UNIVERSITY OF SOUTHAMPTON

New Aromatic Annulation Reactions and their Application in Total Synthesis

by

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A thesis submitted for the degree of Doctor of Philosophy

Department of Chemistry

Faculty of Science

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ABSTRACT

FACULTY OF SCIENCE

CHEMISTRY

Doctor of Philosophy

New Aromatic Annulation Reactions and their Application in Total Synthesis

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This thesis describes new methods for the construction of polycylic molecules.

A new benzannulation reaction involving a tandem Horner-Emmons and Claisen condensation sequence was developed and applied to the syntheses of six arylnaphthalene lignans: taiwanin C, justicidin E, chinensin, retrochinensin, justicidin B and retrojusticidin B.

The tin-mediated addition of aryl radicals to various electron-rich condensed heterocycles was also investigated. 5-*Exo*-trig additions of *N*-tethered aryl radicals to indoles were demonstrated and shown to be more efficient when the radical intermediate was flanked by substituents.

Addition of aryl radicals to C-2 and C-3 of indoles, benzo[*b*]thiophenes and benzo[*b*]furans were also studied and the course followed found to be strongly influenced by the nature of the constituent heteroatom. When a *cis*-alkene was used to tether the arene to the heterocycle a 6-*endo*-trig radical cyclisation pathway was followed, leading to the corresponding polyaromatic system. A notable exception arose when the aryl radical was tethered to C-3 of a benzo[*b*]thiophene or benzo[*b*]furan. In such cases, an addition-elimination-reduction pathway dominated, yielding the corresponding 2-(2-naphthyl)-(thio)phenol.

With an alkane or benzyl ether as the tether, cyclisations generally proceeded *via* 5-*exo*-trig addition of the aryl radical to the tethering carbon. However, with benzo[*b*]furans and *N*-acetyl indoles, C-3 tethered aryl radicals preferentially underwent 6-*endo*-trig addition to C-2 of the heterocycle in a reductive fashion. A total synthesis of demethylhomopterocarpin using this methodology is described.

Two literature reviews are presented. The first outlines previous synthetic routes to the arylnaphthalene lignans. The second is concerned with the addition of carbon-centred radicals to electron-rich heteroaromatic ring systems.

Contents

Preface

The research described in this thesis was carried out under the supervision of Dr. D. C. Harrowven at the University of Southampton between August 2000 and August 2003. No part of this thesis has previously been submitted for a degree.

Acknowledgements

Sorry if this is a bit long or tends towards the soppy side, but there so many people I am indebted to. So, here we go: I'd like to thank (deep breath)...

Neil Wells and Joan Street for their sterling work in keeping the NMR services running. In particular, I'd like to thank Neil for analysing the odd sample or two for me and for teaching me the "joys" of EndNote!

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My in-laws, Terry, Jane and Ali. You are the best friends anyone could wish for.

My family, especially my mum and dad. You've supported me wholeheartedly in everything I've done, and always let me take my own path. I'll never stop being grateful for that.

Finally, my wife, Jo. This thesis is dedicated to you. You've been with me through everything, so there is so much to thank you for, I wouldn't be able to fit it in this entire volume. But, I think you *know* what I want to say here...

Abbreviations

Ac	acetyl
ACN	1,1'-azobis(cyclohexanecarbonitrile)
AIBMe	dimethyl 2,2'-azobis(isobutyrate)
AIBN	2,2'-azobis(isobutyronitrile)
i-Am	isoamyl
amu	atomic mass units
aq.	aqueous
Ar	aryl
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Bs	benzenesulfonyl
Bu	butyl
Bz	benzoyl
t-Bu	*tert*-butyl
celite	Celite 521®
CHN	combustion analysis
CI	chemical ionisation
conc.	concentrated
COSY	correlation spectroscopy
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
decomp.	decomposition
DHP	3,4-dihydro-2*H*-pyran
DIAD	di-isopropylazodicarboxylate
diglyme	diethylene glycol dimethyl ether
DMAP	4-(dimethylamino)pyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide

EI	electron ionisation
eq.	equivalents
ES	electrospray
Et	ethyl
ether	diethyl ether
FT	Fourier transform
GC	gas chromatography
hr(s)	hour(s)
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
hν	visible/ultraviolet radiation
Hz	hertz
IR	infrared
LDA	lithium diisopropylamide
lit.	literature
LRMS	low resolution mass spectrometry
m	*meta*
M	mol dm^{-3}
Me	methyl
min(s)	minute(s)
mol. sieves	molecular sieves
MOM	methoxymethyl
mp	melting point
Ms	methanesulfonyl
MS	mass spectrometry
NBS	*N*-bromosuccinimide
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
[O]	oxidation
o	*ortho*
p	*para*
PCC	pyridinium chlorochromate

petrol	petroleum ether (40/60)
Ph	phenyl
ppm	parts per million
Pr	propyl
i-Pr	isopropyl
PPTS	pyridinium *para*-toluenesulfonate
quant.	quantitative
RSM	recovered starting material
RT	room temperature
SAR	structural activity relationship
SEM	2-trimethylsilylethoxymethoxy
SET	single electron transfer
TBAF	tetrabutylammonium fluoride
TBDMS	*tert*-butyldimethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMS	trimethylsilyl
Ts	*para*-toluenesulfonyl
UV/Vis	ultraviolet/visible spectrometry
Δ	reflux

"I do not know what I may appear to the world, but to myself I seem to have been only like a boy playing on the seashore, and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me."

Isaac Newton

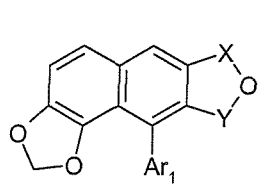
Chapter 1

The Synthesis of Arylnaphthalene Lignans

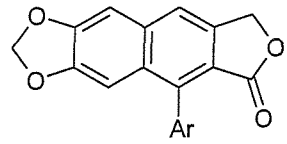
This chapter presents a brief review of the literature concerning the synthesis of arylnaphthalene lignans. Natural sources of the lignans and their observed biological activities are discussed. A new approach to their synthesis is then outlined.

1.1 Background

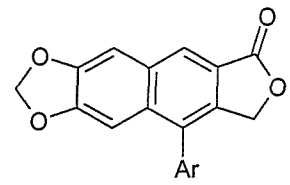
The arylnaphthalene lignan family of natural products occur widely in nature and are often identified as the constituents of tree barks and plants with folkloric medicinal use (**Figure 1**).[1-19]



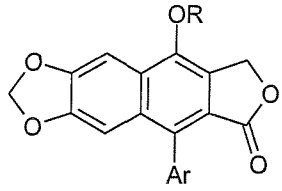
X = CH_2, Y = C(O) retrohelioxanthin **1**
X = C(O), Y = CH_2 helioxanthin **2**



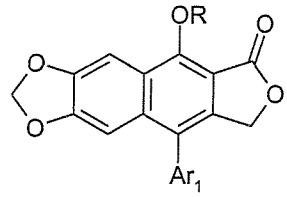
Ar = Ar_1 taiwanin C **3**
Ar = Ar_2 chinensin **4**
Ar = Ar_3 dehydrodeoxypodophyllotoxin **5**



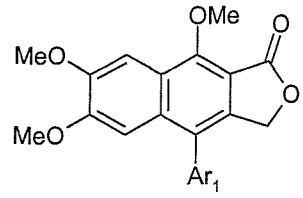
Ar = Ar_1 justicidin E **6**
Ar = Ar_2 retrochinensin **7**



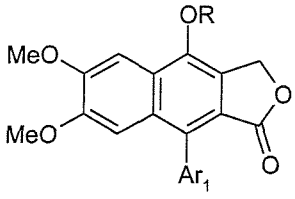
R = H, Ar = Ar_1 taiwanin E **8**
R = H, Ar = Ar_2 chinensinaphthol **9**
R = H, Ar = Ar_3 dehydropodophyllotoxin **10**
R = Me, Ar = Ar_1 justicidin F **11**



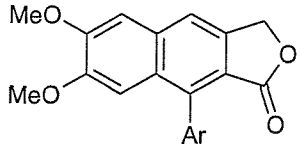
R = H retrotaiwanin E **12**
R = Me justicidin D **13**



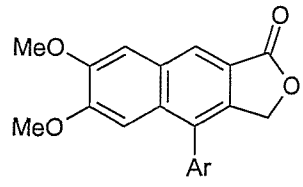
justicidin C **14**



R = H diphyllin **15**
R = Me justicidin A **16**



Ar = Ar_1 justicidin B **17**
Ar = Ar_2 dehydrodimethylretrodendrin **18**



Ar = Ar_1 retrojusticidin B **19**
Ar = Ar_2 dehydrodimethylconidendrin **20**

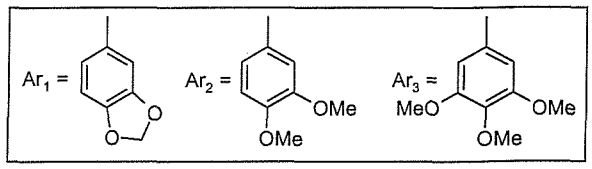


Figure 1

As is evident from **Figure 1**, this class of lignans show considerable variation in the substituents attached to the aromatic rings. The 5, 6, 7 and 8 positions of the naphthalene moiety, as well as the 3', 4' and 5' positions of the attached phenyl ring, are typically substituted with methoxy or methylenedioxy groups, and at the 2 and 3 positions of the naphthalene moiety a γ-lactone is fused.

In addition, this series has been subdivided based on the orientation of the lactone carbonyl. If the lactone carbonyl points toward the phenyl ring the lignan is designated a *lactone*; if the lactone carbonyl points away from the phenyl ring the lignan is designated a *retrolactone* (**Figure 2**).

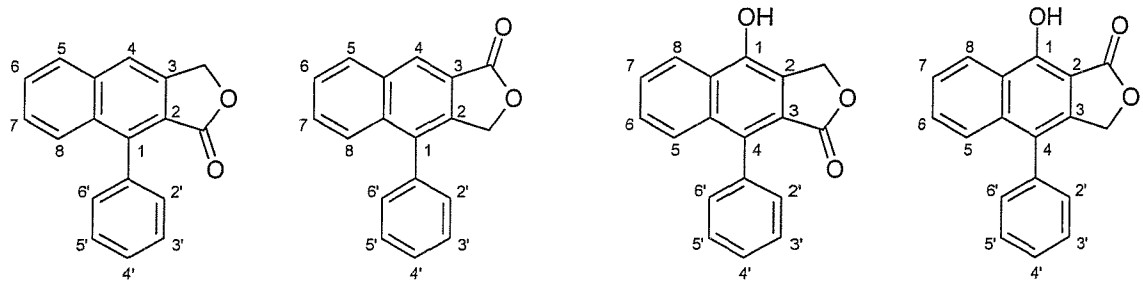


Figure 2

A great amount of effort has gone into synthesising these lignans in order to ascertain their potential as therapeutic agents and leads.[20-25] Numerous biological assays have been conducted and antiplatelet,[26] antiviral,[7,20,21,27-30] cytotoxic,[4,22,31-33] antifungal[23,34] and antidepressant[15] activities have all been reported. In addition, lactones taiwanin C **3**, chinensin **4** and justicidin B **17** are potent bone resorption inhibitors[29] and are lead compounds in the search for new rheumatoid arthritis therapies.[35]

1.2 Synthetic Approaches to the Arylnaphthalene Lignans

Although there are many different syntheses of arylnaphthalene lignans in the literature, the majority can be categorised into three main strategies according to the key step:

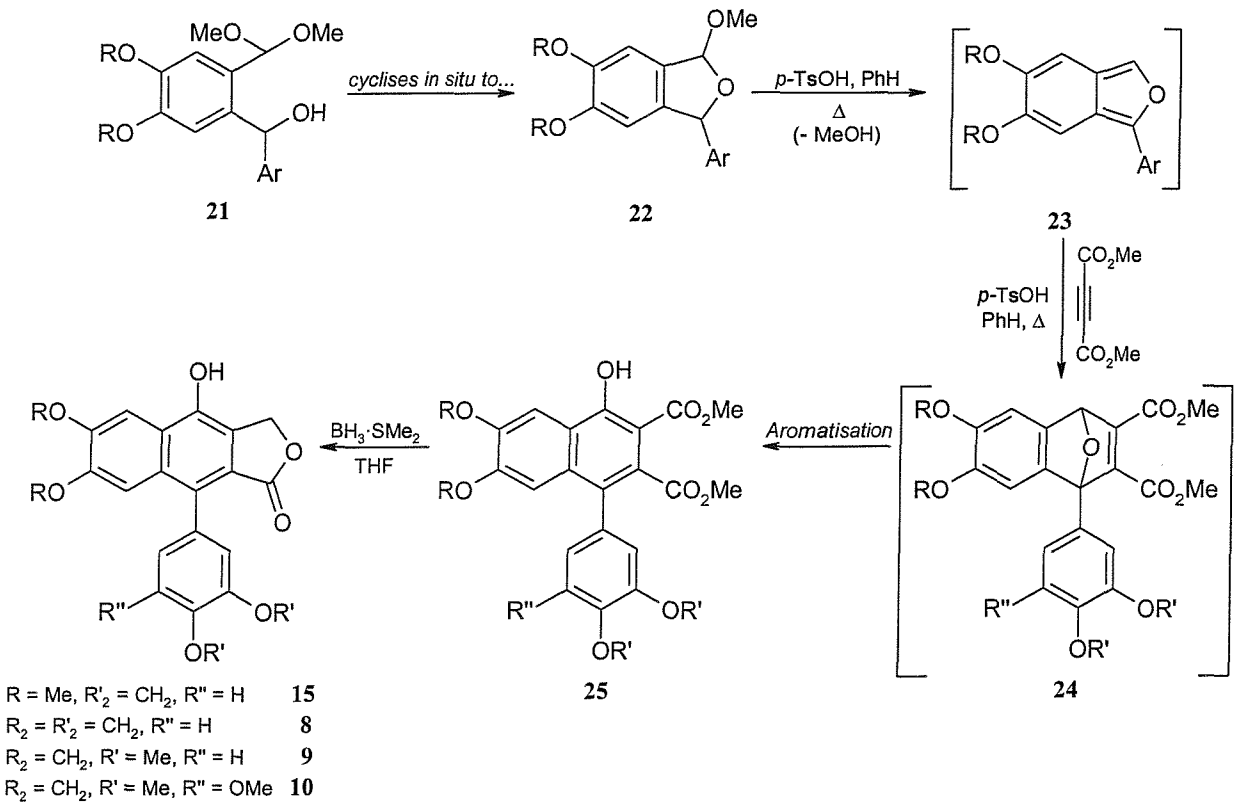
1.2.1 Diels-Alder cycloaddition to a benzo[*c*]furan intermediate

1.2.2 Diels-Alder cycloaddition to a quinodimethane

1.2.3 Michael-addition to 2-(5*H*)-furanone followed by a ring closing protocol to generate the 1-arylnaphthalene skeleton.

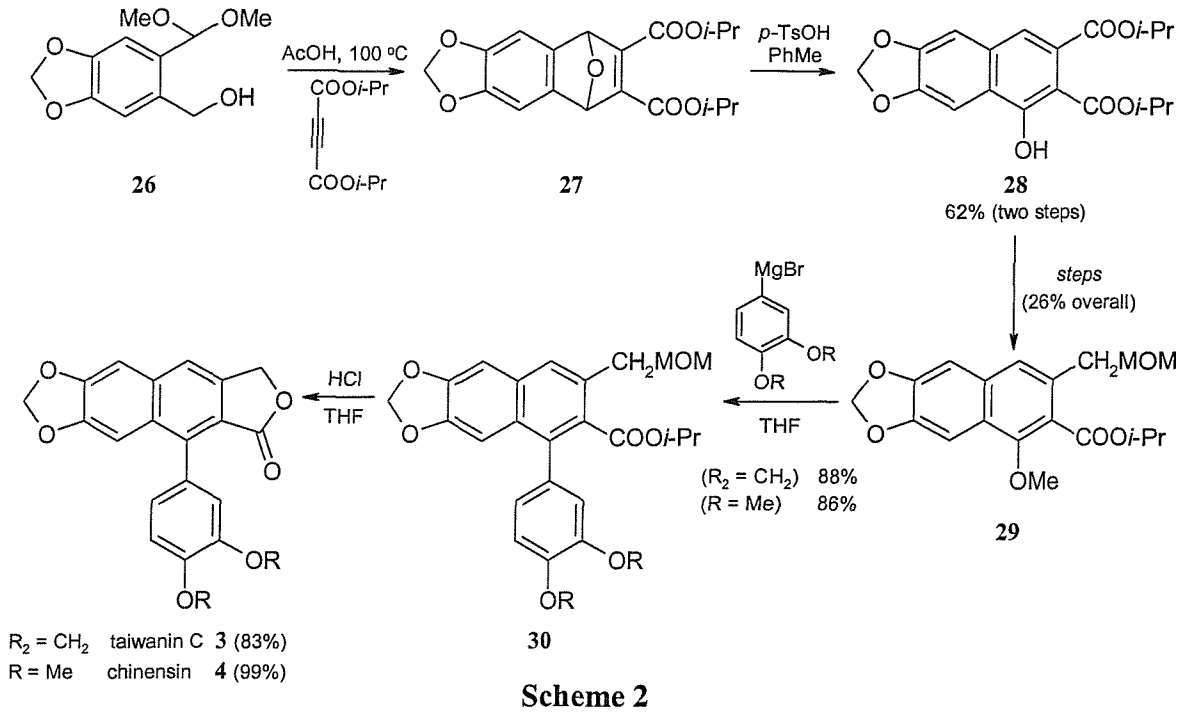
1.2.1 Diels-Alder Cycloaddition to a Benzo[*c*]furan Intermediate

Rodrigo *et al.* were the pioneers of the Diels-Alder cycloaddition approach involving benzo[*c*]furans.[36,37] They generated benzo[*c*]furan **23** by treating dihydrobenzo[*c*]furan **22** with *para*-toluenesulfonic acid in benzene. It was then trapped *in situ* with acetylene dicarboxylate and subsequently aromatised to arylnaphthalene **25**. Manipulation of the terminal ester groups led to syntheses of various lignans in *ca.* 35% overall yield **(Scheme 1)**.



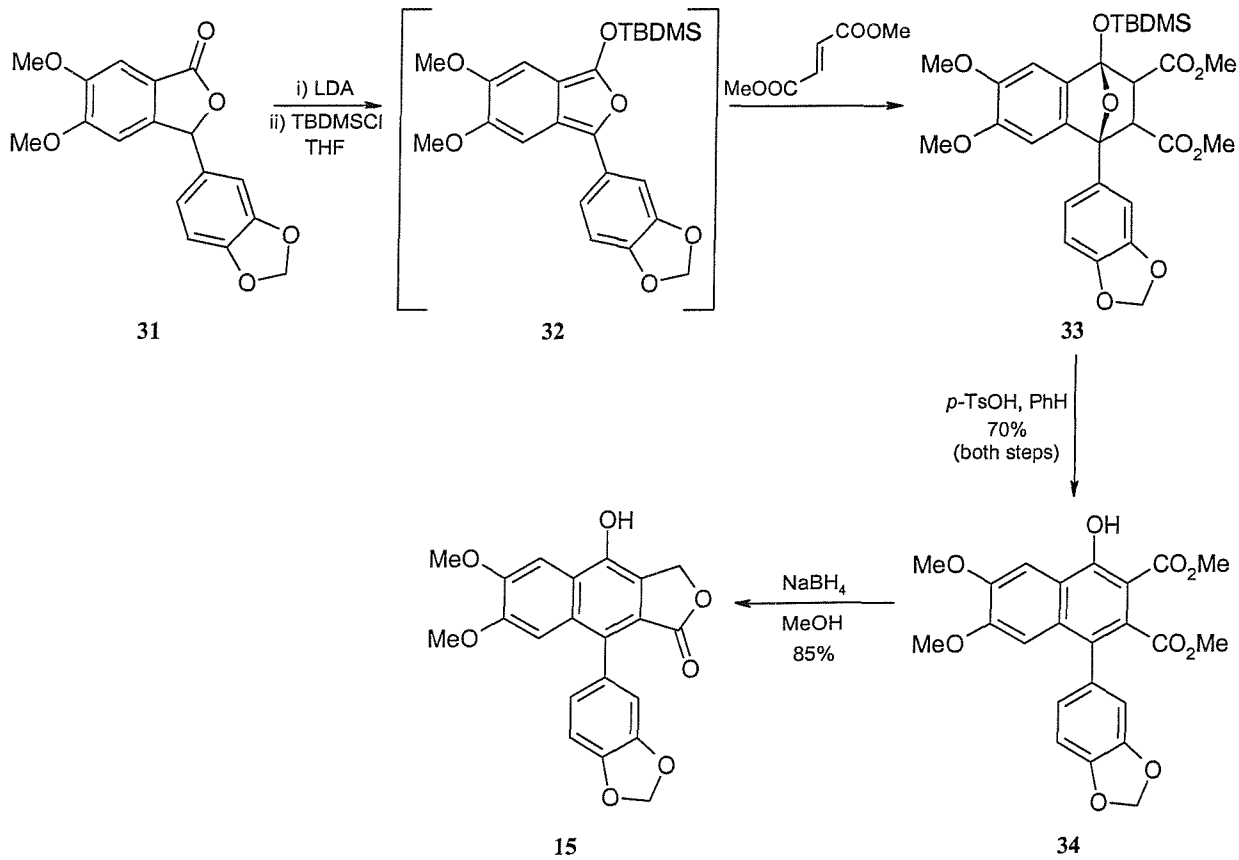
Scheme 1

This methodology is ubiquitous in the literature and has been adopted by others in order to carry out their own research on this class of lignans. In a study of hindered rotation in 1-arylnaphthalenes, Charlton *et al.* used Rodrigo's approach with only a few minor changes,[38] as did Iwasaki *et al.* in their examination of arylnaphthalene lignans as potential antiasthmatic agents.[39] In their syntheses of taiwanin C **3** and chinensin **4**, Hattori *et al.* constructed the naphthalene ring *via* benzo[*c*]furan generation, then used nucleophilic aromatic substitution by an aryl Grignard reagent to furnish the 1-arylnaphthalene skeleton **(Scheme 2)**.[40]



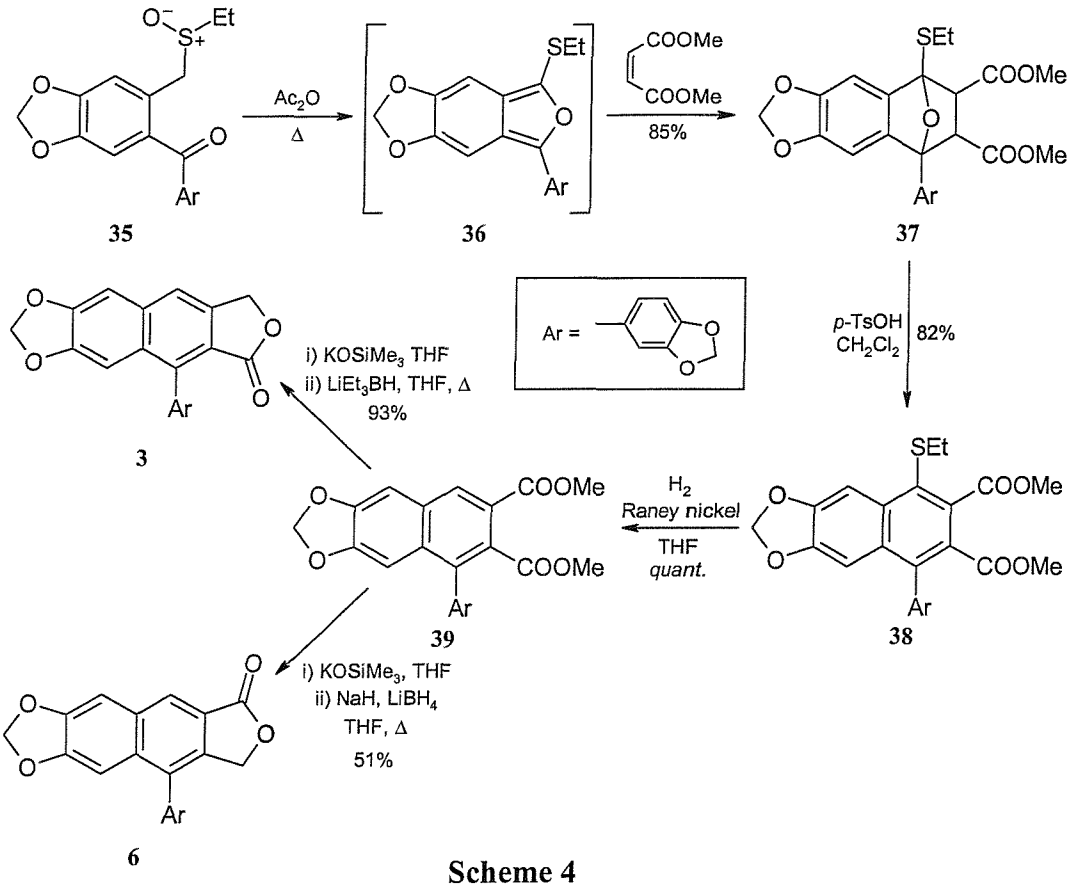
Scheme 2

Different methods have been employed to generate the benzo[*c*]furan intermediate. In their synthesis of diphyllin **15**, Iwao *et al.* generated benzo[*c*]furan **32** from the corresponding γ-lactone **31** (**Scheme 3**).[41] Trapping the benzo[*c*]furan with dimethyl fumarate then yielded Diels-Alder adduct **33**, which was easily converted to 4-aryl-1-naphthol **34** on exposure to acid. Selective reduction of the ester at C-2 using sodium borohydride completed the synthesis.



Scheme 3

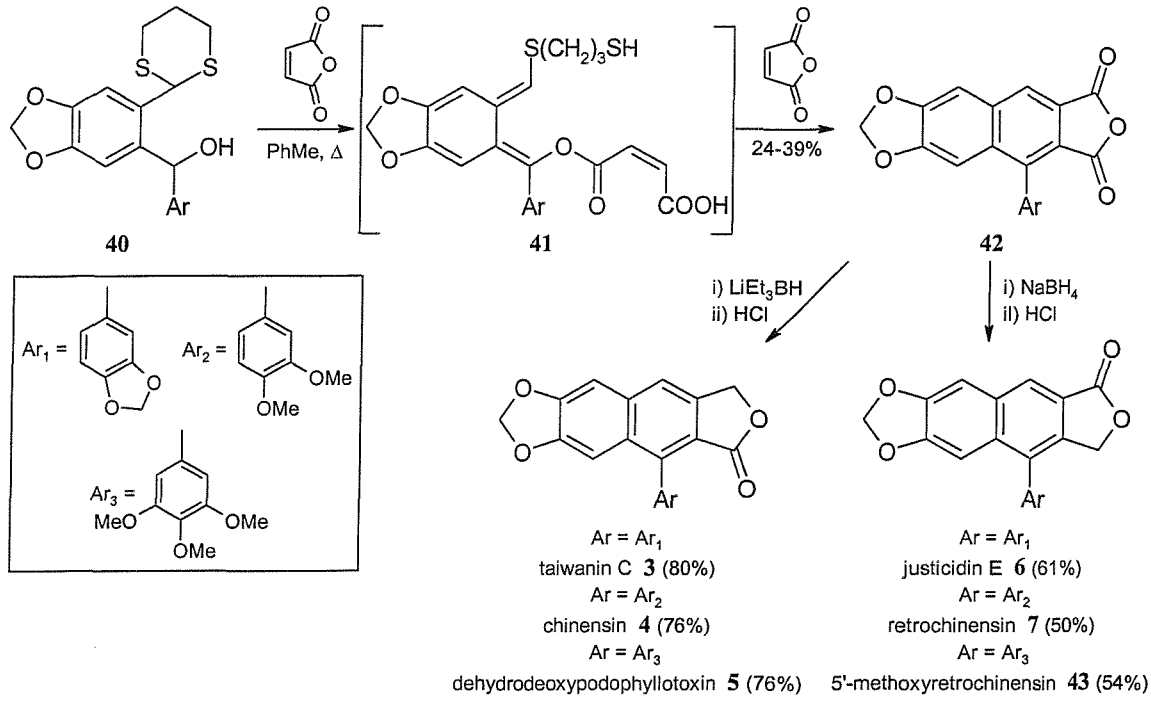
Padwa *et al.* prepared benzo[*c*]furan intermediate **36** *via* a Pummerer rearrangement of **35**.[42,43] After Diels-Alder cycloaddition with dimethyl maleate, the resultant adduct was readily converted to both taiwanin C **3** and justicidin E **6** (**Scheme 4**). Sarkar *et al.* have recently employed this methodology to generate nitrogen containing heterocyclic analogues of 1-arylnaphthalene lignans.[44]



Scheme 4

1.2.2 Diels-Alder Cycloaddition to a Quinodimethane

Another commonly exploited methodology involves Diels-Alder cycloaddition to a quinodimethane. Takano *et al.* generated quinodimethane **41** *in situ* by refluxing thioacetal **40** with maleic anhydride.[45] A second equivalent of maleic anhydride trapped **41** to form 1-arylnaphthalene **42**. Conversion of **42** to the lactones taiwanin C **3**, chinensin **4** and dehydrodeoxypodophyllotoxin **5** and the retrolactones justicidin E **6**, retrochinensin **7** and 5'-methoxyretrochinensin **43** was then achieved by partial reduction of the anhydride with lithium triethylborohydride or sodium borohydride respectively (**Scheme 5**).

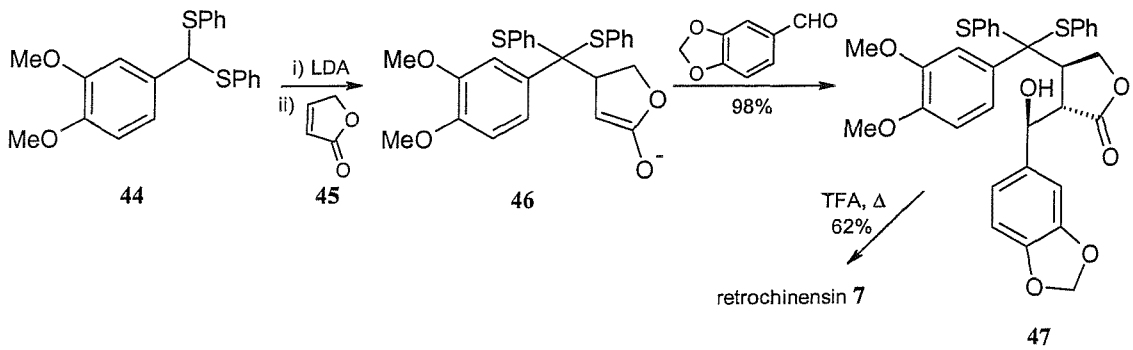


Scheme 5

Various methods of preparing the quinodimethane have been described in the literature: photolysis,[46] thermolysis[47] and chelotropic elimination of sulfur dioxide[48] having all been used. However, the overall strategy remains the same.

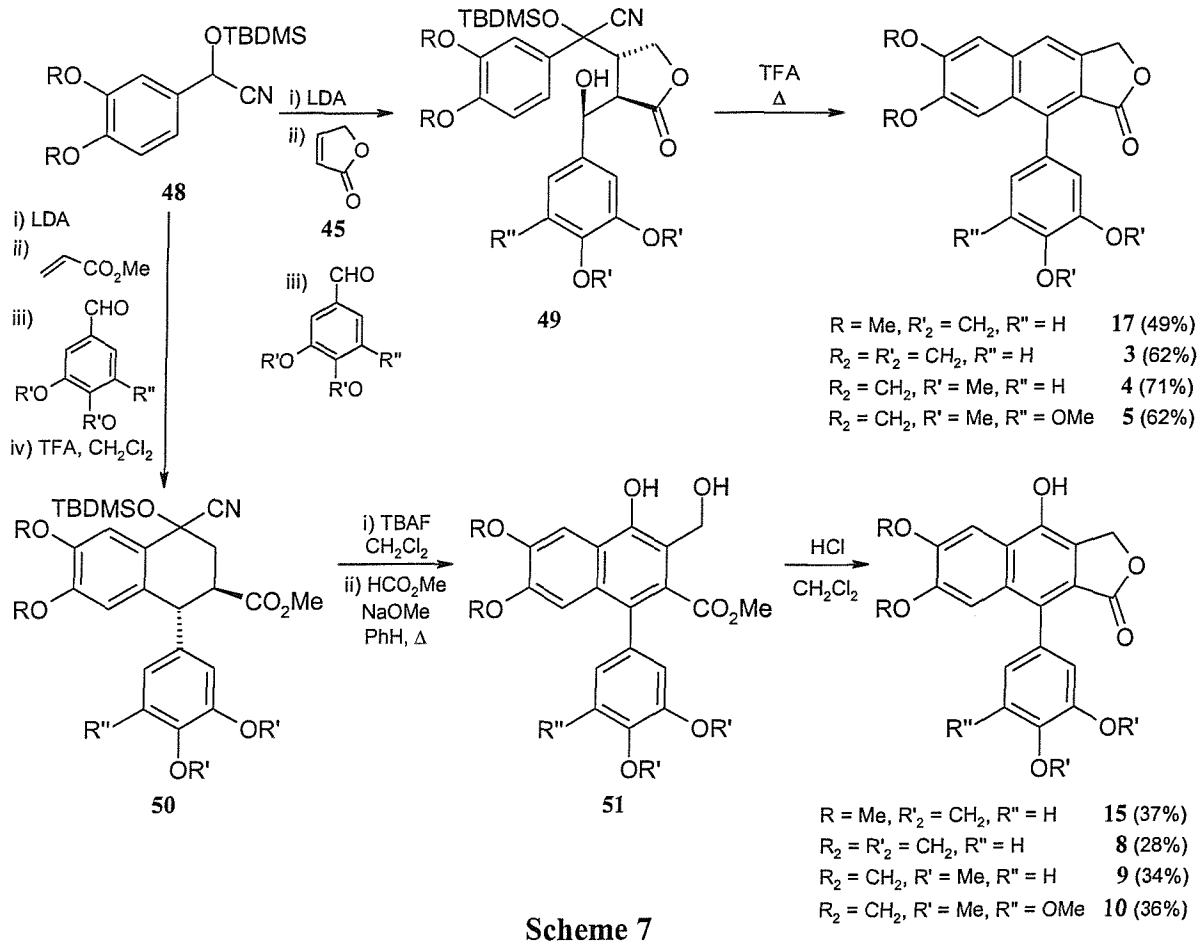
1.2.3 Arylnaphthalene Generation *via* Michael Addition

The most common methodology used to access the arylnaphthalene lignans involves Michael addition of an anion to 2-(5*H*)-furanone **45** followed by trapping with an aryl aldehyde and subsequent naphthalene generation. Ward *et al.* were the pioneers of this strategy and employed it in the synthesis of retrochinensin **7** and other podophyllotoxin analogues (**Scheme 6**).[49-51] Thioacetal **44** was deprotonated and added to 2-(5*H*)-furanone **45** in a Michael fashion to give enolate **46**. The addition of piperonal then trapped the enolate to generate **47**, which was readily converted to retrochinensin **7** by refluxing in TFA.



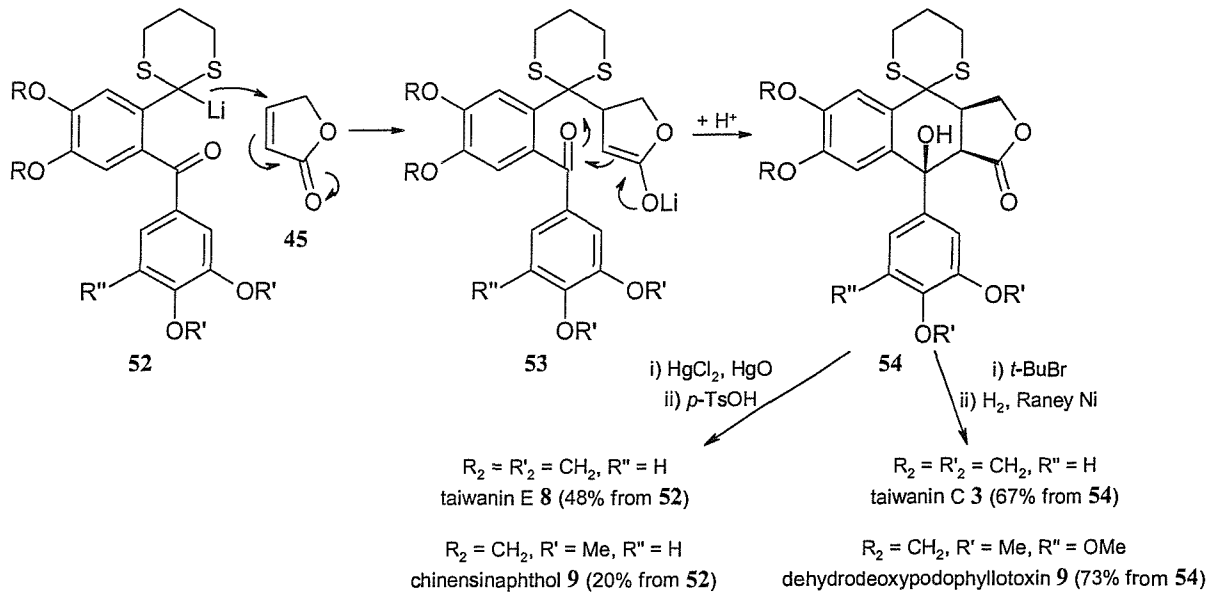
Scheme 6

Iwasaki *et al.* used the same approach with a TBDMS protected cyanohydrin functioning as the acyl anion equivalent.[52,53] Michael addition of **48** to 2-(5*H*)-furanone **45** followed by the addition of an aromatic aldehyde gave lignan precursor **49**. The arylnaphthalene lactones were then obtained by refluxing **49** in TFA. 4-Aryl-1-naphthols were harder to obtain using this route, requiring more tailored conditions and greater functional group manipulation. Nevertheless, Iwasaki *et al.* achieved the syntheses of four 4-aryl-1-naphthol lignans using this methodology (**Scheme 7**).



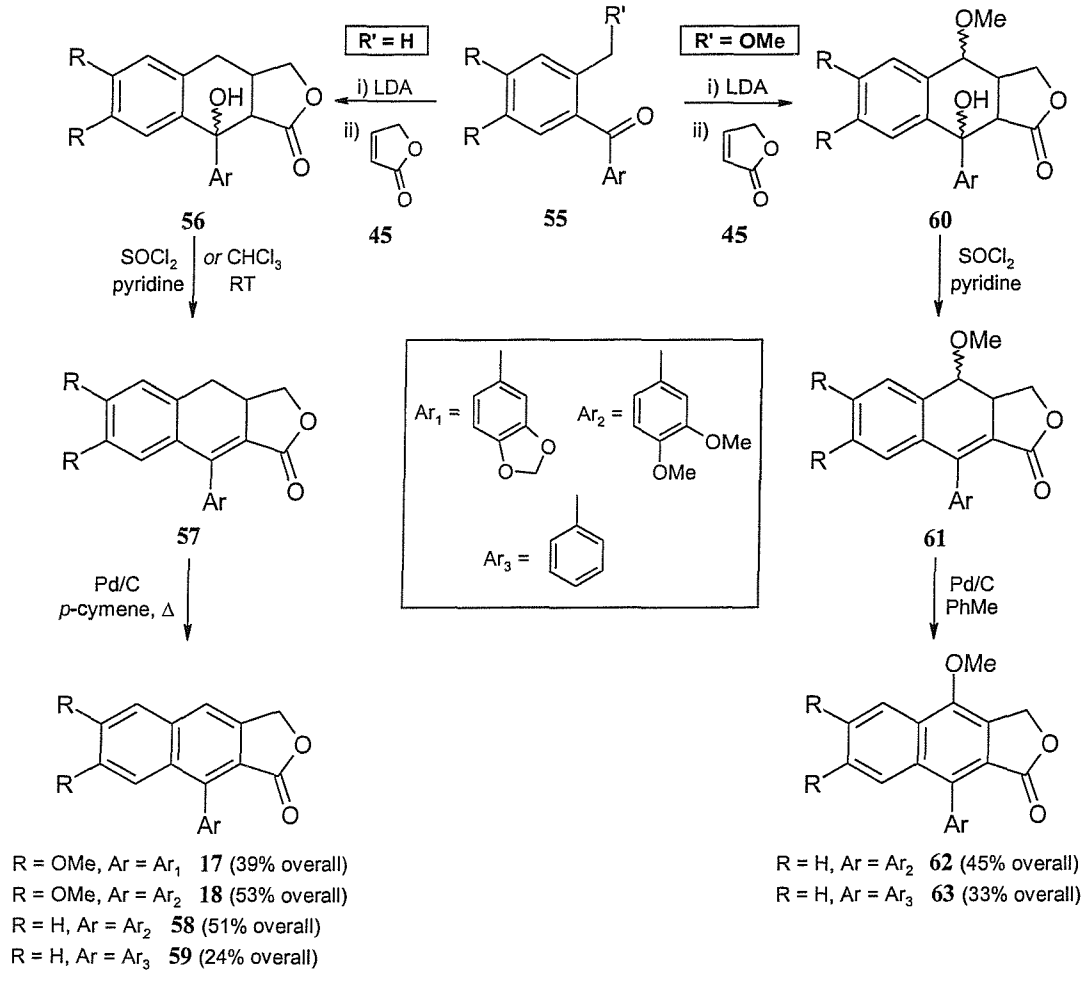
Scheme 7

An innovative progression of this methodology involved the incorporation of the anion and carbonyl trap in the same precursor. In this manner, a *one-step* annulation could be achieved. Harrowven pioneered this Michael initiated ring closure (MIRC) approach using aromatic thioacetals to initiate the cyclisation.[54-56] Upon addition of **52** to 2-(5*H*)-furanone **45**, enolate anion **53** was generated. Addition to the incorporated ketone functionality then gave MIRC adduct **54** on work-up. Removal of the thioacetal moiety allowed a variety of lignans to be prepared, including taiwanins C **3** and E **8**, chinensinaphthol **9** and dehydrodeoxypodophyllotoxin **5** (**Scheme 8**).



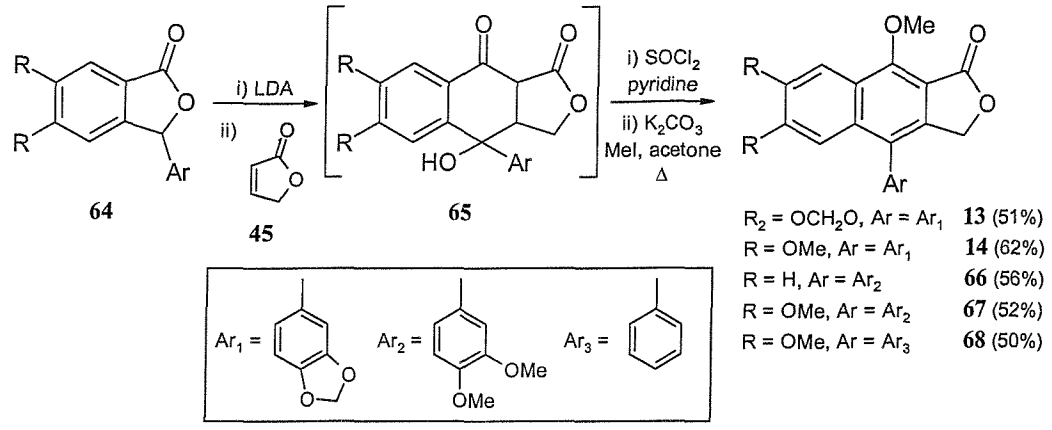
Scheme 8

This approach has been widely used and adapted. Kamal *et al.* used Harrowven's exact procedure to prepare justicidin B **17**,[57] whilst Kobayashi *et al.* used *o*-aroylbenzyllithiums to initiate the MIRC process (**Scheme 9**).[58,59]



Scheme 9

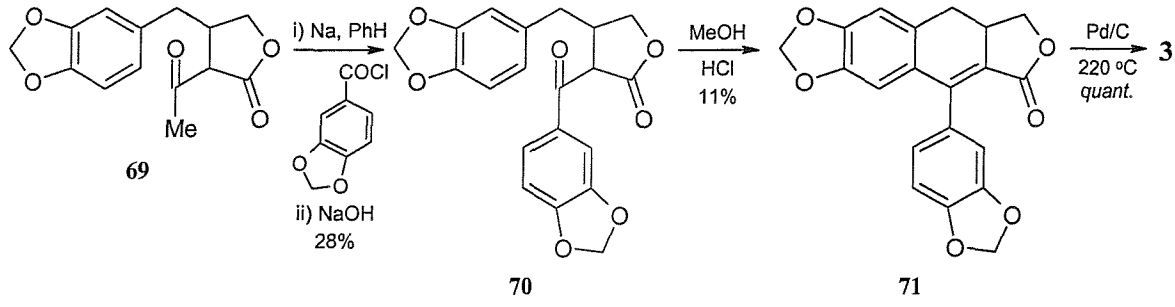
Kobayashi *et al.* also found that 4-aryl-1-naphthol retrolactones could be accessed if a γ-lactone was used as the MIRC precursor. Justicidins C **14** and D **13** were obtained in this manner (**Scheme 10**).[60]



Scheme 10

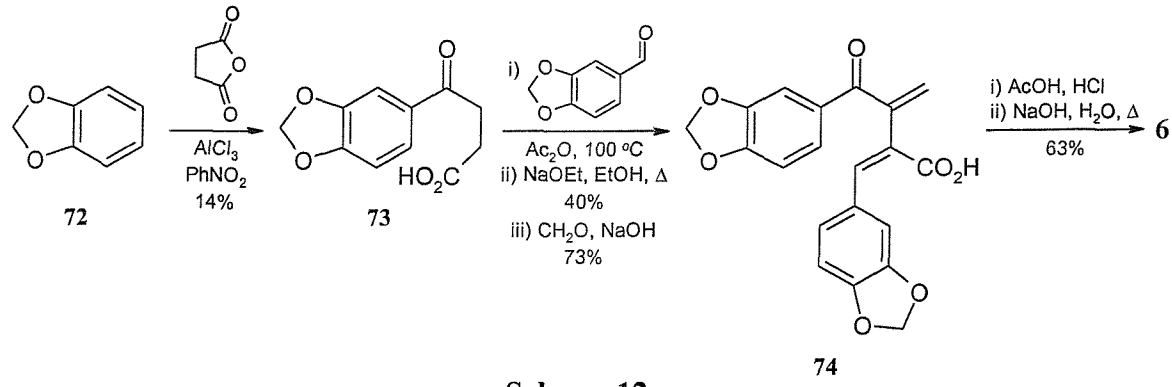
1.2.4 Other Synthetic Routes - Condensation Approaches

The first synthesis of an arylnaphthalene lignan was reported by Haworth and Kelly in 1936.[61] They prepared taiwanin C **3** from butyrolactone **69**[62] in the manner outlined in **Scheme 11**.



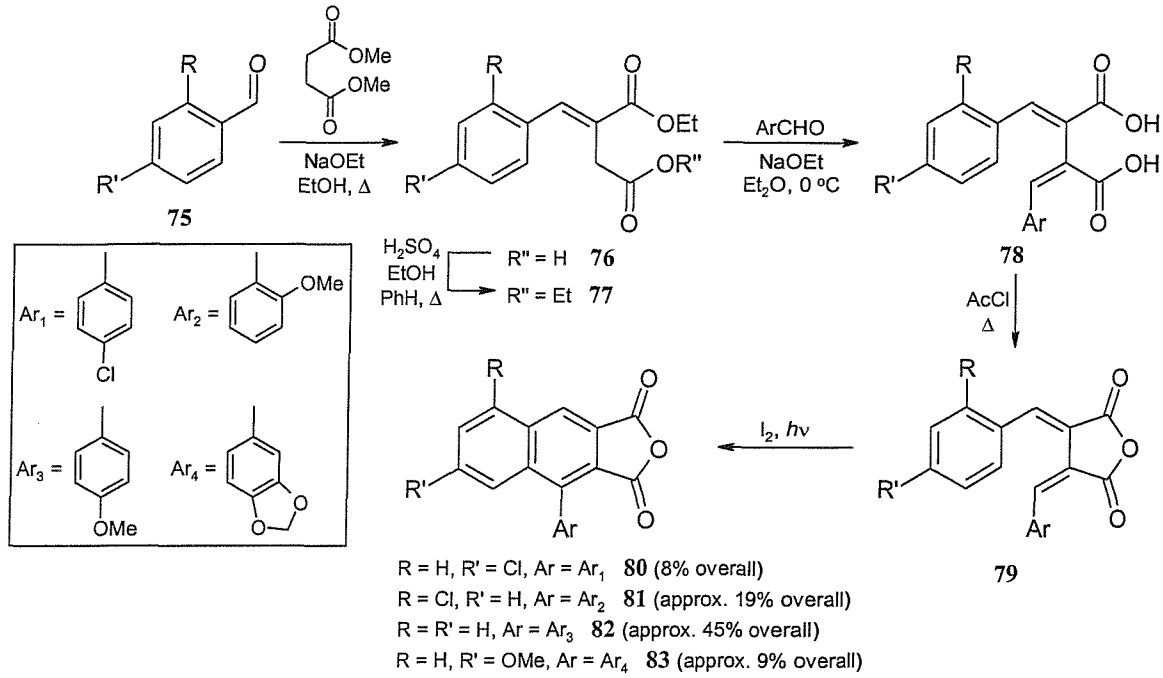
Scheme 11

They also reported the synthesis of justicidin E **6** from benzo[1,3]dioxole **72**. Friedel-Crafts acylation with malonic anhydride accessed **73**, which was condensed successively with piperonal then formaldehyde to yield diene **74**. Refluxing **74** in hydrochloric and acetic acid, then sodium hydroxide, furnished the desired lignan (**Scheme 12**).



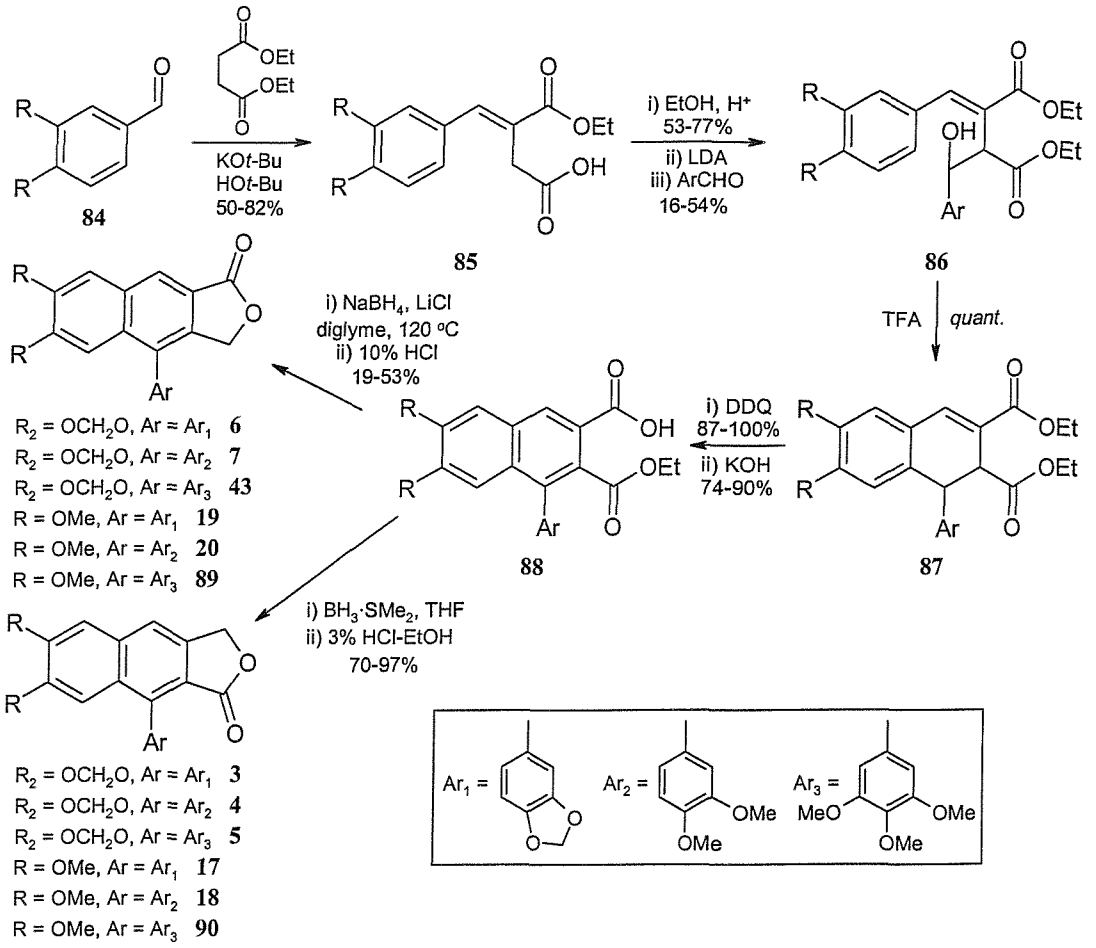
Scheme 12

Baddar *et al.* also achieved the synthesis of 1-arylnaphthalenes using sequential Stobbe condensations to generate diacids **78**.[63] Dehydration followed by exposure to iodine and sunlight gave 1-arylnaphthalenes **80** – **83** **(Scheme 13)**.



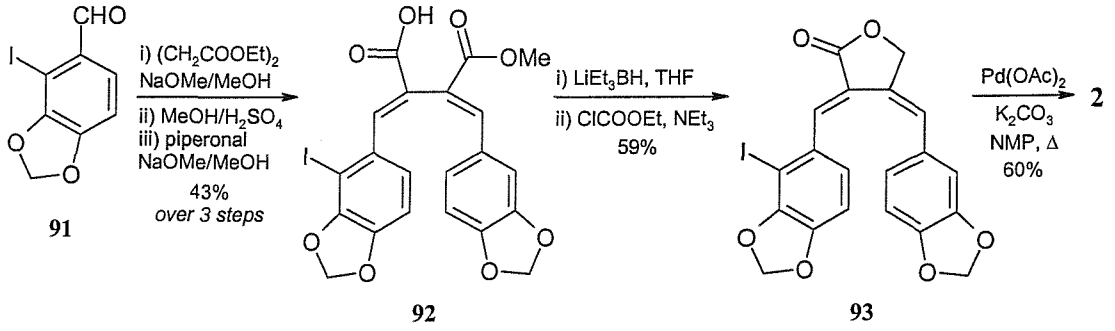
Scheme 13

This approach was further developed by Cow *et al.* as part of their study of the antiviral activity of arylnaphthalene lignans.[27] Their robust route employed a Stobbe condensation to synthesise functionalised styrene **85**. Subsequent esterification and Claisen condensation gave alcohol **86**. Acid-mediated ring closure to **87** and aromatisation with DDQ then achieved arylnaphthalene generation. After partial saponification to half-acid **88**, arylnaphthalene lactones and retrolactones were synthesised from this common intermediate **(Scheme 14)**.



Scheme 14

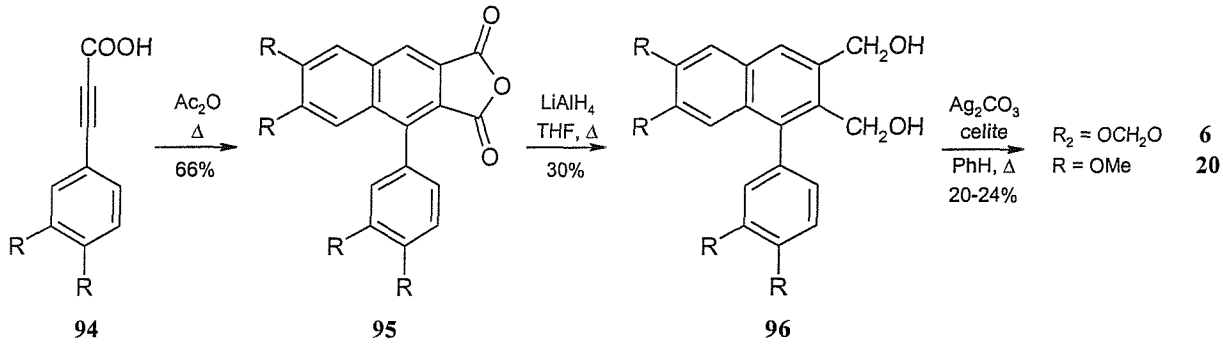
Mizufune *et al.* used sequential Stobbe condensations to generate bisbenzylidene half-ester **92** in their synthesis of helioxanthin **2**.[64] On lactonisation, a regiospecific palladium-catalysed benzannulation constructed the 1-arylnaphthalene skeleton and completed the synthesis (**Scheme 15**).



Scheme 15

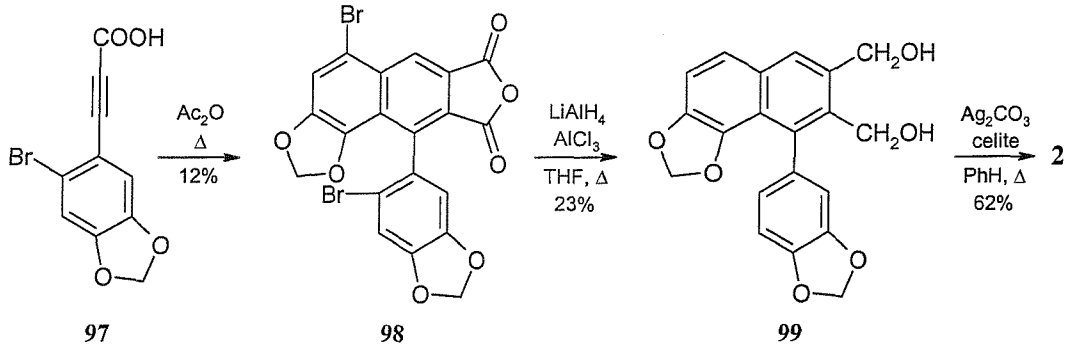
1.2.5 Other Synthetic Routes – Alkyne Dimerisation

Holmes and Stevenson used the thermally-induced dimerisation of **94** to trigger an intramolecular cyclisation leading to arylnaphthalene anhydride **95**.[65] Syntheses of justicidin E **6** and dehydrodimethylconidendrin **20** were then accomplished *via* reduction of the anhydride with lithium aluminium hydride and oxidation of the resultant diol **96** with silver(I) carbonate (**Scheme 16**).



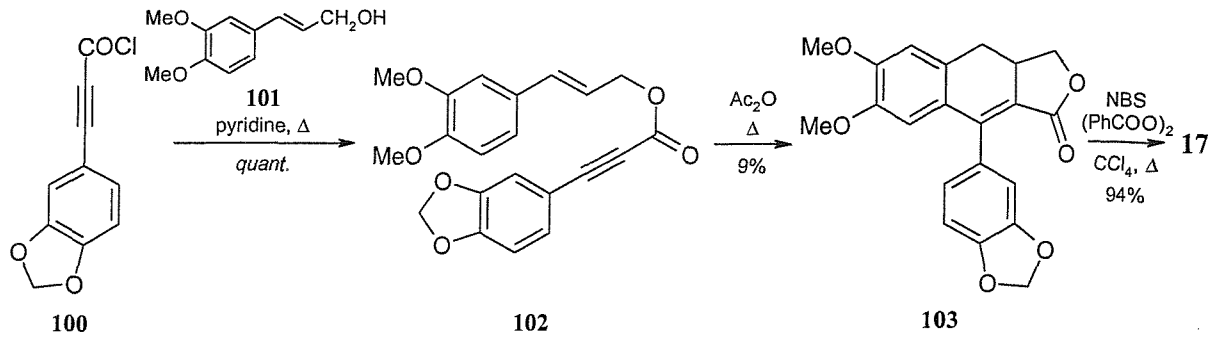
Scheme 16

Helioxanthin **2** was also prepared using this strategy.[66] However, in this instance, it was necessary to incorporate a bromine atom *ortho* to the alkyne moiety in order to achieve the correct regiochemical outcome. Removal of the extraneous bromine atoms was accomplished by the simple expedient of including aluminium trichloride in the reduction step (**Scheme 17**).



Scheme 17

For the synthesis of arylnaphthalene lignans with differing substitution on the phenyl and naphthyl moieties ("mixed" lignans), a different approach was required. Thus Block and Stevenson began the synthesis of justicidin B **17** by esterifying 3,4-dimethoxycinnamyl alcohol **101** with 3,4-methylenedioxyphenylpropiolic chloride **100**, giving ester **102**.[67] An intramolecular electrocyclisation then afforded 3,4-dihydro-1-arylnaphthalene **103**, which readily underwent oxidation to the target lignan **17** (**Scheme 18**).

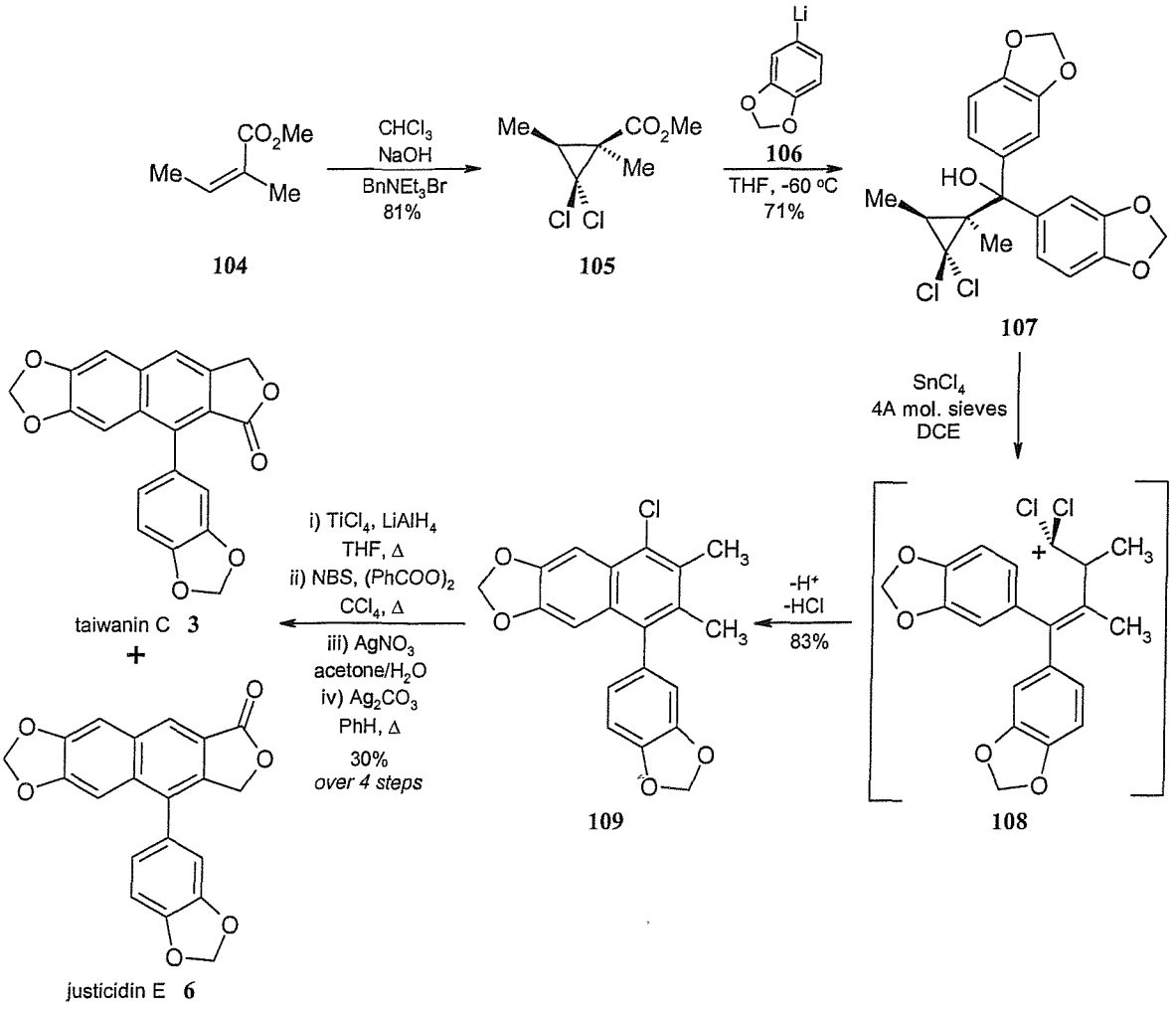


Scheme 18

As is evident from **Schemes 16-18**, the major limitation of this general approach to the arylnaphthalene lignans is the recurrent low yields encountered throughout the synthesis. As the conversion of ester **102** into 3,4-dihydro-1-arylnaphthalene **103** is particularly poor, the synthesis of "mixed" lignans is especially limited.

1.2.6 Other Synthetic Routes – Miscellaneous

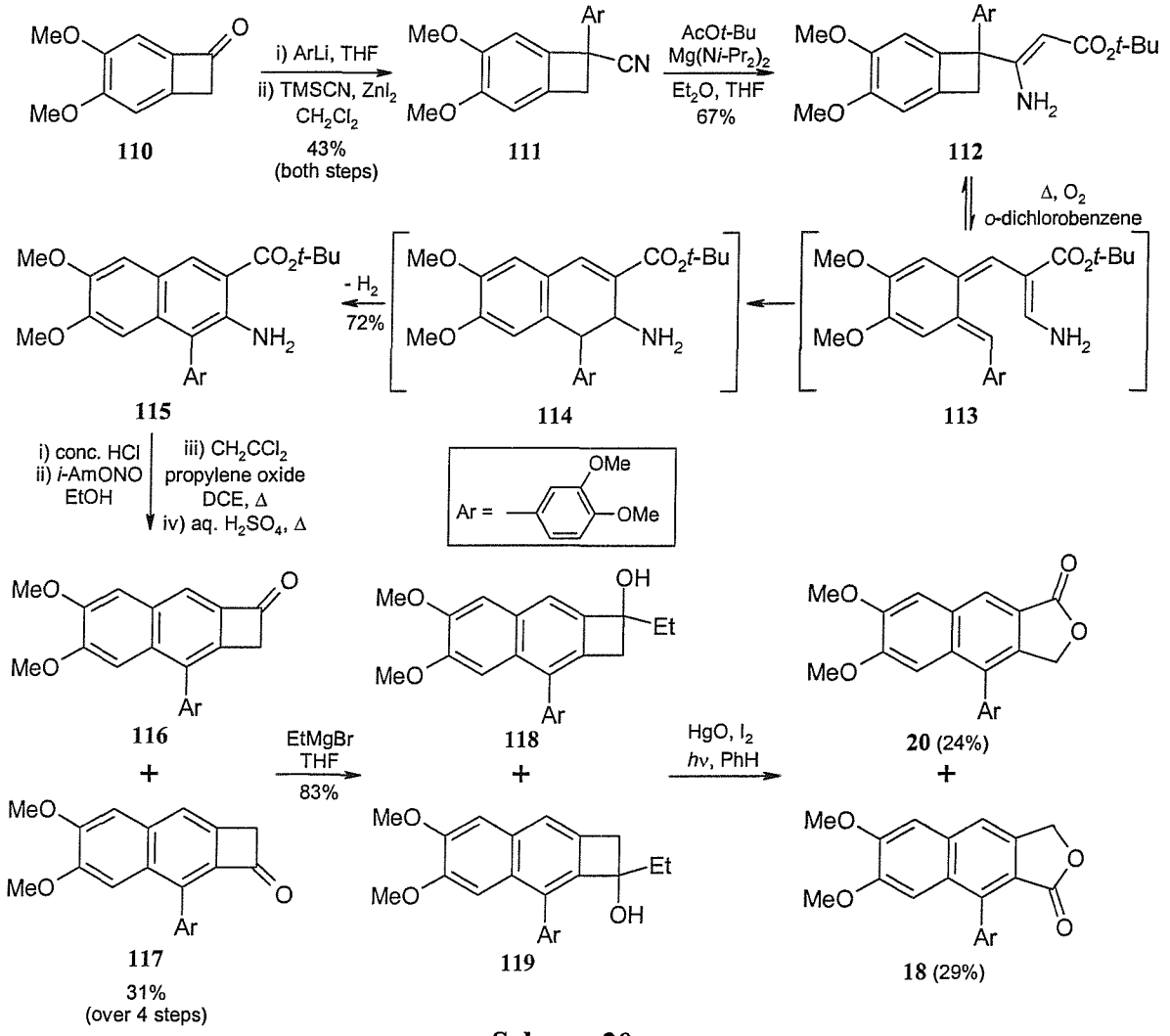
A novel approach to the synthesis of arylnaphthalene lignans has been developed by Tanabe *et al.*, starting with methyl angelate **104** (**Scheme 19**).[68,69]



Scheme 19

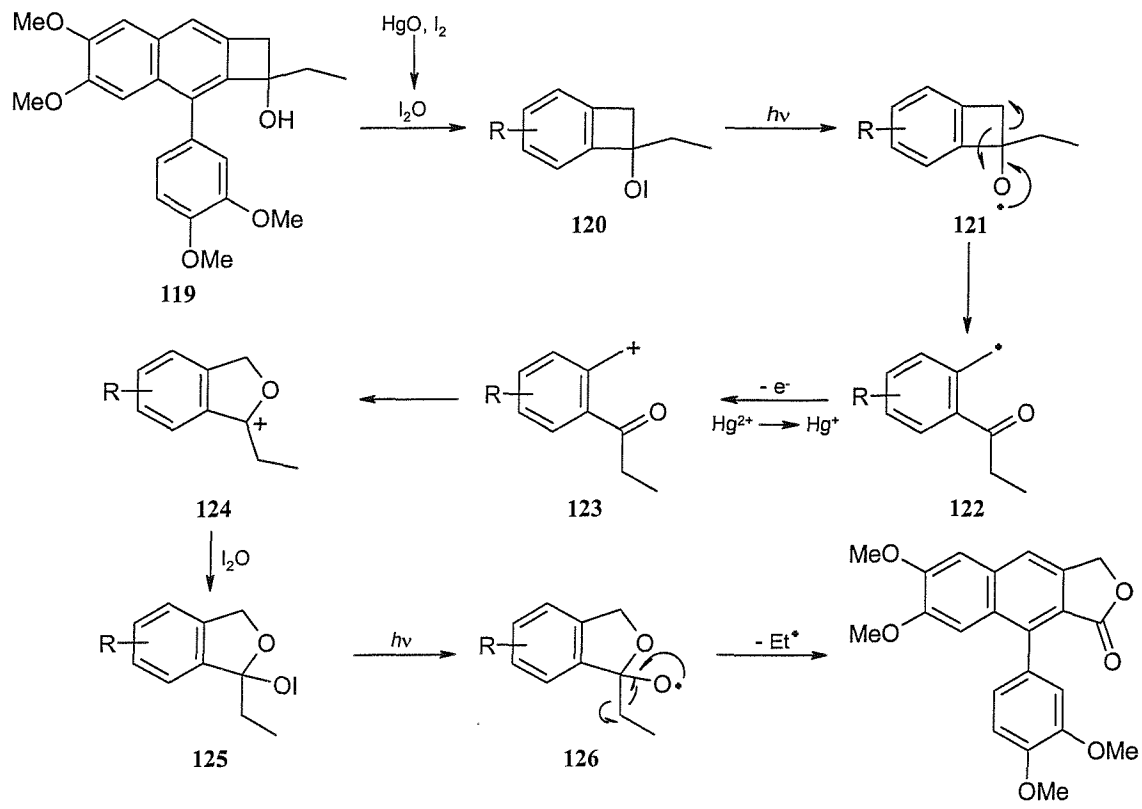
Exposure of methyl angelate **104** to dichlorocarbene gave **105** which, on addition of organolithium **106**, provided aryl-(*gem*-dichlorocyclopropyl)-methanol **107**. 4-Chloro-1-arylnaphthalene **109** was then produced by a regioselective benzannulation *via* **108**. Functionalisation of the terminal methyl groups allowed taiwanin C **3** and justicidin E **6** to be prepared.

The synthesis of dehydrodimethylretrodendrin **18** and dehydrodimethylconidendrin **20** by Kobayashi *et al.* is arguably the most unusual approach to the arylnaphthalene lignans reported to date.[70] Bicyclo[4.2.0]octa-1,3,5-trien-7-one **110** was subject to organolithium addition then transformed into carbonitrile **111**. Grignard addition to the nitrile provided *tert*-butyl propenoate **112**. Thermolysis of **112** in the presence of oxygen then furnished arylnaphthalene **115** *via* the mechanism illustrated (**Scheme 20**). Unfortunately, this route was robbed of its potential elegance by the large number of steps needed to convert **115** into the desired lactones **18** and **20**. However, this route can be adapted to provide access to 1,4-biarylnaphthalenes.



Scheme 20

The mechanism proposed for the conversion of **118** and **119** to lactones **18** and **20** is outlined below in **Scheme 21**.



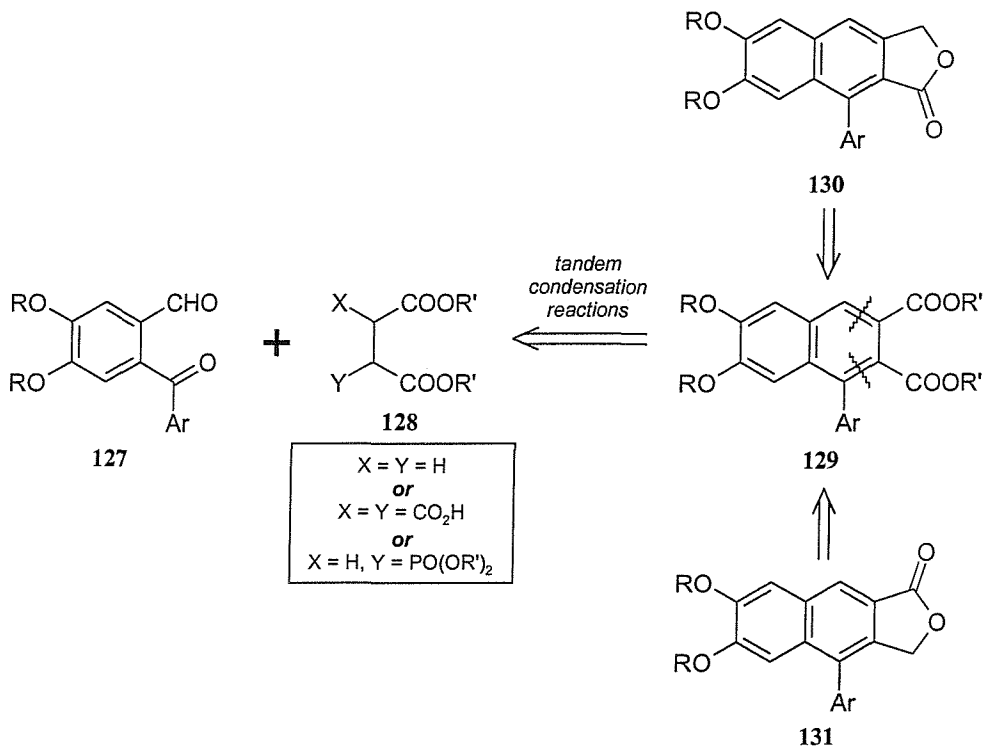
Scheme 21

1.3 Our Aims and Objectives

As has been illustrated, there are many inventive routes towards the arylnaphthalene lignans currently available. Despite this fact, no comprehensive SAR study on the lignans has been forthcoming. Studies conducted thus far have generally focussed on individual lignans, or groups of lignans isolated from a common plant source. As such, the present data on this important sub-group is insufficiently detailed to draw any meaningful conclusions with respect to SAR. A synthetic route to the arylnaphthalene lignans that is amenable to multiple parallel synthesis would therefore contribute greatly to the study of the biological properties of these natural products.

With this objective in mind, we decided to target diesters akin to **129**. These serve as precursors for both the lactone and retrolactone series of arylnaphthalene lignans. We felt that such diesters might be attained *via* a sequential condensation reaction between a ketoaldehyde **127** and a succinate derivative **128**, thus constructing the central arene ring in *one step* (**Scheme 22**). If successful, a multiple parallel synthesis of the arylnaphthalene

lignans would become feasible. Our goal was to achieve the total syntheses of the arylnaphthalene lignans taiwanin C **3**, chinensin **4**, justicidin B **17**, justicidin E **6**, retrochinensin **7** and retrojusticidin B **19** in order to prove the viability of this new methodology.



Scheme 22

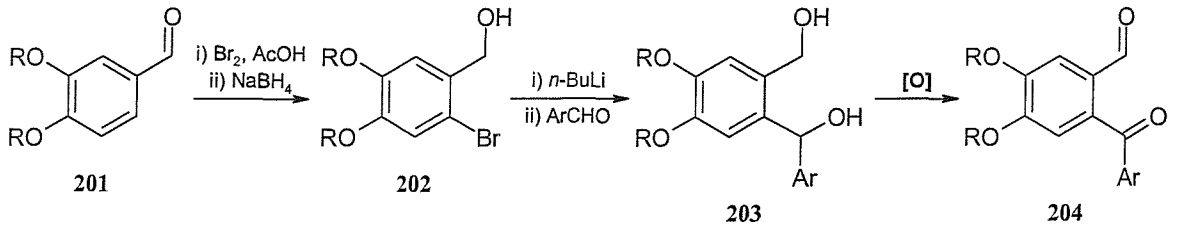
Chapter 2

A New Benzannulation Reaction and its Application in the Multiple Parallel Synthesis of Arylnaphthalene Lignans

This chapter details our successful syntheses of the arylnaphthalene lignans taiwanin C **3**, chinensin **4**, justicidin B **17**, justicidin E **6**, retrochinensin **7** and retrojusticidin B **19**. A new selective oxidation procedure that favours retrolactone formation is also discussed.

2.1 Synthesis of the Ketoaldehydes

In order to develop our new methodology, we first required a synthetic route to the requisite ketoaldehydes. We envisioned a reasonably straightforward synthesis, starting from a functionalised aromatic aldehyde such as **201**. Bromination of the benzene ring and subsequent reduction of the carbonyl functionality would yield benzylic alcohol **202**. Halogen-metal exchange to generate the corresponding organolithium species, followed by addition to a second functionalised aromatic aldehyde, should then give diol **203**. Finally, we hoped that a tandem oxidation of this diol would furnish us with the required ketoaldehyde **204** (**Scheme 23**).

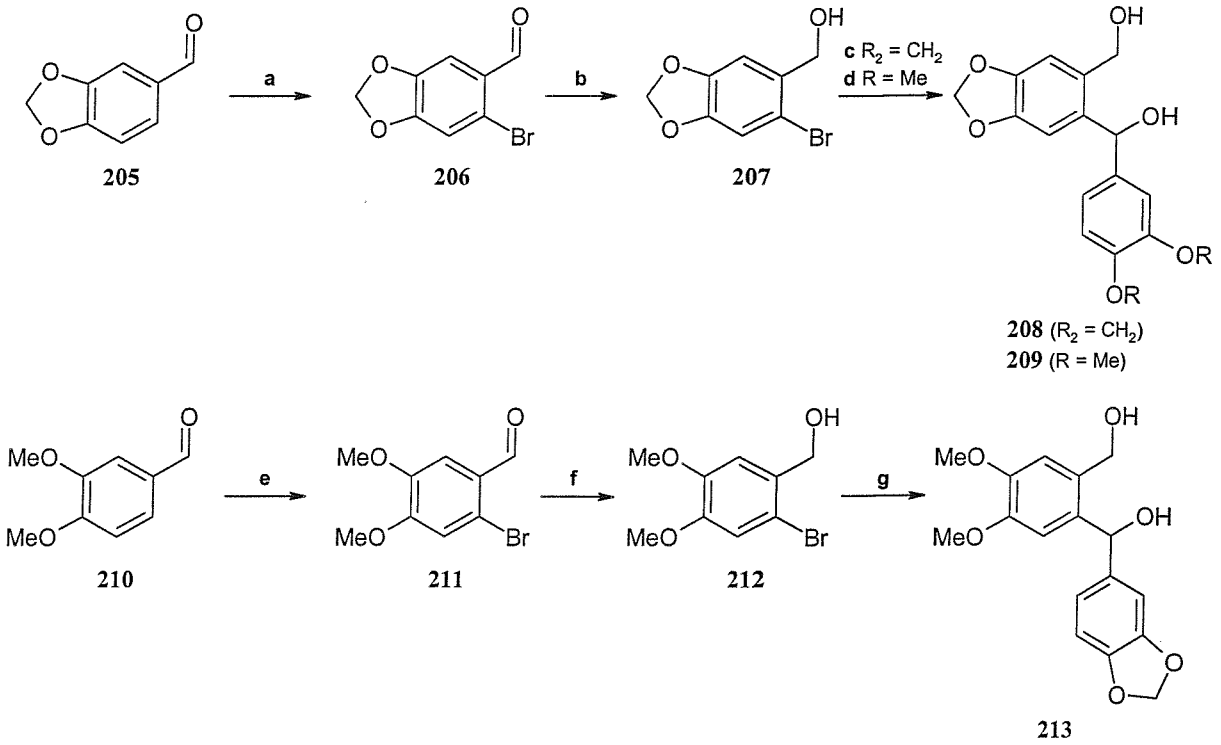


201 **202** **203** **204**

Scheme 23

In practice, the bromination of piperonal **205** and veratraldehyde **210** was unproblematic, as was the reduction of the aldehyde functionality using sodium borohydride. Conversion of the resulting alcohols **207** and **212** to diols **208**, **209** and **213** proved more troublesome. Treating the aryl bromide **207** or **212** with two equivalents of *n*-butyllithium prior to the addition of the aryl aldehyde gave erratic yields. In such cases, the formation of the non-halogenated analogues of **207** and **212** was the primary side reaction. We reasoned that this was due to halogen-metal exchange occurring before deprotonation of the alcohol, resulting in internal protonation of the organolithium species. Fortunately, this problem could be

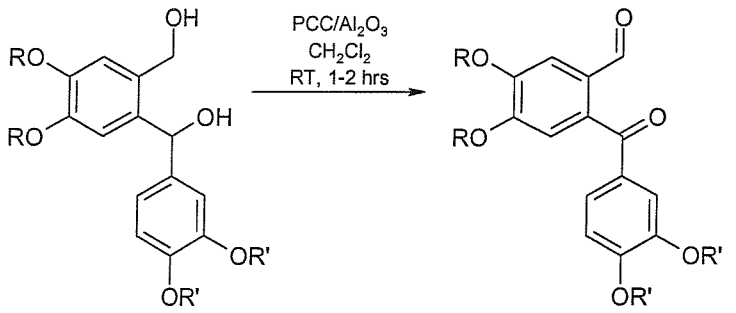
avoided by deprotonating the alcohol with sodium hydride prior to the addition of *n*-butyllithium. Through this simple expedient, high and reproducible yields for the desired diols **208**, **209** and **213** could be realised (**Scheme 24**).



Reagents and Conditions: **a** Br_2, AcOH, RT, 1 hr, 50%. **b** $NaBH_4$, THF, 0 °C, 2 hrs, 86%. **c** 2 eq. *n*-BuLi *then* **205**, THF, -78 °C, 81%. **d** 2 eq. *n*-BuLi *then* **210**, THF, -78 °C, 69%. **e** Br_2, AcOH, RT, 1 hr, 60%. **f** $NaBH_4$, THF, 0 °C, 1 hr, 89%. **g** NaH, *n*-BuLi *then* **205**, THF, -78 °C, 78%

Scheme 24

The optimum conditions for the tandem oxidation of diols **208**, **209** and **213** to ketoaldehydes **214-216** were then sought. A great many oxidants were trialled, but using PCC on alumina proved to be the most consistent and high yielding protocol, and this concluded our route to the ketoaldehydes (**Scheme 25**).



208 (R_2 = R_2' = CH_2)
209 (R_2 = CH_2, R' = Me)
213 (R = Me, R'_2 = CH_2)

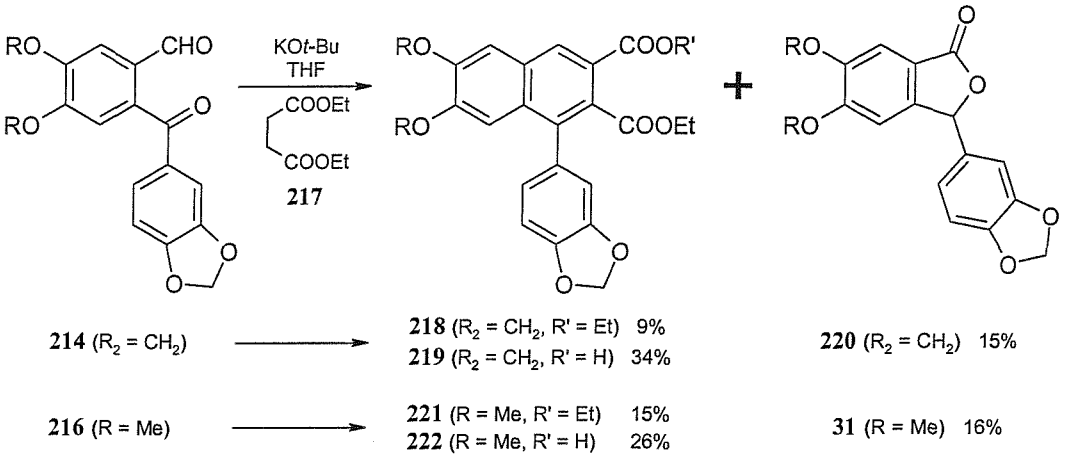
214 (R_2 = R'_2 = CH_2) 61%
215 (R_2 = CH_2, R' = Me) 65%
216 (R = Me, R'_2 = CH_2) 75%

Scheme 25

2.2 Developing the Tandem Condensation Methodology

2.2.1 The Tandem Stobbe-Claisen Condensation

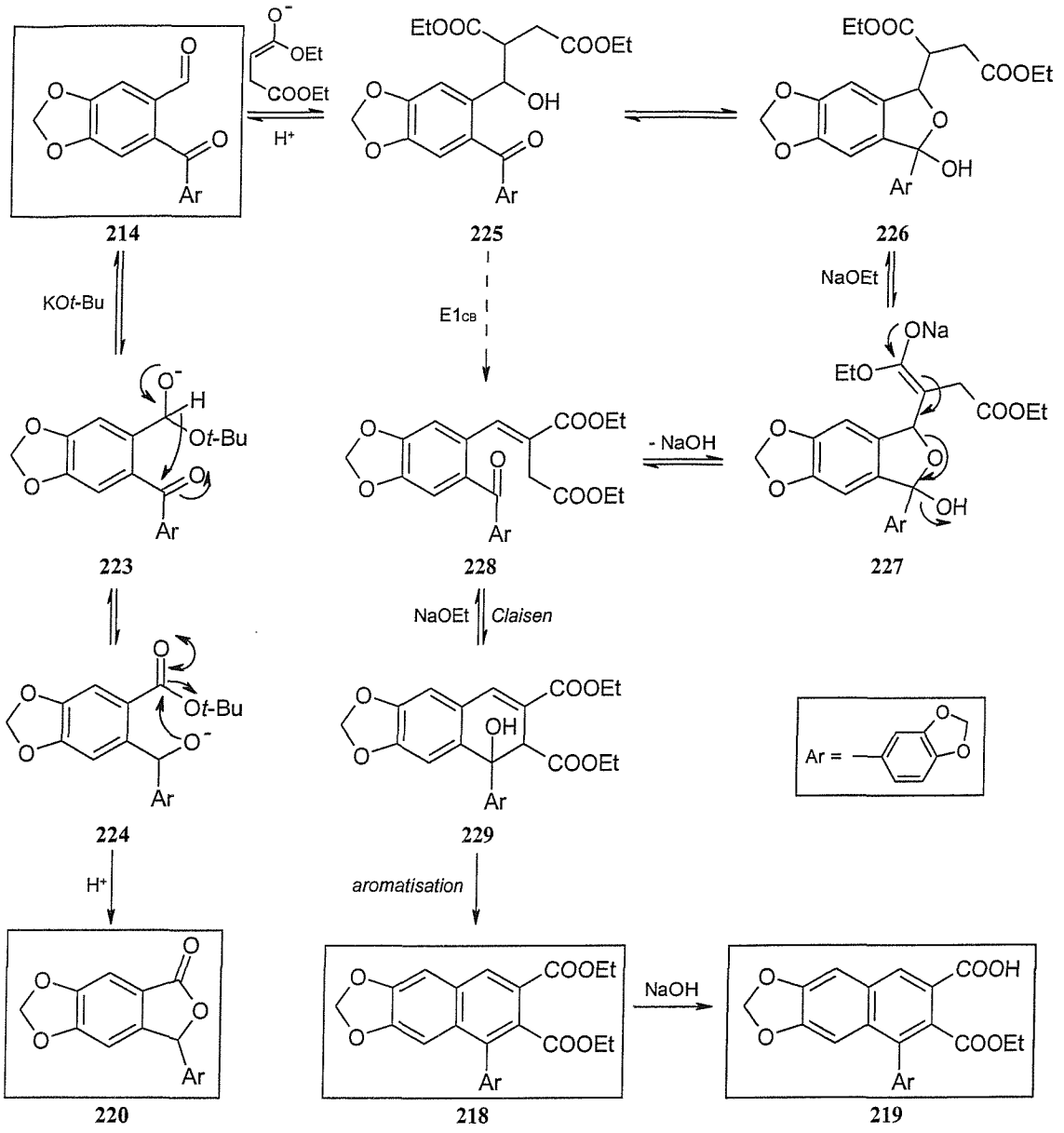
We first attempted to construct the central arene ring by coupling diethyl succinate **217** with ketoaldehyde **214** in a tandem Stobbe/Claisen condensation.[71-75] Unfortunately, this approach was blessed with little success. Attempts to effect the base-induced union of ketoaldehyde **214** and diethyl succinate **217** led to the production of arylnaphthalene diester **218** in a disappointing 9% yield. Indeed, the major product of the reaction was half-acid **219**, which was formed in 34% yield (**Scheme 26**). An additional side product of the reaction was γ-lactone **220** (15% yield), which presumably forms *via* an intramolecular Cannizzaro reaction (**Scheme 27**).[76,77]



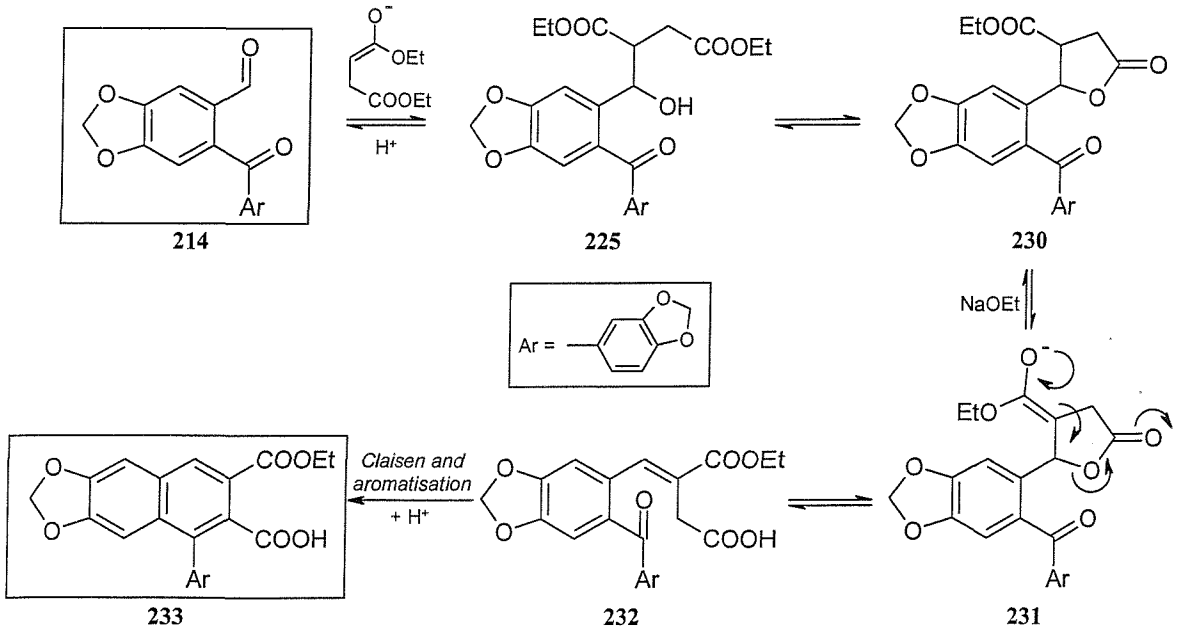
Scheme 26

Intriguingly, the reaction does not follow the normal course for a Stobbe condensation to give half-acid **233** (**Scheme 28**). It is presumed that half-acid **219** arises from saponification of the less hindered ester group at C-3 of **218** by sodium hydroxide, produced *in situ* by arylnaphthalene generation (**Scheme 27**).

A second trial of this methodology with ketoaldehyde **216** gave a similar product mixture (**Scheme 26**). Although various reaction conditions were examined, none could be found that gave better results than using potassium *tert*-butoxide in THF at ambient temperature. Thus, we sought an alternative way of effecting the desired tandem condensation.



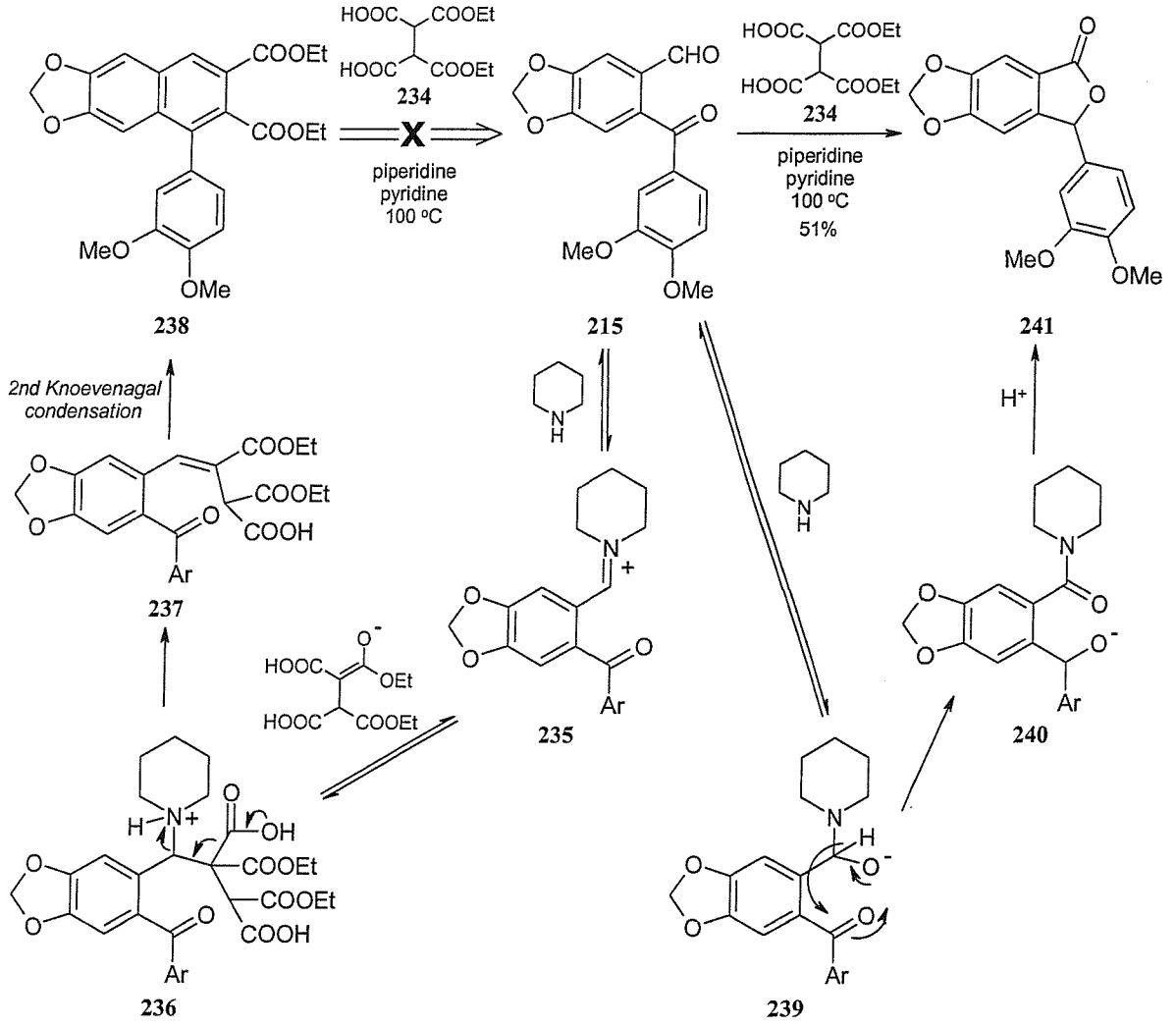
Scheme 27



Scheme 28

2.2.2 The Tandem Knoevenagal Condensation

Our second approach aimed to utilise a tandem Knoevenagal condensation to construct the central arene ring. It was envisioned that ketoaldehyde **215** might undergo a base-induced union with diacid **234**[78] to form diester **238**. Unfortunately, the reaction conditions promoted the intramolecular Cannizzaro reaction, resulting in γ-lactone **241** as the sole identifiable product of the reaction (**Scheme 29**).

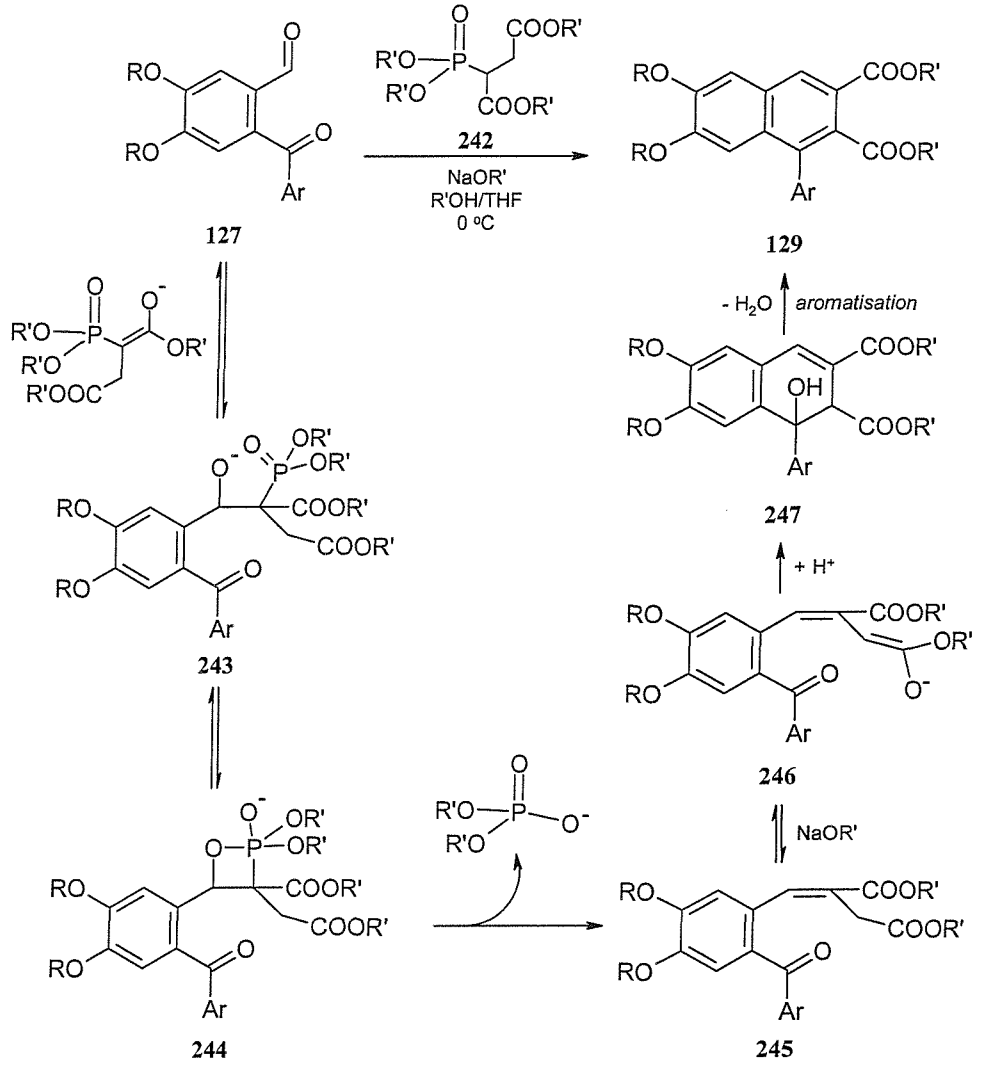


Scheme 29

It became clear, from both this result and our previous attempts, that γ-lactone formation was due to the slow rate of the initial condensation compared to the intramolecular Cannizzaro reaction. Thus, we felt that the problem might be solved if we could find a method of rapidly effecting the condensation between the succinate derivative and the ketoaldehyde.

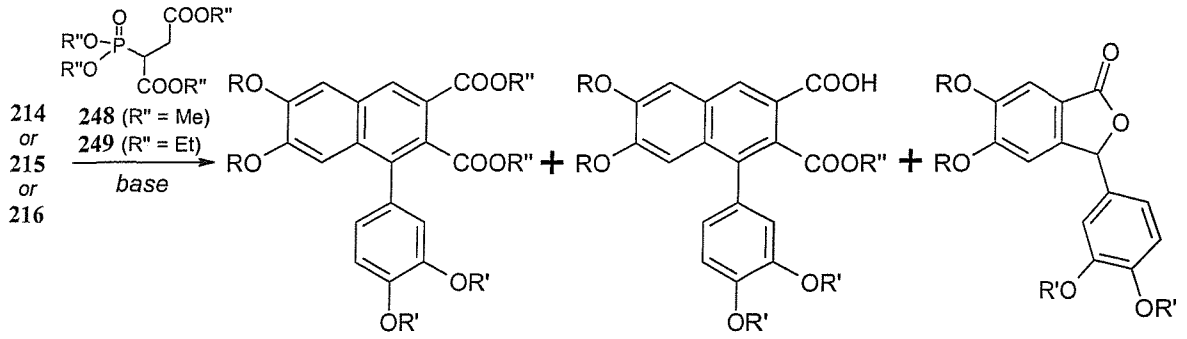
2.2.3 The Tandem Horner-Emmons-Claisen Condensation

On reflection, we speculated that the tandem condensation might be achieved through sequential Horner-Emmons and Claisen condensation reactions. It was our hope that the base-induced union of the aldehyde in **127** with phosphonosuccinate derivative **242** would outpace any intramolecular Cannizzaro reaction, thus ensuring that the tandem-condensation sequence leading to **129** was the dominant reaction pathway (**Scheme 30**). However, the geometry of the first formed alkene **245** was a minor concern, as it would have to form in the correct configuration (or be in dynamic equilibrium) for the annulation sequence to succeed.



Scheme 30

Pleasingly, after experimenting with various reaction conditions, it was found that simply stirring an alcoholic THF solution of the ketoaldehyde and phosphonosuccinate derivative with the corresponding alkoxide base at 0 °C achieved the desired annulation.[79] We thus proceeded to apply the new aromatic annulation reaction to our range of ketoaldehyde substrates with both methyl and ethyl phosphonosuccinate derivatives. The results are summarised in **Scheme 31**.



39 ($R_2 = R'_2 = CH_2$, R" = Me)
218 ($R_2 = R'_2 = CH_2$, R" = Et)
251 ($R_2 = CH_2$, R' = R" = Me)
238 ($R_2 = CH_2$, R' = Me, R" = Et)
253 (R = R" = Me, $R'_2 = CH_2$)
221 (R = Me, $R'_2 = CH_2$, R" = Et)

250 ($R_2 = R'_2 = CH_2$, R" = Me)
219 ($R_2 = R'_2 = CH_2$, R" = Et)
252 ($R_2 = CH_2$, R' = Me, R" = Et)
254 (R = R" = Me, $R'_2 = CH_2$)
222 (R = Me, $R'_2 = CH_2$, R" = Et)

220 ($R_2 = R'_2 = CH_2$)
241 ($R_2 = CH_2$, R' = Me)
31 (R = Me, $R'_2 = CH_2$)

Ketoaldehyde	Phosphonate	Reaction Conditions	Products (Yields)
214	**248**	NaOMe, MeOH, THF, 0 °C, 3 h	**39** (84%), **250** (5%), **220** (4%)
		DBU, LiCl, MeCN, RT, 16 h	**39** (60%)
	249	NaOEt, EtOH, THF, 0 °C, 3 h	**218** (67%), **219** (3%), **220** (5%)
215	**248**	NaOMe, MeOH, THF, 0 °C, 3 h	**251** (65%)
		DBU, LiCl, MeCN, RT, 16 h	**251** (49%)
	249	NaOEt, EtOH, THF, 0 °C, 5 h	**238** (46%), **252** (19%), **241** (9%)
216	**248**	NaOMe, MeOH, THF, 0 °C, 3 h	**253** (56%), **254** (15%), **31** (11%)
		DBU, LiCl, MeCN, RT, 16 h	**253** (70%)
	249	NaOEt, EtOH, THF, 0 °C, 2 h	**221** (68%), **222** (5%)

Scheme 31

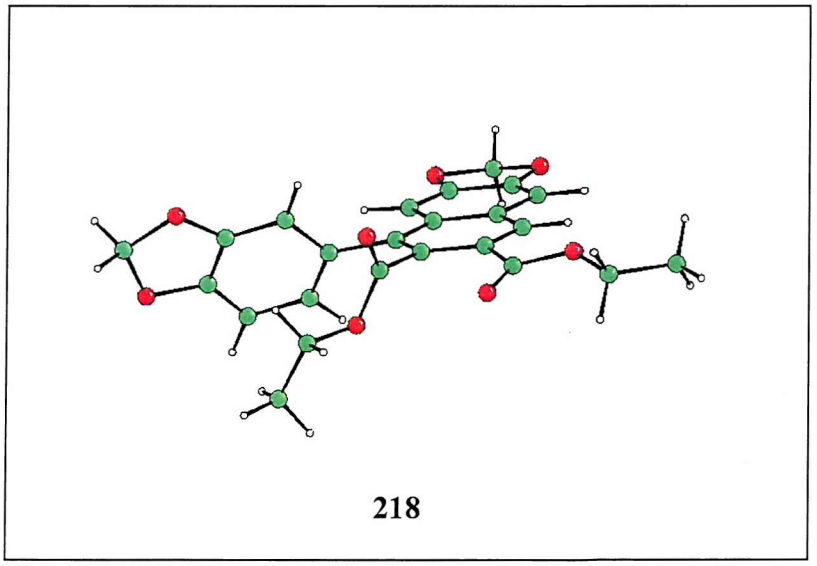
As is evident from the results above, the methodology is versatile and naphthalene construction was achieved over the whole range of substrates used, with the diester always given as the major product in good yield. The corresponding half-acids and γ-lactones were observed as by-products in most cases, but were easily separated from the diester as they remained in the basic aqueous phase during work-up. Nonetheless, we decided to seek an alternative method of effecting the benzannulation reaction in order to elevate the yields still further and avoid the generation of these by-products. Using lithium chloride and DBU in acetonitrile achieved that goal although, in some cases, the yields of the diester were reduced (**Scheme 31**).

2.3 Completing the Total Syntheses

With the requisite diesters to hand, we could now target the arylnaphthalene lignans. All that remained was to chemically differentiate the two ester groups in order to proceed towards the desired lactones and retrolactones. In the past, researchers have found that the ester at C-3 is more reactive and have used this to selectively obtain either the lactone or retrolactone from a diester precursor.[27,43,80] We also hoped to exploit this difference in reactivities for our own end game.

2.3.1 The Ester Dichotomy

In the hope of understanding the different reactivities of the ester groups, we obtained an x-ray crystal structure of arylnaphthalene **218** (**Figure 3**). It became evident that the ester group at C-2 was almost perpendicular to the plane of the naphthalene moiety. The x-ray structure clearly shows that both faces of this ester are blocked from nucleophilic attack, one face by the aryl ring and the opposing face by the adjacent ester group at C-3. The ester group at C-3 (farthest from the aryl ring) is more accessible and hence is more susceptible to nucleophilic attack. A vivid illustration of this fact is that exposure of **218** to potassium hydroxide selectively saponifies the ester group at C-3, but leaves the sterically hindered ester at C-2 untouched.[27] Interestingly, the ester at C-3 is conjugated to the naphthalene. Ordinarily, conjugation reduces the electrophilicity of a carbonyl group, yet this ester is more prone to hydrolysis! Thus, it is steric congestion that slows reaction of the non-conjugated ester at C-2.

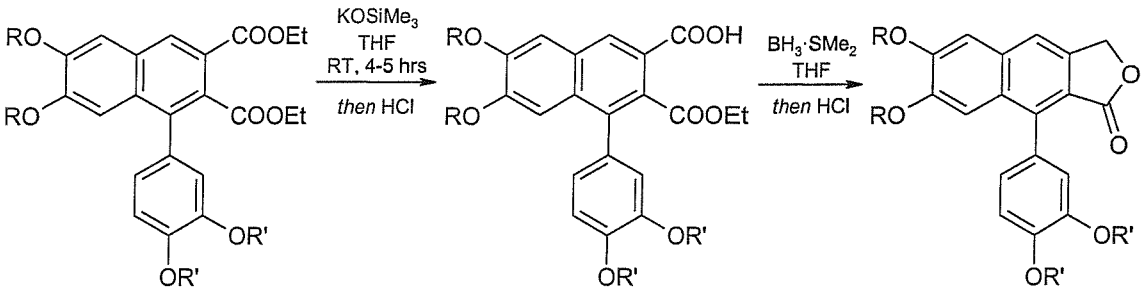


218

Figure 3

2.3.2 Forming the Lactones

Completing the syntheses from this juncture proved relatively straightforward. Diesters **218**, **221** and **238** were saponified with potassium trimethylsilanolate[43] to obtain the corresponding half-acids **219**, **222** and **252**. The procedure of Cow *et al.*, involving treatment of the half-acid with borane-dimethylsulfide complex followed by acidic work-up,[27] was then employed to furnish the desired lignans. In this manner, the syntheses of the arylnaphthalene lignans taiwanin C **3**, chinensin **4** and justicidin B **17** were achieved **(Scheme 32)**.



218 $R_2 = R'_2 = CH_2$
238 $R_2 = CH_2$, R' = Me
221 R = Me, $R'_2 = CH_2$

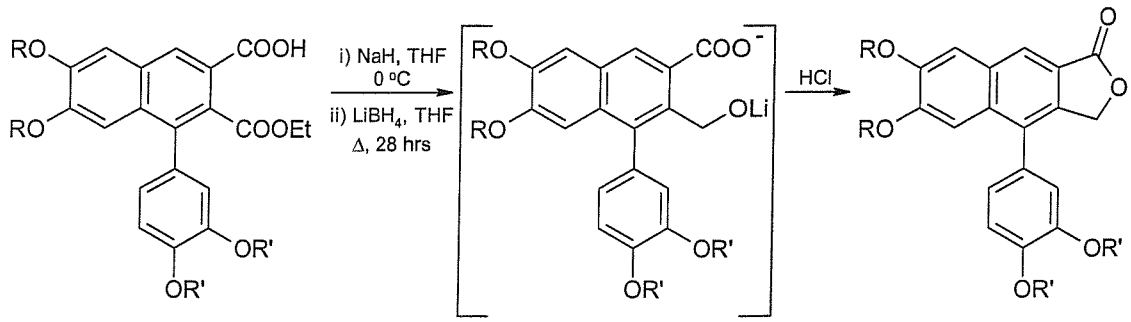
219 $R_2 = R'_2 = CH_2$ (98%)
252 $R_2 = CH_2$, R' = Me (94%)
222 R = Me, $R'_2 = CH_2$ (93%)

3 $R_2 = R'_2 = CH_2$ (87%)
4 $R_2 = CH_2$, R' = Me (97%)
17 R = Me, $R'_2 = CH_2$ (97%)

Scheme 32

2.3.3 Forming the Retrolactones

Efficient formation of the retrolactones proved more challenging. At first, we relied on a method developed by Padwa *et al.*[43] Half-acids **219**, **222** and **252** were deprotonated with sodium hydride then the ester moiety was reduced with lithium borohydride. Finally, addition of aqueous acid induced lactonisation **(Scheme 33)**.



219 $R_2 = R'_2 = CH_2$
252 $R_2 = CH_2$, R' = Me
222 R = Me, $R'_2 = CH_2$

255

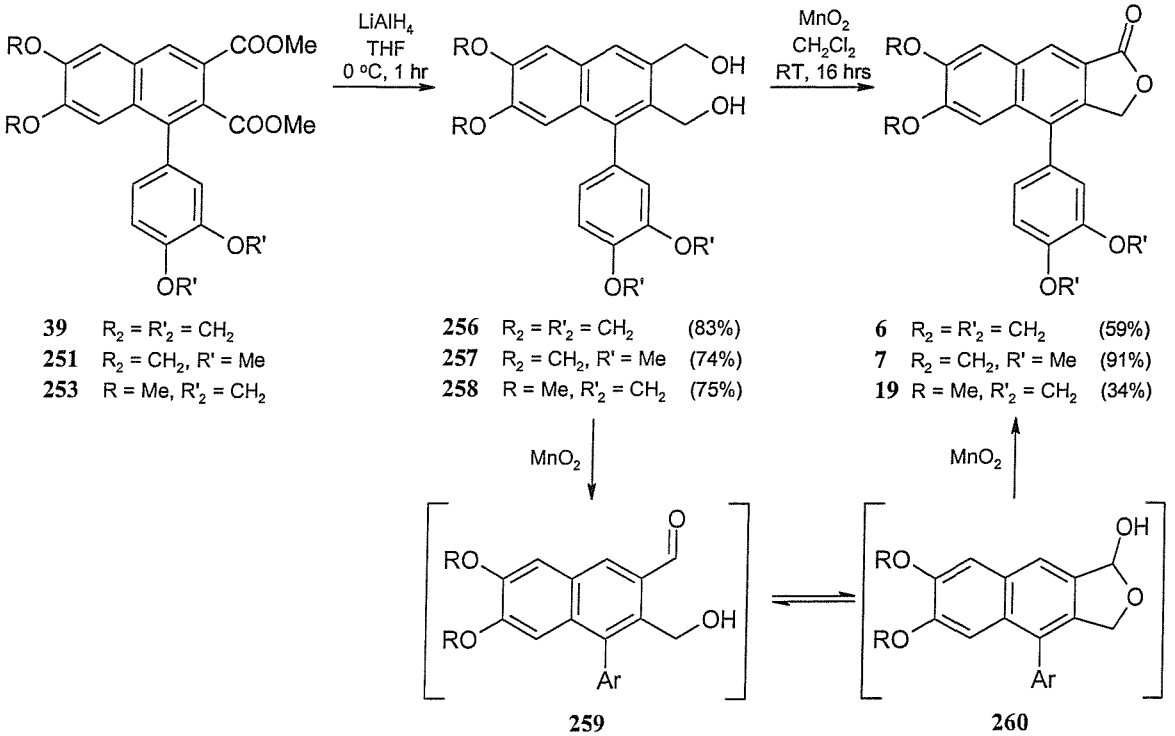
6 $R_2 = R'_2 = CH_2$ (57%)
7 $R_2 = CH_2$, R' = Me (72%)
19 R = Me, $R'_2 = CH_2$ (67%)
(plus 28% **17**)

Scheme 33

Although the retrolactones justicidin E **6**, retrochinensin **7** and retrojusticidin B **19** could be accessed using this methodology, it proved to be an inefficient and non-selective route. The

literature reported yield for the transformation of half-acid **219** to justicidin E **6** could not be reproduced and the yields for the conversion of the remaining half-acids were disappointing. We therefore sought a complimentary end game for our synthesis that would be both high yielding and exclusive for the retrolactone series. Reviewing the literature, we noted that Sammes *et al.*[46] and Holmes and Stevenson[65,66] had prepared retrolactones through the oxidation of diols akin to **256-258** using silver(I) carbonate. Formation of the retrolactone is presumably favoured due to the lower steric encumbrance of the alcohol at C-3 (*c.f.* Section 2.3.1).

To test this alternative route, diesters **39**, **251** and **253** were reduced using lithium aluminium hydride (**Scheme 34**) and the silver(I) carbonate oxidation trialled using diol **256**. Although the overall yield was good (81%), the reaction led to a disappointing 2:1 ratio of justicidin E **6** to taiwanin C **3**, prompting us to seek a more selective oxidation procedure. Pleasingly, it was found that treatment of the diols **256-258** with manganese(IV) oxide (**Scheme 34**) or barium manganate(VI) (**Scheme 35**) induced the required oxidation with much greater selectivity. Manganese(IV) oxide proved to be the more selective protocol, though product yields were consistently higher with barium manganate(VI). In the latter case, the formation of a small amount of the regioisomeric lactones was also observed. Hence, efficient syntheses of the arylnaphthalene lignans justicidin E **6**, retrochinensin **7** and retrojusticidin B **19** were all achieved.



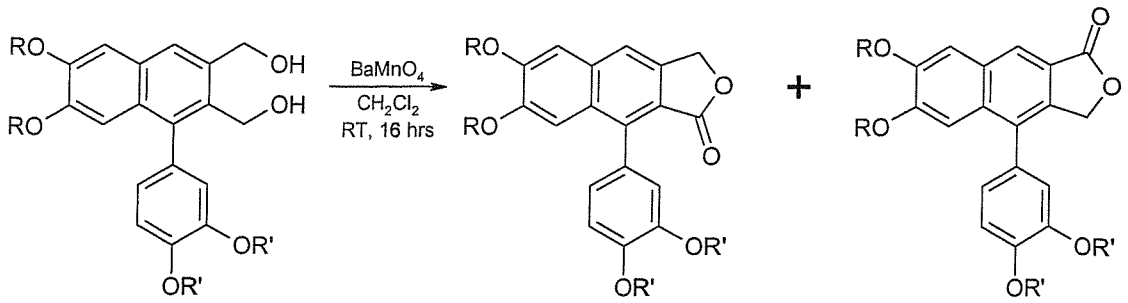
39 $R_2 = R'_2 = CH_2$
251 $R_2 = CH_2$, R' = Me
253 R = Me, $R'_2 = CH_2$

256 $R_2 = R'_2 = CH_2$ (83%)
257 $R_2 = CH_2$, R' = Me (74%)
258 R = Me, $R'_2 = CH_2$ (75%)

6 $R_2 = R'_2 = CH_2$ (59%)
7 $R_2 = CH_2$, R' = Me (91%)
19 R = Me, $R'_2 = CH_2$ (34%)

259 **260**

Scheme 34



256 $R_2 = R'_2 = CH_2$ (59%)
257 $R_2 = CH_2$, R' = Me (91%)
258 R = Me, $R'_2 = CH_2$ (34%)

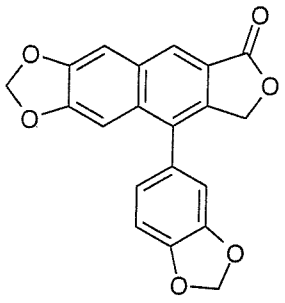
3 $R_2 = R'_2 = CH_2$ (14%)
4 $R_2 = CH_2$, R' = Me (19%)
17 R = Me, $R'_2 = CH_2$ (12%)

6 $R_2 = R'_2 = CH_2$ (71%)
7 $R_2 = CH_2$, R' = Me (80%)
19 R = Me, $R'_2 = CH_2$ (86%)

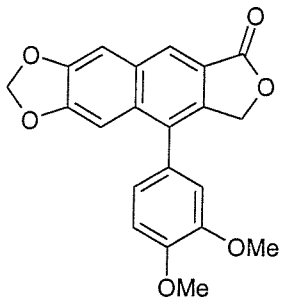
Scheme 35

2.4 Summary

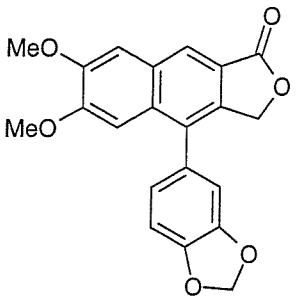
In conclusion, we have developed a new benzannulation reaction featuring a tandem Horner-Emmons and Claisen condensation sequence. The versatility of this new methodology has been proven through the syntheses of six arylnaphthalene lignans: taiwanin C **3**, chinensin **4**, justicidin B **17**, justicidin E **6**, retrochinensin **7** and retrojusticidin B **19** (**Figure 4**). A selective oxidation procedure has also been discovered that readily provides access to the retrolactone series from the corresponding diols. Barium manganate(VI) has been found to be superior to silver(I) carbonate in terms of yield, versatility and selectively.[79,81]



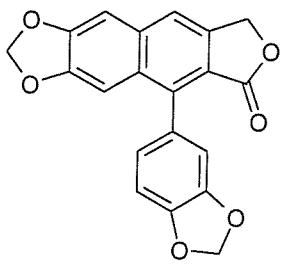
Justicidin E **6**



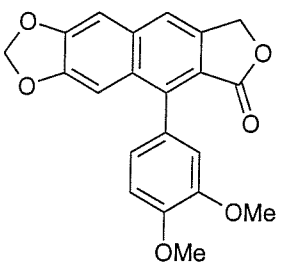
Retrochinensin **7**



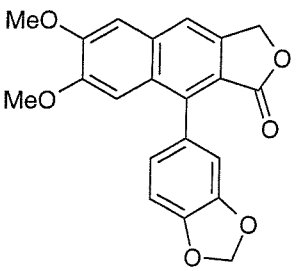
Retrojusticidin B **19**



Taiwanin C **3**



Chinensin **4**



Justicidin B **17**

Figure 4

Chapter 3

Intramolecular Radical Additions to Electron Rich Aromatic Heterocycles and Condensed Heterocycles

This chapter presents a brief summary of the literature concerning the intramolecular cyclisation of carbon centred radicals onto electron rich aromatic heterocycles. Additions to nitrogen-containing heterocycles such as indoles, pyrroles, imidazoles, benzimidazoles, pyrazoles and triazoles are reviewed. Intramolecular radical cyclisations to furans, thiophenes and benzo[*b*]thiophenes are also discussed.

3.1 Background

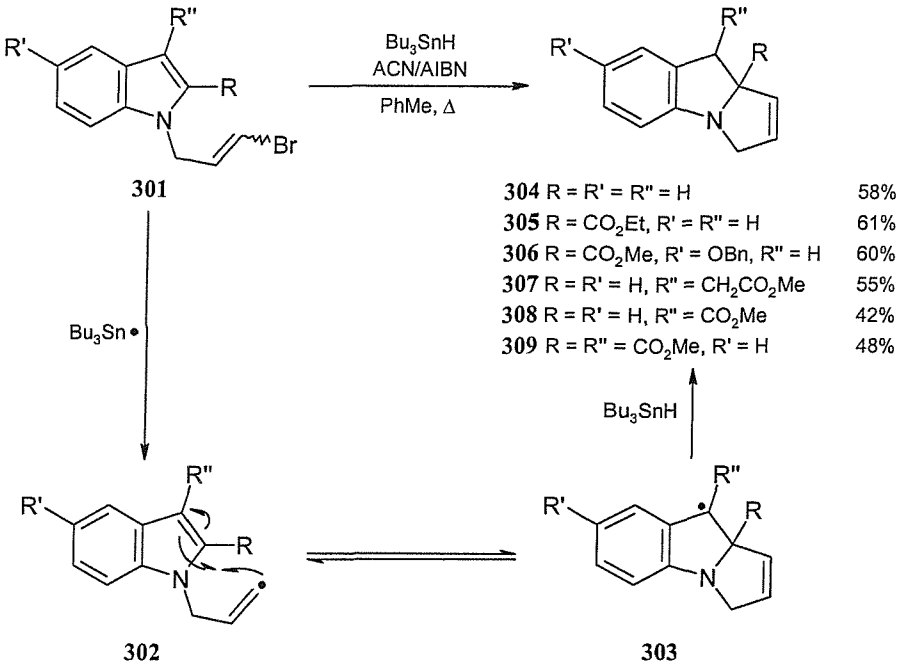
Heterocycles are often the core constituents of biologically active molecules, providing the pharmacophore around which SAR studies are based. As such, new methods of manipulation and functionalisation of heterocycles are vital for the development of future therapeutics. In recent years, the intramolecular addition of carbon centred radicals to aromatic heterocycles has emerged as an important way of introducing new rings and functionalisation. Radical methodology, in particular when employing tri-*n*-butyltin hydride as the mediator, often provides a mild and high-yielding way to add substituents to condensed aromatic ring systems and displays excellent tolerance of functional groups.

This review covers radical cyclisation reactions involving the addition of carbon centred radical intermediates to five-membered heteroaromatic ring systems. This field has developed over the past twelve years from an academic curiosity to an important new weapon in the armoury of the synthetic organic chemist.

3.2 Intramolecular Radical Additions to Nitrogen-Containing Heterocycles

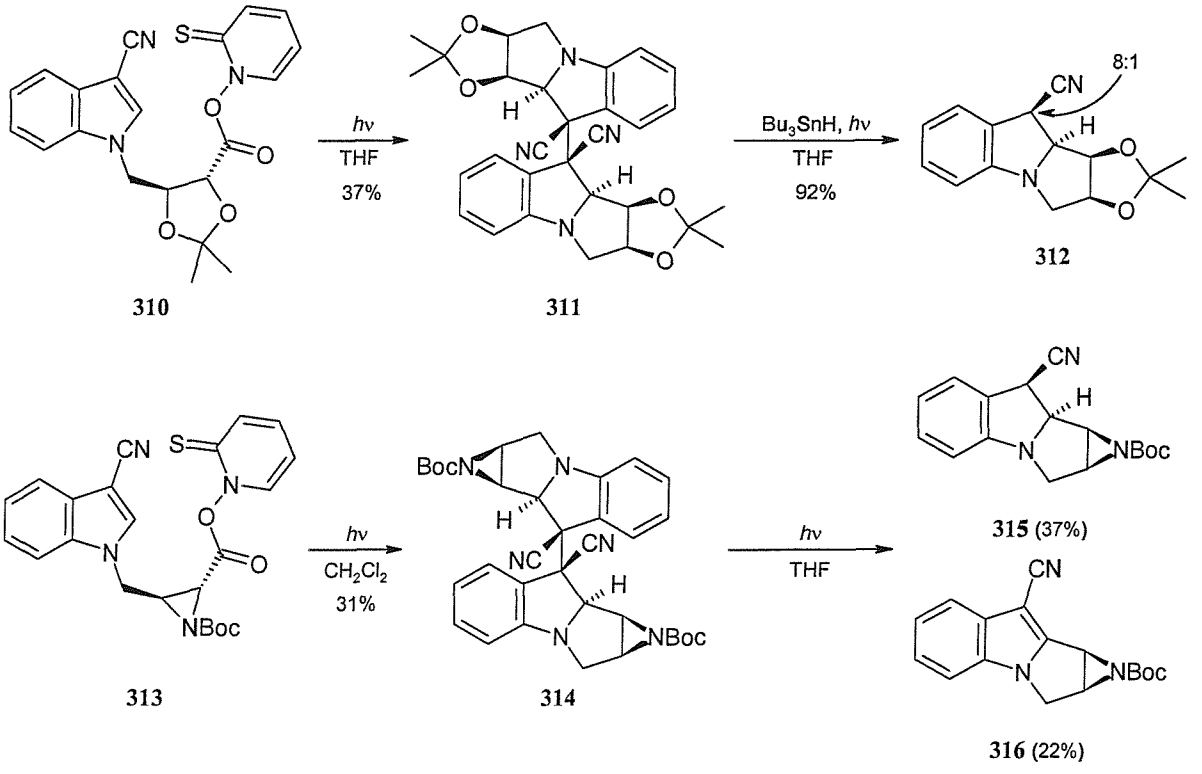
3.2.1 Addition of Carbon Centred Radicals to Indoles

Ziegler and Jeroncic were the first to demonstrate that indoles could act as radical acceptors.[82] A wide range of 9,9a-dihydro-3*H*-pyrrolo[1,2-*a*]indoles were synthesised by the intramolecular addition of an alkenyl radical to C-2 of an indole (**Scheme 36**).



