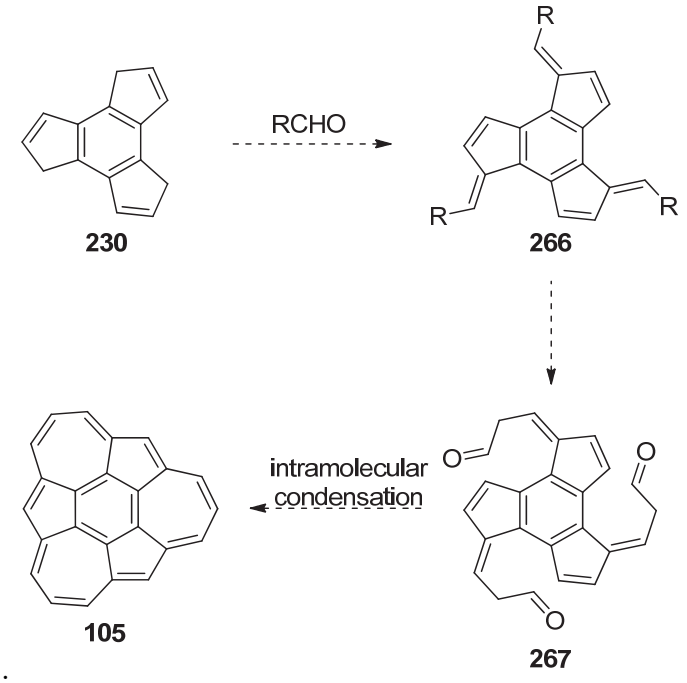
In the first step of the proposed synthesis, nucleophilic substitution of 3-bromopropanal acetal with the trindene trianion **262** would yield the trindene acetal **265**. The trindene trianion was first prepared by addition of *n*BuLi to a solution of trindene at -84 °C followed by addition of 3-bromopropanal acetal. After workup the ^{1}H NMR spectrum of the reaction mixture was analysed. The vinylic region showed signals attributed to unreacted trindene with no other vinylic signals present. This indicated no reaction had occurred to any detectable extent. The reaction was repeated with warming of the reaction mixture to 0 °C however the outcome of the reaction was unchanged. The low reactivity of the trindene trianion towards the aldehyde may be due to solubility in the reaction solvent. The low solubility of the trindene trianion in THF was reported by Katz and Sulsaresk following an attempt to obtain the ^{1}H NMR spectrum.[111] Low solubility is a known issue in the reactivity and characterisation of other polylithiated organic compounds.[128]



Scheme 4.06: Attempted synthesis of **265**.

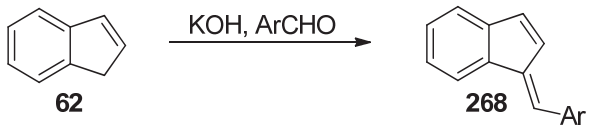
4.3 Trifulvene

The functionalisation of trindene could be achieved under less basic conditions which would avoid the solubility issue of the preformed trindene trianion. Fulvenes are an established class of compounds which may be prepared by the base catalysed condensation of an aldehyde with a cyclopentadiene ring.[129, 130] The condensation reaction of trindene with three equivalents of an aldehyde with would yield the fulvene trimer (trifulvene) **266**. The final ring closing could be accomplished through an intramolecular condensation of trifulvene aldehyde **267** to yield isocoronene **105**.



Scheme 4.07: Proposed synthesis of isocoronene.

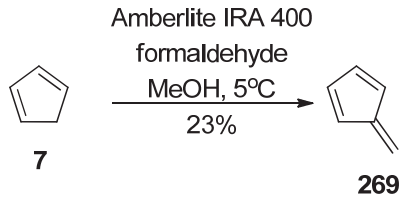
The synthesis of the trifulvene structure **267** has not previously been reported, however the structurally related benzofulvenes **268** have previously been prepared through the base catalysed condensation of indene with an aldehyde. The synthesis of benzofulvenes and fulvenes was first reported by Thiele in 1906 as a series of publications.[131, 132, 133, 134] Under Thiele's reaction conditions, indene and an aromatic aldehyde were heated in the presence of alkoxide or hydroxide base to give a series of benzofulvenes with the general structure of **268**. The authors did not specify the yield of the fulvene derivatives.



Scheme 4.08: Synthesis of benzofulvenes.

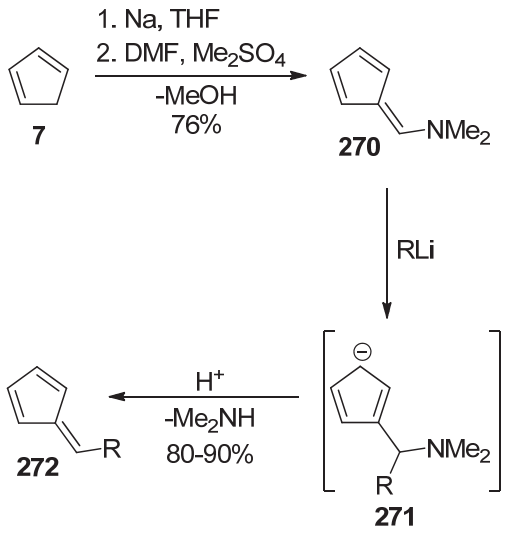
The method developed by Thiele proved unsuitable for the preparation of sensitive fulvenes resulting in low yield with decomposition to resinous material. An improved procedure was developed by McCain who found that anionic exchange resin could be used as the base catalyst.[135] This modification allowed the synthesis of

temperature sensitive fulvenes such as **269**. In the case of fulvene **269**, thermal instability of the product led to partial decomposition during isolation.



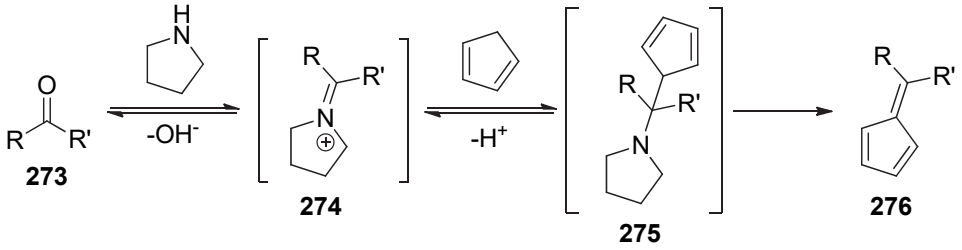
Scheme 4.09: Synthesis of fulvene **269**.[135]

A more widely applicable synthesis of fulvenes was later developed by Hafner.[136] The Hafner fulvene synthesis utilises the dimethylaminofulvene **270** as a common intermediate. The dimethylamino group of **270** is substituted with nucleophiles such as organolithium, hydride and hydroxide to give a range of fulvene derivatives. In the first step of the reaction sequence, cyclopentadiene is deprotonated with sodium metal. The dimethylaminofulvene **270** is then formed through a condensation reaction between the cyclopentadienide anion and DMF - dimethylsulfate complex. The second step of the synthesis involves the conjugate addition of a nucleophile to the exocyclic position of **270** leading to the resonance stabilised anion **271**. Acidification of adduct **271** results in elimination of dimethylamine to give the fulvene product **272** in high yield. This method allows the preparation of sensitive substrates in high yield and is also applicable to benzofulvene derivatives.[137]



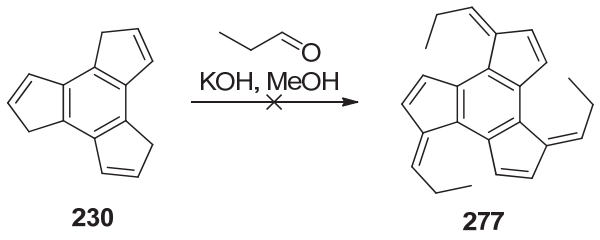
Scheme 4.10: Hafner fulvene synthesis.[136]

The current method of choice for the synthesis of fulvenes was developed by Stone and Little.[138] They found pyrrolidine to be an effective reagent for the synthesis of fulvenes using a wide range of ketones or aldehydes. In particular, the method gave significant improvement in yield over previous methods for reactions involving enolisable or sterically hindered aldehydes. The proposed reaction pathway occurs through activation of the carbonyl compound as an intermediate iminium ion **274**. Pyrrolidine was found to be uniquely effective in comparison to other alkylamines indicating the reactivity is not due solely to pK_a differences. The reactivity of pyrrolidine was therefore attributed to its cyclic structure which improves availability of the nitrogen lone pair for the condensation reaction with the carbonyl to give intermediate **274**.



Scheme 4.11: Stone and Little fulvene synthesis.[138]

The proposed synthesis (Scheme 4.07) would require condensation of trindene with a functionalised alkyl aldehyde to yield a trifulvene intermediate **267**. Since the synthesis of trifulvenes has not previously been reported, a test reaction was first performed using propanal. A methanol solution of propanal, trindene and catalytic KOH was heated under reflux. The reaction mixture was monitored by TLC which showed unreacted trindene only. After 4 hours the crude product was isolated and analysed by ^{1}H NMR. The desired trifulvene **277** would have a characteristic signal in the aromatic region due to the formation of the exocyclic alkene. The vinylic region of the ^{1}H NMR spectrum showed signals attributed to unreacted trindene with no indication of the trifulvene product. Additional signals in the alkyl region were assigned to base catalysed decomposition products of the aldehyde.

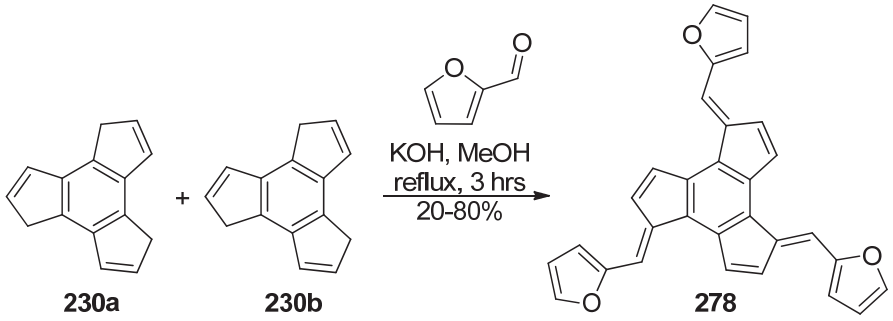


230 **277**

Scheme 4.12: Attempted synthesis of **277**.

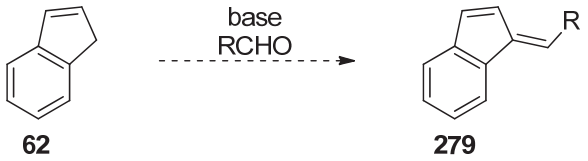
The condensation of trindene with a non-enolisable aldehyde would avoid the potential for competing self-condensation of the starting aldehyde. Furfural was chosen as the non-enolisable aldehyde since the furan ring could be cleaved at a later stage to form the required side chain. A solution of furfural, trindene and catalytic KOH in methanol was heated under reflux and monitored by TLC. As heating was commenced, a rapid colour change of the reaction mixture to dark red was observed. After three hours, TLC indicated consumption of the starting material with formation of a single coloured product. After workup of the reaction mixture, the crude product was purified by column chromatography with a single major product was isolated in high yield. The product appeared as a red solid giving an intense orange colour in solution. The colour of the product is consistent with the intense colour that is common to all fulvene derivatives. Analysis of the ^{1}H NMR spectrum showed several signals in the range of 7.60 to 6.53 ppm. The absence of signals at a lower chemical shift indicates the functionalisation at the benzylic positions of the starting trindene. A singlet was observed at 7.30 ppm which is characteristic of the exocyclic

fulvene proton. Analysis of the ^{13}C NMR spectrum showed a total of ten signals, all appearing in the aromatic region. The number of signals observed is consistent with the formation of a single regioisomer possessing three-fold rotational symmetry. Therefore the structure of the product was assigned as the symmetrical trifulvene **278**. The formation of the trifulvene as a single regioisomer was explained by steric effects. Formation of the alternative regioisomer would be disfavoured since two of the furan rings would be in close proximity. Similarly, the exocyclic alkene groups of trifulvene **278** were assumed to have *E* geometry on the basis of reduced steric interaction. Repetition of the reaction conditions gave the trifulvene in variable yields of 20-80% with the remaining mass balance made up of decomposed material. In addition, the product was occasionally contaminated with impurities that could not be removed by column chromatography. The formation of the impurity was later attributed to a secondary nucleophilic addition of the aldehyde to the trifulvene ring. The variable yield and purity of the trifulvene prompted optimisation of the reaction conditions.



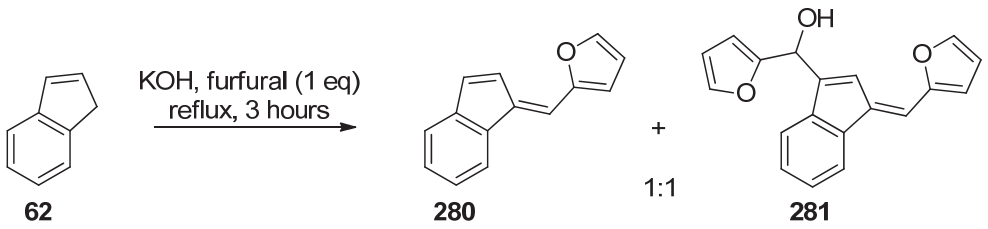
Scheme 4.13: Synthesis of **278**.

Optimisation was first performed by substituting trindene for indene **62** to yield benzofulvene **279**. Indene was chosen for optimisation since the reaction is simplified to a single functionalisation. In addition, indene is commercially available whereas the synthesis of trindene is time consuming and low yielding. It could be expected that optimised conditions for the reaction of indene would be applicable to trindene since they are structurally related and would have similar trends in reactivity.



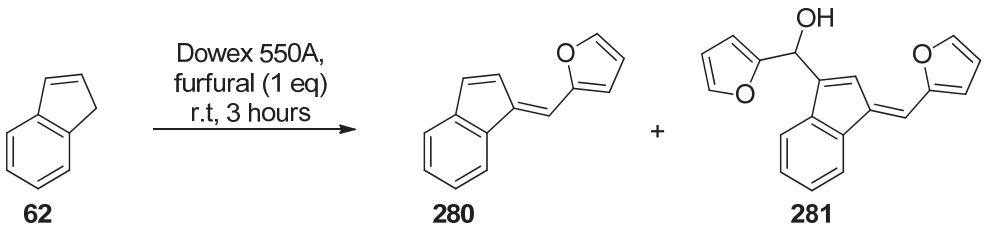
Scheme 4.14: Synthesis of benzofulvene.

Initially, indene and furfural was subject to the reaction conditions used previously for synthesis of trifulvene **278**. An equimolar mixture of indene and furfural with catalytic KOH in methanol was heated under reflux. After 30 minutes TLC indicated complete consumption of the aldehyde with a significant amount of unreacted indene. Two products were observed with an intense yellow colour. The two products were purified by column chromatography and the ^{1}H NMR spectra analysed. The first eluted compound showed the loss of the benzylic signal with new singlet at 7.09 ppm attributed to the exocyclic alkene of a fulvene. The remaining signals and integration were consistent with the desired benzofulvene **280**. The ^{1}H NMR spectrum of the second eluted compound showed signals primarily in the aromatic region. After comparison to the spectrum of isolated fulvene **280**, a singlet at 7.03 ppm was attributed to an exocyclic fulvene position. One signal appeared well separated from the aromatic region, observed as a broad doublet at 6.03 ppm (J = 3.2 Hz). This signal was attributed to the allylic position of the double addition product **281**. This assignment was confirmed by comparison to the reported allylic signal of the equivalent benzaldehyde double addition product, appearing as a doublet at 5.95 ppm (J = 4 Hz).[139] Retrospective analysis of the crude ^{1}H NMR spectrum indicates the desired benzofulvene and the byproduct were formed in equal molar ratio.



Scheme 4.15: Condensation reaction of indene and furfural.

Initial optimisation of the reaction conditions was focussed on determining the optimum base catalyst. Several base catalysts have been reported in the synthesis of fulvenes including hydroxide, alkoxide and alkylamine bases. The use of basic ion exchange resin has been reported to selectively catalyse the initial condensation between cyclopentadiene and an aldehyde, with minimal formation of the double addition product.[135] A strongly basic anion exchange resin (Dowex 550A) was added to an equimolar solution of indene and furfural in methanol at room temperature. The solution rapidly became yellow with TLC indicating complete consumption of the starting aldehyde after three hours. The product ratio was measured by ^{1}H NMR which showed no significant change over the previous run using KOH. The anionic exchange resin was chosen over KOH since the reaction could be run at lower temperature and without significant decomposition. Subsequent optimisation of the reaction was conducted by investigating variables of reaction temperature and addition of reagents.



Scheme 4.16: Basic resin catalysed reaction of indene and furfural.

Conducting a reaction at lower temperature can often reduce the relative rate of an undesired reaction. Therefore the reaction was repeated at 0 °C with Dowex 550A as the base. After complete consumption of the starting aldehyde, the reaction mixture was analysed by ^{1}H NMR. The undesired double addition product was observed as the major product and so the optimal reaction temperature was fixed at 25 °C.

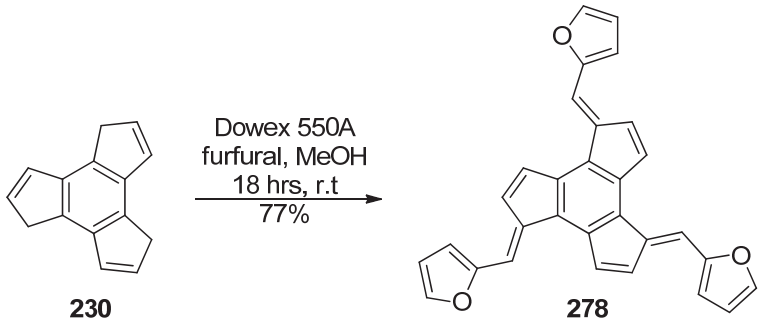
The formation of a secondary reaction product is often influenced by the order and rate in which reagents are added to the reaction mixture. The gradual addition of either the aldehyde or indene to the reaction mixture was therefore considered. The gradual addition of indene would maintain a relatively high concentration of aldehyde in the reaction mixture. This would presumably favour the double addition product and so this modification was not explored. Alternatively, the aldehyde could

be added gradually to indene which would minimise the relative concentration of aldehyde in the reaction mixture. This could favour the desired mono addition product if the rate constant for the secondary reaction is significantly smaller. A solution of furfural was gradually added to a mixture of indene, methanol and Dowex 550A over 18 hours. Analysis of the reaction mixture by TLC showed complete consumption of both furfural and indene. The ^{1}H NMR spectrum indicated the desired fulvene had formed with only trace amount of the double addition byproduct. The reaction mixture was filtered through celite and concentrated to yield the fulvene in nearly quantitative yield and excellent purity.

Reaction conditions	**^{1}H NMR product ratio (280:281)**
room temperature	50:50
0 °C	30:70
room temperature, slow addition of aldehyde	95:5

Table 4.01: Optimisation of benzofulvene synthesis.

The optimised reaction conditions were subsequently applied to the trindene system for the synthesis of trifulvene **278**. Trindene was dissolved in a minimal volume of MeOH followed by the addition of Dowex 550A. A syringe pump was then used to add three equivalents of furfural over 18 hours. After complete consumption of the aldehyde the reaction mixture was filtered through celite and then concentrated to give a red residue. Analysis of the ^{1}H NMR spectrum showed complete consumption of the starting materials. The desired trifulvene was observed as the main product with less than 5% byproducts. Purification by chromatography gave the trifulvene **278** in excellent yield and purity. The synthesis of the furyl trifulvene is a significant step towards the target isocoronene however a suitably functionalised aliphatic trifulvene would allow for a direct route to the final ring closing step.



Scheme 4.17: Optimised synthesis of **278**.

4.4 Condensation reactions of indene and trindene

The literature syntheses of fulvene compounds include numerous examples derived from the condensation reaction of cyclopentadiene with aliphatic aldehydes. In contrast, condensation reactions of indene with aldehydes have been reported almost exclusively with aryl aldehydes. Despite the structural similarities of indene and cyclopentadiene there are significant differences in the reactivity towards condensation reactions. The differences in reactivity could be explained by the lower acidity (pK_a = 20.1) of indene in comparison to cyclopentadiene (pK_a = 16).[140] The difference in pK_a may be rationalised by considering the resonance forms of the conjugate bases of indene and cyclopentadiene. The resonance structures of the cyclopentadienide carbanion **8** shows the carbanion is delocalised equally through all five positions of the ring. In contrast, the significant resonance structures of the indenide anion **282** indicate the carbanion is delocalised at the two benzylic positions only. In analogy to the trindene trianion **262**, the remaining resonance structures (e.g. **282c**) are not significant since aromaticity of the benzene ring is lost. As a consequence of restricted delocalisation, the conjugate base of indene has a reduced resonance stabilisation resulting in the high pK_a value relative to cyclopentadiene. Since the electronic structure of the indene anion is analogous to the trindene trianion (Scheme 4.03), both substrates would be expected to have similar trends in reactivity. From this it may be concluded that indene is better suited as a predictor for the reactivity of trindene.

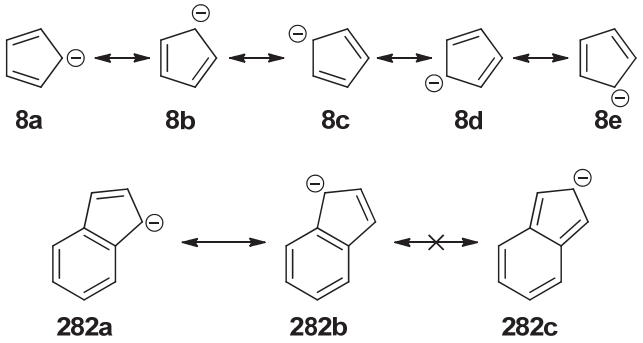
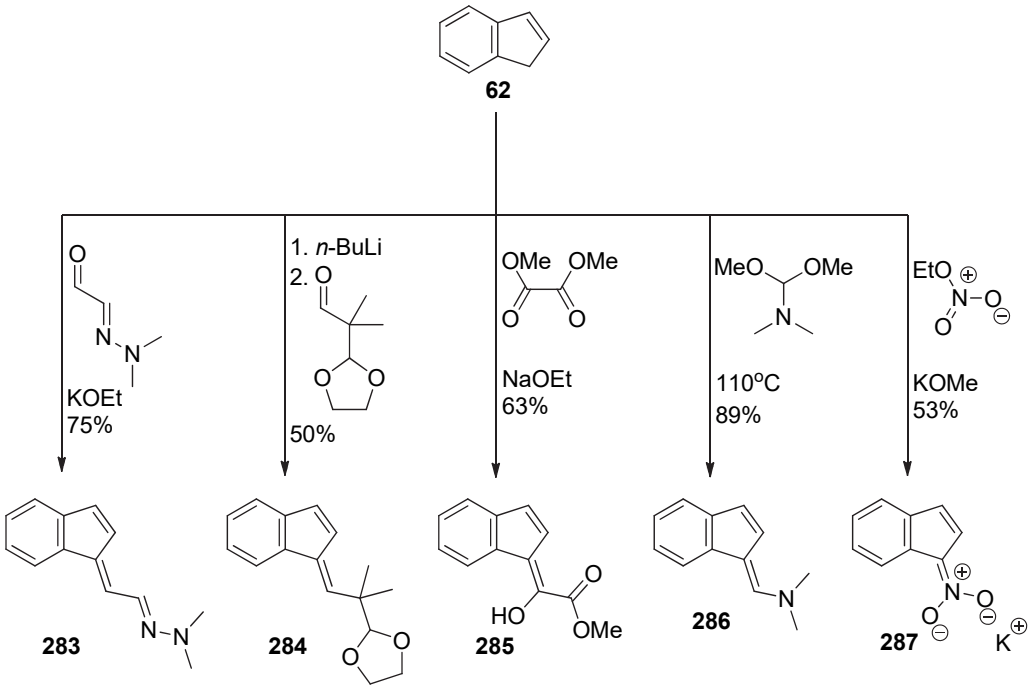


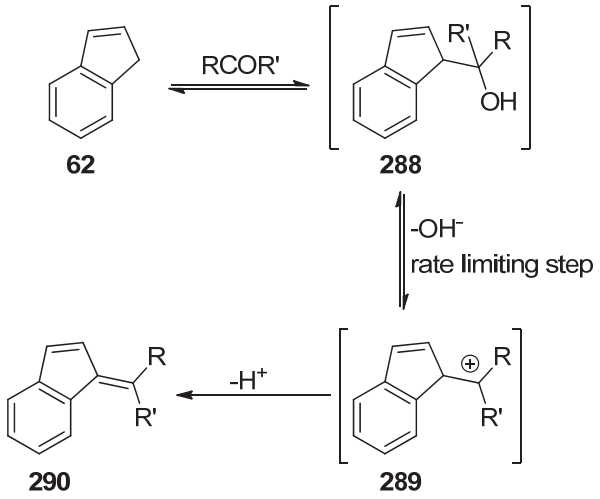
Figure 4.01: Resonance structures of the indenide and cyclopentadienide anions.

In contrast to the numerous reported reactions of indene with aromatic aldehydes, there has been only two reactions involving aliphatic aldehydes reported.[141, 142, 143] In one example, the reaction of indene with glyoxal hydrazone was reported to give benzofulvene **283** in high yield. In the second example, a two-step procedure was reported involving deprotonation of indene with *n*BuLi followed by a condensation with an aldehyde to yield benzofulvene **284**. The acetal side chain of **284** would be ideal as a linking group for the proposed synthesis of isocoronene (Scheme 4.07) however the trindene trianion was previously found to be unreactive (Scheme 4.06). In addition to aldehydes, vinyl triflate derivatives have been used in the synthesis of alkyl benzofulvenes through a condensation reaction with indene.[144] This reaction proceeds through a carbene intermediate and was not investigated. Indene has also been reported to undergo condensation reactions with a range of other electrophiles such as oxalate esters,[145, 146, 147, 148] *N,N*-dimethylformamide dimethyl acetal,[137] and ethyl nitrate[148, 149] to yield benzofulvenes **285** and **286**, and the nitronate analogue **287** respectively.



Scheme 4.18: Condensation reactions of indene.

The overall trend in reactivity for the condensation reactions of indene can be explained using the reaction mechanism proposed by Erden (Scheme 4.19) involving nucleophilic addition to a carbonyl followed by an E_1 elimination reaction.[150] In the first step, the starting indene is in equilibrium with the addition product **288**. The second step involves the reversible elimination of hydroxide to give a carbocation intermediate **289**. The final step is deprotonation of the activated indene ring to yield benzofulvene **290**. The authors identified the rate limiting step as the formation of the carbocation intermediate **289** which is consistent with an E_1 elimination mechanism. As a result, stabilisation of the carbocation intermediate by substituents R and R' is a key factor in determining reaction rate.



