UNIVERSITY OF SOUTHAMPTON

Cyclisation Strategies Towards the Synthesis of Natural Products

By

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A Thesis submitted for the degree of Doctor of Philosophy

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ABSTRACT

FACULTY OF SCIENCE

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Cyclisation Strategies Towards the Synthesis of Natural Products

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This thesis is concerned with the development of cyclisation methodologies which have potential in the synthesis of natural products. A palladium catalysed cyclisation is developed and applied to the synthesis of virola indenone. The structure of virola indenone is redefined and two routes to the natural product are described. A one pot synthesis is also developed.

The use of a radical cyclisation methodology utilising thiyl radicals and a bite back strategy to attempt to control the stereoselectivity is studied. Its scope in the synthesis of aryltetralins and other systems is investigated.

A new method of synthesising biaryls and triaryls through an intramolecular ipso-substitution reaction initiated by the addition of an aryl radical to a benzyl ether is described. A tandem variant of the reaction is also demonstrated.

A literature review of the synthesis of aryl indenones is presented.

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And finally, to Paul Razzell, for being there for the duration.

To Paul,

with all my love

Abbreviations

Ad	Adamantyl
AIBN	azo-*iso*-butyronitrile
amu	atomic mass units
APCI	atmospheric pressure chemical ionisation
aq.	aqueous
Ar	aryl
Bn	benzyl
Bu	butyl
CHN	combustion analysis
CI	chemical ionisation
conc.	concentrated
COSY	correlated spectroscopy
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DMA	*N*,*N*-dimethylacetamide
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
EI	electron impact
eq.	Equivalents
Et	ethyl
FT	Fourier Transform
h	hours
HMPA	hexamethylphosphoramide
HRMS	high resolution mass spectra
IR	infra red
lit.	literature
LRMS	low resolution mass spectra
LDA	lithium diisopropylamide
M	molar
mmol	millimols
Me	methyl
min	minutes

NMR	nuclear magnetic resonance
Ph	phenyl
ppm	parts per million
py	pyridine
THF	tetrahydrofuran
TMEDA	tetramethylethylenediamine
UV	ultra violet

Chapter One

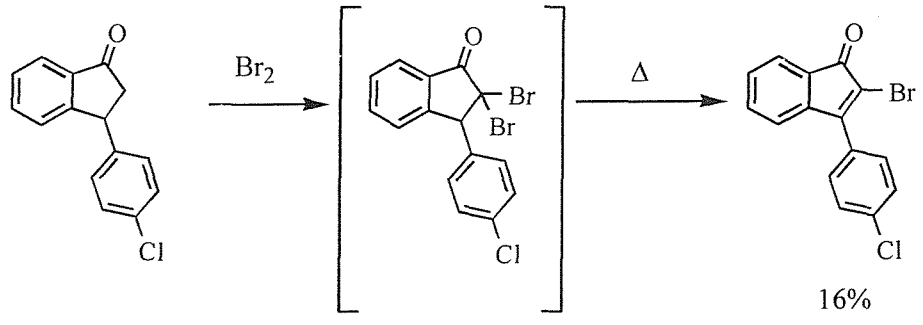
Introduction

The Synthesis of Aryl Indenones

Indenones have been used as fungicides, potential oestrogen binding receptors and fermentation activators. [1-3] They are also useful intermediates in the synthesis of a variety of natural products *e.g.* steroids and gibberellins. [4,5] They can be prepared following traditional synthetic methods or by metal mediated reactions. Summarised below are a selection of the methods available for the synthesis of aryl indenones.

1.1 Elimination of Indanones

Perhaps the most logical precursor to an indenone is the corresponding indanone. This method has a long history and most early examples involved the bromination and dehydrobromination of the corresponding indanone.[6] A typical example is highlighted in Scheme 1.1.[7]



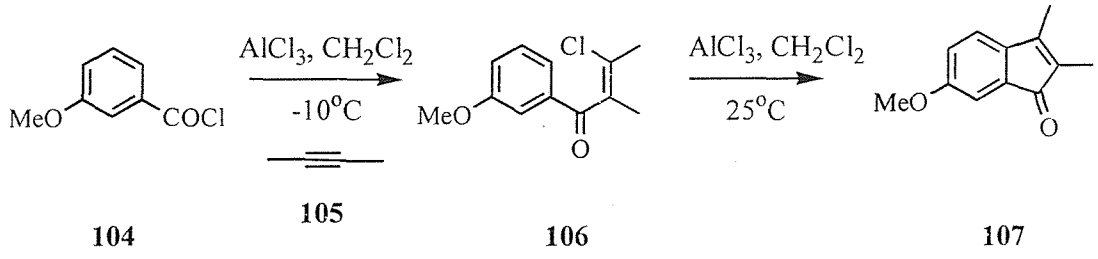
101 **102** **103**

Scheme 1.1

The initial bromination of the indanone **101** resulted in dibromide **102** which was unstable. Immediate heating of **102** provided the aryl indenone **103** in 16% yield. Many examples tell a similar tale of poor yielding reactions. Floyd had more success in the synthesis of indenones *via* this method, as did House in 1969; however, they did not apply the methodology to 3-arylindenones. [6,8]

1.2 Friedel-Crafts Type Cyclisations

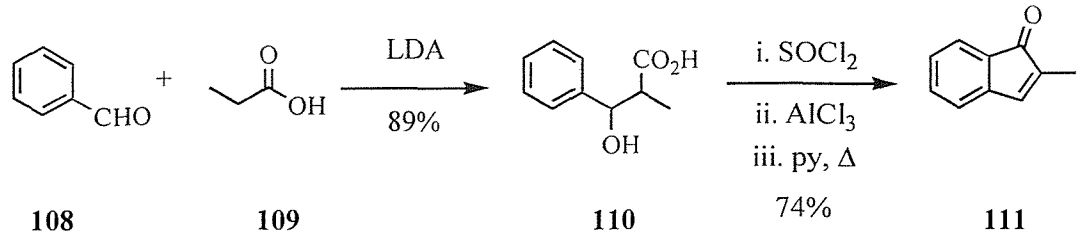
Work has taken place to develop routes to indenones *via* intramolecular Friedel-Crafts cyclisations. Early work laid the foundations for application to the 3-substituted examples. In 1974 Martens effected the synthesis of 2,3-substitued indenones *via* treatment of acid chloride **104** with 2-butyne **105**, a reaction catalysed by aluminium chloride, to give the intermediate β-chlorovinyl ketone **106**.[9] Further treatment of **106** with $AlCl_3$ in DCM gave a 53% yield of indenone **107** (Scheme 1.2).



104 **106** **107**

Scheme 1.2

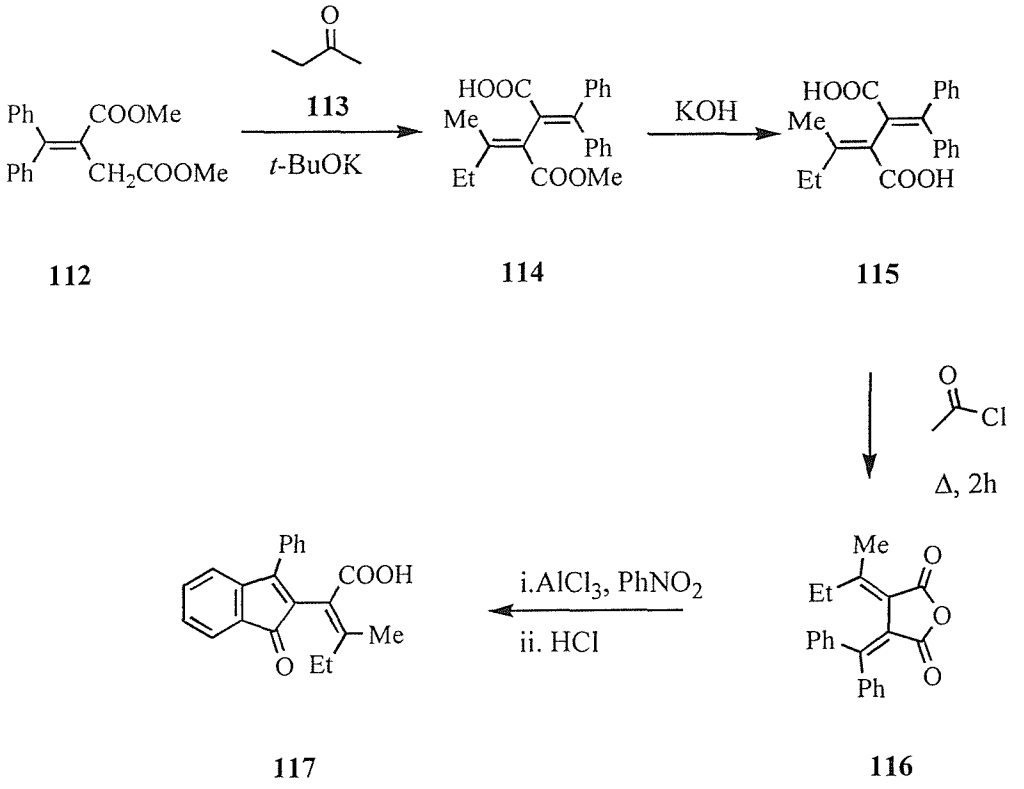
An alternative approach was developed by Floyd and later improved by Galatsis and Manwell.[8,10] They found that direct treatment of **108** with the dianion of propanoic acid accomplished transformation to **110** in 89% yield. A Friedel Crafts acylation with concomitant β-elimination was then successfully effected by treatment of the corresponding acid chloride with aluminium trichloride (Scheme 1.3). However, the reaction was only useful when a substituent was present in the 2-position of the indenone.



108 **109** **110** **111**

Scheme 1.3

In 1991 Banerjee showed that 3-arylindenones could be formed by an intramolecular Friedel-Crafts acylation between an arene and an anhydride.[4] For example, treatment of **116** with aluminium trichloride for 24 h promoted cyclisation to give indenone **117**. Unfortunately, the utility of this route is difficult to assess since no yields or experimental details were given.

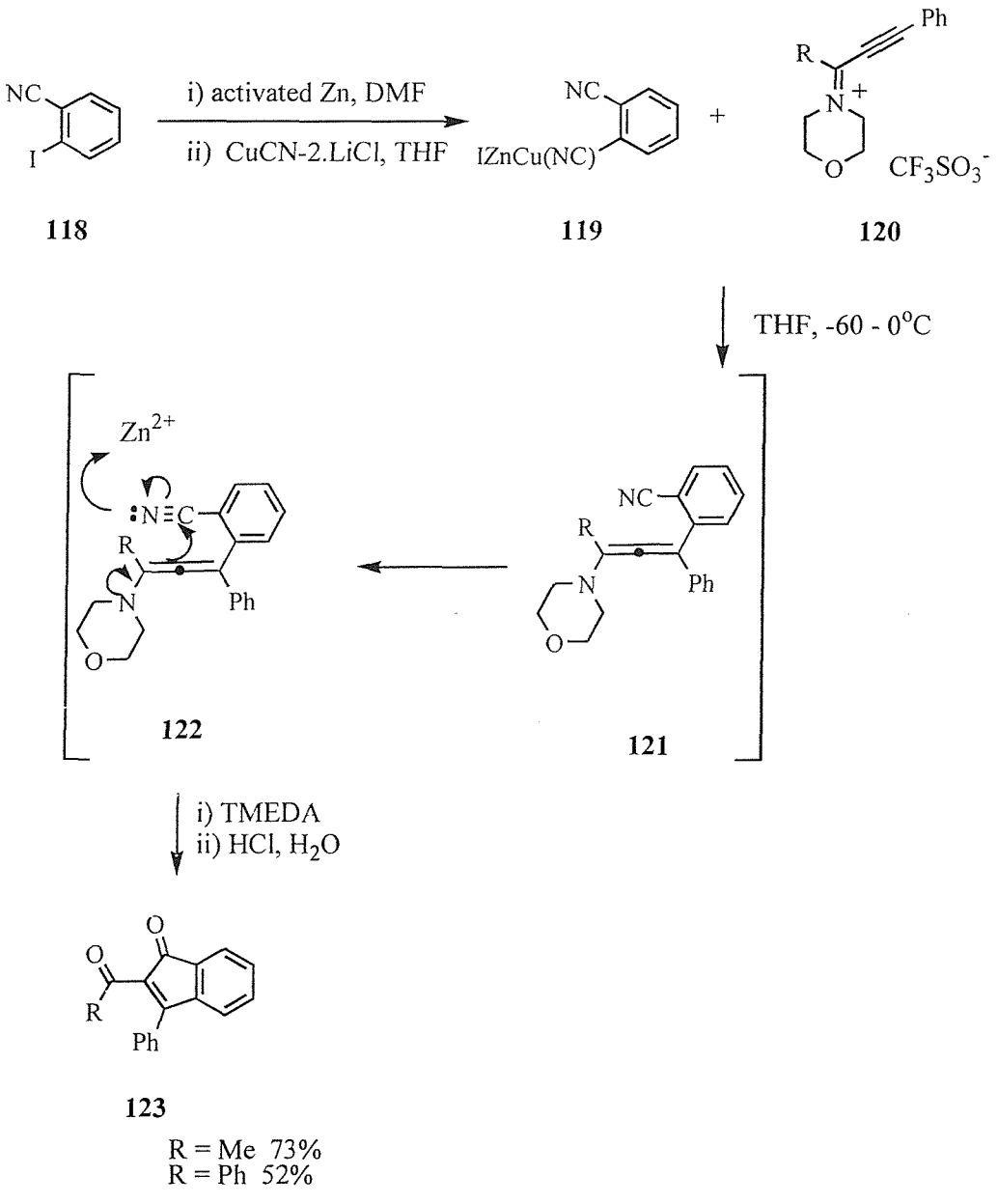


112 **114** **115** **116** **117**

Scheme 1.4

1.3 Use of Transition metals – zinc and copper

A range of transition metals have been used in the synthesis of 3-arylindenones. Brunner found that organozinc and copper reagents can undergo conjugate addition to (2-propynylidene) morpholinium triflates and employed this in the synthesis of several 2-acyl-3-arylindenones.[12] For example, treatment of iodide **118** with activated zinc then CuCN.2LiCl gave a complex to which was added propyne iminium triflate **120**. The intermediate allene **121** cyclised *in situ* to the vicinal cyano moiety giving indenone **123** on work up. Zinc ions are presumed to initiate addition of the enamine to nitrile (Scheme 1.5).



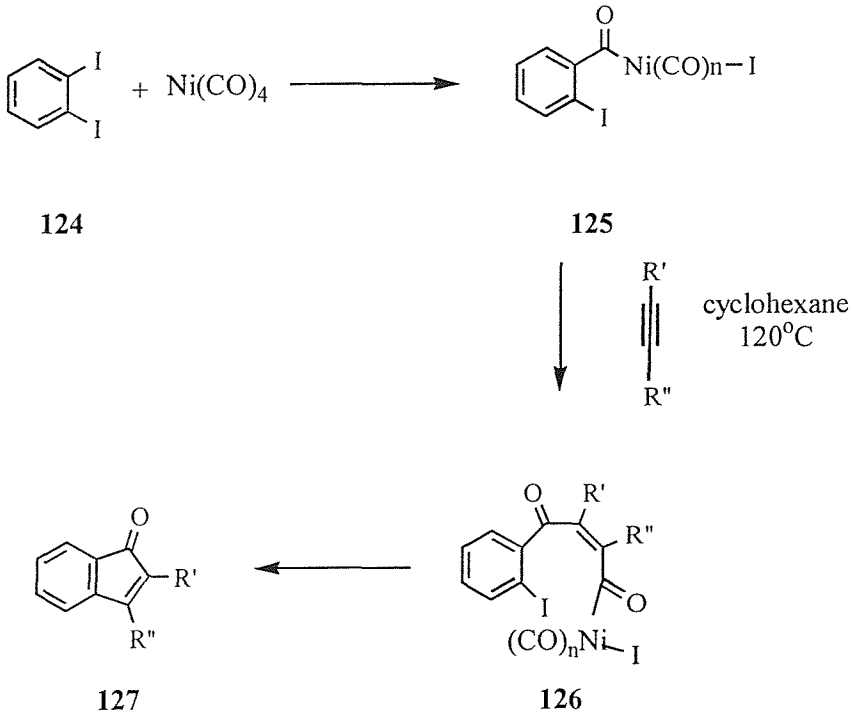
Scheme 1.5

1.4 Use of Transition Metals – Nickel

Liebeskind investigated reactions of nickel carbonyl with iodobenzene.[13] Nickel carbonyl reacts with iodobenzene to produce a benzoylnickel complex which decomposes to benzil in aprotic solvents. However in the prescence of an alkyne, the benzoylnickel intermediate is trapped, undergoing addition to the alkyne. Insertion of

CO follows to yield a nickel complex and subsequent decomposition gives organic products.

In an extension of the reaction it was found that *o*-diiodobenzene gave substituted indenones when treated with 1 equivalent of nickel carbonyl and a substituted alkyne. A number of different substituents were incorporated and some good yields were obtained. When unsymmetrical alkynes were employed both of the possible regioisomers were seen and the reaction was only regioselective when the substituents differed greatly in steric bulk. In such cases the bulkier substituent was found at C-2 of the indenone (Scheme 1.6). This method appears to be a mild and direct route to various substituted indenones. However electron deficient alkynes did not yield any useful products under the reaction conditions.

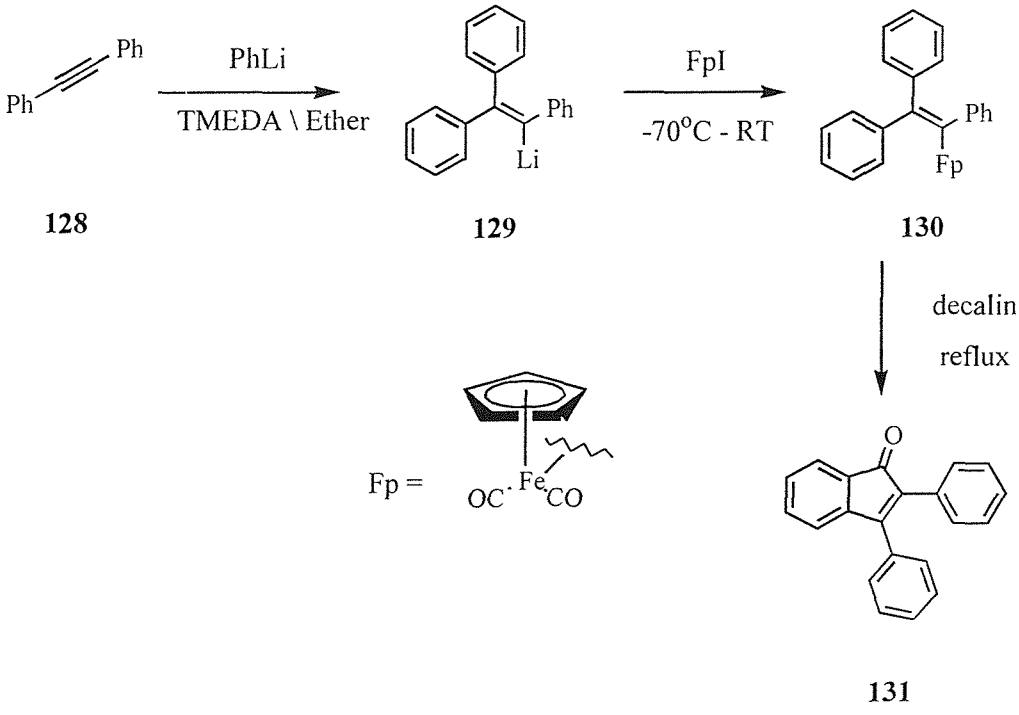


R', R" = Et 89%
R', R" = Ph 51%
R' = Ph R" = Me 67%

Scheme 1.6

1.5 Use of Transition Metals - Iron.

Butler described the thermal reaction of Fp-Aryl (Fp = dicarbonyl-(η^5-cyclopentadienyl)iron) with diarylacetylenes to give 2,3-disubstituted indenones.[14] 2 Molar equivalents of aryllithium with diphenyl acetylene in the prescence of TMEDA followed by metathesis with FpI at low temperature gave the alkenyliron compound **130**. Heating **130** in decalin at reflux for 10 min under N_2 gave indenone **131** cleanly and in good yield (Scheme 1.7). A similar reaction conducted at reflux in xylene or toluene with a molar equivalent of triphenylphosphine gave an improvement in yield. The route was also successful with a naphthyl substitutent on the starting alkyne to produce 2-naphthyl-3-arylindenone in 86% yield.

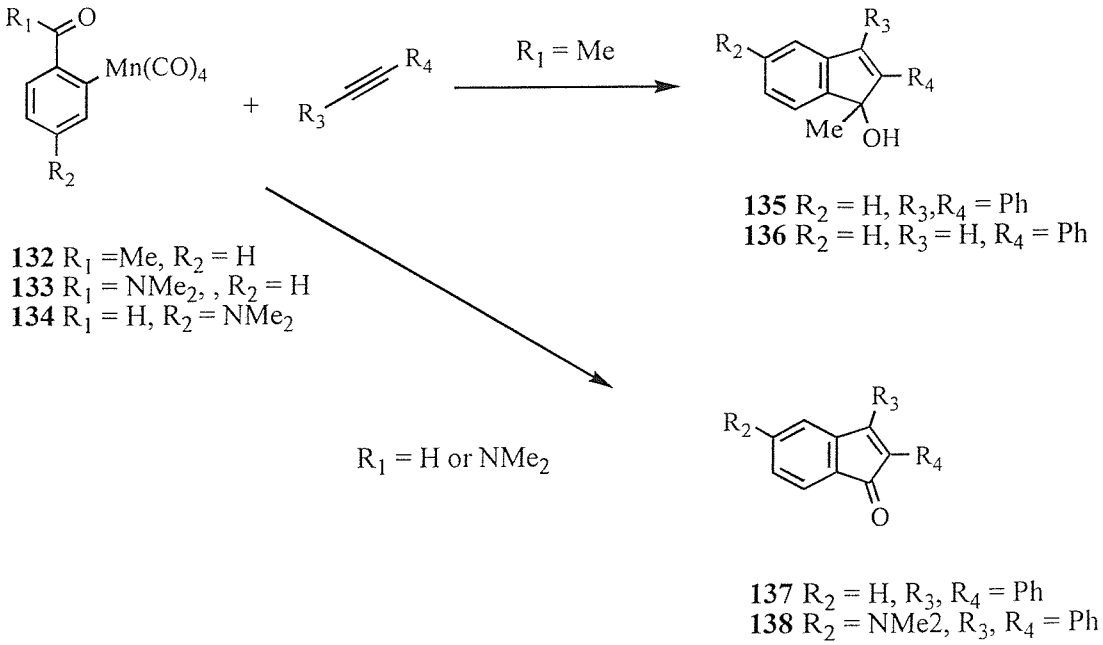


Scheme 1.7

1.5 Use of Transition Metals -Manganese

Robinson and co-workers reported that reactions of *ortho*-manganated aryl carbonyl compounds with alkynes provide an efficient route to indenols and indenones.[15] η^2-(2-Acetylphenyl)tetracarbonylmanganese **132** reacts with diphenylacetylene in benzene under reflux for 8 h to form 2,3-diphenyl-1-methylinden-1-ol **135** in 97% yield. A similar reaction in methanol also gave **135** in 51% yield. While the reaction of *ortho*-manganated *N,N*-dimethylbenzamide **133**, with diphenylacetylene under the same conditions gives the indenone **137** in 56% yield. Similarly, the *ortho*-manganated *p*-dimethylaminobenzaldehyde **134** gives **138** in 46% yield (Scheme 1.8).

It seems likely that an indenol is the first product formed in the reaction and that the indenone is then formed by oxidation. The proposed mechanism involved an initial insertion of the alkyne into the Mn-C bond to give **139**. Intramolecular addition across C=O then gives **140**, which on protonolysis provides the indenol. When aromatic aldehydes and amides were employed, collapse to an indenone is favoured.



132 R_1 =Me, R_2 = H
133 R_1 = NMe_2, , R_2 = H
134 R_1 = H, R_2 = NMe_2

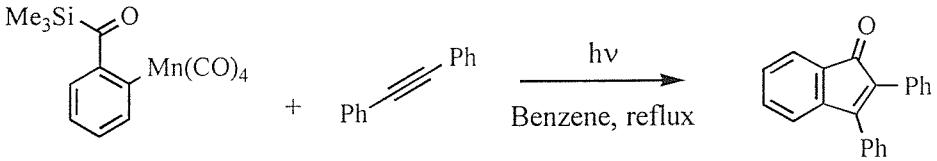
135 R_2 = H, R_3,R_4 = Ph
136 R_2 = H, R_3 = H, R_4 = Ph

137 R_2 = H, R_3, R_4 = Ph
138 R_2 = NMe2, R_3, R_4 = Ph

Scheme 1.8

139 **140**

In 1994 Cambie found that silylated manganese complex **141** and diphenylacetylene in benzene gave **131** in a disappointing 22% yield after photolytic demetallation (Scheme 1.9).[16]

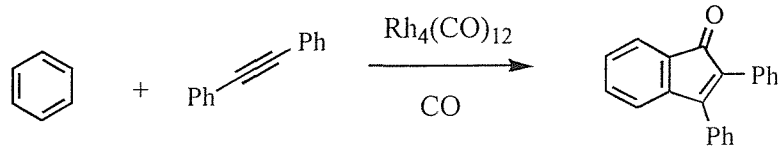


141 **128** **131**

Scheme 1.9

1.7 Use of Transition Metals - Rhodium

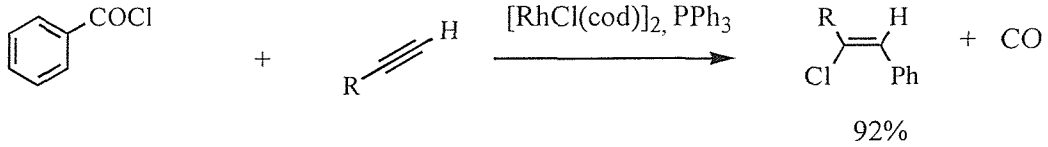
Hong reported in 1979 that the reaction of benzene with diphenylacetylene and carbon monoxide could be catalysed by $Rh_4(CO)_{12}$ and gave 2,3-diphenylindenone in 10% yield together with various side products.[17] The composition of the product mixture varied with the pressure of carbon monoxide, but the yield of the indenone was low in each case studied (Scheme 1.10).



142 **128** **131**

Scheme 1.10

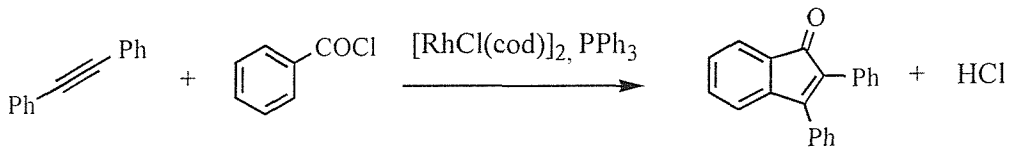
Later, Miura described a much improved route to indenones using rhodium.[18] Aroyl chlorides are known to react with low valent transition metal species, including rhodium and palladium complexes, to produce the corresponding aroyl-chlorometalcomplexes. These may be further transformed into arylchlorometal complexes by decarbonylation at elevated temperatures. He observed that aroyl chlorides react with terminal alkynes in the prescence of $[RhCl(cod)]_2$ and triphenylphosphine to give vinyl chloride derivatives in good yield and in a regio- and stereoselective manner (Scheme 1.11).



143 **144** **145**

Scheme 1.11

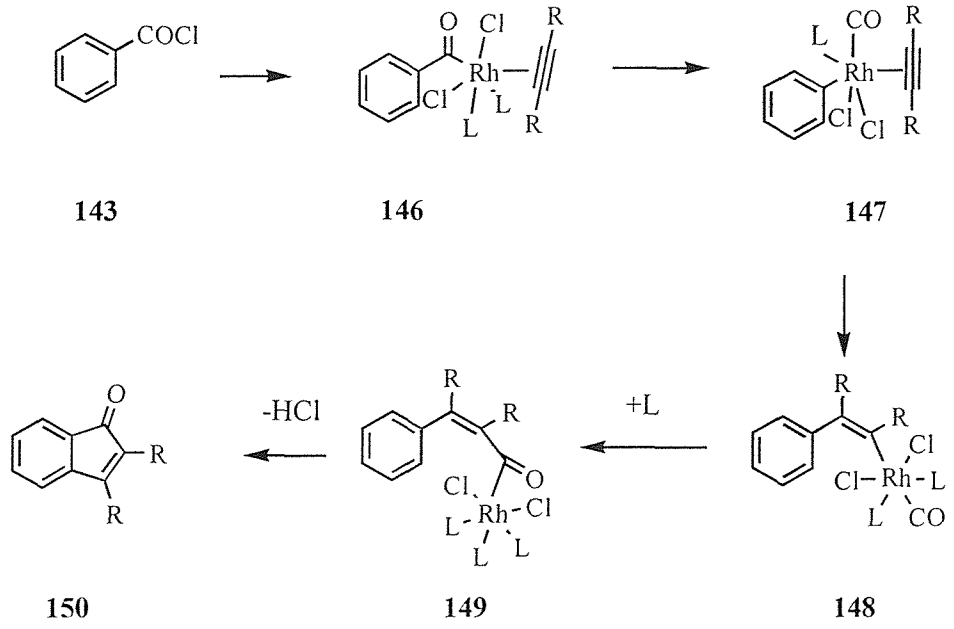
The reaction of aroyl chlorides with disubstituted alkynes was found to proceed without decarbonylation to produce 2,3-disubstituted indenones. No vinyl chloride derivative was detected and yields up to 76% were seen (Scheme 1.12).



128 **143** **131**

Scheme 1.12

Alkyl and phenyl substituted alkynes were sucessfully employed. Where unsymmetrical alkynes were used a 1:1 ratio of regioisomeric 2,3-disubstituted indenones were formed. Yields varied from moderate to low. The mechanism proposed for the formation of these indenones is outlined in Scheme 1.13. Firstly rhodium inserts into the carbon to chlorine bond. Decarbonylation is followed by insertion of the alkyne. Carbon monoxide then reinserts and a subsequent cyclisation involving elimination of HCl generates the indenone.



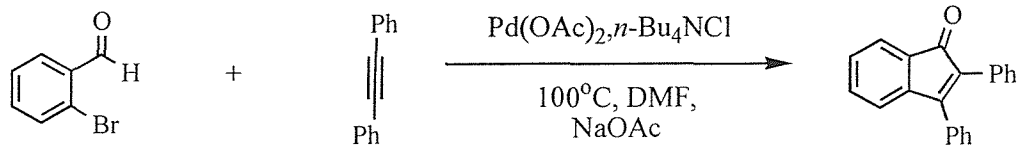
143 **146** **147**

150 **149** **148**

Scheme 1.13

1.8 Use of Transition Metals - Palladium

Heck first reported the palladium catalysed formation of diphenyl indenone from *o*-iodobenzaldehyde **151**and diphenylacetylene **128** in 1989.[19] In 1993 Larock and Doty published a more comprehensive study of the annulation in which the scope and limitations of this chemistry were explored.[20] A wide range of 2,3-disubstitued indenones were reported.

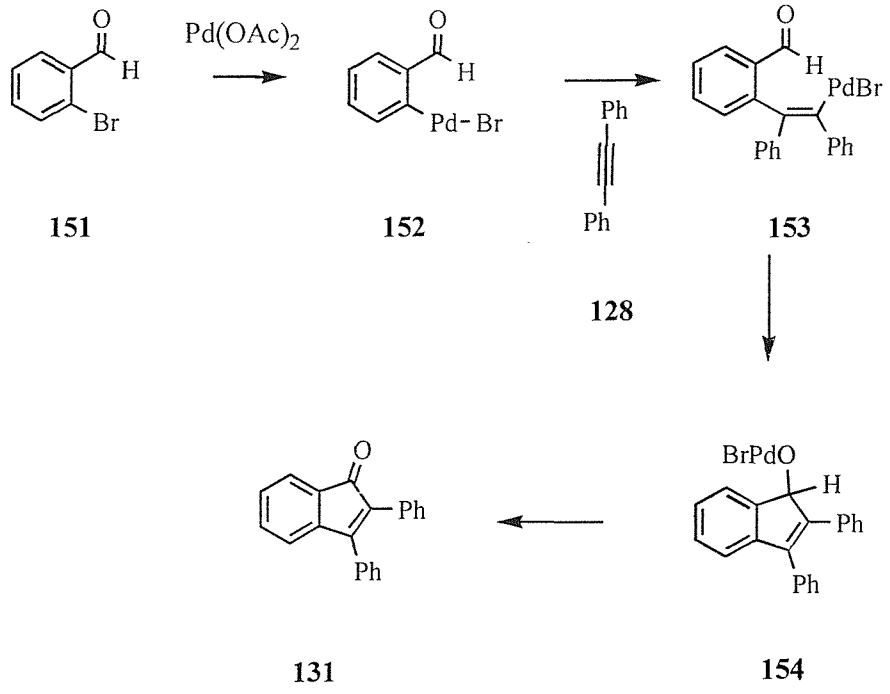


151 **128** **131**

Scheme 1.14

With only 5 mol% of catalyst, an 84% yield of 2,3-diphenylindenone **131** was isolated (Scheme 1.14). The reaction was found to be robust to an increase in scale and changes in substituents. Where regioisomers were possible, less hindered alkynes

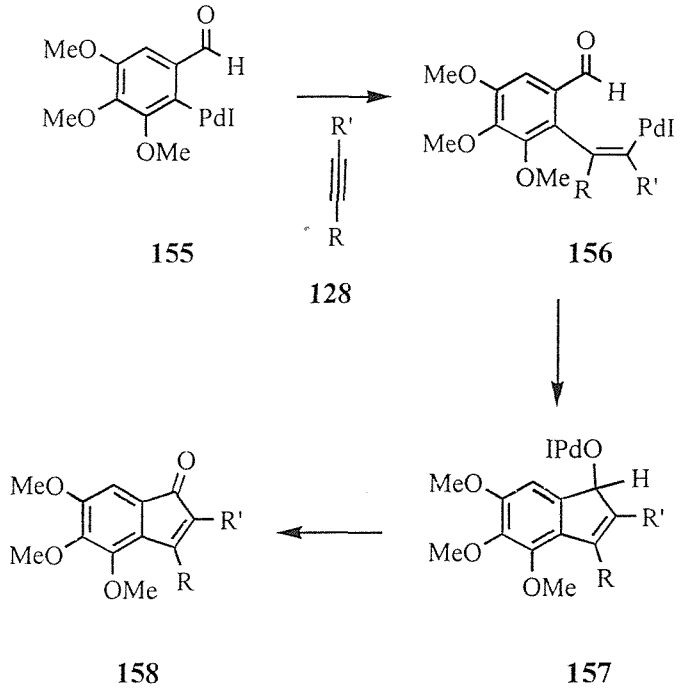
such as 1-phenyl-1-propyne tended to produce a 1:1 mixture of regioisomers, whereas alkynes containing more bulky, tertiary alkyl, trimethylsilyl or other hindering groups were shown to be selective, with the more sterically demanding group in the C-2 position. The most likely mechanism proposed involved addition of the C-Pd bond of the vinyl palladium intermediate **153** across the C=O bond of the aldehyde, followed by β-hydride elimination (Scheme 1.15).



Scheme 1.15

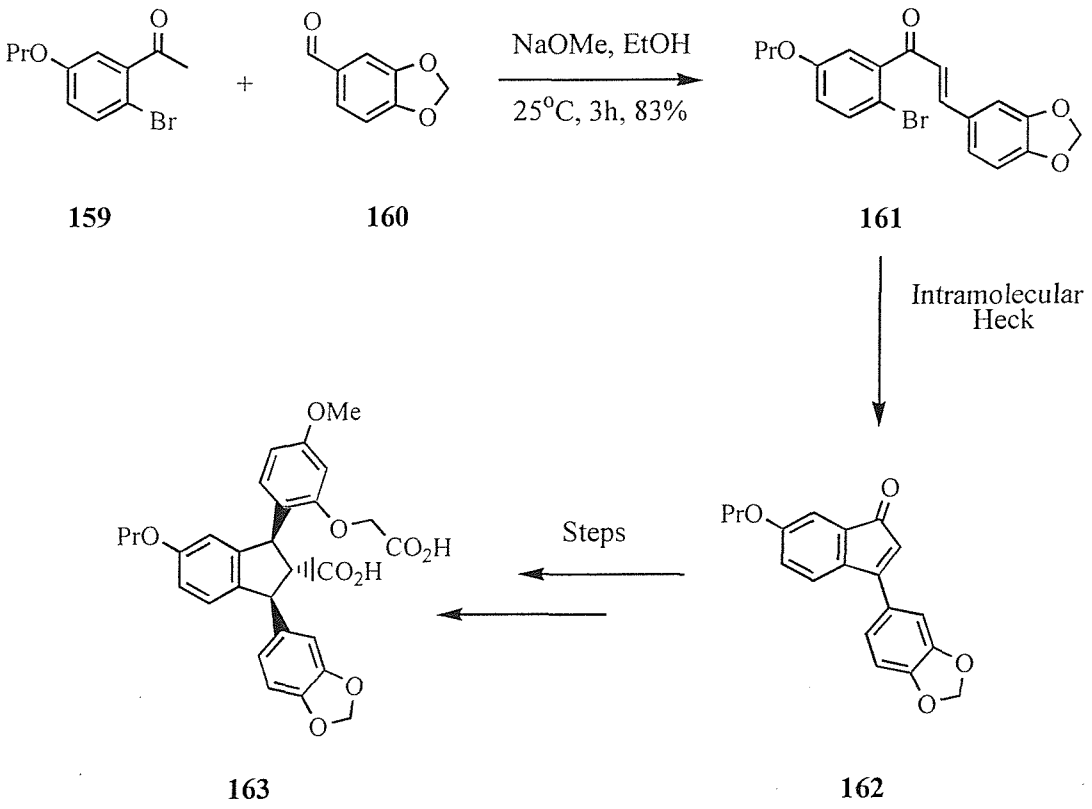
In 1996 Vicente and co-workers investigated palladium assisted formation of carbon to carbon bonds in the synthesis of indenols and indenones.[21] They reported the formation of a wide variety of symmetrical and unsymmetrical 2,3-substituted indenones from palladium complexes. They first isolated an *o*-formylarylpalladium complex **155** which reacted at room temperature with diphenylacetylene to provide the indenone **158** in 77% yield (Scheme 1.16). Again, electron withdrawing groups on the alkyne rendered the reaction unsuccessful while the presence of three donating methoxy groups on the aryl ring gave the most successful results. The reaction was attempted using substoichiometric palladium, but yields were poor. Interestingly, the

only example found to proceed in a regioselective fashion was with 1-phenylpropyne. In this case only 2-phenylindenone was produced. Also, when 1-*t*-butyl-1-propyne was used, a 1:1 mixture of regioisomers was formed. This was in contrast to the observations of Larock.[20]



Scheme 1.16

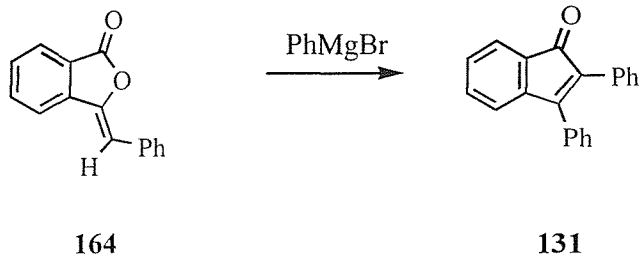
In 1998, Clark required a route to an indenone *en route* to **163**, an indanone natural product which shows constrictor activity of cardiovascular smooth muscle.[22] He successfully performed an intramolecular Heck reaction with enone **161** to give the indenone **162** in 75% yield (Scheme 1.17).



Scheme 1.17

1.9 Use of Grignard Reagents

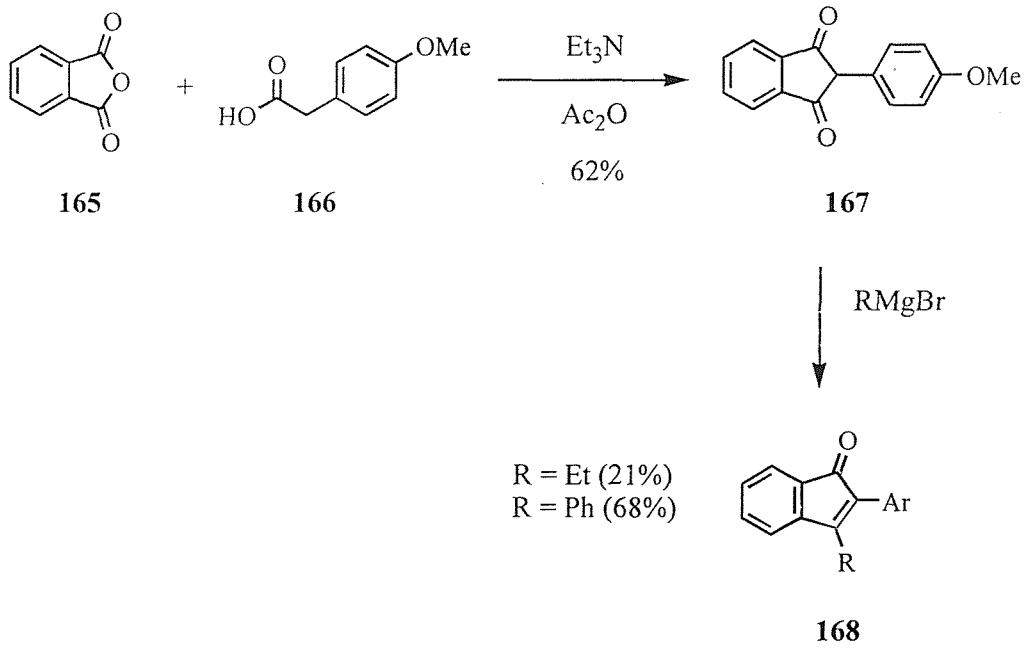
Indenones can be prepared from benzylidenephthalides. Thus, when benylidenephthalide **164** was treated with phenylmagnesium bromide it was converted directly to 2,3-diphenylindenone **131** (Scheme 1.18). The method was first introduced by Shriner and Knox, then developed by Manning and often gives good to acceptable yields.[23,24]



164 **131**

Scheme 1.18

Anstead sought an alternative route to 2- and 3-arylindenones when synthesising substrates to act as oestrogen receptors.[2] The method adopted used a double condensation-decarboxylation reaction between 4-methoxyphenylacetic acid **166** and phthalic anhydride **165** as a first step. The resulting indanedione **167** was then allowed to react with 2 equivalents of Gringard reagent to provide the required indanone **168** (Scheme 1.19).



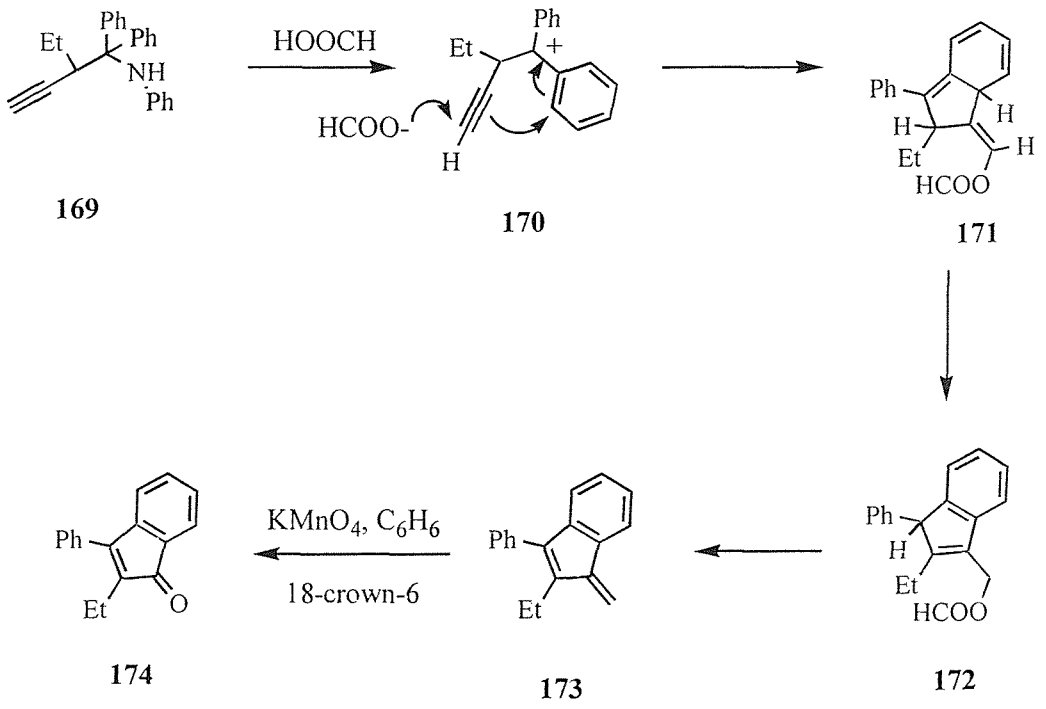
165 **166** **167** **168**

Scheme 1.19

1.10 Miscellaneous Routes

Scheinmann utilised an alternative and indirect route to indenones *via* indenes.[25] Reaction of *N*-phenyl-1,1-diphenyl-2-ethylbut-3-ynylamine **169** in 98% formic acid at room temperature (18 h) followed by hydrolysis gave 2-ethyl-1-methylene-3-phenyl-1*H*-indene **173** in 56% yield. This indene was then treated with potassium

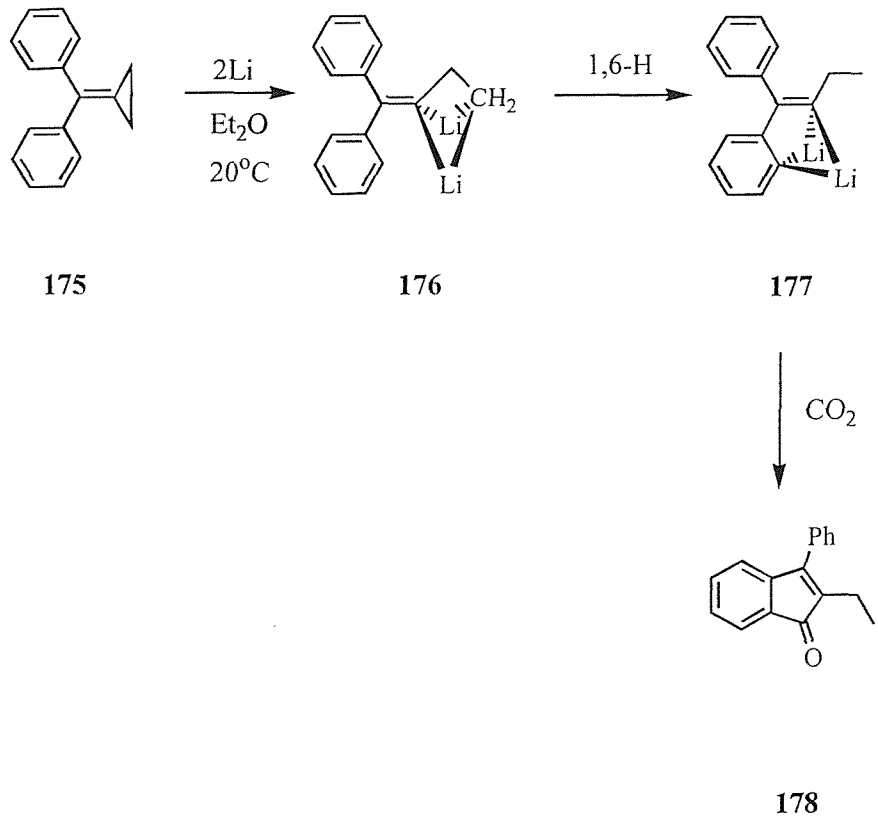
permanganate in benzene containing 18-crown-6 to effect oxidation of the exocyclic double bond to give indenone **174** in 28% yield (Scheme 1.20).