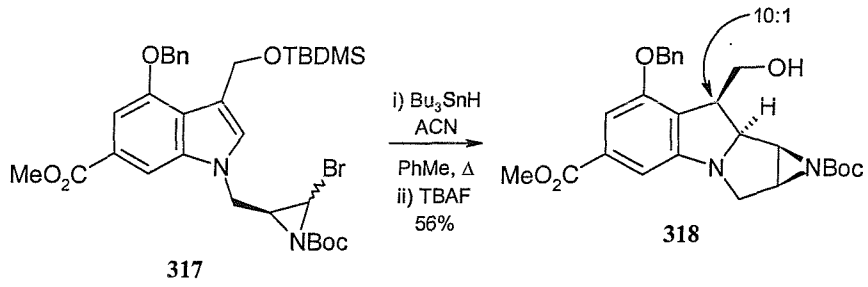
Scheme 36

In a later extension of this work, Ziegler attempted to obtain enantiomerically pure 9,9a-dihydro-3*H*-pyrrolo[1,2-*a*]indoles *via* the addition of chiral dioxolanyl[83] and aziridinyl[84] radicals. However, progress was hampered by the persistent formation of dimeric species such as **311** and **314** (**Scheme 37**).



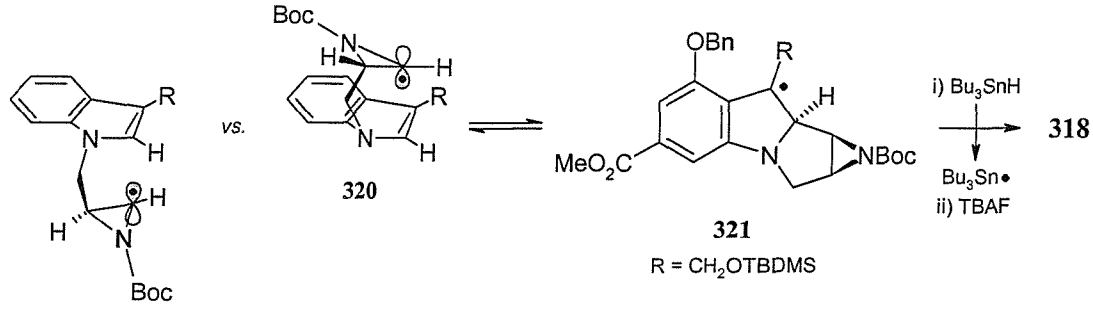
Scheme 37

Although these dimers could be homolysed to enantiomerically pure 9,9a-dihydro-3*H*-pyrrolo[1,2-*a*]indoles **312** and **315**, a method of directly generating chiral 9,9a-dihydro-3*H*-pyrrolo[1,2-*a*]indoles was sought. This was achieved using an aziridinyl bromide as the radical precursor: the cyclisation of **317** forming 9,9a-dihydro-3*H*-pyrrolo[1,2-*a*]indole **318** as a 10:1 mixture of diastereoisomers (**Scheme 38**).[85]



Scheme 38

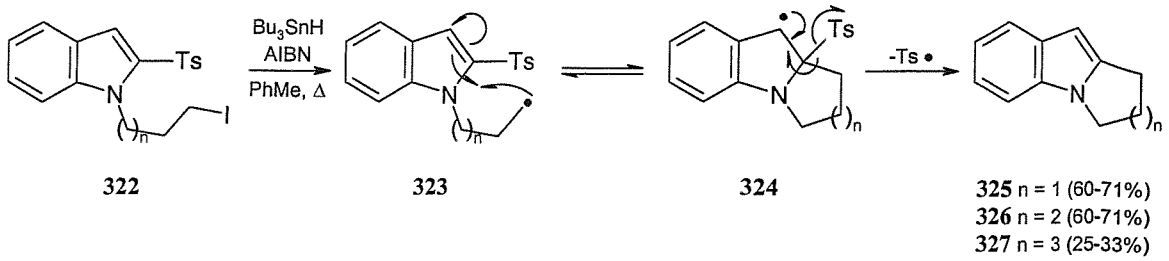
Ziegler *et al.* commented that they had expected the reaction to proceed *via* transition state **319**.[83] However, radical addition proceeded instead *via* the more hindered transition state **320**, bringing the bulky aziridine Boc group much closer to the indole system (**Scheme 39**). The authors suggest that transition state **320** was favoured due to an electronic effect, possibly involving electron transfer. Hydrogen-atom abstraction from tri-*n*-butyltin hydride to the less-hindered convex face of **321** completes the transformation.



NB: Arene functionality has been omitted for clarity

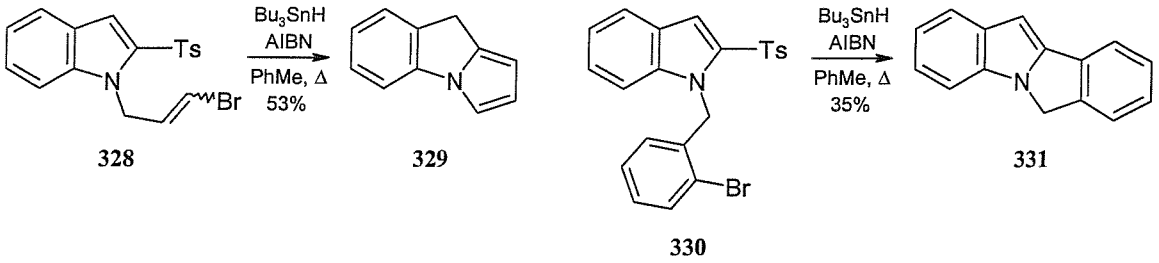
Scheme 39

Caddick *et al.* were next to investigate the intramolecular addition of carbon centred radicals to indoles.[86-89] They showed that fused [1,2-*a*]indoles could be accessed *via* intramolecular addition of an *N*-tethered alkyl radical to C-2 of an indole, followed by the ejection of a tosyl radical from the same site (**Scheme 40**).[86] Aryl sulfides and sulfoxides also function as radical leaving groups for this type of transformation.[87,90]



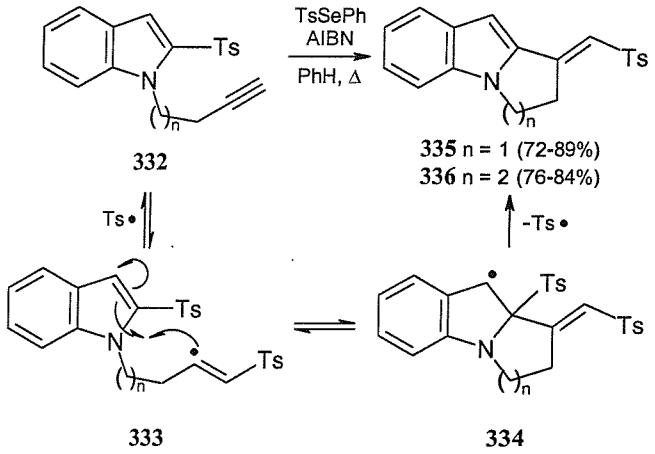
Scheme 40

They later found that these cyclisations could be performed with alkenyl and aryl radicals, providing access to pyrrolo[1,2-*a*]- and isoindolo[1,2-*a*]-indoles (**Scheme 41**).[88]



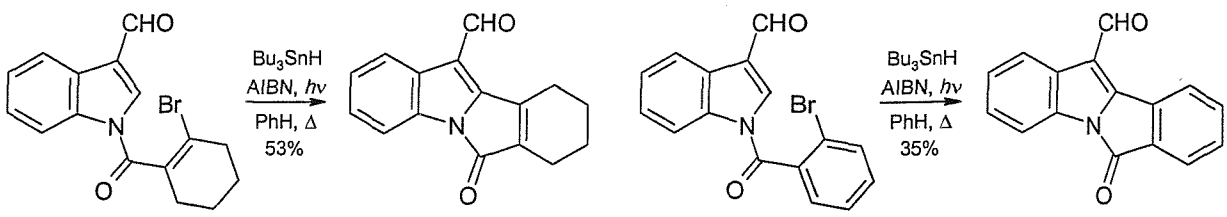
Scheme 41

More recently, and in an interesting twist to the methodology, Caddick *et al.* have found that similar cyclisations can be effected using phenyl-*para*-tolueneselenosulfonate, with a terminal alkene or alkyne serving as the radical precursor.[89,91] Addition of the tosyl radical to the alkene or alkyne results in the formation of a carbon centred radical which undergoes cyclisation in the manner depicted below (**Scheme 42**).



Scheme 42

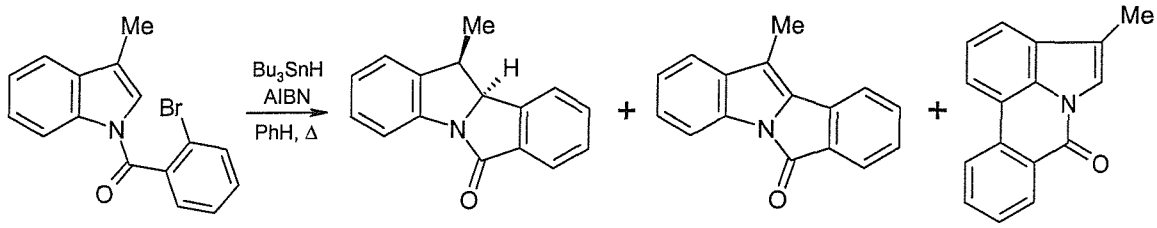
Kraus and Kim have also reported a radical route to isoindolo[1,2-*a*]indoles (**Scheme 43**).[92] They found that cyclisation of a vinyl or aryl radical intermediate to C-2 was followed by rearomatisation of the indole system, even though that position carried no radical leaving group. The mechanism of rearomatisation remains the subject of much debate in the literature, and is discussed in more detail towards the end of this chapter (Section 3.4).



337 338 339 340

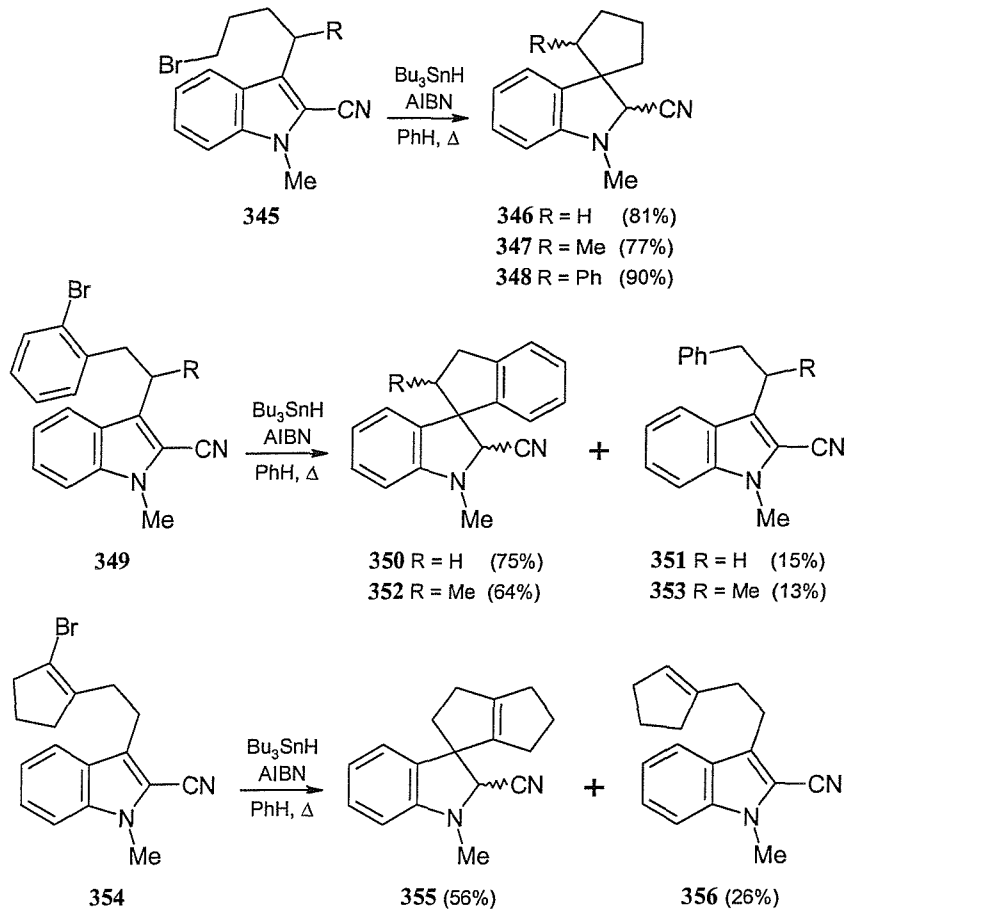
Scheme 43

Curiously, later research by Tsuge and co-workers appeared to contradict the findings of Kraus and Kim (**Scheme 44**).[93] Tin-mediated radical cyclisation of **341** gave dihydro-isoindolo[1,2-*a*]indole **342** as the major product, together with small amounts of the aromatised products **343** and **344** (the latter arising from radical addition to C-7 of the indole). Likewise, Zhang and Pugh observed the products of a reductive pathway when performing related cyclisations a year later.[94]



341 **342** (83%) **343** (3%) **344** (8%)

Scheme 44



345

346 R = H (81%)
347 R = Me (77%)
348 R = Ph (90%)

349

350 R = H (75%)
352 R = Me (64%)

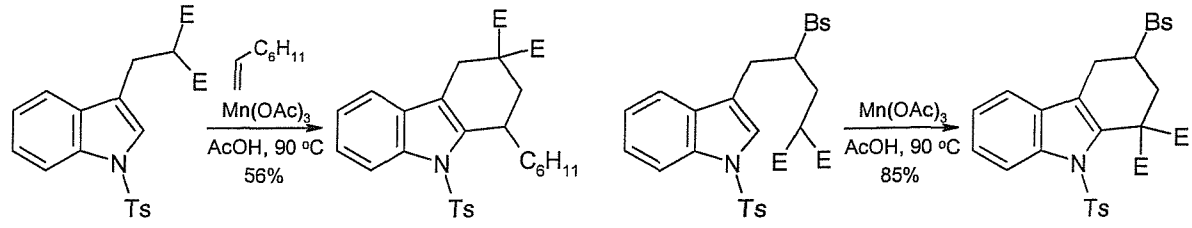
351 R = H (15%)
353 R = Me (13%)

354 **355** (56%) **356** (26%)

Scheme 45

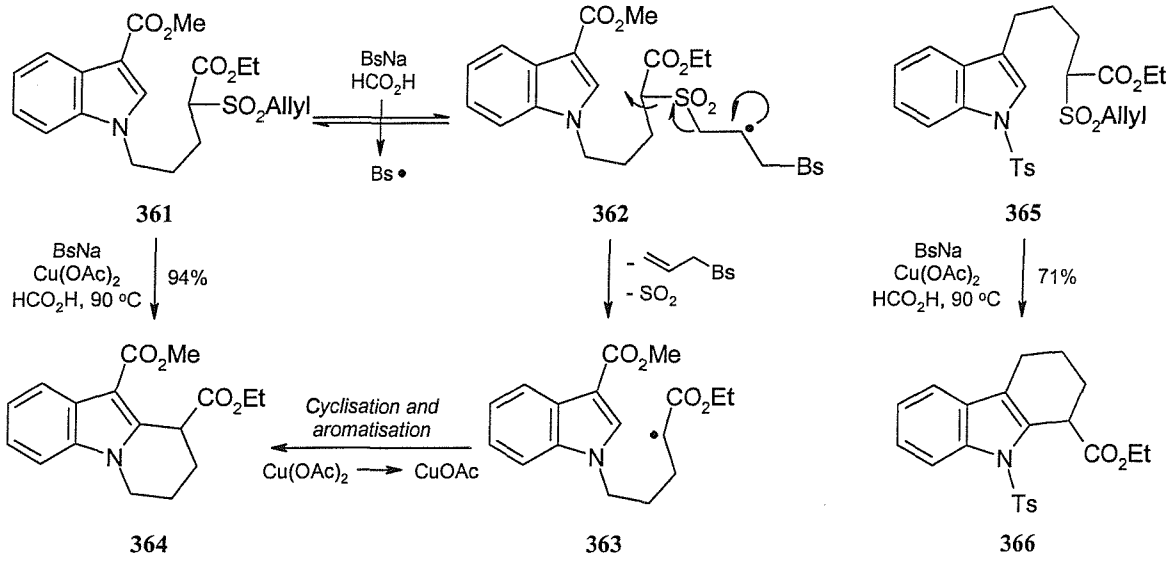
Fang *et al.* were the first to demonstrate that intramolecular radical additions to C-3 of an indole were feasible.[95] Using an alkyl tether between the radical precursor and acceptor, C-3 additions of alkyl, alkenyl and aryl radical intermediates were accomplished over a wide range of substrates (**Scheme 45**).

Later, Chuang and Wang demonstrated that 3-indolylmethyl malonates, on exposure to manganese(III) acetate, could intercept an alkene in a cascade radical cyclisation that culminated in intramolecular addition to C-2 of the indole.[96] 3-Indolylpropyl malonates underwent a similar intramolecular addition (**Scheme 46**). In each case, cyclisation was followed by rearomatisation.



Scheme 46

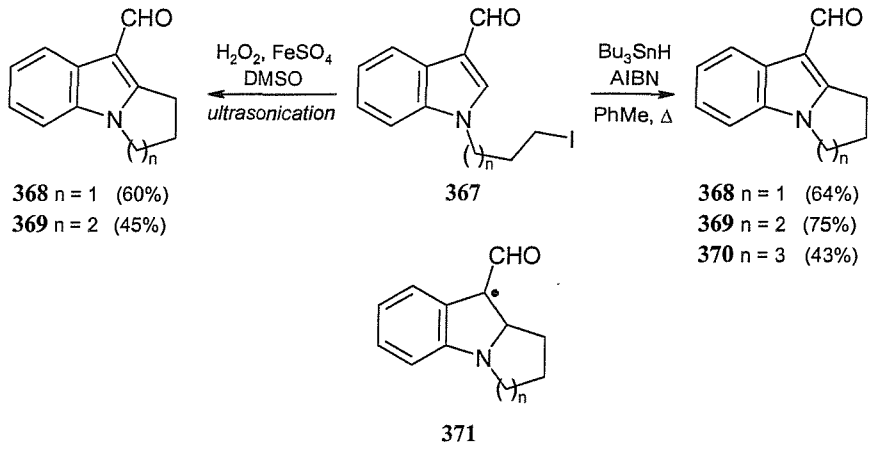
ω-(Allylsulfonylalkyl)indoles were also found to undergo intramolecular cyclisation.[97,98] This time, a benzenesulfonyl radical was used to initiate the process (**Scheme 47**).



Scheme 47

Muchowski *et al.* showed that 5- and 6-*exo*-trig cyclisations to C-2 of an indole could be accomplished with *N*-tethered alkyl iodides using catalytic ferrous sulfate and hydrogen peroxide in DMSO (**Scheme 48**).[99] Methyl radicals, formed from DMSO under the reaction conditions, mediate the process. Again, rearomatisation was observed in the absence of any

radical leaving group; it was assumed that the aromatisation of **371** was facilitated by hydrogen peroxide. Notably, Moody and Norton later showed that the same reaction could be mediated by tri-*n*-butyltin hydride. They also accomplished a 7-*exo*-trig cyclisation in this manner, albeit in moderate yield.[100,101] As in the earlier example of Kraus and Kim,[92] rearomatisation was observed in the absence of an obvious oxidant (**Scheme 48**).



368 n = 1 (60%)
369 n = 2 (45%)

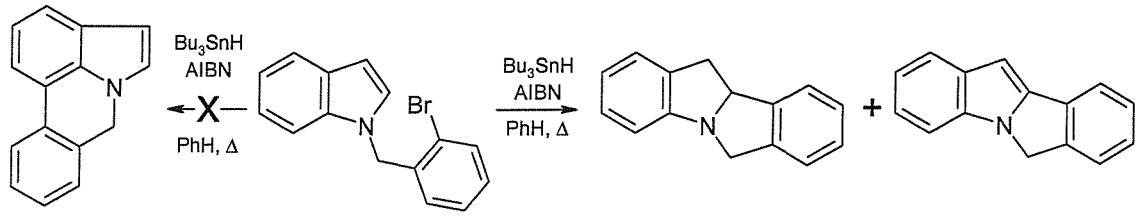
367

368 n = 1 (64%)
369 n = 2 (75%)
370 n = 3 (43%)

371

Scheme 48

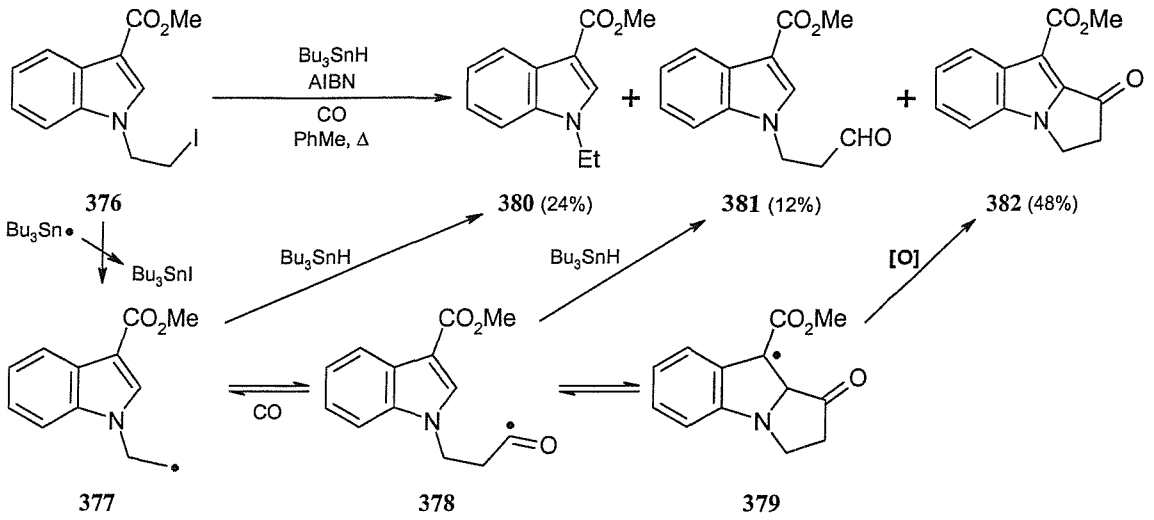
As part of a study towards the synthesis of phenanthridines by radical coupling, Lobo *et al.* reported that, on cyclisation, *N*-bromobenzylindole **372** yielded dihydroisoindolo[1,2-*a*]indole **374** rather than the desired pyrrolophenanthridine **373**. A small amount of the fully aromatic isoindolo[1,2-*a*]indole **375** was also obtained (**Scheme 49**).[102]



373 **372** **374** (47%) **375** (5.6%)

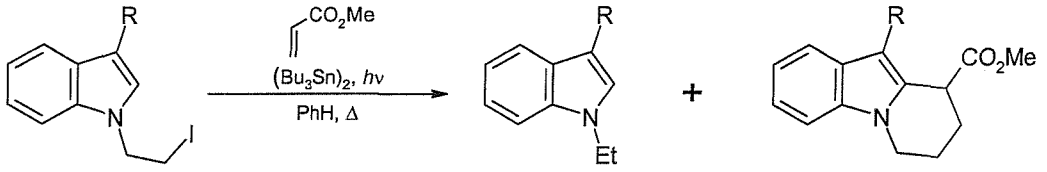
Scheme 49

Miranda *et al.* used this methodology to access 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-ones.[103] On performing the tin-mediated radical cyclisations under an atmosphere of carbon monoxide, they found that carbon monoxide was trapped to create an acyl radical (**377** to **378**). This then underwent cyclisation to C-2 of the indole followed by rearomatisation (**Scheme 50**).



Scheme 50

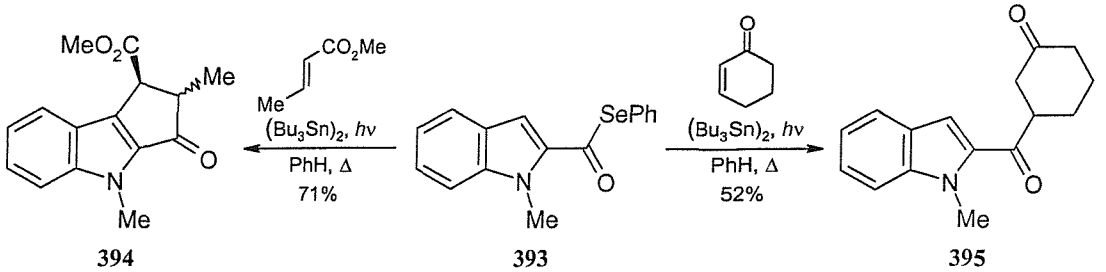
Similar substrates were also employed by Miranda and co-workers to promote sequential 1,4-addition to methyl acrylate, followed by cyclisation to C-2 of the indole. A range of fused [1,2-*a*]indoles were accessed using this methodology (**Scheme 51**).[104]



380 R = CO_2Me	(*traces*)	**384** R = CO_2Me	(60%)
385 R = CHO	(31%)	**386** R = CHO	(45%)
387 R = $COCO_2Et$	(-)	**388** R = $COCO_2Et$	(32%)
389 R = CN	(-)	**390** R = CN	(54%)
391 R = H	(-)	**392** R = H	(15%)

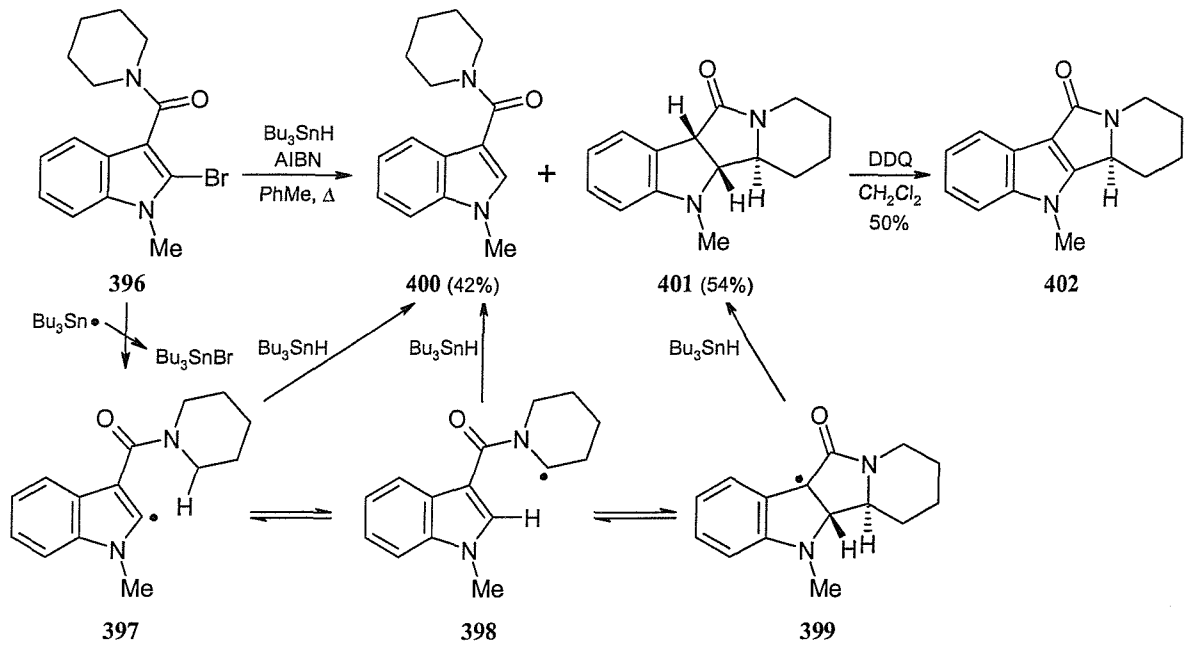
Scheme 51

In related work, Bennasar *et al.* generated 2-indolylacyl radicals directly from the corresponding phenyl selenoesters. 1,4-Additions to a variety of α,β-unsaturated esters, ketones, amides and nitriles were used to trigger cyclisation to C-3 of the indole, leading to a range of fused [2,3-*a*]indoles.[105] Cyclisation was observed in many cases, though products derived from reductive addition were noted with, for example, cyclohexenone (**Scheme 52**).



Scheme 52

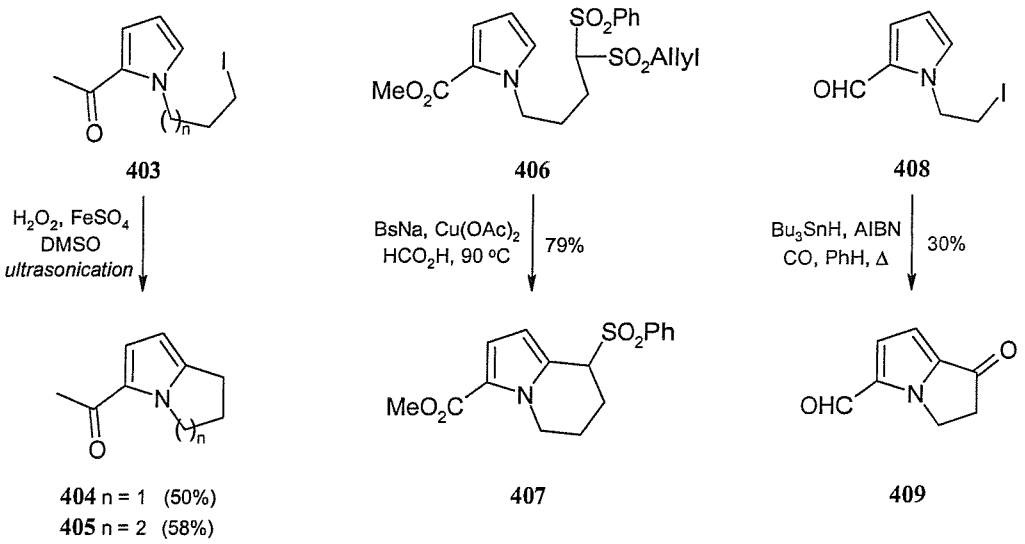
In a recent communication, Gribble *et al.* presented a new synthesis of hexahydropyrrolo[3,4-*b*]indoles using a radical translocation strategy.[106] 2-Bromoindole-3-carboxamide **396** was exposed to tri-*n*-butyltin radical, generating indolyl radical **397** (**Scheme 53**). Hydrogen atom abstraction α- to the nitrogen of the carboxamide then generated alkyl radical **398**, which added to the indole at the C-2 position. Subsequent hydrogen atom abstraction from tri-*n*-butyltin hydride furnished indoline **401**, which was oxidised to the desired hexahydropyrrolo[3,4-*b*]indole **402** with DDQ.



Scheme 53

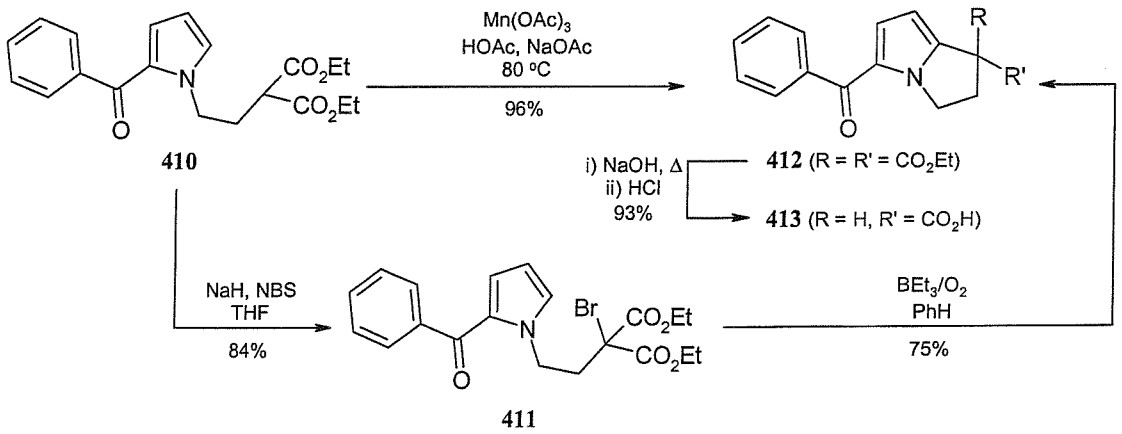
3.2.2 Addition of Carbon Centred Radicals to Pyrroles

Some of the studies described above were extended to, or originated from, work on related pyrrole ring systems. For example, Muchowski *et al.* studied cyclisations to a variety of pyrroles using catalytic ferrous sulfate/hydrogen peroxide/DMSO (left, **Scheme 54**).[99] Chaung *et al.* extended their work on the reaction of α-sulfonyl radicals generated by the addition of benzenesulfonyl radicals (centre, **Scheme 54**),[98] whilst Miranda and colleagues studied intramolecular acyl radical additions to both pyrrole and indole ring systems (right, **Scheme 54**).[103,107] However, some stand-alone studies of intramolecular radical additions to pyrroles have been conducted.



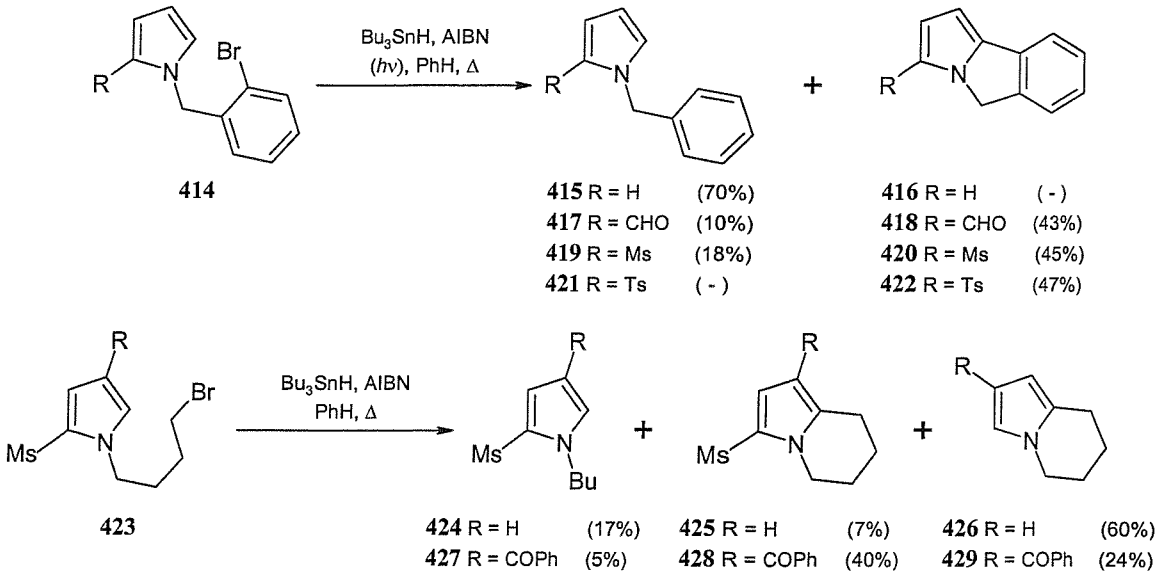
Scheme 54

The earliest example comes from the work of Muchowski, Artis and Cho.[108] In 1992, they showed that a malonate group, tethered to a pyrrole *via* the nitrogen, would undergo cyclisation to C-2 of the pyrrole on exposure to manganese(III) acetate. They also found that the equivalent bromomalonate would give the same reaction when treated with triethylborane and air (**Scheme 55**). In this manner, they managed to obtain the analgesic keterolac **413**.



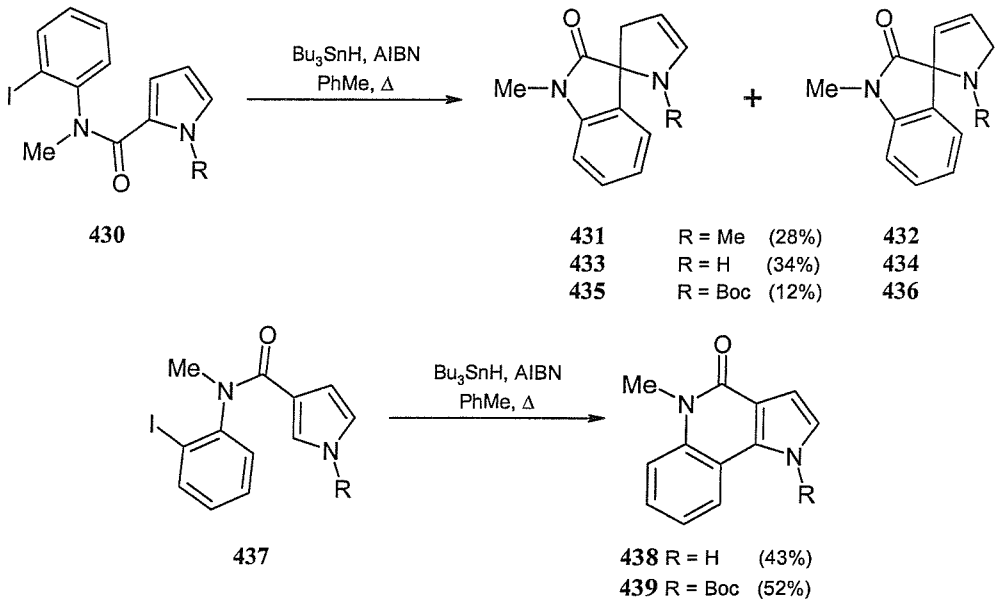
Scheme 55

Later work by Muchowski *et al.* revealed that tri-*n*-butyltin hydride would mediate the cyclisation of *N*-tethered *o*-benzyl and alkyl bromides to C-2 of a pyrrole, as long as the pyrrole was substituted with an electron-withdrawing group (**Scheme 56**).[109] Yet again, upon addition of the carbon centred radical, rearomatisation occurred in the absence of an obvious oxidant.



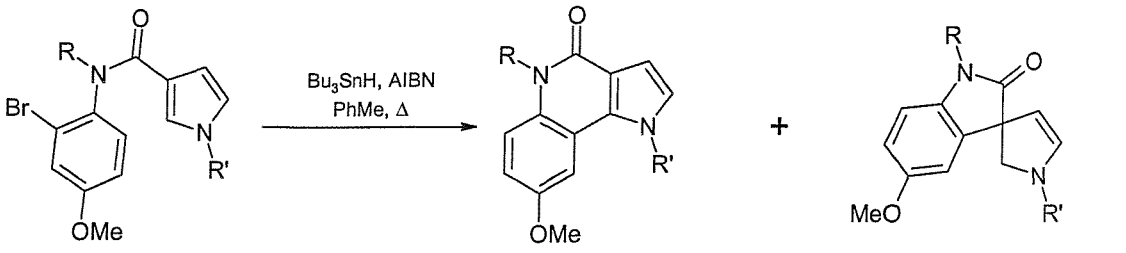
Scheme 56

Jones *et al.* were the first to examine spirocycle formation through the addition of aryl radical intermediates to C-2 of a pyrrole.[110,111] However, when the analogous C-3 spiro-cyclisation was attempted, they observed a 6-*endo*-trig cyclisation to C-2 followed by aromatisation (**Scheme 57**).



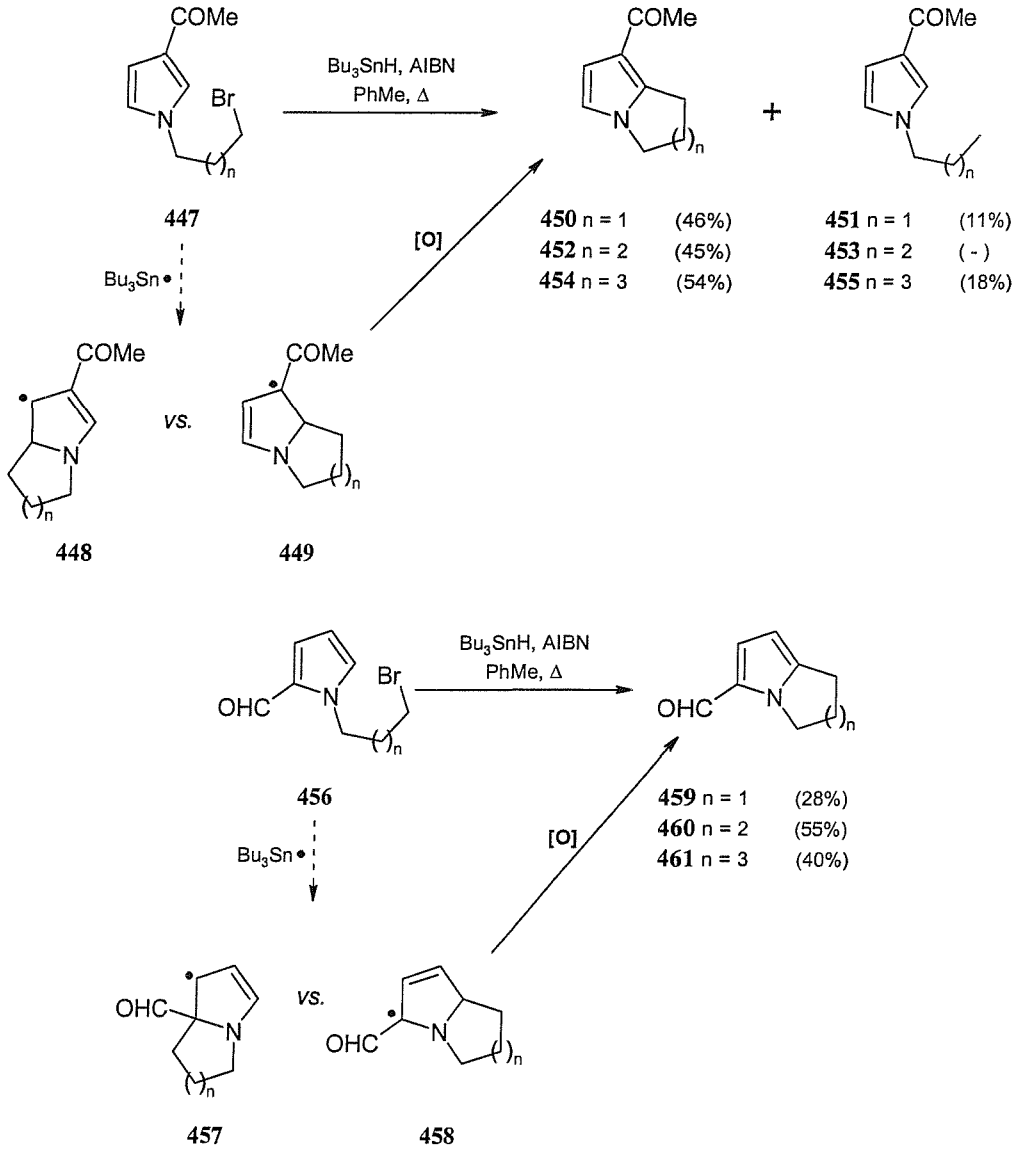
Scheme 57

Further research by Jones and Escolano found that spiro-cyclisation to C-3 of the pyrrole could be achieved with **440** (R' = Boc and R' = CO_2Me).[112] However, yields were low and the formation of minor products derived from cyclisation to C-2 could not be avoided (**Scheme 58**). Yet these results exposed an interesting dichotomy: iodide precursor **437** was analogous to bromide **440** (R' = Boc), yet on cyclisation followed a 6-*endo*-trig mode with rearomatisation exclusively, with C-3 addition unobserved (**Scheme 57**). Jones and Escolano did not account for this dichotomy, but our rationalisation is detailed in Section 3.4.



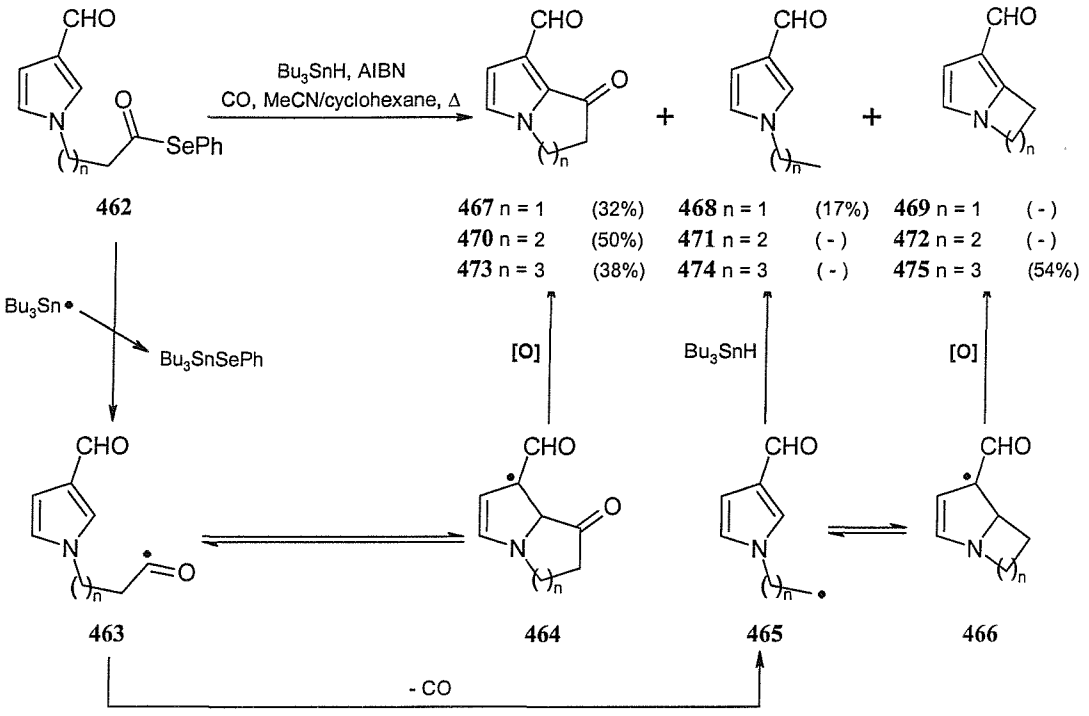
Scheme 58

Bowman *et al.* have published a study on the intramolecular addition of *N*-tethered alkyl radicals to C-2 of a pyrrole.[113,114] 5-, 6- and 7-*exo*-trig cyclisations were shown to be feasible (**Scheme 59**). Most notably, the reaction pathway was always found to proceed *via* the more stabilised product radical intermediate *i.e.* **449** over **448**, and **458** over **457**.



Scheme 59

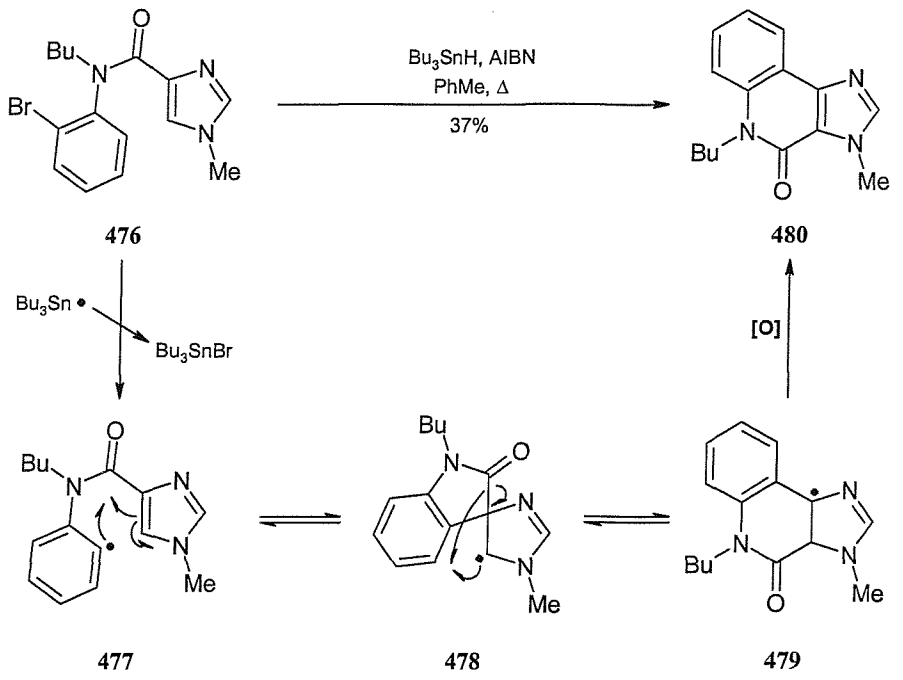
N-tethered acyl radicals initially proved more difficult to cyclise, favouring decarbonylation of the acyl radical.[115] Conducting the reaction in a two-phase solvent system of acetonitrile and cyclohexane under an atmosphere of carbon monoxide was found to lessen this side reaction, and 5-, 6- and 7-*exo*-trig cyclisations to C-2 of the pyrrole were achieved in modest yield (**Scheme 60**).



Scheme 60

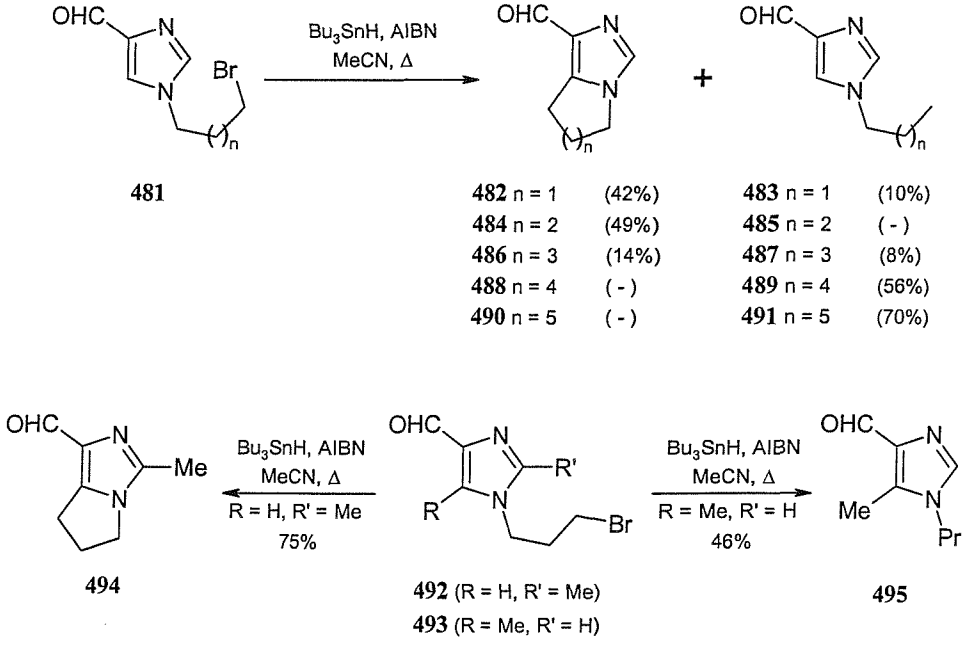
3.2.3 Addition of Carbon Centred Radicals to other Nitrogen-Containing Heterocycles

Suzuki and Kuroda were the first to study intramolecular radical additions to imidazoles.[116] In 1993, they employed a tin-mediated 5-*exo*-trig radical cyclisation to C-4 of an imidazole in order to obtain antiasthmatic agent **480**. The mechanism is notable in that spiro-cyclisation is followed by an acyl shift (**478** to **479**), accounting for the observed regiochemistry (**Scheme 61**).



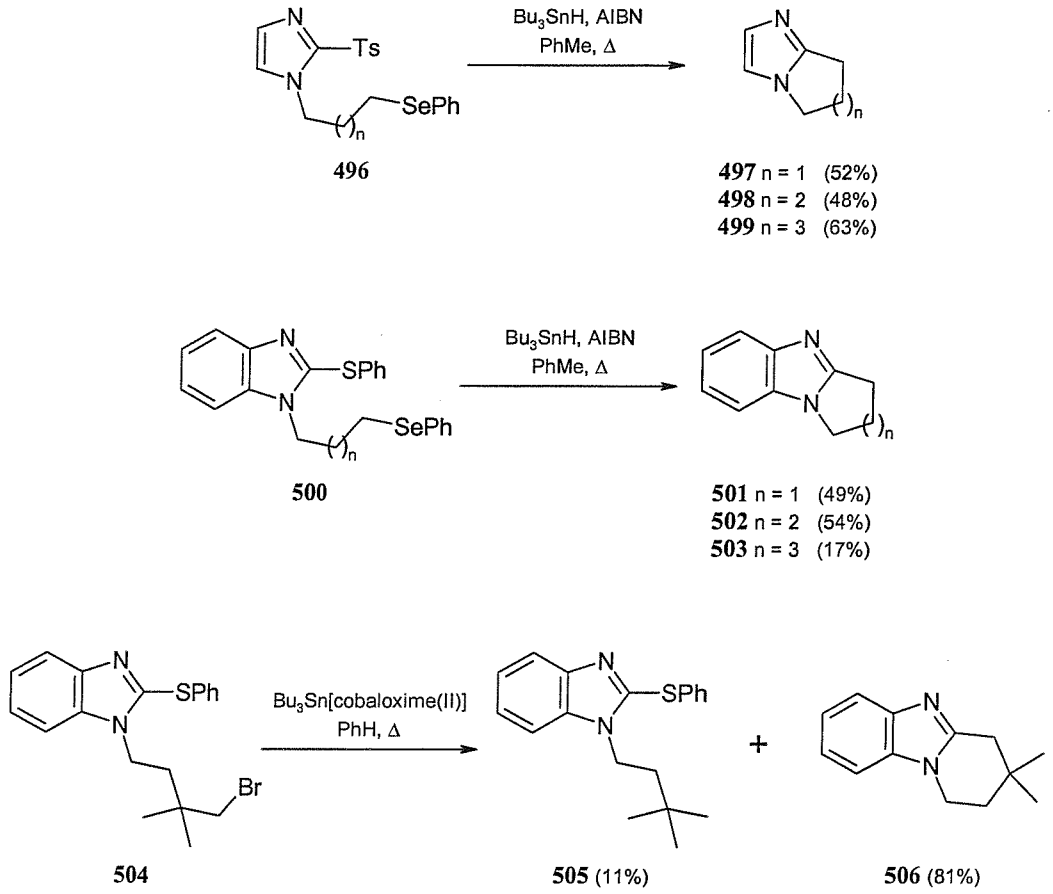
Scheme 61

Some years later, Bowman *et al.* showed that alkyl radical additions to C-5 of an imidazole were facile and outpaced addition to C-2 (**Scheme 62**).[113,114] Tethering the radical donor through the nitrogen led to moderate yields when the C-5 position was free of functionalisation. However, when the C-5 position was blocked by a methyl group, as in **493**, only the reduction product **495** was formed. Attempts were made to achieve 8- and 14-membered cyclisations but, in these instances, only products derived from reduction of the carbon-bromine bond were isolated.



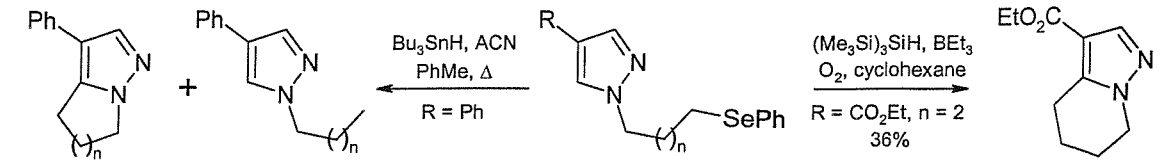
Scheme 62

It was later found additions to C-2 were possible in imidazoles and benzimidazoles, provided that a radical leaving group was incorporated at that position (**Scheme 63**).[90,117,118] Curiously, the 7-*exo*-trig cyclisation mode was the most effective in the imidazole series, yet gave poor results with the corresponding benzimidazole. In that series, the 6-*exo*-trig cyclisation mode was the most effective.



Scheme 63

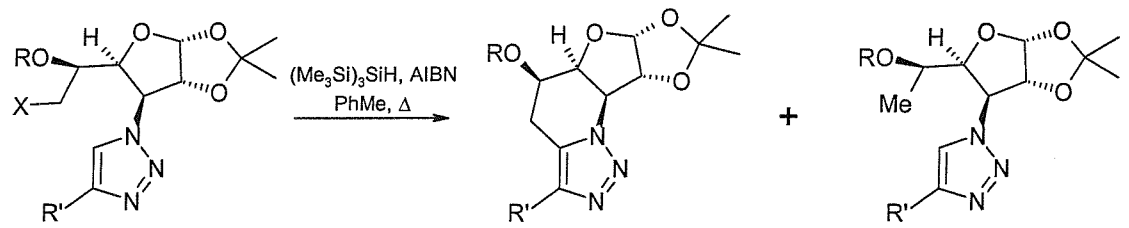
Most recently, intramolecular additions of *N*-tethered alkyl radicals to C-5 of the pyrazole system have been studied.[119] Functional groups on the heterocycle were found to influence the course of the reaction. Phenyl-substituted precursors akin to **507** underwent cyclisation in reasonable yield under tin-mediated radical conditions, whereas for ester-functionalised pyrazole **514**, cyclisation was recalcitrant due to fast hydrogen atom abstraction from tri-*n*-butyltin hydride by the radical intermediates (**Scheme 64**). When *tris*-trimethylsilylsilane and triethylborane were used to mediate the reaction, 6-*exo*-trig cyclisation proved feasible, albeit in low yield.



508 n = 1 (38%) **509** n = 1 (17%) **507** (R = Ph) **515**
510 n = 2 (63%) **511** n = 2 (-) **514** (R = CO_2Et, n = 2)
512 n = 3 (37%) **513** n = 3 (48%)

Scheme 64

Marco-Contelles and Rodriguez-Fernandez have published the only reported examples of intramolecular additions of alkyl radicals to a triazole ring system.[120] In their work towards the synthesis of triazole-piperidinoses, 6-*exo*-trig radical cyclisations were attempted onto C-5 of a functionalised 1,2,3-triazole in order to form the triazole-piperidinose skeleton (**Scheme 65**). Although the yields attained were low, the starting material was recovered in most cases and the authors note that the reactions have yet to be optimised. Thus, future research in this area may be fruitful.



516 R = H, R' = $SiMe_3$, X = Br
519 R = Ac, R' = $SiMe_3$, X = Br
521 R = R' = H, X = I

517 R = H, R' = $SiMe_3$ (36%)
(61% conversion by RSM)
520 R = Ac, R' = $SiMe_3$ (32%)
(78% conversion by RSM)
522 R = R' = H (17%)

518 R = H, R' = $SiMe_3$ (11%)
(19% conversion by RSM)

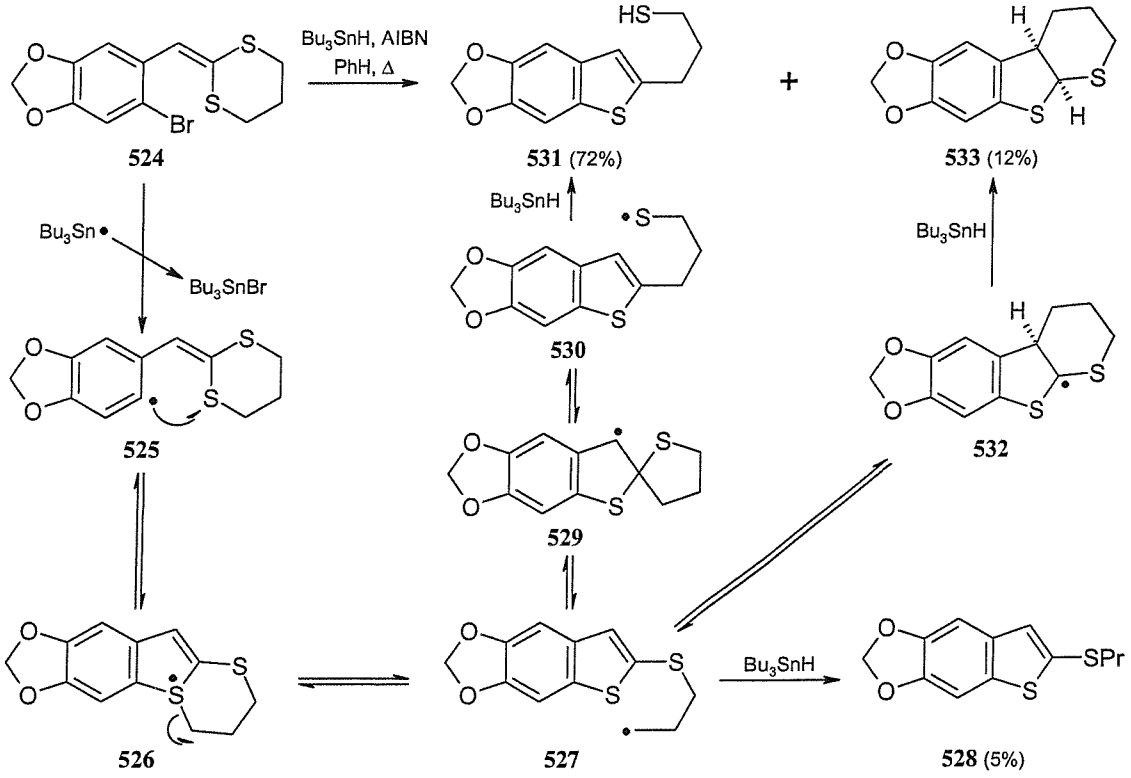
523 R = R' = H (22%)

Scheme 65

3.3 Intramolecular Radical Additions to Oxygen- and Sulfur-Containing Heterocycles

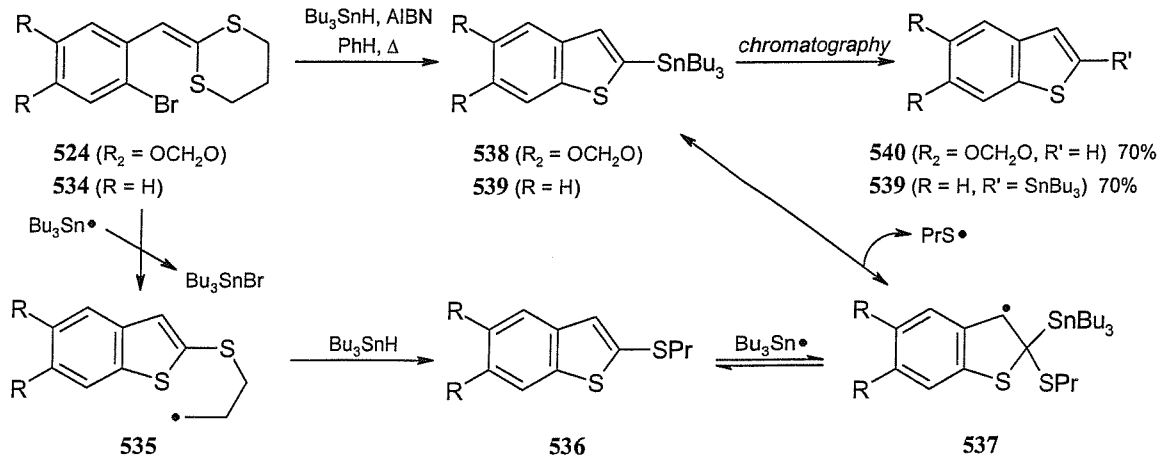
The first examples of intramolecular radical additions to thiophenes and benzo[*b*]thiophenes were published by Harrowven in 1993.[121] Exposure of ketenethioacetal **524** to tri-*n*-butyltin radical promoted cyclisation to sulfur followed by fragmentation to benzo[*b*]thiophene **527** (**Scheme 66**). The resulting alkyl radical then underwent a 5-*exo*-trig cyclisation to C-2 of the benzo[*b*]thiophene. Fragmentation to the more stable thiol radical **530** and quenching by hydrogen atom abstraction from tri-*n*-butyltin hydride gave benzo[*b*]thiophene **531** as the major product. Minor quantities of benzo[*b*]thiophene **528**, formed by the direct quenching of alkyl radical **527**, and tetracyclic thioacetal **533**, from 6-*endo*-trig cyclisation of alkyl radical **527** to the benzo[*b*]thiophene C-3, were also observed.

The reaction achieved the synthesis of a variety of benzo[*b*]thiophenes and thieno[3,2-*b*]thiophenes in good yield, and in each case the by-products accounted for little of the total mass balance.



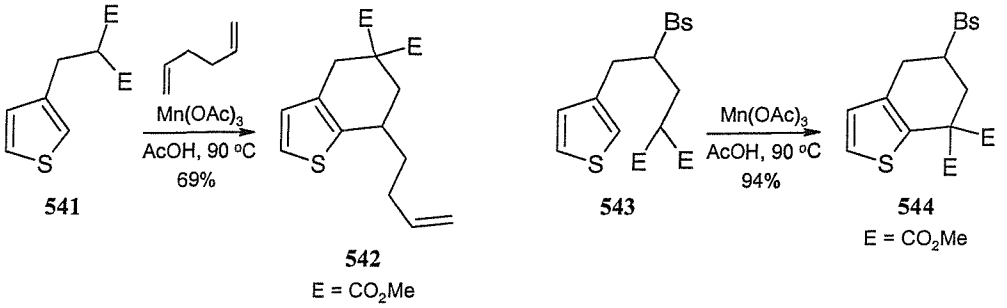
Scheme 66

Further research showed that performing the same reaction in the presence of a high concentration of tri-*n*-butyltin hydride resulted in formation of the corresponding 2-tributylstannylbenzo[*b*]thiophene.[122] In some instances the stannylated benzo[*b*]thiophene could be isolated, as illustrated below for the cyclisation of ketenedithioacetal **534**. In other cases, protodestannylation occurred on work-up, yielding the corresponding C-2 unsubstituted benzo[*b*]thiophene (**Scheme 67**).

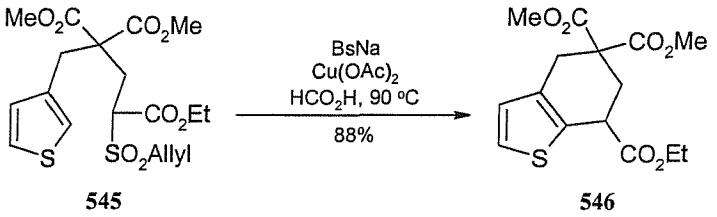


Scheme 67

In 1994, Chuang and Wang extended their study of manganese(III) acetate-initiated radical cyclisations to thiophene derivatives, the highest yielding examples of which are illustrated in **Scheme 68**.[96] In most cases, the yields obtained surpassed those achieved in the indole series. A few years later, Chuang and colleagues also showed that stabilised radicals could undergo intramolecular addition to C-2 of a thiophene (**Scheme 69**).[98]

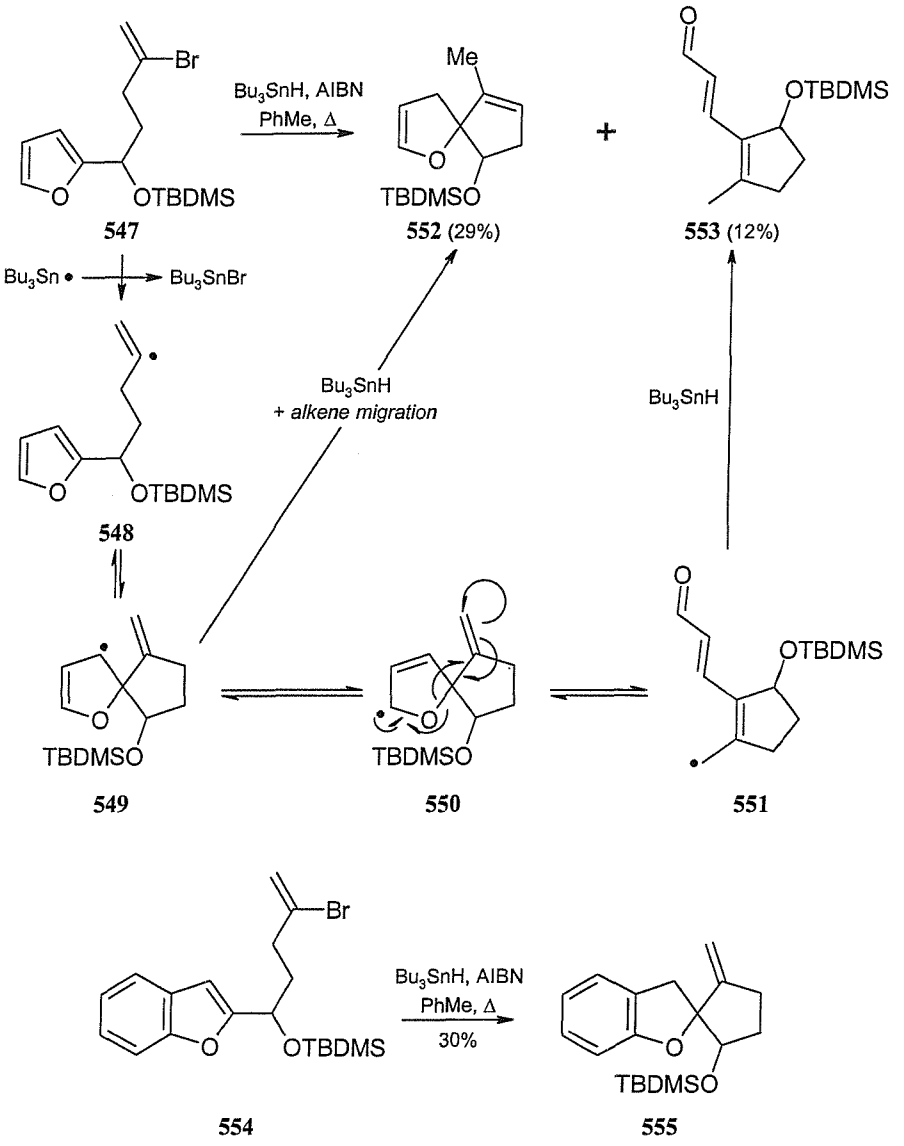


Scheme 68



Scheme 69

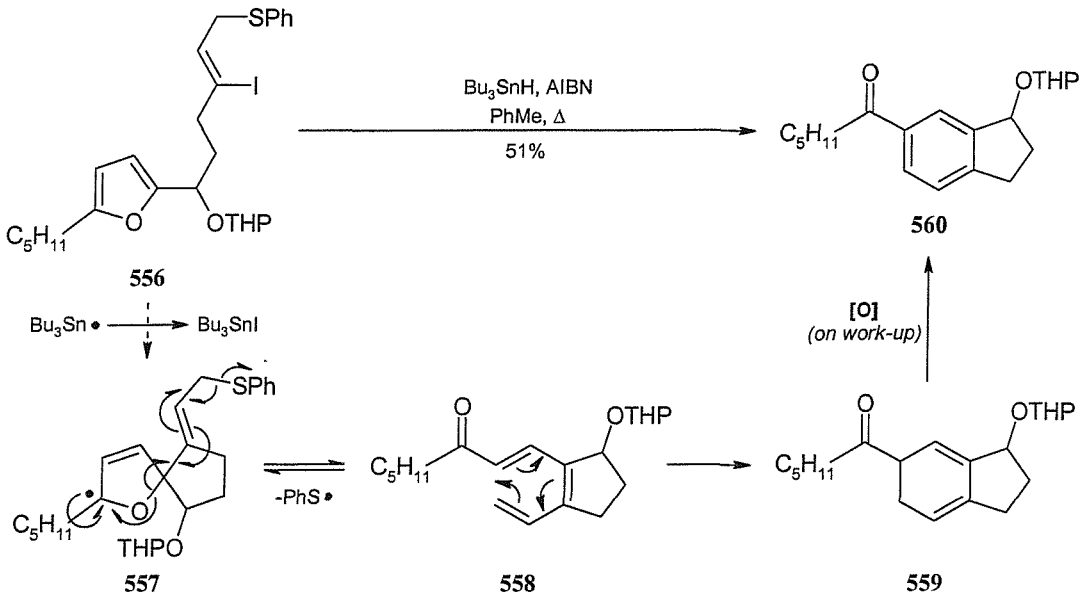
Parsons *et al.* were the first group to study intramolecular additions of carbon-centred radical intermediates to furans and benzo[*b*]furans.[123] In addition to the generation of novel spirocyclic ether **552** from furan **547**, an interesting fragmentation process was observed, culminating in the formation of cyclopentene **553** (**Scheme 70**). However, the analogous benzo[*b*]furan **554** gave, on exposure to tri-*n*-butyltin hydride and AIBN, spirocyclic ether **555** as the sole product of the reaction. Presumably, in this case fragmentation is slow because it would disrupt aromaticity in the benzene ring. Pattenden *et al.* have since employed this methodology in the synthesis of polycycles.[124]



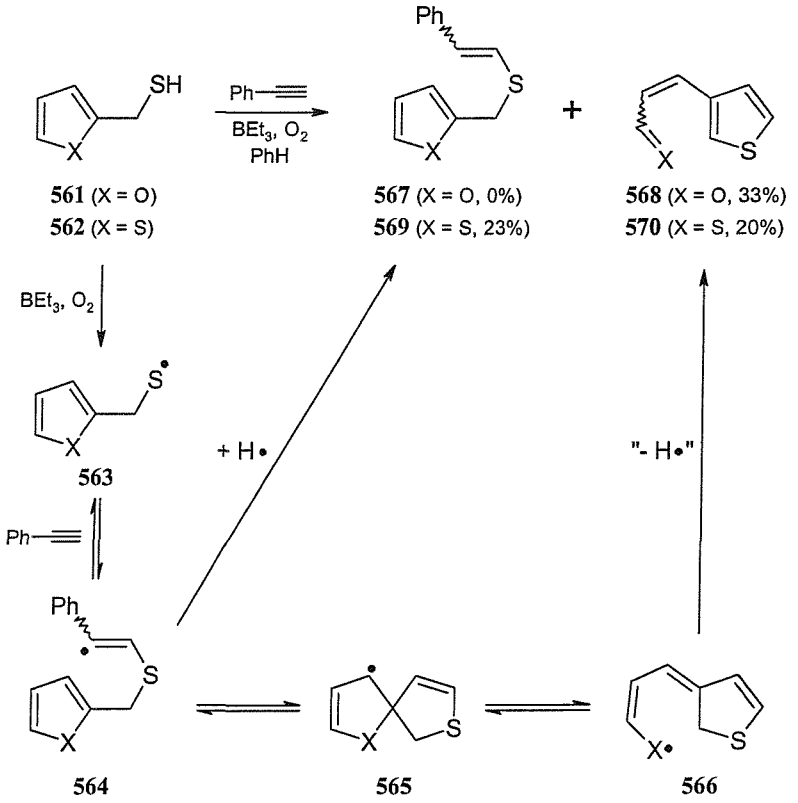
Scheme 70

Parsons and Demircan went on to optimise this fragmentation process to generate indane **560** from furan **556** (**Scheme 71**).[125] Inclusion of the phenyl thioether moiety at the end of the alkene made arene formation possible. Recent attempts to employ this methodology in the synthesis of tricylic ketones have been unsuccessful.[126]

Montevecchi *et al.* have published research detailing the intramolecular addition of transient *β*-sulfanylvinyl radicals to a variety of heterocycles, including thiophenes and furans.[127,128] 2-Heteromethanethiol radical **563** was generated from thiol **561** (and **562**) on treatment with triethylborane and air (**Scheme 72**). Intermolecular trapping of phenylacetylene led to vinyl radical **564**, which underwent either direct quenching *via* hydrogen-atom abstraction or spiro-cyclisation to C-2 of the heterocycle. In the latter case, fragmentation followed to give acrolein **568** (and **570**).

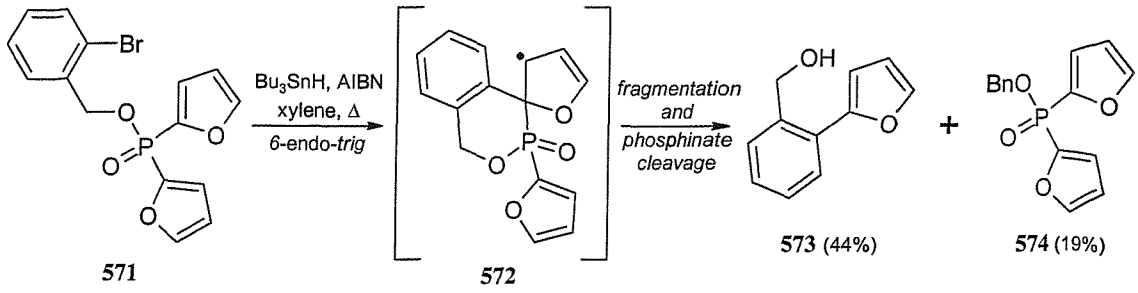


Scheme 71



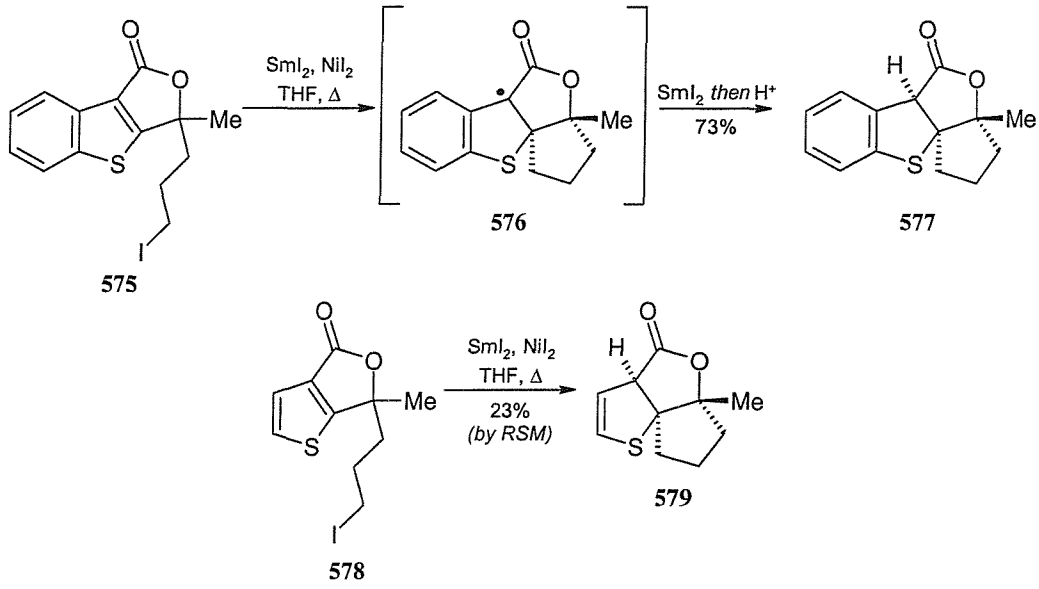
Scheme 72

Clive and Kang achieved the transfer of an aryl group to C-2 of a furan *via* a cyclisation-fragmentation strategy.[129] On abstraction of the bromine atom from **571** by tri-*n*-butyltin radical, cyclisation to C-2 of the furan occurred yielding radical intermediate **572**. The phosphinate tether was then cleaved to give alcohol **573** as the major product, along with a small amount of the reduced material **574** (**Scheme 73**). The mechanism through which the alcohol is liberated is not known; the available evidence suggests that tri-*n*-butyltin hydride has a role in the process.



Scheme 73

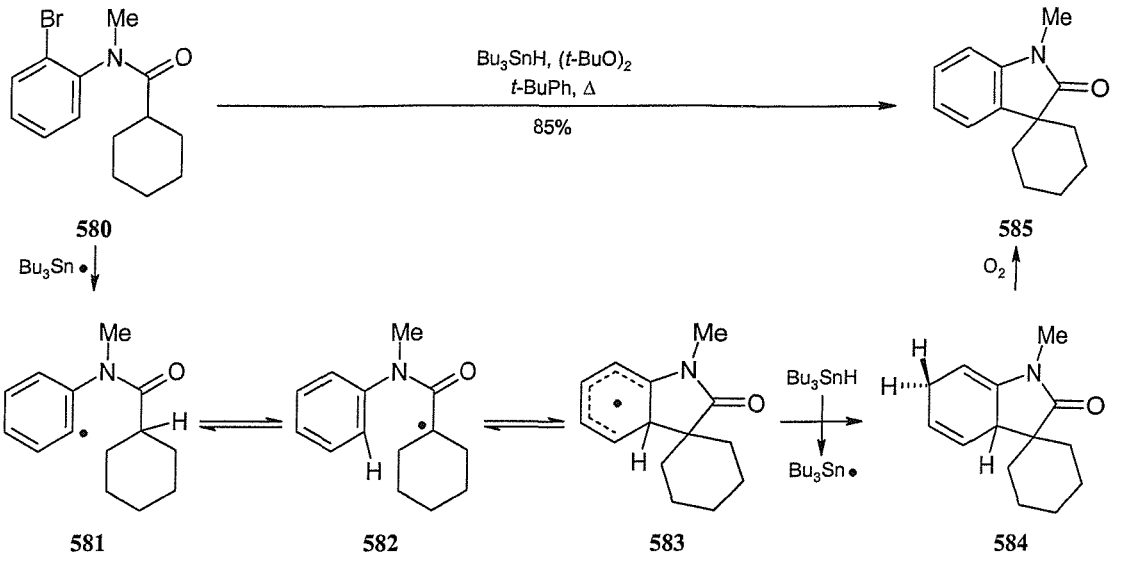
Finally, Molander and St. Jean, Jr. observed the efficient intramolecular addition of an alkyl radical to C-2 of 2,3-fused benzo[*b*]thiophene **575** (**Scheme 74**).[130] In contrast, the analogous cyclisation with thiophene **578** performed poorly. The disappointing yield may be attributed to the instability of tricyclic product **579**.



Scheme 74

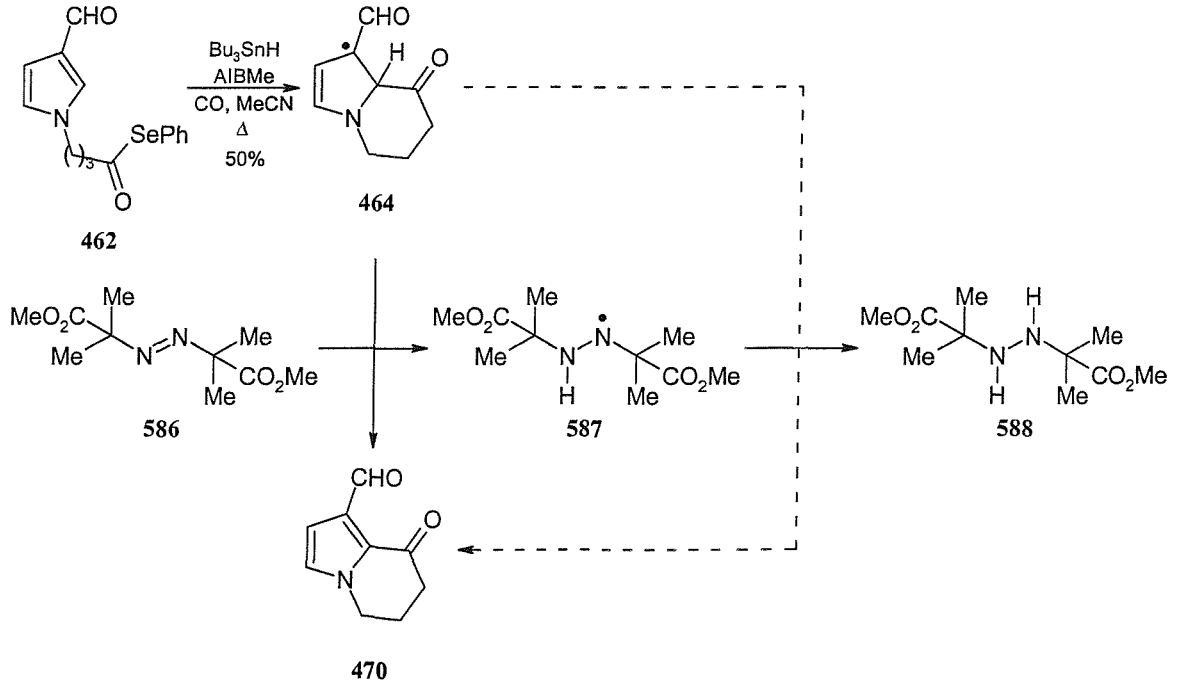
3.4 On the Non-Reducing Pathway of Tin-Mediated Radical Cyclisations

For many of the cyclisations previously discussed, the question arises: what is the mechanistic course leading to rearomatisation of aryl radical intermediates such as **583** (**Scheme 75**)? This question has been much debated in the literature and several different mechanisms have been mooted. In their paper on the radical synthesis of oxindoles, Beckwith and Storey proposed that radical intermediate **583** might abstract a hydrogen atom from tri-*n*-butyltin hydride, leading to dihydro-intermediate **584** which oxidises to **585** on exposure to air (**Scheme 75**).[131] However, they discounted this theory as, when tri-*n*-butyl deuteride was used to mediate the reaction, no deuterium was detected in **585**.



Scheme 75

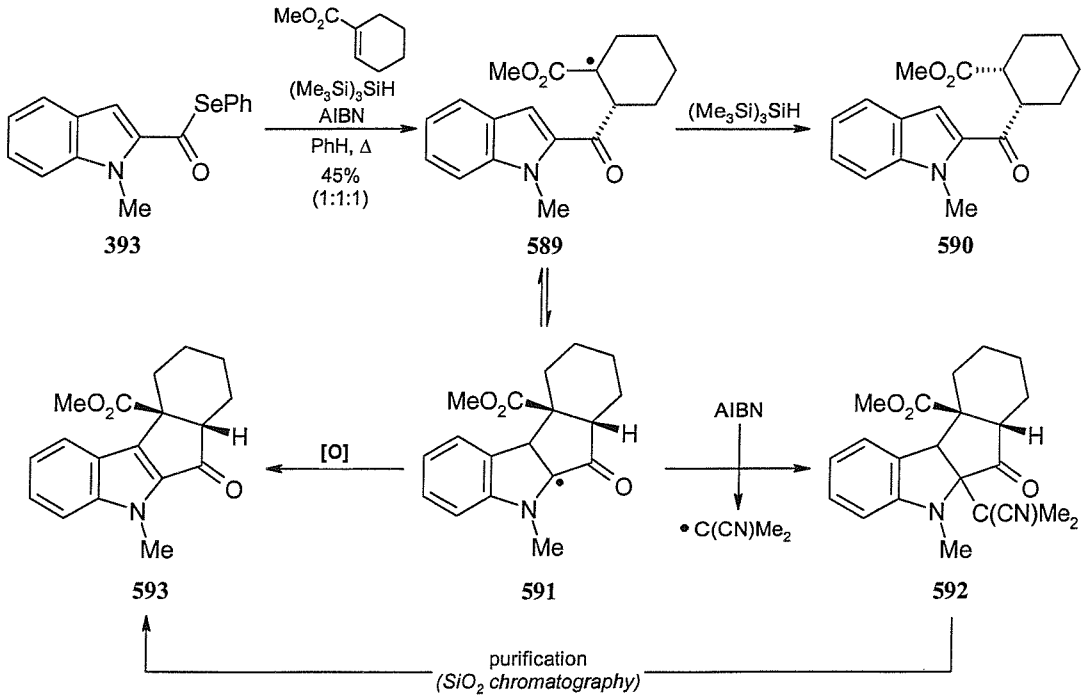
Beckwith and Storey also suggested that the oxidation of radical species such as **583** might be performed by the initiator. This was first proposed by Curran *et al.* in 1994,[132] and has been considered by others. Indeed, in their study of acyl radical cyclisations to pyrroles, Allin *et al.* observed the formation of dihydro-AIBMe **588** when AIBMe **586** was used to initiate the reaction.[115] A mechanism was proposed in which radical intermediate **464** transfers a hydrogen atom to AIBMe (**Scheme 76**). The nitrogen-centred radical **587** thus generated may then either abstract a hydrogen atom from a second equivalent of radical intermediate **464** or be quenched by tri-*n*-butyltin hydride.



Scheme 76

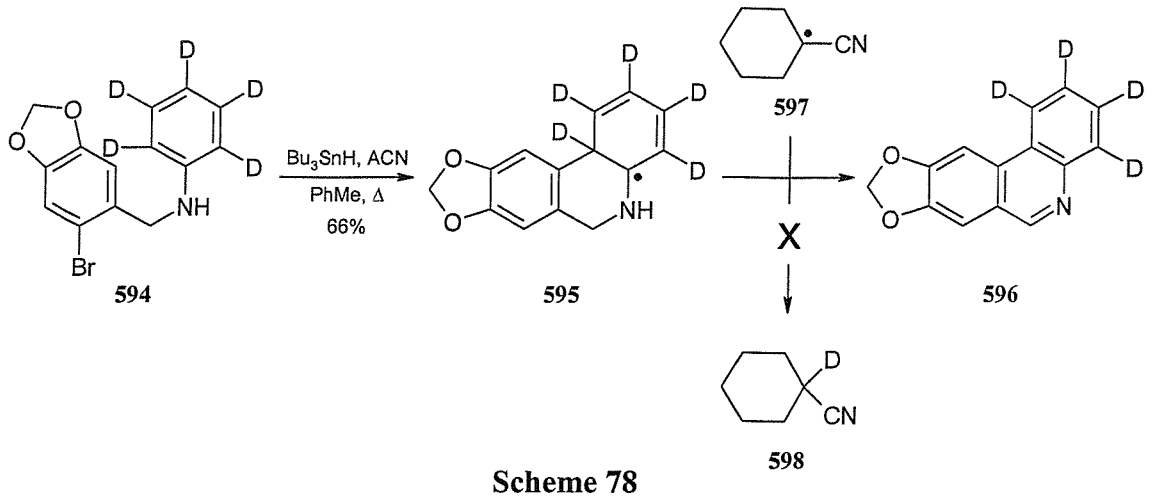
For this process to be ubiquitous, one would expect every non-reducing cyclisation reported in the literature to require at least 0.5 equivalents of initiator. While this may be true in some cases, many non-reducing cyclisations successfully employ as little as 10 mol % AIBN, including those from our own group.[133-140] Hence, the situation is more complex.

Another proposal for the rearomatisation mechanism involves trapping of the product radical with 2-cyano-2-propyl radical (from AIBN). The silicon-mediated cascade cyclisation of **393** with methyl-1-cyclohexenecarboxylate provides support for this mechanism, as adduct **592** was observed in the product mixture. That it was partially converted to **593** on flash chromatography was taken as strong evidence by Bennasar *et al.* that 2-cyano-2-propyl radicals were key participants in the oxidation process (**Scheme 77**).[105] However, this explanation is again limited to those cases where greater than 0.5 equivalents of the initiator are needed. Indeed, the fact that adducts akin to **592** have not been observed as intermediates from other non-reducing radical cyclisations suggests that this is an exceptional case and not a general pathway.



Scheme 77

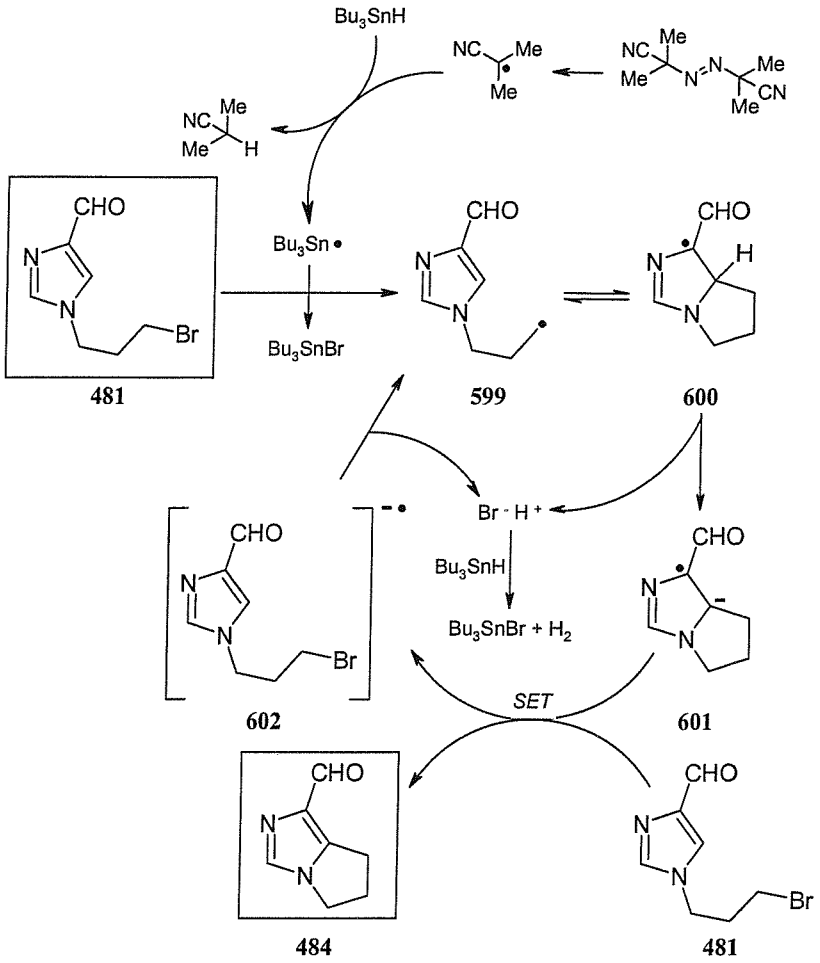
Hydrogen atom abstraction by 2-cyano-2-propyl radical was considered by Lobo *et al.*, though they ultimately discounted this possibility.[102] On cyclisation of deuterated substrate **594** to phenanthridine **596** using tri-*n*-butyltin hydride and ACN, no trace of the expected deuterated ACN fragment **598** was found (**Scheme 78**).



Scheme 78

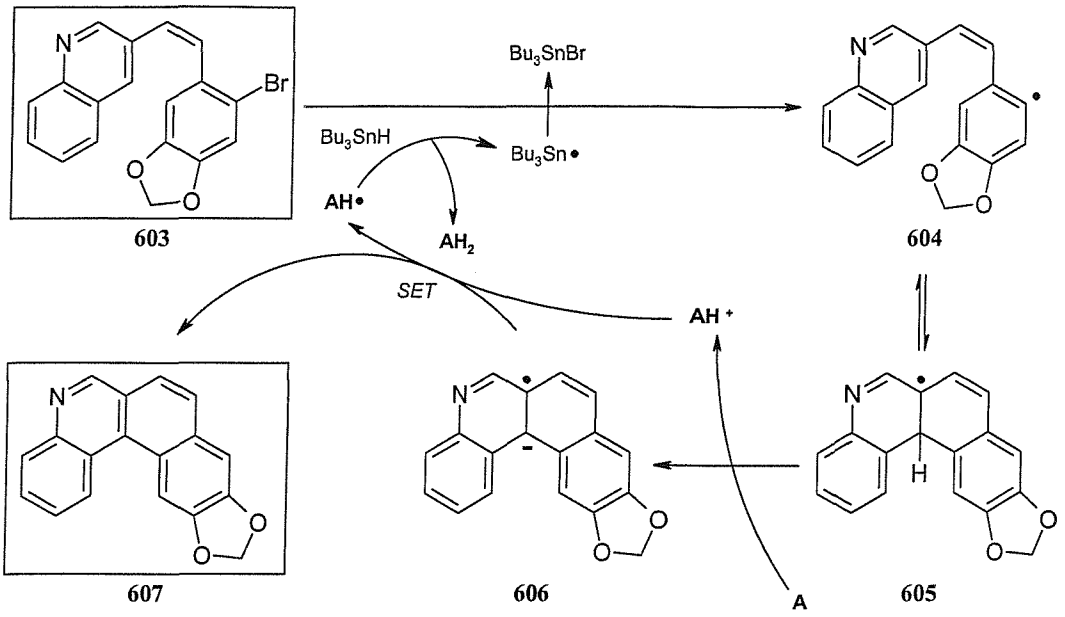
Hydrogen atom abstraction by tri-*n*-butyltin radical has also been considered.[141] However, Bowman argues that this would result in termination of the chain reaction, *ergo* non-reducing cyclisations should require at least 0.5 equivalents of initiator. As has been mentioned previously, this is not always the case. Bowman also noted that, although most non-reducing radical cyclisations take place under inert atmospheres, the removal of all traces of oxygen is difficult to achieve.[142] Under cyclisation conditions, residual oxygen would rapidly form peroxides with any radical species present *i.e.* $Bu_3SnOO^{\bullet}$ and $Me_2(CN)OO^{\bullet}$ for a tri-*n*-butyltin hydride/AIBN-mediated cyclisation. Thus, peroxide-facilitated oxidation of radical intermediates cannot be ruled out. Indeed, such processes may well be significant, depending on how thoroughly reactions are deoxygenated prior to initiation. However, there is very little in the way of literature evidence to provide credence to this theory.

The mechanism that has found greatest support in the literature is the "pseudo $S_{RN}1$" mechanism, first proposed by Bowman *et al.* in 1991 (**Scheme 79**).[101,109,113,114,118,141,142] In this mechanism, illustrated for the cyclisation of *N*-bromoalkyl imidazole **481**,[114] initiation triggers abstraction of a bromine atom from the substrate and cyclisation proceeds as expected. Radical intermediate **600** then loses a proton to generate π^*-radical anion **601**. Single electron transfer (SET) from **601** to radical precursor **481** gives the product **484** and radical anion **602**. Loss of bromide from **602** removes the acquired charge and generates radical intermediate **599**, completing the chain reaction. It should be noted, however, that this mechanism requires sub-stoichiometric amounts of initiator and hence may not hold true for all non-reducing cyclisations.



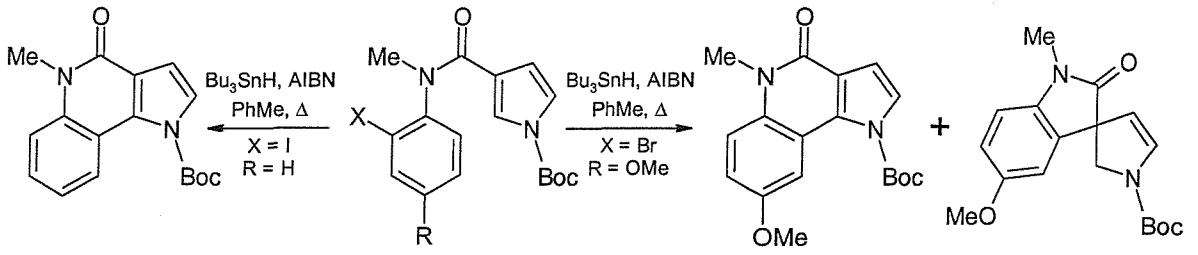
Scheme 79

It was noted earlier that Jones *et al.* observed differences in the cyclisation pathway followed by analogous bromide and iodide radical precursors (**Schemes 57** *and* **58**).[110-112] Harrowven *et al.* also noted differences between iodide and bromide substrates, finding that cyclisations were often more efficient when conducted using iodides as radical precursors. Moreover, substantially more initiator was needed for cyclisation of bromide radical precursors.[137,139] Thus, Harrowven postulates that the pathway illustrated in **Scheme 79** applies only when electron transfer is efficient (*e.g.* with iodides). When SET is inefficient, a different mechanism competes, wherein an "acceptor" in the system (A) removes a proton from **605** to generate π^*-radical anion **606** (**Scheme 80**).[137] The protonated acceptor (AH^+) then receives an electron from **606** to give the product of the non-reducing cyclisation pathway, **607**, and a new radical intermediate, $AH^\bullet$. This in turn abstracts a hydrogen atom from tri-*n*-butyltin hydride to propagate the chain reaction. The identity of this "acceptor" is not known, but it could be a substrate, initiator or product.



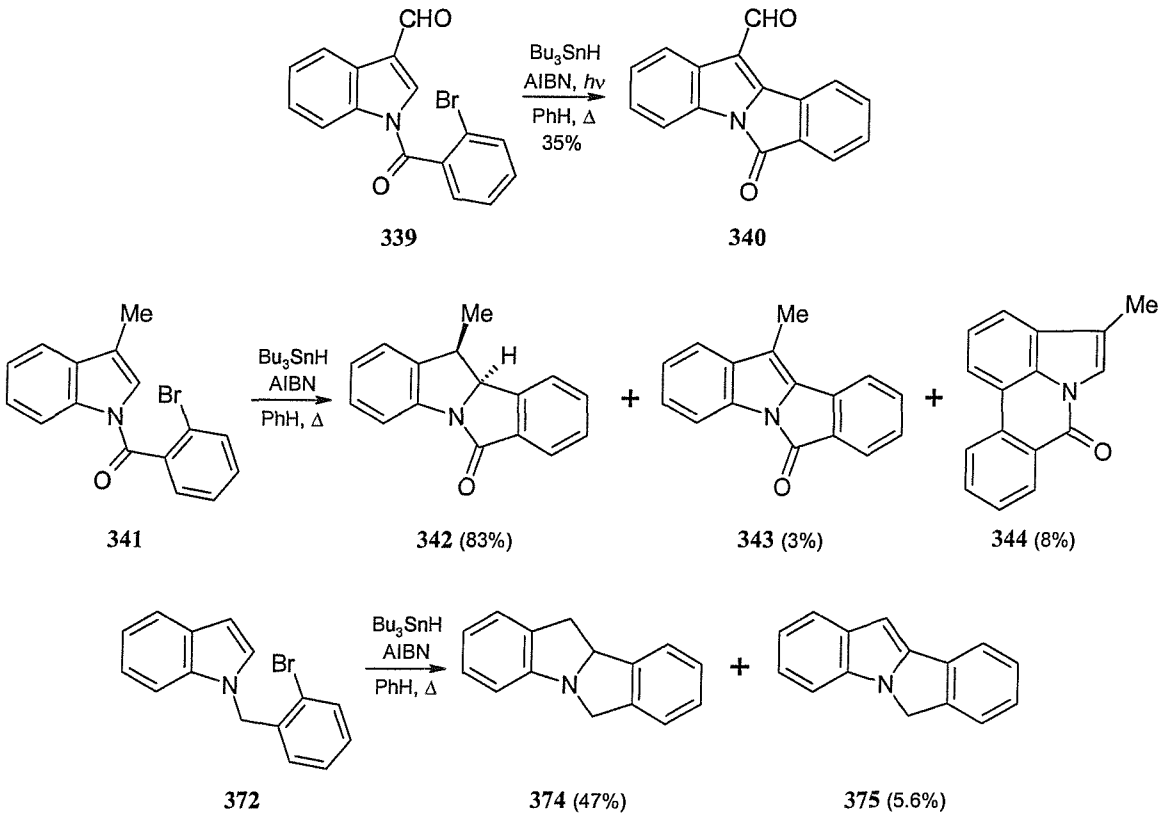
Scheme 80

Hence, the dichotomy observed by Jones *et al.* can be rationalised in terms of the efficiency of electron transfer between the product π^*-radical anion and the radical precursor.[110-112] On cyclisation of iodide **437**, SET is efficient and thus a non-reducing 6-*endo*-trig mode is followed (**Scheme 81**). However, SET to bromide **440** is inefficient and thus the reductive 5-*exo*-trig mode competes, resulting in a 3:2 mixture of C-2 and C-3 cyclisation products, pyrrolo[3,2-*c*]quinoline **441** and spirocycle **442** respectively.



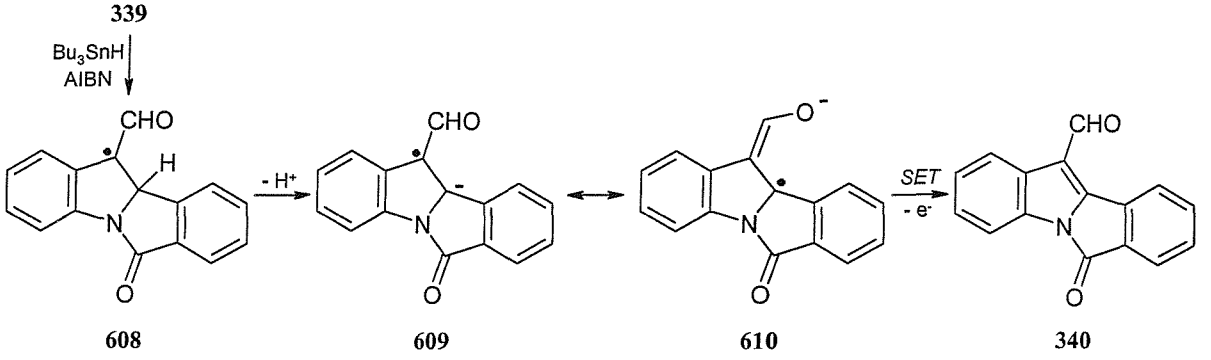
Scheme 81

Whilst compiling this review, it was noted that functionalisation of the heterocycle with an electron-withdrawing group is often necessary in order for a non-reducing radical pathway to proceed. This effect becomes starkly apparent when comparing the radical cyclisations of indole substrates **339**, **341** and **372** (**Scheme 82**). In the case of **339**, a non-reducing cyclisation to **340** is followed in moderate yield.[92] However, on replacing the formyl group with a methyl group or a hydrogen atom (**341** and **372** respectively), the cyclisation favours a reductive process.[93,102]



Scheme 82

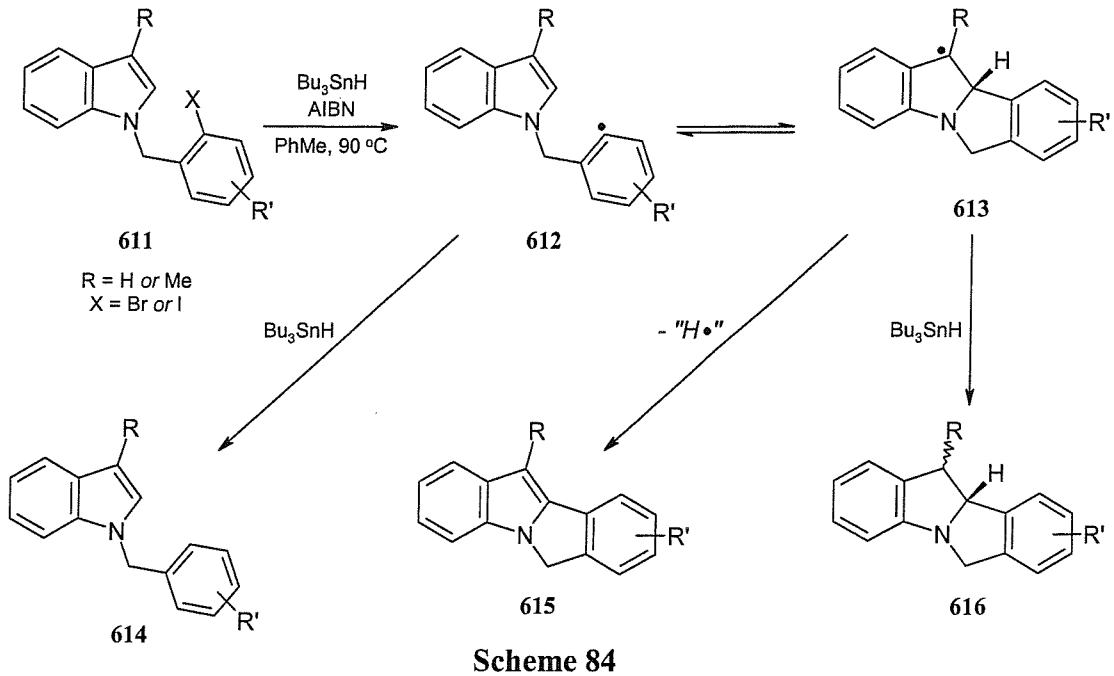
Bowman has speculated that the stabilisation of π^*-radical anions akin to **601** and **606** by electron-withdrawing groups facilitates electron transfer and thus increases the likelihood of a non-reducing cyclisation.[114] We suggest that an electron-withdrawing group also increases the acidity of radical intermediates akin to **608**, in turn encouraging the formation of π^*-radical anion **609/610** (**Scheme 83**). Thus, the presence of an electron-withdrawing group encourages both proton loss from **608** and subsequent electron transfer from **609/610**, facilitating the propagation of a non-reducing cyclisation pathway.



Scheme 83

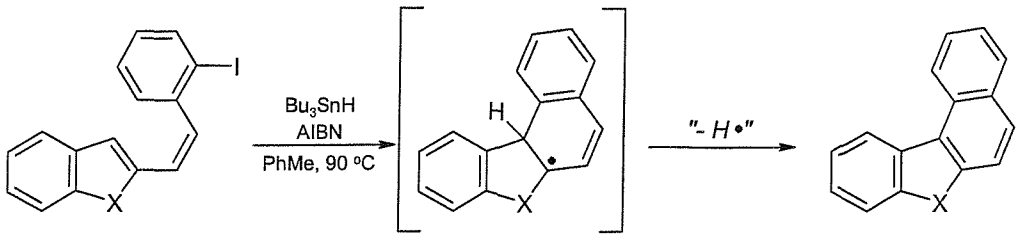
3.5 Our Aims and Objectives

For our own endeavour, we wished to conduct a broad-based examination of the addition of aryl radicals to five-membered aromatic heterocycles. We decided to commence this study with a re-examination of the tin-mediated addition of *N*-tethered aryl radicals to C-2 of an indole (**Scheme 84**). Although this type of cyclisation has been described,[92-94,102] the studies conducted thus far are limited and the effect of substituents on the aryl radical have never been examined. In addition, we wanted to see how the stereochemical outcome of such cyclisations was influenced by the steric bulk of the arene moiety. As the indole C-3 would be either be methylated or unsubstituted, we expected the cyclisations to be reductive in nature, though the formation of products arising from a non-reducing pathway was clearly plausible.



Scheme 84

We also wanted to examine the tin-mediated addition of *cis*-alkene-tethered aryl radicals to the C-2 and C-3 positions of indoles, benzo[*b*]thiophenes and benzo[*b*]furans. Additions of this type have been performed with arenes,[134-136] pyridines[138,143-145] and quinolines,[137,139] but never to five-membered condensed heterocycles. Thus, *cis*-alkenes ***(Z)*-617** to ***(Z)*-619** were expected to yield the corresponding benzo[*c*]carbazole **621**, benzo[*b*]naphtho[1,2-*a*]thiophene **622** and benzo[*b*]naphtho[1,2-*a*]furan **623** respectively *via* a non-reducing radical cyclisation pathway (**Scheme 85**).



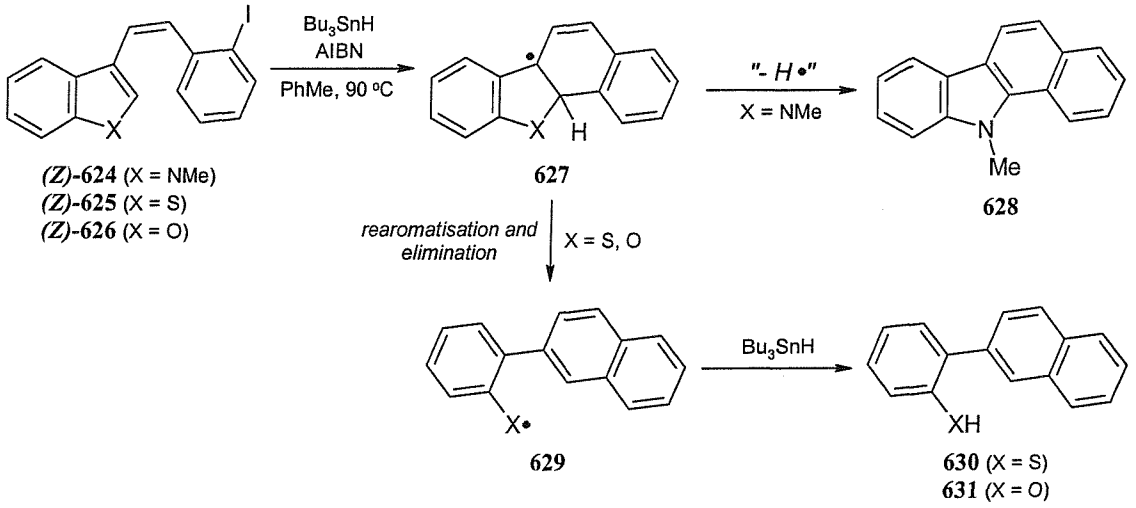
(Z)-**617** (X = NMe)
(Z)-**618** (X = S)
(Z)-**619** (X = O)

620

621 (X = NMe)
622 (X = S)
623 (X = O)

Scheme 85

Of greater interest were the possible structures obtained from cyclisations to C-2 of the heterocycle. For indole ***(Z)*-624**, the reaction was expected to yield the corresponding benzo[*a*]carbazole **628**. However, the work of Montevecchi *et al.*[127,128] and Harrowven and Browne[121,122] suggested that cyclisation to benzo[*b*]thiophene ***(Z)*-625** or benzo[*b*]furan ***(Z)*-626** might follow a different course. Rearomatisation of intermediate **627** *via* ejection of the heteroatom would ultimately result in the formation of the corresponding 2-(2-naphthyl)-phenol **630** or -thiophenol **631** (**Scheme 86**).



(Z)-**624** (X = NMe)
(Z)-**625** (X = S)
(Z)-**626** (X = O)

627

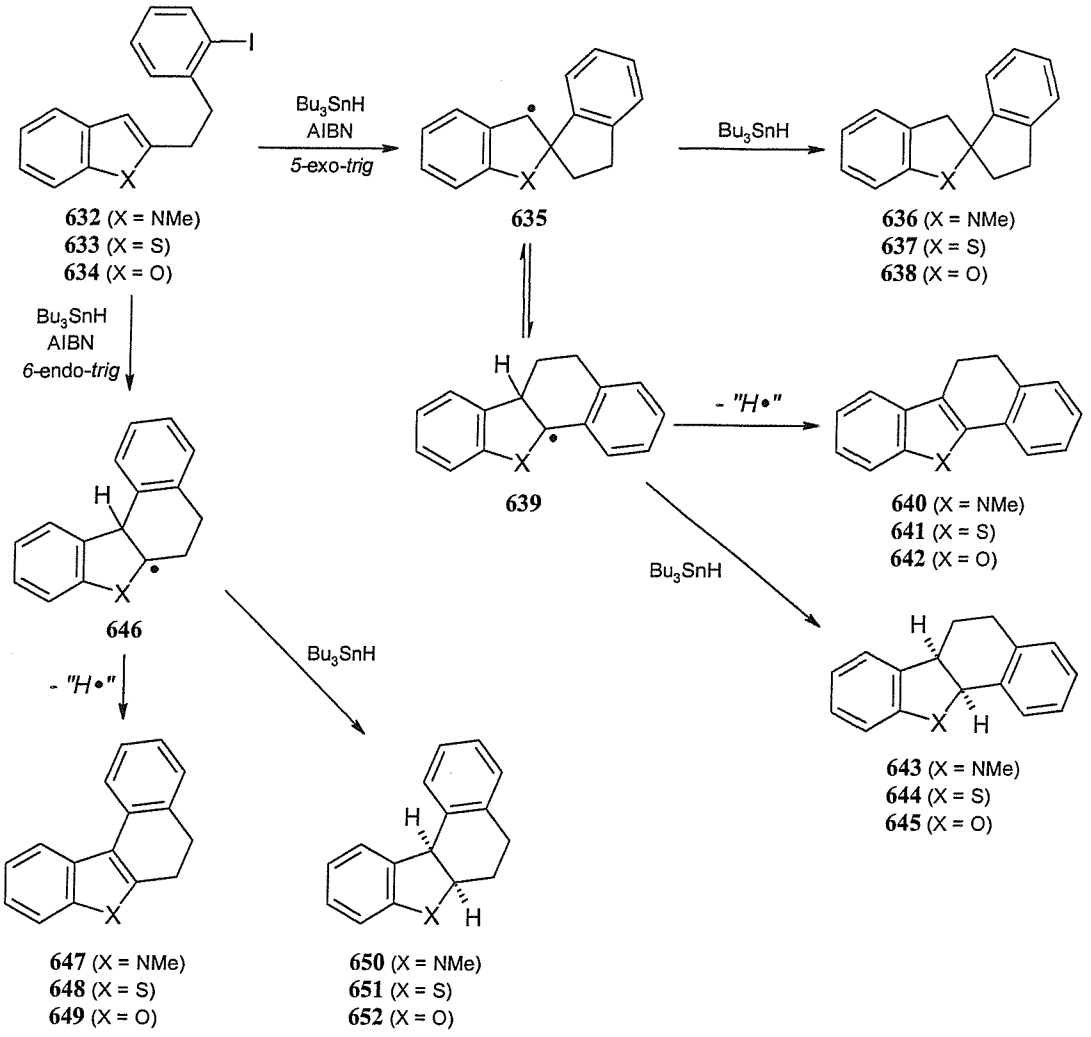
628

629

630 (X = S)
631 (X = O)

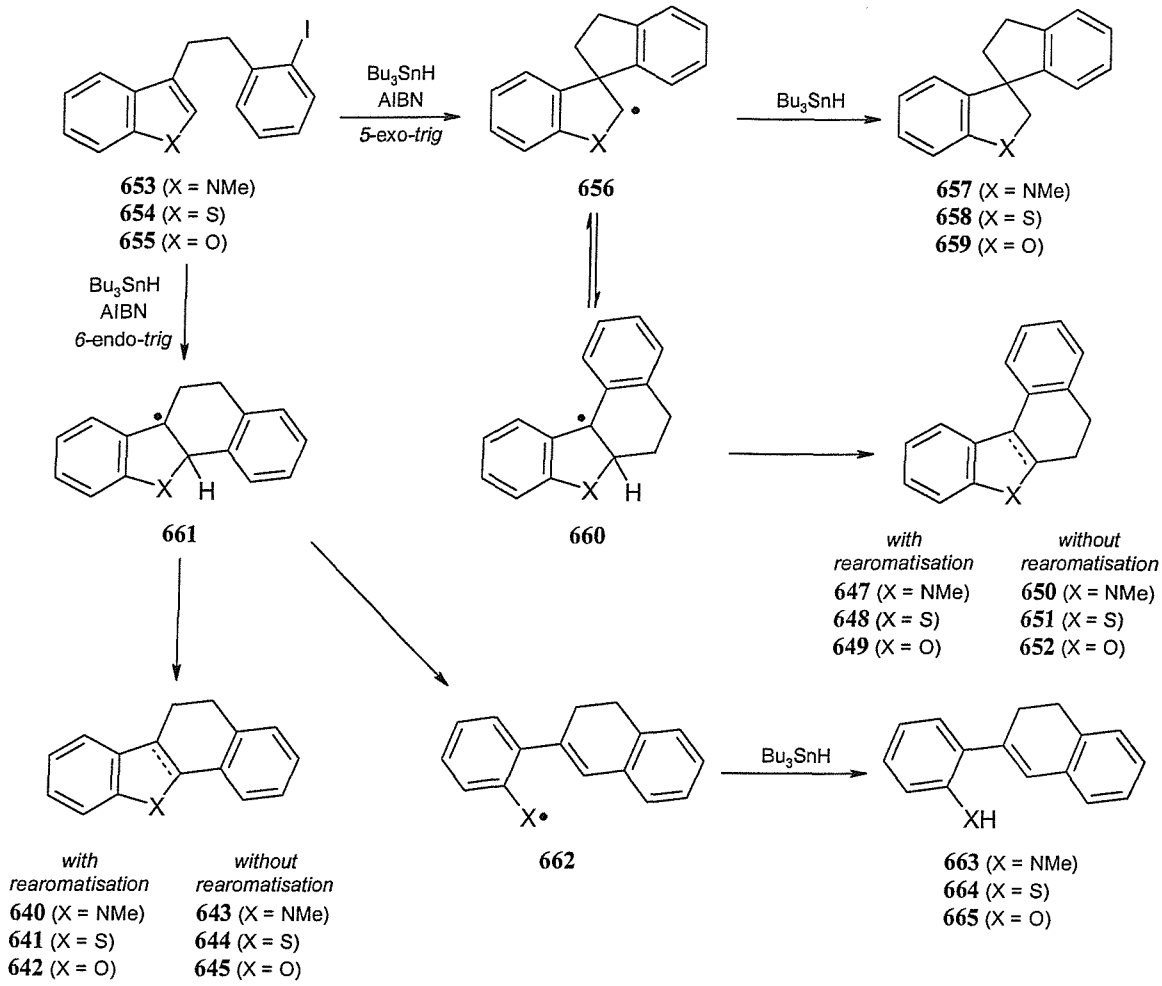
Scheme 86

The effect of conjoining the aryl radical to C-2 or C-3 of the heterocycle with a more flexible alkane tether was also to be examined. It was speculated that 5-*exo*-trig cyclisation could outpace the alternate 6-*endo*-trig cyclisation in some cases. Were this to occur, it was possible that a skeletal rearrangement would follow (**Scheme 87** and **88**).[138] In the circumstances where a 6-*endo*-trig cyclisation arose, the driving force for rearomatisation through the apparent loss of a hydrogen atom would be lessened, so reductive or reductive-elimination pathways could dominate.

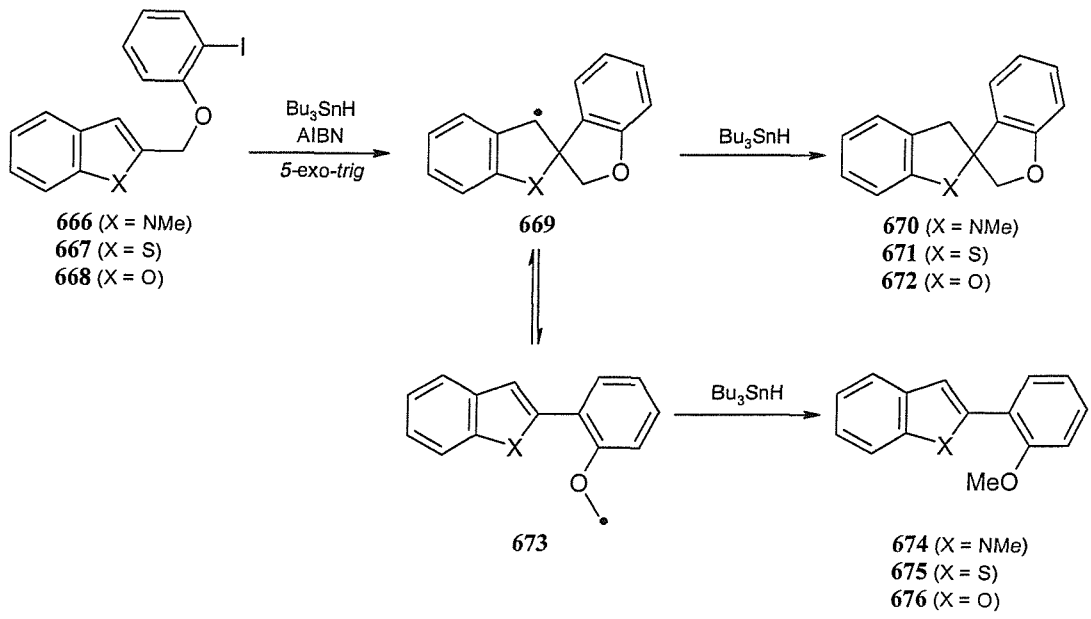


Scheme 87

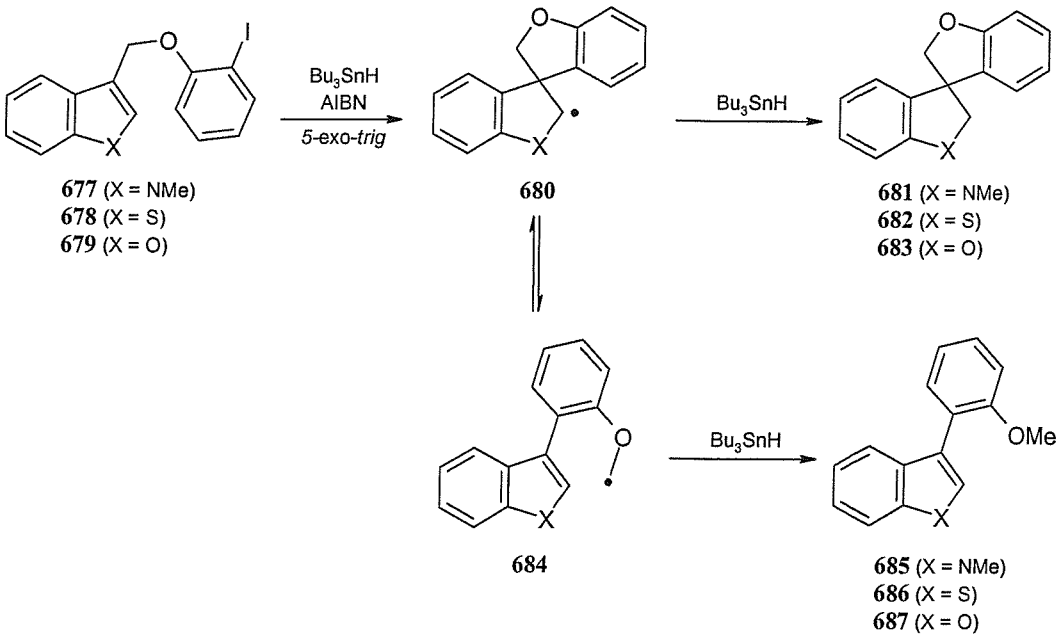
In addition, we wished to examine the effect of replacing one of the methylene units in the alkyl tether with a heteroatom such as oxygen. Based on previous literature evidence,[146] we expected this substitution to bias the reactions towards a 5-*exo*-trig spiro-cyclisation pathway. The fragmentation of radical intermediates **669** or **680** was also thought possible,[140] yielding the corresponding 2- or 3-phenyl-substituted heterocycles (**Scheme 89** and **90**).