Scheme 4.19: Indene condensation reaction mechanism.[150]

The stabilisation of carbocation intermediate **289** as a key requirement is consistent with the reported reactivity of indene towards condensation reactions. With the exception of aldehyde **284**, all of the reported condensation reactions of indene with aldehydes involve carbocation intermediates (**291** to **294**) which are stabilised by conjugation to the adjacent substituents. In contrast, alkyl aldehydes provide no resonance stabilisation of the carbocation intermediate. The condensation reaction of indene with an alkyl aldehyde to yield **284** may be attributed to the use of stoichiometric *n*BuLi as a base in place of catalytic alkoxide. The use of a stronger base may allow the condensation reaction to proceed through an E_2 mechanism which would avoid the formation of carbocation intermediate **289** as the rate limiting step. Likewise, the reactivity of cyclopentadiene towards alkyl aldehydes may be due to the lower pK_a of cyclopentadiene which would allow the condensation reaction to proceed through an E_2 mechanism.

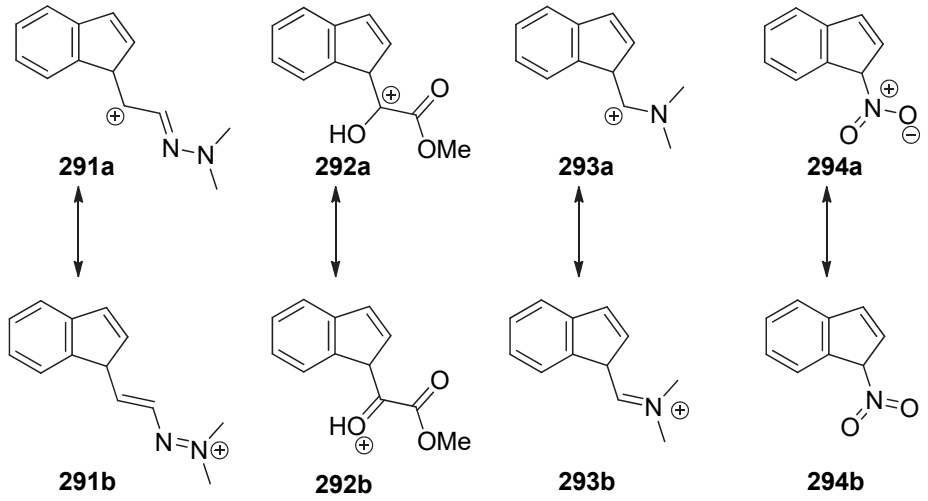
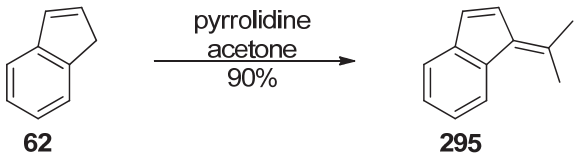


Figure 4.02: Resonance stabilisation of E_1 reaction intermediates.

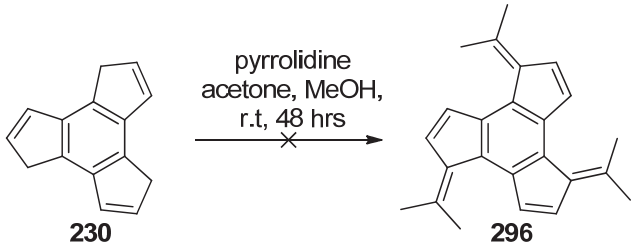
In addition to aryl aldehydes, indene has been shown to undergo condensation reactions with alkyl ketones such as acetone. The enhanced reactivity of alkyl ketones compared to alkyl aldehydes can be explained by the increased stability of the carbocation intermediate **289** (Scheme 4.19) since it is at a tertiary position in the case of a ketone. An alkyl ketone could be used in place of an aldehyde in the proposed synthesis of isocoronene (Scheme 4.07) and so this reaction was investigated. The optimal conditions for the reaction of indene with an alkyl ketone were reported by Stone and Little (Scheme 4.11).[138] The reported procedure was verified with indene **62** in place of trindene. A solution of indene, acetone and pyrrolidine in methanol was kept at room temperature for 48 hours. The crude product was then isolated with the ^{1}H NMR spectrum indicating 90% conversion to the desired benzofulvene **295**.



Scheme 4.20: Synthesis of **295**.

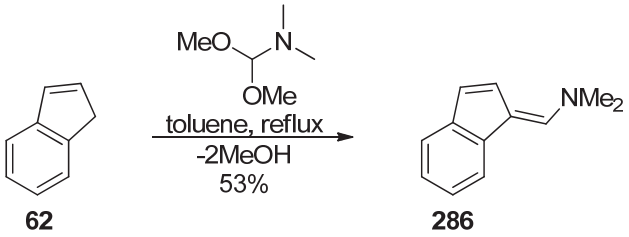
The same reaction conditions for the synthesis of benzofulvene **295** were applied to trindene, with the exception of reactant concentration. Trindene was found to have reduced solubility in methanol and so the reaction was run with greater dilution of

trindene. The concentration of reagents was however maintained. After workup of the reaction mixture, the ^{1}H NMR spectrum of the crude product showed trindene with no fulvene products detected. The difference in reactivity of trindene could be attributed to unfavourable steric interaction within the desired trifulvene **296**. The resonance stabilisation of trifulvene **296** requires a planar geometry. This would result in the methyl substituents being in close proximity to the adjacent ring system. As a result, the planar geometry of **296** is unfavourable and the reaction does not proceed.



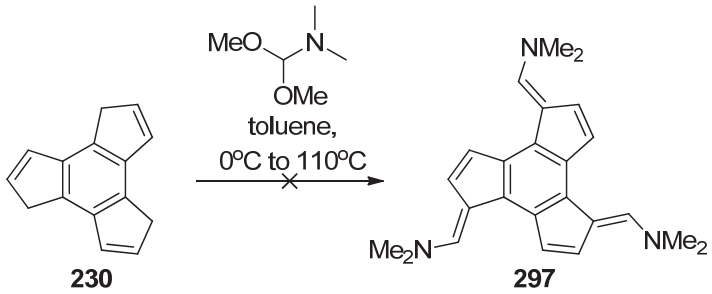
Scheme 4.21: Attempted synthesis of **296**.

The method developed by Hafner provides an alternative synthesis of alkyl fulvenes through a common dimethylamino fulvene intermediate **270** (Scheme 4.10). The synthesis of the benzofulvene analogue **286** has previously been reported through the condensation reaction of indene with the dimethyl acetal of DMF.[137] The Hafner fulvene synthesis could be applied to trindene to introduce the required alkyl side chain. Verification of the dimethylamino benzofulvene synthesis was conducted by following the literature procedure with slight modification.[137] A solution of indene and DMF acetal in toluene was heated under reflux for 18 hours. After workup and purification, a dark blue solid was isolated in good yield. The ^{1}H NMR spectrum of the product showed a singlet at 7.43 ppm which was assigned to the exocyclic fulvene position. Two doublets were observed at 6.84 and 7.07 ppm each with an integration of 1, assigned to the vinylic positions of the five membered ring. Three groups of multiplets were observed at 7.14, 7.49 and 7.61 ppm with integration of 2:1:1 respectively, assigned to the benzene ring.



Scheme 4.22: Synthesis of **286**.

The same reaction conditions used for the synthesis of **286** were applied to trindene towards the synthesis of **297**. A solution of trindene and DMF acetal in toluene was heated under reflux resulting in a rapid colour change from colourless to black. Analysis by TLC indicated consumption of starting material however no UV active product was detected. During workup of the reaction mixture no product could be isolated, indicating complete decomposition of trindene had occurred. The rate of decomposition could be reduced at lower reaction temperature and so the reaction was repeated at room temperature. At room temperature the reaction mixture gradually darkened with analysis by TLC indicating the starting trindene was less rapidly consumed. After 18 hours no UV active products were detected by TLC and the reaction was abandoned. The difference in the reaction outcome in comparison to indene could be explained by the presence of the adjacent ring systems of trindene. This could allow for an intramolecular side reaction leading to decomposition.



Scheme 4.23: Attempted synthesis of **297**.

The observed reactivity of indene and trindene towards electrophiles is summarised below. From these results it was concluded that condensation of trindene with an alkyl substituted electrophile was not feasible and so alternative route to isocoronene was investigated.

Electrophile	Base	Indene	Trindene
furfural	Dowex 550A	80% yield	77% yield
propanal	Dowex 550A	N.R	N.R
acetone	pyrrolidine	90% conversion	N.R
DMF acetal	None	53% yield	decomposition

Table 4.02: Reactivity of indene and trindene.

4.5 Nucleophilic addition to fulvenes

Fulvenes are known to react with nucleophiles at the exocyclic double bond. The reactivity can be explained through fulvene resonance structures. Resonance structure **279a** is a significant contributor since the π electrons from the exocyclic double bond are conjugated within the cyclopentadiene ring leading to aromatic stabilisation. This results in strong polarisation of the double bond and the observed reactivity of fulvenes towards nucleophiles.

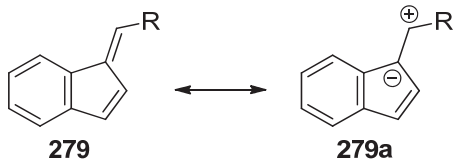
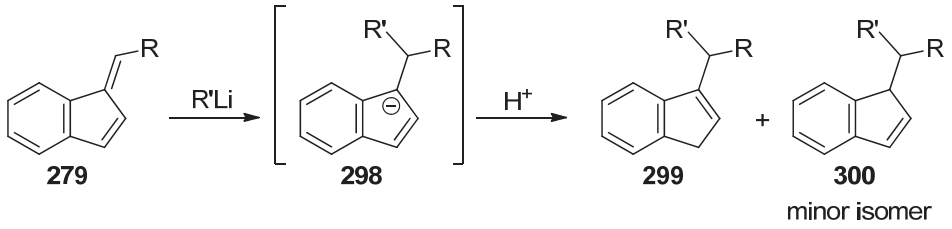


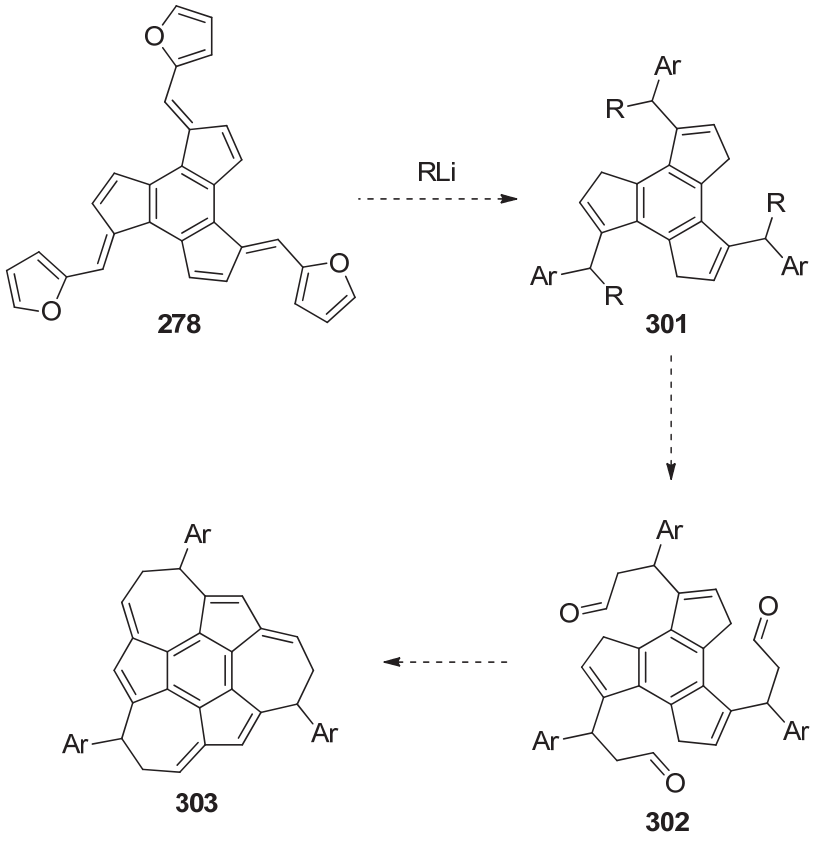
Figure 4.03: Resonance forms of **279**.

Benzofulvene derivatives have been reported to react with strongly nucleophilic organolithium reagents to yield alkylated indene with the general structure of **299**.[151, 152, 153, 154] The reaction proceeds through nucleophilic addition to the exocyclic double bond to form intermediate **298**. The reaction is thermodynamically favourable due to aromatic stabilisation of the anionic intermediate **298**. After the reaction is quenched the alkylated indene **299** is then formed almost exclusively as a single regioisomer with the alkyl substituent at the vinylic position.[153]



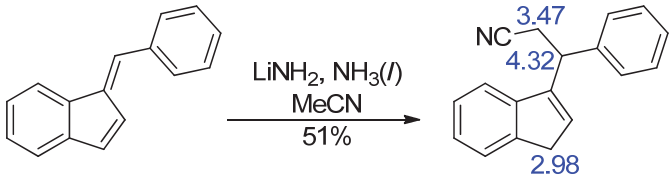
Scheme 4.24: Nucleophilic addition to benzofulvene.

The required carbon linking group could be introduced by nucleophilic addition to the trifulvene **278**. The nucleophile would require a two carbon chain since addition occurs at the exocyclic position of the fulvene. The nucleophile would require a functional group that is inert under the reaction conditions and could be converted to an aldehyde in a subsequent reaction. This would lead to the trialdehyde **302** which could be used in the ring closing reaction through intramolecular condensation to give **303**.



Scheme 4.25: Proposed synthesis of isocoronene ring structure.

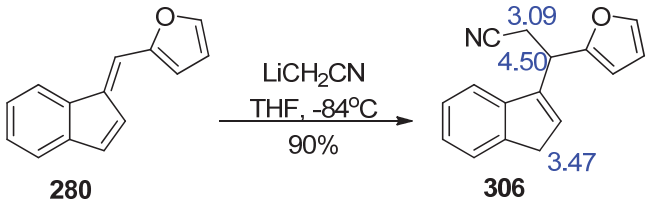
The trifulvene **278** could be expected to have similar reactivity to benzofulvene in nucleophilic addition reactions through the same reasoning introduced in Chapter 4.4 (Figure 4.01). A review of literature shows the nucleophilic addition to benzofulvene occurs with strong carbon nucleophiles such as organolithium reagents. The proposed synthesis (Scheme 4.25) requires the introduction of a functionalised alkyl group however literature examples primarily involve reactions with unfunctionalised alkyl lithium reagents. One notable exception is the reported reaction of lithiated acetonitrile with benzofulvene **304**.[155] Lithiated acetonitrile was prepared by addition of acetonitrile to a suspension of lithium amide in liquid ammonia at an unspecified reaction temperature. Benzofulvene **304** was then added to the reaction mixture and after 3 minutes the reaction was quenched. The crude product was isolated and then recrystallised from methanol to give the alkylated indene **305** in moderate yield.



Scheme 4.26: Nucleophilic addition to benzofulvene with reported ^{1}H NMR assignments (ppm).[155]

Lithiated acetonitrile is suitable as a two carbon nucleophile for the proposed synthesis of isocoronene since the nitrile group may be reduced to an aldehyde at a later stage. The reaction was investigated using the previously prepared benzofulvene **280** in place of the trifulvene **278**. The lithiated acetonitrile reagent was prepared by addition of *n*BuLi to a solution of acetonitrile in THF at -40 °C. The benzofulvene **280** was then added to the prepared solution of lithiated acetonitrile at -84 °C. The reaction was monitored by TLC showing rapid and complete conversion of the starting material to a single colourless product. The reaction was quenched and the product was isolated as a pale yellow oil in high yield. The ^{1}H NMR spectrum of the product showed three new signals in the aliphatic region consistent with the desired alkylation product. The aliphatic signals were observed at 4.50, 3.47 and 3.09 ppm with integration of 1:2:2 respectively. The integration ratio is consistent with the expected regiochemistry of the indene ring since the alternative isomer would have a total of 3 aliphatic protons. The signal at 4.50 ppm was assigned to the position

adjacent to the furan ring based on integration and multiplicity (1H, t, J = 7.2 Hz). The signal at 3.09 ppm appeared as a pair of overlapping doublets (1H+1H, d, J = 7.2 Hz) consistent with diastereotopic protons of the α-nitrile position. The aliphatic signal at 3.47 ppm was therefore assigned to the methylene position of the indene ring. The remaining signals in the aromatic region were consistent with the desired product, integrating to a total of 8 protons with the characteristic fulvene singlet absent. The alkyl signals observed for **306** are consistent with those reported for **305** however assignment of the methylene signals is reversed.[155] The coupling constants of **305** were not reported and so it is likely that the signal assignments were incorrect.



Scheme 4.27: Nucleophilic addition to benzofulvene with ^{1}H NMR signals assigned (ppm).

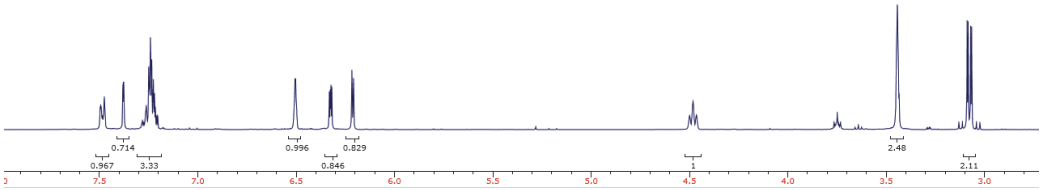
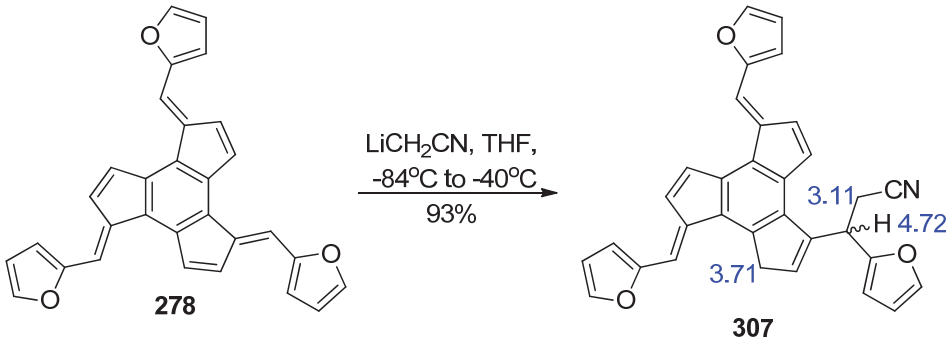


Figure 4.04: ^{1}H NMR spectrum of **306**.

Following the successful synthesis of **306**, the same reaction conditions were applied to the trifulvene **278**. Trifulvene **278** was added to a solution of lithiated acetonitrile at -84 °C with instantaneous colour change observed from yellow to an intensely coloured red solution. After 30 minutes the reaction mixture was quenched and the product was isolated as a red oil. Analysis by TLC indicated the consumption of starting material with the formation of a single product. The ^{1}H NMR spectrum of the product gave a large number of signals in the aromatic region which indicates a loss of symmetry. The desired addition reaction would introduce three new characteristic signals in the aliphatic region as observed for indene **306**. The expected signals were observed at 4.72, 3.71 and 3.11 ppm with integration of 1:2:2

respectively. These signals are comparable to indene **306** in terms of multiplicity, integration and chemical shift. One significant difference was observed for the α-nitrile signal which appeared as a doublet with integration of 2H. This indicates the diasterotopic protons are nearly equivalent and therefore superimposed. Relative to the aliphatic signals, the integration of the aromatic region indicated the addition reaction had occurred exclusively at one of the three fulvene positions and so the product was identified as **307**. The selective formation of the mono addition product could be attributed to the first nucleophilic addition reaction having a deactivating effect on the remaining two fulvene positions.



Scheme 4.28: Nucleophilic addition to trifulvene with ^{1}H NMR signals assigned (ppm).

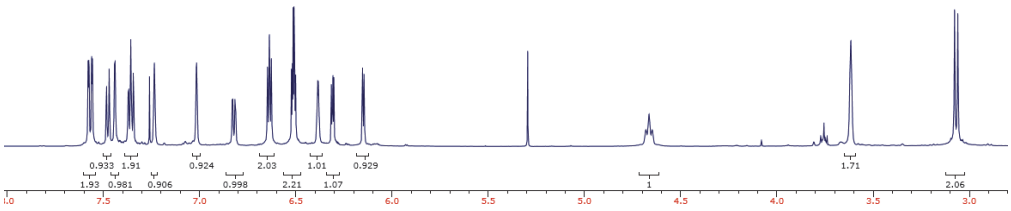
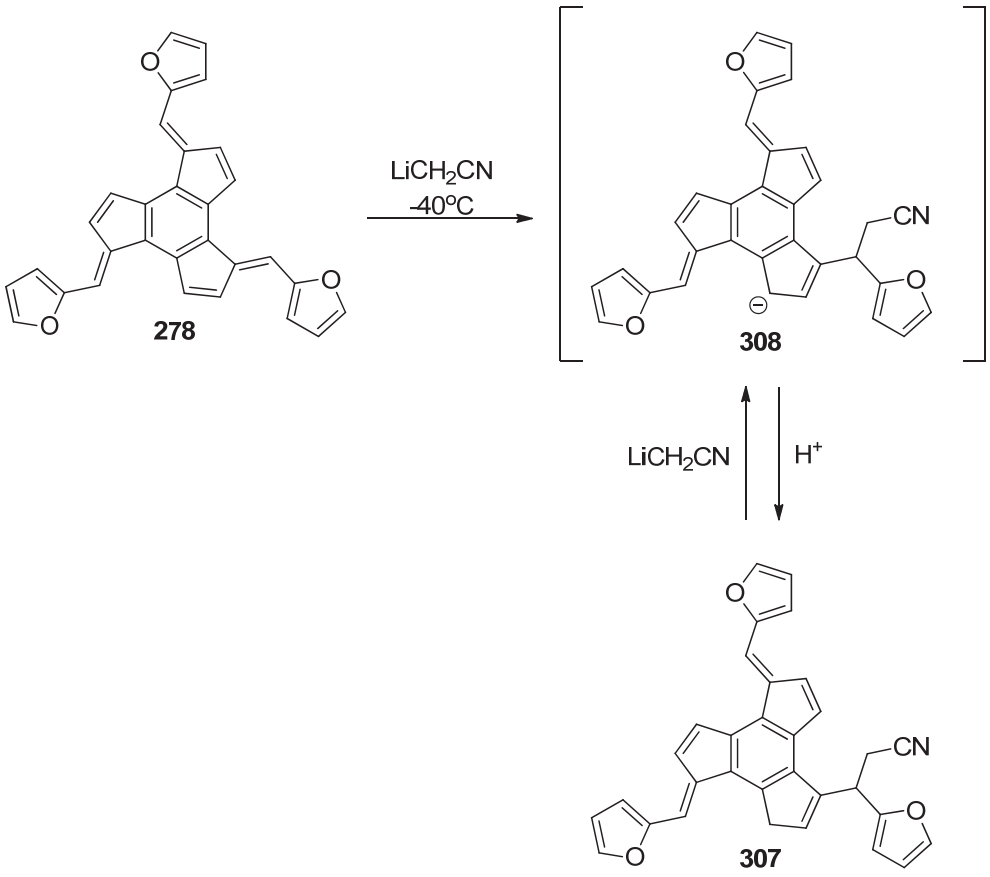


Figure 4.05: ^{1}H NMR spectrum of **307**.

The initial nucleophilic addition of lithiated acetonitrile to trifulvene **278** would lead to the anionic intermediate **308** which after quenching would yield the mono addition product **307**. The exclusive formation of the mono addition product indicates that the nucleophilic addition reaction does not proceed past intermediate **308** despite the presence of a large excess of lithiated acetonitrile. This must be attributed to deactivation of the remaining fulvene positions of **308** towards nucleophilic addition. Deactivation of the fulvene positions of **308** may be explained by the presence of a

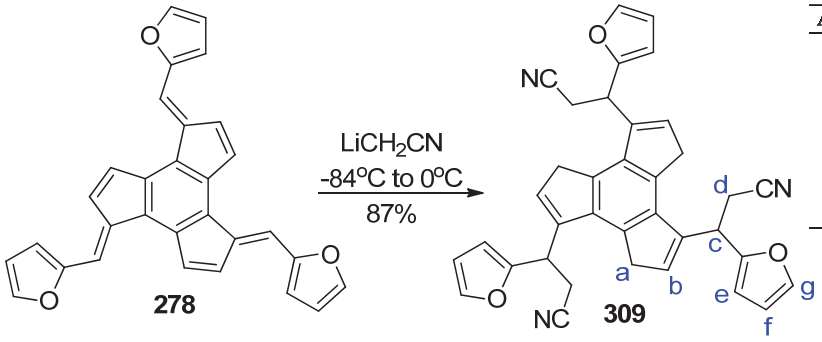
delocalised carbanion. The negative charge of **308** is delocalised through the entire fulvene structure which would greatly reduce reactivity towards a nucleophile. In addition, the negative charge would lead to electrostatic repulsion of the acetonitrile anion. The deactivating effect could be avoided by quenching the intermediate **308** prior to a subsequent nucleophilic addition. To this end, the mono addition product **307** was subject to the same reaction conditions with lithiated acetonitrile. The reaction was monitored by ^{1}H NMR which gave no indication of further nucleophilic addition. The lack of reactivity of **307** towards further addition indicates that lithiated acetonitrile is acting as a base in preference to the desired nucleophilic addition. Deprotonation of **307** would re-form the deactivated intermediate **293** and so further nucleophilic addition would not occur.



Scheme 4.29: Nucleophilic addition to trifulvene.

The deactivation of the first intermediate could be overcome with more forcing conditions such as higher temperature. This is limited by the decomposition of lithiated acetonitrile which is unstable at temperatures above -40 °C. Trifulvene **278**

was added to a large excess of lithiated acetonitrile and the reaction was gradually warmed to 0 °C. The reaction was monitored by TLC which indicated rapid consumption of the starting material followed by gradual consumption of the mono adduct. After 2 hours at 0 °C, the consumption of the mono adduct appeared almost complete by TLC. After workup, the product was isolated as a brown oil. The ^{1}H NMR spectrum showed four major signals in the aromatic region as multiplets with equal integration. These signals were assigned to the furan ring and vinylic position of the desired product **309**. The number of signals indicates the addition reaction had occurred at all three fulvene positions to give a symmetrically substituted product. Three additional signals were observed at 4.70, 3.58 and 3.07 ppm with respective integration of 1:1:3. These signals were assigned to the saturated positions of **309**. All of the signals appeared as broad multiplets which is consistent with the formation of three new stereocentres to give a mixture of three potential diastereomers. The signal at 3.07 ppm appeared as two overlapping multiplets which were assigned to the benzylic methylene and one of the diastereotopic α-nitrile protons. Additional complex signals with low intensity were attributed to unreacted intermediates, byproducts and acetonitrile decomposition products. Attempted purification of the product by silica gel chromatography was not successful and so the crude mixture was used in the subsequent step.