169 **170** **171** **172** **173** **174**

Scheme 1.20

In a study of poly-lithiated organic compounds, Maerker investigated the reaction of benzylidenecyclopropanes with lithium.[26] Diphenylmethylenecyclopropane **175** was taken in dry ether at 20°C and added to a suspension of excess lithium dust under argon. The resulting dilithium **176** underwent a 1,6-hydride shift to give **177** – the mechanism of which was indeterminable. Reaction of **177** with carbon dioxide then gave **178** in 19% yield (Scheme 1.21).



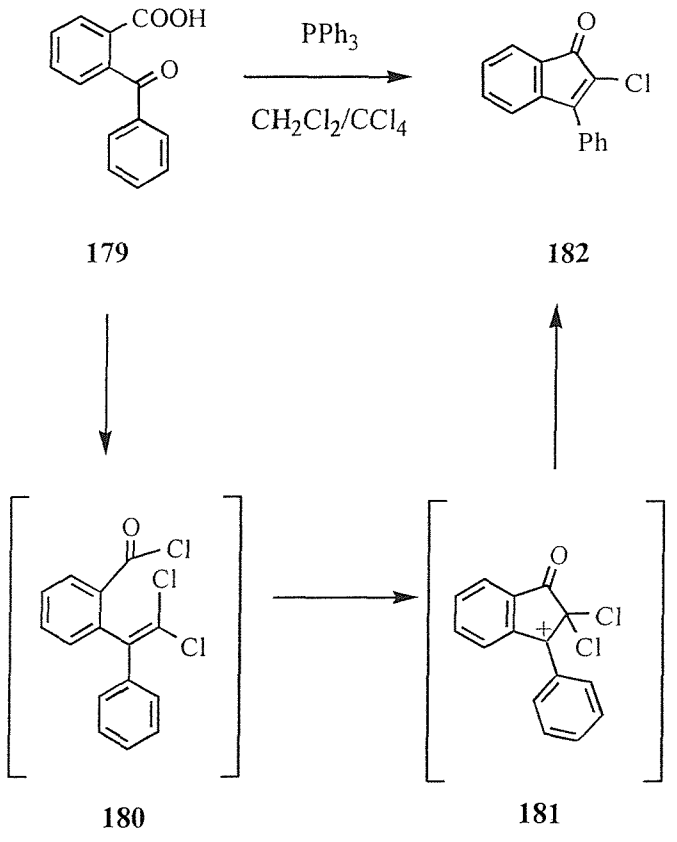
175 **176** **177**

178

Scheme 1.21

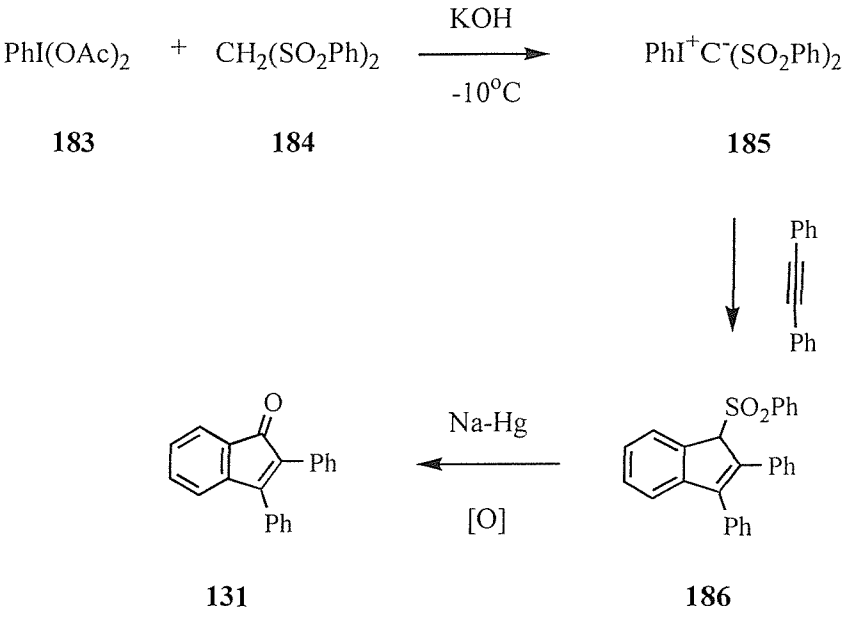
1.11 Wittig type cyclisations

In 1989 Vorbruggen developed a Wittig type cyclisation from keto acid **179** which gave 2-chloro-3-phenylindenone **182** in 37% yield (Scheme 1.21).[27] Although the yield was low the route is simple and direct and may be amenable to optimisation. Presumably, the acid is first converted into acid chloride **180** *en route* to the indenone **182** (Scheme 1.22).



Scheme 1.22

Varvoglis and co-workers showed that phenyliodonium *bis*(phenylsulfonyl)methyllide **185** gives cycloaddition products with alkenes and alkynes.[28] When performing the reaction with alkynes, the indene skeleton was provided. Reduction of the indene with Na amalgam unexpectedly gave the indenone **131**, implicating autooxidation in air (Scheme 1.23). This result was reproducible and a number of examples were successful. Yields were usually in the region of 50 – 60%.



Scheme 1.23

1.12 Conclusion

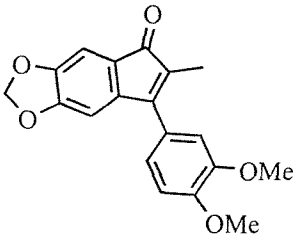
To conclude, many approaches to the aryl indenone have been reported. These range from the classical Friedel-Crafts methodologies to the more recent developments using transition metals. Several miscellaneous methods are also available. This review has not been comprehensive but is intended to provide a useful introduction to the area.

Chapter Two

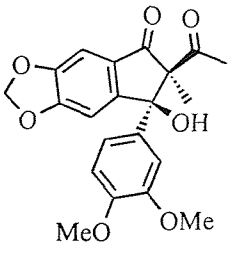
The Synthesis and Identity of Virola Indenone

2.1 Background

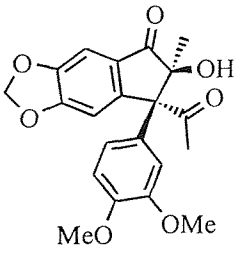
Many compounds have been isolated from the fruit of *Virola sebifera*[29] and *Virola elongata.*[30] Of these a series of arylindenones have attracted particular attention due to their unusual structural features. Most notably, virola indenone **201** is the only reported 3-arylindenone to have been isolated from natural sources and may thus represent the first example of a new class of lignans.



201



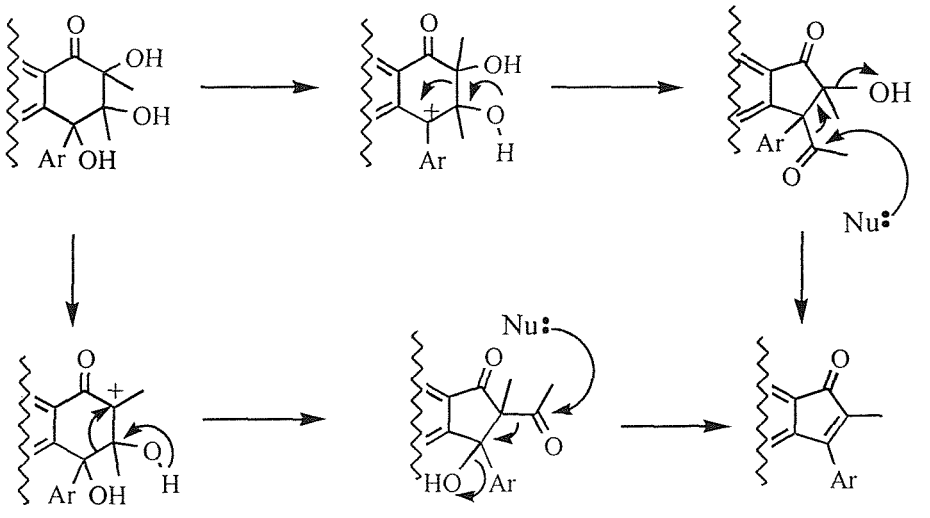
202



203

That virola indenone may be an artifact of the isolation process rather than a true natural product has been noted by Whiting.[31] Thus, loss of acetic acid from **202** provides a plausible route to **201** and this might occur in the fruit or during the extraction process.

Whiting envisioned these compounds as arising through ring contraction of a hypothetical hydroxylated tetralone (Scheme 2.1).



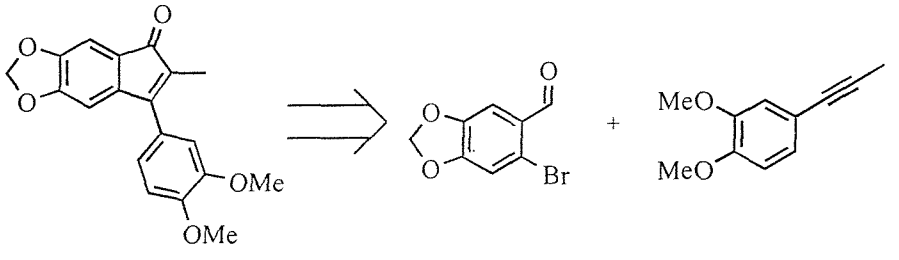
Scheme 2.1

Several reports have appeared in recent years relating to the biological activity of indenones. Klein has investigated the structural requirements for anti-tumour activity in indanone analogues of podophyllotoxin.[32] His investigations focussed on compounds active against human and murine tumour cell lines and led him to conclude that substitution at the C-2 and C-3 position on an indanone is crucial for activity and that these substituents are conformationally sensitive.

Katzenellenbogen considered 2- and 3-substituted aryl indenones as ligands for the oestrogen receptor. He found that they display high binding affinities rendering them potential post coital contraceptives.[33] Hajela then proceeded to investigate this effect in laboratory rats.[34] Indeed, when the substituted indenones were administered post-coitally to female rats, the occurrence of implantation was inhibited by up to 85%.

2.2 Our Preliminary Synthesis of Virola Indenone

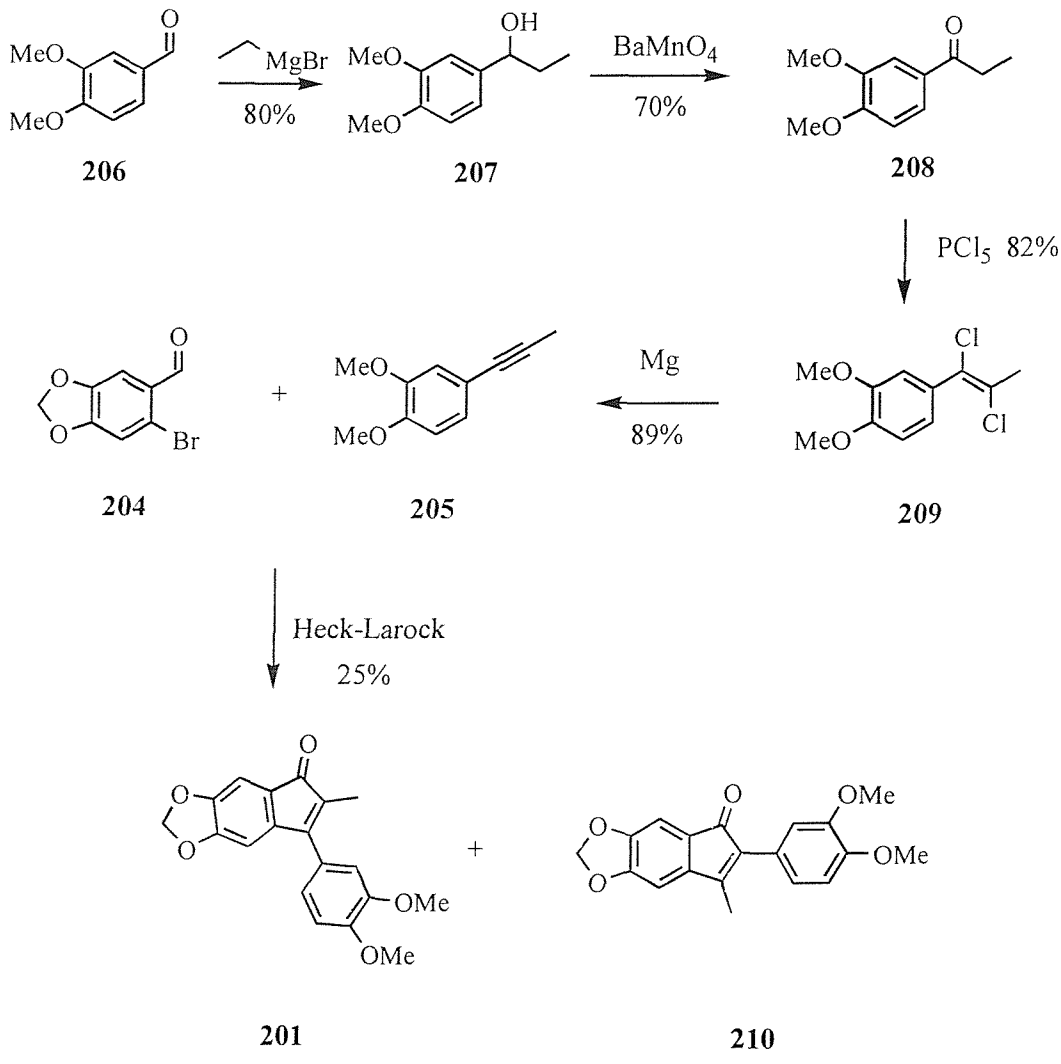
Having considered the literature methods for the synthesis of 3-arylindenones we chose to apply the Heck-Larock annulation to the synthesis of virola indenone **201** as it appeared to be the most direct way of obtaining the natural product.[19, 20] Thus, the palladium coupling of 6-bromopiperonal **204** and aryl alkyne **205** should provide **201** directly, along with the 2-arylindenone regioisomer.



201 **204** **205**

Scheme 2.2

We obtained the alkyne in four steps as shown in Scheme 2.3. Reaction of the aldehyde **206** with ethylmagnesium bromide followed by oxidation with barium manganate provided ketone **208** in good yield. Conversion of the ketone to the dichloride **209** was achieved using phosphorous pentachloride. Stirring **209** with magnesium provided alkyne **205** in 89% yield. We were now in a position to effect the key step. Stirring a DMA solution of **204** and **205** containing sodium carbonate and 5 mol % palladium acetate at 100°C provided a 5:1 mixture of indenone **201** and the corresponding regioisomer **210** in 25% yield.



Scheme 2.3

Separation of **201** and **210** was not trivial but could be achieved using a chromatatron or by selective crystallisation from ethanol. Having obtained pure samples of both **201** and **210**, the spectroscopic and physical characteristics each displayed were compared with those data reported for virola indenone. Numerous discrepancies were revealed. In particular, we noted that the melting point of our synthetic sample of **201** was 142-144°C whereas the reported value was 216°C. There were also discrepancies in the ^{1}H NMR and ^{13}C NMR data while the mass spectra, IR and UV data were in close agreement (Table 2.1).

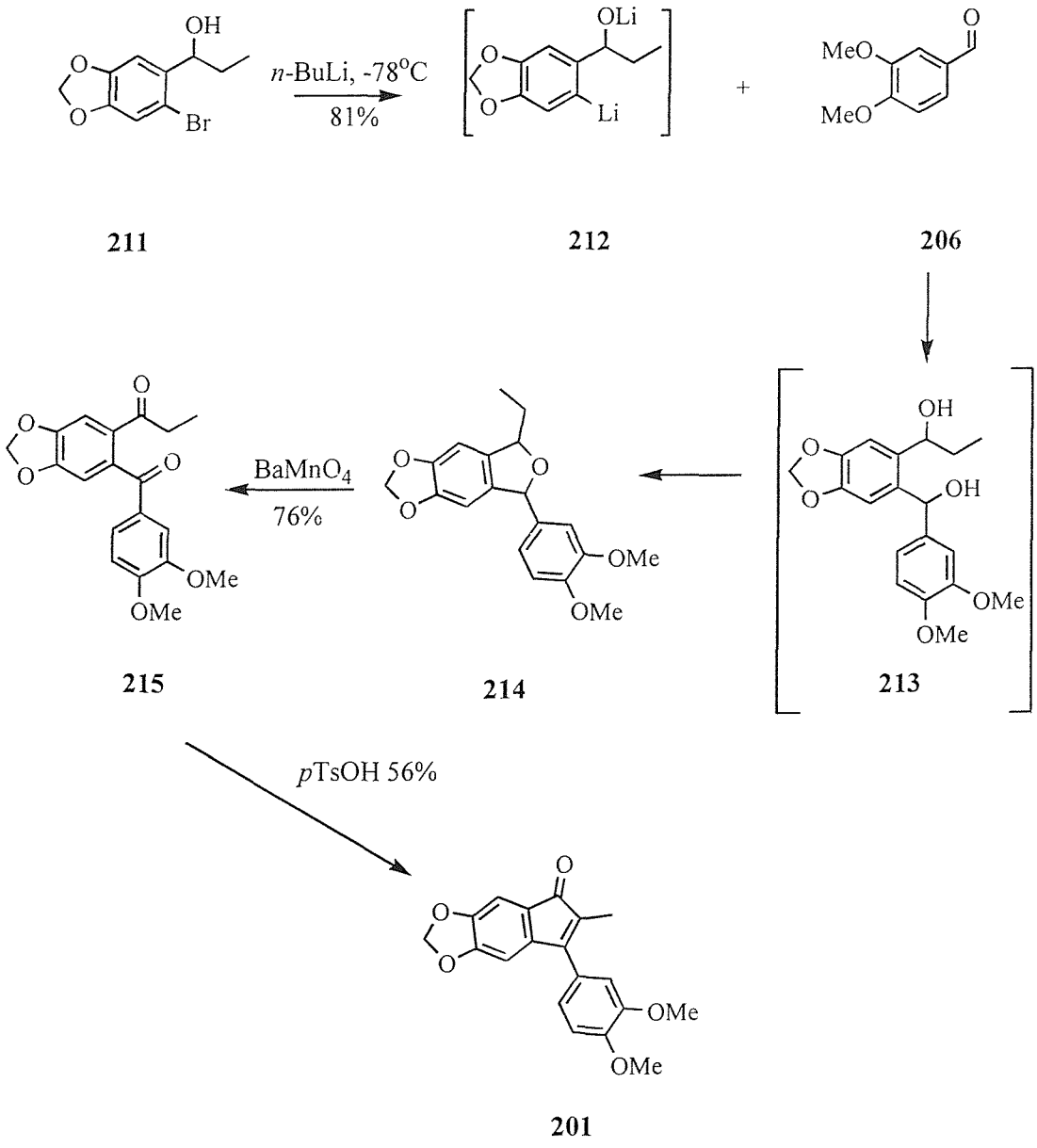
Table 2.1

Characteristics	201	Natural Product
Appearance	red solid	red solid
m. p.(MeOH)	142-144°C	214-216°C
m/e (amu)	MH^+ (APCI) 325	M^+ (EI) 324
IR	CH_2Cl_2 1699, 1598, 1514, 1321	KBr 1692, 1600, 1484-1440
UV (MeOH)	464 (700), 335 (6400) 268 (32000)	340 (7600), 265 (32400)
^1H NMR ($CDCl_3$)	300 MHz	60 MHz
ArH		7.17 (1H, s)
ArH	7.01-6.92 (4H, m)	7.00 (3H, m)
ArH	6.63 (1H, s)	6.69 (1H, s)
2 x ArH	5.98 (2H, s)	6.10 (2H, s)
2 x OMe	3.98 (3H, s), 3.95 (3H, s)	3.89 (3H, s), 3.86 (3H, s)
CMe	1.91 (3H, s)	1.89 (3H, s)
^{13}C NMR ($CDCl_3$)	75.5 MHz	20 MHz
CH_3	56.2, 56.1, 8.9	55.8, 55.7, 18.0
CH_2	102.1	103.5
CH	121.3, 111.3, 111.1, 105.1, 103.6	120.8, 111.7, 108.5, 108.0, 105.9
C	196.9, 152.9, 151.3, 149.9, 149.1, 147.1, 142.4, 129.3, 129.3, 125.3	208.0, 168.6, 159.9, 151.7, 149.3, 148.2, 147.7, 132.4, 128.9, 127.9

We felt sure that our initial synthesis of **201** had proceeded without incident, but thought it wise to secure an alternative route before we drew any conclusions about the identity of virola indenone.

To avoid ambiguity, the new route we adopted followed more traditional lines (Scheme 2.4). It began with 6-bromopiperonal **204** which was treated with ethylmagnesium bromide to give alcohol **211** in 76% yield. The bromoalcohol **211** was then reacted with 2 equivalents of *n*-butyllithium to form a dilithiated

intermediate which, upon exposure to dimethoxybenzaldehyde **206,** gave diol **213**. On work up, this material dehydrated to give the THF **214** as a 1:1 mixture of diastereoisomers. Oxidation of **214** with barium manganate then provided diketone **215** in 76% yield which when exposed to *p*-toluenesulfonic acid in chloroform gave **201** in 56% yield.

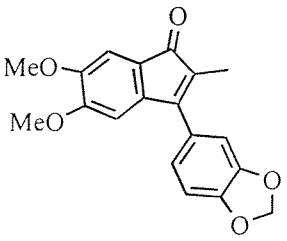


Scheme 2.4

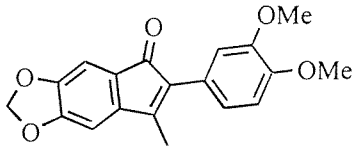
We were pleased to note that the data for our second sample of **201** agreed with that of our first, showing that there had been no errors in our original synthesis.

2.3 Redefinition of the Structure

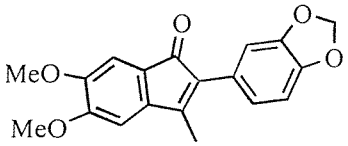
The inconsistencies in the data obtained for our synthetic sample of **201** and those attained for the natural product led us to conclude that the structure proposed for virola indenone was incorrect. Thus, we reassessed the published data and concluded that the most likely structure for virola indenone was **216**, in which the arene substituents are interchanged.



216



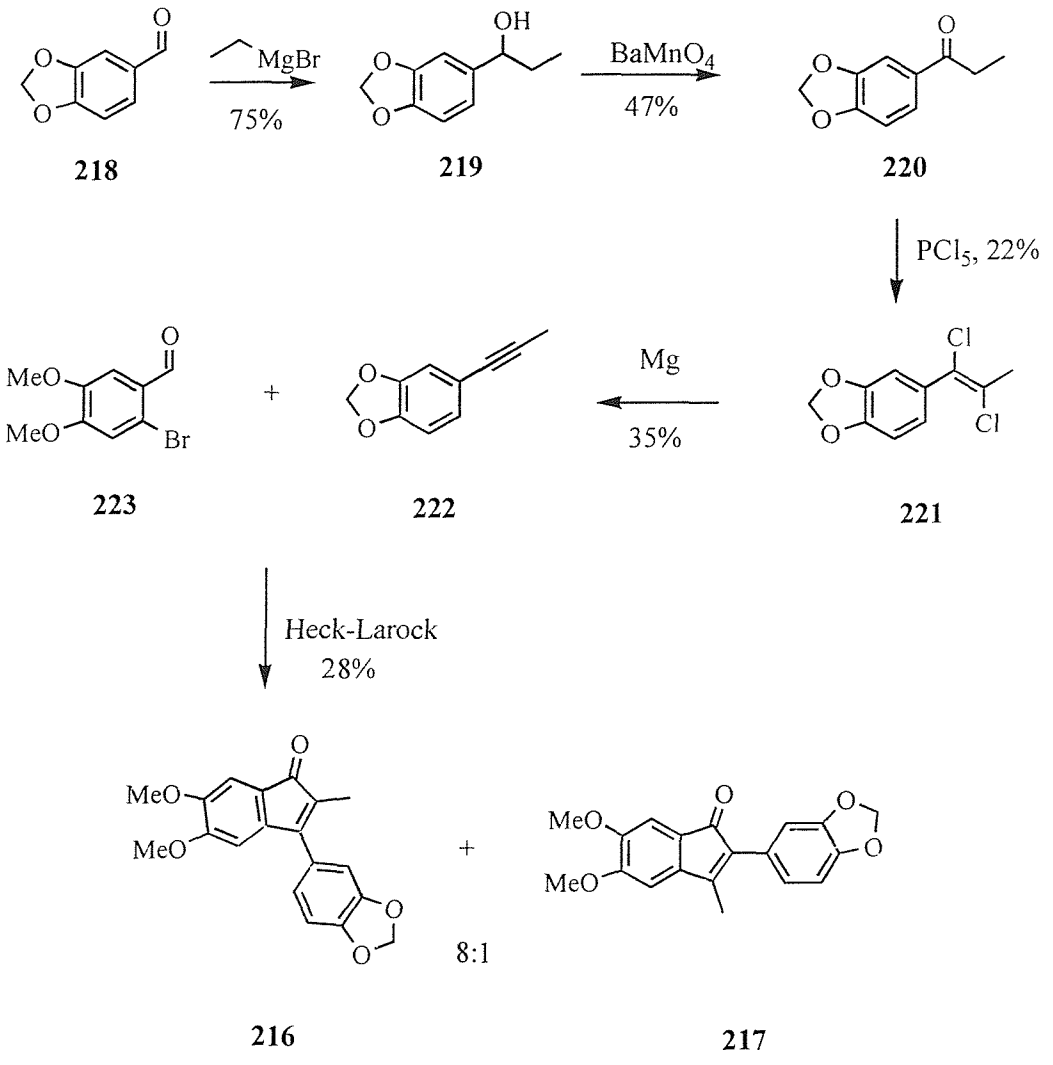
210



217

Our reasoning for favouring **216** over the isomeric indenones **210** and **217** were as follows. The UV/visible spectra obtained for **201** agreed with the data reported in the isolation paper, suggesting the presence of a similar chromophore. Secondly, the chemical shift of the allylic methyl group in **201** and virola indenone were both δ_H 1.89 p.p.m., suggesting attachment at C-2. Thirdly, the biosynthesis of virola indenone proposed by Whiting was equally valid for **216**.[3]

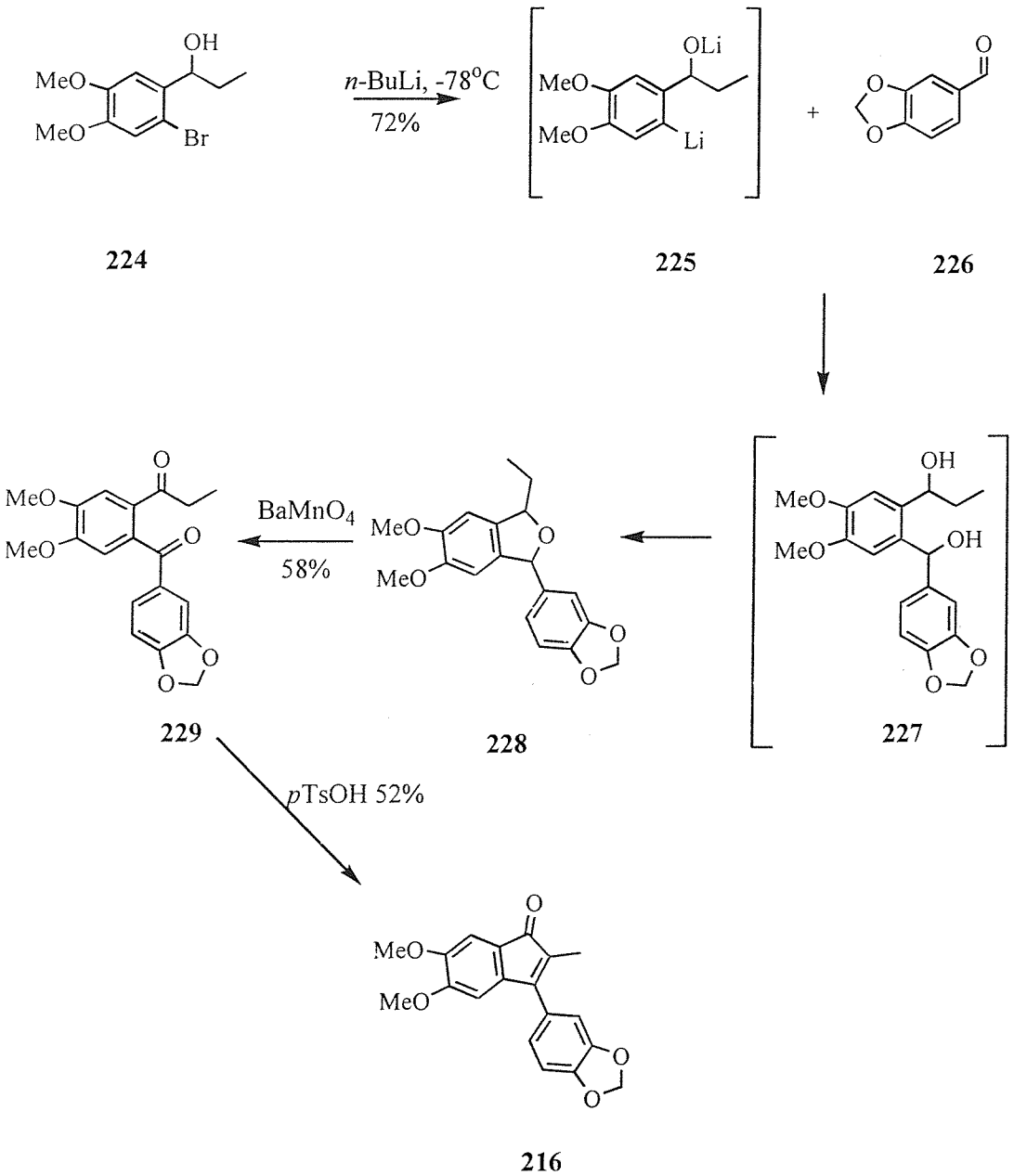
We therefore embarked upon a synthesis of **216** following the strategy used successfully for the synthesis of **201** (Scheme 2.5). Though the yields attained were lower in this sequence, we were nonetheless able to obtain the requisite alkyne **222** and cyclise it under the Heck Larock conditions to give an 8:1 mixture of regioisomers **216** and **217**.



218 **219** **220** **221** **222** **223** **216** **217**

Scheme 2.5

We also synthesised **216** using the more traditional aldol condensation route. The yields were comparable to those attained in the synthesis of **201**, the key cyclisation of **229** to **216** being achieved in 52 % yield (Scheme 2.6).



216

Scheme 2.6

A comparison of the data attained for **216** with that reported in the natural product isolation paper was then undertaken. We were pleased to note that the melting points, IR, UV and mass spectra were in agreement. Likewise the anomalies in the ^{1}H NMR data were within experimental limits given that the original data was recorded using unsophisticated equipment.

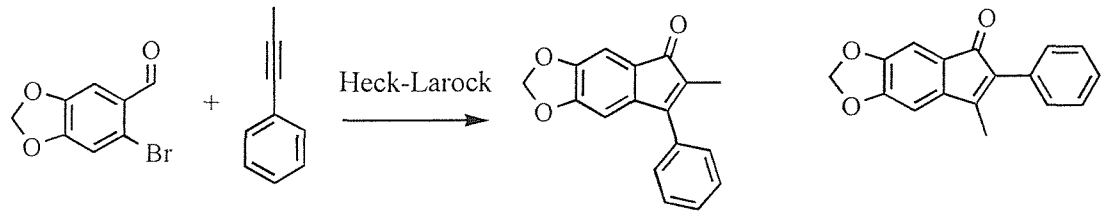
Major discrepancies were nonetheless noted in the ^{13}C NMR spectral data. ^{13}C NMR data attained from **210** and **217** were also compared and these too showed poor correlation. As the ^{13}C NMR data in question was recorded at 20 MHz, we presume an early NMR instrument had been used to attain the values reported. The discrepancies may therefore be attributed to experimental errors. Notably, to locate the signal at 197 p.p.m. coresponding to the carbonyl moiety, we needed to extend the relaxation time between each scan. Clearly, at 20 MHz this signal would have been hard to detect. Thus the signal reported at 208.0 p.p.m. may have been due to noise. Thus we believe that the actual structure of the natural product is indeed **216**.

Table 2.2 Data for all synthetic samples as compared to the natural product.

	201	**Natural product**	**216**	**210**	**217**
Appear-ance	red solid	red solid	red solid	red solid	red solid
m.p. .(MeOH)	142-144°C	214-216°C	214-215°C	198-200°C	187-189°C
m/e (amu)	MH^+ (APCI) 325	M^+ (EI) 324	MH^+ (APCI) 325	MH^+(APCI) 325	M^+(CI) 324
IR	CH_2Cl_2 solution 1699, 1598, 1514, 1321	KBr 1692, 1600, 1484-1440	neat 1685, 1580, 1494, 1460	neat 1702, 1590, 1491, 1354	CH_2Cl_2 solution 1702,1586, 1487,1344
UV (MeOH)	464 (700), 335 (6400) 268 (32000)	340 (7600) 265 (32400)	462 (600) 343 (7100) 273 (32000)	460 (400) 310 (3600), 264 (21800)	488 (700) 314 (3100) 274 (20400)
^{1}H NMR ($CDCl_3$)	300 MHz δ_H	60 MHz δ_H	300 MHz δ_H	300 MHz δ_H	300 MHz δ_H
ArH	7.09- 6.92 (4H, m)	7.17 (1H, s) 7.00 (3H, m)	7.01 (1H, s) 6.95 (3H, m)	7.05 – 6.92 (4H, m)	7.12 (1H, s) 6.90 (3H, m)
ArH	6.63 (1H, s)	6.69 (1H, s)	6.65 (1H, s)	6.71 (1H, s)	6.75 (1H, s)
2 x ArH	5.98 (2H, s)	6.10 (2H, s)	6.09 (2H, s)	5.99 (2H, s)	5.99 (2H, s)
OMe	3.98 (3H, s)	3.89 (3H, s)	3.88 (3H, s)	3.97 (3H, s)	3.96 (3H, s)
OMe	3.95 (3H, s)	3.86 (3H, s)	3.89 (3H, s)	3.97 (3H, s)	3.93 (3H, s)
CMe	1.91 (3H, s)	1.89 (3H, s)	1.91 (3H, s)	2.28 (3H, s)	2.19 (3H, s)
^{13}C NMR ($CDCl_3$)	75.5 MHz δ_C	20 MHz δ_C	75.5 MHz δ_C	100 MHz δ_C	75.5 MHz δ_C
CH_3	56.2, 56.1, 8.9	55.8, 55.7, 18.0	56.4, 56.4, 8.7	56.3, 56.3, 13.1	56.5, 56.5, 12.6
CH_2	102.1	103.5	101.4	102.4	101.1
CH	121.3, 111.3, 111.1, 105.1, 103.6	120.8, 111.7, 108.5, 108.0, 105.9	122.1, 108.7, 108.2, 107.6, 105.6	113.0, 111.4, 105.4, 102.5, 122.5,	123.4, 109.8, 108.3, 107.2, 104.3
C	196.9, 152.9, 151.3, 149.9, 149.1, 147.1, 142.4, 129.3, 129.3, 125.4	208.0, 168.6, 159.9, 151.7, 149.3, 148.2, 147.7, 132.4, 128.9, 127.9	197.6, 152.9, 152.4, 148.4, 148.3, 148.0, 140.2, 129.4, 126.7, 123.6	195.9, 152.2, 152.1, 149.1, 149.0, 147.9, 143.1, 132.5, 124.7, 124.5	196.3 153.1, 152.4, 149.0, 147.6, 147.1, 140.5, 132.0, 128.0, 123.4

2.4 Optimisation of the Cyclisation

When we were making our samples of virola indenone and its isomers, we were disappointed with the yields attained in the Heck-Larock annulation (between 25 and 28%). We thus decided to pursue the optimisation of this reaction, confident that a higher yield could be realised. Optimisation was carried out on the model reaction between **204** and **230** (Scheme 2.7).

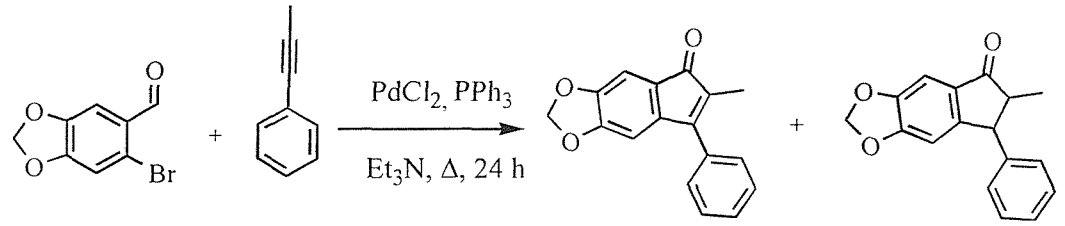


204 **230** **231** **232**

Scheme 2.7

Various palladium catalysts were examined. It was noted that reactions with palladium chloride were generally cleaner than those employing palladium acetate and that two equivalents of PPh_3 was optimal. A range of high boiling solvents were tested including benzene, 1.4-dioxane, toluene, DME and DMF. Best results were attained using toluene at 100°C for 24 h.

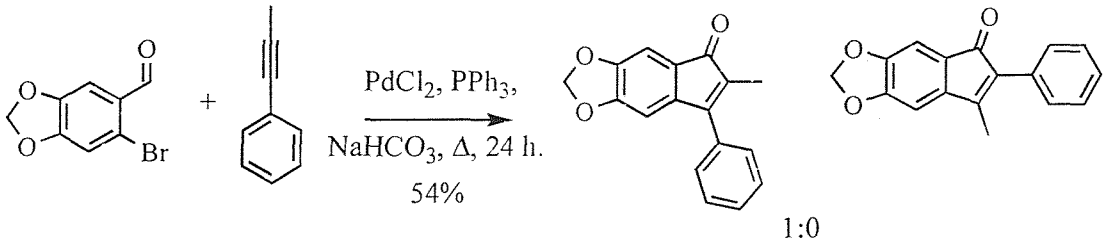
A concentration of 1 mL toluene to every 10 mg of alkyne gave best recovery of product. Surprisingly substituting triethylamine for sodium carbonate led to the production of indanone **233** (Scheme 2.8).



204 **230** **231** **233**

Scheme 2.8

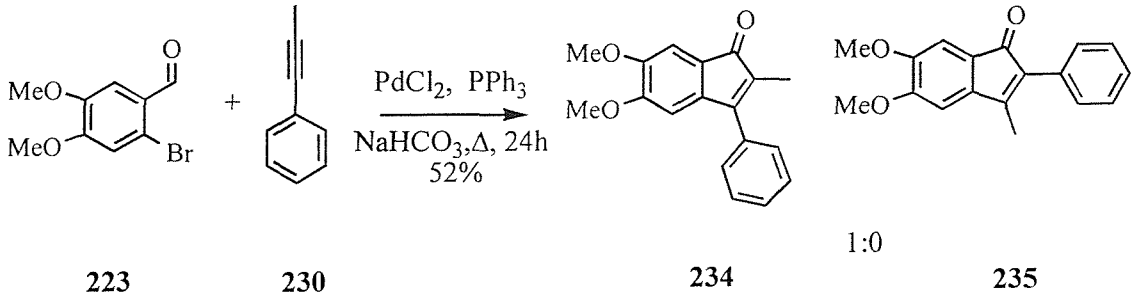
The yield of indenone was improved when sodium hydrogen carbonate was employed as the base. Under these conditions we were pleased to be able to produce a consistent yield of 54% for the annulation step (Scheme 2.9).



204 **230** **231** **232**

Scheme 2.9

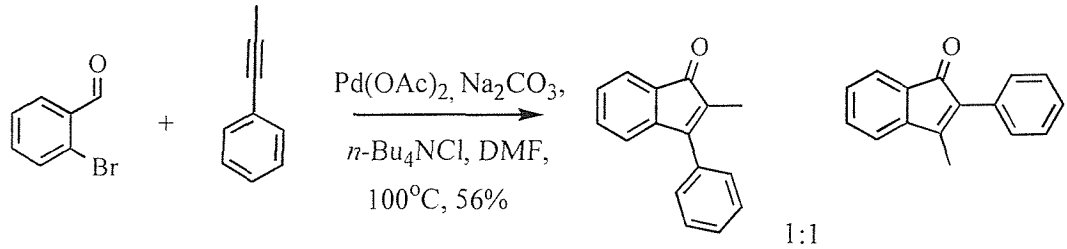
We also had the opportunity to conduct these reactions at high pressure. Success was limited and we were unable to improve on the yields attained using traditional techniques.



223 **230** **234** **235**

Scheme 2.10

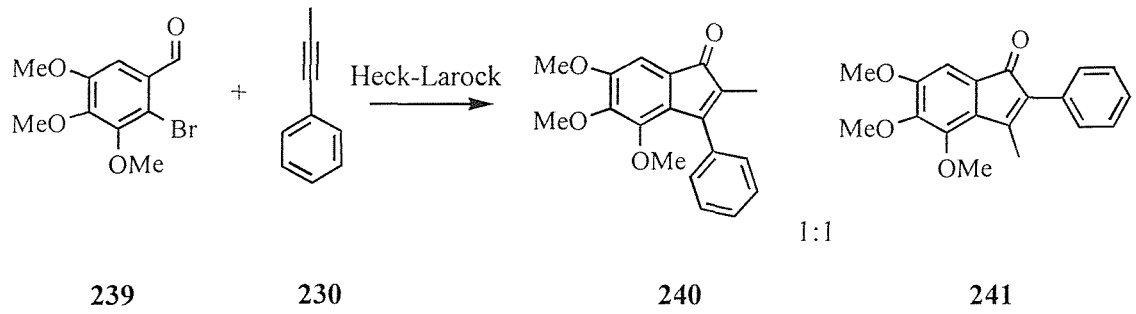
It should be noted that in the Heck-Larock annulation between **204** and **230** we saw no evidence for the formation of regioisomer **232**. Similarly the cyclisation of **223** and **230** provided **234** as the sole product (Scheme 2.10).



236 **230** **237** **238**

Scheme 2.11

We had assumed that the selectivity we observed in the formation of **231** and **234** was governed by the polarisation of the substituted aryl alkyne **230** (Scheme 2.11). However Heck and Larock both reported a 1:1 mixture of regioisomers in the cyclisation of **230** and **236**. These results suggest that the aryl aldehyde governs the regiochemical outcome of the reaction. When we used the trisubstituted aldehyde **239** for the annulation we saw a 1:1 mixture of regioisomers (Scheme 2.12). Overall, we suggest that the reaction is inclined to be selective for the 3-arylindenones when electron rich aldehydes are employed. However, a methoxy group adjacent to the bromine increases steric encumbrance en route to **240** significantly and production of **241** then becomes competitive.

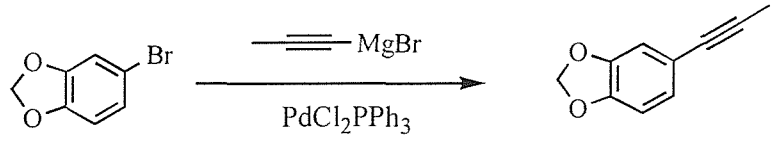


239 **230** **240** **241**

Scheme 2.12

2.5 Our One Pot Approach

We were keen to find an alternative to the four step route to aryl alkyne **222**. A Sonogashira reaction between aryl bromide **242** and propynylmagnesium bromide led us directly to the arylalkyne in 68% yield.[35] We then showed that this reaction could be run efficiently in toluene prompting us to try a one pot synthesis of our natural product.

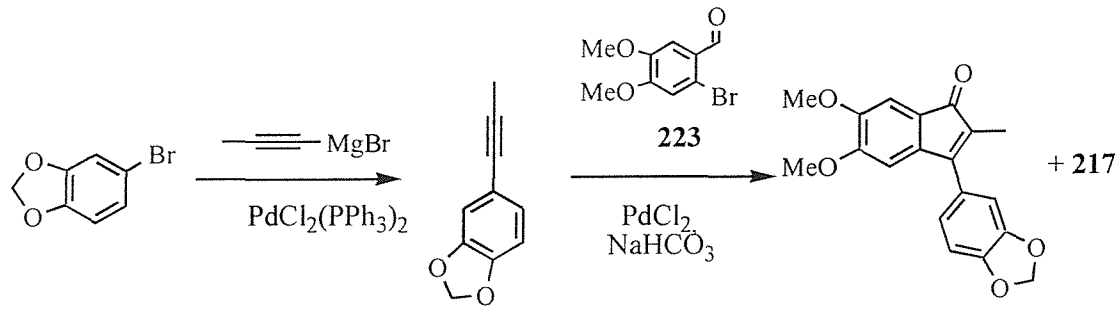


242 **222**

Scheme 2.13

This was achieved, after some optimisation, by warming a toluene solution of aryl bromide **242** and propynylmagnesium bromide in toluene at 60°C together with 20 mol% $PdCl_2(PPh_3)_2$. After 8 h further $PdCl_2$ was added along with aldehyde **223** and $NaHCO_3$. The temperature was raised to 100°C and heating continued for 24 h.

Upon cooling and work up we were pleased to isolate an 8:1 mixture of **216** and **217** in 44% yield.



242 **222** **216**

Scheme 2.14

2.6 Conclusion

We have developed two routes to virola indenone and redefined its structure.[36] We have optimised the Heck Larock annulation for this system and have developed a one pot synthesis of the natural product from commercially available materials.

Chapter Three

Thiyl Mediated Radical Cyclisations in Lignan Natural Product Synthesis

3.1 Background

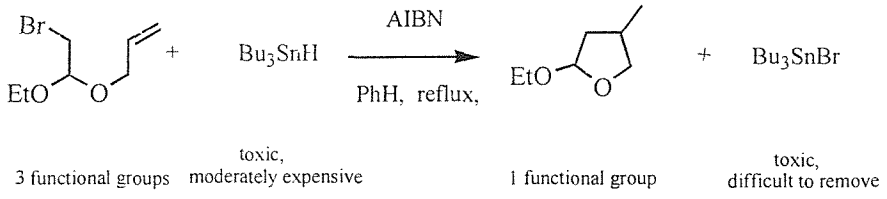
Radical cyclisation reactions are valuable for the construction of both carbocyclic and heterocyclic rings.[37] In the past, radical chemistry has gained a reputation for being capricious and unselective, often giving rise to complex mixtures of products due to their high reactivity. However, the advent of mediators such as tributyltin hydride prompted the development of numerous reactions of synthetic utility.[38] Indeed, it is now appreciated that radical chemistry has significant advantages over more traditional methods in many instances. In particular, radical reactions are conducted under mild, neutral conditions so a wide range of functionalities are tolerated, avoiding the need for protection. They are also useful for the generation of bonds between sterically crowded centres as radical intermediates are unsolvated and reactions proceed *via* early transition states.

The use of trialkyltin hydrides as mediators of radical reactions provides the most popular method to effect radical cyclisations. The tin radical is a powerful atom and group abstractor and a wide variety of radical precursors can be used. Although tributyltin hydride is most commonly employed for cyclisations involving nucleophilic (unstabilised) radicals, it may also be used to generate electrophilic (stabilised) radicals. Thus, reactive aryl and vinyl radicals as well as the more stable allyl and benzyl radicals can all be generated from a suitable radical precursor.[39]

Although these reactions exhibit many benefits, there are several drawbacks associated with the use of organotin compounds. Tin hydrides are highly toxic, as are the stoichiometric amounts of organotin residues produced in their reactions. These

residues can be difficult to remove from the reaction medium and often require specialist workup procedures.[40]

In addition a typical radical cyclisation will expend two functional groups to create one new carbon – carbon bond (Scheme 3.1). When cyclic compounds are formed from acyclic starting materials the stereocontrol is often poor. Thus stannane based methodology has largely been restricted to laboratory scale experiments where toxicity, waste and expense are manageable.[41] Some of these problems are overcome using catalytic variants of the method, though these tend to be less efficient.[42]



Scheme 3.1

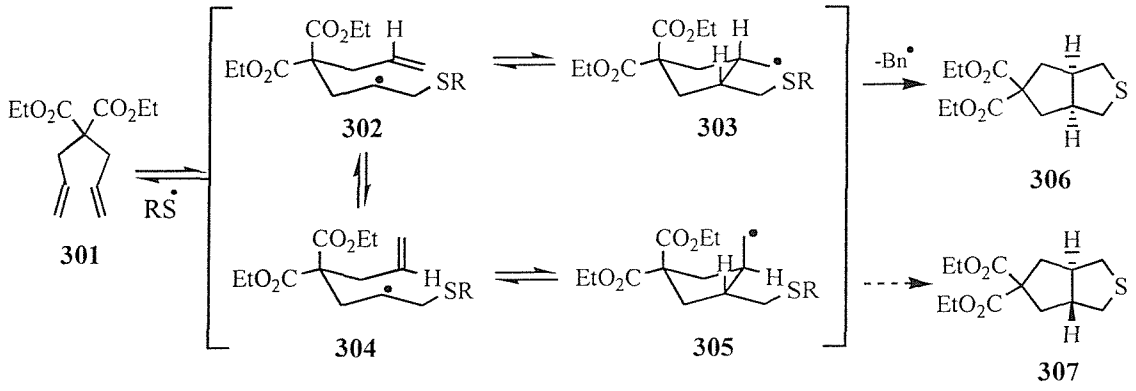
3.2 Radical Cyclisation Reactions

In order to conduct a selective radical cyclisation, one requires selective radical generation, cyclisation and quench. The rate of each cyclisation step must be faster than the rate of quenching by the solvent or other radical trap and the method must convert the cyclic radical into a stable product. The key steps normally involve generation of an initial carbon centred radical, then addition of that reactive centre to an unsaturated moiety to effect an intramolecular cyclisation. Finally atom abstraction from a mediator simultaneously furnishes the product and another radical intermediate to propagate the chain reaction.