Scheme 88



Scheme 89



677 (X = NMe)
678 (X = S)
679 (X = O)

680

681 (X = NMe)
682 (X = S)
683 (X = O)

684

685 (X = NMe)
686 (X = S)
687 (X = O)

Scheme 90

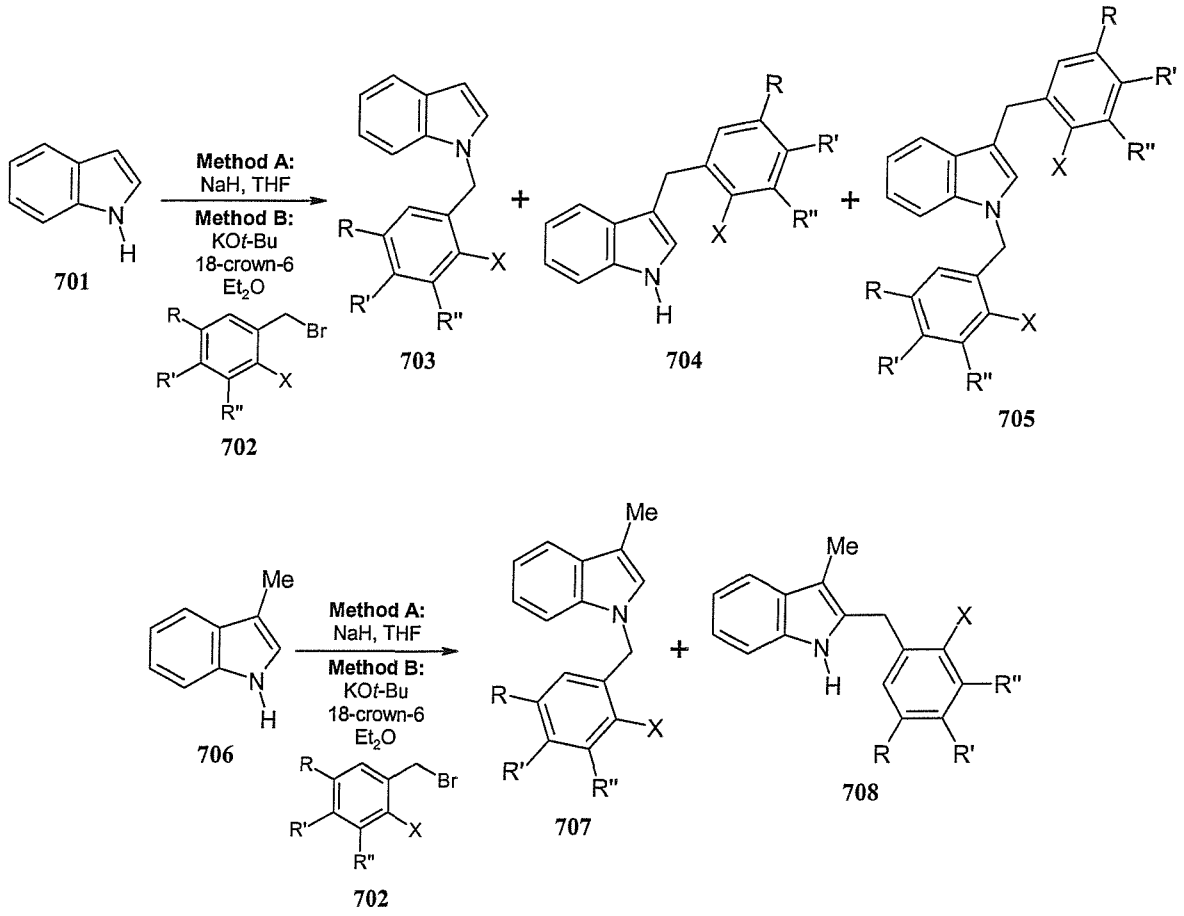
Chapter 4

The Tin-Mediated Radical Synthesis of 10b,11-Dihydro-6H-isoindolo[2,1-a]indoles

This chapter presents our short study of the tin-mediated reductive addition of *N*-tethered aryl radicals to C-2 of an indole to form 10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indoles. The influence of arene functionalisation on the efficiency and stereochemical outcome of the cyclisation is discussed.

4.1 Synthesis of the Radical Precursors

In order to commence our investigation on whether substituents on the aryl ring influence the cyclisation of *N*-(*o*-halobenzyl)indoles, a range of such systems were synthesised. For the *N*-benzylation of indoles **701** and **706**, two general methodologies were employed. Deprotonation with sodium hydride, followed by the addition of a benzyl bromide (**Method A**) worked well in most cases but undesired substitution of the indole at the C-2 and C-3 positions was often observed, and an alternative *N*-benzylation procedure was sought. The method of Guida and Mathre,[147] involving deprotonation of the indole nitrogen with potassium *tert*-butoxide and 18-crown-6 in diethyl ether followed by the addition of a benzyl bromide (**Method B**), was found to be superior in many cases and selectively furnished the desired *N*-benzylated indoles in moderate to good yield (**Scheme 91**).



a (R = R' = R" = H, X = Br)
b (R = R' = R" = H, X = I)
c (RR' = OCH_2O, R" = H, X = Br)
d (RR' = OCH_2O, R" = H, X = I)
e (R = R' = OMe, R" = H, X = Br)
f (R = R' = R" = OMe, X = I)

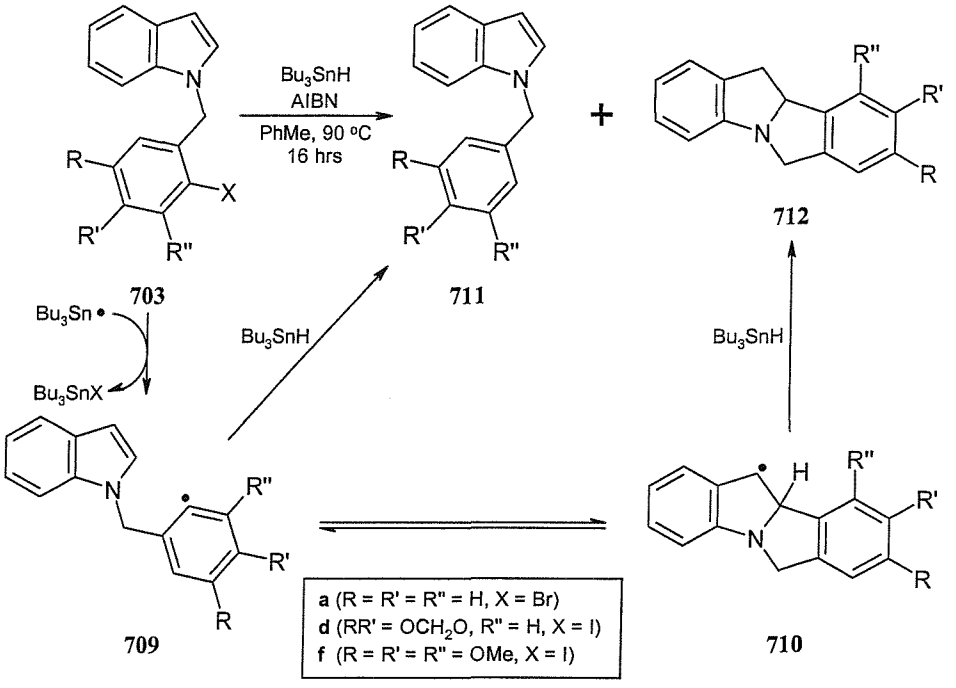
Indole	Aryl Bromide	Benzylation Method	Products (Yields)
701	**702a**	**B**	**703a** (100%)
701	**702d**	**A**	**703d** (20%), **704d** (17%), **705d** (25%) *plus* **701** (14%)
701	**702f**	**B**	**703f** (58%)
706	**702a**	**A**	**707a** (79%)
706	**702b**	**A**	**707b** (99%)
706	**702c**	**B**	**707c** (66%)
706	**702e**	**A**	**707e** (61%), **708e** (18%)
706	**702f**	**B**	**707f** (67%)

Scheme 91

4.2 The Tin-Mediated Radical Cyclisation of *N*-(*o*-Halobenzyl)indoles

Once the desired *N*-(*o*-halobenzyl)indoles had been synthesised, the tin-mediated reductive cyclisation of each radical precursor was effected. Starting with the substrates lacking a methyl substituent at the indole C-3 (group **703**), exposure of **703a** to tri-*n*-butyltin hydride and 20 mol % AIBN in toluene at 90 °C afforded *N*-benzylindole **711a** in 43% yield and the cyclised product **712a** in 32% yield (**Scheme 92**). It is worth noting that 10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indole **712a** was attained in a lower yield than that reported by Lobo *et al.* (47%),[102] though they did not comment on the formation of reduction product **711a**.

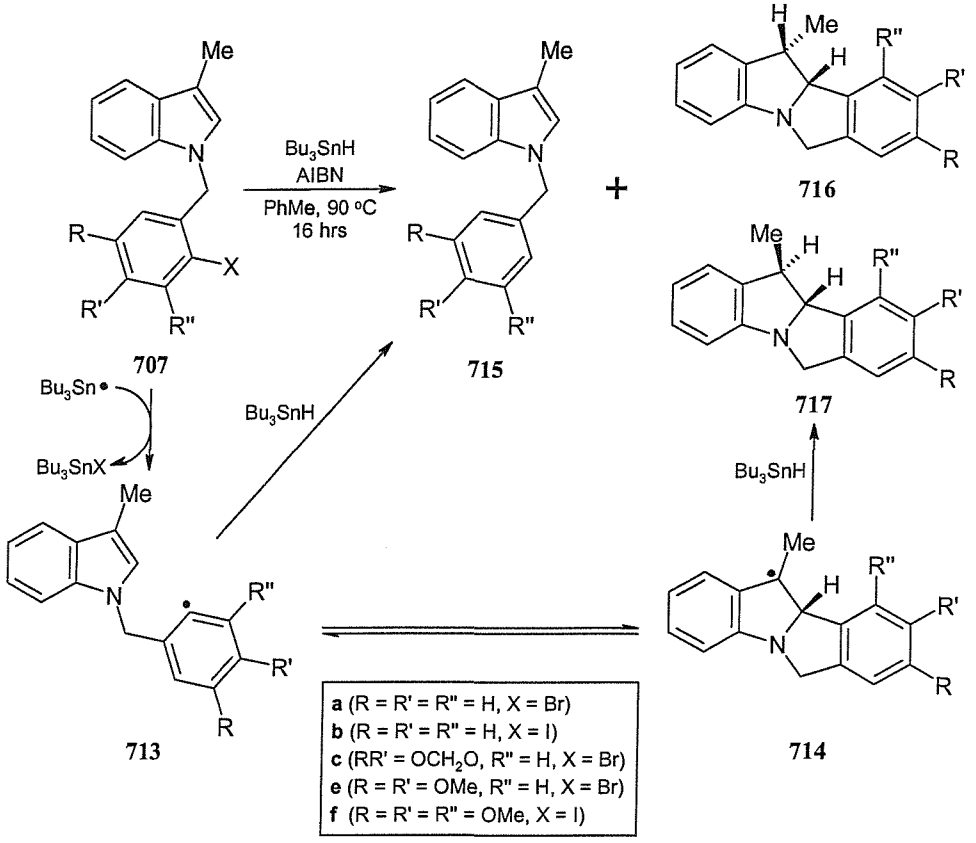
The efficiency of cyclisation did not appear to be greatly affected by functionalisation of the aryl radical with a methylenedioxy group, although a small increase in the isolated yields of both cyclised and reduced materials (**711d** and **712d** respectively) was noted. However, with the trimethoxy-arene **703f**, the product of a reductive cyclisation (**712f**) was formed in 80% yield.



Radical Precursor	Yield of Reduced Product (711)	Yield of Cyclised Product (712)
703a	43%	32%
703d	45%	42%
703f	*trace*	80%

Scheme 92

These results suggest that electron-donating substituents on the attacking aryl radical promote cyclisation to C-2 of the indole. However, it is unclear how an electron-rich arene unit could encourage cyclisation over reduction. It seems more likely that the increase in cyclisation efficiency is steric in origin. Bulky substituents adjacent to the aryl radical hinder the approach of tri-*n*-butyltin hydride and prolong the lifetime of intermediate **709**. Consequently, there is an increased probability that **709** will undergo cyclisation. The effect is most pronounced when a trimethoxy aryl radical is utilised. In this case, a substituent is present either side of the aryl radical, so abstraction of a hydrogen atom from tri-*n*-butyltin hydride is especially encumbered.

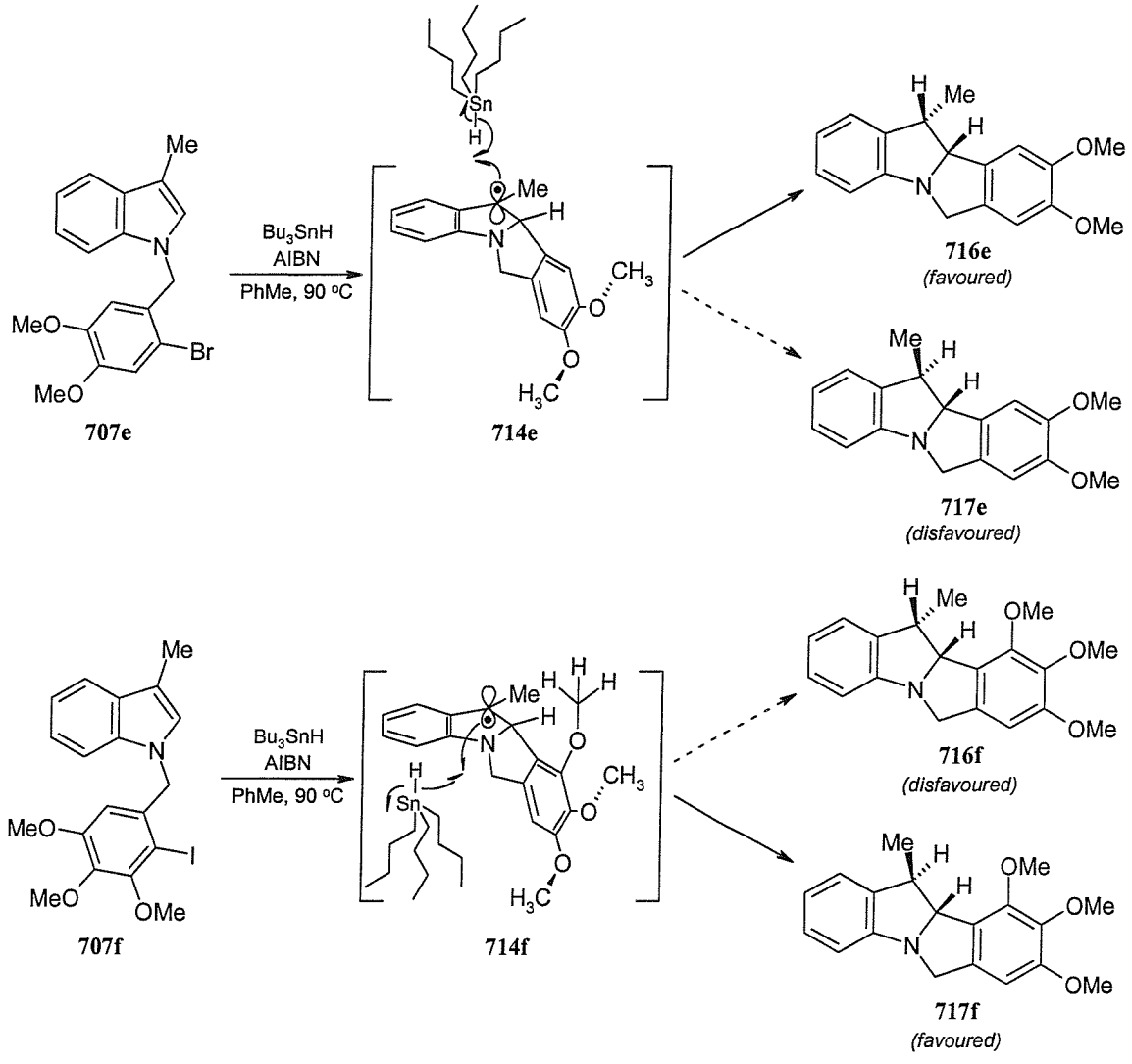


Radical Precursor	Yield of Reduced Product (715)	Yield of Cyclised Products (716:717)
707a	16%	35% (1:1)
707b	11%	38% (1:1)
707c	26%	54% (3:2)
707e	30%	56% (2:1)
707f	*trace*	66% (1:3)

Scheme 93

A similar pattern of results was observed when performing the tin-mediated cyclisations of substrates **707**, where C-3 of the indole was methylated (**Scheme 93**). Cyclisation was markedly more efficient when employing a heavily functionalised arene. In addition, we found that iodide and bromide precursors were equally efficient, giving comparable yields of cyclised and reduced products. Consequently, we employed those substrates that were most conveniently synthesised.

The stereochemical outcome of these reactions was disappointing. Functionality on the arene led to the preferential formation of 10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indoles **716** rather than **717** (**Scheme 94**). Confirmation of this outcome was obtained upon examination of the ^{1}H-NMR spectra of the product mixtures; doublets occurring at 5.2-5.6 ppm (J = 9-10 Hz) were identified as originating from the hydrogen atom at 10*b* of **716**, whilst a broad singlet at 4.7-4.9 ppm was observed for the corresponding hydrogen atom in **717**. However, on cyclisation of *N*-(*o*-halobenzyl)indole **707f**, a reversal in the stereochemical outcome of the reaction was observed, with **717f** and **716f** formed in a 3:1 ratio.



Scheme 94

These results can be explained if hydrogen atom abstraction from tri-*n*-butyltin hydride is assumed to follow the course of lowest steric demand. In most cases, 10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indoles **716** are formed in preference to **717** as hydrogen atom abstraction occurs to the convex face of **714**. However, for **714f**, the methoxy group at C-10 effectively shields the radical intermediate on the convex face. Thus, hydrogen atom abstraction is forced to occur onto the concave face, reversing the stereochemical outcome.

4.3 Summary

In conclusion, we have investigated the tin-mediated radical cyclisation of *N*-(*o*-halobenzyl)indoles. It was found that the efficiency of the reaction was influenced by the degree of substitution on the arene moiety. *Ortho*-substituents in particular promoted cyclisation to a 10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indole over reduction of the starting iodide or bromide. This phenomenon is believed to be due to steric hindrance, which prevents hydrogen atom abstraction from tri-*n*-butyltin hydride by the aryl radical.

Arene substituents also influenced the stereochemical outcome of the cyclisation, with more substituted arenes giving greater selectivity. In most cases, 10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indoles **716** were favoured over **717**. However, the incorporation of an *ortho*-methoxy group on the aryl radical led to a reversal of this trend. In this case, the methoxy group is believed to shield the convex face of radical intermediate **714f** from tri-*n*-butyltin hydride, forcing hydrogen atom abstraction to occur onto the concave face.[148]

Chapter 5

The Tin-Mediated Radical Synthesis of Polyaromatic Systems

This chapter describes cyclisation reactions involving the addition of aryl radical intermediates to C-2 and C-3 of indoles, benzo[*b*]thiophenes and benzo[*b*]furans. Notably, we have found that the nature of the heterocycle heteroatom has a significant influence on the outcome of such reactions.

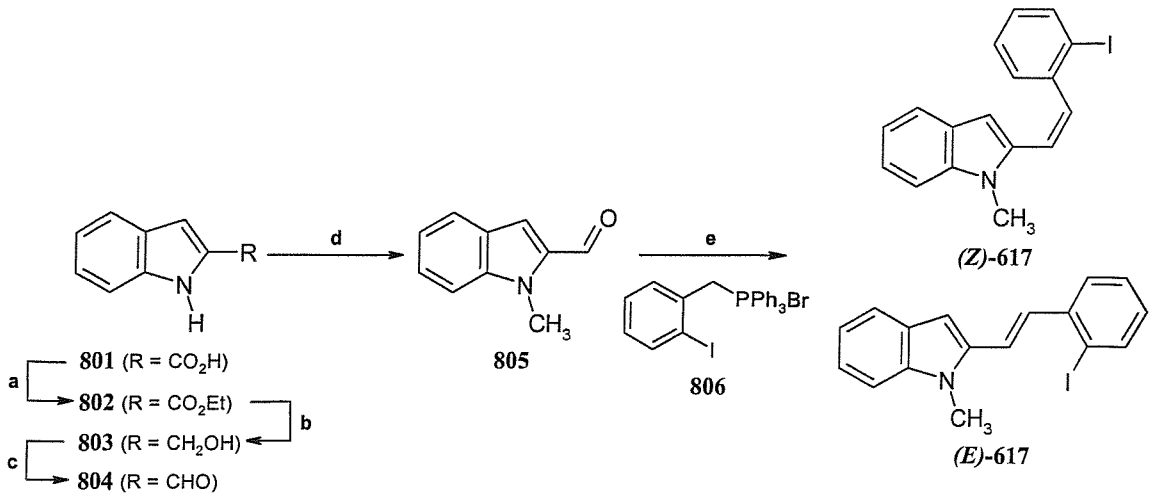
5.1 Synthesis of the Radical Precursors

Before our study could begin, we first needed to synthesise the requisite precursors. The route employed proceeded *via* the corresponding heterocyclic aldehyde. A Wittig reaction conjoined the heterocycle to the aryl radical precursor that, on separation of the alkene diastereoisomers, provided the *cis*-alkenes needed for this research. The *trans*-alkenes also proved useful, as they were hydrogenated to provide the precursors needed for a later study (**Chapter 6**).

5.1.1 Synthesising the C-2 Tethered Radical Precursors

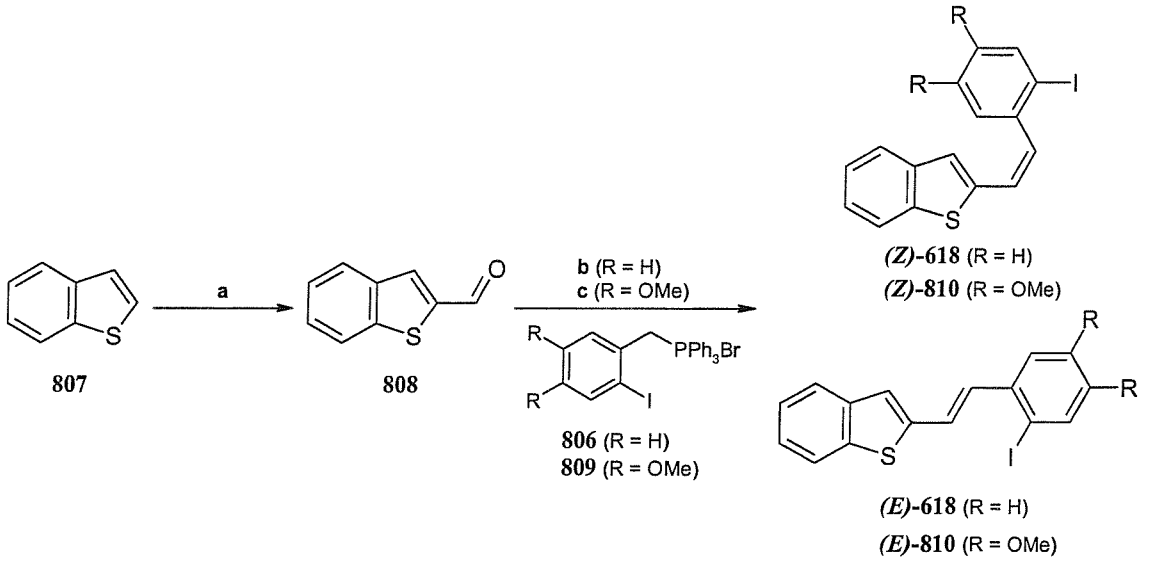
For the synthesis of indole ***(Z)*-617**, accessing the requisite aldehyde **805** proved straightforward. A short sequence of functional-group manipulations successfully transformed indole-2-carboxylic acid **801** into indole-2-carboxaldehyde **804**. Methylation of the indole nitrogen then provided aldehyde **805**. Wittig condensation with triphenylphosphonium salt **806** gave a 1:5.5 mixture of ***(Z)*-617** and ***(E)*-617**, which was readily separated by column chromatography (**Scheme 95**).

Accessing the required aldehyde for the synthesis of benzo[*b*]thiophenes ***(Z)*-618** and ***(Z)*-810** also proved unproblematic. Deprotonation of benzo[*b*]thiophene **807** with *n*-butyllithium followed by the addition of DMF furnished 2-formylbenzo[*b*]thiophene **808**. Wittig condensation with triphenylphosphonium salts **806** and **809** then gave the corresponding *cis*- and *trans*- alkenes in excellent yield (**Scheme 96**). However, column chromatography and successive recrystallisations were required to separate the diastereoisomers in each case.



Reagents and Conditions: **a** H_2SO_4, EtOH, Δ, 16 hrs, 99%. **b** $LiAlH_4$, THF, 0 °C, 1 hr, 96%. **c** $BaMnO_4/MnO_2$, CH_2Cl_2, RT, 16 hrs, 83%. **d** NaH, MeI, THF, RT, 16 hrs, 88%. **e** **806**, KO*t*-Bu, THF, RT, 16 hrs, 14% ***(Z)*-617** *and* 78% ***(E)*-617**.

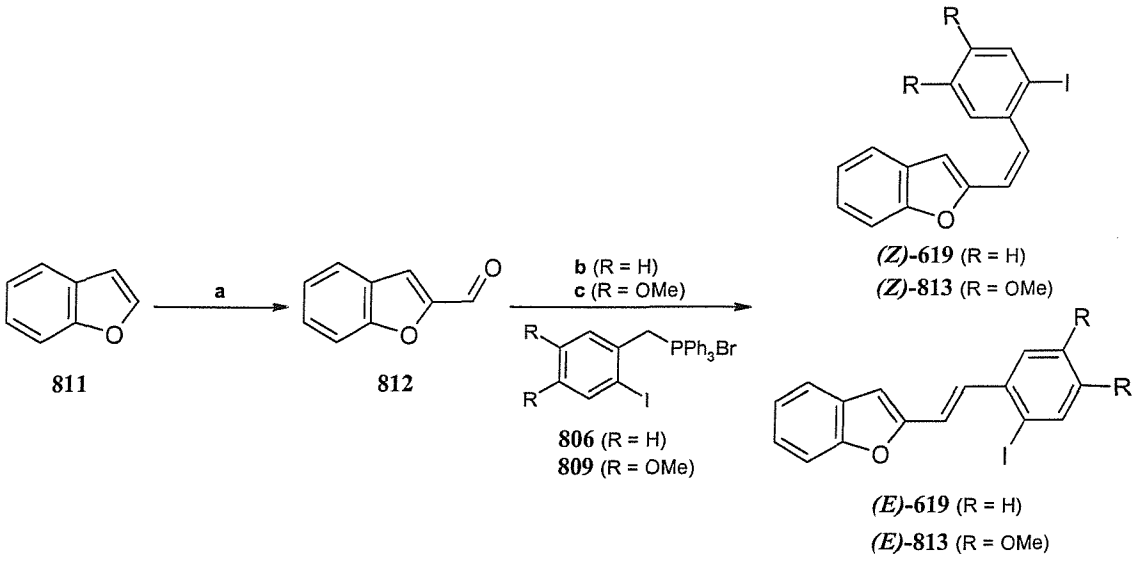
Scheme 95



Reagents and Conditions: **a** *n*-BuLi *then* DMF, THF, -78 °C, 1 hr, 81%. **b** **806**, KO*t*-Bu, THF, RT, 16 hrs, 15% ***(Z)*-618** *and* 71% ***(E)*-618**. **c** **809**, KO*t*-Bu, THF, RT, 16 hrs, 21% ***(Z)*-810** *and* 73% ***(E)*-810**.

Scheme 96

The synthesis of benzo[*b*]furans ***(Z)*-619** and ***(Z)*-813** also began with the parent heterocycle. Various metallation conditions were trialled, eventually leading to the efficient synthesis of 2-formylbenzo[*b*]furan **812**. As before, Wittig condensation with triphenylphosphonium salts **806** and **809** yielded the desired precursors; separation of the *cis*- and *trans*-alkenes being achieved by column chromatography (**Scheme 97**).

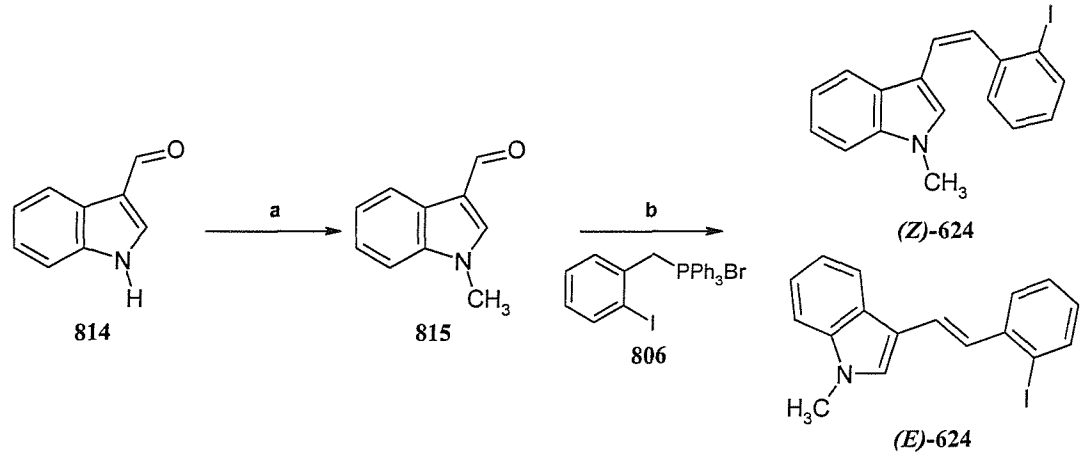


Reagents and Conditions: **a** *n*-BuLi *then* DMF, THF, -10 °C, 1 hr, 84%. **b 806**, KO*t*-Bu, THF, RT, 16 hrs, 42% ***(Z)*-619** *and* 36% ***(E)*-619**. **c 809**, KO*t*-Bu, THF, RT, 16 hrs, 68% ***(Z)*-813** *and* 32% ***(E)*-813**.

Scheme 97

5.1.2 Synthesising the C-3 Tethered Radical Precursors

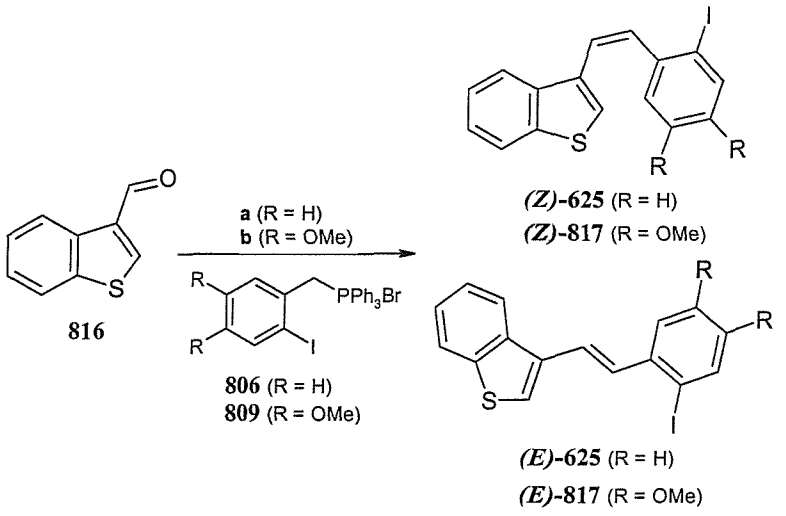
The synthesis of indoles ***(Z)*-624** and ***(E)*-624** was less arduous, as indole-3-carboxaldehyde **814** could be obtained commercially. Methylation of **814** to **815** was followed by Wittig condensation with **806** to give the desired *cis*- and *trans*- alkenes in a 1:1 ratio (**Scheme 98**). The poor yield for this particular Wittig condensation was attributed to the lower nucleophilicity of the carbonyl, resulting from conjugation with the indole nitrogen.



Reagents and Conditions: **a** NaH, MeI, THF, RT, 16 hrs, 99%. **b 806**, KO*t*-Bu, THF, Δ, 64 hrs, 10% ***(Z)*-624** *and* 10% ***(E)*-624**.

Scheme 98

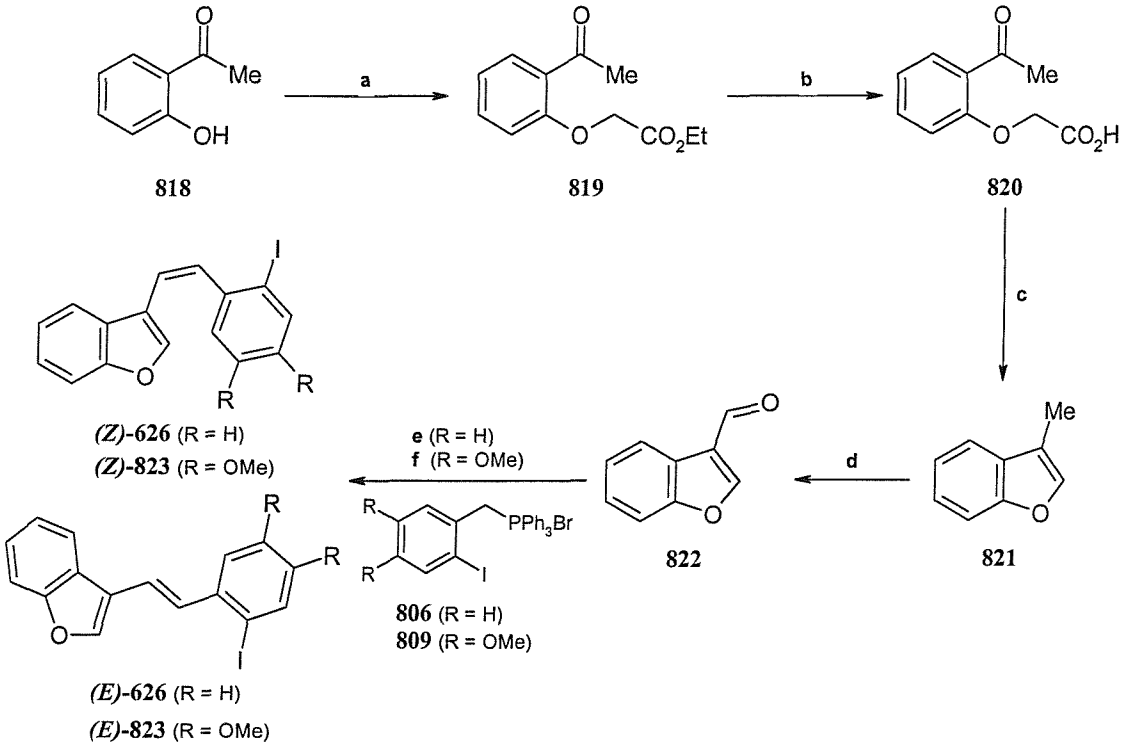
As aldehyde **816** was available commercially, the syntheses of benzo[*b*]thiophenes ***(Z)*-625** and ***(Z)*-817** were also facile. Wittig condensation with triphenylphosphonium salts **806** and **809** provided the corresponding *cis*- and *trans*- alkenes in excellent yield (**Scheme 99**). Again, a combination of column chromatography and successive recrystallisations effected separation of the diastereoisomers.



Reagents and Conditions: **a** **806**, KO*t*-Bu, THF, RT, 16 hrs, 34% ***(Z)*-625** *and* 62% ***(E)*-625**. **b** **809**, KO*t*-Bu, THF, RT, 16 hrs, 38% ***(Z)*-817** *and* 61% ***(E)*-817**.

Scheme 99

For the syntheses of benzo[*b*]furans ***(Z)*-626** and ***(Z)*-823**, 3-formylbenzo[*b*]furan **822** had to be synthesised. Thus, the method of Nielek and Lesiak[149] was employed to access 3-methylbenzo[*b*]furan **821**. Oxidation of the methyl group with selenium dioxide then gave **822** directly.[150] Wittig condensation with triphenylphosphonium salts **806** and **809** furnished the requisite *cis*- and *trans*- alkenes which were readily separated by column chromatography (**Scheme 100**).

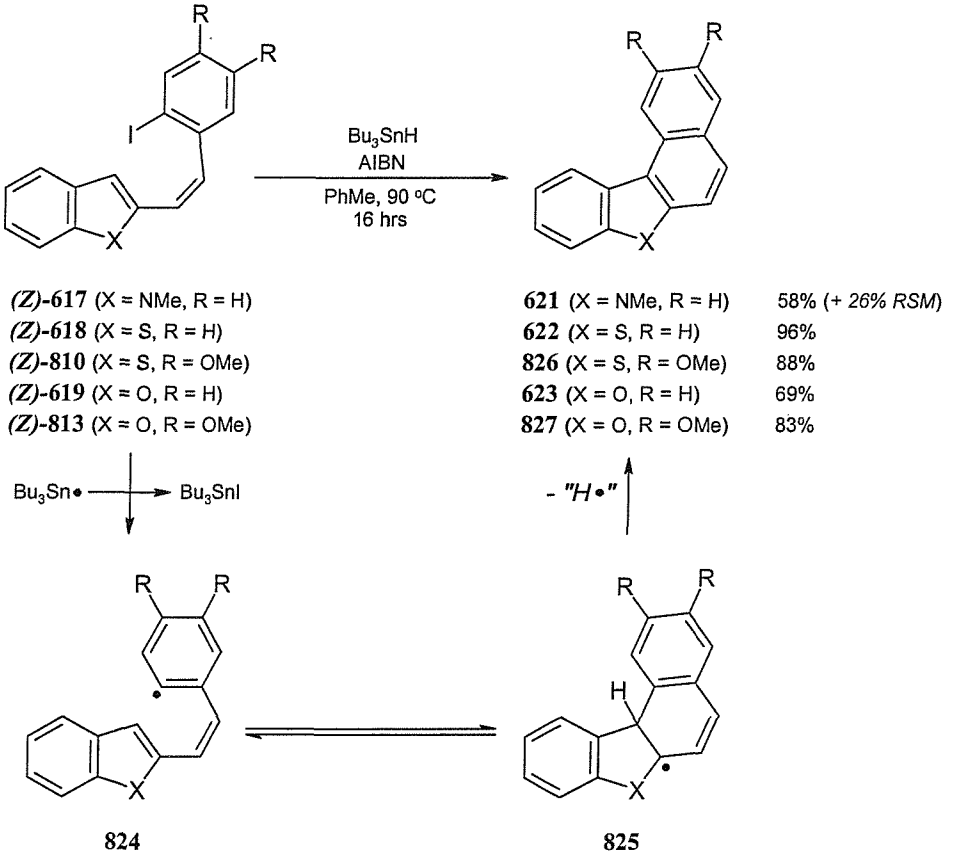


Reagents and Conditions: **a** $BrCH_2CO_2Et$, K_2CO_3, acetone, Δ, 16 hrs, 100%. **b** Na_2CO_3, H_2O, Δ, 1 hr, 92%. **c** NaOAc, Ac_2O, Δ, 3 hrs, 55%. **d** SeO_2, 1,4-dioxane, Δ, 48 hrs, 84%. **e** **806**, KO*t*-Bu, THF, RT, 16 hrs, 57% ***(Z)*-626** *and* 24% ***(E)*-626**. **f** **809**, KO*t*-Bu, THF, RT, 16 hrs, 38% ***(Z)*-823** *and* 51% ***(E)*-823**.

Scheme 100

5.2 C-3 Addition of Alkene-Tethered Aryl Radicals to Five-Membered Condensed Heterocycles

Exposure of precursors ***(Z)*-617**, ***(Z)*-618**, ***(Z)*-619**, ***(Z)*-810** and ***(Z)*-813** to tri-*n*-butyltin hydride and AIBN in toluene at 90 °C successfully furnished the expected polyaromatic heterocycles in moderate to excellent yield *via* a non-reducing radical cyclisation pathway (**Scheme 101**). As noted in our previous study, the use of an electron-rich arene as a radical donor had little influence on the outcome of the reaction. A slight improvement in yield was observed for benzo[*b*]furan ***(Z)*-813** compared to ***(Z)*-619**, but in contrast a small reduction in yield was observed for benzo[*b*]thiophene ***(Z)*-810** in relation to ***(Z)*-618**!



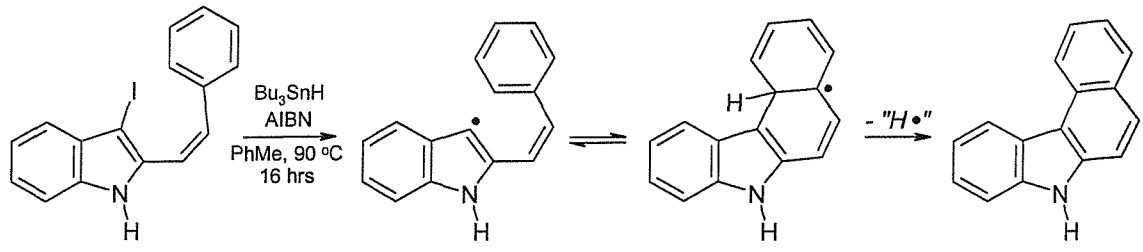
Scheme 101

The most surprising observation in this series was the difficulty encountered in homolysing the carbon-iodine bond in precursor ***(Z)*-617**. The cyclisation was sluggish and yielded a significant quantity of recovered starting material. An alternative radical-mediated synthesis of benzo[*c*]carbazoles was therefore investigated, wherein the roles of radical donor and radical acceptor were reversed.

5.3 Intramolecular Addition of Indolyl Radicals to Arenes

5.3.1 Addition of C-3 Indolyl Radicals to Alkene-Tethered Arenes

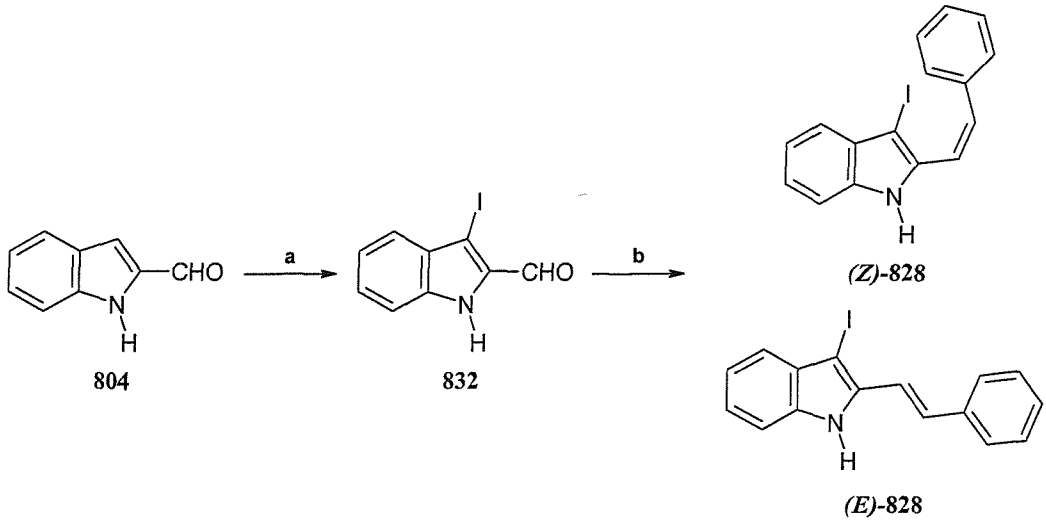
It was hoped that the synthesis of benzo[*c*]carbazole **831** might be accomplished by the cyclisation of alkene ***(Z)*-828** *via* addition of a C-3 indolyl radical to the proximal arene (**Scheme 102**).



(Z)-828 829 830 831

Scheme 102

Thus, the requisite alkene ***(Z)*-828** was synthesised from indole-2-carboxaldehyde **804** *via* iodination at C-3 and Wittig condensation with benzyltriphenylphosphonium chloride. Separation of the *cis*- and *trans*-alkenes was then achieved by column chromatography (**Scheme 103**).

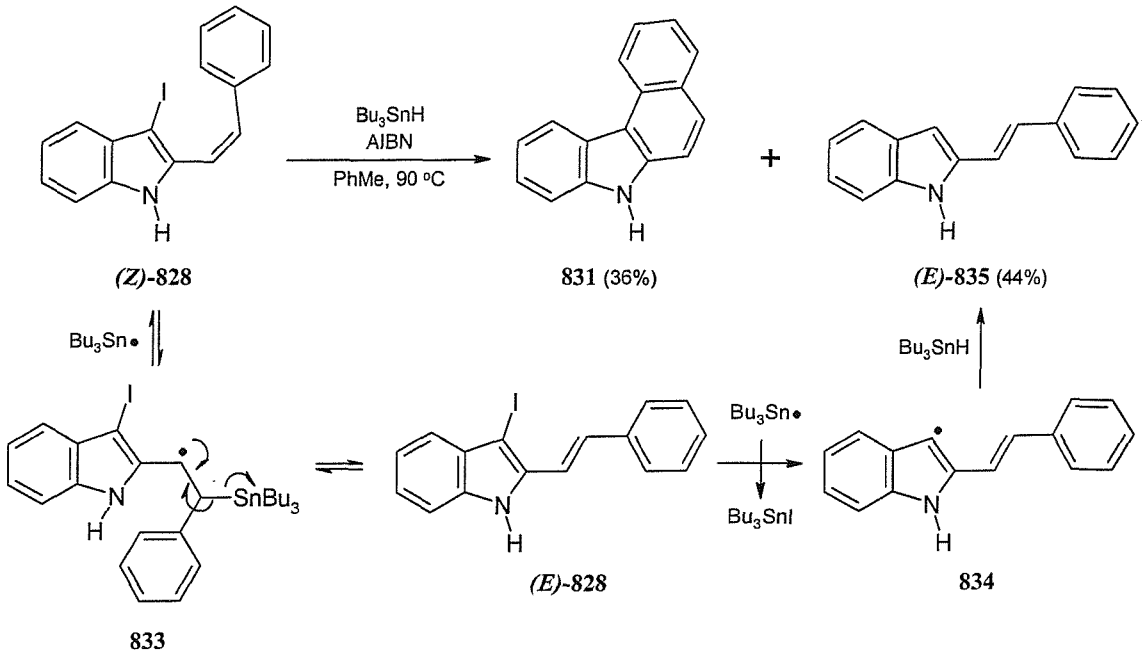


804 832

Reagents and Conditions: **a** I_2, KOH, DMF, RT, 4 hrs, 86%. **b** $BnPPh_3Cl$, NaH, THF, RT, 16 hrs, 61% ***(Z)*-828** *and* 37% ***(E)*-828**

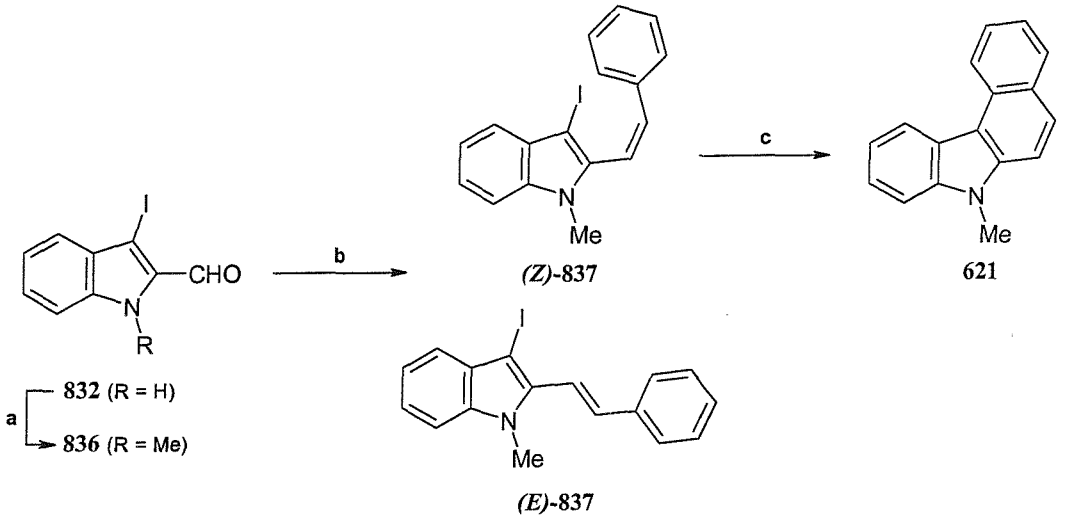
Scheme 103

Surprisingly, exposure of ***(Z)*-828** to tri-*n*-butyltin hydride and AIBN in toluene at 90 °C gave benzo[*c*]carbazole **831** in a disappointing 36% yield. The major product proved to be *trans*-alkene ***(E)*-835**, which was given in 44% yield (**Scheme 104**).



Scheme 104

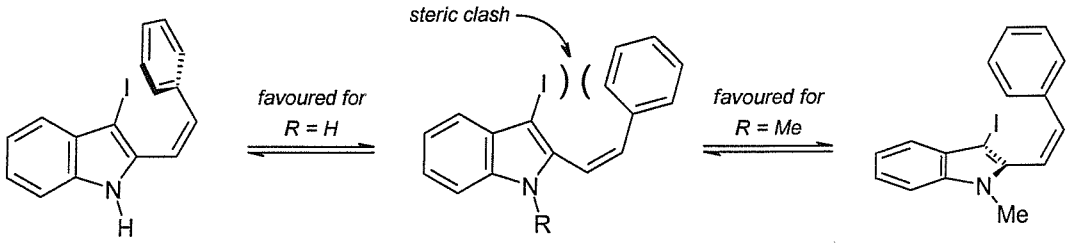
The isomerisation of alkenes under tin-mediated radical cyclisation conditions has been observed previously[139] and can be attributed to the reversible addition of tri-*n*-butyltin radical to the alkene (***(Z)*-828** to **833**). In order to probe this reaction further, the *N*-methylated analogue of ***(Z)*-828** was synthesised *via* methylation of iodinated indole **832**. A Wittig condensation between the resultant aldehyde **836** and benzyltriphenylphosphonium chloride then gave ***(Z)*-837** on separation of the diastereoisomers. Intriguingly, treatment of ***(Z)*-837** with tri-*n*-butyltin hydride and AIBN resulted in efficient conversion to benzo[*c*]carbazole **621** in 95% yield (**Scheme 105**)!



Reagents and Conditions: **a** NaH, MeI, THF, RT, 16 hrs, 98%. **b** $BnPPh_3Cl$, KO*t*-Bu, THF, RT, 16 hrs, 64% ***(Z)*-837** *and* 36% ***(E)*-837**. **c** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 95%.

Scheme 105

These seemingly dichotomous observations may be attributed to polarisation of the alkene by the pendant ring systems. When there are no substituents present on the indole nitrogen, the alkene is presumably conjugated to the indole ring system rather than the arene. As a result, the alkene is polarised and more susceptible to the addition of tri-*n*-butyltin radical. However, when the indole nitrogen is substituted, conjugation of the indole to the alkene is less favourable, so the alkene and arene become co-planar. The alkene is now less polarised and hence the rate of addition of tri-*n*-butyltin radical to the alkene is retarded (**Scheme 106**).

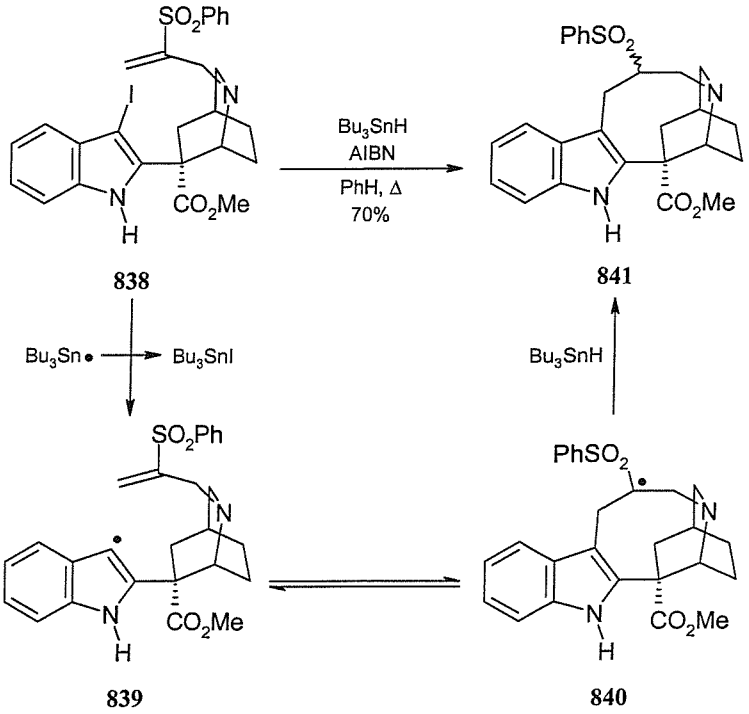


(Z)-828 | *(Z)*-828 (R = H) *(Z)*-837 (R = Me) | *(Z)*-837

Scheme 106

5.3.2 Previously Reported Cyclisation Reactions involving Indolyl Radicals

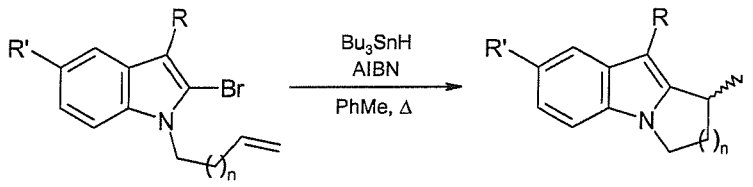
There are only a small number of reports detailing the use of indolyl radicals in cyclisation reactions. The first examples were reported in 1990 by Sundberg and Cherney in work directed towards the synthesis of iboga alkaloid analogues (**Scheme 107**).[151]



Scheme 107

C-3 indolyl radical **839** was generated from iodinated indole **838** by exposure to tri-*n*-butyltin hydride and AIBN. Cyclisation to the alkene moiety then proceeded to furnish the eight-membered ring **841**. For the example illustrated, the yield was pleasing but, unfortunately, this was atypical.

Dobbs, Jones and Veal published further examples, detailing the reductive addition of various substituted and unsubstituted C-2 indolyl radicals to *N*-tethered alkenes (**Scheme 108**).[152]

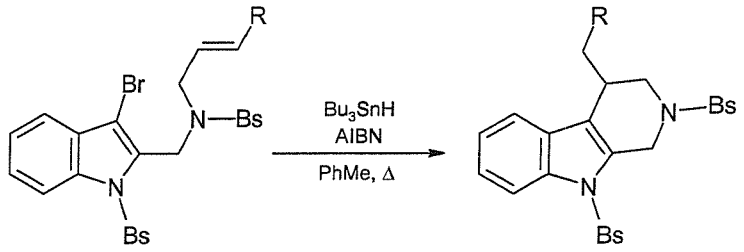


842

843 n = 1, R = R' = H	79%
844 n = 1, R = Me, R' = H	73%
845 n = 1, R = H, R' = OMe	91%
846 n = 2, R = R' = H	74%
847 n = 2, R = Me, R' = H	64%
848 n = 2, R = H, R' = OMe	96%

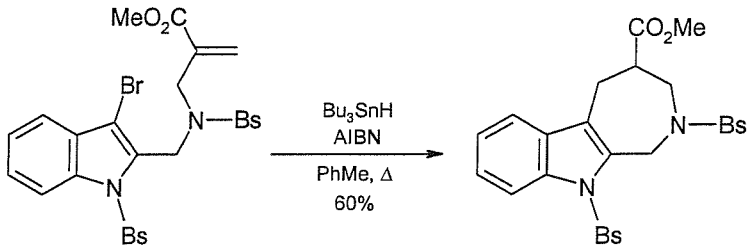
Scheme 108

Mohanakrishnan and Srinivasan then reported a study into the intramolecular addition of C-3 indolyl radicals to C-2 tethered alkenes (**Scheme 109**).[153] Notably, using an α,β-unsaturated ester as the radical acceptor promoted the 7-*endo*-trig cyclisation over the alternate 6-*exo*-trig cyclisation mode.



849 (R = H)
851 (R = CO_2Me)
853 (R = Ph)

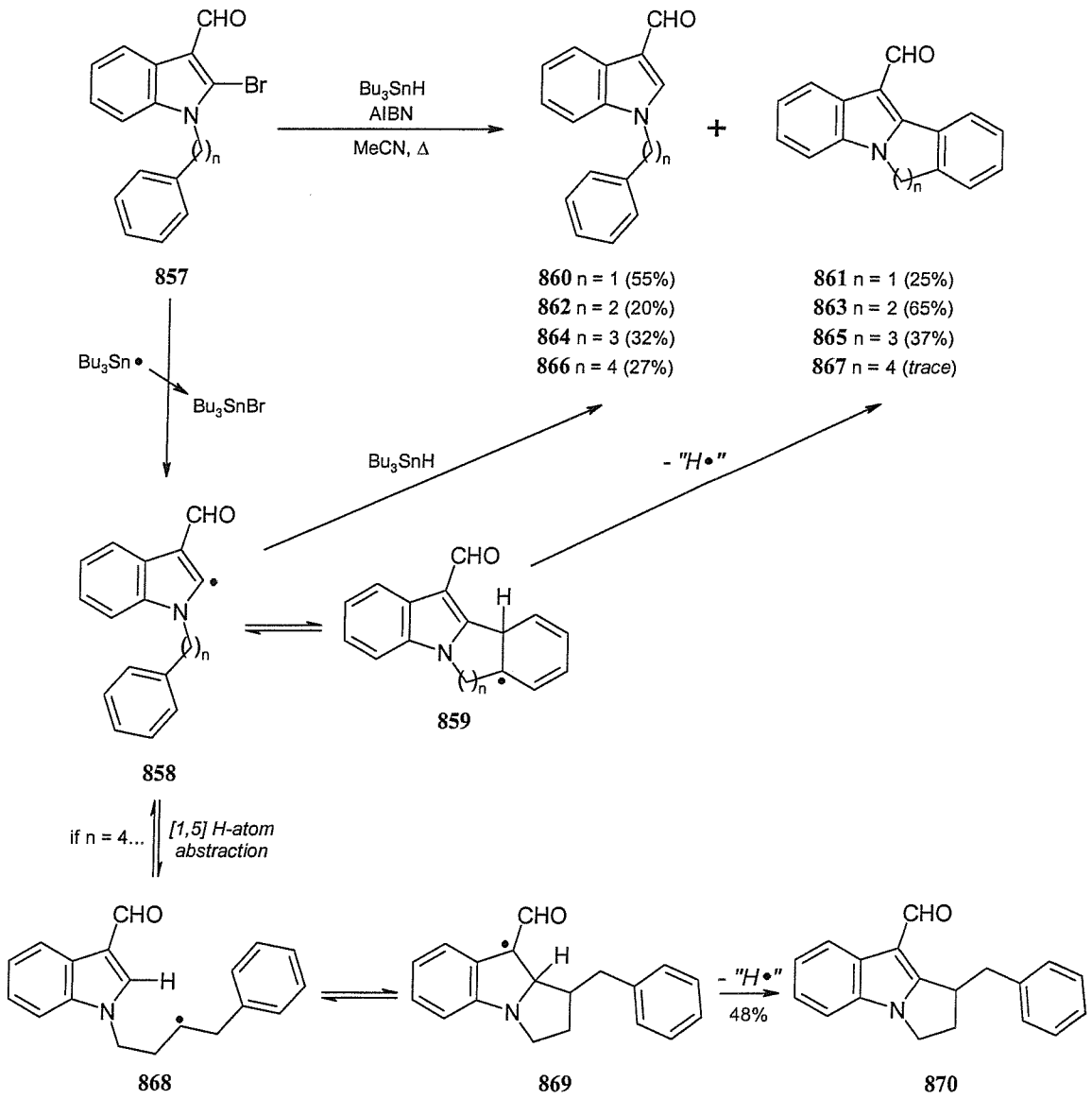
850 (R = H) 40%
852 (R = CO_2Me) 70%
854 (R = Ph) 60%



855 **856**

Scheme 109

Fiumana and Jones pioneered the intramolecular addition of indolyl radicals to arenes (**Scheme 110**).[154] 5-, 6- and 7-*exo*-trig cyclisations all proved viable, although the yield for the 5-*exo*-trig cyclisation was poor. It is presumed that, for these examples, a longer alkane chain length imparts greater flexibility to the system and thus promotes a more efficient cyclisation. Notably, when a four-carbon tether conjoined the arene and the indole, the reaction pursued an alternative pathway. A [1,5]-hydrogen atom abstraction followed by cyclisation of the resulting secondary alkyl radical to C-2 of the indole gave **870** rather than the product of a direct 8-*exo*-trig cyclisation, **867**.

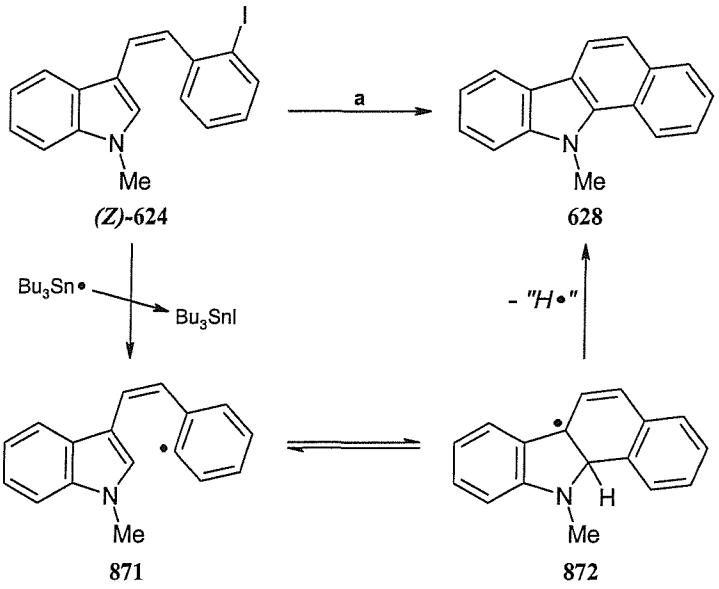


Scheme 110

5.4 C-2 Addition of Alkene-Tethered Aryl Radicals to Five-Membered Condensed Heterocycles

5.4.1 Addition of C-3 Alkene-Tethered Aryl Radicals to Indoles

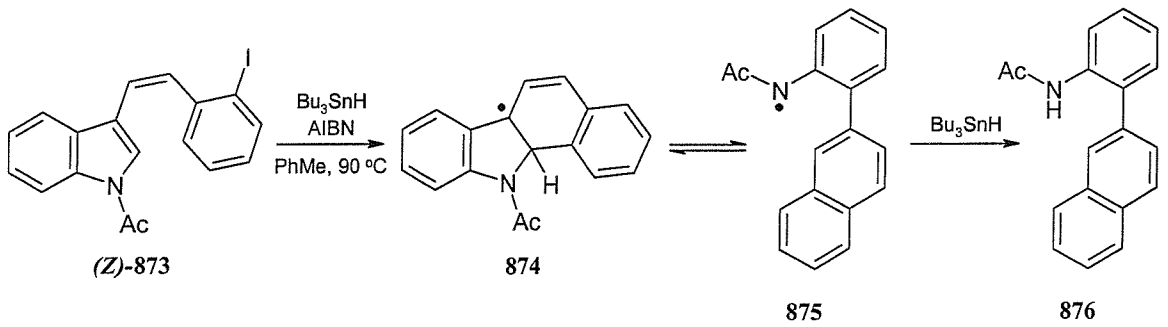
Our attention now turned to the cyclisation of aryl radicals conjoined *via* an alkene tether to C-3 of indoles, benzo[*b*]thiophenes and benzo[*b*]furans. Thus, indole ***(Z)*-624** was exposed to tri-*n*-butyltin hydride and AIBN in toluene at 90 °C. Pleasingly, an efficient cyclisation was observed, yielding benzo[*a*]carbazole **628** in 90% yield *via* a non-reducing pathway (**Scheme 111**).



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 90%.

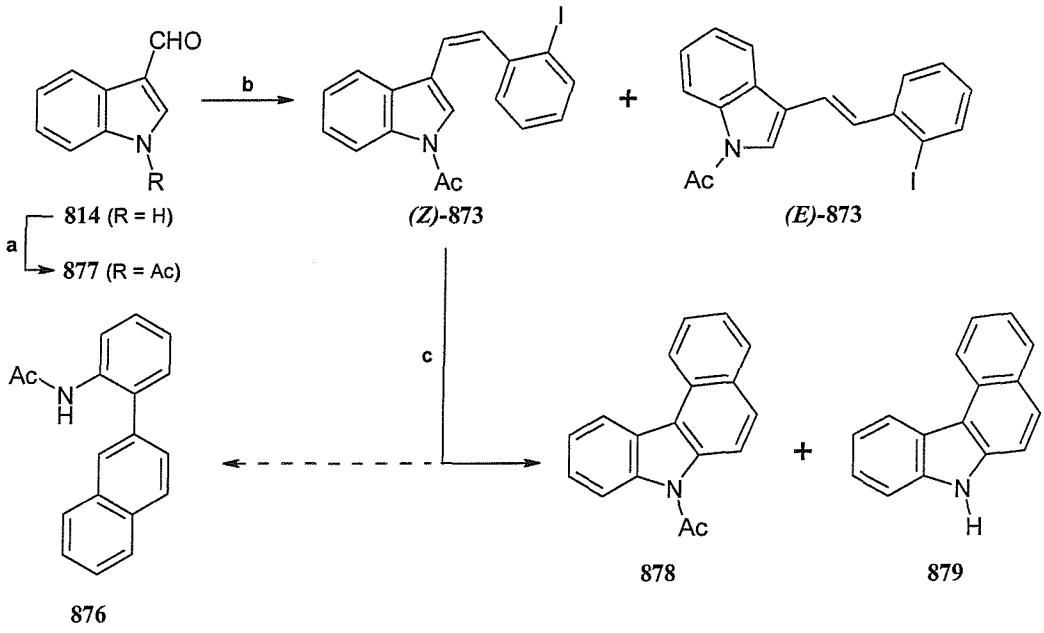
Scheme 111

We then wondered whether the analogous *N*-acetyl substituted indole ***(Z)*-873** would pursue same cyclisation mode, or prove susceptible to an addition-elimination-reduction process, resulting in the formation of *N*-acetyl-2-(2-naphthyl)aniline **876** (**Scheme 112**). It was suspected that this process might be encouraged due to the added stability imparted to nitrogen-centred radical **875** through conjugation to the acetyl group. With this hypothesis in mind, radical precursor ***(Z)*-873** was targeted for synthesis.



Scheme 112

Thus, indole-3-carboxaldehyde **814** was acetylated using the conditions of Bohlmann *et al.*[155] and condensed with Wittig salt **806**. The tin-mediated radical cyclisation of ***(Z)*-873** was then conducted, giving benzo[*c*]carbazoles **878** and **879** in a combined 59% yield (**Scheme 113**). Notably, *N*-acetyl-2-(2-naphthyl)aniline **876** was not observed as a product of the reaction. Presumably, the stability imparted to nitrogen-centred radical **875** through conjugation to the acetyl group is not sufficient to make the addition-elimination-reduction process a viable reaction pathway.



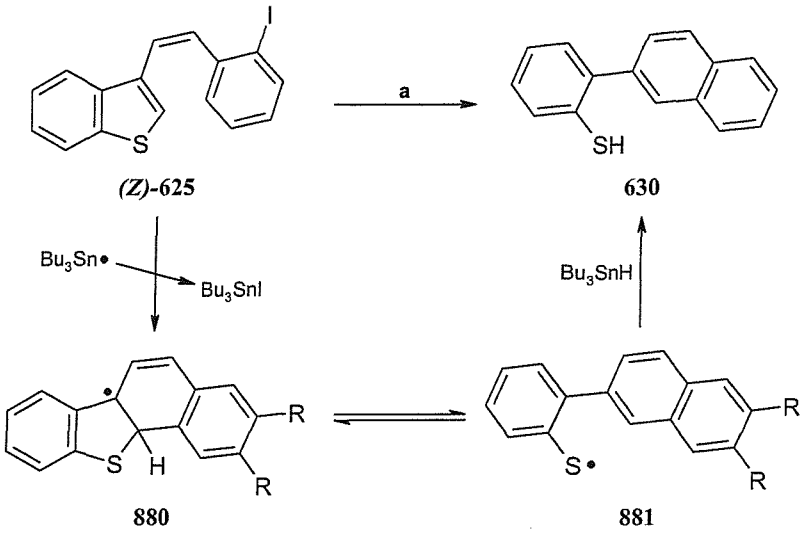
Reagents and Conditions: **a** Ac_2O, NEt_3, DMAP, CH_2Cl_2, RT, 16 hrs, 89%. **b** **806**, KO*t*-Bu, THF, RT, 16 hrs, 25% ***(Z)*-873** *and* 68% ***(E)*-873**. **c** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 31% **878** *and* 28% **879**.

Scheme 113

The partial removal of the acetyl group under the reaction conditions is a curious side-reaction which has also been observed by Kraus and Kim.[92] The mechanism of cleavage is unknown, though it is likely to be a two-electron process mediated by tin rather than radical in nature.

5.4.2 Addition of C-3 Alkene-Tethered Aryl Radicals to Benzo[*b*]thiophenes

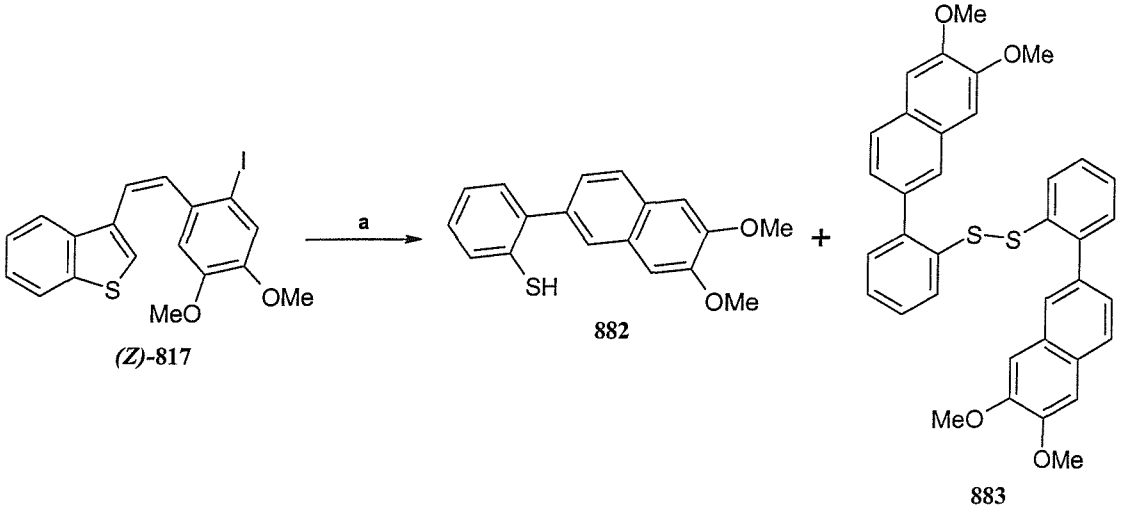
In the benzo[*b*]thiophene series, an entirely different pathway was followed. As anticipated, on exposure of benzo[*b*]thiophene ***(Z)*-625** to tri-*n*-butyltin hydride and AIBN, generation of the aryl radical was followed by cyclisation to C-2. The collapse of intermediate **880** then occurred by the ejection of a thiophenoxy radical leaving group, leading to the reductive formation of 2-(2-naphthyl)thiophenol **630** (**Scheme 114**).



Reagents and Conditions: a Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 98%.

Scheme 114

The cyclisation of benzo[*b*]thiophene ***(Z)*-817** pursued a similar addition-elimination-reduction pathway, though intriguingly thiophenol **882** was formed with it's corresponding dimer **883** as a 1:1 mixture in 97% yield (**Scheme 115**). Since the reaction conditions and concentrations were held constant for the cyclisation of both radical precursors, we attribute this observation to an increased tendency for **882** to undergo aerial oxidation to disulfide **883**. Indeed, on isolation, **882** was found to decompose over several weeks to a complex product mixture.

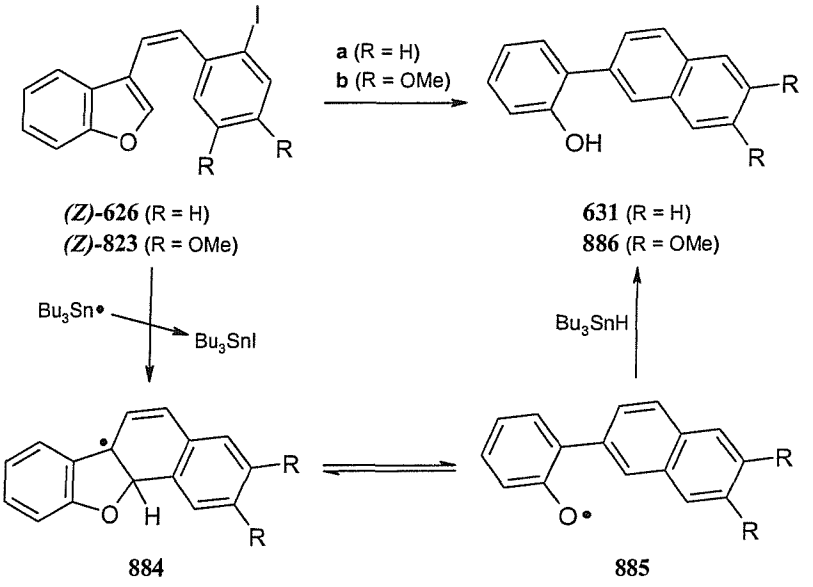


Reagents and Conditions: a Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 52% **882** and 45% **883**

Scheme 115

5.4.3 Addition of C-3 Alkene-Tethered Aryl Radicals to Benzo[*b*]furans

On exposure to tri-*n*-butyltin hydride and AIBN, benzo[*b*]furans ***(Z)*-626** and ***(Z)*-823** were also found to pursue the addition-elimination-reduction pathway, giving 2-(2-naphthyl)phenols **631** and **886** in 35% and 74% yield respectively (**Scheme 116**). Notably, the dimethoxy analogue ***(Z)*-823** gave a much higher yield for the cyclisation. We attribute this to a prolonging of the lifetime of radical intermediate **884**, arising from stabilisation of the carbon centred radical by the substituent methoxy groups.

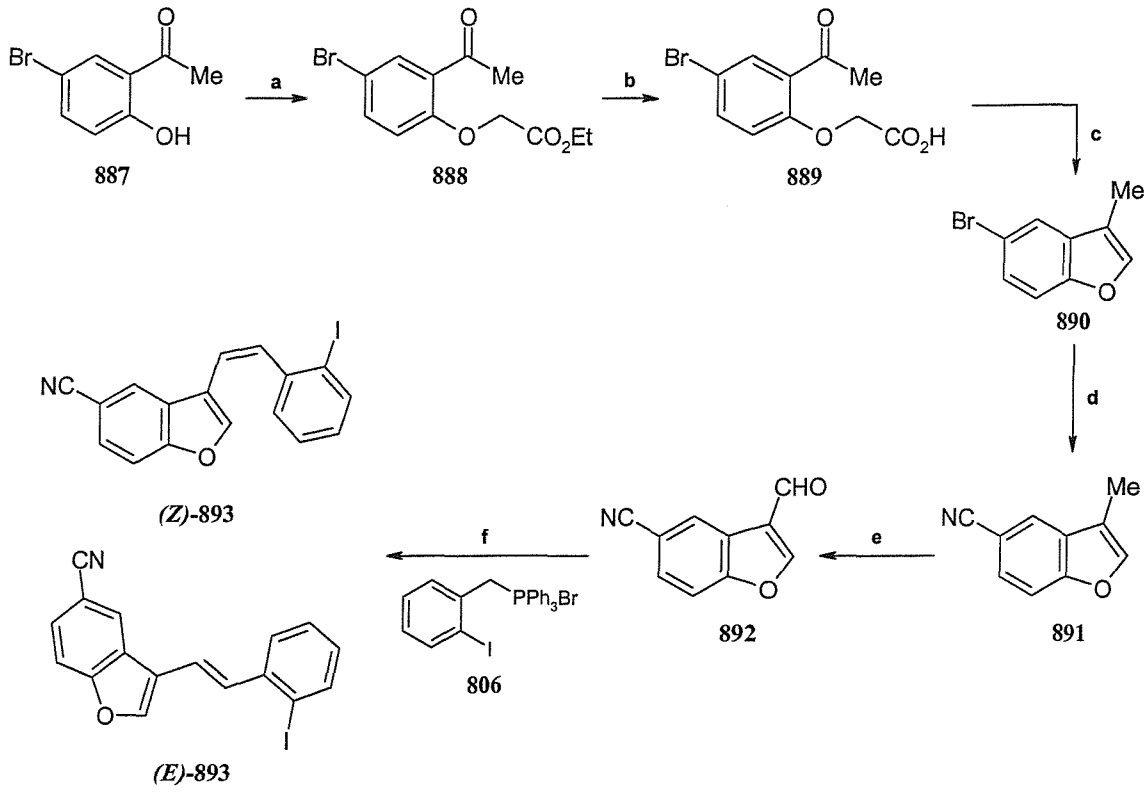


Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 35% **631** *plus* 10% ***(Z)*-626**. **b** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 74%.

Scheme 116

It was felt that the lower yields obtained in the benzo[*b*]furan series could be a consequence of the slower rate of ejection of the phenoxy radical. Thus, we postulated that a substituent capable of stabilising the phenoxy radical intermediate ought to encourage fragmentation and augment the reaction yield. In order to test that hypothesis, 5-cyanobenzo[*b*]furan ***(Z)*-893** was targeted as a cyclisation precursor.

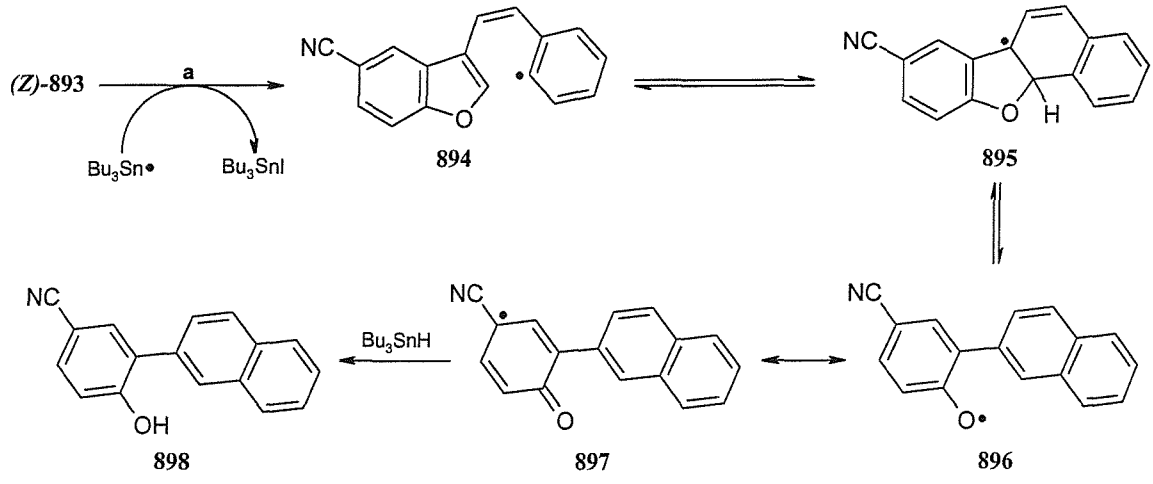
Thus, 5-bromo-3-methylbenzo[*b*]furan **890** was synthesised from 5'-bromo-2'-hydroxyacetophenone **887** using the route of Nielek and Lesiak.[149] Nucleophilic aromatic substitution of the bromide then yielded 3-methylbenzo[*b*]furan-5-carbonitrile **891**.[156] Oxidation of the methyl group with selenium dioxide[150] and subsequent Wittig condensation with triphenylphosphonium salt **806** then furnished desired *cis*-alkene radical precursor ***(Z)*-893**, along with *trans*-analogue ***(E)*-893** (**Scheme 117**).



Reagents and Conditions: **a** $BrCH_2CO_2Et$, K_2CO_3, acetone, Δ, 16 hrs, 100%. **b** Na_2CO_3, H_2O, Δ, 1 hr, 84%. **c** NaOAc, Ac_2O, Δ, 3 hrs, 88%. **d** CuCN, CuI, DMF, 160 °C, 16 hrs, 83%. **e** SeO_2, 1,4-dioxane, Δ, 5 days, 88%. **f** **806**, KO*t*-Bu, THF, RT, 16 hrs, 20% ***(Z)*-893** *and* 79% ***(E)*-893**.

Scheme 117

Pleasingly, treatment of ***(Z)*-893** with tri-*n*-butyltin hydride and AIBN gave 4-hydroxy-3-(2-naphthyl)benzonitrile **898** in 98% yield (**Scheme 118**). Thus, we conclude that stabilisation of the intermediate phenoxy radical does indeed facilitate the conversion of benzo[*b*]furan radical precursors akin to ***(Z)*-626** to their corresponding 2-(2-naphthyl)-phenol.

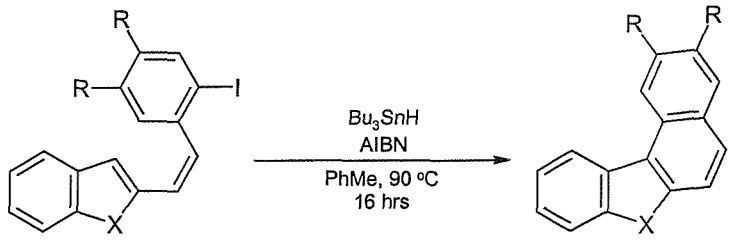


Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 98%.

Scheme 118

5.5 Summary

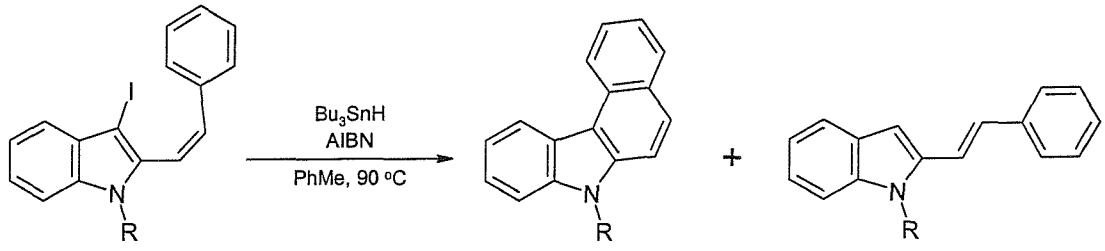
The tin-mediated radical cyclisation of alkenes akin to ***(Z)*-617** have been shown to give the corresponding polyaromatic heterocycles *via* a non-reducing pathway (**Scheme 119**). In this manner, the syntheses of benzo[*c*]carbazole **621**,[148] benzo[*b*]naphtho[1,2-*a*]thiophenes **622** and **826** and benzo[*b*]naphtho[1,2-*a*]furans **623** and **827** were achieved.



***(Z)*-617** (X = NMe, R = H)	**621** (X = NMe, R = H)	58%
***(Z)*-618** (X = S, R = H)	**622** (X = S, R = H)	96%
***(Z)*-810** (X = S, R = OMe)	**826** (X = S, R = OMe)	88%
***(Z)*-619** (X = O, R = H)	**623** (X = O, R = H)	69%
***(Z)*-813** (X = O, R = OMe)	**827** (X = O, R = OMe)	83%

Scheme 119

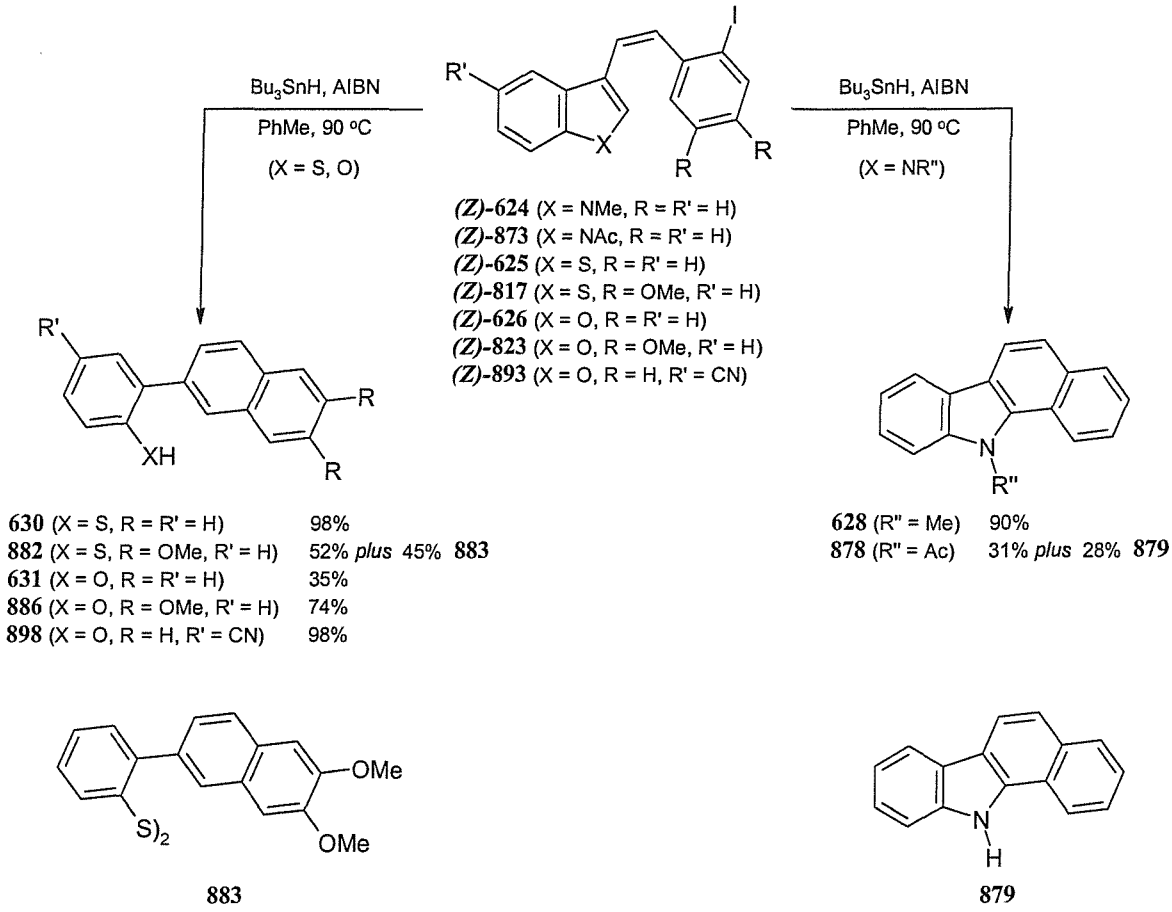
An alternative, higher yielding route to benzo[*c*]carbazoles has also been achieved through addition of a C-3 indolyl radical to an alkene-tethered arene. For these examples, competing addition of the tri-*n*-butyltin radical to the alkene proved detrimental to the cyclisation pathway when the reactions were conducted with the free indole. The simple expedient of substituting the indole nitrogen with a methyl group prevented this side reaction and gave the corresponding benzo[*c*]carbazole **621** in excellent yield **(Scheme 120)**.[148]



***(Z)*-828** (R = H)	**831** (R = H) 36%	***(E)*-835** (R = H) 44%
***(Z)*-837** (R = Me)	**621** (R = Me) 95%	***(E)*-899** (R = Me) *trace*

Scheme 120

The tin-mediated cyclisation of alkenes akin to ***(Z)*-624** were shown to follow different reaction pathways depending on the constituent heteroatom. The indole substrates preferentially underwent a non-reducing cyclisation to form the corresponding benzo[*a*]carbazoles,[148] whereas benzo[*b*]furans and benzo[*b*]thiophenes followed an addition-elimination-reduction pathway to furnish the corresponding 2-(2-naphthyl)-phenols and 2-(2-naphthyl)–thiophenols respectively (**Scheme 121**). Stabilisation of the intermediate phenoxy radical proved necessary for the process to be efficient in the benzo[*b*]furan series.



Scheme 121

Chapter 6

The Tin-Mediated Radical Synthesis of Spirocycles and Other Polycyclic Systems

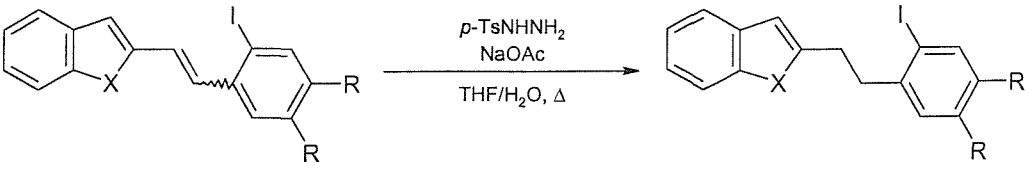
This chapter details the results of our study into the addition of alkane- or ether-tethered aryl radicals to C-2 and C-3 of indoles, benzo[*b*]thiophenes and benzo[*b*]furans. Again, the influence of the constituent heteroatom on the cyclisation pathway is noted. An application of this new methodology in the synthesis of the natural product demethylhomopterocarpin is then described.

6.1 Synthesis of the Radical Precursors

Accessing the alkane-tethered radical precursors for this study proved facile. Di-imide mediated hydrogenation of the alkene precursors from Chapter 5 was readily accomplished in good to excellent yield (**Scheme 122**).

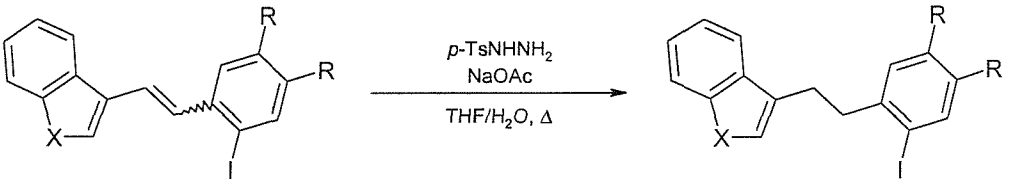
The synthesis of ether **666** commenced with the methylation of indole **802**. Subsequent reduction of the ester group furnished alcohol **907**. A Mitsunobu coupling with 2-iodophenol completed the synthesis in a disappointing 37% overall yield (**Scheme 123**).

The analogous benzo[*b*]thiophene and benzo[*b*]furan ethers **667** and **668** were accessed from the corresponding heterocyclic aldehydes in higher yield. Reduction of these aldehydes followed by a Mitsunobu coupling with 2-iodophenol furnished **667** and **668** in 94% and 85% yield respectively (**Scheme 124**). The syntheses of C-3 tethered ethers **678** and **679** were accomplished in a similar manner (**Scheme 125**). Unfortunately, the indole analogue **677** could not be prepared, as alcohol intermediate **910** proved too unstable.



(E)-**617** (X = NMe, R = H)
(E/Z)-**618** (X = S, R = H)
(E/Z)-**810** (X = S, R = OMe)
(E/Z)-**619** (X = O, R = H)
(E/Z)-**813** (X = O, R = OMe)

632 (X = NMe, R = H)
633 (X = S, R = H)
901 (X = S, R = OMe)
634 (X = O, R = H)
902 (X = O, R = OMe)

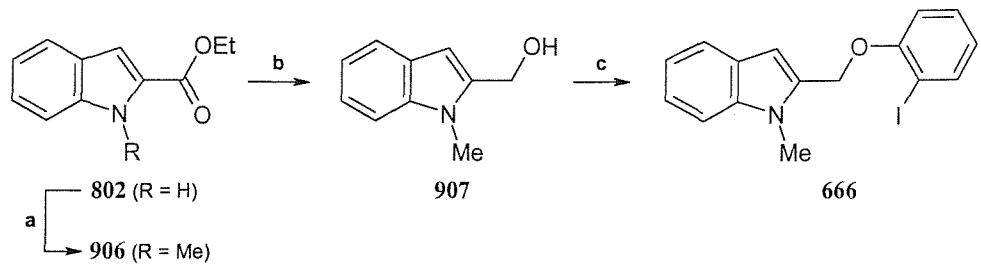


(E)-**624** (X = NMe, R = H)
(E)-**873** (X = NAc, R = H)
(E/Z)-**625** (X = S, R = H)
(E/Z)-**817** (X = S, R = OMe)
(E/Z)-**626** (X = O, R = H)
(E/Z)-**823** (X = O, R = OMe)

653 (X = NMe, R = H)
903 (X = NAc, R = H)
654 (X = S, R = H)
904 (X = S, R = OMe)
655 (X = O, R = H)
905 (X = O, R = OMe)

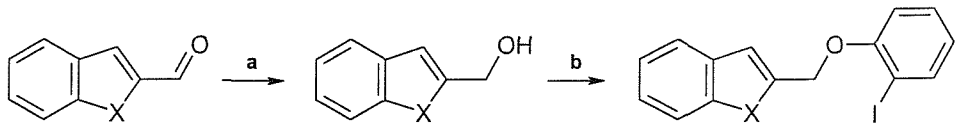
Starting alkene(s)	Reaction time (hrs)	Product (yield)
(E)-617	40	**632** (98%)
(E/Z)-618	40	**633** (95%)
(E/Z)-810	16	**901** (66%)
(E/Z)-619	16	**634** (97%)
(E/Z)-813	40	**902** (77%)
(E)-624	48	**653** (78%)
(E)-873	40	**903** (98%)
(E/Z)-625	40	**654** (94%)
(E/Z)-817	16	**904** (60%)
(E/Z)-626	16	**655** (95%)
(E/Z)-823	40	**905** (90%)

Scheme 122



Reagents and Conditions: **a** MeI, K_2CO_3, acetone, Δ, 48 hrs, 90%. **b** $LiAlH_4$, THF, 0 °C, 1 hr, 97%. **c** 2-iodophenol, PPh_3, DIAD, THF, - 10 °C, 2 hrs, 37%.

Scheme 123

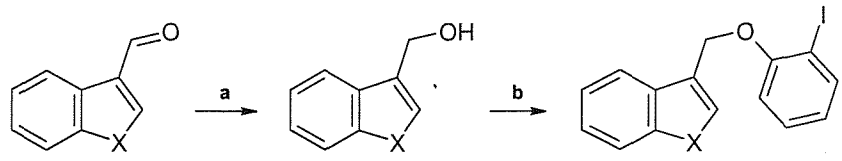


808 (X = S) **908** (X = S) 90% **667** (X = S) 94%

812 (X = O) **909** (X = O) 98% **668** (X = O) 85%

Reagents and Conditions: **a** $NaBH_4$, MeOH, 0 °C, 1 hr. **b** 2-iodophenol, PPh_3, DIAD, THF, - 10 °C, 2 hrs. *Yields given above.*

Scheme 124



814 (X = NMe) **910** (X = NMe) 0% **677** (X = NMe)

816 (X = S) **911** (X = S) 100% **678** (X = S) 82%

822 (X = O) **912** (X = O) 89% **679** (X = O) 68%

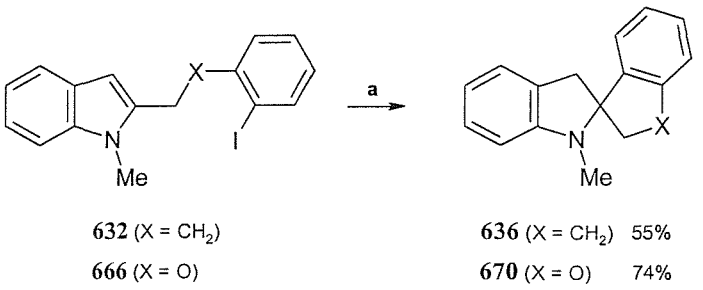
Reagents and Conditions: **a** $NaBH_4$, MeOH, 0 °C, 1 hr. **b** 2-iodophenol, PPh_3, DIAD, THF, - 10 °C, 2 hrs. *Yields given above.*

Scheme 125

6.2 Addition of Alkane- or Ether-Tethered Aryl Radicals to Indoles

6.2.1 Addition of C-2 Alkane- or Ether Tethered Aryl Radicals

Exposure of **632** to tri-*n*-butyltin hydride and AIBN led to a reductive 5-*exo*-trig cyclisation to C-2 of the indole, resulting in the formation of spirocycle **636** in 55% yield. However, ether **666** underwent cyclisation to give spirocycle **670** in a more pleasing 74% yield (**Scheme 126**). This increase in efficiency is attributed to the ether tether promoting 5-*exo*-trig addition of the aryl radical to the indole.[146]



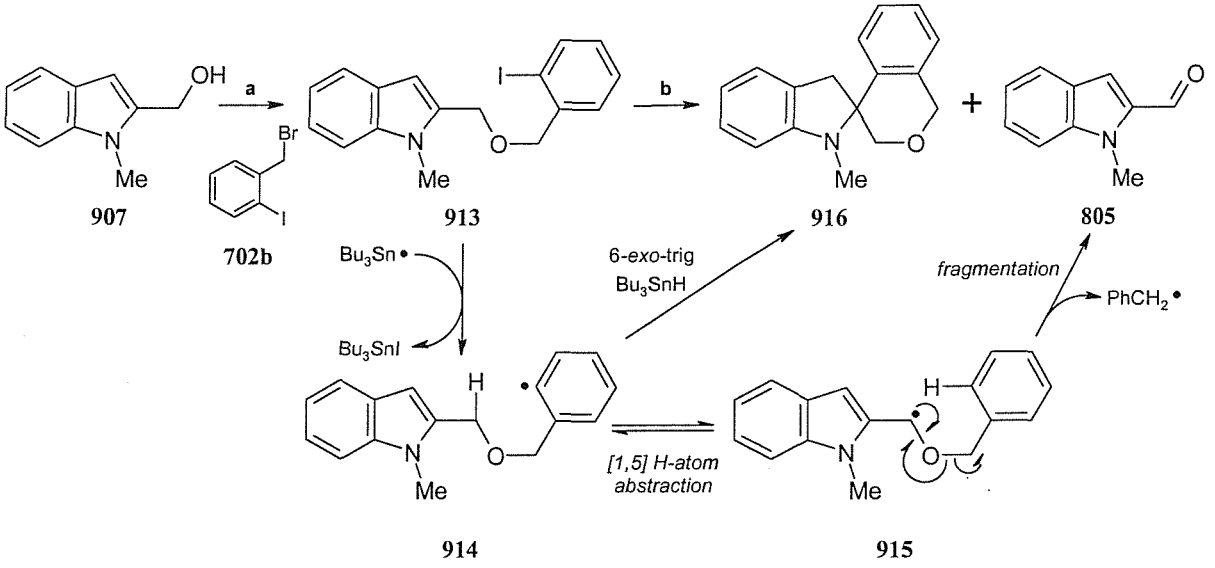
632 (X = CH_2) **636** (X = CH_2) 55%

666 (X = O) **670** (X = O) 74%

Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs. *Yields given above.*

Scheme 126

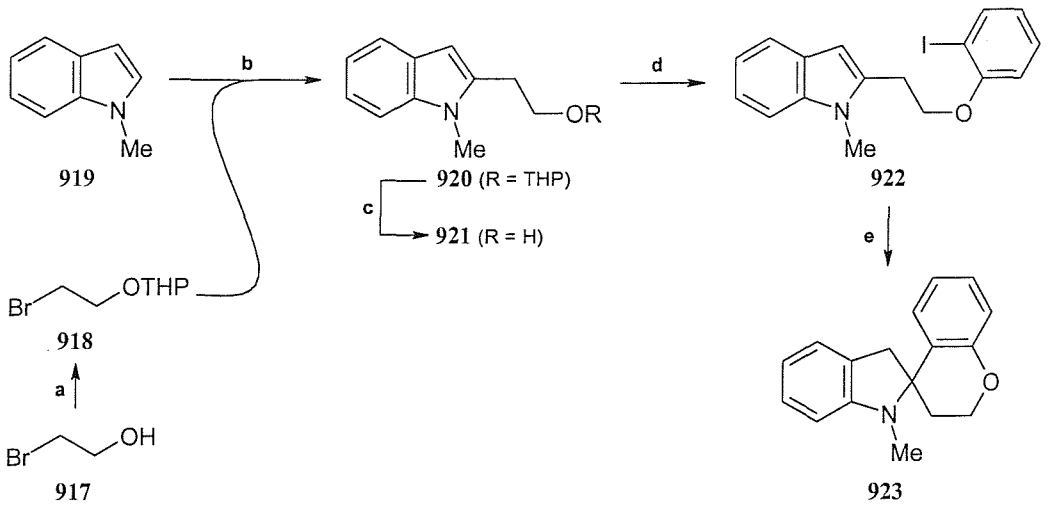
An analogous 6-*exo*-trig cyclisation was also attempted using radical precursor **913**, synthesised from alcohol **907** *via* nucleophilic displacement of bromide **702b**. The yield of spirocycle **916** was lower (43%) than for the analogous 5-*exo*-trig cyclisation (74%), but surprisingly aldehyde **805** (16%) was given as a reaction by-product. Presumably, **805** arises from intramolecular hydrogen atom abstraction leading to radical intermediate **915**, which collapses with the ejection of a benzyl radical (**Scheme 127**).



Reagents and Conditions: **a** NaH, **702b**, THF, RT, 16 hrs, 77%. **b** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 43% **916** *and* 16% **805**

Scheme 127

We postulated that if the position of the heteroatom in the tethering chain was shifted by one methylene unit, fragmentation might be discouraged leading to a more efficient cyclisation. Thus, *N*-methylindole **919** was deprotonated at C-2 and functionalised by nucleophilic displacement of bromide **918** (**Scheme 128**). Acid-mediated deprotection to alcohol **921** and subsequent Mitsunobu coupling with 2-iodophenol then furnished ether **922**. Encouragingly, cyclisation to spirocycle **923** occurred in 42% yield and no products derived from fragmentation were observed.

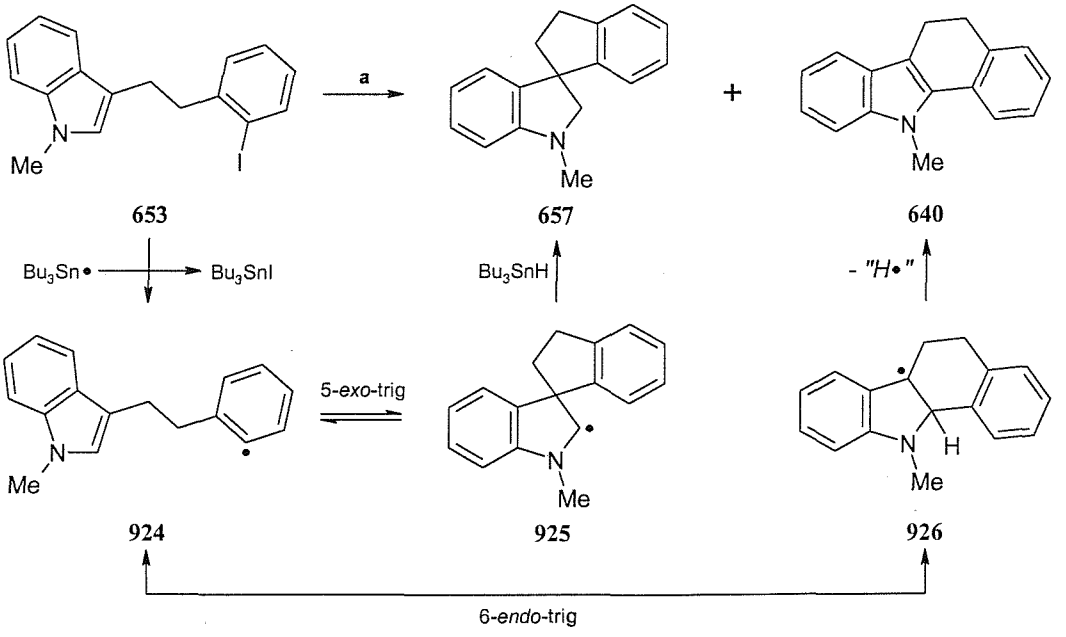


Reagents and Conditions: **a** DHP, *p*-TsOH, Et_2O, RT, 16 hrs, 68%. **b** *n*-BuLi, Et_2O, Δ, 6 hrs, 20% **920** *plus* 51% **919** and 33% **918**. **c** *p*-TsOH.H_2O, MeOH, RT, 16 hrs, 68%. **d** 2-iodophenol, PPh_3, DIAD, THF, -10 °C, 2 hrs, 78%. **e** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 42%

Scheme 128

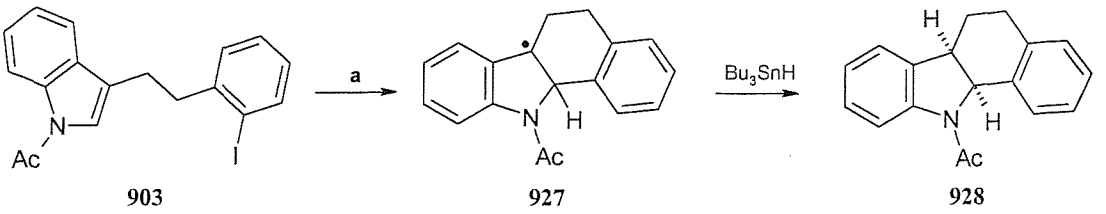
6.2.2 Addition of C-3 Alkane- or Ether Tethered Aryl Radicals

In stark contrast to the C-2 tethered indoles discussed in the previous section, cyclisation of **653** gave a 2:1 mixture of C-3 and C-2 cyclisation products, spirocycle **657** and dihydrobenzo[*a*]carbazole **640**, in 99% overall yield (**Scheme 129**). However, cyclisation of indole amide **903** gave *tetrahydrobenzo[a]carbazole* **928** as the sole isolated product of the reaction in 84% yield (**Scheme 130**)!



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 63% **657** *and* 36% **640**.

Scheme 129



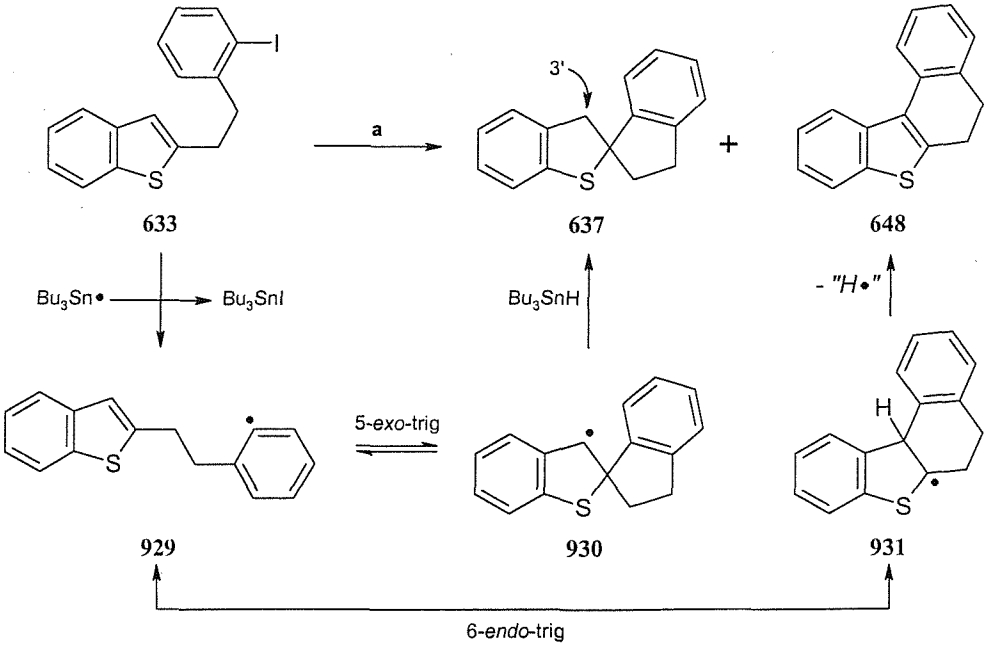
Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 84%.

Scheme 130

From these results, it appears that cyclisation is strongly influenced by the electronic character of the constituent heteroatom. For indole **903**, the nitrogen lone pair is part of the aromatic ring system but is also conjugated to the attached acetate group. Consequently, C-2 of the indole is more δ-positive so the attacking aryl radical, which is nucleophilic in nature, now favours the 6-*endo*-trig cyclisation mode. Conjugation of the nitrogen lone pair to the acetate group also lessens the thermodynamic drive for rearomatisation of radical intermediate **927**. Hence, a reductive cyclisation pathway is followed, leading to tetrahydrobenzo[*a*]carbazole **928**.

6.3 Addition of Alkane- or Ether-Tethered Aryl Radicals to Benzo[*b*]thiophenes

Cyclisation of benzo[*b*]thiophene **633** produced a complex product mixture, from which it proved impossible to isolate any of the constituents in a form pure enough for comprehensive characterisation (**Scheme 131**).

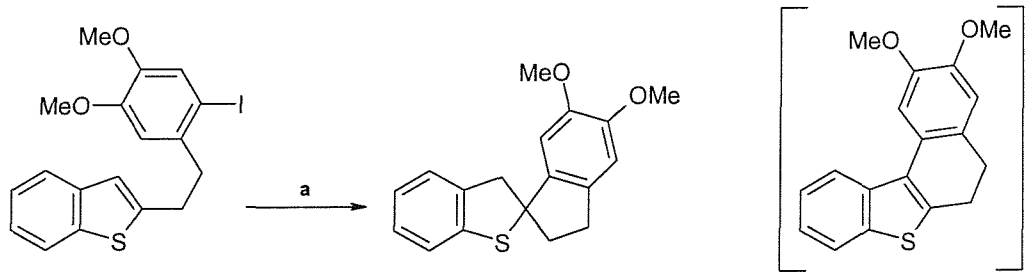


Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 79% by **637**.

Scheme 131

Analysis of the product mixture by ^{1}H-NMR showed doublets at δ_H 3.50 and 3.79 ppm (J = 15.5 Hz) that were attributed to the two hydrogen atoms at C-3' of spirocycle **637**. Triplets at δ_H 3.16 and 3.32 ppm (J = 8.6 Hz) were also observed and assigned as the hydrogen atoms from the saturated portion of dihydrobenzo[*b*]naphtho[1,2-*a*]thiophene **648**. Thus, by ^{1}H-NMR, **637** and **648** appear to be the major components of the product mixture, present in an approximate 3:2 ratio. Pleasingly, GC-CIMS provided further evidence in support of this analysis, giving M^+ signals for the two major components consistent with the formation of **637** (238 amu) and **648** (236 amu).

Cyclisation of benzo[*b*]thiophene **901** also gave a complex product mixture from which spirocycle **932** was isolated in sufficient purity for the ^{1}H-NMR to be fully assigned (**Scheme 132**). Notably, we were unable to identify signals corresponding to dihydrobenzo[*b*]naphtho[1,2-*a*]thiophene **933** in the ^{1}H-NMR of the crude product mixture.

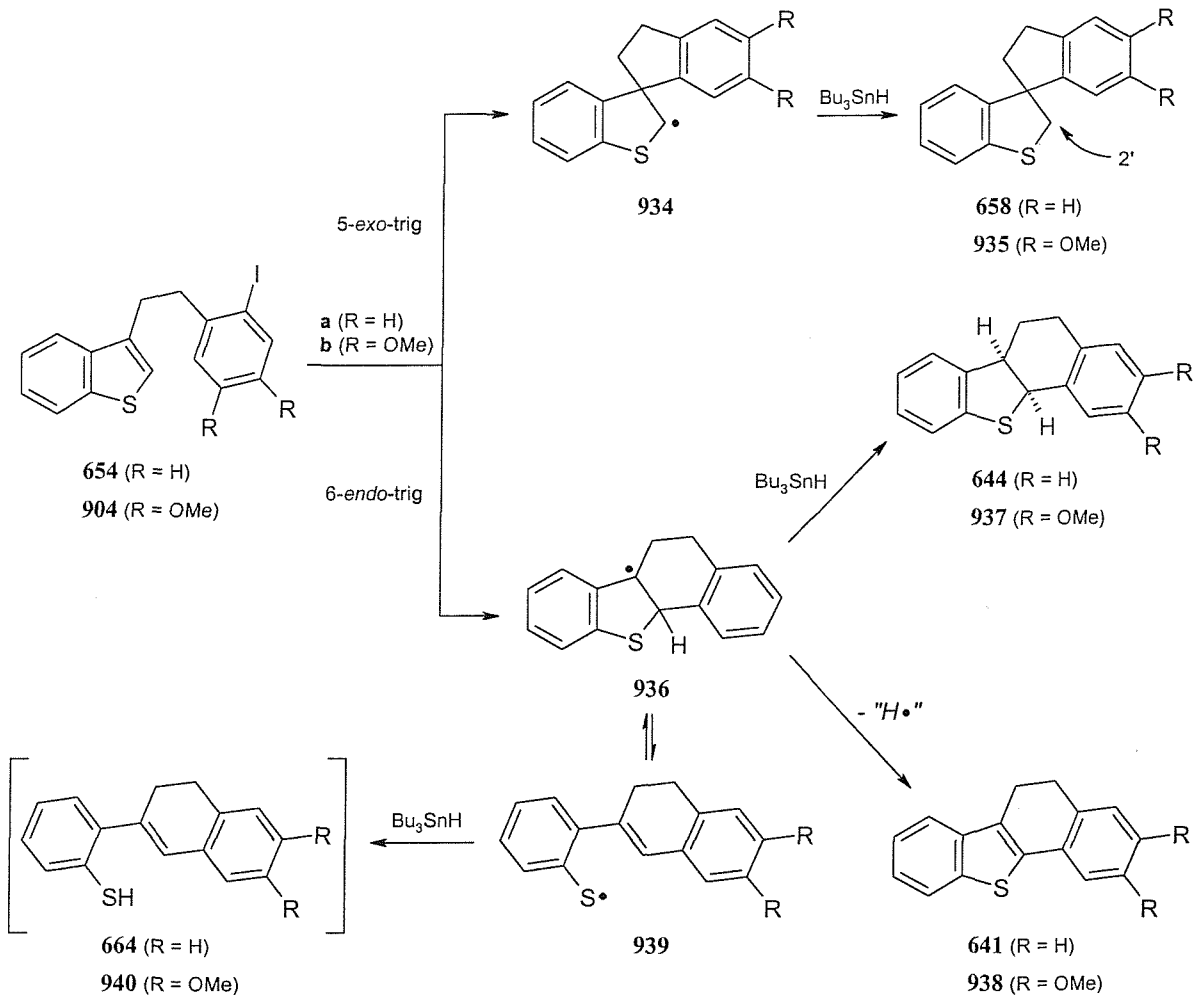


901 **932** **933**

Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 69% by **932**.

Scheme 132

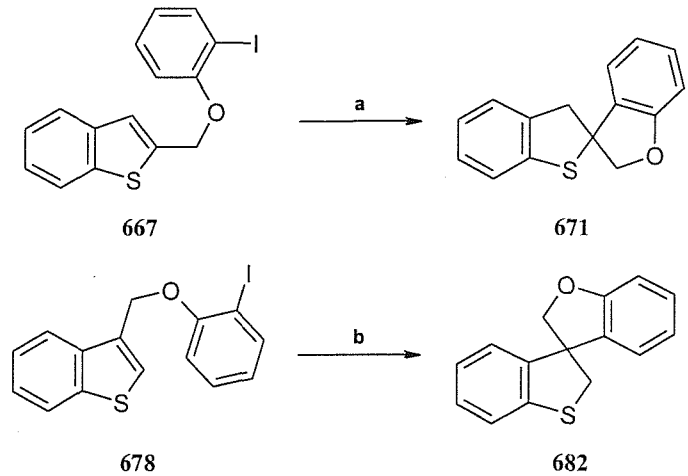
An inseparable product mixture was again obtained on cyclisation of benzo[*b*]thiophene **654** (**Scheme 133**). Analysis by ^{1}H-NMR showed a doublet at δ_H 3.40 ppm (J = 11.0 Hz), attributed to one of the hydrogen atoms at C-2' of spirocycle **658**. In addition, multiplets at δ_H 3.08-3.12 ppm and δ_H 3.12-3.19 ppm corresponding to the hydrogen atoms in the saturated portion of dihydrobenzo[*b*]naphtho[2,1-*d*]thiophene **641** were observed. However, a doublet at δ_H 5.38 ppm (J = 6.9 Hz) also indicated the formation of tetrahydrobenzo[*b*]naphtho[2,1-*d*]thiophene **644**. GC-CIMS confirmed the presence of three major components and supported our suggestion that these were **644** and **658** (238 amu) and **641** (236 amu). **658**, **641** and **644** were formed in an approximate 2:2:1 ratio; cyclisation of benzo[*b*]thiophene **904** gave a similar product distribution. There is no evidence indicating the presence of the addition-elimination-reduction products **664** and **932** in the product mixtures, though they may have been formed as minor by-products.



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 80% by **658**.
b Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 86% by **935**.

Scheme 133

In lieu of these results, the cyclisation of benzo[*b*]thiophenes **667** and **678** were examined. Happily, on exposure to tri-*n*-butyltin hydride and AIBN each underwent 5-*exo*-trig cyclisation smoothly, yielding spirocyclic ethers **671** and **682** in 75% and 90% yield respectively (**Scheme 134**).



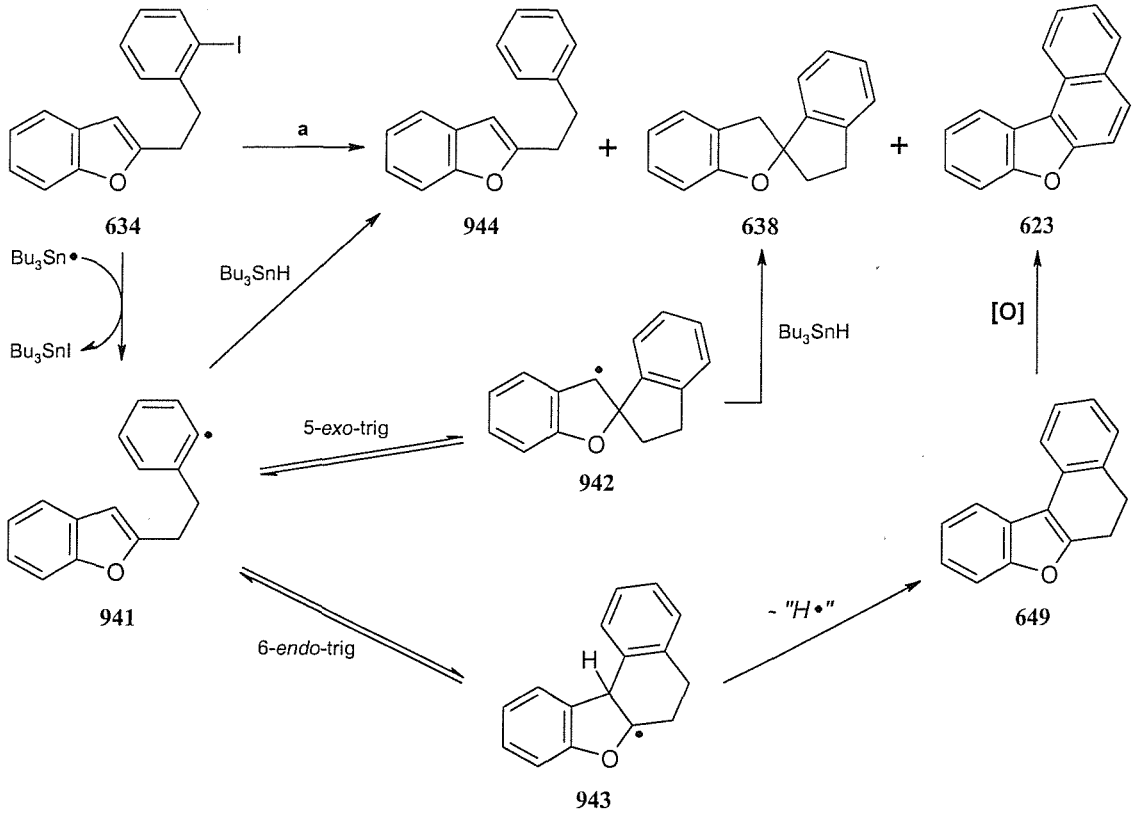
Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 75%.
b Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 90%.

Scheme 134

6.4 Addition of Alkane- or Ether-Tethered Aryl Radicals to Benzo[*b*]furans

6.4.1 Addition of C-2 Alkane- or Ether Tethered Aryl Radicals

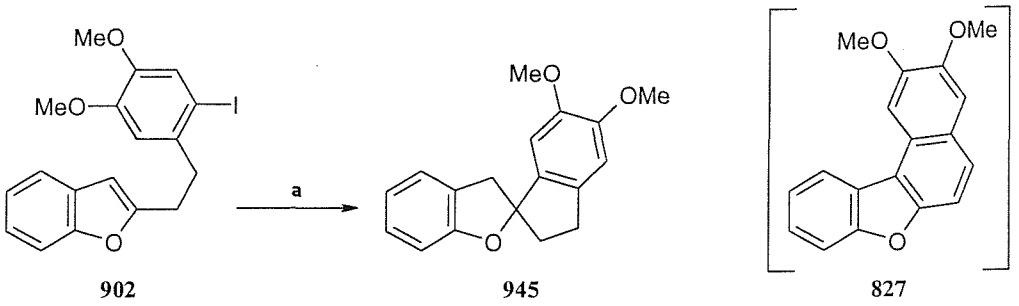
On cyclisation of **634**, 5-*exo*-trig addition to C-2 of the benzo[*b*]furan was the dominant reaction pathway, resulting in the formation of spirocycle **638** in 57% yield. Interestingly, the reaction also gave benzo[*b*]naphtho[1,2-*a*]furan **623** in 9% yield, along with reduction product **944** in 8% yield (**Scheme 135**).



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 8% **944**, 57% **638** *and* 9% **623**.

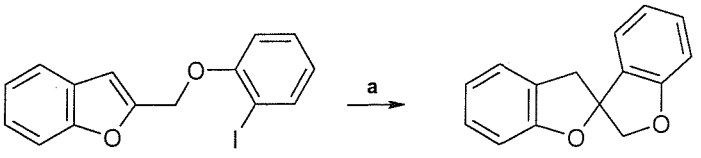
Scheme 135

The formation of **623** was unexpected and presumably arises *via* aerial oxidation of dihydrobenzo[*b*]naphtho[1,2-*a*]furan **649** on work-up. Alternatively, peroxide radicals formed in the reaction mixture may facilitate aromatisation. In either case, the analogous benzo[*b*]naphtho[1,2-*a*]furan **827** was not observed on cyclisation of benzo[*b*]furan **902**. Instead, spirocycle **945** was the sole product of the reaction in 51% yield (**Scheme 136**). 5-*exo*-trig cyclisation was also exclusive on cyclisation of benzo[*b*]furan **668**, giving spirocyclic ether **672** in 52% yield (**Scheme 137**).



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 51% **945**.

Scheme 136

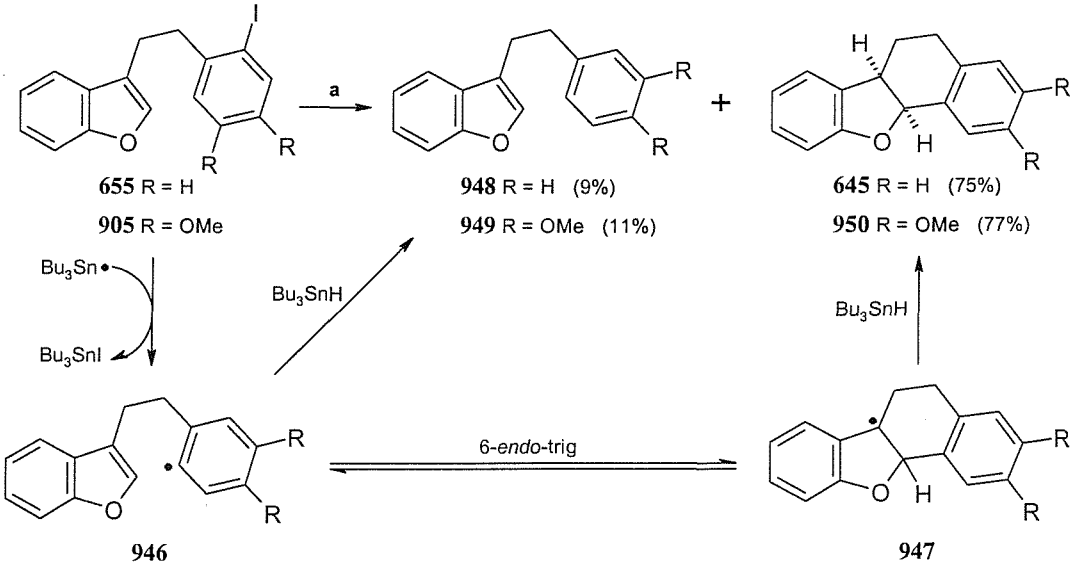


Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 52%.

Scheme 137

6.4.2 Addition of C-3 Alkane- or Ether Tethered Aryl Radicals

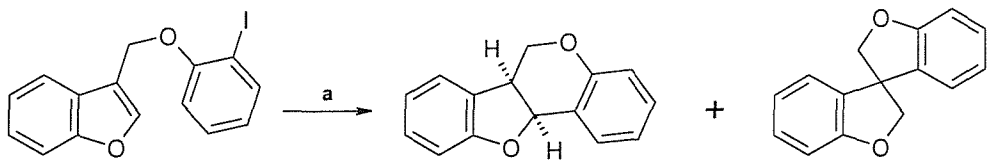
On exposure to tri-*n*-butyltin hydride and AIBN, benzo[*b*]furans **655** and **905** gave tetrahydrobenzo[*b*]naphtho[2,1-*d*]furans **645** and **950** respectively *via* reductive 6-*endo*-trig cyclisation of the aryl radical to C-2 of the benzo[*b*]furan. **948** and **949** were obtained as minor side products (**Scheme 138**).



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs. *Yields given above.*

Scheme 138

In contrast, cyclisation of benzo[*b*]furan ether **679** led to a 1:1 mixture of polycycle **951** and spirocyclic ether **683** (**Scheme 139**). Thus, in accordance with the findings of Smith and Butler,[146] an increased inclination towards 5-*exo*-trig cyclisation was again observed when conjoining the aryl radical to the heterocycle *via* an ether tether.



679 **951** **683**

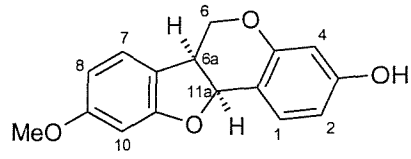
Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 86% (1:1).

Scheme 139

The propensity of these substrates to undergo radical cyclisation to C-2 of the benzo[*b*]furan can again be attributed to the increased electronegativity of the heteroatom. As was observed on cyclisation of indole amide **903**, greater polarisation of the heterocycle at C-2 promotes 6-*endo*-trig cyclisation over the 5-*exo*-trig mode. In addition, the oxygen heteroatom is less able to contribute a lone pair to any forming π-system, so the cyclisation is reductive in nature.