Assignment	δ
a	3.07
b	6.28
c	4.70
d	3.17 and 3.61
e	6.06
f	6.51
g	7.46

Scheme 4.30: Synthesis of **309** with ^{1}H NMR signals assigned (ppm).

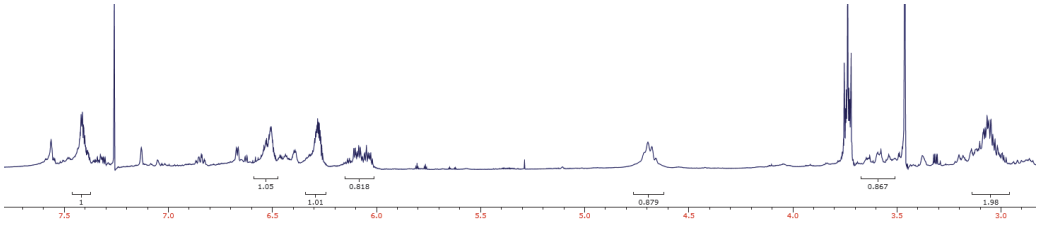
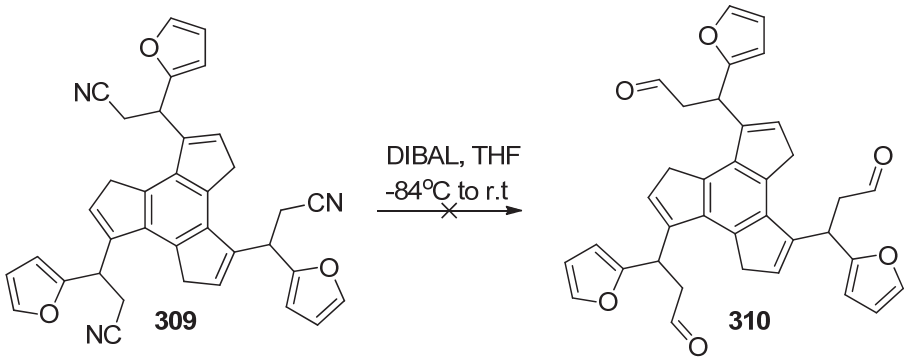


Figure 4.06: ^{1}H NMR spectrum of **309**.

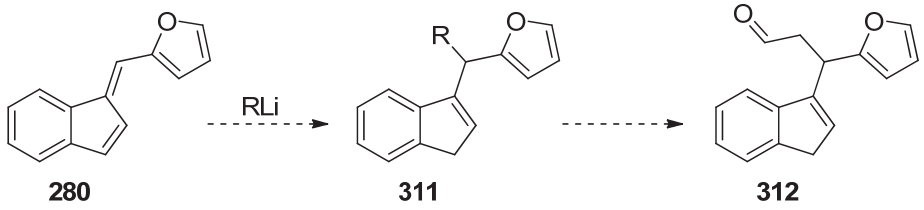
The desired aldehyde **310** could be synthesised by reduction of the nitrile **309** followed by hydrolysis of the imine intermediate. The selective reduction of a nitrile to an imine may be achieved using a stoichiometric amount of DIBAL at low temperature. Three equivalents of DIBAL were added to the nitrile at -84 °C and after two hours the reaction was worked up. The ^{1}H NMR spectrum was analysed which showed signals attributed to unreacted starting material with no additional signals observed. The absence of signals near 10 ppm indicates the desired aldehyde was not formed in significant amount. This result indicates the nitrile has low reactivity towards reduction and so the reaction was repeated with warming to room temperature. After workup the ^{1}H NMR spectrum showed primarily starting material with a minor signal at 9.81 ppm attributed to trace amount of an aldehyde. The relative integration of the signal at 9.81 ppm indicated 8% conversion to the aldehyde. The reaction was repeated with a large excess of DIBAL at room temperature overnight however the ^{1}H NMR spectrum indicated no further conversion to the aldehyde. Alternative methods for the conversion of a nitrile to aldehyde involve hydrogenolysis which is not compatible with the furan and so the reduction was not pursued further.



Scheme 4.31: Attempted synthesis of **310**.

The difficulty encountered with reduction of the nitrile **309** prompted an investigation of alternative aldehyde precursors. A series of test reactions was performed using benzofulvene **280** in place of trifulvene. The benzofulvene was used in place of the trifulvene since it is more readily prepared and the reaction outcome is not complicated by potential reaction intermediates. Organolithium and Grignard reagents have previously been reported to undergo nucleophilic addition to

benzofulvene derivatives.[156,153] Organolithium reagents were reported to give superior yield with shorter reaction time and so the use of Grignard reagents was not investigated.



Scheme 4.32: Model reaction sequence.

A series of functionalised organolithium compounds were synthesised to determine reactivity with benzofulvene **280**. The organolithium reagents would require a two carbon chain with a functional group that could be converted to an aldehyde at a later stage. The main limitation in the choice of functional group is the stability towards the strongly nucleophilic organolithium. Butyllithium was included in the results to compare the reactivity of an unfunctionalised organolithium reagent. Each reaction was monitored by TLC for loss of starting material followed by analysis of the ^{1}H NMR spectrum after workup. The results showed the addition reaction occurred with either lithiated acetonitrile or butyllithium to give complete conversion to the expected indene derivatives. In comparison, the remaining organolithium reagents were found to be completely unreactive with analysis of the reaction mixture showing starting material only. The low reactivity of some reagents could be explained by reduced nucleophilicity. In the case of unhindered primary organolithium reagents, the relative nucleophilicity can be approximated from the pK_a of the conjugate acid. The resonance stabilised negative charge of some organolithium reagents leads to a reduced pK_a and therefore relatively weak nucleophilicity. The difference in reactivity of lithiated acetonitrile compared to the unconjugated nucleophiles indicates the reactivity is not determined by pK_a alone. An alternative explanation for the observed differences in reactivity is the presence of strongly coordinating functional groups. The organolithium reagents found to be reactive include lithiated acetonitrile and butyllithium. The nitrile functional group is well known to have weak coordination through the nitrogen lone pair while the alkyl chain has no potential for coordination. In contrast, the unreactive organolithium

reagents possess carboxylate or ether functional groups which readily coordinate to lithium through the oxygen lone pairs. The reactivity of organolithium reagents is known to be strongly influenced by the formation of clusters which may arise through intermolecular coordination of lithium with functional groups.[157] Following these results the nucleophilic addition to trifulvene **278** was not further investigated due to the apparent limitations. Alternative organometallic nucleophiles such as organozinc or organomagnesium may exhibit greater reactivity however these were not trialled due to time constraints.

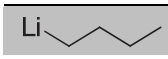
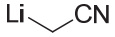
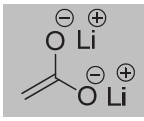
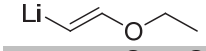
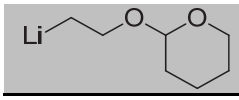
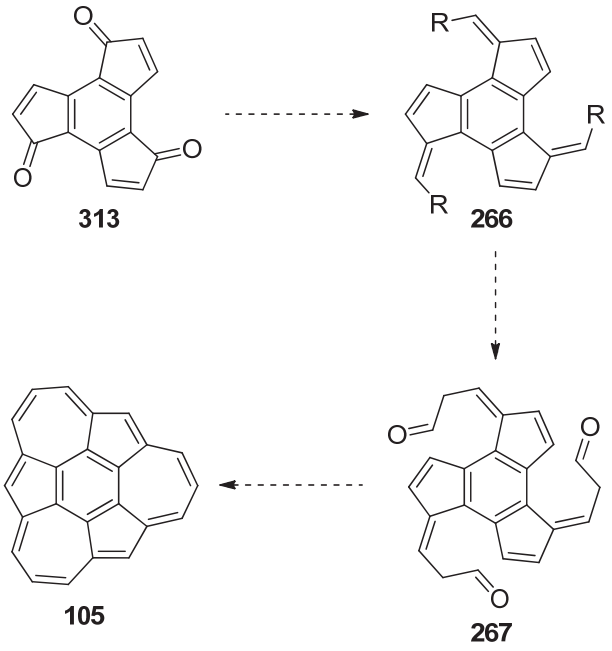
Organolithium	Reaction conditions	^{1}H NMR analysis
	-84°C, 30 minutes	100% conversion
	-84°C, 30 minutes	100% conversion
	THF, reflux	N.R.
	0°C	N.R.
	0°C	N.R.

Table 4.03: Reactivity of organolithium reagents towards benzofulvene **280**.

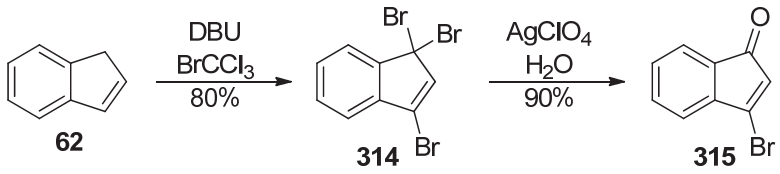
4.6 Trindenone

An alternative approach to the synthesis of trifulvenes is through the Knoevenagel condensation of trindenone **313**. This could allow the synthesis of alkyl trifulvene intermediate **267**, which would lead to isocoronene through an intramolecular condensation reaction.



Scheme 4.33: Proposed synthesis of isocoronene.

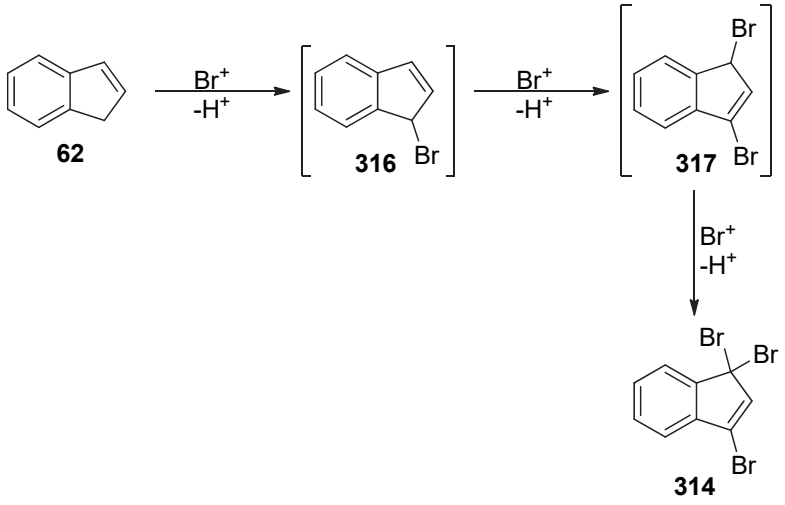
The trindenone structure has not previously been reported in literature however the structurally related bromoindenone **315** may be synthesised from indene in two steps. This reaction sequence could be applied to trindene for the synthesis of trindenone. The first step involves the bromination of indene **62** under basic conditions to give tribromoindene **299**.[158] The geminal dibromide position of **314** may be hydrolysed through the action of a soluble silver salt to give bromoindenone **315**.[159]



Scheme 4.34: Synthesis of bromoindenone.[159]

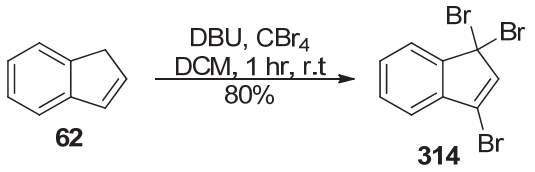
The electrophilic bromination of indene under basic conditions occurs through a stepwise mechanism.[158] In the first step, deprotonation occurs at the active methylene with subsequent bromine addition to give **316**. Intermediate **316** is then deprotonated and the bromination occurs with isomerisation of the alkene to give intermediate **302**. This regioisomer is favoured since bromination occurs at the less hindered position.

Deprotonation of intermediate **317** followed by a third bromination then yields tribromoindene **314**. Tribromoindene does not react further since the remaining protons are not acidic.



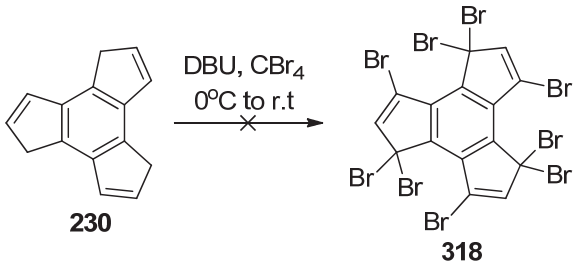
Scheme 4.35: Synthesis of tribromoindene.[158]

The reaction sequence was initially investigated using indene in place of trindene. The reported bromination procedure used $BrCCl_3$ as a source of electrophilic bromine. Since this reagent was not available, it was substituted for CBr_4. A solution of indene and CBr_4 in DCM was cooled to 0 °C and DBU was added dropwise. The reaction was monitored by TLC which indicated consumption of starting material after 30 minutes. The product was isolated from the reaction mixture and the ^1H NMR spectrum was analysed. The absence of a benzylic methylene signal indicated bromination of the five member ring had occurred. Two new singlets were observed at 6.84 and 6.83 ppm in addition to 3 multiplets in the aromatic region. The integration ratio was measured as 1:3:1:2:1 respectively. This is consistent with reported data for **314** with the singlet at 6.84 ppm assigned to the vinylic position.[158] The additional singlet at 6.83 ppm was attributed to bromoform which is produced as a byproduct of the reaction.



Scheme 4.36: Synthesis of tribromoindene.

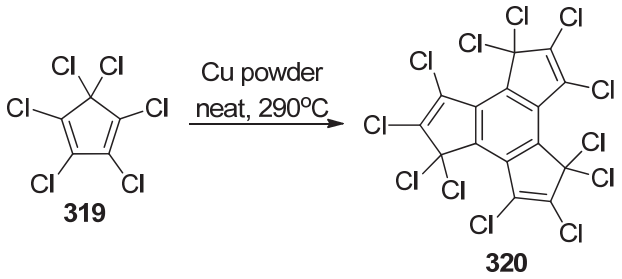
The reaction conditions used for the synthesis of tribromoindene **314** could be applied in the synthesis of the brominated trindene **318**. DBU was added dropwise to a solution of trindene and CBr_4 at 0°C. The reaction mixture rapidly changed from colourless to dark brown during addition of DBU. After addition was complete the black reaction mixture was filtered through celite to remove the insoluble material. The solvent was then removed to yield pale yellow crystalline material. The ^1H NMR spectrum of the crude product was analysed showing a singlet at 6.83 ppm as the only major signal. The singlet could be assigned either to the vinylic position of the desired product or to the bromoform byproduct. The ^{13}C NMR spectrum was analysed with one signal observed at 9.9 ppm, consistent with bromoform. Since bromoform is a liquid at room temperature, the crystalline material isolated from the reaction mixture was attributed to unreacted CBr_4 which gives an upfield ^{13}C NMR signal outside the measured range. The absence of any aromatic signals indicates that trindene has decomposed under the reaction conditions to form an insoluble black material. The reaction was repeated at lower temperatures (-84 to -20°C) and monitored by ^1H NMR during addition of DBU. At lower temperature the rate of decomposition decreased however unreacted trindene and bromoform were the only compounds detected in the ^1H NMR spectrum. The difference in reaction the outcome for trindene and indene must be attributed to differences in geometry since the electronic properties are similar. Bromination of the benzylic positions of trindene could be unfavourable due to close proximity of the adjacent bromide substituents. In comparison, the radical benzylic bromination of trindane to yield hexabromotrindane **224** (Scheme 3.06) was successful however the planar geometry of trindene may lead to unfavourable steric interaction of the bromide substituents. Following this result, an alternative approach to halogenated trindene was investigated.



Scheme 4.37: Attempted synthesis of **318**.

4.7 Perchlorotrindene

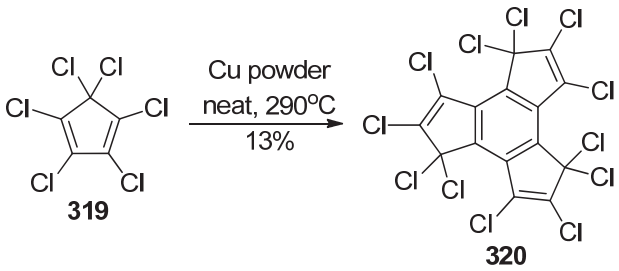
The synthesis of perchlorotrindene **320** has previously been reported from the trimerisation of perchlorocyclopentadiene **319**.[160] The synthesis of **320** was originally reported in 1955 by McBee however the product was incorrectly identified as perchlorofulvalene.[161] The correct structure was later assigned although the correct regioisomer was not confirmed.[162] Final structural assignment of perchlorotrindene was provided by analysis of the ^{13}C NMR spectrum which indicated the compound exists as a single regioisomer with rotational symmetry.[163] The general method for the synthesis of perchlorotrindene involves heating neat perchlorocyclopentadiene **319** at 290 °C for 18 hours in the presence of copper powder. Perchlorocyclopentadiene was then isolated from the crude reaction mixture by trituration and recrystallisation using a solvent such as xylene to give **320** in unspecified yield.[163]



Scheme 4.38: Synthesis of **320**.[163]

Perchlorotrindene was synthesised according to previously reported reaction conditions.[160] A mixture of copper powder and perchlorocyclopentadiene **319** was

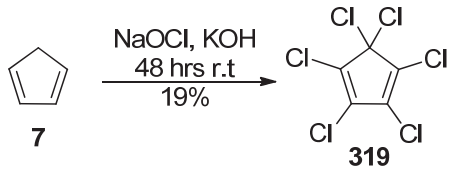
heated at 280°C for 2 hours followed by heating at 290°C for 18 hours. The dark viscous reaction mixture was then cooled to 100°C and diluted with xylene. After cooling to room temperature the precipitate was collected and washed with hexanes. The precipitate was then dissolved in hot DCM and filtered through celite. The filtrate was then concentrated to give a light yellow solid in low yield. The product was slightly soluble in $CDCl_3$ with the ^{13}C NMR spectrum showing five signals consistent with the reported spectrum for perchlorotrindene.[163] Further investigation into the reactivity of perchlorotrindene would require access to perchlorocyclopentadiene however this material was not commercially available due to restrictions on importation. This prompted an investigation into the synthesis of perchlorocyclopentadiene.



Scheme 4.39: Synthesis of **320**.

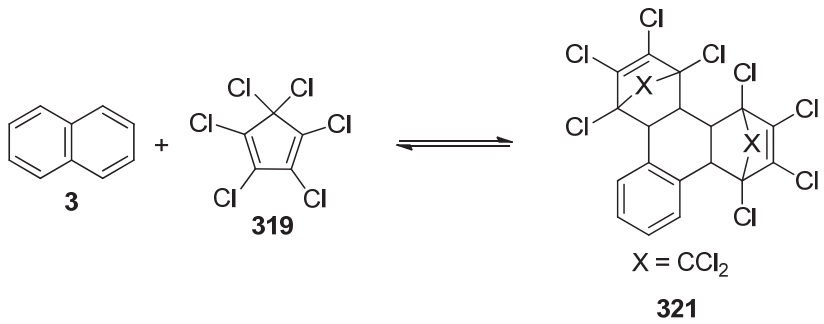
A review has been published which details the various methods of preparing perchlorocyclopentadiene **319**.[164] The most convenient commercial scale preparation involves the radical chlorination of pentane at high temperature however this was not feasible. An alternative lab scale preparation was reported by Straus *et al* in the original synthesis of perchlorocyclopentadiene.[165] The reported synthesis involves the chlorination of cyclopentadiene by reaction with sodium hypochlorite under basic conditions. Following this procedure, a solution of freshly distilled cyclopentadiene in petrol was vigorously stirred with an aqueous solution of sodium hypochlorite. After 48 hours the organic material was isolated as a yellow oil. The ^{13}C NMR spectrum showed the presence of perchlorocyclopentadiene in addition to a significant quantity of unidentified byproducts. The crude product was purified by vacuum distillation to yield a pale yellow oil in low yield. The ^{13}C NMR spectrum of the distillate showed perchlorocyclopentadiene as the major compound however a significant amount of impurities remained after distillation. Improvements on the

original procedure have been reported.[164] In particular, the addition of catalytic sodium sulfamate was reported to suppress side reactions and reduced the reaction time to only 20 minutes.[166] This modification was not investigated in favour of an alternative route to perchlorocyclopentadiene.



Scheme 4.40: Chlorination of cyclopentadiene.

An alternative source of perchlorocyclopentadiene **319** is from the naphthalene-bis(perchlorocyclopentadiene) adduct **321**. The retro Diels Alder reaction of the adduct produces perchlorocyclopentadiene and naphthalene. This was investigated as a source of perchlorocyclopentadiene since the adduct **321** is commercially available and not regulated for shipping.[167]

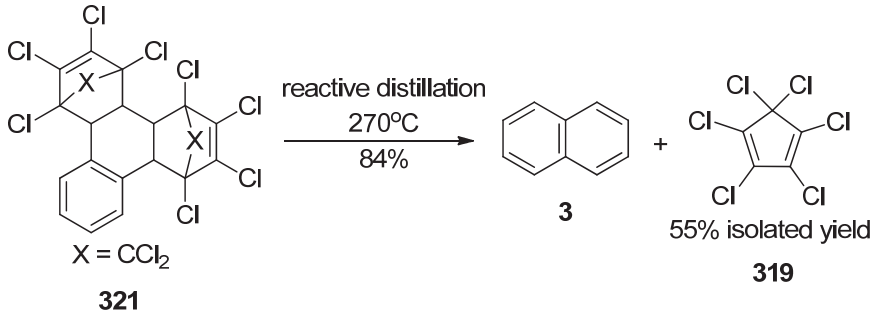


Scheme 4.41: Reversible Diels Alder reaction.

The Diels Alder reaction between perchlorocyclopentadiene and naphthalene is an equilibrium reaction in which the reaction rate and equilibrium constant are dependent on temperature.[168] The retro Diels Alder reaction is favoured at temperatures above 165 °C with rapid dissociation occurring at 300 °C. A sample of solid **321** was heated to 270 °C with distillation under a moderate vacuum (~40 mmHg). The distillate was collected as a semi-crystalline oil in high yield. The ^{13}C NMR spectrum of the distillate indicated a mixture of perchlorocyclopentadiene and naphthalene.

Separation of the mixture could be achieved by vacuum distillation since the boiling point of perchlorocyclopentadiene (239 °C) and naphthalene (218 °C) are significantly different. The mixture was therefore distilled under vacuum (1 mmHg) and the first fraction was analysed by ^{13}C NMR. The observed signals indicated the presence of perchlorocyclopentadiene and naphthalene in approximately the same ratio as the crude mixture. The co-distillation of the two components indicates the mixture exists as an azeotrope.

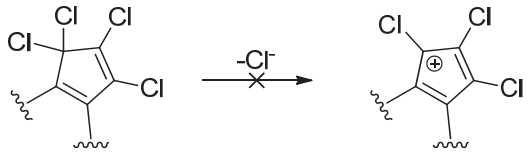
During vacuum distillation of the mixture through a Vigreux column, a white solid was found to crystallise on the walls of the column. The solid was isolated and analysis by ^{13}C NMR showed the presence of naphthalene with a trace amount of perchlorocyclopentadiene. This provided an alternative method for removal of naphthalene from the mixture. The mixture was slowly distilled under vacuum (1 mmHg) through a Vigreux column with the crystallised material removed from the column periodically. After crystallisation was no longer observed, the remaining material was distilled as before. The ^{13}C NMR spectrum of the distillate showed perchlorocyclopentadiene as the major component with approximately 5 mol% naphthalene, estimated from the relative integration of ^{13}C NMR signals corresponding to the fully substituted sp^2 carbon positions. This procedure was conducted on 50 g batches to produce 22 g of perchlorocyclopentadiene in 55% yield. This procedure allowed access to a sufficient quantity of perchlorocyclopentadiene which could be used in the preparation of perchlorotrindene.



Scheme 4.42: Thermolysis of **321**.

Following the synthesis of perchlorotrindene, the desired trindenone structure could be synthesised by hydrolysis of the geminal dichloro positions. Perchlorotrindene

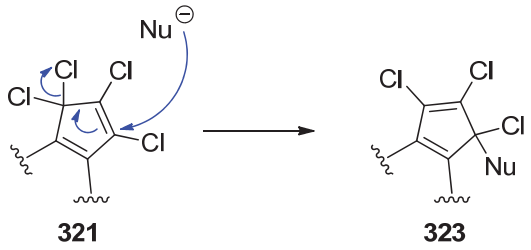
320 has been reported to react with a solution of silver nitrate in ethanol.[163] The reaction was noted to proceed slowly, requiring prolonged heating under reflux. The reaction was used only for the qualitative identification of labile chloride substituents and so characterisation of the product and the yield were not provided. The reaction is similar to the hydrolysis of tribromoindene **314** to yield bromoindenone **315** (Scheme 4.34) and so the product would presumably be the desired perchlorotrindenone **324**. In contrast to **320**, tribromoindene **314** is rapidly hydrolysed to give bromoindenone **315** at room temperature. The low reactivity of the geminal dichloride groups of **320** towards hydrolysis may be explained by considering the mechanism of the initial nucleophilic substitution reaction. One of the potential mechanisms for hydrolysis of **320** is the S_N1 mechanism which could be favoured due to steric hindrance of the geminal dichloride positions. The first step of the S_N1 mechanism is the formation of a carbocation intermediate **322** through loss of a chloride anion. The carbocation intermediate **322** is strongly destabilised due to the anti-aromatic (4n π) electron configuration within the five membered ring. As a result of anti-aromatic destabilisation, the initial formation of carbocation **322** is unfavourable and therefore the S_N1 reaction mechanism unlikely to occur.



Scheme 4.43: Formation of the anti-aromatic carbocation.