Radical cyclisations are especially useful for the synthesis of five membered rings since the 5-*exo*-trig cyclisation is usually faster than reactions leading to other ring sizes. Where cyclisations lead to the creation of a new stereogenic centre, stereoselectivity is usually modest. The Beckwith transition state model, where the intermediate radical is assumed to adopt a chair like conformation, provides a means of predicting the stereochemical course of 5-*exo*-trig cyclisation reactions.[43]

3.3 Thiyl Mediated Radical Cyclisations

Previous work in the group had focussed on developing an alternative to trialkyltin hydride in radical cyclisations. The addition of thiyl radicals to alkenes is both fast and reversible. The normal fate of the intermediate carbon centred radical is to revert back to starting materials or to suffer hydrogen atom quench. For 1,6-dienes radical cyclisation is also possible. Such reactions usually result in complex mixtures. A way was envisaged to control these cyclisations using the "equilibration and bite back strategy" outlined in Scheme 3.2.

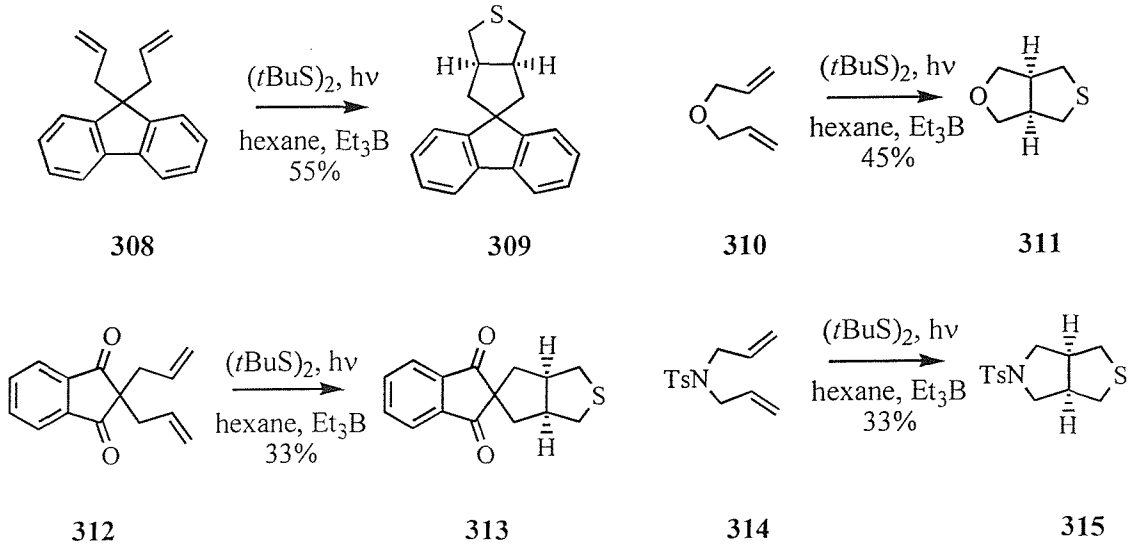


Scheme 3.2

Addition of a thiyl radical to a 1,6-diene **301** would lead to a radical intermediate **302/ 304**. A 5-*exo*-trig cyclisation through the favoured chair like transition state **302**

would provide **303**. A second irreversible 5-*exo*-trig cyclisation involving the homolytic displacement of an alkyl radical from sulfur would generate the fused 5,5-ring system **306**. This fate is not available to the diastereoisomer **305** (derived from cyclisation through conformer **304**) as the intermediate carbon centred radical and the sulfur atom cannot come into close proximity. Overall the cyclisation **301** to **306** would be rendered diastereoselective. It was hoped that the cyclisation **304** to **305** would be reversible so that the homolytic displacement at sulfur would channel all of the substrate **301** through to the bicyclic product **306**.

When we commenced our work this method had been successfully applied to a number of 1,6-dienes as highlighted in Scheme 3.3. Photochemical initiation was found to be more efficient than thermal initiation. The use of di-*t*-butyldisulfide was more effective than other disulfides and thiols (being a poor hydrogen atom donor). Monocyclic side products arising from hydrogen atom quench prior to homolytic displacement at sulfur were minimal under these conditions.



308 **309** **310** **311**

312 **313** **314** **315**

Scheme 3.3

The use of dibenzyldisulfide produced significant amounts of monocycle which was attributed to a facile intramolecular hydrogen atom transfer from the benzylic position (Figure 3.1). Use of *tert*-butyldisulfide increased the yield of co-cyclised product but generation of the monocycle from the *trans* diastereoisomer was still observed. Presumably the hydrogen atoms of the *t*-butyl moiety are less prone to abstraction but can participate in a slow elimination reaction, leading to hydrogen atom transfer (Figure 3.2). *Bis*-(1-adamantyl)disulfide **316** was also investigated as a source of adamantyl thiyl radicals. Abstraction of a hydrogen atom in this case is much less favourable since it would result in the formation of a bridgehead double bond (Figure 3.3). Use of **316** did indeed minimise the formation of monocyclic products but gave virtually no improvement in the yield of bicyclic products. Since **316** is not available commercially, di-*t*-butyl disulphide was subsequently used.

Figure 3.1

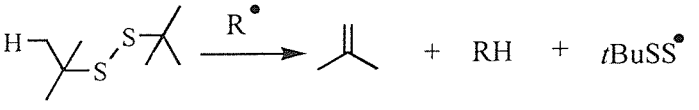
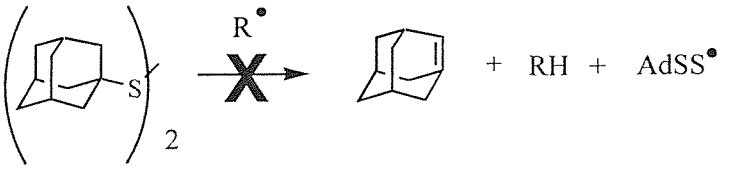


Figure 3.2



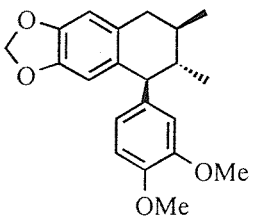
316

Figure 3.3

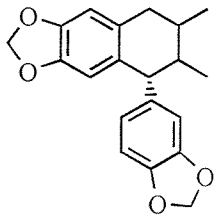
The long reaction times required (typically 24 h of irradiation) were reduced when triethylborane was added to the solution. Switching from a Pyrex photochemical reactor to a quartz vessel was likewise beneficial. The increase in amount of ultra violet light reaching the reaction mixture was apparent from the reduction in reaction times. Hexane was found to be the solvent of choice in these cyclisation reactions. Acetonitrile extended the reaction times slightly but was a useful alternative when more polar substrates, with poor solubility in hexane, were employed. As would be expected, tetrahydrofuran was found to increase the production of monocyclic products through facile hydrogen atom donation.

3.4 Application to Lignan Synthesis

A logical extension of this work would include application in target oriented synthesis and this was our aim. Our targets included the aryltetralin lignans **317** and **321** isolated from the *Myristia Otoba* fruits.[44] **317** has also been isolated from *Virola Elongata*, as have **320** and **322**,[45] while otobain **318** has been found in *Myristica Otoba* fruit and austrobailignan-3 **319** was isolated from *Austrobaileya Scandens*.[46, 47] A range of routes to aryltetralin natural products can be found in the literature and will not be discussed further here.



317



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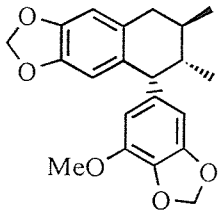

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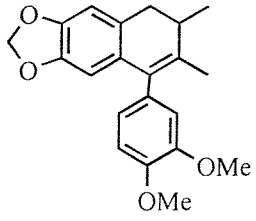
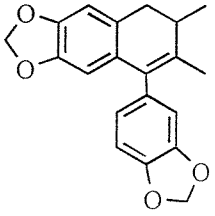
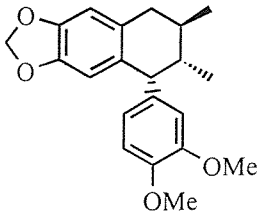


320

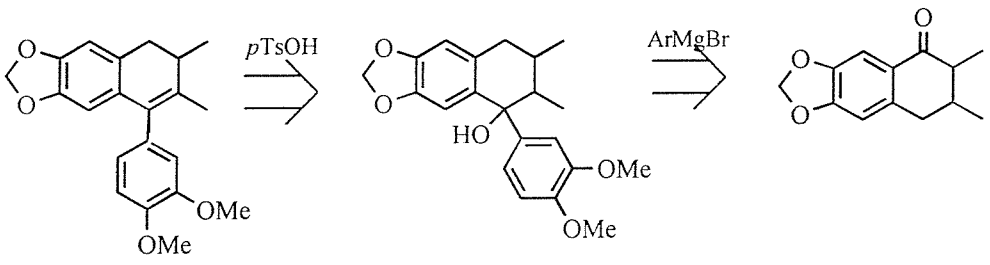


321

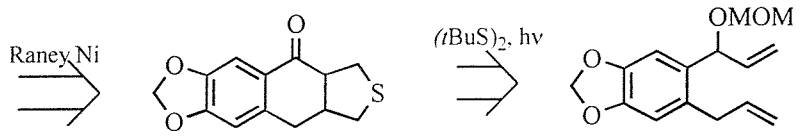


322

Our retrosynthetic analysis sought to produce aryltetralin **320** by dehydration of alcohol **323** formed by union of an aryl Gringard reagent with ketone **324**. The ketone was to originate from the sulfur mediated radical cyclisation of diene **326** followed by treatment with Raney Nickel (Scheme 3.4).



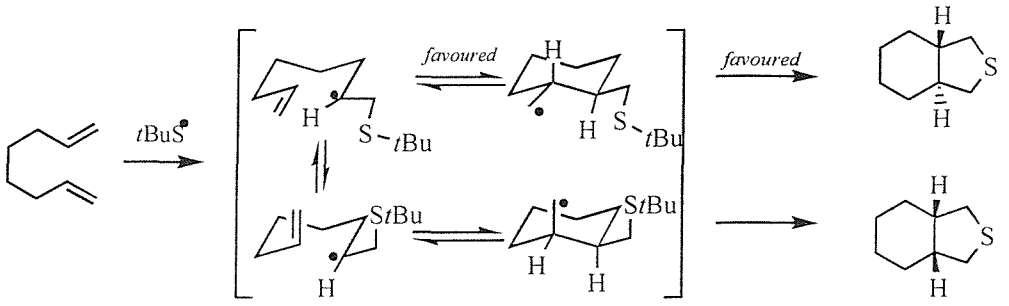
320 323 324



325 326

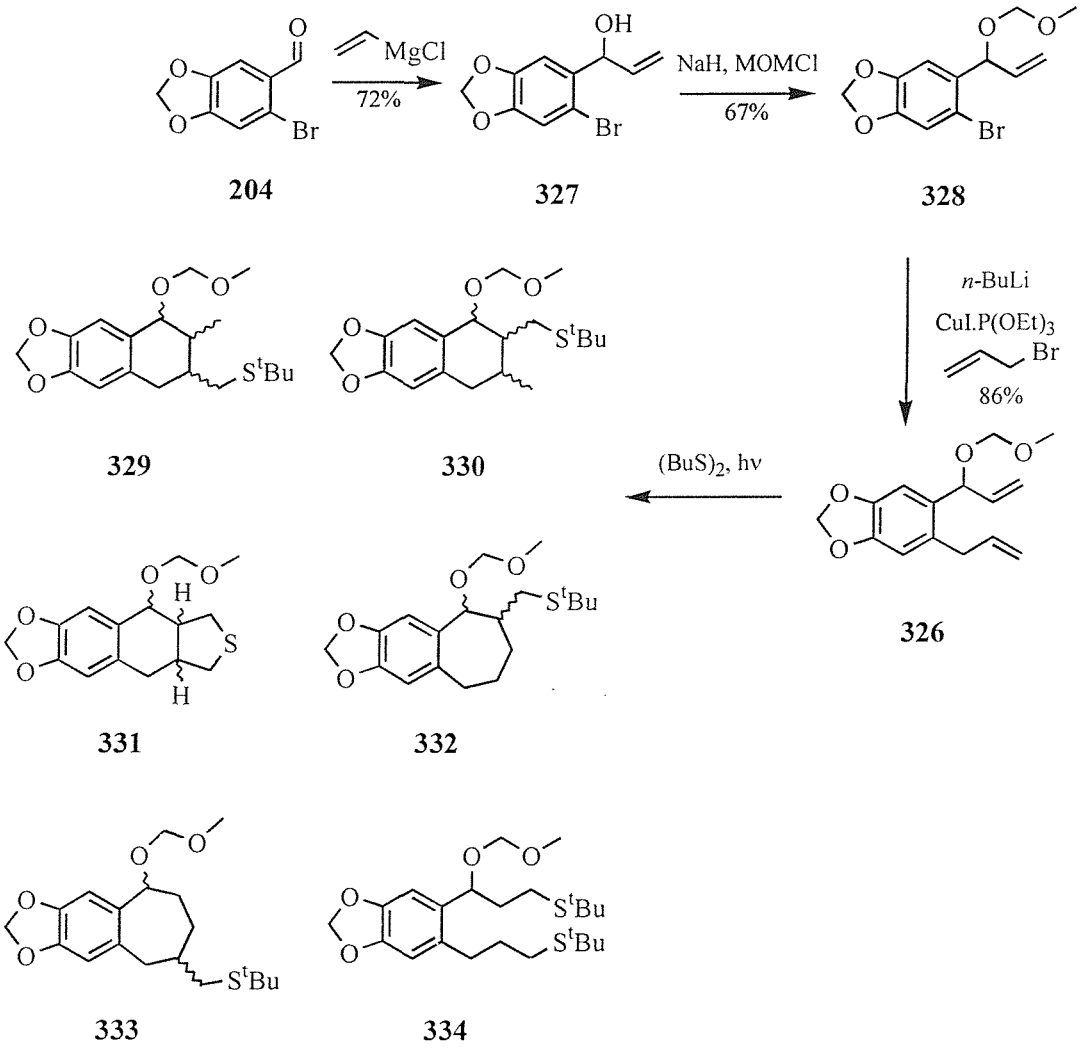
Scheme 3.4

There were several points of interest within the retrosynthetic analysis. Firstly we were curious to see if our method could be used to effect construction of a six membered ring. Moreover, since one would expect ring closure to favour production of a *trans* substituted cyclohexane, would co-cyclisation generate a *trans*-fused product?



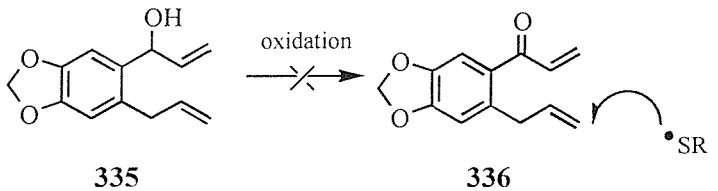
Scheme 3.5

We began by following the synthetic route shown in Scheme 3.6. 6-Bromopiperonal **204** was treated with vinylmagnesium chloride to give **327** in 72% yield. Protection of the alcohol with the methoxymethyl protecting group provided **328** in 86% yield. The allyl moiety was next installed *via* metal-halogen exchange with *t*-butyllithium, transmetallation with CuI.P(OEt)$_3$ and union with allyl bromide to give **326** in 86% yield. Irradiation of a hexane solution of **326** at ambient temperature with triethylborane and di-*t*-butyldisulfide led to a complex and inseparable mixture of products. Notably, no alkene resonances were evident in the proton NMR of the mixture, suggesting that the cyclisation may have proceeded but was unselective. Several regiochemical and stereochemical outcomes can be envisaged and we presume that many are facile (Scheme 3.6).



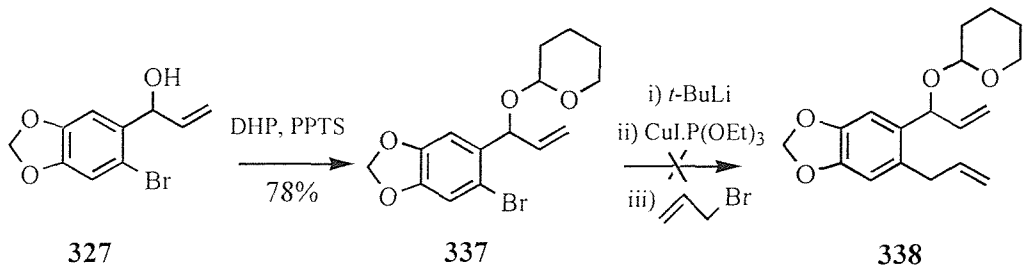
Scheme 3.6

We noted that in this example there was no differentiation between the alkenes. Since the sulfur centred radical is electrophilic, it would be expected to attack an electron rich alkene preferentially. With this in mind we aimed to oxidise alcohol **335** to enone **336** in order to direct attack of the sulfur centred radical to the unconjugated alkene and thus render the reaction selective (Scheme 3.7).



Scheme 3.7

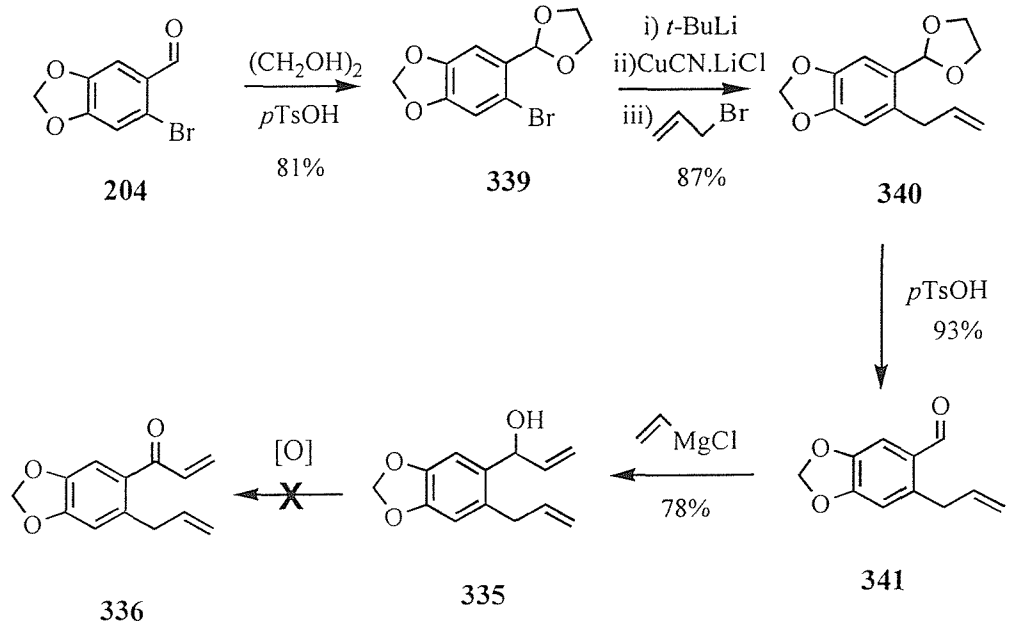
Removal of the MOM protecting group from **326** proved troublesome so we amended our approach and employed a THP protecting group. However the allylation was then unsuccessful so an alternative protection strategy was required (Scheme 3.8).



327 **337** **338**

Scheme 3.8

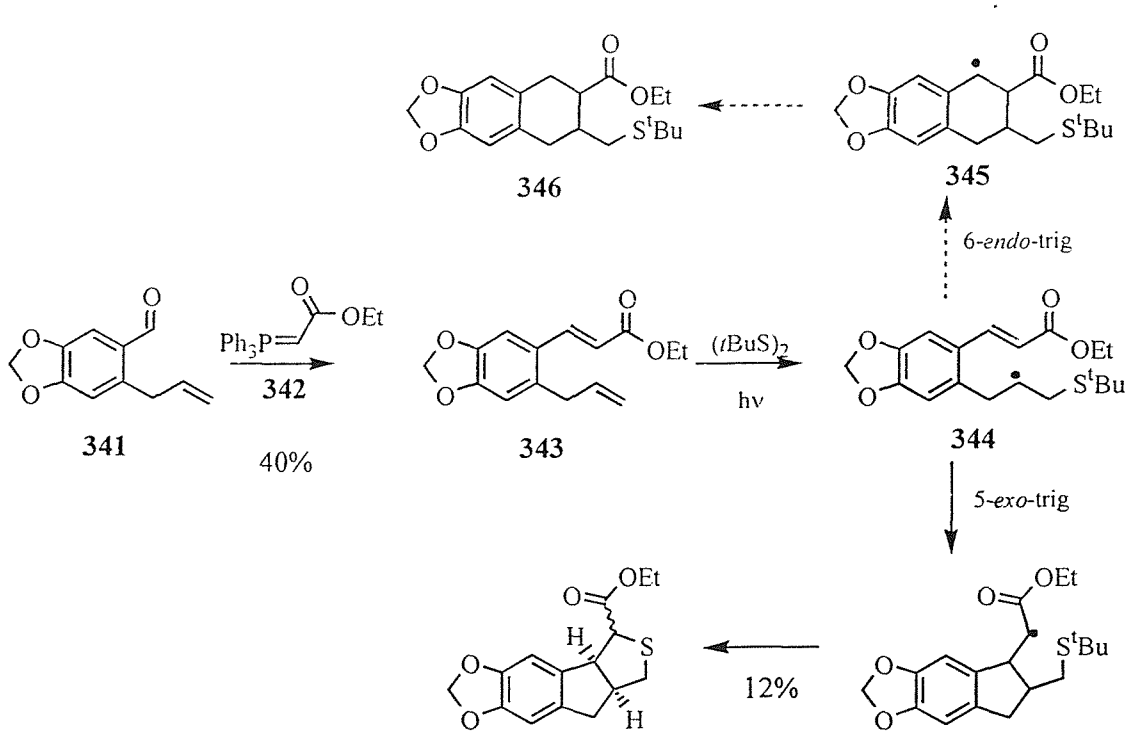
Protection of aldehyde **204** as an acetal and allylation of **339** with CuCN.LiCl and allyl bromide gave **340** in 87% yield. Deprotection under acidic conditions to aldehyde **341** and exposure to vinylmagnesium chloride gave **335**. However, oxidation of **335** to **336** proved intractable most likely due to polymerisation of the α,β-unsaturated ketone.



204 **339** **340** **341** **335** **336**

Scheme 3.9

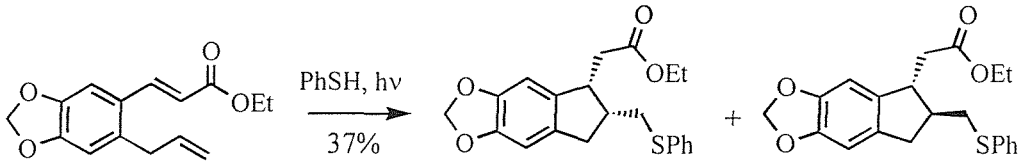
We thus chose to utilise a model system to enable us to make a clearer examination of the cyclisation. A Wittig reaction between aldehyde **341** and ylid **342** gave diene **343**. This molecule satisfied our requirements for differentiation between the alkenes - one being conjugated to the ester and electron poor and the other out of conjugation so, in principle, more likely to be attacked by the electrophilic thiyl radical. Exposure of **343** to di-*t*-butyldisulfide under UV irradiation, as expected led to products derived from attack of the resulting sulfur radical at the more electron rich alkene. (Scheme 3.10).



Scheme 3.10

Due to the planarity of the molecule, we expected the radical **344** to undergo a 6-*endo*-trig cyclisation to form the six membered ring and our desired skeleton **346**. However, in practice the intermediate radical underwent a 5-*exo*-trig cyclisation to intermediate radical **347** which then, underwent homolytic substitution at sulfur to form bicyclic product **348**.

We then attempted the cyclisation again using thiophenol as our radical source. A product was given in 37% yield as an inseparable 1:1 mixture of diastereoisomers. A long range NMR correlation spectroscopy confirmed that this product was a mixture of **349** and **350**, establishing that the 5-*exo*-trig cyclisation dominates in this system.

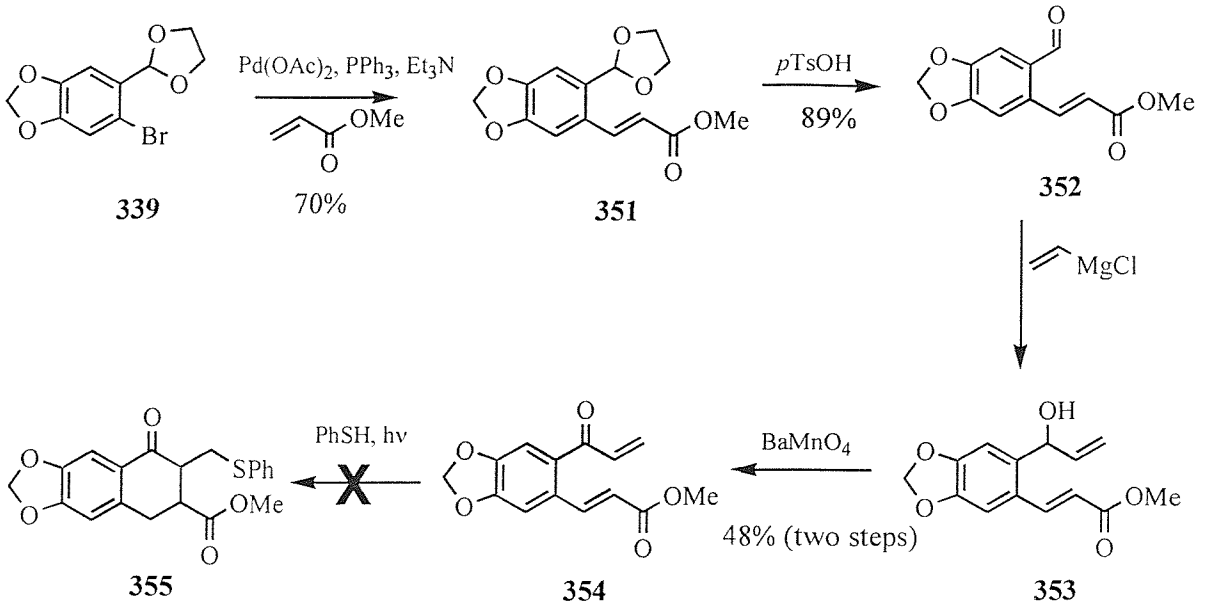


343 **349** **350**

Scheme 3.11

Further model systems were then investigated in an attempt to bias the reaction towards six membered ring formation. We sought to constrain the diene in a more rigid molecule such as **354**. It was hoped that the radical intermediate formed on addition of the thiyl radical to the enone would be better able to effect a 6-*endo*-trig cyclisation as the pathway would be less strained.

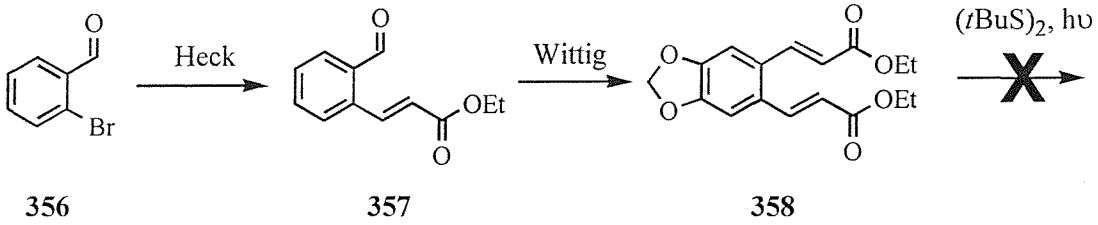
The α,β-unsaturated ketone **354** was synthesised *via* the route shown in Scheme 3.12. Acetal **339** was stirred with methyl acrylate under Heck conditions to give **351** in 70% yield. Deprotection of the acetal under acidic conditions provided **352** in 89% yield. The resulting aldehyde was then treated with vinylmagnesium chloride to give alcohol **353**. Though unstable, this alcohol could be used directly in the following transformation, an oxidation with barium manganate, to give **354** in a yield of 48% over the two steps. Unfortunately cyclisation of **354** was unsuccessful – polymerisation being more facile than cyclisation in this instance.



Scheme 3.12

3.5 Returning to the Methodology.

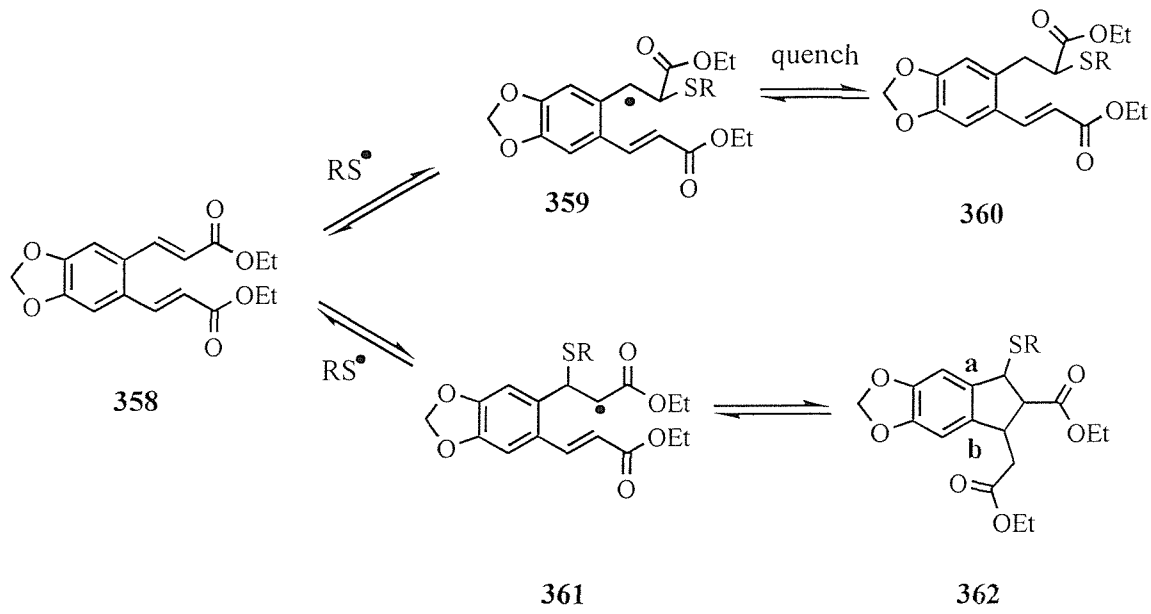
As all attempts to effect the synthesis of a six membered ring had met with failure we chose to further investigate the scope and limitations of the cyclisation.



Scheme 3.13

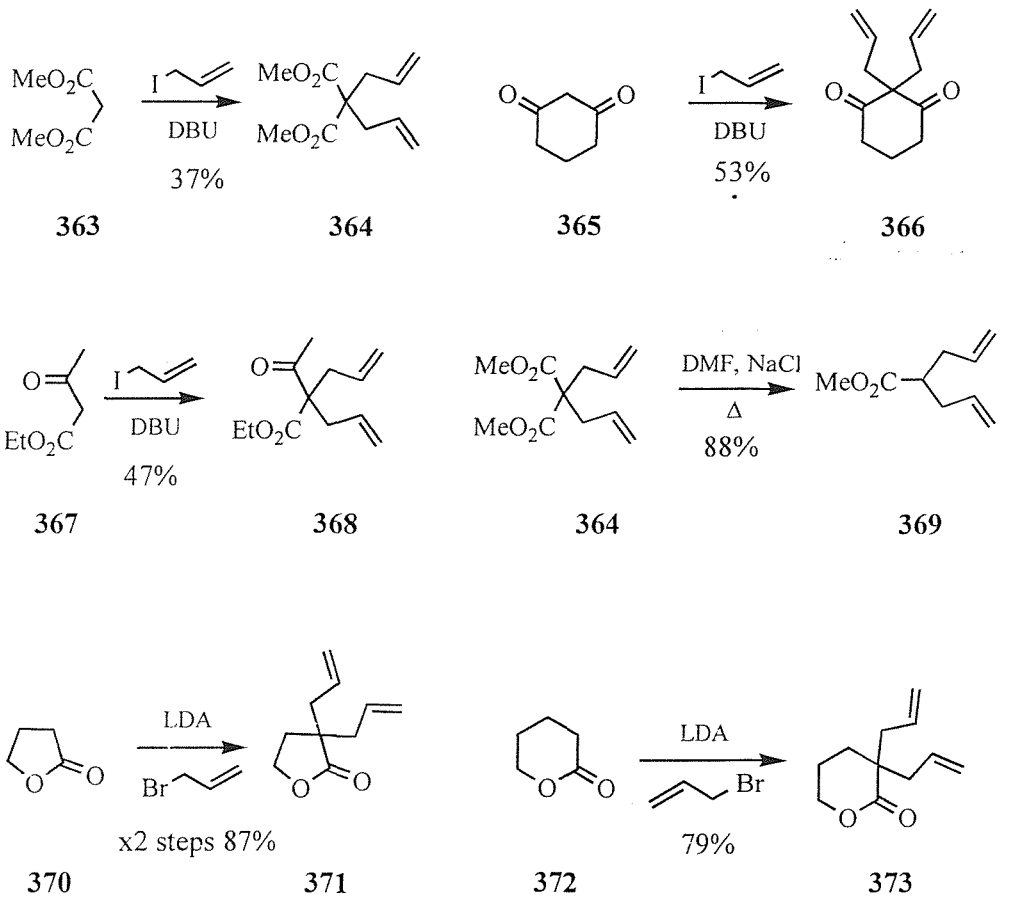
We began by synthesising **358** *via* the sequence depicted in Scheme 3.13. However, all attempts to effect cyclisation of the aromatic substrates using sulfur mediated radical cyclisations failed. One possible explanation is that the cyclisation step will be slow as the product is strained (the bond angle at **a** and **b** is less than its preferred

120°). This may cause the reverse reaction to be faster than the forward reaction (Scheme 3.14).



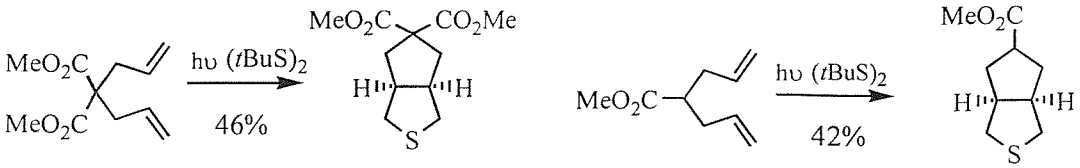
Scheme 3.14

A number of general examples were then attempted to ensure that the method used to conduct the aforementioned experiments did not differ from the original work (Scheme 3.15). The precursors **364**, **366** and **368** were prepared by diallylation of a β-dicarbonyl compound with allyl iodide using DBU as base. Diene **369** was obtained from **364** by decarboxylation with NaCl in refluxing DMF. Dienes **371** and **373** were synthesised by the allylation of **370** and **372** respectively using LDA and quenching with three equivalents of allyl bromide. Where monoallylation occurred, the monoallyated product was subjected to the same reaction conditions to give **371** and **373** respectively.

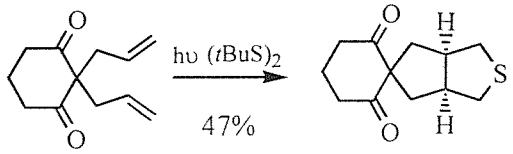


Scheme 3.15

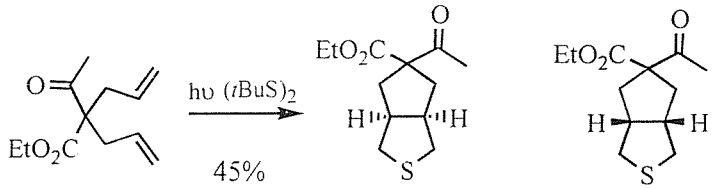
Photolysis of each of the dienes **364**, **366**, **368** and **369** in the presence of di-*t*-butyldisulfide led to the corresponding *cis*-bicyclic products in modest yields. Interestingly, for ester **369**, only one diastereoisomer was given whereas for β-ketoester **368**, two diastereoisomers were given in equal proportion. We were also able to effect the cyclisation with dienes **371** and **373**. In both cases the cyclisation gave a 1:1 mixture of diastereoisomers in modest yields (Scheme 3.16).



364 **374** **369** **375**

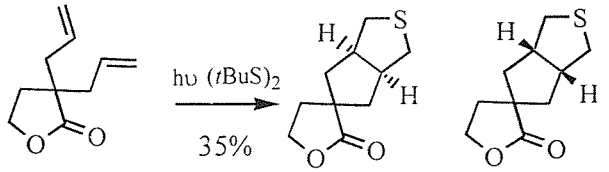


365 **376**



1:1

368 **377** **378**



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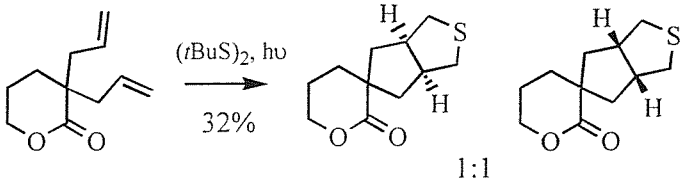
371 **379** **380**

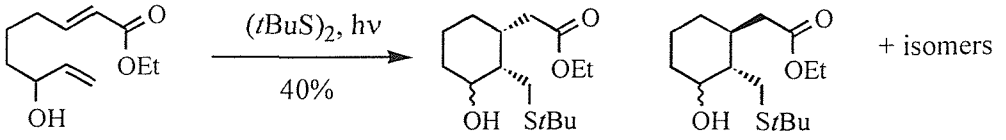


1:1

372 **381** **382**

Scheme 3.15

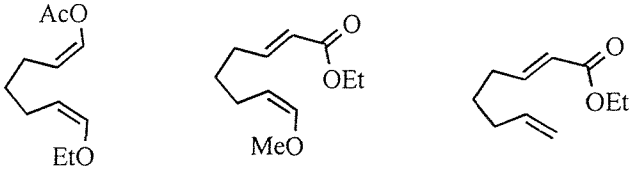
The method was then extended to six ring closures using diene **383**. Here, the products attained were monocycles **384** and **385**. We are unsure why the second cyclisation was disfavoured in this case.



383 **384** **385**

Scheme 3.17

Attempts to cyclise dienes **386** and **387** proved unsuccessful which we presume to be due to steric factors - the alkene being 1,2-disubstituted impedes the addition of di-*t*-dibutyldisulfide considerably. Our failure to effect cyclisation of diene **388** is more puzzling. It may be that the Thorpe-Ingold effect has considerable influence upon the outcome of these reactions.[48] Most successful cyclisations contain a quaternary carbon within the carbon chain of the 1,6-diene, while those that failed do not.

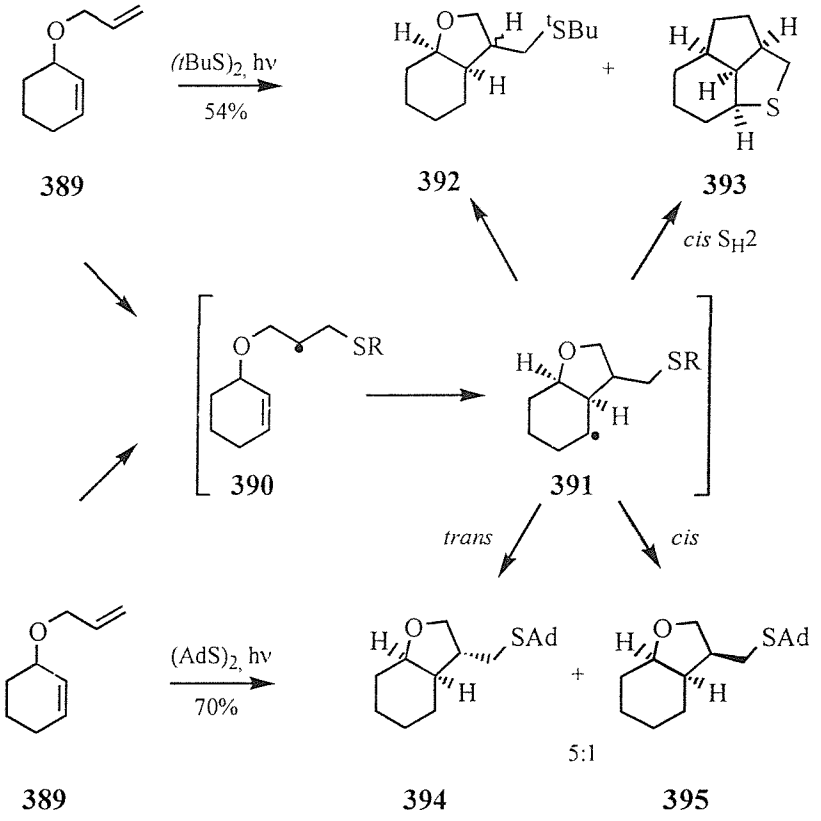


386 **387** **388**

Finally, compound **389** was treated with di-*t*-butyldisulfide. In this case the first cyclisation gave rise to a mixture of *cis* and *trans* isomers. A proportion of the *cis* diastereoisomer then underwent a second cyclisation to give tricycle **393** in 18% yield, while the *trans* diastereoisomer suffered hydrogen atom quench to yield bicycle **392**.

Conducting the reaction with adamantyldisulfide under similar conditions provided a mixture of *cis* and *trans* bicycles **394** and **395** in a 5:1 ratio.

Presumably the steric bulk of the adamantyl group prevents adoption of a conformation that would allow an S_H2 reaction at sulfur to occur. In this case only monocyclic products were given.



Scheme 3.18

3.6 Conclusions

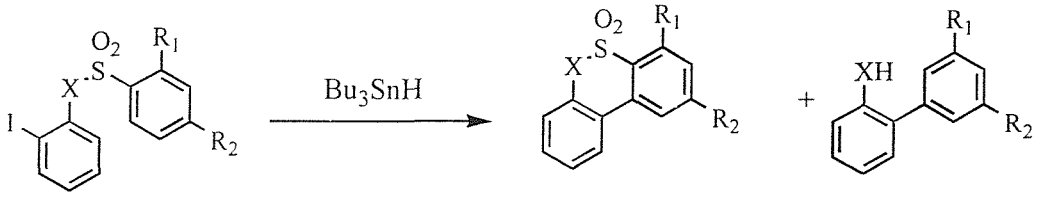
We attempted to construct the aryltetralin skeleton using a thiyl radical cyclisation pioneered in the Harrowven group.[49] Our failure led us to examine further the scope of this cyclisation method. Our studies have shown it to be tolerant of a range of functional groups. Yields were generally modest with 1,6-dienes, suggesting that the first radical cyclisation step (e.g **304** to **305**) is irreversible.

Chapter Four

Intramolecular Radical Cyclisations to Aromatic Systems

4.1 Background

Biaryl moieties are found in many natural product systems and an efficient synthesis of these would have a wide range of applications. There are a number of well known methods for biaryl synthesis, many of which involve transition metal complexes as intermediates.[50] Perhaps the most widely used is the Suzuki reaction, a palladium catalysed cross coupling between an aryl halide and a phenylboronic acid.[51] However these methods are often poor when *ortho* substituted substrates are employed due to steric hindrance. Recent advances in radical based methodologies, such as the *ipso* addition of aryl radicals to aromatics, provide useful alternatives.[52] For example, Motherwell has produced biaryl systems from sulfonamides and sulfonate precursors *via* an aryl migration reaction conducted under standard radical forming conditions (Scheme 4.1).[53]



401 **402** **403**

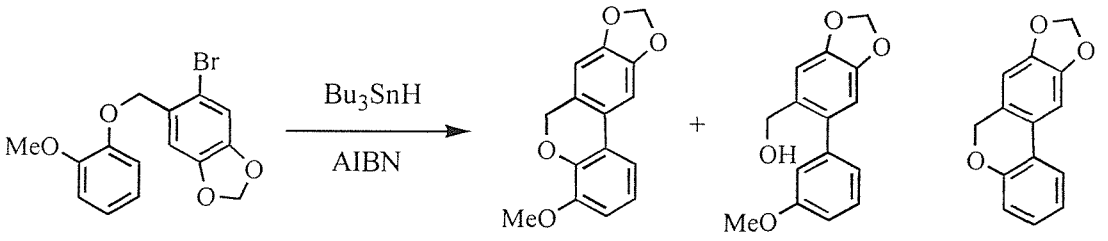
0-63% 0-57%

R_1, R_2 = H or CH_3
X = O or NCH_3

Scheme 4.1

The production of **403** was presumed to occur *via ipso* attack followed by the loss of SO_2. The efficiency of *ipso* attack was greatly influenced by *ortho* substituents on the radical accepting ring. When R_1 = Me and X = NMe, the only identifiable product was **403** in 57% yield.

Use of *o*-bromobenzyl phenyl ethers as precursors to biaryl systems has also been investigated although yields were modest (Scheme 4.2).[54]

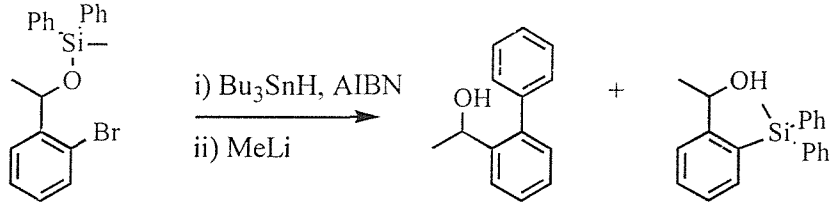


404 **405** **406** **407**

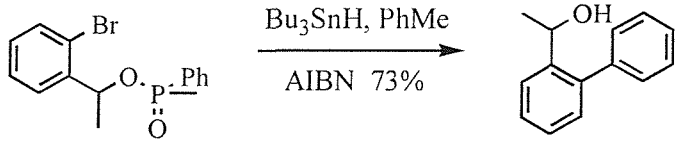
5% 18% 7%

Scheme 4.2

More recently silyl ethers and phosphinates have been used as a tether for aryl migrations (Scheme 4.3).[55, 56]



408 **409** **410**

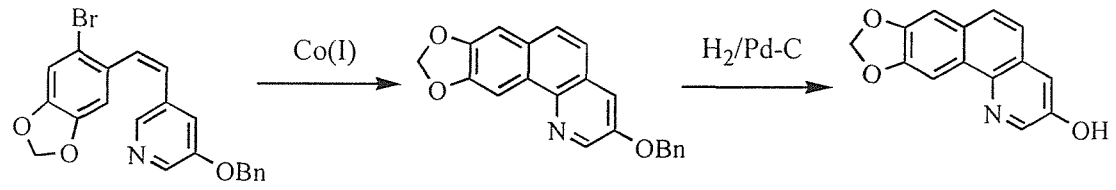


411 **412**

Scheme 4.3

4.2 Cyclisations onto Pyridines

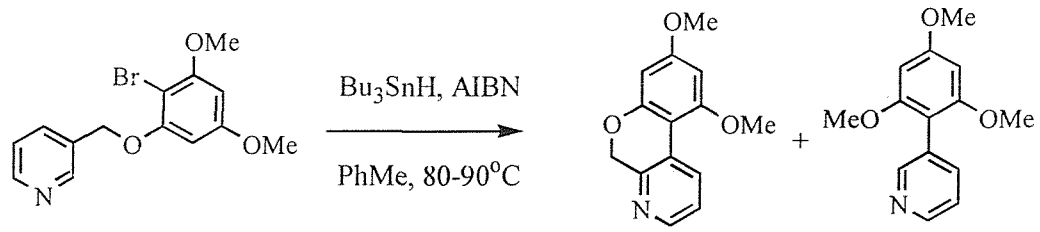
Toddaquinoline **415**, a natural product extracted from the root bark of formosan, has been a target in our group.[57, 58] The successful synthesis of this compound prompted further investigation into radical cyclisations onto pyridines (Scheme 4.4).