6.5 The Total Synthesis of Demethylhomopterocarpin

Polycycle **951** constitutes the core skeleton of a large family of natural occurring compounds called the *pterocarpans*. Thus, we decided to seize the opportunity to apply our newly developed radical methodology to the synthesis of a natural product from this group. Our target was the biologically active pterocarpan, demethylhomopterocarpin **952** (**Figure 5**).



952

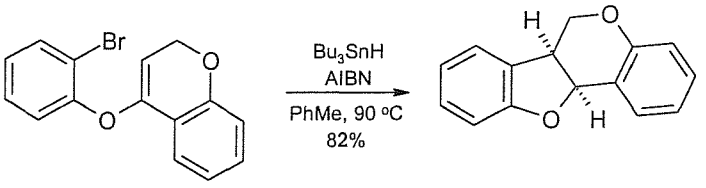
demethylhomopterocarpin

Figure 5

Demethylhomopterocarpin **952**, also known as (±)-medicarpin, has been isolated from the roots of *hedysarum polybotrys*[157] and the heartwoods of *gliricidia sepium*,[158] *maakia amurensis*,[159,160] *dalbergia odorifera*,[161,162] and various *centrolobium* species.[163] Extracts of

dalbergia odorifera are used in Japan as a treatment for "stagnant blood syndrome" and hypercholesterolemia and have been found to show significant activity against platelet aggregation and prostaglandin biosynthesis.[161] In isolation, demethylhomopterocarpin has been found to display antibacterial,[157] insecticidal and antifungal properties.[158]

Although many synthetic strategies towards the pterocarpans have been described in the literature,[164-172] only one has employed a radical cyclisation strategy. Thus, on treatment of enol ether **953** with tri-*n*-butyltin hydride and AIBN in benzene at 80 °C, Santhosh *et al.* achieved the synthesis of 6aS*,11aS*-pterocarpan **951** (**Scheme 140**).[164] Other pterocarpans were afforded in a similar manner. Curiously, the available evidence suggests the reaction proceeds by means of the normally disfavoured 5-*endo*-trig cyclisation pathway.

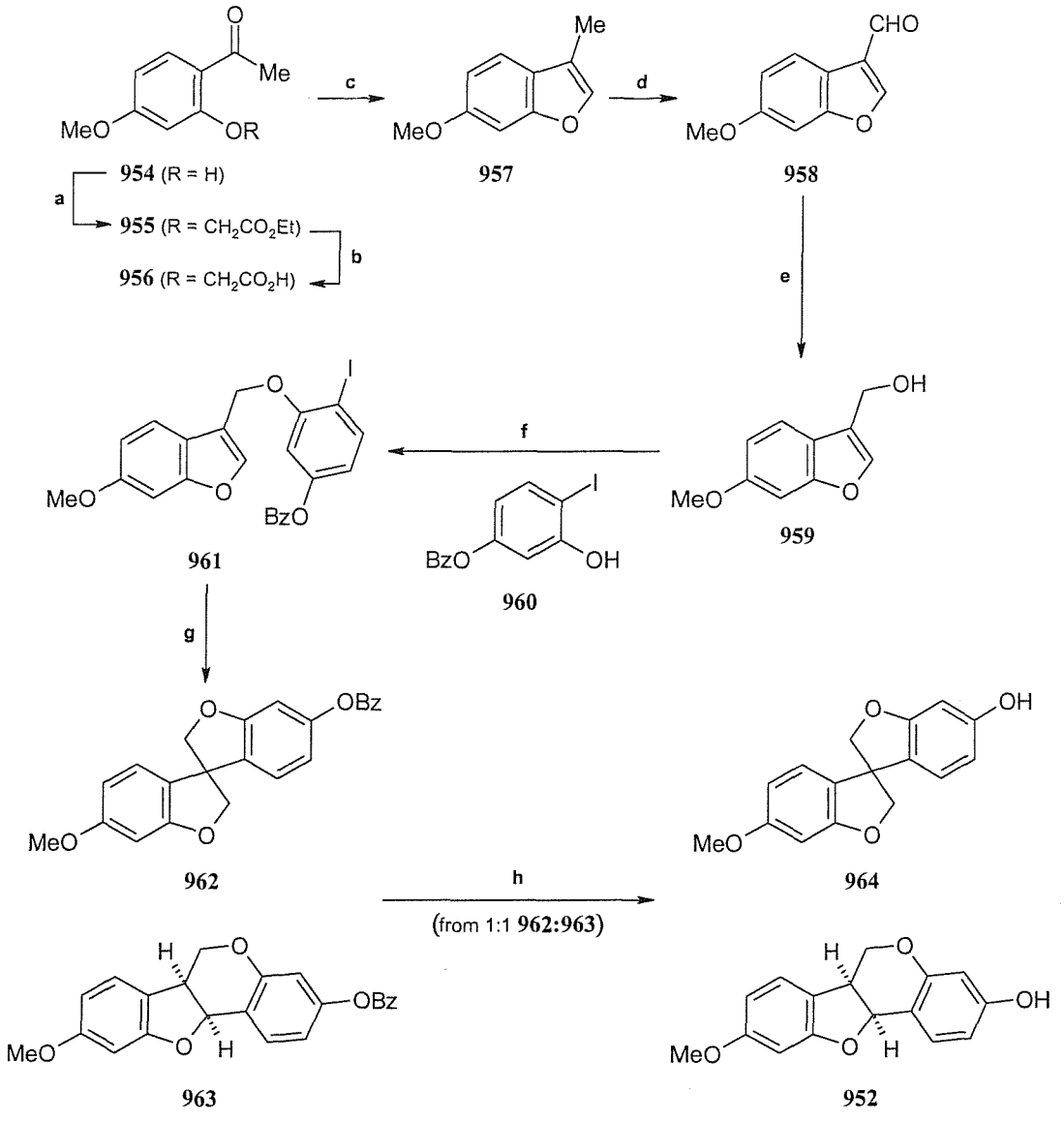


953 **951**

Scheme 140

Our approach required the synthesis of benzo[*b*]furan ether **961** (**Scheme 141**). It was predicted that, on cyclisation, this would yield tetrahydrobenzo[*b*]naphtho[2,1-*d*]furan **963**. Removal of the benzoyl protecting group would then afford demethylhomopterocarpin **952**. Our previous studies suggested that 5-*exo*-trig cyclisation of **961** would compete with the desired outcome, but it was hoped that a way would be found to bias the reaction in favour of the 6-*endo*-trig mode.

Thus, 6-methoxy-3-methylbenzo[*b*]furan **957** was synthesised from 2'-hydroxy-4'-methoxyacetophenone **954** using the method of Nielek and Lesiak.[149] Oxidation of the methyl group[150] furnished 3-formyl-6-methoxybenzo[*b*]furan **958**, which was reduced with sodium borohydride to alcohol **959**. Mitsunobu coupling of this alcohol with 3-hydroxy-4-iodophenyl benzoate **960**[173] provided the desired radical precursor **961** (**Scheme 141**).

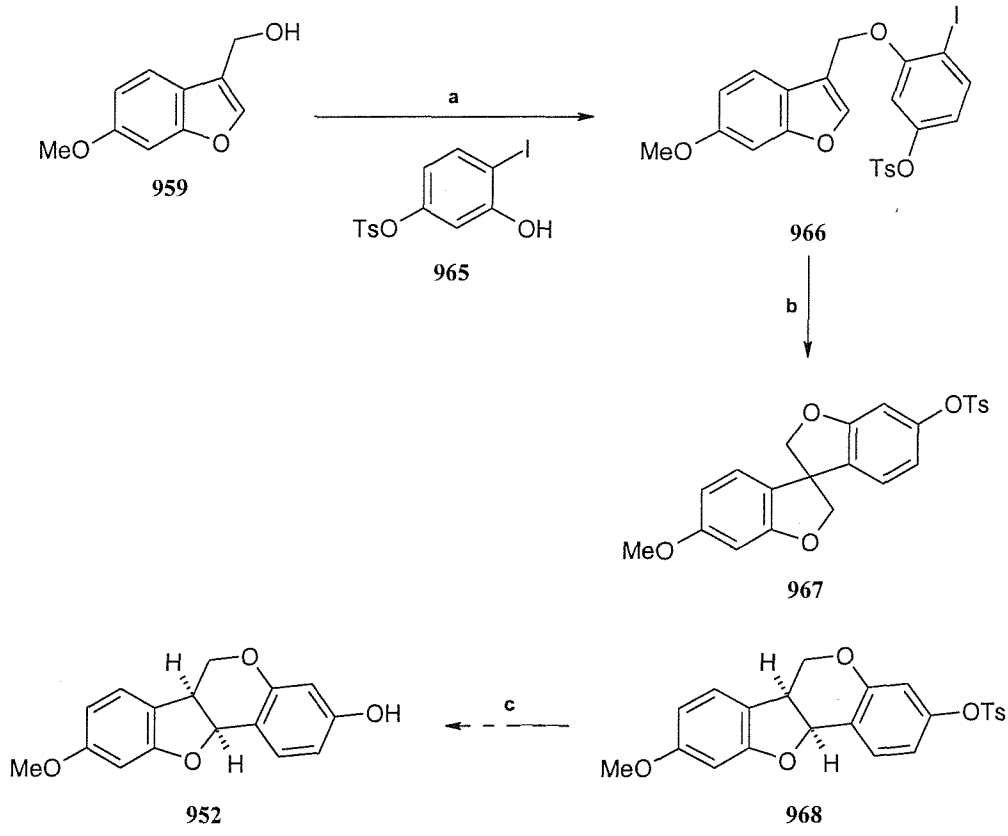


Reagents and Conditions: **a** $BrCH_2CO_2Et$, K_2CO_3, acetone, Δ, 16 hrs, 100%. **b** Na_2CO_3, H_2O, Δ, 1 hr, 97%. **c** NaOAc, Ac_2O, Δ, 3 hrs, 83%. **d** SeO_2, 1,4-dioxane, Δ, 48 hrs, 71%. **e** $NaBH_4$, THF, 0 °C, 1 hr, 95%. **f** **960**, PPh_3, DIAD, THF, -10 °C, 2 hrs, 71%. **g** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 35% **962** *and* 14% **963**. **h** NaOH, MeOH, Δ, 1 hr, 95% (1:1).

Scheme 141

Exposure of **961** to tri-*n*-butyltin hydride and AIBN gave cyclisation adducts **962** and **963** in disappointing 2.5:1 ratio and 49% overall yield. Column chromatography failed to separate tetrahydrobenzo[*b*]naphtho[2,1-*d*]furan **963** from spirocycle **962**, although a pure sample of **962** was eventually obtained for analytical purposes. Consequently, the remainder of the product mixture (consisting of a 1:1 ratio of **962** and **963**) was heated at reflux in methanolic sodium hydroxide to remove the benzoyl group. Pleasingly, the deprotection step was effective, and demethylhomopterocarpin **952** was obtained in a 1:1 ratio with spirocyclic ether **964** in 95% overall yield. Demethylhomopterocarpin **952** was then separated from **964** using HPLC.

3-Hydroxy-4-iodophenyl *para*-toluenesulfonate **965**[173] was also coupled to alcohol **959** to afford the analogous, tosyl-protected benzo[*b*]furan ether **966** (**Scheme 142**). Pleasingly, cyclisation of this precursor gave spirocycle **967** and tetrahydrobenzo[*b*]naphtho[2,1-*d*]furan **968** as a 1.3:1 mixture in 64% overall yield. **968** was then separated from **967** by column chromatography and an attempt was made to remove the tosyl group. Unfortunately, deprotection of **968** failed. Doubtless, given more time, a set of conditions conducive to the removal of the tosyl group would have been found.



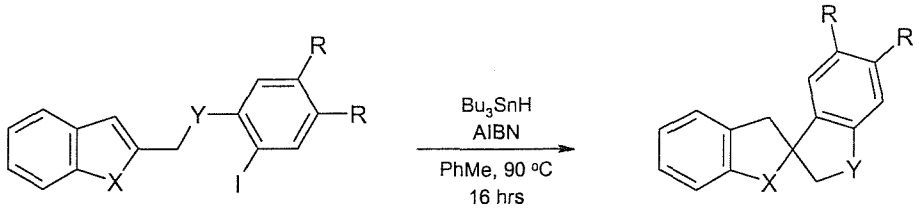
Reagents and Conditions: **a** **965**, PPh_3, DIAD, THF, -10 °C, 2 hrs, 71%. **b** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 36% **967** *and* 28% **968**. **c** KOH, EtOH, H_2O, Δ, 2 hrs.

Scheme 142

The tin-mediated cyclisation of **961** was also attempted in the presence of boron trifluoride etherate. It was hoped that co-ordination of the Lewis acid to the benzo[*b*]furan oxygen would increase the relative electronegativity of the heteroatom, thereby promoting the 6-*endo*-trig cyclisation mode. However, a complex product mixture was obtained on performing the reaction. Analysis of the crude material revealed that the Lewis acid had facilitated cleavage of the ether tether under the reaction conditions. Although discouraging, the use of a milder Lewis acid may help to promote 6-*endo*-trig cyclisation without destroying the radical precursor, so further research is warranted.

6.6 Summary

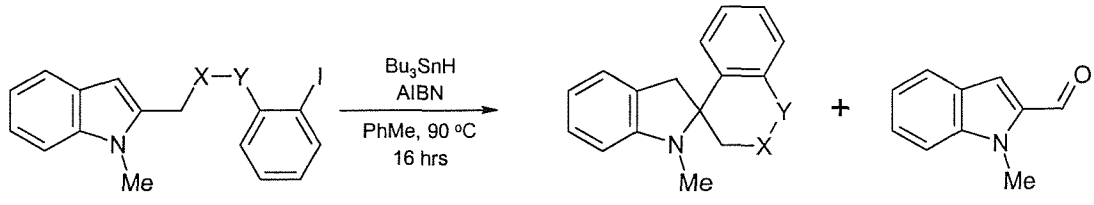
When conjoined to C-2 of a five-membered condensed heterocycle using a dimethylene or benzylic ether tether, aryl radicals favoured 5-*exo*-trig cyclisation to C-2 of the heteroaromatic, leading to the corresponding spirocycle (**Scheme 143**).[148] In general, cyclisations involving benzyl (*o*-iodoaryl)ethers were more efficient than their all carbon analogues.



632 (X = NMe, Y = CH_2, R = H)	**636** (X = NMe, Y = CH_2, R = H)	55%
666 (X = NMe, Y = O, R = H)	**670** (X = NMe, Y = O, R = H)	74%
667 (X = S, Y = O, R = H)	**671** (X = S, Y = O, R = H)	75%
634 (X = O, Y = CH_2, R = H)	**638** (X = O, Y = CH_2, R = H)	57%
902 (X = O, Y = CH_2, R = OMe)	**945** (X = O, Y = CH_2, R = OMe)	51%
668 (X = O, Y = O, R = H)	**672** (X = O, Y = O, R = H)	52%

Scheme 143

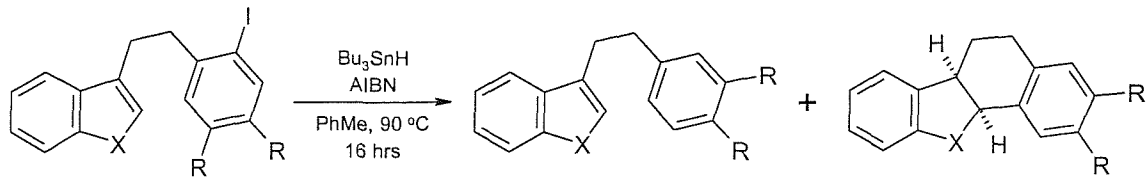
On exposure to tri-*n*-butyltin hydride and AIBN, indoles **913** and **922** were found to undergo 6-*exo*-trig cyclisation to C-2 of the indole (**Scheme 144**).[148] Fragmentation of radical precursor **913** to aldehyde **805** was also observed under the reaction conditions.



			805
913 (X = O, Y = CH_2)	**916** (X = O, Y = CH_2)	43%	(16%)
922 (X = CH_2, Y = O)	**923** (X = CH_2, Y = O)	42%	(-)

Scheme 144

When conjoined to C-3 of a five-membered condensed heterocycle, the cyclisation mode was strongly influenced by the electronic character of the constituent heteroatom. Electronegative heteroatoms such as oxygen promoted cyclisation *via* the 6-*endo*-trig mode. This effect was also noted on cyclisation of indole amide **903** (**Scheme 145**).



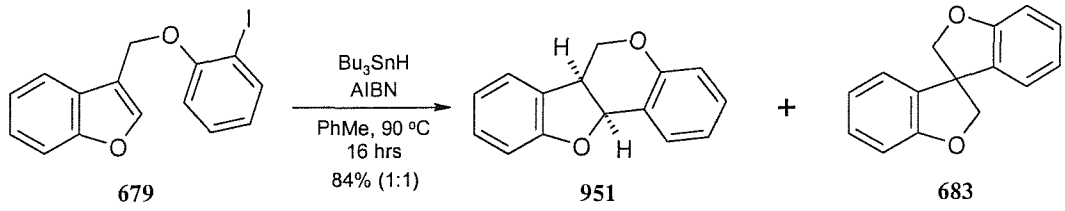
903 (X = NAc, R = H)
655 (X = O, R = H)
905 (X = O, R = OMe)

969 (X = NAc, R = H) (-)
948 (X = O, R = H) 9%
949 (X = O, R = OMe) 11%

928 (X = NAc, R = H) 84%
645 (X = O, R = H) 75%
950 (X = O, R = OMe) 77%

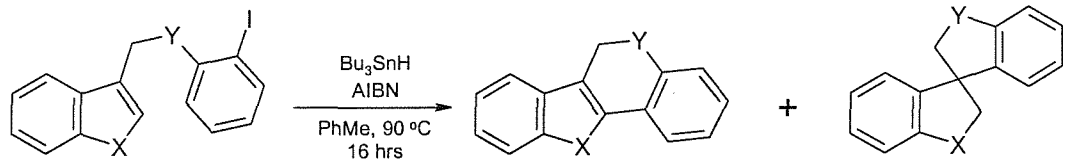
Scheme 145

In contrast, benzo[*b*]furan **679** gave a 1:1 mixture of C-3 and C-2 cyclisation products, **683** and **951** respectively (**Scheme 146**), while indole **653** and benzo[*b*]thiophene **678** preferentially underwent 5-*exo*-trig cyclisation to C-3 of the heterocycle (**Scheme 147**).[148] These results support the findings of Smith and Butler that benzyl ether tethers promote the 5-*exo*-trig cyclisation mode.[146]



679 **951** **683**

Scheme 146



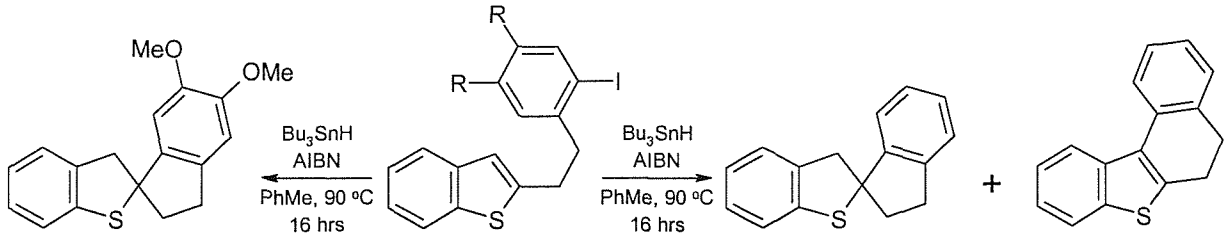
653 (X = NMe, Y = CH_2)
678 (X = S, Y = O)

640 (X = NMe, Y = CH_2) 36%
970 (X = S, Y = H) (-)

657 (X = NMe, R = CH_2) 63%
682 (X = O, R = H) 90%

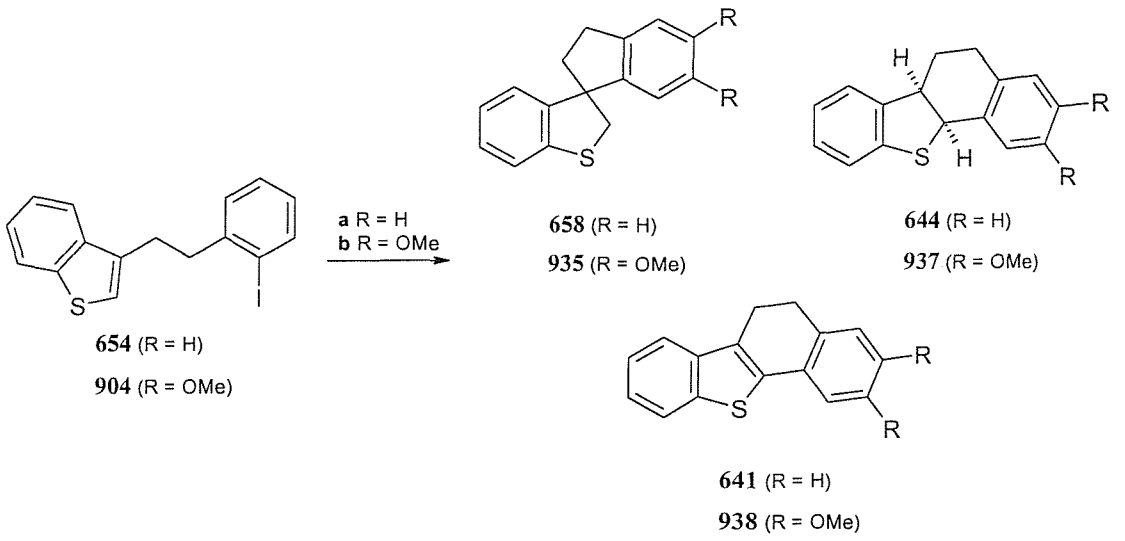
Scheme 147

Tin-mediated cyclisation of benzo[*b*]thiophenes **633** and **901** produced complex product mixtures where the major components were spirocycles **637** and **932** respectively (**Scheme 148**). Complex product mixtures were also obtained when benzo[*b*]thiophenes **654** and **904** were treated in an analogous fashion (**Scheme 149**).



932 (69%) **R = OMe** **633** (R = H) **R = H** **637** (3:2, 79%) **648**
901 (R = OMe)

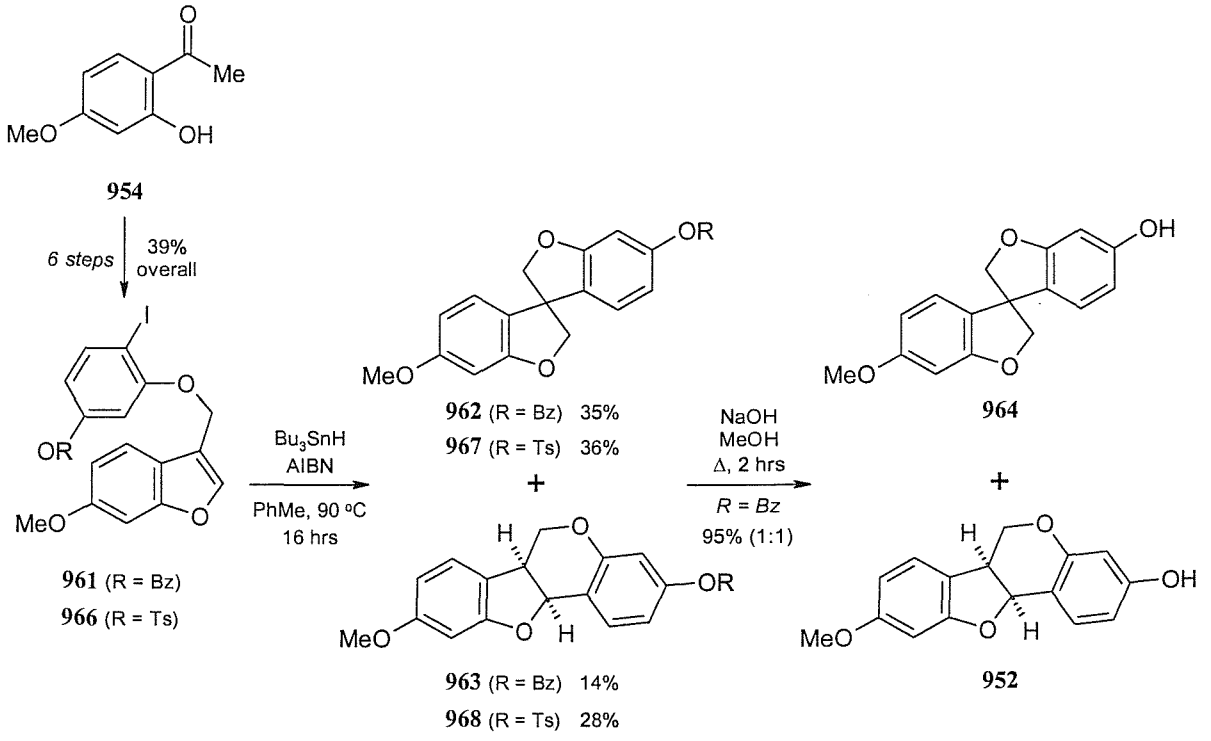
Scheme 148



Reagents and Conditions: **a** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 2:2:1 **658:641:644**, 80%. **b** Bu_3SnH, AIBN, PhMe, 90 °C, 16 hrs, 2:2:1, **935:938:937**, 86%.

Scheme 149

Finally, a synthesis of the natural product demethylhomopterocarpin **952** was achieved from 2'-hydroxy-4'methoxyacetophenone **954**. The tin mediated radical cyclisation of benzo[*b*]furan **961** was employed as the key step (**Scheme 150**).



Scheme 150

Chapter 7

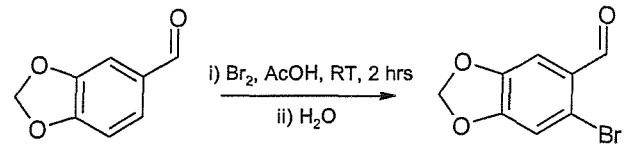
Experimental Section

7.1 General Procedures and Analytical Instrumentation

Where flash chromatography was undertaken, Apollo silica gel (0.040-0.063 mm, 230-400 mesh) was used, slurry packed and ran at low pressure. HPLC was performed using a Kontron Instruments pump with a 10 mm x 250 mm Biosyl D 90/10 column eluting at 3 mL/min. Infrared (IR) spectroscopy was performed using a Bio-Rad FT-IR Goldengate spectrometer or Thermo Mattson Satellite FT-IR spectrometer. Positions of absorption maxima are quoted in cm^{-1}. Letters after give an indication of the relative strength of the peak (w = weak, m = moderate, s = strong, br. = broad, v = very). UV-Vis spectroscopy was performed on a Pye Unicam SP8-400 spectrophotometer, using dichloromethane or methanol as the solvent. ^{1}H, ^{13}C and ^{31}P spectroscopy was performed on a Bruker AC/AM300 or DPX400 spectrometer at operating frequencies indicated in the text. The solvents used are also indicated in the text. Chemical shifts are quoted as δ-values in ppm and multiplicities are reported using the following notation: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, app. = apparent, br. = broad, obsc. = obscured. Chemical ionisation (CI) and electron ionisation (EI) mass spectroscopy was performed on a Thermoquest Trace GCMS spectrometer. Electrospray (ES) mass spectroscopy was performed on a Micromass Platform (MP) spectrometer. High resolution EIMS was performed on a VG Analytical 70-250-SE spectrometer and high resolution ESMS was performed on a Bruker Apex III spectrometer. Combustion analysis was performed by Medac Ltd. Melting points were carried out using a Griffin melting point apparatus and are uncorrected. Benzene, toluene, 1,4-dioxane, ether and THF were distilled from sodium immediately before use. Except in the case of toluene, benzophenone was used as an internal indicator of water content. Chloroform and dichloromethane were distilled from calcium hydride immediately prior to use. All other solvents were used directly from the suppliers.

7.2 Synthetic Procedures for Chapter 2

6-Bromopiperonal (206)



205
mw = 150.13 g mol^{-1}
$C_8H_6O_3$

206
mw = 229.03 g mol^{-1}
$C_8H_5BrO_3$

In accordance with the procedure of Orr *et al.*,[174] to a stirred solution of piperonal **205** (79.2 g, 0.53 mol) in glacial acetic acid (150 mL) at 0 °C was added bromine (31.8 mL, 0.62 mol) in glacial acetic acid (75 mL) over half an hour. After stirring for 2 hours at ambient temperature, the suspended white solid formed was isolated *via* suction filtration and washed with cold glacial acetic acid (10 mL) and water (50 mL). The filtrate was diluted with water (100 mL) and the resultant white solid also isolated *via* suction filtration. The combined solids were recrystallised from aqueous ethanol to afford the product **206** as a white crystalline solid (60.3 g, 0.26 mol, 50%): mp 129-130 °C (ethanol/water), lit. 127-128.5 °C.[175]

FT-IR (neat, cm^{-1}): 1670 s, 1614 w, 1485 s, 1410 m, 1392 w, 1255 s, 1111 m, 1028 s, 977 s, 925 s, 889 m, 837 w, 784 w.

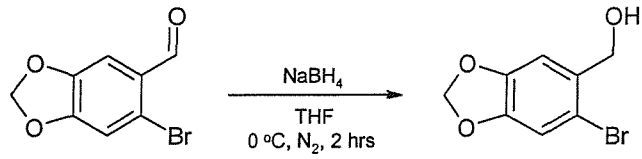
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), MeOH: 325 (5000), 285 (2700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.18 (1H, s, ArC<u>H</u>O), 7.36 (1H, s, Ar<u>H</u>), 7.07 (1H, s, Ar<u>H</u>), 6.09 (2H, s, OC<u>H</u>$_2$O).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 190.8 (<u>C</u>HO), 153.9 (<u>C</u>O (Ar)), 148.3 (<u>C</u>O (Ar)), 128.0 (<u>C</u> (Ar)), 121.9 (<u>C</u>Br (Ar)), 113.5 (<u>C</u>H (Ar)), 108.5 (<u>C</u>H (Ar)), 103.0 (O<u>C</u>H$_2$O).

LRMS (CI) *m/z:* 230 ([M{^{81}Br}]$^+$, 94%), 228 ([M{^{79}Br}]$^+$, 100%)

(6-Bromo-benzo[1,3]dioxol-5-yl)-methanol (**207**)



206
mw = 229.03 g mol^{-1}
$C_8H_5BrO_3$

207
mw = 231.05 g mol^{-1}
$C_8H_7BrO_3$

Following a modified procedure of Mann *et al.*,[48] sodium borohydride (3.03 g, 80.0 mmol) was added portionwise to a stirred solution of **206** (17.3 g, 75.7 mmol) in THF (120 mL) under nitrogen at 0 °C. The resultant white suspension was stirred at 0 °C for 30 minutes, then at ambient temperature for 1.5 hours. Saturated ammonium chloride solution (100 mL) was carefully added and the resultant biphasic mixture diluted with chloroform (200 mL). The aqueous phase was then washed with more chloroform (1 x 200 mL, 1 x 100 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo* to a low-melting waxy solid. Recrystallisation from ether/petrol afforded **207** as white needles (15.0 g, 64.9 mmol, 86%): mp 87-89 °C (ether/petrol), lit. 90 °C (petrol).[176] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3188 br. w, 1732 br. w, 1500 w, 1474 m, 1240 s, 1110 w, 1060 w, 1038 vs, 931 m, 871 w, 852 w, 832 w.

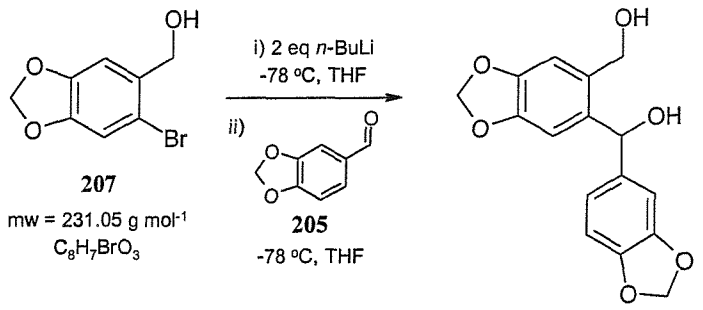
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), MeOH: 295 (5400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 6.98 (1H, s, ArH), 6.95 (1H, s, ArH), 5.97 (2H, s, OCH_2O), 4.61 (2H, d, J = 6.0 Hz, $ArCH_2OH$), 2.36 (1H, t, J = 6.0 Hz, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 147.9 (CO (Ar)), 147.6 (CO (Ar)), 133.2 (C (Ar)), 113.1 (CBr (Ar)), 112.8 (CH (Ar)), 109.2 (CH (Ar)), 101.9 (OCH_2O), 65.0 ($ArCH_2OH$).

LRMS (CI) *m/z:* 232 ($M\{^{81}Br\}^+$, 50%), 230 ($M\{^{79}Br\}^+$, 54%), 214 ($[M\{^{81}Br\} - H_2O]^+$, 66%), 212 ($[M\{^{79}Br\} - H_2O]^+$, 70%), 152 ($[MH - Br]^+$, 40%), 135 ($[MH - Br - H_2O]^+$, 100%).

Benzo[1,3]dioxol-5-yl-(6-hydroxymethyl-benzo[1,3]dioxol-5-yl)-methanol (**208**)



207
mw = 231.05 g mol^{-1}
$C_8H_7BrO_3$

205
-78 °C, THF

208
mw = 302.28 g mol^{-1}
$C_{16}H_{14}O_6$

This procedure was adapted from that of Mann and Piper.[48] To a stirred solution of **207** (10 g, 43.3 mmol) in THF (100 mL) at –78 °C under nitrogen was added *n*-butyllithium (40.2 mL, 90.9 mmol, 2.26 M in hexanes) over 30 minutes, ensuring the reaction temperature never exceeded –70 °C during addition. After stirring the resultant white suspension for 30 minutes, piperonal **205** (6.8 g, 45.4 mmol) was added as a solution in THF (30 mL), again ensuring the temperature never exceeded –65 °C. After stirring for a further 30 minutes, the reaction mixture was quenched at –78 °C by addition of saturated ammonium chloride solution (40 mL) and allowed to warm to ambient temperature, forming a colourless biphasic mixture. After partitioning between ether (140 mL) and water (100 mL), the aqueous phase was extracted with ether (2 x 100 mL). The combined organic phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a pale orange oil. Purification by column chromatography (60% ether in petrol to neat ether) afforded **208** as a pale yellow oil (10.6 g, 35.1 mmol, 81%).

FT-IR (neat, cm^{-1}): 3428 br. w, 1501 w, 1476 s, 1444 w, 1341 w, 1280 m, 1243 s, 1035 vs, 933 m, 805 w, 787 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 292 (5900).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 6.81 (1H, d, J = 1.8 Hz, ArH), 6.80 (1H, dd, J = 8.0, 1.8 Hz, ArH), 6.79 (1H, s, ArH), 6.78 (1H, d, J = 8.0 Hz, ArH), 6.71 (1H, s, ArH), 5.98-5.92 (4H, m, 2 x OCH_2O), 5.88 (1H, br. s, CHOH), 4.60 (1H, br. d, J = 12.3 Hz, ArCHHOH), 4.40 (1H, br. d, J = 12.3 Hz, ArCHHOH). 3.70 (1H, br. s, OH), 2.97 (1H, br. s, OH).

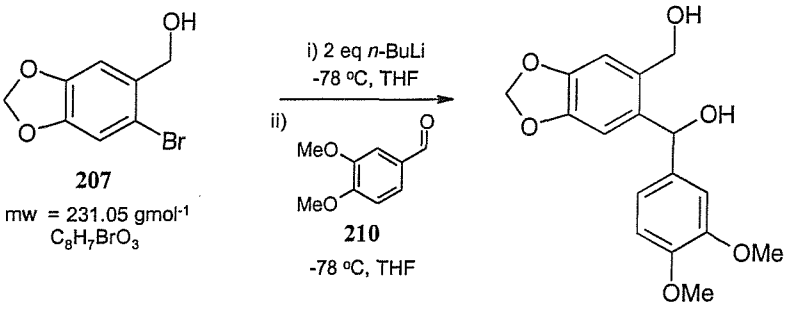
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 147.9 (CO (Ar)), 147.5 (CO (Ar)), 147.0 (2 x CO (Ar)), 136.8 (C (Ar)), 136.6 (C (Ar)), 132.4 (C (Ar)), 119.9 (CH (Ar)), 110.4 (CH (Ar)), 109.1 (CH (Ar)), 108.2 (CH (Ar)), 107.3

(CH (Ar)), 101.4 (OCH_2O), 101.2 (OCH_2O), 73.1 (CHOH), 63.5 ($ArCH_2OH$).

LRMS (CI) *m/z:* 285 ($[MH - H_2O]^+$, 100%), 149 ($[M - C_8H_9O_3]^+$, 47%).

HRMS (EI) *m/z* Found: M^+ 302.0801, $C_{16}H_{14}O_6$ requires 302.0790.

(3,4-Dimethoxyphenyl)-(6-hydroxymethylbenzo[1,3]dioxol-5-yl)-methanol (**209**)



This procedure was adapted from that of Mann and Piper.[48] To a stirred solution of 6-bromopiperonyl alcohol **207** (10 g, 43.3 mmol) in THF (100 mL) at –78 °C under nitrogen was added *n*-butyllithium (40.2 mL, 90.9 mmol, 2.25 M in hexanes) over 30 minutes, ensuring the reaction temperature was maintained at –60 °C to –65 °C during addition. After stirring for 30 minutes, a solution of veratraldehyde **210** (7.55 g, 45.4 mmol) in THF (30 mL) was added under the same restrictions. The reaction mixture was stirred for a further 30 minutes before saturated ammonium chloride solution (50 mL) was added at –78 °C. The resultant biphasic mixture was partitioned between ether (100 mL) and water (100 mL), and the aqueous phase washed with ether (2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (50% ether in petrol to neat ether with 5% methanol) afforded **209** as a white crystalline solid (9.49 g, 29.8 mmol, 69%): mp 41-43 °C (ether/petrol).

FT-IR (neat, cm^{-1}): 2943 w, 2834 w, 1514 m, 1475 m, 1340 w, 1279 m, 1259 s, 1234 m, 1159 w, 1138 s, 1028 vs, 938 w, 844 w, 806 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 285 (6500), 236 (11400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 6.92 (1H, br. s, ArH), 6.85 (1H, dd, J = 8.0, 2.0 Hz, ArH), 6.85 (1H, d, J = 8.0 Hz, ArH), 6.80 (1H, s, ArH), 6.67 (1H, s, ArH), 5.96 (1H, s, CHOH), 5.95-5.91 (2H, m, OCH_2O), 4.65 (1H, br. d, J = 11.8 Hz, ArCHHOH), 4.42 (1H, br. d, J = 11.8 Hz, ArCHHOH), 3.88

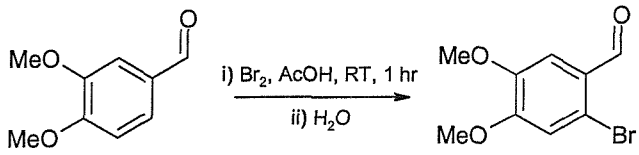
(3H, s, ArOC$\underline{H}_3$), 3.84 (3H, s, ArOC$\underline{H}_3$), 3.71 (1H, br. s, O$\underline{H}$), 2.98 (1H, br. s, O$\underline{H}$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.1 ($\underline{C}$O (Ar)), 148.5 ($\underline{C}$O (Ar)), 147.5 ($\underline{C}$O (Ar)), 147.0 ($\underline{C}$O (Ar)), 136.7 ($\underline{C}$ (Ar)), 135.3 ($\underline{C}$ (Ar)), 132.6 ($\underline{C}$ (Ar)), 118.8 ($\underline{C}$H (Ar)), 111.1 ($\underline{C}$H (Ar)), 110.4 ($\underline{C}$H (Ar)), 109.9 ($\underline{C}$H (Ar)), 109.2 ($\underline{C}$H (Ar)), 101.5 (O$\underline{C}$H$_2$O), 73.0 ($\underline{C}$HOH), 63.4 (Ar$\underline{C}$H$_2$OH), 55.9 (ArO$\underline{C}$H$_3$), 55.8 (ArO$\underline{C}$H$_3$).

LRMS (CI) *m/z:* 301 ([MH - H_2O]$^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 318.1111, $C_{17}H_{18}O_6$ requires 318.1103.

6-Bromoveratraldehyde (**211**)



210
mw = 166.18 g mol^{-1}
$C_9H_{10}O_3$

211
mw = 245.07 g mol^{-1}
$C_9H_9BrO_3$

In accordance with the procedure of Orr *et al.*,[174] to a stirred solution of veratraldehyde **210** (50 g, 0.30 mol) in glacial acetic acid (150 mL) at 0 °C was added bromine (18 mL, 0.35 mol) in glacial acetic acid (60 mL) over half an hour. After stirring for a further hour at ambient temperature, a suspended mass of red solid had formed. This was isolated *via* suction filtration and washed with cold glacial acetic acid (10 mL) and water (100 mL). The filtrate was diluted with water (150 mL) and the resultant white solid also isolated *via* suction filtration. This cycle was repeated until the solid obtained from the filtrate was very dark grey. The combined solids were recrystallised from ethanol (800 mL) to afford **211** as small white needles (44 g, 0.18 mol, 60%): mp 151-152 °C (ethanol/water), lit. 149-151 °C.[177]

FT-IR (neat, cm^{-1}): 1668 s, 1587 w, 1505 s, 1446 w, 1386 w, 1270 vs, 1218 m, 1155 s, 1042 m, 1016 m, 980 w, 869 m.

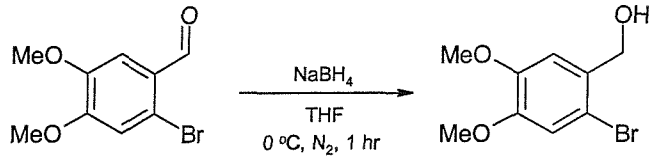
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), MeOH: 319 (5800), 278 (10300), 236 (19100).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.18 (1H, s, ArC$\underline{H}$O), 7.40 (1H, s, Ar$\underline{H}$), 7.05 (1H, s, Ar$\underline{H}$), 3.96 (3H, s, ArOC$\underline{H}_3$), 3.92 (3H, s, ArOC$\underline{H}_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 191.0 (Ar<u>C</u>HO), 154.6 (<u>C</u>O (Ar)), 149.0 (<u>C</u>O (Ar)), 126.7 (<u>C</u> (Ar)), 120.6 (<u>C</u>Br (Ar)), 115.6 (<u>C</u>H (Ar)), 110.5 (<u>C</u>H (Ar)), 56.7 (ArO<u>C</u>H_3), 56.3 (ArO<u>C</u>H_3).

LRMS (CI) *m/z:* 247 ([MH{^{81}Br}]$^+$, 56%), 245 ([MH{^{79}Br}]$^+$, 100%), 167 ([MH - Br]$^+$, 27%).

<u>(2-Bromo-4,5-dimethoxyphenyl)-methanol (**212**)</u>



211
mw = 245.07 g mol^{-1}
$C_9H_9BrO_3$

212
mw = 247.09 g mol^{-1}
$C_9H_{11}BrO_3$

Following a modified procedure of Crombie and Joseph,[178] sodium borohydride (2.27 g, 60.0 mmol) was added portionwise to a stirred solution of **211** (14.0 g, 57.1 mmol) in THF (125 mL) under nitrogen at ambient temperature. After stirring for 1 hour, saturated ammonium chloride solution (100 mL) was added at 0 °C. The resultant biphasic mixture was diluted with ether (100 mL) and water (30 mL) and the organic phase isolated. The aqueous phase was extracted with ether (2 x 100 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo* to a powdery white solid. Recrystallisation from ether/petrol afforded **212** as feathery white strands (12.5 g, 50.7 mmol, 89%): mp 95-96 °C (ether/petrol), lit. 97-98 °C.[179] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3496 w, 1502 s, 1464 w, 1437 w, 1391 w, 1261 s, 1225 w, 1206 m, 1161 s, 1151 s, 1062 m, 1024 m, 856 s.

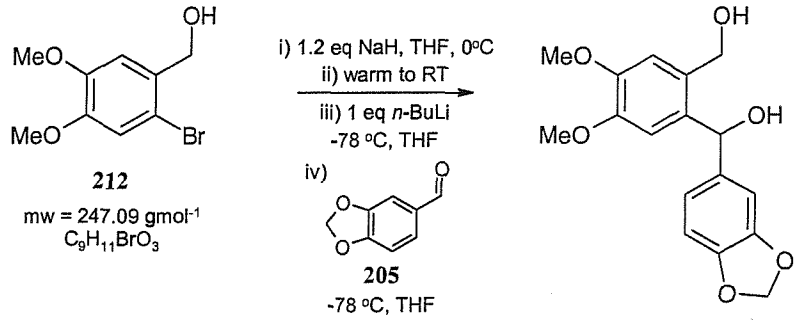
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 286 (4800), 236 (11100).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.03 (1H, s, Ar<u>H</u>), 7.02 (1H, s, Ar<u>H</u>), 4.70 (2H, d, J = 5.0 Hz, ArC<u>H</u>$_2$OH), 3.90 (3H, s, ArOC<u>H</u>$_3$), 3.88 (3H, s, ArOC<u>H</u>$_3$), 1.95 (1H, t, J = 5.0 Hz, ArCH$_2$O<u>H</u>).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.1 (<u>C</u>O (Ar)), 148.7 (<u>C</u>O (Ar)), 132.0 (<u>C</u> (Ar)), 115.5 (<u>C</u>H (Ar)), 112.7 (<u>C</u>Br (Ar)), 112.0 (<u>C</u>H (Ar)), 65.0 (Ar<u>C</u>H$_2$OH), 56.4 (ArO<u>C</u>H_3), 56.2 (ArO<u>C</u>H_3).

LRMS (CI) *m/z:* 248 ([M{^{81}Br}]$^+$, 27%), 246 ([M{^{79}Br}]$^+$, 25%), 231 ([M{^{81}Br} - H_2O]$^+$, 84%), 229 ([MH{^{79}Br} - H_2O]$^+$, 89%), 167 ([M - Br]$^+$, 60%), 150 ([MH – Br - H_2O]$^+$, 100%).

Benzo[1,3]dioxol-5-yl-(2-hydroxymethyl-4,5-dimethoxyphenyl)-methanol (**213**)



212
mw = 247.09 gmol^{-1}
$C_9H_{11}BrO_3$

205
-78 °C, THF

213
mw = 318.33 g mol^{-1}
$C_{17}H_{18}O_6$

This procedure was adapted from that of Mann and Piper.[48] To a stirred solution of petrol washed sodium hydride (1.06 g, 26.6 mmol, 60% dispersion in mineral oil) in THF (25 mL) at 0 °C under nitrogen was added **212** (5.47 g, 22.1 mmol) in THF (50 mL). After the addition of a further quantity of THF (75 mL), the reaction mixture was allowed to warm to ambient temperature and stirred until all effervescence had ceased (30 minutes). This white suspension was then cooled to –78 °C and *n*-butyllithium (16.6 mL, 23.3 mmol, 1.40 M in hexanes) was added over 10 minutes, ensuring the reaction temperature did not exceed –65 °C during addition. After stirring for 30 minutes at –78 °C, a solution of piperonal **205** (3.49 g, 23.3 mmol) in THF (30 mL) was added over 10 minutes under the same restrictions. On stirring for a further 30 minutes at –78 °C, saturated ammonium chloride solution (50 mL) was added followed by ether (100 mL). The two phases were separated and the aqueous phase was extracted with ether (2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (90% ether in petrol to neat ether with 5% methanol) afforded **213** as a colourless oil (5.48 g, 17.2 mmol, 78%).

FT-IR (neat, cm^{-1}): 3374 br. w, 2915 br. w, 1608 w, 1504 m, 1487 m, 1441 m, 1337 w, 1241 s, 1099 s, 1036 s, 929 m, 871 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 290 (6900), 242 (10400).

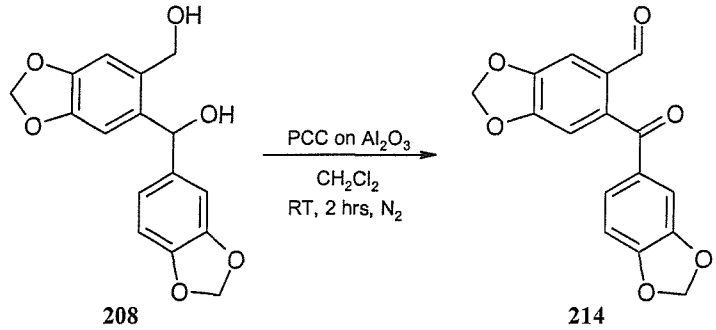
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 6.82 (1H, d, J = 8.1 Hz, ArH), 6.81 (1H, s, ArH), 6.80 (1H, s, ArH), 6.79 (1H, dd, J = 8.1, 1.1 Hz, ArH), 6.77 (1H, d, J = 1.1 Hz, ArH), 6.01 (2H, s, OCH_2O), 5.86 (1H, s, CHOH), 4.55 (1H, br. d, J = 12.1 Hz, ArCHHOH), 4.41 (1H, br. d, J = 12.1 Hz, ArCHHOH), 3.85 (3H, s, $ArOCH_3$), 3.79 (3H, s, $ArOCH_3$), 3.07 (1H, br. s, OH), 1.86 (1H, br. s, OH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 148.5 (CO (Ar)), 148.3 (CO (Ar)), 147.8 (CO (Ar)), 146.9 (CO (Ar)), 137.1 (C (Ar)), 134.9 (C (Ar)), 130.9 (C (Ar)), 119.8 (CH (Ar)), 113.4 (CH (Ar)), 111.9 (CH (Ar)), 108.2 (CH (Ar)), 107.3 (CH (Ar)), 101.2 (OCH_2O), 73.4 (CHOH), 63.4 ($ArCH_2OH$), 56.2 ($ArOCH_3$), 56.1 ($ArOCH_3$).

LRMS (CI) *m/z:* 301 ($[MH - H_2O]^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 318.1101, $C_{17}H_{18}O_6$ requires 318.1103.

Benzo[1,3]dioxol-5-yl-(6-formylbenzo[1,3]dioxol-5-yl)-methanone (**214**)



208
mw = 302.28 g mol^{-1}
$C_{16}H_{14}O_6$

214
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

To a stirred suspension of PCC (2.85 g, 13.2 mmol) on alumina (11.5 g) in dichloromethane (100 mL) at ambient temperature under nitrogen was added diol **208** (1.00 g, 3.31 mmol) in dichloromethane (50 mL). After 2 hours, the reaction mixture was filtered through florisil, washing the filtered solid with dichloromethane (300 mL), and the filtrate concentrated *in vacuo* to a brown oil. Purification by column chromatography (60% ether in petrol up to neat ether) gave **214** as a cream solid (0.61 g, 2.03 mmol, 61%): mp 126-130 °C, lit. 133-134 °C.[180] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 1680 m, 1601 m, 1504 m, 1493 m, 1367 m, 1286 m, 1267 vs, 1098 m, 1035 s, 764 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), MeOH: 317 (10900), 294 (8800).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.82 (1H, s, ArCHO), 7.48 (1H, s, ArH), 7.39 (1H, d, J = 1.7 Hz, ArH), 7.30 (1H, dd, J = 8.2, 1.7 Hz, ArH), 6.92 (1H, s, ArH), 6.84 (1H, d, J = 8.2 Hz, ArH), 6.15 (2H, s, OCH_2O), 6.09 (2H, s, OCH_2O).

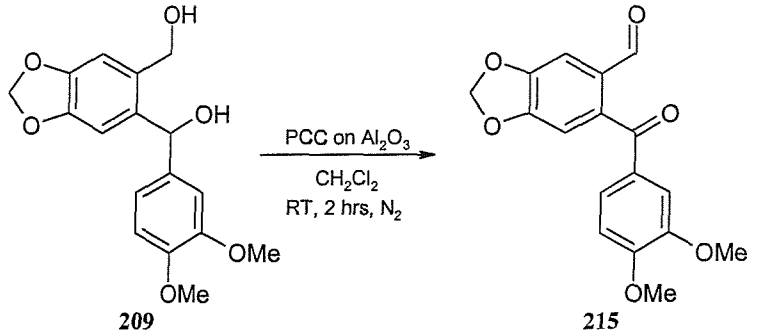
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 193.5 (ArCOAr), 188.7 (ArCHO), 152.8 (CO (Ar)), 151.8 (CO (Ar)), 149.8 (CO (Ar)), 148.6 (CO (Ar)), 139.2 (C (Ar)), 132.2 (C (Ar)), 131.2 (C (Ar)), 127.8 (CH (Ar)), 109.2 (CH (Ar)),

108.9 (CH (Ar)), 108.1 (CH (Ar)), 107.8 (CH (Ar)), 102.8 (OCH_2O), 102.3 (OCH_2O).

LRMS (ES$^+$) *m/z:* 317 ($[M + NH_4]^+$, 85%), 299 (MH^+, 100%).

HRMS (ES$^+$) *m/z* Found: $[M + Na]^+$ 321.0365, $C_{16}H_{10}O_6Na$ requires 321.0369.

3,4-Dimethoxybenzyl-(6-formylbenzo[1,3]dioxol-5-yl)-methanone (**215**)



209
mw = 318.33 g mol^{-1}
$C_{17}H_{18}O_6$

215
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

To a stirred suspension of PCC (8.73 g, 40.5 mmol) on alumina (35 g) in dichloromethane (200 mL) at ambient temperature under nitrogen was added diol **209** (5.15 g, 16.2 mmol) in dichloromethane (50 mL). After 2 hours, the reaction mixture was filtered through florisil, washing the filtered solid with dichloromethane (500 mL), and the filtrate concentrated *in vacuo* to a dark brown solid. Purification by column chromatography (chloroform) gave ketoaldehyde **215** as a mustard yellow solid (3.33 g, 10.6 mmol, 65%): mp 171-173 °C (methanol).

FT-IR (neat, cm^{-1}): 1680 w, 1649 w, 1586 w, 1511 w, 1488 w, 1416 w, 1361 w, 1267 vs, 1228 w, 1126 m, 1037 s, 1022 s, 928 w, 871 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 314 (10200), 280 (10000), 262 (11300), 233 (20400).

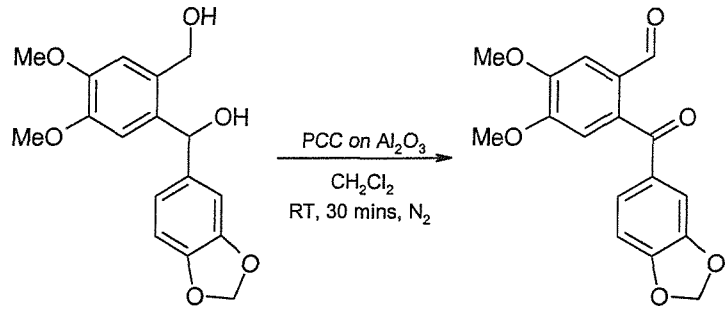
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.83 (1H, s, ArCHO), 7.57 (1H, d, J = 2.0 Hz, ArH), 7.50 (1H, s, ArH), 7.23 (1H, dd, J = 8.4, 2.0 Hz, ArH), 6.95 (1H, s, ArH), 6.85 (1H, d, J = 8.4 Hz, ArH), 6.16 (2H, s, OCH_2O), 3.97 (3H, s, $ArOCH_3$), 3.96 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 193.0 (ArCOAr), 188.7 (ArCHO), 154.2 (CO (Ar)), 151.8 (CO (Ar)), 149.8 (CO (Ar)), 149.5 (CO (Ar)), 139.4 (C (Ar)), 131.4 (C (Ar)), 130.6 (C (Ar)), 126.5 (CH (Ar)), 111.1 (CH (Ar)), 110.1 (CH (Ar)), 109.0 (CH (Ar)), 107.6 (CH (Ar)), 102.8 (OCH_2O), 56.4 ($ArOCH_3$), 56.3 ($ArOCH_3$).

LRMS (CI) *m/z:* 315 (MH^+, 62%), 301 ($[M + NH_4 - CH_3O]^+$, 65%), 299 ($[M - CH_3]^+$, 100%).

CHN Found: C, 64.68; H, 4.48; $C_{17}H_{14}O_6$ requires C, 64.97; H, 4.49.

Benzo[1,3]dioxol-5-yl-(6-formyl-3,4-dimethoxybenzyl)-methanone (**216**)



213
mw = 318.33 g mol^{-1}
$C_{17}H_{18}O_6$

216
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

To a stirred suspension of PCC (12.4 g, 57.4 mmol) on alumina (45 g) in dichloromethane (400 mL) at ambient temperature under nitrogen was added diol **213** (5.48 g, 17.2 mmol) in dichloromethane (50 mL). After 30 minutes, the reaction mixture was filtered through florisil, washing the filtered solid with dichloromethane (400 mL), and the filtrate concentrated *in vacuo* to a yellow solid. Purification by column chromatography (80% chloroform in petrol to neat chloroform) gave **216** as a yellow solid (4.06 g, 12.9 mmol, 75%): mp 157-160 °C, lit. 162-163 °C.[181,182] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 1751 m, 1681 m, 1591 m, 1521 m, 1500 m, 1490 m, 1445 s, 1352 m, 1285 vs, 1270 vs, 1218 s, 1141 m, 1116 s, 1071 w, 1034 vs, 923 m, 869 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 318 (10400), 270 (11500), 240 (20100).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.88 (1H, s, ArC<u>H</u>O), 7.54 (1H, s, Ar<u>H</u>), 7.41 (1H, d, J = 1.8 Hz, Ar<u>H</u>), 7.30 (1H, dd, J = 8.1, 1.8 Hz, Ar<u>H</u>), 6.97 (1H, s, Ar<u>H</u>), 6.84 (1H, d, J = 8.1 Hz, Ar<u>H</u>), 6.10 (2H, s, OC<u>H</u>$_2$O), 4.02 (3H, s, ArOC<u>H</u>$_3$), 3.96 (3H, s, ArOC<u>H</u>$_3$).

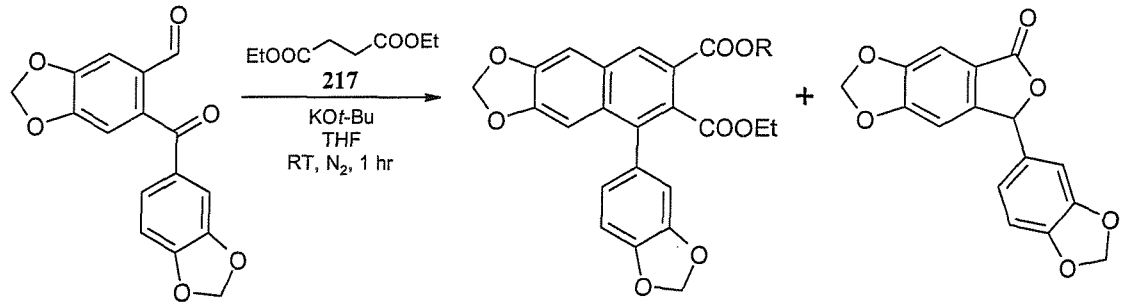
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 194.0 (Ar<u>C</u>OAr), 189.2 (Ar<u>C</u>HO), 153.1 (<u>C</u>O (Ar)), 152.7 (<u>C</u>O (Ar)), 150.7 (<u>C</u>O (Ar)), 148.6 (<u>C</u>O (Ar)), 137.0 (<u>C</u> (Ar)), 132.8 (<u>C</u> (Ar)), 129.1 (<u>C</u> (Ar)), 127.7 (<u>C</u>H (Ar)), 111.2 (<u>C</u>H (Ar)),

109.8 (CH (Ar)), 109.2 (CH (Ar)), 108.1 (CH (Ar)), 102.3 (OCH_2O), 56.6 ($ArOCH_3$), 56.4 ($ArOCH_3$).

LRMS (CI) *m/z:* 315 (MH^+, 88%), 301 ($[M + NH_4 - CH_3O]^+$, 100%), 299 ($[M - CH_3]^+$, 46%).

CHN Found: C, 64.59; H, 4.49; $C_{17}H_{14}O_6$ requires C, 64.97; H, 4.49.

Diethyl 5-benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylate (**218**), 5-Benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylic acid-7-ethyl ester (**219**) and 7-Benzo[1,3]dioxol-5-yl-7*H*-furo[3',4':4,5]benzo[1,2-*d*][1,3]dioxol-5-one (**220**) *via* the Stobbe procedure



214
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

218 (R = Et)
mw = 436.42 g mol^{-1}, $C_{24}H_{20}O_8$

219 (R = H)
mw = 408.36 g mol^{-1}, $C_{22}H_{16}O_8$

220
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

Following the procedure of Gust *et al.*,[183] to a stirred solution of potassium *tert*-butoxide (236 mg, 2.10 mmol) in THF (20 mL) under nitrogen at ambient temperature was added a solution of ketoaldehyde **214** (300 mg, 1.00 mmol) and diethyl succinate **217** (175 µl, 1.05 mmol) in THF (20 mL) over 20 minutes. After stirring for a further hour, the dark brown reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark orange oil. Purification by column chromatography (40-50% ether in petrol) gave diester **218** as an off-white solid (39 mg, 89 µmol, 9%): mp 169-172 °C, lit. 171-172 °C.[27] The aqueous phase was acidified with 6M HCl (15 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale green solid. Purification by column chromatography (40-50% ethyl acetate in petrol with 0.5% acetic acid) gave firstly γ-lactone **220** as an off-white solid (46 mg, 0.15 mmol, 15%): mp 139-142 °C (benzene/petrol), lit. 146-147 °C;[46] then half-acid **219** as a cream solid (140 mg, 0.34 mmol, 34%): mp 223-226 °C, lit. not reported.[27]

*Data for **218**:*

FT-IR (neat, cm^{-1}): 1719 m, 1489 w, 1463 m, 1238 s, 1209 m, 1033 s, 938 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 293 (11600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.39 (1H, s, ArH), 7.24 (1H, s, ArH), 6.90 (1H, d, J = 8.1 Hz, ArH), 6.89 (1H, s, ArH), 6.82 (1H, d, J = 1.5 Hz, ArH), 6.78 (1H, dd, J = 8.1, 1.5 Hz, ArH), 6.10-6.02 (4H, m, OCH_2O), 4.40 (2H, q, J = 7.4 Hz, OCH_2CH_3), 4.13 (2H, q, J = 7.4 Hz, OCH_2CH_3), 1.41 (3H, t, J = 7.4 Hz, OCH_2CH_3), 1.10 (3H, t, J = 7.4 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 169.1 (COOEt), 166.1 (COOEt), 150.3 (CO (Ar)), 148.8 (CO (Ar)), 147.5 (2 x CO (Ar)), 137.1 (C (Ar)), 132.4 (C (Ar)), 130.7 (C (Ar)), 130.1 (CH (Ar)), 130.0 (2 x C (Ar)), 124.0 (CH (Ar)), 123.4 (C (Ar)), 111.1 (CH (Ar)), 108.2 (CH (Ar)), 105.0 (CH (Ar)), 103.4 (CH (Ar)), 101.9 (OCH_2O), 101.3 (OCH_2O), 61.6 (OCH_2CH_3), 61.2 (OCH_2CH_3), 14.4 (OCH_2CH_3), 14.0 (OCH_2CH_3).

LRMS (CI) *m/z:* 436 (M^+, 17%), 391 ($[M - OCH_3]^+$, 100%).

*Data for **219**:*

FT-IR (neat, cm^{-1}): 1689 w, 1487 w, 1457 s, 1238 s, 1106 w, 1039 s, 941 w, 753 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 292 (12200).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.34 (1H, s, ArH), 7.15 (1H, s, ArH), 6.81 (1H, d, J = 7.9 Hz, ArH), 6.79 (1H, s, ArH), 6.73 (1H, d, J = 1.5 Hz, ArH), 6.70 (1H, dd, J = 7.9, 1.5 Hz, ArH), 5.99 (1H, d, J = 1.0 Hz, OCHHO), 5.98 (1H, d, J = 1.0 Hz, OCHHO), 5.97 (1H, d, J = 1.5 Hz, OCHHO), 5.95 (1H, d, J = 1.5 Hz, OCHHO), 4.03 (2H, q, J = 7.2 Hz, OCH_2CH_3), 1.03 (3H, t, J = 7.2 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, D_6-DMSO): 168.0 (COOH), 167.0 (COOEt), 150.2 (CO (Ar)), 148.6 (CO (Ar)), 147.1 (CO (Ar)), 147.0 (CO (Ar)), 136.2 (C (Ar)), 131.3 (C (Ar)), 130.4 (C (Ar)), 130.2 (C (Ar)), 129.6 (C (Ar), CH (Ar)), 124.0 (C (Ar)), 123.5 (CH (Ar)), 110.6 (CH (Ar)), 108.1 (CH (Ar)), 105.0 (CH (Ar)), 102.2 (OCH_2O), 102.0 (CH (Ar)), 101.3 (OCH_2O), 60.4 (OCH_2CH_3), 13.7 (OCH_2CH_3).

LRMS (ES^-) *m/z:* 521 ($[M + CF_3COO]^-$, 9%), 407 ($[M - H]^-$, 10%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 431.0746, $C_{22}H_{16}O_8Na$ requires 431.0737.

*Data for **220**:*

FT-IR (neat, cm^{-1}): 2881 w, 1754 m, 1734 w, 1499 w, 1474 w, 1463 w, 1455 w, 1317 m, 1251 m, 1242 m, 1089 m, 1037 s, 1030 s, 927 s.

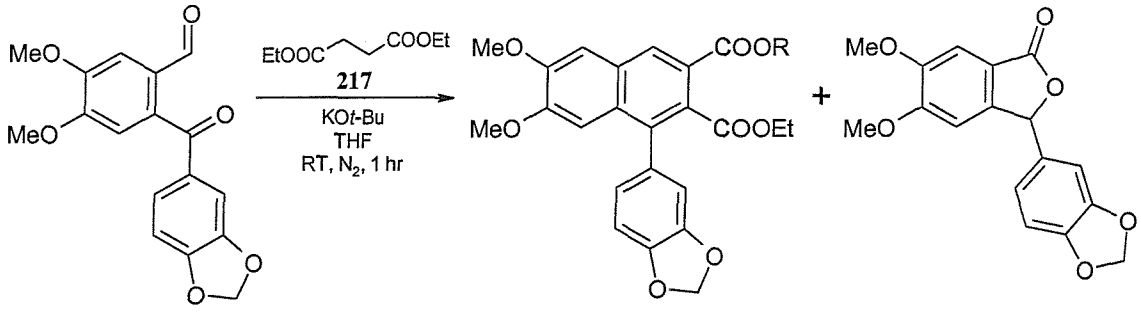
UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 291 (11400), 260 (13400), 252 (13600).

^{1}H NMR δ_H ppm (300 MHz, C_6D_6): 7.12 (1H, s, ArH), 6.49 (1H, d, J = 7.7 Hz, ArH), 6.46 (1H, d, J = 1.8 Hz, ArH), 6.39 (1H, dd, J = 7.7, 1.8 Hz, ArH), 6.09 (1H, s, ArH), 5.56 (1H, s, CHOC(O)), 5.23 (2H, s, OCH_2O), 5.17 (1H, d, J = 1.1 Hz, OCHHO), 5.12 (1H, d, J = 1.1 Hz, OCHHO).

^{13}C NMR δ_C ppm (75 MHz, C_6D_6): 169.4 (ArCOO), 153.6 (CO (Ar)), 148.8 (CO (Ar)), 148.6 (CO (Ar)), 146.5 (CO (Ar)), 131.1 (C (Ar)), 128.3 (C (Ar)), 121.4 (CH (Ar)), 120.1 (C (Ar)), 108.5 (CH (Ar)), 107.4 (CH (Ar)), 104.1 (CH (Ar)), 102.5 (CH (Ar)), 102.4 (OCH_2O), 101.3 (OCH_2O), 81.7 (CHOC(O)).

LRMS (CI) *m/z:* 316 ($[M + NH_4]^+$, 7%), 299 (MH^+, 100%).

Diethyl 6,7-dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylate (**221**), 6,7-Dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylic acid 2-ethyl ester (**222**) and 3-Benzo[1,3]dioxol-5-yl-5,6-dimethoxy-3*H*-isobenzofuran-1-one (**31**) *via* the Stobbe procedure



216
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

221 (R = Et)
mw = 452.46 g mol^{-1}, $C_{25}H_{24}O_8$

222 (R = H)
mw = 424.41 g mol^{-1}, $C_{23}H_{20}O_8$

31
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

In accordance with the Stobbe procedure of Gust *et al.*,[183] to a stirred solution of potassium *tert*-butoxide (225 mg, 2.0 mmol) in THF (20 mL) under nitrogen at ambient temperature was added a solution of **216** (300 mg, 0.96 mmol) and diethyl succinate **217** (170 µl, 1.0 mmol) in THF (20 mL) over 20 minutes. After stirring for a further hour, the reaction mixture was diluted with water (20 mL) and extracted with ether (3 x 50 mL). The

combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange semi-solid. Purification by column chromatography (50-60% ether in petrol) gave diester **221** as an off-white solid (64 mg, 0.14 mmol, 15%): mp 192-194 °C, lit. 195-197 °C.[27] The aqueous phase was acidified with 6M HCl (10 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark yellow gum. Purification by column chromatography (40-50% ethyl acetate in petrol with 0.5% acetic acid) gave firstly γ-lactone **31** as an off-white solid (49 mg, 0.16 mmol, 16%): mp 156-158 °C (ethyl acetate/petrol), lit. 157.5-158 °C;[41] then half-acid **222** as a cream solid (106 mg, 0.25 mmol, 26%): mp 200-202 °C, lit. not reported.[27]

*Data for **221**:*

FT-IR (neat, cm^{-1}): 2975 w, 2903 w, 2846 w, 1727 m, 1703 m, 1617 w, 1500 m, 1473 m, 1434 s, 1342 w, 1318 w, 1284 m, 1232 vs, 1200 s, 1161 s, 1139 m, 1110 m, 1093 m, 1030 s, 1005 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 290 (13600), 258 (51300).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.42 (1H, s, Ar<u>H</u>), 7.23 (1H, s, Ar<u>H</u>), 6.89 (1H, d, J = 7.7 Hz, Ar<u>H</u>), 6.85 (1H, s, Ar<u>H</u>), 6.84 (1H, d, J = 1.0 Hz, Ar<u>H</u>), 6.80 (1H, dd, J = 7.7, 1.0 Hz, Ar<u>H</u>), 6.05 (1H, s, OC<u>H</u>HO), 6.00 (1H, s, OCH<u>H</u>O), 4.37 (2H, q, J = 7.2 Hz, OC<u>H</u>$_2$CH$_3$), 4.12 (2H, q, J = 7.2 Hz, OC<u>H</u>$_2$CH$_3$), 4.00 (3H, s, ArOC<u>H</u>$_3$), 3.78 (3H, s, ArOC<u>H</u>$_3$), 1.39 (3H, t, J = 7.2 Hz, OCH$_2$C<u>H</u>$_3$), 1.09 (3H, t, J = 7.2 Hz, OCH$_2$C<u>H</u>$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 169.1 (<u>C</u>OOEt), 166.0 (<u>C</u>OOEt), 151.7 (<u>C</u>O (Ar)), 150.4 (<u>C</u>O (Ar)), 147.3 (<u>C</u>O (Ar)), 147.3 (<u>C</u>O (Ar)), 136.3 (<u>C</u> (Ar)), 130.6 (<u>C</u> (Ar)), 130.3 (<u>C</u> (Ar)), 129.5 (<u>C</u>H (Ar)), 128.4 (2 x <u>C</u> (Ar)), 123.8 (<u>C</u>H (Ar)), 123.1 (<u>C</u> (Ar)), 110.9 (<u>C</u>H (Ar)), 108.1 (<u>C</u>H (Ar)), 107.3 (<u>C</u>H (Ar)), 105.2 (<u>C</u>H (Ar)), 101.2 (O<u>C</u>H$_2$O), 61.3 (O<u>C</u>H$_2$CH$_3$), 61.0 (O<u>C</u>H$_2$CH$_3$), 56.0 (ArO<u>C</u>H$_3$), 55.8 (ArO<u>C</u>H$_3$), 14.3 (OCH$_2$<u>C</u>H$_3$), 13.9 (OCH$_2$<u>C</u>H$_3$).

LRMS (CI) *m/z:* 452 (M^+, 100%), 407 ([M - OCH_2CH_3]$^+$, 73%), 379 ([M - $COOCH_2CH_3$]$^+$, 33%).

Data for 222:

FT-IR (neat, cm^{-1}): 2961 w, 2918 w, 2844 w, 1723 m, 1678 m, 1617 w, 1504 m, 1475 m, 1431 s, 1342 w, 1294 w, 1236 vs, 1207 s, 1163 m, 1146 m, 1111 m, 1097 m, 1037 s, 1008 m, 932 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 290 (14000), 259 (47500).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.55 (1H, s, ArH), 7.27 (1H, s, ArH), 6.92 (1H, d, J = 7.9 Hz, ArH), 6.89 (1H, s, ArH), 6.87 (1H, d, J = 1.5 Hz, ArH), 6.83 (1H, dd, J = 7.9, 1.5 Hz, ArH), 6.08 (1H, d, J = 1.5 Hz, OCHHO), 6.04 (1H, d, J = 1.5 Hz, OCHHO), 4.15 (2H, q, J = 7.2 Hz, OCH_2CH_3), 4.04 (3H, s, $ArOCH_3$), 3.81 (3H, s, $ArOCH_3$), 1.16 (3H, t, J = 7.2 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 171.5 (COOH), 169.1 (COOEt), 152.2 (CO (Ar)), 150.7 (CO (Ar)), 147.5 (CO (Ar)), 147.5 (CO (Ar)), 136.6 (C (Ar)), 131.3 (C (Ar)), 130.8 (C (Ar)), 130.7 (CH (Ar)), 130.5 (C (Ar)), 128.5 (C (Ar)), 124.0 (CH (Ar)), 121.8 (C (Ar)), 111.0 (CH (Ar)), 108.3 (CH (Ar)), 107.6 (CH (Ar)), 105.5 (CH (Ar)), 101.4 (OCH_2O), 61.4 (OCH_2CH_3), 56.2 ($ArOCH_3$), 56.0 ($ArOCH_3$), 14.0 (OCH_2CH_3).

LRMS (ES^-) *m/z:* 537 ($[M + CF_3COO]^-$, 97%), 356 (100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 447.1056, $C_{23}H_{20}O_8Na$ requires 447.1050.

Data for 31:

FT-IR (neat, cm^{-1}): 1734 m, 1685 m, 1459 s, 1292 w, 1237 s, 1160 w, 1136 w, 1038 m, 941 w, 905 w, 837 s, 799 w.

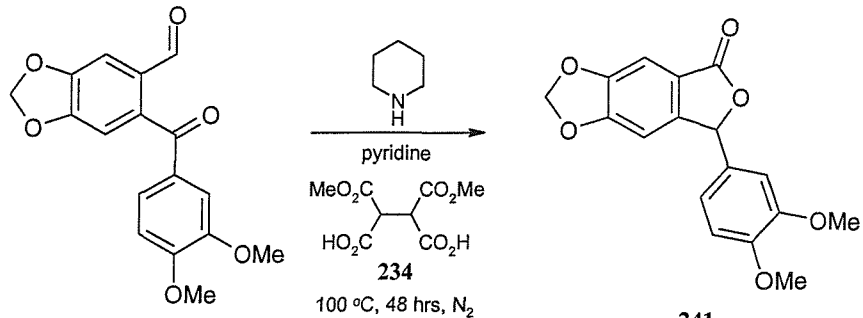
UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 300 (9700), 254 (43400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.31 (1H, s, ArH), 6.81-6.77 (2H, m, ArH), 6.67 (1H, s, ArH), 6.57 (1H, d, J = 1.2 Hz, ArH), 6.18 (1H, s, CHOC(O)), 5.94 (1H, d, J = 1.2 Hz, OCHHO), 5.93 (1H, d, J = 1.2 Hz, OCHHO), 3.94 (3H, s, $ArOCH_3$), 3.88 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 171.0 (ArCOO), 155.2 (CO (Ar)), 150.9 (CO (Ar)), 149.0 (CO (Ar)), 148.7 (CO (Ar)), 144.2 (C (Ar)), 130.4 (C (Ar)), 121.8 (CH (Ar)), 118.0 (C (Ar)), 108.6 (CH (Ar)), 107.5 (CH (Ar)), 106.0 (CH (Ar)), 104.2 (CH (Ar)), 101.6 (OCH_2O), 82.4 (CHOC(O)), 56.6 ($ArOCH_3$), 56.5 ($ArOCH_3$).

LRMS (CI) *m/z:* 315 (MH^+, 100%).

7-(3,4-Dimethoxyphenyl)-7*H*-furo[3',4':4,5]benzo[1,2-*d*][1,3]dioxol-5-one (**241**)



215
mw = 314.30 g mol^{-1}
$C_{17}H_{14}O_6$

241
mw = 314.30 g mol^{-1}
$C_{17}H_{14}O_6$

This procedure was based on the Knoevenagal methodology of Gensler and Berman.[184] A pre-dried boiling tube under nitrogen was charged with ketoaldehyde **215** (200 mg, 0.64 mmol) and diacid **234**[78] (297 mg, 1.27 mmol) in pyridine (5 mL). Piperidine (126 μL, 1.27 mmol) was added and the reaction mixture stirred and heated at 100 °C under nitrogen for 48 hours. On cooling to ambient temperature, the reaction mixture was carefully added to a stirred solution of concentrated hydrochloric acid (10 mL) on ice (20 g), producing a yellow precipitate that was isolated by extraction with ether (3 x 50 mL). The combined ether phases were then washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (60%-80% ether in petrol) gave **241** as a white solid (101 mg, 0.32 mmol, 51%): mp 173-174 °C.

FT-IR (neat, cm^{-1}): 1733 s, 1518 w, 1475 w, 1460 w, 1323 m, 1256 m, 1234 w, 1142 w, 1102 m, 1023 vs, 954 w, 935 m, 878 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 300 (4500), 285 (4700), 229 (10600).

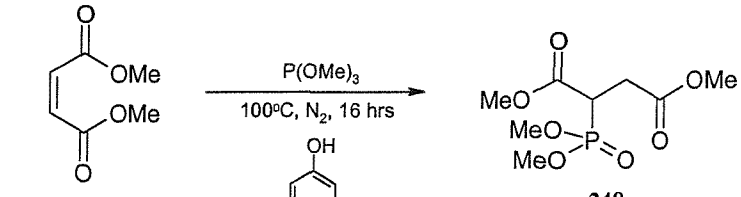
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.25 (1H, s, ArH), 6.87 (1H, d, J = 1.0 Hz, ArH), 6.86 (1H, s, ArH), 6.68-6.64 (2H, m, ArH), 6.21 (1H, s, CHOC(O)), 6.12 (1H, d, J = 1.2 Hz, OCHHO), 6.11 (1H, d, J = 1.2 Hz, OCHHO), 3.89 (3H, s, $ArOCH_3$), 3.82 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 170.2 (ArCOO), 154.0 (CO (Ar)), 150.1 (CO (Ar)), 149.6 (CO (Ar)), 149.6 (CO (Ar)), 146.6 (C (Ar)), 128.8 (C (Ar)), 120.2 (CH (Ar)), 119.6 (C (Ar)), 111.2 (CH (Ar)), 109.8 (CH (Ar)), 104.2 (CH (Ar)), 102.9 (OCH_2O), 102.7 (CH (Ar)), 82.4 (CHOC(O)), 56.1 ($ArOCH_3$), 56.1 ($ArOCH_3$).

LRMS (CI) *m/z:* 332 ([M + NH_4]$^+$, 13%), 315 (MH^+, 100%).

HRMS (ES$^+$) *m/z* Found: $[2M + Na]^+$ 651.1473, $C_{34}H_{28}O_{12}Na$ requires 651.1493.

2-(Dimethoxyphosphoryl)-dimethyl succinate (**248**)



mw = 144.13 gmol^{-1}
$C_6H_8O_4$

248

mw = 254.18 gmol^{-1}
$C_8H_{15}O_7P$

Using the procedure of Trost and Melvin,[185] a molten mixture of dimethyl maleate (4.34 mL, 34.7 mmol), phenol (8.19 g, 87 mmol) and trimethylphosphite (5.12 mL, 43.4 mmol) was stirred at 100 °C for 16 hours under nitrogen. On cooling to ambient temperature, the reaction mixture was purified by column chromatography (90% ether in petrol to 10% methanol in ether) to give **248** as a colourless oil (8.87 g, 34.7 mmol, 100%). The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3015 w, 2970 w, 1737 vs, 1438 w, 1365 m, 1259 w, 1228 s, 1217 s, 1161 w, 1027 s, 850 w, 825 w.

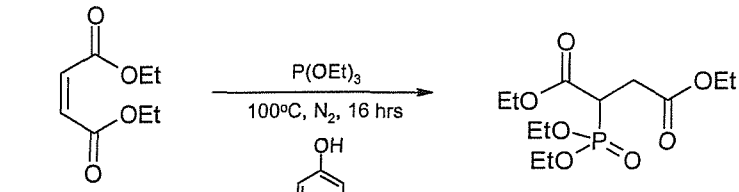
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 3.81 (3H, d, J = 6.8 Hz, P(O)OC$\underline{H}_3$), 3.77 (3H, d, J = 0.8 Hz, COOC$\underline{H}_3$), 3.76 (3H, d, J = 6.8 Hz, P(O)OC$\underline{H}_3$), 3.68 (3H, s, COOC$\underline{H}_3$), 3.49 (1H, ddd, J = 24.3, 11.2, 3.7 Hz, P(O)C$\underline{H}$COOCH$_3$), 3.07 (1H, ddd, J = 17.6, 11.2, 7.7 Hz, C$\underline{H}$HCOOCH$_3$), 2.80 (1H, ddd, J = 17.6, 9.7, 3.7 Hz, CH$\underline{H}$COOCH$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 171.8 (d, J = 18.9 Hz, P(O)CH$\underline{C}$OOCH$_3$), 168.9 (CH$_2\underline{C}$OOCH$_3$), 53.8 [2 x (d, J = 6.4 Hz, P(O)O$\underline{C}$H$_3$)], 53.3 (COO$\underline{C}$H$_3$), 52.6 (COO$\underline{C}$H$_3$), 40.8 (d, J = 131.6 Hz, P(O)$\underline{C}$HCOOCH$_3$), 31.4 (d, J = 1.9 Hz, $\underline{C}$H$_2$COOCH$_3$).

^{31}P NMR δ_P ppm (121.5 MHz, $CDCl_3$): 24.5.

LRMS (CI) *m/z:* 255 (MH^+, 100%), 223 ($[MH - CH_3OH]^+$, 82%), 195 ($[M - COOCH_3]^+$, 54%).

2-(Diethoxyphosphoryl)-diethyl succinate (**249**)



mw = 172.18 gmol^{-1}
$C_8H_{12}O_4$

249
mw = 310.28 gmol^{-1}
$C_{12}H_{23}O_7P$

Using the procedure of Harvey,[186] a molten mixture of diethyl maleate (4.7 mL, 29 mmol), phenol (7.25 g, 77 mmol) and triethylphosphite (6.22 mL, 36.3 mmol) was stirred at 100 °C for 16 hours under nitrogen. On cooling to ambient temperature, the reaction mixture was purified by column chromatography (neat ether to 10% methanol in ether) to give **249** as a pale yellow oil (8.97 g, 28.9 mmol, 100%). The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 2985 w, 1736 vs, 1370 w, 1321 w, 1257 s, 1211 m, 1161 s, 1023 vs, 971 s.

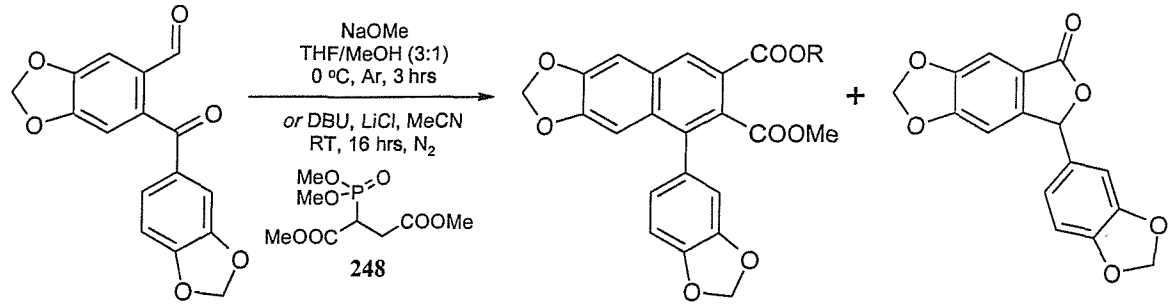
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 4.20 (2H, qd, J = 7.0, 2.9 Hz, P(O)OC$\underline{H}_2$CH$_3$), 4.13 (2H, qd, J = 7.0, 2.9 Hz, P(O)OC$\underline{H}_2$CH$_3$), 4.11 (2H, q, J = 7.0 Hz, COOC$\underline{H}_2$CH$_3$), 4.10 (2H, q, J = 7.0 Hz, COOC$\underline{H}_2$CH$_3$), 3.42 (1H, ddd, J = 23.9, 11.4, 3.3 Hz, P(O)C$\underline{H}$COOEt), 3.03 (1H, ddd, J = 17.6, 11.4, 7.4 Hz, C$\underline{H}$HCOOEt), 2.75 (1H, ddd, J = 17.6, 9.2, 3.3 Hz, CH$\underline{H}$COOEt), 1.32 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.30 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$), 1.26 (3H, t, J = 7.0 Hz, COOCH$_2$C$\underline{H}_3$), 1.22 (3H, t, J = 7.0 Hz, P(O)OCH$_2$C$\underline{H}_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 171.2 (d, J = 19 Hz, P(O)CH$\underline{C}$OOEt), 168.4 (d, J = 5.6 Hz, CH$_2\underline{C}$OOEt), 63.0 (d, J = 3.4 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 62.9 (d, J = 3.4 Hz, P(O)O$\underline{C}$H$_2$CH$_3$), 61.7 (COO$\underline{C}$H$_2$CH$_3$), 61.1 (COO$\underline{C}$H$_2$CH$_3$), 41.3 (d, J = 131 Hz, P(O)$\underline{C}$HCOOEt), 31.6 (d, J = 1.8 Hz, $\underline{C}$H$_2$COOEt), 16.3 (d, J = 3.4 Hz, P(O)OCH$_2\underline{C}$H$_3$), 16.2 (d, J = 3.4 Hz, P(O)OCH$_2\underline{C}$H$_3$), 14.1 (COOCH$_2\underline{C}$H$_3$), 14.0 (COOCH$_2\underline{C}$H$_3$).

^{31}P NMR δ_P ppm (121.5 MHz, $CDCl_3$): 21.9.

LRMS (CI) *m/z:* 311 (MH^+, 100%), 265 ([M - OCH_2CH_3]$^+$, 48%), 237 ([MH - CH_2CH_3 - OCH_2CH_3]$^+$, 38%), 209 ([MH - 2CH_2CH_3 - OCH_2CH_3]$^+$, 6%).

Dimethyl 5-benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylate (**39**), 5-Benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylic acid-7-methyl ester (**250**) and 7-Benzo[1,3]dioxol-5-yl-7*H*-furo[3',4':4,5]benzo[1,2-*d*][1,3]dioxol-5-one (**220**)



214
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

39 (R = Me)
mw = 408.36 g mol^{-1}, $C_{22}H_{16}O_8$

250 (R = H)
mw = 394.34 g mol^{-1}, $C_{21}H_{14}O_8$

220
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

Sodium (126 mg, 5.5 g-atom) was added portionwise to anhydrous methanol (8 mL) stirring vigorously at ambient temperature under argon. On consumption of the metal the solution was cooled (0 °C) and ketoaldehyde **214** (400 mg, 1.34 mmol) and phosphonate **248** (680 mg, 2.68 mmol) in THF (32 mL) and methanol (10 mL) were added *via* a dropping funnel over 20 minutes. After stirring at 0 °C for a further 3 hours, the reaction mixture was diluted with water (50 mL) and extracted with 1:1 THF/ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (40-60% ether in petrol) gave diester **39** as a white solid (462 mg, 1.13 mmol, 84%): mp 217-219 °C, lit. 218-219 °C.[46] The aqueous phase was acidified with 6 M HCl (50 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (40% ethyl acetate in petrol with 0.5% acetic acid) gave first γ-lactone **220** (14 mg, 47 μmol, 4%) then half-acid **250** (26 mg, 66 μmol, 5%): mp 234-237 °C, lit. 243-244 °C,[46] both as white solids. The data for **220** has been stated previously.

Alternatively, a flask containing anhydrous lithium chloride (87 mg, 2.06 mmol) under nitrogen was charged with ketoaldehyde **214** (150 mg, 0.50 mmol) in acetonitrile (15 mL). To this stirred suspension was added phosphonate **248** (256 mg, 1.01 mmol) in acetonitrile (5 mL), followed by DBU (0.31 mL, 2.06 mmol). After stirring at ambient temperature for 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (50 mL) and 1:1 THF/ether (2 x 50 mL). The combined organic phases were dried ($MgSO_4$)

and concentrated *in vacuo* to give a yellow oil. Purification by column chromatography (40-50% ether in petrol) gave **39** as a cream solid (123 mg, 0.30 mmol, 60%).

*Data for **39**:*

FT-IR (neat, cm^{-1}): 1723 w, 1711 w, 1488 w, 1462 m, 1450 m, 1280 w, 1262 m, 1242 vs, 1214 m, 1147 w, 1039 s, 930 w, 891 w, 851 w, 800 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 296 (13700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.37 (1H, s, ArH), 7.21 (1H, s, ArH), 6.88 (1H, d, J = 8.1 Hz, ArH), 6.87 (1H, s, ArH), 6.77 (1H, d, J = 1.5 Hz, ArH), 6.76 (1H, dd, J = 8.1 Hz, 1.5 Hz, ArH), 6.20-6.00 (4H, m, OCH_2O), 3.92 (3H, s, $COOCH_3$), 3.66 (3H, s, $COOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 166.5 (2 x $ArCOOCH_3$), 150.4 (CO (Ar)), 148.9 (CO (Ar)), 147.5 (2 x CO (Ar)), 137.1 (C (Ar)), 132.5 (C (Ar)), 130.5 (2 x C (Ar)), 130.1 (CH (Ar)), 130.0 (C (Ar)), 123.8 (CH (Ar)), 122.9 (C (Ar)), 110.9 (CH (Ar)), 108.3 (CH (Ar)), 105.0 (CH (Ar)), 103.5 (CH (Ar)), 101.9 (OCH_2O), 101.4 (OCH_2O), 52.7 ($COOCH_3$), 52.4 ($COOCH_3$).

LRMS (CI) *m/z:* 408 (M^+, 100%), 377 ($[M - OCH_3]^+$, 62%).

*Data for **250**:*

FT-IR (neat, cm^{-1}): 2960 w, 1735 w, 1688 w, 1455 s, 1261 w, 1237 s, 1219 w, 1106 w, 1038 s, 939 w, 895 w, 812 m, 798 m.

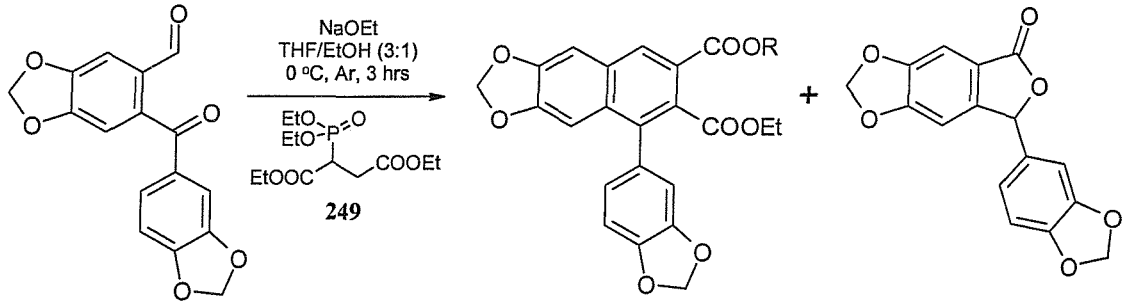
UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 294 (11500).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.32 (1H, s, ArH), 7.13 (1H, s, ArH), 6.79 (1H, d, J = 8.0 Hz, ArH), 6.77 (1H, s, ArH), 6.69 (1H, d, J = 1.7 Hz, ArH), 6.66 (1H, dd, J = 8.0 Hz, 1.7 Hz, ArH), 5.98 (1H, d, J = 0.7 Hz, OCHHO), 5.97 (1H, d, J = 0.7 Hz, OCHHO), 5.96 (1H, d, J = 1.1 Hz, OCHHO), 5.94 (1H, d, J = 1.1 Hz, OCHHO), 3.54 (3H, s, $COOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 174.6 (ArCOOH), 172.3 ($ArCOOCH_3$), 155.0 (CO (Ar)), 153.5 (CO (Ar)), 152.1 (2 x CO (Ar)), 141.5 (C (Ar)), 136.9 (C (Ar)), 135.4 (C (Ar)), 135.0 (C (Ar)), 134.7 (C (Ar)), 128.7 (C (Ar)), 128.5 (2 x CH (Ar)), 115.6 (CH (Ar)), 112.9 (CH (Ar)), 109.7 (CH (Ar)), 108.0 (CH (Ar)), 106.6 (OCH_2O), 106.1 (OCH_2O), 57.0 ($COOCH_3$).

LRMS (ES$^-$) *m/z:* 787 ([2M - H]$^-$, 18%), 507 ([M + CF_3COO]$^-$, 33%), 393 ([M - H]$^-$, 12%), 184 (75%), 133 (100%).

Diethyl 5-benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylate (**218**), 5-Benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylic acid-7-ethyl ester (**219**) and 7-Benzo[1,3]dioxol-5-yl-7*H*-furo[3',4':4,5]benzo[1,2-*d*][1,3]dioxol-5-one (**220**)



249

214
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

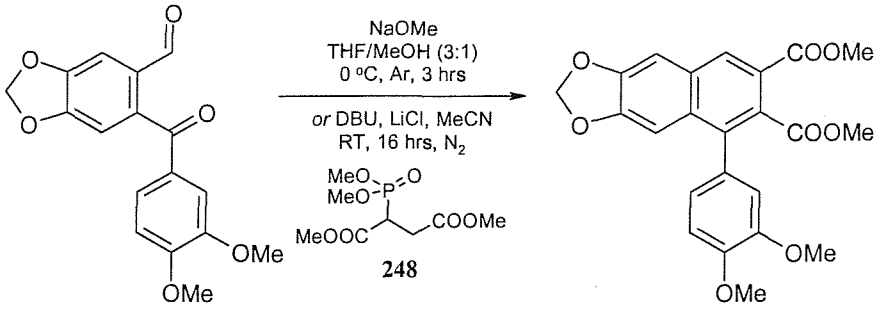
218 (R = Et)
mw = 436.42 g mol^{-1}, $C_{24}H_{20}O_8$

219 (R = H)
mw = 408.36 g mol^{-1}, $C_{22}H_{16}O_8$

220
mw = 298.25 g mol^{-1}
$C_{16}H_{10}O_6$

Sodium (126 mg, 5.5 g-atom) was added portionwise to anhydrous ethanol (8 mL) stirring vigorously at ambient temperature under argon. On consumption of the metal the solution was cooled (0 °C) and ketoaldehyde **214** (400 mg, 1.34 mmol) and phosphonate **249** (832 mg, 2.68 mmol) in THF (32 mL) and ethanol (10 mL) were added *via* a dropping funnel over 20 minutes. After stirring at 0 °C for a further 3 hours, the reaction mixture was diluted with water (50 mL) and extracted with 1:1 THF/ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (40-50% ether in petrol) gave diester **218** as a white solid (394 mg, 0.90 mmol, 67%). The aqueous phase was acidified with 6 M HCl (50 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a brown solid. Purification by column chromatography (40% ethyl acetate in petrol with 0.5% acetic acid) gave first γ-lactone **220** (18 mg, 60 μmol, 5%) then half-acid **219** (14 mg, 34 μmol, 3%), both as white solids. The data for **218**, **219** and **220** has been stated previously.

Dimethyl 6,7-methylenedioxy-1-(3,4-dimethoxyphenyl)-naphthalene-2,3-dicarboxylate (251)



215
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

251
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

Sodium (150 mg, 6.52 g-atom) was added portionwise to anhydrous methanol (12 mL) stirring vigorously at ambient temperature under argon. On consumption of the metal the solution was cooled (0 °C) and ketoaldehyde **215** (500 mg, 1.59 mmol) and phosphonate **248** (810 mg, 3.18 mmol) in THF (50 mL) and methanol (12 mL) were added *via* a dropping funnel over 20 minutes. After stirring at 0 °C for a further 3 hours, the reaction mixture was concentrated *in vacuo* and the solid residue partitioned between water (50 mL) and 1:1 THF/ether (200 mL). The aqueous layer was extracted with 1:1 THF/ether (2 x 100 mL), then the combined organic phases washed with saturated sodium bicarbonate solution (2 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to an orange semi-solid. Purification by column chromatography (50-60% ether in petrol) gave diester **251** as a sparingly soluble pale yellow solid (84 mg, 0.20 mmol, 12%): mp 252-254 °C, lit. 248-250 °C.[187] The combined aqueous phases were acidified with 6 M HCl (50 mL) and extracted with chloroform (3 x 100 mL). The combined chloroform phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a yellow solid. Purification by column chromatography (30-40% ethyl acetate in petrol with 0.5% acetic acid) yielded a further quantity of diester **251** (355mg, 0.79 mmol, 53%). The observed data is consistent with literature values.

Alternatively, a flask containing anhydrous lithium chloride (166 mg, 3.92 mmol) under nitrogen was charged with ketoaldehyde **215** (300 mg, 0.96 mmol) and acetonitrile (30 mL). To this stirred suspension was added phosphonate **248** (486 mg, 1.91 mmol) in acetonitrile (10 mL), followed by DBU (0.6 mL, 3.92 mmol). After stirring at ambient temperature for 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with 1:1 THF/ether (50 mL) and dichloromethane (2 x 50 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give a dark orange

oil. Purification by column chromatography (60-80% ether in petrol) gave **251** as a pale yellow solid (199 mg, 0.47 mmol, 49%).

FT-IR (neat, cm^{-1}): 1731 w, 1716 m, 1518 w, 1457 s, 1332 w, 1256 m, 1235 s, 1212 m, 1130 m, 1024 s, 929 m, 886 w, 849 m, 835 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 300 (10700), 254 (50400).

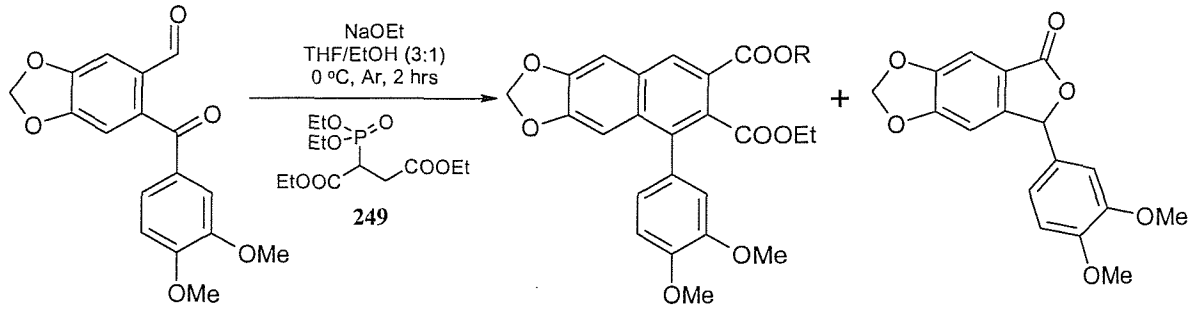
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.39 (1H, s, ArH), 7.22 (1H, s, ArH), 6.96 (1H, d, J = 7.9 Hz, ArH), 6.88 (1H, s, ArH), 6.87 (1H, dd, J = 7.9, 1.0 Hz, ArH), 6.85 (1H, d, J = 1.0 Hz, ArH), 6.06 (2H, s, OCH_2O), 3.95 (3H, s, $COOCH_3$), 3.93 (3H, s, $COOCH_3$), 3.85 (3H, s, $ArOCH_3$), 3.63 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 169.8 ($ArCOOCH_3$), 166.5 ($ArCOOCH_3$), 150.4 (CO (Ar)), 148.9 (CO (Ar)), 148.8 (CO (Ar)), 148.6 (CO (Ar)), 137.4 (C (Ar)), 132.5 (C (Ar)), 130.5 (C (Ar)), 130.0 (CH (Ar)), 129.4 (C (Ar)), 125.7 (C (Ar)), 122.9 (C (Ar)), 122.8 (CH (Ar)), 113.5 (CH (Ar)), 110.8 (CH (Ar)), 105.0 (CH (Ar)), 103.5 (CH (Ar)), 101.9 (OCH_2O), 56.1 ($ArOCH_3$), 56.0 ($ArOCH_3$), 52.6 ($COOCH_3$), 52.4 ($COOCH_3$).

LRMS (CI) *m/z:* 424 (M^+, 100%), 393 ($[M - OCH_3]^+$, 91%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 871.2249, $C_{46}H_{40}O_{16}Na$ requires 871.2209.

Diethyl 6,7-methylenedioxy-1-(3,4-dimethoxyphenyl)-naphthalene-2,3-dicarboxylate (**238**), 6,7-Methylenedioxy-1-(3,4-dimethoxyphenyl)-naphthalene-2,3-dicarboxylic acid 2-ethyl ester (**252**) and 7-(3,4-Dimethoxyphenyl)-7*H*-furo[3',4':4,5]benzo[1,2-*d*][1,3]dioxol-5-one (**241**)



215
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

238 (R = Et)
mw = 452.46 g mol^{-1}, $C_{25}H_{24}O_8$

252 (R = H)
mw = 424.41 g mol^{-1}, $C_{23}H_{20}O_8$

241
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

Sodium (150 mg, 6.52 g-atom) was added portionwise to anhydrous ethanol (10 mL) stirring vigorously at ambient temperature under argon. On consumption of the metal the solution was cooled (0 °C) and ketoaldehyde **215** (500 mg, 1.59 g-atom) and phosphonate

249 (987 mg, 3.18 mmol) in THF (50 mL) and ethanol (12 mL) were added *via* a dropping funnel over 20 minutes. After stirring at 0 °C for a further 2 hours, the reaction mixture was concentrated *in vacuo* and the solid residue partitioned between water (50 mL) and 1:1 THF/ether (200 mL). The aqueous layer was washed with 1:1 THF/ether (2 x 100 mL), then the combined organic phases washed with saturated sodium bicarbonate solution (2 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (50-60% ether in petrol) gave diester **238** as a pale yellow solid (332 mg, 0.73 mmol, 46%): mp 159-162 °C, lit. not reported.[27,188] The combined aqueous phases were acidified with 6 M HCl (50 mL) and extracted with chloroform (3 x 100 mL). The combined chloroform phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (40-50% ethyl acetate in petrol with 0.5% acetic acid) gave γ-lactone **241** (45mg, 0.14 mmol, 9%) then half-acid **252** (125 mg, 0.30 mmol, 19%): mp 200-203 °C, lit. not reported,[27,188] both as white solids. The observed data for **238** and **252** is consistent with literature values. [27,188] The data for **241** has been stated previously.

*Data for **238**:*

FT-IR (neat, cm^{-1}): 1727 m, 1710 m, 1515 w, 1460 s, 1412 w, 1321 w, 1272 w, 1256 s, 1235 vs, 1207 s, 1157 m, 1144 m, 1030 s, 941 w, 869 w, 851 w, 811 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 300 (14800), 258 (59600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.39 (1H, s, ArH), 7.23 (1H, s, ArH), 6.95 (1H, d, J = 8.2 Hz, ArH), 6.88 (1H, dd, J = 8.2, 2.0 Hz, ArH), 6.87 (1H, s, ArH), 6.85 (1H, d, J = 2.0 Hz, ArH), 6.05 (2H, s, OCH_2O), 4.39 (2H, q, J = 7.2 Hz, OCH_2CH_3), 4.15-3.99 (2H, m, OCH_2CH_3), 3.95 (3H, s, $ArOCH_3$), 3.85 (3H, s, $ArOCH_3$), 1.40 (3H, t, J = 7.2 Hz, OCH_2CH_3), 1.04 (3H, t, J = 7.2 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 169.3 (ArCOOEt), 166.1 (ArCOOEt), 150.3 (CO (Ar)), 148.8 (2 x CO (Ar)), 148.6 (CO (Ar)), 137.3 (C (Ar)), 132.5 (C (Ar)), 130.7 (C (Ar)), 130.0 (CH (Ar)), 130.0 (C (Ar)), 129.6 (C (Ar)), 123.4 (C (Ar)), 122.9 (CH (Ar)), 113.7 (CH (Ar)), 110.8 (CH (Ar)), 105.0 (CH (Ar)), 103.5 (CH (Ar)), 101.9 (OCH_2O), 61.6 (OCH_2CH_3), 61.2 (OCH_2CH_3), 56.1 (2 x $ArOCH_3$), 14.4 (OCH_2CH_3), 14.0 (OCH_2CH_3).

LRMS (CI) *m/z:* 452 (M^+, 100%), 407 ($[M - OCH_2CH_3]^+$, 84%), 379 ($[M - COOCH_2CH_3]^+$, 31%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 927.2828, $C_{50}H_{48}O_{16}Na$ requires 927.2835.

*Data for **252**:*

FT-IR (neat, cm^{-1}): 1743 m, 1687 m, 1460 s, 1286 w, 1236 vs, 1159 w, 1139 w, 1037 m, 942 w, 907 w, 849 w, 835 w, 770 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 304 (17600), 254 (73400).

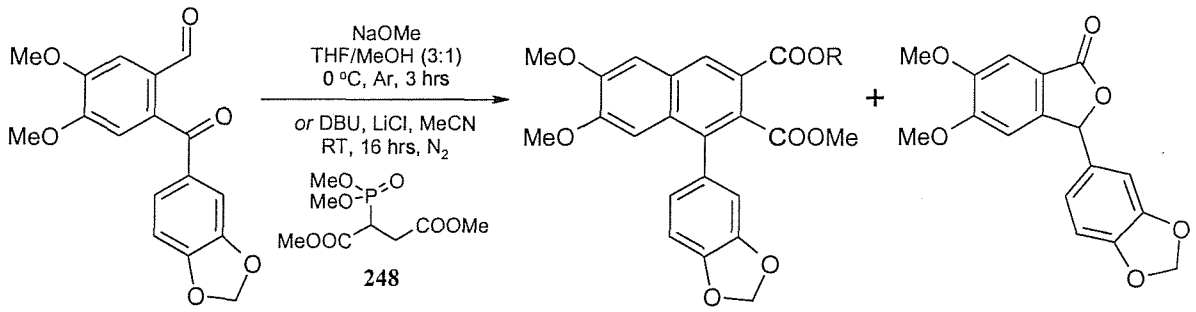
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.24 (1H, s, ArH), 7.05 (1H, s, ArH), 6.79 (1H, d, J = 8.0 Hz, ArH), 6.70 (1H, dd, J = 8.0, 1.7 Hz, ArH), 6.69 (1H, s, ArH), 6.68 (1H, d, J = 1.7 Hz, ArH), 5.89 (2H, s, OCH_2O), 3.94-3.83 (2H, m, OCH_2CH_3), 3.78 (3H, s, $ArOCH_3$), 3.67 (3H, s, $ArOCH_3$), 0.90 (3H, t, J = 7.2 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 174.0 (ArCOOH), 172.4 (ArCOOEt), 154.9 (CO (Ar)), 153.4 (2 x CO (Ar)), 153.2 (CO (Ar)), 141.7 (C (Ar)), 137.0 (C (Ar)), 135.6 (C (Ar)), 134.9 (CH (Ar)), 134.6 (C (Ar)), 134.4 (C (Ar)), 128.7 (C (Ar)), 127.6 (CH (Ar)), 118.4 (CH (Ar)), 115.6 (CH (Ar)), 109.6 (CH (Ar)), 108.0 (CH (Ar)), 106.6 (OCH_2O), 65.8 (OCH_2CH_3), 60.7 (2 x $ArOCH_3$), 18.7 (OCH_2CH_3).

LRMS (ES^-) *m/z:* 537 ($[M + CF_3COO]^-$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 447.1048, $C_{23}H_{20}O_8Na$ requires 447.1050.

Dimethyl 6,7-dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylate (**253**), 6,7-Dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylic acid 2-methyl ester (**254**) and 3-Benzo[1,3]dioxol-5-yl-5,6-dimethoxy-3*H*-isobenzofuran-1-one (**31**)



216
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

253 (R = Me)
mw = 424.41 g mol^{-1}, $C_{23}H_{20}O_8$

254 (R = H)
mw = 410.38 g mol^{-1}, $C_{22}H_{18}O_8$

31
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

Sodium (150 mg, 6.52 g-atom) was added portionwise to anhydrous methanol (10 mL) stirring vigorously at ambient temperature under argon. On consumption of the metal the solution was cooled (0 °C) and ketoaldehyde **216** (500 mg, 1.59 mmol) and phosphonate **248** (810 mg, 3.18 mmol) in THF (50 mL) and methanol (12 mL) were added *via* a dropping funnel over 20 minutes. After stirring at 0 °C for a further 3 hours, the solution was concentrated *in vacuo* and the solid residue partitioned between water (50 mL) and 1:1 THF/ether (200 mL). The aqueous layer was washed with 1:1 THF/ether (2 x 100 mL), then the combined organic phases washed with saturated sodium bicarbonate solution (2 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (40-50% ether in petrol) gave diester **253** as a white solid (376 mg, 0.89 mmol, 56%): mp 169-171 °C, lit. 169-170 °C.[189] The combined aqueous phases were acidified with 6 M HCl (50 mL) and extracted with chloroform (3 x 100 mL). The combined chloroform phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (30-50% ethyl acetate in petrol with 0.5% acetic acid) gave γ-lactone **31** (53 mg, 0.17 mmol, 11%); then half-acid **254** (98 mg, 0.24 mmol, 15%): mp 251-253 °C, lit. 255-256 °C,[189] both as white solids. The observed data for **253** and **254** is consistent with literature values.[189] The data for **31** has been stated previously.

Alternatively, a flask containing anhydrous lithium chloride (166 mg, 3.92 mmol) under nitrogen was charged with ketoaldehyde **216** (300 mg, 0.96 mmol) in acetonitrile (30 mL). To this stirred suspension was added phosphonate **248** (486 mg, 1.91 mmol) in acetonitrile (10 mL), followed by DBU (0.60 mL, 3.92 mmol). After stirring at ambient temperature for 16 hours, the reaction mixture was diluted with water (20 mL) and extracted with ether (2 x

50 mL) and 1:1 THF/ether (50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to give an orange oil. Purification by column chromatography (50-60% ether in petrol) gave **253** as a white solid (284 mg, 0.67 mmol, 70%).

*Data for **253**:*

FT-IR (neat, cm^{-1}): 1722 br. m, 1501 w, 1491 w, 1436 m, 1240 s, 1202 m, 1161 m, 1144 w, 1115 w, 1034 m, 1014 w, 866 w, 849 m, 800 s, 785 s, 763 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 290 (10300), 256 (43900).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.44 (1H, s, ArH), 7.24 (1H, s, ArH), 6.91 (1H, d, J = 7.9 Hz, ArH), 6.87 (1H, s, ArH), 6.84 (1H, d, J = 1.2 Hz, ArH), 6.81 (1H, dd, J = 7.9, 1.2 Hz, ArH), 6.08 (1H, d, J = 1.5 Hz, OCHHO), 6.04 (1H, d, J = 1.5 Hz, OCHHO), 4.03 (3H, s, $COOCH_3$), 3.94 (3H, s, $COOCH_3$), 3.80 (3H, s, $ArOCH_3$), 3.68 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 169.9 ($COOCH_3$), 166.6 ($COOCH_3$), 151.9 (CO (Ar)), 150.7 (CO (Ar)), 147.6 (CO (Ar)), 147.4 (CO (Ar)), 136.6 (C (Ar)), 130.8 (C (Ar)), 130.6 (C (Ar)), 130.3 (C (Ar)), 129.7 (CH (Ar)), 128.6 (C (Ar)), 123.8 (CH (Ar)), 122.7 (C (Ar)), 110.8 (CH (Ar)), 108.3 (CH (Ar)), 107.5 (CH (Ar)), 105.5 (CH (Ar)), 101.4 (OCH_2O), 56.2 ($ArOCH_3$), 56.0 ($ArOCH_3$), 52.6 ($COOCH_3$), 52.4 ($COOCH_3$).

LRMS (CI) *m/z:* 424 (M^+, 36%), 393 ($[M - OCH_3]^+$, 100%).

*Data for **254**:*

FT-IR (neat, cm^{-1}): 1730 m, 1679 m, 1474 m, 1436 m, 1361 w, 1345 w, 1239 s, 1209 m, 1112 w, 1097 w, 1047 m, 1014 w, 911 w, 850 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 288 (13000), 258 (51300).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.42 (1H, s, ArH), 7.18 (1H, s, ArH), 6.85 (1H, d, J = 8.0 Hz, ArH), 6.81 (1H, s, ArH), 6.79 (1H, d, J = 1.0 Hz, ArH), 6.76 (1H, dd, J = 8.0, 1.0 Hz, ArH), 6.02 (1H, s, OCHHO), 5.98 (1H, s, OCHHO), 3.97 (3H, s, $COOCH_3$), 3.74 (3H, s, $ArOCH_3$), 3.60 (3H, s, $ArOCH_3$).

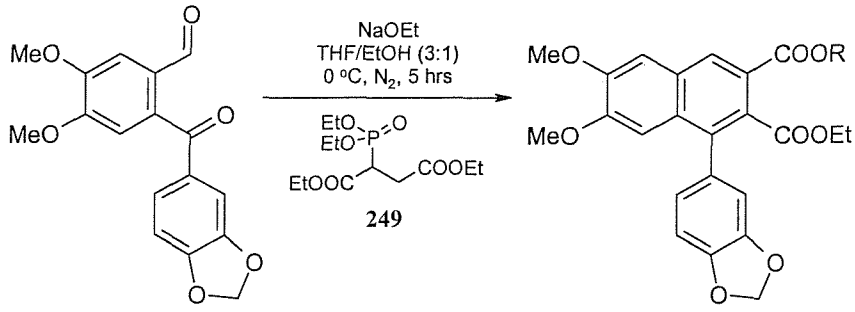
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 174.7 (ArCOOH), 172.7 ($ArCOOCH_3$), 156.4 (CO (Ar)), 155.2 (CO (Ar)), 152.2 (CO (Ar)), 152.0 (CO (Ar)), 141.0

(C (Ar)), 135.4 (C (Ar)), 135.3 (C (Ar)), 135.1 (C (Ar)), 134.7 (CH (Ar)), 133.3 (C (Ar)), 128.5 (CH (Ar)), 128.4 (C (Ar)), 115.5 (CH (Ar)), 112.9 (CH (Ar)), 112.1 (CH (Ar)), 110.1 (CH (Ar)), 106.0 (OCH_2O), 60.8 ($ArOCH_3$), 60.6 ($ArOCH_3$), 57.0 ($COOCH_3$).

LRMS (ES$^-$) *m/z:* 523 ($[M + CF_3COO]^-$, 100%).

HRMS (ES$^+$) *m/z* Found: $[M + Na]^+$ 433.0896, $C_{22}H_{18}O_8Na$ requires 433.0894.

Diethyl 6,7-dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylate (**221**) and 6,7-Dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylic acid 2-ethyl ester (**222**)



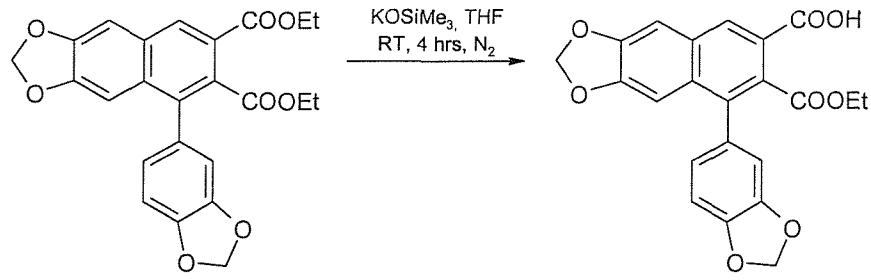
216
mw = 314.29 g mol^{-1}
$C_{17}H_{14}O_6$

221 (R = Et)
mw = 452.46 g mol^{-1}, $C_{25}H_{24}O_8$

222 (R = H)
mw = 424.41 g mol^{-1}, $C_{23}H_{20}O_8$

Sodium (75 mg, 3.26 g-atom) was added portionwise to anhydrous ethanol (5 mL) stirring vigorously at ambient temperature under nitrogen. On consumption of the metal the solution was cooled (0 °C) and ketoaldehyde **216** (250 mg, 0.80 mmol) and phosphonate **249** (493 mg, 1.60 mmol) in THF (20 mL) and ethanol (7 mL) were added *via* a dropping funnel over 20 minutes. After stirring at 0 °C for a further 5 hours, the reaction mixture was concentrated *in vacuo* and the solid residue partitioned between water (50 mL) and 1:1 THF/ether (100 mL). The aqueous layer was washed with 1:1 THF/ether (2 x 50 mL), then the combined organic phases washed with saturated sodium bicarbonate solution (2 x 30 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a mustard yellow solid. Purification by column chromatography (50-60% ether in petrol) gave diester **221** as a white solid (246 mg, 0.54 mmol, 68%). The combined aqueous phases were acidified with 6 M HCl (25 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (40-50% ethyl acetate in petrol with 0.5% acetic acid) gave half-acid **222** as a white solid (16 mg, 38 μmol, 5%). The data for **221** and **222** has been stated previously.

5-Benzo[1,3]dioxol-5-yl-naphtho[2,3-*d*][1,3]dioxole-6,7-dicarboxylic acid-7-ethyl ester (219)

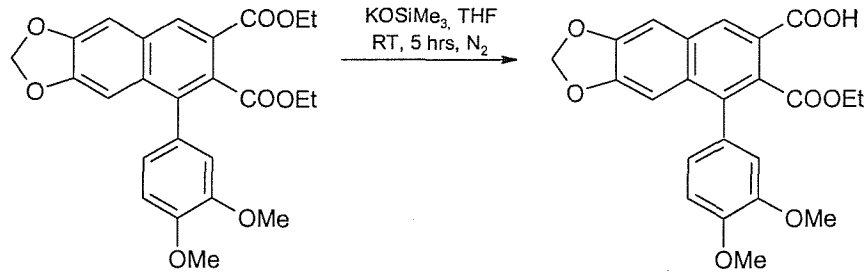


218
mw = 436.42 g mol^{-1}
$C_{24}H_{20}O_8$

219
mw = 408.36 g mol^{-1}
$C_{22}H_{16}O_8$

Following the procedure of Padwa *et al.*,[43] to a stirred solution of diester **218** (200 mg, 0.46 mmol) in THF (20 mL) at ambient temperature under nitrogen was added potassium trimethylsilanolate (260 mg, 2.0 mmol). After stirring for 4 hours at ambient temperature, the solution was acidified with 5% HCl (35 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform extracts were dried ($MgSO_4$) and concentrated *in vacuo* to a pale green solid. Purification by column chromatography (40% ethyl acetate in petrol with 0.5% acetic acid) gave **219** as a cream solid (185 mg, 0.45 mmol, 98%). The data for **219** has been stated previously.

6,7-Methylenedioxy-1-(3,4-dimethoxyphenyl)-naphthalene-2,3-dicarboxylic acid 2-ethyl ester (252)

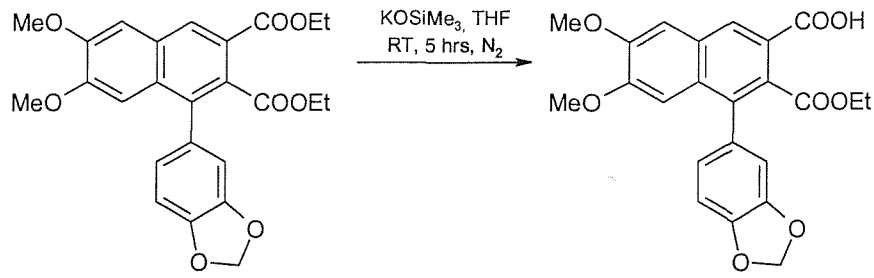


238
mw = 452.46 g mol^{-1}
$C_{25}H_{24}O_8$

252
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

Following the procedure of Padwa *et al.*,[43] to a stirred solution of diester **238** (205 mg, 0.45 mmol) in THF (20 mL) at ambient temperature under nitrogen was added potassium trimethylsilanolate (260 mg, 2.00 mmol). After stirring for a further 5 hours, the solution was acidified with 5% HCl (50 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give **252** as a white solid (186 mg, 0.44 mmol, 97%). The data for **252** has been stated previously.

6,7-Dimethoxy-1-(benzo[1,3]dioxol-5-yl)-naphthalene-2,3-dicarboxylic acid 2-ethyl ester (222)

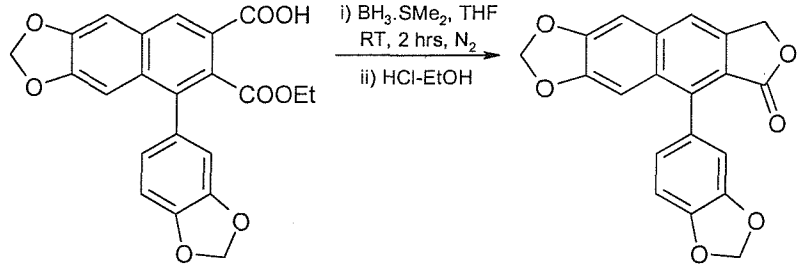


221
mw = 452.46 g mol^{-1}
$C_{25}H_{24}O_8$

222
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

Following the procedure of Padwa *et al.*,[43] to a stirred solution of diester **221** (246 mg, 0.54 mmol) in THF (30 mL) at ambient temperature under nitrogen was added potassium trimethylsilanolate (308 mg, 2.40 mmol). After stirring for 5 hours at ambient temperature, the solution was acidified with 5% HCl (50 mL) and extracted with chloroform (3 x 50 mL). The combined chloroform extracts were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give **222** as a white solid (215 mg, 0.51 mmol, 93%). The data for **222** has been stated previously.

Taiwanin C (3)



219
mw = 408.36 g mol^{-1}
$C_{22}H_{16}O_8$

3
mw = 348.31 g mol^{-1}
$C_{20}H_{12}O_6$

Following the procedure of Cow *et al.*,[27] to a stirred solution of **219** (50 mg, 0.12 mmol) in THF (4 mL) at ambient temperature under nitrogen was added borane-dimethyl sulfide complex (122 μL, 1.22 mmol, 10.0 M solution in dimethylsulfide). The yellow reaction mixture was then stirred at ambient temperature for 2 hours before acidifying with 3% HCl in ethanol (formed by adding 0.25 mL acetyl chloride to 4.75 mL anhydrous ethanol). Once effervescence had ceased, the solvent was removed *in vacuo* and the residue dissolved in chloroform (25 mL), washed with saturated sodium bicarbonate solution (3 x 25 mL) and water (25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a pale yellow solid. Purification by column chromatography (5-10% ethyl acetate in toluene) gave taiwanin C **3** as a white

solid (37 mg, 0.11 mmol, 87%): mp 267-270 °C, lit. 272-273 °C.[55] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 2919 w, 2850 w, 1763 s, 1612 w, 1489 m, 1469 s, 1457 m, 1366 w, 1336 w, 1257 m, 1234 m, 1203 m, 1152 m, 1048 w, 1033 s, 1012 s, 930 m, 874 m, 797 m, 750 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 340 (4700), 288 (12400), 251 (50300).

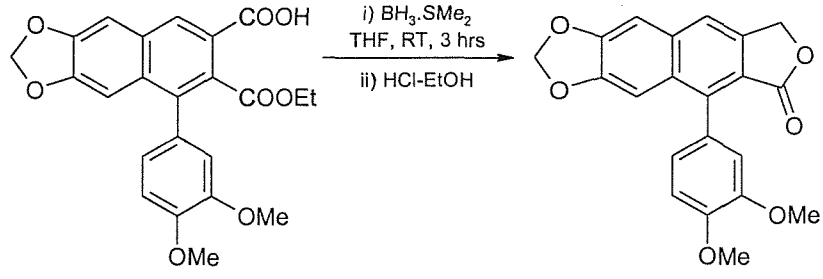
^{1}H NMR δ_H ppm (300 MHz, D_6-DMSO): 7.93 (1H, s, ArH), 7.52 (1H, s, ArH), 7.03 (1H, d, J = 7.7 Hz, ArH), 6.88 (1H, s, ArH), 6.87 (1H, d, J = 1.5 Hz, ArH), 6.73 (1H, dd, J = 7.7, 1.5 Hz, ArH), 6.18 (1H, d, J = 2.6 Hz, OCHHO), 6.17 (1H, d, J = 2.6 Hz, OCHHO), 6.13 (1H, d, J = 1.1 Hz, OCHHO), 6.12 (1H, d, J = 1.1 Hz, OCHHO), 5.42 (2H, s, CH_2OCO).

^{13}C NMR δ_C ppm (75 MHz, D_6-DMSO): 169.1 (CH_2OCO), 149.5 (CO (Ar)), 148.3 (CO (Ar)), 146.9 (2 x (CO (Ar)), 140.2 (C (Ar)), 138.6 (C (Ar)), 134.2 (C (Ar)), 129.3 (C (Ar)), 128.3 (C (Ar)), 123.2 (CH (Ar)), 119.5 (CH (Ar)), 118.4 (C (Ar)), 110.4 (CH (Ar)), 107.9 (CH (Ar)), 103.7 (CH (Ar)), 102.1 (CH (Ar)), 102.1 (OCH_2O), 101.1 (OCH_2O), 67.9 (CH_2OCO).

LRMS (CI) *m/z:* 349 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 371.0527, $C_{20}H_{12}O_6Na$ requires 371.0526.