Alternatively, the hydrolysis of **320** may occur through an S_N2 reaction mechanism. This would avoid the anti-aromatic carbocation intermediate and therefore the mechanism is thermodynamically favourable. In contrast to the S_N1 mechanism, steric hindrance is a key factor in reactions which proceed through an S_N2 mechanism. Due to steric hindrance, the S_N2 reaction is unlikely to occur through direct substitution at the geminal dichloride position of **321**. The issue of steric hindrance could be alleviated if the reaction proceeded through an S_N2' reaction mechanism. Through the S_N2' reaction mechanism, the nucleophile reacts at the vinyl chloride positions with the concurrent shift of the alkene position and elimination of a chloride anion. In comparison to the geminal dichloride position, the

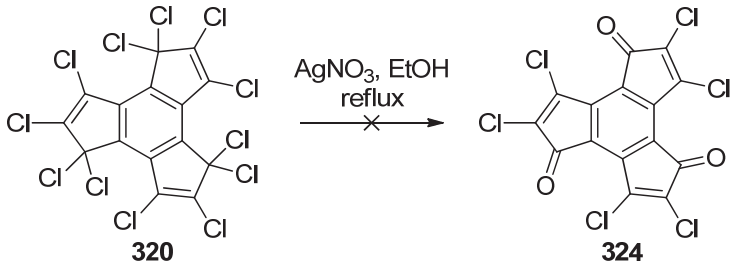
vinyl chloride position is far less hindered due to the trigonal planar geometry. As a result, the nucleophilic substitution of perchlorotrindene **320** would be likely to occur through an S_N2' mechanism since the alternatives are unfavourable. The reduced reactivity of **320** could therefore be attributed to the steric environment surrounding the benzylic vinyl chloride positions. The same mechanistic reasoning could be applied to the hydrolysis reaction of tribromoindene **314** (Scheme 4.34). It could therefore be concluded that hydrolysis of **314** would occur primarily through an S_N2' reaction mechanism. Therefore the greater reactivity of **314** could be attributed to reduced steric effects at the benzylic vinyl halide position due to the absence of the adjacent ring system present in perchlorotrindene.



Scheme 4.44: Proposed S_N2' reaction mechanism.

Following the previously reported reaction conditions, perchlorotrindene was added to a solution of silver nitrate in ethanol.[163] After heating under reflux, a very slow colour change was observed from colourless to yellow. After 48 hours the starting material was consumed with the formation of a strongly yellow coloured product. The reaction mixture was filtered through a short plug of silica gel and the eluent was concentrated to yield a yellow solid. The ^{13}C NMR spectrum of the product showed numerous signals indicating a mixture of products had formed. A group of three signals between 180.7 and 183.4 ppm were assigned to the desired ketone functional group. Two groups of signals in the ranges of 59.6 to 60.1 ppm and 15.2 to 15.6 ppm were assigned to alkyl substituents, attributed to the formation of a diethyl acetal. The acetal may form through reaction of ethanol with either the starting material or through condensation with the ketone position of the desired product. The presence of an acetal was supported by a group of signals between 104.8 and 105.4 ppm, subsequently assigned to the benzylic acetal position. The presence of ethoxy substituents was further verified by the ^{1}H NMR spectrum which showed two groups

of multiplets in the range of 3.18 to 3.50 ppm and 1.17 to 1.23 ppm with integration of 2:3 respectively. In addition to the ethyl acetal signals, the ^{1}H NMR spectrum showed signals at 4.88 ppm (q, J = 7.2 Hz) and 1.59 ppm (t, J = 7.2 Hz) with integration of 2:3 respectively. These signals were attributed to an ethyl vinyl ether functional group. A similar functional group transformation has been reported for the reaction of sodium methoxide with perchlorocyclopentadiene to give dimethyl acetal and methyl vinyl ether products.[169] Following this result, an attempt was made to hydrolyse the acetal groups to give the desired trindenone. The crude product was dissolved in a mixture of acetone and concentrated HCl followed by heating under reflux. The reaction was monitored by ^{13}C NMR which indicated the acetal groups were not hydrolysed after extended reaction time. The stability of the acetal groups towards acidic hydrolysis is comparable to the hydrolytic stability of perchlorotrindene **320** and may be explained through the same mechanistic reasoning. Following this result it was concluded that ethanol is unsuitable as a solvent in the hydrolysis of perchlorotrindene.

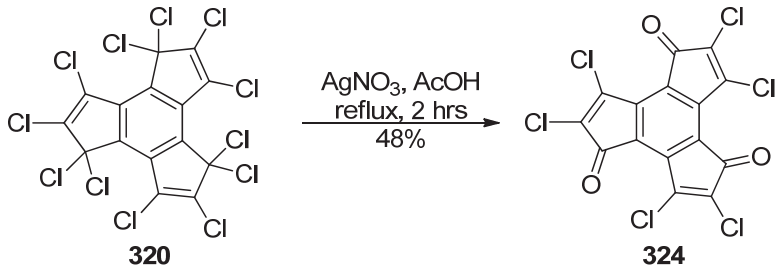


320 **324**

Scheme 4.45: Hydrolysis of perchlorotrindene.

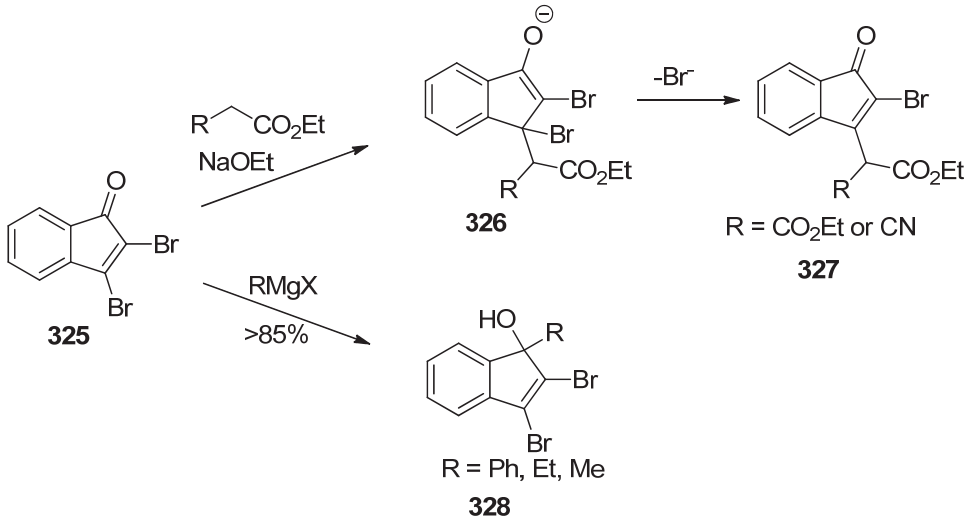
The formation of diethyl acetal products from the hydrolysis of perchlorotrindene was attributed to the nucleophilic reactivity of the solvent. Using a non-nucleophilic solvent would therefore reduce the potential for side reactions. In addition to nucleophilicity, the major limiting factor in the choice of reaction solvent was the required solubility of both silver nitrate and perchlorotrindene. The use of acetone as the reaction solvent was initially considered since it was previously used in the hydrolysis of tribromoindene **314**. A solution of silver nitrate in acetone was added to perchlorotrindene and the reaction mixture was heated under reflux. After 48 hours, no reaction was detected by TLC and so the reaction was abandoned.

Acetic acid was considered next as a reaction solvent since the relatively high boiling point would allow a higher reaction temperature. Similar to ethanol, acetic acid is a weak nucleophile which could lead to the formation of an acetate derived acetal. Unlike the previously observed diethyl acetal, the acetate acetal could undergo hydrolysis through reaction at the carbonyl position of the acetate to give the desired benzylic ketone. This mode of hydrolysis would occur more readily since it avoids the formation of a destabilised carbocation intermediate and is not inhibited by steric effects (Scheme 4.43). Accordingly, a mixture of perchlorotrindene and silver nitrate in acetic acid was heated under reflux. As the reaction temperature reached 100 °C, a rapid colour change was observed from colourless to intense yellow. The reaction was monitored by TLC which indicated complete consumption of the starting material with the formation of a yellow product after 2 hours. The reaction mixture was then filtered through celite and the yellow filtrate collected. The filtrate was then diluted in water and extracted with DCM to give an orange solid in low yield. The aqueous layer and the filter cake remained strongly coloured however further extraction with organic solvents did not provide additional product. The use of sodium carbonate solution to wash the organic extract caused a rapid colour change from yellow to dark brown. This was attributed to partial decomposition of the product under basic conditions. The isolated product was found to have low solubility in both $CDCl_3$ and acetone while addition of DMSO led to a rapid colour change from yellow to black, indicating decomposition. As a result the ^{13}C NMR spectrum could not be obtained since a suitable NMR solvent was not available. Analysis of the IR spectrum showed a strong signal at 1722 cm^{-1}, consistent with the formation of the desired ketone **324**. Further characterisation was not possible and so the product was carried through to the next step.



Scheme 4.46: Synthesis of trindenone.

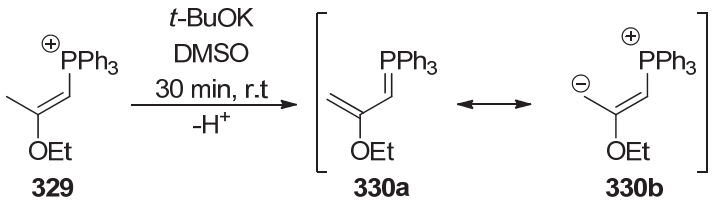
The nucleophilic addition to an enone such as trindenone may occur through a 1,2 addition directly to the carbonyl group or through a Michael addition. The regioselectivity for the addition could be predicted from the electronic properties of the nucleophile. The 1,2-addition would be favoured with a hard nucleophile while a soft nucleophile would favour the 1,4-addition. This trend in reactivity has been reported in the reaction of dibromoindenone **307** with carbon nucleophiles.[170, 171, 172, 173] Liebermann has shown the enolates of malonic and cyanoacetic esters react through a 1,4 addition-elimination mechanism to yield the substituted indenones **327** in unspecified yield. In contrast, Simonis reported reaction of **325** with Grignard reagents to give the tertiary alcohols **328** through 1,2 nucleophilic addition. It could be expected that perchlorotrindenone **324** would have the same reactivity towards nucleophiles.



Scheme 4.47: Reactivity of indenone towards nucleophiles.

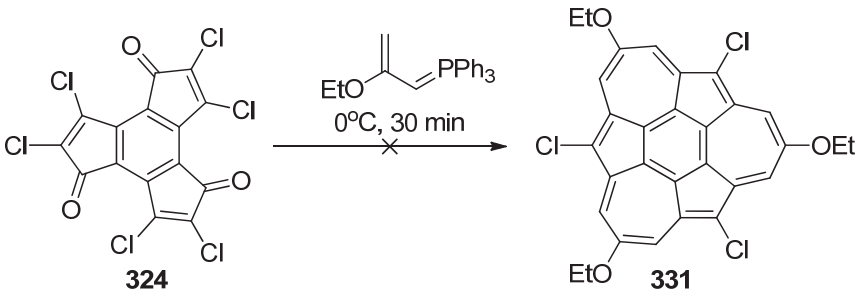
The reaction of trindenone **324** with a soft nucleophile was first explored. The conjugated Wittig reagent **330** has previously been used as a three carbon linking group for the annulation of a cyclic enone.[174, 175] The resonance structures of **330** indicate the terminal carbon would act as a soft nucleophile in the Michael reaction. In addition, the triphenylphosphonium group is able to participate in the Wittig reaction with the ketone to form an alkene bond. This allows for both ends of the carbon chain to participate in bond forming reactions. This allows the annulation of

enones by linking 1 and 4 carbon positions. This reagent could be used for introducing the three carbon linking chain to perchlorotrindenone **324**.



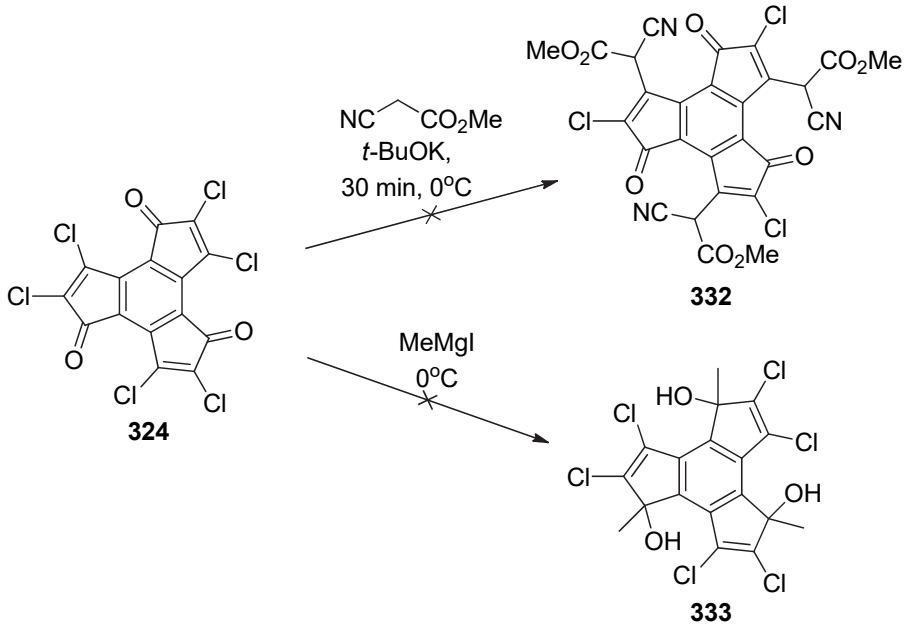
Scheme 4.48: Preparation of Wittig reagent.

Isocoronene **331** could be synthesised by annulation of trindenone with the Wittig reagent **330**. The Wittig reagent was generated by addition of phosphonium salt **329** to a solution of *t*-BuOK in THF. A solution of trindenone was then added at -84 °C. A rapid colour change to red to and then very dark purple was observed. Analysis of the reaction mixture by TLC indicated consumption of the starting material. The reaction mixture was then quenched resulting in a colour change from dark purple to black with the formation of dark insoluble material. After workup, the ^{1}H NMR spectrum was analysed. The desired isocoronene **331** has six equivalent vinylic protons which would be observed as a singlet in the ^{1}H NMR spectrum. Several multiplets were observed in the aromatic region at 7.43 to 7.78 ppm however these signals were attributed to triphenylphosphine byproducts. The crude product was purified by silica gel chromatography however no reaction products attributed to trindenone were isolated. The absence of reaction products indicates decomposition of the starting material and so alternative nucleophiles were considered.



Scheme 4.49: Attempted synthesis of **331**.

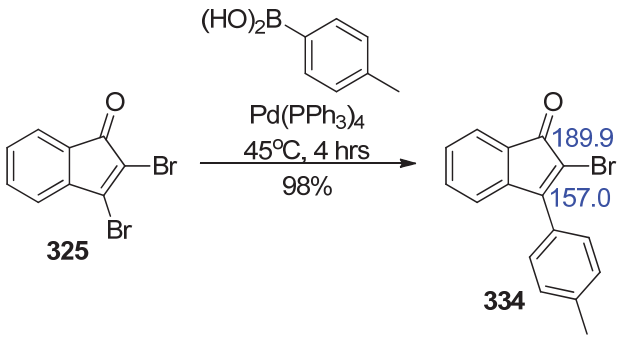
The reactivity of perchlorotrindenone towards other carbon nucleophiles was investigated next. The structurally related dibromoindenone **325** has previously been shown to react with a Grignard reagent or with a cyanoacetate ester (Scheme 4.47) and so these reactions were applied to trindenone **324**. A solution of the trindenone was cooled to -84 °C and methylmagnesium iodide was then added. After addition of the Grignard reagent, the reaction mixture changed colour from yellow to dark brown. After 30 minutes, the reaction mixture was analysed by TLC which indicated decomposition had occurred. The reaction of perchlorotrindenone with methyl cyanoacetate was examined next. The nucleophile was first generated by addition of methyl cyanoacetate to sodium hydride. The resulting solution was cooled to -84 °C and perchlorotrindenone was added. The reaction mixture changed colour to dark brown with TLC indicating decomposition had occurred. The decomposition of trindenone in each of the attempted reactions could be attributed to a low stability under basic conditions. These results prompted an investigation into alternative bond forming reactions under non-basic reaction conditions.



Scheme 4.50: Reactivity of trindenone towards nucleophiles.

An alternative approach to the introduction of an alkyl chain is through a metal catalysed cross coupling reaction. Coupling reactions may be conducted under mildly basic conditions which could minimise the decomposition of the trindenone. The

Suzuki coupling of dibromoindenone **325** has been reported using a series of aryl boronic acids to give monosubstituted indenone **334** in excellent yields.[176, 177] The coupling reaction occurs selectively at the electron deficient vinyl bromide resulting in excellent regioselectivity. The Suzuki coupling reaction could be applied to trindenone **324** to introduce the required three carbon linking group.



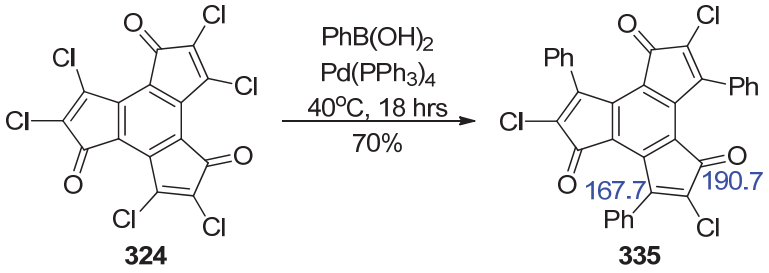
Scheme 4.51: Suzuki coupling of dibromoindenone with selected ^{13}C NMR signals assigned.[177]

The Suzuki coupling of trindenone **324** was initially investigated using phenylboronic acid. A mixture of trindenone and phenylboronic acid in dioxane was degassed and $Pd(PPh_3)_4$ was added resulting in a colour change to dark green. An aqueous solution of K_2CO_3 was then added and the mixture heated to 40 °C. After 18 hours the reaction mixture was worked up and the crude product was isolated by silica gel filtration. The orange eluent was collected to yield a red solid which was fully soluble in $CDCl_3$. Analysis by TLC indicated the starting material had been consumed with the formation of a single yellow product.

The ^1H NMR spectrum showed a series of complex multiplets (7.75 to 7.00 ppm) as the only significant signals detected. These signals were attributed to phenyl groups derived from phenylboronic acid. Two impurities that may be present are phenylboronic acid and biphenyl however comparison to literature spectra indicated these compounds were not present in detectable amount.

The ^{13}C NMR spectrum showed a signal at 190.7 ppm which was assigned to the carbonyl position of the trindenone product. A second signal at 155.0 ppm was assigned to the vinylic γ-carbonyl position of **335** which is characteristic of the enone structure. These signals are comparable to the reported ^{13}C NMR spectrum for indenone **334**. The presence of a single carbonyl signal in the ^{13}C NMR spectrum is

consistent with the symmetrical structure of **335**. The symmetrical structure of **335** has a total of 33 carbon atoms with 11 non-equivalent carbon atoms present. In comparison, the number of signals observed in the ^{13}C NMR spectrum is significantly greater than 11. This may be attributed to rotational restriction about the single bond of the phenyl substituent. Due to the surrounding steric environment, the phenyl substituents of **335** would be perpendicular to the plane of the trindenone ring system since the planar conformation is unfavourable. This would lead to the presence of rotamers due to the high rotational energy barrier about the single bond of the phenyl substituents. The potential for rotamers of **335** would explain the complexity of ^{1}H NMR and ^{13}C NMR signals attributed to the phenyl substituents. The synthesis of **335** demonstrates the feasibility of introducing a side chain through a cross coupling reaction. The coupling reaction could therefore be used to introduce a 3 carbon linking chain towards the formation of the isocoronene ring system. Due to time constraints, further work towards the synthesis of isocoronene was not attempted.



324 **335**

Scheme 4.52: Suzuki coupling of perchlorotrindenone with selected ^{13}C NMR signal assignments.

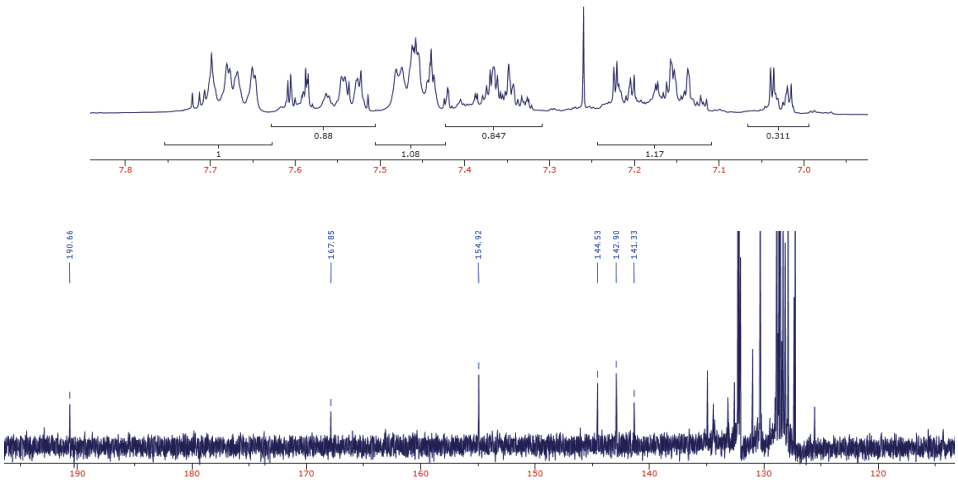


Figure 4.08: ^{1}H NMR and ^{13}C NMR spectra of **335**.

Chapter 5

Conclusions

Isocoronene **105** represents a unique group of non-alternant corannulenes in which the peripheral ring is isolated from the central benzene ring by formal single bonds. The fixed conjugated circuit opens the potential for superaromaticity, an elusive type of aromaticity which has not yet been demonstrated in any known compound. The aromaticity of isocoronene has been studied computationally however the results are inconsistent. The synthesis of isocoronene would allow for characterisation of its physical properties, providing decisive evidence towards aromaticity.

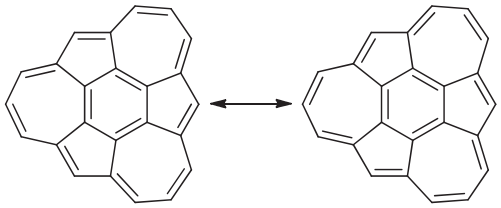
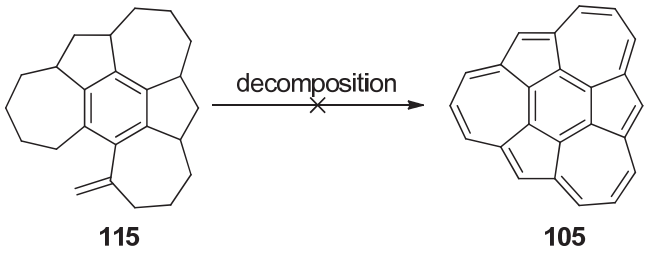


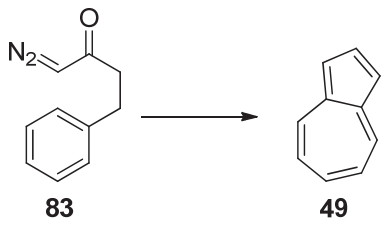
Figure 5.01: Isocoronene resonance structures.

The structures of non-alternant PAHs such as isocoronene provide synthetically challenging targets due to the presence of odd numbered ring systems. There has been one attempted synthesis of isocoronene reported by Hellwinkel in 1985. The synthetic approach involved a 17 step annulation sequence of a central benzene ring with the final ring closing of **115** resulting in decomposition in every attempt. The analysis of alternative synthetic strategies which have been successful in the synthesis of the structurally related azulene and azupyrene could therefore provide valuable leads towards the synthesis of isocoronene.



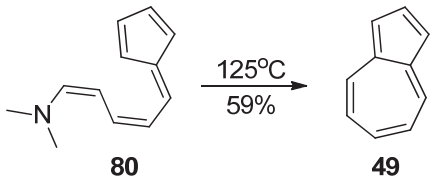
Scheme 5.02: Attempted synthesis of isocoronene.

One of the ring forming strategies involves the stepwise annulation of a benzene ring, followed by a Buchner ring expansion. This reaction sequence has been applied to the synthesis of vetivazulene by Plattner and in the Anderson synthesis of azupyrene. The Scott synthesis of azulene **49** gave significant improvement in yield by combining the annulation and ring expansion in a single step through an intramolecular Buchner reaction of diazoketone **83**.



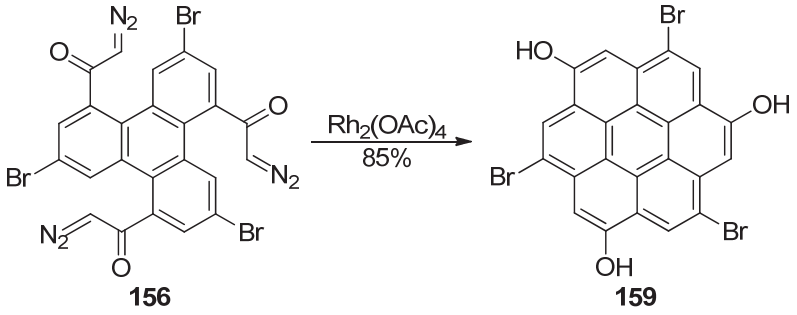
Scheme 5.03: Scott synthesis of azulene.

A second ring forming strategy involves the annulation of a five membered cyclopentadiene ring to form an azulene ring system. This is achieved through the synthesis of the dimethylaminofulvene **80** followed by intramolecular condensation to azulene **49**. This strategy was used in the Jutz synthesis of azupyrene and in the Ziegler-Hafner synthesis of azulene.



Scheme 5.04: Ziegler-Hafner synthesis of azulene.

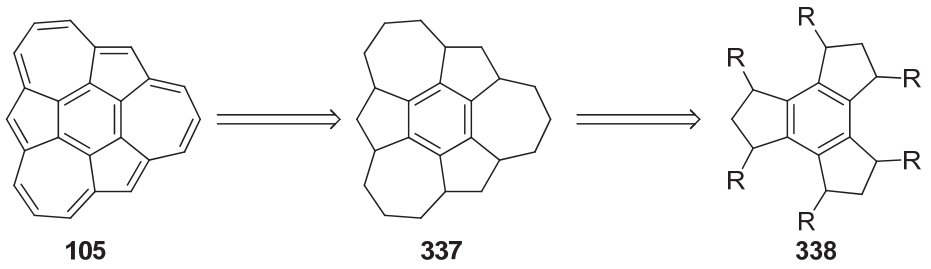
The initial synthetic approach towards isocoronene utilised the intramolecular Buchner ring expansion strategy. The first stage of the synthesis required preparation of the diiodide intermediate. A high yielding synthetic sequence was developed to provide large scale quantities of the diiodide in three steps from methyl anthranilate. The second stage of the synthesis required cyclotrimerisation of the diiodide followed by conversion to the diazoketone **156**. The literature procedure for cyclotrimerisation required extensive optimisation to provide triphenylene in consistent yield with minimal purification. The triphenylene diazoketone **156** was successfully synthesised from the triphenylene ester in two steps. In the final stage of the synthesis, the diazoketone was subjected to rhodium catalysed Buchner reaction conditions. a single product was isolated in high yield from the reaction mixture. The product was identified as coronene derivative **159** which indicated the C-H insertion is favoured over the desired Buchner ring expansion. The preference for C-H insertion is attributed to reduced electron density of the aromatic ring. This trend in reactivity of the carbene intermediate may be rationalised using HSAB theory



Scheme 5.05: Synthesis of coronene.