413 **414** **415**

Scheme 4.4

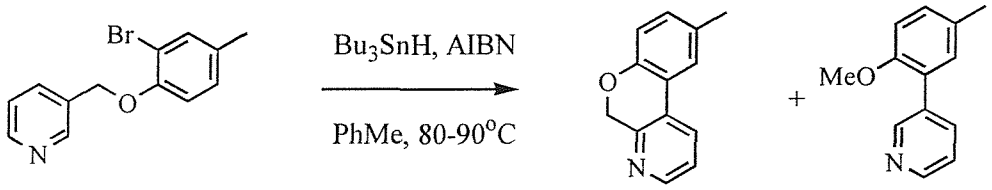
After some initial failures, treatment of aryl bromides **416** and **419** with tributyltin hydride and AIBN in toluene at 80°C for 24 h provided products derived from *ipso*-substitution albeit in low yield (Scheme 4.5 and 4.6).



18% 13%

416 **417** **418**

Scheme 4.5



19% 16%

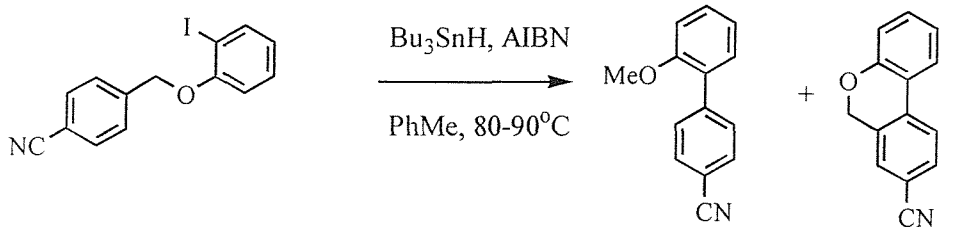
419 **420** **421**

Scheme 4.6

4.3 Extension of the methodology

We felt that this methodology had great potential especially if it could be extended to *ipso*-substitutions involving phenyl rings. To that end a series of benzyl 2-iodophenyl ethers were prepared from 2-iodophenol and various benzyl halides. These were either commercially available or synthesised from the corresponding benzyl alcohol by treatment with phosphorous tribromide in benzene.

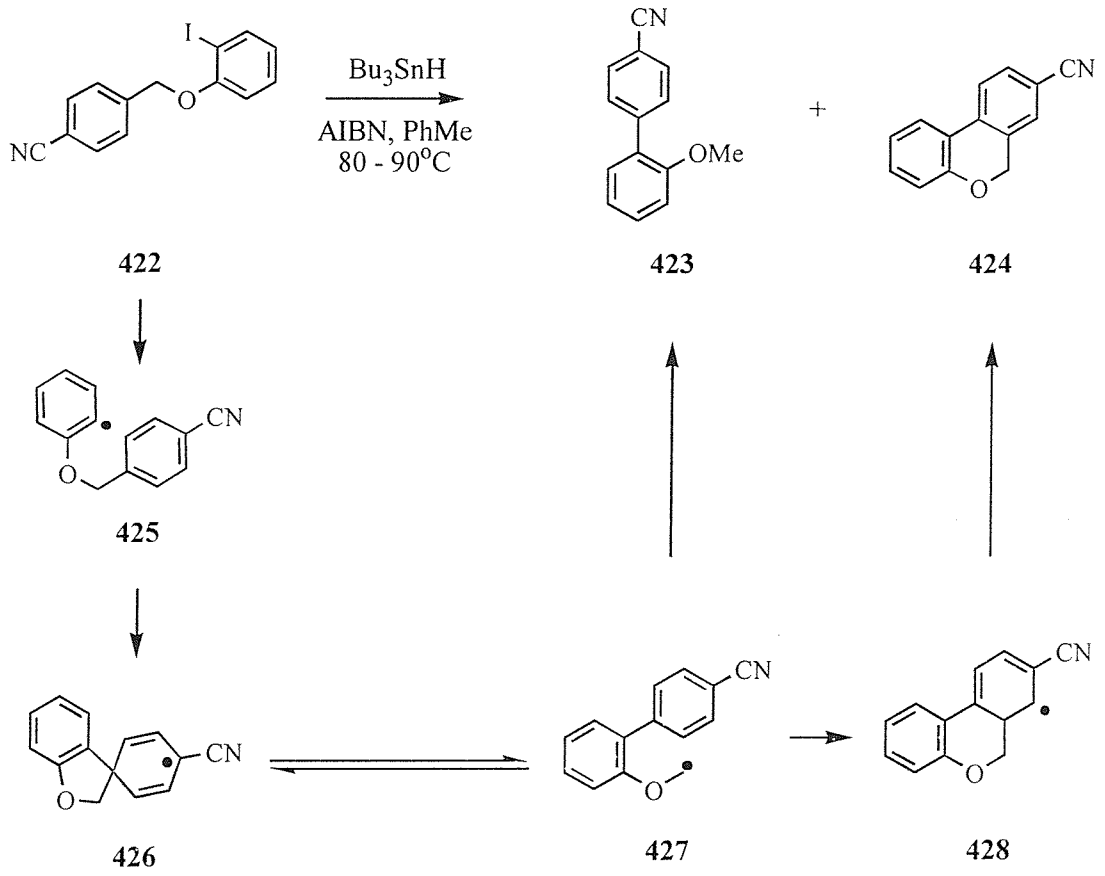
Reaction of **422** with tributyltin hydride and AIBN in toluene provided aryl methyl ether **423** in 73% yield together with a trace of tricycle **424** (Scheme 4.7).



422 **423** (73%) **424** (trace)

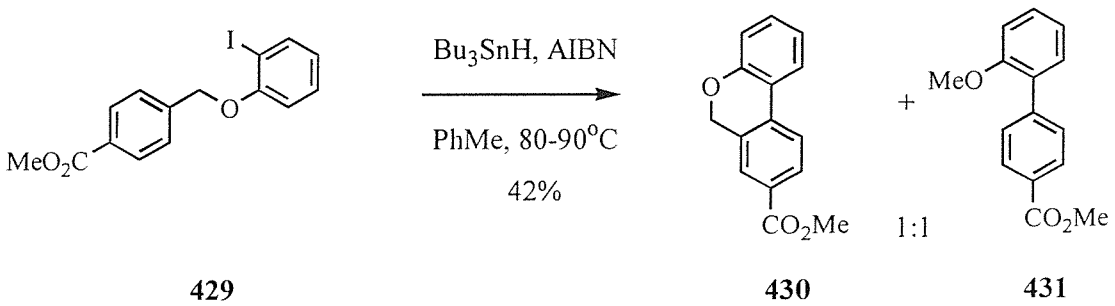
Scheme 4.7

Production of **423** and **424** were presumed to be a result of a 5-*exo*-trig cyclisation *via ipso* attack. Spirocycle **426** then fragments to **427** to re-establish the aromatic ring. A hydrogen atom abstraction from tributyltin hydride gives methyl ether **423**. The radical intermediate **427** may also add to the arene *via* either a 5-*exo*-trig cyclisation leading back to spirocycle **426** or a slower 6-*endo*/*exo*-trig course to **428** providing benzo[c]chromene **424** (Scheme 4.8).



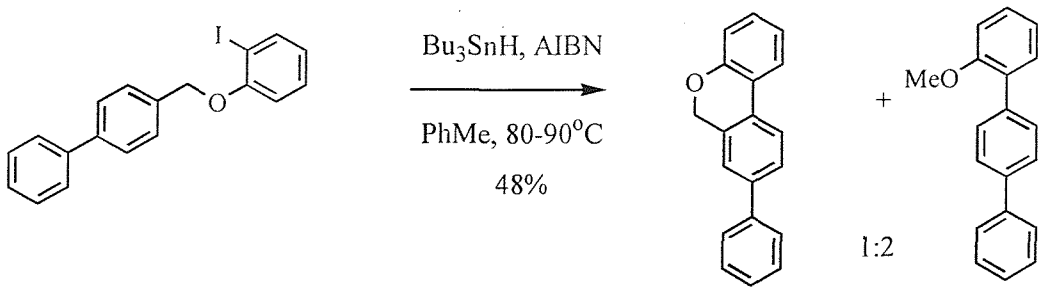
Scheme 4.8

We were pleased to be able to apply the cyclisation to a number of substrates. Thus, ester **429** gave **430** and **431** in moderate yield and we saw cyclisation to the terphenyls **433** and **434** in 16% and 32% respectively (Scheme 4.9 and 4.10). Unfortunately the complete separation of the two products was not possible in these examples.



429 **430** **431**

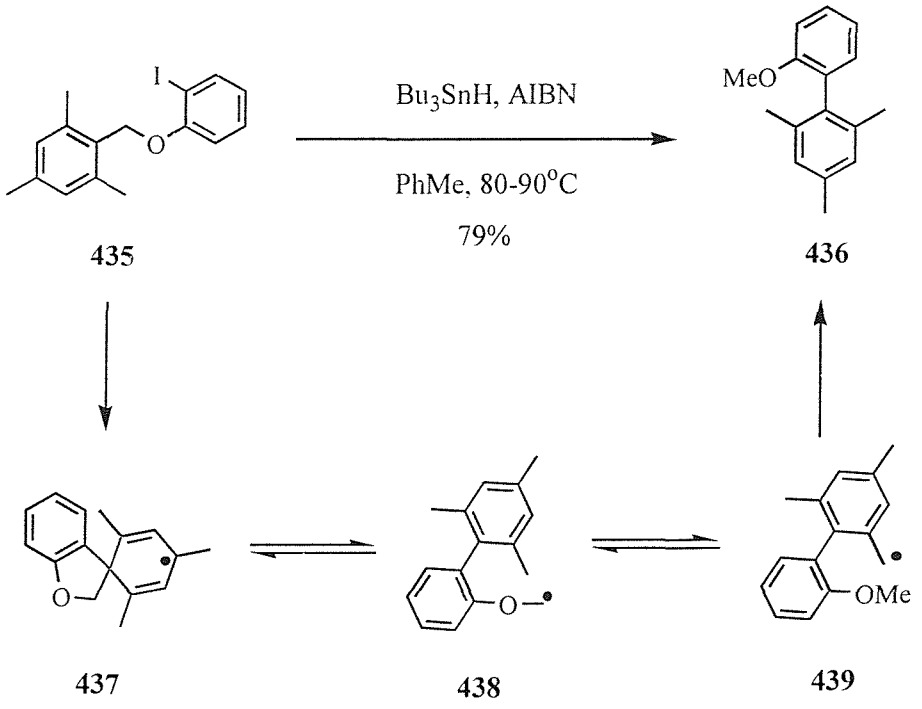
Scheme 4.9



432 **433** **434**

Scheme 4.10

Methyl substituents at the *ortho* position were then shown to block the 6-*endo*-trig pathway. Hence, exposure of 2,4,6-trimethylbenzyl ether **435** to tributyltin hydride under standard radical forming conditions gave methyl ether **436** in good yield (Scheme 4.11).

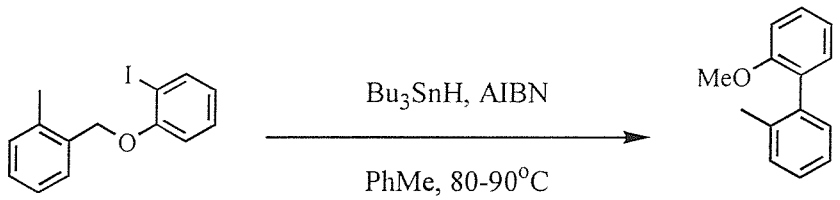


435 **436** **437** **438** **439**

Scheme 4.11

We believe that the intermediate radical **438** may abstract a hydrogen atom from a proximal methyl group to give **439** which is then quenched by tributyltin hydride (Scheme 4.11). Intramolecular hydrogen atom abstraction may also occur when one

ortho-methyl substituent is present on the benzyl ether. Thus, *o*-tolyl ether **440** provided biaryl methyl ether **441** as the major product in 47% yield (Scheme 4.12).

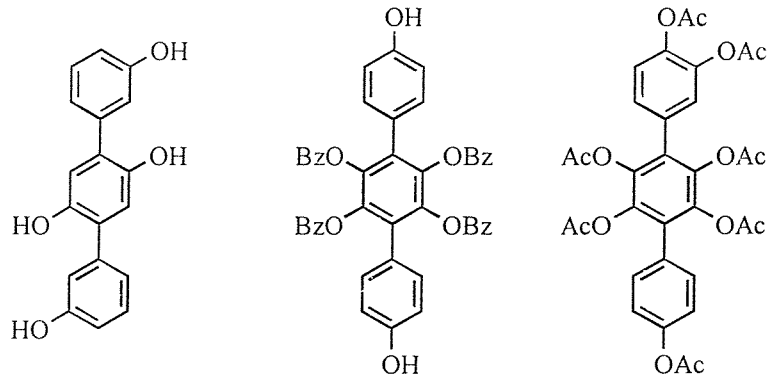


440 **441**

Scheme 4.12

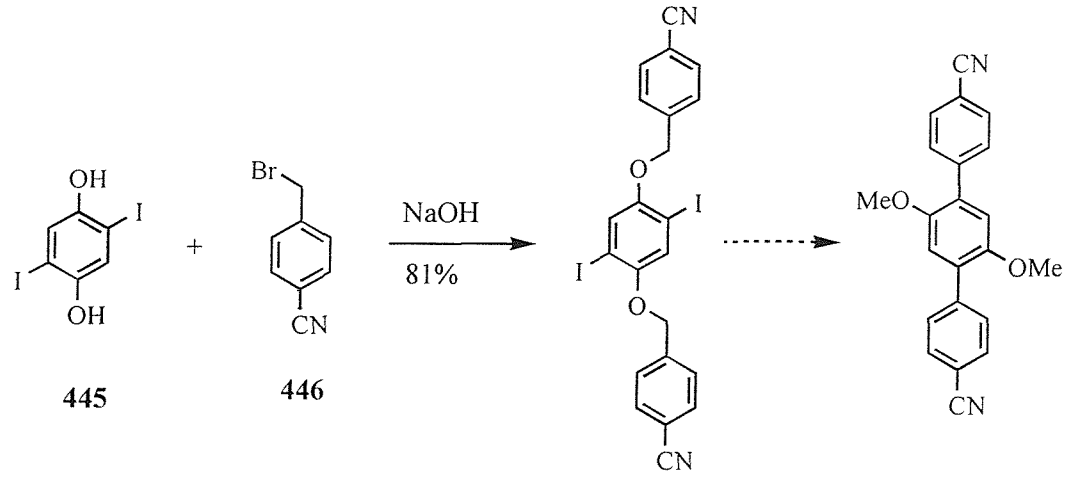
4.4 Synthesis of terphenyls

Terphenyl systems are also present in a number of natural products, including the simple terphenyls **442** –**444**.[59]



442 **443** **444**

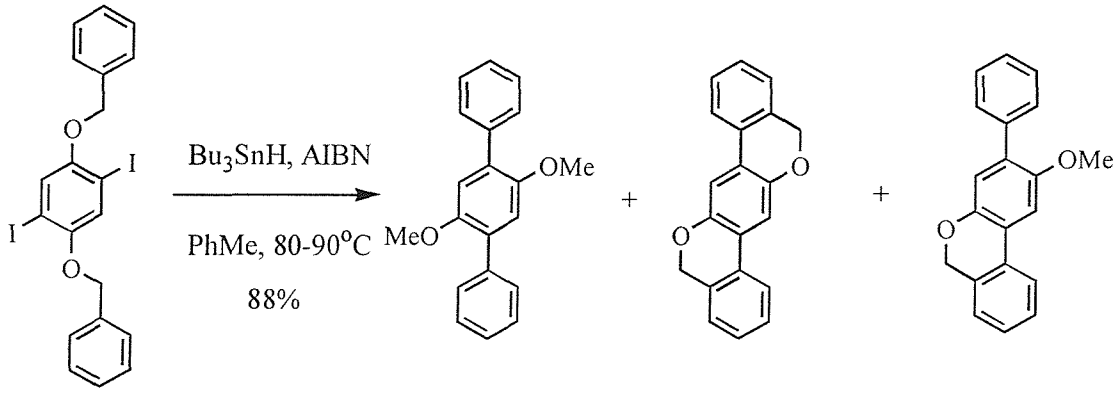
We attempted to target this class of compounds using a tandem variant of the reaction. By treating 2,4-diiodo-1,3-diphenol with 4-cyano benzyl bromide **446** we were able to prepare the *bis* ether **447** which was set up for sequential cyclisation. Unfortunately, we found this compound to be insoluble in all regular solvents. Its molecular weight and melting point were beyond the parameters of our instruments so we were unable to fully characterise the material. Moreover, its insolubility in refluxing toluene or benzene prevented us from taking the compound through the tandem *ipso*-substitution step (Scheme 4.13).



445 **446** **447** m.p. >270°C

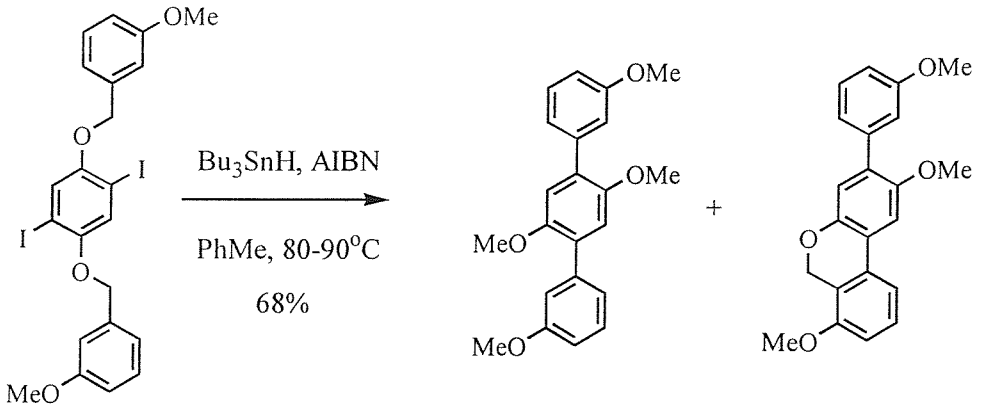
Scheme 4.13

We were, however, able to effect such a reaction on other substrates. The cyclisation and fragmentation of *bis* ether **448** appeared to be successful but the resulting mixture of compounds could not be separated. Likewise, the products from the *p*-methoxy substrate **452** were also inseparable. In both cases we were able to use ^{13}C NMR data to confirm the absence of starting material. These data also provided evidence in support of the products **449 – 451** and **453 – 454**. Furthermore analysis of the product mixture by GC mass spectrometry allowed us to confirm that the molecular weight of each component was in agreement with the assignments made (Scheme 4.14 and 4.15).



448 **449** **450** **451**

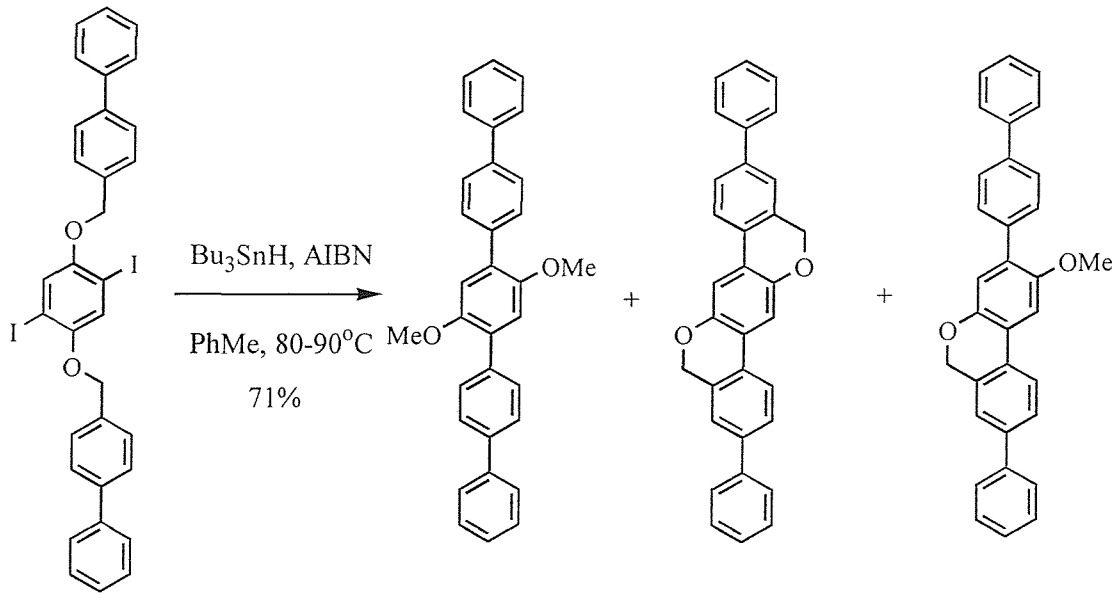
Scheme 4.14



452 **453** **454**

Scheme 4.15

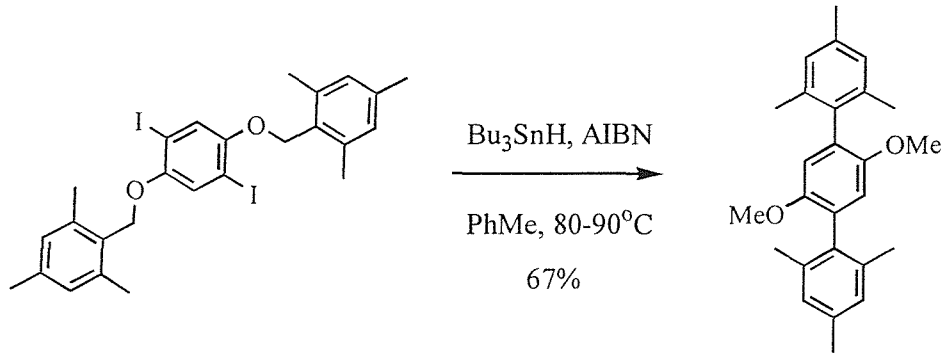
The success of the cyclisation of **432** to terphenyls **433** and **434** prompted us to try a tandem version of this cyclisation as it would provide a route to the pentaphenyl moiety, a class of compounds that has found applications as laser dyes.[60] Thus, we synthesised compound **455** and treated it under our radical forming conditions. The resulting products again proved inseparable by column chromatography but were yellow solids that appeared to fluoresce in solution. Attempts to separate these compounds by recrystallisation also failed. However, GC-MS showed that all three components of the product mixture had molecular masses consistent with **456** – **458**.



455 **456** **457** **458**

Scheme 4.16

As before, the reaction produced only one product when two *ortho* methyl substituents were present in the benzyl ether. Thus cyclisation of **459** gave terphenyl **460** as the only isolated product in 67% yield (Scheme 4.17).

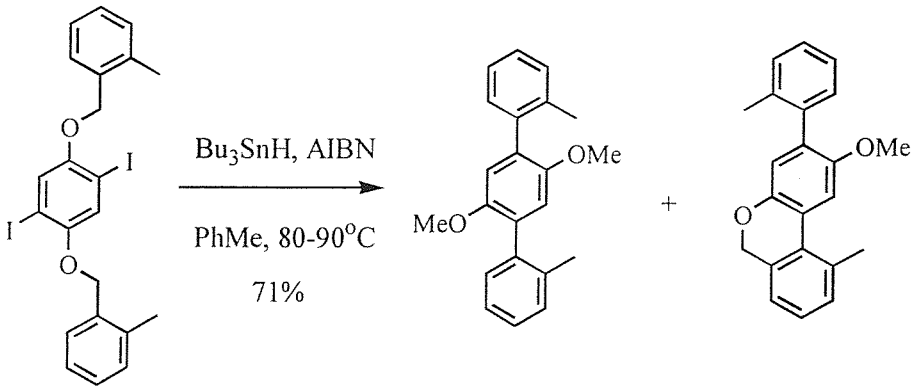


459 **460**

Scheme 4.17

We had noted that selectivity was poorer when only one *ortho*-methyl group was present in the benzyl ether (Scheme 4.12). The tandem variant of that cyclisation *e.g* with **461**, unsurprisingly gave a complex mixture of products attributed to **462** and

463. Again we were unable to effect the complete separation of these compounds though data attained on the mixture helps confirm our assignment (Scheme 4.18).



461 **462** **463**

Scheme 4.18

4.5 Conclusions

We have uncovered a new method of synthesising biaryls and triaryls through an intramolecular *ipso*-substitution reaction initiated by the addition of an aryl radical to a benzyl ether.[61] A tandem variant of the reaction has also been demonstrated. Whilst there are some issues relating to the separation of the products, the reaction has much potential in natural product synthesis.

Chapter Five

Experimental

Experimental

5.1 General Experimental

Reactions requiring anhydrous conditions were conducted in flame dried apparatus under a positive nitrogen atmosphere. Dry solvents were prepared by standard methods and where necessary commercial reagents were purified by distillation or recrystallisation prior to use.

Organic extracts were concentrated at aspirator pressure using a Büchi-type rotary evaporator. All reaction mixtures were magnetically stirred and monitored by thin layer chromatography using Machery-Nagel polygram Sil G/UV_{254} precoated aluminium sheets, layer thickness 0.25 mm. Compounds were visualised firstly by UV irradiation, then by heating plates exposed to solutions of either phosphomolybdic acid in ethanol or dinitrophenol in sulfuric acid. Column chromatography was performed on 230-400 Mesh 60H silica gel (Machery-Nagel), slurry packed and run under low pressure. Petrol refers to petroleum ether b.p. 40-60°C and ether refers to diethyl ether.

Melting points were determined on a Griffin melting point apparatus and are uncorrected. UV spectra were recorded on a Pye Unicam (PU8800 or SP800) UV-vis spectrometer. Maxima are reported as λ_{max} (nm) followed in parenthesis by the extinction coefficient, ε ($dm^3mol^{-1}cm^{-1}$).

IR spectra were recorded on a Perkin Elmer 1600 series spectrometer using NaCl cells, or a Nicolet Impact 400 spectrophotometer (1 milliwatt helium neon laser at 633

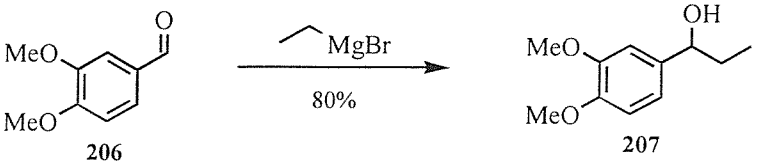
nm). Details are reported as ν_{max} (cm^{-1}) followed by a description using the following abbreviations: s = strong, m = medium, w = weak and br = broad.

^{1}H NMR spectra were recorded on a Bruker AC300 (300MHz) spectrometer or a DPX 400 (400 MHz) spectrometer as stated. Chemical shifts are quoted as δ values (p.p.m.) relative to residual $CHCl_3$ (δ_H = 7.27 p.p.m.). Multiplicities are described using the abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad and app = apparent.

^{13}C NMR were recorded on a Bruker AC300 (75MHz) spectrometer or a DPX400 (400MHz) spectrometer as stated. Chemical shifts are quoted as δ values (p.p.m.) relative to residual $CHCl_3$ (δ_C = 77.2 p.p.m.).

Mass Spectra were recorded under the supervision of Dr. J.A. Ballantine at the EPSRC Mass Spectrometry Centre, University of Wales, Swansea or Dr. G.J. Langley at the University of Southampton using a variety of instruments. Signals are reported as values in atomic mass units followed in parenthesis by the peak intensity relative to the base peak (100%).

1-(3,4-Dimethoxyphenyl)propan-1-ol 207[62]



206 $C_9H_{10}O_3$ 166

207 $C_{11}H_{16}O_3$ 196

Prepared by the method of Roberti.[62] 3,4-Dimethoxybenzaldehyde **206** (5.0 g, 30 mmol) was stirred in THF (60 mL) under N_2. Ethylmagnesium bromide (12 mL of a 3M solution) was added *via* syringe over 10 min. The mixture was left to stir for 1h. After this time the solution was quenched with water (30 mL) and extracted with ether (3 x 20 mL). The organic layer was separated, dried ($MgSO_4$) and solvent removed *in vacuo*. The product was purified by column chromotography (40% ether in petrol) to give **207** as a clear oil (4.71 g, 24 mmol, 80%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.80 (1H, s, Ar*H*), 6.72 (2H, s, 2 x Ar*H*), 4.38 (1H, t, *J* 6.6 Hz, C*H*OH), 3.75 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 2.78 (1H, br s, O*H*), 1.71 (1H, app. qd, *J* 7.3, 6.6 Hz, C*H*HCH$_3$), 1.61 (1H, app. qd, *J* 7.3, 6.6 Hz, CH*H*CH$_3$), 0.83 (3H, t, *J* 7.3 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 148.9 (*C* (Ar)), 148.5 (*C* (Ar)), 138.6 (*C* (Ar)), 118.7 (*C*H (Ar)), 110.6 (*C*H (Ar)), 109.1 (*C*H (Ar)), 75.7 (*C*HOH), 55.9 (OCH_3), 55.8 (OCH_3), 31.9 (*C*H$_2$), 10.3 (*C*H$_3$) p.p.m.

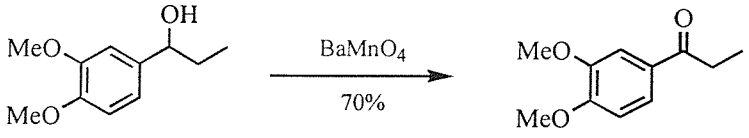
FT-IR ν_{max} (neat film) 3490brs, 2836s, 1607s, 1517s, 1483s, 1318m, 1158s, 1101m, 1027s, 979m, 858m cm^{-1}.

UV λ_{max} (MeOH) 279 (3500), 238 (3000) nm.

LRMS (APCI) 196 ([M]$^+$, 11%), 180 (10), 179 (100), 166 (14) amu.

These data were fully consistent with those reported in the literature.[62]

1-(3,4-Dimethoxyphenyl)propan-1-one 208[63]



207
$C_{11}H_{16}O_3$ 196

208
$C_{11}H_{14}O_3$ 194

Compound **207** (3.0 g, 15 mmol) and $BaMnO_4$ (19.2 g, 75 mmol) in dry CH_2Cl_2 were stirred under a nitrogen atmosphere for 48 h. The mixture was then filtered through a plug of celite and the solvent removed *in vacuo*. The product was purified *via* column chromatography (10% ether in petrol) to give **208** as colourless crystals (2.03 g, 11 mmol, 70 %).

m.p. 60-61°C (petrol), lit[63] 59-60 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.54 (1H, d with fine splitting, *J* 8.2 Hz, Ar*H*), 7.49 (1H, br s with fine splitting, Ar*H*), 6.84 (1H, d with fine splitting, *J* 8.2 Hz, Ar*H*), 3.87 (6H, s, 2 x O*CH*$_3$), 2.91 (2H, q, *J* 7.2 Hz, *CH*$_2$), 1.17 (3H, t, *J* 7.2 Hz, *CH*$_3$) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 199.5 (*C*=O), 153.1 (*C* (Ar)), 149.1 (*C* (Ar)), 130.2 (*C* (Ar)), 122.6 (*C*H (Ar)), 110.2 (*C*H (Ar)), 110.1 (*C*H (Ar)), 56.1 (O*C*H$_3$), 56.0 (O*C*H$_3$), 31.3 (*C*H$_2$), 8.6 (*C*H$_3$) p.p.m.

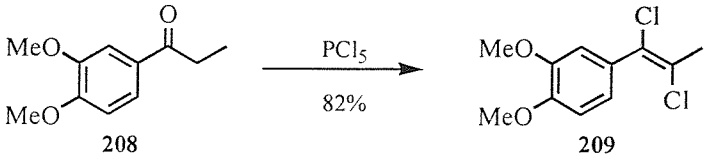
FT-IR ν_{max} (nujol) 1667s, 1515s, 1377s, 1280s, 1204s, 1083m, 1017m, 875m, 798s, 722m cm^{-1}.

UV λ_{max} (MeOH) 299 (28000), 273 (46800), 226 (44800) nm.

LRMS (APCI) 195 ([M+H]$^+$, 100%) amu.

These data are fully consistent with those reported in the literature.[63]

(*E*)-1,2-Dichloro-1-(3,4-dimethoxyphenyl)propene 209[64]



208 $C_{11}H_{14}O_3$ 194 **209** $C_{11}H_{12}Cl_2O_2$ 246

Prepared by the method of Engler.[64] Compound **208** (1.55 g, 8.46 mmol) was refluxed in toluene (40 mL) together with PCl_5 (3.52 g, 16.9 mmol) under a nitrogen atmosphere for 48 h. The reaction was diluted with ether (40 mL) and washed with saturated sodium bicarbonate solution (2 x 20 mL) and then brine (2 x 20mL). The organic layer was dried ($MgSO_4$), concentrated *in vacuo* and purified *via* column chromatography (5% ether in petrol) to give **209** as a colourless oil (1.71 g, 6.93 mmol, 82%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.06 (1H, dd, *J* 8.4, 1.8 Hz, Ar*H*), 6.99 (1H, d, *J* 1.8 Hz, Ar*H*), 6.86 (1H, d, *J* 8.4 Hz, Ar*H*), 3.87 (6H, s, 2 x OCH_3), 2.38 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 149.3 (*C* (Ar)), 148.4 (*C* (Ar)), 129.8 (*C* (Ar)), 126.9 (Ar*C*Cl), 126.2 (=*C*Cl), 122.3 (*C*H (Ar)), 112.4 (*C*H (Ar)), 110.7 (*C*H (Ar)), 56.1 (OCH_3), 56.0 (OCH_3), 24.4 (CH_3) p.p.m.

Some additional signals attributed to ca. 8% of the *cis* isomer were also observed.

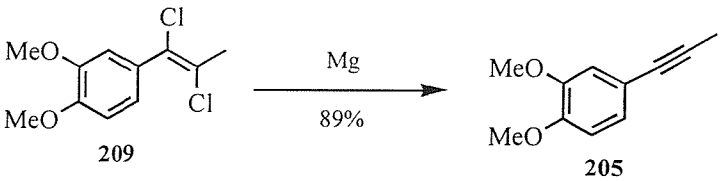
FT-IR ν_{max} (neat film) 3012s, 2836s, 2589w, 2029w, 1601s, 1464s, 1326m, 1167s, 1027s, 859m cm^{-1}.

UV λ_{max} (MeOH) 285 (30500), 262 (37600), 231inf. (31000) nm.

LRMS (APCI) 246 ($[M]^+$, 100%) amu.

These data were fully consistent with those reported in the literature.[64]

1,2-Dimethoxy-4-(prop-1-ynyl)benzene 205[64]



209
$C_{11}H_{12}Cl_2O_2$ 246

205
$C_{11}H_{12}O_2$ 176

Prepared by the method of Engler.[64] Activated magnesium turnings (737 mg, 30.4 mmol) were stirred in THF (40 mL) and 1,2-dibromoethane (0.2 mL, 1.2 mmol) was added *via* syringe. A solution of compound **209** (1.5 g, 6.07 mmol) in THF (10 mL) was added *via* syringe over 10 min and after the initial reaction had subsided, the temperature was increased to reflux for 16 h. The mixture was then filtered, diluted with water (20 mL) and extracted with ether (3 x 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product was purified *via* column chromatography (2% ether in petrol) to give **205** as colourless crystals (0.95 g, 5.39 mmol, 89%).

m.p. 47-48°C (petrol), lit[64] 49-51°C.

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.96 (1H, d with fine splitting, *J* 8.4 Hz, Ar*H*), 6.88 (1H, s with fine splitting, Ar*H*), 6.74 (1H, d, *J* 8.4 Hz, Ar*H*), 3.85 (6H, s, 2 x OCH_3), 1.98 (3H, s, CH_3) p.p.m.

^{13}C NMR (300 MHz, $CDCl_3$) δ_C 148.9 (*C* (Ar)), 148.6 (*C* (Ar)), 124.6 (*C*H (Ar)), 116.4 (*C* (Ar)), 114.4 (*C*H (Ar)), 111.1 (*C*H (Ar)), 84.2 (*C*≡C), 79.7 (C≡*C*), 55.9 (2 x OCH_3), 4.3 (CH_3) p.p.m.

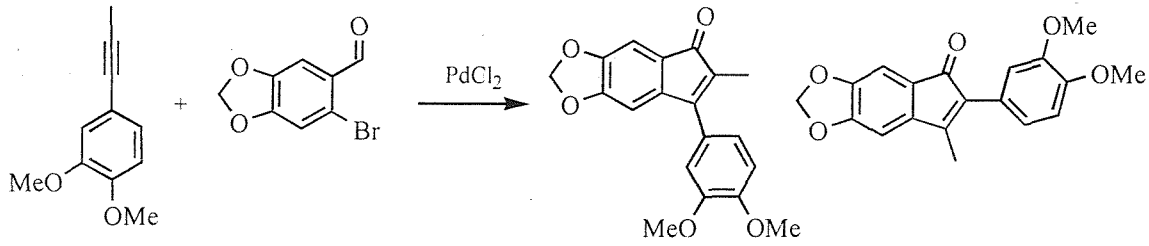
FT-IR ν_{max} (nujol) 2032w, 1838w, 1723w, 1600s, 1513s, 1483s, 1377m, 1212s, 1135s, 863s, 763s, 722m cm^{-1}.

UV λ_{max} (MeOH) 278 (9300), 283 (9600), 256 (30900), 223 (16400) nm.

LRMS (APCI) 176 ($[M]^+$, 100%) amu.

These data were fully consistent with those reported in the literature.[64]

7-[3,4-Dimethoxyphenyl]-6-methyl-5*H*-indeno[5,6-d][1,3]dioxol-5-one 201[29] and 6-[3,4-Dimethoxyphenyl]-7-methyl-5*H*-indeno[5,6-d][1,3]dioxol-5-one 210



205 **204** **201** **210**

$C_{11}H_{12}O_2$ 176 $C_8H_5BrO_3$ 227 $C_{19}H_{16}O_5$ 324 $C_{19}H_{16}O_5$ 324

Prepared by a method analogous to that of Larock.[20] 6-Bromopiperonal (0.286 g, 1.24 mmol) was stirred in DMA (20 mL) together with *n*-Bu_4NBr (0.805 g, 2.5 mmol), Na_2CO_3 (1.06 g, 0.01M), $Pd(OAc)_2$ (0.028 g, 0.12 mmol) and alkyne **204** (0.440 g, 2.5 mmol). The temperature was maintained at 100°C and the mixture stirred under a nitrogen atmosphere for 3h. The solution was diluted with ether (30 mL) and washed with saturated ammonium chloride (2 x 45 mL). The organic layer was separated and dried ($MgSO_4$) and the solvent removed *in vacuo*. Components were purified *via* column chromatography to give **201** and **210** as a 5:1 mixture of red solids which were separable by selective crystallisation from ethanol ([**201** 85 mg, 0.262 mmol, 21%], [**210** 17 mg, 0.052 mmol, 4%]).

Data for **201**

m.p. 142-144°C (MeOH), lit[29] 214-216°C (MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.09 – 6.92 (4H, m, 4 x Ar*H*), 6.63 (1H, s, Ar*H*), 5.98 (2H, s, OCH_2O), 3.98 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 1.91 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$), δ_C 196.9 (*C*=O), 152.9 (Ar*C*=CCH_3), 151.3 (*C* (Ar)), 149.9 (*C* (Ar)), 149.1 (*C* (Ar)), 147.1 (*C* (Ar)), 142.4 (*C* (Ar)), 129.3 (2 x *C*(Ar)), 125.4 (ArC=*C*CH_3), 121.3 (*C*H (Ar)), 111.3 (*C*H (Ar)), 111.1 (*C*H (Ar)), 105.1 (*C*H (Ar)), 103.6 (*C*H (Ar)), 102.1 (O*C*H_2O), 56.2 (O*C*H_3), 56.1 (O*C*H_3), 8.9 (*C*H_3) p.p.m.

LRMS (APCI) 325 ($[M+H]^+$, 100%).

FT-IR ν_{max} ($CDCl_3$) 2923m, 1699s, 1598m, 1514s, 1321m, 1237s, 1140m, 1027s, 921m, 758m cm^{-1}.

UV-vis λ_{max} ($CHCl_3$) 464 (700), 335 (6400), 268 (32000), 219 (11000) nm.

HRMS (EI^+) Found 324.1004 $C_{19}H_{16}O_5$ requires 324.0998 amu

CHN Found C 69.86 H 5.13 $C_{19}H_{16}O_5$ requires C 70.36 H 4.97.

Data for **210**

m.p. 198 - 200°C (ethanol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.05 – 6.92 (4H, m, 4 x Ar*H*), 6.71 (1H, s, Ar*H*), 5.99 (2H, s, OCH_2O), 3.97 (6H, s, 2 x OCH_3), 2.28 (3H, s, CH_3) p.p.m.

^{13}C NMR (100 MHz, $CDCl_3$) δ_C 195.9 (*C*=O), 152.2 (*C* (Ar)), 152.1 (Ar*C*=CCH_3), 149.1 (*C* (Ar)), 149.0 (*C* (Ar)), 147.9 (*C* (Ar)), 143.1 (*C* (Ar)), 132.5 (*C* (Ar)), 124.7 (ArC=*C*CH_3), 124.5 (*C* (Ar)), 122.5 (*C*H

(Ar)), 113.0 (*C*H (Ar)), 111.4 (*C*H(Ar), 105.1 (*C*H (Ar)), 102.5 (*C*H (Ar)), 102.4 (OCH_2), 56.3 (2 x OCH_3), 13.1 (CH_3) p.p.m.

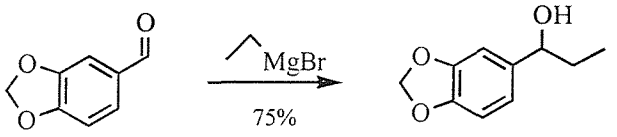
FT-IR ν_{max} (neat) 2947w, 2883w, 1702m, 1590m, 1491s, 1354m, 1221s, 1030s, 927m, 808w cm^{-1}.

UV-vis λ_{max} (CH_2Cl_2) 460 (400), 310 (3600), 264 (21800) nm.

LRMS (APCI) 325 ($[MH]^+$, 100%) amu.

HRMS (EI) Found 324.0999, $C_{19}H_{16}O_5$ requires 324.0998 amu.

1-Benzo[1,3]dioxol-5-yl-propan-1-ol 219 [65]



218 $C_8H_6O_3$ 150

219 $C_{10}H_{12}O_3$ 180

Prepared by the method of Orcutt.[65] Piperonal **218** (7.0 g, 46 mmol) was stirred in THF at 0°C. Ethylmagnesium bromide (15.5 mL of a 3M solution in ether) was added *via* syringe over 10 min and the solution was allowed to stir for 1h. The reaction mixture was diluted with ether (50 mL) and washed with water (2 x 20 mL) and brine (2 x 20 mL). The organic layer was dried ($MgSO_4$) and the solvent was removed *in vacuo* to give **219** as a pale yellow oil (6.27 g, 34 mmol, 75%).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 6.82 (1H, s, Ar*H*), 6.74 (2H, s, 2 x Ar*H*), 5.91 (2H, s, OCH_2O), 4.44 (1H, t, *J* 6.2 Hz, C*H*OH), 2.51 (1H, br s, O*H*), 1.81 – 1.59 (2H, m, CH_2CH_3), 0.86 (3H, t, *J* 7.3 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.8 (*C* (Ar)), 146.9 (*C* (Ar)), 138.9 (*C* (Ar)), 119.5 (*C*H (Ar)), 108.1 (*C*H (Ar)), 106.6 (*C*H (Ar)), 101.2 (OCH_2O), 75.9 (*C*HOH), 31.9 (CH_2), 10.3 (CH_3) p.p.m.

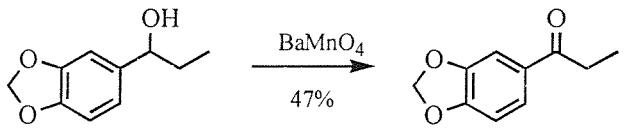
FT-IR ν_{max} (neat film) 3416br, 2969s, 1684m, 1609m, 1506s, 1437s, 1247s, 1039s, 976w, 812w cm^{-1}.

UV λ_{max} (MeOH) 286 (2800), 239 (2200) nm.

LRMS (APCI) 180 ($[M]^+$, 6%), 163 (100) amu.

These data were consistent with those reported in the literature.[65]

1-(Benzo[1,3]dioxol-5-yl)-propan-1-one 220[66]



219 $C_{10}H_{12}O_3$ 180

220 $C_{10}H_{10}O_3$ 178

Compound **219** (4.0 g, 22 mmol) was stirred in dry CH_2Cl_2 (30 mL) together with activated $BaMnO_4$ (38.2 g, 44mmol) for 16 h at ambient temperature. The reaction mixture was filtered through a plug of celite and the solvent removed *in vacuo*. The product was purified *via* column chromatography to give **220** as colourless crystals (1.85 g, 0.01M, 47%) which were recrystallised from petrol.

m.p. 33-34°C (petrol), lit[66] 36-37°C

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.36 (1H, dd, *J* 8.2, 1.6 Hz, Ar*H*), 7.23 (1H, d, *J* 1.6 Hz, Ar*H*), 6.64 (1H, d, *J* 8.2 Hz, Ar*H*), 5.85 (2H, s, OCH_2O), 2.74 (2H, q, *J* 7.3 Hz, CH_2), 1.03 (3H, t, *J* 7.3 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 198.6 (*C*=O), 151.5 (*C* (Ar)), 148.1 (*C* (Ar)), 131.7 (*C* (Ar)), 124.4 (*C*H (Ar)), 107.7 (*C*H (Ar)), 107.6 (*C*H (Ar)), 101.9 (OCH_2O), 31.4 (CH_2), 8.3 (CH_3) p.p.m.

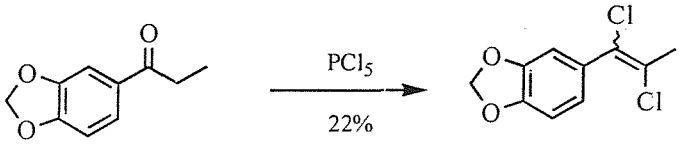
FT-IR ν_{max} (nujol) 1882w, 1749w, 1673s, 1604s, 1441s, 1216s, 1138m, 1043s, 972m, 827w cm^{-1}.

UV λ_{max} (MeOH) 307 (11000), 272 (10500), 233 (10500) nm.

LRMS (APCI) 179 ($[MH]^+$, 100%) 149 (28) amu.