Chinensin (**4**)



252
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

4
mw = 364.35 g mol^{-1}
$C_{21}H_{16}O_6$

Following the procedure of Cow *et al.*,[27] to a stirred solution of half acid **252** (60 mg, 0.14 mmol) in THF (3 mL) at ambient temperature under argon was added borane-dimethylsulfide complex (140 μL, 1.40 mmol, 10.0 M solution in dimethylsulfide). The yellow reaction mixture was then stirred at ambient temperature for 3 hours before acidifying with 3% HCl in ethanol (formed by adding 0.25 mL acetyl chloride to 4.75 mL

anhydrous ethanol). Once effervescence had ceased, the solvent was removed *in vacuo* and the residue dissolved in chloroform (25 mL), washed with saturated sodium bicarbonate solution (3 x 25 mL) and water (25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10% ethyl acetate in toluene) gave chinensin **4** as a white solid (50 mg, 0.137 mmol, 97%): mp 224-226 °C, lit. 224-228 °C.[11,80] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 1762 s, 1738 s, 1491 w, 1462 m, 1366 m, 1245 m, 1229 s, 1217 s, 1202 s, 1155 w, 1132 w, 1032 m, 1018 m, 937 w, 873 w, 802 w, 762 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 340 (5500), 300 (10600), 250 (46600).

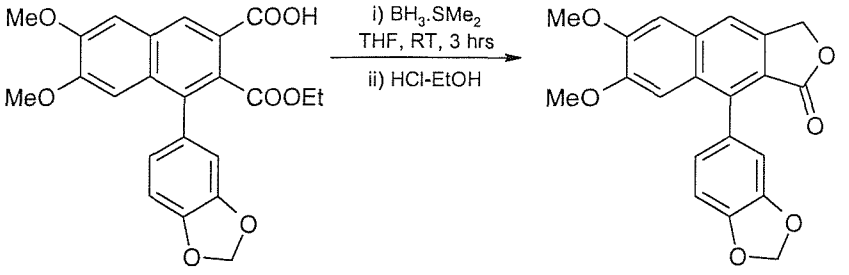
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.70 (1H, s, Ar<u>H</u>), 7.21 (1H, s, Ar<u>H</u>), 7.12 (1H, s, Ar<u>H</u>), 7.03 (1H, d, J = 8.1 Hz, Ar<u>H</u>), 6.91 (1H, dd, J = 8.1, 1.8 Hz, Ar<u>H</u>), 6.87 (1H, d, J = 1.8 Hz, Ar<u>H</u>), 6.08 (2H, s, OC<u>H</u>$_2$O), 5.38 (2H, s, C<u>H</u>$_2$OCO), 3.98 (3H, s, ArOC<u>H</u>$_3$), 3.87 (3H, s, ArOC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 170.0 (CH_2O<u>C</u>O), 150.1 (<u>C</u>O (Ar)), 149.0 (<u>C</u>O (Ar)), 148.8 (<u>C</u>O (Ar)), 148.7 (<u>C</u>O (Ar)), 140.6 (<u>C</u> (Ar)), 140.0 (<u>C</u> (Ar)), 134.8 (<u>C</u> (Ar)), 130.6 (<u>C</u> (Ar)), 127.3 (<u>C</u> (Ar)), 122.6 (<u>C</u>H (Ar)), 119.1 (<u>C</u>H (Ar)), 118.9 (<u>C</u> (Ar)), 113.5 (<u>C</u>H (Ar)), 110.9 (<u>C</u>H (Ar)), 103.9 (<u>C</u>H (Ar)), 103.8 (<u>C</u>H (Ar)), 102.0 (O<u>C</u>H$_2$O), 68.1 (<u>C</u>H$_2$OCO), 56.1 (ArO<u>C</u>H$_3$), 56.0 (ArO<u>C</u>H$_3$).

LRMS (CI) *m/z:* 365 (MH^+, 65%), 364 (M^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 387.0843, $C_{21}H_{16}O_6Na$ requires 387.0839.

Justicidin B (17)



222

mw = 424.41 g mol^{-1}

$C_{23}H_{20}O_8$

17

mw = 364.35 g mol^{-1}

$C_{21}H_{16}O_6$

Following the procedure of Cow *et al.*,[27] to a stirred solution of half-acid **222** (30 mg, 71 μmol) in THF (1.5 mL) at ambient temperature under nitrogen was added borane-dimethyl sulfide complex (80 μL, 0.8 mmol, 10.0 M solution in dimethylsulfide). The reaction mixture was then stirred at ambient temperature for 3 hours before acidifying with 3% HCl in ethanol (formed by adding 0.25 mL acetyl chloride to 4.75 mL anhydrous ethanol). Once effervescence had ceased, the solvent was removed *in vacuo* and the residue dissolved in chloroform (25 mL), washed with saturated sodium bicarbonate solution (3 x 25 mL) and water (25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10% ethyl acetate in toluene) gave justicidin B **17** as a white solid (25 mg, 69 μmol, 97%): mp 227-229 °C, lit. 235-238 °C.[17,190] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 1759 s, 1506 s, 1481 m, 1439 m, 1387 w, 1343 w, 1262 s, 1239 s, 1217 s, 1198 s, 1158 m, 1044 s, 1021 m, 1002 m, 932 w, 876 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 340 (3100), 286 (8300), 252 (38000).

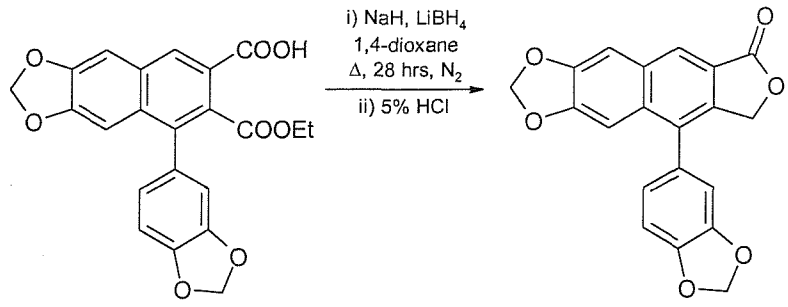
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.71 (1H, s, ArH), 7.19 (1H, s, ArH), 7.12 (1H, s, ArH), 6.98 (1H, d, J = 7.7 Hz, ArH), 6.86 (1H, d, J = 1.2 Hz, ArH), 6.84 (1H, dd, J = 7.7, 1.2 Hz, ArH), 6.10 (1H, d, J = 1.0 Hz, OCHHO), 6.05 (1H, d, J = 1.0 Hz, OCHHO), 5.39 (2H, s, CH_2OCO), 4.06 (3H, s, $ArOCH_3$), 3.82 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 169.9 (CH_2OCO), 151.9 (CO (Ar)), 150.2 (CO (Ar)), 147.7 (2 x CO (Ar)), 139.7 (2 x C (Ar)), 133.3 (C (Ar)), 129.0 (C (Ar)), 128.5 (C (Ar)), 123.6 (CH (Ar)), 118.6 (C (Ar)), 118.5 (CH (Ar)), 110.7 (CH (Ar)), 108.4 (CH (Ar)), 106.1 (CH (Ar)), 105.9 (CH (Ar)), 101.4 (OCH_2O), 68.2 (CH_2OCO), 56.2 (OCH_3), 56.0 (OCH_3).

LRMS (CI) *m/z:* 365 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 387.0842, $C_{21}H_{16}O_6Na$ requires 387.0839.

Justicidin E (**6**)



219

mw = 408.36 g mol^{-1}
$C_{22}H_{16}O_8$

6

mw = 348.31 g mol^{-1}
$C_{20}H_{12}O_6$

This procedure was adapted from that of Padwa *et al.*[43] To a stirred solution of half-acid **219** (50 mg, 0.12 mmol) and petrol washed sodium hydride (39 mg, 0.97 mmol, 60% dispersion in mineral oil) in 1,4-dioxane (2.3 mL) at ambient temperature under nitrogen was added lithium borohydride (485 μL, 0.97 mmol, 2.0 M solution in THF). Once effervescence had ceased, the reaction mixture was stirred at reflux for 28 hours, cooled to 0 °C and carefully acidified with 5% HCl (10 mL). The biphasic mixture was then extracted with dichloromethane (3 x 25 mL) and the combined organic layers washed with saturated sodium bicarbonate solution (25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (5-10% ethyl acetate in toluene) gave justicidin E **6** as a white solid (24 mg, 69 μmol, 57%): mp 264-268 °C, lit. 265-269 °C.[80,191-193] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 2920 w, 1757 s, 1498 w, 1458 vs, 1245 s, 1207 m, 1025 s, 1007 m, 931 m, 858 w, 805 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 300 (9500), 244 (33800).

^{1}H NMR δ_H ppm (300 MHz, D_6-DMSO): 8.34 (1H, s, ArH), 7.62 (1H, s, ArH), 7.08 (1H, d, J = 8.1 Hz, ArH), 7.03 (1H, d, J = 1.5 Hz, ArH), 6.99 (1H, s, ArH), 6.89 (1H, dd, J = 8.1, 1.5 Hz, ArH), 6.18 (2H, s, OCH_2O), 6.12 (2H, s, OCH_2O), 5.32 (1H, d, J = 14.7 Hz, CHHOCO), 5.25 (1H, d, J = 14.7 Hz, CHHOCO).

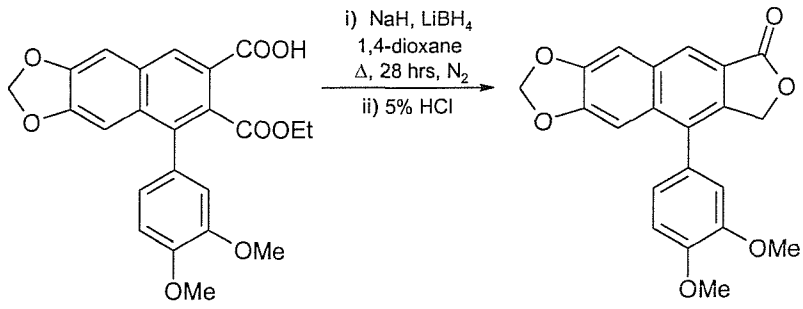
^{13}C NMR δ_C ppm (75 MHz, D_6-DMSO): 170.8 (CH_2OCO), 150.4 (CO (Ar)), 148.0 (CO (Ar)), 147.9 (CO (Ar)), 147.3 (CO (Ar)), 138.7 (C (Ar)), 132.6 (C (Ar)),

132.1 (C (Ar)), 131.0 (C (Ar)), 129.1 (C (Ar)), 124.1 (CH (Ar)), 123.0 (CH (Ar)), 121.2 (C (Ar)), 109.7 (CH (Ar)), 108.9 (CH (Ar)), 105.2 (CH (Ar)), 102.3 (OCH_2O), 101.4 (OCH_2O), 100.9 (CH (Ar)), 69.3 (CH_2OCO).

LRMS (CI) *m/z:* 349 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 371.0525, $C_{20}H_{12}O_6Na$ requires 371.0526.

Retrochinensin (7)



252
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

7
mw = 364.35 g mol^{-1}
$C_{21}H_{16}O_6$

This procedure was adapted from that of Padwa *et al.*[43] To a stirred solution of half-acid **252** (68 mg, 0.16 mmol) and petrol washed sodium hydride (51 mg, 1.27 mmol, 60% dispersion in mineral oil) in 1,4-dioxane (3 mL) at ambient temperature under nitrogen was added lithium borohydride (0.64 mL, 1.27 mmol, 2.0 M solution in THF). Once effervescence had ceased, the reaction mixture was stirred at reflux for 28 hours, cooled to 0 °C and carefully acidified with 5% HCl (10 mL). The biphasic mixture was then extracted with dichloromethane (4 x 20 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10% ethyl acetate in toluene) gave retrochinensin **7** as a white solid (42 mg, 0.115 mmol, 72%): mp 234-236 °C, lit. 233-235 °C.[80] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 1755 m, 1742 m, 1515 w, 1464 m, 1369 w, 1255 m, 1245 m, 1230 s, 1206 m, 1133 m, 1035 s, 1024 s, 942 w, 919 m, 831 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 306 (9000), 248 (33900).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.26 (1H, s, ArH), 7.30 (1H, s, ArH), 7.11 (1H, s, ArH), 7.04 (1H, d, J = 8.1 Hz, ArH), 6.91 (1H, dd, J = 8.1, 1.8 Hz, ArH), 6.85 (1H, d, J = 1.8 Hz, ArH), 6.10 (2H, s, OCH_2O), 5.24 (1H, d,

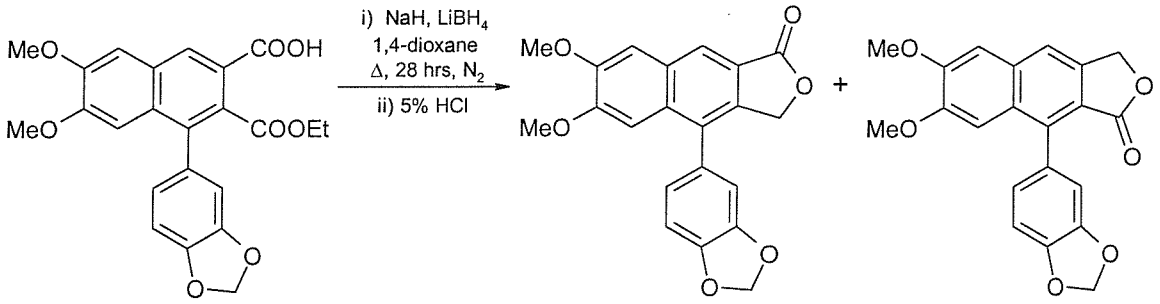
J = 14.7 Hz, CHHOCO), 5.18 (1H, d, J = 14.7 Hz, CHHOCO), 3.99 (3H, s, $ArOCH_3$), 3.89 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 171.7 (CH_2OCO), 150.6 (CO (Ar)), 149.5 (CO (Ar)), 149.2 (CO (Ar)), 148.5 (CO (Ar)), 138.5 (C (Ar)), 133.6 (C (Ar)), 133.1 (C (Ar)), 131.4 (C (Ar)), 128.7 (C (Ar)), 124.7 (CH (Ar)), 121.8 (CH (Ar)), 121.8 (C (Ar)), 112.3 (CH (Ar)), 111.8 (CH (Ar)), 105.4 (CH (Ar)), 102.2 (CH (Ar)), 102.0 (OCH_2O), 69.7 (CH_2OCO), 56.2 ($ArOCH_3$), 56.2 ($ArOCH_3$).

LRMS (CI) *m/z:* 365 (MH^+, 73%), 364 (M^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 387.0844, $C_{21}H_{16}O_6Na$ requires 387.0839.

Retrojusticidin B (**19**) and Justicidin B (**17**)



222
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

19
mw = 364.35 g mol^{-1}
$C_{21}H_{16}O_6$

17

This procedure was adapted from that of Padwa *et al.*[43] To a stirred solution of **222** (140 mg, 0.33 mmol) and petrol washed sodium hydride (105 mg, 2.62 mmol, 60% dispersion in mineral oil) in 1,4-dioxane (6.25 mL) at 0 °C under nitrogen was added lithium borohydride (0.94 mL, 2.62 mmol, 2.0 M solution in THF). Once effervescence had ceased, the reaction mixture was stirred at reflux for 28 hours, cooled to 0 °C and carefully acidified with 5% HCl (15 mL). The biphasic mixture was then extracted with dichloromethane (4 x 20 mL) and the combined organic layers dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (5-15% ethyl acetate in toluene) gave first retrojusticidin B **19** (80 mg, 0.22 mmol, 67%): mp 216-220 °C, lit. 218-220 °C;[194] then justicidin B **17** (34 mg, 0.09 mmol, 28%), both as white solids. The data for **17** has been stated previously .The observed data for **19** is consistent with literature values.

*Data for retrojusticidin B **19**:*

FT-IR (neat, cm^{-1}): 2948 w, 2919 w, 2849 w, 1750 s, 1505 m, 1483 m, 1457 m, 1435 m, 1385 w, 1345 w, 1263 m, 1240 s, 1230 s, 1154 m, 1113 w, 1037 s, 1006 m, 930 w, 908 w, 862 w, 832 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 310 (8000), 252 (65600).

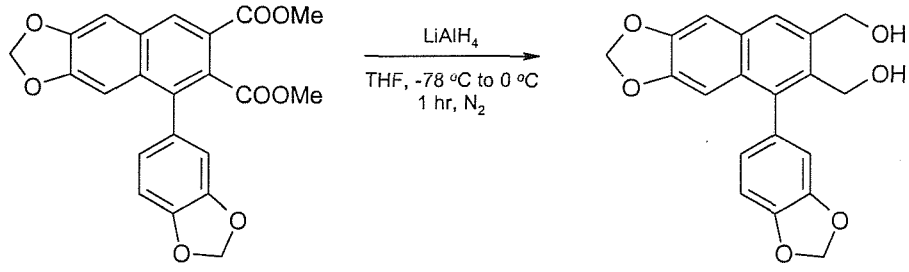
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.30 (1H, s, ArH), 7.30 (1H, s, ArH), 7.10 (1H, s, ArH), 6.99 (1H, d, J = 8.4 Hz, ArH), 6.85 (1H, d, J = 1.7 Hz, ArH), 6.84 (1H, dd, J = 8.4, 1.7 Hz, ArH), 6.11 (1H, d, J = 1.2 Hz, OCHHO), 6.08 (1H, d, J = 1.2 Hz, OCHHO), 5.21 (2H, s, CH_2OCO), 4.05 (3H, s, $ArOCH_3$), 3.86 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 171.8 (CH_2OCO), 152.2 (CO (Ar)), 150.3 (CO (Ar)), 148.5 (CO (Ar)), 147.8 (CO (Ar)), 138.1 (C (Ar)), 132.1 (C (Ar)), 131.8 (C (Ar)), 130.0 (C (Ar)), 129.9 (C (Ar)), 124.4 (CH (Ar)), 122.9 (CH (Ar)), 121.5 (C (Ar)), 109.7 (CH (Ar)), 109.2 (CH (Ar)), 107.8 (CH (Ar)), 104.1 (CH (Ar)), 101.6 (OCH_2O), 69.7 (CH_2OCO), 56.2 ($ArOCH_3$), 56.1 ($ArOCH_3$).

LRMS (CI) *m/z:* 364 (M^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 387.0842, $C_{21}H_{16}O_6Na$ requires 387.0839.

6,7-Methylenedioxy-1-(3,4-methylenedioxy)naphthalene-2,3-dimethanol (**256**)



39
mw = 408.36 g mol^{-1}
$C_{22}H_{16}O_8$

256
mw = 352.34 g mol^{-1}
$C_{20}H_{16}O_6$

To a stirred solution of diester **39** (250 mg, 0.61 mmol) in THF (50 mL) at –78 °C under nitrogen was added lithium aluminium hydride (95 mg, 2.51 mmol). On allowing the reaction mixture to warm to 0 °C over 1 hour, water (1 mL) was added. Once effervescence had ceased, 15% NaOH (1 mL) and water (1 mL) were added and the resultant grey suspension stirred vigorously at ambient temperature for 16 hours. After stirring over anhydrous $MgSO_4$ for 2.5 hours, the reaction mixture was filtered and concentrated *in vacuo*

to a white solid. Purification by column chromatography (90% ether in petrol to neat ether with 5% methanol) gave **256** as a white solid (179 mg, 0.51 mmol, 83%): mp 176-179 °C, lit. 183-185 °C.[46]

FT-IR (neat, cm^{-1}): 3349 br. w, 1504 w, 1486 m, 1459 s, 1234 s, 1038 s, 1013 m, 939 m, 885 w, 802 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 332 (3300), 294 (12400).

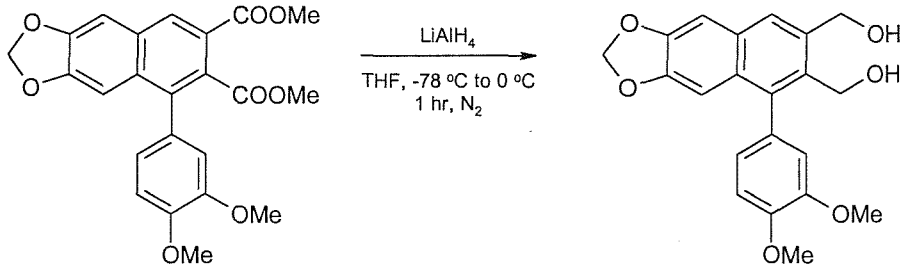
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.65 (1H, s, ArH), 7.10 (1H, s, ArH), 6.93 (1H, d, J = 8.1 Hz, ArH), 6.85-6.70 (3H, m, ArH), 6.13-5.89 (4H, m, OCH_2O), 4.87 (2H, s, CH_2OH), 4.61 (2H, s, CH_2OH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 148.2 (CO (Ar)), 147.9 (CO (Ar)), 147.8 (CO (Ar)), 147.1 (CO (Ar)), 139.6 (C (Ar)), 135.9 (C (Ar)), 133.6 (C (Ar)), 132.6 (C (Ar)), 130.2 (2 x C (Ar)), 128.2 (CH (Ar)), 123.6 (CH (Ar)), 110.9 (CH (Ar)), 108.5 (CH (Ar)), 103.9 (CH (Ar)), 103.8 (CH (Ar)), 101.3 (2 x OCH_2O), 65.4 (CH_2OH), 60.8 (CH_2OH).

LRMS (CI) *m/z:* 321 ($[M - CH_2OH]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 727.1798, $C_{40}H_{32}O_{12}Na$ requires 727.1786.

6,7-Methylenedioxy-1-(3,4-dimethoxyphenyl)naphthalene-2,3-dimethanol (**257**)



251
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

257
mw = 368.39 g mol^{-1}
$C_{21}H_{20}O_6$

To a stirred solution of diester **251** (100 mg, 0.24 mmol) in THF (50 mL) at –78 °C under argon was added lithium aluminium hydride (37 mg, 0.97 mmol). On allowing the reaction mixture to warm to 0 °C over 1 hour, water (0.40 mL) was added. Once effervescence had ceased, 15% NaOH (0.40 mL) and water (0.40 mL) were added and the resultant grey suspension stirred vigorously at ambient temperature for 16 hours. After stirring over anhydrous $MgSO_4$ for 2.5 hours, the reaction mixture was filtered and concentrated *in vacuo* to a pale yellow solid. Purification by column chromatography (90% ether in petrol to neat

ether with 5% methanol) gave **257** as a white solid (64 mg, 0.17 mmol, 74%): mp 179-182 °C, lit. 184 °C.[10,195] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3430 br. w, 2943 w, 1515 w, 1462 s, 1248 s, 1229 m, 1203 w, 1139 m, 1025 s, 1006 w, 941 m, 907 w, 884 w, 851 w, 763 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 314 (2000), 274 (12800), 238 (60400).

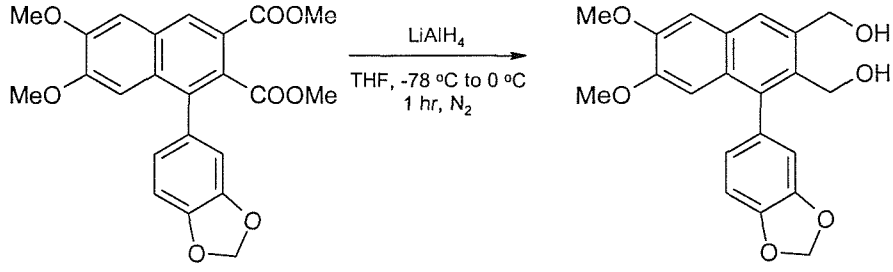
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.68 (1H, s, ArH), 7.13 (1H, s, ArH), 7.00 (1H, d, J = 7.7 Hz, ArH), 6.85 (1H, dd, J = 7.7, 2.0 Hz, ArH), 6.84 (1H, d, J = 2.0 Hz, ArH), 6.76 (1H, s, ArH), 6.01 (2H, s, OCH_2O), 4.91 (2H, s, CH_2OH), 4.62 (2H, s, CH_2OH), 3.98 (3H, s, $ArOCH_3$), 3.86 (3H, s, $ArOCH_3$), 2.64 (2H, br. s, 2 x CH_2OH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 148.8 (CO (Ar)), 148.3 (CO (Ar)), 148.0 (CO (Ar)), 147.8 (CO (Ar)), 139.8 (C (Ar)), 135.8 (C (Ar)), 133.5 (C (Ar)), 131.3 (C (Ar)), 128.0 (C (Ar)), 128.0 (CH (Ar)), 122.3 (C (Ar)), 122.3 (CH (Ar)), 113.3 (CH (Ar)), 111.1 (CH (Ar)), 103.8 (CH (Ar)), 103.7 (CH (Ar)), 101.2 (OCH_2O), 65.5 (CH_2OH), 61.0 (CH_2OH), 56.1 ($ArOCH_3$), 56.1 ($ArOCH_3$).

LRMS (CI) *m/z:* 368 (M^+, 4%), 351 ($[MH - H_2O]^+$, 62%), 350 ($[M - H_2O]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 759.2427, $C_{42}H_{40}O_{12}Na$ requires 759.2412.

6,7-Dimethoxy-1-(3,4- methylenedioxyphenyl)naphthalene-2,3-dimethanol (**258**)



253
mw = 424.41 g mol^{-1}
$C_{23}H_{20}O_8$

258
mw = 368.39 g mol^{-1}
$C_{21}H_{20}O_6$

To a stirred solution of diester **253** (275 mg, 0.65 mmol) in THF (20 mL) at –78 °C under nitrogen was added lithium aluminium hydride (100 mg, 2.66 mmol). On allowing the reaction mixture to warm to 0 °C over 1 hour, water (1 mL) was added. Once effervescence had ceased, 15% NaOH (1 mL) and water (1 mL) were added and the resultant grey suspension stirred vigorously at ambient temperature for 16 hours. After stirring over

anhydrous $MgSO_4$ for 2.5 hours, the reaction mixture was filtered and concentrated *in vacuo* to a white solid. Purification by column chromatography (90% ether in petrol to neat ether with 5% methanol) gave **258** as a white solid (180 mg, 0.49 mmol, 75%): mp 191-193 °C (benzene/petrol), lit. 191 °C.[196]

FT-IR (neat, cm^{-1}): 3320 br. w, 2768 w, 1509 m, 1485 w, 1456 w, 1434 m, 1259 w, 1233 s, 1201 w, 1155 m, 1037 m, 1005 m, 984 m, 928 w, 851 vs.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 331 (6100), 289 (14600), 246 (78500).

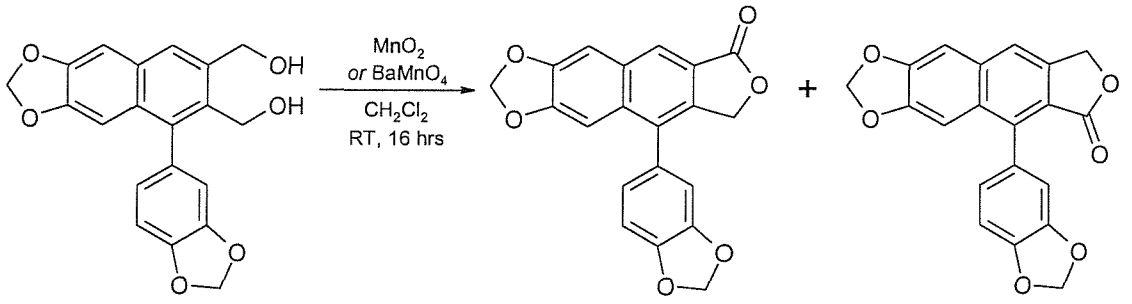
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.64 (1H, s, ArH), 7.09 (1H, s, ArH), 6.93 (1H, d, J = 7.7 Hz, ArH), 6.80 (1H, d, J = 1.7 Hz, ArH), 6.75 (1H, dd, J = 7.7, 1.7 Hz, ArH), 6.72 (1H, s, ArH), 6.08 (1H, d, J = 1.5 Hz, OCHHO), 6.03 (1H, d, J = 1.5 Hz, OCHHO), 4.83 (2H, s, CH_2OH), 4.57 (2H, s, CH_2OH), 3.98 (3H, s, $ArOCH_3$), 3.73 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 150.2 (CO (Ar)), 150.0 (CO (Ar)), 148.1 (CO (Ar)), 147.3 (CO (Ar)), 139.2 (C (Ar)), 136.1 (C (Ar)), 133.6 (C (Ar)), 132.9 (C (Ar)), 129.2 (C (Ar)), 129.0 (C (Ar)), 127.7 (CH (Ar)), 123.9 (CH (Ar)), 111.2 (CH (Ar)), 108.7 (CH (Ar)), 106.7 (CH (Ar)), 106.4 (CH (Ar)), 101.6 (OCH_2O), 65.6 (CH_2OH), 61.1 (CH_2OH), 56.4 (OCH_3), 56.3 (OCH_3).

LRMS (CI) *m/z:* 351 ($[MH - H_2O]^+$, 100%), 350 ($[M - H_2O]^+$, 79%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 759.2444, $C_{42}H_{40}O_{12}Na$ requires 759.2412.

Justicidin E (**6**) and Taiwanin C (**3**): Oxidative Route



256
mw = 352.34 g mol^{-1}
$C_{20}H_{16}O_6$

6
mw = 348.31 g mol^{-1}
$C_{20}H_{12}O_6$

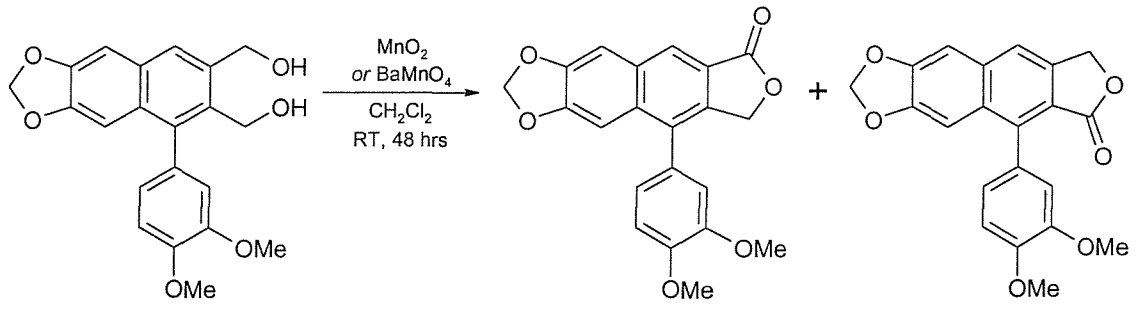
3

To a stirred solution of diol **256** (175 mg, 0.50 mmol) in dichloromethane (25 mL) under argon at ambient temperature was added activated manganese dioxide (2.59 g, 29.8 mmol). The resultant black suspension was stirred for 16 hours then filtered through celite, washing

through with chloroform (250 mL). Concentration of the filtrate *in vacuo* yielded a mustard solid. Purification by column chromatography (5% ethyl acetate in toluene) gave justicidin E **6** as a white solid (102 mg, 0.29 mmol, 59%).

Alternatively, to a stirred solution of diol **256** (50 mg, 0.14 mmol) in dichloromethane (10 mL) under nitrogen at ambient temperature was added barium manganate (364 mg, 1.42 mmol). The resultant black suspension was stirred for 16 hours then filtered through celite, washing through with chloroform (150 mL). The pale yellow filtrate was concentrated *in vacuo* to a cream solid. Purification by column chromatography (5-10% ethyl acetate in toluene) gave firstly justicidin E **6** (35 mg, 0.10 mmol, 71%) then taiwanin C **3** (7.0 mg, 20 μmol, 14%), both as white solids. The data for **3** and **6** has been stated previously.

Retrochinensin (**7**) and Chinensin (**4**): Oxidative Route



257
mw = 368.39 g mol^{-1}
$C_{21}H_{20}O_6$

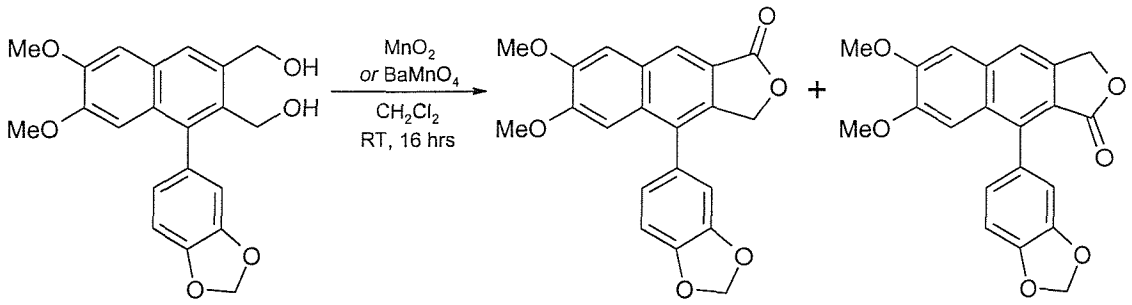
7
mw = 364.35 g mol^{-1}
$C_{21}H_{16}O_6$

4

To a stirred solution of diol **257** (20 mg, 54 μmol) in dichloromethane (10 mL) under argon at ambient temperature was added activated manganese dioxide (284 mg, 3.26 mmol). The resultant black suspension was stirred for 48 hours then filtered through celite, washing through with chloroform (100 mL). Concentration of the filtrate *in vacuo* gave retrochinensin **7** as a white solid (18 mg, 49 μmol, 91%).

Alternatively, to a stirred solution of diol **257** (20 mg, 54 μmol) in dichloromethane (5 mL) under argon at ambient temperature was added barium manganate (140 mg, 0.54 mmol). The resultant black suspension was stirred for 48 hours then filtered through celite, washing through with chloroform (100 mL). The pale yellow filtrate was concentrated *in vacuo* to a cream solid. Purification by column chromatography (5-10% ethyl acetate in toluene) gave first retrochinensin **7** (15.7 mg, 43 μmol, 80%), then chinensin **4** (3.7 mg, 10 μmol, 19%), both as white solids. The data for 4 and 7 has been stated previously.

Retrojusticidin B (**19**) and Justicidin B (**17**): Oxidative Route



258

mw = 368.39 g mol^{-1}

$C_{21}H_{20}O_6$

19

17

mw = 364.35 g mol^{-1}

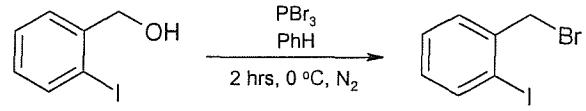
$C_{21}H_{16}O_6$

To a stirred solution of diol **258** (145 mg, 0.39 mmol) in dichloromethane (30 mL) under nitrogen at ambient temperature was added activated manganese dioxide (2.09 g, 24 mmol). The resultant black suspension was stirred for 16 hours then filtered through celite, washing through with chloroform (200 mL). Concentration of the filtrate *in vacuo* yielded an orange semi-solid. Purification by column chromatography (5-10% ethyl acetate in toluene) gave retrojusticidin B **19** as a white solid (62 mg, 0.17 mmol, 44%).

Alternatively, to a stirred solution of diol **258** (25 mg, 68 μmol) in dichloromethane (10 mL) under nitrogen at ambient temperature was added barium manganate (174 mg, 0.68 mmol). The resultant black suspension was stirred for 16 hours then filtered through celite, washing through with chloroform (150 mL). The filtrate was concentrated *in vacuo* to a white solid. Purification by column chromatography (5-10% ethyl acetate in toluene) gave first retrojusticidin B **19** (21 mg, 58 μmol, 86%); then justicidin B **17** (3 mg, 8 μmol, 12%), both as white solids. The data for **17** and **19** has been stated previously.

7.3 Synthetic Procedures for Chapter 4

2-Iodobenzyl bromide (**702b**)



mw = 234.04 g mol^{-1}
C_7H_7IO

702b

mw = 296.93 g mol^{-1}
C_7H_6BrI

To a stirred solution of 2-iodobenzyl alcohol (4.0 g, 17.1 mmol) in benzene (20 mL) at 0 °C under nitrogen was added phosphorus tribromide (0.57 mL, 6.0 mmol) over 5 minutes. After 2 hours, the reaction mixture was diluted with dichloromethane (50 mL), washed with water (30 mL) and saturated sodium bicarbonate solution (30 mL) then dried ($MgSO_4$). Concentration *in vacuo* gave **702b** as a colourless oil that crystallised on standing to a white solid (4.78 g, 16.1 mmol, 94%): mp 54-56 °C, lit. 55-56 °C (petrol).[197] The observed data is consistent with literature values.[198]

FT-IR (neat, cm^{-1}): 3060 w, 1583 w, 1561 w, 1467 w, 1435 w, 1274 w, 1217 w, 1199 w, 1091 w, 1044 w, 1012 w, 945 w, 867 w, 814 w, 755 w, 717 w.

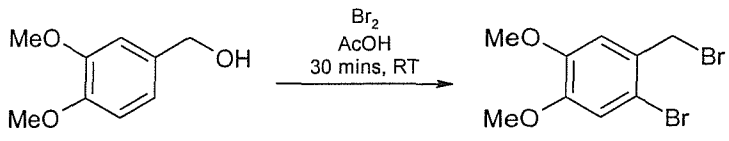
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 224 (10600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.87 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.48 (1H, dd, J = 7.5, 1.7 Hz, ArH), 7.35 (1H, app. td, J = 7.5, 1.2 Hz, ArH), 6.99 (1H, app. td, J = 8.0, 1.7 Hz, ArH), 4.61 (2H, s, ArCH_2Br).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.3 (C (Ar)), 140.2 (CH (Ar)), 130.7 (CH (Ar)), 130.3 (CH (Ar)), 129.1 (CH (Ar)), 100.3 (CI (Ar)), 39.0 (CH_2Br).

LRMS (CI) *m/z:* 298 ([M{^{81}Br}]$^+$, 2%), 296 ([M{^{79}Br}]$^+$, 2%), 234 ([M – Br + NH_4]$^+$, 14%), 217 ([M - Br]$^+$, 27%), 90 ([M – Br – I]$^+$, 100%).

6-Bromo-3,4-dimethoxybenzyl bromide (**702e**)



mw = 168.19 g mol^{-1}
$C_9H_{12}O_3$

702e

mw = 309.98 g mol^{-1}
$C_9H_{10}Br_2O_2$

In accordance with the procedure of Orr *et al.*,[174] to a stirred solution of 3,4-dimethoxybenzyl alcohol (1.64 g, 9.75 mmol) in acetic acid (3 mL) at 0 °C was added a

solution of bromine (0.60 mL, 11.7 mmol) in acetic acid (1.6 mL) *via* dropping funnel over 5 minutes. The reaction mixture was stirred at ambient temperature for 30 minutes, then diluted with water (50 mL) and filtered. The isolated precipitate was washed sequentially with water (50 mL), acetic acid (2 mL) and ice cold ethanol (2 mL) then dried under high vacuum to afford **702e** as a white solid (2.16 g, 6.97 mmol, 71%): mp 78-81 °C, lit. 82-84 °C (ether).[199] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 2965 w, 2930 w, 2905 w, 2838 w, 1598 w, 1501 w, 1434 w, 1382 w, 1342 w, 1260w, 1224 w, 1205 w, 1166 w, 1116 w, 1029 w, 968 w, 861 w, 797 w, 727 w, 677 w.

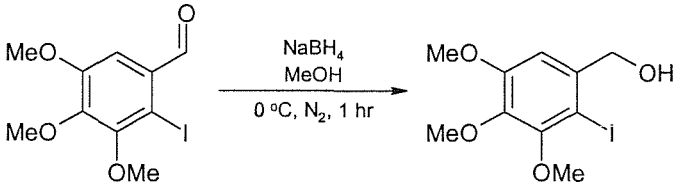
UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 282 (3200), 250 (5800).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.02 (1H, s, Ar<u>H</u>), 6.93 (1H, s, Ar<u>H</u>), 4.59 (2H, s, Ar<u>C</u>H_2Br), 3.88 (3H, s, ArOC<u>H</u>$_3$), 3.87 (3H, s, ArOC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 150.0 (<u>C</u>O (Ar)), 148.7 (<u>C</u>O (Ar)), 128.9 (<u>C</u> (Ar)), 115.8 (<u>C</u>H (Ar)), 115.1 (<u>C</u>Br (Ar)), 113.4 (<u>C</u>H (Ar)), 56.4 (ArO<u>C</u>H_3), 56.3 (ArO<u>C</u>H_3), 34.4 (Ar<u>C</u>H_2Br).

LRMS (CI) *m/z:* 250 ([MH{^{81}Br} - Br + NH_4]$^+$, 17%), 248 ([MH{^{79}Br} - Br + NH_4]$^+$, 25%), 232 ([MH{^{81}Br} – Br]$^+$, 98%), 230 ([MH{^{79}Br} – Br]$^+$, 100%).

<u>2-Iodo-3,4,5-trimethoxybenzyl alcohol (**969**)</u>



mw = 322.09 g mol^{-1}
$C_{10}H_{11}IO_4$

969

mw = 324.11 g mol^{-1}
$C_{10}H_{13}IO_4$

To a stirred solution of 2-iodo-3,4,5-trimethoxybenzaldehyde (1.54 g, 4.79 mmol) in methanol (20 mL) at 0 °C was added sodium borohydride (200 mg, 5.27 mmol). The reaction mixture was stirred at ambient temperature for 1 hour then concentrated *in vacuo*. Water (25 mL) was added and the resultant suspension extracted with ether (3 x 50 mL). The combined ether layers were dried ($MgSO_4$) and concentrated *in vacuo* to give **969** as a colourless oil that crystallised on standing to a waxy white solid (1.44 g, 4.43 mmol, 92%): mp 54-57 °C, lit. 56.5-57.5 °C.[200] The observed data is consistent with literature values.

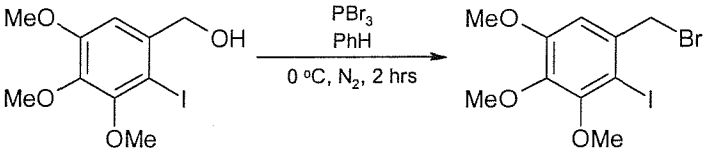
FT-IR (neat, cm^{-1}): 3411 br. w, 2937 w, 2848 w, 1563 w, 1477 w, 1446 w, 1425 w, 1390 w, 1322 w, 1237 w, 1194 w, 1158 w, 1105 w, 1077 w, 1009 w, 960 w, 918 w, 843 w, 800 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 6.91 (1H, s, ArH), 4.61 (2H, d, J = 6.2 Hz, $ArCH_2OH$), 3.86 (3H, s, $ArOCH_3$), 3.85 (6H, s, 2 x $ArOCH_3$), 2.60 (1H, t, J = 6.2 Hz, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.1 (CO (Ar)), 153.0 (CO (Ar)), 141.4 (CO (Ar)), 138.6 (C (Ar)), 108.0 (CH (Ar)), 84.6 (CI (Ar)), 69.4 (CH_2OH), 61.2 ($ArOCH_3$), 61.0 ($ArOCH_3$), 56.3 ($ArOCH_3$).

LRMS (CI) *m/z:* 324 (M^+, 84%), 307 ($[MH - H_2O]^+$, 100%), 198 ($[MH - I]^+$, 60%), 181 ($[MH - H_2O - I]^+$, 66%).

2-Iodo-3,4,5-trimethoxybenzyl bromide (**702f**)



969
mw = 324.11 g mol^{-1}
$C_{10}H_{13}IO_4$

702f
mw = 387.01 g mol^{-1}
$C_{10}H_{12}BrIO_3$

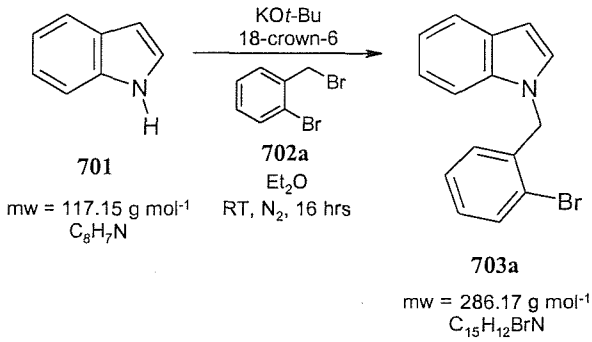
To a stirred solution of 2-iodo-3,4,5-trimethoxybenzyl alcohol **969** (1.44 g, 4.43 mmol) in benzene (20 mL) at 0 °C under nitrogen was added phosphorus tribromide (0.15 mL, 1.55 mmol) over 5 minutes. The solution was stirred at ambient temperature for 2 hours, diluted with dichloromethane (50 mL), washed with water (30 mL) and saturated sodium bicarbonate solution (30 mL) then dried ($MgSO_4$). Concentration *in vacuo* yielded **702f** as a mustard yellow solid that quickly decomposed at room temperature (1.62 g, 4.19 mmol, 95%). As a result, only partial data could be obtained.

^{1}H NMR δ_H ppm (300 MHz, C_6D_6): 6.42 (1H, s, ArH), 4.33 (2H, s, $ArCH_2Br$), 3.61 (3H, s, $ArOCH_3$), 3.56 (3H, s, $ArOCH_3$), 3.14 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, C_6D_6): 154.4 (CO (Ar)), 143.1 (CO (Ar)), 136.0 (CO (Ar)), 110.2 (CH (Ar)), 107.0 (C (Ar)), 89.1 (CI (Ar)), 60.7 ($ArOCH_3$), 60.6 ($ArOCH_3$), 55.7 ($ArOCH_3$), 39.9 (CH_2Br).

LRMS (CI) *m/z*: 307 ($[MH - Br]^+$, 78%), 181 ($[MH - Br - I]^+$, 100%).

N-(2-bromobenzyl)-indole (**703a**)



The procedure of Guida and Mathre was followed.[147] To a stirred solution of 18-crown-6 (119 mg, 0.45 mmol) in ether (10 mL) under nitrogen was added potassium *tert*-butoxide (578 mg, 5.15 mmol) followed by indole **701** (525 mg, 4.48 mmol). On stirring for 15 minutes at ambient temperature the solution was cooled to 0 °C and 2-bromobenzyl bromide **702a** (0.69 mL, 5.15 mmol) was added. After 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 25 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (2.5-5% ether in petrol) gave **703a** as a colourless oil that crystallised on standing to a waxy white solid (1.28 g, 4.48 mmol, 100%): mp 37-38 °C, lit. 39 °C.[201] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3055 w, 2921 w, 1613 w, 1568 w, 1513 w, 1462 w, 1439 w, 1349 w, 1334 w, 1317 w, 1258 w, 1184 w, 1025 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 276 (5600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.71 (1H, dd, J = 7.1, 1.2 Hz, ArH), 7.65-7.60 (1H, m, ArH), 7.30-7.12 (6H, m, ArH), 6.63 (1H, d, J = 3.0 Hz, ArH), 6.58-6.53 (1H, m, ArH), 5.42 (2H, s, NCH_2Ar).

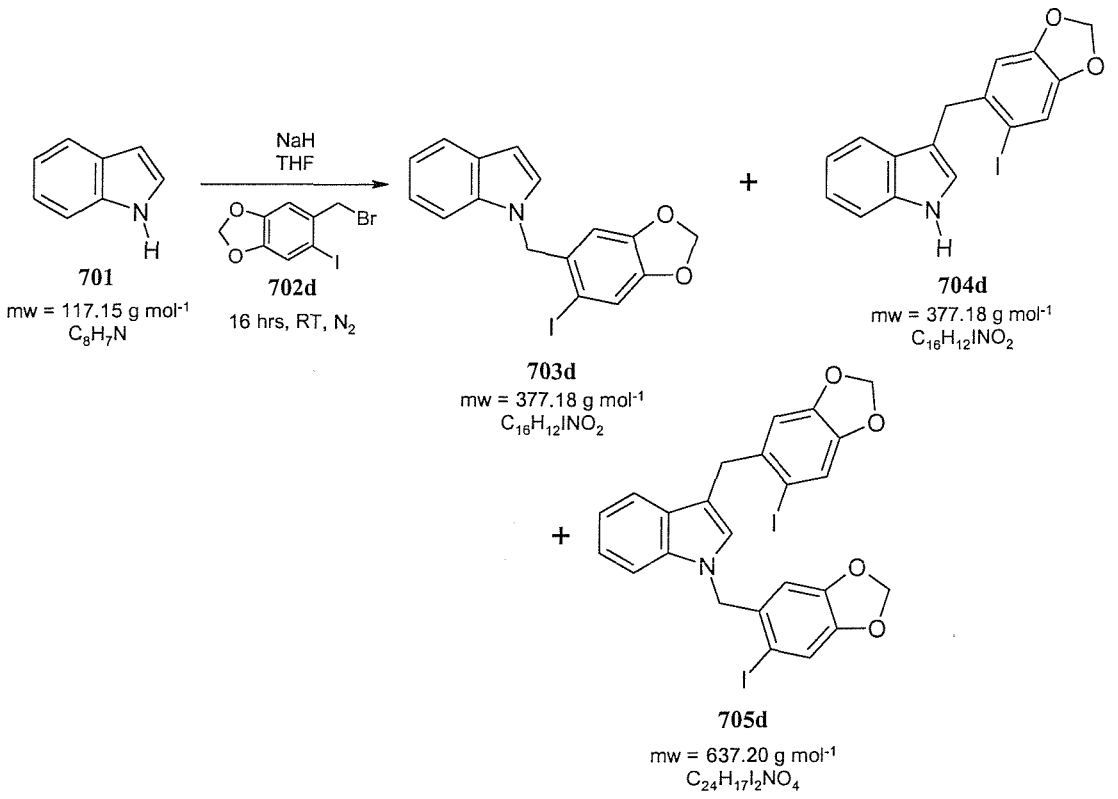
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.4 (C (Ar)), 136.9 (C (Ar)), 136.4 (C (Ar)), 132.9 (CH (Ar)), 129.2 (CH (Ar)), 128.8 (CBr (Ar)), 128.5 (CH (Ar)), 128.2 (CH (Ar)), 128.0 (CH (Ar)), 122.1 (CH (Ar)), 121.2 (CH (Ar)), 119.9 (CH (Ar)), 109.8 (CH (Ar)), 102.3 (CH (Ar)), 50.3 (NCH_2Ar).

LRMS (CI) *m/z*: 288 ($[M\{^{81}Br\}H]^+$, 88%), 286 ($[M\{^{79}Br\}H]^+$, 100%), 206 ($[MH - Br]^+$, 79%).

1-(6-Iodobenzo[1,3]dioxol-5-ylmethyl)-1*H*-indole (**703d**),

3-(6-Iodobenzo[1,3]dioxol-5-ylmethyl)-1*H*-indole (**704d**) and

1,3-*Bis*-(6-iodobenzo[1,3]dioxol-5-ylmethyl)-1*H*-indole (**705d**)



To a stirred suspension of petrol-washed sodium hydride (65 mg, 1.62 mmol, 60% dispersion in mineral oil) in THF (30 mL) at 0 °C under nitrogen was added indole **701** (170 mg, 1.47 mmol). After stirring for a further hour at 0 °C, 2-iodopiperonyl bromide **702d** (0.50 g, 1.47 mmol) in THF (15 mL) was added over 10 minutes. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (10-50% toluene in petrol) gave firstly **703d** as a white solid (109 mg, 0.29 mmol, 20%): mp 132-133 °C; then **705d** as a buff solid (233 mg, 0.37 mmol, 25%): mp 182-185 °C; thirdly recovered indole **701** as a white crystalline solid (24 mg, 0.20 mmol, 14%); and finally **704d** as a white solid (95 mg, 0.25 mmol, 17%): mp 127-128 °C.

*Data for **703d**:*

FT-IR (neat, cm^{-1}): 2901 w, 1504 w, 1461 w, 1435 w, 1313 w, 1258 w, 1227 w, 1105 w, 1034 w, 922 w, 862 w, 763 w, 743 w, 718 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 270 (14700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.69 (1H, dd, J = 7.5, 1.2 Hz, ArH), 7.31 (1H, s, ArH), 7.26 (1H, dd, J = 8.2, 1.7 Hz, ArH), 7.22 (1H, app. td, J = 8.2, 1.2 Hz, ArH), 7.16 (1H, app. td, J = 7.5, 1.7 Hz, ArH), 7.12 (1H, d, J = 3.3 Hz, NCH=CH), 6.60 (1H, dd, J = 3.3, 0.7 Hz, NCH=CH), 6.07 (1H, s, ArH), 5.90 (2H, s, OCH_2O), 5.24 (2H, s, NCH_2Ar).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.1 (CO (Ar)), 148.1 (CO (Ar)), 136.3 (C (Ar)), 133.2 (C (Ar)), 128.9 (C (Ar)), 128.3 (CH (Ar)), 122.1 (CH (Ar)), 121.3 (CH (Ar)), 120.0 (CH (Ar)), 118.8 (CH (Ar)), 109.9 (CH (Ar)), 108.2 (CH (Ar)), 102.4 (CH (Ar)), 101.9 (OCH_2O), 85.1 (CI (Ar)), 55.1 (NCH_2Ar).

LRMS (CI) *m/z*: 378 (MH^+, 100%), 251 ($[MH - I]^+$, 74%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 776.9707, $C_{32}H_{24}I_2N_2O_4Na$ requires 776.9718.

*Data for **704d**:*

FT-IR (neat, cm^{-1}): 3401 w, 2915 w, 2855 w, 1498 w, 1473 w, 1454 w, 1222 w, 1033 w, 928 w, 916 w, 873 w, 763 w, 746 w, 733 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 278 (22000).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.98 (1H, s, NH), 7.55 (1H, d, J = 7.7 Hz, ArH), 7.38 (1H, d, J = 8.0 Hz, ArH), 7.31 (1H, s, ArH), 7.23 (1H, app. td, J = 8.0, 1.2 Hz, ArH), 7.11 (1H, app. td, J = 7.7, 1.2 ArH), 6.94 (1H, d, J = 1.2 Hz, ArH), 6.70 (1H, s, ArH), 5.91 (2H, s, OCH_2O), 4.12 (2H, s, $ArCH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 148.6 (CO (Ar)), 146.9 (CO (Ar)), 137.2 (C (Ar)), 136.6 (C (Ar)), 127.4 (C (Ar)), 123.0 (CH (Ar)), 123.0 (CH (Ar)), 119.7 (CH (Ar)), 119.4 (CH (Ar)), 118.6 (CH (Ar)), 114.7 (C (Ar)), 111.3 (CH (Ar)), 110.0 (CH (Ar)), 101.6 (OCH_2O), 88.2 (CI (Ar)), 37.0 ($ArCH_2Ar$).

LRMS (CI) *m/z*: 378 (MH^+, 56%), 251 ($[MH - I]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 776.9707, $C_{32}H_{24}I_2N_2O_4Na$ requires 776.9718.

*Data for **705d**:*

FT-IR (neat, cm^{-1}): 2955 w, 2920 w, 2855 w, 1499 w, 1465 w, 1427 w, 1330 w, 1233 w, 1099 w, 1036 w, 931 w, 862 w, 824 w, 750 w, 732 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 284 (13800).

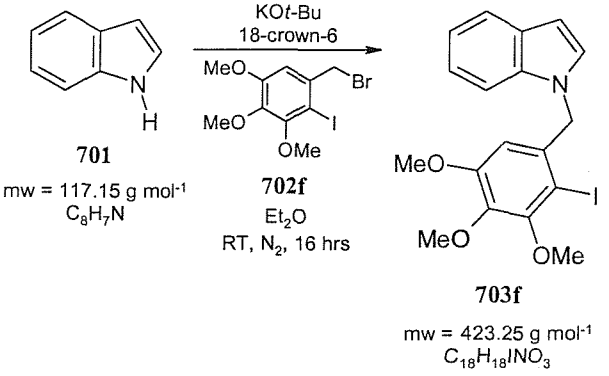
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.56 (1H, d, J = 7.7 Hz, ArH), 7.33-7.07 (5H, m, ArH), 6.83 (1H, s, ArH), 6.74 (1H, s, ArH), 6.07 (1H, s, ArH), 5.92 (2H, s, OCH_2O), 5.90 (2H, s, OCH_2O), 5.18 (2H, s, NCH_2Ar), 4.12 (2H, s, $ArCH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 148.9 (CO (Ar)), 147.9 (CO (Ar)), 146.8 (CO (Ar)), 136.9 (CO (Ar)), 136.7 (C (Ar)), 133.0 (CH (Ar)), 128.2 (C (Ar)), 126.9 (CH (Ar)), 125.3 (C (Ar)), 122.2 (CH (Ar)), 119.5 (2 x CH (Ar)), 118.6 (CH (Ar)), 118.5 (CH (Ar)), 114.2 (C (Ar)), 109.9 (C (Ar)), 109.8 (CH (Ar)), 108.1 (CH (Ar)), 101.7 (OCH_2O), 101.5 (OCH_2O), 84.7 (2 x CI (Ar)), 54.9 (NCH_2Ar), 36.9 ($ArCH_2Ar$).

LRMS (ES^+) *m/z*: 637 (M^+, 6%), 191 (63%), 171 (97%), 153 (100%), 142 (56%), 130 (82%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 659.9162, $C_{24}H_{17}I_2NO_4Na$ requires 659.9139.

N-(2-Iodo-3,4,5-trimethoxybenzyl)-indole (**703f**)



The procedure of Guida and Mathre was followed.[147] To a stirred solution of 18-crown-6 (40 mg, 0.15 mmol) in ether (5 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (194 mg, 1.73 mmol) followed by indole **701** (176 mg, 1.50 mmol). After 15 minutes, the solution was cooled to 0 °C and 2-iodo-3,4,5-trimethoxybenzyl bromide **702f** (670 mg, 1.73 mmol) was added as a solution in ether (5 mL). After a further 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 25 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (5-50% ether in petrol) gave **703f** as a colourless oil (368 mg, 0.87 mmol, 58%).

FT-IR (neat, cm^{-1}): 2934 w, 2849 w, 1562 w, 1479 w, 1461 w, 1425 w, 1388 w, 1318 w, 1242 w, 1194 w, 1161 w, 1102 w, 1033 w, 1004 w, 963 w, 922 w, 834 w, 803 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 276 (9700).

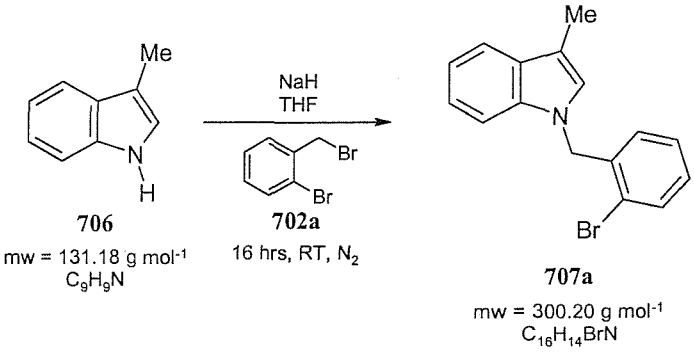
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.70 (1H, br. d, J = 7.2 Hz, ArH), 7.29 (1H, br. d, J = 8.0 Hz, ArH), 7.22 (1H, td, J = 7.2, 1.4 Hz, ArH), 7.16 (1H, td, J = 8.0, 1.4 Hz, ArH), 7.14 (1H, d, J = 3.1 Hz, ArH), 6.62 (1H, d, J = 3.1 Hz, ArH), 5.90 (1H, s, ArH), 5.31 (2H, s, NCH_2Ar), 3.95 (3H, s, $ArOCH_3$), 3.87 (3H, s, $ArOCH_3$), 3.47 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.3 (CO (Ar)), 153.3 (CO (Ar)), 141.5 (CO (Ar)), 136.5 (C (Ar)), 135.4 (C (Ar)), 128.8 (C (Ar)), 128.4 (CH (Ar)), 122.1 (CH (Ar)), 121.2 (CH (Ar)), 119.9 (CH (Ar)), 109.9 (CH (Ar)), 107.3 (CH (Ar)), 102.4 (CH (Ar)), 84.9 (CI (Ar)), 61.2 ($ArOCH_3$), 61.1 ($ArOCH_3$), 56.0 ($ArOCH_3$), 55.4 (NCH_2Ar).

LRMS (CI) *m/z:* 424 (MH^+, 78%), 297 ($[MH - I]^+$, 96%), 181 (100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 446.0217, $C_{18}H_{18}INO_3Na$ requires 446.0224.

N-(2-bromobenzyl)-3-methylindole (**707a**)



706
mw = 131.18 g mol^{-1}
C_9H_9N

702a
16 hrs, RT, N_2

707a
mw = 300.20 g mol^{-1}
$C_{16}H_{14}BrN$

To a stirred suspension of petrol-washed sodium hydride (192 mg, 4.8 mmol, 60% dispersion in mineral oil) in THF (80 mL) at 0 °C under nitrogen was added 3-methylindole **706** (525 mg, 4.0 mmol). After stirring for 1 hour at ambient temperature, the solution was cooled to 0 °C and 2-bromobenzyl bromide **702a** (0.56 mL, 4.2 mmol) was added over 5 minutes. The solution was stirred for 16 hours, then diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (5% ether in petrol) gave **707a** as large white plates (948 mg, 3.16 mmol, 79%): mp 99-101 °C (petrol).

FT-IR (neat, cm^{-1}): 3050 w, 2911 w, 1465 w, 1438 w, 1425 w, 1385 w, 1349 w, 1333 w, 1199 w, 1182 w, 1021 w, 1012 w, 787 w, 746 w, 661 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 280 (6800), 227 (24000).

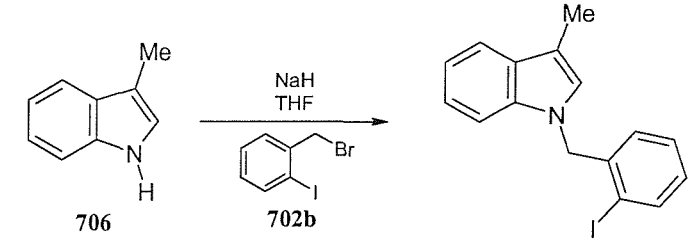
^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 7.70-7.50 (2H, m, ArH), 7.33-6.98 (6H, m, ArH), 6.63-6.49 (1H, m, ArH), 5.40 (2H, s, NCH_2Ar), 2.32 (3H, s, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, D_6-acetone): 137.6 (C (Ar)), 136.8 (C (Ar)), 132.8 (CH (Ar)), 129.2 (CH (Ar)), 129.1 (C (Ar)), 128.3 (CH (Ar)), 127.9 (CH (Ar)), 126.3 (CH (Ar)), 121.9 (C (Ar)), 121.6 (CH (Ar)), 118.9 (2 x CH (Ar)), 110.6 (CBr (Ar)), 109.6 (CH (Ar)), 49.4 (NCH_2Ar), 8.93 ($ArCH_3$).

LRMS (CI) *m/z*: 302 ($[M\{^{81}Br\}H]^+$, 65%), 300 ($[M\{^{79}Br\}H]^+$, 100%), 220 ($[M - Br]^+$, 51%).

CHN Found: C, 63.87; H, 4.70; N, 4.60; $C_{16}H_{14}BrN$ requires C, 64.02; H, 4.70; N, 4.66.

N-(2-iodobenzyl)-3-methylindole (**707b**)



To a stirred suspension of petrol-washed sodium hydride (192 mg, 4.8 mmol, 60% dispersion in mineral oil) in THF (80 mL) at 0 °C under nitrogen was added 3-methylindole **706** (525 mg, 4.0 mmol). After 1 hour the solution was cooled to 0 °C and 2-iodobenzyl bromide **702b** (1.25 g, 4.2 mmol) in THF (20 mL) was added over 5 minutes. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (5% ether in petrol) gave **707b** as large white plates (1.38 g, 3.98 mmol, 99%): mp 94-96 °C (petrol).

FT-IR (neat, cm^{-1}): 2910 w, 1561 w, 1462 w, 1435 w, 1329 w, 1195 w, 1179 w, 1008 w, 737 w, 649 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 274 (8700), 226 (36900).

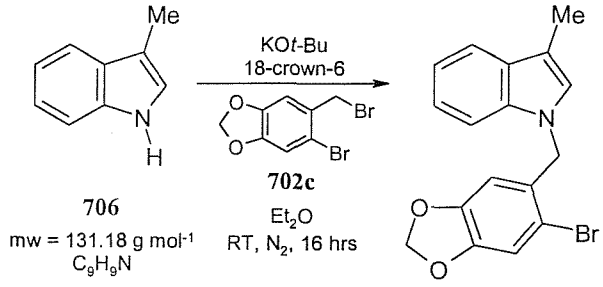
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.89 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.64 (1H, dd, J = 7.7, 1.2 Hz, ArH), 7.23-7.12 (4H, m, ArH), 6.97 (1H, app. td, J = 8.0, 1.2 Hz, ArH), 6.90 (1H, d, J = 1.0 Hz, ArH), 6.50 (1H, dd, J = 7.7, 1.4 Hz, ArH), 5.26 (2H, s, NCH_2Ar), 2.38 (3H, d, J = 1.2 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.1 (C (Ar)), 139.6 (CH (Ar)), 136.9 (C (Ar)), 129.5 (CH (Ar)), 129.2 (C (Ar)), 129.0 (CH (Ar)), 127.9 (CH (Ar)), 126.1 (CH (Ar)), 122.2 (CH (Ar)), 119.4 (CH (Ar)), 119.3 (CH (Ar)), 111.6 (C (Ar)), 109.8 (CH (Ar)), 97.3 (CI (Ar)), 55.1 (NCH_2Ar), 10.0 ($ArCH_3$).

LRMS (CI) *m/z*: 348 (MH^+, 100%), 221 ($[MH - I]^+$, 76%)

CHN Found: C, 55.51; H, 4.08; N, 4.02; $C_{16}H_{14}IN$ requires C, 55.35; H, 4.06; N, 4.03.

N-(2'-Bromo-4',5'-methylenedioxybenzyl)-3-methylindole (**707c**)



The procedure of Guida and Mathre was followed.[147] To a stirred solution of 18-crown-6 (48 mg, 0.18 mmol) in ether (5 mL) under nitrogen was added potassium *tert*-butoxide (230 mg, 2.05 mmol) followed by 3-methyl-indole **706** (233 mg, 1.78 mmol). After 15 minutes the solution was cooled to 0 °C and 6-bromo-4,5-methylenedioxybenzyl bromide **702c** (597 mg, 2.05 mmol) was added. After 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 25 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a brown solid. Purification by column chromatography (2.5-20% ether in petrol) gave **707c** as a white solid that gave large white prisms on recrystallisation (407 mg, 1.18 mmol, 66%): mp 177-179 °C (ether/petrol).

FT-IR (neat, cm^{-1}): 2912 w, 2887 w, 2857 w, 1614 w, 1479 w, 1467 w, 1429 w, 1384 w, 1362 w, 1331 w, 1238 w, 1192 w, 1154 w, 1102 w, 1036 w, 934 w, 856 w, 832 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 278 (14300).

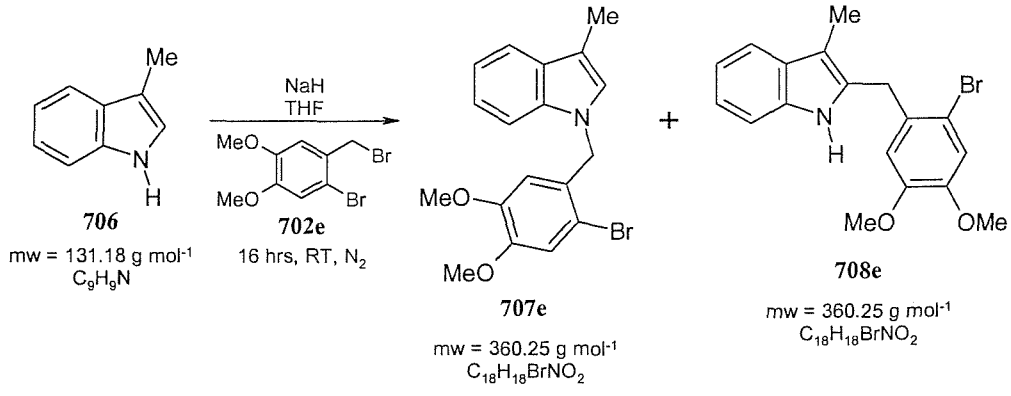
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.63 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.26-7.20 (1H, obsc. m, ArH), 7.22 (1H, ddd, J = 8.0, 6.1, 1.2 Hz, ArH), 7.16 (1H, ddd, J = 8.0, 6.1, 2.1 Hz, ArH), 7.06 (1H, s, ArH), 6.90 (1H, br. d, J = 0.9 Hz, ArH), 6.10 (1H, s, ArH), 5.90 (2H, s, OCH_2O), 5.24 (2H, s, NCH_2Ar), 2.38 (3H, d, J = 0.9 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 148.0 (CO (Ar)), 147.9 (CO (Ar)), 136.6 (C (Ar)), 130.5 (C (Ar)), 129.1 (C (Ar)), 125.9 (CH (Ar)), 122.0 (CH (Ar)), 119.3 (CH (Ar)), 119.2 (CH (Ar)), 112.8 (CH (Ar)), 112.6 (C (Ar)), 111.5 (CBr (Ar)), 109.6 (CH (Ar)), 108.3 (CH (Ar)), 101.9 (OCH_2O), 49.8 (NCH_2Ar), 9.9 (CH_3).

LRMS (CI) *m/z:* 346 ([M{^{81}Br}H]$^+$, 84%), 344 ([M{^{79}Br}H]$^+$, 96%), 264 ([MH - Br]$^+$, 73%), 215 (100%).

CHN Found C, 59.30; H, 4.09; N, 4.05; $C_{17}H_{14}BrNO_2$ requires C, 59.32; H, 4.10; N, 4.07.

N-(6-Bromo-3,4-dimethoxybenzyl)-3-methylindole (**707e**) and
2-(6-Bromo-3,4-dimethoxy-benzyl)-3-methylindole (**708e**)



To a stirred suspension of petrol-washed sodium hydride (192 mg, 4.8 mmol, 60% dispersion in mineral oil) in THF (80 mL) at 0 °C under nitrogen was added 3-methylindole **706** (525 mg, 4.0 mmol). After 1 hour at ambient temperature, the solution was cooled to 0 °C and 6-bromo-3,4-dimethoxybenzyl bromide **702e** (1.30 g, 4.2 mmol) in THF (20 mL) was added over 5 minutes. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (10-60% ether in petrol) gave **707e** as a pale yellow oil (879 mg, 2.44 mmol, 61%); then **708e** as a white solid that yielded small white needles on recrystallisation (266 mg, 0.74 mmol, 18%): mp 166-167 °C (ether/petrol).

Data for 707e:

FT-IR (neat, cm^{-1}): 2935 w, 2838 w, 1503 w, 1463 w, 1434 w, 1382 w, 1351 w, 1329 w, 1258 w, 1207 w, 1179 w, 1157 w, 1028 w, 1013 w, 853 w, 801 w, 734 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 276 (10400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.60 (1H, dd, J = 7.7, 1.2 Hz, Ar$\underline{H}$), 7.27 (1H, dd, J = 7.7, 1.2 Hz, Ar$\underline{H}$), 7.20 (1H, app. td, J = 7.7, 1.2 Hz, Ar$\underline{H}$), 7.13 (1H, app. td, J = 7.7, 1.2 Hz, Ar$\underline{H}$), 7.06 (1H, s, Ar$\underline{H}$), 6.89 (1H, d, J = 1.2 Hz, Ar$\underline{H}$), 6.23 (1H, s, Ar$\underline{H}$), 5.26 (2H, s, NC$\underline{H}_2$Ar), 3.87 (3H, s, ArOC$\underline{H}_3$), 3.54 (3H, s, ArOC$\underline{H}_3$), 2.36 (3H, s, ArC$\underline{H}_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.1 (C(Ar)), 148.9 (C(Ar)), 136.8 (C(Ar)), 129.0 (C(Ar)), 125.8 (CH(Ar)), 121.9 (CH(Ar)), 119.2 (CH(Ar)), 119.1 (CH(Ar)), 116.0 (C(Ar)), 115.6 (CH(Ar)), 112.6 (C(Ar)), 111.4 (CH(Ar)), 111.3 (C(Ar)), 109.6 (CH(Ar)), 56.4 (ArOCH$_3$), 56.0 (ArOCH$_3$), 49.7 (NCH$_2$Ar), 9.9 (ArCH$_3$).

LRMS (CI) *m/z*: 362 ([MH{^{81}Br}]$^+$, 89%), 360 ([MH{^{79}Br}]$^+$, 100%), 280 ([M - Br]$^+$, 28%).

HRMS (ES$^+$) *m/z* Found: [M + Na]$^+$ 382.0421, $C_{18}H_{18}[^{79}Br]NO_2Na$ requires 382.0413.

Data for 708e:

FT-IR (neat, cm^{-1}): 3405 w, 2907 w, 2865 w, 1502 w, 1461 w, 1431 w, 1342 w, 1255 w, 1220 w, 1212 w, 1158 w, 1100 w, 1042 w, 1022 w, 962 w, 842 w, 798 w, 740 w, 635 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 270 (13500).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.78 (1H, br. s, N$\underline{H}$), 7.55 (1H, dd, J = 7.0, 1.7 Hz, Ar$\underline{H}$), 7.25 (1H, dd, J = 7.1, 1.7 Hz, Ar$\underline{H}$), 7.13 (1H, app. td, J = 7.1, 1.7 Hz, Ar$\underline{H}$), 7.11 (1H, td, J = 7.0, 1.7 Hz, Ar$\underline{H}$), 7.07 (1H, s, Ar$\underline{H}$), 6.65 (1H, s, Ar$\underline{H}$), 4.16 (2H, s, ArC$\underline{H}_2$Ar), 3.87 (3H, s, ArOC$\underline{H}_3$), 3.74 (3H, s, ArOC$\underline{H}_3$), 2.36 (ArC$\underline{H}_3$).

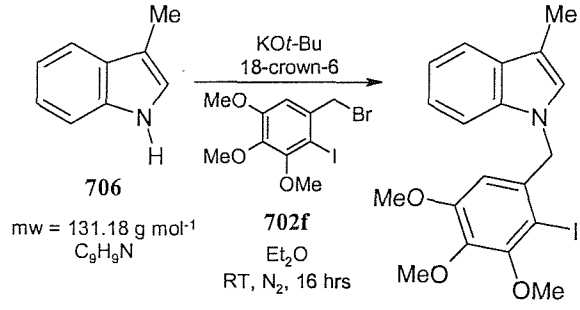
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 149.2 (C(Ar)), 148.9 (C(Ar)), 135.9 (C(Ar)), 132.6 (C(Ar)), 130.8 (C(Ar)), 129.6 (C(Ar)), 121.8 (CH(Ar)),

119.5 (CH (Ar)), 118.7 (CH (Ar)), 116.0 (CH (Ar)), 114.4 (C (Ar)), 113.6 (CH (Ar)), 111.1 (CH (Ar)), 108.4 (CBr (Ar)), 56.6 ($ArOCH_3$), 56.5 ($ArOCH_3$), 32.7 ($ArCH_2Ar$), 9.1 ($ArCH_3$).

LRMS (CI) *m/z*: 362 ($[MH\{^{81}Br\}]^+$, 81%), 360 ($[MH\{^{79}Br\}]^+$, 100%), 282 ($[MH-Br]^+$, 65%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 741.0923, $C_{36}H_{36}[^{79}Br]_2N_2O_4Na$ requires 741.0934.

N-(2'-Iodo-3',4',5'-trimethoxybenzyl)-3-methylindole (**707f**)



The procedure of Guida and Mathre was followed.[147] To a stirred solution of 18-crown-6 (40 mg, 0.15 mmol) in ether (5 mL) under nitrogen was added potassium *tert*-butoxide (194 mg, 1.73 mmol) followed by 3-methyl-indole **706** (197 mg, 1.50 mmol). After stirring for 15 minutes at ambient temperature the solution was cooled to 0 °C and 2-iodo-3,4,5-trimethoxybenzyl bromide **702f** (670 mg, 1.73 mmol) in ether (5 mL) added. After 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 25 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (2.5-50% ether in petrol) gave **707f** as a colourless oil (437 mg, 1.0 mmol, 67%).

FT-IR (neat, cm^{-1}): 3050 w, 2970 w, 2934 w, 2887 w, 2858 w, 1616 w, 1561 w, 1467 w, 1421 w, 1388 w, 1339 w, 1317 w, 1265 w, 1238 w, 1190 w, 1157 w, 1100 w, 1008 w, 922 w, 832 w, 801 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 276 (11700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.62 (1H, d, J = 7.7 Hz, ArH), 7.24 (1H, dd, J = 8.0, 1.7 Hz, ArH), 7.20 (1H, td, J = 8.0, 1.2 Hz, ArH), 7.14 (1H, ddd, J = 8.0, 7.7, 1.7 Hz, ArH), 6.89 (1H, br. d, J = 0.9 Hz, ArH), 5.95 (1H, s,

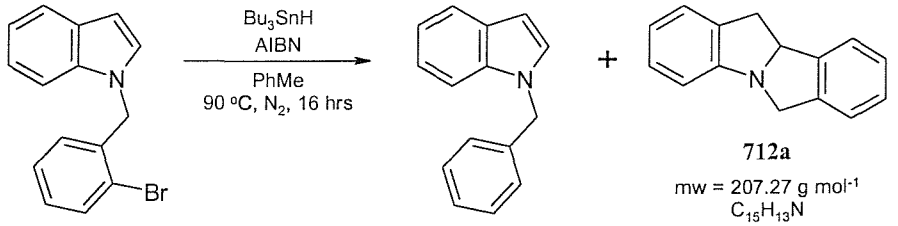
ArH), 5.23 (2H, s, NCH_2Ar), 3.93 (3H, s, $ArOCH_3$), 3.85 (3H, s, $ArOCH_3$), 3.47 (3H, s, $ArOCH_3$), 2.37 (3H, d, $J = 0.9$ Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.2 (CO (Ar)), 153.2 (CO (Ar)), 141.5 (CO (Ar)), 136.9 (C (Ar)), 135.7 (C (Ar)), 129.0 (C (Ar)), 125.9 (CH (Ar)), 122.0 (CH (Ar)), 119.3 (CH (Ar)), 119.2 (CH (Ar)), 111.5 (C (Ar)), 109.7 (CH (Ar)), 107.4 (CH (Ar)), 84.9 (CI (Ar)), 61.1 (OCH_3), 61.0 (OCH_3), 56.1 (OCH_3), 55.1 (NCH_2Ar), 9.9 (CH_3).

LRMS (CI) *m/z:* 438 (MH^+, 28%), 311 ($[MH - I]^+$, 52%), 181 (100%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 897.0840, $C_{38}H_{40}I_2N_2O_6Na$ requires 897.0868.

N-Benzyl-indole (**711a**) and 10*b*,11-Dihydro-6*H*-isoindolo[2,1-*a*]indole (**712a**)



703a
mw = 286.17 g mol^{-1}
$C_{15}H_{12}BrN$

711a
mw = 207.27 g mol^{-1}
$C_{15}H_{13}N$

712a
mw = 207.27 g mol^{-1}
$C_{15}H_{13}N$

To a stirred solution of **703a** (0.8 g, 2.80 mmol) in toluene (80 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.90 mL, 3.36 mmol) followed by AIBN (92 mg, 0.56 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (40 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (100 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5-20% ether in petrol followed by 2.5-10% toluene in petrol) gave firstly recovered **703a** as a colourless oil that crystallised on standing to a waxy white solid (80 mg, 0.28 mmol, 10%); then **711a** as a buff solid that gave large colourless prisms on recrystallisation (247 mg, 1.19 mmol, 43%): mp 44-46 °C (petrol), lit. 40-42 °C (ethanol);[202] and finally **712a** as a pale yellow oil which crystallised on standing to small yellow needles (184 mg, 0.89 mmol, 32%): mp 74-77 °C, lit. 82-85 °C.[102] The observed data for **711a** and **712a** is consistent with literature values.

*Data for **711a**:*

FT-IR (neat, cm^{-1}): 3124 w, 3101 w, 3054 w, 3026 w, 2937 w, 1610 w, 1587 w, 1509 w, 1485 w, 1463 w, 1441 w, 1353 w, 1337 w, 1318 w, 1257 w, 1179 w, 1078 w, 1010 w, 925 w, 865 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 310 (2100), 262 (13500).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.70 (1H, dd, J = 7.0, 1.1 Hz, ArH), 7.37-7.26 (4H, m, ArH), 7.23 (1H, td, J = 7.0, 1.1 Hz, ArH), 7.19-7.12 (4H, m, ArH), 6.61 (1H, dd, J = 3.3, 0.8 Hz, ArH), 5.36 (2H, s, NCH_2Ar).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 137.7 (2 x C (Ar)), 136.5 (C (Ar)), 128.9 (2 x CH (Ar)), 128.5 (CH (Ar)), 127.8 (CH (Ar)), 126.9 (2 x CH (Ar)), 121.9 (CH (Ar)), 121.2 (CH (Ar)), 119.7 (CH (Ar)), 109.9 (CH (Ar)), 101.9 (CH (Ar)), 50.2 (NCH_2Ar).

LRMS (CI) *m/z:* 207 (M^+, 100%).

*Data for **712a**:*

FT-IR (neat, cm^{-1}): 3068 w, 3038 w, 2919 w, 2879 w, 2855 w, 1601 w, 1478 w, 1458 w, 1345 w, 1271 w, 1252 w, 1218 w, 1197 w, 1164 w, 1117 w, 1056 w, 1025 w, 935 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 286 (3800).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.35-7.22 (4H, m, ArH), 7.15 (1H, d, J = 8.2 Hz, ArH), 7.11 (1H, d, J = 7.0 Hz, ArH), 6.84 (1H, d, J = 7.7 Hz, ArH), 6.82 (1H, td, J = 7.5, 0.9 Hz, ArH), 5.24 (1H, br. d, J = 9.8 Hz, NCH), 4.67 (1H, dd, J = 15.0, 1.4 Hz, NCHHAr), 4.54 (1H, d, J = 15.0 Hz, NCHHAr), 3.57 (1H, dd, J = 15.7, 9.8 Hz, ArCHH), 3.40 (1H, dd, J = 15.7, 2.8 Hz, ArCHH).

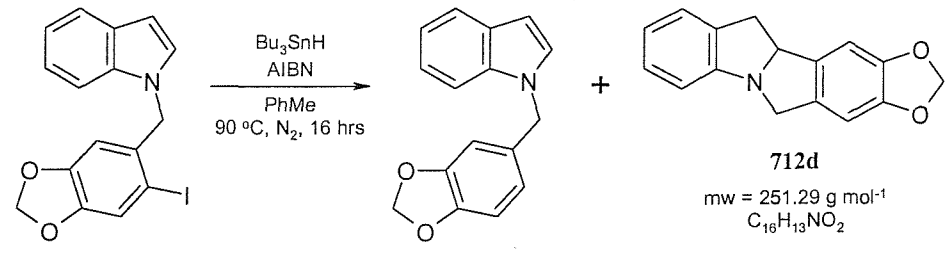
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.5 (C (Ar)), 144.0 (C (Ar)), 140.0 (C (Ar)), 129.9 (C (Ar)), 127.8 (CH (Ar)), 127.8 (CH (Ar)), 127.5 (CH (Ar)), 125.0 (CH (Ar)), 122.8 (CH (Ar)), 122.4 (CH (Ar)), 120.7 (CH (Ar)), 112.1 (CH (Ar)), 69.7 (NCH), 59.3 (NCH_2Ar), 35.4 ($ArCH_2$).

LRMS (CI) *m/z:* 208 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 208.1121, $C_{15}H_{14}N$ requires 208.1121.

N-(3,4-Methylenedioxybenzyl)-indole (**711d**) and

8,9-Methylenedioxy-10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indole (**712d**)



703d

mw = 377.18 g mol^{-1}
$C_{16}H_{12}INO_2$

711d

mw = 251.29 g mol^{-1}
$C_{16}H_{13}NO_2$

712d

mw = 251.29 g mol^{-1}
$C_{16}H_{13}NO_2$

To a stirred solution of **703d** (50 mg, 0.13 mmol) in toluene (5 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (47 mg, 0.16 mmol) followed by AIBN (4 mg, 27 μmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5-20% ether in petrol) gave firstly **711d** as a pale yellow oil (15 mg, 60 μmol, 45%); then **712d** as a pale yellow oil (14 mg, 56 μmol, 42%).

*Data for **711d**:*

FT-IR (neat, cm^{-1}): 2960 w, 2917 w, 2849 w, 1498 w, 1484 w, 1463 w, 1439 w, 1432 w, 1323 w, 1314 w, 1268 w, 1233 w, 1178 w, 1036 w, 937 w, 921 w, 802 w, 732 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 310 (1300), 270 (9400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.65 (1H, app. d, J = 7.5 Hz, ArH), 7.31 (1H, d, J = 7.5 Hz, ArH), 7.20 (1H, app. td, J = 7.5, 1.2 Hz, ArH), 7.13 (1H, d, J = 3.3 Hz, NCH=CH), 7.12 (1H, app. td, J = 7.5, 1.2 Hz, ArH), 6.75 (1H, d, J = 8.0 Hz, ArH), 6.65 (1H, dd, J = 8.0, 1.2 Hz, ArH), 6.60 (1H, d, J = 1.2 Hz, ArH), 6.56 (1H, dd, J = 3.3, 0.9 Hz, NCH=CH), 5.92 (2H, s, OCH_2O), 5.23 (2H, s, NCH_2Ar).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 148.5 (CO (Ar)), 147.5 (CO (Ar)), 136.6 (C (Ar)), 131.8 (C (Ar)), 129.2 (C (Ar)), 128.5 (CH (Ar)), 122.1 (CH (Ar)), 121.4 (CH (Ar)), 120.6 (CH (Ar)), 120.0 (CH (Ar)), 110.1 (CH (Ar)), 108.8

(CH (Ar)), 107.9 (CH (Ar)), 102.1 (CH (Ar)), 101.5 (OCH_2O), 50.4 (NCH_2Ar).

LRMS (CI) *m/z*: 252 (MH^+, 100%).

HRMS (EI) *m/z* Found: M^+ 251.0946, $C_{16}H_{13}NO_2$ requires 251.0946.

*Data for **712d**:*

FT-IR (neat, cm^{-1}): 2916 w, 2849 w, 1601 w, 1497 w, 1473 w, 1461 w, 1327 w, 1309 w, 1289 w, 1267 w, 1196 w, 1153 w, 1139 w, 1106 w, 1059 w, 1033 w, 930 w, 749 w, 722 w, 673 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 284 (9400), 224 (12600).

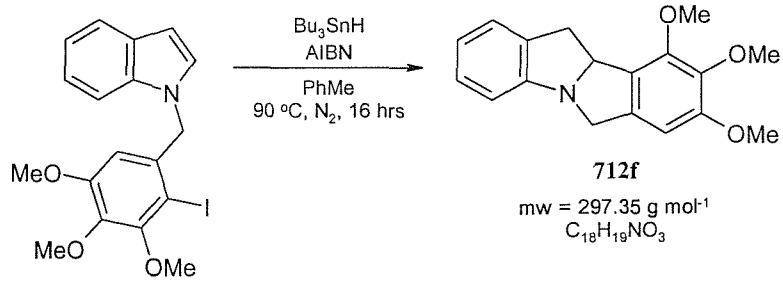
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.16-7.06 (2H, m, ArH), 6.83-6.76 (2H, m, ArH), 6.73 (1H, s, ArH), 6.64 (1H, s, ArH), 5.94 (1H, d, J = 1.4 Hz, OCHHO), 5.91 (1H, d, J = 1.4 Hz, OCHHO), 5.12 (1H, app. d, J = 9.4 Hz, NCH), 4.55 (1H, dd, J = 14.6, 2.1 Hz, NCHHAr), 4.40 (1H, d, J = 14.6 Hz, NCHHAr), 3.48 (1H, dd, J = 15.7, 9.4 Hz, ArCHH), 3.30 (1H, dd, J = 15.7, 2.1 Hz, ArCHH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 154.5 (CO (Ar)), 148.2 (CO (Ar)), 148.0 (C (Ar)), 137.1 (C (Ar)), 132.8 (C (Ar)), 130.0 (C (Ar)), 128.1 (CH (Ar)), 125.2 (CH (Ar)), 121.2 (CH (Ar)), 112.5 (CH (Ar)), 103.5 (CH (Ar)), 103.1 (CH (Ar)), 101.8 (OCH_2O), 69.8 (NCH), 59.6 (NCH_2Ar), 35.6 ($ArCH_2$).

LRMS (CI) *m/z*: 252 (MH^+, 100%).

HRMS (EI) *m/z* Found: $[MH]^+$ 252.1017, $C_{16}H_{14}NO_2$ requires 252.1019.

8,9,10-Trimethoxy-10*b*,11-dihydro-6*H*-isoindolo[2,1-*a*]indole (**712f**)



703f
mw = 423.25 g mol^{-1}
$C_{18}H_{18}INO_3$

712f
mw = 297.35 g mol^{-1}
$C_{18}H_{19}NO_3$

To a stirred solution of indole **703f** (226 mg, 0.53 mmol) in toluene (15 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.20 mL, 0.74 mmol) followed

by AIBN (20 mg, 0.12 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10-40% ether in petrol) gave **712f** as a white crystalline solid (126 mg, 0.42 mmol, 80%): mp 117-120 °C.

FT-IR (neat, cm^{-1}): 2927 w, 1589 w, 1463 w, 1412 w, 1332 w, 1259 w, 1238 w, 1190 w, 1106 w, 1079 w, 1047 w, 1022 w, 1004 w, 963 w, 926 w, 836 w, 760 w, 742 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.13 (1H, t, J = 8.0 Hz, ArH), 7.11 (1H, d, J = 8.0 Hz, ArH), 6.81 (1H, t, J = 7.3 Hz, ArH), 6.80 (1H, d, J = 7.3 Hz, ArH), 6.52 (1H, s, ArH), 5.33 (1H, br. d, J = 9.4 Hz, NCH), 4.58 (1H, dd, J = 14.5, 1.2 Hz, NCHHAr), 4.44 (1H, d, J = 14.5 Hz, NCHHAr), 4.00 (3H, s, $ArOCH_3$), 3.85 (3H, s, $ArOCH_3$), 3.83 (3H, s, $ArOCH_3$), 3.58 (1H, dd, J = 16.2, 3.8 Hz, ArCHH), 3.48 (1H, dd, J = 16.2, 9.4 Hz, ArCHH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.5 (CO (Ar)), 154.3 (CO (Ar)), 149.5 (CO (Ar)), 141.0 (C (Ar)), 135.4 (C (Ar)), 130.6 (C (Ar)), 127.7 (CH (Ar)), 127.6 (C (Ar)), 124.9 (CH (Ar)), 120.7 (CH (Ar)), 112.1 (CH (Ar)), 101.4 (CH (Ar)), 69.0 (NCHAr), 61.2 (OCH_3), 60.7 (OCH_3), 59.9 (NCH_2Ar), 56.4 (OCH_3), 34.6 ($ArCH_2$).

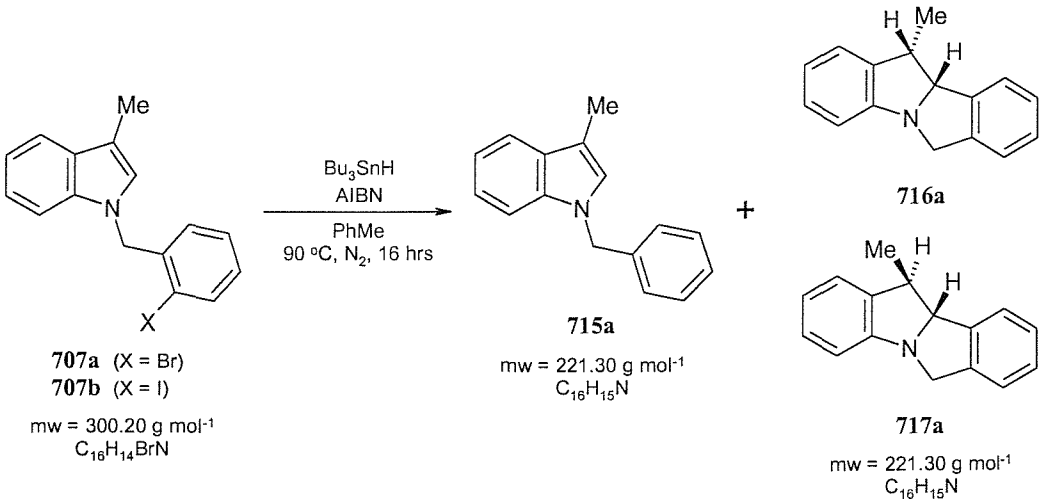
LRMS (CI) *m/z:* 298 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 298.1434, $C_{18}H_{20}NO_3$ requires 298.1438.

N-(Benzyl)-3-methyl-indole (**715a**),

11-Methyl-10*b*R*,11R*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**716a**) and

11-Methyl-10*b*R*,11S*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**717a**)



707a (X = Br)
707b (X = I)

mw = 300.20 g mol^{-1}
$C_{16}H_{14}BrN$

715a

mw = 221.30 g mol^{-1}
$C_{16}H_{15}N$

716a

717a

mw = 221.30 g mol^{-1}
$C_{16}H_{15}N$

To a stirred solution of **707a** (600 mg, 2.0 mmol) in toluene (45 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (700 mg, 2.40 mmol) followed by AIBN (66 mg, 0.40 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (2-20% ether in petrol, then 5-15% toluene in petrol) gave firstly recovered **707a** as a white solid (95 mg, 0.32 mmol, 16%); then **715a** as a white waxy solid (47 mg, 0.21 mmol, 11%): mp 68-69 °C, lit. 72-73.5 °C (petrol);[203] and finally a 1:1 mixture of **716a** and **717a** as a yellow oil, inseparable by chromatography (170 mg, 0.77 mmol, 38%). The observed data for **715a** is consistent with literature values.[204]

Alternatively, to a stirred solution of **707b** (700 mg, 2.0 mmol) in toluene (45 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (700 mg, 2.40 mmol) followed by AIBN (66 mg, 0.40 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (1-10% ether in petrol, then 2.5-10% toluene in petrol) gave firstly recovered **707b** as a white solid (93 mg, 0.27 mmol, 13%); then **715a** as a white waxy solid (73 mg, 0.33 mmol,

16%); and finally a 1:1 mixture of **716a** and **717a** as a yellow oil, inseparable by chromatography (157 mg, 0.71 mmol, 35%). NMR assignments for **716a** and **717a** were confirmed by ^{1}H-^{1}H and ^{1}H-^{13}C COSY experiments.

Data for 715a:

FT-IR (neat, cm^{-1}): 3030 w, 2914 w, 2850 w, 1466 w, 1452 w, 1439 w, 1387 w, 1356 w, 1329 w, 1258 w, 1178 w, 1011 w, 730 w, 694 w, 669 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 276 (6900).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.64 (1H, dd, J = 6.8, 1.4 Hz, ArH), 7.37-7.26 (4H, m, ArH), 7.22 (1H, app. td, J = 6.8, 1.4 Hz, ArH), 7.19-7.12 (3H, m, ArH), 6.93 (1H, br. d, J = 0.9 Hz, ArH), 5.30 (2H, s, $ArCH_2Ph$), 2.39 (3H, d, J = 0.9 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 138.1 (C (Ar)), 136.8 (C (Ar)), 129.1 (C (Ar)), 128.9 (2 x CH (Ar)), 127.7 (CH (Ar)), 127.0 (2 x CH (Ar)), 126.0 (CH (Ar)), 121.8 (CH (Ar)), 119.2 (CH (Ar)), 119.0 (CH (Ar)), 111.0 (C (Ar)), 109.6 (CH (Ar)), 49.9 ($ArCH_2Ph$), 9.9 ($ArCH_3$).

LRMS (CI) *m/z*: 222 (MH^+, 100%), 130 ($[M - C_6H_5CH_2]^+$, 11%), 91 ($C_6H_5CH_2^+$, 44%).

HRMS (EI) *m/z* Found: M^+ 221.1207, $C_{16}H_{15}N$ requires 221.1205.

Data for 716a/717a:

FT-IR (neat, cm^{-1}): 3065 w, 3031 w, 2957 w, 2920 w, 2857 w, 2243 w, 1602 w, 1478 w, 1450 w, 1345 w, 1266 w, 1025 w, 907 w, 730 w, 684 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 280 (5100), 232 (15000).

^{1}H NMR Signals observed for **716a**: δ_H ppm (300 MHz, $CDCl_3$): 7.45-7.05 (6H + 6H, m, ArH, **716a** *and* **717a**), 6.92-6.81 (2H + 2H, m, ArH, **716a** *and* **717a**), 5.40 (1H, d, J = 9.9 Hz, NCH), 4.69 (1H , app. dd, J = 14.6, 1.6 Hz, NCHHAr), 4.56 (1H, dd, J = 14.6, 1.4 Hz, NCHHAr), 3.78 (1H, dq, J = 9.9, 7.1 Hz, $ArCHCH_3$), 1.40 (3H, d, J = 7.1 Hz, $ArCHCH_3$).

Signals observed for **717a**: δ_H ppm (300 MHz, $CDCl_3$): 4.86 (1H, app. s, NCH), 4.69 (1H, app. dd, J = 14.6, 1.6 Hz, NCHHAr), 4.53 (1H, d,

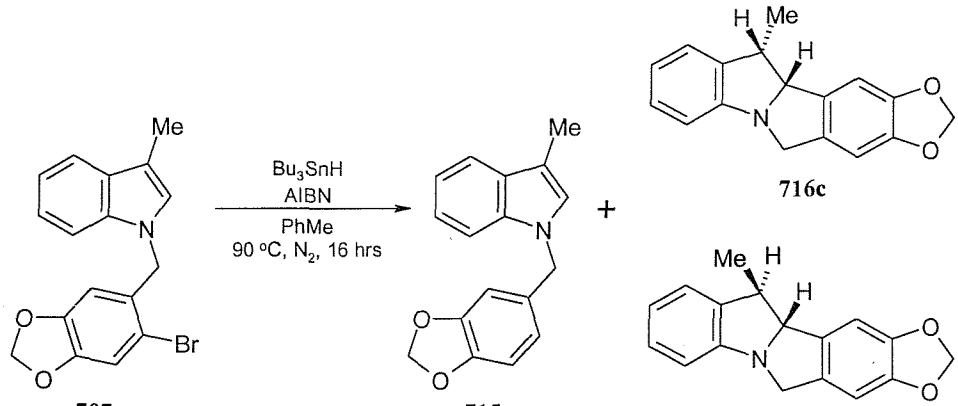
J = 14.6 Hz, NCHHAr), 3.70 (1H, qd, J = 7.1, 3.1 Hz, ArCHCH$_3$), 1.58 (3H, d, J = 7.1 Hz, ArCHCH$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 153.8 (C (Ar)), 153.6 (C (Ar)), 143.6 (C (Ar)), 140.8 (C (Ar)), 139.9 (2 x C (Ar)), 136.1 (C (Ar)), 136.0 (C (Ar)), 128.1 (CH (Ar)), 127.9 (CH (Ar)), 127.8 (CH (Ar)), 127.6 (CH (Ar)), 127.5 (CH (Ar)), 126.8 (CH (Ar)), 124.8 (CH (Ar)), 124.2 (CH (Ar)), 123.7 (CH (Ar)), 123.0 (CH (Ar)), 123.0 (CH (Ar)), 122.3 (CH (Ar)), 120.9 (CH (Ar)), 120.6 (CH (Ar)), 112.4 (CH (Ar)), 112.0 (CH (Ar)), 78.3 (NCH, **717a**), 74.2 (NCH, **716a**), 59.2 (NCH$_2$Ar, **717a**), 59.1 (NCH$_2$Ar, **716a**), 43.2 (ArCHCH$_3$, **717a**), 39.4 (ArCHCH$_3$, **716a**), 22.8 (ArCHCH$_3$, **717a**), 17.3 (ArCHCH$_3$, **716a**).

LRMS (CI) *m/z*: 222 (MH^+, 100%).

HRMS (EI) *m/z* Found: M^+ 221.1196, $C_{16}H_{15}N$ requires 221.1205.

N-(3',4'-Methylenedioxybenzyl)-3-methylindole (**715c**),
8,9-Methylenedioxy-11-methyl-10*b*R*,11R*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**716c**) and
8,9-Methylenedioxy-11-methyl-10*b*R*,11S*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**717c**)



707c
mw = 344.21 g mol^{-1}
$C_{17}H_{14}BrNO_2$

715c
mw = 265.31 g mol^{-1}
$C_{17}H_{15}NO_2$

716c

717c
mw = 265.31 g mol^{-1}
$C_{17}H_{15}NO_2$

To a stirred solution of indole **707c** (300 mg, 0.87 mmol) in toluene (20 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.28 mL, 1.05 mmol) followed by AIBN (29 mg, 0.17 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (15 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5-20% ether in petrol) gave firstly recovered **707c** as a white solid (61 mg, 0.18 mmol, 20%); then **715c**

as a buff solid (56 mg, 0.21 mmol, 24%); and finally a 3:2 mixture of **716c** and **717c** as a yellow oil, inseparable by chromatography (125 mg, 0.47 mmol, 54%). **715c** proved to be unstable at ambient temperature and, as such, only partial data could be obtained.

Data for 715c:

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$): 7.71 (1H, dd, J = 8.0, 1.0 Hz, ArH), 7.27 (1H, td, J = 8.0, 1.0 Hz, ArH), 7.21-7.15 (2H, m, ArH), 7.10 (1H, br. d, J = 0.5 Hz, ArH), 7.05 (1H, td, J = 7.5, 1.0 Hz, ArH), 6.95-6.89 (2H, m, ArH), 6.00 (2H, s, OCH_2O), 4.93 (2H, s, NCH_2Ar), 2.28 (3H, s, $ArCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 152.9 (CO (Ar)), 148.4 (CO (Ar)), 136.2 (C (Ar)), 136.0 (C (Ar)), 128.4 (C (Ar)), 126.8 (CH (Ar)), 126.3 (C (Ar)), 125.9 (2 x CH (Ar)), 123.7 (CH (Ar)), 120.4 (CH (Ar)), 113.2 (CH (Ar)), 106.1 (CH (Ar)), 102.6 (CH (Ar)), 102.3 (OCH_2O), 30.1 (NCH_2Ar), 9.7 ($ArCH_3$).

Data for 716c/717c:

FT-IR (neat, cm^{-1}): 2958 w, 2920 w, 2983 w, 2866 w, 1602 w, 1500 w, 1461 w, 1371 w, 1343 w, 1301 w, 1263 w, 1198 w, 1151 w, 1122 w, 1006 w, 939 w, 865 w, 833 w, 799 w, 740 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 282 (12200).

^{1}H NMR Signals observed for **716c**: δ_H ppm (300 MHz, $CDCl_3$): 7.15 (1H, br. t, J = 8.0 Hz, ArH), 7.09 (1H, br. t, J = 7.3 Hz, ArH), 6.85 (1H, d, J = 7.3 Hz, ArH), 6.81 (1H, d, J = 8.0 Hz, ArH), 6.81 (1H, s, ArH), 6.66 (1H, s, ArH), 5.95 (2H, s, OCH_2O), 5.27 (1H, d, J = 9.4 Hz, NCH), 4.56 (1H, app. dt, J = 14.1, 2.3 Hz, NCHHAr), 4.41 (1H, dd, J = 14.1, 1.7 Hz, NCHHAr), 3.72-3.56 (1H + 1H, m, $ArCHCH_3$, **716c** *and* **717c**), 1.36 (3H, d, J = 7.3 Hz, $ArCHCH_3$).

Signals observed for **717c**: δ_H ppm (300 MHz, $CDCl_3$): 7.15 (1H, br. t, J = 8.0 Hz, ArH), 7.09 (1H, br. t, J = 7.3 Hz, ArH), 6.86 (1H, d, J = 7.3 Hz, ArH), 6.80 (1H, d, J = 8.0 Hz, ArH), 6.76 (1H, s, ArH), 6.64 (1H, s, ArH), 5.97 (1H, d, J = 1.4 Hz, OCHHO), 5.92 (1H, d, J = 1.4 Hz, OCHHO), 4.72

(1H, app. s, NC<u>H</u>), 4.56 (1H, app. dt, J = 14.1, 2.3 Hz, NC<u>H</u>HAr), 4.39 (1H, d, J = 14.1 Hz, NCH<u>H</u>Ar), 1.50 (3H, d, J = 7.3 Hz, ArCHC<u>H</u>$_3$).

^{13}C NMR Signals observed for **716c**: δ_C ppm (75 MHz, $CDCl_3$): 153.5 (<u>C</u>O (Ar)), 147.1 (<u>C</u>O (Ar)), 136.3 (<u>C</u> (Ar)), 135.7 (<u>C</u> (Ar)), 132.5 (<u>C</u> (Ar)), 132.4 (<u>C</u> (Ar), 127.7 (<u>C</u>H (Ar)), 124.1 (<u>C</u>H (Ar)), 120.5 (<u>C</u>H (Ar)), 111.8 (<u>C</u>H (Ar)), 103.2 (<u>C</u>H (Ar)), 102.5 (<u>C</u>H (Ar)), 101.3 (O<u>C</u>H$_2$O), 73.9 (N<u>C</u>H), 59.0 (N<u>C</u>H$_2$Ar), 39.4 (Ar<u>C</u>HCH$_3$), 17.1 (ArCH<u>C</u>H$_3$).

Signals observed for **717c**: δ_C ppm (75 MHz, $CDCl_3$): 153.6 (<u>C</u>O (Ar)), 147.5 (<u>C</u>O (Ar)), 136.3 (<u>C</u> (Ar)), 135.7 (<u>C</u> (Ar)), 133.4 (<u>C</u> (Ar)), 132.4 (<u>C</u> (Ar), 127.9 (<u>C</u>H (Ar)), 123.5 (<u>C</u>H (Ar)), 120.8 (<u>C</u>H (Ar)), 112.2 (<u>C</u>H (Ar)), 104.9 (<u>C</u>H (Ar)), 103.1 (<u>C</u>H (Ar)), 101.3 (O<u>C</u>H$_2$O), 78.0 (N<u>C</u>H), 59.0 (N<u>C</u>H$_2$Ar), 42.9 (Ar<u>C</u>HCH$_3$), 22.5 (ArCH<u>C</u>H$_3$).

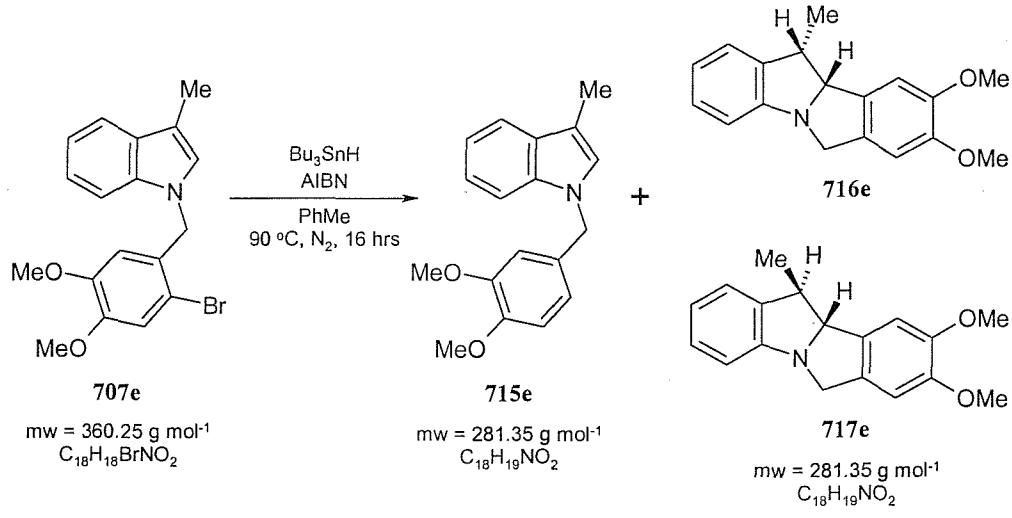
LRMS (CI) *m/z:* 266 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 266.1173, $C_{17}H_{16}NO_2$ requires 266.1176.

<u>*N*-(3,4-Dimethoxybenzyl)-3-methyl-indole (**715e**),</u>

<u>8,9-Dimethoxy-11-methyl-10*b*R*,11R*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**716e**) and</u>

<u>8,9-Dimethoxy-11-methyl-10*b*R*,11S*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**717e**)</u>



707e
mw = 360.25 g mol^{-1}
$C_{18}H_{18}BrNO_2$

715e
mw = 281.35 g mol^{-1}
$C_{18}H_{19}NO_2$

717e
mw = 281.35 g mol^{-1}
$C_{18}H_{19}NO_2$

To a stirred solution of indole **707e** (600 mg, 1.67 mmol) in toluene (40 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (583 mg, 2.0 mmol) followed by AIBN (55 mg, 0.33 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and

concentrated *in vacuo* to a yellow oil. Purification by column chromatography (10-60% ether in petrol) gave firstly **715e** as a pale yellow oil (141 mg, 0.50 mmol, 30%); then a 2:1 mixture of **716e** and **717e** as a pale brown oil, inseparable by chromatography (260 mg, 0.92 mmol, 56%).

Data for 715e:

FT-IR (neat, cm^{-1}): 2930 w, 2915 w, 2834 w, 1513 w, 1463 w, 1439 w, 1419 w, 1255 w, 1234 w, 1138 w, 1025 w, 736 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 276 (8200), 227 (25800).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.61 (1H, app. d, J = 8.0 Hz, ArH), 7.30 (1H, app. d, J = 8.0 Hz, ArH), 7.20 (1H, app. td, J = 8.0, 1.2 Hz, ArH), 7.13 (1H, app. td, J = 8.0, 1.2 Hz, ArH), 6.89 (1H, br. d, J = 0.9 Hz, ArH), 6.80 (1H, d, J = 8.0 Hz, ArH), 6.71 (1H, app. s, ArH), 6.69 (1H, dd, J = 8.0, 2.0 Hz, ArH), 5.20 (2H, s, NCH_2Ar), 3.86 (3H, s, $ArOCH_3$), 3.81 (3H, s, $ArOCH_3$), 2.36 (3H, d, J = 0.9 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.3 (CO (Ar)), 148.6 (CO (Ar)), 136.8 (C (Ar)), 130.4 (C (Ar)), 129.1 (C (Ar)), 125.8 (CH (Ar)), 121.7 (CH (Ar)), 119.5 (CH (Ar)), 119.2 (CH (Ar)), 118.9 (CH (Ar)), 111.3 (CH (Ar)), 110.9 (C (Ar)), 110.4 (CH (Ar)), 109.6 (CH (Ar)), 56.1 ($ArOCH_3$), 56.0 ($ArOCH_3$), 49.7 ($ArCH_2Ar$), 9.8 ($ArCH_3$).

LRMS (CI) *m/z*: 282 (MH^+, 100%).

HRMS (EI) *m/z* Found: M^+ 281.1414, $C_{18}H_{19}NO_2$ requires 281.1416.

Data for 716e/717e:

FT-IR (neat, cm^{-1}): 2955 w, 2930 w, 2859 w, 1604 w, 1503 w, 1478 w, 1459 w, 1450 w, 1344 w, 1302 w, 1273 w, 1215 w, 1189 w, 1127 w, 1102 w, 1062 w, 1026 w, 1008 w, 992 w, 836 w, 757 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 282 (12900), 226 (21400).

^{1}H NMR Signals observed for **716e**: δ_H ppm (300 MHz, $CDCl_3$): 7.19-7.04 (2H + 2H, m, ArH, **716e** *and* **717e**), 6.89-6.71 (4H + 4H, m, ArH, **716e** *and* **717e**), 5.33 (1H, d, J = 9.4 Hz, NCH), 4.61 (1H, app. d, J = 13.8 Hz, NCHHAr), 4.44 (1H, app. dd, J = 13.8 Hz, NCHHAr), 3.89 (3H, s, $ArOCH_3$), 3.86 (3H, s,

$ArOCH_3$), 3.74-3.58 (1H + 1H, m, $ArCHCH_3$, **716e** *and* **717e**), 1.40 (3H, d, J = 7.3 Hz, $ArCHCH_3$).

Signals observed for **717e**: δ_H ppm (300 MHz, $CDCl_3$): 4.77 (1H, app. s, NCH), 4.61 (1H, app. d, J = 13.8 Hz, NCHHAr), 4.43 (1H, app. dd, J = 13.8 Hz, NCHHAr), 3.90 (3H, s, $ArOCH_3$), 3.84 (3H, s, $ArOCH_3$), 1.52 (3H, d, J = 7.3 Hz, $ArCHCH_3$).

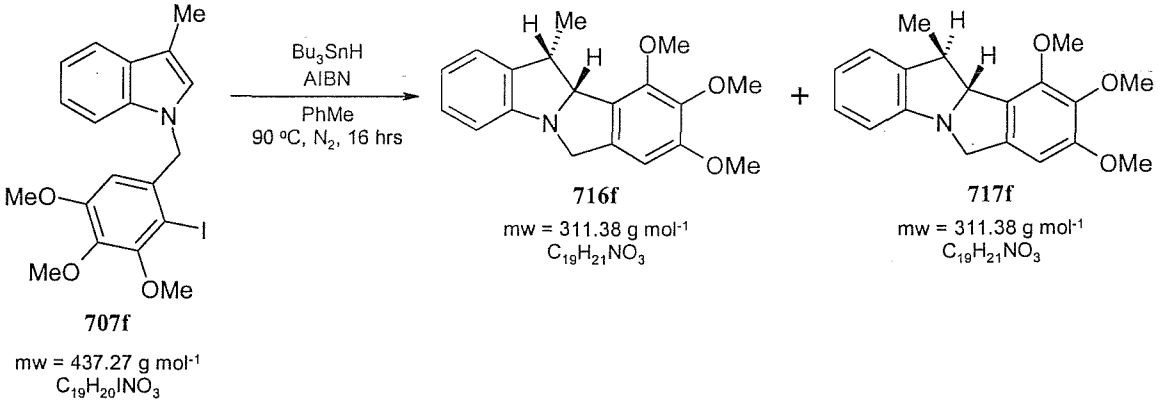
^{13}C NMR Signals observed for **716e**: δ_C ppm (100 MHz, $CDCl_3$): 153.6 (CO (Ar)), 149.3 (CO (Ar)), 148.4 (C (Ar)), 136.0 (C (Ar)), 132.4 (C (Ar)), 131.4 (C (Ar)), 127.9 (CH (Ar)), 123.7 (CH (Ar)), 120.6 (CH (Ar)), 112.0 (CH (Ar)), 107.8 (CH (Ar)), 105.6 (CH (Ar)), 74.3 (NCH), 59.4 (NCH_2Ar), 56.3 (OCH_3), 56.1 (OCH_3), 39.5 ($ArCHCH_3$), 17.4 ($ArCHCH_3$).

Signals observed for **717e**: δ_C ppm (100 MHz, $CDCl_3$): 153.8 (CO (Ar)), 149.1 (CO (Ar)), 148.4 (C (Ar)), 135.0 (C (Ar)), 131.4 (C (Ar)), 131.2 (C (Ar)), 128.0 (CH (Ar)), 124.2 (CH (Ar)), 120.9 (CH (Ar)), 112.4 (CH (Ar)), 105.8 (CH (Ar)), 105.1 (CH (Ar)), 78.5 (NCH), 59.4 (NCH_2Ar), 56.3 (OCH_3), 56.2 (OCH_3), 42.9 ($ArCHCH_3$), 22.8 ($ArCHCH_3$).

LRMS (CI) *m/z*: 282 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 282.1486, $C_{18}H_{20}NO_2$ requires 282.1489.

8,9,10-Trimethoxy-11-methyl-10*b*R*,11R*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**716f**) and 8,9,10-Trimethoxy-11-methyl-10*b*R*,11S*-dihydro-6*H*-isoindolo[2,1-*a*]indole (**717f**)



707f
mw = 437.27 g mol^{-1}
$C_{19}H_{20}INO_3$

716f
mw = 311.38 g mol^{-1}
$C_{19}H_{21}NO_3$

717f
mw = 311.38 g mol^{-1}
$C_{19}H_{21}NO_3$

To a stirred solution of indole **707f** (300 mg, 0.69 mmol) in toluene (16 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.22 mL, 0.82 mmol) followed by AIBN (23 mg, 0.14 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and

concentrated *in vacuo* to a yellow oil. Purification by column chromatography (20-30% ether in petrol) gave firstly a 1:3 mixture of **716f** and **717f** as a colourless semi-solid (131 mg, 0.42 mmol, 61%); then **717f** as a buff solid (10 mg, 0.03 mmol, 5%): mp 125-127 °C. NMR assignments for **716f** and **717f** were confirmed by ^{1}H-^{1}H and ^{1}H-^{13}C COSY experiments.

*Data for **716f/717f**:*

FT-IR (neat, cm^{-1}): 2959 w, 2937 w, 2893 w, 2863 w, 1601 w, 1476 w, 1413 w, 1331 w, 1268 w, 1216 w, 1190 w, 1006 w, 1070 w, 984 w, 940 w, 922 w, 841 w, 762 w, 744 w.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 278 (4200).

^{1}H NMR Signals observed for **716f**: δ_H ppm (300 MHz, $CDCl_3$): 5.58 (1H, dd, J = 8.9, 1.4 Hz, NC<u>H</u>), 4.72 (1H, d, J = 13.4 Hz, NC<u>H</u>H), 4.35 (1H, dd, J = 13.4, 2.3 Hz, NCH<u>H</u>), 4.02 (3H, s, ArOC<u>H</u>$_3$), 3.88 (3H, s, ArOC<u>H</u>$_3$), 3.87 (3H, s, ArOC<u>H</u>$_3$), 0.83 (3H, d, J = 7.0 Hz, ArCHC<u>H</u>$_3$). All remaining signals were obscured.

Signals observed for **717f**: δ_H ppm (300 MHz, $CDCl_3$): 7.13 (1H, t, J = 7.7 Hz, Ar<u>H</u>), 7.08 (1H, d, J = 7.3 Hz, Ar<u>H</u>), 6.82 (1H, t, J = 7.3 Hz, Ar<u>H</u>), 6.77 (1H, d, J = 7.7 Hz, Ar<u>H</u>), 6.50 (1H, s, Ar<u>H</u>), 4.90 (1H, br. s, NC<u>H</u>), 4.58 (1H, dd, J = 14.3, 1.2 Hz, NC<u>H</u>H), 4.40 (1H, d, J = 14.3 Hz, NCH<u>H</u>), 3.99 (3H, s, ArOC<u>H</u>$_3$), 3.84 (3H, s, ArOC<u>H</u>$_3$), 3.82 (3H, s, ArOC<u>H</u>$_3$), 3.88-3.71 (1H, m, ArC<u>H</u>CH$_3$), 1.54 (3H, d, J = 7.0 Hz, ArCHC<u>H</u>$_3$).

^{13}C NMR Signals observed for **716f**: δ_C ppm (100 MHz, $CDCl_3$): 154.7 (<u>C</u>O (Ar)), 153.0 (<u>C</u>O (Ar)), 149.6 (<u>C</u>O (Ar)), 141.4 (<u>C</u> (Ar)), 140.9 (<u>C</u> (Ar)), 139.1 (<u>C</u> (Ar)), 128.2 (<u>C</u>H (Ar)), 124.9 (<u>C</u>H (Ar)), 124.2 (<u>C</u> (Ar)), 121.0 (<u>C</u>H (Ar)), 113.2 (<u>C</u>H (Ar)), 101.4 (<u>C</u>H (Ar)), 74.0 (N<u>C</u>HAr), 61.7 (ArO<u>C</u>H$_3$), 60.7 (ArO<u>C</u>H$_3$), 60.3 (N<u>C</u>H$_2$Ar), 56.6 (ArO<u>C</u>H$_3$), 41.2 (Ar<u>C</u>HCH$_3$), 20.7 (ArCH<u>C</u>H$_3$).

Signals observed for **717f**: δ_C ppm (100 MHz, $CDCl_3$): 154.6 (<u>C</u>O (Ar)), 154.2 (<u>C</u>O (Ar)), 149.7 (<u>C</u>O (Ar)), 141.4 (<u>C</u> (Ar)), 136.7 (<u>C</u> (Ar)), 135.5 (<u>C</u> (Ar)), 128.1 (<u>C</u>H (Ar)), 128.0 (<u>C</u> (Ar)), 124.4 (<u>C</u>H (Ar)), 121.0 (<u>C</u>H (Ar)), 112.5 (<u>C</u>H (Ar)), 101.8 (<u>C</u>H (Ar)), 78.1 (N<u>C</u>HAr), 61.4 (ArO<u>C</u>H$_3$), 60.9

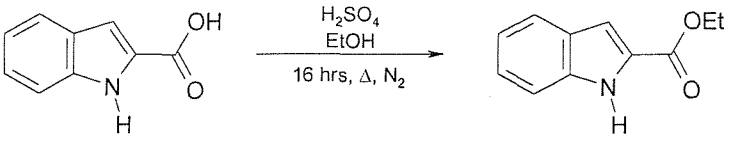
($ArO\underline{C}H_3$), 60.1 ($N\underline{C}H_2Ar$), 56.6 ($ArO\underline{C}H_3$), 42.7 ($Ar\underline{C}HCH_3$), 22.4 ($ArCH\underline{C}H_3$).

LRMS (CI) *m/z:* 312 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 312.1590, $C_{19}H_{22}NO_3$ requires 312.1594.

7.4 Synthetic Procedures for Chapter 5

2-(Ethoxycarbonyl)-indole (**802**)



801
mw = 161.16 g mol^{-1}
$C_9H_7NO_2$

802
mw = 189.21 g mol^{-1}
$C_{11}H_{11}NO_2$

In accordance with the procedure of Fagan *et al.*,[205] a solution of indole-2-carboxylic acid **801** (4.0 g, 24.8 mmol) and concentrated sulfuric acid (0.6 mL) in ethanol (60 mL) under nitrogen was heated at reflux for 16 hours. On cooling to ambient temperature, the reaction mixture was reduced to approximately one-third *in vacuo* and poured into saturated sodium bicarbonate solution (100 mL) at 0 °C. The resulting precipitate was isolated by extraction with ether (1 x 200 mL, 2 x 100 mL), then the combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to give **802** as a white fibrous solid (4.66 g, 24.6 mmol, 99%): mp 119-121 °C, lit. 120-121 °C.[205] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3307 m, 1687 s, 1526 m, 1381 w, 1339 w, 1307 m, 1246 s, 1200 s, 1145 m, 1020 s, 932 w, 820 w, 770 m, 743 s, 662 s.

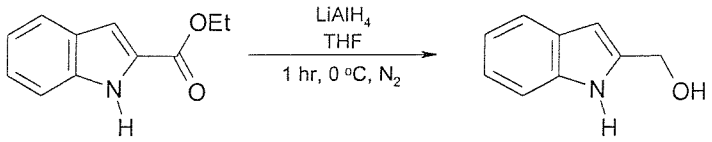
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 286 (28400), 224 (23400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.31 (1H, br. s, NH), 7.72 (1H, dd, J = 7.9, 1.0 Hz, ArH), 7.46 (1H, dd, J = 8.2, 1.0 Hz, ArH), 7.35 (1H, ddd, J = 8.2, 7.0, 1.0 Hz, ArH), 7.29-7.25 (1H, m, ArH), 7.18 (1H, ddd, J = 7.9, 7.0, 1.0 Hz, ArH), 4.46 (2H, q, J = 7.2 Hz, $COOCH_2CH_3$), 1.45 (3H, t, J = 7.2 Hz, $COOCH_2CH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 162.5 (COOEt), 137.1 (C (Ar)), 127.6 (2 x C (Ar)), 125.5 (CH (Ar)), 122.8 (CH (Ar)), 120.9 (CH (Ar)), 112.1 (CH (Ar)), 108.8 (CH (Ar)), 61.3 ($COOCH_2CH_3$), 14.6 ($COOCH_2CH_3$).

LRMS (CI) *m/z*: 189 (M^+, 100%), 143 ([MH - EtOH]$^+$, 44%), 115 ([M - COOEt]$^+$, 14%).

2-(Hydroxymethyl)-indole (**803**)



802
mw = 189.21 g mol^{-1}
$C_{11}H_{11}NO_2$

803
mw = 147.18 g mol^{-1}
C_9H_9NO

To a stirred solution of **802** (8.0 g, 42.3 mmol) in THF (200 mL) at –78 °C under nitrogen was added lithium aluminium hydride (3.53 g, 93 mmol). The reaction mixture was warmed to 0 °C then stirred for 1 hour. Water (5 mL) was added, followed by 15% sodium hydroxide (5 mL) and water (5 mL) once effervescence had ceased. On stirring for 4 hours, $MgSO_4$ (15 g) was added. After 16 hours the white suspension was filtered and concentrated *in vacuo* to a pale orange solid. Recrystallisation from benzene/petrol gave **803** as pale orange needles (5.99 g, 40.7 mmol, 96%): mp 70-71 °C (benzene/petrol), lit. 75-76 °C.[206] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3374 m, 3269 br. m, 3046 w, 2905 w, 2848 w, 1453 m, 1382 w, 1338 w, 1230 m, 1206 w, 1136 m, 1056 s, 1006 s, 927 w, 888 w, 821 w, 737 vs, 631 s, 618 s.

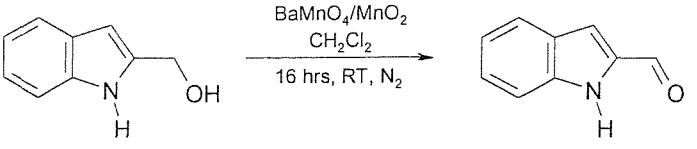
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 266 (8700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.36 (1H, br. s, NH), 7.60 (1H, d, J = 7.7 Hz, ArH), 7.25 (1H, br. d, J = 7.9 Hz, ArH), 7.20 (1H, td, J = 7.9, 1.5 Hz, ArH), 7.14 (1H, td, J = 7.7, 1.5 Hz, ArH), 6.37 (1H, s, ArH), 4.66 (2H, s, $ArCH_2OH$), 2.58 (1H, br. s, CH_2OH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 137.7 (C (Ar)), 136.5 (C (Ar)), 128.1 (C (Ar)), 122.4 (CH (Ar)), 120.8 (CH (Ar)), 120.1 (CH (Ar)), 111.3 (CH (Ar)), 100.8 (CH (Ar)), 58.6 (CH_2OH).

LRMS (CI) *m/z*: 148 (MH^+, 100%), 130 ($[MH - H_2O]^+$, 74%).

Indole-2-carboxaldehyde (**804**)



803
mw = 147.18 g mol^{-1}
C_9H_9NO

804
mw = 145.16 g mol^{-1}
C_9H_7NO

This procedure was adapted from that of Meyer and Kruse.[207] To a stirred solution of 2-(hydroxymethyl)-indole **803** (5.99 g, 40.7 mmol) in dichloromethane (150 mL) under nitrogen was added barium manganate (10 g, 40 mmol) followed by activated manganese dioxide (85 g, 0.98 mol). The resultant black suspension was stirred for 16 hours then filtered through celite. The solids were washed with chloroform (500 mL), followed by hot acetone (500 mL), then both filtrates were concentrated *in vacuo* to dark brown solids. Column chromatography of the combined residues (10-30% ether in petrol) gave **804** as a flaky pearlescent solid (4.93 g, 33.9 mmol, 83%): mp 136-138 °C, lit. 139-140 °C (benzene/hexane).[206] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3170 br. m, 2853 m, 1649 s, 1525 s, 1426 m, 1362 m, 1338 s, 1252 m, 1230 m, 1154 w, 1122 m, 1002 w, 983 w, 937 w, 897 w, 855 w, 819 s, 744 s.