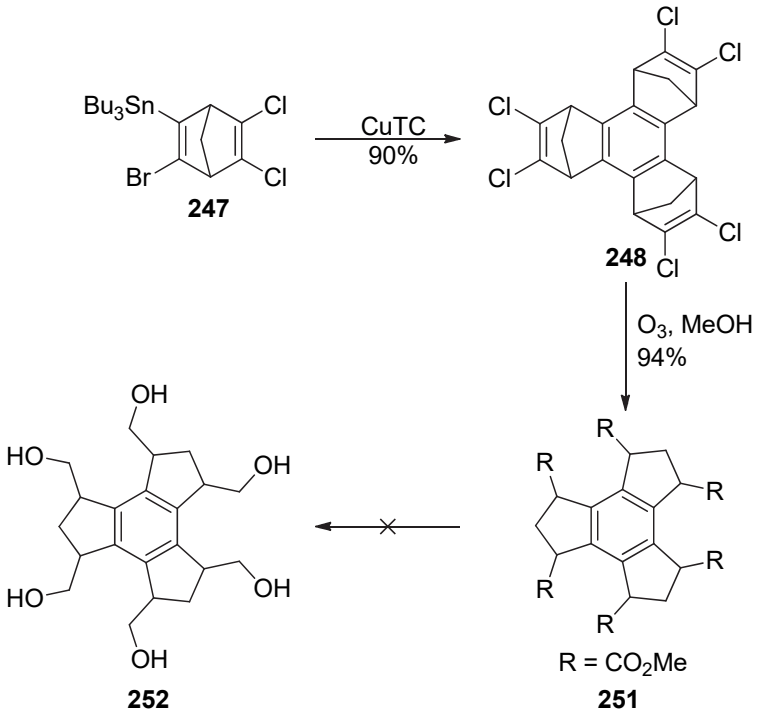
Although the desired isocoronene was not synthesised from the triphenylene diazoketone, the procedure provides a valuable route to functionalised coronene derivatives. The methods currently available are particularly limited in functional group tolerance and substitution patterns. As such, this reaction sequence could be used to develop a general methodology for the synthesis of coronene derivatives with excellent functional group tolerance and substitution patterns limited only by the triphenylene precursor. This would allow the synthesis of numerous coronene derivatives that are currently inaccessible.

An alternative approach towards the synthesis of isocoronene was investigated since the Buchner ring expansion strategy was unsuccessful. The trindane ring system **338** was chosen as an intermediate structure since it forms part of the isocoronene substructure. The isocoronene ring structure could be accessed from trindane by linking of the benzylic positions with three carbon chains.



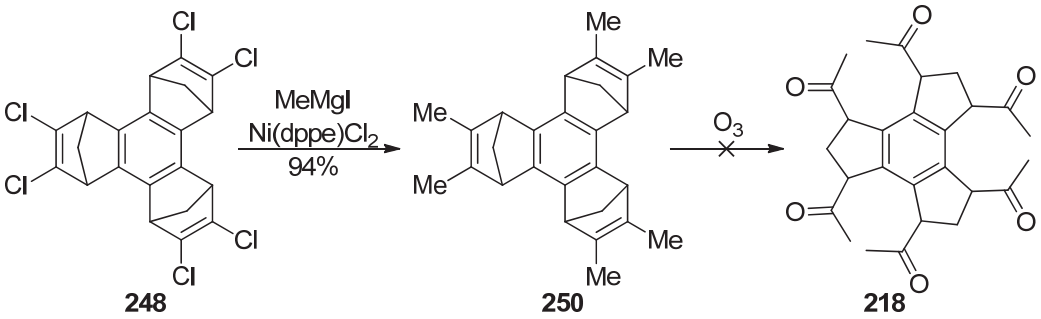
Scheme 5.06: Retrosynthesis of isocoronene.

The initial approach to the synthesis of the trindane derivative was through ozonolysis of a norbornadiene trimer **248**. Synthesis of the trimer began with preparation of the bromostannane **247** in four steps from cyclopentadiene. Cyclotrimerisation of the bromostannane under Stille coupling conditions then gave the norbornadiene trimer **248**. This sequence was repeated on large scale to provide a 10 g batch of the trimer. Ozonolysis of the hexachloride in the presence of methanol gave the hexacarboxytrindane methyl ester **251**. Reduction of the ester groups gave a product that could not be characterised by ^{1}H-NMR due to extreme signal broadening. Attempts at converting the hydroxy substituents to leaving groups did not provide conclusive results and so an alternative route was investigated.



Scheme 5.07: Attempted synthesis of **252**.

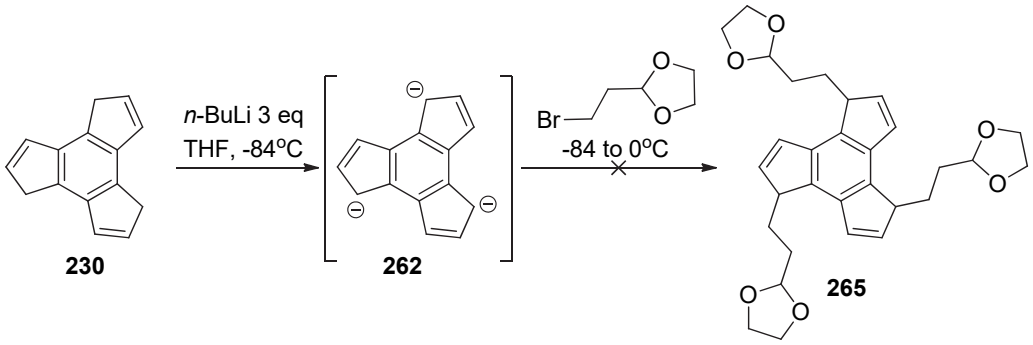
The hexamethyl norbornadiene trimer **250** was synthesised through Kumada coupling of the hexachloride **248**. Ozonolysis would then provide the acyl substituted trindane **218** which could be used directly in a subsequent ring closing step. Ozonolysis of the hexamethyl trimer was attempted using a range of reaction conditions and workup procedures. In each case, the reaction gave a crude product that could not be characterised by ^{1}H-NMR due to extreme signal broadening. This result is in contrast to the successful ozonolysis of the hexachloro trimer. The difference in reaction outcome was attributed to the formation of a stable polymeric ozonide. Ozonolysis of the hexachloride may proceed through an alternative mechanism which avoids polymerisation.



Scheme 5.08: Attempted synthesis of **218**.

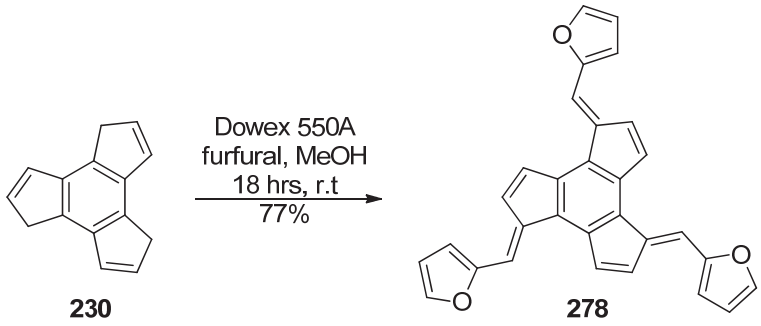
The issues encountered in the synthesis of hexasubstituted trindane derivatives were attributed to the sterically crowded nature of the substituents. The close proximity of the opposing benzylic substituents allows for undesired interactions of reaction intermediates. An alternative synthesis of trindane derivatives was subsequently investigated.

The synthesis of trindane derivative with three benzylic substituents was explored. Trindene was chosen as an intermediate since it could be functionalised at the three active methylene groups. The active methylene positions of trindene were deprotonated with *n*-BuLi to give the trindene trianion **262**. The trindene trianion was found to be completely unreactive in the nucleophilic substitution of an alkyl halide. This result is in contrast to the reported alkylation reactions of indene under similar reaction conditions. The unreactive nature of the trianion was attributed to the low solubility in the reaction solvent. The low solubility was previously reported following unsuccessful attempts at characterising the trianion by ^{1}H NMR. The low solubility of the trindene trianion limits its synthetic potential and so alternative reaction conditions were investigated.



Scheme 5.09: Attempted synthesis of **265**.

The structurally related indene is known to undergo condensation reactions with aldehydes under mildly basic conditions and so the same reaction conditions were applied to trindene **230**. The trifulvene ring system **278** was synthesised from the base catalysed condensation of trindene with an aryl aldehyde. The trifulvene structure has not been reported previously in literature and as such it represents a new class of fulvene compounds.

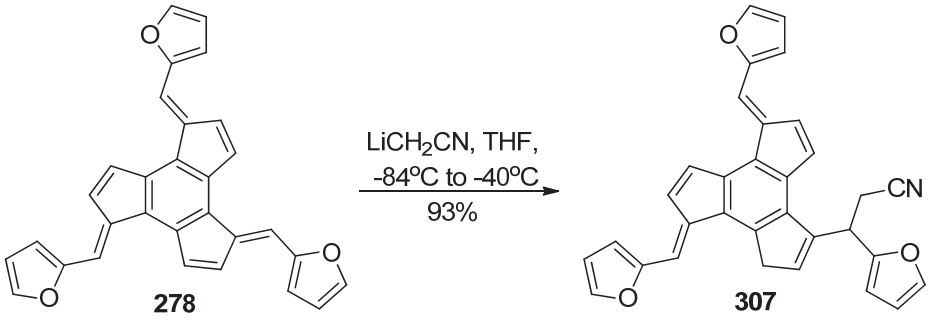


Scheme 5.10: Synthesis of **278**.

The reactivity of trindene towards aldehydes and ketones was further investigated utilising a range of reaction conditions and reagents. It was concluded that trindene is unreactive or unstable towards condensation reactions with electrophiles other than aryl aldehydes. Aryl aldehydes are not suitable for the direct introduction of the required three carbon linking group and so alternative methods of functionalisation were explored.

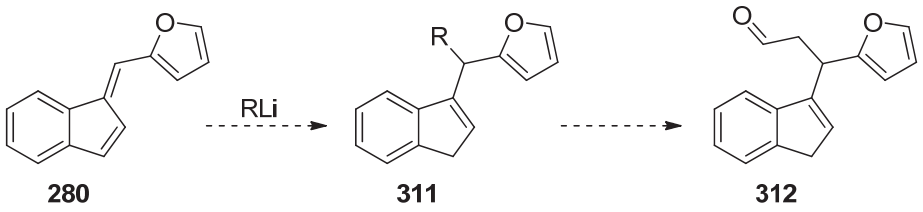
Benzofulvenes are known to undergo addition reactions with strong carbon nucleophiles and so these reaction conditions were applied to trifulvene **278**. Trifulvene was found to react with lithiated acetonitrile at -40 °C to selectively form

the mono-addition product **307**. This result indicates a strong deactivation following the first addition reaction. The deactivation was attributed to the formal negative charge of the first reaction intermediate. The negative charge may reduce the electrophilicity of the remaining fulvene positions in addition to electrostatic repulsion of lithiated acetonitrile. Increasing the reaction temperature to 0 °C and using a large excess of lithiated acetonitrile resulted in partial conversion to the desired trindene derivative. Subsequently, the nitrile groups were found to be unreactive towards reduction, even under forcing conditions.



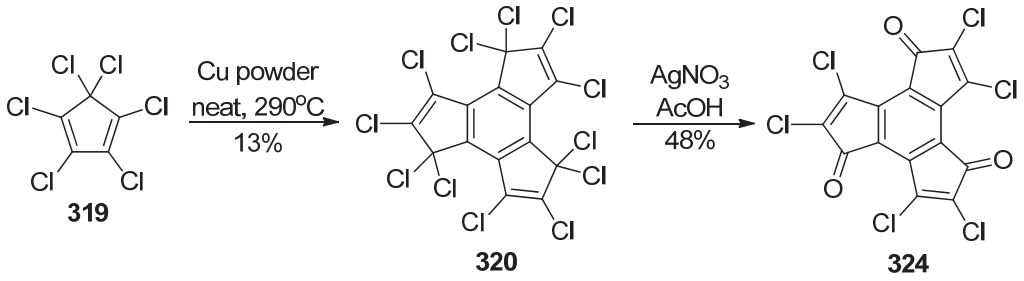
Scheme5.11: Synthesis of **307**.

The nucleophilic addition of a range of organolithium reagents was investigated using benzofulvene **280** as a model substrate. Benzofulvene reacted rapidly with lithiated acetonitrile or *n*-BuLi to give complete conversion to the alkylated indene derivatives. In contrast, all other organolithium reagents were completely unreactive towards benzofulvene. The reduced reactivity was not consistent with a lower *p*Ka of the organolithium reagent and so an alternative explanation was proposed. The unreactive organolithium species each possessed a functional group which is capable of coordination to lithium. In comparison, lithiated acetonitrile possesses a nitrile which is weakly coordinating while *n*-BuLi has no coordinating groups. The reduced reactivity could be attributed to the formation of organolithium aggregates due to the presence of coordinating functional groups. Following this result, further investigation into the synthesis and reactivity of trifulvenes was halted.



Scheme 5.12: Nucleophilic addition to benzofulvene.

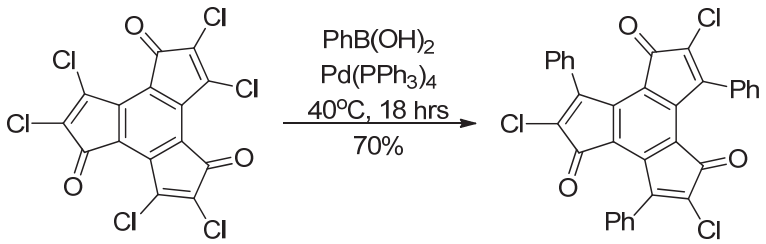
The synthesis and reactivity of the previously unknown trindenone structure **324** was explored. The presence of the benzylic ketone groups of trindenone would allow the introduction of a linking group through a nucleophilic addition reaction. The perchlorinated trindene **320** was prepared in low yield by the cyclotrimerisation of perchlorocyclopentadiene **319** at 290 °C in the presence of copper. The benzylic ketone groups were then introduced by hydrolysis of the geminal chloro positions. The geminal chlorides were found to have greatly reduced reactivity in comparison to the structurally related tribromoindene. This was attributed to an energetically unfavourable S_N1 mechanism since the steric effects of the adjacent ring system prevent S_N2 from occurring. An investigation into silver mediated hydrolysis conditions showed that perchlorotrindene reacted rapidly with silver nitrate and acetic acid under reflux. Analysis by TLC indicated the reaction gave a single yellow product attributed to **324**. Characterisation by ^{13}C NMR was not possible due to low solubility.



Scheme 5.13: Synthesis of **305**.

The reaction of trindenone **324** with a range of nucleophiles led to rapid decomposition to form dark insoluble material in each attempt. This result suggests trindenone **324** is not stable under basic conditions and so alternative methods of functionalisation were explored. Trindenone **324** was shown to participate in a

Suzuki coupling reaction with phenylboronic acid. The coupling is regioselective at the electron deficient vinyl chloride resulting in functionalisation at the desired benzylic position to give trindene **335**. The product was readily soluble in $CDCl_3$ which allowed characterisation by ^{13}C NMR to confirm the presence of the enone structure of **335**. This result gave indirect structural confirmation of the starting material **324**. The successful coupling of phenylboronic acid to trindenone indicates the Suzuki coupling reaction is a potential route towards the target isocoronene structure.



324 **335**

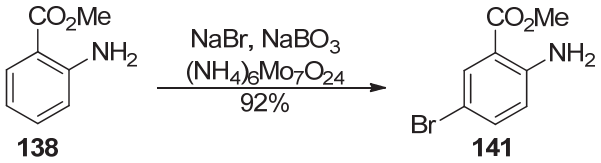
Scheme 5.14: Synthesis of **335**.

Chapter 6

Experimental

All reactions involving moisture or air-sensitive reagents were performed under a positive pressure of nitrogen. Materials were obtained from commercial sources and used without further purification unless otherwise stated. NMR experiments were performed on a Bruker UltraShield Avance III 400 spectrometer (^{1}H, 400.1 MHz; ^{13}C, 100.6 MHz). Chemical shifts (δ) are expressed in ppm with reference to the solvent resonances of $CDCl_3$ (^{1}H, 7.26 ppm; ^{13}C, 77.16 ppm), $(CD_3)_2CO$ (^{1}H, 2.05 ppm; ^{13}C, 29.84 ppm) and $(CD_3)_2SO$ (^{1}H, 2.50 ppm; ^{13}C, 39.52 ppm). Resonance patterns are reported with the following notations: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets), dt (doublet of triplets) and td (triplet of doublets). Infrared spectra were recorded on a Perkin Elmer Fourier Transform-IR spectrometer 100 equipped with a ZnSe-diamond crystal ATR accessory; spectra were acquired between 4000-650 cm-1. Column/flash chromatography was achieved using SiliaFlash® P60 silica gel (230-400 mesh, SiliaCycle, Canada) with the solvents stated. Electrospray ionisation (ESI^+) HRMS analyses were performed using a Thermo Fisher Scientific LTQ Orbitrap XL at Curtin University. Atmospheric solids analysis probe ($ASAP^+$) HRMS analyses were performed using a Waters Xevo QTof and were conducted by Dr Celine Kelso of the Department of Chemistry, University of Wollongong. TLC was performed on Merck aluminium backed silica gel 60 F254 sheets and visualised by using short-wave UV light (λ = 254 nm) and potassium permanganate or ninhydrin stains. Solvents (tetrahydrofuran, dichloromethane and acetonitrile) were dried using methods described in Armarego and Chai. Petrol refers to the fraction of alkanes that boils between 40-60°C.

Methyl-5-bromoanthranilate

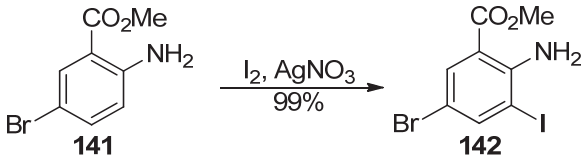


138 **141**

A mixture of methyl anthranilate (15.1 g, 0.1 mol), potassium bromide (14.28 g, 0.12 mol) and ammonium molybdate tetrahydrate (1.24 g, 1 mmol) in acetic acid (100 mL) was stirred under ambient atmosphere. Sodium perborate tetrahydrate (16.15 g, 0.105 mol) was then added and the reaction was placed in a water bath at room temperature. After 3 hours, the brown reaction mixture was poured slowly into a solution of 5% sodium metabisulfite (400 mL) with vigorous stirring to form a loose precipitate. The precipitate was filtered and washed with water to yield methyl 5-bromoanthranilate (21.15 g, 92%) as a tan solid of sufficient purity. The spectroscopic data matches the reported literature values.[71]

^{1}H NMR (400 MHz, $CDCl_3$) 7.96 (1 H, d, J = 2.4 Hz), 7.32 (1 H, dd, J = 2.4 and 8.8 Hz), 6.55 (1 H, d, J = 8.8 Hz), 3.87 (3 H, s) ppm.

Methyl-5-bromo-3-iodoanthranilate



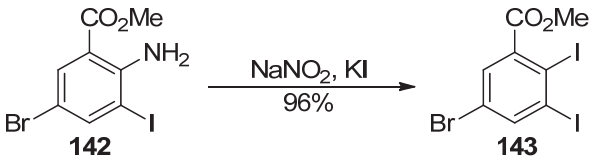
141 **142**

A solution of methyl 5-bromoanthranilate (21.15 g, 92.0 mmol) in methanol (500 mL) was cooled on ice and iodine (23.5 g, 92.6 mmol) was added. Finely powdered silver nitrate (15.8 g, 93.0 mmol) was then added portion wise with vigorous stirring. After the reaction was complete by TLC (approximately 90 minutes), 5% sodium bicarbonate solution (100 mL) was added followed by sodium metabisulfite solution (5%, 100 mL). The mixture was concentrated under reduced pressure to remove most of the methanol and the precipitate was filtered and reserved. The filtrate was diluted with brine (200 mL) and extracted with EtOAc (3x 100mL). The organic extracts were combined with the reserved precipitate and thoroughly mixed. The insoluble

material was removed by filtration and washed with fresh EtOAc. The filtrate was dried and concentrated under reduced pressure yielding methyl 5-bromo-3-iodoanthranilate (32.5 g, 99%) as a light brown powder, essentially pure by NMR. The spectral properties match those reported.[73]

^{1}H NMR (400 MHz, $CDCl_3$) 8.01 (1H, d, J = 2.4 Hz), 7.89 (1H, d, J = 2.4 Hz), 3.89 (3H, s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 167.0 (C), 148.9 (C), 145.6 (CH), 134.2 (CH), 111.8 (C), 107.4 (C), 86.5 (C), 52.4 (CH_3) ppm; ATR IR: 3457, 3340, 1698 cm^{-1}.

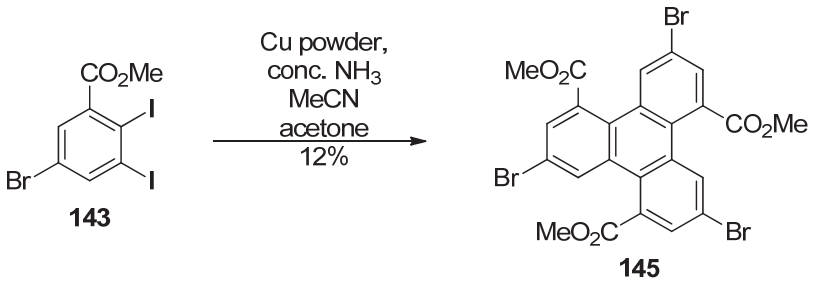
Methyl 5-bromo-2,3-diiodobenzoate



Sodium nitrite (11 g, 0.16 mol) was dissolved in concentrated sulfuric acid (150 mL) at 0°C. A solution of methyl 5-bromo-3-iodoanthranilate (32.5 g, 91.3 mmol) in acetic acid (200 mL) was added slowly with mixing while the reaction temperature was kept below 10°C. The dark viscous mixture was slowly poured into an ice cold solution of potassium iodide (40 g) in water (300 mL) with vigorous stirring. The black reaction mixture was then heated to 80°C for 1 hour until no further gas evolution was observed. The mixture was then diluted with sodium metabisulfite solution (5%, 100 mL) and water (300 mL) then extracted with dichloromethane (3 x 150 mL). The extract was washed with water (2 x 100 mL), followed by saturated Na_2CO_3 solution (200 mL) then dried and the solvent removed yielding methyl 5-bromo-2,3-diiodobenzoate (40.92 g, 87.7 mmol, 96%) as a brown solid used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 2.3 Hz, 1H), 7.60 (d, J = 2.3 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.71 (C), 143.48 (CH), 141.23 (C), 131.60 (CH), 122.68 (C), 113.11 (C), 105.65 (C), 53.32 (CH_3); HRMS: (ESI$^+$) *m/z* $C_8H_6BrI_2O_2^+$ requires 466.7640, not detected.

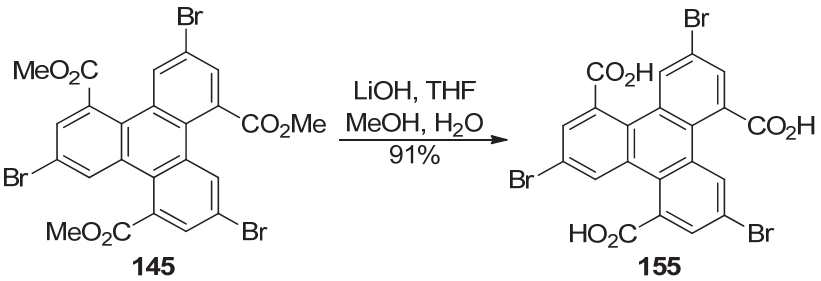
Trimethyl 3,7,11-tribromotriphenylene-1,5,9-tricarboxylate



A mixture of Cu powder (Sigma Aldrich, 7 g, 110 mmol) and 30% aqueous ammonia (6 mL) was sonicated in a sealed vial for 4 hours. A flask containing powdered diiodide **143** (14 g, 30 mmol) was evacuated and kept under nitrogen. Acetonitrile (10 mL) and acetone (10 mL) were then added to the diiodide with stirring. The copper/ammonia slurry was then poured into the reaction flask with vigorous stirring. The reaction was monitored for initiation as indicated by a rise in temperature. Immediately after initiation, the flask was placed into an ice bath and vigorous stirring continued. After 1 hour, the reaction mixture was allowed to warm to room temperature. After 18 hours, the beige coloured slurry was concentrated under reduced pressure then suspended in DCM (100 mL) and filtered through celite. The dark filtrate was then washed with HCl (1 M, 100 mL), dried and again filtered through celite. The dark red filtrate was then concentrated under reduced pressure (foam) yielding a brown resin as the crude product which consisted of approximately equal proportions of the two triphenylene regioisomers. The desired isomer was isolated by trituration with boiling EtOAc (100 mL) followed by cooling on ice and filtration, yielding **145** as a waxy white solid (0.775 g, 12%).

^{1}H NMR (400 MHz, $CDCl_3$) 8.17 (3H, d, J = 2.0 Hz), 7.93 (3H, d, J = 2.0 Hz), 3.97 (9 H, s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 169.9 (C), 132.8 (C), 132.6 (CH), 132.0 (CH), 131.3 (C), 126.5 (C), 121.1 (C), 53.4 (CH_3) ppm; ATR IR: 1710 cm^{-1}; HRMS: (ASAP$^+$), *m/z* $C_{24}H_{16}Br_3O_6^+$ calculated for 636.8497, found 636.8508.

3,7,11-tribromotriphenylene-1,5,9-tricarboxylic acid

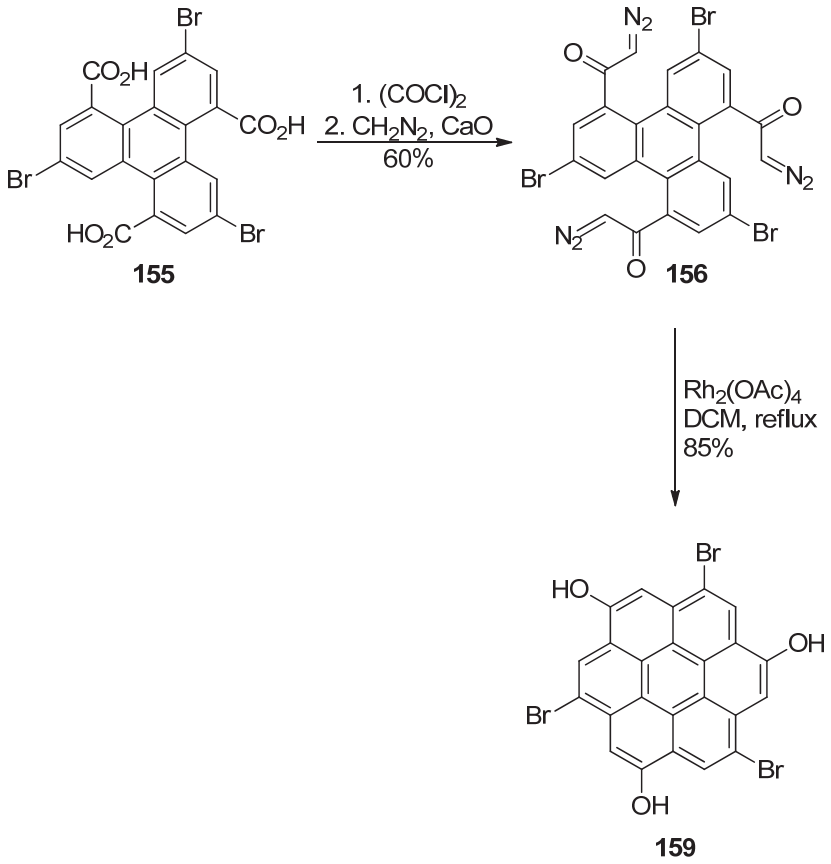


145 **155**

A mixture of triphenylene ester **145** (100 mg, 0.16 mmol), MeOH (20 mL), THF (20 mL), water (10 mL) and LiOH.H_2O (200 mg, 4.76 mmol) was heated under reflux for 3 hours. After completion of the reaction which was indicated by dissolution of the starting material and TLC (EtOAc). The clear colourless solution was neutralised with HCl (1 M, 100 mL) then extracted with EtOAc (3x 20 mL). The combined extracts were washed with brine (20 mL) then dried and the solvent removed yielding the triacid **155** as a white solid (85 mg, 91%) which did not require further purification.