These data were consistent with those reported in the literature.[66]

5-[-1,2-Dichloro-1-propenyl]-1,3-benzodioxole 221



220 $C_{10}H_{10}O_3$ 178

221 $C_{10}H_8Cl_2O_2$ 230

Prepared in accordance with the method of Engler.[64] Compound **220** (5.02 g, 28 mmol) was stirred in toluene (40 mL) at reflux together with PCl_5 (11.7 g, 56 mmol) for 8 h. The mixture was diluted with ether (40 mL) and washed with saturated sodium bicarbonate solution (2 x 20 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was purified *via* column chromatography to give a 1:1 mixture of *cis* and *trans* isomers of **221** as a colourless oil (1.48 g, 6.43 mmol, 22%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.97 (6H, m, 6 x Ar*H*), 6.04 (4H, s with fine splitting, OCH_2O), 2.43 (3H, s, CH_3), 2.19 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.9 (*C* (Ar)), 147.7 (*C* (Ar)), 147.5, (*C* (Ar)), 147.2 (*C* (Ar)), 130.8 (*C* (Ar)), 130.7 (*C* (Ar)), 128.8 (=*C*Cl), 126.4

(=CCl), 123.4 (*C*H (Ar)), 123.1 (*C*H (Ar)), 109.6 (*C*H (Ar)), 109.4 (*C*H (Ar)), 108.1 (*C*H (Ar)), 107.8 (*C*H (Ar)), 107.8 (=*C*Cl), 106.9 (=*C*Cl), 101.4 (OCH_2O), 101.3 (OCH_2O), 24.2 (CH_3), 23.9 (CH_3) p.p.m.

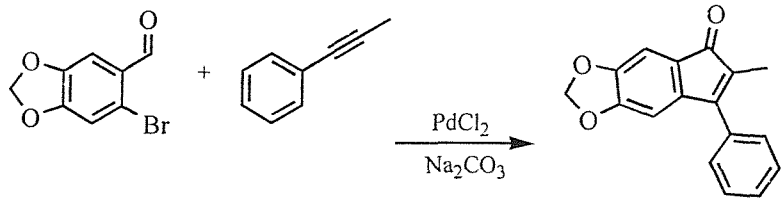
FT-IR ν_{max} (neat film) 2899m, 1838m, 1608m, 1503s, 1434s, 1341m, 1248s, 1099m, 1040s, 936s, 842w, 748m cm^{-1}.

UV λ_{max} (MeOH) 293 (4200), 258 (4300), 230 (3300) nm.

LRMS (APCI) 230 ($[M]^+$, 100%) 214 (23), 196 (37) amu.

HRMS (EI^+) Found 229.9898, $C_{10}H_8Cl_2O_2$ requires 229.9901 amu.

6-Methyl-7-phenyl-5*H*-indeno[5,6-d][1,3]-dioxol-5-one 231



204 $C_8H_5BrO_3$ 227

230 C_9H_8 116

231 $C_{17}H_{12}O_3$ 264

Prepared by a modified method of Larock.[20] Compound **204** (495 mg, 2.16 mmol), 1-phenylpropene **230** (500 mg, 4.32 mmol) and sodium hydrogen carbonate (724 mg , 8.63 mmol) were stirred in toluene (30 mL) together with triphenylphosphine (281 mg, 1.08 mmol) and palladium chloride (95 mg, 0.54 mmol). The mixture was heated at reflux for 48 h after which time it was diluted with water (40 mL) and extracted with ether (3 x 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by column chromatography (5% ether in petrol) to gave **231** as a red solid (615 mg, 2.33 mmol, 54 %).

m.p. 162-165°C (MeOH)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.42 (5H, m, 5 x Ar*H*), 7.08 (1H, s, Ar*H*), 6.59 (1H, s, Ar*H*), 6.02 (2H, s, OCH_2O), 2.37 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 195.2 (*C*=O), 152.9 (*C* (Ar)), 151.9 (*C* (Ar)), 147.7 (*C* (Ar)), 142.5 (*C* (Ar)), 132.5 (*C* (Ar)), 131.4 (*C*=CAr), 129.5 (2 x *C*H (Ar)), 128.9 (2 x *C*H (Ar)), 127.6 (*C*H (Ar)), 124.5 (*C*=CCH_3), 104.8 (*C*H (Ar)), 102.4(*C*H (Ar)), 102.1 (OCH_2O), 12.8 (CH_3) p.p.m.

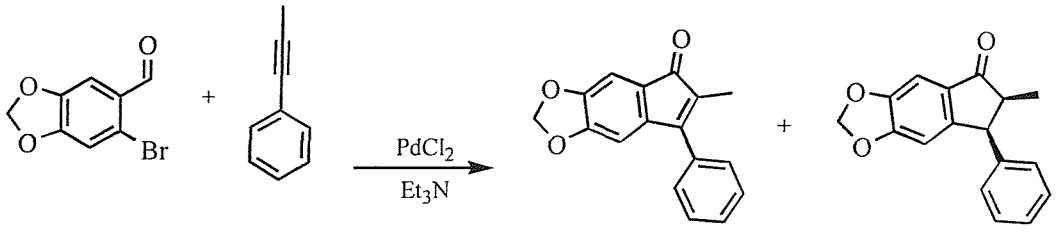
FT-IR ν_{max} (neat) 2903m, 2251w, 1709s, 1591s, 1448s, 1379m, 1261s, 1218m, 1871m, 852w cm^{-1}.

UV-vis λ_{max} (MeOH) 473 (378), 332 (7900), 296 (22700), 231 (9500), 214 (7600) nm.

LRMS (APCI) 265 ($[M]^+$, 100%), 249 (9), 215 (8), 157 (7) amu.

HRMS (EI) Found 264.0780, $C_{17}H_{12}O_3$ requires 264.0786 amu.

6-Methyl-7-phenyl-5*H*-indeno[5,6-d][1,3]-dioxol-5-one 231 and rel-(6*S*, 7*S*)-6-Methyl-7-phenyl-6,7-dihydro-5*H*-indeno-[5,6-d][1,3]dioxol-5-one 233



204 $C_8H_5BrO_3$ 229 | **230** C_9H_8 116 | **231** $C_{17}H_{12}O_3$ 264 | **233** $C_{17}H_{14}O_3$ 266

Prepared by a method modified from Larock.[20] 6-Bromopiperonal (495 mg, 2.16 mmol), 1-phenylpropyne (500 mg, 4.3 mmol), triethylamine (1.74 g 8.64 mmol) and palladium chloride (38 mg, 0.11 mmol) were stirred together under reflux in toluene

(30 mL) for 36 h. The mixture was cooled, diluted with ether (20 mL) and washed with sulfuric acid (30 mL of a 2M aqueous solution) and then brine (2 x 20 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. Components were separated by column chromatography (5% ether in petrol) to give **231** as a red solid (62 mg, 0.23 mmol, 11%), data as reported previously, then **233** as a cream solid (68 mg, 0.24mmol, 12%).

m.p. 185-187°C (petrol).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.38 (4H, m, 4 x Ar*H*), 7.23 (2H, m, 2 x Ar*H*), 6.62 (1H, s, Ar*H*), 6.14 (2H, s, OCH_2O), 3.93 (1H, d, *J* 4.4 Hz, ArC*H*), 2.64 (1H, qd, *J* 7.3, 4.4 Hz, C*H*CH_3), 1.37 (3H, d, *J* 7.3 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 205.9 (*C*=O), 154.5 (*C* (Ar)), 153.7 (*C* (Ar)), 148.8 (*C* (Ar)), 142.9 (*C* (Ar)), 131.0 (*C* (Ar)), 129.1 (2 x *C*H (Ar)), 128.0 (2 x *C*H (Ar)), 127.3 (*C*H (Ar)), 105.8 (*C*H (Ar)), 102.4 (*C*H (Ar)), 102.1 (OCH_2O), 53.9 (*C*HC=O), 53.8 (*C*HAr), 14.7 (CH_3) p.p.m.

FT-IR ν_{max} (neat) 2905m, 1791s, 1608m, 1471s, 1294s, 1265s, 1101w, 1035s, 939m, 871w, 815w, 701m cm^{-1}.

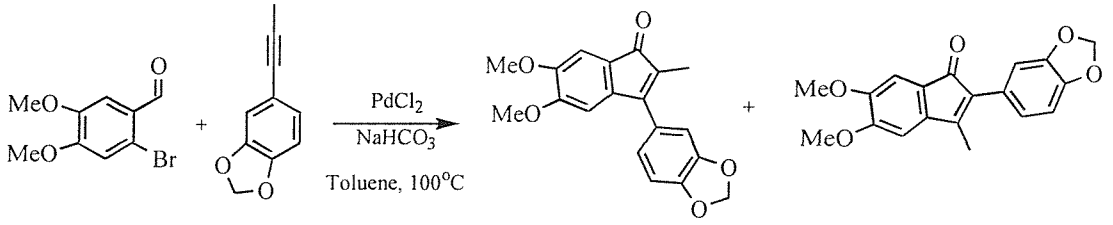
UV λ_{max} (MeOH) 317 (1800), 268 (1600), 234 (3300) nm.

LRMS (APCI) 267 ($[MH]^+$, 100%) amu

HRMS (EI^+) Found 266.0929, $C_{17}H_{14}O_3$ requires 266.0942 amu.

3-(1,3-Benzodioxol-5-yl)-5,6-dimethoxy-1*H*-indenone 216 and

2-(1,3-benzodioxol-5-yl)-3-methyl-5,6-dimethoxy-1*H*-1-indenone 217



223 $C_9H_9BrO_3$ 244

222 $C_{10}H_8O_2$ 160

216 $C_{19}H_{16}O_5$ 324

217 $C_{19}H_{16}O_5$ 324

Alkyne **222** (340 mg, 1.21mmol), 3,4-dimethoxy-6-bromobenzaldehyde (148 mg, 0.61 mmol) and sodium hydrogen carbonate (406 mg, 4.84 mmol) were stirred in toluene (30 mL) together with palladium chloride (53 mg, 0.30 mmol) and triphenylphosphine (155 mg, 0.61 mmol). The mixture was refluxed for 36 h then cooled, diluted with ether (30 mL) and washed with water (20 mL) and brine (20 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent was removed *in vacuo*. Separation by column chromotography gave firstly **216** (102 mg, 0.32 mmol, 52%) and then **217** (11 mg, 0.03 mmol, 6%) both as red solids.

Data for **216**

m.p. 214-215°C

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.01 (1H, s, Ar*H*), 6.95 – 6.79 (3H, m, 3 x Ar*H*), 6.65 (1H, s, Ar*H*), 6.09 (2H, s, OCH_2O), 3.88 (6H, s, 2 x OCH_3), 1.91 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 197.6 (*C*=O), 152.9 (*C* (Ar)), 152.4 (*C* (Ar)), 148.4 (*C* (Ar)), 148.3 (*C* (Ar)), 148.0 (*C* (Ar)), 140.2 (*C* (Ar)), 129.4 (*C* (Ar)), 126.7 (*C*=CAr), 123.6 (*C*=CCH_3), 122.1 (*C*H (Ar)), 108.7 (*C*H (Ar)), 108.2 (*C*H (Ar)), 107.6 (*C*H (Ar)), 105.6 (*C*H (Ar)), 101.4 (OCH_2O), 56.4 (2 x OCH_3), 8.7 (CH_3) p.p.m.

FT-IR ($CDCl_3$) ν_{max} 2914s, 1685m, 1579m, 1494m, 1460s, 1361m, 1245m, 1095w, 1016w, 927w cm^{-1}.

UV-vis ($CHCl_3$) λ_{max} 462 (600), 341 (7100), 273 (32000).

LRMS (APCI) 325 ($[MH]^+$,100%), 162 (10), 104 (25) amu.

HRMS (EI^+) Found 324.1006, $C_{19}H_{16}O_5$ requires 324.0997 amu.

Data for **217**

m.p. 187 - 189°C (ethanol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.12 (1H, s, Ar*H*), 6.92 – 6.87 (3H, m, 3 x Ar*H*), 6.75 (1H, s, Ar*H*), 5.99 (2H, s, OCH_2O), 3.96 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 2.19 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 196.3 (*C*=O), 153.1 (*C* (Ar)), 152.4 (*C* (Ar)), 149.0 (*C* (Ar)), 147.6 (*C* (Ar)), 147.1 (*C* (Ar)), 140.5 (*C* (Ar)), 132.0 (*C* (Ar)), 128.0 (*C*=CAr), 125.3 (*C*=CCH_3), 123.4 (*C*H (Ar)), 109.8 (*C*H (Ar)), 108.3 (*C*H (Ar)), 107.2 (*C*H (Ar)), 104.3 (*C*H (Ar)), 101.1 (OCH_2O), 56.5 (2 x OCH_3), 12.6 (CH_3) p.p.m.

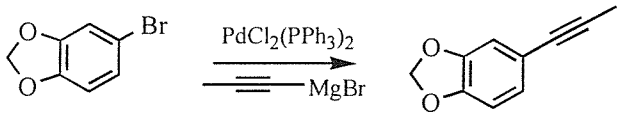
FT-IR ($CHCl_3$) ν_{max} 2912m, 1702m, 1586s, 1487s, 1344m, 1286s, 1040s 934m, 798m cm^{-1}.

UV-vis λ_{max} ($CHCl_3$) 488 (700), 314 (3100), 274 (20400) nm.

LRMS (APCI) 325 ($[MH]^+$, 100%), 324 $[M]^+$ (33) amu.

HRMS $(EI)^+$ Found 324.0987 $C_{19}H_{16}O_5$ requires 324.0997 amu.

5-(1-Propynyl)-1,3-benzodioxole 222[67]



242 **222**

$C_7H_5BrO_2$ 201 $C_{10}H_8O_2$ 160

Compound **242** (2 g, 9.9 mmol) was stirred in toluene (40 mL) together with $PdCl_2(PPh_3)_2$ (1.39 g, 1.98 mmol) and CuI (18 mg, 0.09mmol) and the mixture was heated to 60°C. Propynylmagnesium bromide was added *via* syringe and the mixture stirred at this temperature for 15 h. The mixture was diluted with ether (40 mL), washed with water (2 x 20 mL) and brine (2 x 20 mL). The organic layers were separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was purified by column chromotography (1% $CHCl_2$ in petrol) to give **222** as a clear oil (1.097 g, 6.85 mmol, 69%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.19 (2H, m, 2 x Ar*H*), 7.09 (1H, dd, *J* 8.4, 1.8 Hz, Ar*H*), 5.92 (2H, s, OCH_2O), 2.03 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.4 (2 x *C* (Ar)), 125.9 (*C*H (Ar)), 117.5 (*C* (Ar)) 111.7 (*C*H (Ar)), 108.5 (*C*H (Ar)), 101.3 (OCH_2O), 84.1 ($C{\equiv}CCH_3$), 79.1 ($C{\equiv}CCH_3$), 4.4 (CH_3) p.p.m.

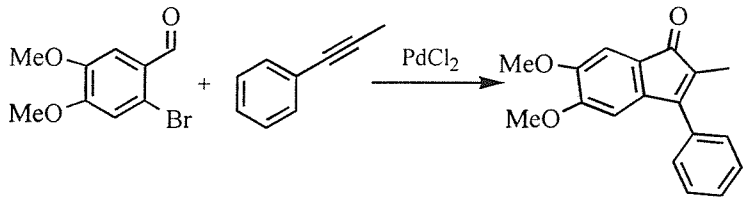
FT-IR λ_{max} (neat) 2916m, 2362m, 1654m, 1489s, 1329s, 1246s, 1213s, 1101m, 1039s, 936m, 808m cm^{-1}.

UV ($CHCl_3$) λ_{max} 299 (6600), 261 (11900) nm.

LRMS (APCI) 161 (100% $[M+H]^+$), 131 (14) amu.

These data are consistent with those published in the literature.[67]

5,6-Dimethoxy-2-methyl-3-phenyl-1*H*-1-indenone 234



223 **230** **234**

$C_9H_9BrO_3$ 245 C_9H_8 116 $C_{18}H_{16}O_3$ 280

Prepared by a modified method of Larock.[20] Alkyne **230** (100 mg, 0.86 mmol) was stirred in toluene (10 mL) together with 3,4-dimethoxy-6-bromobenzaldehyde **223** (104 mg, 0.43 mmol), $PdCl_2$ (15 mg, 0.043 mmol), triphenylphosphine (47 mg, 0.086 mmol) and sodium hydrogen carbonate (144 mg, 1.72 mmol). The mixture was heated with stirring at 100°C for 24h. The solution was diluted with ether (10 mL) then washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromotography (20% ether in petrol) gave **234** as a red solid (62 mg, 0.221 mmol, 52%) and a single regioisomer.

m.p. 187-189°C (ethanol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.47-7.32 (5H, m, 5 x Ar*H*), 7.19 (1H, s, Ar*H*), 6.76 (1H, s, Ar*H*), 3.99 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 2.29 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 153.8 (*C* (Ar)), 153.5 (*C* (Ar)), 148.9 (*C* (Ar)), 140.8 (*C* (Ar)), 132.8 (C=CCH_3), 131.8 (*C* (Ar)), 129.5 (2 x *C*H (Ar)), 128.4 (2 x *C*H (Ar)), 127.5 (*C*H (Ar)), 122.5 (C=CCH_3), 107.1 (*C*H (Ar)), 104.3 (*C*H (Ar)), 56.5 (2 x OCH_3), 12.7 (CH_3) p.p.m. A peak corresponding to the carbonyl carbon was not observed in this spectra.

FT-IR ν_{max} ($CHCl_3$) 2838w, 1703s, 1589s, 1490s, 1415w, 1380w, 1292m, 1122w, 1030m, 877w cm^{-1}.

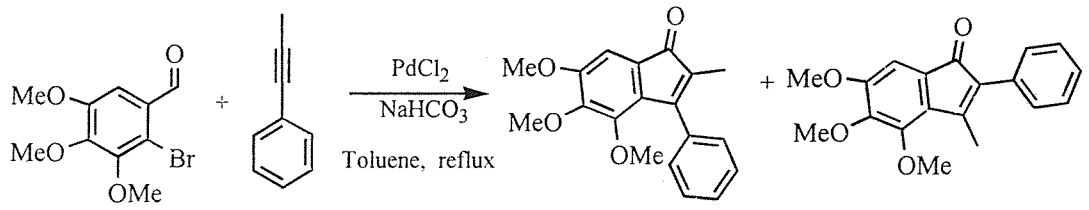
UV-vis λ_{max} ($CHCl_3$) 464 (924), 300 (44000), 275 (19000) nm.

LRMS (APCI) 281 ($[MH]^+$, 100%), 280 ($[M]^+$,19%) amu.

HRMS (EI^+) Found 280.1111, $C_{18}H_{16}O_3$ requires 280.1010 amu.

2-Methyl-4,5,6-tri(methyloxy)-3-phenyl-1*H*-indenone 240

3-Methyl-4,5,6-tri(methyloxy)-2-phenyl-1*H*-indenone 241



239 $C_{10}H_{11}IO_4$ 321

230 C_9H_8 116

240 $C_{19}H_{18}O_4$ 310

241 $C_{19}H_{18}O_4$ 310

Prepared by a modification of a method described by Larock.[20] Compound **239** (404 mg, 1.25 mmol), compound **230** (291 mg, 2.5 mmol), sodium hydrogen carbonate (840 mg, 5 mmol), triphenylphosphine (131 mg, 0.25 mmol) and palladium chloride (44 mg, 0.12 mmol) were stirred together at reflux in toluene (30 mL) for 48 h. The reaction mixture was diluted with ether (30 mL) and washed with water (2 x 20 mL) and brine (2 x 20 mL). The organic layer was separated, dried ($MgSO_4$) and concentrated *in vacuo*. Components were separated by column chromotography (5% ether in petrol) to give **240** and **241** a red solid (147 mg, 0.47 mmol, 38%) comprising an inseparable 1:1 mixture of **240** and **241**.

m.p. 154-157°C (MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.41 (10H, m, 10 x Ar*H*), 7.06 (2H, s, Ar*H*), 7.05 (2H, s, Ar*H*), 3.86-3.92 (15H, m, 5 x OCH_3), 3.38 (3H, s, OCH_3), 2.48 (3H, s, CH_3), 1.79 (3H, s, CH_3) p.p.m.

^{13}C NMR (75 MHz, $CDCl_3$) δ_C 197.3 (*C*=O), 195.6 (*C*=O), 156.2 (*C* (Ar)), 155.6 (*C* (Ar)), 154.4 (*C* (Ar)), 153.7 (*C* (Ar)), 149.3 (*C* (Ar)), 148.6 (*C* (Ar)), 147.5 (*C* (Ar)), 147.0 (*C* (Ar)), 135.5 (*C* (Ar)), 135.4 (*C*H (Ar)), 134.1 (*C* (Ar)), 132.7 (*C* (Ar)), 131.2 (*C* (Ar)), 131.4 (*C* (Ar)), 130.9 (*C* (Ar)), 130.7 (*C* (Ar)), 130.4 (*C*H (Ar)), 129.7 (*C*H (Ar)), 128.9 (*C* (Ar)), 128.7 (*C*H (Ar)), 128.4 (2 x *C*H (Ar)), 128.2 (2 x *C*H (Ar)), 127.9 (*C*H (Ar)), 127.6 (*C*H (Ar)), 104.9 (*C*HAr), 104.3 (*C*HAr), 61.5 (O*C*H_3), 61.3 (O*C*H_3), 61.2 (O*C*H_3), 61.1 (O*C*H_3), 56.6 (2 x O*C*H_3), 15.5 (*C*H_3), 8.6 (*C*H_3) p.p.m.

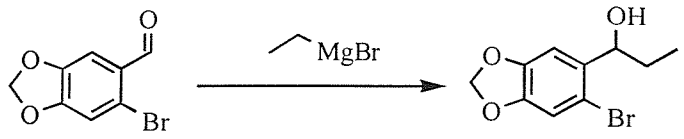
FT-IR ν_{max} (nujol) 2361s, 1682m, 1471s, 1372s, 1321s, 1158w, 1101m cm^{-1}.

UV-Vis λ_{max} (MeOH) 447 (700), 340 (7200), 325 (7800), 271 (32300), 265 (29250), 223 inf. (17400) nm.

LRMS (APCI) 311 ($[M+H]^+$, 100%), 279 (13), 263 (31) amu.

HRMS (EI^+) Found 310.1211, $C_{19}H_{18}O_4$ requires 310.1205 amu.

6-Bromo-1-(Benzo[1,3]dioxol-5-yl)-propan-1-ol 211



204 **211**

$C_8H_5BrO_3$ 228 $C_{10}H_{11}BrO_3$ 258

Aldehyde **204** (10 g, 43 mmol) was cooled in THF (100 mL) to 0°C. Ethylmagnesium bromide (14.3 mL of a 3M solution in ether) was added *via* syringe over 5 min and the solution stirred for 1 h. The reaction was diluted with water (20 mL), and extracted into ether (3 x 30 mL). The organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to give **211** (10.914 g, 42 mmol, 98%) as a colourless solid.

m.p. 92 - 93°C (methanol)

^{1}H NMR (300MHz, $CDCl_3$) δ_H 7.11 (1H, s, Ar*H*), 6.92 (1H, s, Ar*H*), 5.95 (2H, s, OCH_2O), 4.92 (1H, t, *J* 7.3 Hz, OC*H*), 2.24 (1H, br s, O*H*), 1.78 – 1.70 (2H, m, CH_2), 0.98 (3H, t, *J* 7.7 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.6 (*C* (Ar)), 147.3 (*C* (Ar)), 137.0 (*C* (Ar)), 112.3 (*C* (Ar)), 112.3 (*C*H (Ar)), 107.2 (*C*H (Ar)), 101.6 (O*C*H_2), 74.0 (O*C*H), 30.7 (*C*H_2), 10.2 (*C*H_3) p.p.m.

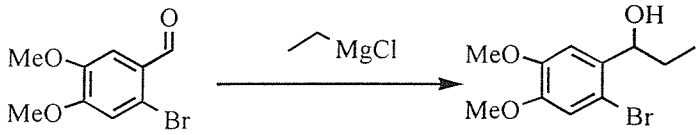
FT-IR ν_{max} (nujol) 2919s, 1503s, 1375s, 1239s, 1312m, 1282m, 1157m, 1041s, 980s, 839s, 721m cm^{-1}.

UV λ_{max} ($CHCl_3$) 289 (1400), 256 (1500) nm.

LRMS (APCI) 260 ([M]$^+$, ^{81}Br, 96%), 258 ([M]$^+$, ^{79}Br, 94%), 243 (100), 241 (98) amu.

CHN Found C 46.32 H 4.21, $C_{10}H_{11}BrO_3$ requires C 46.36 H 4.28.

1-[2-Bromo-4,5-dimethoxyphenyl]-propan-1-ol 224



223 **224**

$C_9H_9BrO_3$ 244 $C_{11}H_{15}BrO_3$ 274

Aldehyde **223** (2.0 g, 8.1 mmol) was stirred in THF (50 mL) at 0°C. Ethylmagnesium chloride (5.83 mL of a 1.4M solution in hexane) was added *via* syringe over 2 min. The mixture was stirred at ambient temperature for 1 h. The solution was diluted with water (20 mL) and extracted with ether (3 x 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting oil was purified by column chromotography to give **224** as a colourless oil (1.92 g, 7 mmol, 86%).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 7.19 (1H, s, Ar*H*), 6.92 (1H, s, Ar*H*), 4.89 (1H, t, *J* 7.2 Hz, OC*H*), 3.88 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 2.18 (1H, brs, O*H*), 1.72 – 1.74 (2H, m, CH_2), 0.98 (3H, t, *J* 7.4 Hz, CH_3) p.p.m.

^{13}C NMR (300MHz, $CDCl_3$) δ_C 148.6 (*C* (Ar)), 148.5 (*C* (Ar)), 135.6 (*C* (Ar)), 115.1 (*C*H (Ar)), 111.7 (*C* (Ar)), 109.7 (*C*H (Ar)), 73.9 (O*C*H), 56.1 (OCH_3), 55.9 (OCH_3), 30.7 (CH_2), 10.1 (CH_3) p.p.m.

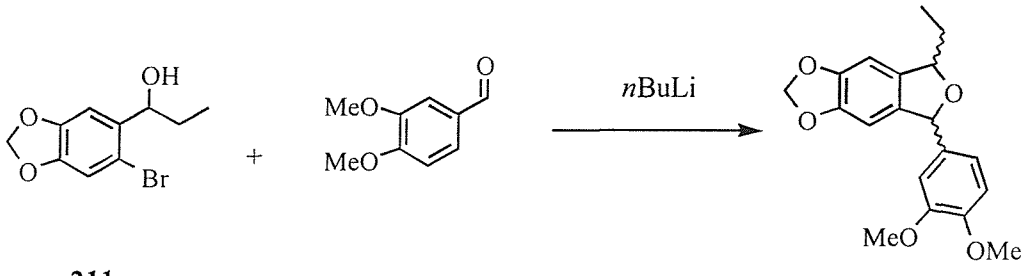
FT-IR (neat) ν_{max} 2969w, 2916w, 1605m, 1499s, 1456w, 1378m, 1257s, 1246s, 967w, 870w, 793m cm^{-1}.

UV λ_{max} (MeOH) 396 (1000), 242 (3500), 224 (3900) nm.

LRMS (CI) 274 ($[M]^+$, 7%), 258 (44), 178 (100) amu.

HRMS (EI) Found 274.0203 $C_{11}H_{15}O_3{}^{79}Br$ requires 274.0205 amu.

5-(3,4-Dimethoxyphenyl)-7-ethyl-(-5,7-dihydro[1,3]-dioxolo[4,5-f]isobenzofuran 214



211 **206** **214**

$C_{10}H_{11}BrO_3$ 258 $C_9H_{10}O_3$ 166 $C_{19}H_{20}O_5$ 328

Alcohol **211** (2.0 g, 7.7 mmol) was stirred in THF (50 mL) under N_2 at -78°C. *n*-butyllithium (7.7 ml of a 1.5 M solution) was added *via* syringe over 2 min. The mixture was allowed to stir for 1h after which time aldehyde **206** (1.27 g, 7.7 mmol) was added as a solution in THF (10 mL) *via* syringe over 1 min. The mixture was allowed to warm to ambient temperature, stirred for 30 min then diluted with water (20 mL) and extracted into ether (3 x 30 mL). The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (40% ether in petrol) to give **214** as an unstable oil and an inseparable 1:1 mixture of diastereoisomers (989 mg, 2.6 mmol, 62%).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 7.14 (1H, s, Ar*H*), 6.79 (2H, s, 2 x Ar*H*), 6.75 – 6.59 (6H, m, 6 x Ar*H*), 6.52 (1H, s, Ar*H*), 6.49 (1H, s, OC*H*Ar), 6.23 (1H, s, OC*H*Ar), 5.80 (2H, s, OCH_2O), 5.72 (2H, s, OCH_2O), 5.03 – 4.97 (1H, m, $OCHCH_2$), 4.72 – 4.63 (1H, m, $OCHCH_2$), 3.73 (6H, s, 2 x OCH_3), 3.67 (6H, s, 2 x OCH_3), 1.93 – 1.78 (1H, m, C*H*H), 1.77 – 1.46 (2H, m, 2 x CH*H*), 1.44 – 1.41 (1H, m, C*H*H), 0.92 (3H, t, *J* 6.8 Hz, CH_3), 0.71 (3H, t, *J* 6.8 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 149.1 (2 x *C* (Ar)), 147.9 (2 x *C* (Ar)), 147.7 (2 x *C* (Ar)), 136.1 (2 x *C* (Ar)), 135.3 (2 x *C* (Ar)), 134.8 (2 x *C* (Ar)), 120.2 (2 x *C*H (Ar)), 110.9 (2 x *C*H (Ar)), 110.8 (2 x *C*H (Ar)), 100.9 (2 x *C* (Ar)), 102.9 (2 x *C*H (Ar)), 101.6 (2 x O*C*H$_2$O + 2 x *C*H (Ar)), 85.1 (2 x O*C*HAr), 83.9 (2 x O*C*HCH$_2$), 56.1 (2 x O*C*H$_3$), 55.9 (2 x O*C*H$_3$), 28.9 (2 x *C*H$_2$), 9.5 (2 x *C*H$_3$) p.p.m.

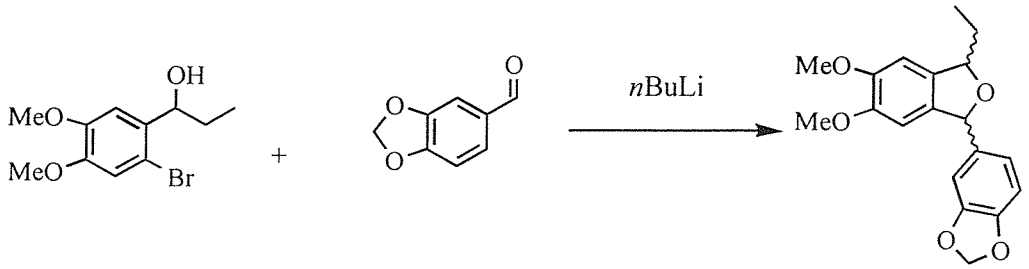
FT-IR ν_{max} (neat) 2955w, 2929w, 2858w, 1588w, 1521m, 1434m, 1255s, 1029s, 927m, 860w, 756w cm^{-1}.

UV λ_{max} (CH_2Cl_2) 277 (5600), 224 (9400) nm.

LRMS (CI) 328 ([M]$^+$, 29%), 299 (100) amu.

HRMS Found 328.1309, $C_{19}H_{20}O_5$ requires 328.1311 amu.

5-(3-Ethyl-5,6-dimethoxy-1,3-dihydro-2-benzofuran-1-yl)-1,3-benzodioxole 228



224 **226** **228**

$C_{11}H_{15}BrO_3$ 274 $C_8H_6O_3$ 150 $C_{19}H_{20}O_5$ 328

Alcohol **224** (1.09 g, 3.9 mmol) was stirred in THF (50 mL) under N_2 at -78°C. *n*-Butyllithium (7.8 ml of a 1.5 M solution) was added *via* syringe over 2 min. The mixture was allowed to stir for 1h after which time aldehyde **226** (630 mg, 3.9 mmol) was added as a solution in THF (10 mL) *via* syringe over 1 min. The mixture was allowed to warm to ambient temperature and stirred for 30 min. The mixture was diluted with water (20 mL), extracted into ether (3 x 30 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The product was purified by column chromatography (40% ether in petrol) to give **228** as an unstable oil and an inseparable mixture of diastereoisomers (691 mg, 2.1 mmol, 54%).

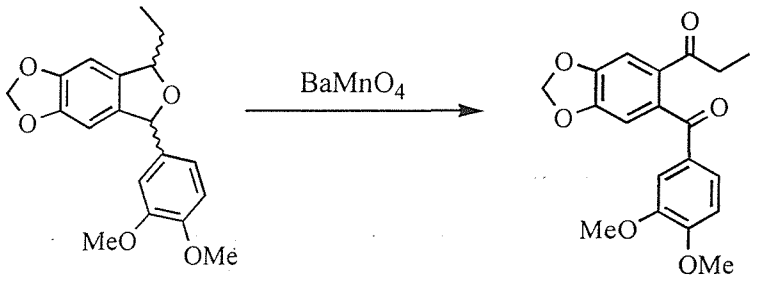
^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.93 (2H, s, 2 x Ar*H*), 6.91 – 6.72 (7H, m, 7 x Ar*H*), 6.69 (1H, s, Ar*H*), 6.61 (1H, s, OC*H*Ar), 6.37 (1H, s, OC*H*Ar), 5.93 (2H, s, OCH_2O), 5.90 (2H, s, OCH_2O), 5.18 – 5.11 (1H, m, OC*H*CH_2), 4.86 – 4.77 (1H, m, OC*H*CH_2), 3.88 (6H, s, 2 x OCH_3), 3.81 (6H, s, 2 x OCH_3), 2.08 – 1.95 (1H, m, C*H*H), 1.89 – 1.62 (2H, m, 2 x CH*H*), 1.62 – 1.46 (1H, m, CH*H*), 1.06 (3H, t, *J* 7.3 Hz, CH_3), 0.87 (3H, t, *J* 7.3 Hz, CH_3) p.p.m.

FT-IR ν_{max} (neat) 2939w, 2847w, 1598w, 1490s, 1244m, 1224s, 1101w, 1045s, 927w, 753s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 294 (5600), 241 (7900) nm.

LRMS (EI) 328 ($[M]^+$, 27%), 299 (100) amu.

1-(6-{[3,4-Dimethoxyphenyl]carbonyl}-1,3-benzodioxol-5-yl)-1-propanone 215



214 **215**

$C_{19}H_{20}O_5$ 328 $C_{19}H_{18}O_6$ 342

THF **214** (420 mg, 1.2 mmol) was stirred in DCM (30 mL) together with barium manganate (1.64 g, 6.4 mmol) at ambient temperature for 18 h. The heterogeneous mixture was then filtered through a plug of celite, and the residual solids washed with $CHCl_3$ (150 mL). The combined filtrate and washings were then concentrated *in vacuo* to give **215** a yellow solid which was recrystallised from $CHCl_3$ (321 mg, 0.92 mmol, 76%).

m.p. 126-128 °C ($CHCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.58 (1H, s with fine splitting, Ar*H*), 7.28 (1H, s with fine splitting, Ar*H*), 7.11 (1H, d with fine splitting, *J* 6.9 Hz, Ar*H*), 6.85 (1H, s, Ar*H*), 6.79 (1H, d, *J* 6.9 Hz, Ar*H*), 6.15 (2H, s, OCH_2O), 3.97 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 2.84 (2H, q, *J* 7.2 Hz, CH_2), 1.07 (3H, t, *J* 7.2 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 200.1 (*C*=O), 195.8 (*C*=O), 153.4 (*C* (Ar)), 150.4 (*C* (Ar)), 149.3 (*C* (Ar)), 148.5 (*C* (Ar)), 137.0 (*C* (Ar)), 132.4 (*C* (Ar)), 130.4 (*C* (Ar)), 124.9 (*C*H (Ar)), 110.7 (*C*H (Ar)), 109.9 (*C*H (Ar)), 108.8 (*C*H (Ar)), 108.6 (*C*H (Ar)), 102.6 (OCH_2), 56.2 (OCH_3), 56.1 (OCH_3), 33.2 (CH_2), 8.3 (CH_3) p.p.m.

FT-IR ν_{max} (neat) 2943w, 1680s, 1643s, 1499s, 1441m, 1375s, 1255s, 1177s, 1029s, 979w, 930m, 806m cm^{-1}.

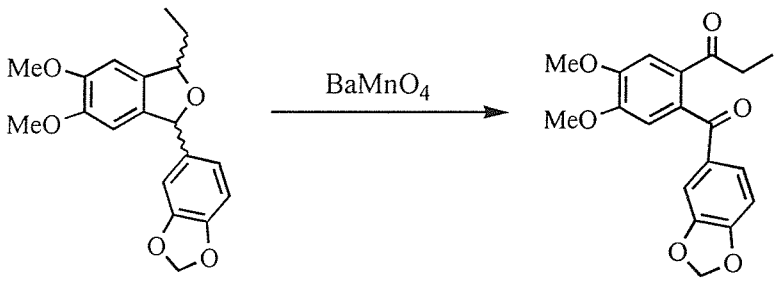
UV λ_{max} (CH_2Cl_2) 296 (1100), 262 (1200), 218 (2900) nm.

LRMS (CI) 343 ($[M+H]^+$, 2%), 324 (100) amu.

HRMS Found 342.1102, $C_{19}H_{18}O_6$ requires 342.1103 amu.

CHN Found C 66.53 H 5.25, $C_{19}H_{18}O_6$ requires C 66.66 H 5.29.

1-[2-(1,3-Benzodioxol-5-ylcarbonyl)-4,5-dimethoxyphenyl-1-propanone 229



228 **229**

$C_{19}H_{20}O_5$ 328 $C_{19}H_{18}O_6$ 342

THF **228** (810 mg, 2.36 mmol) was stirred in DCM (30 mL) together with barium manganate (2.64 g, 10 mmol) at ambient temperature for 18 h. The heterogeneous mixture was then filtered through a plug of celite, and the residual solids washed with $CHCl_3$ (150 mL). The combined filtrate and washings were then concentrated *in vacuo* to give **229** as a yellow solid which was recrystallised from $CHCl_3$ (470 mg, 1.37 mmol, 58%).

m.p. 165-168°C (ethanol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.21 (1H, s, Ar*H*), 7.15 (1H, s, Ar*H*), 7.12 (1H, d, *J* 7.1 Hz, Ar*H*), 6.91 (1H, s, Ar*H*), 6.68 (1H, d, *J* 7.1 Hz, Ar*H*), 5.98 (2H, s, OCH_2O), 3.93 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 2.78 (2H, q, *J* 7.7 Hz, CH_2), 0.99 (3H, t, *J* 7.7 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 200.5 (*C*=O), 196.1 (*C*=O), 152.1 (2 x *C* (Ar)), 149.7 (*C* (Ar)), 148.6 (*C* (Ar)), 135.2 (*C* (Ar)), 132.7 (*C* (Ar)), 130.8 (*C* (Ar)), 126.4 (*C*H (Ar)), 111.7 (*C*H (Ar)), 111.3 (*C*H (Ar)), 109.2 (*C*H (Ar)), 108.2 (*C*H (Ar)), 102.3 (OCH_2), 56.7 (OCH_3), 56.6 (OCH_3), 33.5 (CH_2), 8.6 (CH_3) p.p.m.

FT-IR ν_{max} (neat) 2914w, 1676m, 1647m, 1590w, 1565w, 1363m, 1288s, 1198m, 1132w, 1020m, 872m, 814m cm^{-1}.

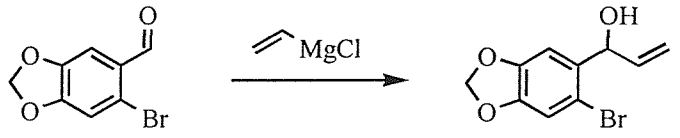
UV λ_{max} (CH_2Cl_2) 296 (1400), 262 (1200), 218 (2900) nm.

LRMS (CI) 342 ($[M]^+$, 6%), 324 (100) amu.

HRMS Found 342 1104, $C_{19}H_{18}O_6$ requires 342.1103 amu.

CHN Found C 66.57 H 5.32, $C_{19}H_{18}O_6$ requires C 66.66 H 5.32.

1-(6-Bromo-1,3-benzodioxol-5-yl)-2-propen-1-ol 327



204 **327**

$C_8H_5O_3Br$ 229 $C_{10}H_9O_3Br$ 257

A THF solution (30 mL) of 6-bromopiperonal **204** (15.0 g, 0.065 mol) was stirred under N_2 at 0°C and vinylmagnesium chloride (37.7 mL of a 1.7M solution in THF) was slowly added *via* syringe. The solution was warmed to ambient temperature and it was stirred for a further 1 h. The reaction was then diluted with water (30 mL), extracted with ether (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was recrystallised from ethanol to give **327** as a white solid (11.8 g, 0.045 mol, 70%).

m.p. 65-67°C (ethanol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.03 (1H, s, Ar*H*), 6.99 (1H, s, Ar*H*), 6.00 (2H, s, OC*H*$_2$O), 5.99 (1H, obs ddd, *J* 17.2, 8.4, 5.1 Hz, C*H*CH$_2$), 5.55 (1H, dd with fine splitting, *J* 5.1, 3.3 Hz, *H*COH), 5.41 (1H, d, *J* 17.2 Hz, CHCH*H*), 5.23 (1H, d, *J* 10.0 Hz, CHC*H*H), 2.08 (1H, d, *J* 3.3 Hz, O*H*) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.9 (2 x *C* (Ar)), 138.5 (=*C*HCHOH), 135.0 (*C* (Ar)), 115.5 (CH=*C*H$_2$), 113.0 (*C*Br (Ar)), 112.6 (*C*H (Ar)), 107.9 (*C*H (Ar)), 101.9 (O*C*H$_2$O), 73.4 (*C*HOH) p.p.m.

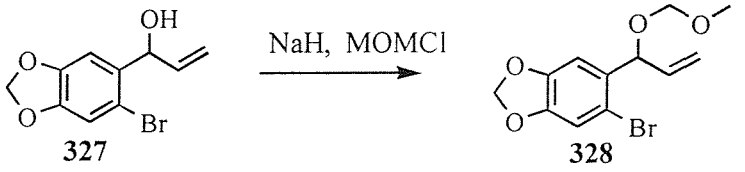
FT-IR ν_{max} (nujol) 3208brs, 2916m, 1692w, 1503m, 1468s 1305w, 1241s, 1039s, 922m, 862w cm^{-1}.

UV λ_{max} (MeOH) 293 (20000), 241 (23000), 219 inf (19000) nm

LRMS (APCI) 258 ([MH(^{81}Br)]$^+$, 100%) 256 (MH(^{79}Br), 87) 240 (57), 160 (82), 150 (9), 134 (8) amu.

HRMS (CI) Found [M]$^+$ 255.9735, $C_{10}H_9O_3Br$ requires 255.9735 amu.

5-Bromo-6(1-{[(methyloxy)methyl]oxy}-2-propenyl)-1,3-benzodioxole 338



327 **328**

$C_{10}H_9O_3Br$ 257 $C_{12}H_{13}O_4Br$ 301

Prepared by a method analogous to that of Winkle.[68] NaH (144 mg of a 60% dispersion in mineral oil, 6.03 mmol) under a N_2 atmosphere was washed with petrol (3 x 10 mL). Dry ether (25 mL) and DMF (5 mL) were added followed, after 15 min, by a solution of **327** (1.55 g, 6.03 mmol) in ether (5 mL). The reaction mixture was then allowed to stir overnight. The solution was diluted with water (20 mL), extracted into ether (3 x 20 mL), the organic layer dried ($MgSO_4$) and solvent removed *in vacuo*. The product was isolated by column chromatography (15% ether in petrol) to give **328** as a clear oil (1.21 g, 4.01 mmol, 67%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.95 (2H, s, 2 x Ar*H*), 6.01 – 5.96 (2H m, OCH_2O), 5.86 (1H, ddd, *J* 16.5, 10.3, 6.0 Hz, $CHCH_2$), 5.48 (1H, d, *J* 6.0 Hz, $CHOCH_2$), 5.35 (1H, app. d, *J* 16.5 Hz, =C*H*H), 5.23 (1H, app. d *J* 10.3 Hz, =CH*H*), 4.70 (1H, d, *J* 6.6 Hz, OC*H*HOMe), 4.61 (1H, d, *J* 6.6 Hz, OCH*H*OMe), 3.41 (3H, s, OCH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.9 (2 x *C* (Ar)), 136.9 (*C*H=CH_2), 133.3 (*C* (Ar)), 116.6 (=*C*H_2), 113.3 (*C* (Ar)), 112.5 (*C*H (Ar)), 108.2 (*C*H (Ar)), 101.9 (Ar*C*H_2O), 94.1 (O*C*H_2OMe), 76.7 (*C*HOH), 55.8 (O*C*H_3) p.p.m.

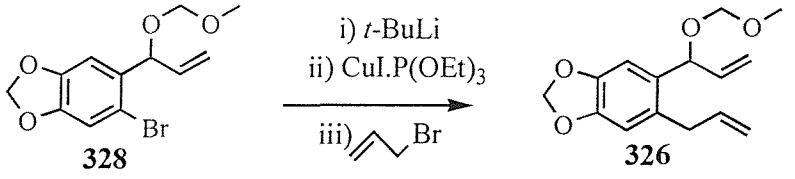
FT-IR ν_{max} (neat) 3082w, 2890m, 2360w, 1607w, 1502s, 1476s, 1237s, 1150s, 1034s, 980m, 859w cm^{-1}.

UV λ_{max} (MeOH) 294 (20100), 241 (22000), 217 inf. (21000) nm.

LRMS (EI) 303 ([MH(^{81}Br)]$^+$, 5%), 302 ([M(^{81}Br)]$^+$, 35%), 301 ([MH(^{79}Br)]$^+$, 37%), 300 ([M(^{79}Br)]$^+$, 27%), 270 (25), 255 (30), 241 (15), 229 (17), 215 (6), 160 (100), 148 (45) amu.

HRMS (CI) Found [M]$^+$ 299.9997, $C_{12}H_{13}O_4Br$ requires 299.9997 amu.

5-(1-[{(Methyloxy)methyl]oxy}-2-propenyl)-6-(2-propenyl)-1,3-benzodioxole 326



328 $C_{12}H_{10}O_4Br$ 301

326 $C_{15}H_{18}O_4$ 262

A solution of **328** (932 mg, 3.1 mmol) in THF (30 mL) was stirred under N_2 at -78°C. *t*-BuLi (3.48 mL, 0.89 M solution in pentane) was slowly added to produce a red solution which was stirred for 10 min. A THF (10 mL) solution of $CuI.P(OEt)_3$ was then added over 10 min giving rise to a pale yellow solution. After 1 h allyl bromide (0.268 mL, 3.1 mmol) was added, neat over 5 min producing a dark green solution which was then warmed to ambient temperature. The mixture was diluted with water (20 mL) and washed with ammonia solution

until the washings were no longer blue (5 x 20 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was purified by column chromatography (10% ether in petrol) to give **326** as a colourless oil (700 mg, 2.67 mmol, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.94 (1H, s, Ar*H*), 6.65 (1H, s, Ar*H*), 6.00 (4H, m, 2 x CH_2=C*H* & ArOC*H*$_2$O), 5.29 (1H, m, C*H*OCH_2), 5.24 (1H, brd with fine splitting, *J* 16.0 Hz, CH=CH*H*), 5.19 (1H, brd with fine splitting, *J* 11.4 Hz, CH=C*H*H), 5.07 (1H, d with fine splitting, *J* 11.4 Hz, CH=C*H*H), 5.00 (1H, d with fine splitting, *J* 16.0 Hz, CH=CH*H*), 4.67 (1H, d, *J* 6.6 Hz, OC*H*HO) 4.56 (1H, d, *J* 6.6 Hz, OCH*H*O), 3.39 (5H, app. s, OC*H*$_3$ & Ar C*H*$_2$) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) 147.2 (*C* (Ar)), 146.6 (*C* (Ar)), 138.1 (*C*H=CH_2), 137.2 (*C*H=CH_2), 131.9 (*C* (Ar)), 131.2 (*C* (Ar)), 116.3 (CH=*C*H$_2$), 116.1 (CH=*C*H$_2$), 109.7 (*C*H (Ar)), 107.6, (*C*H (Ar)), 101.1 (ArO*C*H$_2$O), 93.6 (O*C*H$_2$OMe), 74.0 (Ar*C*H), 55.6 (Ar*C*H$_2$), 36.6 (O*C*H$_3$) p.p.m.