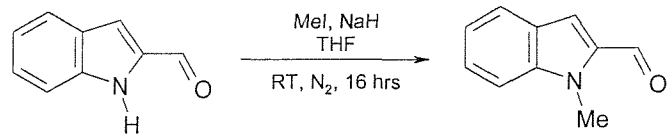
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 300 (28700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.88 (1H, s, ArC<u>H</u>O), 9.80 (1H, br. s, N<u>H</u>), 7.77 (1H, dd, J = 8.2, 1.0 Hz, Ar<u>H</u>), 7.53 (1H, dd, J = 8.2, 1.0 Hz, Ar<u>H</u>), 7.42 (1H, ddd, J = 8.2, 7.0, 1.0 Hz, Ar<u>H</u>), 7.33-7.29 (1H, m, Ar<u>H</u>), 7.20 (1H, ddd, J = 8.2, 7.0, 1.0 Hz, Ar<u>H</u>).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 182.6 (Ar<u>C</u>HO), 138.5 (<u>C</u> (Ar)), 136.1 (<u>C</u> (Ar)), 127.6 (<u>C</u>H (Ar)), 127.5 (<u>C</u> (Ar)), 123.6 (<u>C</u>H (Ar)), 121.4 (<u>C</u>H (Ar)), 115.5 (<u>C</u>H (Ar)), 112.9 (<u>C</u>H (Ar)).

LRMS (CI) *m/z*: 145 (M^+, 100%), 117 ([MH - CHO]$^+$, 10%).

N-Methylindole-2-carboxaldehyde (**805**)



804

mw = 145.16 g mol^{-1}
C_9H_7NO

805

mw = 159.19 g mol^{-1}
$C_{10}H_9NO$

To a stirred suspension of petrol-washed sodium hydride (465 mg, 19.4 mmol) in THF (150 mL) at 0 °C under nitrogen was added indole-2-carboxaldehyde **7** (2.55 g, 17.6 mmol). After stirring for 30 minutes at ambient temperature, methyl iodide (1.64 mL, 26.4 mmol) was added. After 16 hours, the reaction mixture was diluted with water (100 mL) and extracted with ether (1 x 200 mL, 2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (10-20% ether in petrol) gave **805** as a white solid (2.46 g, 15.4 mmol, 88%): mp 80-81 °C, lit. 83-85 °C.[208] The observed data for **805** is consistent with literature values.

FT-IR (neat, cm^{-1}): 2955 w, 2924 w, 2856 w, 2822 w, 2727 w, 1659 vs, 1610 s, 1518 s, 1468 s, 1395 s, 1353 s, 1317 m, 1183 m, 1156 m, 1114 s, 910 s, 845 s, 801 s.

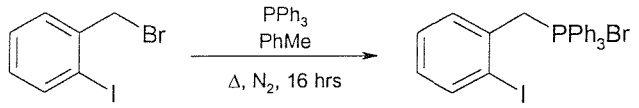
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 286 (19900).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.90 (1H, s, ArC<u>H</u>O), 7.75 (1H, app. d, J = 8.1 Hz, Ar<u>H</u>), 7.46-7.38 (2H, m, Ar<u>H</u>), 7.25 (1H, s, Ar<u>H</u>), 7.20 (1H, ddd, J = 8.1, 6.6, 1.5 Hz, Ar<u>H</u>), 4.10 (3H, s, NC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 183.1 (Ar<u>C</u>HO), 141.0 (<u>C</u> (Ar)), 135.8 (<u>C</u> (Ar)), 127.1 (<u>C</u>H (Ar)), 126.4 (<u>C</u> (Ar)), 123.5 (<u>C</u>H (Ar)), 121.1 (<u>C</u>H (Ar)), 117.6 (<u>C</u>H (Ar)), 110.5 (<u>C</u>H (Ar)), 31.7 (N<u>C</u>H$_3$).

LRMS (CI) *m/z:* 160 (MH^+, 100%), 130 ($[M - CHO]^+$, 19%).

2-Iodobenzyltriphenylphosphonium bromide (**806**)



702b
mw = 296.93 g mol^{-1}
C_7H_6BrI

806
mw = 559.22 g mol^{-1}
$C_{25}H_{21}BrIP$

A solution of 2-iodobenzyl bromide **702b** (4.29 g, 14.4 mmol) and triphenylphosphine (3.97 g, 15.1 mmol) in toluene (200 mL) was heated at reflux under nitrogen for 16 hours. On cooling to ambient temperature, the suspension was filtered and the isolated white solid washed with petrol (100 mL) to yield **806** as a white solid (7.59 g, 13.6 mmol, 94%): mp 266-268 °C, lit. 265-266 °C.[209] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3055 w, 3001 w, 2949 w, 2852 w, 2759 w, 1585 w, 1483 w, 1436 s, 1391 m, 1319 w, 1156 w, 1106 vs, 1018 w, 996 w, 833 s.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 254 (7500).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.83-7.72 (3H, m, ArH), 7.70-7.51 (13H, m, ArH), 7.43 (1H, d, J = 7.5, 1.2 Hz, ArH), 7.17 (1H, t, J = 7.5 Hz, ArH), 6.94 (1H, t, J = 7.7 Hz, ArH), 5.54 (2H, d, J = 13.8 Hz, $ArCH_2PPh_3$).

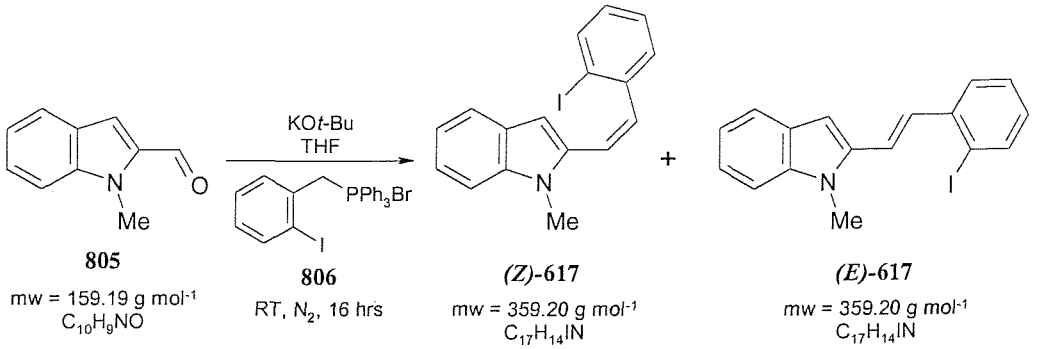
^{13}C NMR δ_C ppm (75 MHz, D_6-DMSO): 140.1 (CH (Ar)), 135.5 (3 x CH (Ph)), 134.1 (d, J = 10.0 Hz, 6 x CH (Ph)), 131.1 (CH (Ar)), 131.1 (CH (Ar)), 130.9 (d, J = 8.3 Hz, C (Ar)), 130.6 (d, J = 11.6 Hz, 6 x CH (Ph)), 130.4 (CH (Ar)), 117.1 (d , J = 85 Hz, 3 x C (Ph)), 105.3 (d, J = 6.8 Hz, CI (Ar)), 33.7 (d, J = 48 Hz, $ArCH_2PPh_3$).

^{31}P NMR δ_P ppm (121.5 MHz, $CDCl_3$): 23.3.

LRMS (ES^+) *m/z:* 479 ($[M - Br]^+$, 100%).

2-[(*Z*)-2-(2-Iodophenyl)vinyl]-1-methyl-1*H*-indole (***(Z)*-617**) and

2-[(*E*)-2-(2-Iodophenyl)vinyl]-1-methyl-1*H*-indole (***(E)*-617**)



To a stirred suspension of **806** (2.0 g, 3.58 mmol) in THF (75 mL) under nitrogen was added potassium *tert*-butoxide (383 mg, 3.41 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of indole **805** (517 mg, 3.25 mmol) in THF (25 mL) added. After 16 hours, the reaction mixture was diluted with water (100 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (2.5-5% ether in petrol) yielded firstly ***(Z)*-617** as a yellow oil that crystallised on standing to small yellow needles (168 mg, 0.47 mmol, 14%): mp 80-84 °C; then ***(E)*-617** as a yellow solid that gave yellow prisms on recrystallisation (911 mg, 2.54 mmol, 78%): mp 106-108 °C (ether/petrol).

*Data for **(Z)-617**:*

FT-IR (neat, cm^{-1}): 3050 w, 2919 w, 2850 w, 1630 w, 1580 w, 1462 s, 1430 m, 1319 s, 1148 m, 1117 w, 1013 m, 909 m, 779 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 306 (15200).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.93 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.46 (1H, app. d, J = 7.5 Hz, ArH), 7.28 (1H, obsc. dd, J = 7.5, 1.7 Hz, ArH), 7.26 (1H, obsc. d, J = 7.5 Hz, ArH), 7.19 (1H, td, J = 8.0, 1.2 Hz, ArH), 7.18 (1H, td, J = 7.5, 1.2 Hz, ArH), 7.06 (1H, td, J = 7.5, 1.2 Hz, ArH), 6.97 (1H, td, J = 7.5, 1.7 Hz, ArH), 6.71 (1H, d, J = 12.0 Hz, ArCH=CHAr), 6.66 (1H, d, J = 12.0 Hz, ArCH=CHAr), 6.22 (1H, s, ArH), 3.62 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 141.7 (2 x C (Ar)), 139.3 (CH (Ar)), 137.5 (C (Ar)), 135.6 (ArCH=CHAr), 130.0 (CH (Ar)), 129.2 (CH (Ar)), 128.3 (CH (Ar)), 127.9 (C (Ar)), 122.0 (CH (Ar)), 120.8 (CH (Ar)), 120.1

(CH (Ar)), 119.9 (ArCH=CHAr), 109.4 (CH (Ar)), 102.6 (CH (Ar)), 99.8 (CI (Ar)), 30.2 (NCH_3).

LRMS (CI) *m/z:* 360 (MH^+, 81%), 232 ($[M - I]^+$, 100%), 217 ($[M - I - CH_3]^+$, 21%).

HRMS (EI) *m/z* Found: M^+ 359.0174, $C_{17}H_{14}IN$ requires 359.0171.

Data for (E)-617:

FT-IR (neat, cm^{-1}): 3104 w, 3065 w, 2935 w, 2906 w, 1626 s, 1567 w, 1529 m, 1475 m, 1452 s, 1430 m, 1375 m, 1332 m, 1253 m, 1134 m, 1073 m, 1006 s, 951 s, 810 m, 792 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 336 (34900).

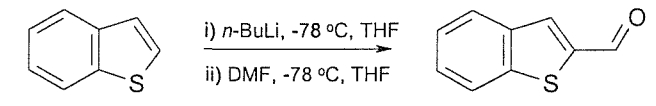
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.91 (1H, dd, J = 7.7, 0.9 Hz, ArH), 7.66 (1H, dd, J = 7.7, 1.6 Hz, ArH), 7.65 (1H, app. d, J = 8.0 Hz, ArH), 7.41 (1H, d, J = 15.7 Hz, ArCH=CHAr), 7.39 (1H, app. t, J = 7.7 Hz, ArH), 7.33 (1H, app. d, J = 8.2 Hz, ArH), 7.25 (1H, td, J = 8.2, 1.2 Hz, ArH), 7.15 (1H, td, J = 8.0, 1.2 Hz, ArH), 7.05 (1H, d, J = 15.7 Hz, ArCH=CHAr), 6.99 (1H, td, J = 7.7, 1.6 Hz, ArH), 6.91 (1H, s, ArH), 3.85 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.4 (C (Ar)), 140.0 (CH (Ar)), 138.5 (C (Ar)), 138.0 (C (Ar)), 134.3 (ArCH=CHAr), 129.3 (CH (Ar)), 128.7 (CH (Ar)), 128.0 (C (Ar)), 126.2 (CH (Ar)), 122.3 (CH (Ar)), 120.8 (CH (Ar)), 120.2 (CH (Ar), ArCH=CHAr), 109.4 (CH (Ar)), 100.6 (CI (Ar)), 100.4 (CH (Ar)), 30.3 (NCH_3).

LRMS (CI) *m/z:* 360 (MH^+, 72%), 232 ($[M - I]^+$, 100%), 217 ($[M - I - CH_3]^+$, 58%).

CHN Found C, 56.78; H, 3.90; N, 3.88; $C_{17}H_{14}IN$ requires C, 56.84; H, 3.93; N, 3.90.

2-Formylbenzo[*b*]thiophene (**808**)



807
mw = 134.20 g mol^{-1}
C_8H_6S

808
mw = 162.21 g mol^{-1}
C_9H_6OS

In a modified procedure to that of Shirley and Danzig,[210] to a stirred solution of benzo[*b*]thiophene **807** (10.0 g, 74.5 mmol) in THF (200 mL) under nitrogen at –78 °C was added *n*-butyllithium (37.3 mL, 82 mmol, 2.20 M solution in hexanes) over 10 minutes,

ensuring that the temperature of the reaction mixture did not exceed –65 °C. After stirring at –78 °C for 1 hour, a solution of DMF (6.1 mL, 78.2 mmol) in THF (50 mL) was added over 10 minutes, again ensuring that the temperature did not exceed –65 °C. The reaction mixture was warmed to ambient temperature, stirred for 16 hrs, then diluted with saturated ammonium chloride solution (100 mL) and extracted with ether (2 x 200 mL, 1 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (10-40% ether in petrol) yielded **808** as a yellow oil that crystallized on standing to a pale yellow solid (9.84 g, 60.7 mmol, 81%): mp 32 °C, lit. 34-34.5 °C (ethanol).[210] The observed data is consistent with literature values.[211]

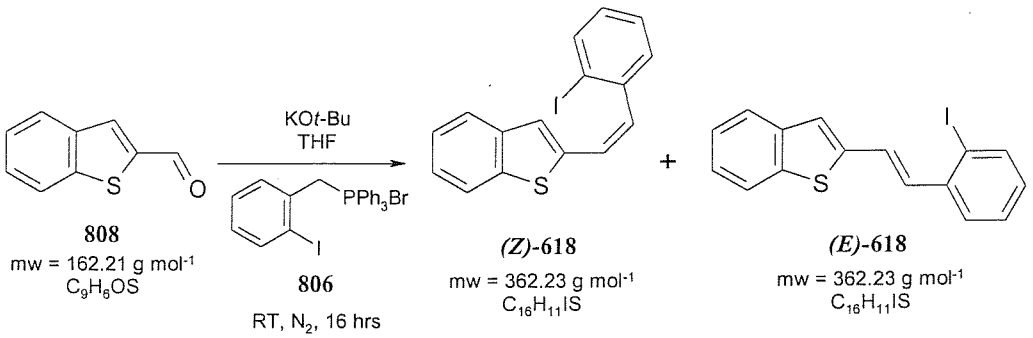
FT-IR (neat, cm^{-1}): 3057 w, 2819 w, 1669 vs, 1593 w, 1517 m, 1432 w, 1323 w, 1256 w, 1225 m, 1136 s, 867 w, 841 w, 749 m, 726 m, 659 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.12 (1H, s, ArC<u>H</u>O), 8.04 (1H, d, J = 0.8 Hz, Ar<u>H</u>), 7.95 (1H, dd, J = 7.4, 1.1 Hz, Ar<u>H</u>), 7.91 (1H, dd, J = 7.7, 1.1 Hz, Ar<u>H</u>), 7.52 (1H, td, J = 7.4, 1.1 Hz, Ar<u>H</u>), 7.45 (1H, td, J = 7.7, 1.1 Hz, Ar<u>H</u>).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 185.1 (Ar<u>C</u>HO), 143.8 (<u>C</u> (Ar)), 143.1 (<u>C</u> (Ar)), 139.0 (<u>C</u> (Ar)), 134.9 (<u>C</u>H (Ar)), 128.6 (<u>C</u>H (Ar)), 126.7 (<u>C</u>H (Ar)), 125.7 (<u>C</u>H (Ar)), 123.7 (<u>C</u>H (Ar)).

LRMS (CI) *m/z:* 180 ($[M + NH_4]^+$, 5%), 162 (M^+, 100%), 134 ($[MH - CHO]^+$, 37%).

<u>2-[(*Z*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]thiophene (***(Z)*-618**) and 2-[(*E*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]thiophene (***(E)*-618**)</u>



To a stirred suspension of **806** (2.84 g, 5.08 mmol) in THF (50 mL) under nitrogen was added potassium *tert*-butoxide (622 mg, 5.54 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of 2-

formylbenzo[*b*]thiophene **808** (750 mg, 4.62 mmol) in THF (50 mL) was added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a colourless semi-solid. Purification by column chromatography (0.5-5% ethyl acetate in petrol, followed by 1-2% toluene in petrol) and successive recrystallisation of the mixed fractions (ethyl acetate/hexane, then hexane) eventually isolated ***(Z)*-618** as a pale yellow solid (258 mg, 0.71 mmol, 15%): mp 81-83 °C; and ***(E)*-618** as a yellow solid that, on further recrystallisation, gave colourless prisms (1.19 g, 3.29 mmol, 71%): mp 130-132 °C (petrol).

*Data for **(Z)-618**:*

FT-IR (neat, cm^{-1}): 3054 w, 2956 w, 2920 w, 2852 w, 1624 w, 1583 w, 1556 w, 1461 m, 1429 m, 1388 w, 1326 w, 1279 w, 1244 w, 1208 w, 1154 w, 1109 w, 1041 w, 1010 s, 946 m, 864 m, 840 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 292 (26600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.98 (1H, dd, J = 7.9, 1.2 Hz, ArH), 7.68 (1H, dd, J = 6.5, 1.7 Hz, ArH), 7.62 (1H, dd, J = 7.6, 1.2 Hz, ArH), 7.45 (1H, dd, J = 7.9, 1.9 Hz, ArH), 7.38 (1H, td, J = 7.4, 1.2 Hz, ArH), 7.30 (1H, td, J = 7.4, 1.7 Hz, ArH), 7.25 (1H, obsc. td, J = 7.4, 1.7 Hz, ArH), 7.24 (1H, s, ArH), 7.11 (1H, app. td, J = 7.9, 1.2 Hz, ArH), 6.91 (1H, d, J = 11.9 Hz, ArCH=CHAr), 6.58 (1H, d, J = 11.9 Hz, ArCH=CHAr).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 141.4 (C (Ar)), 140.5 (C (Ar)), 139.6 (C (Ar)), 139.3 (CH (Ar)), 138.9 (C (Ar)), 133.7 (ArCH=CHAr), 130.8 (CH (Ar)), 129.7 (CH (Ar)), 128.5 (CH (Ar)), 126.0 (CH (Ar)), 125.1 (ArCH=CHAr), 124.9 (CH (Ar)), 124.4 (CH (Ar)), 123.6 (CH (Ar)), 122.2 (CH (Ar)), 99.9 (CI (Ar)).

LRMS (EI) *m/z:* 362 (M^+, 57%), 235 ($[M - I]^+$, 98%), 202 (61%), 189 (62%), 117 (100%).

HRMS (EI) *m/z* Found: M^+ 361.9629, $C_{16}H_{11}IS$ requires 361.9626.

Data for (E)-618:

FT-IR (neat, cm^{-1}): 3057 w, 3024 w, 1618 w, 1581 w, 1453 m, 1429 m, 1312 w, 1280 w, 1243 w, 1226 w, 1200 w, 1146 w, 1011 m, 944 vs, 864 w, 847 w, 818 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 322 (35200), 258 (20100).

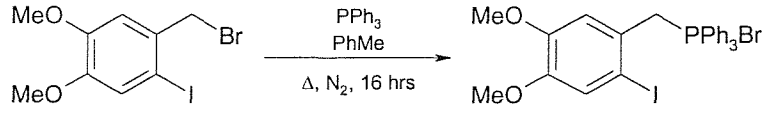
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.90 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.84-7.77 (1H, m, ArH), 7.77-7.70 (1H, m, ArH), 7.62 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.40-7.32 (3H, m, ArH), 7.31 (1H, s, ArH), 7.26 (1H, d, J = 15.8 Hz, ArH), 7.19 (1H, d, J = 15.8 Hz, ArH), 6.98 (1H, td, J = 7.4, 1.5 Hz, ArH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 142.6 (C (Ar)), 140.3 (C (Ar)), 140.0 (CH (Ar)), 139.7 (C (Ar)), 139.3 (C (Ar)), 134.5 (ArCH=CHAr), 129.5 (CH (Ar)), 128.7 (CH (Ar)), 126.3 (CH (Ar)), 125.2 (CH (Ar) *and* ArCH=CHAr), 124.7 (CH (Ar)), 124.2 (CH (Ar)), 123.8 (CH (Ar)), 122.5 (CH (Ar)), 100.6 (CI (Ar)).

LRMS (CI) *m/z:* 362 (M^+, 35%), 235 ($[M - I]^+$, 100%).

CHN Found C, 53.14; H, 3.07; $C_{16}H_{11}IS$ requires C, 53.05; H, 3.06.

4,5-Dimethoxy-2-iodobenzyltriphenylphosphonium bromide (**809**)



mw = 356.98 g mol^{-1}
$C_9H_{10}BrIO_2$

809
mw = 619.27 g mol^{-1}
$C_{27}H_{25}BrIO_2P$

A solution of 4,5-dimethoxy-2-iodobenzyl bromide (6.07 g, 17.0 mmol) and triphenylphosphine (4.68 g, 17.8 mmol) in toluene (250 mL) under nitrogen was heated at reflux for 16 hours. On cooling to ambient temperature, the suspension was filtered and the isolated solid washed with petrol (150 mL) to yield **809** as a powdery cream solid (8.31 g, 13.4 mmol, 79%): mp > 250 °C.

FT-IR (neat, cm^{-1}): 3007 w, 2967 w, 2929 w, 2839 w, 2776 w, 1589 w, 1501 s, 1470 w, 1438 vs, 1375 w, 1335 w, 1256 s, 1211 s, 1163 m, 1139 w, 1111 s, 1017 m, 997 w, 956 w, 854 m, 836 m, 795 w, 762 vs, 736 s, 690 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.84-7.75 (3H, m, PhH), 7.70-7.59 (12H, m, PhH), 7.07 (1H, d, J = 2.2 Hz, ArH), 7.00 (1H, s, ArH), 5.42 (2H, d, J = 13.2 Hz, $ArCH_2PPh_3$), 3.79 (3H, s, $ArOCH_3$), 3.50 (3H, s, $ArOCH_3$).

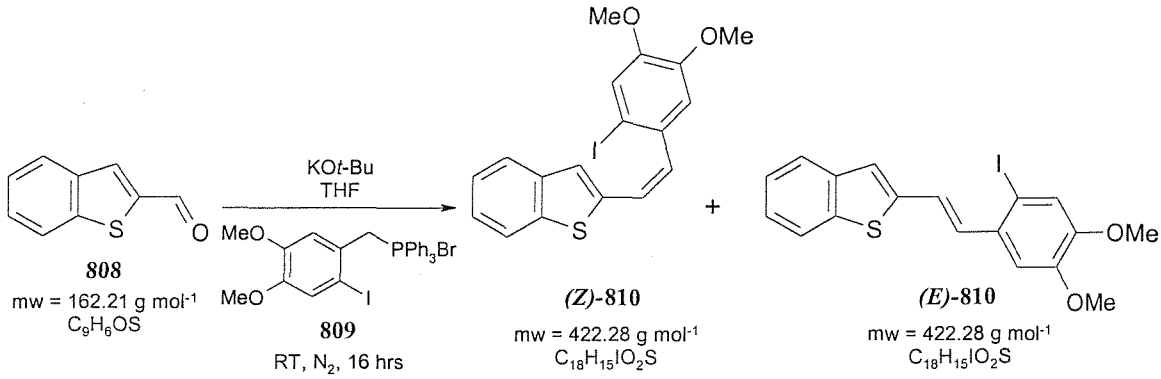
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.6 (2 x CO (Ar)), 135.2 (d, J = 3.4 Hz, 3 x CH (Ph)), 134.6 (d, J = 9.5 Hz, 6 x CH (Ph)), 130.2 (d, J = 12.4 Hz, 6 x CH (Ph)), 122.4 (d, J = 9.0 Hz, C (Ar)), 121.0 (d, J = 3.4 Hz, CH (Ar)), 117.2 (d, J = 84.8 Hz, 3 x C (Ph)), 115.0 (d, J = 3.9 Hz, CH (Ar)), 92.6 (d, J = 7.7 Hz, CI (Ar)), 56.4 (2 x $ArOCH_3$), 35.4 (d, J = 47.4 Hz, $ArCH_2PPh_3$).

^{31}P NMR δ_P ppm (121.5 MHz, $CDCl_3$): 22.6.

LRMS (ES^+) *m/z:* 539 ($[M - Br]^+$, 100%).

CHN Found: C, 52.03; H, 4.15; $C_{27}H_{25}BrIO_2P$ requires C, 52.37; H, 4.07.

2-(*Z*)-2-(4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]thiophene (***(Z)*-810**) and
2-(*E*)-2-(4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]thiophene (***(E)*-810**)



To a stirred suspension of **809** (3.55 g, 5.73 mmol) in THF (80 mL) under nitrogen was added potassium *tert*-butoxide (674 mg, 6.00 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of 2-formylbenzo[*b*]thiophene **808** (643 mg, 3.96 mmol) in THF (80 mL) was added. After 16 hours, the reaction mixture was diluted with water (100 mL) and extracted with ether (2 x 200 mL, 1 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (10-40% ether in petrol) gave ***(Z)*-810** as a pale yellow solid that yielded large yellow prisms on recrystallisation (355 mg, 0.84 mmol, 21%): mp 124-125 °C (hexane); then ***(E)*-810** as a yellow solid that gave fine yellow needles on recrystallisation (1.22 g, 2.89 mmol, 73%): mp 134-136 °C (ethyl acetate/hexane).

Data for ***(Z)-810****:*

FT-IR (neat, cm^{-1}): 3078 w, 3006 w, 2964 w, 2927 w, 2835 w, 1591 w, 1562 w, 1495 s, 1460 m, 1438 m, 1392 w, 1355 m, 1323 m, 1251 vs, 1205 vs, 1176 m, 1157 s, 1110 w, 1026 m, 858 m, 841 m, 785 m, 755 vs, 726 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.68 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.63 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.37 (1H, s, ArH), 7.29 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.26 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.25 (1H, s, ArH), 6.97 (1H, s, ArH), 6.86 (1H, d, J = 11.8 Hz, ArCH=CHAr), 6.52 (1H, d, J = 11.8 Hz, ArCH=CHAr), 3.95 (3H, s, $ArOCH_3$), 3.77 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 149.8 (CO (Ar)), 149.7 (CO (Ar)), 140.8 (C (Ar)), 139.9 (C (Ar)), 139.2 (C (Ar)), 133.9 (ArCH=CHAr), 133.6 (C (Ar)), 126.2 (CH (Ar)), 125.2 (CH (Ar)), 125.1 (CH (Ar)), 124.7 (ArCH=CHAr), 123.8 (CH (Ar)), 122.5 (CH (Ar)), 121.7 (CH (Ar)), 113.8 (CH (Ar)), 88.3 (CI (Ar)), 56.6 ($ArOCH_3$), 56.4 ($ArOCH_3$).

LRMS (EI) *m/z:* 422 (M^+, 11%), 296 ($[MH - I]^+$, 56%), 221 (55%), 208 (100%).

CHN Found: C, 51.04; H, 3.66; $C_{18}H_{15}IO_2S$ requires C, 51.20; H, 3.58.

Data for ***(E)-810****:*

FT-IR (neat, cm^{-1}): 3051 w, 3004 w, 2932 w, 2838 w, 1592 m, 1556 w, 1497 s, 1461 m, 1432 s, 1378 m, 1348 w, 1324 m, 1255 vs, 1203 s, 1163 s, 1023 m, 976 m, 944 s, 856 m, 844 m, 801 s, 741 vs, 723 s, 670 m.

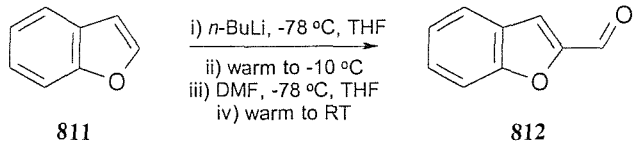
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.83-7.77 (1H, m, ArH), 7.75-7.69 (1H, m, ArH), 7.38-7.30 (2H, m, ArH), 7.29 (2H, s, ArH), 7.17 (1H, d, J = 15.8 Hz, ArCH=CHAr), 7.12 (1H, s, ArH), 7.09 (1H, d, J = 15.8 Hz, ArCH=CHAr), 3.96 (3H, s, $ArOCH_3$), 3.90 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 150.0 (2 x CO (Ar)), 143.1 (C (Ar)), 140.6 (C (Ar)), 139.5 (C (Ar)), 134.7 (ArCH=CHAr), 132.5 (C (Ar)), 125.2 (CH (Ar)), 124.9 (CH (Ar)), 123.9 (CH (Ar)), 123.6 (CH (Ar) *and* ArCH=CHAr), 122.7 (CH (Ar)), 122.1 (CH (Ar)), 108.8 (CH (Ar)), 89.9 (CI (Ar)), 56.6 ($ArOCH_3$), 56.4 ($ArOCH_3$).

LRMS (CI) *m/z:* 422 (M^+, 14%), 296 ($[MH - I]^+$, 67%), 208 (88%), 134 (100%).

CHN Found: C, 51.36; H, 3.67; $C_{18}H_{15}IO_2S$ requires C, 51.20; H, 3.58.

2-Formylbenzo[*b*]furan (**812**)



811
mw = 118.14 g mol^{-1}
C_8H_6O

812
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

In accordance with the procedure of Cugnon de Sévricourt and Robba,[212] to a stirred solution of benzo[*b*]furan **811** (5 g, 42.3 mmol) in THF (100 mL) under nitrogen at –78 °C was added *n*-butyllithium (21.1 mL, 46.5 mmol, 2.2 M solution in hexanes) over 5 minutes. After allowing to warm to –10 °C over 1 hour, the solution was again cooled to -78 °C and DMF (3.6 mL, 46.5 mmol) was added over 5 minutes. The reaction mixture was stirred for 16 hours at ambient temperature, then diluted with saturated ammonium chloride solution (50 mL) and extracted with ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (10-20% ether in petrol) gave **812** as a yellow oil (5.22 g, 35.7 mmol, 84%). The observed data is consistent with literature values.[213]

FT-IR (neat, cm^{-1}): 1680 vs, 1610 m, 1555 s, 1477 w, 1448 w, 1348 w, 1328 w, 1288 m, 1257 w, 1196 w, 1152 w, 1119 s, 1005 w, 947 s, 884 m, 831 s, 750 s, 733 s.

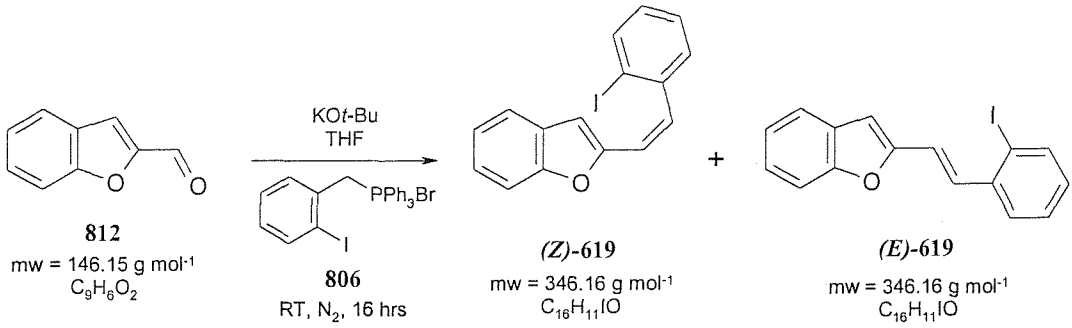
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.89 (1H, s, ArC<u>H</u>O), 7.77 (1H, dd, J = 8.1, 1.2 Hz, Ar<u>H</u>), 7.63 (1H, app. d, J = 8.3 Hz, Ar<u>H</u>), 7.59 (1H, d, J = 0.5 Hz, Ar<u>H</u>), 7.55 (1H, td, J = 8.3, 1.2 Hz, Ar<u>H</u>), 7.37 (1H, app. t, J = 8.1 Hz, Ar<u>H</u>).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 179.9 (Ar<u>C</u>HO), 156.4 (<u>C</u>O (Ar)), 152.8 (<u>C</u> (Ar)), 129.4 (<u>C</u>H (Ar)), 126.8 (<u>C</u> (Ar)), 124.4 (<u>C</u>H (Ar)), 123.8 (<u>C</u>H (Ar)), 118.1 (<u>C</u>H (Ar)), 112.8 (<u>C</u>H (Ar)).

LRMS (CI) *m/z:* 164 ([M + NH_4]$^+$, 23%), 146 (M$^+$, 100%), 118 ([MH – CHO]$^+$, 15%).

2-(*Z*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]furan (***(Z)*-619**) and

2-(*E*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]furan (***(E)*-619**)



812
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

806
RT, N_2, 16 hrs

***(Z)*-619**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

***(E)*-619**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

To a stirred suspension of **806** (1.95 g, 3.76 mmol) in THF (40 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (461 mg, 4.10 mmol). On stirring for 1 hour, the reaction mixture was cooled to 0 °C and a solution of **812** (0.50 g, 3.42 mmol) in THF (40 mL) added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale yellow semi-solid. Purification by column chromatography (1% ether in petrol followed by 0.25-1% ether in petrol) gave firstly ***(Z)*-619** as a pale yellow oil (495 mg, 1.43 mmol, 42%); then ***(E)*-619** as a white solid that on recrystallisation gave large colourless needles (430 mg, 1.24 mmol, 36%): mp 65-67 °C (hexane).

*Data for **(Z)-619**:*

FT-IR (neat, cm^{-1}): 3058 w, 2958 w, 2868 w, 1583 w, 1557 w, 1449 m, 1429 m, 1391 w, 1346 w, 1291 w, 1256 m, 1197 w, 1162 w, 1145 w, 1125 w, 1105 w, 1042 w, 1011 s, 946 m, 890 w, 873 w, 846 w, 806 s, 730 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.96 (1H, dd, J = 8.1, 1.1 Hz, ArH), 7.51 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.46 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.36 (1H, td, J = 7.4, 1.1 Hz, ArH), 7.33 (1H, d, J = 7.4 Hz, ArH), 7.25 (1H, td, J = 8.1, 1.5 Hz, ArH), 7.18 (1H, td, J = 7.7, 1.1 Hz, ArH), 7.06 (1H, td, J = 7.4, 1.5 Hz, ArH), 6.63 (1H, d, J = 12.5 Hz, ArCH=CHAr), 6.59 (1H, d, J = 12.5 Hz, ArCH=CHAr), 6.44 (1H, s, ArH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 154.7 (C (Ar)), 153.8 (C (Ar)), 141.9 (C (Ar)), 139.3 (CH (Ar)), 135.0 (ArCH=CHAr), 130.5 (CH (Ar)), 129.7 (CH (Ar)), 128.9 (C (Ar)), 128.3 (CH (Ar)), 125.1 (ArCH=CHAr), 123.3 (CH (Ar)), 121.3 (CH (Ar)), 119.7 (CH (Ar)), 111.5 (CH (Ar)), 106.9 (CH (Ar)), 99.6 (CI (Ar)).

LRMS (CI) *m/z:* 347 (MH^+, 70%), 220 ($[MH - I]^+$, 68%), 189 (94%), 63 (100%).

HRMS (EI) *m/z* Found: M^+ 345.9853, $C_{16}H_{11}IO$ requires 345.9855.

*Data for **(E)-619**:*

FT-IR (neat, cm^{-1}): 3055 w, 1610 w, 1579 w, 1543 w, 1458 m, 1432 m, 1132 w, 1292 w, 1255 m, 1196 w, 1122 w, 1104 w, 1011 s, 951 vs, 886 w, 828 w, 788 s, 745 vs, 707 m.

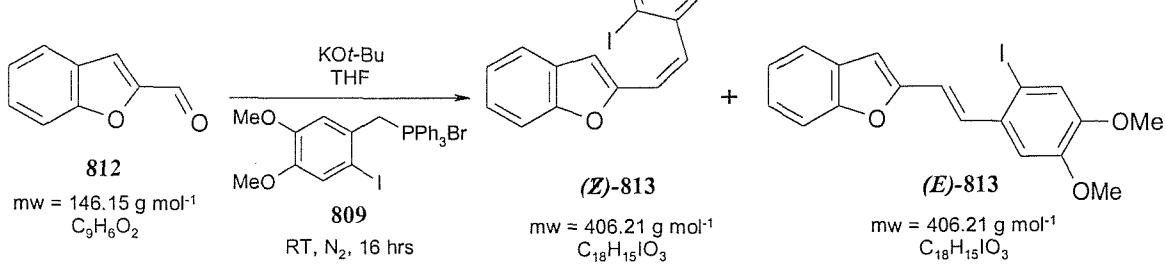
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.93 (1H, dd, J = 8.1, 1.1 Hz, ArH), 7.63 (1H, dd, J = 8.1, 1.5 Hz, ArH), 7.56 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.53 (1H, dd, J = 8.1, 0.8 Hz, ArH), 7.52 (1H, d, J = 15.8 Hz, ArCH=CHAr), 7.37 (1H, app. t, J = 7.7 Hz, ArH), 7.32 (1H, td, J = 8.1, 1.5 Hz, ArH), 7.23 (1H, td, J = 7.7, 0.8 Hz, ArH), 6.99 (1H, td, J = 7.7, 1.5 Hz, ArH), 6.91 (1H, d, J = 15.8 Hz, ArCH=CHAr), 6.76 (1H, s, ArH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 154.5 (C (Ar)), 154.0 (C (Ar)), 139.4 (CH (Ar)), 139.2 (C (Ar)), 133.1 (ArCH=CHAr), 128.8 (CH (Ar)), 128.5 (C (Ar)), 127.9 (CH (Ar)), 125.6 (CH (Ar)), 124.4 (ArCH=CHAr), 122.4 (CH (Ar)), 120.4 (CH (Ar)), 118.7 (CH (Ar)), 110.6 (CH (Ar)), 105.5 (CH (Ar)), 100.0 (CI (Ar)).

LRMS (CI) *m/z:* 347 (MH^+, 90%), 220 ($[MH - I]^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 345.9860, $C_{16}H_{11}IO$ requires 345.9855.

2-(*Z*)-2-(4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]furan (***(Z)*-813**) and 2-(*E*)-2-(4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]furan (***(E)*-813**)



To a stirred suspension of **809** (560 mg, 0.90 mmol) in THF (12 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (101 mg, 0.90 mmol). On stirring for 1 hour, the reaction mixture was cooled to 0 °C and a solution of **812** (120 mg,

0.82 mmol) in THF (12 mL) was added. After 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (10-50% ether in petrol) gave firstly ***(Z)*-813** as a pale yellow solid that gave on recrystallisation large white prisms (228 mg, 0.56 mmol, 68%): mp 134-136 °C (ethyl acetate/hexane); then ***(E)*-813** as a pale yellow solid that on recrystallisation gave fine white needles (108 mg, 0.27 mmol, 32%): mp 146-149 °C (ethyl acetate/hexane).

*Data for **(Z)-813**:*

FT-IR (neat, cm^{-1}): 3003 w, 2934 w, 2836 w, 1501 s, 1451 s, 1434 m, 1414 m, 1369 m, 1309 m, 1262 s, 1208 vs, 1164 s, 1124 m, 1039 m, 1025 s, 1004 m, 935 m, 880 m, 829 s, 801 m, 780 m, 755 vs, 673 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.49-7.45 (1H, m, ArH), 7.36-7.31 (1H, m, ArH), 7.34 (1H, s, ArH), 7.24 (1H, td, J = 7.1, 1.7 Hz, ArH), 7.18 (1H, td, J = 7.4, 1.4 Hz, ArH), 7.12 (1H, s, ArH), 6.56 (1H, d, J = 12.4 Hz, ArCH=CHAr), 6.53 (1H, s, ArH), 6.50 (1H, d, J = 12.4 Hz, ArCH=CHAr), 3.94 (3H, s, $ArOCH_3$), 3.74 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.4 (CO (Ar)), 153.6 (CO (Ar)), 149.3 (CO (Ar)), 148.9 (CO (Ar)), 134.5 (ArCH=CHAr), 133.4 (C (Ar)), 128.7 (C (Ar)), 124.9 (CH (Ar)), 123.1 (CH (Ar)), 121.1 (CH (Ar)), 121.0 (CH (Ar)), 118.5 (ArCH=CHAr), 113.0 (CH (Ar)), 111.1 (CH (Ar)), 106.9 (CH (Ar)), 88.2 (CI (Ar)), 56.3 ($ArOCH_3$), 56.1 ($ArOCH_3$).

LRMS (CI) *m/z:* 407 (MH^+, 13%), 280 ($[MH - I]^+$, 100%).

CHN Found: C, 53.34; H, 3.70; $C_{18}H_{15}IO_3$ requires C, 53.22; H, 3.72.

*Data for **(E)-813**:*

FT-IR (neat, cm^{-1}): 3051 w, 2996 w, 2935 w, 2851 w, 1496 s, 1449 m, 1439 m, 1381 m, 1334 m, 1255 vs, 1210 vs, 1189 vs, 1164 vs, 1108 w, 1025 s, 838 s, 799 vs, 747 m, 733 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.55 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.52 (1H, dd, J = 7.4, 1.1 Hz, ArH), 7.44 (1H, d, J = 16.2 Hz, ArCH=CHAr), 7.31 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.30 (1H, s, ArH), 7.23 (1H, td, J = 7.4, 1.1 Hz,

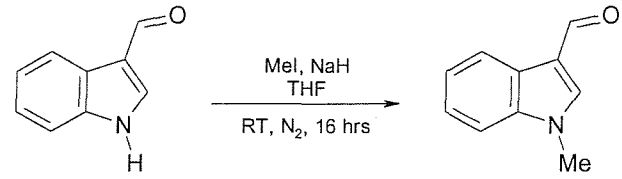
ArH), 7.12 (1H, s, ArH), 6.80 (1H, d, J = 16.2 Hz, ArCH=CHAr), 6.72 (1H, s, ArH), 3.96 (3H, s, $ArOCH_3$), 3.90 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.1 (CO (Ar)), 154.9 (CO (Ar)), 149.8 (CO (Ar)), 149.7 (CO (Ar)), 133.6 (ArCH=CHAr), 132.3 (C (Ar)), 129.2 (C (Ar)), 124.9 (CH (Ar)), 123.1 (CH (Ar)), 121.9 (CH (Ar)), 121.0 (CH (Ar)), 117.6 (ArCH=CHAr), 111.3 (CH (Ar)), 108.3 (CH (Ar)), 105.5 (CH (Ar)), 89.9 (CI (Ar)), 56.3 ($ArOCH_3$), 56.1 ($ArOCH_3$).

LRMS (CI) *m/z:* 406 (M^+, 11%), 280 ($[MH - I]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 835.0012, $C_{36}H_{30}I_2O_6Na$ requires 835.0024.

N-Methylindole-3-carboxaldehyde (**815**)



814
mw = 145.16 g mol^{-1}
C_9H_7NO

815
mw = 159.19 g mol^{-1}
$C_{10}H_9NO$

In accordance with the procedure of Ward *et al.*,[214] to a stirred suspension of petrol-washed sodium hydride (465 mg, 19.4 mmol) in THF (150 mL) at 0 °C under nitrogen was added indole-3-carboxaldehyde **814** (2.55 g, 17.6 mmol). On stirring for 30 minutes at ambient temperature, methyl iodide (1.64 mL, 26.4 mmol) was added. After 16 hours, the reaction mixture was diluted with water (100 mL) and extracted with ether (1 x 200 mL, 2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark brown oil. Purification by column chromatography (90% ether in petrol to 5% methanol in ether) gave **815** as a brown crystalline solid (2.77 g, 17.4 mmol, 99%): mp 59-60 °C, lit. 60-63 °C (benzene/petrol).[214]

FT-IR (neat, cm^{-1}): 3103 w, 3060 w, 2804 w, 1638 vs, 1613 m, 1534 s, 1468 s, 1381 s, 1333 m, 1257 w, 1190 m, 1123 m, 1073 s, 786 s.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 290 (18800), 239 (19300).

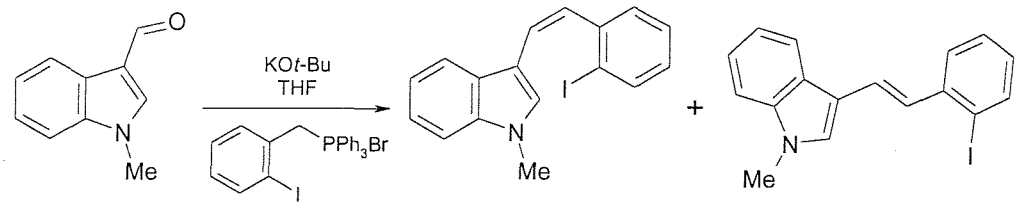
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.94 (1H, s, ArCHO), 8.32-8.27 (1H, m, ArH), 7.61 (1H, s, ArH), 7.36-7.28 (3H, m, ArH), 3.81 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 184.6 (ArCHO), 139.6 (CH (Ar)), 138.0 (C (Ar)), 125.3 (C (Ar)), 124.2 (CH (Ar)), 123.1 (CH (Ar)), 122.1 (CH (Ar)), 118.1 (C (Ar)), 110.1 (CH (Ar)), 33.8 (NCH_3).

LRMS (CI) *m/z:* 160 (MH^+, 100%).

3-[(*Z*)-2-(2-Iodophenyl)vinyl]-1-methyl-1*H*-indole (***(Z)*-624**) and

3-[(*E*)-2-(2-Iodophenyl)vinyl]-1-methyl-1*H*-indole (***(E)*-624**)



815
mw = 159.19g mol^{-1}
$C_{10}H_9NO$

806
Δ, N_2, 64 hrs

***(Z)*-624**
mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

***(E)*-624**
mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

To a stirred suspension of **806** (6.04 g, 10.8 mmol) in THF (200 mL) under nitrogen was added potassium *tert*-butoxide (1.16 g, 10.4 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of indole **815** (1.5 g, 9.42 mmol) in THF (50 mL) added. After 16 hours, the reaction was heated to reflux for 48 hours. On cooling to ambient temperature, the reaction mixture was diluted with water (100 mL) and extracted with ether (1 x 200 mL, 2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale brown oil. Purification by column chromatography (5-30% ether in petrol) gave firstly ***(Z)*-624** as a yellow oil that crystallised on standing to small yellow needles (323 mg, 0.90 mmol, 10%): mp 58-59 °C; then ***(E)*-624** as a yellow solid that gave yellow prisms on recrystallisation (330 mg, 0.92 mmol, 10%): mp 127-130 °C (ether/petrol).

*Data for **(Z)-624**:*

FT-IR (neat, cm^{-1}): 3103 w, 3050 w, 2936 w, 1632 m, 1531 s, 1476 s, 1476 s, 1422 m, 1377 m, 1336 m, 1318 m, 1224 s, 1204 w, 1152 w, 1118 m, 1059 m, 1011 s, 959 w, 886 w, 825 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 306 (17100).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.96 (1H, dd, J = 7.9, 1.3 Hz, ArH), 7.51 (1H, td, J = 7.9, 1.0 Hz, ArH), 7.46 (1H, dd, J = 7.7, 1.7 Hz, ArH), 7.29-7.19 (3H, m, ArH), 7.12 (1H, ddd, J = 8.0, 6.4, 1.7 Hz, ArH), 6.97 (1H, td, J = 7.9, 1.7 Hz, ArH), 6.86 (1H, d, J = 11.6 Hz, ArCH=CHAr), 6.67 (1H, s, ArH), 6.38 (1H, d, J = 11.6 Hz, ArCH=CHAr), 3.65 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 143.7 (C (Ar)), 139.3 (CH (Ar)), 136.5 (C (Ar)), 130.2 (CH (Ar)), 129.3 (CH (Ar)), 128.6 (CH (Ar)), 128.3 (CH (Ar)), 128.2 (ArCH=CHAr), 127.7 (C (Ar)), 122.2 (CH (Ar)), 122.1 (ArCH=CHAr),

119.9 (CH (Ar)), 119.4 (CH (Ar)), 111.2 (C (Ar)), 109.4 (CH (Ar)), 100.2 (CI (Ar)), 33.1 (NCH_3).

LRMS (CI) *m/z:* 360 (MH^+, 100%), 232 ($[M - I]^+$, 82%), 217 ($[M - I - CH_3]^+$, 39%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 741.0222, $C_{34}H_{28}I_2N_2Na$ requires 741.0234.

*Data for **(E)-624**:*

FT-IR (neat, cm^{-1}): 3104 w, 3065 w, 3048 w, 3005 w, 2931 w, 2906 w, 1626 s, 1567 w, 1528 m, 1452 s, 1430 m, 1374 m, 1344 m, 1252 m, 1134 m, 1072 m, 1006 m, 952 s, 811 m, 791 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 322 (32700).

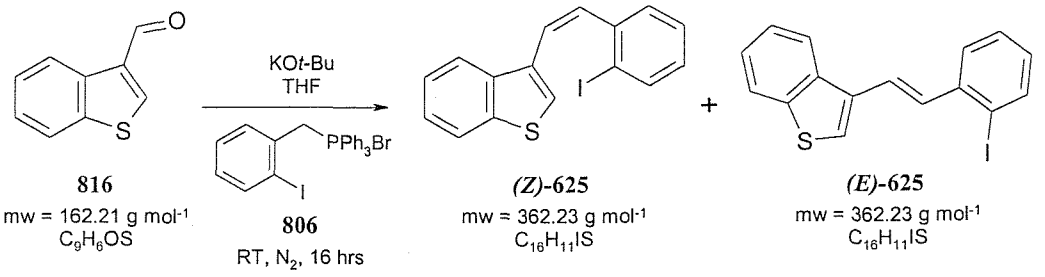
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.11 (1H, dd, J = 6.7, 2.0 Hz, ArH), 7.90 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.68 (1H, dd, J = 8.0, 1.5 Hz, ArH), 7.37 (1H, d, J = 16.1 Hz, ArCH=CHAr), 7.38-7.27 (5H, m, ArH), 7.20 (1H, d, J = 16.1 Hz, ArCH=CHAr), 6.93 (1H, td, J = 8.0, 1.7 Hz, ArH), 3.80 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 141.6 (C (Ar)), 139.7 (CH (Ar)), 138.0 (C (Ar)), 129.6 (CH (Ar)), 128.5 (CH (Ar)), 128.5 (CH (Ar)), 128.1 (ArCH=CHAr), 126.1 (C (Ar)), 125.4 (CH (Ar)), 124.7 (CH (Ar)), 122.6 (CH (Ar)), 120.7 (CH (Ar)), 120.7 (ArCH=CHAr), 114.0 (C (Ar)), 109.8 (CH (Ar)), 100.4 (CI (Ar)), 33.1 (NCH_3).

LRMS (CI) *m/z:* 360 (MH^+, 56%), 232 ($[M - I]^+$, 100%), 217 ($[M - I - CH_3]^+$, 17%).

CHN Found C, 56.88; H, 3.91; N, 3.86; $C_{17}H_{14}IN$ requires C, 56.84; H, 3.93; N, 3.90.

3-[(*Z*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]thiophene (***(Z)*-625**) and
3-[(*E*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]thiophene (***(E)*-625**)



To a stirred suspension of **806** (7.0 g, 12.5 mmol) in THF (100 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (1.66 g, 14.8 mmol). After 1 hour, the

reaction mixture was cooled to 0 °C and a solution of 3-formylbenzo[*b*]thiophene **816** (2.0 g, 12.3 mmol) in THF (50 mL) was added. After 16 hours, the reaction mixture was diluted with water (100 mL) and extracted with ether (1 x 200 mL, 2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (2.5-10% ether in petrol) yielded firstly mixed fractions of ***(Z)*-625** and ***(E)*-625** in a 1:1 ratio as a colourless oil that crystallised on standing to a white solid (3.03 g, 8.34 mmol, 68%); then ***(E)*-625** as a white solid that on recrystallisation gave colourless prisms (1.25 g, 3.46 mmol, 28%): mp 96-98 °C (ether/petrol). Consecutive recrystallisations (ether/petrol) of the mixed fractions gave a small sample of ***(Z)*-625** as a clear oil from the mother liquor (132 mg, 0.36 mmol, 3%).

*Data for **(Z)-625***:

FT-IR (neat, cm^{-1}): 3058 w, 3015 w, 2916 w, 2849 w, 1581 w, 1556 w, 1508 w, 1456 m, 1425 s, 1315 w, 1256 w, 1076 w, 1011 s, 862 w, 829 s, 790 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.92 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.85 (1H, dd, J = 7.0, 1.8 Hz, ArH), 7.79 (1H, dd, J = 7.0, 1.8 Hz, ArH), 7.40 (1H, ddd, J = 7.4, 7.0, 1.8 Hz, ArH), 7.37 (1H, ddd, J = 7.4, 7.0, 1.8 Hz, ArH), 7.20 (1H, dd, J = 7.7, 1.9 Hz ArH), 7.13 (1H, td, J = 7.7, 1.1 Hz ArH), 7.00 (1H, s, ArH), 6.91 (1H, td, J = 7.7, 1.9 Hz ArH), 6.87 (1H, d, J = 11.8 Hz, ArCH=CHAr), 6.73 (1H, d, J = 11.8 Hz, ArCH=CHAr).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 142.0 (C (Ar)), 139.8 (C (Ar)), 139.4 (CH (Ar)), 138.7 (C (Ar)), 135.4 (ArCH=CHAr), 131.6 (C (Ar)), 130.2 (CH (Ar)), 129.1 (CH (Ar)), 128.3 (CH (Ar)), 125.0 (ArCH=CHAr), 124.7 (CH (Ar)), 124.4 (CH (Ar)), 123.2 (CH (Ar)), 122.9 (CH (Ar)), 122.2 (CH (Ar)), 99.8 (CI (Ar)).

LRMS (CI) *m/z:* 363 (MH^+, 23%), 235 ($[M - I]^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 361.9626, $C_{16}H_{11}IS$ requires 361.9626.

*Data for **(E)-625***:

FT-IR (neat, cm^{-1}): 3050 w, 3001 w, 1625 w, 1556 w, 1503 w, 1453 m, 1424 s, 1361 w, 1238 m, 1208 w, 1184 w, 1162 w, 1086 w, 1010 m, 950 vs, 883 w, 838 m.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 310 (24600).

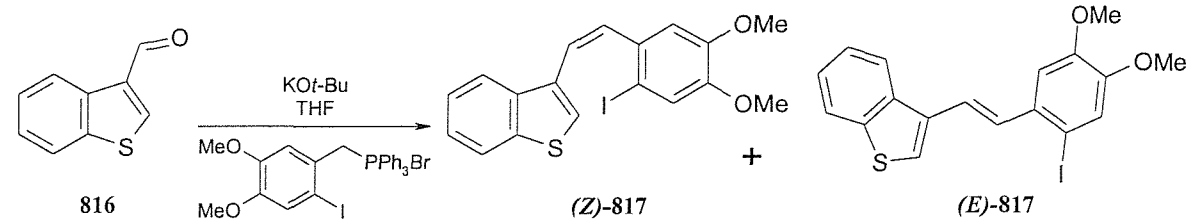
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$): 8.13 (1H, d, *J* = 7.8 Hz, ArH), 7.95 (2H, d, *J* = 7.8 Hz, 2 x ArH), 7.74 (1H, dd, *J* = 7.8, 1.5 Hz, ArH), 7.69 (1H, s, ArH), 7.53 (1H, td, *J* = 7.8, 1.2 Hz, ArH), 7.50-7.41 (3H, m, 2 x ArH *and* ArCH=CHAr), 7.29 (1H, d, *J* = 16.1 Hz, ArCH=CHAr), 7.04 (1H, td, *J* = 7.8, 1.5 Hz, ArH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 141.0 (C (Ar)), 140.9 (2 x C (Ar)), 140.1 (CH (Ar)), 138.0 (C (Ar)), 134.2 (CH (Ar)), 129.5 (CH (Ar)), 128.9 (CH (Ar)), 126.6 (CH (Ar)), 125.1 (ArCH=CHAr), 124.9 (ArCH=CHAr), 124.2 (CH (Ar)), 123.7 (CH (Ar)), 123.4 (CH (Ar)), 122.5 (CH (Ar)), 100.8 (CI (Ar)).

LRMS (CI) *m/z:* 362 (M^+, 50%), 235 ($[M - I]^+$, 100%).

CHN Found C, 53.26; H, 3.07; $C_{16}H_{11}IS$ requires C, 53.05; H, 3.06.

3-[(*Z*)-2-(4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]thiophene (***(Z)*-817**) and
3-[(*E*)-2- (4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]thiophene (***(E)*-817**)



816
mw = 162.21 g mol^{-1}
C_9H_6OS

809
RT, N_2, 16 hrs

***(Z)*-817**
mw = 422.28 g mol^{-1}
$C_{18}H_{15}IO_2S$

***(E)*-817**
mw = 422.28 g mol^{-1}
$C_{18}H_{15}IO_2S$

To a stirred suspension of **809** (2.10 g, 3.39 mmol) in THF (45 mL) under nitrogen was added potassium *tert*-butoxide (380 mg, 3.39 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of 3-formylbenzo[*b*]thiophene **816** (500 mg, 3.08 mmol) in THF (45 mL) was added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (5-50% ether in petrol) gave firstly ***(Z)*-817** as a waxy yellow solid (494 mg, 1.17 mmol, 38%): mp 47-50 °C; then ***(E)*-817** as a white solid that gave fine white needles on recrystallisation (799 mg, 1.89 mmol, 61%): mp 183-185 °C (ether/petrol).

*Data for **(Z)-817**:*

FT-IR (neat, cm^{-1}): 3076 w, 3001 w, 2953 w, 2905 w, 2834 w, 1590 w, 1498 s, 1462 s, 1424 m, 1367 w, 1314 w, 1249 s, 1234 s, 1207 s, 1160 m, 1098 w, 1019 m, 954 w, 856 m, 793 m, 760 s, 736 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.87-7.82 (1H, m, ArH), 7.75-7.68 (1H, m, ArH), 7.40-7.32 (2H, m, ArH), 7.28 (1H, s, ArH), 7.15 (1H, d, J = 1.2 Hz, ArH), 6.79 (1H, dd, J = 11.9, 1.2 Hz, ArCH=CHAr), 6.70 (1H, d, J = 11.9 Hz, ArCH=CHAr), 6.67 (1H, s, ArH), 3.87 (3H, s, $ArOCH_3$), 3.32 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 149.3 (CO (Ar)), 149.2 (CO (Ar)), 140.1 (C (Ar)), 138.6 (C (Ar)), 135.7 (ArCH=CHAr), 134.1 (C (Ar)), 132.4 (C (Ar)), 124.8 (CH (Ar)), 124.7 (CH (Ar)), 123.0 (CH (Ar)), 122.8 (2 x CH (Ar)), 122.7 (CH (Ar)), 121.5 (ArCH=CHAr), 112.8 (CH (Ar)), 88.6 (CI (Ar)), 56.4 ($ArOCH_3$), 55.8 ($ArOCH_3$).

LRMS (CI) *m/z:* 423 (MH^+, 25%), 296 ($[MH - I]^+$, 80%), 221 (84%), 208 (100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 444.9729, $C_{18}H_{15}IO_2SNa$ requires 444.9729.

*Data for **(E)-817**:*

FT-IR (neat, cm^{-1}): 3111 w, 3008 w, 2933 w, 2903 w, 1592 m, 1498 s, 1461 m, 1425 m, 1384 m, 1322 m, 1258 s, 1241 s, 1202 vs, 1171 vs, 1087 m, 1040 m, 1018 s, 977 m, 945 s, 879 m, 839 m, 809 m, 787 m, 771 vs, 731 s, 708 m.

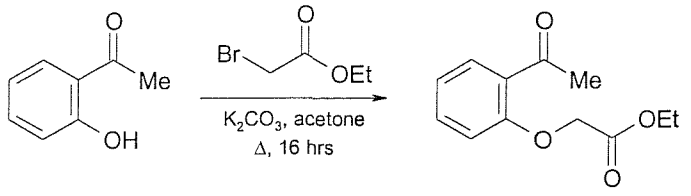
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.09 (1H, app. d, J = 7.4 Hz, ArH), 7.91 (1H, dd, J = 8.1, 1.2 Hz, ArH), 7.62 (1H, s, ArH), 7.49 (1H, td, J = 8.1, 1.2 Hz, ArH), 7.42 (1H, td, J = 7.4, 1.2 Hz, ArH), 7.34 (1H, d, J = 16.0 Hz, ArCH=CHAr), 7.31 (1H, s, ArH), 7.20 (1H, s, ArH), 7.14 (1H, d, J = 16.0 Hz, ArCH=CHAr), 3.99 (3H, s, $ArOCH_3$), 3.91 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 150.1 (CO (Ar)), 149.9 (CO (Ar)), 141.1 (C (Ar)), 138.0 (C (Ar)), 134.3 (C (Ar)), 134.1 (ArCH=CHAr), 133.4 (C (Ar)), 125.0 (CH (Ar)), 124.9 (CH (Ar)), 123.4 (ArCH=CHAr), 123.2 (CH (Ar)), 122.5 (CH (Ar)), 122.4 (CH (Ar)), 122.1 (CH (Ar)), 109.0 (CH (Ar)), 89.7 (CI (Ar)), 56.6 ($ArOCH_3$), 56.5 ($ArOCH_3$).

LRMS (CI) *m/z:* 423 (MH^+, 14%), 296 ($[MH - I]^+$, 100%), 221 (54%), 208 (41%).

CHN Found: C, 51.26; H, 3.67; $C_{18}H_{15}IO_2S$ requires C, 51.20; H, 3.58.

Ethyl (2-acetylphenoxy)acetate (**819**)



818
mw = 136.15 g mol^{-1}
$C_8H_8O_2$

819
mw = 222.24 g mol^{-1}
$C_{12}H_{14}O_4$

In a slightly modified procedure to that of Nielek and Lesiak,[149] a stirred suspension of 2'-hydroxyacetophenone **818** (4.42 mL, 36.7 mmol), ethyl bromoacetate (4.27 mL, 38.5 mmol) and potassium carbonate (15.2 g, 0.11 mol) in acetone (100 mL) was heated at reflux under a $CaCl_2$ drying tube for 16 hours. Upon cooling to ambient temperature, the reaction mixture was filtered and the filtrate concentrated *in vacuo*. The white solid obtained was suspended in water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to yield **819** as a colourless oil that crystallised on standing to a waxy white solid (8.12 g, 36.5 mmol, 100%): mp 45-48 °C, lit. 40-50.5 °C.[149] The observed data is consistent with literature values.

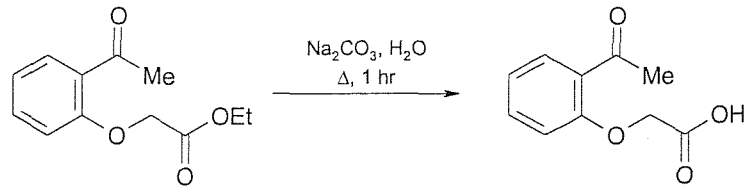
FT-IR (neat, cm^{-1}): 2980 w, 2932 w, 1756 vs, 1667 vs, 1597 s, 1578 w, 1489 m, 1453 m, 1431 m, 1410 m, 1359 m, 1301 m, 1240 s, 1205 vs, 1166 s, 1133 s, 1081 s, 1027 m, 968 m, 837 m, 761 vs, 693 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.78 (1H, dd, J = 7.9, 1.9 Hz, ArH), 7.46 (1H, ddd, J = 7.9, 7.6, 1.9 Hz, ArH), 7.06 (1H, td, J = 7.9, 1.0 Hz, ArH), 6.84 (1H, d, J = 7.6, 1.0 Hz, ArH), 4.74 (2H, s, ArOC$\underline{H}_2$COOEt), 4.29 (2H, q, J = 7.1 Hz, OC$\underline{H}_2$CH$_3$), 2.73 (3H, s, ArCOC$\underline{H}_3$), 1.32 (3H, t, J = 7.1 Hz, OCH$_2$C$\underline{H}_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 199.9 (Ar$\underline{C}$OCH$_3$), 168.3 ($\underline{C}$OOEt), 157.1 ($\underline{C}$O (Ar)), 133.7 ($\underline{C}$H (Ar)), 130.8 ($\underline{C}$H (Ar)), 128.9 ($\underline{C}$ (Ar)), 121.8 ($\underline{C}$H (Ar)), 112.3 ($\underline{C}$H (Ar)), 65.6 (ArO$\underline{C}$H$_2$COOEt), 61.7 (O$\underline{C}$H$_2$CH$_3$), 32.2 (ArCO$\underline{C}$H$_3$), 14.3 (OCH$_2$$\underline{C}H_3$).

LRMS (Cl) *m/z:* 223 (MH^+, 100%), 149 ($[M - C_3H_5O_2]^+$, 63%).

Ethyl (2-acetylphenoxy)acetic acid (**820**)



819

mw = 222.24 g mol^{-1}
$C_{12}H_{14}O_4$

820

mw = 194.19 g mol^{-1}
$C_{10}H_{10}O_4$

Following the procedure of Nielek and Lesiak,[149] a stirred suspension of **819** (8.23 g, 37 mmol) and sodium carbonate (4.35 g, 40.7 mol) in water (66 mL) was heated at reflux for 1 hour. On cooling to 0 °C, the reaction mixture was acidified with concentrated HCl until effervescence ceased. The resultant cream precipitate was collected by filtration, washed with water (150 mL) and dried under air flow to give **820** as a cream solid (6.63 g, 34.1 mmol, 92%): mp 112-115 °C, lit. 114-114.5 °C (H_2O).[149] The observed data is consistent with literature values.

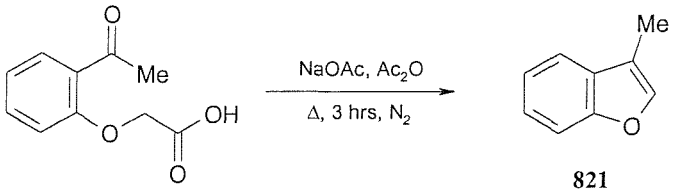
FT-IR (neat, cm^{-1}): 3427 br. m, 2651 m, 2486 m, 2325 w, 1980 w, 1700 s, 1643 s, 1596 s, 1486 m, 1455 m, 1423 w, 1362 m, 1288 s, 1240 vs, 1170 m, 1135 m, 1058 s, 1010 m, 974 m, 843 m, 767 s, 736 m, 658 m.

^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 7.68 (1H, dd, J = 7.6, 1.9 Hz, ArH), 7.52 (1H, ddd, J = 8.3, 7.4, 1.9 Hz, ArH), 7.12 (1H, app. d, J = 8.3 Hz, ArH), 7.06 (1H, td, J = 7.6, 1.0 Hz, ArH), 4.91 (2H, s, $ArOCH_2COOH$), 2.66 (3H, s, $ArCOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, D_6-acetone): 199.3 ($ArCOCH_3$), 169.8 (COOH), 158.0 (CO (Ar)), 134.2 (CH (Ar)), 130.6 (CH (Ar)), 129.3 (C (Ar)), 121.8 (CH (Ar)), 113.6 (CH (Ar)), 65.5 ($ArOCH_2COOH$), 31.8 ($ArCOCH_3$).

LRMS (ES$^-$) *m/z:* 387 ([2M - H]$^-$, 100%), 307 ([M + CF_3COO]$^-$, 14%).

3-Methylbenzo[*b*]furan (**821**)



820

mw = 194.19 g mol^{-1}

$C_{10}H_{10}O_4$

821

mw = 132.16 g mol^{-1}

C_9H_8O

Following the procedure of Nielek and Lesiak,[149] a stirred suspension of **820** (6.40 g, 33 mmol) and sodium acetate (11.48 g, 0.14 mol) in acetic anhydride (21.8 mL, 0.23 mol) was heated at reflux for 3 hours under nitrogen. On cooling to ambient temperature, the reaction mixture was poured onto water (75 mL) and extracted with benzene (3 x 50 mL). The combined organic phases were washed with saturated sodium carbonate solution (2 x 50 mL) and brine (50 mL), dried ($CaCl_2$) and concentrated *in vacuo* to a black oil. Distillation under reduced pressure gave **821** as a colourless oil (2.38 g, 18.0 mmol, 55%). The observed data is consistent with literature values.[215]

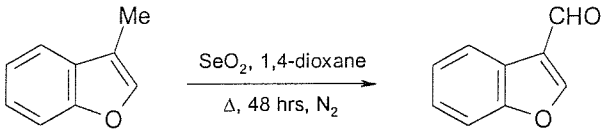
FT-IR (neat, cm^{-1}): 3058 w, 3039 w, 1535 w, 1474 w, 1452 m, 1348 w, 1329 w, 1248 m, 1174 m, 1126 m, 1103 m, 1029 m, 1007 w, 932 w, 898 w, 859 m, 767 m, 745 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.60 (1H, dd, J = 7.4, 1.6 Hz, ArH), 7.53 (1H, dd, J = 7.4, 1.4 Hz, ArH), 7.47 (1H, q, J = 1.2 Hz, ArH), 7.36 (1H, td, J = 7.4, 1.6 Hz, ArH), 7.31 (1H, td, J = 7.4, 1.4 Hz, ArH), 2.31 (3H, d, J = 1.2 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.4 (C (Ar)), 141.5 (CH (Ar)), 129.2 (C (Ar)), 124.3 (CH (Ar)), 122.4 (CH (Ar)), 119.6 (CH (Ar)), 115.8 (C (Ar)), 111.5 (CH (Ar)), 8.1 ($ArCH_3$).

LRMS (CI) *m/z:* 132 (M^+, 100%).

3-Formylbenzo[*b*]furan (**822**)



821
mw = 132.16 g mol^{-1}
C_9H_8O

822
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

In accordance with the procedure of Zaidlewicz *et al.*,[150] a solution of **821** (2.20 g, 16.6 mmol) and selenium dioxide (2.12 g, 19.1 mmol) in 1,4-dioxane (25 mL) was heated at reflux for 48 hours under nitrogen. On cooling to ambient temperature, the reaction mixture was filtered through celite and the resultant filtrate concentrated *in vacuo* to a black oil. Distillation under reduced pressure gave **822** as a colourless oil that crystallised on standing to a white solid (2.05 g, 14.0 mmol, 84%): mp 40-41 °C, lit. 38-39 °C (petrol).[150] The observed data is consistent with literature values.[150,213]

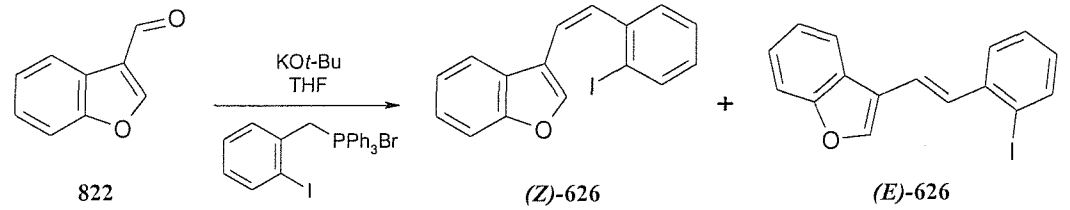
FT-IR (neat, cm^{-1}): 3129 w, 3086 w, 3041 w, 2875 w, 1665 vs, 1592 w, 1553 s, 1479 m, 1448 s, 1399 w, 1371 m, 1338 w, 1274 m, 1240 m, 1182 w, 1137 m, 1117 s, 1074 s, 1013 w, 952 w, 858 m, 847 m, 784 s, 762 s.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.2 (1H, s, ArC<u>H</u>O), 8.29 (1H, s, Ar<u>H</u>), 8.23-8.19 (1H, m, Ar<u>H</u>), 7.60-7.55 (1H, m, Ar<u>H</u>), 7.44 (1H, td, J = 7.1, 1.9 Hz, Ar<u>H</u>), 7.40 (1H, td, J = 7.6, 1.7 Hz, Ar<u>H</u>).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 185.0 (Ar<u>C</u>HO), 156.1 (<u>C</u> (Ar)), 155.6 (<u>C</u>H (Ar)), 126.4 (<u>C</u>H (Ar)), 125.0 (<u>C</u>H (Ar)), 123.8 (<u>C</u> (Ar)), 123.1 (<u>C</u> (Ar)), 122.7 (<u>C</u>H (Ar)), 111.8 (<u>C</u>H (Ar)).

LRMS (CI) *m/z:* 146 (M^+, 100%).

3-[(*Z*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]furan (***(Z)*-626**) and
3-[(*E*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]furan (***(E)*-626**)



822
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

806
RT, N_2, 16 hrs

***(Z)*-626**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

***(E)*-626**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

To a stirred suspension of **806** (1.95 g, 3.76 mmol) in THF (40 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (461 mg, 4.10 mmol). On stirring for

1 hour, the reaction mixture was cooled to 0 °C and a solution of **822** (0.50 g, 3.42 mmol) in THF (40 mL) was added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale yellow semi-solid. Purification by column chromatography (2.5% ether in petrol followed by 0.25-0.5% ether in petrol) gave firstly ***(Z)*-626** as a colourless oil (679 mg, 1.96 mmol, 57%); then ***(E)*-626** as a white solid that on recrystallisation gave large white needles (288 mg, 0.83 mmol, 24%): mp 78-79 °C (hexane).

*Data for **(Z)-626***:

FT-IR (neat, cm^{-1}): 3057 w, 2916 w, 2849 w, 1557 w, 1451 m, 1431 m, 1261 w, 1229 w, 1192 m, 1106 s, 1011 s, 947 w, 876 w, 857 m, 804 m, 740 vs, 707 s.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.95 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.45 (1H, dd, J = 8.1, 1.1 Hz, ArH), 7.32-7.25 (4H, m, ArH), 7.20 (1H, td, J = 7.4, 1.1 Hz, ArH), 7.17 (1H, td, J = 8.1, 1.1 Hz, ArH), 6.98 (1H, td, J = 7.7, 1.5 Hz, ArH), 6.72 (1H, d, J = 12.1 Hz, ArCH=CHAr), 6.66 (1H, d, J = 12.1 Hz, ArCH=CHAr).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.0 (C (Ar)), 143.6 (CH (Ar)), 142.3 (C (Ar)), 139.3 (CH (Ar)), 134.8 (ArCH=CHAr), 130.0 (CH (Ar)), 129.2 (CH (Ar)), 128.4 (CH (Ar)), 126.8 (C (Ar)), 124.6 (CH (Ar)), 122.8 (CH (Ar)), 120.4 (CH (Ar)), 119.6 (ArCH=CHAr), 117.0 (C (Ar)), 111.5 (CH (Ar)), 99.6 (CI (Ar)).

LRMS (CI) *m/z:* 347 (MH^+, 53%), 220 ($[MH - I]^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 345.9851, $C_{16}H_{11}IO$ requires 345.9855.

*Data for **(E)-626***:

FT-IR (neat, cm^{-1}): 3137 w, 3061 w, 1639 m, 1582 w, 1549 w, 1450 s, 1433 m, 1277 w, 1240 m, 1210 w, 1185 w, 1155 w, 1108 s, 1081 m, 1008 m, 950 s, 857 m, 788 m, 772 m, 740 vs, 704 m, 652 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.13-8.07 (1H, m, ArH), 7.92 (1H, dd, J = 8.1, 1.5 Hz, ArH), 7.81 (1H, s, ArH), 7.67 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.59-7.54 (1H, m, ArH), 7.50 (1H, d, J = 16.6 Hz, ArCH=CHAr), 7.44-7.35 (3H,

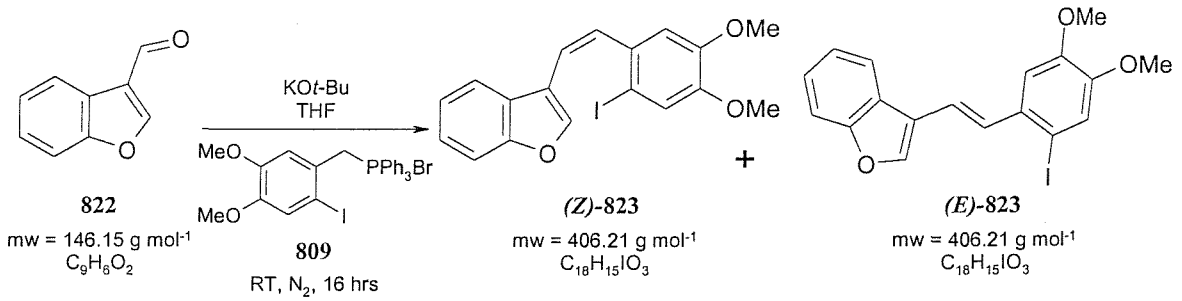
m, ArH), 7.08 (1H, d, J = 16.6 Hz, ArCH=CHAr), 6.99 (1H, td, J = 7.7, 1.5 Hz, ArH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 156.2 (C (Ar)), 144.6 (CH (Ar)), 140.6 (C (Ar)), 139.8 (CH (Ar)), 133.2 (ArCH=CHAr), 129.1 (CH (Ar)), 128.7 (CH (Ar)), 125.9 (CH (Ar)), 125.6 (C (Ar)), 125.1 (CH (Ar)), 123.6 (CH (Ar)), 121.4 (CH (Ar)), 121.3 (ArCH=CHAr), 119.6 (C (Ar)), 112.0 (CH (Ar)), 100.7 (CI (Ar)).

LRMS (CI) *m/z:* 347 (MH^+, 36%), 220 ($[MH - I]^+$, 74%), 63 (100%).

CHN Found: C, 55.63; H, 3.27; $C_{16}H_{11}IO$ requires C, 55.52; H, 3.20.

3-[(*Z*)-2-(4,5-Dimethoxy-2-iodophenyl)vinyl]-benzo[*b*]furan (***(Z)*-823**) and
3-[(*E*)-2-(4,5-Dimethoxy-2-iodophenyl]-benzo[*b*]furan (***(E)*-823**)



822
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

***(Z)*-823**
mw = 406.21 g mol^{-1}
$C_{18}H_{15}IO_3$

***(E)*-823**
mw = 406.21 g mol^{-1}
$C_{18}H_{15}IO_3$

To a stirred suspension of **809** (1.86 g, 3.01 mmol) in THF (40 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (338 mg, 3.01 mmol). On stirring for 1 hour, the reaction mixture was cooled to 0 °C and a solution of **822** (400 mg, 2.74 mmol) in THF (40 mL) was added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark yellow semi-solid. Purification by column chromatography (5-50% ether in petrol followed) gave firstly ***(Z)*-823** as a yellow oil (426 mg, 1.05 mmol, 38%); then ***(E)*-823** as a yellow solid that on recrystallisation gave yellow prisms (564 mg, 1.39 mmol, 51%): mp 141-143 °C (ethyl acetate/hexane).

*Data for **(Z)-823**:*

FT-IR (neat, cm^{-1}): 3002 w, 2959 w, 2933 w, 2836 w, 1592 w, 1556 w, 1497 s, 1451 m, 1253 s, 1206 vs, 1152 m, 1104 m, 1026 m, 740 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.43 (1H, app. d, J = 8.1 Hz, ArH), 7.38 (1H, s, ArH), 7.30 (1H, s, ArH), 7.26 (1H, td, J = 7.1, 1.7 Hz, ArH), 7.22 (1H, app. d, J = 7.1 Hz, ArH), 7.14 (1H, ddd, J = 8.1, 7.1, 1.0 Hz, ArH), 6.76 (1H, s,

ArH), 6.64 (1H, d, J = 11.9 Hz, ArCH=CHAr), 6.60 (1H, d, J = 11.9 Hz, ArCH=CHAr), 3.88 (3H, s, $ArOCH_3$), 3.38 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 155.3 (CO (Ar)), 149.5 (CO (Ar)), 149.3 (CO (Ar)), 143.8 (CH (Ar)), 135.0 (ArCH=CHAr), 134.4 (C (Ar)), 126.9 (C (Ar)), 124.9 (CH (Ar)), 123.1 (CH (Ar)), 121.6 (CH (Ar)), 121.0 (CH (Ar)), 119.1 (ArCH=CHAr), 117.5 (C (Ar)), 113.0 (CH (Ar)), 111.8 (CH (Ar)), 88.3 (CI (Ar)), 56.6 ($ArOCH_3$), 56.0 ($ArOCH_3$).

LRMS (CI) *m/z:* 407 (MH^+, 47%), 280 ($[MH - I]^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 406.0065, $C_{18}H_{15}IO_3$ requires 406.0066.

*Data for **(E)-823**:*

FT-IR (neat, cm^{-1}): 3080 w, 2636 w, 2908 w, 1496 s, 1463 m, 1450 s, 1383 m, 1272 m, 1255 s, 1207 m, 1184 s, 1163 s, 1109 s, 1025 m, 936 s, 851 m, 806 m, 752 vs.

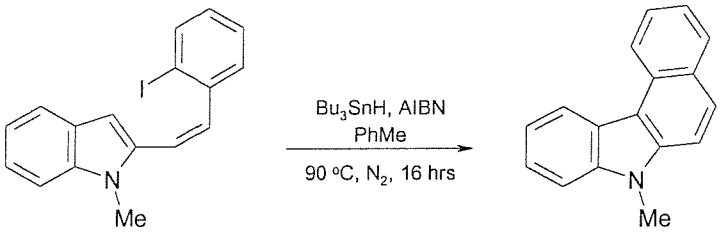
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.13-8.06 (1H, m, ArH), 7.80 (1H, s, ArH), 7.59-7.52 (1H, m, ArH), 7.45-7.36 (3H, m, 2 x ArH *and* ArCH=CHAr), 7.31 (1H, s, ArH), 7.16 (1H, s, ArH), 6.97 (1H, d, J = 16.2 Hz, ArCH=CHAr), 3.98 (3H, s, $ArOCH_3$), 3.91 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 156.4 (CO (Ar)), 150.1 (CO (Ar)), 149.7 (CO (Ar)), 144.4 (CH (Ar)), 133.4 (ArCH=CHAr), 133.4 (C (Ar)), 125.9 (C (Ar)), 125.3 (CH (Ar)), 123.7 (CH (Ar)), 122.0 (CH (Ar)), 121.6 (CH (Ar)), 119.9 (C (Ar)), 119.7 (ArCH=CHAr), 112.2 (CH (Ar)), 108.4 (CH (Ar)), 89.6 (CI (Ar)), 56.6 ($ArOCH_3$), 56.4 ($ArOCH_3$).

LRMS (CI) *m/z:* 407 (MH^+, 28%), 280 ($[MH - I]^+$, 100%).

CHN Found: C, 53.22; H, 3.77; $C_{18}H_{15}IO_3$ requires C, 53.22; H, 3.72.

N-Methyl-7*H*-benzo[*c*]carbazole (**621**)



(Z)-**617**
mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

621
mw = 231.30 g mol^{-1}
$C_{17}H_{13}N$

To a stirred solution of indole ***(Z)*-617** (140 mg, 0.39 mmol) in toluene (11 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.13 mL, 0.47 mmol) followed by AIBN (13 mg, 0.08 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (0.5-1% ether in petrol followed by 5-10% toluene in petrol) gave firstly recovered ***(Z)*-617** as a yellow oil that crystallised on standing to yellow needles (37 mg, 0.10 mmol, 26%); then **621** as a buff solid that gave large orange prisms on recrystallisation (52 mg, 0.22 mmol, 58%): mp 116-119 °C (petrol), lit. 118-119 °C (methanol).[216] The data for (*Z*)-**9** has been stated previously.

FT-IR (neat, cm^{-1}): 3060 w, 2926 w, 1620 m, 1584 m, 1525 m, 1475 s, 1424 m, 1385 m, 1329 m, 1283 m, 1247 m, 1213 m, 1145 m, 1087 w, 1018 w, 941 w, 800 vs, 747 m, 729 vs, 710 m, 677 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 318 (9000), 264 (31100).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.84 (1H, d, *J* = 8.2 Hz, ArH), 8.63 (1H, d, *J* = 8.0 Hz, ArH), 8.05 (1H, d, *J* = 7.9 Hz, ArH), 7.93 (1H, d, *J* = 8.9 Hz, ArH), 7.75 (1H, ddd, *J* = 8.2, 6.8, 1.4 Hz, ArH), 7.65 (1H, d, *J* = 8.9 Hz, ArH), 7.57 (1H, d, *J* = 7.9 Hz, ArH), 7.56 (1H, ddd, *J* = 7.9, 7.0, 1.4 Hz, ArH), 7.51 (1H, ddd, *J* = 8.0, 6.8, 1.2 Hz, ArH), 7.43 (1H, ddd, *J* = 7.9, 7.0, 1.4 Hz, ArH), 3.97 (3H, s, NCH_3).

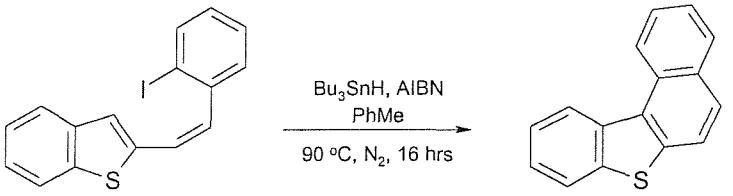
^{13}C NMR δ_C ppm (75 Hz, $CDCl_3$): 140.0 (C (Ar)), 138.6 (C (Ar)), 130.1 (C (Ar)), 129.4 (CH (Ar)), 129.0 (C (Ar)), 127.4 (CH (Ar)), 127.1 (CH (Ar)), 124.2 (CH (Ar)), 123.6 (C (Ar)), 123.3 (CH (Ar)), 122.9 (CH (Ar)), 122.2

(CH (Ar)), 119.9 (CH (Ar)), 115.0 (C (Ar)), 110.7 (CH (Ar)), 109.3 (CH (Ar)), 29.4 (NCH_3).

LRMS (CI) *m/z*: 232 (MH^+, 100%).

CHN Found: C, 88.09; H, 5.61; N, 6.10; $C_{17}H_{13}N$ requires C, 88.28; H, 5.66; N, 6.05.

Benzo[*b*]naphtho[1,2-*a*]thiophene (**622**)



(Z)-**618**
mw = 362.23 g mol^{-1}
$C_{16}H_{11}IS$

622
mw = 234.32 g mol^{-1}
$C_{16}H_{10}S$

To a stirred solution of ***(Z)*-618** (100 mg, 0.28 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.09 mL, 0.33 mmol) followed by AIBN (9 mg, 0.06 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (1% ether in petrol) gave **622** as a yellow solid that on recrystallisation yielded yellow needles (63 mg, 0.27 mmol, 96%): mp 101-104 °C (hexane), lit. 103.5 °C (hexane).[217]

FT-IR (neat, cm^{-1}): 3052 w, 3031 w, 1585 m, 1509 m, 1461 m, 1434 m, 1362 m, 1337 w, 1311 w, 1292 w, 1212 m, 1159 w, 1140 m, 1113 w, 1066 w, 1025 w, 947 m, 889 m, 852 w, 795 vs, 780 vs.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 338 (4300), 306 (13800).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.04 (1H, d, *J* = 8.6 Hz, ArH), 8.90 (1H, d, *J* = 8.6 Hz, ArH), 8.10-8.02 (2H, m, ArH), 7.95 (1H, d, *J* = 8.6 Hz, ArH), 7.92 (1H, d, *J* = 8.6 Hz, ArH), 7.77 (1H, ddd, *J* = 8.6, 6.9, 1.4 Hz, ArH), 7.68-7.58 (2H, m, ArH), 7.54 (1H, ddd, *J* = 8.6, 6.9, 1.2 Hz, ArH).

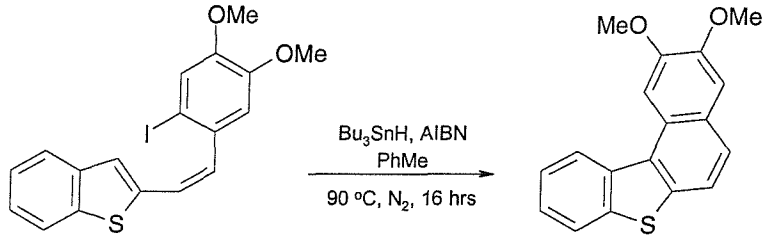
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 139.9 (C (Ar)), 138.8 (C (Ar)), 136.9 (C (Ar)), 132.1 (C (Ar)), 130.8 (C (Ar)), 129.6 (CH (Ar)), 129.2 (C (Ar)), 128.0

(CH (Ar)), 127.3 (CH (Ar)), 125.4 (CH (Ar)), 125.1 (CH (Ar)), 125.0 (CH (Ar)), 124.9 (CH (Ar)), 123.4 (2 x CH (Ar)), 121.2 (CH (Ar)).

LRMS (EI) *m/z:* 234 (M^+, 10%), 202 (29%), 189 (33%), 117 (40%), 104 (27%).

HRMS (EI) *m/z* Found: M^+ 234.0506, $C_{16}H_{10}S$ requires 234.0503.

2,3-Dimethoxybenzo[*b*]naphtho[1,2-*a*]thiophene (**826**)



***(Z)*-810**
mw = 422.28 g mol^{-1}
$C_{18}H_{15}IO_2S$

826
mw = 294.37 g mol^{-1}
$C_{18}H_{14}O_2S$

To a stirred solution of ***(Z)*-810** (50 mg, 0.12 mmol) in toluene (5 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.04 mL, 0.14 mmol) followed by AIBN (4 mg, 26 μmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (5 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (10-20% ether in petrol) gave **826** as a yellow solid (28 mg, 95 μmol, 79%): mp 172-174 °C.

FT-IR (neat, cm^{-1}): 3005 w, 2965 w, 2938 w, 2843 w, 1591 w, 1513 m, 1484 m, 1434 m, 1403 m, 1379 m, 1359 m, 1255 s, 1220 s, 1200 s, 1170 vs, 1102 vs, 1034 m, 1006 s, 960 w, 904 w, 855 s, 818 m, 793 s, 770 m, 737 s, 715 m.

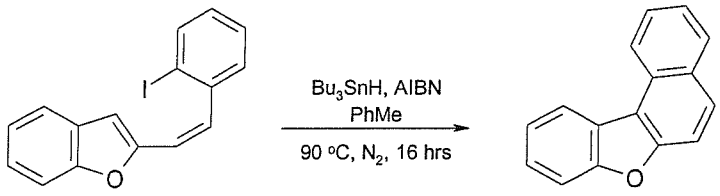
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.70 (1H, d, J = 8.1 Hz, ArH), 8.28 (1H, s, ArH), 8.01 (1H, dd, J = 7.9, 1.2 Hz, ArH), 7.81 (1H, d, J = 8.6 Hz, ArH), 7.77 (1H, d, J = 8.6 Hz, ArH), 7.62 (1H, td, J = 8.1, 1.2 Hz, ArH), 7.51 (1H, td, J = 7.9, 0.7 Hz, ArH), 7.34 (1H, s, ArH), 4.21 (3H, s, $ArOCH_3$), 4.08 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 150.2 (CO (Ar)), 148.3 (CO (Ar)), 140.0 (C (Ar)), 137.1 (C (Ar)), 136.7 (C (Ar)), 128.4 (C (Ar)), 127.6 (C (Ar)), 126.7 (CH (Ar)), 126.2 (C (Ar)), 125.2 (CH (Ar)), 124.8 (CH (Ar)), 124.2 (CH (Ar)), 123.5 (CH (Ar)), 119.4 (CH (Ar)), 108.5 (CH (Ar)), 103.4 (CH (Ar)), 56.2 ($ArOCH_3$), 56.0 ($ArOCH_3$).

LRMS (CI) *m/z:* 294 (M^+, 100%).

CHN Found: C, 73.65; H, 4.80; $C_{18}H_{14}O_2S$ requires C, 73.44; H, 4.79.

Benzo[*b*]naphtho[1,2-*a*]furan (**623**)



***(Z)*-619**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

623
mw = 218.25 g mol^{-1}
$C_{16}H_{10}O$

To a stirred solution of ***(Z)*-619** (40 mg, 0.12 mmol) in toluene (3 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (40 μL, 0.15 mmol) followed by AIBN (4 mg, 24 μmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (5 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (0.25-0.5% ether in petrol) gave **623** as a yellow oil that crystallised on standing to a pale yellow solid (18 mg, 0.08 mmol, 69%): mp 36-39 °C, lit. 40-41.5 °C (methanol).[218] The observed data is consistent with literature values.[219]

FT-IR (neat, cm^{-1}): 3058 w, 2952 w, 2923 m, 2854 w, 1626 w, 1585 w, 1525 w, 1460 m, 1377 m, 1252 m, 1214 s, 1151 w, 1102 w, 1037 w, 1015 w, 997 m, 855 w, 802 s, 735 vs, 677 m.

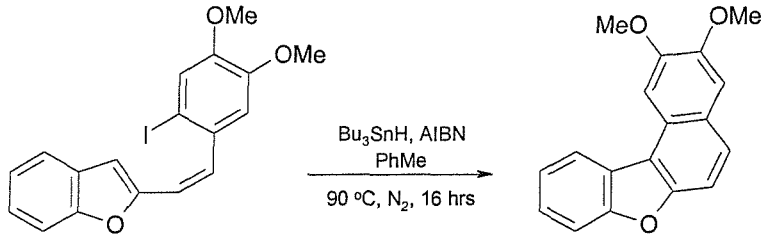
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.64 (1H, d, J = 8.5 Hz, ArH), 8.45-8.39 (1H, m, ArH), 8.05 (1H, d, J = 8.1 Hz, ArH), 7.96 (1H, d, J = 8.8 Hz, ArH), 7.79 (1H, d, J = 8.8 Hz, ArH), 7.76 (1H, dd, J = 8.5, 1.5 Hz, ArH), 7.75-7.69 (1H, m, ArH), 7.57 (1H, ddd, J = 8.1, 7.0, 1.1 Hz, ArH), 7.56-7.45 (2H, m, ArH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 156.3 (C (Ar)), 154.8 (C (Ar)), 130.9 (C (Ar)), 129.7 (CH (Ar)), 129.5 (C (Ar)), 129.0 (CH (Ar)), 127.6 (CH (Ar)), 126.3 (CH (Ar)), 125.4 (C (Ar)), 124.8 (CH (Ar)), 123.9 (CH (Ar)), 123.6 (CH (Ar)), 122.4 (CH (Ar)), 17.8 (C (Ar)), 113.2 (CH (Ar)), 112.3 (CH (Ar)).

LRMS (CI) *m/z:* 218 (M^+, 100%).

HRMS (EI) *m/z* Found: M^+ 218.0733, $C_{16}H_{10}O$ requires 218.0732.

2,3-Benzo[*b*]naphtho[1,2-*a*]furan (**827**)



***(Z)*-813**

mw = 406.21 g mol^{-1}

$C_{18}H_{15}IO_3$

827

mw = 278.31 g mol^{-1}

$C_{18}H_{14}O_3$

To a stirred solution of ***(Z)*-813** (100 mg, 0.25 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.08 mL, 0.30 mmol) followed by AIBN (8 mg, 50 μmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to an orange semi-solid. Purification by column chromatography (10-30% ether in petrol) gave **827** as a buff solid that yielded on recrystallisation small tan plates (58 mg, 0.21 mmol, 83%): sublimes over 190 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 3062 w, 2960 w, 2906 w, 2832 w, 1523 m, 1493 s, 1453 m, 1434 w, 1380 m, 1270 vs, 1210 m, 1160 m, 1151 m, 744 s.

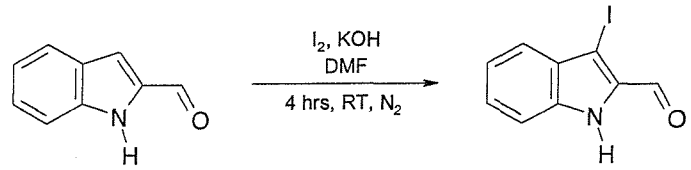
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.31-8.24 (1H, m, ArH), 7.85 (1H, s, ArH), 7.78 (1H, d, J = 8.8 Hz, ArH), 7.73-7.66 (1H, m, ArH), 7.63 (1H, d, J = 8.8 Hz, ArH), 7.50 (1H, td, J = 7.4, 1.8 Hz, ArH), 7.47 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.32 (1H, s, ArH), 4.18 (3H, s, $ArOCH_3$), 4.06 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 156.3 (CO (Ar)), 154.2 (CO (Ar)), 150.9 (CO (Ar)), 148.4 (CO (Ar)), 127.3 (CH (Ar)), 126.2 (C (Ar)), 126.1 (CH (Ar)), 125.3 (C (Ar)), 124.9 (C (Ar)), 123.3 (CH (Ar)), 121.8 (CH (Ar)), 117.1 (C (Ar)), 112.3 (CH (Ar)), 110.8 (CH (Ar)), 108.6 (CH (Ar)), 103.3 (CH (Ar)), 56.4 ($ArOCH_3$), 56.3 ($ArOCH_3$).

LRMS (CI) *m/z:* 278 (M^+, 30%), 192 (100%).

HRMS (EI) *m/z* Found: M^+ 278.0943, $C_{18}H_{14}O_3$ requires 278.0943.

3-Iodoindole-2-carboxaldehyde (**832**)



804
mw = 145.16 g mol^{-1}
C_9H_7NO

832
mw = 271.05 g mol^{-1}
C_9H_6INO

Following the procedure of Hibino *et al.*,[220,221] to a stirred suspension of indole-2-carboxaldehyde **804** (300 mg, 2.07 mmol) and powdered potassium hydroxide (420 mg, 7.46 mmol) in DMF (10 mL) at ambient temperature under nitrogen was added a solution of iodine (525 mg, 2.07 mmol) in DMF (10 mL) *via* dropping funnel over 10 minutes. The reaction mixture was stirred in darkness for 4 hours then poured into a rapidly stirring solution of sodium bisulfite (3.1 g) and concentrated ammonia (25 mL) in water (470 mL), yielding a pale yellow precipitate. Filtration and recrystallisation of the isolated solid from ethanol gave **832** as small orange needles (483 mg, 1.78 mmol, 86% over two crops): mp 191-192 °C, lit. 193-194 °C (ethanol). The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3292 br. w, 2841 w, 1642 m, 1613 w, 1567 w, 1502 m, 1445 w, 1411 m, 1360 w, 1222 m, 1150 m, 1122 w, 1039 m, 932 w, 908 w, 878 w, 856 m, 739 vs, 648 s.

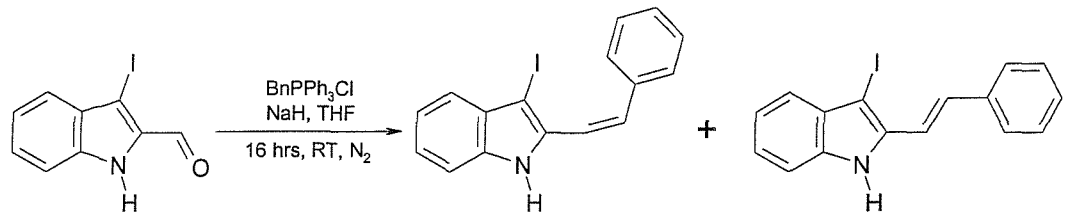
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 312 (17500), 229 (10500).

^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 11.4 (1H, br. s, NH), 9.89 (1H, s, ArCHO), 7.62-7.55 (2H, m, ArH), 7.46 (1H, ddd, J = 8.2, 6.9, 1.2 Hz, ArH), 7.27 (1H, ddd, J = 8.2, 6.9, 1.2 Hz, ArH).

^{13}C NMR δ_C ppm (100 MHz, D_6-acetone): 183.6 (ArCHO), 139.3 (C (Ar)), 135.3 (C (Ar)), 131.7 (C (Ar)), 129.1 (CH (Ar)), 124.0 (CH (Ar)), 123.0 (CH (Ar)), 114.6 (CH (Ar)), 72.0 (CI (Ar)).

LRMS (CI) *m/z*: 271 (M^+, 100%), 242 ([M - CHO]$^+$, 9%).

(*Z*)-3-Iodo-2-Styryl-1*H*-indole (***(Z)*-828**) and (*E*)-3-Iodo-2-Styryl-1*H*-indole (***(E)*-828**)



832
mw = 271.05 g mol^{-1}
C_9H_6INO

***(Z)*-828**
mw = 345.18 g mol^{-1}
$C_{16}H_{12}IN$

***(E)*-828**
mw = 345.18 g mol^{-1}
$C_{16}H_{12}IN$

To a stirred suspension of petrol-washed sodium hydride (190 mg, 4.78 mmol, 60% dispersion in mineral oil) in THF (90 mL) at ambient temperature under nitrogen was added benzyltriphenylphosphonium chloride (1.56 g, 4.00 mmol). After gentle warming with a heat gun, the reaction mixture was left to stir at ambient temperature for 16 hours, then cooled to 0 °C and a solution of 3-iodo-indole-2-carboxaldehyde **832** (900 mg, 3.32 mmol) in THF (50 mL) added. After 16 hours, the reaction mixture was diluted with water (150 mL) and extracted with ether (3 x 150 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (10-20% ether in petrol) gave firstly ***(Z)*-828** as a black solid (700 mg, 2.03 mmol, 61%): mp 60-61 °C (decomp.); then ***(E)*-828** as a yellow solid (422 mg, 1.22 mmol, 37%): mp 95-98 °C (decomp.).

*Data for **(Z)-828**:*

FT-IR (neat, cm^{-1}): 3375 s, 3060 w, 3014 w, 2958 w, 2921 w, 2855 w, 1441 m, 1296 m, 1226 m, 1021 m, 774 s, 749 vs, 697 vs.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 322 (18800), 224 (24900).

^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 10.16 (1H, br. s, NH), 7.38-7.24 (7H, m, ArH and PhH), 7.17 (1H, app. td, J = 7.1, 1.7 Hz, ArH), 7.12 (1H, app. td, J = 7.1, 1.4 Hz, ArH), 6.82 (1H, d, J = 12.2 Hz, ArCH=CHPh), 6.61 (1H, d, J = 12.2 Hz, ArCH=CHPh).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 137.5 (C (Ar)), 136.5 (C (Ar)), 135.5 (C (Ph)), 130.7 (C (Ar)), 130.6 (CH (Ph)), 129.5 (2 x CH (Ph)), 128.9 (2 x CH (Ph)), 128.6 (ArCH=CHPh), 124.6 (CH (Ar)), 121.6 (CH (Ar)), 121.2 (CH (Ar)), 120.8 (CH (Ar)), 111.4 (ArCH=CHPh), 65.6 ((CI (Ar)).

LRMS (CI) *m/z*: 345 (M^+, 24%), 218 ([M - I]$^+$, 100%).

HRMS (ES$^+$) *m/z* Found: [MH]$^+$ 346.0090, $C_{16}H_{13}IN$ requires 346.0087.

*Data for **(E)-828**:*

FT-IR (neat, cm^{-1}): 3391 s, 3040 w, 3014 w, 2921 w, 2844 w, 1444 w, 1410 m, 1359 w, 1329 m, 1298 m, 1224 s, 1147 w, 1038 m, 937 s, 744 vs, 682 vs.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 340 (16100), 262 (14700), 224 (10900).

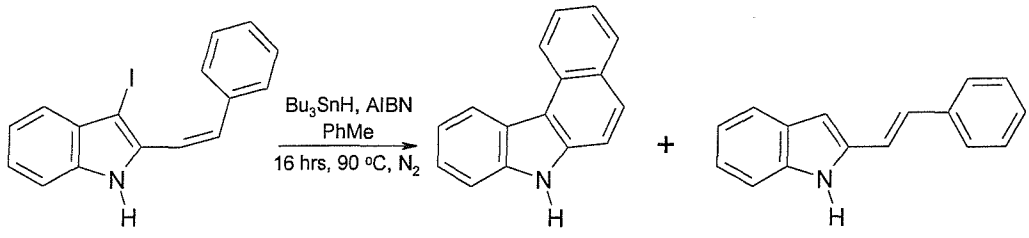
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.50 (1H, br. s, NH), 7.57 (2H, app. d, J = 7.4 Hz, PhH), 7.43 (1H, app. d, J = 7.7 Hz, ArH), 7.42 (2H, app t, J = 7.4 Hz, PhH), 7.36-7.30 (1H, m, PhH), 7.33 (1H, app. d, J = 7.2 Hz, ArH), 7.27 (1H, td, J = 7.7, 1.3 Hz, ArH), 7.22 (1H, d, J = 16.6 Hz, ArCH=CHPh), 7.19 (1H, td, J = 7.2, 1.5 Hz, ArH), 6.94 (1H, d, J = 16.6 Hz, ArCH=CHPh).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 136.7 (C (Ar)), 136.4 (C (Ar)), 136.4 (C (Ph)), 131.5 (C (Ar)), 128.9 (2 x CH (Ph)), 128.8 (CH (Ph)), 128.2 (ArCH=CHPh), 126.6 (2 x CH (Ph)), 124.3 (CH (Ar)), 121.2 (CH (Ar)), 121.0 (CH (Ar)), 118.5 (CH Ar)), 110.8 (ArCH=CHPh), 64.3 (CI (Ar)).

LRMS (CI) *m/z*: 345 (M^+, 21%), 218 ($[M - I]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 346.0088, $C_{16}H_{13}IN$ requires 346.0087.

7*H*-Benzo[*c*]carbazole (**831**) and (*E*)-2-Styryl-1*H*-indole (***(E)*-835**)



***(Z)*-828**
mw = 345.18 g mol^{-1}
$C_{16}H_{12}IN$

831
mw = 217.27 g mol^{-1}
$C_{16}H_{11}N$

***(E)*-835**
mw = 219.29 g mol^{-1}
$C_{16}H_{13}N$

To a stirred solution of ***(Z)*-828** (300 mg, 0.87 mmol) in toluene (30 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (306 mg, 1.05 mmol) followed by AIBN (15 mg, 0.09 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (20 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10-30% ether in petrol) gave firstly ***(E)*-835** as a white solid (68 mg, 0.31 mmol, 36%): mp 207-

208 °C, lit. 208-210 °C;[222] then **831**, also as a white solid (84 mg, 0.38 mmol, 44%): mp 133-136 °C, lit. 134-136 °C.[223,224] The observed data for **831** and ***(E)*-835** is consistent with the literature values.

*Data for **831**:*

FT-IR (neat, cm^{-1}): 3425 m, 3048 w, 2916 w, 2849 w, 1616 w, 1588 w, 1529 w, 1489 w, 1465 m, 1447 m, 1357 m, 1328 m, 1274 m, 1243 m, 1209 m, 1143 w, 1044 w, 804 s, 739 vs, 681 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 350 (2700), 315 (11100), 258 (36400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.82 (1H, d, J = 8.2 Hz, ArH), 8.60 (1H, d, J = 7.7 Hz, ArH), 8.32 (1H, br. s, NH), 8.04 (1H, d, J = 8.2 Hz, ArH), 7.88 (1H, d, J = 8.9 Hz, ArH), 7.75 (1H, ddd, J = 8.2, 6.9, 1.2 Hz, ArH), 7.57 (1H, d, J = 8.9 Hz, ArH), 7.54 (1H, d, J = 7.7 Hz, ArH), 7.53 (1H, ddd, J = 8.2, 6.9, 1.2 Hz, ArH), 7.49 (1H, ddd, J = 7.7, 6.7, 1.3 Hz, ArH), 7.43 (1H, ddd, J = 7.7, 6.7, 1.3 Hz, ArH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 138.9 (C (Ar)), 137.5 (C (Ar)), 129.7 (2 x C (Ar)), 129.5 (CH (Ar)), 127.8 (CH (Ar)), 127.4 (CH (Ar)), 125.3 (CH (Ar)), 124.8 (C (Ar)), 123.7 (CH (Ar)), 123.5 (CH (Ar)), 122.5 (CH (Ar)), 120.7 (CH (Ar)), 115.8 (C (Ar)), 113.0 (CH (Ar)), 111.6 (CH (Ar)).

LRMS (CI) *m/z*: 217 (M^+, 100%).

HRMS (EI) *m/z* Found: M^+ 217.0891, $C_{16}H_{11}N$ requires 217.0892.

*Data for ***(E)*-835**:*

FT-IR (neat, cm^{-1}): 3414 w, 3030 w, 1591 w, 1489 w, 1446 w, 1415 m, 1342 m, 1292 m, 1236 m, 1126 m, 955 s, 786 s, 750 vs, 692 vs, 652 vs.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 338 (24800), 256 (6500).

^{1}H NMR δ_H ppm (400 MHz, D_6-acetone): 10.50 (1H, br. s, NH), 7.60-7.52 (3H, m, ArH and PhH), 7.41-7.34 (3H, m, ArH and PhH), 7.31 (1H, d, J = 16.6 Hz, ArCH=CHPh), 7.27 (1H, tt, J = 7.3, 2.0 Hz, PhH), 7.22 (1H, d, J = 16.6 Hz,

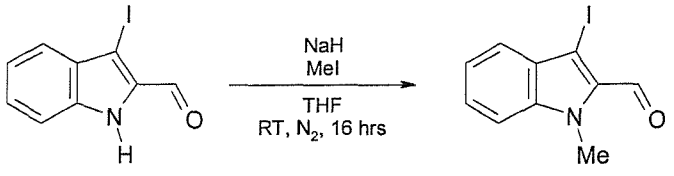
ArCH=CHPh), 7.14 (1H, ddd, J = 8.0, 7.0, 1.0 Hz, ArH), 7.03 (1H, ddd, J = 8.0, 7.0, 1.0 Hz, ArH), 6.65 (1H, d, J = 1.7 Hz, ArH).

^{13}C NMR δ_C ppm (100 MHz, D_6-acetone): 139.0 (C (Ar)), 138.7 (C (Ar)), 138.2 (C (Ph)), 130.4 (C (Ar)), 130.0 (2 x CH (Ph)), 128.7 (CH (Ph)), 128.4 (ArCH=CHPh), 127.5 (2 x CH (Ph)), 123.6 (CH (Ar)), 121.5 (CH (Ar)), 120.8 (CH (Ar)), 120.7 (CH Ar)), 112.1 (ArCH=CHPh), 104.6 (CH (Ar)).

LRMS (CI) *m/z*: 219 (M^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 220.1124, $C_{16}H_{14}N$ requires 220.1121.

3-Iodo-1-methyl-indole-2-carboxaldehyde (**836**)



832
mw = 271.05 g mol^{-1}
C_9H_6INO

836
mw = 285.08 g mol^{-1}
$C_{10}H_8INO$

Following the procedure of Dupas *et al.*,[225] to a stirred suspension of petrol-washed sodium hydride (130 mg, 3.25 mmol, 60% dispersion in mineral oil) in THF (30 mL) at 0 °C under nitrogen was added indole **832** (0.8 g, 2.95 mmol). After stirring at 0 °C for 5 minutes, methyl iodide (0.92 mL, 14.8 mmol) was added. The suspension was stirred for 16 hours at ambient temperature, then water (25 mL) was added. The reaction mixture was extracted with ether (3 x 50 mL), and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5-20% ether in petrol) gave **836** as a white fibrous solid (0.82 g, 2.88 mmol, 98%): mp 114-117 °C.

FT-IR (neat, cm^{-1}): 2924 w, 2815 w, 1648 s, 1608 m, 1464 m, 1386 m, 1344 m, 1319 m, 1235 w, 1176 m, 1122 m, 1104 m, 927 w, 866 m, 736 s, 721 s.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 342 (7800), 310 (23000), 235 (18600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 9.98 (1H, s, ArCHO), 7.57 (1H, app. dt, J = 8.2, 1.2 Hz, ArH), 7.47 (1H, ddd, J = 8.4, 7.0, 1.2 Hz, ArH), 7.34 (1H, d, J = 8.4 Hz, ArH), 7.25 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, ArH), 4.08 (3H, s, CH_3).

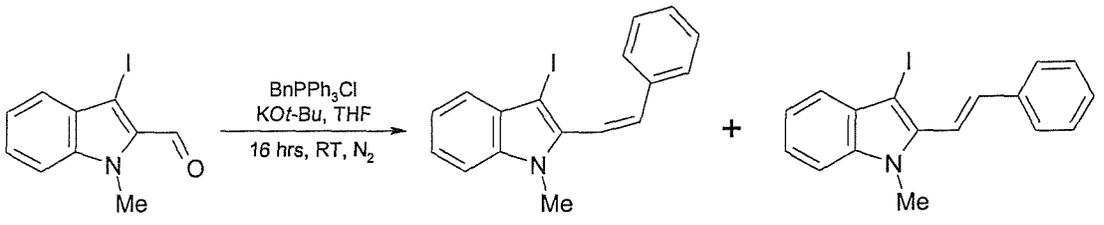
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 184.8 (Ar<u>C</u>HO), 140.6 (<u>C</u> (Ar)), 131.5 (<u>C</u> (Ar)), 129.8 (<u>C</u> (Ar)), 128.2 (<u>C</u>H (Ar)), 123.8 (<u>C</u>H (Ar)), 121.9 (<u>C</u>H (Ar)), 110.8 (<u>C</u>H (Ar)), 75.4 (<u>C</u>I (Ar)), 32.0 (<u>C</u>H_3).

LRMS (CI) *m/z:* 285 (M^+, 100%), 159 ($[MH - I]^+$, 44%), 130 ($[MH - I - CHO]^+$, 30%).

CHN Found: C, 42.37; H, 2.86; N, 4.89; $C_{10}H_8INO$ requires C, 42.13; H, 2.83; N, 4.91.

<u>(*Z*)-3-Iodo-1-methyl-2-styryl-indole (***(Z)*-837**) and</u>

<u>(*E*)-3-Iodo-1-methyl-2-styryl-indole (***(E)*-837**)</u>



836
mw = 285.08 g mol^{-1}
C_9H_6INO

***(Z)*-837**
mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

***(E)*-837**
mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

To a stirred suspension of potassium *tert*-butoxide (216 mg, 1.93 mmol) in THF (50 mL) under nitrogen was added benzyltriphenylphosphonium chloride (0.82 g, 2.10 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of 3-iodo-1-methyl-indole-2-carboxaldehyde **836** (0.50 g, 1.75 mmol) in THF (50 mL) added. After 16 hours, the reaction mixture was diluted with water (150 mL) and extracted with ether (3 x 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil. Purification by column chromatography (2.5-10% ether in petrol) gave firstly ***(Z)*-837** as a black solid that gave large black prisms on recrystallisation (401 mg, 1.12 mmol, 64%): mp 111-113 °C (chloroform); then ***(E)*-837** as a pale brown solid that gave long brown needles on recrystallisation (225 mg, 0.63 mmol, 36%): mp 85-87 °C (chloroform).

Data for ***(Z)*-837***:

FT-IR (neat, cm^{-1}): 3050 w, 3015 w, 2918 w, 1459 m, 1442 m, 1392 m, 1333 m, 1226 m, 1181 w, 1153 m, 1134 w, 1099 w, 1011 w, 935 m, 767 s, 738 vs, 688 vs.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 298 (12300).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.49 (1H, dd, J = 8.0, 1.4 Hz, ArH), 7.31-7.17 (6H, m, ArH), 7.11-7.06 (2H, m, ArH), 6.94 (1H, d, J = 12.2 Hz, ArCH=CHPh), 6.53 (1H, d, J = 12.2 Hz, ArCH=CHPh), 3.43 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 138.5 (C (Ar)), 137.8 (C (Ar)), 136.6 (C (Ar)), 136.4 (ArCH=CHPh), 130.6 (C (Ar)), 128.7 (4 x CH (Ar)), 128.3 (CH (Ar)), 122.9 (CH (Ar)), 121.0 (CH (Ar)), 120.6 (CH (Ar)), 119.4 (ArCH=CHPh), 110.0 (CH (Ar)), 59.3 (CI (Ar)), 31.7 (NCH_3).

LRMS (CI) *m/z*: 360 (MH^+, 43%), 233 ($[MH - I]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 741.0222, $C_{34}H_{28}I_2N_2Na$ requires 741.0234.

*Data for **(E)-837**:*

FT-IR (neat, cm^{-1}): 3060 w, 3025 w, 2926 w, 1461 m, 1444 w, 1426 w, 1377 m, 1342 w, 1312 w, 1227 m, 1155 m, 1101 w, 1071 w, 1008 w, 920 m, 736 vs, 688 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 330 (26200), 258 (20200).

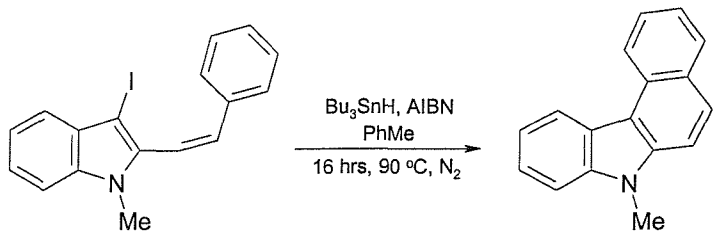
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.60 (2H, app. d, J = 7.0 Hz, ArH), 7.51-7.28 (6H, m, ArH), 7.31 (1H, d, J = 16.4 Hz, ArCH=CHPh), 7.22 (1H, td, J = 7.7, 2.1 Hz, ArH), 7.15 (1H, d, J = 16.4 Hz, ArCH=CHPh), 3.89 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 138.7 (C (Ar)), 137.4 (C (Ar)), 137.0 (C (Ar)), 134.7 (ArCH=CHPh), 130.9 (C (Ar)), 129.0 (2 x CH (Ar)), 128.5 (CH (Ar)), 126.8 (2 x CH (Ar)), 123.5 (CH (Ar)), 121.6 (CH (Ar)), 120.9 (CH (Ar)), 117.9 (ArCH=CHPh), 109.7 (CH (Ar)), 60.1 (CI (Ar)), 32.0 (NCH_3).

LRMS (CI) *m/z*: 233 ($[MH - I]^+$, 100%).

CHN Found: C, 56.79; H, 3.92; N, 3.88; $C_{17}H_{14}IN$ requires C, 56.84; H, 3.93; N, 3.90.

N-Methylbenzo[*c*]carbazole (**621**) from ***(Z)*-837**



***(Z)*-837**

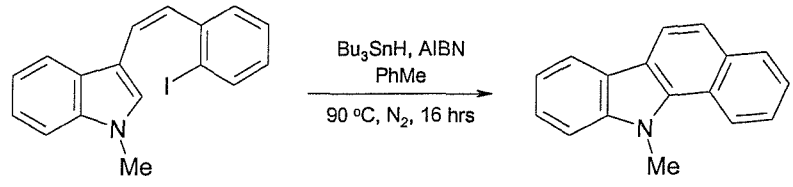
mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

621

mw = 231.30 g mol^{-1}
$C_{17}H_{13}N$

To a stirred solution of ***(Z)*-837** (295 mg, 0.82 mmol) in toluene (30 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (285 mg, 0.98 mmol) followed by AIBN (27 mg, 0.16 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (20 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to an off-white solid. Purification by column chromatography (5-10% ether in petrol) gave **621** as a buff solid that yielded large orange prisms on recrystallisation (180 mg, 0.78 mmol, 95%): mp 116-119 °C (petrol), lit. 118-119 °C (methanol).[216] The data for **621** has been stated previously.

N-Methyl-7*H*-benzo[*a*]carbazole (**628**)



***(Z)*-624**

mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

628

mw = 231.30 g mol^{-1}
$C_{17}H_{13}N$

To a stirred solution of indole ***(Z)*-624** (285 mg, 0.79 mmol) in toluene (15 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.26 mL, 0.95 mmol) followed by AIBN (24 mg, 0.16 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10% ether in petrol) gave **628** as a pale yellow solid (164 mg, 0.71 mmol, 90%): mp 169-171 °C (petrol), lit. 171-172.5 °C (ethyl acetate).[226]

FT-IR (neat, cm^{-1}): 3053 w, 2935 w, 2855 w, 1593 w, 1557 w, 1527 w, 1476 m, 1421 w, 1400 w, 1380 w, 1354 w, 1329 m, 1277 w, 1251 w, 1232 w, 1165 w, 1134 m, 1057 w, 951 w, 808 s.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 350 (4000), 330 (5200), 294 (24900), 270 (40500), 244 (42200).

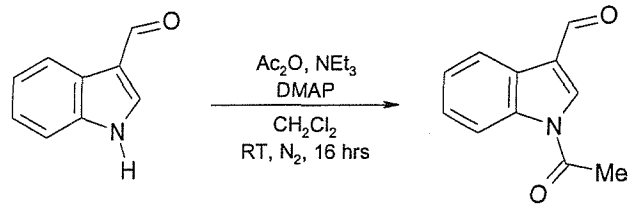
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.72 (1H, d, J = 8.1 Hz, ArH), 8.20 (1H, d, J = 8.5 Hz, ArH), 8.20 (1H, d, J = 7.7 Hz, ArH), 8.08 (1H, dd, J = 7.7, 1.8 Hz, ArH), 7.70 (1H, d, J = 8.5 Hz, ArH), 7.65-7.50 (4H, m, ArH), 7.36 (1H, ddd, J = 8.1, 7.0, 1.5 Hz, ArH), 4.39 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.8 (C (Ar)), 135.6 (C (Ar)), 133.7 (C (Ar)), 129.6 (CH (Ar)), 125.3 (CH (Ar)), 124.9 (CH (Ar)), 124.8 (CH (Ar)), 123.1 (C (Ar)), 122.9 (C (Ar)), 122.2 (CH (Ar)), 120.6 (CH (Ar)), 119.8 (CH (Ar)), 119.6 (CH (Ar)), 119.3 (CH (Ar)), 119.1 (C (Ar)), 109.1 (CH (Ar)), 34.1 (NCH_3).

LRMS (CI) *m/z:* 231 (M^+, 100%), 216 ($[M - CH_3]^+$, 37%).

HRMS (ES^+) *m/z* Found: $[2M + Na]^+$ 485.1997, $C_{34}H_{26}N_2Na$ requires 485.1988.

N-Acetylindole-3-carboxaldehyde (**877**)



814
mw = 145.16 g mol^{-1}
C_9H_7NO

877
mw = 187.20 g mol^{-1}
$C_{11}H_9NO_2$

In accordance with the procedure of Bohlmann *et al.*,[155] to a stirred solution of indole-3-carboxaldehyde **814** (1.0 g, 6.89 mmol) in CH_2Cl_2 (14 mL) under nitrogen was added triethylamine (1.15 mL, 8.27 mmol) followed by DMAP (84 mg, 0.69 mmol). After 16 hours, the reaction mixture was diluted with dichloromethane (50 mL) and washed sequentially with 1 M hydrochloric acid (2 x 25 mL) and saturated sodium bicarbonate solution (2 x 25 mL). After drying ($MgSO_4$) and concentration *in vacuo*, the resulting white solid was recrystallised from benzene/hexane (two crops) to give **877** as small peach needles (1.15 g, 6.13 mmol, 89%): mp 163-165 °C (benzene/petrol), lit. 162-163 °C (ether/petrol).[155] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3123 w, 3080 w, 3026 w, 2931 w, 2845 w, 2770 w, 1731 s, 1668 vs, 1607 m, 1548 m, 1446 s, 1406 m, 1370 s, 1321 s, 1205 vs, 1170 s, 1125 vs, 1010 vs, 938 m, 770 vs, 751 vs.

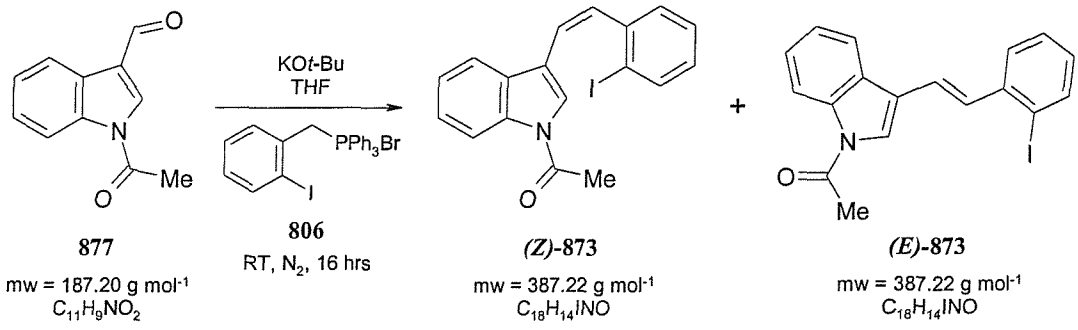
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.1 (1H, s, ArC<u>H</u>O), 8.38 (1H, dd, J = 7.1, 1.7 Hz, Ar<u>H</u>), 8.25 (1H, dd, J = 7.4, 1.9 Hz, Ar<u>H</u>), 8.04 (1H, s, Ar<u>H</u>), 7.45 (1H, td, J = 7.4, 1.7 Hz, Ar<u>H</u>), 7.41 (1H, td, J = 7.1, 1.9 Hz, Ar<u>H</u>), 2.72 (3H, s, ArCOC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 185.8 (Ar<u>C</u>HO), 168.7 (Ar<u>C</u>OCH$_3$), 136.5 (<u>C</u> (Ar)), 135.4 (<u>C</u>H (Ar)), 127.0 (<u>C</u>H (Ar)), 126.2 (<u>C</u> (Ar)), 125.6 (<u>C</u>H (Ar)), 122.8 (<u>C</u> (Ar)), 122.1 (<u>C</u>H (Ar)), 116.5 (<u>C</u>H (Ar)), 24.1 (ArCO<u>C</u>H$_3$).

LRMS (CI) *m/z:* 188 (MH^+, 46%), 145 ([MH - CH_3CO]$^+$, 28%), 116 ([MH - CH_3CO - CHO]$^+$, 25%).

<u>3-[(*Z*)-2-(2-Iodophenyl)vinyl]-1-acetyl-1*H*-indole (***(Z)*-873**) and</u>

<u>3-[(*E*)-2-(2-Iodophenyl)vinyl]-1-acetyl-1*H*-indole (***(E)*-873**)</u>



877
mw = 187.20 g mol^{-1}
$C_{11}H_9NO_2$

806

***(Z)*-873**
mw = 387.22 g mol^{-1}
$C_{18}H_{14}INO$

***(E)*-873**
mw = 387.22 g mol^{-1}
$C_{18}H_{14}INO$

To a stirred suspension of **806** (1.48 g, 2.64 mmol) in THF (35 mL) under nitrogen was added potassium *tert*-butoxide (300 mg, 2.64 mmol). The reaction mixture was stirred at ambient temperature for 1 hour, then cooled to 0 °C and a solution of **877** (450 mg, 2.40 mmol) in THF (35 mL) added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (10-60% ether in petrol) gave firstly ***(Z)*-873** as a white solid that gave colourless needles on recrystallisation (229 mg, 0.59 mmol, 25%): mp 110-111 °C (hexane); then ***(E)*-873** as a white solid that gave small white prisms on recrystallisation (636 mg, 1.64 mmol, 68%): mp 145-146 °C (hexane).