^{1}H NMR (400 MHz, acetone) 8.59 (3H, d, J = 1.9 Hz), 8.06 (3H, d, J = 1.9 Hz) ppm; ^{13}C NMR (100 MHz, acetone) 170.9 (C), 132.8 (CH), 132.4 (CH), 132.1 (C), 126.8 (C), 121.5 (C) ppm; ATR IR: 1667 cm^{-1}. HRMS: (ESI$^+$) *m/z* $C_{21}H_{10}Br_3O_6^+$ requires 594.8027, not detected.

3,7,11-Tribromo-1,5,9-coronenetriol



Triphenylene triacid (100 mg, 0.17 mmol) was suspended in DCM (20 mL) with sonication. Oxalyl chloride (71 mg, 0.56 mmol) was added followed by DMF (10 mg). The reaction was complete after 2 hours, as indicated by dissolution of the starting material to give a clear yellow solution. The solvent was removed under reduced pressure then the residue was taken up in DCM and concentrated again yielding a pale yellow solid which was used in the subsequent reaction.

The diazomethane solution was prepared following a literature procedure.[180] A biphasic mixture of KOH solution (40%, 3 mL) and ether (10 mL) was cooled in an ice bath. *N*-Nitroso-*N*-methylurea (1.00 g, 9.7 mmol) was added to the biphasic mixture with stirring. After most of the solid had dissolved, the yellow organic layer was decanted and dried over KOH pellets with continued cooling. After 1 hour the solution was decanted to a dry flask with continued cooling.

Dry CaO (50 mg, 0.89 mmol) was added to the diazomethane solution with stirring at 0°C. After 5 minutes, a solution of the acid chloride in DCM (10 mL) was added

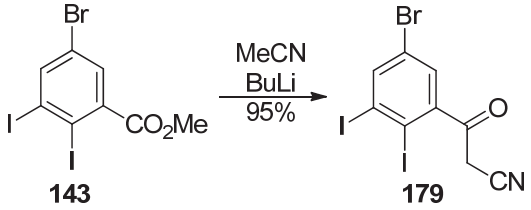
dropwise with stirring and the reaction was allowed to warm to room temperature. After 1 hour excess diazomethane was removed with a stream of nitrogen and the reaction mixture was filtered through celite. The solvent was removed under reduced pressure and the crude yellow solid was purified by column chromatography (50% DCM, 49% petrol, 1% AcOH). The diazoketone was collected as a distinct yellow band, yielding **156** as a yellow solid after removal of the solvent (70 mg, 0.10 mmol, 60%) used for the subsequent reaction without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) 8.49 (3H, br s), 7.79 (3H, br s), 5.42 (3H, br s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 189.7 (C), 139.6 (C), 132.8 (CH), 131.2 (CH), 125.8 (C), 121.5 (C), 58.5 (CH) ppm; ATR IR: 2101, 1612 cm^{-1}

A solution of $Rh_2(OAc)_4$ (5 mg) in DCM (100 mL) was heated under reflux under N_2. A solution of diazoketone **156** (70 mg, 0.10 mmol) in DCM (20 mL) was then added portionwise over 5 minutes. After addition was complete the reaction mixture was cooled on ice and the precipitate was isolated by filtration to yield coronene **159** as a dark orange solid (50 mg, 0.085 mmol, 85%).

^{1}H NMR (400 MHz, DMSO) 11.35 (3OH, s, D_2O exchangeable), 9.05 (3H, s), 8.17 (3H, s) ppm; ^{13}C NMR (100 MHz, DMSO) 153.0 (C), 128.4 (C), 123.9 (CH), 121.0 (C), 118.9 (C), 118.3 (C), 115.8 (C), 105.1 (CH) ppm; ATR IR: 3280, 1604 cm^{-1}.

3-(5-Bromo-2,3-diiodophenyl)-3-oxopropanenitrile

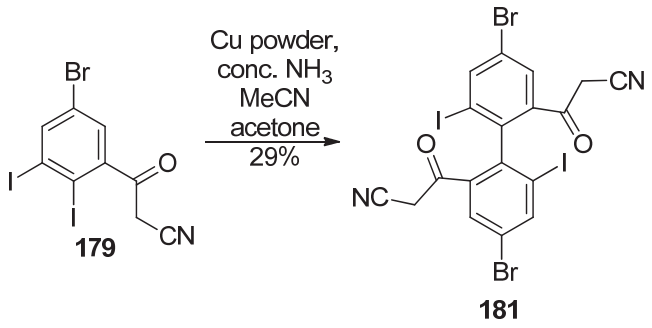


A solution of acetonitrile (0.2 mL, 3.8 mmol) in THF (10 mL) was cooled to -84°C and *n*BuLi (1.6 M, 1.9 mL, 3.0 mmol) was added dropwise. After 30 minutes the reaction mixture had become pale orange and cloudy. A solution of the diiodide **143** (0.466 g, 1.0 mmol) in THF (5 mL) was then added dropwise over 5 minutes, resulting in a dark homogeneous solution. After 15 minutes, the reaction was quenched with aqueous HCl (1M, 30 mL) and then warmed to room temperature.

The reaction mixture was diluted with EtOAc (50 mL) and the organic phase was separated, washed with HCl (1 M, 30 mL) then brine (50 mL) and then dried and concentrated to yield **179** as an off white crystalline solid (0.451 g, 95%).

R_F 0.15 (20:80 EtOAc:petrol); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 2.2 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 3.99 (s, 2H); ^{13}C NMR (101 MHz, Acetone) δ 193.40 (C), 148.13 (C), 143.76 (CH), 130.10 (CH), 123.34 (C), 114.48 (C), 113.52 (C), 104.05 (C), 32.23 (CH_2); ATR IR: 2266, 1710 cm^{-1}; HRMS: (ESI^+) *m/z* not detected.

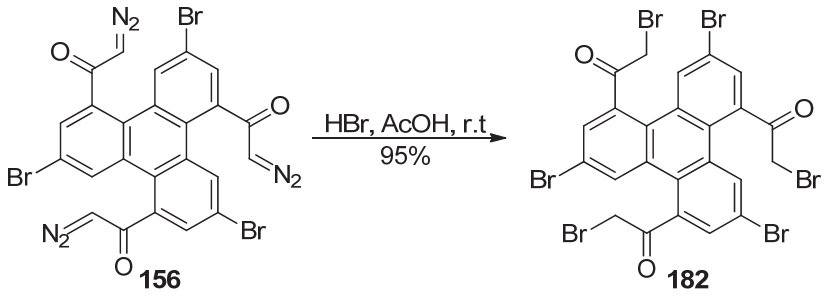
*Biphenyl ketonitrile **181***



A mixture of the diiodide **179** (0.200 g, 0.42 mmol), acetonitrile (0.3 mL), acetone (0.3 mL) and aqueous ammonia (30%, 0.1 mL) was cooled on ice under N_2. Copper powder (0.2 g, 3.1 mmol) was then added with vigorous stirring. After 3 hours, the reaction mixture was diluted in DCM (50 mL), filtered through celite and concentrated to yield a pale yellow residue (0.045 g). The crude product was purified by silica gel chromatography (50:50 EtOAc/petrol) to yield **181** as a colourless crystalline solid (0.042 g, 29%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 1.8 Hz, 1H), 7.85 (d, *J* = 1.8 Hz, 1H), 4.03 (s, 1H), 4.02 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.02 (C), 146.10 (CH), 145.14 (C), 136.35 (C), 131.47 (CH), 123.20 (C), 112.96 (C), 103.92 (C), 30.77 (CH_2); ATR IR: 2256, 1708 cm^{-1}.

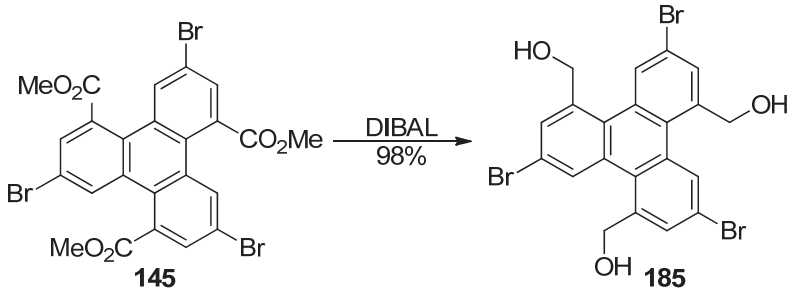
3,7,11-Tribromo-1,5,9-tri(bromoacetyl)triphenylene



The triphenylene diazoketone **156** (0.030 g, 45 μmol) was suspended in AcOH (0.5 mL) and cooled on ice. Aqueous HBr (48%, 0.1 mL) was then added and the reaction was warmed to room temperature with subsequent gas evolution observed. After 45 minutes, gas evolution had ceased, and the reaction was diluted in water (10 mL) and DCM (20 mL). The organic layer was separated then washed with Na_2CO_3 (saturated, 10 mL), dried and concentrated to yield a pale yellow solid. The crude product was purified by silica gel chromatography (10:90 EtOAc:petrol) to yield a white solid (0.020 g, 53%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 1.9 Hz, 1H), 7.87 (d, *J* = 1.9 Hz, 1H), 4.16 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.34 (C), 138.79 (C), 132.79 (CH), 132.21 (CH), 130.97 (C), 126.17 (C), 123.31 (C), 34.52 (CH_2).

3,7,11-Tribromo-1,5,9-tri(hydroxymethyl)triphenylene

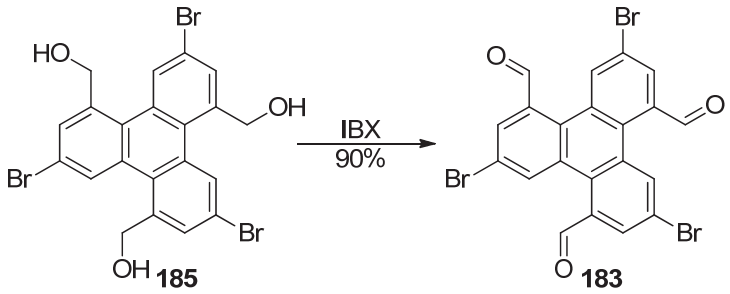


A solution of triester **145** (300 mg, 0.469 mmol) in THF (50 mL) was cooled to -84°C and DIBAL (~1.7 M in toluene, 3 mL, 11 eq) was added. The reaction was warmed to 0°C and after 3 hours, quenched with MeOH (1 mL). The mixture was diluted in HCl (1 M, 20 mL) and water (300 mL) then extracted with EtOAc (3 x 20

mL). The organic extract was dried and concentrated to give **185** as a white solid (255 mg, 0.459 mmol, 98%).

R_F 0.15 (20:80 EtOAc:petrol); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (d, J = 2.1 Hz, 3H), 7.95 (d, J = 2.1 Hz, 3H), 5.96 (t, J = 5.2 Hz, 3OH), 4.85 (d, J = 5.3 Hz, 6H); ^{13}C NMR (101 MHz, DMSO) δ 140.38 (C), 133.01 (CH), 131.40 (C), 129.40 (CH), 128.94 (C), 120.21 (C), 63.15 (CH_2); ATR IR: 3282 and 1578 cm^{-1}; HRMS: (ESI$^+$) *m/z* $C_{21}H_{16}Br_3O_3^+$ requires 552.8650, not detected.

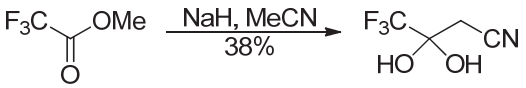
3,7,11-Tribromo-1,5,9-tri(formyl)triphenylene



The triol **185** (34 mg, 61 μmol) and IBX (85 mg, 0.30 mmol) were dissolved in DMSO (10 mL). After 2 hours the reaction was diluted with aqueous $NaHCO_3$ (5%, 20 mL) and extracted with DCM (2x 20 mL). The organic extract was washed with 5% $NaHCO_3$ (2x 10 mL) then dried and concentrated to yield **183** as a pale yellow solid (30 mg, 55 μmol, 90%).

R_F 0.6 (20:80 EtOAc: petrol); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.41 (s, 3H), 8.34 (d, J = 2.0 Hz, 3H), 8.18 (d, J = 2.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.52 (CH), 136.49 (C), 135.72 (CH), 133.72 (CH), 130.49 (C), 129.45 (C), 123.03 (C); ATR IR:1683 cm^{-1}; HRMS: (ESI$^+$) *m/z* $C_{21}H_{10}Br_3O_3^+$ requires 546.8180, not detected.

Trifluoroacetylacetonitrile hydrate

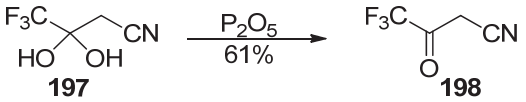


196 **197**

A solution of methyl trifluoroacetate (10 mL, 0.10 mol) and acetonitrile (8.4 mL, 0.16 mol) was added dropwise to a suspension of NaH (~60% in parrafin, 6.4 g, 0.16 mol) in THF (100 mL). The reaction mixture was heated to 65 °C until gas evolution had ceased (2 hours). The brown reaction mixture was carefully poured into water (200 mL) and extracted with ether (2x 50 mL). The organic extracts were dried and concentrated and the brown oil was purified by vacuum distillation (50 °C @ 1.5 mmHg) yielding **197** as a colourless oil (5.9 g, 38 mmol, 38%). The oil rapidly became yellow with no significant loss of purity after storage at -20 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.75 (br s, 2OH), 2.98 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 123.07 (C, q, J = 289.3 Hz), 116.11 (C), 90.74 (C, q, J = 32.0 Hz), 25.97 (CH_2).

Trifluoroacetylacetonitrile

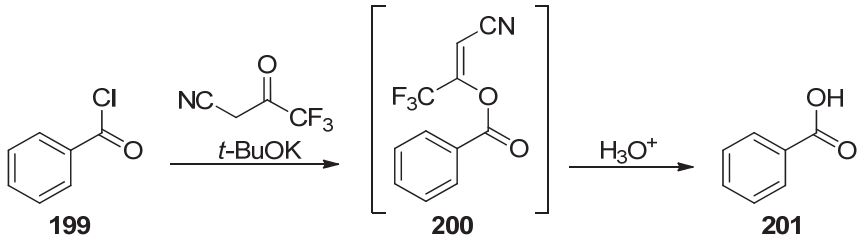


197 **198**

P_2O_5 (with indicator, 10.0 g, 35.2 mmol) was added portionwise with vigorous stirring to a solution of the ketone hydrate **197** (10.0 g, 64.5 mmol) in ether (150 mL). After 1 hour, the ether was decanted and the residue was washed with ether (20 mL) and then discarded. Fresh P_2O_5 (10.0 g, 35.2 mmol) was added to the ether solution and then decanted after 1 hour. The procedure was repeated two more times at which point the added P_2O_5 did not show any colour change from the presence of water. The decanted ether was concentrated under reduced pressure and the brown oil was purified by vacuum distillation (50 °C @ 1.2 mmHg) to give **198** as a colourless oil (5.4 g, 39.3 mmol 61%) which decomposed after prolonged storage at room temperature.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.93 (s, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 179.60 (C, q, *J* = 39.5 Hz), 114.76 (C, q, *J* = 290.5 Hz), 110.33 (C), 27.50 (CH_2); ATR IR: 2277, 1783cm^{-1}.

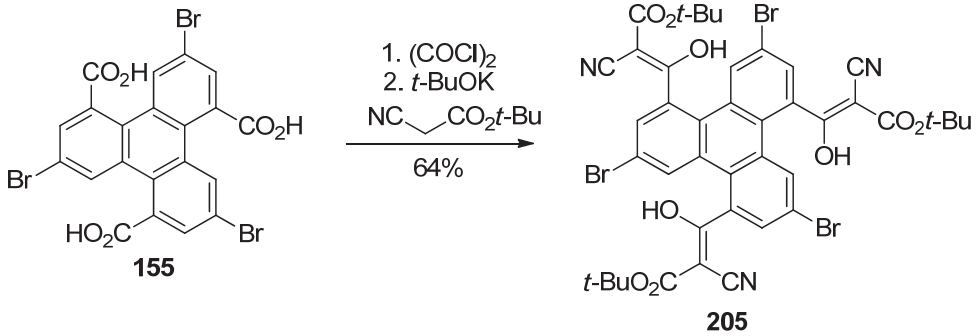
Attempted synthesis of 2-benzoyl-trifluoroacetylacetonitrile



199 **200** **201**

A solution of trifluoroacetylacetonitrile (0.343 g, 2.5 mmol) in THF (5 mL) was added to a solution of *t*BuOK (0.247 g, 2.2 mmol) in THF (10 mL) at room temperature. After 30 minutes, the reaction was cooled on ice and a solution of benzoyl chloride (0.281 g, 2 mmol) in THF (5 mL) was added dropwise. The reaction was then warmed to room temperature and after 2 hours the reaction was quenched with HCl (1 M, 20 mL), diluted with water (100 mL) and extracted with EtOAc (50 mL). The organic extract was then washed with brine (20 mL), dried and concentrated to yield a pale yellow residue. The ^{1}H NMR spectrum of the crude product showed benzoic acid as a single major product.

Triphenylene ketonitrile ***205***



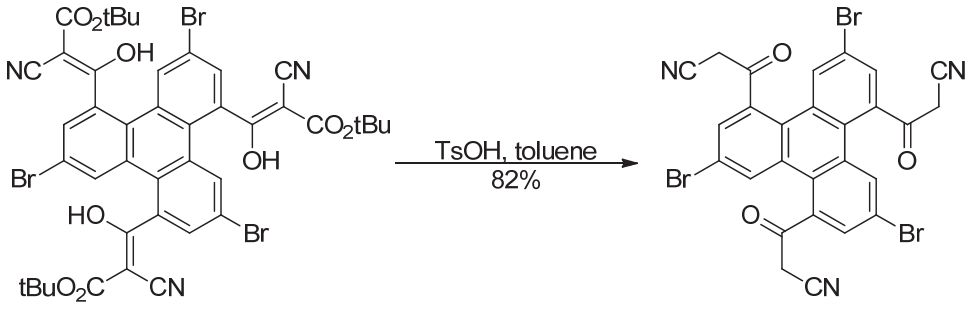
155 **205**

t-Butylcyanoacetate (340 µL, 2.38 mmol) in THF (10 mL) was added to a solution of *t*BuOK (250 mg, 2.23 mmol) in THF (50 mL). After 30 minutes the solution was

cooled to 0 °C and a solution of the acid chloride **155** (222 mg, 0.34 mmol) in THF (10 mL) was added dropwise. The reaction was warmed to room temperature and after 2 hours the reaction was quenched with HCl (1 M, 20 mL) then diluted with water (100 mL) and extracted with DCM (3x 30 mL). The organic extracts were dried and the solvent removed to give a pale yellow residue. The crude product was triturated with diethyl ether (10 mL) to yield **205** as a white solid (212 mg, 0.22 mmol, 64%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 2.0 Hz, 3H), 7.92 (d, *J* = 1.9 Hz, 3H), 1.63 (s, 27H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.17 (C), 169.94 (C), 133.33 (CH), 133.01 (CH), 131.89 (C), 131.41 (C), 127.00 (C), 121.42 (C), 113.90 (C), 86.80 (C), 84.50 (C), 28.16 (CH_3); ATR IR: 2227, 1656, 1572 cm^{-1}; HRMS (ESI^{+}) *m/z* $C_{42}H_{37}Br_3N_3O9^{+}$ requires 964.0080, found 964.0074.

*Triphenylene ketonitrile **174***

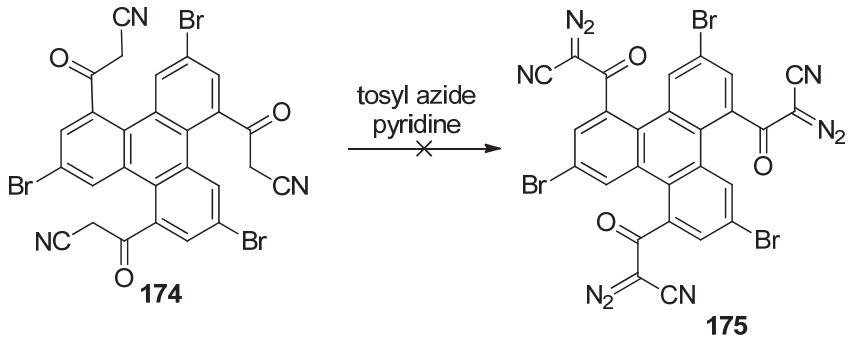


205 **174**

Triphenylene ester **205** (120 mg, 0.124 mmol) was suspended in toluene (50 mL) and tosic acid (20 mg, 0.116 mmol) was added. The mixture was then heated to 100 °C for 18 hours. The reaction was cooled to room temperature then diluted with EtOAc (50 mL), washed with water (50 mL) then dried and the solvent removed under reduced pressure to yield **174** as a white solid (68 mg, 0.102 mmol, 82%). The keto tautomer is favoured in $CDCl_3$.

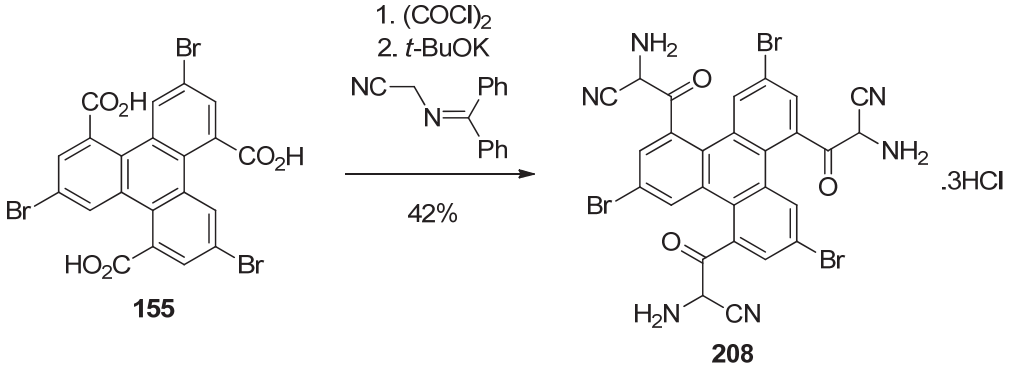
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 1.9 Hz, 3H), 7.92 (d, *J* = 1.9 Hz, 3H), 3.68 (s, 6H); ATR IR: 2217, 1703 cm^{-1}.

*Attempted synthesis of triphenylene diazoketonitrile **175***



A solution of the ketonitrile **174** (0.200 g, 0.30 mmol) and tosyl azide (0.200 g, 1.01 mmol) in acetonitrile (20 mL) was cooled on ice. Pyridine (0.300 g, 3.79 mmol) was then added and the reaction was warmed to room temperature. A rapid colour change from pale yellow to dark red was observed. After 12 hours, the reaction mixture was concentrated to give a large quantity of dark red residue. The residue was not appreciably soluble in organic or aqueous solvent.

*Triphenylene aminoketonitrile **208***



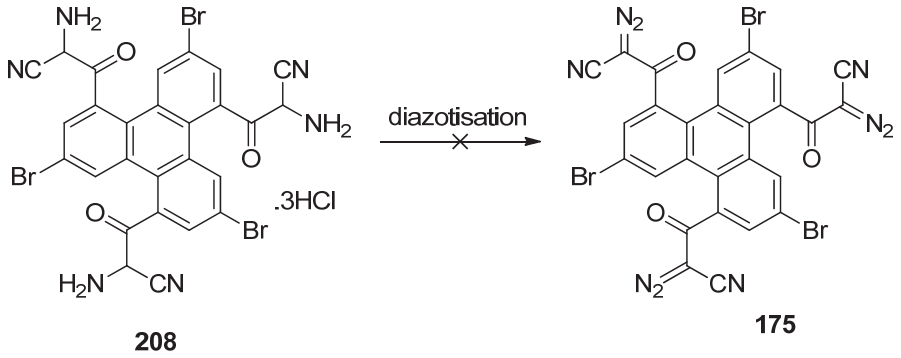
Triphenylene triacid **155** (200 mg, 0.34 mmol) was suspended in DCM (20 mL) and oxalyl chloride (173 mg, 1.36 mmol) was added followed by DMF (10 mg). The reaction was complete after 1 hour, as indicated by dissolution of the starting material to give a clear yellow solution. The solvent was removed and the resulting yellow solid used without further purification.

A solution of *t*BuOK (150 mg, 1.34 mmol) in THF (20 mL) was cooled to -84 °C. To the reaction flask was added a solution of *N*-(diphenylmethylene)aminoacetonitrile (330 mg, 1.5 mmol) in THF (10 mL). After 30 minutes, a solution of the acid

chloride (222mg, 0.34 mmol) in THF (10 mL) was added dropwise and the reaction was allowed to warm to room temperature. After 30 minutes the reaction was quenched with HCl (3M, 20 mL) and the mixture was concentrated to dryness (water bath T< 40 °C). The residue was taken up in water (100 mL) and extracted with Et_2O (3x 20 mL). The organic extracts were discarded and the aqueous layer was concentrated to dryness. The residue was suspended in MeOH (20 mL) and the insoluble material was removed by filtration and discarded. The filtrate was then concentrated to give **208** as a pale yellow solid (115 mg, 0.14 mmol, 42%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.63 (d, J = 2.0 Hz, 3H), 7.93 (d, J = 2.0 Hz, 3H), 3.48 (q, J = 6.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO) δ 167.75 (C), 133.98 (C), 133.36 (C), 131.11 (CH), 130.68 (C), 126.79 (CH), 120.92 (C), 116.55 (C), 84.01 (C); ATR IR: 2185, 1652 cm^{-1}; HRMS: (ESI$^+$) *m/z* $C_{27}H_{16}Br_3N_6O_3^+$ requires 708.8834, not detected.