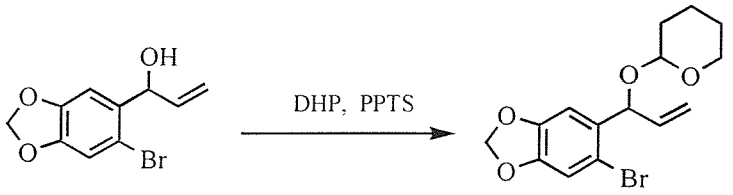
FT-IR ν_{max} (neat) 2891s, 2316w, 1501s, 1407m, 1236s, 1150s, 1033s, 934m, 869m cm^{-1}.

UV λ_{max} (MeOH) 290 (24000), 242 (28300), 220 inf. (23000) nm.

LRMS (APCI) 262 ($[M]^+$, 100%) amu.

HRMS (CI) Found $[M]^+$ 262.1205, $C_{15}H_{18}O_4$ requires 262.1205 amu.

1-(6-Bromo-1,3-benzodioxol-5-yl)allyl tetrahydro-2*H*-pyran-2-yl ether 337



327 **337**

$C_{10}H_9O_3Br$ 257 $C_{15}H_{17}BrO_4$ 340

A solution of **327** (6.0 g, 23 mmol) was stirred in dry chloroform (40 mL) together with 3,4-dihydro-2*H*-pyran (3.36 g, 39 mmol) and pyridinium *para*-toluenesulfonate (1.0 g, 3 mmol) under a nitrogen atmosphere for 18 h. The mixture was diluted with ether (40 mL), washed with brine (3 x 20 mL), the organic layer dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by column chromatography (5% ether in petrol) gave **337** as a clear oil and a 1:1 mixture of diastereoisomers (5.65 g, 16 mmol, 72%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.09 (1H, s, Ar*H*), 6.99 (2H, s, 2 x Ar*H*), 6.97 (1H, s, Ar*H*), 5.95 (4H, s, 2 x ArOC*H*$_2$O), 5.96 (1H, obs. ddd, *J* 17.0, 10.3, 5.1 Hz, C*H*=CH$_2$), 5.73 (1H, ddd, *J* 17.3, 10.1, 6.9 Hz, C*H*=CH$_2$) 5.60 (1H, app. d, *J* 5.1 Hz, ArC*H*O), 5.45 (1H, app. d, *J* 6.9 Hz, ArC*H*O), 5.38 (1H, d with fine splitting, *J* 17.1 Hz, =C*H*H), 5.30 (1H, d with fine splitting, *J* 17.1 Hz, =C*H*H), 5.21 (1H, d with fine splitting, *J* 10.3 Hz, =CH*H*), 5.15 (1H, d with fine splitting, *J* 10.3 Hz, =CH*H*), 4.86 (1H, t, *J* 2.7 Hz, OC*H*O), 4.50 (1H, t, *J* 3.2 Hz, OC*H*O), 3.95 (1H, ddd, *J* 12.6, 7.8, 3.2 Hz, OC*H*H), 3.72 (1H, ddd, *J* 11.4, 8.8, 2.7 Hz, OC*H*H), 3.59-3.43 (2H, m, 2 x OCH*H*), 1.95-1.41 (12H, m, 2 x C*H*$_2$C*H*$_2$C*H*$_2$) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 147.9 (*C* (Ar)), 147.9 (*C* (Ar)), 147.8 (*C* (Ar)), 147.6 (*C* (Ar)), 137.6 (*C*H=CH_2), 136.7 (*C*H=CH_2), 134.3 (*C* (Ar)), 133.5 (*C* (Ar)), 117.0 (=*C*H_2), 115.5 (=*C*H_2), 113.9 (*C*Br (Ar)), 112.6 (*C*Br (Ar)), 112.4 (*C*H (Ar)), 112.3 (*C*H (Ar)), 108.2 (*C*H (Ar)), 108.1 (*C*H (Ar)), 101.9 (Ar*C*H_2O), 101.8 (Ar*C*H_2O), 95.8 (Ar*C*H), 95.6 (Ar*C*H), 76.4 (O*C*HO), 75.9 (O*C*HO) 62.5 (CH_2*C*H_2O), 62.0 (CH_2*C*H_2O), 30.7 (*C*$H_2$$CH_2$O), 30.5 (*C*$H_2$$CH_2$O), 25.6 (2 x *C*$H_2$$CH_2$O), 19.5 ($CH_2$*C*$H_2$$CH_2$), 19.2 ($CH_2$*C*$H_2$$CH_2$) p.p.m.

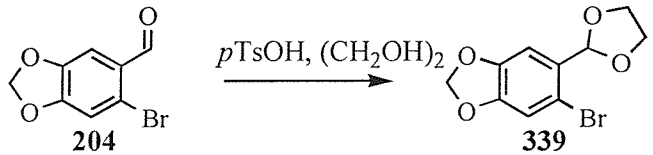
FT-IR ν_{max} (neat) 3426 br, 2941s, 1724w, 1502s, 1476s, 1409m, 1286s, 1037s, 967m, 933m cm^{-1}.

UV λ_{max} (MeOH) 293 (16100), 242 (17200), 223 inf. (12700) nm.

LRMS (APCI) 342 ([M(^{81}Br)]$^+$, 100%) 340 ([M(^{79}Br)]$^+$, 81%) amu.

HRMS (CI) Found $[M]^+$ 340.0310, $C_{15}H_{17}O_4Br^{79}$ requires 340.0310 amu.

5-Bromo-6-(1,3-dioxolan-2-yl)1,3-benzodioxole[69] 339



204 $C_8H_5O_3Br$ 229

339 $C_{10}H_9O_4Br$ 273

A solution of 6-Bromopiperonal **204** (6.90 g, 0.03 mol), *p*-toluenesulfonic acid (0.573 g, 0.003 mol) and 1,2-ethanediol (3.74 g, 0.06 mol), in toluene (30 mL) was refluxed under a soxhlet filled with 3Å molecular sieves. The reaction was continued for 4 h then allowed to cool, diluted with ether (50 mL) and washed with 2M NaOH (2 x 20 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent removed *in vacuo* to give **339** as a white solid which was recrystallised from petrol (6.58 g, 0.024 mol, 80%).

m.p. 65-67°C (petrol), lit[69] 68°C

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.11 (1H, s, Ar*H*), 7.05 (1H, s, Ar*H*), 5.95 (1H, s, OC*H*O), 5.90 (2H, s, OCH_2O), 4.17 – 3.98 (4H, m, CH_2CH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 149.1 (*C* (Ar)), 147.6 (*C* (Ar)), 130.1 (*C* (Ar)), 114.0 (*C* (Ar)), 113.3 (*C*H (Ar)), 107.8 (*C*H (Ar)), 102.6 (OCHO), 102.1 (OCH_2O), 65.5 (2 x OCH_2) p.p.m.

The NMR Spectra also show peaks corresponding to ca. 2% of starting material.

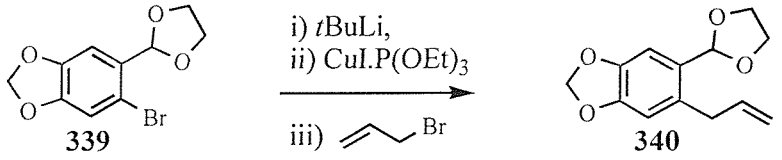
FT-IR ν_{max} (nujol) 2919s, 1847w, 1624m, 1504s, 1247s, 1124s, 951s, 838s, 721m cm^{-1}.

UV λ_{max} (MeOH) 292 (2400), 242 (3000), 217 inf, (2100) nm.

LRMS (APCI) 274 ([M(^{81}Br)]$^+$, 51%), 273([MH (^{79}Br)]$^+$, 100%), 272 ([M(^{79}Br)]$^+$, 29%), 271 (29) amu.

These data are fully consistent with those reported in the literature.[69]

5-Allyl-6-(1,3-dioxalan-2-yl)-1,3-benzodioxole 340



339
$C_{10}H_9O_4Br$ 273

340
$C_{13}H_{14}O_4$ 234

A solution of **339** (1.01 g, 5.22mmol) in THF (30 mL) was stirred under nitrogen at -78°C. *t*-Butyllithium (6.5 mL of a 1.2 M solution in hexanes) was added dropwise over 5 min producing a yellow solution. After 15 min. CuI.P(OEt)$_3$ (1.84 g 5.22 mmol) in THF (5 mL) was added dropwise over 5 min and the mixture was then stirred for a further 15 min. Allyl bromide (0.8 mL, 10.4 mmol) was added neat over 1 min producing a red black solution which was allowed to stir for 10 min at -78°C before being warmed to ambient temperature. The mixture was diluted with ether (20 mL) and washed with ammonia solution (6 x 20 mL) until the washings were no longer blue. The organic layer was dried ($MgSO_4$) and the solvent removed *in vacuo* to give **340** as cream crystals (1.08 g, 3.96 mmol, 89%) which were recrystallised from petrol.

m.p. 52-55°C (petrol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.09 (1H, s, Ar*H*), 6.68 (1H, s, Ar*H*), 5.95 (2H, s, OCH_2O), 5.93 – 5.96 (1H, obs. m, C*H*=CH$_2$), 5.92 (1H, s, OC*H*O), 5.07 (1H, d with fine splitting, *J* 10.4, =C*H*H), 5.02 (1H, d with fine splitting, *J* 17.8, =CH*H*), 4.20 – 3.97 (4H, m, OCH_2CH_2), 3.45 (2H, d, *J* 6.3 Hz, ArCH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 148.2 (*C* (Ar)), 146.2 (*C* (Ar)), 137.3 (*C*H=CH_2), 132.6 (*C* (Ar)), 128.8 (*C* (Ar)), 116.0 (=*C*H_2), 110.0 (*C*H (Ar)), 106.6 (*C*H (Ar)), 101.2 (OCH_2O + OCHO), 65.3 (OCH_2CH_2O), 36.3 ($ArCH_2$) p.p.m.

FT-IR ν_{max} (nujol) 1847w, 1687w, 1481s, 1377s, 1320m, 1233s, 1088s, 1036s, 955s, 809m, 713m cm^{-1}.

UV λ_{max} (MeOH) 286 (12800), 237 (18700), 217 inf. (12400) nm.

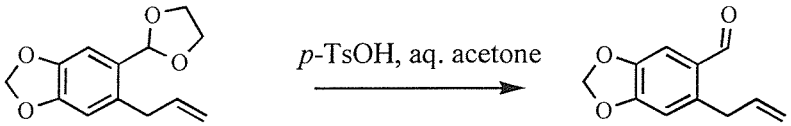
LRMS (APCI) 235 ($[MH]^+$, 60%) 173 (100) amu.

HRMS (CI) Found $[M]^+$ 235.0970, $C_{13}H_{14}O_4$ requires 235.0970 amu.

Alternative procedure for synthesis of **340**

A solution of compound **339** (7.30 g, 0.026 mol) in THF (40 mL) at -78°C was stirred under nitrogen. *tert*-Butyllithium (17.3 mL of a 1.5 M solution in THF) was added over 10 min and the mixture allowed to stir for 10 min. A preformed solution of CuCN (2.41 g, 0.026 mol) and LiCl (1.09 g, 0.026 mol) in THF (10 mL) was then added over 10 min. After a further 10 min allyl bromide (9.43 g, 0.078 mol) was added as a solution in THF (10 mL) over 10 min. The solution was stirred for 15 min and then warmed to ambient temperature, poured into water (40 mL) and diluted with ether (30 mL). The organic layer was washed with ammonia solution (5 x 20 mL) until the washings were no longer blue. The organic layer was then dried ($MgSO_4$) and the solvent removed *in vacuo* to yield **340** as a white solid (5.30 g, 0.022 mol, 87 %).

6-(2-Propenyl-1,3-benzodioxole)-5 carbaldehyde 341[70]



340
$C_{13}H_{14}O_4$ 234

341
$C_{11}H_{10}O_3$ 190

Acetal **340** (140 mg, 0.597 mmol) was stirred in 10% aqueous acetone (30 mL) together with *p*-toluenesulfonic acid (125 mg, 0.71 mmol) for 18 h. The mixture was diluted with water (40 mL) and extracted with ether (4 x 20 mL). The combined organic phases were dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was purified by column chromatography (10% ether in petrol) to give **341** as a yellow oil (91 mg, 0.57 mmol, 80%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 10.06 (1H, s, C*H*O), 7.28 (1H, s, Ar*H*), 6.62 (1H, s, Ar*H*), 6.09 – 5.92 (1H, obs. m, C*H*=CH_2), 6.04 (2H, s, OCH_2O), 5.12 (1H, d with fine splitting, *J* 10.4 Hz, =C*H*H), 4.95 (1H, d with fine splitting, *J* 17.0 Hz, =CH*H*), 3.71 (2H, d, *J* 6.3 Hz, ArCH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 189.5 (*C*HO), 152.6 (*C* (Ar)), 147.1 (*C* (Ar)), 139.8 (*C* (Ar)), 137.1 (*C*H=CH_2), 128.5 (*C* (Ar)), 116.7 (=*C*H_2), 110.6 (*C*H (Ar)), 108.4 (*C*H (Ar)), 102.1 (O*C*H_2O), 36.1 (Ar*C*H_2) p.p.m.

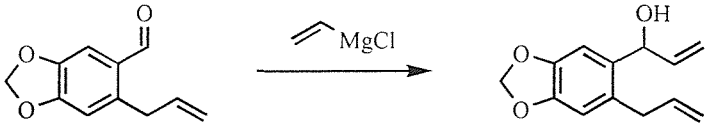
FT-IR ν_{max} (neat) 2904s, 2627w, 2100w, 1676s, 1608s, 1482s, 1259s, 1153m, 996m, 879m, 754m cm^{-1}.

UV λ_{max} (MeOH) 320 (8360), 280 (7600), 238 (14200) nm.

LRMS (APCI) 190 ($[M]^+$, 100%), 173 (22) amu.

These data are fully consistent with those reported in the literature.[70]

1,6-Allyl-(1,3-benzodioxol-5-yl)-2-propen-1-ol 335



341
$C_{11}H_{10}O_3$ 190

335
$C_{13}H_{14}O_3$ 218

A solution of **341** (500 mg, 2.63 mmol) in THF (30 mL) was stirred under a nitrogen atmosphere at 0°C. Vinylmagnesium chloride (2.64 mL of a 1.2M solution in THF) was added over 10 min and the mixture stirred for 1 h. The solution was poured into water (20 mL), extracted with ether (3 x 20 mL), the organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was purified by flash chromotography (20 % ether in petrol) to give **335** as a colourless oil (450 mg, 2.06 mmol, 78%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.98 (1H, s, Ar*H*), 6.67 (1H, s, Ar*H*), 6.08 – 5.90 (2H, obs. m., 2 x C*H*=CH_2), 5.94 (2H, s, OCH_2O), 5.44 – 5.38 (1H, obs. m., C*H*OH), 5.35 (1H, d with fine splitting, *J* 17.0 Hz, =C*H*H), 5.22 (1H, d with fine splitting, *J* 10.3 Hz, =CH*H*), 5.09 (1H, d with fine splitting, *J* 9.9 Hz, =CH*H*), 5.01 (1H, d with fine splitting, *J* 16.9 Hz, =C*H*H), 3.41 (2H, app. d, *J* 5.9 Hz, ArCH_2), 1.83 (1H, d, *J* 3.6 Hz, O*H*) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$), δ_C 147.9 (*C* (Ar)), 147.1 (*C* (Ar)), 139.9 (*C*H=CH_2), 137.6 (*C*H=CH_2), 133.9 (*C* (Ar)), 130.8 (*C* (Ar)), 116.1 (=*C*H_2), 115.0 (=*C*H_2), 110.1 (*C*H (Ar)), 107.1 (*C*H (Ar)), 101.1 (O*C*H_2O), 71.0 (*C*HOH), 36.7 (Ar*C*H_2) p.p.m.

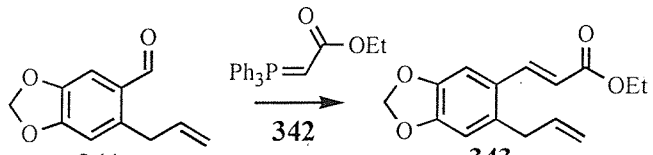
FT-IR ν_{max} (neat) 3374 br, 2893m, 1637m, 1502s, 1107m, 1039s, 990m, 867m, 809m cm^{-1}.

UV λ_{max} (MeOH) 287 (28100), 242 (29200), 221 inf. (16500) nm.

LRMS (APCI) 218 ($[M]^+$, 11%) 201(79), 173 (65), 160 (100) amu.

HRMS (CI) Found $[M]^+$ 218.0943, $C_{13}H_{14}O_3$ requires 218.0943 amu.

Ethyl (*E*)-3-(6-allyl-1,3-benzodioxol-5-yl)-2-propenoate 341



341 $C_{11}H_{10}O_3$ 190 **343** $C_{15}H_{16}O_4$ 260

Compound **341** (1.09 g, 5.73 mmol) was stirred in CH_2Cl_2 (30 mL) together with **342** (4.00 g, 0.011 mol) (which had been prepared by stirring carboethoxymethylenetriphenylphosphonium bromide with 10 equivalents of 2M NaOH in 30 ml CH_2Cl_2) under a nitrogen atmosphere at ambient temperature for 48 h. The solvent was removed *in vacuo* and the products separated by column chromotography (100% petrol) to give **343** as colourless crystals (600 mg, 2.3 mmol, 40%).

m.p. 78-80°C

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (1H, d, *J* 15.8 Hz, ArC*H*=CH), 7.07 (1H, s, Ar*H*), 6.69 (1H, s, Ar*H*), 6.23 (1H, d, *J* 15.8 Hz, ArCH=C*H*), 5.95 (2H, s, OCH_2O), 5.95-5.75 (1H, obs. m, C*H*=CH_2), 5.08 (1H, d with fine splitting, *J* 9.9 Hz, =C*H*H), 5.01 (1H, d with fine splitting, *J* 15.9 Hz, =CH*H*), 4.26 (2H, q, *J* 7.2 Hz, C$H_2$$CH_3$), 3.46 (2H, d, *J* 6.2 Hz, ArCH_2), 1.34 (3H, t, *J* 7.2 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 167.3 (*C*=O), 149.6 (*C* (Ar)), 146.9 (*C* (Ar)), 142.5 (Ar*C*H=), 136.7 (*C*H=CH_2), 134.8 (*C* (Ar)), 126.7 (*C* (Ar)), 120.5 (ArCH=*C*H), 117.4 (=CH_2), 109.7 (*C*H (Ar)), 105.8 (*C*H (Ar)), 101.5 (OCH_2O), 60.5 (OCH_2CH_3), 37.6 ($ArCH_2$), 14.4 (CH_3) p.p.m.

NMR Spectra contain additional peaks due to presence of ca. 10% of the *cis* isomer.

FT-IR ν_{max} (nujol) 1687s, 1683m, 1462s, 1258s, 1169m, 1038s, 974m, 854m, 722m cm^{-1}.

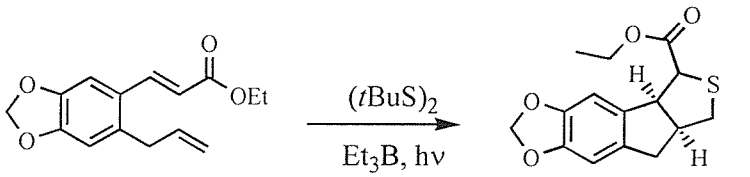
UV λ_{max} (MeOH) 332 (158000), 293 (133000), 238 (141000), 220 inf. (130000) nm.

LRMS (APCI) 260 ($[M]^+$, 100%), 231 (9), 215 (20) 186 (33) amu.

HRMS (CI) Found $[M+H]^+$ 261.1127, $C_{15}H_{16}O_4$ requires 260.1049 amu

CHN Found C 69.21 H 6.24, $C_{15}H_{16}O_4$ requires C 69.22 H 6.24.

Ethyl 4b,7,7a,8-tetrahydro-5*H*-thieno[3',4':1,2]-indeno-[5,6-d][1,3]dioxole-5- carboxylate 348



343
$C_{15}H_{16}O_4$ 260

348
$C_{15}H_{16}O_4S$ 292

A solution of diene **343** (100 mg, 0.38 mmol), in acetonitrile (20 mL) containing di-*tert*-butyl disulfide (342 g, 1.92 mmol) and triethylborane (0.385 mL of a 1M solution in hexanes) was stirred and irradiated in a quartz photochemical reactor

for 4 h. The solution was quenched with sat. NH_4Cl (20 mL), extracted with ether (3 x 20 mL) and washed with brine (2 x 20 mL). The organic layer was dried ($MgSO_4$), and solvent removed *in vacuo*. Components were separated by column chromatography (2% ether in petrol) to give **348** as a colourless oil (9 mg, 0.065 mmol, 13 %).

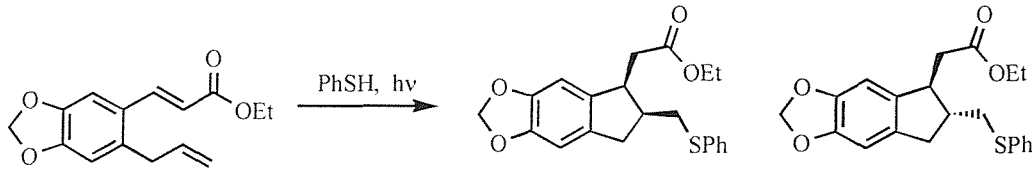
^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.69 (1H, s, Ar*H*), 6.63 (1H, s, Ar*H*), 5.94 (2H, s, OCH_2O), 4.24 (2H, q, *J* 7.3 Hz, OCH_2CH$_3$), 4.12 (1H, app. d, *J* 7.3 Hz, C*H*C=O), 3.89 (1H, m, ArC*H*), 3.56 (1H, app. dddd, *J* 11.4, 7.3, 8.2, 4.0 Hz, C*H*CH$_2$S), 3.33 (1H, dd, *J* 11.4, 6.9 Hz, ArC*H*H), 3.15 (1H, dd, *J* 16.0, 8.2 Hz, C*H*HS), 2.78 (1H, dd, *J* 16.0, 4.0 Hz, CH*H*S), 2.70 (1H, dd, *J* 11.4, 4.0 Hz, ArC*H*H), 1.21-1.48 (3H, t, *J* 7.3 Hz, CH_3) p.p.m.

The spectrum contains some additional signals presumed to be alkane (petrol) residues.

UV λ_{max} (MeOH) 295 (8400), 235 inf. (8200), 217 (13400) nm.

LRMS (APCI) 292 ([M]$^+$, 53%), 218 (100) amu.

Ethyl 2-[6-(phenylthiomethyl)-6,7-dihydro-5*H*-indeno[5,6-d][1,3]dioxol-5-yl-acetate 349 350



343 $C_{15}H_{16}O_4$ 260

349 $C_{21}H_{22}O_4S$ 370

350 $C_{21}H_{22}O_4S$ 370

A solution of **343** (330 mg, 1.27 mmol) in acetonitrile (20 mL) containing thiophenol (838 mg, 2.54 mmol) and triethylborane (1.27 mL, 1.27 mmol) was stirred and irradiated in a quartz photochemical reactor for 8 h. NH_4Cl (30 mL) was added and the reaction mixture extracted with ether (3 x 30 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo*. Purification by column chromotography (5% ether in petrol) gave a major component (60 mg, 0.16 mmol, 12 %) comprising a 1:1 mixture of diastereoisomers assigned as **349** and **350**.

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.41-7.21 (10H, m, 5 x Ar*H*), 6.71 (4H, s, 4 x Ar*H*), 5.95 (2H, s, OCH_2O), 5.94 (2H, s, OCH_2O), 4.17 (2H, q, *J* 7.0 Hz, OCH_2), 4.15 (2H, q, *J* 7.0 Hz, OCH_2), 3.60 – 3.64 (1H, mC*H*H), 3.39 – 3.44 (1H, m, CH*H*), 3.24-3.06 (3H, m, C*H* + CH_2), 2.97-2.71 (5H, m, 2 x CH_2 + C*H*), 2.65 (2H, dd, *J* 15.3, 6.6 Hz, CH_2), 2.52 (2H, dd, *J* 6.6, 2.8 Hz, CH_2), 2.45 (2H, dd, *J* 15.3, 8.4, Hz, CH_2), 1.27 (6H, t, *J* 6.9 Hz, 3 x CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 172.7 (*C*=O), 172.5 (*C*=O), 147.2 (*C* (Ar)), 147.0 (*C* (Ar)), 146.8 (*C* (Ar)), 146.7 (*C* (Ar)), 138.2 (*C* (Ar)), 137.3 (*C* (Ar)), 136.7, (*C* (Ar)), 136.3 (*C* (Ar)), 134.8 (*C* (Ar)), 134.6 (*C* (Ar)), 129.5 (2 x *C*H (Ar)), 129.1 (2 x *C*H (Ar)), 129.1 (2 x *C*H (Ar)), 129.0 (2 x *C*H (Ar)), 126.2 (*C*H (Ar)), 126.0 (*C*H (Ar)), 105.5 (*C*H (Ar)), 105.5 (*C*H (Ar)), 105.0 (*C*H (Ar)), 104.9 (*C*H (Ar)), 101.1 (O*C*H_2O), 101.1 (O*C*H_2O), 60.7 (2 x *C*H_2CH$_3$), 47.0 (*C*H), 45.1 (*C*H), 43.3 (*C*H), 42.8 (*C*H), 40.1 (*C*H_2), 38.8 (*C*H_2), 36.9 (*C*H_2), 36.6 (*C*H_2), 34.9 (*C*H_2), 34.7 (*C*H_2), 14.3 (2 x *C*H_3) p.p.m.

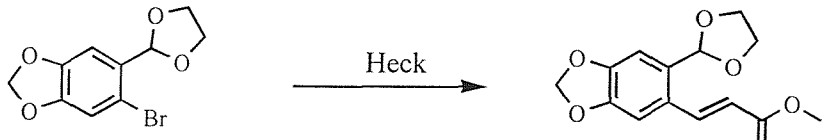
FT-IR ν_{max} (neat) 2903brd, 1728s, 1583w, 1474s, 1438m, 1372m, 1251s, 1147m, 1039s, 909s cm^{-1}.

UV λ_{max} (MeOH) 294 (22200), 254 (23500), 227 inf. (17000) nm.

LRMS (CI) 370 ($[M]^+$, 28%), 325 (12), 260 (29), 172 (100) amu.

HRMS (EI) Found $[M]^+$ 370.1251, $C_{21}H_{22}O_4S$ requires 370.1238 amu.

Methyl (*E*)-3-[6-(1,3-dioxolan-2-yl)-1,3-benzodioxol-5-yl]-2-propenoate 351



339 $C_{10}H_9O_4Br$ 272

351 $C_{14}H_{14}O_6$ 278.08

Prepared in accordance with the procedure of Heck.[71] Compound **339** (2.72 g, 10 mmol) was stirred with heating to 80°C under a nitrogen atmosphere together with palladium acetate (22 mg, 0.1 mmol), methyl acrylate (1.07 g, 12.5 mmol), triethylamine (1.26 g, 12.5 mmol) and triphenylphosphine (52 mg, 0.2 mmol). After 8 h the mixture was cooled, diluted with ether (40 mL) and water (20 mL) and the organic layer separated. The aqueous layer was washed with ether (3 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product was purified by column chromotography (10% ether in petrol) to give **351** as white crystals (1.94 g, 6.97 mmol, 70%).

m.p. 38-40°C (ethanol)

^{1}H NMR. (300 MHz, $CDCl_3$) δ_H 8.02 (1H, d, *J* 15.8 Hz, C*H*=CH), 7.12 (1H, s, Ar*H*), 7.05 (1H, s, Ar*H*), 6.25 (1H, d, *J* 15.8 Hz, CH=C*H*), 6.0 (1H, s, OC*H*O), 5.99 (2H, s, OCH_2OAr), 4.10 (4H, m, OCH_2CH_2O), 3.78 (3H, s, OCH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_H 167.5 (*C*=O), 149.4 (*C* (Ar)), 148.6 (*C* (Ar)), 141.1 (ArCH=CH), 131.9 (*C* (Ar)), 127.8 (*C* (Ar)), 118.2 (ArCH=*C*H), 109.2 (*C*H (Ar)), 107.1 (*C*H (Ar)), 102.6 (O*C*HO), 101.8 (OCH_2O), 65.5 (2 x OCH_2), 51.8 (OCH_3) p.p.m.

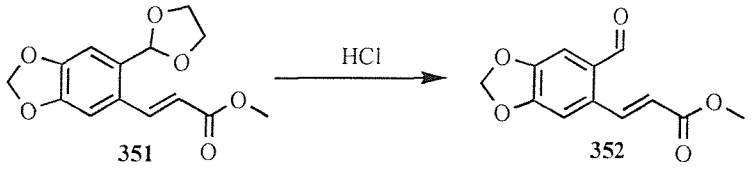
FT-IR ν_{max} (nujol) 1716s, 1635s, 1501s, 1461s, 1376s, 1190s, 1093s, 1035s, 975m, 930m, 858m cm^{-1}.

UV λ_{max} (MeOH) 302 (18400), 273 (25700), 229 (34000) nm.

LRMS (CI) 278 ($[M]^+$, 100%), 219 (100), 205 (85), 175 (86) amu.

HRMS (EI) Found $[M]^+$ 278.0777, $C_{14}H_{14}O_6$ requires 278.0790 amu.

Methyl (*E*)-3-(4,5-[methylenedioxy]-2-formylphenyl)propenoate 352[72]



351 $C_{14}H_{14}O_6$ 278 352 $C_{12}H_{10}O_5$ 234

Acetal **351** (2.0 g, 7.1 mmol) was stirred in THF (20 mL) at ambient temperature. Hydrochloric acid (0.5 mL of a 2M solution) was added and the reaction allowed to stir for 15 min. The precipated product was collected by filtration to give **352** as cream crystals (1.54 g, 6.58 mmol, 90%).

m.p. 182-183°C ($CHCl_3$) lit[72] 178-180 ($CHCl_3$/ hexane).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 10.26 (1H, s, C*H*O), 8.45 (1H, d, *J* 15.8 Hz, ArC*H*=CH), 7.37 (1H, s, Ar*H*), 7.06 (1H, s, Ar*H*), 6.33 (1H, d, *J* 15.8 Hz, ArCH=C*H*), 6.13 (2H, s, OCH_2O), 3.84 (3H, s, OCH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 188.9 (*C*HO), 167.1 (*C*=O), 152.7 (*C* (Ar)), 149.7 (*C* (Ar)), 139.8 (ArCH=CH), 133.8 (*C* (Ar)), 129.7 (*C* (Ar)), 121.9 (ArCH=*C*H), 109.2 (*C*H (Ar)), 106.9 (*C*H (Ar)), 102.6 (OCH_2O), 52.1 (OCH_3) p.p.m.

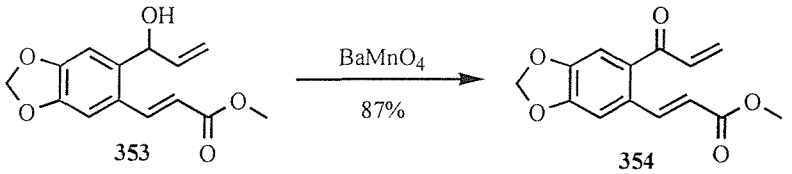
FT-IR ν_{max} (nujol) 1745m, 1668s, 1607s, 1488s, 1432m, 1239m, 1178m, 1061m, 975w, 866w, 787w cm^{-1}.

UV λ_{max} (MeOH) 320 (51400), 263 (91200), 234 (94700) nm.

LRMS (APCI) 235 ($[M+H]^+$, 18%), 203 (100), 175 (78) amu.

These data were consistent with those reported in the literature.[72]

Methyl (*E*)-3-(6-acryloyl-1,3-benzodioxole-5-yl)-2-propenoate 354



$C_{14}H_{14}O_5$ 262 $C_{14}H_{12}O_5$ 260

Compound **353** (50 mg, 0.19 mmol) was stirred at ambient temperature in CH_2Cl_2 (30 mL) together with $BaMnO_4$ (243 mg, 0.95 mmol) under a nitrogen atmosphere for 7 h. The mixture was filtered through a plug of celite and solvent removed from the filtrate *in vacuo*. The product was purified by column chromatography to give **354** as cream crystals (43 mg, 0.16 mmol, 87%).

m.p. 70-72°C (ethanol).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.84 (1H, d, *J* 15.6 Hz, ArC*H*=CH), 7.08 (1H, s, Ar*H*), 6.98 (1H, s, Ar*H*), 6.75 (1H, dd, *J* 17.3, 10.6 Hz, C*H*=CHH), 6.22 (1H, d, *J* 15.6, ArCH=C*H*), 6.18 (1H, d, *J* 17.3 Hz, CH=CH*H*), 6.04 (1H, d, *J*, 10.6 Hz, CH=C*H*H), 6.05 (2H, s, OCH_2O), 3.73 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 193.7 (Ar*C*=O), 167.1 (CH_3OC=O), 152.7 (*C* (Ar)), 149.7 (*C* (Ar)), 142.4 (Ar*C*H=CH), 136.0 (ArCH=*C*H), 133.7 (*C* (Ar)), 132.0 (CH=*C*H_2), 129.9 (*C* (Ar)), 119.0 (*C*H=CH_2), 109.1 (*C*H (Ar)), 106.8 (*C*H (Ar)), 102.4 (O*C*H_2O), 51.8 (*C*H_3) p.p.m.

The NMR spectra also contain signals relating to compound **352**.

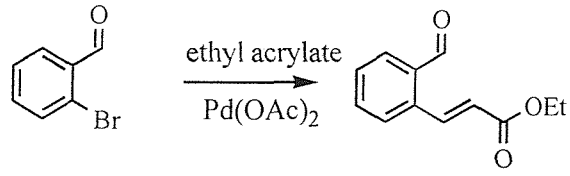
FT-IR ν_{max} (neat film) 3019s, 2903m, 1718s, 1610s, 1437s, 1041s, 1264s, 1176s, 1090m, 972m, 856w cm^{-1}.

UV λ_{max} (MeOH) 320 (70400), 236 (150900) nm.

LRMS (CI) 261 (54%, $[M+H]^+$), 175 (100) amu.

HRMS (EI) Found $[M]^+$ 260.0677, $C_{14}H_{12}O_5$ requires 260.0685 amu.

Ethyl-3-[2-formylphenyl]-2-propenoate 357[73]



356 **357**

C_7H_5BrO 184 $C_{12}H_{12}O_3$ 204

2-Bromobenzaldehyde **356** (10 g, 54 mmol) was stirred with heating to 100°C under a nitrogen atmosphere together with palladium acetate (1.03 g, 5.4 mmol), ethyl acrylate (6.49 g, 54 mmol), triethylamine (6.54g, 54 mmol) and triphenylphosphine (2.83g, 10.8 mmol). After 16 h the mixture was cooled, diluted with ether (50 mL) and water (50 mL) and the organic layer separated. The aqueous layer was washed with ether (2 x 30 mL), the combined organic layers were dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was purified by column chromotography (10% ether in petrol) to give **357** as a colourless oil (6.23 g, 30 mmol, 56%).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 10.21 (1H, s, C*H*O), 8.44 (1H, d, *J* 15.8 Hz, =C*H*), 7.78 (1H, d, *J* 7.7 Hz, Ar*H*), 7.58 – 7.42 (3H, m, 3 x Ar*H*), 6.29 (1H, d, *J* 15.8 Hz, =C*H*), 4.18 (2H, q, *J* 6.9 Hz, CH_2), 1.24 (3H, t, *J* 6.9 Hz, CH_3) p.p.m.

^{13}C NMR (300MHz, $CDCl_3$) δ_C 191.8 (*C*HO), 166.1 (O*C*=O), 140.9 (=*C*H), 136.3 (*C* (Ar)), 133.9 (=*C*H), 133.8 (*C* (Ar)), 133.1 (*C*H (Ar)), 132.4 (*C*H (Ar)), 128.2 (*C*H (Ar)), 125.6 (*C*H (Ar)), 60.2 (CH_2), 14.2 (CH_3) p.p.m.

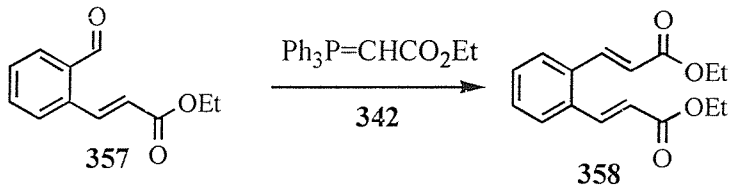
FT-IR ν_{max} (neat) 2981s, 1710s, 1636s, 1481s, 1392m, 1317m, 1281s, 1034s, 888m, 819m, 764m cm^{-1}.

UV λ_{max} (CH_2Cl_2) 293 (7700), 254 (14000), 221 (22600) nm.

LRMS (APCI) 246 ($[MCH_3CN]^+$, 100%), 205 ($[MH]^+$, 38%), 120 (48) amu.

These data were fully consistent with those reported in the literature.[73]

Ethyl 3-(2-[3-ethoxy-3-oxo-1-propenyl]phenyl)-2-propenoate 358[74]



357 $C_{12}H_{12}O_3$ 204

358 $C_{16}H_{18}O_4$ 274

Aldehyde **357** (4.24 g, 27 mmol) was stirred in CH_2Cl_2 (40 mL) together with ylid **342** (4.004 g, 0.011 mol), (prepared by stirring carboethoxymethylene-triphenylphosphonium bromide with 10 equivalents of 2M NaOH in CH_2Cl_2 (30 mL)) under a nitrogen atmosphere at ambient temperature for 48 h. The solvent was removed *in vacuo* and the products separated by column chromotography (20% ether in petrol) to give **358** as yellow crystals (2.83 g, 10 mmol, 38%).

m.p. 81°C (petrol), lit[74] 74°C (hexane)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (2H, d, *J* 15.8 Hz, 2 x =C*H*), 7.41 – 7.34 (2H, m, Ar*H*), 7.24 – 7.14 (2H, m, Ar*H*), 6.17 (2H, d, *J* 15.8 Hz, 2 x =C*H*), 4.09 (4H, q, *J* 6.9 Hz, 2 x CH_2), 1.18 (6H, t, *J* 6.9 Hz, 2 x CH_3) p.p.m.

^{13}C NMR (300MHz, $CDCl_3$) δ_C 166.1 (2 x O*C*=O), 141.4 (2 x =*C*H), 134.1 (2 x *C* (Ar)), 130.0 (2 x =*C*H), 127.5 (2 x *C*H (Ar)), 121.7 (2 x *C*H (Ar)), 60.5 (2 x *C*H_2), 14.2 (2 x *C*H_3) p.p.m.

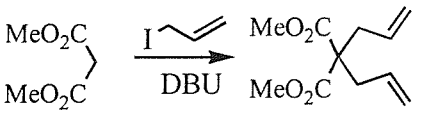
FT-IR (CH_2Cl_2) ν_{max} 2983s, 1706s, 1635s, 1478m, 1308s, 1185s, 1095m, 1034s, 977s, 867m cm^{-1}.

UV (CH_2Cl_2) 300 (42700), 265 (55300) nm.

LRMS (APCI) 292 ($[M+NH_4]^+$, 100%), 274 ($[M]^+$, 14%), 246 (34) amu.

These data were consistent with those reported in the literature.[74]

Dimethyl 2,2-diallylmalonate 364[75]



363 $C_5H_8O_4$ 132

364 $C_{11}H_{16}O_4$ 212

Allyl bromide (5.19 mL, 60 mmol) was stirred in acetone (50 mL) together with NaI (9.1 g, 60 mmol) for 20 min. Dimethyl malonate **363** (2.0 g, 15 mmol) was then added *via* syringe and the mixture stirred at ambient temperature for 20 min. DBU (4.48 mL, 30 mmol) was then added *via* syringe and the whole was allowed to stir for 24 h. The mixture was diluted with water (20 mL) and extracted into ether (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$) concentrated *in vacuo* and purified by column

chromotography (5% ether in petrol) to give **364** as a colourless oil (1.21 g, 5.6 mmol, 37%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.68-5.55 (2H, m, 2 x =C*H*), 5.09 (2H, d, *J* 15.8 Hz, 2 x =C*H*H), 5.08 (2H, d, *J* 11.8 Hz, 2 x =CH*H*), 3.67 (6H, s, 2 x OCH_3), 2.63 (4H, d, *J* 7.3 Hz, 2 x CH_2) p.p.m.

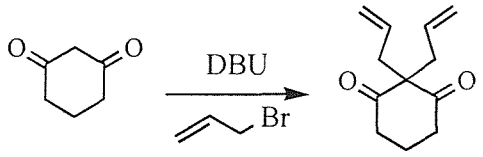
^{13}C NMR (300MHz, $CDCl_3$) δ_C 171.2 (2 x *C*=O), 132.3 (2 x =*C*H), 119.3 (2 x =CH_2), 57.7 (*C*CH_2), 52.4 (2 x OCH_3), 37.0 (2 x *C*H_2) p.p.m.

FT-IR ν_{max} (neat) 2951m, 1732s, 1639m, 1436mm, 1325m, 1218m, 1144m, 1030w, 994w, 854w cm^{-1}.

LRMS (CI) 213 ($[M+H]^+$, 100%) amu.

These data were consistent with those reported in the literature.[75]

2,2-Diallyl-1,3-cyclohexandione 366[76]



365 $C_6H_8O_2$ 112

366 $C_{12}H_{16}O_2$ 192

Allyl bromide (9.24 mL, 106 mmol) was stirred in acetone (100 mL) together with NaI (12.1 g, 106 mmol) for 20 min. Dione **365** (3 g, 26.7 mmol) was then added as a solution in acetone (10 mL) *via* syringe and the mixture stirred at ambient temperature for 20 min. DBU (7.98 mL, 53.4 mmol) was then added *via* syringe and the whole was allowed to stir for 24 h. The mixture was diluted with water (20 mL) and extracted into ether (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo*

and purified by column chromotography (10% ether in petrol) to give **366** as a colourless oil (2.75g, 14 mmol, 53%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.56 – 5.39 (2H, m, 2 x =C*H*), 4.92 (4H, app.d, *J* 13.1 Hz, 2 x =CH_2), 2.54 – 2.40 (8H, m, 4 x CH_2), 1.91 – 1.80 (2H, m, $CH_2CH_2CH_2$) p.p.m.

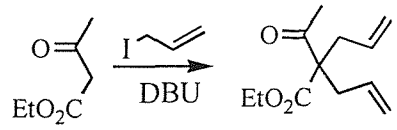
^{13}C NMR (300MHz, $CDCl_3$) δ_C 210.4 (2 x *C*=O), 132.5 (2 x *C*H=CH_2), 119.4 (2 x =*C*H_2), 68.3 (*C*C=O), 40.9 (2 x CH*C*H_2), 40.1 (2 x *C*H_2C=O), 16.5 ($CH_2CH_2CH_2$) p.p.m.

FT-IR ν_{max} (neat) 3078m, 2921m, 1722s, 1639s, 1461m, 1337m, 1258m, 1212s, 1093w, 999m cm^{-1}.

LRMS (CI) 193 ($[MH]^+$, 23%), 164 (11), 151 (19) amu.

These data were fully consistent with those reported in the literature.[76]

Ethyl-2-acetyl-2-allyl-4-penteneoate 368[77]



367 $C_6H_{10}O_3$ 130

368 $C_{12}H_{18}O_3$ 210

Allyl bromide (5.19 mL, 60 mmol) was stirred in acetone (50 mL) together with NaI (9.1 g, 60 mmol) for 20 min. **367** (1.95 g, 15 mmol) was then added *via* syringe and the mixture stirred at ambient temperature for 20 min. DBU (4.48 mL, 30 mmol) was then added *via* syringe and the whole was allowed to stir for 24 h. The mixture was diluted with water (20 mL) and extracted into ether (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried

($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (5% ether in petrol) to give **368** as a colourless oil (1.503 g, 7.1 mmol, 47%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.52 (2H, m, 2 x =C*H*), 5.04 (2H, d, *J* 15.8 Hz, =C*H*H), 5.01 (2H, d, *J* 11.4 Hz, =CH*H*), 4.12 (2H, q, *J* 7.1 Hz, C*H*$_2$CH$_3$), 2.46 – 2.65 (4H, m, 2 x C*H*$_2$CH), 2.11 (3H, s, CH$_3$C=O), 1.26 (3H, t, *J* 7.1 Hz, CH$_2$C*H*$_3$) p.p.m.

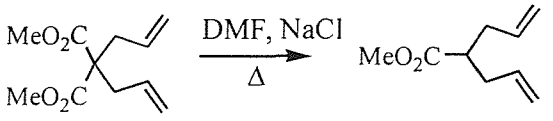
^{13}C NMR (75.5MHz, $CDCl_3$) δ_C 204.1 (*C*=O), 171.5 (O*C*=O), 132.3 (2 x =*C*H), 119.2 (2 x =*C*H$_2$), 63.2 (*C*CH$_2$), 61.4 (*C*H$_2$CH$_3$), 36.1 (2 x CH*C*H$_2$), 27.0 (*C*H$_3$C=O), 14.2 (CH$_2$*C*H$_3$) p.p.m.

FT-IR ν_{max} (neat) 2949m, 1729brs, 1453m, 1433s, 1253s, 1205s, 1161m, 1084m, 1022w, 907w, cm^{-1}.

LRMS (CI) 211 ([MH]$^+$, 100%) amu.

These data were fully consistent with those reported in the literature.[77]

Methyl 2-allyl-4-pentenoate 368[78]



364 $C_{11}H_{16}O_4$ 212

369 $C_9H_{14}O_2$ 154

Compound **364** (500 mg, 2.3 mmol) was stirred in DMSO (40 mL) together with NaCl (151 mg, 2.53 mmol) and H_2O (0.165 mL, 9.2 mmol) and the mixture heated to reflux for 28 h. The mixture was diluted with ether (30 mL) and washed with water (20 mL). The organic layer was washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (10% ether in petrol) to give **369** as a colourless oil (311 mg, 2.0 mmol, 88%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.74 (2H, m, 2 x =C*H*), 5.10-4.98 (4H, m, =CH_2), 3.63 (3H, s, OCH_3), 2.54 (1H, m, C*H*), 2.35 (2H, ddd, *J* 10.1, 7.1, 6.6 Hz, CHCH_2), 2.28 (2H, ddd, *J* 10.1, 7.1, 6.6 Hz, CHCH_2) p.p.m.

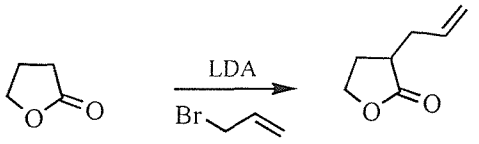
^{13}C NMR (75.5MHz, $CDCl_3$) δ_C 175.5 (*C*=O), 135.3 (2 x =*C*H), 117.1 (2 x =*C*H_2), 51.5 (O*C*H_3), 45.1 (*C*H), 35.9 (2 x CHCH_2) p.p.m.

FT-IR ν_{max} (neat) 2950s, 1738s, 1642s, 1441s, 1369s, 1267s, 1139s, 994s, 832m cm^{-1}.

LRMS (CI) 155 ([MH]$^+$, 100%) amu.

These data were fully consistent with those reported in the literature.[78]

3-Allyltetrahydro-2-furanone[79]



370

$C_4H_6O_2$ 86 $C_7H_{10}O_2$ 126

Diisopropylamine (0.812 mL, 10 mmol) was stirred in THF (40 mL) at -78°C under a nitrogen atmosphere. *n*-BuLi (13.3 mL of a 1.5M solution) was added *via* syringe over 2 min and the mixture allowed to warm to ambient temperature. The solution was then cooled to -78°C and the lactone was added as a solution in THF (5 mL). The mixture was stirred at -78°C for 10 min and allyl bromide (3.63 mL, 30 mmol) added *via* syringe. After warming to ambient temperature over 1h, water (20 mL) was added and the mixture extracted with ether (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried

($MgSO_4$), concentrated *in vacuo* and the product purified *via* column chromatography to give the monoallylated product as a colourless oil (510 mg, 4 mmol, 41%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.82 – 5.66 (1H, m, =C*H*), 5.11 (1H, d, *J* 12.5 Hz, =C*H*H), 5.05 (1H, d, *J* 9.9 Hz, =CH*H*), 4.31 (1H, app. td, *J* 8.8, 2.9 Hz, OC*H*H), 4.21 – 4.11 (1H, m, OCH*H*), 2.68-2.43 (2H, m, CH_2), 2.39 -2.14 (2H, m, CH_2), 2.07 – 1.97 (1H, m, C*H*) p.p.m.