*Data for **(Z)-873**:*

FT-IR (neat, cm^{-1}): 1704 vs, 1626 w, 1604 w, 1556 w, 1540 w, 1450 s, 1431 m, 1409 w, 1362 m, 1343 m, 1343 s, 1323 s, 1302 m, 1217 vs, 1156 m, 1035 w, 1009 vs, 937 m, 872 w, 754 vs, 735 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.42 (1H, d, J = 8.1 Hz, ArH), 7.97 (1H, dd, J = 7.9, 1.0 Hz, ArH), 7.46 (1H, dd, J = 7.4, 1.2 Hz, ArH), 7.37 (1H, td, J = 7.1, 1.2 Hz, ArH), 7.33 (1H, obsc. dd, J = 7.1, 1.7 Hz, ArH), 7.27 (1H, td, J = 7.9, 1.0 Hz, ArH), 7.24 (1H, td, J = 7.4, 1.2 Hz, ArH), 7.00 (1H, td, J = 7.9, 1.7 Hz, ArH), 6.91 (1H, s, ArH), 6.78 (1H, dd, J = 11.9, 1.0 Hz, ArH), 6.68 (1H, d, J = 11.9 Hz, ArH), 2.37 (3H, s, $NCOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 168.8 ($NCOCH_3$), 142.8 (C (Ar)), 139.7 (CH (Ar)), 135.7 (C (Ar)), 135.0 (ArCH=CHAr), 130.2 (CH (Ar)), 130.1 (C (Ar)), 129.5 (CH (Ar)), 128.6 (CH (Ar)), 125.9 (ArCH=CHAr), 124.1 (CH (Ar)), 123.7 (CH (Ar)), 121.1 (CH (Ar)), 119.6 (CH (Ar)), 118.0 (C (Ar)), 116.9 (CH (Ar)), 99.8 (CI (Ar)), 24.1 ($NCOCH_3$).

LRMS (CI) *m/z:* 388 (MH^+, 26%), 261 ($[MH - I]^+$, 86%), 218 ($[MH - I - CH_3CO]^+$, 49%).

CHN Found: C, 56.30; H, 3.75; N, 3.69; $C_{18}H_{14}INO$ requires C, 55.83; H, 3.64; N, 3.62.

*Data for **(E)-873**:*

FT-IR (neat, cm^{-1}): 3142 w, 3063 w, 1693 vs, 1637 m, 1603 w, 1556 w, 1447 s, 1372 s, 1348 s, 1329 m, 1298 m, 1220 vs, 1155 m, 1126 m, 1092 w, 1017 m, 1007 m, 949 s, 932 m, 785 m, 745 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.52 (1H, app. d, J = 7.1 Hz, ArH), 8.05-7.99 (1H, m, ArH), 7.92 (1H, dd, J = 8.1, 1.2 Hz, ArH), 7.66 (1H, dd, J = 7.9, 1.4 Hz, ArH), 7.57 (1H, s, ArH), 7.51-7.35 (4H, m, ArH *and* ArCH=CHAr), 7.07 (1H, d, J = 16.2 Hz, ArH), 6.99 (1H, td, J = 7.6, 1.4 Hz, ArH), 2.68 (3H, s, $NCOCH_3$).

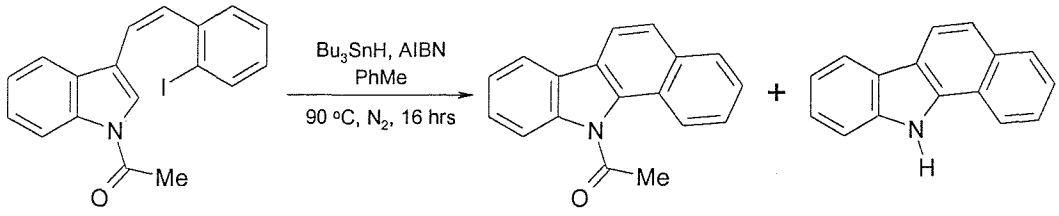
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 168.8 ($NCOCH_3$), 140.9 (C (Ar)), 140.1 (CH (Ar)), 137.0 (C (Ar)), 133.8 (ArCH=CHAr), 129.4 (CH (Ar)), 128.9 (CH (Ar)), 128.9 (C (Ar)), 126.2 (CH (Ar) *and* ArCH=CHAr), 124.6

(CH (Ar)), 124.4 (CH (Ar)), 122.9 (CH (Ar)), 120.9 (C (Ar)), 120.6 (CH (Ar)), 117.3 (CH (Ar)), 100.8 (CI (Ar)), 24.5 ($NCOCH_3$).

LRMS (CI) *m/z:* 388 (MH^+, 4%), 261 ($[MH - I]^+$, 11%), 218 ($[MH - I - CH_3CO]^+$, 11%).

CHN Found: C, 56.06; H, 3.68; N, 3.71; $C_{18}H_{14}INO$ requires C, 55.83; H, 3.64; N, 3.62.

N-Acetyl-7*H*-benzo[*a*]carbazole (**878**) and 7*H*-Benzo[*a*]carbazole (**879**)



(Z)-**873**
mw = 387.22 g mol^{-1}
$C_{18}H_{14}INO$

878
mw = 259.31 g mol^{-1}
$C_{18}H_{13}NO$

879
mw = 217.27 g mol^{-1}
$C_{16}H_{11}N$

To a stirred solution of ***(Z)*-873** (150 mg, 0.39 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.13 mL, 0.47 mmol) followed by AIBN (12 mg, 0.08 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (10-40% ether in petrol) gave firstly **878** as a tan solid that yielded large yellow needles on recrystallisation (31 mg, 0.12 mmol, 31%): mp 104-106 °C (hexane); then **879** as a tan solid that yielded fine tan needles on recrystallisation (24 mg, 0.11 mmol, 28%): mp 217-219 °C (benzene/hexane), lit. 226-228 °C.[227] The observed data for **879** is consistent with literature values.[228]

*Data for **878**:*

FT-IR (neat, cm^{-1}): 3068 w, 2930 w, 1704 s, 1461 m, 1428 m, 1378 s, 1362 s, 1320 m, 1275 m, 1252 s, 1214 s, 1173 m, 1067 m, 1030 m, 994 m, 965 m, 858 m, 820 s, 758 s, 735 vs, 693 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.22 (1H, dd, J = 8.1, 1.4 Hz, ArH), 8.10 (1H, d, J = 8.6 Hz, ArH), 8.07 (1H, dd, J = 7.4, 1.2 Hz, ArH), 8.04 (1H, dd, J = 8.3,

1.4 Hz, ArH), 8.02 (1H, app. d, J = 8.1 Hz, ArH), 7.88 (1H, d, J = 8.6 Hz, ArH), 7.63 (1H, td, J = 8.1, 1.4 Hz, ArH), 7.55 (1H, td, J = 8.1, 1.2 Hz, ArH), 7.54 (1H, td, J = 8.3, 1.4 Hz, ArH), 7.46 (1H, td, J = 7.4, 1.2 Hz, ArH), 2.70 (3H, s, $NCOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 172.9 ($NCOCH_3$), 140.1 (2 x C (Ar)), 134.9 (C (Ar)), 133.7 (2 x C (Ar)), 129.5 (CH (Ar)), 127.2 (CH (Ar)), 126.2 (CH (Ar)), 125.6 (CH (Ar)), 125.5 (CH (Ar)), 124.5 (C (Ar)), 124.4 (CH (Ar)), 123.7 (CH (Ar)), 119.8 (CH (Ar)), 118.4 (CH (Ar)), 114.8 (CH (Ar)), 27.6 ($NCOCH_3$).

LRMS (CI) *m/z:* 260 (MH^+, 11%), 217 ($[MH\text{-}COCH_3]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 282.0886, $C_{18}H_{13}NONa$ requires 282.0889.

*Data for **879**:*

FT-IR (neat, cm^{-1}): 3432 m, 3051 w, 1561 w, 1530 w, 1492 w, 1461 m, 1442 m, 1384 m, 1330 m, 1308 m, 1280 m, 1239 m, 1208 w, 1152 w, 1123 w, 1095 w, 1016 w, 930 w, 817 s, 784 w, 735 vs.

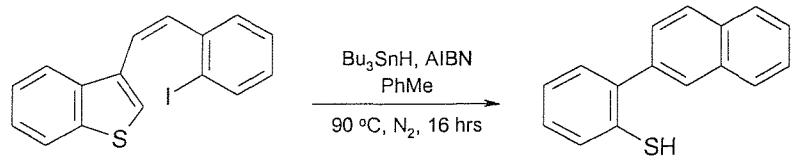
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.78 (1H, br. s, NH), 8.16 (1H, d, J = 8.6 Hz, ArH), 8.18-8.10 (2H, m, ArH), 8.04 (1H, dd, J = 7.2, 1.7 Hz, ArH), 7.69 (1H, d, J = 8.6 Hz, ArH), 7.64-7.52 (3H, m, ArH), 7.47 (1H, td, J = 7.1, 1.2 Hz, ArH), 7.34 (1H, td, J = 7.1, 1.2 Hz, ArH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 138.5 (C (Ar)), 134.9 (C (Ar)), 132.4 (C (Ar)), 129.1 (CH (Ar)), 125.6 (CH (Ar)), 125.2 (CH (Ar)), 124.9 (CH (Ar)), 124.2 (C (Ar)), 121.1 (C (Ar)), 120.5 (CH (Ar)), 120.2 (CH (Ar)), 120.0 (CH (Ar)), 119.9 (CH (Ar)), 119.4 (CH (Ar)), 118.4 (C (Ar)), 111.1 (CH (Ar)).

LRMS (CI) *m/z:* 217 (M^+, 100%).

CHN Found: C, 88.49; H, 5.03; N, 6.49; $C_{16}H_{11}N$ requires C, 88.45; H, 5.10; N, 6.44.

2-(2-Naphthyl)thiophenol (**630**)



***(Z)*-625**
mw = 362.23 g mol^{-1}
$C_{16}H_{11}IS$

630
mw = 236.30 g mol^{-1}
$C_{16}H_{12}S$

To a stirred solution of ***(Z)*-625** (107 mg, 0.30 mmol) in toluene (8 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (95 μL, 0.35 mmol) followed by AIBN (9 mg, 0.06 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (0.25-0.5% ether in petrol) gave **630** as a yellow oil (68 mg, 0.29 mmol, 98%).

FT-IR (neat, cm^{-1}): 3016 w, 2961 w, 2924 w, 2570 w, 1478 m, 1454 m, 1439 m, 1036 m, 944 m, 896 m, 856 m, 817 s, 725 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.98 (1H, d, J = 8.1 Hz, ArH), 7.97-7.91 (3H, m, ArH), 7.62 (1H, dd, J = 8.5, 1.9 Hz, ArH), 7.60 (1H, t, J = 6.2 Hz, ArH), 7.57 (1H, t, J = 6.2 Hz, ArH), 7.48-7.43 (1H, m, ArH), 7.43-7.36 (1H, m, ArH), 7.33-7.26 (2H, m, ArH), 3.48 (1H, s, ArSH).

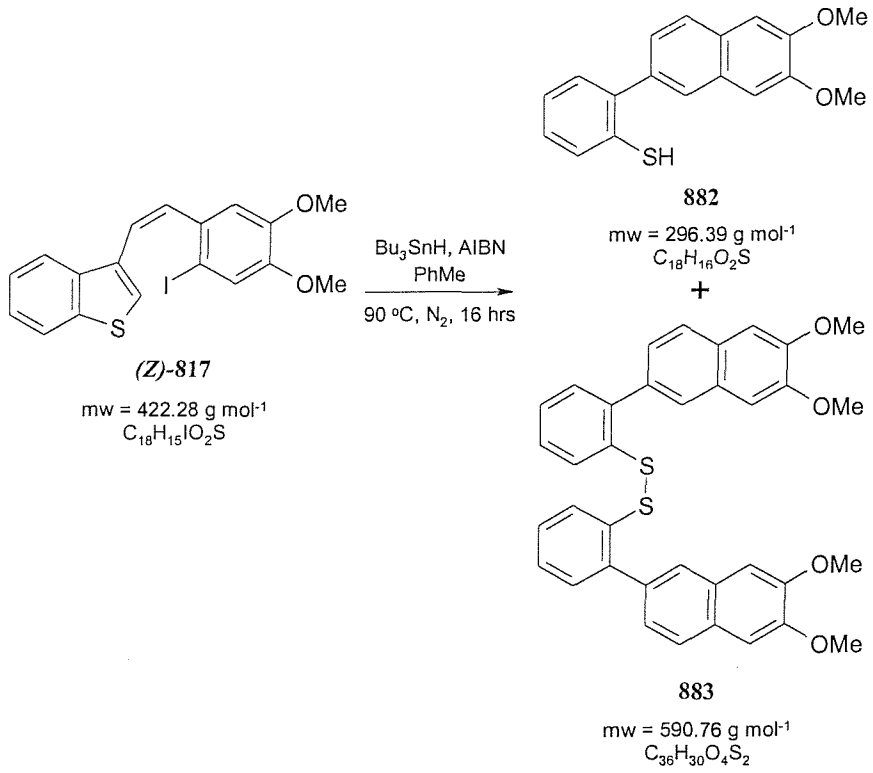
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.4 (CS (Ar)), 138.4 (C (Ar)), 133.4 (C (Ar)), 132.7 (C (Ar)), 131.1 (C (Ar)), 130.8 (CH (Ar)), 129.6 (CH (Ar)), 128.2 (CH (Ar)), 128.1 (2 x CH (Ar)), 128.1 (CH (Ar)), 127.8 (CH (Ar)), 127.3 (CH (Ar)), 126.4 (CH (Ar)), 126.3 (CH (Ar)), 125.7 (CH (Ar)).

LRMS (CI) *m/z:* 236 (M^+, 90%), 235 (100%), 234 (98%).

HRMS (EI) *m/z* Found: M^+ 236.0650, $C_{16}H_{12}S$ requires 236.0660.

2-(6,7-Dimethoxy-2-naphthyl)thiophenol (**882**) and

2-(6,7-Dimethoxy-2-naphthyl)thiophenol dimer (**883**)



To a stirred solution of ***(Z)*-817** (400 mg, 0.95 mmol) in toluene (25 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.31 mL, 1.14 mmol) followed by AIBN (29 mg, 0.19 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (5-10% ether in petrol) gave **882** as a colourless oil (146 mg, 0.49 mmol, 52%); then **883**, also as a colourless oil (125 mg, 0.21 mmol, 45%).

*Data for **882**:*

FT-IR (neat, cm^{-1}): 3058 w, 3000 w, 2956 w, 2932 w, 2854 w, 2562 w, 1510 s, 1495 vs, 1462 w, 1435 w, 1414 w, 1253 vs, 1196 w, 1163 m, 1131 m, 1036 w, 1007 w, 895 w, 855 m, 748 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.79 (1H, d, J = 8.3 Hz, ArH), 7.73 (1H, d, J = 1.4 Hz, ArH), 7.42 (1H, obsc. dd, J = 8.3, 1.4 Hz, ArH), 7.43-7.39 (1H, m, ArH), 7.36-7.31 (1H, m, ArH), 7.26 (1H, td, J = 6.7, 1.0 Hz, ArH), 7.23

(1H, td, J = 6.7, 1.0 Hz, ArH), 7.19 (1H, s, ArH), 7.18 (1H, s, ArH), 4.06 (3H, s, $ArOCH_3$), 4.04 (3H, s, $ArOCH_3$), 3.47 (1H, s, ArSH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 149.9 (2 x CO (Ar)), 140.7 (CS (Ar)), 136.8 (C (Ar)), 131.1 (C (Ar)), 130.7 (CH (Ar)), 129.4 (CH (Ar)), 129.1 (C (Ar)), 128.5 (C (Ar)), 127.8 (CH (Ar)), 126.6 (CH (Ar)), 126.5 (CH (Ar)), 125.6 (CH (Ar)), 125.5 (CH (Ar)), 106.6 (CH (Ar)), 106.2 (CH (Ar)), 56.0 ($ArOCH_3$), 55.9 ($ArOCH_3$).

LRMS (CI) *m/z:* 296 (M^+, 16%), 295 (78%), 294 (59%), 208 (100%).[229]

HRMS (EI) *m/z* Found: M^+ 294.0711, $C_{18}H_{14}O_2S$ requires 294.0713.[229]

*Data for **883**:*

FT-IR (neat, cm^{-1}): 2956 w, 2926 w, 2854 w, 1509 m, 1491 s, 1461 m, 1435 w, 1413 m, 1258 vs, 1196 w, 1163 m, 1131 m, 1034 w, 1007 w, 895 w, 855 m, 749 m, 732 w.

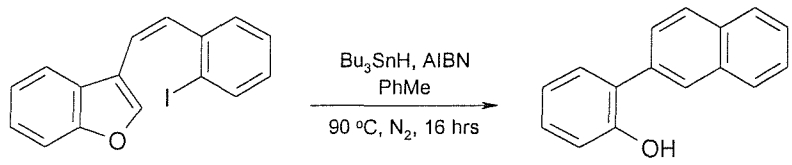
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.76 (2H, d, J = 8.3 Hz, ArH), 7.71 (2H, d, J = 1.4 Hz, ArH), 7.69-7.62 (2H, m, ArH), 7.39 (2H, dd, J = 8.3, 1.4 Hz, ArH), 7.35-7.26 (6H, m, ArH), 7.19 (2H, s, ArH), 7.16 (2H, s, ArH), 4.05 (6H, s, $ArOCH_3$), 4.04 (6H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 150.3 (4 x CO (Ar)), 141.9 (2 x CS (Ar)), 136.0 (2 x C (Ar)), 135.7 (2 x C (Ar)), 130.7 (2 x CH (Ar)), 129.3 (2 x C (Ar)), 129.0 (2 x C (Ar)), 128.5 (2 x CH (Ar)), 127.6 (2 x CH (Ar)), 127.5 (2 x CH (Ar)), 126.9 (2 x CH (Ar)), 126.6 (2 x CH (Ar)), 126.3 (2 x CH (Ar)), 107.0 (2 x CH (Ar)), 106.6 (2 x CH (Ar)), 56.3 (4 x $ArOCH_3$).

LRMS (ES^+) *m/z:* 613 ($[M + Na]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$, 613.1483, $C_{36}H_{30}O_4S_2Na$ requires 613.1478.

2-(2-Naphthyl)phenol (**631**)



***(Z)*-626**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

631
mw = 220.27 g mol^{-1}
$C_{16}H_{12}O$

To a stirred solution of ***(Z)*-626** (155 mg, 0.45 mmol) in toluene (15 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.15 mL, 0.54 mmol) followed by AIBN (14 mg, 0.09 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (1-10% ether in petrol) gave firstly recovered ***(Z)*-626** as a colourless oil (16 mg, 0.05 mmol, 10%, data as stated previously); then **631** as a white solid that on recrystallisation from hexane yielded radial clusters of white needles (35 mg, 0.16 mmol, 35%): mp 94-97 °C (hexane), lit. 97 °C (petrol).[230] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3524 s, 3058 w, 1586 w, 1500 m, 1466 w, 1449 s, 1430 w, 1328 m, 1277 s, 1252 m, 1180 s, 1101 s, 1049 w, 1026 w, 944 w, 901 m, 866 m, 830 s, 811 s, 755 vs, 681 w, 657 w.

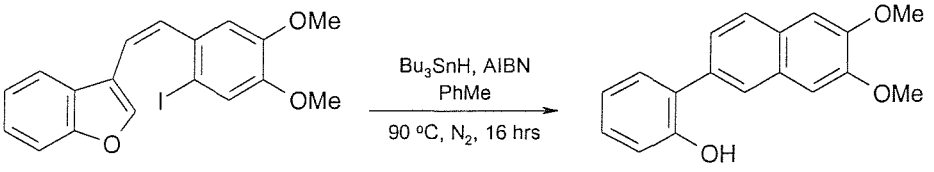
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.01 (1H, d, J = 8.1 Hz, ArH), 7.99 (1H, app. s, ArH), 7.94 (1H, d, J = 9.3 Hz, ArH), 7.92 (1H, d, J = 9.3 Hz, ArH), 7.63 (1H, dd, J = 8.6, 1.2 Hz, ArH), 7.59 (1H, td, J = 6.9, 1.2 Hz, ArH), 7.56 (1H, td, J = 6.9, 1.2 Hz, ArH), 7.40 (1H, dd, J = 8.6, 1.2 Hz, ArH), 7.35 (1H, td, J = 9.3, 1.7 Hz, ArH), 7.09 (1H, obsc. td, J = 9.3, 1.7 Hz, ArH), 7.07 (1H, d, J = 8.1 Hz, ArH), 5.40 (1H, br. s, ArOH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 152.8 (COH), 134.7 (C (Ar)), 133.8 (C (Ar)), 132.9 (C (Ar)), 130.7 (CH (Ar)), 129.4 (CH (Ar)), 129.3 (CH (Ar)), 128.2 (CH (Ar)), 128.0 (CH (Ar)), 127.9 (CH (Ar)), 127.3 (CH (Ar)), 126.8 (CH (Ar)), 126.6 (CH (Ar)), 121.1 (CH (Ar)), 1116.1 (CH (Ar)). One aromatic quaternary carbon is unobserved.

LRMS (CI) *m/z:* 238 ($[M + NH_4]^+$, 26%), 220 (M^+, 100%).

HRMS (EI) *m/z* Found: M^+ 220.0885, $C_{16}H_{12}O$ requires 220.0888.

2-(6,7-Dimethoxy-2-naphthyl)phenol (**886**)



(Z)-**823**
mw = 406.21 g mol^{-1}
$C_{18}H_{15}IO_3$

886
mw = 280.32 g mol^{-1}
$C_{18}H_{16}O_3$

To a stirred solution of ***(Z)*-823** (258 mg, 0.64 mmol) in toluene (15 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.21 mL, 0.77 mmol) followed by AIBN (20 mg, 0.13 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Column chromatography (50-60% ether in petrol) gave **886** as a white solid that yielded on recrystallisation small white prisms (132 mg, 0.47 mmol, 74%): mp 144-146 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 3429 m, 2998 w, 2942 w, 2834 w, 1614 w, 1504 m, 1487 m, 1447 m, 1410 m, 1374 w, 1347 m, 1278 w, 1240 vs, 1195 s, 1164 s, 1125 vs, 1103 m, 999 m, 885 m, 864 s, 829 m, 814 m, 763 s, 742 m.

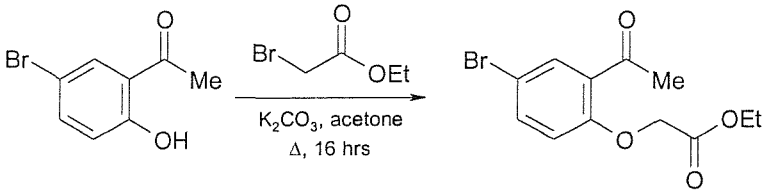
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.81 (1H, d, J = 7.4 Hz, ArH), 7.80 (1H, d, J = 1.7 Hz, ArH), 7.46 (1H, dd, J = 8.3, 1.7 Hz, ArH), 7.36 (1H, dd, J = 7.9, 1.7 Hz, ArH), 7.32 (1H, td, J = 7.9, 1.7 Hz, ArH), 7.17 (1H, s, ArH), 7.15 (1H, s, ArH), 7.06 (1H, d, J = 8.3 Hz, ArH), 7.05 (1H, td, J = 7.4, 1.7 Hz, ArH), 5.53 (1H, br. s, ArOH), 4.04 (3H, s, $ArOCH_3$), 4.02 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 152.8 (COH), 150.1 (CO (Ar)), 150.0 (CO (Ar)), 132.9 (C (Ar)), 130.6 (CH (Ar)), 129.6 (C (Ar)), 129.2 (CH (Ar)), 128.7 (C (Ar)), 128.5 (C (Ar)), 127.6 (CH (Ar)), 126.5 (CH (Ar)), 125.5 (CH (Ar)), 121.0 (CH (Ar)), 116.0 (CH (Ar)), 106.5 (CH (Ar)), 106.3 (CH (Ar)), 56.1 (2 x $ArOCH_3$).

LRMS (CI) *m/z:* 281 (MH^+, 100%).

CHN Found: C, 76.93; H, 5.72: $C_{18}H_{16}O_3$ requires C, 77.13; H, 5.75.

Ethyl (2-acetyl-4-bromophenoxy)acetate (**888**)



887

mw = 215.05 mol^{-1}
$C_8H_7BrO_2$

888

mw = 301.14g mol^{-1}
$C_{12}H_{13}BrO_4$

Following the procedure of Nielek and Lesiak,[149] a stirred suspension of 5'-bromo-2'-hydroxyacetophenone **887** (5.0 g, 23.3 mmol), ethyl bromoacetate (2.70 mL, 24.5 mmol) and potassium carbonate (9.67 g, 70 mmol) in acetone (100 mL) was heated at reflux under a $CaCl_2$ drying tube for 16 hours. On cooling to ambient temperature, the reaction mixture was filtered and the filtrate concentrated *in vacuo*. The white solid obtained was suspended in water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a colourless oil that crystallised on standing to give **888** as a waxy white solid (7.03 g, 23.3 mmol, 100%): mp 41-43 °C, lit. not reported. The observed data is consistent with literature values.[231]

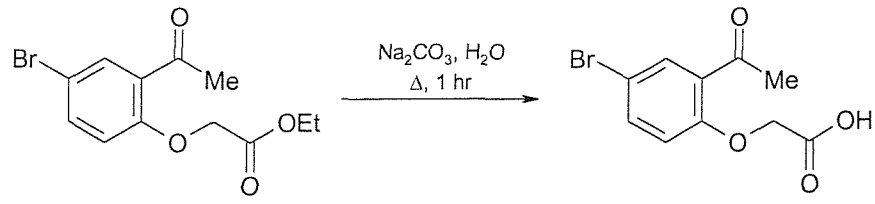
FT-IR (neat, cm^{-1}): 2984 w, 2928 w, 1760 vs, 1660 vs, 1593 w, 1484 m, 1434 w, 1400 m, 1356 w, 1289 m, 1206 vs, 1150 s, 1075 s, 1019 m, 977 w, 945 w, 906 w, 877 w, 814 s, 765 m, 700 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.87 (1H, d, J = 2.6 Hz, ArH), 7.52 (1H, dd, J = 8.8, 2.6 Hz, ArH), 6.72 (1H, d, J = 8.8 Hz, ArH), 4.71 (2H, s, $ArOCH_2COOEt$), 4.28 (2H, q, J = 7.4 Hz, OCH_2CH_3), 2.70 (3H, s, $ArCOCH_3$), 1.31 (3H, t, J = 7.4 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 198.3 ($ArCOCH_3$), 167.9 (COOEt), 156.1 (CO (Ar)), 136.1 (CH (Ar)), 133.5 (CH (Ar)), 130.7 (C (Ar)), 114.5 (CBr (Ar)), 114.3 (CH (Ar)), 65.8 ($ArOCH_2COOEt$), 61.9 (OCH_2CH_3), 32.1 ($ArCOCH_3$), 14.3 (OCH_2CH_3).

LRMS (CI) *m/z:* 303 ($[MH\{^{81}Br\}]^+$, 17%), 301 ($[MH\{^{79}Br\}]^+$, 16%).

Ethyl (2-acetyl-4-bromophenoxy)acetic acid (**889**)



888

mw = 301.14 g mol^{-1}
$C_{12}H_{13}BrO_4$

889

mw = 273.08 g mol^{-1}
$C_{10}H_9BrO_4$

Following the procedure of Nielek and Lesiak,[149] a suspension of **888** (6.90 g, 22.9 mmol) and sodium carbonate (2.67 g, 25.2 mmol) in water (41 mL) was heated at reflux for 1 hour. On cooling to 0 °C, the reaction mixture was acidified with concentrated HCl until effervescence ceased. The resultant cream precipitate was collected by filtration, washed with water (150 mL) and dried under air flow. Recrystallisation from ethanol (two crops) gave **889** as small cream needles (5.24 g, 19.2 mmol, 84%): mp 181-182 °C, lit. not reported. The observed data is consistent with literature values.[231]

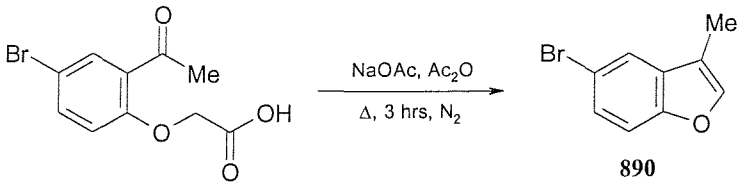
FT-IR (neat, cm^{-1}): 2888 br. w, 1743 s, 1714 m, 1656 s, 1588 w, 1484 s, 1423 m, 1397 m, 1355 w, 1280 m, 1225 vs, 1157 s, 1076 s, 1061 m, 977 w, 913 m, 895 m, 818 s, 753 m, 677 m.

^{1}H NMR δ_H ppm (300 MHz, D_6-DMSO): 13.22 (1H, br. s, COOH), 7.77 (1H, dd, J = 8.8, 2.6 Hz, ArH), 7.64 (1H, d, J = 2.6 Hz, ArH), 7.09 (1H, d, J = 8.8 Hz, ArH), 4.86 (2H, s, $ArOCH_2COOH$), 2.60 (3H, s, $ArCOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, D_6-DMSO): 197.9 ($ArCOCH_3$), 170.0 (COOH), 156.2 (CO (Ar)), 135.8 (CH (Ar)), 131.7 (CH (Ar)), 130.0 (C (Ar)), 116.0 (CH (Ar)), 112.6 (CBr (Ar)), 65.3 ($ArOCH_2COOH$), 31.6 ($ArCOCH_3$).

LRMS (ES^-) *m/z:* 547 ([2M{$^{81}Br_2$} - H]$^-$, 48%), 545 ([2M{^{81}Br}{^{79}Br} - H]$^-$, 100%), 543 ([2M{$^{79}Br_2$} - H]$^-$, 48%), 387 ([M{^{81}Br} + CF_3COO]$^-$, 43%), 385 ([M{^{79}Br} + CF_3COO]$^-$, 48%), 273 ([M{^{81}Br} – H]$^-$, 15%), 271 ([M{^{79}Br} – H]$^-$, 15%).

5-Bromo-3-methylbenzo[*b*]furan (**890**)



889
mw = 273.08 g mol^{-1}
$C_{10}H_9BrO_4$

890
mw = 211.06 g mol^{-1}
C_9H_7BrO

Following the procedure of Nielek and Lesiak,[149] a suspension of **889** (4.93 g, 18.1 mmol) and sodium acetate (6.31 g, 76.9 mmol) in acetic anhydride (12 mL, 0.13 mol) was heated at reflux for 3 hours under nitrogen. On cooling to ambient temperature, the reaction mixture was poured into water (50 mL) and extracted with ether (3 x 50 mL). The combined organic phases were washed with saturated sodium carbonate solution (2 x 50 mL) and brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a red oil. Purification by column chromatography (1-2% ether in petrol) gave **890** as a colourless oil (3.35 g, 15.9 mmol, 88%). The observed data is consistent with literature values.[231]

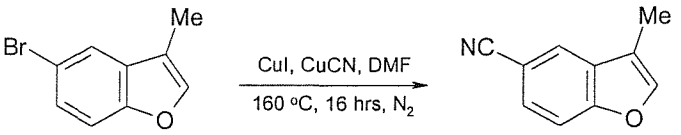
FT-IR (neat, cm^{-1}): 2920 w, 2860 w, 1589 w, 1440 vs, 1385 w, 1327 w, 1307 w, 1285 m, 1250 w, 1187 s, 1080 vs, 1045 w, 993 w, 864 s, 780 vs, 727 s.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.66 (1H, d, J = 1.8 Hz, ArH), 7.41 (1H, app. s, ArH), 7.39 (1H, dd, J = 8.5, 1.8 Hz, ArH), 7.33 (1H, d, J = 8.5 Hz, ArH), 2.22 (3H, d, J = 1.5 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 154.1 (C (Ar)), 142.8 (CH (Ar)), 131.2 (C (Ar)), 127.1 (CH (Ar)), 122.4 (CH (Ar)), 115.5 (C (Ar), CBr (Ar)), 113.0 (CH (Ar)), 8.0 ($ArCH_3$).

LRMS (CI) *m/z:* 212 ([M{^{81}Br}]$^+$, 95%), 210 ([M{^{79}Br}]$^+$, 100%).

3-Methyl-1-benzo[*b*]furan-5-carbonitrile (**891**)



890
mw = 211.06 g mol^{-1}
C_9H_7BrO

891
mw = 157.17 g mol^{-1}
$C_{10}H_7NO$

Following the procedure of Sall *et al.*,[156] a stirred suspension of **890** (2.0 g, 9.48 mmol), copper iodide (1.82 g, 9.57 mmol) and copper cyanide (1.74 g, 19.4 mmol) in DMF (35 mL) under nitrogen was heated at 160 °C for 16 hours. On cooling to ambient temperature, the reaction mixture was filtered through celite and the celite rinsed with ether (200 mL). The

resultant filtrate was washed with 2 M HCl (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a pale green semi-solid. Purification by column chromatography (5-30% ether in petrol) gave firstly recovered **890** as a colourless oil (91 mg, 0.43 mmol, 5%); then **891** as a colourless oil that crystallised on standing to a white solid. Recrystallisation from hexane gave **891** as small white prisms (1.24 g, 7.88 mmol, 83%): mp 64-65 °C (hexane).

FT-IR (neat, cm^{-1}): 3124 w, 3104 w, 2989 w, 2965 w, 2931 w, 2225 s, 1621 w, 1590 w, 1453 s, 1383 w, 1343 w, 1296 w, 1195 s, 1120 w, 1071 vs, 993 w, 909 w, 886 s, 816 s, 795 vs, 746 m, 654 m.

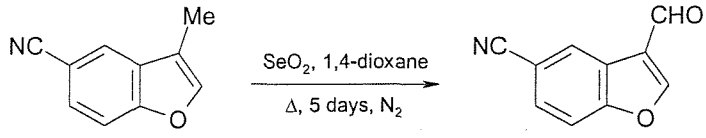
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.88-7.85 (1H, m, ArH), 7.57 (1H, dd, J = 8.8, 1.8 Hz, ArH), 7.53 (1H, d, J = 1.8 Hz, ArH), 7.51 (1H, d, J = 8.8 Hz, ArH), 2.26 (3H, d, J = 1.5 Hz, $ArCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 157.1 (CO (Ar)), 143.7 (CH (Ar)), 129.9 (C (Ar)), 128.0 (CH (Ar)), 124.8 (CH (Ar)), 119.7 (C (Ar)), 115.5 (C (Ar)), 112.7 (CH (Ar)), 106.3 (CN), 8.0 ($ArCH_3$).

LRMS (CI) *m/z:* 175 ($[M + NH_4]^+$, 12%), 157 (M^+, 69%), 63 (100%).

CHN Found: C, 76.32; H, 4.58; N, 9.00; $C_{10}H_7NO$ requires C, 76.42; H, 4.49; N, 8.91.

3-Formyl-1-benzo[*b*]furan-5-carbonitrile (**892**)



891
mw = 157.17 g mol^{-1}
$C_{10}H_7NO$

892
mw = 171.16 g mol^{-1}
$C_{10}H_5NO_2$

Following the procedure of Zaidlewicz *et al.*,[150] a solution of **891** (1.0 g, 6.36 mmol) and selenium dioxide (1.23 g, 11.1 mmol) in 1,4-dioxane (10 mL) was heated at reflux for 5 days under nitrogen. On cooling to ambient temperature, the reaction mixture was filtered through celite and the filtrate concentrated *in vacuo* to a red oil. Purification by column chromatography (10-30% ether in petrol) gave **892** as white solid that yielded on recrystallisation small white needles (957 mg, 5.59 mmol, 88%): mp 158-160 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 3149 w, 3089 w, 3042 w, 2857 w, 2768 w, 2233 m, 1666 vs, 1618 w, 1552 s, 1463 m, 1447 m, 1396 w, 1352 m, 1326 w, 1275 w, 1254 w, 1198 w, 1120 vs, 1058 m, 891 m, 826 s, 787 vs, 706 m.

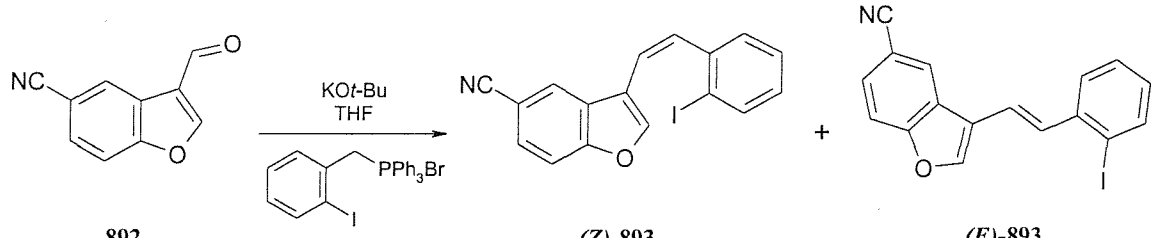
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.21 (1H, s, ArC<u>H</u>O), 8.56 (1H, app. t, J = 1.0 Hz, Ar<u>H</u>), 8.44 (1H, s, Ar<u>H</u>), 7.71 (1H, dd, J = 8.6, 1.0 Hz, Ar<u>H</u>), 7.68 (1H, d, J = 8.6 Hz, Ar<u>H</u>).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 184.3 (Ar<u>C</u>HO), 157.3 (<u>C</u> (Ar)), 156.7 (<u>C</u>H (Ar)), 130.1 (<u>C</u>H (Ar)), 128.0 (<u>C</u>H (Ar)), 124.0 (<u>C</u> (Ar)), 123.2 (<u>C</u> (Ar)), 118.8 (<u>C</u> (Ar)), 113.3 (<u>C</u>H (Ar)), 109.2 (<u>C</u>N).

LRMS (CI) *m/z:* 189 ($[M + NH_4]^+$, 85%), 171 (M^+, 100%).

CHN Found: C, 69.88; H, 2.86; N, 8.18; $C_{10}H_5NO_2$ requires C, 70.18; H, 2.94; N, 8.18.

<u>3-[(*Z*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]furan-5-carbonitrile (***(Z)*-893**) and 3-[(*E*)-2-(2-Iodophenyl)vinyl]-benzo[*b*]furan-5-carbonitrile (***(E)*-893**)</u>



892
mw = 171.16 g mol^{-1}
$C_{10}H_5NO_2$

mw = 371.17 g mol^{-1}
$C_{17}H_{10}INO$

mw = 371.17 g mol^{-1}
$C_{17}H_{10}INO$

To a stirred suspension of **806** (1.80 g, 3.21 mmol) in THF (40 mL) at ambient temperature under nitrogen was added potassium *tert*-butoxide (377 mg, 3.36 mmol). On stirring for 1 hour, the reaction mixture was cooled to 0 °C and a solution of **892** (0.50 g, 2.92 mmol) in THF (40 mL) was added. After 16 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (5-40% ether in petrol) gave firstly ***(Z)*-893** as a white solid that on recrystallisation gave small white prisms (211 mg, 0.57 mmol, 20%): mp 86-88 °C (ethyl acetate/hexane); then ***(E)*-893** as a white solid that on recrystallisation gave granular white prisms (859 mg, 2.31 mmol, 79%): mp 128-131 °C (ethyl acetate/hexane).

Data for (Z)-893:

FT-IR (neat, cm^{-1}): 3141 w, 3082 w, 3033 w, 2925 w, 2227 m, 1464 m, 1444 m, 1429 m, 1404 m, 1286 m, 1196 m, 1086 vs, 1014 m, 880 m, 824 m, 806 s, 763 s, 749 vs, 696 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.98 (1H, d, J = 8.1 Hz, ArH), 7.55 (1H, dd, J = 8.6, 1.4 Hz, ArH), 7.51 (1H, dd, J = 8.6, 0.7 Hz, ArH), 7.46 (1H, d, J = 0.7 Hz, ArH), 7.39 (1H, s, ArH), 7.25-7.18 (2H, m, ArH), 7.08-6.99 (1H, m, ArH), 6.76 (1H, d, J = 11.7 Hz, ArCH=CHAr), 6.65 (1H, d, J = 11.7, 0.7 Hz, ArCH=CHAr).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 156.6 (CO (Ar)), 145.5 (CH (Ar)), 141.8 (C (Ar)), 139.5 (CH (Ar)), 136.3 (ArCH=CHAr), 129.8 (CH (Ar)), 129.6 (CH (Ar)), 128.5 (CH (Ar)), 128.3 (CH (Ar)), 127.4 (C (Ar)), 125.9 (CH (Ar)), 119.4 (C (Ar)), 118.3 (ArCH=CHAr), 117.2 (C (Ar)), 112.8 (CH (Ar)), 106.8 (CN), 99.3 (CI (Ar)).

LRMS (CI) *m/z:* 371 (M^+, 4%), 245 ($[MH - I]^+$, 100%).

CHN Found: C, 55.03; H, 2.73; N, 3.77; $C_{17}H_{10}INO$ requires C, 55.01; H, 2.72; N, 3.77.

Data for (E)-893:

FT-IR (neat, cm^{-1}): 3128 w, 3060 w, 3039 w, 2228 m, 1639 m, 1458 s, 1434 m, 1101 vs, 1068 m, 1011 m, 951 s, 878 m, 807 s, 790 s, 771 vs, 709 m.

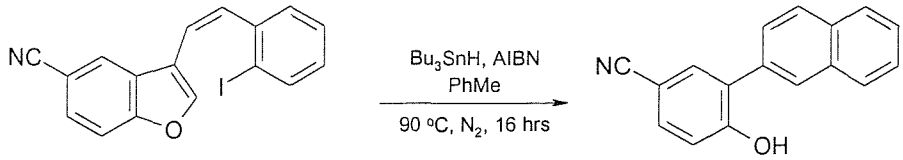
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.35 (1H, app. s, ArH), 7.91 (1H, s, ArH), 7.90 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.69-7.59 (3H, m, ArH), 7.40 (1H, d, J = 16.2 Hz, ArCH=CHAr), 7.39 (1H, app. t, J = 7.4 Hz, ArH), 7.01 (1H, td, J = 7.7, 1.5 Hz, ArH), 6.99 (1H, d, J = 16.2 Hz, ArCH=CHAr).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 157.6 (CO (Ar)), 145.9 (CH (Ar)), 139.9 (C (Ar)), 139.9 (CH (Ar)), 134.9 (ArCH=CHAr),129.6 (CH (Ar)), 128.8 (CH (Ar)), 128.7 (CH (Ar)), 126.5 (C (Ar)), 126.4 (CH (Ar)), 126.0 (CH (Ar)), 119.5 (C (Ar)), 119.5 (ArCH=CHAr), 113.2 (CH (Ar)), 107.5 (CN), 100.7 (CI (Ar)). One quaternary carbon remains unobserved.

LRMS (CI) *m/z:* 371 (M^+, 6%), 245 ($[MH - I]^+$, 100%).

CHN Found: C, 54.90; H, 2.68; N, 3.73; $C_{17}H_{10}INO$ requires C, 55.01; H, 2.72; N, 3.77.

4-Hydroxy-3-(2-naphthyl)benzonitrile (**898**)



(Z)-893
mw = 371.17 g mol^{-1}
$C_{17}H_{10}INO$

898
mw = 245.28 g mol^{-1}
$C_{17}H_{11}NO$

To a stirred solution of ***(Z)*-893** (150 mg, 0.40 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.13 mL, 0.48 mmol) followed by AIBN (12 mg, 0.08 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (20-40% ether in petrol) gave **898** as a white solid that on recrystallisation yielded granular white prisms (96 mg, 0.39 mmol, 98%): mp 180-182 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 3301 br. m, 3068 w, 2222 s, 1599 m, 1503 m, 1439 w, 1409 w, 1355 w, 1338 w, 1271 s, 1237 m, 1199 m, 1167 m, 1132 m, 1115 s, 953 w, 916 w, 892 , 864 m, 825 s, 755 vs.

^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 9.62 (1H, br. s, ArOH), 8.13 (1H, d, J = 1.9 Hz, ArH), 8.00-7.91 (3H, m, ArH), 7.83 (1H, d, J = 2.1 Hz, ArH), 7.79 (1H, dd, J = 8.6, 1.9 Hz, ArH), 7.65 (1H, dd, J = 8.6, 2.1 Hz, ArH), 7.56 (1H, t, J = 6.4 Hz, ArH), 7.53 (1H, t, J = 6.2 Hz, ArH), 7.21 (1H, d, J = 8.6 Hz, ArH).

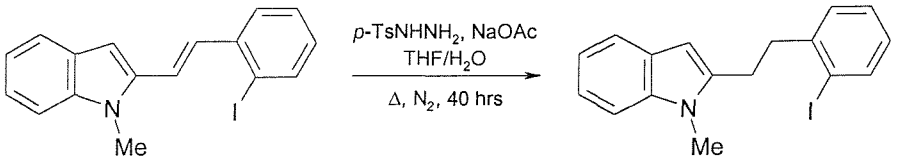
^{13}C NMR δ_C ppm (75 MHz, D_6-acetone): 159.1 (CO (Ar)), 135.6 (CH (Ar)), 134.9 (C (Ar)), 134.1 (C (Ar)), 133.6 (CH (Ar)), 133.5 (C (Ar)), 130.4 (C (Ar)), 128.9 (2 x CH (Ar)), 128.2 (2 x CH (Ar)), 128.1 (CH (Ar)), 126.9 (CH (Ar)), 126.8 (CH (Ar)), 119.6 (C (Ar)), 117.8 (CH (Ar)), 104.0 (CN).

LRMS (ES$^-$) *m/z:* 449 (71%), 358 ([M + CF_3COO]$^-$, 13%), 326 (100%).

CHN Found: C, 83.38; H, 4.42; N, 5.66; $C_{17}H_{11}NO$ requires C, 83.25; H, 4.52; N, 5.71.

7.5 Synthetic Procedures for Chapter 6

2-[2-(2-Iodophenyl)ethyl]-1-methyl-1*H*-indole (**632**)



***(E)*-617**

mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

632

mw = 361.22 g mol^{-1}
$C_{17}H_{16}IN$

A rapidly stirred solution of ***(E)*-617** (400 mg, 1.11 mmol), *para*-toluenesulfonohydrazide (1.24 g, 6.66 mmol) and sodium acetate (546 mg, 6.66 mmol) in THF (10 mL) and water (10 mL) was heated at reflux for 40 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (1.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark yellow solid. Purification by column chromatography (5-10% ether in petrol) gave **632** as a pale yellow solid that yielded colourless needles on recrystallisation (394 mg, 1.09 mmol, 98%): mp 77 °C (petrol).

FT-IR (neat, cm^{-1}): 3048 w, 2930 w, 2899 w, 2839 w, 1541 w, 1466 s, 1449 m, 1434 m, 1403 m, 1328 m, 1311 m, 1010 s, 787 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 266 (14800).

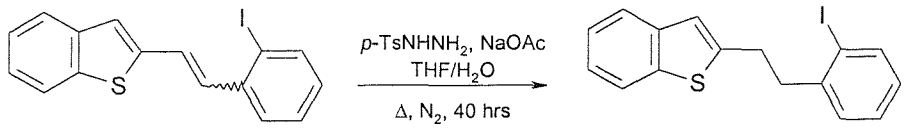
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.88 (1H, dd, J = 7.7, 0.9 Hz, ArH), 7.60 (1H, app. d, J = 7.5 Hz, ArH), 7.34-7.18 (4H, m, ArH), 7.12 (1H, td, J = 7.7, 1.2 Hz, ArH), 6.96 (1H, td, J = 8.0, 2.1 Hz, ArH), 6.38 (1H, s, ArH), 3.68 (3H, s, NCH_3), 3.22-3.13 (2H, m, $ArCH_2CH_2Ar$), 3.10-3.02 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 144.0 (C (Ar)), 140.1 (C (Ar)), 139.8 (CH (Ar)), 137.5 (C (Ar)), 129.8 (CH (Ar)), 128.7 (CH (Ar)), 128.4 (CH (Ar)), 128.0 (C (Ar)), 120.9 (CH (Ar)), 120.1 (CH (Ar)), 119.5 (CH (Ar)), 109.0 (CH (Ar)), 100.5 (CI (Ar)), 99.3 (CH (Ar)), 40.6 ($ArCH_2CH_2Ar$), 29.8 (NCH_3), 27.7 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 362 (MH^+, 87%), 234 ($[M - I]^+$, 90%), 144 ($[C_{10}H_{10}N]^+$, 100%).

CHN Found C, 56.30; H, 4.42; N, 3.83; $C_{17}H_{16}IN$ requires C, 56.53; H, 4.46; N, 3.88.

2-[2-(2-Iodophenyl)ethyl]-benzo[*b*]thiophene (**633**)



***(Z/E)*-618**
mw = 362.33 g mol^{-1}
$C_{16}H_{11}IS$

633
mw = 364.24 g mol^{-1}
$C_{16}H_{13}IS$

A rapidly stirred solution of ***(Z/E)*-618** (655 mg, 1.81 mmol), *para*-toluenesulfonohydrazide (3.04 g, 16.3 mmol) and sodium acetate (1.34 g, 16.3 mmol) in THF (14 mL) and water (14 mL) was heated at reflux for 40 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (2.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (2.5% ether in petrol) gave **633** as a colourless oil that crystallised on standing to small white needles (628 mg, 1.72 mmol, 95%): mp 70-73 °C.

FT-IR (neat, cm^{-1}): 3056 w, 2947 w, 2924 w, 2854 w, 1561 w, 1449 m, 1433 m, 1310 w, 1206 m, 1154 w, 1121 w, 1062 w, 1007 s, 935 w, 838 m, 821 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 278 (5200).

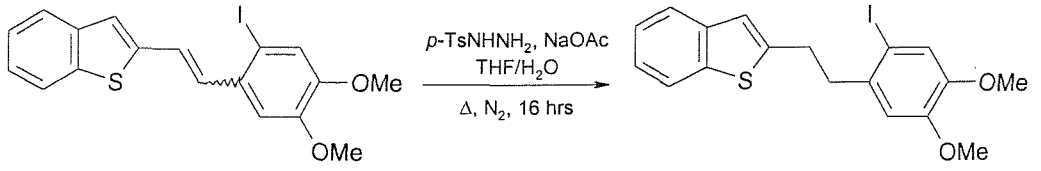
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.89 (1H, dd, J = 7.9, 1.2 Hz, ArH), 7.82 (1H, dd, J = 7.6, 1.0 Hz, ArH), 7.71 (1H, dd, J = 7.4, 1.2 Hz, ArH), 7.36 (1H, td, J = 7.2, 1.4 Hz, ArH), 7.34-7.23 (3H, m, ArH), 7.08 (1H, d, J = 0.5 Hz, ArH), 6.95 (1H, ddd. J = 7.9, 7.0, 1.4 Hz, ArH), 3.29-3.11 (4H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 145.0 (C (Ar)), 143.5 (C (Ar)), 140.3 (C (Ar)), 139.8 (CH (Ar)), 139.6 (C (Ar)), 129.7 (CH (Ar)), 128.6 (CH (Ar)), 128.4 (CH (Ar)), 124.3 (CH (Ar)), 123.8 (CH (Ar)), 123.0 (CH (Ar)), 122.4 (CH (Ar)), 121.2 (CH (Ar)), 100.6 (CI (Ar)), 42.7 ($ArCH_2CH_2Ar$), 31.5 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 364 (M^+, 16%), 237 ($[M - I]^+$, 99%), 147 ($C_9H_7S^+$, 100%).

CHN Found: C, 52.75; H, 3.64; $C_{16}H_{13}IS$ requires C, 52.76; H, 3.60.

2-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]-1-benzo[*b*]thiophene (**901**)



***(Z/E)*-810**

mw = 422.28 g mol^{-1}
$C_{18}H_{15}IO_2S$

901

mw = 424.30 g mol^{-1}
$C_{18}H_{17}IO_2S$

A rapidly stirred solution of ***(Z/E)*-810** (1.05 g, 2.49 mmol), *para*-toluenesulfonohydrazide (4.18 g, 22.4 mmol) and sodium acetate (1.84 g, 22.4 mmol) in THF (20 mL) and water (20 mL) was heated at reflux for 16 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (3.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark yellow oil. Purification by column chromatography (10-30% ether in petrol) gave **901** as a yellow oil (694 mg, 1.64 mmol, 66%).

FT-IR (neat, cm^{-1}): 3057 w, 2999 w, 2932 w, 2837 w, 1595 w, 1567 w, 1500 s, 1457 m, 1434 m, 1376 m, 1333 w, 1251 s, 1210 s, 1160 s, 1098 w, 1065 w, 1027 m, 949 w, 910 w, 853 m, 824 m, 793 m, 744 s, 725 s.

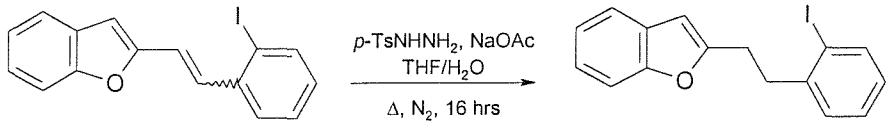
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.80 (1H, dd, J = 7.9, 1.0 Hz, ArH), 7.68 (1H, dd, J = 7.0, 1.4 Hz, ArH), 7.34 (1H, td, J = 7.9, 1.4 Hz, ArH), 7.28 (1H, obsc. td, J = 7.0, 1.0 Hz, ArH), 7.26 (1H, s, ArH), 7.03 (1H, s, ArH), 6.69 (1H, s, ArH), 3.87 (3H, s, $ArOCH_3$), 3.73 (3H, s, $ArOCH_3$), 3.22-3.14 (2H, m, $ArCH_2CH_2Ar$), 3.14-3.06 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 149.3 (CO (Ar)), 148.2 (CO (Ar)), 144.9 (C (Ar)), 140.2 (C (Ar)), 139.5 (C (Ar)), 135.9 (C (Ar)), 124.3 (CH (Ar)), 123.8 (CH (Ar)), 123.0 (CH (Ar)), 122.3 (CH (Ar)), 121.7 (CH (Ar)), 121.4 (CH (Ar)), 112.5 (CH (Ar)), 88.0 (CI (Ar)), 56.3 ($ArOCH_3$), 56.0 ($ArOCH_3$), 42.3 ($ArCH_2CH_2Ar$), 31.7 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 298 ($[MH - I]^+$, 52%), 151 ($C_9H_{11}O_2^+$, 100%), 147 ($C_9H_7S^+$, 64%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 446.9886, $C_{18}H_{17}IO_2SNa$ requires 446.9886.

2-[2-(2-Iodophenyl)ethyl]-benzo[*b*]furan (**634**)



(Z/E)-**619**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

634
mw = 348.18 g mol^{-1}
$C_{16}H_{13}IO$

A rapidly stirred solution of ***(Z/E)*-619** (500 mg, 1.44 mmol), *para*-toluenesulfonohydrazide (2.42 g, 13 mmol) and sodium acetate (1.07 g, 13 mmol) in THF (10 mL) and water (10 mL) was heated at reflux for 16 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (2.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (1-2% ether in petrol) gave **634** as a colourless oil (488 mg, 1.40 mmol, 97%).

FT-IR (neat, cm^{-1}): 3058 w, 2958 w, 2930 w, 2866 w, 1600 w, 1586 w, 1562 w, 1466 m, 1454 s, 1434 m, 1253 m, 1178 w, 1145 w, 1104 w, 1011 m, 944 w, 798 w, 755 vs.

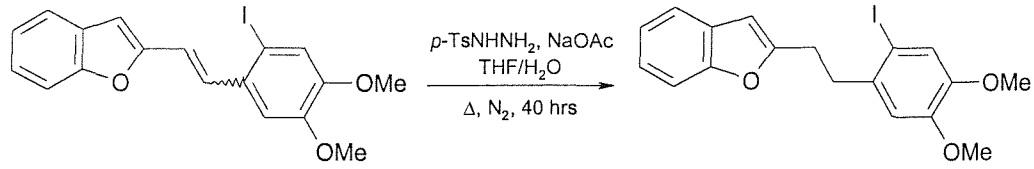
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.87 (1H, d, J = 8.1, 1.2 Hz, ArH), 7.51 (1H, dd, J = 7.1, 1.9 Hz, ArH), 7.48 (1H, app. d, J = 8.1 Hz, ArH), 7.31-7.18 (4H, m, ArH), 6.93 (1H, td, J = 7.4, 1.9 Hz, ArH), 6.43 (1H, s, ArH), 3.25-3.16 (2H, m, $ArCH_2CH_2Ar$), 3.14-3.06 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 158.0 (CO (Ar)), 154.5 (C (Ar)), 143.5 (C (Ar)), 139.7 (CH (Ar)), 129.6 (CH (Ar)), 129.0 (C (Ar)), 128.6 (CH (Ar)), 128.3 (CH (Ar)), 123.5 (CH (Ar)), 122.6 (CH (Ar)), 120.5 (CH (Ar)), 111.0 (CH (Ar)), 102.7 (CH (Ar)), 100.5 (CI (Ar)), 39.2 ($ArCH_2CH_2Ar$), 29.2 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 349 (MH^+, 14%), 222 ($[MH - I]^+$, 20%), 131 ($C_9H_7O^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 348.0013, $C_{16}H_{13}IO$ requires 348.0011.

2-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]-1-benzo[*b*]furan (**902**)



***(Z/E)*-813**
mw = 406.21 g mol^{-1}
$C_{18}H_{15}IO_3$

902
mw = 408.23 g mol^{-1}
$C_{18}H_{17}IO_3$

A rapidly stirred solution of ***(Z/E)*-813** (150 mg, 0.37 mmol), *para*-toluenesulfonohydrazide (0.62 g, 3.32 mmol) and sodium acetate (0.27 g, 3.32 mmol) in THF (5 mL) and water (5 mL) was heated at reflux for 40 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (1.0 g) was added. After 2 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 25 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale yellow oil. Purification by column chromatography (toluene) gave **902** as a pale yellow oil (117 mg, 0.29 mmol, 77%).

FT-IR (neat, cm^{-1}): 3002 w, 2932 w, 2838 w, 1596 w, 1503 s, 1453 m, 1376 w, 1255 vs, 1214 s, 1161 s, 1027 m, 944 w, 912 w, 854 w, 795 m, 738 s.

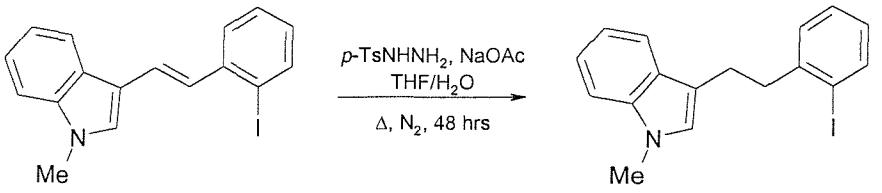
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.50-7.42 (2H, m, ArH), 7.23 (1H, td, J = 7.4, 1.7 Hz, ArH), 7.23 (1H, s, ArH), 7.17 (1H, td, J = 7.4, 1.4 Hz, ArH), 6.60 (1H, s, ArH), 6.37 (1H, s, ArH), 3.85 (3H, s, $ArOCH_3$), 3.65 (3H, s, $ArOCH_3$), 3.17-3.08 (2H, m, $ArCH_2CH_2Ar$), 3.07-2.97 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 158.1 (CO (Ar)), 155.1 (CO (Ar)), 149.7 (CO (Ar)), 148.4 (CO (Ar)), 136.2 (C (Ar)), 129.2 (C (Ar)), 123.7 (CH (Ar)), 122.9 (CH (Ar)), 121.9 (CH (Ar)), 120.8 (CH (Ar)), 112.7 (CH (Ar)), 111.1 (CH (Ar)), 103.3 (CH (Ar)), 88.1 (CI (Ar)), 56.6 ($ArOCH_3$), 56.1 ($ArOCH_3$), 39.1 ($ArCH_2CH_2Ar$), 29.7 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 408 (M^+, 3%), 281 ($[M - I]^+$, 63%), 277 (76%), 151 ($C_9H_{11}O_2^+$, 97%), 131 ($C_9H_7O^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 431.0120, $C_{18}H_{17}IO_3Na$ requires 431.0114.

3-[2-(2-Iodophenyl)ethyl]-1-methyl-1*H*-indole (**653**)



***(E)*-624**

mw = 359.20 g mol^{-1}
$C_{17}H_{14}IN$

653

mw = 361.22 g mol^{-1}
$C_{17}H_{16}IN$

A rapidly stirred solution of ***(E)*-624** (500 mg, 1.39 mmol), *para*-toluenesulfonohydrazide (2.33 g, 12.5 mmol) and sodium acetate (1.03 g, 12.5 mmol) in THF (11 mL) and water (11 mL) was heated at reflux for 48 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (1.5 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (5-10% ether in petrol) gave **653** as a yellow crystalline solid (390 mg, 1.08 mmol, 78%): mp 50-52 °C.

FT-IR (neat, cm^{-1}): 3052 w, 2941 w, 2924 w, 2855 w, 1574 w, 1559 w, 1463 s, 1435 m, 1376 m, 1323 m, 1264 w, 1240 w, 1200 w, 1142 m, 1126 w, 1060 w, 1005 s, 838 w, 788 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 266 (10800).

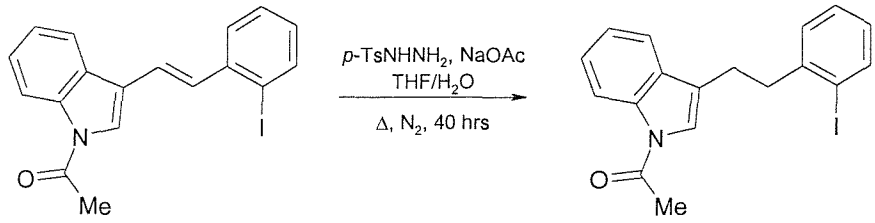
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.89 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.75 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.38-7.24 (4H, m, ArH), 7.18 (1H, ddd, J = 8.1, 7.0, 1.5 Hz, ArH), 6.94 (1H, ddd, J = 8.1, 7.0, 1.5 Hz, ArH), 6.91 (1H, s, ArH), 3.79 (3H, s, NCH_3), 3.19-3.11 (2H, m, $ArCH_2CH_2Ar$), 3.11-3.03 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 145.0 (C (Ar)), 139.6 (CH (Ar)), 137.2 (C (Ar)), 130.1 (C (Ar)), 129.7 (CH (Ar)), 128.5 (CH (Ar)), 128.0 (CH (Ar)), 126.5 (CH (Ar)), 121.7 (CH (Ar)), 119.3 (CH (Ar)), 118.8 (CH (Ar)), 114.4 (C (Ar)), 109.4 (CH (Ar)), 100.7 (CI (Ar)), 42.2 ($ArCH_2CH_2Ar$), 32.8 (NCH_3), 26.2 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 362 (MH^+, 29%), 234 ($[M - I]^+$, 21%), 144 ($C_{10}H_{10}N^+$, 100%).

CHN Found: C, 56.25; H, 4.48; N, 3.77; $C_{17}H_{16}IN$ requires C, 56.53; H, 4.46; N, 3.88.

3-[2-(2-Iodophenyl)ethyl]-1-acetyl-1*H*-indole (**903**)



(E)-873
mw = 387.22 g mol^{-1}
$C_{18}H_{14}INO$

903
mw = 389.23 g mol^{-1}
$C_{18}H_{16}INO$

A rapidly stirred solution of ***(E)*-873** (500 mg, 1.29 mmol), *para*-toluenesulfonohydrazide (2.16 g, 11.6 mmol) and sodium acetate (0.95 g, 11.6 mmol) in THF (10 mL) and water (10 mL) was heated at reflux for 40 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (2.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10-30% ether in petrol) gave **903** as a white solid that yielded small white prisms on recrystallisation (493 mg, 1.27 mmol, 98%): mp 66-68 °C (hexane).

FT-IR (neat, cm^{-1}): 3433 w, 2944 w, 1691 s, 1606 w, 1561 w, 1448 s, 1383 s, 1335 m, 1246 m, 1212 m, 1147 w, 1012 m, 932 w, 750 vs, 662 m.

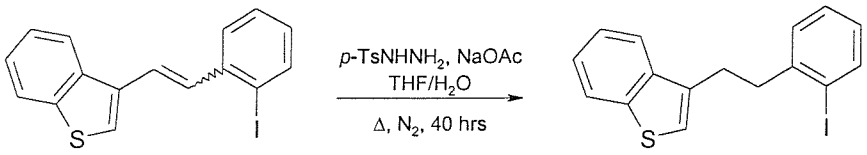
H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.44 (1H, app. br. d, J = 6.7 Hz, ArH), 7.85 (1H, dd, J = 7.6, 1.4 Hz, ArH), 7.62 (1H, dd, J = 7.4, 1.4 Hz, ArH), 7.37 (1H, td, J = 7.4, 1.2 Hz, ArH), 7.30 (1H, td, J = 7.4, 1.4 Hz, ArH), 7.26 (1H, td, J = 7.6, 1.4 Hz, ArH), 7.18 (1H, dd, J = 7.6, 1.7 Hz, ArH), 7.16 (1H, s, ArH), 6.92 (1H, td, J = 7.6, 1.7 Hz, ArH), 3.15-3.07 (2H, m, $ArCH_2CH_2Ar$), 3.02-2.93 (2H, m, $ArCH_2CH_2Ar$), 2.59 (3H, s, $NCOCH_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 168.8 ($NCOCH_3$), 144.4 (C (Ar)), 140.0 (CH (Ar)), 136.4 (C (Ar)), 131.0 (C (Ar)), 130.1 (CH (Ar)), 128.9 (CH (Ar)), 128.5 (CH (Ar)), 125.7 (CH (Ar)), 123.9 (CH (Ar)), 122.5 (CH (Ar)), 122.4 (C (Ar)), 119.5 (CH (Ar)), 117.1 (CH (Ar)), 100.8 (CI (Ar)), 41.1 ($ArCH_2CH_2Ar$), 26.2 ($ArCH_2CH_2Ar$), 24.5 ($NCOCH_3$).

LRMS (Cl) *m/z:* 390 (MH^+, 34%), 263 ($[MH - I]^+$, 31%), 130 (77%).

CHN Found: C, 55.63; H, 4.15; N, 3.70; $C_{18}H_{16}INO$ requires C, 55.54; H, 4.14; N, 3.60.

3-[2-(2-Iodophenyl)ethyl]-benzo[*b*]thiophene (**654**)



***(Z/E)*-625**

mw = 362.33 g mol^{-1}
$C_{16}H_{11}IS$

654

mw = 364.24 g mol^{-1}
$C_{16}H_{13}IS$

A rapidly stirred solution of ***(Z/E)*-625** (1.88 g, 5.19 mmol), *para*-toluenesulfonohydrazide (8.70 g, 46.7 mmol) and sodium acetate (3.83 g, 46.7 mmol) in THF (40 mL) and water (40 mL) was heated at reflux for 40 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (5.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (2.5% ether in petrol) gave **654** as a colourless oil which crystallised on standing to small white needles (1.77 g, 4.86 mmol, 94%): mp 38-40 °C.

FT-IR (neat, cm^{-1}): 3057 w, 2949 w, 1454 m, 1426 m, 1365 w, 1269 w, 1162 w, 1042 w, 1009 s, 934 w, 842 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 280 (4000), 250 (8000).

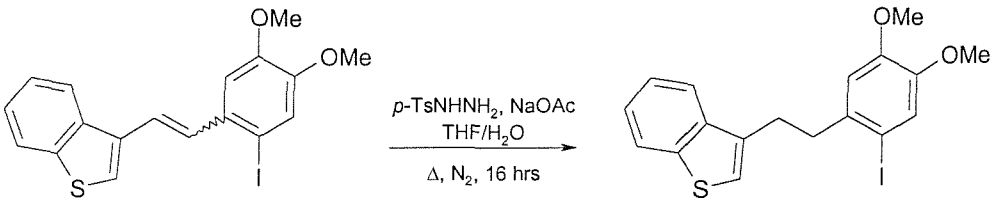
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.94-7.85 (3H, m, ArH), 7.43 (1H, td, J = 7.7, 1.5 Hz, ArH), 7.39 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.28 (1H, dd, J = 7.4, 1.1 Hz, ArH), 7.21 (1H, dd, J = 7.7, 1.8 Hz, ArH), 7.14 (1H, s, ArH), 6.91 (1H, td, J = 7.4, 1.8 Hz, ArH), 3.17 (4H, app. s, Ar(CH_2)$_2$Ar).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 144.1 (C (Ar)), 140.5 (C (Ar)), 139.6 (CH (Ar)), 138.9 (C (Ar)), 135.7 (C (Ar)), 129.6 (CH (Ar)), 128.5 (CH (Ar)), 128.1 (CH (Ar)), 124.2 (CH (Ar)), 123.9 (CH (Ar)), 122.9 (CH (Ar)), 121.8 (2 x CH (Ar)), 100.4 (CI (Ar)), 40.7 (ArCH_2CH_2Ar), 29.3 (ArCH_2CH_2Ar).

LRMS (CI) *m/z:* 365 (MH^+, 16%), 237 ([M - I]$^+$, 95%), 147 ($C_9H_7S^+$, 100%).

CHN Found: C, 52.72; H, 3.69; $C_{16}H_{13}IS$ requires C, 52.76; H, 3.60.

3-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]-benzo[*b*]thiophene (**904**)



***(Z/E)*-817**

mw = 422.28 g mol^{-1}
$C_{18}H_{15}IO_2S$

904

mw = 424.29 g mol^{-1}
$C_{18}H_{17}IO_2S$

A rapidly stirred solution of ***(Z/E)*-817** (750 mg, 1.78 mmol), *para*-toluenesulfonohydrazide (2.98 g, 16.0 mmol) and sodium acetate (1.31 g, 16.0 mmol) in THF (10 mL) and water (10 mL) was heated at reflux for 16 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (2.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (10-30% ether in petrol) gave **904** as a white solid. Recrystallisation from hexane gave **904** as small white prisms (453 mg, 1.07 mmol, 60%): mp 115-117 °C (hexane).

FT-IR (neat, cm^{-1}): 3079 w, 3059 w, 2998 w, 2966 w, 2934 w, 2902 w, 2845 w, 1594 w, 1568 w, 1500 vs, 1462 m, 1429 m, 1371 m, 1312 w, 1264 m, 1250 s, 1201 vs, 1160 vs, 1020 s, 859 m, 843 m, 796 s, 761 s, 739 vs, 723 s.

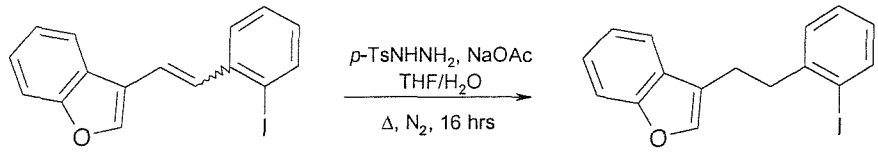
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.89-7.80 (2H, m, ArH), 7.40 (1H, td, J = 7.1, 1.4 Hz, ArH), 7.34 (1H, td, J = 7.1, 1.7 Hz, ArH), 7.23 (1H, s, ArH), 7.06 (1H, s, ArH), 6.53 (1H, s, ArH), 3.85 (3H, s, $ArOCH_3$), 3.70 (3H, s, $ArOCH_3$), 3.08 (4H, br. s, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 149.6 (CO (Ar)), 148.4 (CO (Ar)), 140.8 (C (Ar)), 139.3 (C (Ar)), 136.9 (C (Ar)), 136.1 (C (Ar)), 124.6 (CH (Ar)), 124.3 (CH (Ar)), 123.3 (CH (Ar)), 122.3 (CH (Ar)), 122.2 (CH (Ar)), 122.1 (CH (Ar)), 112.9 (CH (Ar)), 88.2 (CI (Ar)), 56.6 ($ArOCH_3$), 56.2 ($ArOCH_3$), 40.7 ($ArCH_2CH_2Ar$), 29.8 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 297 ($[M - I]^+$, 54%), 151 ($C_9H_{11}O_2^+$, 100%).

CHN Found: C, 50.77; H, 4.04; $C_{18}H_{17}IO_2S$ requires C, 50.95; H, 4.04.

3-[2-(2-Iodophenyl)ethyl]-benzo[*b*]furan (**655**)



***(Z/E)*-626**
mw = 346.16 g mol^{-1}
$C_{16}H_{11}IO$

655
mw = 348.18 g mol^{-1}
$C_{16}H_{13}IO$

A rapidly stirred solution of ***(Z/E)*-626** (532 mg, 1.54 mmol), *para*-toluenesulfonohydrazide (2.59 g, 13.9 mmol) and sodium acetate (1.14 g, 13.9 mmol) in THF (10 mL) and water (10 mL) was heated at reflux for 16 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (2.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (1-2% ether in petrol) gave **655** as a colourless oil (510 mg, 1.46 mmol, 95%).

FT-IR (neat, cm^{-1}): 3054 w, 2929 w, 2861 w, 1585 w, 1561 w, 1452 s, 1363 w, 1276 w, 1184 m, 1091 s, 1010 s, 929 w, 857 m, 795 w, 735 vs.

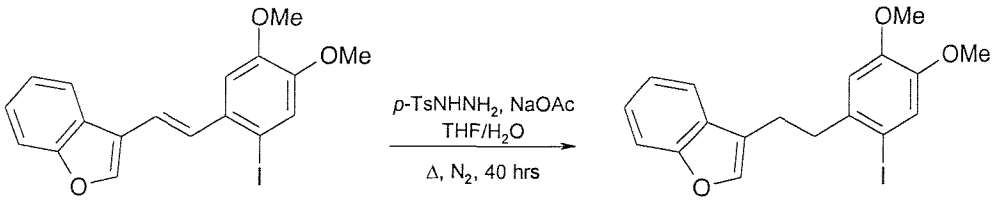
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.89 (1H, dd, J = 8.1, 1.1 Hz, ArH), 7.68 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.53 (1H, dd, J = 7.4, 1.1 Hz, ArH), 7.45 (1H, s, ArH), 7.35 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.31 (1H, obsc. dd, J = 7.4, 1.8 Hz, ArH), 7.29 (1H, td, J = 7.4, 1.1 Hz, ArH), 7.23 (1H, td, J = 7.7, 1.8 Hz, ArH), 6.95 (1H, td, J = 8.1, 1.1 Hz, ArH), 3.19-3.11 (2H, m, $ArCH_2CH_2Ar$), 3.04-2.96 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.5 (C (Ar)), 144.2 (C (Ar)), 141.6 (CH (Ar)), 139.8 (CH (Ar)), 129.8 (CH (Ar)), 128.6 (CH (Ar)), 128.3 (CH (Ar) *and* C (Ar)), 124.4 (CH (Ar)), 122.5 (CH (Ar)), 120.0 (CH (Ar)), 119.7 (C (Ar)), 111.7 (CH (Ar)), 100.6 (CI (Ar)), 40.8 ($ArCH_2CH_2Ar$), 24.6 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 349 (MH^+, 32%), 221 ($[M-I]^+$, 42%), 131 ($C_9H_7O^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 348.0002, $C_{16}H_{13}IO$ requires 348.0011.

3-[2-(4,5-Dimethoxy-2-iodophenyl)ethyl]-benzo[*b*]furan (**905**)



***(Z/E)*-823**

mw = 406.21 g mol^{-1}

$C_{18}H_{15}IO_3$

905

mw = 408.23 g mol^{-1}

$C_{18}H_{17}IO_3$

A rapidly stirred solution of ***(Z/E)*-823** (450 mg, 1.11 mmol), *para*-toluenesulfonohydrazide (1.86 g, 10 mmol) and sodium acetate (820 mg, 10 mmol) in THF (10 mL) and water (10 mL) was heated at reflux for 40 hours under nitrogen. On cooling to ambient temperature, potassium carbonate (2.0 g) was added. After 2 hours, the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (10-30% ether in petrol) gave **905** as a white solid that yielded on recrystallisation fine white needles (410 mg, 1.0 mmol, 90%): mp 96-98 °C (hexane).

FT-IR (neat, cm^{-1}): 3060 w, 2913 w, 2836 w, 1505 s, 1450 s, 1435 m, 1377 m, 1255 m, 1216 vs, 1165 s, 1090 s, 1029 s, 860 m, 805 m, 735 vs.

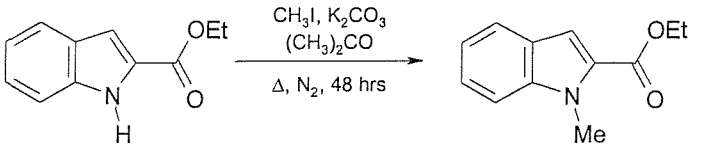
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.62 (1H, dd, J = 7.1, 1.7 Hz, ArH), 7.47 (1H, dd, J = 7.4, 1.4 Hz, ArH), 7.39 (1H, s, ArH), 7.30 (1H, td, J = 7.1, 1.4 Hz, ArH), 7.24 (1H, td, J = 7.4, 1.7 Hz, ArH), 7.23 (1H, s, ArH), 6.60 (1H, s, ArH), 3.85 (3H, s, $ArOCH_3$), 3.70 (3H, s, $ArOCH_3$), 3.08-3.00 (2H, m, $ArCH_2CH_2Ar$), 2.97-2.89 (2H, m, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 155.8 (CO (Ar)), 149.7 (CO (Ar)), 148.4 (CO (Ar)), 141.9 (CH (Ar)), 136.8 (C (Ar)), 128.6 (C (Ar)), 124.6 (CH (Ar)), 122.7 (CH (Ar)), 122.1 (CH (Ar)), 120.2 (CH (Ar)), 119.9 (C (Ar)), 112.9 (CH (Ar)), 111.9 (CH (Ar)), 88.2 (CI (Ar)), 56.6 ($ArOCH_3$), 56.2 ($ArOCH_3$), 40.7 ($ArCH_2CH_2Ar$), 25.0 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 281 ($[M - I]^+$, 66%), 151 ($C_9H_{11}O_2^+$, 99%), 131 ($C_9H_7O^+$, 100%).

CHN Found: C, 52.82; H, 4.18; $C_{18}H_{17}IO_3$ requires C, 52.96; H, 4.20.

Ethyl *N*-methylindole-2-carboxylate (**906**)



802

mw = 189.21 g mol^{-1}
$C_{11}H_{11}NO_2$

906

mw = 203.24 g mol^{-1}
$C_{12}H_{13}NO_2$

In accordance with the procedure of Sukari and Vernon,[232] a suspension of ethyl indole-2-carboxylate **802** (4.0 g, 21.1 mmol), potassium carbonate (23.4 g, 0.17 mol) and methyl iodide (16 mL, 0.26 mol) in acetone (200 mL) under nitrogen was heated at reflux for 48 hours. On cooling to ambient temperature, the suspension was filtered and concentrated *in vacuo* to a white solid. Water (200 mL) was added and the resultant suspension extracted with ether (1 x 200 mL, 2 x 100 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow solid. Recrystallisation from ethanol gave **906** as a white crystalline solid (3.87 g, 19.0 mmol, 90%): mp 61-63 °C (ethanol), lit. 59-60.5 °C (ethanol).[232] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3057 w, 2986 w, 2942 w, 2876 w, 1695 vs, 1514 m, 1469 m, 1448 m, 1400 m, 1249 s, 1222 vs, 1165 s, 1130 s, 1091 s, 1009 m, 809 m.

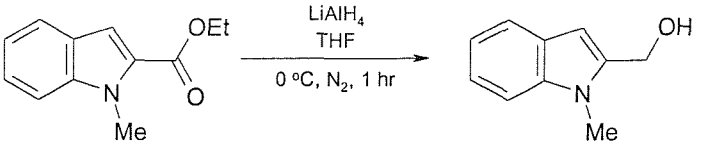
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 279 (22200).

H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.70 (1H, dd, J = 8.0, 1.0 Hz, ArH), 7.43-7.34 (2H, m, ArH), 7.33 (1H, s, ArH), 7.17 (1H, ddd, J = 8.0, 6.1, 1.8 Hz, ArH), 4.40 (2H, q, J = 7.1 Hz, OCH_2CH_3), 4.10 (3H, s, NCH_3), 1.44 (3H, t, J = 7.1 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 162.4 (COOEt), 139.8 (C (Ar)), 128.2 (C (Ar)), 126.0 (C (Ar)), 125.1 (CH (Ar)), 122.7 (CH (Ar)), 120.7 (CH (Ar)), 110.4 (CH (Ar)), 110.2 (CH (Ar)), 60.7 (OCH_2CH_3), 31.8 (OCH_2CH_3), 14.6 (NCH_3).

LRMS (CI) *m/z:* 204 (MH^+, 100%), 175 ($[MH - CH_2CH_3]^+$, 27%), 158 ($[M - OCH_2CH_3]^+$, 15%), 130 ($[M - COOCH_2CH_3]^+$, 13%).

N-Methyl-2-(hydroxymethyl)-indole (**907**)



906

mw = 203.24 g mol^{-1}
$C_{12}H_{13}NO_2$

907

mw = 161.20 g mol^{-1}
$C_{10}H_{11}NO$

To a stirred solution of ethyl *N*-methylindole-2-carboxylate **906** (3.0 g, 14.8 mmol) in THF (75 mL) at –78 °C under nitrogen was added lithium aluminium hydride (1.12 g, 29.6 mmol). The reaction mixture was warmed to 0 °C and stirred for 1 hour. Water (1.1 mL) was then added, followed by 15% sodium hydroxide (1.1 mL) and water (1.1 mL) once effervescence had ceased. After stirring for 2 hours at ambient temperature, anhydrous magnesium sulfate (10 g) was added. The resultant white suspension was stirred for 16 hours then filtered and concentrated *in vacuo* to give **907** as a pink crystalline solid (2.31 g, 14.3 mmol, 97%): mp 90 °C, lit. 92-93 °C.[233] The observed data is consistent with literature values.

FT-IR (neat, cm^{-1}): 3195 br. m, 1467 m, 1395 m, 1367 m, 1340 m, 1316 w, 1237 w, 1140 m, 1005 m, 984 s, 958 m, 906 w, 843 w, 799 m, 779 s.

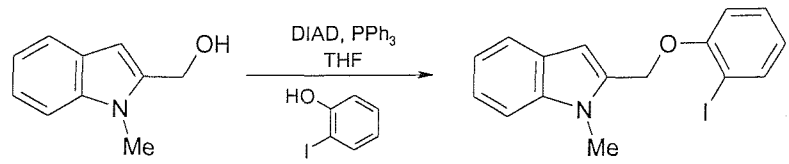
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 266 (14600).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.64 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.34 (1H, app. dd, J = 7.7, 1.0 Hz, ArH), 7.29 (1H, ddd, J = 7.7, 6.6, 1.1 Hz, ArH), 7.17 (1H, ddd, J = 7.7, 6.6, 1.0 Hz, ArH), 6.44 (1H, s, ArH), 4.72 (2H, d, J = 5.5 Hz, $ArCH_2OH$), 3.73 (3H, s, NCH_3), 2.21 (1H, t, J = 5.5 Hz, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 138.8 (C (Ar)), 138.3 (C (Ar)), 127.3 (C (Ar)), 122.1 (CH (Ar)), 121.0 (CH (Ar)), 119.8 (CH (Ar)), 109.4 (CH (Ar)), 101.4 (CH (Ar)), 57.5 (CH_2OH), 29.9 (NCH_3).

LRMS (CI) *m/z:* 162 (MH^+, 100%), 144 ($[MH - H_2O]^+$, 64%).

2-(2-Iodophenoxymethyl)-1-methyl-1*H*-indole (**666**)



907

mw = 161.20 g mol^{-1}
$C_{10}H_{11}NO$

666

mw = 363.19 g mol^{-1}
$C_{16}H_{14}INO$

To a stirred solution of alcohol **907** (400 mg, 2.48 mmol), 2-iodophenol (656 mg, 2.98 mmol) and triphenylphosphine (782 mg, 2.98 mmol) in THF (20 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.54 mL, 2.73 mmol) over 10 minutes. After stirring for 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a green oil. Purification by column chromatography (2.5-5% ether in petrol) yielded **666** as a white solid that gave pale pink needles on recrystallisation (330 mg, 0.91 mmol, 37%): mp 169-171 °C (ether/petrol).

FT-IR (neat, cm^{-1}): 3065 w, 2939 w, 1568 w, 1465 m, 1437 m, 1402 m, 1380 m, 1340 m, 1314 w, 1275 m, 1234 s, 1160 m, 1147 m, 1119 w, 1046 w, 1016 m, 993 vs, 861 m, 794 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 262 (8400).

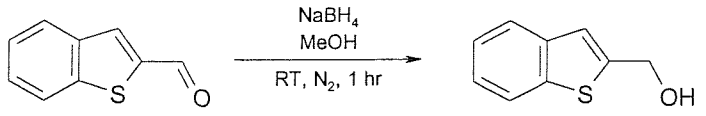
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.80 (1H, dd, J = 7.8, 1.7 Hz, ArH), 7.64 (1H, d, J = 7.8 Hz, ArH), 7.38 (1H, d, J = 8.0 Hz, ArH), 7.33 (1H, td, J = 7.8, 1.7 Hz, ArH), 7.29 (1H, td, J = 8.0, 1.2 Hz, ArH), 7.15 (1H, td, J = 8.0, 1.0 Hz, ArH), 7.03 (1H, dd, J = 8.0, 1.0 Hz, ArH), 6.76 (1H, td, J = 7.8, 1.2 Hz, ArH), 6.63 (1H, s, ArH), 5.28 (2H, s, $ArCH_2OAr$), 3.90 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 156.8 (CO (Ar)), 139.9 (CH (Ar)), 138.4 (C (Ar)), 134.0 (C (Ar)), 129.6 (CH (Ar)), 127.2 (C (Ar)), 123.3 (CH (Ar)), 122.4 (CH (Ar)), 121.2 (CH (Ar)), 119.8 (CH (Ar)), 112.9 (CH (Ar)), 109.5 (CH (Ar)), 103.8 (CH (Ar)), 87.0 (CI (Ar)), 63.8 ($ArCH_2OAr$), 30.7 (NCH_3).

LRMS (CI) *m/z:* 364 (MH^+, 35%), 237 ($[MH - I]^+$, 100%).

CHN Found C, 52.85; H, 3.89; N, 3.84; $C_{16}H_{14}INO$ requires C, 52.91; H, 3.89; N, 3.85.

2-(Hydroxymethyl)-benzo[*b*]thiophene (**908**)



808
mw = 162.21 g mol^{-1}
C_9H_6OS

908
mw = 164.23 g mol^{-1}
C_9H_8OS

In accordance with the procedure of Takeshita *et al.*,[234] to a stirred solution of 2-formylbenzo[*b*]thiophene **808** (5.0 g, 30.8 mmol) in methanol (500 mL) at 0 °C was added sodium borohydride (1.29 g, 34.0 mmol). The reaction mixture was stirred at ambient temperature for 1 hour then concentrated *in vacuo*. The resultant white semi-solid was recrystallised from petrol to yield **908** as small white needles (4.56 g, 27.8 mmol, 90%): mp 102 °C (petrol), lit. 99-100 °C (petrol).[235] The observed data is consistent with literature values.[236]

FT-IR (neat, cm^{-1}): 3272 br. w, 3057 w, 2915 w, 2859 w, 1456 w, 1435 w, 1362 w, 1237 w, 1124 w, 1102 w, 1004 s, 938 w, 838 s.

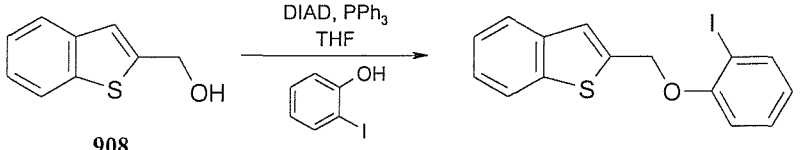
UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 278 (4700), 250 (14700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.85-7.80 (1H, m, ArH), 7.76-7.70 (1H, m, ArH), 7.37 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.33 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.19 (1H, d, J = 0.8 Hz, ArH), 4.91 (2H, d, J = 0.8 Hz, $ArCH_2OH$), 2.31 (1H, br. s, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 144.9 (C (Ar)), 140.1 (C (Ar)), 139.7 (C (Ar)), 124.5 (2 x CH (Ar)), 123.7 (CH (Ar)), 122.7 (CH (Ar)), 121.7 (CH (Ar)), 61.0 ($ArCH_2OH$).

LRMS (CI) *m/z:* 164 (M^+, 92%), 147 ($[MH - H_2O]^+$, 100%).

2-(2-Iodophenoxymethyl)-benzo[*b*]thiophene (**667**)



908
mw = 164.23 g mol^{-1}
C_9H_8OS

667
mw = 366.22 g mol^{-1}
$C_{15}H_{11}IOS$

To a stirred solution of alcohol **908** (300 mg, 1.83 mmol), 2-iodophenol (484 mg, 2.20 mmol) and triphenylphosphine (577 mg, 2.20 mmol) in THF (15 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.40 mL, 2.01 mmol) over 10 minutes.

After 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5-10% ether in petrol) yielded **667** as a colourless oil which crystallised on standing to a white solid (633 mg, 1.73 mmol, 94%): mp 91-93 °C.

FT-IR (neat, cm^{-1}): 3051 w, 2924 w, 2869 w, 1583 m, 1566 m, 1472 s, 1454 s, 1439 s, 1368 s, 1275 s, 1240 s, 1188 m, 1141 m, 1120 m, 1048 m, 1007 s, 862 m, 822 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\ mol^{-1}\ cm^{-1}$), CH_2Cl_2: 274 (6100).

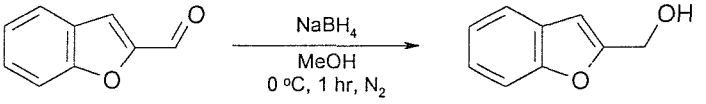
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.89-7.76 (3H, m, ArH), 7.43-7.33 (3H, m, ArH), 7.32 (1H, td, J = 8.1, 7.4, 1.7 Hz, ArH), 6.95 (1H, dd, J = 8.1, 1.2 Hz, ArH), 6.78 (1H, td, J = 7.4, 1.2 Hz, ArH), 5.40 (2H, d, J = 1.0 Hz, $ArCH_2OAr$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 157.0 (CO (Ar)), 140.3 (C (Ar)), 140.0 (C (Ar)), 139.9 (CH (Ar)), 139.5 (C (Ar)), 129.6 (CH (Ar)), 124.7 (CH (Ar)), 124.6 (CH (Ar)), 123.9 (CH (Ar)), 123.5 (CH (Ar)), 122.9 (CH (Ar)), 122.6 (CH (Ar)), 113.1 (CH (Ar)), 87.2 (CI (Ar)), 67.1 ($ArCH_2OAr$).

LRMS (CI) *m/z:* 366 (M^+, 3%), 240 ($[MH - I]^+$, 11%), 147 ($C_9H_7S^+$, 100%).

CHN Found: C, 49.56; H, 3.06; $C_{15}H_{11}IOS$ requires C, 49.20; H, 3.03.

2-(Hydroxymethyl)benzo[*b*]furan (**909**)



812
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

909
mw = 148.16 g mol^{-1}
$C_9H_8O_2$

To a stirred solution of **812** (4.0 g, 27.4 mmol) in methanol (300 mL) at 0 °C was added sodium borohydride (1.14 g, 30 mmol). The reaction mixture was stirred at ambient temperature for 1 hour then concentrated *in vacuo*. Water (100 mL) was added and the resultant aqueous suspension was extracted with ether (3 x 100mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to yield **909** as a yellow oil (3.96 g, 26.7 mmol, 98%). The observed data is consistent with literature values.[237]

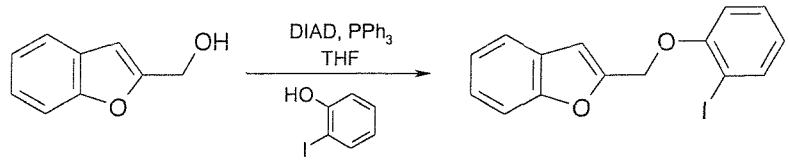
FT-IR (neat, cm^{-1}): 3332 br. m, 2929 w, 2867 w, 1604 w, 1587 w, 1453 s, 1254 s, 1175 m, 1133 m, 1062 w, 1007 s, 937 s, 875 w, 808 s, 730 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.60-7.55 (1H, m, ArH), 7.51-7.47 (1H, m, ArH), 7.31 (1H, td, J = 7.4, 1.4 Hz, ArH), 7.25 (1H, td, J = 7.4, 1.4 Hz, ArH), 6.67 (1H, d, J = 0.7 Hz, ArH), 4.78 (2H, s, $ArCH_2OH$), 2.41 (1H, br. s, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 156.6 (C (Ar)), 155.2 (C (Ar)), 128.3 (C (Ar)), 124.5 (CH (Ar)), 123.0 (CH (Ar)), 121.3 (CH (Ar)), 111.4 (CH (Ar)), 104.3 (CH (Ar)), 58.2 ($ArCH_2OH$).

LRMS (CI) *m/z:* 148 (M^+, 31%), 131 ($[MH - H_2O]^+$, 100%).

2-(2-Iodophenoxymethyl)-1-benzo[*b*]furan (**668**)



909
mw = 148.16 g mol^{-1}
$C_9H_8O_2$

668
mw = 350.15 g mol^{-1}
$C_{15}H_{11}IO_2$

To a stirred solution of alcohol **909** (250 mg, 1.69 mmol), 2-iodophenol (446 mg, 2.03 mmol) and triphenylphosphine (532 mg, 2.03 mmol) in THF (15 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.37 mL, 1.86 mmol) over 10 minutes. After 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5% ether in petrol) gave **668** as a colourless oil (503 mg, 1.44 mmol, 85%).

FT-IR (neat, cm^{-1}): 3061 w, 2936 w, 2866 w, 1581 w, 1470 s, 1452 s, 1375 w, 1285 m, 1242 s, 120 s, 1182 m, 1135 w, 1121 w, 1049 m, 1017 s, 946 m, 877 w, 853 w, 809 m, 736 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.83 (1H, dd, J = 7.7, 1.8 Hz, ArH), 7.60 (1H, dd, J = 7.4, 1.1 Hz, ArH), 7.53 (1H, dd, J = 8.1, 1.1 Hz, ArH), 7.37-7.29 (2H, m, ArH), 7.26 (1H, td, J = 7.4, 1.1 Hz, ArH), 6.99 (1H, dd, J = 8.1, 1.5 Hz, ArH), 6.87 (1H, d, J = 0.8 Hz, ArH), 6.78 (1H, td, J = 7.7, 1.5 Hz, ArH), 5.25 (2H, s, $ArCH_2OAr$).

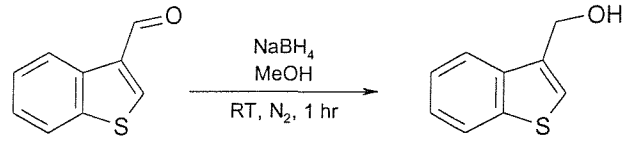
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 157.5 (C (Ar)), 155.6 (C (Ar)), 152.9 (C (Ar)), 140.0 (CH (Ar)), 129.9 (CH (Ar)), 128.5 (C (Ar)), 125.0 (CH (Ar)), 123.9

(CH (Ar)), 123.3 (CH (Ar)), 121.7 (CH (Ar)), 113.7 (CH (Ar)), 111.8 (CH (Ar)), 106.5 (CH (Ar)), 87.5 (CI (Ar)), 64.9 ($ArCH_2OAr$).

LRMS (CI) *m/z:* 351 (MH^+, 3%), 223 ($[M-I]^+$, 19%), 131 ($C_9H_7O^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 349.9809, $C_{15}H_{11}IO_2$ requires 349.9804.

3-(Hydroxymethyl)-benzo[*b*]thiophene (**911**)



816

mw = 162.21 g mol^{-1}
C_9H_6OS

911

mw = 164.23 g mol^{-1}
C_9H_8OS

To a stirred solution of 3-formylbenzo[*b*]thiophene **816** (1.0 g, 6.16 mmol) in methanol (100 mL) at 0 °C was added sodium borohydride (257 mg, 6.78 mmol). The reaction mixture was stirred at ambient temperature for 1 hour then concentrated *in vacuo*. The resultant white semi-solid was recrystallised from petrol to yield **911** as a white solid (1.01 g, 6.15 mmol, 100%). A second recrystallisation from petrol gave white needles: mp 42-44 °C (petrol).

FT-IR (neat, cm^{-1}): 3225 br. s, 3103 w, 2915 w, 2867 w, 1460 m, 1428 m, 1366 m, 1313 w, 1225 m, 1139 w, 1091 m, 1058 s, 995 s, 854 w, 811 w, 771 s, 751 vs.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 278 (2300), 246 (5500).

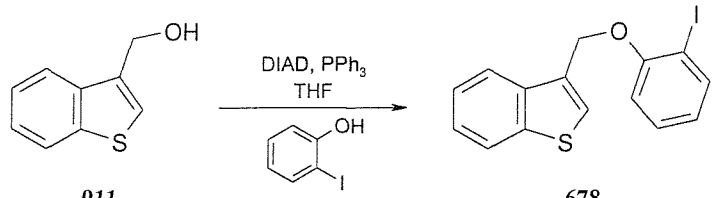
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.90-7.86 (1H, m, ArH), 7.84-7.80 (1H, m, ArH), 7.41 (1H, td, J = 7.0, 1.8 Hz, ArH), 7.38 (1H, td, J = 7.0, 1.5 Hz, ArH), 7.33 (1H, s, ArH), 4.85 (2H, s, CH_2OH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.8 (C (Ar)), 137.7 (C (Ar)), 136.0 (C (Ar)), 124.6 (CH (Ar)), 124.2 (CH (Ar)), 123.8 (CH (Ar)), 122.9 (CH (Ar)), 122.0 (CH (Ar)), 59.6 (CH_2OH).

LRMS (CI) *m/z:* 164 (M^+, 94%), 147 ($[MH - H_2O]^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 164.0288, C_9H_8OS requires 164.0296.

3-(2-Iodophenoxymethyl)-benzo[*b*]thiophene (**678**)



911
mw = 164.23 g mol^{-1}
C_9H_8OS

678
mw = 366.22 g mol^{-1}
$C_{15}H_{11}IOS$

To a stirred solution of alcohol **911** (700 mg, 4.26 mmol), 2-iodophenol (1.13 g, 5.11 mmol) and triphenylphosphine (1.34 g, 5.11 mmol) in THF (15 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.92 mL, 4.69 mmol) over 10 minutes. After 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a colourless oil. Purification by column chromatography (5-10% ether in petrol) yielded **678** as a colourless oil that crystallised on standing to a white solid (1.27 g, 3.48 mmol, 82%): mp 54-56 °C.

FT-IR (neat, cm^{-1}): 3057 w, 1582 w, 1569 w, 1475 m, 1452 m, 1435 m, 1323 w, 1276 s, 1248 s, 1157 w, 1121 w, 1059 s, 1015 s, 825 m, 775 m.

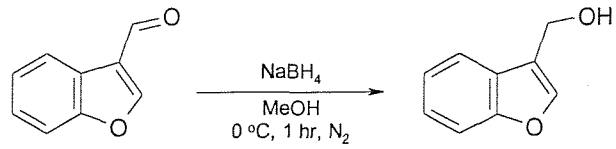
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.93 (1H, dd, J = 7.2, 1.5 Hz, ArH), 7.91 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.83 (1H, dd, J = 7.2, 1.5 Hz, ArH), 7.62 (1H, s, ArH), 7.45 (1H, td, J = 7.2, 1.5 Hz, ArH), 7.41 (1H, td, J = 7.2, 1.5 Hz, ArH), 7.32 (1H, ddd, J = 8.4, 7.4, 1.5 Hz, ArH), 6.98 (1H, dd, J = 8.4, 1.2 Hz, ArH), 6.76 (1H, td, J = 7.4, 1.2 Hz, ArH), 5.38 (2H, s, $ArCH_2OAr$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 157.2 (CO (Ar)), 140.8 (C (Ar)), 139.8 (CH (Ar)), 137.6 (C (Ar)), 131.4 (C (Ar)), 129.7 (CH (Ar)), 125.1 (CH (Ar)), 124.8 (CH (Ar)), 124.4 (CH (Ar)), 123.2 (CH (Ar)), 123.1 (CH (Ar)), 122.3 (CH (Ar)), 112.7 (CH (Ar)), 87.0 (CI (Ar)), 66.3 ($ArCH_2OAr$).

LRMS (CI) *m/z:* 366 (M^+, 4%), 240 ([MH - I]$^+$, 10%), 147 ($C_9H_7S^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 365.9582, $C_{15}H_{11}IOS$ requires 365.9575.

3-(Hydroxymethyl)-benzo[*b*]furan (**912**)



822
mw = 146.15 g mol^{-1}
$C_9H_6O_2$

912
mw = 148.16 g mol^{-1}
$C_9H_8O_2$

To a stirred solution of **822** (0.50 g, 3.42 mmol) in methanol (30 mL) at 0 °C was added sodium borohydride (142 mg, 3.75 mmol). The reaction mixture was stirred at ambient temperature for 1 hour then concentrated *in vacuo*. Water (25 mL) was added and the resultant aqueous suspension was extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to an off-white solid. Recrystallisation from hexane gave **912** as fine orange needles (452 mg, 3.05 mmol, 89%): mp 45-46 °C (hexane), lit. 46-47 °C (petrol).[230] The observed data is consistent with literature values.[238]

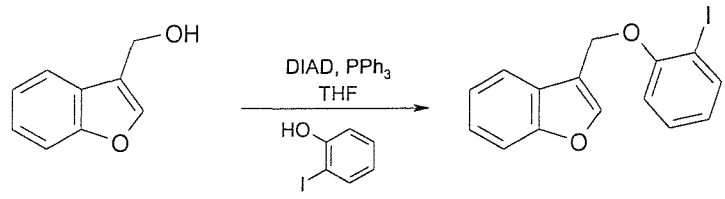
FT-IR (neat, cm^{-1}): 3219 br. m, 2924 w, 2880 w, 1584 w, 1479 w, 1449 s, 1359 w, 1318 w, 1301 w, 1281 m, 1189 m, 1151 w, 1097 s, 1077 m, 999 vs, 931 w, 855 m, 814 m, 735 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.67 (1H, dd, J = 7.4, 1.5 Hz, ArH), 7.59 (1H, s, ArH), 7.51 (1H, app. d, J = 7.4 Hz, ArH), 7.34 (1H, td, J = 7.4, 1.5 Hz, ArH), 7.28 (1H, td, J = 7.4, 1.1 Hz, ArH), 4.81 (2H, s, $ArCH_2OH$), 2.28 (1H, br. s, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.7 (C (Ar)), 142.5 (CH (Ar)), 126.9 (C (Ar)), 124.8 (CH (Ar)), 122.9 (CH (Ar)), 120.5 (C (Ar)), 120.1 (CH (Ar)), 111.7 (CH (Ar)), 55.9 ($ArCH_2OH$).

LRMS (CI) *m/z:* 148 (M^+, 100%), 131 ($[MH - H_2O]^+$, 88%).

3-(2-Iodophenoxymethyl)-1-benzo[*b*]furan (**679**)



912
mw = 148.16 g mol^{-1}
$C_9H_8O_2$

679
mw = 350.15 g mol^{-1}
$C_{15}H_{11}IO_2$

To a stirred solution of alcohol **912** (250 mg, 1.69 mmol), 2-iodophenol (446 mg, 2.03 mmol) and triphenylphosphine (532 mg, 2.03 mmol) in THF (15 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.37 mL, 1.86 mmol) over 10 minutes. After 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a yellow oil. Purification by column chromatography (5% ether in petrol) gave **679** as a colourless oil (401 mg, 1.15 mmol, 68%).

FT-IR (neat, cm^{-1}): 1581 w, 1469 m, 1451 m, 1284 m, 124 m, 1187 w, 1101 m, 1048 m, 1016 m, 858 w, 805 w, 736 vs.

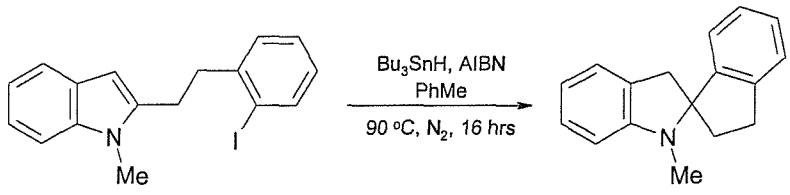
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.82 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.79 (1H, obsc. d, J = 8.1, 1.1 Hz, ArH), 7.78 (1H, s, ArH), 7.53 (1H, dd, J = 7.0, 1.1 Hz, ArH), 7.40-7.26 (3H, m, ArH), 6.98 (1H, dd, J = 8.1, 1.5 Hz, ArH), 6.77 (1H, td, J = 7.7, 1.1 Hz, ArH), 5.29 (2H, s, $ArCH_2OAr$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 157.5 (C (Ar)), 156.0 (C (Ar)), 143.6 (CH (Ar)), 140.1 (CH (Ar)), 129.9 (CH (Ar)), 127.0 (C (Ar)), 125.2 (CH (Ar)), 123.5 (CH (Ar)), 123.3 (CH (Ar)), 120.8 (CH (Ar)), 116.9 (C (Ar)), 113.1 (CH (Ar)), 112.0 (CH (Ar)), 87.3 (CI (Ar)), 63.1 ($ArCH_2OAr$).

LRMS (CI) *m/z:* 223 ([M – I]$^+$, 13%), 148 (27%), 131 ($C_9H_7O^+$, 100%).

HRMS (EI) *m/z* Found: M$^+$ 349.9808, $C_{15}H_{11}IO_2$ requires 349.9804.

1'-Methylspiro(indane-1,2'-indoline) (**636**)



632

mw = 361.22 g mol^{-1}
$C_{17}H_{16}IN$

636

mw = 235.33 g mol^{-1}
$C_{17}H_{17}N$

To a stirred solution of indole **632** (250 mg, 0.69 mmol) in toluene (20 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.22 mL, 0.83 mmol) followed by AIBN (23 mg, 0.14 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (15 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (1-2% ether in petrol) gave **636** as a colourless oil (89 mg, 0.38 mmol, 55%).

FT-IR (neat, cm^{-1}): 3047 w, 3024 w, 2942 w, 2852 w, 1606 m, 1483 s, 1369 m, 1312 m, 1190 m, 1154 w, 1118 w, 1080 w, 1005 m, 897 w, 855 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 278 (4900).

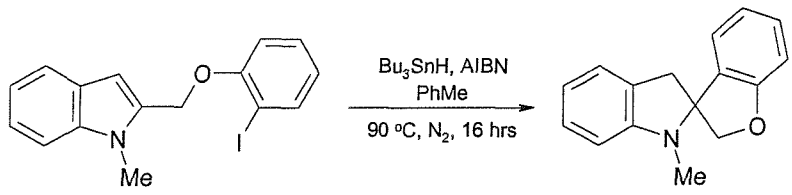
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.32-7.23 (4H, m, ArH), 7.18 (1H, t, J = 7.5 Hz, ArH), 7.10 (1H, d, J = 7.0 Hz, ArH), 6.72 (1H, t, J = 7.3 Hz, ArH), 6.44 (1H, d, J = 7.7 Hz, ArH), 3.25 (1H, d, J = 15.5 Hz, ArCHH), 3.17 (1H, d, J = 15.5 Hz, ArCHH), 3.03-2.95 (2H, m, $ArCH_2$), 2.61 (3H, s, NCH_3), 2.45-2.32 (1H, m, $ArCH_2CHH$), 2.16 (1H, dt, J = 13.1, 5.6 Hz, $ArCH_2CHH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 152.4 (C (Ar)), 145.8 (C (Ar)), 143.4 (C (Ar)), 128.1 (CH (Ar)), 127.9 (C (Ar)), 127.8 (CH (Ar)), 126.9 (CH (Ar)), 125.0 (CH (Ar)), 124.2 (CH (Ar)), 123.4 (CH (Ar)), 117.1 (CH (Ar)), 105.6 (CH (Ar)), 79.7 (C), 43.8 ($ArCH_2$), 34.0 ($ArCH_2$), 29.6 ($ArCH_2CH_2$), 29.3 (NCH_3).

LRMS (CI) *m/z:* 236 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 236.1432, $C_{17}H_{18}N$ requires 236.1434.

2,3-Dihydro-1'-methylspiro(benzofuran-3,2'-indoline) (**670**)



666

mw = 363.19 g mol^{-1}
$C_{16}H_{14}INO$

670

mw = 237.30 g mol^{-1}
$C_{16}H_{15}NO$

To a stirred solution of **666** (170 mg, 0.47 mmol) in toluene (12 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.15 mL, 0.56 mmol) followed by AIBN (15 mg, 0.10 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (2.5-10% ether in petrol) gave **670** as a white crystalline solid (83 mg, 0.35 mmol, 74%): mp 124-125 °C.

FT-IR (neat, cm^{-1}): 3048 w, 2951 w, 2928 w, 2880 w, 2811 w, 1596 s, 1473 s, 1368 m, 1309 m, 1228 m, 1193 m, 1108 w, 1076 w, 1019 w, 971 s, 879 m, 834 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 270 (8100), 238 (9700).

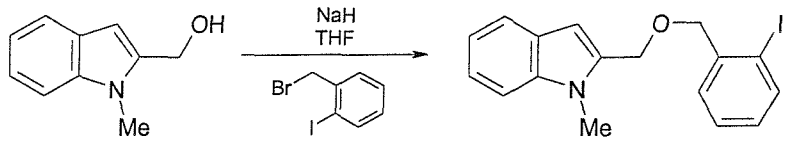
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.27 (1H, td, J = 8.2, 1.4 Hz, ArH), 7.20-7.10 (3H, m, ArH), 6.91 (1H, dd, J = 8.2, 1.0 Hz, ArH), 6.89 (1H, td, J = 7.5, 1.0 Hz, ArH), 6.75 (1H, t, J = 7.5 Hz, ArH), 6.40 (1H, d, J = 7.8 Hz, ArH), 4.76 (1H, d, J = 10.3 Hz, ArOCHH), 4.40 (1H, d, J = 10.3 Hz, ArOCHH), 3.52 (1H, d, J = 15.7 Hz, ArCHH), 3.30 (1H, d, J = 15.7 Hz, ArCHH), 2.54 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 160.2 (CO (Ar)), 151.4 (C (Ar)), 130.3 (CH (Ar)), 128.4 (C (Ar)), 128.2 (CH (Ar)), 127.0 (C (Ar)), 124.1 (CH (Ar)), 123.9 (CH (Ar)), 121.2 (CH (Ar)), 118.0 (CH (Ar)), 110.4 (CH (Ar)), 106.4 (CH (Ar)), 79.6 ($ArCH_2OAr$), 76.3 (C), 42.5 ($ArCH_2$), 29.4 (NCH_3).

LRMS (CI) *m/z:* 238 (MH^+, 100%).

HRMS (EI) *m/z* Found: M^+ 237.1153, $C_{16}H_{15}NO$ requires 237.1154.

2-(2-Iodobenzyloxymethyl)-1-methyl-1*H*-indole (**913**)



907
mw = 161.20 g mol^{-1}
$C_{10}H_{11}NO$

913
mw = 377.22 g mol^{-1}
$C_{17}H_{16}INO$

To a stirred suspension of petrol-washed sodium hydride (72 mg, 2.98 mmol) in THF (25 mL) at 0 °C under nitrogen was added **907** (400 mg, 2.48 mmol). After stirring for 30 minutes at ambient temperature, the solution was again cooled to 0 °C and 2-iodobenzyl bromide **7xx** (773 mg, 2.60 mmol) added as a solution in THF (25 mL) over 5 minutes. On stirring at ambient temperature for 16 hours, the reaction mixture was diluted with water (25 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a yellow solid. Purification by column chromatography (5-20% ether in petrol) gave **913** as a pink solid that yielded small pink needles on recrystallisation (718 mg, 1.90 mmol, 77%): mp 88-89 °C.

FT-IR (neat, cm^{-1}): 3043 w, 2945 w, 2918 w, 2893 w, 2854 w, 2797 w, 1469 s, 1438 m, 1396 m, 1363 s, 1340 s, 1213 m, 1146 m, 1067 s, 1009 s, 941 w, 909 w, 854 w, 808 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 244 (15700).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.86 (1H, dd, J = 7.7, 1.1 Hz, ArH), 7.76 (1H, d, J = 8.1 Hz, ArH), 7.45 (1H, dd, J = 7.7, 1.8 Hz, ArH), 7.41-7.33 (2H, m, ArH), 7.28 (1H, td, J = 8.1, 1.1 Hz, ArH), 7.16 (1H, td, J = 8.1, 1.1 Hz, ArH), 7.03 (1H, td, J = 7.7, 1.8 Hz, ArH), 6.59 (1H, s, ArH), 4.82 (2H, s, $ArCH_2$), 4.57 (2H, s, $ArCH_2$), 3.85 (3H, s, NCH_3).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 140.4 (C (Ar)), 139.5 (CH (Ar)), 138.4 (C (Ar)), 135.6 (C (Ar)), 129.6 (CH (Ar)), 129.4 (CH (Ar)), 128.4 (CH (Ar)), 127.3 (C (Ar)), 122.1 (CH (Ar)), 121.0 (CH (Ar)), 119.7 (CH (Ar)), 109.4 (CH (Ar)), 103.4 (CH (Ar)), 98.5 (CI (Ar)), 75.5 ($ArCH_2$), 64.9 ($ArCH_2$), 30.3 (NCH_3).

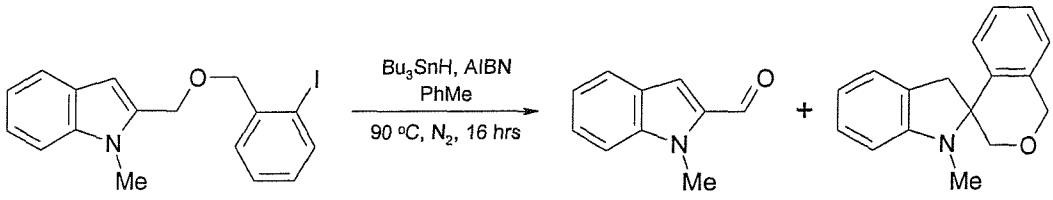
LRMS (CI) *m/z:* 378 (MH^+, 13%), 220 (18%), 144 ($C_{10}H_{10}N^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 400.0170, $C_{17}H_{16}INONa$ requires 400.0169

CHN Found: C, 54.10; H, 4.31; N, 3.65; $C_{17}H_{16}INO$ requires C, 54.13; H, 4.28; N, 3.71.

N-Methylindole-2-carboxaldehyde (**805**) and

1'-Methylspiro(2-benzopyran-4,2'-indoline) (**916**)



913

mw = 377.22 g mol^{-1}

$C_{17}H_{16}NOI$

805

mw = 159.19 g mol^{-1}

$C_{10}H_9NO$

916

mw = 251.33 g mol^{-1}

$C_{17}H_{17}NO$

To a stirred solution of indole **913** (500 mg, 1.33 mmol) in toluene (40 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.43 mL, 1.60 mmol) followed by AIBN (41 mg, 0.27 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to an orange oil. Purification by column chromatography (2.5-10% ether in petrol) gave firstly **916** as a colourless oil which crystallised on standing to white needles (143 mg, 0.57 mmol, 43%): mp 90-93 °C; then **805** as a white solid (34 mg, 0.21 mmol, 16%): mp 80 °C, lit. 83-85 °C.[208] The data for **805** has been stated previously.

*Data for **916**:*

FT-IR (neat, cm^{-1}): 3054 w, 3024 w, 2958 w, 2939 w, 2831 w, 1662 w, 1604 s, 1485 vs, 1448 s, 1370 m, 1321 m, 1268 w, 1206 w, 1183 m, 1106 s, 1079 m, 1015 m, 1003 m, 948 m, 906 s, 847 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 286 (4400), 230 (9400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.55-7.50 (1H, m, ArH), 7.30-7.26 (2H, m, ArH), 7.17 (1H, app. t, J = 7.4 Hz, ArH), 7.11-7.03 (2H, m, ArH), 6.70 (1H, td, J = 7.4, 0.8 Hz, ArH), 6.41 (1H, app. d, J = 7.7 Hz, ArH), 4.85 (2H, d, J = 2.2 Hz, $ArCH_2OCH_2$), 3.95 (1H, dd, J = 11.4, 0.8 Hz, $ArCH_2OCHH$), 3.86 (1H, dd, J = 11.4, 2.2 Hz, $ArCH_2OCHH$), 3.40 (1H, d, J = 16.2 Hz, ArCHH), 3.22 (1H, d, J = 16.2 Hz, ArCHH), 2.66 (3H, s, NCH_3).

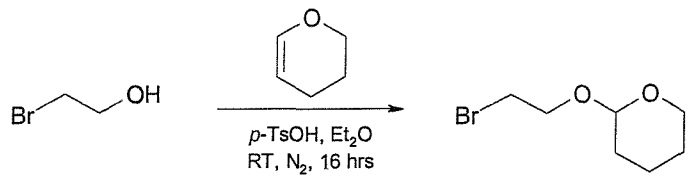
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 152.0 (C (Ar)), 137.9 (C (Ar)), 135.5 (C (Ar)), 128.0 (CH (Ar)), 127.4 (2 x CH (Ar)), 126.6 (C (Ar)), 126.5 (CH (Ar)),

124.4 (CH (Ar)), 124.0 (CH (Ar)), 117.3 (CH (Ar)), 105.3 (CH (Ar)), 70.5 (OCH_2Ar), 68.7 (OCH_2), 66.6 (C), 43.7 ($ArCH_2$), 30.1 (NCH_3).

LRMS (CI) *m/z:* 251 (M^+, 100%), 236 ($[M - CH_3]^+$, 83%).

CHN Found: C, 81.13; H, 6.90; N, 5.51; $C_{17}H_{17}NO$ requires C, 81.24; H, 6.82; N, 5.57.

2-(2-Bromoethoxy)tetrahydro-2*H*-pyran (**918**)



917
mw = 124.97 g mol^{-1}
C_2H_5BrO

918
mw = 209.08 g mol^{-1}
$C_7H_{13}BrO_2$

In accordance with the procedure of Maeyama *et al.*,[239] to a stirred solution of 2-bromoethanol **917** (1.14 mL, 16 mmol) in ether (50 mL) at ambient temperature under nitrogen was added 3,4-dihydro-2*H*-pyran (2.20 mL, 24 mmol) and *para*-toluenesulfonic acid (152 mg, 0.8 mmol). After stirring for 16 hours, the reaction mixture was washed with saturated sodium bicarbonate solution (3 x 25 mL) and brine (25mL). On drying ($MgSO_4$) and removal of the solvent *in vacuo* a pale yellow oil was obtained. Purification by column chromatography (5-10% ether in petrol) gave **918** as a colourless oil (2.27 g, 10.8 mmol, 68%). The observed data is consistent with literature values.[239]

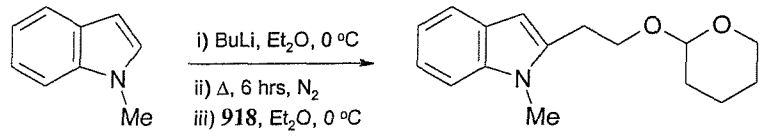
FT-IR (neat, cm^{-1}): 2942 w, 2870 w, 1441 w, 1385 w, 1352 w, 1275 w, 1200 w, 1120 s, 1076 m, 1027 vs, 977 m, 904 m, 869 m, 814 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 4.68 (1H, t, J = 3.1 Hz, OCHO), 4.03 (1H, dt, J = 11.5, 6.2 Hz, $OCHHCH_2Br$), 3.92 (1H, ddd, J = 11.2, 7.9, 3.3 Hz, OCHOCHH), 3.78 (1H, dt, J = 11.5, 6.2 Hz, $OCHHCH_2Br$), 3.58-3.48 (3H, m, OCH_2CH_2Br *and* OCHOCHH), 1.93-1.49 (6H, m, $OCH_2CH_2CH_2CH_2$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 99.3 (OCHO), 67.9 (OCH_2CH_2Br), 62.3 (OCH_2), 31.2 (OCH_2CH_2Br), 30.8 ($OCH_2CH_2CH_2CH_2$), 25.8 ($OCH_2CH_2CH_2CH_2$), 19.7 ($OCH_2CH_2CH_2CH_2$).

LRMS (CI) *m/z:* 210 ($[M\{^{81}Br\}]^+$, 6%), 208 ($[M\{^{79}Br\}]^+$, 6%), 85 ($C_5H_9O^+$, 100%).

1-Methyl-2-[2-(tetrahydro-2*H*-pyran-2-yloxy)ethyl]-1*H*-indole (**920**)



919
mw = 131.18 g mol^{-1}
C_9H_9N

920
mw = 259.35 g mol^{-1}
$C_{16}H_{21}NO_2$

In accordance with the procedure of Jones and Fresneda,[240] to a stirred solution of *N*-methyl indole **919** (0.58 mL, 4.55 mmol) in ether (30 mL) at 0 °C under nitrogen was added *n*-butyllithium (2.16 mL, 5 mmol, 2.32 M solution in hexanes) over 5 minutes. The reaction mixture was heated at reflux for 6 hours then cooled to 0 °C. A solution of **918** (1.0 g, 4.78 mmol) in ether (30 mL) was added over 5 minutes, then after 16 hours the reaction mixture was diluted with water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a dark brown oil. Purification by column chromatography (2.5-30% ether in petrol) gave firstly recovered *N*-methyl indole **919** (304 mg, 2.32 mmol, 51%); then recovered **918** as a colourless oil (334 mg, 1.59 mmol, 33%); and finally **920** as a colourless oil (235 mg, 0.91 mmol, 20%).

FT-IR (neat, cm^{-1}): 2938 w, 2868 w, 1544 w, 1467 m, 1439 w, 1400 w, 1350 w, 1317 w, 1133 m, 1119 m, 1076 m, 1030 vs, 972 m, 904 w, 869 w, 813 w, 773 w, 746 s.

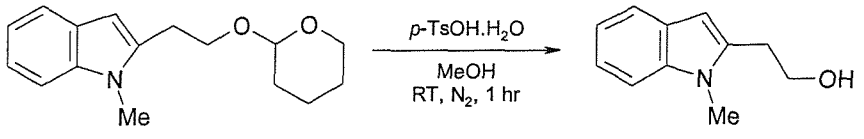
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.57 (1H, app. d, J = 8.1 Hz, ArH), 7.30 (1H, dd, J = 8.1, 1.1 Hz, ArH), 7.20 (1H, ddd, J = 8.1, 7.0, 1.1 Hz, ArH), 7.10 (1H, ddd, J = 8.1, 7.0, 1.1 Hz, ArH), 6.34 (1H, s, ArH), 4.68 (1H, dd, J = 4.1, 2.6 Hz, OCHO), 4.12 (1H, dt, J = 9.6, 7.4 Hz, OCHHCH$_2$Ar), 3.92-3.83 (1H, m, OCHOCHH), 3.77 (1H, dt, J = 9.6, 7.4 Hz, OCHHCH$_2$Ar), 3.73 (3H, s, NCH$_3$), 3.58-3.49 (1H, m, OCHOCHH), 3.11 (2H, t, J = 7.4 Hz, OCH$_2$CH$_2$Ar), 1.93-1.51 (6H, m, OCH$_2$CH$_2$CH$_2$CH$_2$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 138.2 (C (Ar)), 137.4 (C (Ar)), 128.0 (C (Ar)), 120.9 (CH (Ar)), 120.0 (CH (Ar)), 119.4 (CH (Ar)), 109.0 (CH (Ar)), 99.5 (CH (Ar)), 99.2 (OCHO), 66.9 (OCH$_2$CH$_2$Ar), 62.6 (OCH$_2$), 30.8 (OCH$_2$CH$_2$CH$_2$CH$_2$), 29.8 (NCH$_3$), 27.7 (OCH$_2$CH$_2$Ar), 25.6 (OCH$_2$CH$_2$CH$_2$CH$_2$), 19.8 (OCH$_2$CH$_2$CH$_2$CH$_2$).

LRMS (CI) *m/z:* 260 (MH^+, 61%), 175 ([MH - $C_5H_9O]^+$, 77%), 159 ([MH - $C_5H_9O_2]^+$, 74%), 144 ($C_{10}H_{10}N^+$, 100%), 85 ($C_5H_9O^+$, 87%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$, 282.1465, $C_{16}H_{21}NO_2Na$ requires 282.1464.

2-(1-Methyl-1*H*-indol-2-yl)ethanol (**921**)



920

mw = 259.35 g mol^{-1}
$C_{16}H_{21}NO_2$

921

mw = 175.23 g mol^{-1}
$C_{11}H_{13}NO$

To a stirred solution of **920** (195 mg, 0.75 mmol) in methanol (20 mL) at ambient temperature under nitrogen was added *para*-toluenesulfonic acid monohydrate (8 mg, 0.04 mmol). After 1 hour, the reaction mixture was concentrated *in vacuo*. Saturated sodium bicarbonate solution (25 mL) was added and the resultant suspension extracted with ether (3 x 25 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale brown oil. Purification by column chromatography (50-60% ether in petrol) gave **921** as a colourless oil that crystallised on standing to large colourless prisms (90 mg, 0.51 mmol, 68%): mp 58-61 °C, lit. 60-61 °C.[241] The observed data is consistent with literature values.