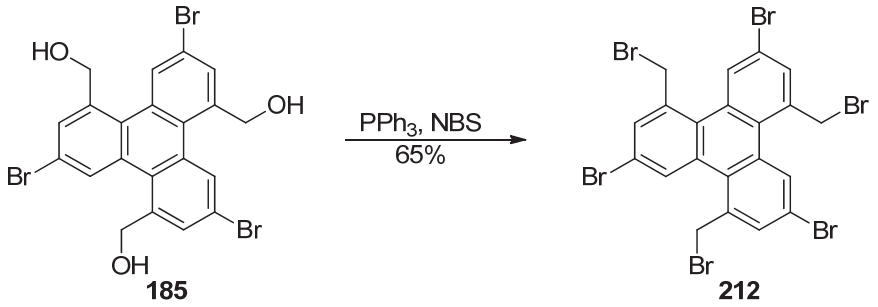
*Attempted synthesis of triphenylene diazoketonitrile **175***



208 **175**

t-Butyl nitrite (45 µL, 0.37 mmol) was added to a solution of the amine **208** (0.050 g, 0.06 mmol) in acetic acid (5 mL). The mixture was then warmed to 50 °C resulting in a colour change to a yellow homogeneous solution. After 1 hour, the reaction mixture was diluted in water (100 mL) and extracted with EtOAc (2x 30 mL). The extracts were washed with saturated Na_2CO_3 (50 mL) then brine (50 mL), dried and concentrated to yield a yellow residue (0.067 g). Analysis of the crude reaction product by ^{1}H NMR indicated consumption of starting material with formation of a complex mixture.

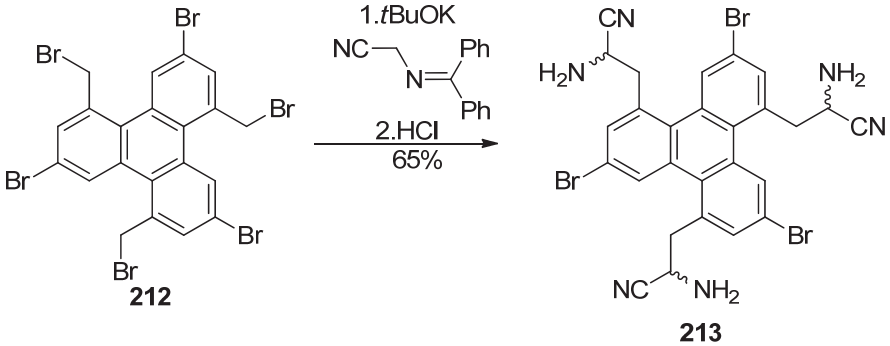
3,7,11-Tribromo-1,5,9-tri(bromomethyl)triphenylene



Triphenylene triol **185** (470 mg, 0.847 mmol) and PPh_3 (888 mg, 3.39 mmol) were dissolved in THF (50 mL). The mixture was cooled on ice and a solution of NBS (510 mg, 2.86 mmol) in THF (10 mL) was added portionwise. The reaction mixture was then allowed to warm to room temperature and after 1 hour diluted with DCM (200 mL). The reaction mixture was filtered through a short plug of silica gel and the eluent was concentrated to give a white solid. The solid was triturated with methanol (10 mL) to yield **212** as a poorly soluble white solid (408 mg, 0.549 mmol, 65%).

R_F 0.8 (20:80 EtOAc:petrol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (d, J = 2.1 Hz, 3H), 8.13 (d, J = 2.0 Hz, 3H), 5.17 (s, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 137.38 (C), 136.15 (CH), 131.74 (C), 130.58 (CH), 129.23 (C), 121.18 (C), 36.63 (CH_2).

3,7,11-Tribromo-1,5,9-tri(2-amino-2-cyanoethyl)triphenylene

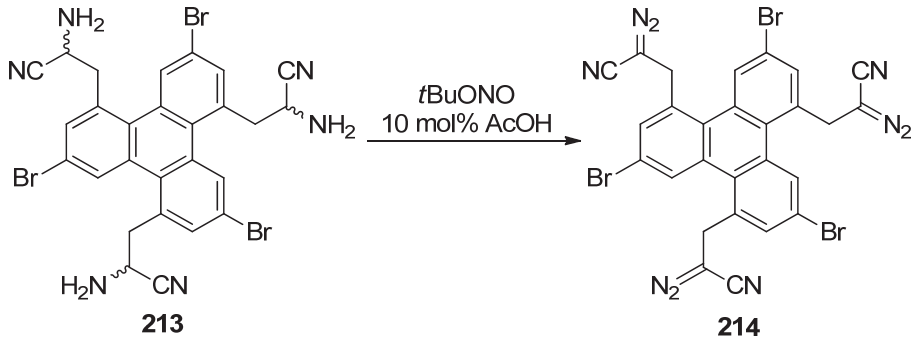


A solution of *t*BuOK (270 mg, 2.41 mmol) in THF (20 mL) was cooled to -84 °C. To this was added a solution of *N*-(diphenylmethylene)aminoacetonitrile (550 mg, 2.5

mmol) in THF (10 mL). After 30 minutes, powdered triphenylene hexabromide **212** (408 mg, 0.549 mmol) was added portionwise. The reaction mixture was allowed to warm to room temperature and after 1 hour, quenched with HCl (1M, 100 mL). The mixture was extracted with diethyl ether (3x 50 mL) and the organic extracts were discarded. The aqueous layer was basified with KOH (1M, 110 mL) and extracted with EtOAc (3x 80 mL). The organic extracts were dried and the solvent removed under reduced pressure yielding **213** as a pale yellow residue (239 mg, 0.357 mmol, 65%) isolated as a mixture of diastereomers.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 – 8.21 (m, 3H), 7.76 – 7.71 (m, 3H), 3.97 (q, *J* = 7.4 Hz, 3H), 3.77 – 3.66 (m, 6H). ^{13}C NMR (101 MHz, DMSO) δ 136.31 (C), 133.14 (CH), 131.73 (C), 129.61 (C), 128.10 (CH), 122.47 (C), 119.90 (C), 44.08 (CH), 40.28 (CH_2). ATR IR: 3374, 3306, 2229 cm^{-1}; HRMS: (ESI^+) *m/z* $C_{27}H_{22}Br_3N_6^+$ requires 666.9456, not detected.

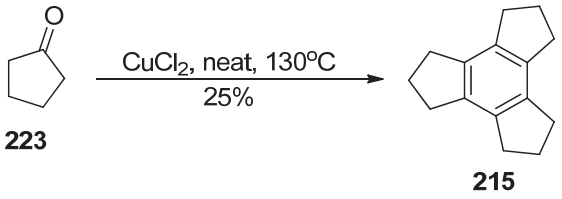
Attempted synthesis of 3,7,11-tribromo-1,5,9-tri(2-cyano-2-diazoethyl)triphenylene



*t*BuONO (50 µL, 0.42 mmol) was added to a solution of the amine **213** (20 mg, 30 µmol) and AcOH (10 µL, 0.17 mmol) in $CDCl_3$ (2 mL). The solution was warmed to 50 °C for 20 minutes and the reaction monitored by ^{1}H NMR.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 2.0 Hz, 3H), 7.76 (d, *J* = 1.9 Hz, 3H), 4.21 (s, 6H).

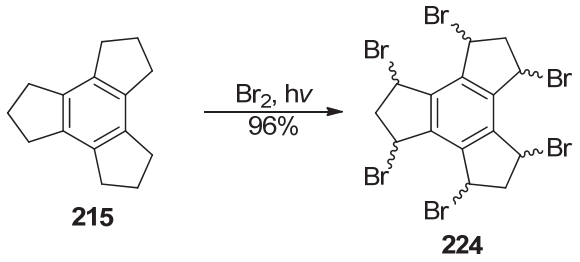
Trindane



A mixture of cyclopentanone (45 mL, 0.508 mol) and anhydrous $CuCl_2$ (8 g, 0.060 mol) was heated under reflux. After 18 hours the mixture was diluted with DCM (200 mL), silica gel (100 g) was then added and the volatiles were removed under reduced pressure. The silica adsorbed crude product was subject to silica gel filtration using petrol as the eluent. The light yellow eluent was filtered again through silica gel and the colourless eluent was concentrated to give **215** as a colourless crystalline solid (8.32 g, 25%). The spectroscopic data matches the reported literature values.[110]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.84 (t, *J* = 7.4 Hz, 12H), 2.13 (p, *J* = 7.4 Hz, 6H).

1,3,4,6,7,9-Hexabromotrindane

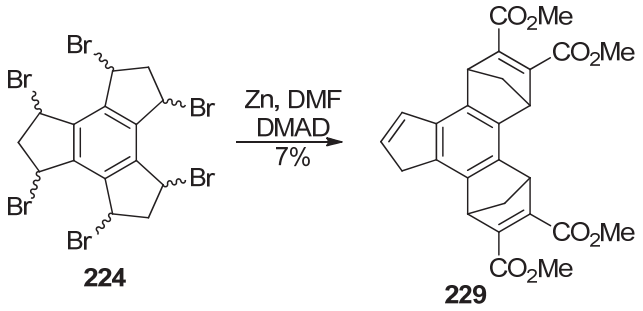


The synthesis of hexabromotrindane was conducted with slight modification to the literature procedure.[111] A solution of trindane **215** (6.31 g, 31.8 mmol) in $CHCl_3$ (150 mL) was cooled on ice and irradiated with a 500 W tungsten halogen lamp. A solution of bromine (5.4 mL) in $CHCl_3$ (50 mL) was then added over a period of 3 hours with significant evolution of HBr observed. The reaction was allowed to warm to room temperature and after 3 hours heated under reflux. After a further 2 hours, the reaction was cooled to room temperature and then quenched with sodium metabisulfite solution (5%, 100 mL). The organic layer was then separated and

neutralised with saturated Na_2CO_3 solution (100 mL) then dried and concentrated under reduced pressure producing a large volume of foam. After 40 minutes under reduced pressure the foam had solidified. The crude product was obtained as a light brown powder (20.42 g, 30.4 mmol, 96%) which was used without further purification. The spectroscopic data matches the literature values for **224** with additional signals attributed to unidentified byproducts.[111]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.96 – 5.36 (m, 6H), 3.50 – 2.98 (m, 6H).

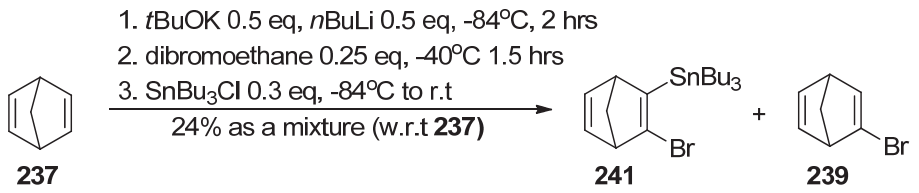
Attempted synthesis of norbornadiene trimer



A mixture of zinc powder (0.460 g, 7.0 mmol) and DMF (50 mL) was sonicated for 30 minutes. DMAD (1.8 g, 12.7 mmol) was then added followed by a solution of the hexabromide **224** (0.671 g, 1.0 mmol) in DMF (5 mL). The mixture was sonicated for a further 5 hours and then diluted in water (100 mL) and brine (100 mL). The mixture was extracted with EtOAc (3x 30 mL) and the extracts were washed with water (50 mL) then brine (50 mL), dried and concentrated to yield a light brown residue which was purified by silica gel flash chromatography (0-50% EtOAc:petrol) to yield a pale yellow residue which was further purified by trituration with ice cold MeOH (5 mL) to give **229** as a white solid (0.034 g, 7%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.97 – 6.88 (m, 1H), 6.54 – 6.44 (m, 1H), 4.45 – 4.43 (m, 1H), 4.42 – 4.38 (m, 2H), 4.36 – 4.33 (m, 1H), 3.79 – 3.73 (m, 6H), 3.43 – 3.36 (m, 2H), 2.57 – 2.51 (m, 2H), 2.26 – 2.20 (m, 2H).

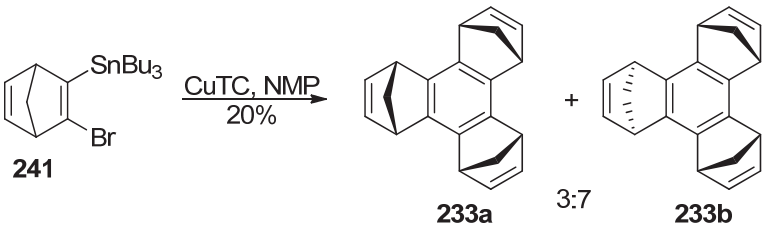
2-Bromo-3-(tributylstannyl)norbornadiene



The synthesis of the norbornadiene bromostannane was carried out according to the literature procedure.[117] A solution of *t*BuOK (1.627 g, 14.50 mmol) in THF (50 mL) was cooled to -84 °C and freshly distilled norbornadiene (2.949 mL, 29.00 mmol) was added. *n*BuLi (1.6 M in hexanes, 9.063 mL, 14.50 mmol) was then added dropwise over 2 hours resulting in a colour change to yellow. After addition was complete, the bright yellow opaque reaction mixture was warmed to -40 °C. After 1 hour, the light brown homogeneous reaction mixture was cooled to -84 °C and 1,2-dibromoethane (0.628 mL, 7.25 mmol) was added dropwise resulting in the formation of a white precipitate. The reaction mixture was then warmed to -40 °C and after 90 minutes, the colourless reaction mixture was cooled to -84 °C. Tributyltin chloride (2.360 mL, 8.70 mmol) was then added and the reaction was allowed to warm slowly to room temperature. After 18 hours, the reaction mixture was diluted in water (50 mL) and brine (50 mL) then extracted with Et_2O (3x 50 mL). The extracts were dried and concentrated to yield **241** as a pale yellow oil (3.20 g, 24%) which was used without further purification. The spectroscopic data matches the reported literature values.[118]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.86 – 6.82 (m, 1H), 6.67 – 6.63 (m, 1H), 3.80 – 3.70 (m, 1H), 3.53 – 3.48 (m, 1H), 2.21 – 2.17 (m, 1H), 2.01 – 1.96 (m, 1H), 1.37 – 1.24 (m, 12H), 1.05 – 0.95 (m, 6H), 0.95 – 0.84 (m, 9H).

Benzotris(norbornadiene)

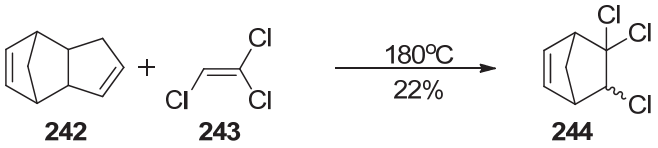


241 233a 233b

The synthesis of the norbornadiene trimer was carried out according to the literature procedure.[117] A solution of the norbornadiene bromostannane **241** (3.20 g, 6.96 mmol) in dry and degassed NMP (20 mL) was cooled to -20 °C. CuTC (1.326 g, 6.96 mmol) was then added and after 1 hour the reaction mixture was allowed to warm to room temperature. After 18 hours the reaction was quenched by addition of aqueous ammonia (10%, 50 mL) then diluted in brine (20 mL) and extracted with Et_2O (3x 20 mL). The extracts were dried and concentrated to give a red oil which was dissolved in petrol (100 mL) and filtered through a short plug of silica gel. The eluent was concentrated to yield **233** as a pale yellow oil (0.270 g, 43%) isolated as a mixture of stereoisomers. The spectroscopic data matches the literature values for a mixture of *syn* and *anti* isomers in a ratio of 3:7 respectively.[115]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.70 – 6.65 (m, 3H), 6.62 – 6.56 (m, 3H), 3.92 – 3.83 (m, 6H), 2.26 – 2.16 (m, 3H), 2.11 – 1.97 (m, 3H).

5,5,6-Trichloronorbornene



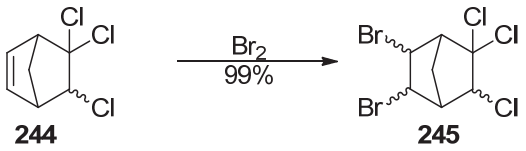
242 243 244

A mixture of dicyclopentadiene (15 mL, 0.111 mol) and trichloroethylene (50 mL, 0.555 mol) was heated to 180 °C in a sealed tube. After 24 hours, the reaction mixture was cooled and concentrated under reduced pressure. The dark residue was subject to vacuum distillation (80-90 °C @ 1 mmHg) with the first fraction being collected. The product partially crystallised in the condenser and gentle warming of the condenser was used to prevent blockage. The distillate was obtained as a pale

yellow semi crystalline oil (9.50 g, 48.1 mmol, 22%) as a mixture of two diastereomers of **244**. The product was of sufficient purity for the subsequent reaction. The spectroscopic data matches the reported literature values.[120]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.38 – 6.23 (m, 4H), 4.77 (d, *J* = 3.5 Hz, 1H), 4.19 (d, *J* = 2.7 Hz, 1H), 3.57 – 3.51 (m, 1H), 3.49 – 3.45 (m, 1H), 3.26 – 3.21 (m, 1H), 3.06 – 3.01 (m, 1H), 2.33 – 2.27 (m, 1H), 2.11 – 2.05 (m, 1H), 2.00 – 1.89 (m, 2H).

2,2,3-Trichloro-5,6-dibromonorbornane

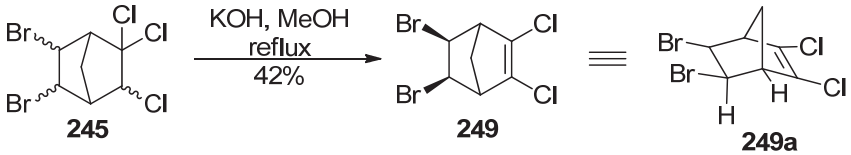


244 **245**

The synthesis of 2,2,3-trichloro-6,5-dibromonorbornane was carried out according to the previously published procedure.[119] A solution of trichloronorbornene **244** (9.50 g, 48.1 mmol) in DCM (100 mL) was cooled to 0 °C and Br_2 (2.5 mL, 48.8 mmol) in DCM (20 mL) was added dropwise. The reaction was allowed to warm to room temperature and after 1 hour, quenched with sodium metabisulfite solution (5%, 100 mL). The organic layer was dried and then concentrated to yield **245** as a pale yellow oil (17.10 g, 47.9 mmol, 99%) as a mixture of stereoisomers of sufficient purity.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.95 – 4.15 (m, 3H), 3.28 – 2.75 (m, 2H), 2.62 – 2.19 (m, 2H).

5,6-Dibromo-2,3-dichloronorbornene



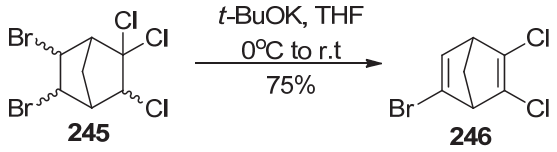
245 **249** **249a**

A solution of KOH (10 g) in MeOH (200 mL) was added to a solution of norbornane **245** (22.0 g, 61.6 mmol) in MeOH (100 mL). After 18 hours, the reaction mixture

was diluted with DCM (200 mL) and filtered through a short silica plug. The eluent was concentrated to give a white solid (8.30 g, 25.9 mmol, 42%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.25 (d, *J* = 2.1 Hz, 2H), 3.19 (t, *J* = 1.8 Hz, 2H), 2.41 – 2.34 (m, 1H), 2.20 – 2.12 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.74 (C), 59.19 (CH), 50.64 (CH), 42.21 (CH_2).

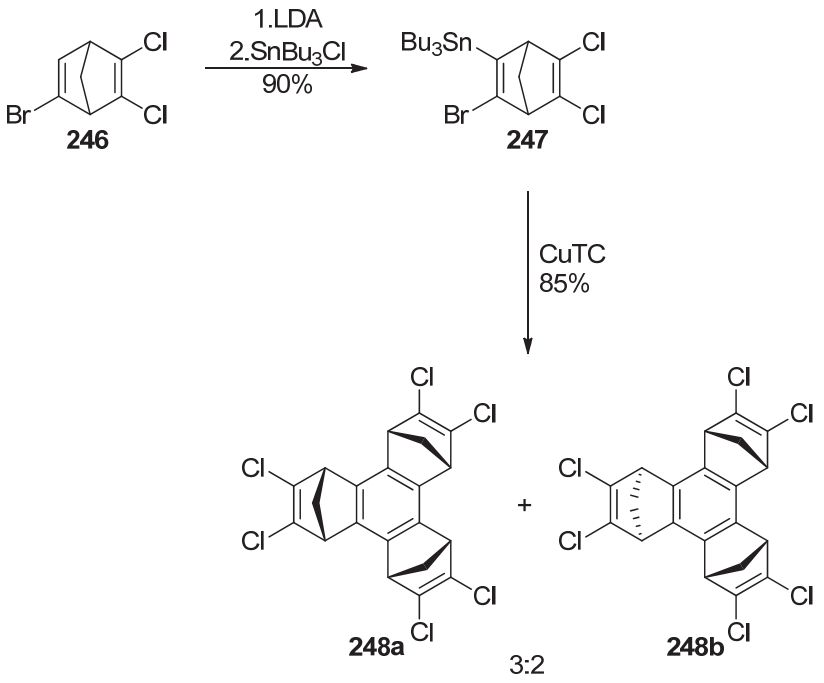
5-Bromo-2,3-dichloronorbornadiene



The synthesis of 4-bromo-1,2-dichloronorbornadiene was carried out according to the previously published procedure.[119] A solution of the norbornane **245** (17.10 g, 47.9 mmol) in THF (150 mL) was cooled to 0 °C and *t*BuOK (11.70 g, 104.3 mmol) was added portionwise with vigorous stirring. The dark reaction mixture was then warmed to room temperature and after 1 hour the reaction mixture was diluted with petrol (250 mL) and subject to silica gel filtration. The colourless eluent was concentrated under reduced pressure (product is moderately volatile) to yield **246** as a colourless oil (8.62 g, 35.9 mmol, 75%) of high purity.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84 (d, *J* = 3.1 Hz, 1H), 3.52 – 3.49 (m, 1H), 3.49 – 3.46 (m, 1H), 2.54 – 2.50 (m, 1H), 2.50 – 2.45 (m, 1H).

Benzotris(5,6-dichloronorbornadiene)



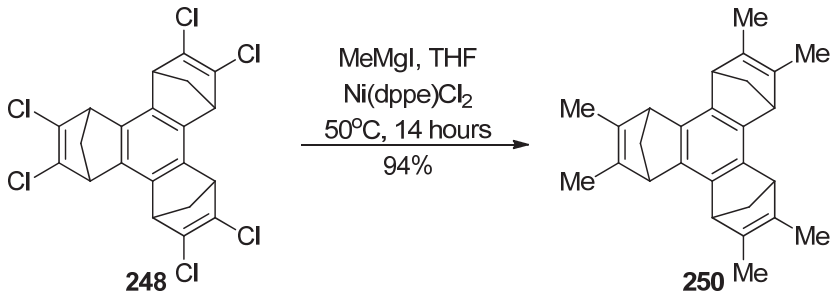
The synthesis of 4,5-dichloro-2-tributylstannyl-1-bromonorbornadiene was carried out with minor modification of the previously published procedure.[119] A solution of diisopropylamine (17.0 mL, 0.121 mol) in THF (100 mL) was cooled to 0 °C and *n*BuLi (1.6 M in hexane, 63 mL, 0.108 mol) was added dropwise. After 15 minutes, the cloudy solution was cooled to -84 °C and the norbornadiene **246** (20.285 g, 84.5 mmol) in THF (50 mL) was added dropwise. After 1 hour, $SnBu_3Cl$ (23.0 mL, 84.8 mmol) was added dropwise. The brown reaction mixture was allowed to warm to room temperature and after 2 hours the reaction was quenched with water (300 mL) and extracted with petrol (5x 100 mL). The extracts were then subject to silica gel filtration and the eluent concentrated under reduced pressure to give **247** as a pale yellow oil (40.49 g, 76.5 mmol, 90%) which was used without further purification.

R_F 0.95 (petrol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.61 – 3.49 (m, 2H), 2.43 – 2.33 (m, 2H), 1.59 – 1.22 (m, 12H), 1.12 – 1.00 (m, 6H), 0.90 (t, J = 7.3 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.50 (C), 146.22 (C), 139.83 (C), 137.56 (C), 69.21 (CH_2), 66.09 (CH), 63.11 (CH), 29.20 (CH_2), 27.40 (CH_2), 13.83 (CH_3), 10.19 (CH_2).

A solution of the norbornadiene **247** (40.49 g, 76.5 mmol) in degassed NMP (400 mL) was cooled to -15 °C and CuTC (15.25 g, 80 mmol) was added portionwise. After 3 hours, the reaction was quenched with ammonia (10%, 150 mL) then diluted with water (800 mL) and extracted with DCM (4x 100 mL). The extracts were dried and then concentrated to yield a brown solid with an oily residue. The crude product was triturated with petrol (100 mL) to yield **248** as a light brown solid (10.34 g, 21.7 mmol, 85%) isolated as a mixture of stereoisomers. The spectroscopic data matches the reported literature values.[119]

R_F 0.5 (petrol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.93 – 3.84 (m, 6H), 2.70 – 2.62 (m, 3H), 2.28 – 2.21 (m, 3H).

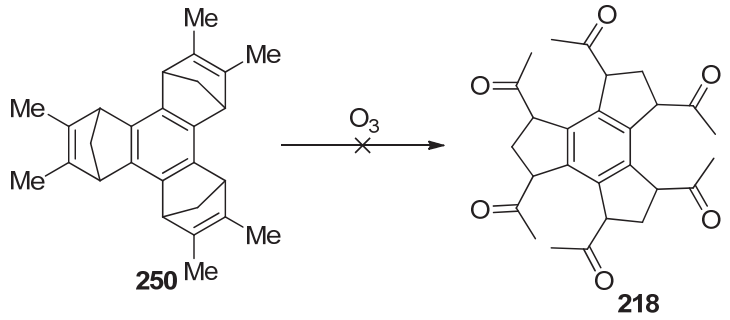
Benzotris(5,6-dimethylnorbornadiene)



The hexachloride **248** (2.00 g, 4.19 mmol) was added to MeMgI (1M in ether, 50 mL) followed by Ni(dppe)Cl_2 (110 mg, 5 mol%). The mixture was then sealed and heated to 50 °C. After 14 hours, the reaction was cooled and quenched with saturated NH_4Cl then diluted with ether (50 mL) and washed with HCl (1 M, 50 mL). The organic layer was dried and subject to silica gel filtration using petrol as the eluent. The eluent was concentrated to yield **250** as a light brown oil (1.40 g, 3.95 mmol, 94%). The spectroscopic data matches the reported literature values.[119]

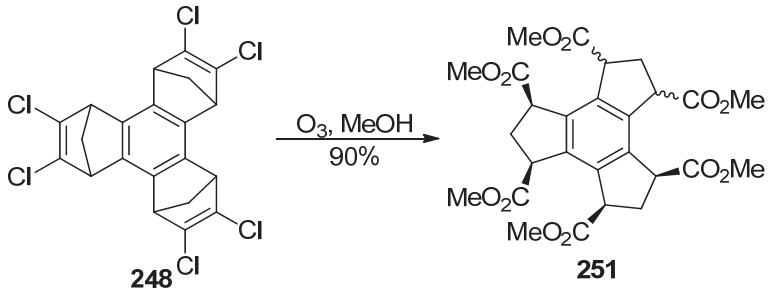
R_F 0.2 (petrol) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.58 – 3.48 (m, 6H), 2.23 – 2.12 (m, 3H), 2.03 – 1.87 (m, 3H), 1.72 – 1.65 (m, 18H).