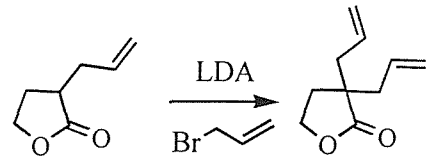
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 179.1 (*C*=O), 134.5 (=*C*H), 117.8 (=*C*H_2), 66.7 (O*C*H_2), 38.9 (*C*H_2), 34.4 (*C*H_2), 27.9 (*C*H) p.p.m.

FT-IR ν_{max} 2910s, 1771s, 1641m, 1453m, 1374s, 1306w, 1212s, 1166s, 998m, 918s cm^{-1}.

LRMS (CI) 144 ($[M+NH_4]^+$, 100%), 127 ($[MH]^+$, 77%) amu.

These data were fully consistent with those reported in the literature.[79]

3,3-Diallyltetrahydro-2-furanone 371[80]



371

$C_7H_{10}O_2$ 126 $C_{10}H_{14}O_2$ 166

Diisopropylamine (0.594 mL, 5.5 mmol) was stirred in THF (40 mL) at -78°C under a nitrogen atmosphere. *n*-BuLi (3.3 mL of a 1.25 M solution) was added *via* syringe over 2 min and the mixture allowed to warm to ambient temperature. The solution was the cooled to -78°C and the allyllactone (347 mg, 2.75mmol)

was added as a solution in THF (5 mL). After 10 min allyl bromide (0.714 mL, 7.5 mmol) was added *via* syringe. The mixture was then warmed to ambient temperature over 30 min and was stirred for a further 1 h. Water (20 mL) was then added and the mixture extracted with ether (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (5% ether in petrol) to give **371** product as a colourless oil (327 mg, 1.96 mmol, 87%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.87 – 5.71 (2H, m, 2 x =C*H*), 5.15 (2H, d, *J* 15.8 Hz 2 x =C*H*H), 5.11 (2H, d, *J* 11.4 Hz, 2 x =CH*H*) 4.20 (2H, t, *J* 7.3 Hz, OCH_2), 2.65 – 2.24 (4H, m, CH_2CH_2), 2.16 (2H, t, *J* 7.3 Hz, CH_2) p.p.m.

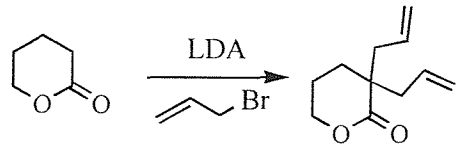
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 180.6 (*C*=O), 132.7 (2 x =*C*H), 119.8 (2 x =CH_2), 65.5 (OCH_2), 46.2 (*C*CH_2), 41.0 (2 x *C*H_2CH), 30.5 (CH_2) p.p.m.

FT-IR ν_{max} (neat) 2910s, 1771s, 1374s, 1306w, 1212s, 1022s, 955m, 822w cm^{-1}.

LRMS (CI) 184 ([M+NH_4]$^+$, 100%), 167 ([MH]$^+$, 93%) amu.

These data were fully consistent with those reported in the literature.[80]

3,3-Diallyltetrahydro-2*H*-2-pyranone 373[80]



372 $C_5H_8O_2$ 100

373 $C_{11}H_{16}O_2$ 180

Diisopropylamine (4.32 mL, 50 mmol) was stirred in THF (40 mL) at -78°C under a nitrogen atmosphere. *n*-BuLi (34 mL of a 1.4 M solution) was added *via* syringe over 2 min and the mixture allowed to warm to ambient temperature. The solution was then cooled to -78°C and the lactone (2.0 g, 20 mmol) was added as a solution in THF (5 mL). After 10 min allyl bromide (5.1 mL, 60 mmol) was added *via* syringe. The mixture was allowed to warm to ambient temperature over 30 min then stirred for 1 h. Water (20 mL) was added and the mixture was extracted with ether (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography to give the *bis*-allylated product as a colourless oil (2.84 g, 15.7 mmol, 87%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.82 – 5.66 (2H, m, 2 x =C*H*), 5.11 (2H, d, *J* 9.8 Hz, 2 x =C*H*H), 5.10 (2H, d, *J* 18.3 Hz, 2 x =CH*H*), 4.31 – 4.22 (2H, m, OCH_2), 2.54 (2H, dd, *J* 13.1, 6.6 Hz, CH_2CH=), 2.19 (2H, dd, *J* 13.6, 8.1 Hz, CH_2CH=), 1.81 (4H, m, CH_2CH_2) p.p.m.

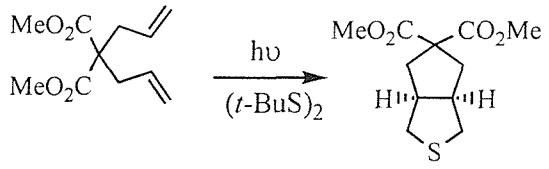
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 175.2 (*C*=O), 133.3 (2 x =*C*H), 119.3 (2 x *C*H_2=), 70.4 (O*C*H_2), 46.0 (*C*C=O), 43.9 (2 x *C*H_2CH=), 28.6 (*C*H_2), 21.1 (*C*H_2) p.p.m.

FT-IR ν_{max} (neat) 2934s, 1726s, 1638m, 1438m, 1231s, 1166s, 1085m, 996m, 638w cm^{-1}.

LRMS (CI) 181 ($[M+H]^+$, 100%), 198.2 ($[M+NH_4]^+$, 60%), 139 (31) amu.

These data were fully consistent with those reported in the literature.[80]

Dimethyl *cis*-perhydrocyclopentathiophene-5,5-dicarboxylate 374



364 $C_{11}H_{16}O_4$ 212

374 $C_{11}H_{16}O_4S$ 244

Compound **364** (500 mg, 2.3 mmol) was stirred in hexane (90 mL) together with (tBuS)$_2$ (2.27 mL, 11.5 mmol) under hν irradiation in a quartz vessel for 36 h. The mixture was partitioned between water (20 mL) and ether (20 mL) and the aqueous phase was extracted further with ether (2 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (5% ether in petrol) to give **374** as a colourless oil (258 mg, 0.94 mmol, 46%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.73 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 2.93 – 2.77 (4H, m, 2 x CH_2), 2.59 – 2.44 (4H, m, 2 x CH_2), 1.98 – 1.87 (2H, m, 2 x CH) p.p.m.

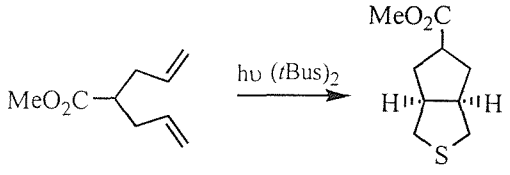
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 52.8 (CCH_2), 52.7 (2 x OCH_3), 46.7 (2 x CH_2), 39.9 (2 x CH), 38.4 (2 x CH_2) p.p.m.

FT-IR ν_{max} (neat) 2934m, 1713s, 1640m, 1442m, 1278s, 1208s, 1096m, 992m, 921s, 855w cm^{-1}.

LRMS (CI) 262 ($[M+NH_4]^+$, 36%), 245 ($[MH]^+$, 100%) 213 (76) amu.

HRMS (CI) Found $[M]^+$ 244.0771, $C_{11}H_{16}O_4S$ requires 244.0769 amu.

Methyl *cis*-perhydrocyclopentathiophene-5-carboxylate 375



369 $C_9H_{14}O_2$ 154

375 $C_9H_{14}O_2S$ 186

Compound **369** (1 g, 6.4 mmol) was stirred in hexane (90 mL) together with $(t\text{BuS})_2$ (5.69 g, 32 mmol) under hν irradiation for 36 h in a quartz photochemical cell. Water (20 mL) was added and the mixture extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (5% ether in petrol) to give a single diastereoisomer of **375** as a colourless oil (500mg, 2.7 mmol, 42%).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 3.71 (3H s, OCH_3), 2.87 – 2.68 (4H, m, 2 x $SCHH$+ 2 x CH), 2.68 – 2.59 (1H, m, CHC=O), 2.58 – 2.51 (2H, m, 2 x $SCHH$), 2.21 – 2.09 (2H, m, CH_2), 1.71 - 1.58 (2H, m, CH_2) p.p.m.

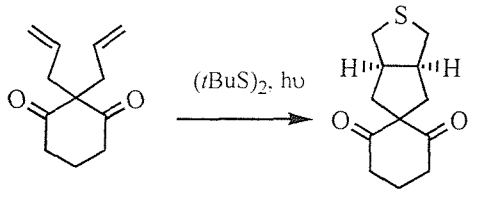
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 175.4 (C=O), 51.7 (OCH_3), 47.5 (2 x CH), 45.0 ($CHCO_2CH_3$), 38.5 (2 x CH_2), 36.2 (2 x CH_2) p.p.m.

FT-IR ν_{max} (neat) 2935w, 1723s, 1453w, 1258m, 1190m, 1153m, 1060w, 931w cm^{-1}.

LRMS (CI) 186 ($[M]^+$, 100%), 155 (79), 126 (80) amu.

HRMS (EI) Found $[M]^+$ 186.0715, $C_9H_{14}O_2S$ requires 186.0715 amu.

***cis*-~Spiro[2,2-(perhydrocyclopentathiophene)-5,2'-(-1',3'-cyclohexanedione] 376**



365 **376**

$C_{12}H_{16}O_2$ 192 $C_{12}H_{16}O_2S$ 224

Compound **365** (1.0 g, 5.2 mmol) was stirred in hexane (90 mL) together with (*t*-BuS)$_2$ (4.62 mL, 25 mmol) under hν irradiation in a quartz vessel for 24 h. Water (20 mL) was added and the mixture extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and by column chromotography (10% ether in petrol) to give **376** as a colourless oil (407 mg, 1.8 mmol, 46%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.91 – 2.84 (4H, m, 2 x CH_2S), 2.71 – 2.48 (6H, m, 2x C*H* + 2 x CH_2C=O), 2.23 (2H, app. q., *J* 5.14 Hz, $CH_2CH_2CH_2$), 1.93 (4H, app. q, *J* 7.7 Hz, 2 x CCH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 208.5 (*C*=O), 207.5 (*C*=O), 74.4 (*C*C=O), 47.6 (2 x CH_2CH), 38.6 (CH_2C=O), 38.1 (2 x CH_2S), 37.5 (2 x CH_2CH), 37.3 (CH_2C=O), 18.0 ($CH_2CH_2CH_2$) p.p.m.

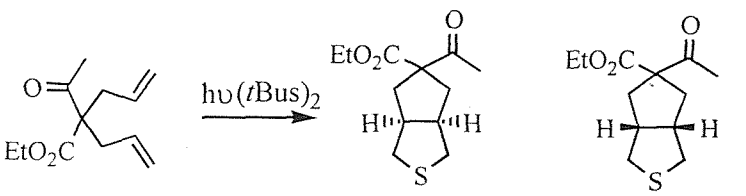
NMR Spectra also contain peaks due to petrol residues.

FT-IR ν_{max} (neat) 2959m, 2359m, 1724s, 1633s, 1458m, 1437m, 1276w, 1032w cm^{-1}.

LRMS (CI) 224 ($[M]^+$, 100%) amu.

HRMS (CI) Found $[M]^+$ 225.0957, $C_{12}H_{17}O_2S$ requires 225.0949 amu

5-Acetyl-5-carboethoxy-2-thiabicyclo[3.3.0]octane 377, 378



368 $C_{12}H_{18}O_3$ 210

377 $C_{12}H_{18}O_3S$ 242

378 $C_{12}H_{18}O_3S$ 242

Compound **368** (500 mg, 2.3 mmol) was stirred in hexane (90 mL) together with (tBuS)$_2$ (2.27 mL, 11.5 mmol) under hν irradiation in a quartz vessel for 24 h. Water (20 mL) was added and the mixture was extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (10% ether in petrol) to give **377** and **378** as a colourless oil (250 mg, 0.94 mmol, 45%).and a 1:1 mixture of diastereoisomers

^{1}H NMR (300MHz, $CDCl_3$) δ_H 4.24 – 4.11 (4H, m, CH_2CH_3), 2.98 – 2.71 (8H, m, 4 x SCH_2), 2.52 – 2.41 (8H, m, 4 x CH_2), 2.14 (6H, s, CH_3C=O), 2.0 – 1.82 (4H, m, 4 x $CHCH_2$), 1.36 – 1.24 (6H, m, 2 x CH_2CH_3) p.p.m.

^{13}C NMR (75.5MHz, $CDCl_3$) δ_C 204.1 (C=O), 203.6 (C=O), 172.7 (OC=O), 172.1 (OC=O), 68.6 (CCH_2), 67.8 (CCH_2), 61.6 (2 x CH_2CH_3),

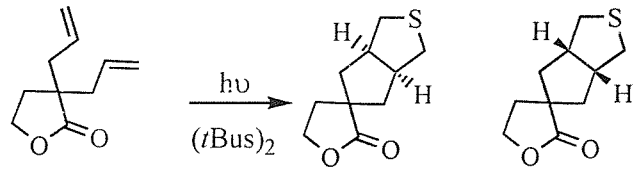
46.8 (2 x SCH_2), 46.7 (2 x SCH_2), 38.7 (2 x CH_3), 38.3 (2 x CH_2), 38.2 (2 x $C{=}OCH_3$), 26.9 (2 x $CHCH_2$), 25.9 (2 x $CHCH_2$), 14.1 (2 x CH_2CH_3) p.p.m.

FT-IR ν_{max} (neat) 2974m, 1712br, 1444m, 1354m, 1241s, 1197s, 1086m, 1017m, 859w cm^{-1}.

LRMS (CI) 260 ($[M+NH_4]^+$, 34%) 243 ($[MH]^+$, 100%), 197 (85) amu.

HRMS (EI) Found $[M]^+$ 242.9743, $C_{12}H_{18}O_3S$ requires 242.9767 amu.

Spiro[(perhydrofuran-2-one)-3,5'-(2'thiabicyclo[3.3.0]octane)] 379, 380



371 **379** **380**

1:1

$C_{10}H_{14}O_2$ 166 $C_{10}H_{14}O_2S$ 198 $C_{10}H_{14}O_2S$ 198

Compound **371** (385 mg, 2.3 mmol) was stirred in hexane (90 mL) together with (tBuS)$_2$ (1.9 mL, 7.6 mmol) under hν irradiation in a quartz vessel for 18 h. Water (20 mL) was added and the mixture was extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (5% ether in petrol) to give firstly **379** as a colourless solid (80 mg, 0.4 mmol, 18%) followed by **380** (80 mg, 0.4 mmol, 18%).

Data for **379**

m.p. 85 - 87°C (ethanol)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 4.21 (2H, t, *J* 6.9 Hz, OCH_2), 3.19 – 3.07 (2H, m, 2 x C*H*), 2.89 (2H, dd, *J* 12.1, 6.6 Hz, SCH_2), 2.49 (2H, d, *J* 9.4 Hz, SCH_2), 2.31 – 2.19 (4H, m, 2 x CCH_2), 1.49 (2H, dd, *J* 6.6, 6.9 Hz, CCH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 181.9 (*C*=O), 66.1 (OCH_2), 50.0 (CCH_2), 47.1 (2 x *C*H), 41.9 (2 x SCH_2), 38.8 (2 x CCH_2), 35.6 (CCH_2) p.p.m.

FT-IR ν_{max} (neat) 2935w, 1760s, 1450w, 1370m, 1115m, 1019s, 910w, 733m cm^{-1}.

LRMS (CI) 216 ($[M+NH_4]^+$, 100%), 198 ($[MH]^+$, 64%) amu.

HRMS (EI) Found $[M]^+$ 198.0712, $C_{10}H_{14}O_2S$ requires 198.0715 amu.

Data for **380**

m.p. 85 - 6°C (ethanol)

^{1}H NMR (300 MHz, CDCl3) δ_H 4.26 (2H, t, *J* 6.9 Hz, OCH_2), 2.97 – 2.78 (4H, m, 2 x C*H*,SCH_2), 2.55 (2H, app.d, *J* 10.3 Hz, SCH_2), 2.07 (2H, t, *J* 6.9 Hz CCH_2), 2.04 – 1.77 (4H, m, 2 x CH_2) p.p.m.

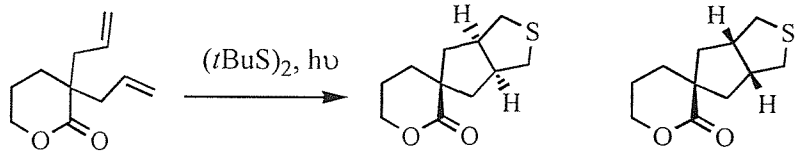
^{13}C NMR (75.5 MHz, CDCl3) δ_C 180.9 (*C*=O), 65.4 (OCH_2), 50.0 (CCH_2), 47.1 (2 x *C*H), 41.9 (2 x SCH_2), 38.3 (2 x CCH_2), 35.4 (CCH_2) p.p.m.

FT-IR ν_{max} (neat) 2860w, 1760s, 1450w, 1371m, 1176m, 1019s, 910w, 733s cm^{-1}.

LRMS (CI) 216 ($[M+NH_4]^+$, 26%), 199 ($[MH]^+$, 100%) amu.

HRMS (EI) Found $[M]^+$ 198.0713, $C_{10}H_{14}O_2S$ requires 198.0715 amu.

Spiro[(perhydropyran-2-one)3,5'-(2'-thiabicyclo[3.3.0]octane)] 381, 382



372 **381** **382**

$C_{11}H_{16}O_2$ 180 $C_{11}H_{16}O_2S$ 212 $C_{11}H_{16}O_2S$ 212

Compound **372** (524 mg, 2.8 mmol) was stirred in hexane (90 mL) together with (tBuS)$_2$ (2.7 mL, 14 mmol) under hν irradiation in a quartz photochemical reactor for 24 h. Water (20 mL) was added and the mixture extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (5% ether in petrol) to give **381** (98 mg, 0.46 mmol, 16%) and **382** as colourless oils (97 mg, 0.45 mmol, 16%).

Data for **381**

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 4.33 – 4.20 (2H, m, OC*H*$_2$), 3.14 – 3.04 (2H, m, 2 x C*H*), 2.82 (2H, dd, *J* 10.2, 7.3 Hz, 2 x C*H*HS), 2.47 (2H, d, *J*10.2 Hz, 2 x CH*H*S), 2.36 (2H, dd, *J* 12.8, 7.7 Hz, 2 x CC*H*H), 1.92 – 1.78 (4H, m, C*H*$_2$C*H*$_2$), 1.1.36 – 1.23 (2H, m, 2 x CCH*H*) p.p.m.

^{13}C NMR (100 MHz, $CDCl_3$) δ_C 177.7 (*C*=O), 71.7 (O*C*H$_2$), 52.4 (*C*CH$_2$), 48.8 (2 x *C*HCH$_2$), 46.3 (2 x *C*H$_2$CH), 40.1 (2 x *C*H$_2$S), 35.1 (*C*H$_2$CH$_2$), 23.1 (CH$_2$*C*H$_2$) p.p.m.

The spectrum contain an unidentifiable contaminant (ca 10%).

Assignments were confirmed by a C-H correlation experiment

FT-IR ν_{max} (neat) 2956s, 2358w, 2250w, 1731s, 1456m, 1351m, 1268m, 1153s, 1089s, 982w cm^{-1}.

LRMS (CI) 213 ([MH]$^+$, 100%), 113 (52) amu.

Data for **382**

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 4.28 (2H, app. t, *J* 5.5 Hz, OCH_2), 2.85 – 2.76 (4H, m, 2 x C*H* + 2 x CH*H*S), 2.57 (2H, app. d, *J* 9.6 Hz, 2 x C*H*HS), 2.03 (2H, dd, *J* 12.5, 6.8 Hz, 2 x CC*H*H), 1.91 (2H, dd, *J* 12.5, 5.2 Hz, 2 x CCH*H*), 1.87 – 1.78 (2H, m, CH_2CH_2), 1.74 – 1.67 (2H, m, CH_2CH_2) p.p.m.

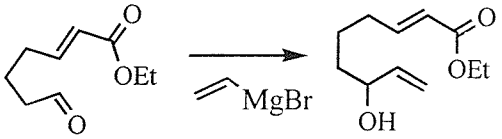
^{13}C NMR (100 MHz, $CDCl_3$) δ_C 176.2 (*C*=O), 70.1 (OCH_2), 50.9 (CCH_2), 46.9 (2 x *C*H), 44.4 (2 x CH_2), 38.4 (2 x CH_2), 31.9 (CH_2CH_2), 21.4 (CH_2CH_2) p.p.m.

FT-IR ν_{max} (neat) 2948m, 2358w, 1722s, 1442w, 1344w, 1257m, 1155s, 1104m, 972w cm^{-1}.

LRMS (CI) 213 ($[MH]^+$, 100%) amu.

HRMS (CI) Found $[M]^+$ 212.0869, $C_{11}H_{16}O_2S$ requires 212.871 amu.

Ethyl 7-hydroxy-2,8-nonadienoate 383



383a **383**

$C_9H_{14}O_3$ 170 $C_{11}H_{18}O_3$ 198

Aldehyde **383a** (2.0 g, 11.8 mmol) was stirred in dry THF (40 mL) at 0°C. Vinylmagnesium bromide (15 mL of a 0.79M solution in hexane) was added *via* syringe over 5 min and the mixture was allowed to stir for 1 h at ambient temperature. The mixture was then diluted with water (20 mL) and extracted with ether (4 x 20 mL).

The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide **383** as a colourless oil (1.0 g, 5 mmol, 43%).

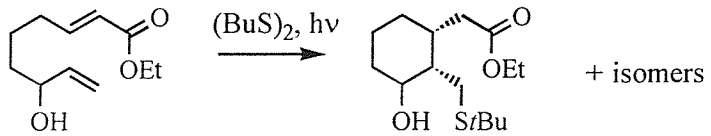
^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.9 (1H, dt, *J* 15.8, 6.6 Hz, CH_2CH=), 5.73 – 5.91 (2H, m, CH=CH_2 + CH=CH), 5.12 (1H, d, *J* 17.1 Hz, CH=CHH), 4.98 (1H, d, *J* 10.3 Hz, CH=CHH), 4.18 (2H, q, *J* 6.9 Hz, OCH_2), 4.10 (1H, m, CHOH), 2.21 – 2.24 (2H, m, CH_2), 1.86 (1H, brs, OH), 1.58- 1.52 (4H, m, CH_2CH_2), 1.29 (3H, t, *J* 6.9Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 166.8 (C=O), 149.1 (CH_2CH=), 141.2 (CH=CH_2), 121.5 (CH=CH), 114.6 (CH=CH_2), 72.7 (OCH_2), 60.3 ($CHOH$), 36.3 (CH_2CH=), 32.1 (CH_2), 23.8 (CH_2), 14.3 (CH_3) p.p.m.

FT-IR ν_{max} (neat) 3434brd, 2980s, 2863s, 1720s, 1445s, 1128m, 1042s, 988s, 858w cm^{-1}.

LRMS (CI) 199 ($[MH]^+$, 28%), 181 (100), 153 (12), 135 (31), 107 (73) amu.

Ethyl-2-{2-[(*tert*-butylthio)methyl]-3-hydroxycyclohexyl}acetate 384



383 **384**

$C_{11}H_{18}O_3$ 198 $C_{15}H_{28}O_3S$ 288

Compound **383** (1.0 g, 5 mmol) was stirred in hexane (90 mL) together with (tBuS)$_2$ (4.57 mL, 25 mmol) under hν irradiation in a quartz vessel for 24 h. Water (20 mL) was added and the mixture extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo*. and purified

by column chromotography (10% ether in petrol) to give **384** as a colourless oil and as an inseparable mixture of diastereoisomers (544 mg, 2.0 mmol, 40%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 4.30 – 4.02 (2H, m, OCH_2), 2.53 – 1.48 (14H, m, 6 x CH_2 + 2 x CH), 1.43 - 1.25 (12H, m, 4 x CH_3) p.p.m.

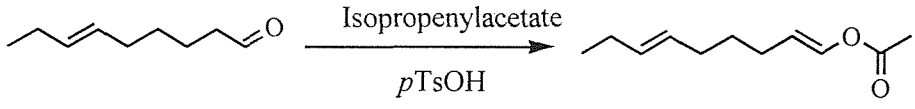
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C major diastereoisomer 171.9 (C=O), 68.1 (OCH_2), 61.5 ($CHOH$), 48.1 (CH_2C=O), 45.4 (CH_2S), 43.7 (SC), 39.7 (CH), 32.3 (CH), 31.3 (CH_3), 31.0 (CH_3), 30.9 (CH_3), 30.7 (CH_2), 30.1 (CH_2), 19.7 (CH_2), 14.4 (CH_3) p.p.m.

The spectra also contained signals corresponding to other diastereoisomers

FT-IR ν_{max} (neat) 3465br, 2959s, 1654w, 1724s, 1458s, 1364s, 1266m, 1164s, 1095m, 912m, 733s cm^{-1}.

HRMS (CI) Found $[MH]^+$ 289.1839, $C_{15}H_{29}O_3S$ requires 289.1837 amu.

1*E*,6*E*-Nonadienyl acetate 386



386a $C_9H_{16}O$ 140

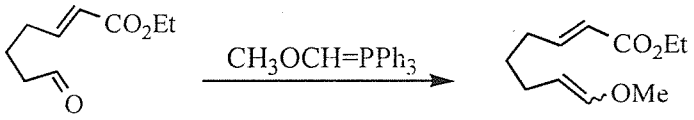
386 $C_{11}H_{18}O_2$ 182

Nonenal **386a** (200 mg, 1.42 mmol) was stirred at reflux in isopropenyl acetate (30 mL) together with *p*-TsOH (2 mg, 0.13 mmol) for 22 h. The mixture was diluted with ether (30 mL) washed with water (2 x 20 mL) and then brine (2 x 20 mL). The organic layer was dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (10% ether in petrol) to give **386** as a colourless oil which deteriorated upon standing (120 mg, 0.65 mmol, 46%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.90 (1H, d, *J* 6.2 Hz, =C*H*), 5.51 – 5.25 (2H, m, C*H*=C*H*), 4.87 (1H, app. q. *J* 7.2 Hz, =C*H*), 2.16 (3H, s, CH_3C=O), 2.22– 1.99 (6H, m, 3 x CH_2), 1.44 (2H, app. quin, *J* 7.4 Hz, CH_2), 0.95 (3H, t, *J* 7.7 Hz, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 168.2 (*C*=O), 134.3 (=*C*H), 132.2 (=*C*H) 128.7 (=*C*H), 114.1 (=*C*H), 29.4 (*C*H_3), 26.6 (*C*H_2), 24.1 (*C*H_2), 20.8 (*C*H_2), 20.7 (*C*H_2), 14.9 (*C*H_3) p.p.m.

Ethyl (2*E*,7*EZ*)-8-methoxy-2,7-octadienoate 387[81]



383a **387**

$C_9H_{14}O_3$ 170 $C_{11}H_{18}O_3$ 198

The Wittig salt, $MeOCH_2ClPPh_3$ (1.21 g, 3.52 mmol) was stirred in dry THF (30 mL) under a nitrogen atmosphere. *t*BuOK (394 mg, 3.52 mmol) was added and the reaction stirred for 1 h giving a bright red solution. Compound **383a** (300 mg, 1.76 mmol) was added dropwise *via* syringe as a solution in THF (10 mL) and the resulting orange solution to stirred for 1 h. The mixture was poured into water (20 mL) and extracted into ether (3 x 20 mL). The combined organic layers were then washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (20% ether in petrol) to give **387** as a colourless oil and an inseparable 3:2 mixture of *cis* and *trans* isomers (229 mg, 1.16 mmol, 66%).

^{1}H NMR (300 MHz, $CDCl_3$), δ_H 7.0 – 6.81 (1H, m, C*H*=CHC=O), 6.25 (1H, d, *J* 12.5 Hz, C*H*=CHOCH$_3$ (*trans*)), 5.85 (1H, d, *J* 6.2 Hz,C*H*=CHOCH$_3$

(*cis*)), 5.78 (1H, d, *J* 15.8 Hz, C*H*CO_2Et), 4.64 (1H, dt, *J* 12.5, 7.3 Hz, CH_2CH= (*trans*)), 4.23 (1H, dt, *J* 6.9, 6.2 Hz, CH_2CH= (*cis*)), 4.12 (2H, q, *J* 6.9 Hz, CH_2CH_3), 3.52 (3H, s, OCH_3), 3.45 (3H, s, OCH_3), 2.18 (2H, dt, *J* 6.9, 6.2 Hz, CH_2CH= (*cis*)), 2.04 (2H, dt, *J* 7.3, 6.9 Hz, CH_2CH= (*trans*)) 1.85 (2H, dt, *J* 6.9, 6.9 Hz, CH_2CH=C=O), 1.48 (2H, quin, *J* 7.1 Hz, $CH_2CH_2CH_2$), 1.24 (3H, t, *J* 6.9 Hz, CH_2CH_3) p.p.m.

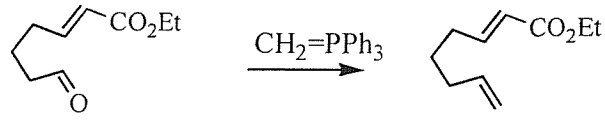
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 166.7 (CO_2), 149.3 (CH=$CHCO_2$), 147.6 (CH=$CHOCH_3$), 122.3 ($CHCO_2$), 102.0 (CH_2CH=$CHOCH_3$), 60.2 (CH_2CH_3), 55.9 (OCH_3), 31.4 (CH_2CH=CHO) 29.1 (CH_2CH=C=O), 28.1 ($CH_2CH_2CH_2$), 14.3 (CH_2CH_3) p.p.m. ^{13}C NMR spectra also contains signals relating to the *trans* isomer.

FT-IR ν_{max} (neat) 2932m, 2855w, 1718s, 1653s, 1454w, 1367m, 1266s, 1136s, 1042m, 935m cm^{-1}.

LRMS (CI) 199 ($[MH]^+$, 98%), 184 (100), 167 (88), 138 (32), 75 (28) amu.

These data are fully consistent with those published in the literature.[81]

Ethyl (2*E*)-2,7-octadienoate 388[82]



383a **388**

$C_9H_{14}O_3$ 170 $C_{10}H_{16}O_2$ 168

The Wittig salt $BrCH_2PPh_3$ (3.15 g, 7.5 mmol) was stirred in THF (40 mL) at -78°C under a nitrogen atmosphere. *n*-BuLi (5.35 mL of a 1.44 mol solution in hexanes) was added dropwise over 1 min *via* syringe and the mixture stirred at this temperature for 15 min. The whole was allowed to warm to ambient temperature over 90 min then cooled

to -78°C. **383a** (1 g, 5 mmol) was added as a solution in THF (10 mL) *via* syringe over 1 min and the reaction allowed to warm to ambient temperature over 30 min then stirred for 15 h. The mixture was diluted with ether (30 mL), washed with water (30 mL) and brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (5% ether in petrol) to give **388** as a colourless oil (537 mg, 3.1 mmol, 64%).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.92 (1H, dt, *J* 15.4, 6.9 Hz, CH_2CH=), 5.87 – 5.71 (2H, m, =C*H*, CH_2=C*H*), 5.02 (1H, d, *J* 17.1 Hz, =C*H*H), 4.97 (1H, d, *J* 9.9 Hz, =CH*H*), 4.38 (2H, q, *J* 7.1 Hz, CH_2CH_3), 2.21 (2H, dt, *J* 7.7, 6.6 Hz, CH_2CH), 2.07 (2H, dt, *J* 7.7, 6.6 Hz, CH_2CH), 1.56 (2H, app. quin, *J* 7.7 Hz, $CH_2CH_2CH_2$), 1.28 (3H, t, *J*, 7.1 Hz CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 166.8 (*C*=O), 149.1 (CH_2CH=), 138.1 CH_2=*C*H), 121.6 (*C*H=CH), 115.2 (=*C*H_2), 64.2 (O*C*H_2), 33.2 (*C*H_2CH), 31.6 (*C*H_2CH), 27.2 ($CH_2CH_2CH_2$), 14.4 (*C*H_3) p.p.m.

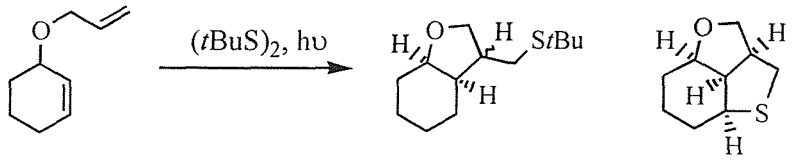
FT-IR ν_{max} (neat) 2931m, 1720s, 1652m, 1309m, 1264s, 1175s, 1041m, 978m, 911m cm^{-1}.

LRMS (CI) 186 ($[M+NH_4]^+$, 82%), 169 ($[MH]^+$, 100%) amu.

These data are consistent with those published in the literature.[83]

***tert*-Butyl perhydrobenzo[*b*]furan-3-ylmethyl sulfide 392,**

rel-(2aR,7bS) Perhydro[1]benzothiolo[4,3-bc]furan 393



389 **392** **393**

$C_9H_{14}O$ 138 $C_{13}H_{24}OS$ 228 $C_9H_{14}OS$ 170

Compound **389** (1.0 g, 7.2 mmol) was stirred in hexane (90 mL) together with $(t\text{BuS})_2$ (6.94 mL, 36 mmol) under hν irradiation in a quartz vessel for 24 h. Water (20 mL) was added and the mixture was extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromotography (10% ether in petrol) to give **392** (590 mg, 2.5 mmol, 36%) and **393** (220 mg, 1.3 mmol, 18%) as colourless oils.

Data for **392** a 1:1 mixture of diasteroisomers

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 4.12 (1H, app.t, *J* 5.14 Hz, OC*H*), 4.02 – 3.92 (3H, m, OC*H*, OCH_2), 3.62 – 3.53 (2H, m, OCH_2), 2.68 (1H, app.dd, *J* 10.2, 6.9 Hz, CH_2CH), 2.61 – 2.47 (4H, m, 2 x CH_2CH, SCH_2), 2.18 – 2.06 (1H, m, $CHCH_2$), 2.01 – 1.80 (4H, m, SCH_2, CH_2), 1.71 – 1.36 (10H, m, 5 x CH_2), 1.33 (20H, m, 3 x CH_3, CH_2), 1.21 – 1.09 (2H, m, CH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 78.4 (OCH), 76.3 (OCH), 72.2 (OCH_2), 70.9 (OCH_2), 44.5 (CH), 43.7 (CH), 43.6 (CH), 42.1 (CCH_3), 41.9 (CCH_3), 40.1 (CH), 32.4 (SCH_2), 31.1 (2 x CH_3), 30.9 (4 x CH_3), 28.5 (SCH_2), 28.2 (CH_2), 27.7 (CH_2), 26.4 (CH_2), 24.5 (CH_2), 23.8 (CH_2), 21.5 (CH_2), 21.1 (CH_2), 20.5 (CH_2) p.p.m.

FT-IR ν_{max} 2928s, 2241m, 1720w, 1458s, 1363s, 1239w, 1182s, 1120m, 1022s, 990m 910s cm^{-1}.

LRMS (CI) 229 ($[MH]^+$, 33%), 57 (100) amu.

HRMS (EI) Found $[M]^+$ 228.1548, $C_{13}H_{24}OS$ requires 228.1548 amu.

Data for **393**

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.96 – 3.82 (2H, m, OC*H*, OC*H*H), 3.77 (1H, d with fine splitting, *J* 6.9 Hz, OCH*H*), 3.55 – 3.48 (1H, m, C*H*S), 3.15 (1H, app.q, *J* 6.9 Hz, CH_2CHCH_2), 2.96 (1H, dd, *J* 9.4, 5.1 Hz, CHC*H*CH), 2.73 (1H, app. d, *J* 10.2 Hz, SC*H*H), 2.63 – 2.54 (1H, m *J* 7.7 Hz, SCH*H*), 2.17 – 1.96 (2H, m, CH_2), 1.91 – 1.67 (2H, m, CH_2), 1.64 – 1.46 (2H, m, CH_2) p.p.m.

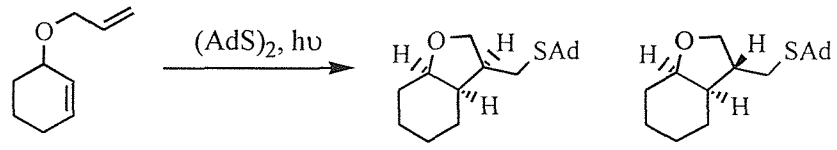
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 77.9 (O*C*H), 75.3 (OCH_2), 50.0 (S*C*H), 47.7 (*C*H), 47.3 (*C*H), 39.8 (SCH_2), 28.1 (CH_2), 26.7 (CH_2), 15.1 (CH_2) p.p.m.

FT-IR ν_{max} (neat) 2995s, 1713m, 1442m, 1270m, 1164w, 1078s, 1029s, 907s cm^{-1}.

LRMS (CI) 171 ($[MH]^+$, 100%) amu.

Adamantyl rel-(3S,3aR,7aR)-perhydrobenzo[b]furan-3-ylmethyl sulfide 394

Adamantyl rel-(3R,3aR,7aR)-perhydrobenzo[b]furan-3-ylmethyl sulfide 395



389 **394** **395**

$C_9H_{14}O$ 138 $C_{19}H_{30}OS$ 306 $C_{19}H_{30}OS$ 306

Compound **389** (1.01 g, 7.3 mmol) was stirred in hexane (90 mL) together with $(AdS)_2$ (12.1 g, 21.5 mmol) under hν irradiation in a quartz vessel for 24 h. Water (20 mL) was added and the mixture was extracted with ether (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (10% ether in petrol) to give **394** (1.30 g, 4.2 mmol, 58%) and **395** (260 mg, 0.84 mmol, 11%) as colourless oils.

Data for **394**

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 4.04 (1H, app. t, *J* 7.7 Hz, OC*H*), 3.78 (1H, dd, *J* 9.5, 6.1 Hz, OC*H*H), 3.42 (1H, dd, *J* 7.7, 6.1 Hz, OCH*H*), 2.50 (1H, dd, *J* 9.4, 8.5 Hz, OCH_2CH), 2.32 (1H, dd, *J* 11.1, 8.5, Hz, $CHCH_2S$), 2.06 – 1.86 (6H, m, 3 x CH_2), 1.85 - 1.63 (10H, m, 5 x CH_2), 1.62 – 1.50 (5H, m, CH_2 + 3 x CH), 1.49 – 1.05 (4H, m, 2 x CH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 77.6 (*O*CH), 72.3 (OCH_2), 44.8 (OCH*C*H), 44.3 (S*C*), 43.7 (3 x CH_2), 43.7 (OCH_2CH), 36.4 (3 x CH_2), 30.0 (3 x CH), 29.6 (SCH_2), 28.3 (CH_2), 27.8 (CH_2), 23.9 (CH_2), 21.1 (CH_2) p.p.m.

FT-IR ν_{max} (neat) 2903s, 2848m, 1448m, 1342w, 1299m, 1155w, 1043s, 1022s, 976w, 855w cm^{-1}.

LRMS (CI) 307 ($[M]^+$, 8%), 170 (10), 135 (100) amu.

HRMS (EI) Found $[M]^+$ 306.2019, $C_{19}H_{30}OS$ requires 306.2017 amu.

Data for **395**

^{1}H NMR (300 MHz, CDCl3) δ_H 4.05 – 3.91 (2H, m, OC*H* + OC*H*H), 3.61 – 3.52 (1H, m, OCH*H*), 2.62 – 2.46 (2H, m, OCH_2CH + $CHCH_2S$), 2.13 – 2.00 (6H, m, 3 x CH_2), 1.95 – 1.82 (10H, m, 5 x CH_2), 1.81 – 1.70 (5H, m, CH_2 + 3 x C*H*), 1.68 – 1.36 (4H, m, 2 x CH_2) p.p.m.

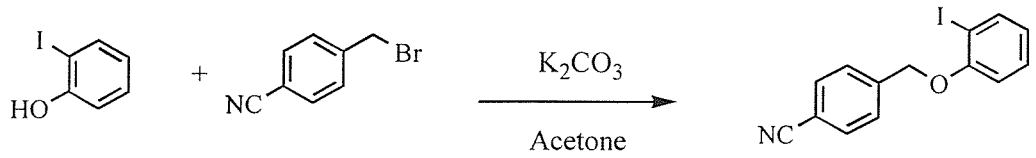
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 78.4 (O*C*H), 70.9 (OCH_2), 44.2 (OCH*C*H), 43.9 (S*C*), 43.7 (3 x CH_2), 40.1 (OCH_2CH), 36.4 (3 x CH_2), 29.8 (3 x *C*H), 28.6 (SCH_2), 24.5 (CH_2), 23.7 (CH_2), 21.6 (CH_2), 20.6 (CH_2) p.p.m.

FT-IR ν_{max} (neat) 2903s, 2848w, 1448m, 1342m, 1299m, 1155w, 1101w, 1022s, 976w, 855w cm^{-1}.

LRMS (CI) 307 ($[M]^+$, 22%), 171 (34), 135 (100) amu.

HRMS (EI) Found $[M]^+$ 306.2019, $C_{19}H_{30}OS$ requires 306.2017 amu.

4-(2'Iodophenoxy)methylbenzonitrile 422



422

C_6H_5IO 220 C_8H_6BrN 195 $C_{14}H_{10}INO$ 335

Benzonitrile **422** was prepared using a modification of the method of Sheppard.[83] 2-Iodophenol (2.29g, 10.41 mmol), potassium carbonate (1.83 g, 13.26 mmol) and 4-cyanobenzyl bromide (2.00g, 10.20 mmol) were stirred in acetone (20 mL) at ambient temperature for 16 h. The mixture was filtered and the solvent removed *in vacuo* to give **422** as a colourless solid (3.04 g, 9.07 mmol 89%).

m.p. 75 – 77 °C (EtOH)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.86 (1H, d, *J* 7.7 Hz, Ar*H*), 7.75 (2H, d, *J* 8.5 Hz, 2 x Ar*H*), 7.64 (2H, d, *J* 8.5 Hz, 2 x Ar*H*), 7.31 (1H, app. t, *J* 8.5 Hz, Ar*H*), 6.83 (1H, d, *J* 8.4 Hz, Ar*H*), 6.81 (1H, app. t, *J* 7.7 Hz, Ar*H*), 5.23 (2H, s, O*CH*$_2$) p.p.m.

^{13}C NMR (100 MHz, $CDCl_3$) δ_C 157.1 (*C* (Ar)), 142.3 (*C* (Ar)), 140.1 (*C*H (Ar)), 132.9 (2 x *C*H (Ar)), 129.9 (*C*H (Ar)), 127.7 (2 x *C*H (Ar)), 123.7 (*C*H (Ar)), 119.1 (*C*≡N), 112.9 (*C* (Ar)), 112.8 (*C*H (Ar)), 87.1 (*C*I (Ar)), 70.2 (O*C*H$_2$) p.p.m.

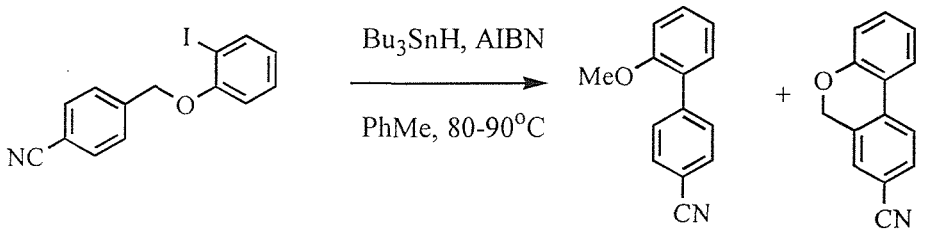
FT-IR ν_{max} (neat) 2372w, 2339w, 2220m, 1734m, 1586w, 1476m, 1362m, 1248s, 1129m, 1014s, 819s, 752s cm^{-1}.

LRMS (CI) 335 ([M]$^+$, 29%), 116 (100) amu.

CHN Found C 50.05 H 3.03 N 4.16, $C_{14}H_{10}INO$ requires C 50.17 H 3.01 N 4.18.

4-(2'-Methoxyphenyl)benzocarbonitrile 423[84]

6*H*-benzo[*c*]chromene-8-carbonitrile 424



422 **423** **424**

$C_{14}H_{10}INO$ 335 $C_{14}H_{11}NO$ 209 $C_{14}H_9NO$ 207

Nitrile **422** (800 mg, 2.39 mmol), tri-*n*-butyltin hydride (1.04 g, 3.58 mmol) and azo-*bis*-isobutyronitrile (60 mg, 0.36 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was cooled to ambient temperature, aqueous potassium fluoride (10% w/v, 20 mL) was added and the mixture stirred for 24 h. The mixture was then extracted with ether (3 x 20 mL) and the combined organic phases washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (10% ether in petrol) to provide **423** (364 mg, 1.74 mmol, 73%) and **424** (<4.94 mg, <0.02 mmol, <1%) as colourless oils.

Data for **423**

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.72 (4H, m, 4 x Ar*H*), 7.46 (1H, t, *J* 7.7 Hz, Ar*H*), 7.34 (1H, d, *J* 7.7 Hz, Ar*H*), 7.14 (1H, t, *J* 7.3 Hz, Ar*H*), 7.06 (1H, d, *J* 8.4 Hz, Ar*H*), 3.89 (1H, s, OCH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 156.4 (*C* (Ar)), 143.5 (*C* (Ar)), 131.9 (2 x *C*H (Ar)), 130.8 (*C* (Ar)), 130.4 (*C*H (Ar)), 130.1 (2 x *C*H (Ar)), 128.7 (*C* (Ar)), 121.2 (*C*H (Ar)), 119.3 (*C*≡N), 111.5 (*C*H (Ar)), 110.5 (*C*H (Ar)), 55.7 (O*C*H_3) p.p.m.

FT-IR ν_{max} (neat) 2978w, 2835w, 2210m, 1600m, 1481m, 1429w, 1262m, 1029m, 824m, 757s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 292 (1900), 262 (2900), 233 (3000) nm.

LRMS (CI) 209 ($[M]^+$, 100%), 194 (45), 140 (52) amu.

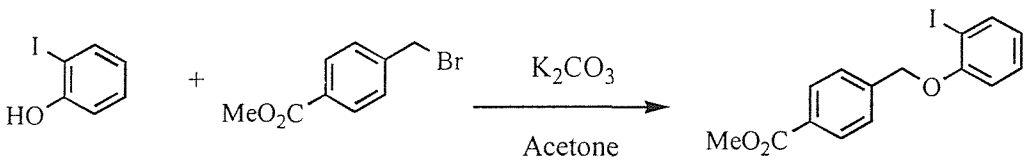
These data were consistent with those reported in the literature.[84]

Data for **424**

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.79 (1H, d, *J* 8.5 Hz, Ar*H*), 7.75 (1H, d, *J* 8.5 Hz, Ar*H*), 7.67 (1H, d, *J* 7.7 Hz, Ar*H*), 7.47 (1H, s, Ar*H*), 7.32 (1H, t, *J* 7.7 Hz, Ar*H*), 7.10 (1H, t, *J* 7.4 Hz, Ar*H*), 6.98 (1H, d, *J* 8.1 Hz, Ar*H*), 5.12 (2H, s, OCH_2) p.p.m.

This spectra is contaminated with **423** and residual tin compounds.