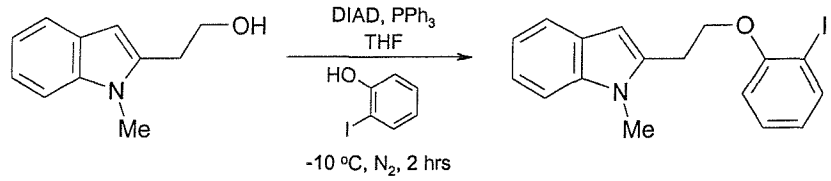
FT-IR (neat, cm^{-1}): 3302 br. w, 3055 w, 2935 w, 2879 w, 1468 s, 1433 m, 1407 w, 1362 w, 1344 m, 1315 m, 1281 w, 1234 w, 1194 m, 1138 m, 1063 s, 1012 s, 859 w, 768 m, 745 vs, 721 vs, 671 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.59 (1H, app. d, J = 7.7 Hz, ArH), 7.32 (1H, app. d, J = 8.1 Hz, ArH), 7.22 (1H, ddd, J = 8.1, 6.9, 1.2 Hz, ArH), 7.13 (1H, ddd, J = 7.7, 6.9, 1.2 Hz, ArH), 6.37 (1H, s, ArH), 3.95 (2H, t, J = 6.4 Hz, $ArCH_2CH_2OH$), 3.71 (3H, s, NCH_3), 3.05 (2H, t, J = 6.4 Hz, $ArCH_2CH_2OH$), 1.80 (1H, br. s, $ArCH_2CH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 137.7 (C (Ar)), 137.3 (C (Ar)), 127.9 (C (Ar)), 121.2 (CH (Ar)), 120.1 (CH (Ar)), 119.7 (CH (Ar)), 109.2 (CH (Ar)), 100.1 (CH (Ar)), 61.5 ($ArCH_2CH_2OH$), 30.3 ($ArCH_2CH_2OH$), 29.8 (NCH_3).

LRMS (CI) *m/z:* 176 (MH^+, 100%), 158 ([MH – $H_2O]^+$, 34%), 144 (MH – H_2O – $CH_2]^+$, 74%).

2-[2-(2-iodophenoxy)ethyl]-1-methyl-1*H*-indole (**922**)



921

mw = 175.23 g mol^{-1}
$C_{11}H_{13}NO$

922

mw = 377.22 g mol^{-1}
$C_{17}H_{16}INO$

To a stirred solution of alcohol **921** (118 mg, 0.67 mmol), 2-iodophenol (177 mg, 0.80 mmol) and triphenylphosphine (210 mg, 0.80 mmol) in THF (15 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.15 mL, 0.74 mmol) over 5 minutes. After 2 hours, the reaction mixture was concentrated *in vacuo* to an orange oil and purified by column chromatography (5-10% ether in petrol) to give **922** as a colourless oil (196 mg, 0.52 mmol, 78%).

FT-IR (neat, cm^{-1}): 3054 w, 2923 w, 1580 w, 1543 w, 1464 s, 1438 m, 1316 w, 1276 m, 1243 s, 1121 w, 1049 m, 1016 s, 907 w, 775 w, 750 vs.

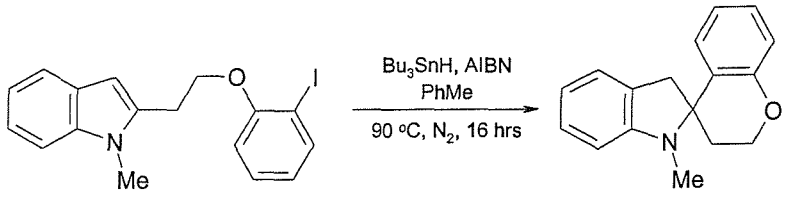
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.81 (1H, dd, J = 7.9, 1.7 Hz, ArH), 7.59 (1H, dd, J = 7.6, 0.7 Hz, ArH), 7.33 (1H, dd, J = 7.4, 1.4 Hz, ArH), 7.32 (1H, td, J = 7.6, 1.7 Hz, ArH), 7.23 (1H, td, J = 8.3, 1.4 Hz, ArH), 7.12 (1H, td, J = 7.9, 1.0 Hz, ArH), 6.85 (1H, dd, J = 8.3, 1.2 Hz, ArH), 6.75 (1H, td, J = 7.4, 1.2 Hz, ArH), 6.44 (1H, d, J = 0.7 Hz, ArH), 4.35 (2H, t, J = 7.2 Hz, $ArCH_2CH_2O$), 3.80 (3H, s, NCH_3), 3.37 (2H, t, J = 7.2 Hz, $ArCH_2CH_2O$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 157.4 (CO (Ar)), 139.8 (CH (Ar)), 137.5 (C (Ar)), 137.0 (C (Ar)), 129.7 (CH (Ar)), 128.0 (C (Ar)), 123.1 (CH (Ar)), 121.2 (CH (Ar)), 120.2 (CH (Ar)), 119.7 (CH (Ar)), 112.5 (CH (Ar)), 109.2 (CH (Ar)), 100.1 (CH (Ar)), 86.8 (CI (Ar)), 68.7 ($ArCH_2CH_2O$), 30.1 (NCH_3), 27.1 ($ArCH_2CH_2O$).

LRMS (CI) *m/z:* 378 (MH^+, 76%), 250 ($[M - I]^+$, 75%), 158 ($[MH - C_6H_5IO]^+$, 43%), 144 ($C_{10}H_{10}N^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$, 400.0169, $C_{17}H_{16}INONa$ requires 400.0169.

1'-Methylspiro(1-benzopyran-4,2'-indoline) (**923**)



922
mw = 377.22 g mol^{-1}
$C_{17}H_{16}INO$

923
mw = 251.33 g mol^{-1}
$C_{17}H_{17}NO$

To a stirred solution of **922** (150 mg, 0.40 mmol) in toluene (20 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.13 mL, 0.48 mmol) followed by AIBN (12 mg, 0.08 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (1-2.5% ether in petrol) gave **923** as a pale yellow oil (42 mg, 0.17 mmol, 42%).

FT-IR (neat, cm^{-1}): 3028 w, 2945 w, 2874 w, 1606 m, 1581 w, 1484 s, 1450 m, 1371 m, 1305 m, 1249 m, 1219 m, 1120 m, 1053 m, 1019 w, 967 w, 941 w, 916 w, 888 w, 849 w, 810 w, 745 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.49 (1H, dd, J = 7.9, 1.7 Hz, ArH), 7.21 (1H, td, J = 7.1, 1.7 Hz, ArH), 7.19 (1H, t, J = 7.6 Hz, ArH), 7.08 (1H, d, J = 7.1 Hz, ArH), 6.93 (1H, td, J = 8.1, 1.0 Hz, ArH), 6.88 (1H, dd, J = 8.1, 1.0 Hz, ArH), 6.71 (1H, t, J = 7.6 Hz, ArH), 6.44 (1H, d, J = 7.6 Hz, ArH), 4.42 (1H, ddd, J = 11.5, 4.3, 2.6 Hz, OCHH), 4.29 (1H, td, J = 11.5, 1.9 Hz, OCHH), 3.34 (1H, d, J = 15.7 Hz, ArCHH), 3.17 (1H, d, J = 15.7 Hz, ArCHH), 2.60 (3H, s, NCH_3), 2.32 (1H, td, J = 13.6, 4.3 Hz, OCH_2CHH), 1.86 (1H, dt, J = 13.6, 1.9 Hz, OCH_2CHH).

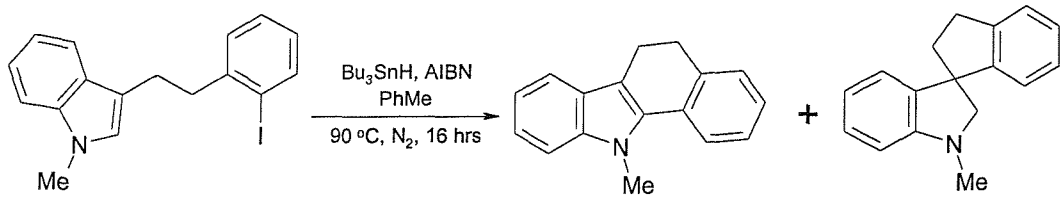
^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.7 (CO (Ar)), 151.8 (C (Ar)), 128.8 (CH (Ar)), 128.1 (CH (Ar)), 127.6 (CH (Ar)), 126.6 (C (Ar)), 126.0 (C (Ar)), 124.5 (CH (Ar)), 121.0 (CH (Ar)), 117.2 (CH (Ar)), 117.0 (CH (Ar)), 105.4 (CH (Ar)), 66.7 (C), 64.1 (OCH_2), 46.9 ($ArCH_2$), 28.9 (NCH_3), 28.2 (OCH_2CH_2).

LRMS (CI) *m/z:* 252 (MH^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$, 252.1385, $C_{17}H_{18}NO$ requires 252.1383.

11-Methyl-5,6-dihydro-11*H*-benzo[*a*]carbazole (**640**) and

1'-Methylspiro(indane-1,3'-indoline) (**657**)



653

mw = 361.22 g mol^{-1}
$C_{17}H_{16}IN$

640

mw = 233.31 g mol^{-1}
$C_{17}H_{15}N$

657

mw = 235.33 g mol^{-1}
$C_{17}H_{17}N$

To a stirred solution of indole **653** (297 mg, 0.82 mmol) in toluene (15 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.27 mL, 0.98 mmol) followed by AIBN (25 mg, 0.16 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (15 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (1-2% ether in petrol) gave firstly **640** as a white solid (69 mg, 0.30 mmol, 36%): mp 130-132 °C, lit. 133 °C (ethanol);[242] then **657** as a white solid (122 mg, 0.52 mmol, 63%): mp 122-125 °C. The observed data for **640** is consistent with literature values.

*Data for **640**:*

FT-IR (neat, cm^{-1}): 3049 w, 2946 w, 2918 w, 2890 w, 2835 w, 1600 w, 1537 w, 1491 m, 1464 s, 1423 m, 1367 s, 1342 s, 1307 m, 1279 m, 1254 m, 1226 m, 1153 m, 1119 m, 1009 m, 916 w, 831 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 314 (19600), 238 (26500).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$): 7.55 (1H, d, J = 7.5 Hz, Ar<u>H</u>), 7.49 (1H, d, J = 7.9 Hz, Ar<u>H</u>), 7.26 (1H, d, J = 7.9 Hz, Ar<u>H</u>), 7.24 (1H, obsc. d, J = 7.5 Hz, Ar<u>H</u>), 7.21 (1H, t, J = 7.5 Hz, Ar<u>H</u>), 7.15 (1H, t, J = 7.9 Hz, Ar<u>H</u>), 7.10 (1H, t, J = 7.5 Hz, Ar<u>H</u>), 7.05 (1H, t, J = 7.9 Hz, Ar<u>H</u>), 3.94 (3H, s, NC<u>H</u>$_3$), 2.93-2.86 (2H, m, ArC<u>H</u>$_2$CH$_2$Ar), 2.86-2.79 (2H, m, ArCH$_2$C<u>H</u>$_2$Ar).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 139.7 (<u>C</u> (Ar)), 138.6 (<u>C</u> (Ar)), 135.5 (<u>C</u> (Ar)), 130.1 (<u>C</u> (Ar)), 129.1 (<u>C</u>H (Ar)), 127.0 (<u>C</u>H (Ar)), 126.7 (<u>C</u>H (Ar)), 126.4 (<u>C</u> (Ar)), 122.8 (<u>C</u>H (Ar)), 122.5 (<u>C</u>H (Ar)), 119.9 (<u>C</u>H (Ar)), 119.2

(CH (Ar)), 114.3 (C (Ar)), 109.8 (CH (Ar)), 33.0 (NCH_3), 31.2 ($ArCH_2CH_2Ar$), 20.6 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 233 (M^+, 100%).

CHN Found: C, 87.45; H, 6.48; N, 5.93; $C_{17}H_{15}N$ requires C, 87.52; H, 6.48; N, 6.00.

*Data for **657**:*

FT-IR (neat, cm^{-1}): 2936 m, 2851 w, 2806 w, 1602 m, 1486 s, 1453 m, 1355 m, 1268 s, 1242 m, 1118 m, 1084 m, 1022 m, 946 m, 837 s.

UV-Vis λ_{max} (ε_{max}), nm ($dm^3\,mol^{-1}\,cm^{-1}$), CH_2Cl_2: 290 (4100), 244 (11800).

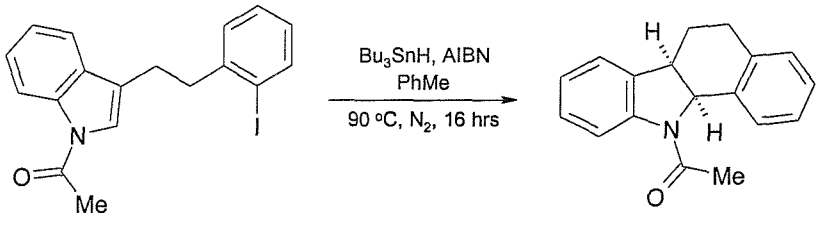
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$): 7.18-6.98 (6H, m, ArH), 6.63 (1H, t, J = 7.3 Hz, ArH), 6.33 (1H, d, J = 7.3 Hz, ArH), 4.22 (1H, d, J = 8.8 Hz, NCHH), 3.50 (1H, app. br. s, NCHH), 2.68-2.45 (2H, obsc. m, $ArCH_2CH_2$), 2.55 (3H, s, NCH_3), 1.95-1.86 (1H, m, $ArCH_2CHH$), 1.80-1.69 (1H, m, $ArCH_2CHH$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 153.6 (C (Ar)), 141.7 (C (Ar)), 135.1 (C (Ar)), 134.1 (C (Ar)), 130.5 (CH (Ar)), 128.8 (CH (Ar)), 128.3 (CH (Ar)), 128.1 (CH (Ar)), 126.1 (CH (Ar)), 124.8 (CH (Ar)), 118.5 (CH (Ar)), 107.3 (CH (Ar)), 68.7 (NCH_2), 40.6 (NCH_3), 31.3 ($ArCH_2CH_2$), 30.2 (C), 28.2 ($ArCH_2CH_2$).

LRMS (CI) *m/z:* 235 (M^+, 100%).

HRMS (ES^+) *m/z* Found: $[MH]^+$ 236.1434, $C_{17}H_{18}N$ requires 236.1434.

N-Acetyl-5,6,6aS*,11aS*-tetrahydrobenzo[*a*]carbazole (**928**)



903

mw = 389.23 g mol^{-1}
$C_{18}H_{16}INO$

928

mw = 263.34 g mol^{-1}
$C_{18}H_{17}NO$

To a stirred solution of **903** (300 mg, 0.77 mmol) in toluene (20 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.25 mL, 0.92 mmol) followed by AIBN (23 mg, 0.15 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (15 mL) was added and the biphasic

mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (10-40% ether in petrol) gave **928** as a white solid that yielded white prisms on recrystallisation (171 mg, 0.65 mmol, 84%): mp 110-112 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 2957 w, 2921 w, 1646 s, 1597 w, 1475 m, 1455 m, 1394 s, 1328 w, 1313 w, 1269 m, 1234 w, 1197 w, 1151 w, 1121 w, 1081 w, 1015 w, 929 w, 829 w, 755 vs, 715 w.

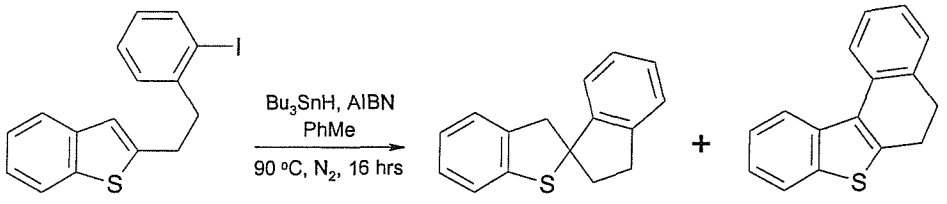
^{1}H NMR δ_H ppm (400 MHz, D_6-DMSO at 100 °C): 7.56 (1H, d, J = 8.0 Hz, ArH), 7.41 (1H, d, J = 7.3 Hz, ArH), 7.24 (1H, app. d, J = 7.5 Hz, ArH), 7.19-7.10 (3H, m, ArH), 7.07 (1H, dd, J = 6.8, 1.0 Hz, ArH), 7.04 (1H, td, J = 7.5, 1.0 Hz, ArH), 5.71 (1H, d, J = 8.8 Hz, NCH), 3.99 (1H, app. dd, J = 14.7, 6.5 Hz, ArCH), 2.67-2.62 (2H, m, $ArCH_2$), 2.37 (3H, s, $NCOCH_3$), 2.42-2.32 (1H, m, $ArCH_2CHH$), 1.98-1.89 (1H, m, $ArCH_2CHH$).

^{13}C NMR δ_C ppm (100 MHz, D_6-DMSO at 100 °C): 168.1 ($NCOCH_3$), 141.8 (C (Ar)), 138.1 (C (Ar)), 135.7 (C (Ar)), 135.1 (C (Ar)), 127.2 (CH (Ar)), 126.8 (CH (Ar)), 126.5 (CH (Ar)), 126.4 (CH (Ar)), 125.8 (CH (Ar)), 123.4 (CH (Ar)), 123.2 (CH (Ar)), 116.7 (CH (Ar)), 60.7 (NCH), 39.3 (ArCH), 25.4 ($NCOCH_3$), 23.3 ($ArCH_2CH_2$), 22.8 ($ArCH_2CH_2$).

LRMS (CI) *m/z:* 264 (MH^+, 100%), 220 ($[M - COCH_3]^+$, 14%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 286.1206, $C_{18}H_{17}NONa$ requires 286.1202.

2',3'-Dihydrospiro(indane-1,2'-benzo[*b*]thiophene) (**637**) and
5,6-Dihydrobenzo[*b*]naphtho[1,2-*a*]thiophene (**648**)



633
mw = 364.24 g mol^{-1}
$C_{16}H_{13}IS$

637
mw = 238.35 g mol^{-1}
$C_{16}H_{14}S$

648
mw = 236.34 g mol^{-1}
$C_{16}H_{12}S$

To a stirred solution of **633** (400 mg, 1.10 mmol) in toluene (30 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.36 mL, 1.32 mmol) followed by AIBN (34 mg, 0.22 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic

mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (1-2.5% ether in petrol) gave a yellow oil (206 mg, 0.86 mmol, 79% by **637**). This was shown to be a complex mixture of products by NMR, with **637** and **648** as the major components in an approximate 3:2 ratio.

*Observable data for **637**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.90-7.06 (8H, m, ArH), 3.79 (1H, d, J = 15.5 Hz, ArCHH), 3.50 (1H, d, J = 15.5 Hz, ArCHH). All remaining signals were obscured.

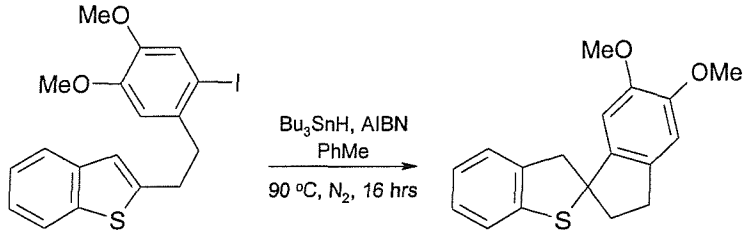
LRMS (GC-CI) *m/z:* 238 (M^+, 100%).

*Observable data for **648**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.90-7.06 (8H, m, ArH), 3.32 (2H, t, J = 8.6 Hz, $ArCH_2CH_2Ar$), 3.16 (2H, t, J = 8.6 Hz, $ArCH_2CH_2Ar$).

LRMS (GC-CI) *m/z:* 236 (M^+, 100%).

2',3'-Dihydro-5,6-dimethoxyspiro(indane-1,2'-benzo[*b*]thiophene) (**932**)



901
mw = 424.30 g mol^{-1}
$C_{18}H_{17}IO_2S$

932
mw = 298.41 g mol^{-1}
$C_{18}H_{18}O_2S$

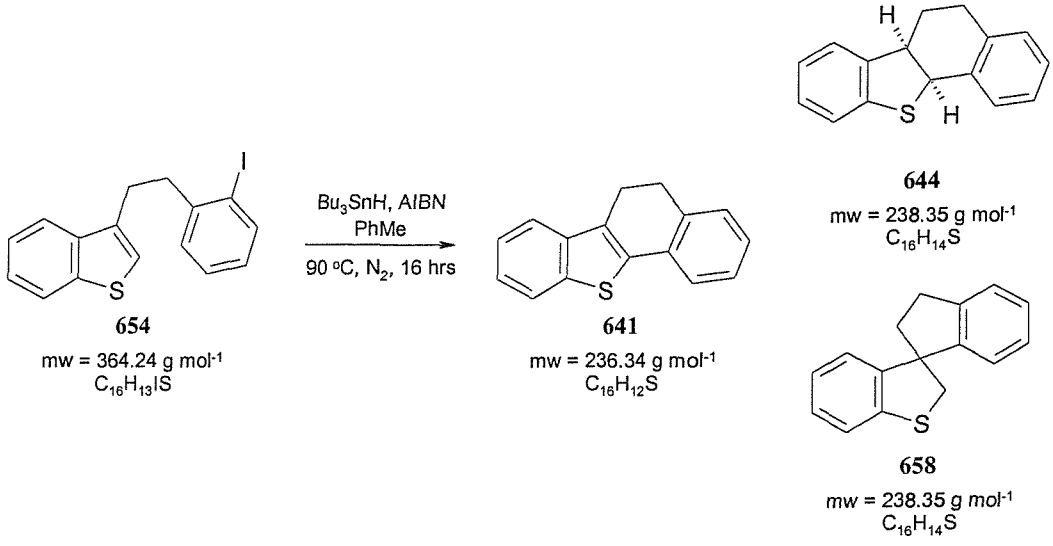
To a stirred solution of **901** (240 mg, 0.57 mmol) in toluene (30 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.18 mL, 0.68 mmol) followed by AIBN (18 mg, 0.11 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (5-30% ether in

petrol) gave a yellow oil (117 mg, 0.39 mmol, 69% by **932**). This was shown to be a complex mixture of products by NMR, with **932** as the major component.

*Observable data for **932**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.33-7.25 (1H, m, ArH), 7.20 (1H, t, J = 8.1 Hz, ArH), 7.17 (1H, t, J = 8.1 Hz, ArH), 7.12-7.04 (1H, m, ArH), 6.96 (1H, s, ArH), 6.78 (1H, s, ArH), 3.89 (3H, s, $ArOCH_3$), 3.83 (3H, s, $ArOCH_3$), 3.70 (1H, d, J = 15.8 Hz, ArCHH), 3.36 (1H, d, J = 15.8 Hz, ArCHH), 3.02 (1H, dt, J = 15.8, 7.4 Hz, ArCHH), 2.89 (1H, ddd, J = 15.8, 7.7, 4.4 Hz, ArCHH), 2.64 (1H, ddd, J = 13.2, 7.7, 4.4 Hz, $ArCH_2CHH$), 2.33 (1H, dt, J = 13.2, 7.4 Hz, $ArCH_2CHH$).

5,6-Dihydrobenzo[*b*]naphtho[2,1-*d*]thiophene (**641**),
5,6,6aS^*,11aS^*-Tetrahydrobenzo[*b*]naphtho[2,1-*d*]thiophene (**644**) and
2',3'-Dihydrospiro(indane-1,3'-benzo[*b*]thiophene) (**658**)



To a stirred solution of **654** (1.0 g, 2.75 mmol) in toluene (40 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.89 mL, 3.30 mmol) followed by AIBN (85 mg, 0.35 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (1-2% ether in petrol) gave a yellow oil (527 mg, 2.21 mmol, 80% by **658**). This was shown to be a complex

mixture of products by NMR, with **641, 644** and **658** as the major components in an approximate 2:1:2 ratio.

*Observable data for **641**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.99-7.05 (8H, m, ArH), 3.19-3.12 (2H, m, $ArCH_2CH_2Ar$), 3.12-3.08 (2H, m, $ArCH_2CH_2Ar$).

LRMS (GC-CI) *m/z:* 236 (M^+, 100%).

*Observable data for **644**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.99-7.05 (8H, m, ArH), 5.38 (1H, d, J = 6.9 Hz, SCH). All remaining signals were obscured.

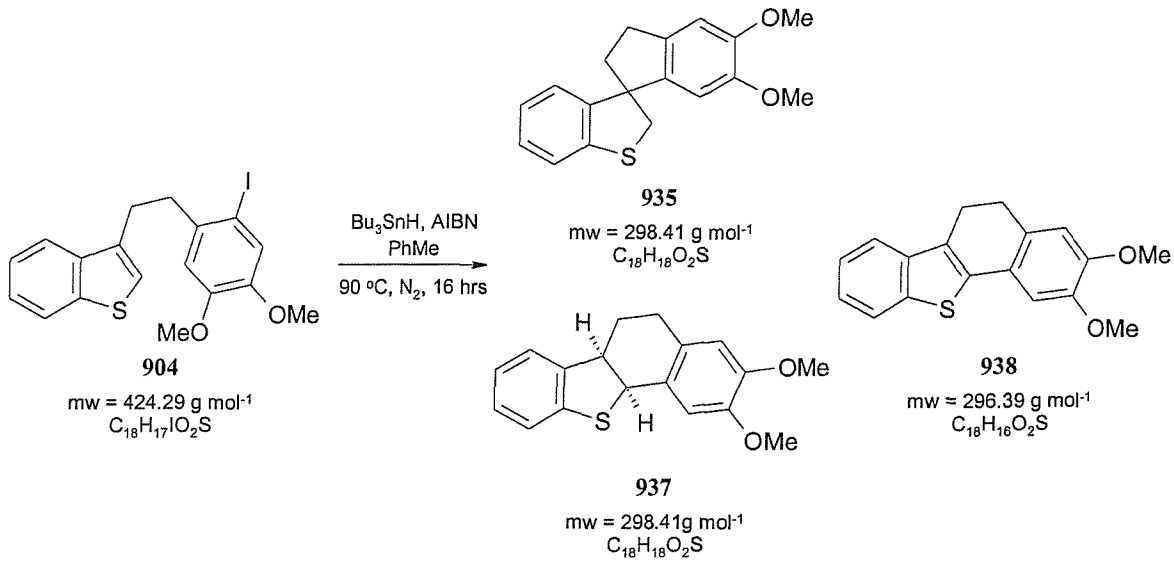
LRMS (GC-CI) *m/z:* 238 (M^+, 89%), 223 (100%).

*Observable data for **658**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.99-7.05 (8H, m, ArH), 3.40 (1H, d, J = 11.0 Hz, ArCHH). All remaining signals were obscured.

LRMS (GC-CI) *m/z:* 238 (M^+, 100%).

2',3'-Dihydro-5,6-dimethoxyspiro(indane-1,3'-benzo[*b*]thiophene) (**935**), 2,3-Dimethoxy-5,6,6aS^*,11aS^*-tetrahydrobenzo[*b*]naphtho[2,1-*d*]thiophene (**937**) and 5,6-Dihydro-2,3-dimethoxybenzo[*b*]naphtho[2,1-*d*]thiophene (**938**)



To a stirred solution of **904** (300 mg, 0.71 mmol) in toluene (17 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.23 mL, 0.85 mmol) followed by AIBN (22 mg, 0.14 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow semi-solid. Purification by column chromatography (5-10% ether in petrol) gave a yellow oil (182 mg, 0.61 mmol, 86% by **935**). This was shown to be a complex mixture of products by NMR, with **935, 937** and **938** as the major components in an approximate 2:1:2 ratio. Further chromatography elucidated **935** in sufficient purity that the ^{1}H-NMR could be fully assigned.

*Observable data for **935**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.28 (1H, obsc. d, J = 7.4 Hz, ArH), 7.18 (1H, td, J = 7.7, 1.5 Hz, ArH), 7.04 (1H, td, J = 7.4, 1.1 Hz, ArH), 6.84 (1H, s, ArH), 6.83 (1H, d, J = 7.7 Hz, ArH), 6.68 (1H, s, ArH), 3.91 (3H, s, $ArOCH_3$), 3.80 (3H, s, $ArOCH_3$), 3.49 (1H, d, J = 11.0 Hz, ArCHH), 3.31 (1H, d, J = 11.0 Hz, ArCHH), 3.08-2.93 (2H, m, $ArCH_2$), 2.68 (1H, ddd, J = 12.9, 7.4, 3.7 Hz, $ArCH_2CHH$), 2.07 (1H, dt, J = 12.9, 7.7 Hz, $ArCH_2CHH$).

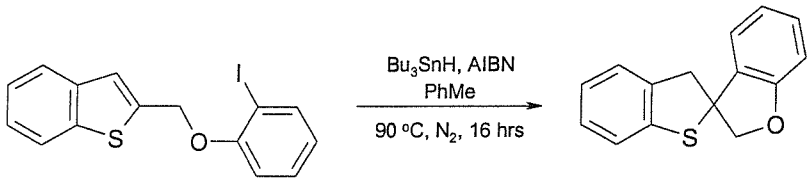
*Observable data for **937**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 5.28 (1H, d, J = 7.0 Hz, SC<u>H</u>). All remaining signals were obscured.

*Observable data for **938**:*

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 3.17 (2H, t, J = 8.5 Hz, ArC<u>H</u>$_2$CH$_2$Ar), 3.17-3.08 (2H, m, ArCH$_2$C<u>H</u>$_2$Ar). All remaining signals were obscured.

<u>2,2',3,3'-Tetrahydrospiro(benzofuran-3,2'-benzo[*b*]thiophene) (**671**)</u>



667
mw = 366.22 g mol^{-1}
$C_{15}H_{11}IOS$

671
mw = 240.33 g mol^{-1}
$C_{15}H_{12}OS$

To a stirred solution of **667** (400 mg, 1.09 mmol) in toluene (30 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.35 mL, 1.31 mmol) followed by AIBN (34 mg, 0.22 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (2.5-5% ether in petrol) gave **671** as a colourless oil that crystallised on standing to a waxy white solid (196 mg, 0.82 mmol, 75%): mp 60-64 °C.

FT-IR (neat, cm^{-1}): 3056 w, 2935 w, 2885 w, 2831 w, 1599 m, 1476 s, 1461 s, 1319 m, 1235 m, 1173 m, 1112 m, 1061 m, 1018 m, 969 s, 859 w, 825 w, 799 w.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 274 (7400).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.40 (1H, dd, J = 7.6, 1.4 Hz, Ar<u>H</u>), 7.29-7.09 (5H, m, Ar<u>H</u>), 6.96 (1H, td, J = 7.4, 1.0 Hz, Ar<u>H</u>), 6.90 (1H, app. d, J = 8.1 Hz, Ar<u>H</u>), 4.84 (1H, d, J = 9.8 Hz, ArOC<u>H</u>H), 4.70 (1H, d,

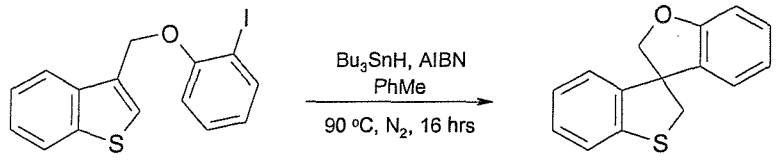
J = 9.8 Hz, ArOCHH), 3.78 (1H, d, J = 15.7 Hz, ArCHH), 3.51 (1H, d, J = 15.7 Hz, ArCHH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 159.5 (CO (Ar)), 140.6 (C (Ar)), 137.4 (2 x C (Ar)), 130.0 (CH (Ar)), 128.2 (CH (Ar)), 125.0 (CH (Ar)), 124.7 (CH (Ar)), 123.7 (CH (Ar)), 122.1 (CH (Ar)), 121.5 (CH (Ar)), 110.5 (CH (Ar)), 85.6 ($ArOCH_2$), 65.4 (C), 49.2 ($ArCH_2$).

LRMS (EI) *m/z:* 240 (M^+, 100%), 147 ($C_9H_7S^+$, 61%).

HRMS (EI) *m/z* Found: M^+ 240.0606, $C_{15}H_{12}OS$ requires 240.0609.

2,2',3,3'-Tetrahydrospiro(benzofuran-3,3'-benzo[*b*]thiophene) (**682**)



678
mw = 366.22 g mol^{-1}
$C_{15}H_{11}IOS$

682
mw = 240.33 g mol^{-1}
$C_{15}H_{12}OS$

To a stirred solution of **678** (1.0 g, 2.73 mmol) in toluene (75 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.88 mL, 3.28 mmol) followed by AIBN (84 mg, 0.55 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then cooled to ambient temperature. 10% Potassium fluoride solution (50 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (100 mL), the organic phase was isolated, washed with water (3 x 100 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (1-5% ether in petrol) gave **682** as a pale yellow oil (593 mg, 2.47 mmol, 90%).

FT-IR (neat, cm^{-1}): 3058 w, 2970 w, 2922 w, 2880 w, 1596 m, 1477 s, 1459 s, 1365 w, 1321 w, 1280 w, 1208 s, 1151 w, 1056 w, 1014 w, 985 m, 948 m, 861 w, 825 m.

UV-Vis λ_{max} (ε_{max}), nm (dm^3 mol^{-1} cm^{-1}), CH_2Cl_2: 272 (17200), 242 (10300).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.34-7.19 (4H, m, ArH), 7.10 (1H, td, J = 7.4, 1.2 Hz, ArH), 7.02-6.94 (3H, m, ArH), 4.90 (1H, d, J = 9.1 Hz, ArOCHH), 4.32 (1H, dd, J = 9.1, 1.0 Hz, ArOCHH), 3.65 (1H, dd, J = 11.2, 1.0 Hz, ArSCHH), 3.50 (1H, d, J = 11.2 Hz, ArSCHH).

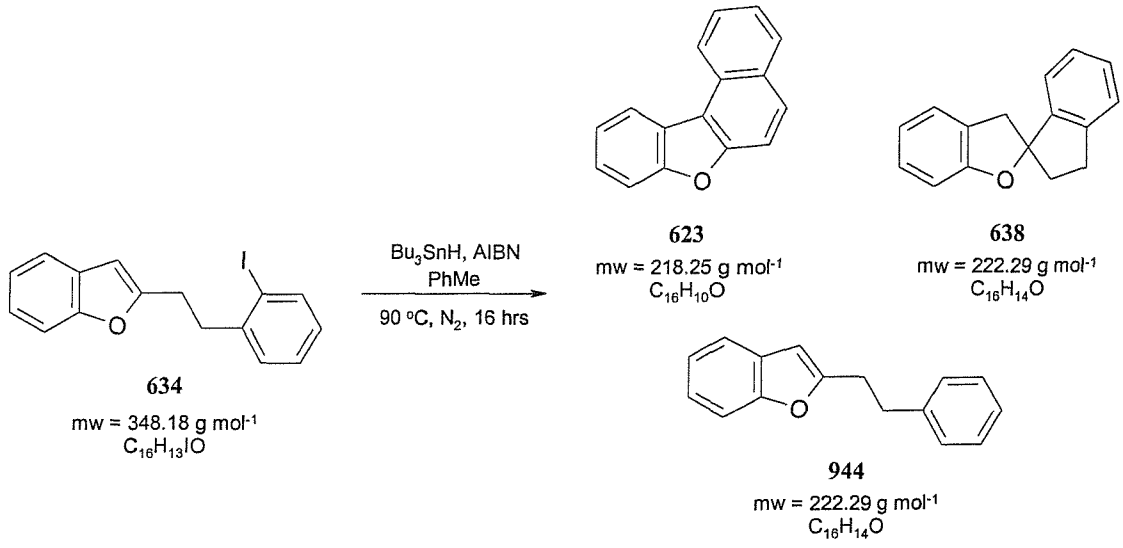
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 160.9 (CO (Ar)), 143.5 (C (Ar)), 142.0 (C (Ar)), 136.9 (C (Ar)), 129.9 (CH (Ar)), 129.0 (CH (Ar)), 125.6 (CH (Ar)), 125.0

(CH (Ar)), 124.4 (CH (Ar)), 123.1 (CH (Ar)), 122.1 (CH (Ar)), 110.5 (CH (Ar)), 82.7 ($ArOCH_2$), 62.0 (C), 45.8 ($ArSCH_2$).

LRMS (EI) *m/z:* 240 (M^+, 100%).

HRMS (EI) *m/z* Found: M^+ 240.0608, $C_{15}H_{12}OS$ requires 240.0609.

Benzo[*b*]naphtho[1,2-*a*]furan (**623**), 2',3'-Dihydrospiro(indane-1,2'-benzo[*b*]furan) (**638**) and 2-(2-Phenethyl)-1-benzo[*b*]furan (**944**)



634
mw = 348.18 g mol^{-1}
$C_{16}H_{13}IO$

623
mw = 218.25 g mol^{-1}
$C_{16}H_{10}O$

638
mw = 222.29 g mol^{-1}
$C_{16}H_{14}O$

944
mw = 222.29 g mol^{-1}
$C_{16}H_{14}O$

To a stirred solution of **634** (418 mg, 1.20 mmol) in toluene (20 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.39 mL, 1.44 mmol) followed by AIBN (37 mg, 0.24 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (1-20% ether in petrol) gave firstly **623** as a yellow oil that crystallised on standing to a pale yellow solid (23 mg, 0.11 mmol, 9%, data as stated previously); then **944** as a pale yellow oil in approximately 90% purity (20 mg, 0.09 mmol, 8%); and finally **638** as a pale yellow oil (153 mg, 0.69 mmol, 57%). The observed data for **944** is consistent with literature values.[243]

*Data for **638**:*

FT-IR (neat, cm^{-1}): 3028 w, 2924 w, 2850 w, 1598 w, 1478 s, 1459 m, 1324 w, 1240 s, 1153 w, 1100 w, 1015 w, 994 w, 938 w, 918 w, 869 m, 750 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.38-7.23 (5H, m, ArH), 7.19 (1H, t, J = 8.1 Hz, ArH), 6.93 (1H, t, J = 7.4 Hz, ArH), 6.80 (1H, d, J = 8.1 Hz, ArH), 3.64 (1H, d, J = 15.8 ArCHH), 3.44 (1H, d, J = 15.8 Hz, ArCHH), 3.22 (1H, dt, J = 15.8, 8.1 Hz, ArCHHCH_2), 2.98 (1H, ddd, J = 15.8, 8.1, 4.1 Hz, ArCHHCH_2), 2.66 (1H, ddd, J = 13.6, 8.1, 4.1 Hz, ArCH_2CHH), 2.35 (1H, ddd, J = 13.6, 8.1, 7.0 Hz, ArCH_2CHH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 159.1 (CO (Ar)), 145.0 (C (Ar)), 143.9 (C (Ar)), 129.3 (CH (Ar)), 128.5 (CH (Ar)), 127.3 (CH (Ar)), 127.2 (C (Ar)), 125.2 (CH (Ar)), 125.0 (CH (Ar)), 123.1 (CH (Ar)), 120.5 (CH (Ar)), 109.7 (CH (Ar)), 96.9 (C), 41.2 (ArCH_2), 40.7 (ArCH_2CH_2), 30.0 (ArCH_2CH_2).

LRMS (CI) *m/z:* 223 (MH^+, 100%).

HRMS (EI) *m/z* Found: M^+ 222.1044, $C_{16}H_{14}O$ requires 222.1045.

*Data for **944**:*

FT-IR (neat, cm^{-1}): 3063 w, 3029 w, 2955 w, 2927 w, 2864 w, 1602 w, 1586 w, 1496 w, 1454 s, 1316 w, 1253 m, 1179 w, 945 w, 797 w, 750 vs.

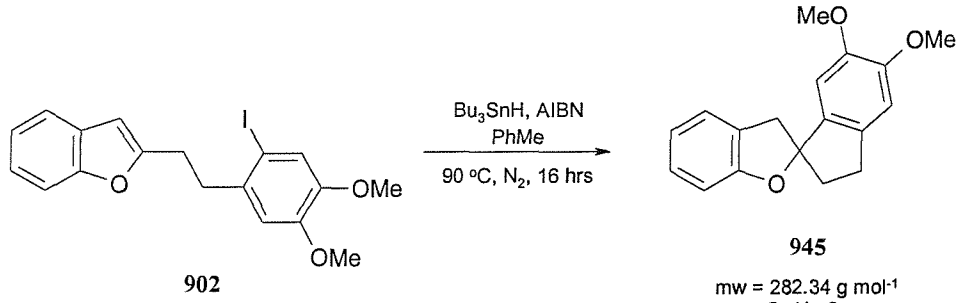
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.53-7.43 (2H, m, ArH), 7.36-7.16 (7H, m, ArH), 6.39 (1H, s, ArH), 3.11 (4H, app. s, ArCH_2CH_2Ar).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 158.9 (CO (Ar)), 141.3 (C (Ar)), 130.0 (C (Ar)), 128.9 (2 x CH (Ar)), 128.8 (2 x CH (Ar)), 126.6 (CH (Ar)), 123.6 (CH (Ar)), 122.9 (CH (Ar)), 120.7 (CH (Ar)), 111.2 (CH (Ar)), 102.8 (CH (Ar)), 34.4 (ArCH_2CH_2Ar), 30.8 (ArCH_2CH_2Ar). One quaternary carbon remains unobserved.

LRMS (CI) *m/z:* 223 (MH^+, 54%), 131 ($C_9H_7O^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 222.1050, $C_{16}H_{14}O$ requires 222.1045.

2',3'-Dihydro-5,6-dimethoxyspiro(indane-1,2'-benzo[*b*]furan) (**945**)



902

mw = 408.23 g mol^{-1}

$C_{18}H_{17}IO_3$

945

mw = 282.34 g mol^{-1}

$C_{18}H_{18}O_3$

To a stirred solution of **902** (100 mg, 0.25 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (80 μL, 0.29 mmol) followed by AIBN (8 mg, 0.05 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a pale yellow oil. Column chromatography (10-20% ether in petrol) gave **945** as a colourless oil (35 mg, 0.12 mmol, 51%).

FT-IR (neat, cm^{-1}): 2995 w, 2935 w, 2834 w, 1597 w, 1500 s, 1478 s, 1460 s, 1414 w, 1340 m, 1312 s, 1291 m, 1260 s, 1240 vs, 1213 s, 1184 m, 1158 m, 1114 m, 1099 m, 1037 m, 954 w, 912 w, 868 s, 817 w, 801 w, 760 vs.

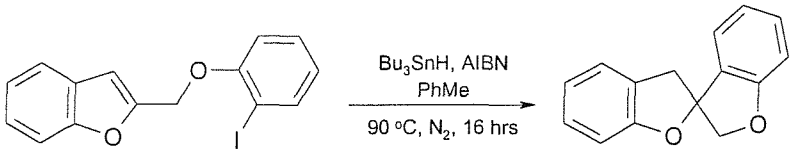
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.25 (1H, dd, J = 7.4, 1.2 Hz, ArH), 7.17 (1H, t, J = 7.9 Hz, ArH), 6.90 (1H, td, J = 7.4, 1.0 Hz, ArH), 6.82 (2H, s, ArH), 6.79 (1H, d, J = 7.9 Hz, ArH), 3.90 (3H, s, $ArOCH_3$), 3.82 (3H, s, $ArOCH_3$), 3.59 (1H, d, J = 16.2 Hz, $ArCHH$), 3.47 (1H, d, J = 16.2 Hz, $ArCHH$), 3.12 (1H, dt, J = 15.5, 8.1 Hz, $ArCHH$), 2.88 (1H, ddd, J = 15.5, 8.1, 4.3 Hz, $ArCHH$), 2.61 (1H, ddd, J = 13.6, 8.1, 4.3 Hz, $ArCH_2CHH$), 2.33 (1H, ddd, J = 13.6, 8.1, 6.5 Hz, $ArCH_2CHH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 158.9 (CO (Ar)), 150.5 (CO (Ar)), 148.9 (CO (Ar)), 136.2 (CO (Ar)), 136.1 (C (Ar)), 128.4 (CH (Ar)), 127.0 (C (Ar)), 124.9 (CH (Ar)), 120.4 (CH (Ar)), 109.7 (CH (Ar)), 107.5 (CH (Ar)), 105.6 (CH (Ar)), 97.6 (C), 56.2 ($ArOCH_3$), 56.2 ($ArOCH_3$), 41.4 ($ArCH_2$), 41.3 ($ArCH_2$), 29.7 ($ArCH_2CH_2$).

LRMS (CI) *m/z*: 282 (M^+, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 305.1146, $C_{18}H_{18}O_3Na$ requires 305.1148.

2,2',3,3'-Tetrahydrospiro(benzo[*b*]furan-3,2'-benzo[*b*]furan) (**672**)



668

mw = 350.15 g mol^{-1}
$C_{15}H_{11}IO_2$

672

mw = 224.26 g mol^{-1}
$C_{15}H_{12}O_2$

To a stirred solution of **668** (400 mg, 1.14 mmol) in toluene (40 mL) at ambient temperature under nitrogen was The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (2.5% ether in petrol) gave **672** as a white solid that yielded on recrystallisation small white prisms (134 mg, 0.60 mmol, 52%): mp 85-86 °C (hexane).

FT-IR (neat, cm^{-1}): 3054 w, 2926 w, 1592 m, 1475 s, 1321 m, 1250 s, 1229 s, 1189 w, 1154 w, 1050 w, 1035 w, 1015 w, 973 s, 939 w, 875 s, 831 s, 755 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.38-7.30 (2H, m, ArH), 7.28 (1H, app. d, J = 7.4 Hz, ArH), 7.21 (1H, td, J = 8.1, 0.7 Hz, ArH), 7.01-6.93 (3H, m, ArH), 6.80 (1H, app. d, J = 7.7 Hz, ArH), 4.91 (1H, d, J = 10.7 Hz, OCHH), 4.46 (1H, d, J = 10.7 Hz, OCHH), 3.78 (1H, d, J = 16.2 Hz, ArCHH), 3.47 (1H, d, J = 16.2 Hz, ArCHH).

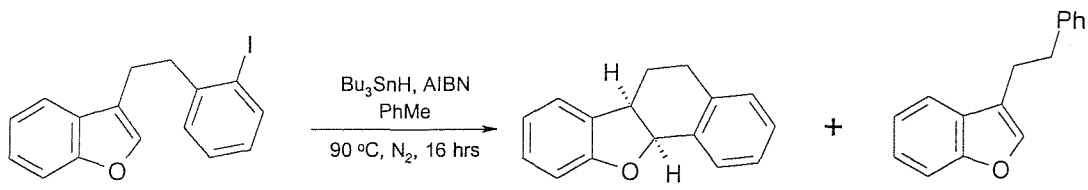
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 160.9 (CO (Ar)), 158.6 (CO (Ar)), 131.6 (CH (Ar)), 129.1 (CH (Ar)), 128.9 (C (Ar)), 126.1 (C (Ar)), 125.0 (CH (Ar)), 124.0 (CH (Ar)), 121.8 (CH (Ar)), 121.3 (CH (Ar)), 111.2 (CH (Ar)), 110.1 (CH (Ar)), 93.1 (C), 83.1 (OCH_2), 40.1 ($ArCH_2$).

LRMS (CI) *m/z:* 225 (MH^+, 100%).

CHN Found: C, 80.07; H, 5.49; $C_{15}H_{12}O_2$ requires C, 80.34; H, 5.39.

5,6,6aS*,11aS*-Tetrahydrobenzo[*b*]naphtho[2,1-*d*]furan (**645**) and

3-(2-Phenylethyl)-1-benzo[*b*]furan (**948**)



655

mw = 348.18 g mol^{-1}

$C_{16}H_{13}IO$

645

mw = 222.29 g mol^{-1}

$C_{16}H_{14}O$

948

mw = 222.29 g mol^{-1}

$C_{16}H_{14}O$

To a stirred solution of **655** (418 mg, 1.20 mmol) in toluene (20 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.39 mL, 1.44 mmol) followed by AIBN (37 mg, 0.24 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (4-20% toluene in petrol) gave firstly **948** as a pale yellow oil (24 mg, 0.11 mmol, 9%); then **645** as a yellow oil (199 mg, 0.90 mmol, 75%). The observed data for **948** is consistent with literature values.[244]

*Data for **645**:*

FT-IR (neat, cm^{-1}): 3026 w, 2927 w, 2858 w, 1596 w, 1476 s, 1460 m, 1359 w, 1328 w, 1222 m, 1184 w, 1109 w, 1080 w, 1015 w, 930 m, 911 s, 859 w, 817 w, 775 w, 740 vs.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.65 (1H, dd, J = 7.0, 1.8 Hz, ArH), 7.43-7.31 (3H, m, ArH), 7.24 (1H, app. d, J = 7.0 Hz, ArH), 7.23 (1H, td, J = 7.7, 1.1 Hz, ArH), 6.99 (1H, td, J = 7.4, 1.1 Hz, ArH), 6.89 (1H, d, J = 8.1 Hz, ArH), 5.76 (1H, d, J = 8.5 Hz, OCH), 3.59 (1H, td, J = 8.5, 5.5 Hz, ArCH), 2.86-2.66 (2H, m, $ArCH_2$), 2.20-2.09 (1H, m, $ArCH_2CHH$), 1.97-1.84 (1H, m, $ArCH_2CHH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 159.6 (CO (Ar)), 139.1 (C (Ar)), 133.7 (C (Ar)), 131.6 (C (Ar)), 130.5 (CH (Ar)), 128.7 (CH (Ar)), 128.5 (2 x CH (Ar)), 126.9 (CH (Ar)), 124.6 (CH (Ar)), 120.8 (CH (Ar)), 109.8 (CH (Ar)), 82.0 (OCH), 41.3 (ArCH), 28.3 ($ArCH_2CH_2$), 27.8 ($ArCH_2CH_2$).

LRMS (CI) *m/z:* 240 ($[M + NH_4]^+$, 14%), 223 (MH^+, 100%).

HRMS (EI) *m/z* Found: M^+ 222.1046, $C_{16}H_{14}O$ requires 222.1045.

*Data for **948**:*

FT-IR (neat, cm^{-1}): 3062 w, 3026 w, 2924 w, 2855 w, 1496 w, 1453 s, 1363 w, 1280 w, 1184 w, 1092 m, 857 w, 750 vs, 723 w.

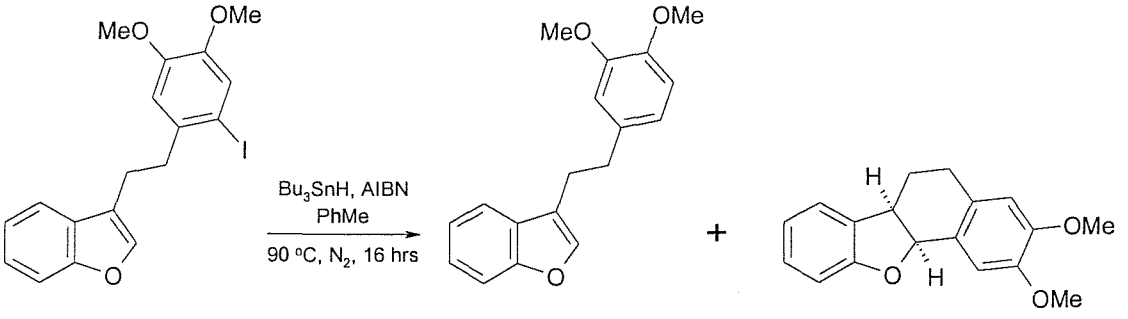
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.57 (1H, dd, J = 7.7, 1.4 Hz, ArH), 7.50 (1H, dd, J = 7.4, 1.2 Hz, ArH), 7.38 (1H, s, ArH), 7.37-7.21 (7H, m, ArH), 3.04 (4H, app. s, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 155.7 (CO (Ar)), 142.0 (C (Ar)), 141.7 (CH (Ar)), 128.8 (4 x CH (Ar)), 128.6 (C (Ar)), 126.5 (CH (Ar)), 124.5 (CH (Ar)), 122.7 (CH (Ar)), 120.2 (C (Ar)), 119.9 (CH (Ar)), 111.9 (CH (Ar)), 35.8 ($ArCH_2CH_2Ar$), 26.0 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 223 (MH^+, 100%), 131 ($C_9H_7O^+$, 66%).

3-[2-(3,4-Dimethoxyphenyl)ethyl]-1-benzo[*b*]furan (**949**) and

2,3-Dimethoxy-5,6,6aS^*,11aS^*-tetrahydrobenzo[*b*]naphtho[2,1-*d*]furan (**950**)



905
mw = 408.23 g mol^{-1}
$C_{18}H_{17}IO_3$

949
mw = 282.34 g mol^{-1}
$C_{18}H_{18}O_3$

950
mw = 282.34 g mol^{-1}
$C_{18}H_{18}O_3$

To a stirred solution of **905** (150 mg, 0.37 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.12 mL, 0.44 mmol) followed by AIBN (11 mg, 0.07 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a yellow oil. Column chromatography (20-50% ether in petrol) gave firstly **949** as a pale yellow oil (12 mg, 43 μmol, 11%); then **950** as a white solid that

yielded on recrystallisation granular white prisms (80 mg, 0.28 mmol, 77%): mp 92-95 °C (hexane).

*Data for **949**:*

FT-IR (neat, cm^{-1}): 2996 w, 2932 m, 2857 w, 2835 w, 1591 w, 1510 vs, 1453 s, 1418 w, 1358 w, 1336 w, 1261 s, 1236 s, 1185 w, 1155 m, 1091 w, 1030 m, 857 w, 811 w, 747 s.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.55 (1H, dd, J = 7.1, 1.4 Hz, ArH), 7.49 (1H, dd, J = 7.4, 1.4 Hz, ArH), 7.37 (1H, s, ArH), 7.32 (1H, td, J = 7.1, 1.4 Hz, ArH), 7.26 (1H, obsc. td, J = 7.4, 1.4 Hz, ArH), 6.83 (1H, d, J = 8.3 Hz, ArH), 6.77 (1H, dd, J = 8.3, 1.9 Hz, ArH), 6.71 (1H, d, J = 1.9 Hz, ArH), 3.89 (3H, s, $ArOCH_3$), 3.84 (3H, s, $ArOCH_3$), 2.99 (4H, app. s, $ArCH_2CH_2Ar$).

^{13}C NMR δ_C ppm (100 Hz, $CDCl_3$): 156.8 (CO (Ar)), 150.4 (CO (Ar)), 149.0 (CO (Ar)), 142.9 (CH (Ar)), 135.7 (2 x C (Ar)), 125.7 (CH (Ar)), 123.8 (CH (Ar)), 121.8 (CH (Ar)), 121.4 (C (Ar)), 121.1 (CH (Ar)), 113.4 (CH (Ar)), 113.0 (CH (Ar)), 112.9 (CH (Ar)), 57.5 ($ArOCH_3$), 57.3 ($ArOCH_3$), 36.5 ($ArCH_2CH_2Ar$), 27.3 ($ArCH_2CH_2Ar$).

LRMS (CI) *m/z:* 300 ($[M + NH_4]^+$, 10%), 283 (MH^+, 47%), 151 ($C_9H_{11}O_2^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 305.1144, $C_{18}H_{18}O_3Na$ requires 305.1148.

*Data for **950**:*

FT-IR (neat, cm^{-1}): 3008 w, 2936 w, 2834 w, 1516 s, 1474 m, 1453 m, 1359 m, 1259 m, 1236 vs, 1195 m, 1122 s, 1078 m, 1015 m, 893 s, 872 s, 849 m, 813 s, 755 vs.

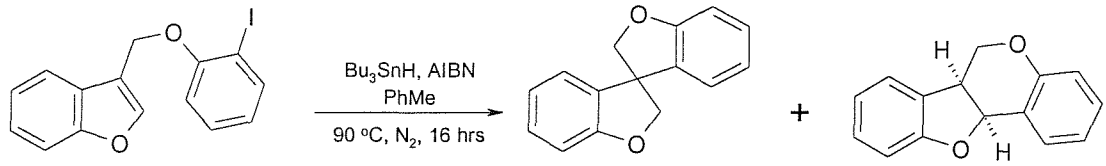
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.27 (1H, d, J = 7.4 Hz, ArH), 7.16 (1H, td, J = 7.7, 1.1 Hz, ArH), 7.07 (1H, s, ArH), 6.92 (1H, td, J = 7.4, 1.1 Hz, ArH), 6.82 (1H, d, J = 7.7 Hz, ArH), 6.66 (1H, s, ArH), 5.62 (1H, d, J = 8.1 Hz, OCH), 3.95 (3H, s, $ArOCH_3$), 3.89 (3H, s, $ArOCH_3$), 3.69-3.59 (1H, m, ArCH), 2.74-2.56 (2H, m, $ArCH_2$), 2.13-2.02 (1H, m, $ArCH_2CHH$), 1.88-1.75 (1H, m, $ArCH_2CHH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 159.4 (CO (Ar)), 149.0 (CO (Ar)), 147.9 (CO (Ar)), 131.7 (C (Ar)), 131.4 (C (Ar)), 128.5 (CH (Ar)), 125.2 (C (Ar)), 124.5 (CH (Ar)), 120.7 (CH (Ar)), 112.6 (CH (Ar)), 111.2 (CH (Ar)), 109.8 (CH (Ar)), 82.0 (OCH), 56.2 ($ArOCH_3$), 56.1 ($ArOCH_3$), 41.1 (ArCH), 28.0 ($ArCH_2CH_2$), 27.5 ($ArCH_2CH_2$).

LRMS (CI) *m/z:* 283 (MH^+, 100%).

CHN Found: C, 76.36; H, 6.43; $C_{18}H_{18}O_3$ requires C, 76.57; H, 6.43.

2,2',3,3'-Tetrahydrospiro(benzo[*b*]furan-3,3'-benzo[*b*]furan) (**683**) and 6aS^*,11aS^*-Dihydro-6*H*-benzo[4,5]furo[3,2-*c*]chromene (6aS^*,11aS^*-pterocarpan) (**951**)



679
mw = 350.15 g mol^{-1}
$C_{15}H_{11}IO_2$

683
mw = 224.26 g mol^{-1}
$C_{15}H_{12}O_2$

951
mw = 224.26 g mol^{-1}
$C_{15}H_{12}O_2$

To a stirred solution of **679** (300 mg, 0.86 mmol) in toluene (30 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (0.28 mL, 1.03 mmol) followed by AIBN (27 mg, 0.17 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (25 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (50 mL), the organic phase was isolated, washed with water (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (1% ether in petrol) yielded a 1:1 mixture of **683** and **951** as a white solid (166 mg, 0.74 mmol, 86%) Recrystallisations from ethyl acetate/hexane and further chromatography failed to separate the two components. The observable data for **951** is consistent with the literature.[245] The NMR assignments for **683** and **951** were confirmed by ^{1}H-^{1}H and ^{1}H-^{13}C COSY experiments.

^{1}H NMR Signals observed for **683**: δ_H ppm (300 MHz, $CDCl_3$): 7.34-7.18 (5H, m, ArH, **683** *and* **951**), 7.08 (2H, dd, J = 7.4, 1.1 Hz, ArH), 7.01-6.87 (7H, m, ArH, **683** *and* **951**), 4.71 (2H, d, J = 9.6 Hz, OCHH), 4.57 (2H, d, J = 9.6 Hz, OCHH).

Signals observed for **951**: δ_H ppm (300 MHz, $CDCl_3$): 7.59 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.09 (1H, td, J = 7.4, 1.1 Hz, ArH), 5.56 (1H, d, J = 6.2 Hz,

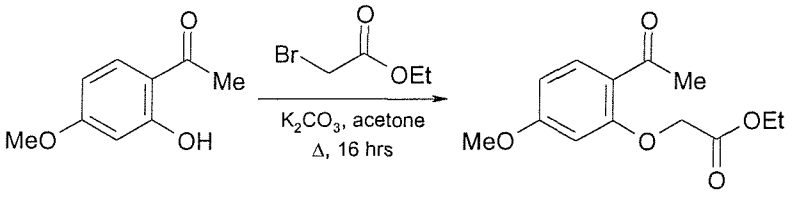
OCH), 4.39-4.27 (1H, m, ArOCHH), 3.75-3.63 (2H, m, ArOCHH *and* ArCH).

^{13}C NMR Signals observed for **683**: δ_C ppm (75 MHz, $CDCl_3$): 160.1 (2 x CO (Ar)), 129.5 (2 x CH (Ar)), 124.2 (2 x CH (Ar)), 121.8 (2 x CH (Ar)), 110.0 (2 x CH (Ar)), 83.6 (2 x OCH_2), 56.3 (C). One of the quaternary carbons remains unobserved.

Signals observed for **951**: δ_C ppm (75 MHz, $CDCl_3$): 159.4 (CO (Ar)), 155.6 (CO (Ar)), 131.3 (CH (Ar)), 130.3 (CH (Ar)), 129.4 (CH (Ar)), 127.2 (C (Ar)), 124.9 (CH (Ar)), 121.9 (CH (Ar)), 121.1 (CH (Ar)), 120.2 (C (Ar)), 117.6 (CH (Ar)), 110.4 (CH (Ar)), 77.8 (OCH), 66.5 ($ArOCH_2$), 40.5 (ArCH).

LRMS (CI) *m/z:* 242 ($[M + NH_4]^+$, 10%), 225 (MH^+, 100%), 224 (M^+, 100%).

Ethyl (2-acetyl-5-methoxyphenoxy)acetate (**955**)



954

mw = 166.18 mol^{-1}
$C_9H_{10}O_3$

955

mw = 252.27g mol^{-1}
$C_{13}H_{16}O_5$

Following the procedure of Nielek and Lesiak,[149] a suspension of 2'-hydroxy-4'-methoxyacetophenone **954** (5.0 g, 30.1 mmol), ethyl bromoacetate (3.50 mL, 31.6 mmol) and potassium carbonate (12.5 g, 90 mmol) in acetone (100 mL) was heated at reflux under a $CaCl_2$ drying tube for 16 hours. On cooling to ambient temperature, the reaction mixture was filtered and the filtrate concentrated *in vacuo*. The white solid obtained was suspended in water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to give **955** as a colourless oil that crystallised on standing to a waxy white solid (7.58 g, 30.1 mmol, 100%): mp 73-74 °C, lit. 73 °C.[246] The observed data is consistent with literature values.

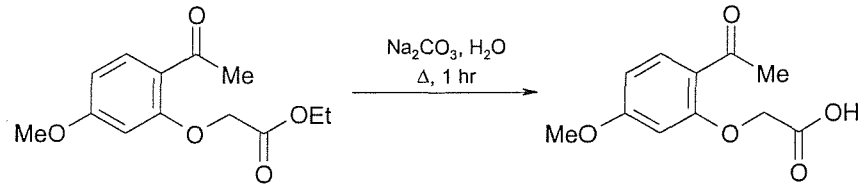
FT-IR (neat, cm^{-1}): 2988 w, 1760 m, 1732 m, 1647 m, 1600 vs, 1576 m, 1504 w, 1429 w, 1364 w, 1328 w, 1261 vs, 1198 s, 1127 m, 1080 w, 1053 m, 1027 s, 962 m, 869 w, 826 m, 700 w, 674 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.86 (1H, d, J = 8.6 Hz, ArH), 6.57 (1H, dd, J = 8.6, 2.1 Hz, ArH), 6.32 (1H, d, J = 2.1 Hz, ArH), 4.70 (2H, s, $ArOCH_2COOEt$), 4.29 (2H, q, J = 7.1 Hz, OCH_2CH_3), 3.84 (3H, s, $ArOCH_3$), 2.69 (3H, s, $ArCOCH_3$), 1.31 (3H, t, J = 7.1 Hz, OCH_2CH_3).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 198.1 ($ArCOCH_3$), 168.4 (COOEt), 164.7 (CO (Ar)), 159.4 (CO (Ar)), 133.3 (CH (Ar)), 122.0 (C (Ar)), 106.4 (CH (Ar)), 99.5 (CH (Ar)), 65.9 ($ArOCH_2COOEt$), 62.0 (OCH_2CH_3), 56.0 ($ArOCH_3$), 32.5 ($ArCOCH_3$), 14.5 (OCH_2CH_3).

LRMS (CI) *m/z:* 253 (MH^+, 100%), 237 ($[M - CH_3]^+$, 41%).

Ethyl (2-acetyl-5-methoxyphenoxy)acetic acid (**956**)



955

mw = 252.27 g mol^{-1}

$C_{13}H_{16}O_5$

956

mw = 224.21 g mol^{-1}

$C_{11}H_{12}O_5$

Following the procedure of Nielek and Lesiak,[149] a suspension of **955** (5.0 g, 19.8 mmol) and sodium carbonate (2.31 g, 21.8 mmol) in water (35 mL) was heated at reflux for 1 hour. On cooling to 0 °C, the reaction mixture was acidified with concentrated HCl until effervescence ceased. The resultant cream precipitate was collected by filtration, washed with water (150 mL) and dried under air flow to give **956** as a cream solid (4.29 g, 19.1 mmol, 97%): mp 122-124 °C, lit. 126 °C (benzene/ethanol).[246] The observed data is consistent with literature values.

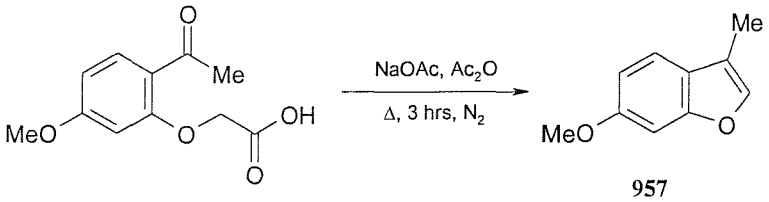
FT-IR (neat, cm^{-1}): 3488 w, 3179 br. w, 1699 m, 1633 m, 1587 s, 1504 w, 1467 w, 1442 w, 1413 m, 1362 m, 1334 m, 1319 m, 1293 m, 1254 vs, 1205 vs, 1183 s, 1127 s, 1052 s, 1022 s, 964 vs, 821 vs, 753 w, 678 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.83 (1H, d, J = 8.8 Hz, ArH), 6.65 (1H, dd, J = 8.8, 2.4 Hz, ArH), 6.46 (1H, d, J = 2.4 Hz, ArH), 4.76 (2H, s, $ArOCH_2COOH$), 3.89 (3H, s, $ArOCH_3$), 2.64 (3H, s, $ArCOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 203.0 (Ar<u>C</u>OCH$_3$), 174.8 (<u>C</u>OOH), 169.3 (<u>C</u>O (Ar)), 164.1 (<u>C</u>O (Ar)), 137.8 (<u>C</u>H (Ar)), 125.9 (<u>C</u> (Ar)), 110.9 (<u>C</u>H (Ar)), 104.3 (<u>C</u>H (Ar)), 70.4 (ArO<u>C</u>H$_2$COOH), 60.4 (ArO<u>C</u>H$_3$), 36.5 (ArCO<u>C</u>H$_3$).

LRMS (ES$^-$) *m/z:* 447 ([2M-H]$^-$, 100%), 337 ([M + CF_3COO]$^-$, 71%), 223 ([M – H]$^-$, 23%).

<u>6-Methoxy-3-methylbenzo[*b*]furan (**957**)</u>



956

mw = 224.21 g mol^{-1}
$C_{11}H_{12}O_5$

957

mw = 162.19 g mol^{-1}
$C_{10}H_{10}O_2$

Following the procedure of Nielek and Lesiak,[149] a suspension of **956** (4.0 g, 17.8 mmol) and sodium acetate (6.23 g, 76 mmol) in acetic anhydride (12 mL, 0.13 mol) under nitrogen was heated at reflux for 3 hours. On cooling to ambient temperature, the reaction mixture was poured into water (50 mL) and extracted with ether (3 x 50 mL). The combined organic phases were washed with saturated sodium carbonate solution (2 x 50 mL) and brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a red oil. Purification by column chromatography (1-5% ether in petrol) gave **957** as a white solid that formed small white prisms on recrystallisation (2.41 g, 14.9 mmol, 83%): mp 60 °C (hexane), lit. 58 °C.[246,247] The observed data is consistent with literature values.[248]

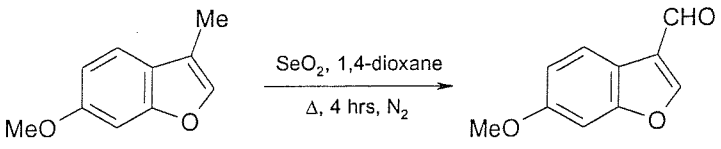
FT-IR (neat, cm^{-1}): 3125 w, 3002 w, 2972 w, 2944 w, 2839 w, 1621 m, 1584 m, 1488 s, 1437 s, 1388 w, 1331 m, 1292 m, 1264 m, 1228 s, 1187 m, 1142 vs, 1130 s, 1080 s, 1066 m, 1025 s, 931 s, 810 vs, 791 s.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.42 (1H, d, J = 8.3 Hz, Ar<u>H</u>), 7.37-7.35 (1H, m, Ar<u>H</u>), 7.04 (1H, d, J = 2.4 Hz, Ar<u>H</u>), 6.93 (1H, ddd, J = 8.3, 2.4, 1.0 Hz, Ar<u>H</u>), 3.88 (3H, s, ArOC<u>H</u>$_3$), 2.25 (3H, s, ArC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 158.4 (<u>C</u>O (Ar)), 156.6 (<u>C</u>O (Ar)), 140.9 (<u>C</u>H (Ar)), 122.9 (<u>C</u> (Ar)), 119.9 (<u>C</u>H (Ar)), 115.9 (<u>C</u> (Ar)), 111.7 (<u>C</u>H (Ar)), 96.4 (<u>C</u>H (Ar)), 56.1 (ArO<u>C</u>H$_3$), 8.3 (Ar<u>C</u>H$_3$).

LRMS (CI) *m/z:* 163 (MH$^+$, 100%), 147 ([M – CH_3]$^+$, 72%).

3-Formyl-6-methoxybenzo[*b*]furan (**958**)



957

mw = 162.19 g mol^{-1}
$C_{10}H_{10}O_2$

958

mw = 176.17 g mol^{-1}
$C_{10}H_8O_3$

Following the procedure of Zaidlewicz *et al.*,[150] a solution of **957** (2.20 g, 13.6 mmol) and selenium dioxide (1.73 g, 15.6 mmol) in 1,4-dioxane (20 mL) under nitrogen was heated at reflux for 4 hours. On cooling to ambient temperature, the reaction mixture was filtered through celite and concentrated *in vacuo* to a red oil. Purification by column chromatography (5-30% ether in petrol) gave **958** as an orange solid that yielded orange prisms on recrystallisation (1.71 g, 9.7 mmol, 71%): mp 74-76 °C (methanol).

FT-IR (neat, cm^{-1}): 3134 w, 3086 w, 2998 w, 2946 w, 2837 w, 1671 m, 1621 m, 1591 m, 1556 m, 1494 s, 1426 m, 1390 w, 1330 w, 1281 m, 1232 m, 1189 w, 1149 s, 1133 s, 1068 s, 1022 s, 928 m, 810 vs, 724 m.

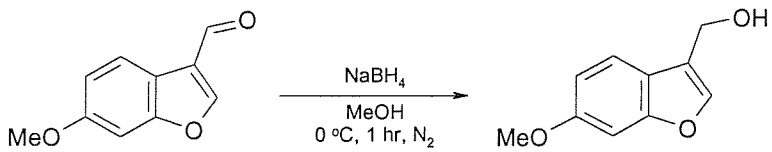
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 10.11 (1H, s, ArC<u>H</u>O), 8.18 (1H, s, Ar<u>H</u>), 8.03 (1H, d, J = 8.6 Hz, Ar<u>H</u>), 7.06 (1H, d, J = 2.4 Hz, Ar<u>H</u>), 7.00 (1H, dd, J = 8.6, 2.4 Hz, Ar<u>H</u>), 3.87 (3H, s, ArOC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 185.2 (Ar<u>C</u>HO), 159.7 (<u>C</u>O (Ar)), 157.5 (<u>C</u>O (Ar)), 155.0 (<u>C</u>H (Ar)), 124.2 (<u>C</u> (Ar)), 123.1 (<u>C</u>H (Ar)), 116.5 (<u>C</u> (Ar)), 114.1 (<u>C</u>H (Ar)), 96.5 (<u>C</u>H (Ar)), 56.2 (ArO<u>C</u>H$_3$).

LRMS (CI) *m/z:* 176 (M^+, 100%), 161 ($[M - CH_3]^+$, 37%).

CHN Found: C, 68.32; H, 4.61; $C_{10}H_8O_3$ requires C, 68.18; H, 4.58.

3-(Hydroxymethyl)-6-methoxybenzo[*b*]furan (**959**)



958

mw = 176.17 g mol^{-1}
$C_{10}H_8O_3$

959

mw = 178.19 g mol^{-1}
$C_{10}H_{10}O_3$

To a stirred solution of **958** (0.60 g, 3.41 mmol) in THF (30 mL) at 0 °C was added sodium borohydride (142 mg, 3.75 mmol). The reaction mixture was stirred at ambient temperature for 1 hour then concentrated *in vacuo*. The resultant yellow semi-solid was suspended in

water (25 mL) and extracted with ether (3 x 50mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to give **959** as a pale yellow solid that yielded fine white plates on recrystallisation (0.58 g, 3.25 mmol, 95%): mp 63-64 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 3325 br. m, 2971 w, 2946 w, 2919 w, 2871 w, 1623 m, 1585 m, 1491 s, 1441 s, 1309 m, 1287 m, 1260 w, 1225 s, 1143 vs, 1081 vs, 1012 vs, 932 s, 810 vs, 781 s, 709 m, 665 w.

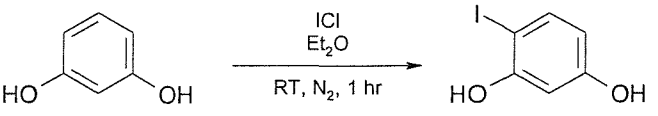
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.52 (1H, d, J = 8.6 Hz, ArH), 7.52-7.50 (1H, m, ArH), 7.03 (1H, d, J = 2.2 Hz, ArH), 6.91 (1H, dd, J = 8.6, 2.2 Hz, ArH), 4.79 (2H, d, J = 4.3 Hz, $ArCH_2OH$), 3.86 (3H, s, $ArOCH_3$), 1.98 (1H, t, J = 4.3 Hz, $ArCH_2OH$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 158.4 (CO (Ar)), 156.8 (CO (Ar)), 141.5 (CH (Ar)), 120.5 (C (Ar)), 120.2 (CH (Ar)), 112.0 (CH (Ar)), 96.2 (CH (Ar)), 56.0 ($ArCH_2OH$), 55.9 ($ArOCH_3$). One quaternary carbon remains unobserved.

LRMS (CI) *m/z:* 178 (M^+, 100%), 161 ($[MH - H_2O]^+$, 85%).

CHN Found: C, 67.25; H, 5.64; $C_{10}H_{10}O_3$ requires C, 67.41; H, 5.66.

4-Iodoresorcinol (**970**)



mw = 110.11 g mol^{-1}
$C_6H_6O_2$

970

mw = 236.0 g mol^{-1}
$C_6H_5IO_2$

In accordance with the procedure of Sakamoto *et al.*,[173] to a stirred solution of resorcinol (10 g, 91 mmol) in ether (100 mL) at ambient temperature under nitrogen was added iodine monochloride (4.56 mL, 91 mmol) over 5 minutes. The reaction mixture was stirred for 1 hour at ambient temperature then washed with saturated sodium bicarbonate solution (100 mL) and saturated sodium thiosulfate solution (100 mL). Drying ($MgSO_4$) and concentration *in vacuo* yielded a black oil. Purification by column chromatography (2.5-30% ethyl acetate in toluene) gave firstly **970** as a white powdery solid (11.18 g, 47 mmol, 52%): mp 69-73 °C, lit. 67-70 °C;[249] then recovered resorcinol (0.81 g, 7.3 mmol, 8%). The observed data is consistent with literature values.[173,249]

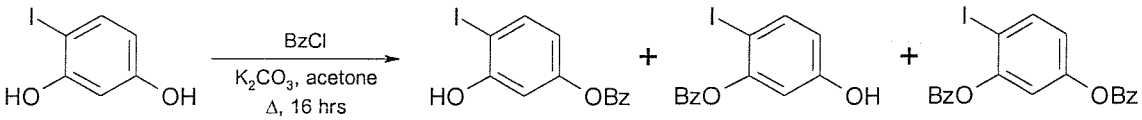
FT-IR (neat, cm^{-1}): 3161 br. m, 2889 w, 1584 m, 1511 w, 1445 m, 1374 m, 1293 m, 1243 s, 1213 s, 1185 s, 1114 m, 1021 w, 976 m, 937 w, 820 vs, 768 m, 700 s.

^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 8.95 (1H, br. s, ArOH), 8.57 (1H, br. s, ArOH), 7.45 (1H, d, J = 8.5 Hz, ArH), 6.52 (1H, d, J = 2.6 Hz, ArH), 6.23 (1H, dd, J = 8.5, 2.6 Hz, ArH).

^{13}C NMR δ_C ppm (75 MHz, D_6-acetone): 159.8 (CO (Ar)), 158.0 (CO (Ar)), 139.7 (CH (Ar)), 110.2 (CH (Ar)), 103.4 (CH (Ar)), 71.4 (CI (Ar)).

LRMS (EI) *m/z:* 236 (M^+, 100%).

3-Hydroxy-4-iodophenyl benzoate (**960**), 5-Hydroxy-2-iodophenyl benzoate (**971**) and 3-(Benzoyloxy)-4-iodophenyl benzoate (**972**)



970 mw = 236.0 g mol^{-1} $C_6H_5IO_2$

960 mw = 340.11 g mol^{-1} $C_{13}H_9IO_3$

971 mw = 340.11 g mol^{-1} $C_{13}H_9IO_3$

972 mw = 444.22 g mol^{-1} $C_{20}H_{13}IO_4$

Following the procedure of Sakamoto *et al.*,[173] a suspension of **970** (660 mg, 2.80 mmol), benzoyl chloride (0.36 mL, 3.10 mmol) and potassium carbonate (1.41 g, 10.2 mmol) in acetone (20 mL) under a $CaCl_2$ drying tube was heated at reflux for 16 hours. On cooling to ambient temperature, the reaction mixture was filtered and concentrated *in vacuo*. The white solid obtained was suspended in water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were then dried ($MgSO_4$) and concentrated *in vacuo* to a white semi-solid. Purification by column chromatography (5-50% ether in petrol) gave firstly **972** as a colourless oil that crystallised on standing to a white solid (131 mg, 0.30 mmol, 11%): mp 171-173 °C, lit. 176-178 °C;[250] then **960** as a white solid that gave small white prisms on recrystallisation (572 mg, 1.68 mmol, 60%): mp 163-165 °C (ethyl acetate/hexane), lit. 160-164 °C;[250] and finally **971** as a white solid that gave fine white needles on recrystallisation (140 mg, 0.41 mmol, 15%): mp 159-161 °C (ethyl acetate/hexane). The observed data for **960** and **972** is consistent with literature values.

*Data for **960**:*

FT-IR (neat, cm^{-1}): 3330 br. m, 1700 s, 1604 m, 1575 w, 1489 w, 1450 w, 1417 m, 1343 w, 1315 m, 1264 s, 1181 m, 1152 s, 1116 m, 1090 m, 1065 m, 1018 m, 958 m, 885 m, 832 w, 791 m, 701 vs, 685 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.23-8.17 (2H, m, PhH), 7.70 (1H, d, J = 8.8 Hz, ArH), 7.67 (1H, tt, J = 7.4, 1.5 Hz, PhH), 7.53 (2H, app. t, J = 7.4 Hz, PhH), 6.89 (1H, d, J = 2.6 Hz, ArH), 6.63 (1H, dd, J = 8.8, 2.6 Hz, ArH), 5.71 (1H, br. s, ArOH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 165.2 (OCOPh), 155.9 (CO (Ar)), 152.6 (CO (Ar)), 138.6 (CH (Ar)), 134.1 (CH (Ar)), 130.4 (2 x CH (Ar)), 129.2 (C (Ar)), 128.8 (2 x CH (Ar)), 116.2 (CH (Ar)), 109.3 (CH (Ar)), 81.9 (CI (Ar)).

LRMS (CI) *m/z:* 340 (M^+, 4%), 214 ($[MH - I]^+$, 15%), 105 ($C_7H_5O^+$, 100%).

*Data for **971**:*

FT-IR (neat, cm^{-1}): 3309 br. m, 1706 vs, 1600 m, 1584 m, 1484 m, 1434 m, 1356 w, 1303 m, 1268 vs, 1230 vs, 1169 vs, 1121 s, 1087 s, 1067 s, 1020 s, 1001 m, 962 m, 881 m, 837 m, 801 m, 702 vs, 681 s.

^{1}H NMR δ_H ppm (300 MHz, D_6-acetone): 9.02 (1H, br. s, ArOH), 8.27-8.20 (2H, m, PhH), 7.77 (1H, tt, J = 7.4, 2.2 Hz, PhH), 7.70 (1H, d, J = 8.8 Hz, ArH), 7.63 (2H, app. t, J = 7.4 Hz, ArH), 6.91 (1H, d, J = 2.6 Hz, ArH), 6.69 (1H, dd, J = 8.8, 2.6 Hz, ArH).

^{13}C NMR δ_C ppm (100 MHz, D_6-acetone): 165.0 (OCOPh), 160.2 (CO (Ar)), 153.6 (CO (Ar)), 140.5 (CH (Ar)), 135.2 (CH (Ar)), 131.4 (2 x CH (Ar)), 130.7 (C (Ar)), 130.1 (2 x CH (Ar)), 116.9 (CH (Ar)), 112.5 (CH (Ar)), 78.0 (CI (Ar)).

LRMS (CI) *m/z:* 341 (MH^+, 5%), 214 ($[MH - I]^+$, 7%), 105 ($C_7H_5O^+$, 100%).

CHN Found: C, 46.31; H, 2.75; $C_{13}H_9IO_3$ requires C, 45.91; H, 2.67.

Data for 972:

FT-IR (neat, cm^{-1}): 3063 w, 1737 vs, 1600 w, 1583 w, 1469 w, 1451 w, 1403 w, 1314 w, 1244 s, 1175 w, 1148 s, 1119 m, 1076 m, 1054 s, 1019 s, 895 m, 828 w, 796 m, 695 vs.

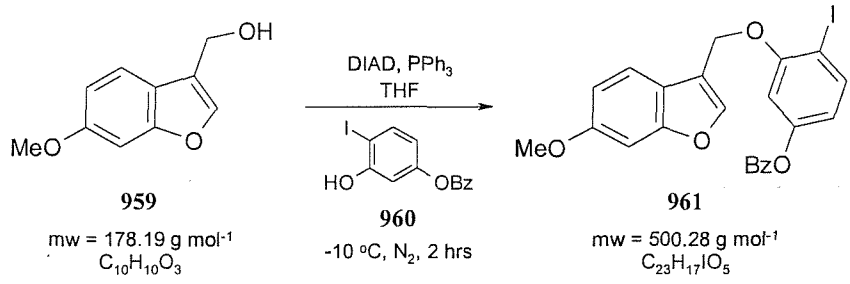
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.33-8.25 (2H, m, PhH), 8.23-8.17 (2H, m, PhH), 7.93 (1H, d, J = 8.8 Hz, ArH), 7.69 (1H, tt, J = 7.4, 1.5 Hz, PhH), 7.67 (1H, tt, J = 7.4, 1.5 Hz, PhH), 7.56 (2H, app. t, J = 7.4 Hz, PhH), 7.53 (2H, app. t, J = 7.4 Hz, PhH), 7.28 (1H, d, J = 2.6 Hz, ArH), 7.01 (1H, dd, J = 8.8, 2.6 Hz, ArH).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 164.7 (OCOPh), 164.2 (OCOPh), 151.9 (CO (Ar)), 151.8 (CO (Ar)), 139.6 (CH (Ar)), 134.2 (CH (Ar)), 134.1 (CH (Ar)), 130.7 (2 x CH (Ar)), 130.4 (2 x CH (Ar)), 129.1 (C (Ar)), 129.0 (C (Ar)), 128.9 (2 x CH (Ar)), 128.8 (2 x CH (Ar)), 121.4 (CH (Ar)), 117.5 (CH (Ar)), 86.4 (CI (Ar)).

LRMS (CI) *m/z:* 444 (M^+, 10%), 105 ($C_7H_5O^+$, 100%).

HRMS (EI) *m/z* Found: M^+ 443.9842, $C_{20}H_{13}IO_4$ requires 443.9859.

4-Iodo-3-[(6-methoxy-1-benzo[*b*]furan-3-yl)methoxy]phenyl benzoate (**961**)



To a stirred solution of alcohol **959** (100 mg, 0.56 mmol), **960** (200 mg, 0.59 mmol) and triphenylphosphine (176 mg, 0.67 mmol) in THF (10 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.12 mL, 0.62 mmol) over 10 minutes. After 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a yellow oil. Purification by column chromatography (10-30% ether in petrol, then 80% toluene in petrol to neat toluene) gave **961** as a white solid (198 mg, 0.40 mmol, 71%): mp 137-139 °C.

FT-IR (neat, cm^{-1}): 3069 w, 2945 w, 2841 w, 1728 s, 1628 w, 1588 m, 1494 m, 1475 m, 1462 m, 1437 m, 1404 m, 1316 m, 1257 vs, 1225 s, 1165 s, 1145 vs, 1114 s, 1081 s, 1066 s, 1011 vs, 932 m, 839 m, 801 s, 777 m, 706 vs, 686 m.

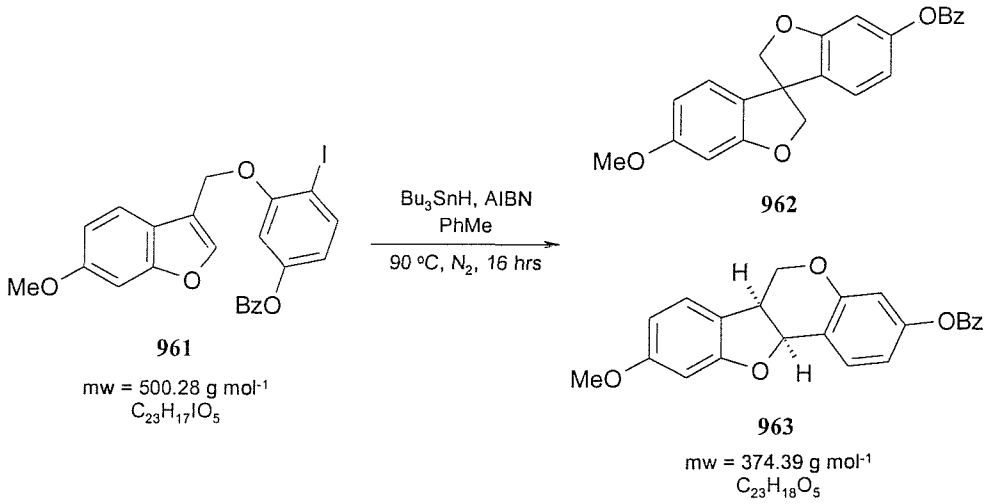
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.25-8.19 (2H, m, PhH), 7.84 (1H, d, J = 8.6 Hz, ArH), 7.72-7.67 (1H, m, PhH), 7.69 (1H, s, ArH), 7.64 (1H, d, J = 8.6 Hz, ArH), 7.59-7.51 (2H, m, PhH), 7.06 (1H, d, J = 2.1 Hz, ArH), 6.95 (1H, dd, J = 8.6, 2.1 Hz, ArH), 6.92 (1H, d, J = 2.6 Hz, ArH), 6.70 (1H, dd, J = 8.6, 2.6 Hz, ArH), 5.25 (2H, d, J = 1.0 $ArCH_2O$), 3.88 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 165.0 (PhCOO), 158.5 (CO (Ar)), 157.9 (CO (Ar)), 156.8 (CO (Ar)), 152.3 (CO (Ar)), 142.4 (CH (Ar)), 139.7 (CH (Ar)), 134.0 (CH (Ph)), 130.4 (2 x CH (Ph)), 129.3 (C (Ph)), 128.8 (2 x CH (Ph)), 120.7 (CH (Ar)), 120.0 (C (Ar)), 116.4 (CH (Ar)), 116.1 (C (Ar)), 112.2 (CH (Ar)), 107.0 (CH (Ar)), 96.3 (CH (Ar)), 82.8 (CI (Ar)), 63.1 ($ArCH_2O$), 55.9 ($ArOCH_3$).

LRMS (CI) *m/z:* 501 (MH^+, 18%), 374 ($[MH - I]^+$, 14%), 122 ($C_7H_6O_2^+$, 56%), 105 ($C_7H_5O^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 523.0008, $C_{23}H_{17}IO_5Na$ requires 523.0013.

6-Benzoyloxy-6'-methoxy-2,2',3,3'-tetrahydrospiro(benzo[*b*]furan-3,3'-benzo[*b*]furan) (**962**) and 3-Benzoyloxy-9-methoxy-6aS^*,11aS^*-dihydro-6*H*-benzo[4,5]furo[3,2-*c*]-chromene (**963**)



To a stirred solution of **961** (75 mg, 0.15 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (48 μL, 0.18 mmol) followed by AIBN (5 mg, 0.03 mmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (5-20%

ether in petrol) yielded firstly **962** as a white solid (12 mg, 32 μmol, 21%): mp 146-148 °C; then a 1:1 mixture of **962** and **963** as a white solid (16 mg, 43 μmol, 28%).

*Data for **962**:*

FT-IR (neat, cm^{-1}): 3063 w, 2926 w, 2838 w, 1729 s, 1620 m, 1599 m, 1491 s, 1454 m, 1435 m, 1332 m, 1266 m, 1248 vs, 1149 m, 1133 s, 1120 vs, 1105 s, 1082 m, 1057 s, 1028 s, 989 m, 969 s, 891 m, 829 m, 705 s, 690 m.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 8.23-8.18 (2H, m, PhH), 7.66 (1H, tt, J = 7.4, 1.4 Hz, PhH), 7.53 (2H, app. t, J = 7.4 Hz, PhH), 7.09 (1H, d, J = 8.6 Hz, ArH), 7.00 (1H, d, J = 8.1 Hz, ArH), 6.78 (1H, dd, J = 8.6, 1.9 Hz, ArH), 6.76 (1H, d, J = 1.9 Hz, ArH), 6.51 (1H, dd, J = 8.1, 2.4 Hz, ArH), 6.48 (1H, d, J = 2.4 Hz, ArH), 4.74 (1H, d, J = 9.3 Hz, ArOCHH), 4.72 (1H, d, J = 9.3 Hz, ArOCHH), 4.58 (1H, d, J = 9.3 Hz, ArOCHH), 4.57 (1H, d, J = 9.3 Hz, ArOCHH), 3.81 (3H, s, $ArOCH_3$).

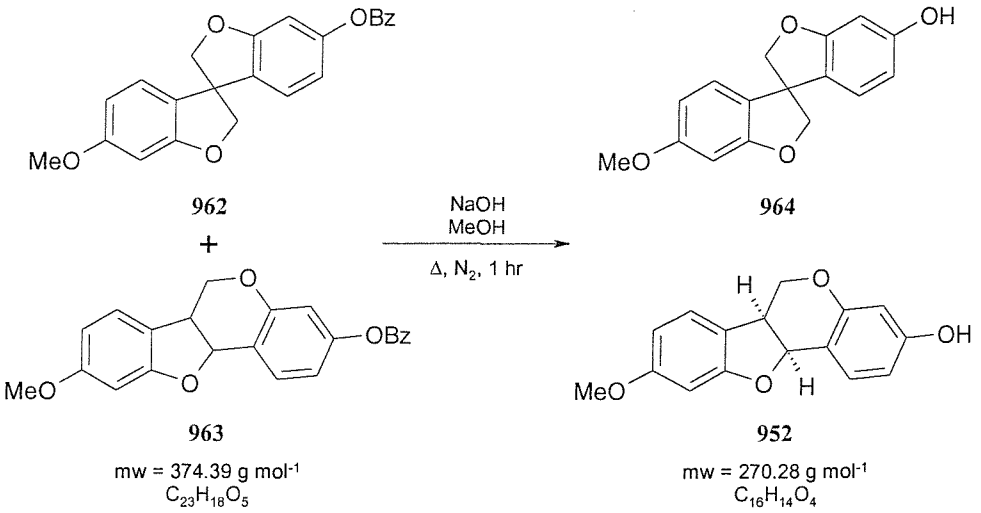
Signals observed for **963**: δ_H ppm (300 MHz, $CDCl_3$): 8.25-8.19 (2H, m, PhH), 7.67 (1H, tt, J = 7.4, 1.4 Hz, PhH), 7.54 (2H, app. t, J = 7.4 Hz, PhH), 7.62 (1H, d, J = 8.3 Hz, ArH), 7.00 (1H, d, J = 8.8 Hz, ArH), 6.96 (1H, dd, J = 8.3, 2.4 Hz, ArH), 6.87 (1H, d, J = 2.4 Hz, ArH), 6.55-6.47 (2H, m, ArH), 5.58 (1H, d, J = 6.4 Hz, OCH), 4.32 (1H, dd, J = 11.0, 4.3 Hz, ArOCHH), 3.69 (1H, dd, J = 11.0 Hz, ArOCHH), 3.63 (1H, ddd, J = 11.0, 6.4, 4.3 Hz, ArCH), 3.82 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 165.5 (PhCOO), 161.8 (2 x CO (Ar)), 161.3 (CO (Ar)), 152.3 (CO (Ar)), 134.1 (CH (Ph)), 130.6 (2 x CH (Ph)), 129.8 (C (Ar)), 129.5 (C (Ph)), 129.0 (2 x CH (Ph)), 124.7 (CH (Ar)), 124.6 (CH (Ar)), 123.2 (C (Ar)), 115.3 (CH (Ar)), 108.0 (CH (Ar)), 104.7 (CH (Ar)), 96.7 (CH (Ar)), 84.8 ($ArOCH_2$), 84.7 ($ArOCH_2$), 66.3 (C), 56.0 ($ArOCH_3$).

LRMS (CI) *m/z:* 375 (MH^+, 18%), 105 ($C_7H_5O^+$, 100%), 77 ($C_6H_5^+$, 81%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 397.1052, $C_{23}H_{18}O_5Na$ requires 397.1046.

3-Hydroxy-9-methoxy-6aS*,11aS*-dihydro-6*H*-benzo[4,5]furo[3,2-*c*]chromene (Demethylhomopterocarpin) (**952**) and 6-Hydroxy-6'-methoxy-2,2',3,3'-tetrahydrospiro-(benzo[*b*]furan-3,3'-benzo[*b*]furan) (**964**)



A solution of a 1:1 mixture of **962/963** (16 mg, 43 μmol) and sodium hydroxide (13 mg, 0.32 mmol) in methanol (5 mL) under nitrogen was heated at reflux for 1 hour. On cooling to ambient temperature, the reaction mixture was concentrated *in vacuo,* suspended in saturated sodium bicarbonate solution (10 mL) and extracted with ether (3 x 10 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a pale yellow solid. Purification by column chromatography (40-50% ether in petrol) gave a 1:1 mixture of **952** and **964** as a white solid (11 mg, 41 μmol, 95%). The two components were subsequently separated by HPLC (25% ethyl acetate in hexane). The observed data for demethylhomopterocarpin **952** is consistent with the literature.[158]

*Data for **952**:* (white solid, mp 194-197 °C, lit. 195-197 °C.[172])

FT-IR (neat, cm^{-1}): 3383 m, 2940 w, 2926 w, 1601 vs, 1599 s, 1500 vs, 1472 s, 1448 m, 1347 m, 1278 m, 1209 m, 1154 s, 1114 s, 1084 m, 1029 m, 949 m, 907 w, 839 w, 797 w, plus residual acetone signals.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.42 (1H, d, J = 8.3 Hz, ArH), 7.16 (1H, d, J = 8.8 Hz, ArH), 6.69 (1H, ddd, J = 8.3, 2.4, 0.7 Hz, ArH), 6.48 (1H, dd, J = 8.8, 2.4, 0.7 Hz, ArH), 6.47 (1H, d, J = 2.4 Hz, ArH), 6.44 (1H, d, J = 2.4 Hz, ArH), 5.52 (1H, d, J = 6.4 Hz, OCH), 4.87 (1H, s, ArOH), 4.26 (1H, app. dd, J = 10.5, 4.5 Hz, ArOCHH), 3.79 (3H, s, $ArOCH_3$), 3.65 (1H, app. t, J = 10.5 Hz, ArOCHH), 3.55 (1H, ddd, J = 10.5, 6.7, 4.5 Hz, ArCH).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 162.2 (CO (Ar)), 161.9 (CO (Ar)), 159.8 (CO (Ar)), 157.8 (CO (Ar)), 133.2 (CH (Ar)), 126.0 (CH (Ar)), 120.6 (C (Ar)), 113.0 (C (Ar)), 110.6 (CH (Ar)), 107.0 (CH (Ar)), 104.0 (CH (Ar)), 97.3 (CH (Ar)), 79.5 (OCH), 67.2 ($ArOCH_2$), 55.8 ($ArOCH_3$), 40.5 (ArCH).

LRMS (EI) *m/z:* 270 (M^+, 100%), 255 ($[M - CH_3]^+$, 27%).

HRMS (EI) *m/z* Found: M^+ 270.0884, $C_{16}H_{14}O_4$ requires 270.0892.

*Data for **964**:* (colourless oil).

FT-IR (neat, cm^{-1}): 3408 br. w, 2938 w, 2885 w, 2839 w, 1619 s, 1501 vs, 1466 m, 1332 m, 1290 m, 1199 m, 1169 w, 1144 s, 1114 s, 1078 m, 1028 w, 980 w, 925 w, 831 w, 801 w, 768 w.

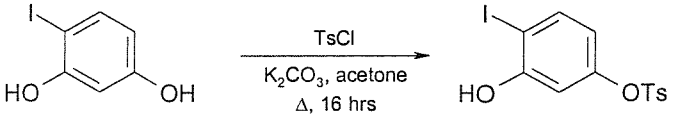
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 6.96 (1H, dd, J = 8.1, 0.7 Hz, ArH), 6.91 (1H, d, J = 8.8 Hz, ArH), 6.49 (1H, dd, J = 8.1, 2.2 Hz, ArH), 6.47 (1H, d, J = 2.2 Hz, ArH), 6.40 (1H, d, J = 2.4 Hz, ArH), 6.39 (1H, dd, J = 8.8, 2.4 Hz, ArH), 4.82 (1H, s, ArOH), 4.69 (2H, app. d, J = 9.3 Hz, 2 x ArOCHH), 4.52 (1H, d, J = 9.3 Hz, ArOCHH), 4.51 (1H, d, J = 9.3 Hz, ArOCHH), 3.81 (3H, s, $ArOCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 161.4 (2 x CO (Ar)), 161.3 (CO (Ar)), 157.0 (CO (Ar)), 124.4 (CH (Ar)), 124.1 (CH (Ar)), 123.6 (C (Ar)), 123.2 (C (Ar)), 108.6 (CH (Ar)), 107.5 (CH (Ar)), 97.7 (CH (Ar)), 96.2 (CH (Ar)), 84.4 ($ArOCH_2$), 76.7 ($ArOCH_2$), 55.6 ($ArOCH_3$), 55.2 (C).

LRMS (EI) *m/z:* 270 (M^+, 100%), 255 ($[M - CH_3]^+$, 21%).

HRMS (EI) *m/z* Found: M^+ 270.0890, $C_{16}H_{14}O_4$ requires 270.0892.

3-Hydroxy-4-iodophenyl *para*-toluenesulfonate (**965**)



970
mw = 236.0 g mol^{-1}
$C_6H_5IO_2$

965
mw = 390.19 g mol^{-1}
$C_{13}H_{11}IO_4S$

In accordance with the procedure of Sakamoto *et al.*,[173] a suspension of **970** (1.0 g, 4.24 mmol), *p*-toluenesulfonyl chloride (890 mg, 4.66 mmol) and potassium carbonate (1.76 g, 12.7 mmol) in acetone (20 mL) under a $CaCl_2$ drying tube was heated at reflux for 16 hours. On cooling to ambient temperature, the reaction mixture was filtered and

concentrated *in vacuo*. The white solid obtained was suspended in water (50 mL) and extracted with ether (3 x 50 mL). The combined ether phases were dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (1-3% ethyl acetate in toluene, followed by 80% toluene in petrol to 3% ethyl acetate in toluene) gave **965** as a white solid that yielded pale orange prisms on recrystallisation (971 mg, 2.49 mmol, 59%): mp 114-116 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 3414 br. w, 1596 w, 1576 w, 1491 w, 1414 m, 1361 s, 1337 m, 1270 w, 1192 s, 1180 vs, 1132 s, 1116 s, 1090 s, 1027 w, 969 s, 858 m, 829 s, 815 vs, 727 s, 703 m, 658 vs.

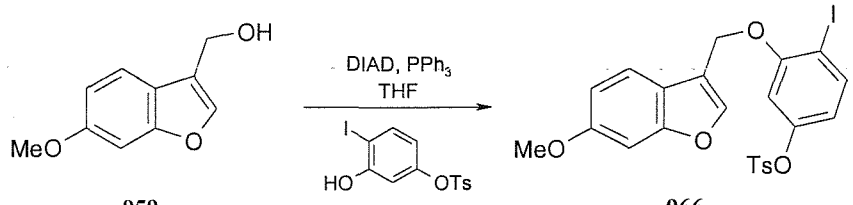
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.72 (2H, d, J = 8.3 Hz, ArH), 7.56 (1H, d, J = 8.6 Hz, ArH), 7.33 (2H, d, J = 8.3 Hz, ArH), 6.67 (1H, d, J = 2.6 Hz, ArH), 6.38 (1H, dd, J = 8.6, 2.6 Hz, ArH), 5.63 (1H, br. s, ArOH), 2.45 (3H, s, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 155.8 (CO (Ar)), 151.1 (CO (Ar)), 145.9 (C (Ar)), 138.6 (CH (Ar)), 132.1 (C (Ar)), 130.1 (2 x CH (Ar)), 128.7 (2 x CH (Ar)), 116.5 (CH (Ar)), 109.7 (CH (Ar)), 83.6 (CI (Ar)), 21.9 ($ArCH_3$).

LRMS (ES^-) *m/z*: 389 ($[M - H]^-$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 412.9318, $C_{13}H_{11}IO_4SNa$ requires 412.9315.

4-Iodo-3-[(6-methoxy-1-benzo[*b*]furan-3-yl)methoxy]phenyl *para*-toluenesulfonate (**966**)



959 mw = 178.19 g mol^{-1} $C_{10}H_{10}O_3$

965 -10 °C, N_2, 2 hrs

966 mw = 550.37 g mol^{-1} $C_{23}H_{19}IO_6S$

To a stirred solution of alcohol **959** (175 mg, 0.98 mmol), **965** (402 mg, 1.03 mmol) and triphenylphosphine (308 mg, 1.18 mmol) in THF (15 mL) at –10 °C under nitrogen was added di-isopropylazodicarboxylate (0.21 mL, 1.08 mmol) over 10 minutes. After 2 hours at –10 °C, the reaction mixture was concentrated *in vacuo* to a yellow oil. Purification by column chromatography (10-30% ether in petrol) gave **966** as a white solid that yielded fine white plates on recrystallisation (385 mg, 0.70 mmol, 71%): mp 120-122 °C (ethyl acetate/hexane).

FT-IR (neat, cm^{-1}): 2993 w, 2938 w, 2830 w, 1628 w, 1591 m, 1573 w, 1491 m, 1475 m, 1437 w, 1399 m, 1372 s, 1278 m, 1192 s, 1180 s, 1141 vs, 1115 s, 1090 s, 1017 s, 934 m, 861 s, 816 vs, 790 vs, 735 s, 697 m, 653 s.

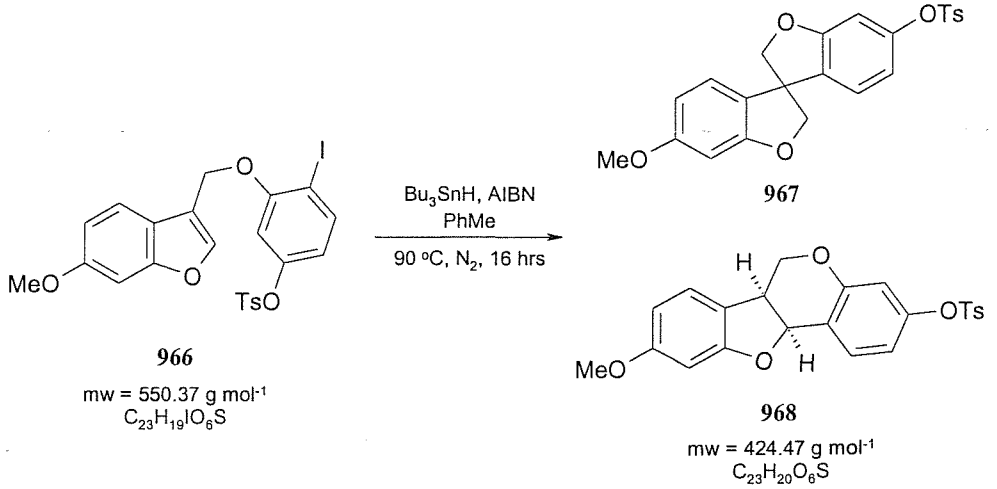
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.69 (2H, d, J = 8.3 Hz, ArH), 7.64 (1H, d, J = 8.6 Hz, ArH), 7.63 (1H, s, ArH), 7.61 (1H, d, J = 8.6 Hz, ArH), 7.31 (2H, d, J = 8.3 Hz, ArH), 7.06 (1H, d, J = 2.4 Hz, ArH), 6.95 (1H, dd, J = 8.6, 2.4 Hz, ArH), 6.75 (1H, d, J = 2.4 Hz, ArH), 6.31 (1H, dd, J = 8.6, 2.4 Hz, ArH), 5.16 (2H, s, $ArCH_2OAr$), 3.88 (3H, s, $ArOCH_3$), 2.46 (3H, s, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 158.6 (CO (Ar)), 157.8 (CO (Ar)), 156.7 (CO (Ar)), 150.7 (CO (Ar)), 145.8 (C (Ar)), 142.7 (CH (Ar)), 139.7 (CH (Ar)), 132.1 (C (Ar)), 130.0 (2 x CH (Ar)), 128.7 (2 x CH (Ar)), 120.6 (CH (Ar)), 119.8 (C (Ar)), 116.5 (CH (Ar)), 115.7 (C (Ar)), 112.2 (CH (Ar)), 107.5 (CH (Ar)), 96.2 (CH (Ar)), 84.6 (CI (Ar)), 63.0 ($ArCH_2OAr$), 55.9 ($ArOCH_3$), 21.9 ($ArCH_3$).

LRMS (ES^+) *m/z:* 573 ($[M + Na]^+$, 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 572.9845, $C_{23}H_{19}IO_6SNa$ requires 572.9839.

6'-Methoxy-2,2',3,3'-tetrahydrospiro(benzo[*b*]furan-3,3'-benzo[*b*]furan)-6-yl *para*-toluenesulfonate (**967**) and 9-Methoxy-6aS^*,11aS^*-dihydro-6*H*-benzo[4,5]furo[3,2-*c*]chromen-3-yl *para*-toluenesulfonate (**968**)



To a stirred solution of **966** (150 mg, 0.27 mmol) in toluene (10 mL) at ambient temperature under nitrogen was added tri-*n*-butyltin hydride (89 μL, 0.33 mmol) followed by AIBN (8 mg, 54 μmol). The reaction mixture was stirred for 16 hours at 90 °C, then allowed to cool to ambient temperature. 10% Potassium fluoride solution (10 mL) was added and the biphasic mixture stirred vigorously for 24 hours. Following dilution with ether (25 mL), the

organic phase was isolated, washed with water (3 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo* to a white solid. Purification by column chromatography (5-20% ether in petrol) gave firstly **967** as a pale yellow oil (41 mg, 97 μmol, 36%); then **968**, also as a pale yellow oil (32 mg, 75 μmol, 28%).

*Data for **967**:*

FT-IR (neat, cm^{-1}): 2955 w, 2931 w, 2883 w, 1598 s, 1496 s, 1484 s, 1445 w, 1374 s, 1329 w, 1279 w, 1256 w, 1196 vs, 1179 vs, 1148 s, 1114 w, 1095 vs, 1028 w, 1005 w, 979 m, 964 m, 857 m, 825 s, 735 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.76 (2H, d, J = 8.3 Hz, ArH), 7.34 (2H, d, J = 8.3 Hz, ArH), 6.93 (1H, d, J = 8.8 Hz, ArH), 6.91 (1H, d, J = 8.1 Hz, ArH), 6.54 (1H, dd, J = 8.8, 2.4 Hz, ArH), 6.52 (1H, d, J = 2.4 Hz, ArH), 6.47 (1H, dd, J = 8.1, 2.2 Hz, ArH), 6.45 (1H, d, J = 2.2 Hz, ArH), 4.68 (1H, d, J = 9.3 Hz, ArOCHH), 4.67 (1H, d, J = 9.3 Hz, ArOCHH), 4.53 (1H, d, J = 9.3 Hz, ArOCHH), 4.50 (1H, d, J = 9.3 Hz, ArOCHH), 3.79 (3H, s, $ArOCH_3$), 2.47 (3H, s, $ArCH_3$).

^{13}C NMR δ_C ppm (75 MHz, $CDCl_3$): 161.6 (CO (Ar)), 161.5 (CO (Ar)), 160.7 (CO (Ar)), 150.5 (CO (Ar)), 145.6 (C (Ar)), 132.7 (C (Ar)), 130.6 (C (Ar)), 130.0 (2 x CH (Ar)), 128.6 (2 x CH (Ar)), 124.4 (CH (Ar)), 124.3 (CH (Ar)), 122.6 (C (Ar)), 115.7 (CH (Ar)), 107.8 (CH (Ar)), 104.9 (CH (Ar)), 96.4 (CH (Ar)), 84.4 (2 x $ArOCH_2$), 66.0 (C), 55.7 ($ArOCH_3$), 21.9 ($ArCH_3$).

LRMS (ES^+) *m/z:* 871 ([2M + Na], 16%), 447 ([M + Na], 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 447.0864, $C_{23}H_{20}O_6SNa$ requires 447.0873.

*Data for **968**:*

FT-IR (neat, cm^{-1}): 2959 w, 2925 w, 2855 w, 1496 w, 1463 w, 1446 w, 1377 w, 1260 m, 1192 w, 1179 w, 1146 w, 1106 m, 1090 s, 1027 s, 949 w, 865 w, 800 vs, 720 w.

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$): 7.75 (2H, d, J = 8.3 Hz, ArH), 7.45 (1H, d, J = 8.1 Hz, ArH), 7.33 (2H, d, J = 8.3 Hz, ArH), 7.14 (1H, d, J = 8.1 Hz, ArH), 6.69 (1H, dd, J = 8.1, 2.4 Hz, ArH), 6.65 (1H, d, J = 2.4 Hz, ArH), 6.47 (1H, dd, J = 8.1, 2.4 Hz, ArH), 6.45 (1H, d, J = 2.4 Hz, ArH), 5.47 (1H,

d, J = 5.7 Hz, OC<u>H</u>), 4.28-4.20 (1H, m, ArOC<u>H</u><u>H</u>), 3.78 (3H, s, ArOC<u>H</u>$_3$), 3.58-3.53 (2H, m, ArOCH<u>H</u> *and* ArC<u>H</u>), 2.46 (3H, s, ArC<u>H</u>$_3$).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$): 161.3 (<u>C</u>O (Ar)), 160.4 (<u>C</u>O (Ar)), 156.2 (<u>C</u>O (Ar)), 150.4 (<u>C</u>O (Ar)), 145.4 (<u>C</u> (Ar)), 135.8 (<u>C</u> (Ar)), 129.8 (2 x <u>C</u>H (Ar)), 128.5 (2 x <u>C</u>H (Ar)), 125.5 (<u>C</u>H (Ar)), 124.8 (<u>C</u>H (Ar)), 119.1 (<u>C</u> (Ar)), 118.6 (<u>C</u> (Ar)), 115.7 (<u>C</u>H (Ar)), 111.5 (<u>C</u>H (Ar)), 106.7 (<u>C</u>H (Ar)), 97.0 (<u>C</u>H (Ar)), 77.8 (O<u>C</u>H), 66.7 (ArO<u>C</u>H$_2$), 55.5 (ArO<u>C</u>H$_3$), 39.4 (Ar<u>C</u>H), 21.7 (Ar<u>C</u>H$_3$).

LRMS (ES^+) *m/z:* 871 ([2M + Na], 10%), 447 ([M + Na], 100%).

HRMS (ES^+) *m/z* Found: $[M + Na]^+$ 447.0866, $C_{23}H_{20}O_6SNa$ requires 447.0873.

Appendix

X-Ray Crystallography: Data Collection Summary for ***218***

2191349 Compound 02srf002 02-06-07

Formula: C_{24} H_{20} O_8

Crystal Class: Monoclinic
Space Group: P 1 21/c 1

a	7.8044(6)	alpha	90
b	24.705(2)	beta	100.163(3)
c	10.5309(11)	gamma	90

Volume 1998.5
Z 4

Radiation type Mo K\a Wavelength 0.710730
Dx 1.45 Mr 436.42
Mu 0.110 Temperature (K) 120
Size 0.30 x 0.30 x 0.05

Colour: colourless Shape: block

Cell from 3194 Reflections, Theta Range 3 to 26

Standard Interval: 0 Standard Count: 0
Diffractometer type KAPPACCD, Scan type OMEGA
Absorption type: multi-scan Transmission range: 0.97 0.97
Reflections measured: 6405 Independent reflections: 3769
Rint 0.0004 Theta max 25.85
Hmin, Hmax -9 9
Kmin, Kmax -30 28
Lmin, Lmax -11 12

Refinement on Fsqd
R-factor 0.061 Weighted R-factor 0.141
Max shift/su 0.0014
Delta Rho min -0.29 Delta Rho max 0.71
Reflections used 1147 sigma(I) limit 3.00
Number of parameters 290 Goodness of fit 0.889
Weights: Chebychev polymial with 3 parameters, Carruthers & Watkin

Atom	x/a	y/b	z/c	U(iso)
O6	-0.0029(8)	0.3353(2)	0.4056(6)	0.0384
C2	-0.1104(12)	0.3413(4)	0.4895(9)	0.0324
O5	-0.1797(8)	0.3045(2)	0.5369(6)	0.0421
C4	-0.1484(11)	0.4004(3)	0.5087(8)	0.0304
C5	-0.2467(11)	0.4293(3)	0.4083(8)	0.0261
C6	-0.296(1)	0.4020(3)	0.2782(8)	0.0277
C7	-0.4022(11)	0.3554(3)	0.2664(8)	0.0301
C8	-0.4273(12)	0.3298(3)	0.1491(9)	0.0327
O8	-0.517(1)	0.2836(3)	0.1149(7)	0.0635
C10	-0.5055(16)	0.2751(5)	-0.0199(11)	0.0631
O7	-0.3922(9)	0.3150(2)	-0.0584(6)	0.0441
C12	-0.3566(12)	0.3478(3)	0.0473(9)	0.0365
C13	-0.2572(12)	0.3937(4)	0.051(1)	0.0505
C15	-0.2305(11)	0.4211(3)	0.1724(8)	0.0359
C16	-0.2888(11)	0.4851(3)	0.4240(8)	0.0293
C17	-0.2277(11)	0.5092(3)	0.5457(8)	0.0306
C18	-0.1262(11)	0.4795(3)	0.6455(8)	0.0264
C19	-0.0861(11)	0.4259(3)	0.6283(8)	0.0269
C20	0.0368(11)	0.3971(4)	0.7288(8)	0.0307
O4	.0.0696(8)	0.4253(2)	0.8416(6)	0.0394
C22	0.2016(12)	0.4024(3)	0.9415(8)	0.0380
C23	0.2431(14)	0.4442(4)	1.0469(9)	0.0550
O3	0.1060(8)	0.3545(2)	0.7165(6)	0.0435
C26	-0.2665(12)	0.5647(3)	0.5671(8)	0.0351
C27	-0.3593(11)	0.5929(3)	0.4679(8)	0.0257
O2	-0.4142(8)	0.6456(2)	0.4630(6)	0.0409
C29	-0.4926(13)	0.6566(3)	0.3306(9)	0.0392
O1	-0.5170(8)	0.6043(2)	0.2681(5)	0.0363
C31	-0.4216(12)	0.5678(3)	0.3496(8)	0.0303
C32	-0.3904(11)	0.5155(3)	0.3254(8)	0.0296
C33	0.0183(12)	0.2798(3)	0.362(1)	0.0447
C35	0.1079(14)	0.2842(4)	0.248(1)	0.0491

Atom	x/a	y/b	z/c	U(iso)
H71	-0.4567	0.3411	0.3413	0.0349
H101	-0.6280	0.2775	-0.0767	0.0843
H102	-0.4629	0.2369	-0.0342	0.0843
H131	-0.2032	0.4061	-0.0286	0.0575
H151	-0.1574	0.4558	0.1832	0.0417
H181	-0.0823	0.4974	0.7318	0.0308
H221	0.1589	0.3679	0.9765	0.0448
H222	0.3119	0.3932	0.9067	0.0448
H231	0.3328	0.4304	1.1202	0.0641
H232	0.1336	0.4529	1.0823	0.0641
H233	0.2865	0.4782	1.0125	0.0641
H261	-0.2219	0.5834	0.6530	0.0385
H291	-0.6075	0.6768	0.3276	0.0527
H292	-0.4144	0.6813	0.2889	0.0527
H321	-0.4405	0.4985	0.2387	0.0312
H331	0.0884	0.2574	0.4314	0.0643
H332	-0.0985	0.2617	0.3337	0.0643
H351	0.1307	0.2475	0.2121	0.0600
H352	0.2275	0.3023	0.2754	0.0600
H353	0.0406	0.3066	0.1777	0.0600

Atom	u(11)	u(22)	u(33)	(u23)	(u13)	u(12)
O6	0.044(4)	0.022(3)	0.048(4)	-0.009(3)	0.003(3)	0.005(3)
C2	0.034(6)	0.028(5)	0.032(6)	-0.005(4)	-0.004(5)	0.007(5)
O5	0.049(4)	0.022(3)	0.051(4)	0.001(3)	-0.003(3)	-0.005(3)
C4	0.036(5)	0.020(4)	0.033(6)	-0.002(4)	0.002(4)	-0.006(4)
C5	0.027(5)	0.027(5)	0.025(5)	-0.003(4)	0.007(4)	-0.003(4)
C6	0.029(5)	0.026(5)	0.025(5)	0.003(4)	-0.005(4)	0.010(4)
C7	0.039(5)	0.026(5)	0.023(5)	0.007(4)	0.002(4)	-0.002(4)
C8	0.052(6)	0.013(4)	0.027(6)	-0.008(4)	-0.010(5)	-0.005(4)
O8	0.080(6)	0.054(5)	0.056(5)	-0.004(4)	0.010(4)	-0.012(4)
C10	0.076(8)	0.068(8)	0.041(8)	-0.013(6)	-0.001(6)	-0.004(6)
O7	0.071(5)	0.023(3)	0.035(4)	-0.008(3)	0.003(3)	-0.010(3)
C12	0.038(5)	0.034(6)	0.035(6)	-0.006(5)	-0.000(5)	0.005(5)
C13	0.035(6)	0.045(6)	0.062(7)	-0.009(6)	-0.017(5)	-0.007(5)
C15	0.039(5)	0.032(5)	0.035(6)	-0.006(5)	0.000(5)	-0.010(4)
C16	0.037(5)	0.016(5)	0.034(6)	-0.005(4)	0.004(4)	-0.005(4)
C17	0.036(5)	0.013(5)	0.040(6)	-0.001(4)	0.000(5)	-0.001(4)
C18	0.030(5)	0.029(5)	0.019(5)	-0.002(4)	0.003(4)	-0.005(4)
C19	0.028(5)	0.018(5)	0.033(6)	0.001(4)	0.002(4)	-0.003(4)
C20	0.035(5)	0.032(6)	0.025(6)	0.006(4)	0.003(4)	0.001(5)
O4	0.047(4)	0.044(4)	0.023(4)	-0.004(3)	-0.004(3)	0.013(3)
C22	0.045(6)	0.040(6)	0.026(6)	0.010(4)	-0.001(5)	0.014(5)
C23	0.069(7)	0.055(7)	0.034(6)	-0.008(5)	-0.010(6)	0.020(6)
O3	0.054(4)	0.029(4)	0.041(4)	-0.004(3)	-0.010(3)	0.008(3)
C26	0.040(6)	0.040(6)	0.026(6)	0.000(4)	0.007(5)	-0.008(5)
C27	0.036(5)	0.019(4)	0.024(5)	-0.001(4)	0.011(4)	0.002(4)
O2	0.059(4)	0.029(3)	0.033(4)	0.001(3)	0.005(3)	0.014(3)
C29	0.057(7)	0.030(5)	0.032(6)	0.012(4)	0.011(5)	0.013(5)
O1	0.048(4)	0.028(3)	0.032(4)	0.006(3)	0.002(3)	0.006(3)
C31	0.038(5)	0.027(5)	0.024(6)	0.003(4)	-0.002(4)	-0.001(4)
C32	0.039(6)	0.023(5)	0.025(5)	-0.002(4)	0.001(4)	0.008(4)
C33	0.045(6)	0.022(5)	0.066(7)	-0.003(5)	0.007(6)	0.013(5)
C35	0.061(7)	0.033(6)	0.052(7)	-0.015(5)	0.006(6)	0.004(5)

O6	C2	1.331(11)	
O6	C33	1.47(1)	
C2	O5	1.21(1)	
C2	C4	1.509(12)	
C4	C5	1.389(11)	
C4	C19	1.416(11)	
C5	C6	1.515(12)	
C5	C16	1.434(11)	
C6	C7	1.411(11)	
C6	C15	1.388(11)	
C7	C8	1.371(12)	
C7	H71	1.023	
C8	O8	1.35(1)	
C8	C12	1.364(12)	
O8	C10	1.453(12)	
C10	O7	1.429(13)	
C10	H101	1.036	
C10	H102	1.023	
O7	C12	1.36(1)	
C12	C13	1.369(12)	
C13	C15	1.426(12)	
C13	H131	1.052	
C15	H151	1.023	
C16	C17	1.417(11)	
C16	C32	1.408(11)	
C17	C18	1.407(11)	
C17	C26	1.429(11)	
C18	C19	1.379(11)	
C18	H181	1.015	
C19	C20	1.480(11)	
C20	O4	1.36(1)	
C20	O3	1.20(1)	
O4	C22	1.452(9)	
C22	C23	1.510(12)	
C22	H221	1.008	
C22	H222	1.018	
C23	H231	1.006	
C23	H232	1.014	
C23	H233	0.998	
C26	C27	1.354(11)	
C26	H261	1.021	
C27	O2	1.370(9)	
C27	C31	1.399(12)	
O2	C29	1.45(1)	
C29	O1	1.45(1)	
C29	H291	1.022	
C29	H292	1.015	
O1	C31	1.371(9)	
C31	C32	1.348(11)	
C32	H321	1.019	
C33	C35	1.490(14)	
C33	H331	1.002	
C33	H332	1.011	
C35	H351	1.013	
C35	H352	1.028	
C35	H353	0.998	

C2 . O6 . C33 . 115.7(7)
O6 . C2 . O5 . 124.8(8)
O6 . C2 . C4 . 111.0(8)
O5 . C2 . C4 . 124.0(9)
C2 . C4 . C5 . 119.4(7)
C2 . C4 . C19 . 120.4(7)
C5 . C4 . C19 . 120.3(7)
C4 . C5 . C6 . 118.5(7)
C4 . C5 . C16 . 120.9(8)
C6 . C5 . C16 . 120.4(8)
C5 . C6 . C7 . 119.6(8)
C5 . C6 . C15 . 120.3(7)
C7 . C6 . C15 . 120.1(7)
C6 . C7 . C8 . 116.3(8)
C6 . C7 . H71 . 122.066
C8 . C7 . H71 . 121.588
C7 . C8 . O8 . 127.9(9)
C7 . C8 . C12 . 123.0(8)
O8 . C8 . C12 . 109.1(8)
C8 . O8 . C10 . 105.3(8)
O8 . C10 . O7 . 109.0(8)
O8 . C10 . H101 . 110.294
O7 . C10 . H101 . 110.549
O8 . C10 . H102 . 110.744
O7 . C10 . H102 . 111.280
H101 . C10 . H102 . 104.952
C10 . O7 . C12 . 103.0(7)
C8 . C12 . O7 . 113.2(8)
C8 . C12 . C13 . 123.4(8)
O7 . C12 . C13 . 123.3(9)
C12 . C13 . C15 . 114.5(9)
C12 . C13 . H131 . 121.345
C15 . C13 . H131 . 124.118
C6 . C15 . C13 . 122.5(8)
C6 . C15 . H151 . 118.216
C13 . C15 . H151 . 119.216
C5 . C16 . C17 . 117.5(8)
C5 . C16 . C32 . 122.7(8)
C17 . C16 . C32 . 119.8(7)
C16 . C17 . C18 . 120.7(7)
C16 . C17 . C26 . 120.0(8)
C18 . C17 . C26 . 119.3(8)
C17 . C18 . C19 . 120.9(8)
C17 . C18 . H181 . 119.871
C19 . C18 . H181 . 119.190
C4 . C19 . C18 . 119.7(8)
C4 . C19 . C20 . 120.0(7)
C18 . C19 . C20 . 120.0(8)
C19 . C20 . O4 . 112.1(8)
C19 . C20 . O3 . 126.2(8)
O4 . C20 . O3 . 121.6(8)
C20 . O4 . C22 . 115.6(6)
O4 . C22 . C23 . 107.3(7)
O4 . C22 . H221 . 110.949
C23 . C22 . H221 . 110.593
O4 . C22 . H222 . 111.289
C23 . C22 . H222 . 109.303
H221 . C22 . H222 . 107.375
C22 . C23 . H231 . 111.241
C22 . C23 . H232 . 109.221
H231 . C23 . H232 . 107.913
C22 . C23 . H233 . 110.638
H231 . C23 . H233 . 109.198
H232 . C23 . H233 . 108.551
C17 . C26 . C27 . 118.0(8)
C17 . C26 . H261 . 121.712
C27 . C26 . H261 . 120.193
C26 . C27 . O2 . 129.8(8)
C26 . C27 . C31 . 121.0(8)
O2 . C27 . C31 . 109.2(7)
C27 . O2 . C29 . 107.0(6)
O2 . C29 . O1 . 105.7(6)
O2 . C29 . H291 . 109.955
O1 . C29 . H291 . 112.127
O2 . C29 . H292 . 110.194
O1 . C29 . H292 . 112.375
H291 . C29 . H292 . 106.560
C29 . O1 . C31 . 106.8(6)
C27 . C31 . O1 . 109.4(7)
C27 . C31 . C32 . 123.1(8)
O1 . C31 . C32 . 127.5(8)
C16 . C32 . C31 . 118.0(8)
C16 . C32 . H321 . 121.148
C31 . C32 . H321 . 120.819
O6 . C33 . C35 . 106.2(7)
O6 . C33 . H331 . 111.399
C35 . C33 . H331 . 110.755
O6 . C33 . H332 . 111.133
C35 . C33 . H332 . 108.949
H331 . C33 . H332 . 108.411
C33 . C35 . H351 . 112.033
C33 . C35 . H352 . 109.950
H351 . C35 . H352 . 106.337
C33 . C35 . H353 . 112.206
H351 . C35 . H353 . 108.619
H352 . C35 . H353 . 107.425

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