Attempted synthesis of 1,3,4,6,7,9-hexaacetyltrindane



A solution of the hexamethyl norbornadiene trimer **250** (350 mg, 0. mmol) in DCM (100 mL) was cooled to -84 °C. Ozonised oxygen was passed through the solution until a blue colour became apparent. The excess ozone was removed by passing a stream of oxygen until the solution became colourless. Thiourea (0.20 g, 2.6 mmol) was then added and the reaction mixture was allowed to warm to room temperature. After 1 hour, the mixture was washed with water (100 mL), dried and concentrated to yield a pale brown oil (0.420 g).

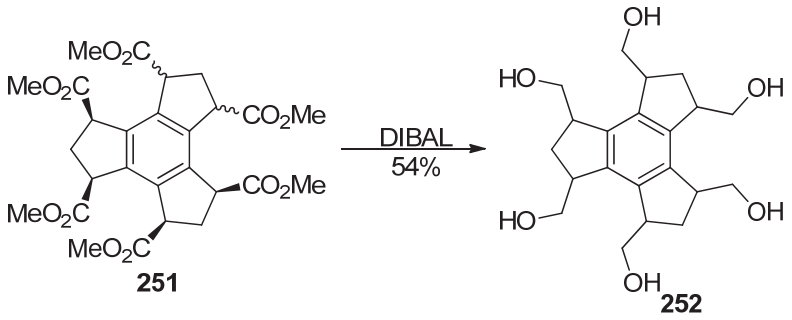
Hexamethyl trindane-1,3,4,6,7,9-carboxylate



A solution of the hexachloride **248** (385 mg, 0.81 mmol) in DCM (80 mL) and MeOH (20 mL) was cooled to -84 °C. Ozonised oxygen was passed through the solution until a blue colour became apparent. The excess ozone was removed by passing a stream of oxygen until the solution became colourless. The reaction mixture was allowed to warm to room temperature and the solvent removed to yield **251** as a pale yellow semi solid (420 mg, 0.77 mmol, 95%) isolated as a mixture of diastereomers. The spectroscopic data matches the reported literature values.[122]

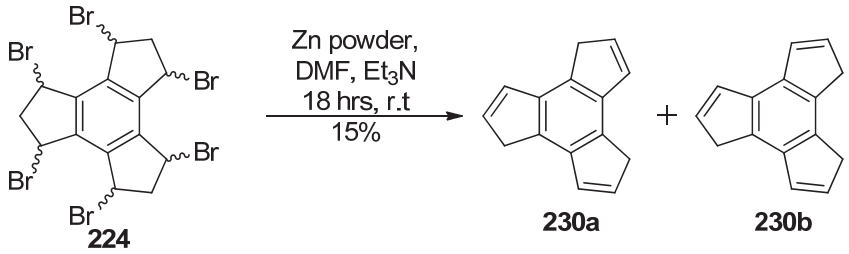
^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.39 – 3.90 (m, 6H), 3.73 – 3.57 (m, 18H), 2.99 – 2.54 (m, 6H). ATR IR: 1703 cm^{-1}.

1,3,4,6,7,9-Hexa(hydroxymethyl)trindane



A solution of the hexamethyl ester **251** (0.185 g, 0.34 mmol) in THF (15 mL) was cooled to -84 °C. DIBAL (~2 M in toluene, 6 mL, 18 mmol) was added dropwise and then reaction was warmed to room temperature. After 1 hour, the reaction was quenched by addition of MeOH (1 mL) then diluted with HCl (1 M, 100 mL) and extracted with EtOAc (3x 30 mL). The extracts were washed with brine (50 mL), dried and concentrated to yield an off white residue (0.070 g).

Trindene

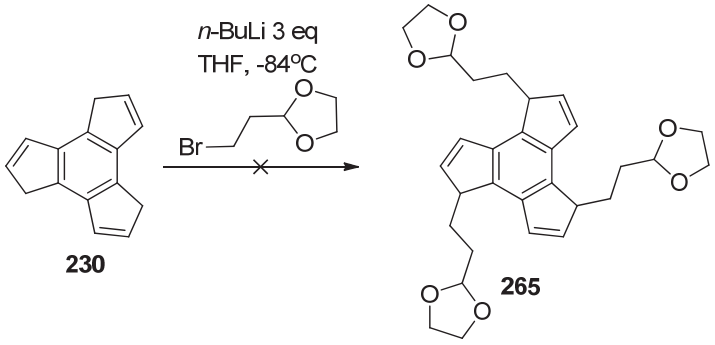


Zn powder (7.5 g, 110 mmol) in degassed DMF (200 mL) was cooled on ice with vigorous stirring. The solid hexabromide **224** (11.2 g, 16.7 mmol) and triethylamine (4 mL, 28.7 mmol) were added concurrently portionwise over 15 minutes. The dark reaction mixture was then allowed to warm to room temperature. After 18 hours, the reaction mixture was filtered through celite and the filtrate was diluted with brine (200 mL) and water (300 mL). The mixture was then extracted with petrol (3x 150 mL) and the organic extracts were passed through a short plug of silica gel (5:95 EtOAc:petrol). The colourless eluent was concentrated to give **230** as a colourless

crystalline solid (0.48 g, 2.50 mmol, 15%) isolated as a mixture of regioisomers. The spectroscopic data matches the reported literature values.[111]

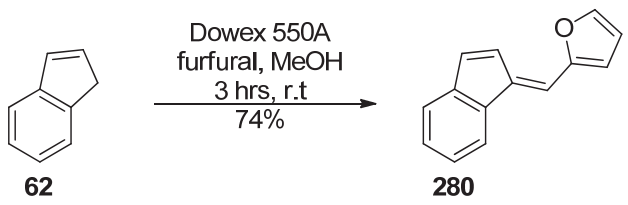
R_F = 0.7 (petrol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 – 7.01 (m, 3H), 6.69 – 6.53 (m, 3H), 3.61 – 3.45 (m, 6H).

*Attempted synthesis of trindene acetal **265***



The trindenyl trianion was prepared according to the literature procedure.[111] A solution of trindene **230** (0.050 g, 0.26 mmol) in THF (10 mL) was cooled to -84 °C and *n*BuLi (1.6 M, 0.57 mL, 0.91 mmol) was added dropwise. The mixture was warmed to 0 °C for 1 hour and then cooled to -84 °C. A solution of 3-bromopropanal acetal (0.282 g, 1.56 mmol) in THF (2 mL) was then added dropwise and the mixture warmed to 0 °C. After 1 hour the reaction was quenched by addition of HCl (1M, 10 mL) then diluted in water (100 mL) and extracted with EtOAc (3x 20 mL). The extracts were dried and then concentrated to give a pale yellow oil with analysis by ^{1}H NMR showing unreacted trindene as the major component.

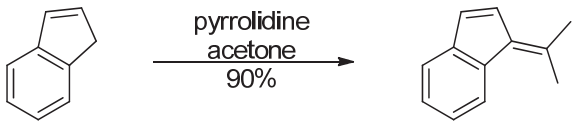
6-Furylbenzofulvene



6-Furylbenzofulvene was synthesised following a modified literature procedure.[181] A solution of furfural (5.30 g, 55.2 mmol) in methanol (25 mL) was added dropwise over 18 hours to a solution of indene (5.80 g, 49.9 mmol) in methanol (40 mL) with Dowex 550A resin (6 g). Halfway through the addition the product started to precipitate as a yellow solid. After addition was complete, the mixture was stirred for an additional 2 hours then diluted with DCM (150 mL) and filtered through celite. The yellow filtrate was concentrated and the yellow solid was recrystallised from methanol (15 mL) yielding **280** as a yellow solid (7.17 g, 36.9 mmol, 74%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 – 7.56 (m, 2H), 7.37 (d, *J* = 5.5 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.25 – 7.15 (m, 2H), 7.09 (s, 1H), 6.97 (dd, *J* = 5.6, 1.5 Hz, 1H), 6.67 (d, *J* = 3.4 Hz, 1H), 6.51 (dd, *J* = 3.4, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.42 (C), 144.84 (CH), 142.18 (C), 137.54 (C), 136.71 (C), 133.67 (CH), 127.40 (CH), 125.03 (CH), 121.16 (CH), 119.10 (CH), 115.04 (CH), 114.29 (CH), 112.41 (CH).

6,6-Dimethylbenzofulvene

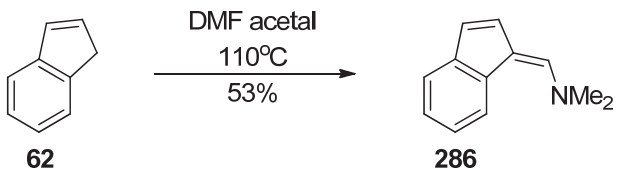


62 **295**

Pyrrolidine (0.541 g, 7.6 mmol) was added to a solution of indene (0.581 g, 5.0 mmol) and acetone (0.441 g, 7.6 mmol) in methanol (5 mL). After 48 hours, the reaction mixture was concentrated under reduced pressure to yield the crude product as a yellow oil (0.891 g). Analysis of the ^{1}H NMR spectrum indicated 90% conversion of indene to the benzofulvene **295**. The spectroscopic data matches the reported literature values.[178]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 – 7.74 (m, 1H), 7.37 – 7.33 (m, 1H), 7.25 – 7.20 (m, 2H), 6.87 (d, *J* = 5.6 Hz, 1H), 6.80 (d, *J* = 5.4 Hz, 1H), 2.44 (s, 3H), 2.31 (s, 3H).

6-(Dimethylamino)benzofulvene

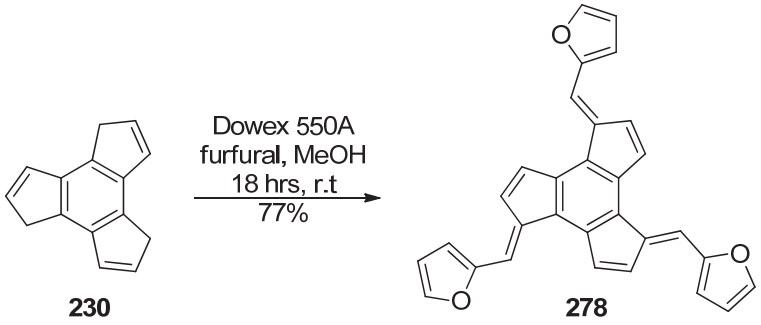


62 **286**

The dimethylamino benzofulvene was synthesised according to the literature procedure.[137] A solution of indene (0.581 g, 5.0 mmol) and DMF dimethyl acetal (1.192 g, 10 mmol) in toluene (5 mL) was heated under reflux. After 18 hours, the reaction mixture was diluted in DCM (100 mL) and filtered through a short plug of silica gel. The eluent was then concentrated under reduced pressure to yield **286** as a dark red oil (0.730 g, 85%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.59 (m, 1H), 7.51 – 7.46 (m, 1H), 7.43 (s, 1H), 7.16 – 7.12 (m, 2H), 7.06 (d, *J* = 5.3 Hz, 1H), 6.84 (d, *J* = 5.2 Hz, 1H), 3.27 (s, 6H).

Tris(furyl)trifulvene

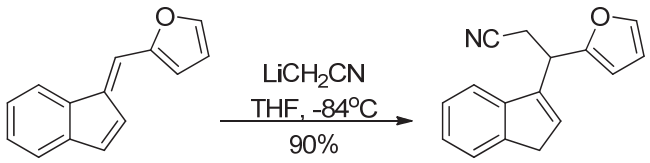


230 **278**

A solution of furfural (160 mg, 1.67 mmol) in methanol (20 mL) was added dropwise over 18 hours (syringe pump) to a solution of trindene **230** (100 mg, 0.52 mmol) in methanol (30 mL) with Dowex 550A resin (3 g). After addition was complete the mixture was stirred for an additional 2 hours then diluted with DCM (100 mL) and filtered through celite. The filtrate was concentrated under reduced pressure and purified by silica gel chromatography to yield **278** as a dark red solid (170 mg, 0.40 mmol, 77%) isolated as a single regioisomer.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (m, 6H), 7.47 (dd, *J* = 5.8, 1.5 Hz, 3H), 7.30 (s, 3H), 6.67 (d, *J* = 3.3 Hz, 3H), 6.53 (dd, *J* = 3.4, 1.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.68 (C), 144.41 (CH), 137.20 (C), 135.33 (C), 130.91 (CH), 130.40 (CH), 127.54 (C), 115.81 (CH), 114.58 (CH), 112.33 (CH). ATR IR: 1615 cm^{-1}.

3-(Furyl)-3-(indenyl)propanenitrile

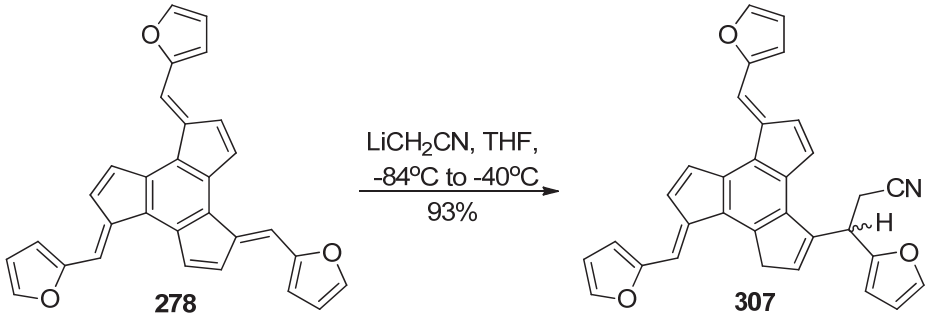


280 **306**

A solution of acetonitrile (0.246 g, 6.0 mmol) in THF (20 mL) was cooled to -84 °C and *n*BuLi (1.6 M in hexane, 2.5 mL, 4.0 mmol) was added dropwise. After 45 minutes, a solution of benzofulvene **280** (0.380 g, 2.0 mmol) in THF (5 mL) was added dropwise. After 30 minutes, the reaction mixture was poured into HCl (1M, 50 mL) then diluted with water (100 mL) and extracted with DCM (50 mL). The extract was dried and concentrated to yield **306** as a pale yellow oil (0.412 g, 88%). The spectroscopic data matches the reported literature values.[155]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.48 (m, 1H), 7.41 – 7.37 (m, 1H), 7.31 – 7.20 (m, 3H), 6.54 – 6.49 (m, 1H), 6.37 – 6.31 (m, 1H), 6.25 – 6.20 (m, 1H), 4.50 (t, 1H, *J* = 7.2 Hz), 3.47 (m, 2H), 3.09 (1H+1H, d, *J* = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.53 (C), 144.36 (C), 143.13 (C), 142.32 (CH), 141.46 (C), 130.78 (CH), 126.26 (CH), 125.29 (CH), 124.14 (CH), 119.27 (CH), 118.08 (C), 110.59 (CH), 107.51 (CH), 38.03 (CH_2), 35.22 (CH), 21.74 (CH_2).

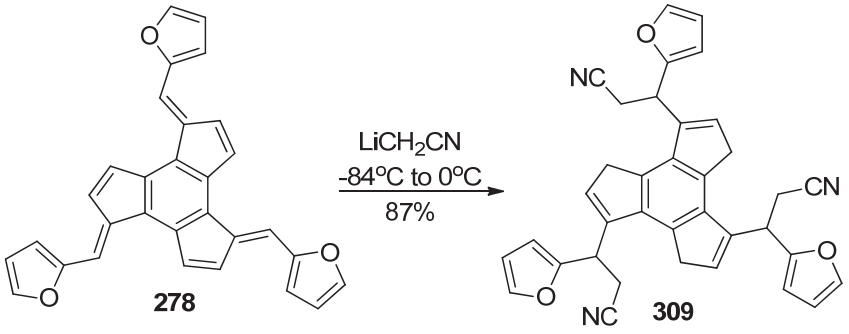
*Tris(furyl)trifulvene monoadduct **307***



A solution of acetonitrile (60 μL, 1.15 mmol) in THF (10 mL) was cooled to -84 °C and *n*BuLi (1.6 M in hexane, 0.6 mL, 0.96 mmol) was added dropwise. After 45 minutes a solution of trifulvene **278** (64 mg, 0.15 mmol) in THF (10 mL) was added dropwise. The intensely coloured reaction mixture was warmed to -40 °C for 30 minutes and then quenched with NH_4Cl (saturated, 10 mL). The reaction was diluted with water (100 mL) then extracted with DCM (50 mL). The organic extract was dried and then concentrated to yield **307** as a red oil (66 mg, 0.14 mmol, 93%).

R_F 0.25 (20:80 EtOAc:petrol); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (dd, *J* = 10.3, 1.8 Hz, 2H), 7.53 (d, *J* = 5.7 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.39 (d, *J* = 5.7 Hz, 1H), 7.29 (s, 1H), 7.10 (s, 1H), 6.86 (dd, *J* = 5.8, 1.5 Hz, 1H), 6.67 (dd, *J* = 3.5, 1.6 Hz, 2H), 6.55 – 6.50 (m, 2H), 6.45 – 6.43 (m, 1H), 6.31 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.16 (d, *J* = 3.3 Hz, 1H), 4.72 (t, *J* = 6.9 Hz, 1H), 3.71 (m, 2H), 3.11 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.64 (C), 153.63 (C), 152.77 (C), 144.60 (CH), 144.52 (CH), 142.43 (CH), 142.35 (C), 137.27 (C), 137.21 (C), 137.13 (C), 134.62 (C), 133.92 (C), 133.88 (C), 130.86 (CH), 130.69 (C), 130.55 (CH), 130.44 (CH), 130.00 (CH), 128.95 (C), 128.71 (CH), 118.22 (C), 116.24 (CH), 114.91 (CH), 114.78 (CH), 112.43 (CH), 112.42 (CH), 110.84 (CH), 37.16 (CH_2), 36.31 (CH), 22.20 (CH_2).

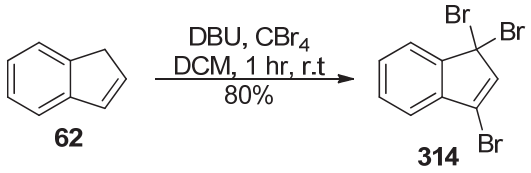
Tris(3-(furyl)propanenitrile)indene



A solution of acetonitrile (60 µL, 1.15 mmol) in THF (10 mL) was cooled to -84 °C and *n*BuLi (1.6 M in hexane, 0.6 mL, 0.96 mmol) was added dropwise. After 45 minutes a solution of trifulvene **278** (44 mg, 0.10mmol) in THF (10 mL) was added dropwise. The reaction mixture was warmed to 0 °C for 2 hours and then quenched with NH_4Cl (saturated 10 mL). The reaction was diluted with water (100 mL) then extracted with DCM (50 mL). The organic extract was dried and then concentrated to yield **309** a brown oil (48 mg, 0.087 mmol, 87%). Attempts at purification by silica gel chromatography resulted in loss of the desired product.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.38 (m, 3H), 6.56 – 6.49 (m, 3H), 6.32 – 6.25 (m, 3H), 6.14 – 5.99 (m, 3H), 4.69 (d, *J* = 7.2 Hz, 3H), 3.69 – 3.49 (m, 6H), 3.24 – 2.96 (m, 6H).

1,1,3-Tribromoindene

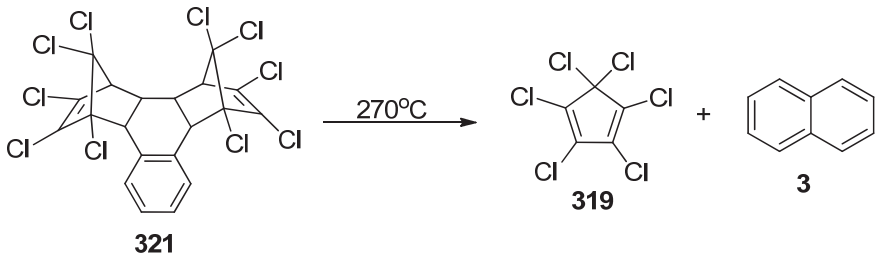


A solution of indene (0.116 g, 1.0 mmol) and carbon tetrabromide (1.324 g, mmol) in DCM (10 mL) was cooled on ice. DBU (0.5 mL) was then added dropwise over 5 minutes and the reaction was warmed to room temperature. After 30 minutes, the reaction was diluted in DCM (50 mL) and washed with HCl (1 M, 50 mL) then dried and concentrated to yield a brown solid which was triturated with ice cold MeOH (5

mL) to yield **314** as a colourless crystalline solid (0.282 g, 80%). The spectroscopic data matches the reported literature values.[159]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.67 (m, 1H), 7.40 – 7.36 (m, 2H), 7.27 – 7.23 (m, 1H), 6.82 (s, 1H).

Perchlorocyclopentadiene

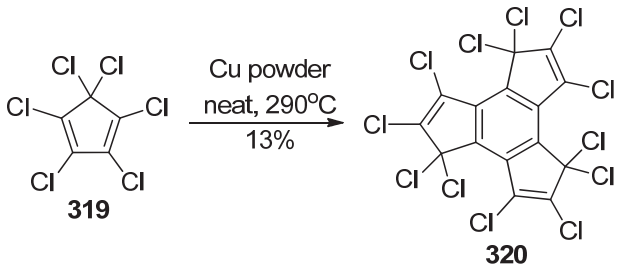


321 **319** **3**

Naphthalene-*bis*(hexachlorocyclopentadiene) adduct (50.00 g, 74.2 mmol) was heated to 270 °C and distilled under reduced pressure (240 mmHg). After distillation had ceased the remaining black tarry residue was dissolved in toluene (20 mL) before cooling to allow for cleaning. The semi crystalline distillate (42.1 g) was distilled under reduced pressure (80 °C @ 1.2 mmHg) through a vigreux column. The naphthalene which crystallised on the column was periodically rinsed off and discarded. The process was repeated as required to yield **319** as a pale yellow oil (22.4 g, 82.1 mmol, 55%) containing approximately 5% naphthalene impurity determined by ^{13}C NMR. The spectroscopic data matches the reported literature values.[179]

^{13}C NMR (101 MHz, $CDCl_3$) δ 133.14 (C), 128.62 (C), 81.72 (C).

Perchlorotrindene

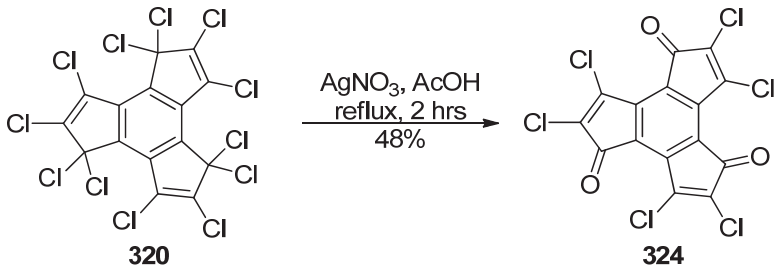


319 320

A mixture of perchlorocylopentadiene (6 mL, 10.2 g, 37.4 mmol) and Cu powder (0.3 g) was heated to 270 °C for 2 hours and then 290 °C for 24 hours. The black tarry reaction mixture was cooled to 120 °C and dissolved in xylene (20 mL). The mixture was then cooled to 0 °C and the precipitate collected by filtration and washed with petrol (3x 20 mL). The light brown solid was dissolved in DCM (150 mL) and filtered through celite. The filtrate was concentrated yielding **320** as a pale yellow solid (1.02 g, 1.68 mmol, 13%). The spectroscopic data matches the reported literature values.[163]

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.39 (C), 134.85 (C), 133.40 (C), 127.39 (C), 79.58 (C).

Perchlorotrindenone

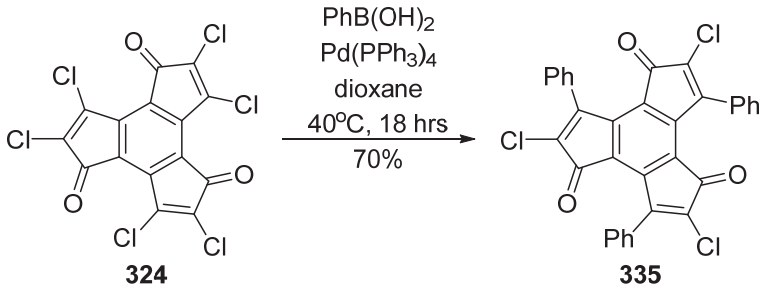


320 324

A mixture of perchlorocyclopentadiene **320** (600 mg, 0.992 mmol) and $AgNO_3$ (1.65 g, 9.71 mmol) in AcOH (50 mL) was heated under reflux. After 2 hours, the reaction mixture was cooled then diluted with DCM (200 mL) and filtered. The filtrate was concentrated under reduced pressure yielding a poorly soluble yellow solid (210 mg, 0.480 mmol, 48%). NMR spectra could not be obtained due to the low solubility and absence of hydrogen substituents.

ATR IR: 1722 cm^{-1}.

2,5,8-Trichloro-3,6,9-triphenyltrindenone



324 **335**

A mixture of trindenone **324** (50 mg, 0.113 mmol) and phenylboronic acid (45 mg, 0.369 mmol, 3.2 eq) in dioxane (5 mL) was degassed and $Pd(PPh_3)_4$ (20 mg, 15 mol%) added. The mixture rapidly changed colour from yellow to dark green/black. Aqueous K_2CO_3 (1 M, 1 mL) was then added and the reaction flask was sealed and heated to 40 °C. After 18 hours the reaction mixture was diluted with water (50 mL) and extracted with DCM (50 mL). The organic extract was filtered through a short plug of silica and the orange fraction collected. The solvent was removed to yield **335** as an orange solid (45 mg, 79 μmol, 70%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.33 (m, 6H), 7.24 – 7.14 (m, 6H), 7.05 – 7.00 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.71 (C), 154.97 (C), 144.57 (C), 142.94 (C), 134.95 (C), 130.33 (CH), 128.34 (CH), 127.91 (CH), 125.60 (C).

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