Methyl 4-[(2'iodophenoxy)methyl]benzoate 429



429

C_6H_5IO 220 $C_9H_9BrO_2$ 228 $C_{15}H_{13}IO_3$ 368

Ester **429** was prepared using a modification of the method of Sheppard.[83] 2-Iodophenol (1.17g, 5.3 mmol), potassium carbonate (1.83 g, 13.26 mmol) and methyl 4-(bromomethyl)benzoate (1.95g, 14.12 mmol) were stirred in acetone (20 mL) at ambient temperature for 16 h. The mixture was filtered and the solvent removed *in vacuo* to give **429** as a colourless solid (3.04 g, 9.07 mmol 89%).

m.p. 95 - 97°C (ether)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.09 (2H, d, *J* 8.0 Hz, 2 x Ar*H*), 7.82 (1H, d, *J* 7.3 Hz, Ar*H*), 7.60 (2H, d, *J* 8.0 Hz, 2 x Ar*H*), 7.30 (1H, t, *J* 7.7 Hz, Ar*H*), 6.86 (1H, d, *J* 7.7 Hz, Ar*H*), 6.78 (1H, t, *J* 7.7 Hz, Ar*H*), 5.18 (2H, s, OCH_2), 3.94 (3H, s, OCH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 166.9 (*C*=O), 156.9 (*C* (Ar)), 141.8 (*C* (Ar)), 139.7 (*C*H (Ar)), 130.1 (2 x *C*H (Ar)), 129.7 (*C* (Ar)), 129.6 (*C*H (Ar)), 126.8 (2 x *C*H(Ar)), 123.2 (*C*H(Ar)), 112.7 (*C*H(Ar)), 86.8 (*C*I (Ar)), 70.2 (OCH_2), 52.3 (OCH_3) p.p.m.

FT-IR ν_{max} (neat) 2992w, 1710s, 1619w, 1581w, 1486m, 1453m, 1272s, 1233m, 1100m, 1005m, 738s cm^{-1}.

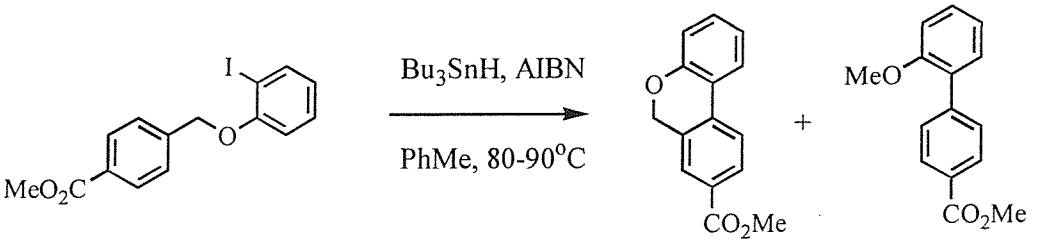
UV λ_{max} (CH_2Cl_2) 260 (3000), 220 (15000) nm.

LRMS (CI) 368 ($[M]^+$, 15%), 149 (100) amu.

CHN Found C 48.87 H 3.51, $C_{15}H_{13}IO_3$ requires C 48.93 H 3.56.

Methyl 6*H*-benzo[*c*]chromene-8-carboxylate 430

Methyl 4-(2'-methoxyphenyl) benzoate 431[85]



429

$C_{15}H_{13}IO_3$ 368

430

$C_{15}H_{12}O_3$ 240

431

$C_{15}H_{14}O_3$ 242

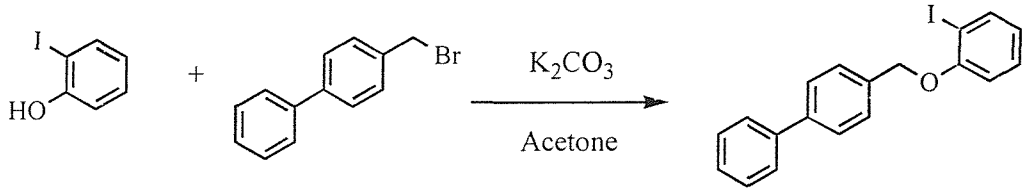
Ester **429** (800 mg, 2.17 mmol), tri-*n*-butyltin hydride (1.27 g, 4.35 mmol) and azobisisobutyronitrile (50 mg, 0.31 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium

fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide a colourless oil comprising of **430** and **431** as an inseparable 1:1 mixture (221 mg, 0.91 mmol, 42%).

GC-MS Retention time 12.07 min (CI) 242 ($[M]^+$, 100%), 211 (48), 168 (44), 139 (52) amu.

Retention time 12.76 min (CI) 240 ($[M]^+$, 100%) 209 (11), 181 (24), 152 (72) amu.

4'-[(2'-Iodophenoxy)methyl]biphenyl 432



432

C_6H_5IO 220 $C_{13}H_{11}Br$ 246 $C_{19}H_{15}IO$ 386

Benzonitrile **432** was prepared using a modification of the method of Sheppard.[83] 2-Iodophenol (1.68 g, 7.65 mmol), potassium carbonate (1.51 g, 10.94 mmol) and 4-(bromomethyl)biphenyl (1.80g, 7.29 mmol) were stirred in acetone (20 mL) at ambient temperature for 16 h. The mixture was filtered and the solvent removed *in vacuo* to give **432** as a colourless solid (2.08 g, 5.39 mmol, 74%).

m.p. 99 - 100°C (ethanol).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.91 (1H, d, *J* 7.7 Hz, Ar*H*), 7.71 – 7.59 (6H, m, 6 x Ar*H*), 7.53 (2H, app. t, *J* 7.7 Hz, 2 x Ar*H*), 7.42 (1H, d, *J* 8.0 Hz,

Ar*H*), 7.30 (1H, m, Ar*H*), 6.93 (1H, d, *J* 8.1 Hz, Ar*H*), 6.78 (1H, t, *J* 7.7 Hz, Ar*H*), 5.22 (2H, s, OCH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 157.4 (*C* (Ar)), 140.9 (*C* (Ar)), 139.7 (*C*H (Ar)), 135.7 (*C* (Ar)), 129.6 (*C*H (Ar)), 129.0 (2 x *C*H (Ar)), 127.7 (2 x (*C*H (Ar)), 127.5 (3 x *C*H (Ar)), 127.5 (2 x *C*H (Ar)), 127.3 (*C* (Ar)), 123.1 (*C*H (Ar)), 112.9 (*C*H (Ar)), 87.1 (*C*I (Ar)), 70.7 (*OC*H_2) p.p.m.

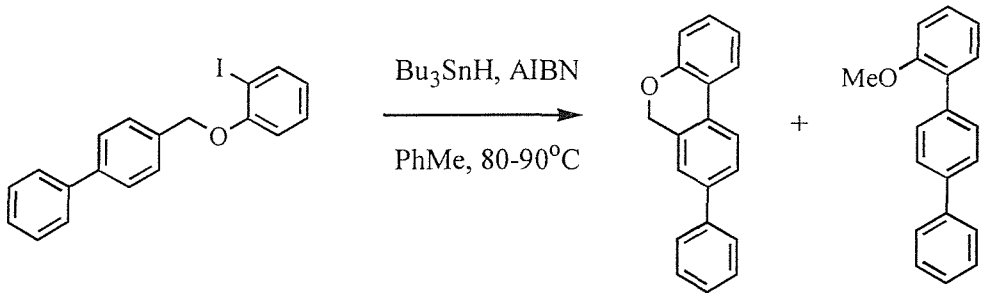
FT-IR ν_{max} (neat) 2975w, 3032w, 1736m, 1547w, 1480s, 1378s, 1250s, 1122w, 1065m, 768s, 691m cm^{-1}.

UV λ_{max} (CH_2Cl_2) 272 (33000) nm.

LRMS (CI) 386 ([M]$^+$, 2%), 167 (100) amu.

8-Phenyl-6*H*-benzo[*c*]chromene 433

4'-(2"-Methoxyphenyl)biphenyl 434[86]



432 $C_{19}H_{15}IO$ 386

433 $C_{19}H_{14}O$ 258

434 $C_{19}H_{16}O$ 260

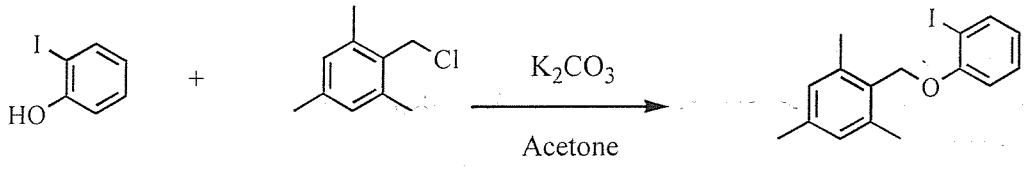
Iodide **432** (800 mg, 2.07 mmol), tri-*n*-butyltin hydride (905 mg, 3.11 mmol) and azo-*bis*-isobutyronitrile (60 mg, 0.37 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column

chromatography (20% ether in petrol) to provide a colourless oil comprising of a 1:2 mixture of **433** and **434** (5.37 mg, 2.28 mmol, 48%).

GC-MS Retention time 13.54 min (CI) 260 ([M]$^+$, 100%), 215 (22) amu.

Retention time 14.35 min (CI) 258 ([M]$^+$, 100%), 226 (19) amu.

1-[(2'-Iodophenoxy)methyl]2,4,6-trimethylbenzene 435



435

C_6H_5IO 220 $C_{10}H_{13}Cl$ 168 $C_{16}H_{17}IO$ 352

Benzonitrile **435** was prepared using a modification of the method of Sheppard.[83] 2-Iodophenol (2.74 g, 12.45 mmol), potassium carbonate (2.79 g, 20.16 mmol) and 2,4,6-trimethylbenzyl chloride (2.00g, 11.86 mmol) were stirred in acetone (20 mL) at ambient temperature for 16 h. The mixture was filtered and the solvent removed *in vacuo* to give **435** as a colourless solid (2.54 g, 7.23 mmol, 61%).

m.p. 56 - 58°C

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.86 (1H, d, *J* 7.7 Hz, Ar*H*), 7.39 (1H, t, *J* 8.1 Hz, Ar*H*), 7.05 (1H, d, *J* 8.1 Hz, Ar*H*), 6.97 (2H, s, 2 x Ar*H*), 6.78 (1H, t, *J* 7.7 Hz, Ar*H*), 5.11 (2H, s, OCH_2), 2.46 (6H, s, 2 x CH_3), 2.39 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 158.1 (*C* (Ar)), 139.7 (*C* (Ar)), 139.7 (*C*H (Ar)), 138.4 (*C* (Ar)), 138.3 (2 x *C* (Ar)), 129.6 (*C*H (Ar)), 129.2 (2 x

*C*H (Ar)), 122.9 (*C*H (Ar)), 112.9 (*C*H (Ar)), 87.2 (*C*I (Ar), 66.2 (OCH_2), 21.3 (2 x CH_3), 19.9 (CH_3) p.p.m.

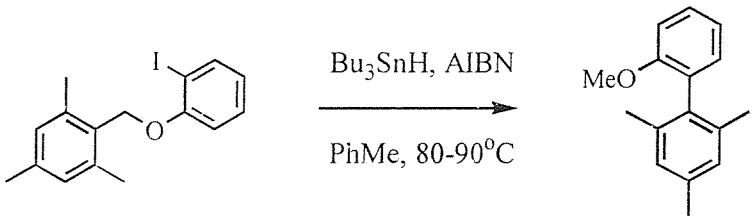
FT-IR ν_{max} (neat) 2963w, 2920w, 1610w, 1457m, 1381w, 1276m, 1243m, 1014m, 990m, 905s, 747s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 275 (3000), 229 (13600) nm

LRMS (CI) 352 ($[M]^+$, 8%), 209 (14), 133 (100) amu.

CHN Found C 54.53 H 4.82, $C_{16}H_{17}IO$ requires C 54.56 H 4.87.

1-(2'-Methoxyphenyl)-2,4,6-trimethylbenzene 436[87]



435 **436**

$C_{16}H_{17}IO$ 352 $C_{16}H_{18}O$ 226

Iodide **435** (800 mg, 2.27 mmol), tri-*n*-butyltin hydride (990 mg, 3.41 mmol) and azo-*bis*-isobutyronitrile (60 mg, 0.37 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide **436** as a colourless solid (405 mg, 1.79 mmol, 79%).

m.p. 48 - 50°C (ethanol)

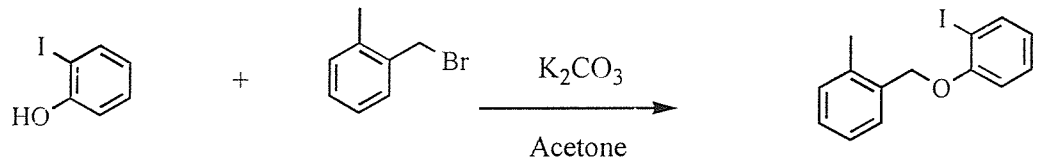
^{1}H NMR (300 MHz, CDCl3) δ_H 7.43 - 7.35 (1H, m, Ar*H*), 7.10 – 7.02 (3H, m, 3 x Ar*H*), 6.98 (2H, s, 2 x Ar*H*), 3.79 (3H, s, OCH_3), 2.38 (3H, s, CH_3), 2.04 (6H, s, 2 x CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 156.9 (*C* (Ar)), 136.7 (4 x *C* (Ar)), 135.4 (*C* (Ar)), 131.1 (*C*H (Ar)), 128.6 (*C*H (Ar)), 128.1 (2 x *C*H (Ar)), 120.8 (*C*H (Ar)), 110.9 (*C*H (Ar)), 55.6 (O*C*H_3), 21.3 (*C*H_3), 20.6 (2 x *C*H_3) p.p.m.

FT-IR ν_{max} (neat) 2968w, 2825w, 1596w, 1505w, 1448m, 1376w, 1233s, 1105m, 1062s, 1024s, 790s, 743s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 260 (2200), 218 (3700) nm.

1-[(2'-Iodophenoxy)methyl}2-methylbenzene 440



440

C_6H_5IO 220 C_8H_9Br 184 $C_{14}H_{13}IO$ 324

Iodide **435** was prepared using a modification of the method of Sheppard.[83] 2-Iodophenol (2.62 g, 11.94 mmol), potassium carbonate (2.79 g, 20.16 mmol) and 2-methylbenzyl bromide (2.00g, 10.86 mmol) were stirred in acetone (20 mL) at ambient temperature for 16 h. The mixture was filtered and the solvent removed *in vacuo* to give **440** as a colourless oil (1.05 g, 3.24 mmol, 21%).

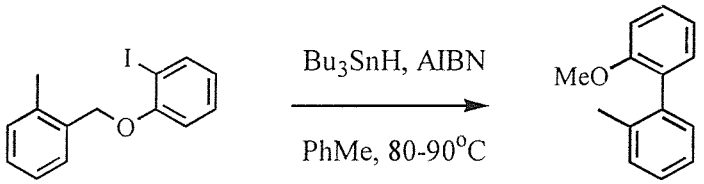
^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.82 (1H, dd, *J* 7.7, 1.1 Hz, Ar*H*), 7.59 (1H, m, Ar*H*), 7.38 – 7.21 (4H, m, 4 x Ar*H*), 6.94 (1H, d, *J* 7.3 Hz, Ar*H*), 6.76 (1H, t, *J* 7.7 Hz, Ar*H*), 5.16 (2H, s, OCH_2), 2.45 (3H, s, CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 157.4 (*C* (Ar)), 139.7 (*C*H (Ar)), 136.3 (*C* (Ar)), 134.5 (*C* (Ar)), 130.4 (*C*H (Ar)), 129.6 (*C*H (Ar)), 128.3 (*C*H (Ar)), 128.3 (*C*H (Ar)), 126.1 (*C*H (Ar)), 122.9 (*C*H (Ar)), 112.6 (*C*H Ar)), 86.8 (*C* (Ar)), 69.5 (OCH_2), 19.2 (CH_3) p.p.m.

FT-IR ν_{max} (neat) 2979w, 2865w, 1471s, 1431m, 1374w, 1268s, 1229s, 1048m, 1021m, 735s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 260 (1900), 212 (7100) nm.

1-(2'-Methoxyphenyl)-2-methylbenzene 441[88]



440 $C_{14}H_{13}IO$ 324

441 $C_{14}H_{14}O$ 198

Iodide **440** (800 mg, 2.46 mmol), tri-*n*-butyltin hydride (1.24 g, 3.69 mmol) and azo-*bis*-isobutyronitrile (100 mg, 0.45 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL), the combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo*, and purified by column

chromatography (20% ether in petrol) to provide **441** as a colourless oil (228 mg, 1.15 mmol, 47%).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 7.47 – 7.21 (6H, m, 6 x Ar*H*), 7.18 – 7.04 (2H, m, Ar*H*), 3.87 (3H, s, O*CH*$_3$), 2.29 (3H, s, *CH*$_3$) p.p.m.

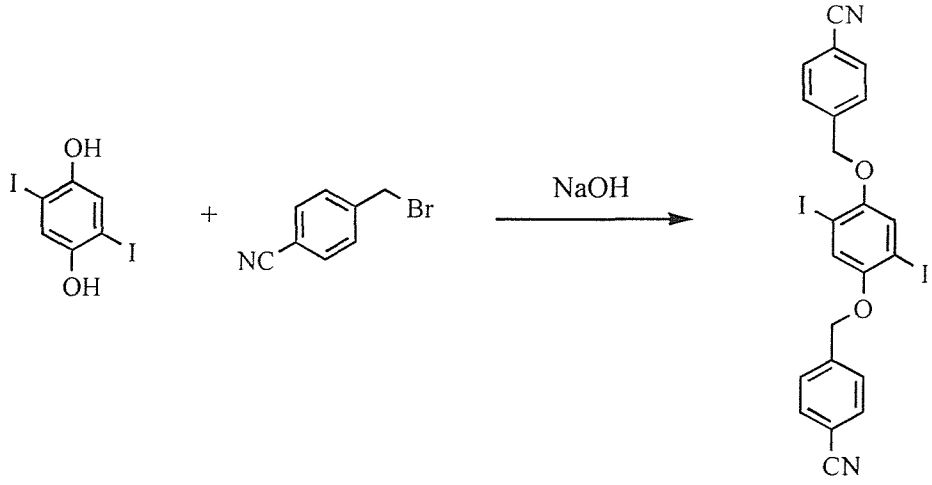
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 138.1 (*C* (Ar)), 131.6 (*C*H (Ar)), 130.1 (*C* (Ar)), 129.7 (*C*H (Ar)), 129.2 (*C*H (Ar)), 128.7 (*C* (Ar)), 128.3 (*C*H (Ar)), 127.4 (*C*H (Ar)), 125.6 (*C*H (Ar)), 125.5 (*C* (Ar)), 120.5 (*C*H (Ar)), 110.7 (*C*H (Ar)), 55.5 (O*C*H$_3$), 20.9 (*C*H$_3$) p.p.m.

FT-IR ν_{max} (neat) 2935w, 2909w, 1489m, 1453m, 1308w, 1237s, 1167w, 1030m, 999w, 876w, 743s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 254 (2600), 215 (4000) nm.

LRMS (CI) 198 ([M]$^+$, 26%), 175 (100) amu.

<u>1,4,-*bis*-(4-cyanobenzyoxy)-2,5-diiodo benzene 447</u>



445 $C_6H_4I_2O_2$ 362

446 C_8H_6BrN 195

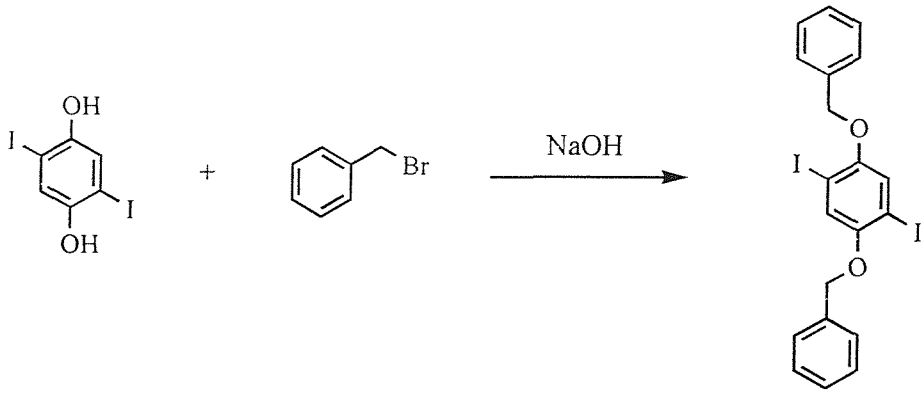
447 $C_{22}H_{14}I_2N_2O_2$ 592

Diiodide **447** was prepared using a procedure adapted from Hunig.[89] 2,5-Diiodohydroquinone (3.718 g, 10.2 mmol) was dissolved in NaOH (12.8 ml of a 2M solution) and ethanol (40 mL) then treated with 4-cyanobenzyl bromide (5.99 g, 30.5 mmol). The mixture was heated at reflux for 1 h then cooled and filtered to give **447** as a pink solid. (2.891 g, 4.8 mmol, 47%).

m.p. > 270°C

Due to the high boiling point and insoluble nature of this compound, no further data was obtained.

1,4-*bis*benzyloxy-2,5-diiodobenzene 448[89]



445 **448**

$C_6H_4I_2O_2$ 362 C_7H_7Br 170 $C_{20}H_{16}I_2O_2$ 542

Diiodide **448** was prepared using the procedure of Hunig.[89] 2,5-Diiodohydroquinone (1.5 g, 4.1 mmol) was dissolved in NaOH (5.1 mL of a 2M solution) and ethanol (40 mL) and treated with benzyl bromide (2.1 g, 12.3 mmol). The mixture was heated at reflux for 1 h then cooled and the precipitated solid filtered. The crude product was recrystallised from toluene to give **448** as a white solid (1.273 g, 2.3 mmol, 57%).

m.p. 171 - 172°C (toluene)

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.69 – 7.21 (12H, m, 12 x Ar*H*), 5.24 (4H, s, 2 x OCH_2) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 154.9 (2 x *C* (Ar)), 137.1 (2 x *C* (Ar)), 128.7 (4 x *C*H (Ar)), 128.2 (2 x *C*H (Ar)), 127.4 (4 x *C*H (Ar)), 123.6 (2 x *C*H (Ar)), 87.3 (2 x *C*l (Ar)), 72.2 (2 x OCH_2) p.p.m.

FT-IR ν_{max} (neat) 3441w, 1475s, 1444w, 1347s, 1219s, 1050s, 1014s, 906w, 845s, 789m, 732s cm^{-1}.

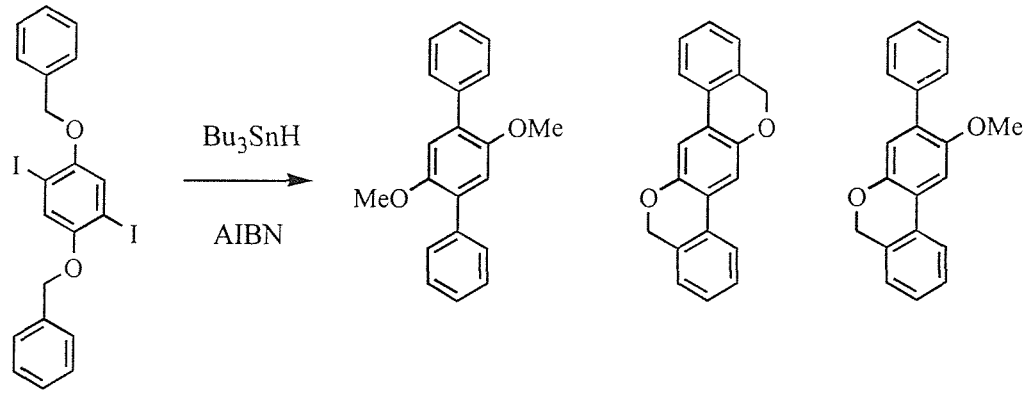
UV λ_{max} (CH_2Cl_2) 281 (1400), 242 (8200) nm.

LRMS (CI) 542 ($[M]^+$, 4%), 91 (100) amu.

2'5'-Dimethoxy-*p*-terphenyl 449

5,12-Dihydrobenzo[*c*]isochromeno-[3,4-g]chromene 450

2-Methoxy-3-phenyl- 6*H*-benzo[*c*]chromene 451



448 **449** **450** **451**

$C_{20}H_{16}I_2O_2$ 542 $C_{20}H_{18}O_2$ 290 $C_{20}H_{16}O_2$ 288 $C_{20}H_{14}O_2$ 286

Diiodide **448** (273 mg, 0.5 mmol), tri-*n*-butyltin hydride (218 mg, 0.75 mmol) and azo-*bis*-isobutyronitrile (12 mg, 0.07 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium

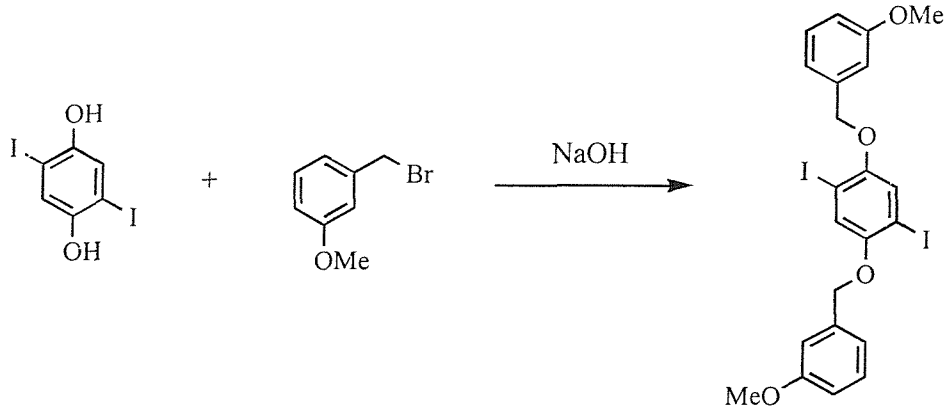
fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide a coulourless oil comprising of **449**, **450** and **451** as a 1:4:6 mixture (129 mg, 0.44 mmol, 88%).

GC-MS Retention time 6.67 (EI) 290 ($[M]^+$, 100%), 275 (28) amu

Retention time 7.14 (EI) 288 ($[M]^+$, 100%) 197 (62) amu

Retention time 8.26 (EI) 287 ($[M+H]^+$, 33%) amu.

1,4-*bis*(3-methoxybenzyloxy)-2,5-diiodobenzene 452



445 **452**

$C_6H_4I_2O_2$ 362 C_8H_9BrO 200 $C_{22}H_{20}I_2O_4$: 602

Diiodide **452** was prepared using a procedure adapted from Hunig.[89] Diiodohydroquinone (2.328 g, 6.4 mmol) was dissolved in NaOH (8.03 ml of a 2M solution) and ethanol (40 mL) and treated with 3-methoxybenzyl bromide (3.86 g, 19.2 mmol). The mixture was heated at reflux for 1 h then cooled and filtered. The crude product was recrystallised from DCM/petrol to give **452** as a colourless solid (3.12 g, 5.1 mmol, 81%).

m.p. 140 - 141°C (DCM/petrol)

^{1}H NMR (300MHz, $CDCl_3$) δ_H 7.41 – 7.27 (4H, m, 4 x Ar*H*), 7.12 (2H, s, 2 x Ar*H*), 7.07 (2H, d, *J* 8.1 Hz, 2 x Ar*H*), 6.95 – 6.36 (2H, m, 2 x Ar*H*), 5.07 (4H, s, 2 x OCH_2), 3.86 (6H, s, 2 x OCH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 159.9 (2 x *C* (Ar)), 152.8 (2 x *C* (Ar)), 137.9 (2 x *C* (Ar)), 129.7 (2 x *C*H (Ar)), 123.5 (2 x *C*H (Ar)), 119.4 (2 x *C*H (Ar)), 113.9 (2 x *C*H (Ar)), 112.6 (2 x *C*H (Ar)), 86.6 (2 x *C*I (Ar)), 71.8 (2 x OCH_2), 55.4 (2 x OCH_3) p.p.m.

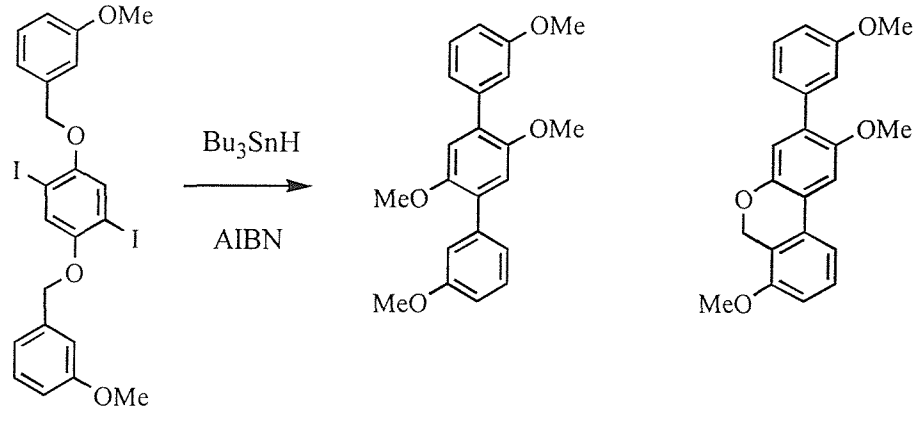
FT-IR ν_{max} (neat) 2960w, 2883w, 1608m, 1485m, 1367m, 1250s, 1163s, 1040s, 840s, 789s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 312 (1400), 281 (1600), 235 (4700) nm.

CHN Found C 43.85 H 3.30, $C_{22}H_{20}O_2I_4$ requires C 43.88 H 3.35.

2',3,3",5-Tetramethoxy-*p*-terphenyl 453

2,7-Dimethoxy-8-(3-methoxyphenyl)-benzo[*c*]chromene 454



452 **453** **454**

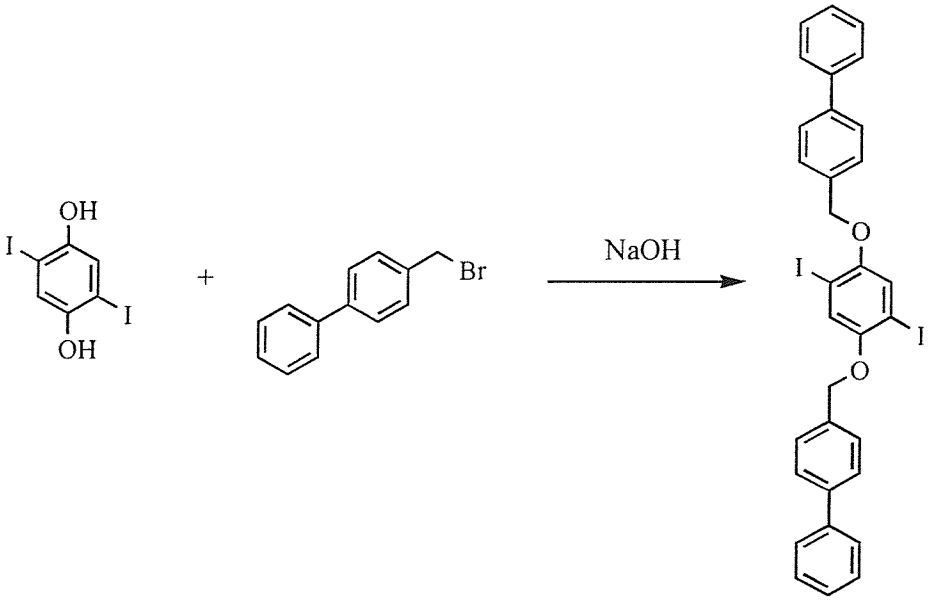
$C_{22}H_{20}I_2O_4$ 602 $C_{22}H_{22}O_4$ 350 $C_{22}H_{20}O_4$ 348

Iodide **452** (1.242 mg, 2.0 mmol), tri-*n*-butyltin hydride (873 mg, 3.0 mmol) and azobisisobutyronitrile (48 mg, 0.3 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide a colourless oil comprising of a 2:3 mixture of **453** and **454** (237 mg, 0.67 mmol, 33%).

GCMS Retention time 17.07 (CI) 350 ($[M]^+$, 38%) 121 (100) amu.

Retention time 16.81 (CI) 348 ($[M]^+$, 100%) amu

1,4-*bis*-*p*-Biphenyloxy-2,5-diiodobenzene 455



445 **455**

$C_6H_4I_2O_2$ 362 $C_{13}H_{11}Br$ 246 $C_{32}H_{24}I_2O_2$ 694

Diiodide **455** was prepared using a procedure adapted from Hunig.[89] 2,5-Diiodohydroquinone (2.328 g, 6.4 mmol) was dissolved in NaOH (8.03 ml of a 2M solution) and ethanol (40 mL) and treated with 4-(bromomethyl)biphenyl (3.98 g, 19.2 mmol). After heating at reflux for 1 h the mixture was then cooled, filtered and the resulting solid recrystallised from DCM/petrol to give **455** as a colourless solid (2.97 g, 4.2 mmol, 66%).

m.p. 236 - 238°C (DCM/petrol)

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.59 – 7.38 (14H, m, 14 x Ar*H*), 7.36 – 7.24 (2H, m, 2 x Ar*H*), 7.25 – 7.16 (2H, m, 2 x Ar*H*), 7.11 (2H, s, 2 x Ar*H*) 4.98 (4H, s, 2 x OCH_2) p.p.m.

^{13}C NMR (100 MHz, CDCl3) δ_C 154.1 (2 x *C* (Ar)), 142.2 (2 x *C* (Ar)), 140.1 (2 x *C* (Ar)), 135.4 (2 x *C* (Ar)), 129.2 (4 x *C*H (Ar)), 128.1 (4 x *C*H (Ar)), 127.7 (5 x *C*H (Ar)), 127.5 (5 x *C*H (Ar)), 124.1 (2 x *C*H (Ar)), 87.1 (2 x *C*I (Ar)), 72.3 (2 x O*C*H_2) p.p.m.

FT-IR ν_{max} (neat) 2955w, 2863w, 1480m, 1449w, 1342m, 1193s, 1055s, 999s, 871w 773s cm^{-1}.

UV λ_{max} (CH_2Cl_2) 292 (1000), 232 (9000) nm.

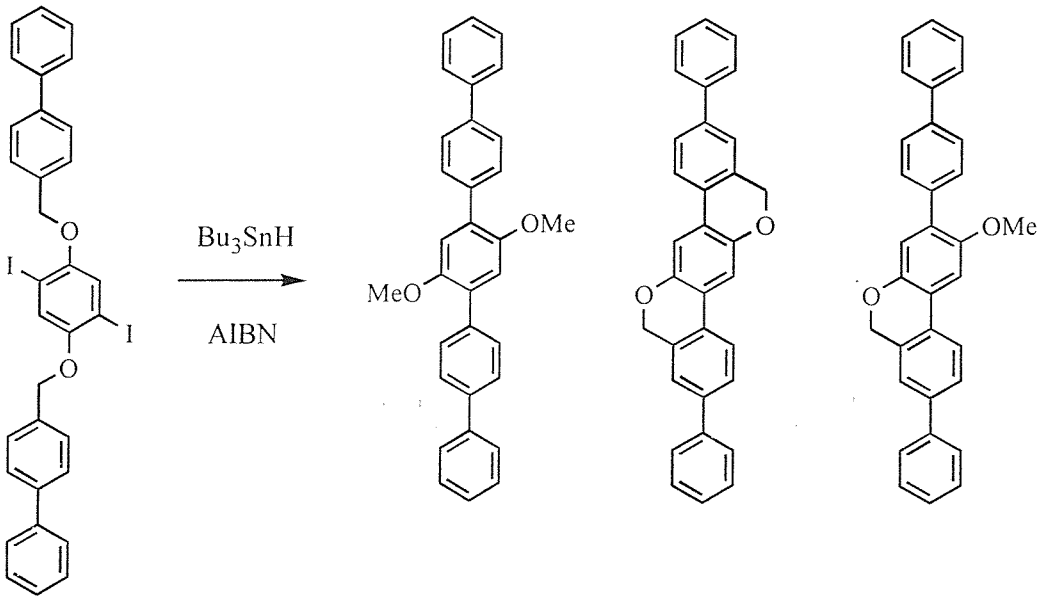
CHN Found C 55.71 H 3.47, $C_{32}H_{24}O_2I_2$ requires C 55.35 H 3.48.

The high molecular weight prevented a satisfactory mass spectra from being obtained.

2",5", Dimethoxypentaphenyl 456

Pentaphenyl 457

8-*p*-Biphenyl-7-methoxy-3-phenyl-benzo[*c*]chromene 458



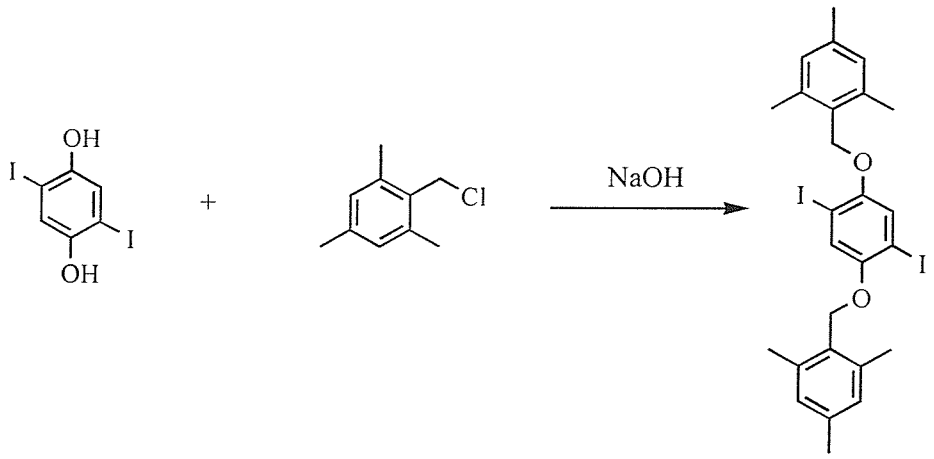
455 **456** **457** **458**

$C_{32}H_{24}I_2O_2$ 694 $C_{32}H_{26}O_2$ 442 $C_{32}H_{24}O_2$ 440 $C_{32}H_{22}O_2$ 438

Diiodide **455** (2.162 g, 3.1 mmol), tri-*n*-butyltin hydride (1.35 g, 4.6 mmol) and azobisisobutyronitrile (74 mg, 0.4 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide a colourless oil comprising a mixture of **456**, **457** and **458** (532 mg, 1.2 mmol, 38%).

LRMS (EI) 442 ($[M]^+$, 7%), 440 ($[M]^+$, 15%), 438 ($[M]^+$, 13%) 167 (100) amu.

2,5-*bis*-(2,4,6-Trimethylbenzyloxy)-1,4-diiodobenzene 459



445 **459**

$C_6H_4I_2O_2$ 362 $C_{10}H_{13}Cl$ 168 $C_{26}H_{28}I_2O_2$ 626

Diiodide **459** was prepared using a procedure adapted from Hunig.[89] Diiodohydroquinone (3.0 g, 8.3 mmol) was dissolved in NaOH (10.3 ml of a 2M solution) and ethanol (40 mL) and treated with 2,4,6-trimethylbenzyl chloride (2.79 g, 16.6 mmol). The mixture was heated at reflux for 1 h then cooled, filtered and the resulting solid recrystallised from (ethanol) to give **459** as a colourless solid. (3.27 g, 5.2 mmol, 63%).

m.p. 230-232°C (ethanol)

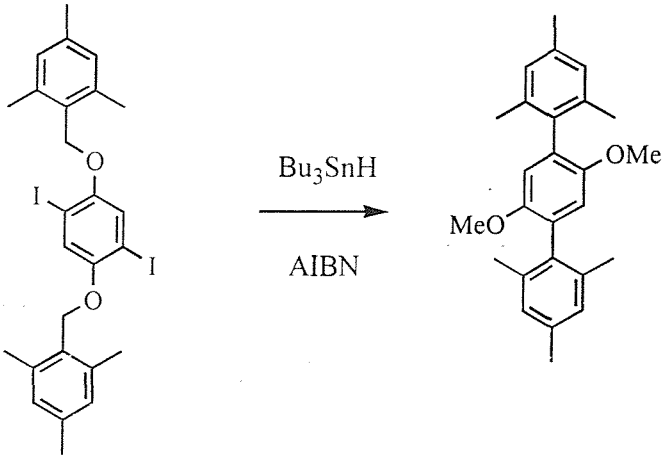
^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.18 (4H, s, 4 x Ar*H*), 6.78 (2H, s, 2 x Ar*H*), 4.52 (4H, s, 2 x OCH_2), 2.26 (12H, s, 4 x CH_3), 2.15 (6H, s, 2 x CH_3) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 153.4 (2 x *C* (Ar)), 138.5 (2 x *C* (Ar)), 138.4 (4 x *C* (Ar)), 129.3 (2 x *C* (Ar)), 129.2 (4 x *C*H (Ar)), 123.7 (2 x *C*H (Ar)), 86.7 (2 x *C*I (Ar)), 67.3 (2 x OCH_2), 21.2 (2 x CH_3), 19.9 (4 x CH_3) p.p.m.

FT-IR ν_{max} (neat) 2924w, 2842w, 1731m, 1454s, 1362m, 1342s, 1198s, 1055m, 988s, 830s, 763m cm^{-1}.

UV λ_{max} (CH_2Cl_2) 302 (1100), 228 (5000) amu.

2', 2",4',4",6', 6"-hexamethyl-2',5'-methoxy-*p*-terphenyl 460



459 **460**

$C_{26}H_{28}I_2O_2$ 626 $C_{26}H_{30}O_2$ 374

Diiodide **459** (1.166 g, 1.86 mmol), tri-*n*-butyltin hydride (811 mg, 2.79 mmol) and azo-*bis*-isobutyronitrile (44 mg, 0.3 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was then cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide **460** as a colourless solid (466 mg, 1.2 mmol, 67%).

m.p. 210 - 212°C (ethanol).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.06 (4H, s, 4 x Ar*H*), 6.73 (2H, s, 2 x Ar*H*), 3.73 (6H, s, 2 x OC*H*$_3$), 2.45 (6H, s, 2 x C*H*$_3$), 2.17 (12H, s, 4 x C*H*$_3$) p.p.m.

^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 150.7 (2 x *C* (Ar)), 136.7 (4 x *C* (Ar)), 136.6 (2 x *C* (Ar)), 135.4 (2 x *C* (Ar)), 129.1 (2 x *C* (Ar)), 128.6 (4 x *C*H (Ar)), 113.9 (2 x *C*H (Ar)), 56.2 (2 x OCH$_3$), 21.2 (2 x *C*H$_3$), 20.3 (4 x *C*H$_3$) p.p.m.

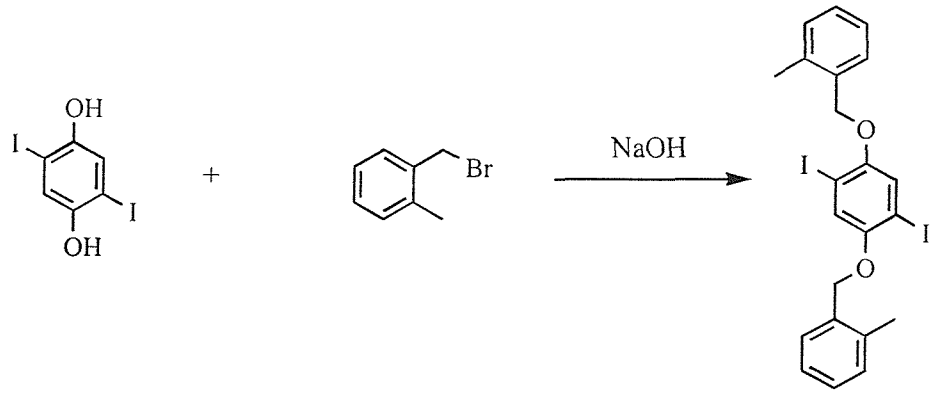
FT-IR ν_{max} (neat) 2929w, 2852w. 1511m, 1480m, 1378m, 1203s, 1060s, 866m, 845s, 778m, 732w cm^{-1}.

UV λ_{max} (CH_2Cl_2) 293 (2400), 222 (5200) nm.

LRMS (CI) 374 ([M]$^+$, 100%) amu.

HRMS Found 374.2249, $C_{26}H_{30}O_2$ requires 374.2245 amu.

1,4-*bis*-(2-Methylbenzyloxy)-2,5-diiodobenzene 461



445 **461**

$C_6H_4I_2O_2$ 362 C_8H_9Br 184 $C_{22}H_{20}I_2O_2$ 570

Diiodide **461** was prepared using a procedure adapted from Hunig.[89] 2,5-Diiodohydroquinone (3.5 g, 9.6 mmol) was dissolved in NaOH (12.8 ml of a 2M

solution) and ethanol (40 mL) and treated with 2-methylbenzyl bromide (5.29 g, 28.8 mmol). The mixture was heated at reflux for 1 h then cooled, filtered and the solid recrystallised from DCM/petrol to give **461** as a colourless solid. (2.97 g, 5.2 mmol, 54%).

m.p. 188 – 190 °C (DCM/petrol).

^{1}H NMR (300MHz, $CDCl_3$) δ_H 7.59 – 7.49 (2H, m, 2 x Ar*H*), 7.37 – 7.18 (8H, m, Ar*H*), 5.06 (4H, s, 2 x OCH_2), 2.46 (6H, s, 2 x CH_3), p.p.m.

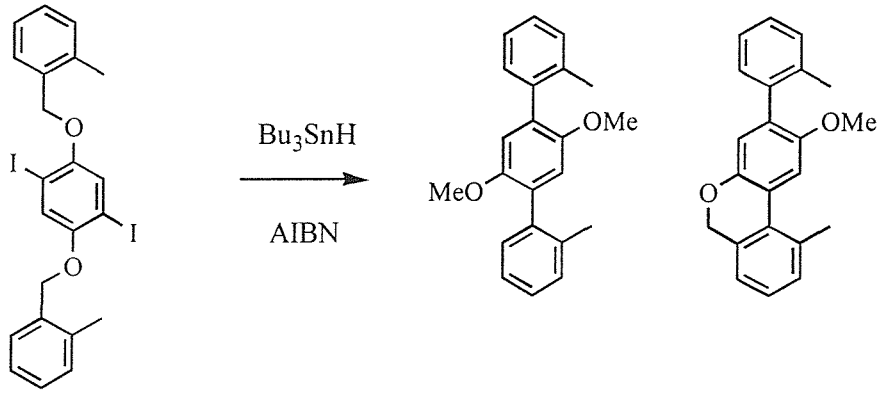
^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 153.1 (2 x *C* (Ar)), 136.5 (2 x *C* (Ar)), 135.2 (2 x *C* (Ar)), 130.4 (2 x *C*H (Ar)), 128.6 (2 x *C*H (Ar)), 128.4 (2 x *C*H (Ar)), 126.2 (2 x *C*H (Ar)), 123.4 (2 x *C*H (Ar)), 86.4 (2 x *C*I (Ar)), 70.2 (2 x O*C*H_2), 19.2 (2 x *C*H_3) p.p.m.

FT-IR ν_{max} (neat) 2960w, 2847w, 1485m, 1352s, 1219s, 1055m, 840m, 830m cm^{-1}.

UV λ_{max} (CH_2Cl_2) 292 (4000), 223 (10000) nm.

2,2"-Dimethyl-2',5'-dimethoxy-*p*-terphenyl 462

5-Methyl-7-methoxy-8-(2-methylphenyl)-benzo[*c*]chromene 463



461 $C_{22}H_{20}I_2O_2$ 570

462 $C_{22}H_{22}O_2$ 318

463 $C_{22}H_{20}O_2$ 316

Diiodide **461** (1.796 g, 3.3 mmol), tri-*n*-butyltin hydride (1.44 g, 4.95 mmol) and azo-*bis*-isobutyronitrile (79 mg, 0.5 mmol) were stirred in toluene (40 mL) at 85°C for 20 h. The mixture was cooled to ambient temperature and aqueous potassium fluoride (10% w/v, 20 mL) was added. The mixture was stirred for 24 h then extracted with ether (3 x 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (20% ether in petrol) to provide a colourless oil comprising a 2:1 **462** and **463** as inseparable colourless oils (640 mg, 2.0 mmol, 61%).

GC-MS Retention time 13.62 min (CI) 318 ($[M]^+$, 100%) amu

Retention time 15.04 min (CI) 316 ($[M\}^+$, 100%) amu.

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