UNIVERSITY OF SOUTHAMPTON

INTRAMOLECULAR RADICAL ADDITIONS TO PYRIDINES, QUINOLINES AND ISOQUINOLINES

BY

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A Thesis submitted for the Degree of Doctor of Philosophy

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ABSTRACT

FACULTY OF SCIENCE

CHEMISTRY

Doctor of Philosophy

Intramolecular Radical Additions to Pyridines, Quinolines and Isoquinolines

By Benjamin Josiah Sutton

This thesis is concerned with the development of intramolecular radical additions onto nitrogen containing heteroaromatics. Notably, 6-*exo*/*endo*-trig radical cyclisations to C-2, C-3 and C-4 of pyridines and quinolines and C-3 and C-4 of isoquinolines have all been shown to be facile processes at neutral p*H*. Cyclisations follow a chain pathway in which aromaticity in the heteroaromatic is re-established through loss of a hydrogen atom.

5-*exo*/*endo*-Trig radical cyclisations to quinolines fail and appear to be more akin to 5-*endo*-trig processes than 5-*exo*-trig processes. Reactions that employ aryl iodides as radical precursors generally proceed more efficiently than related cyclisations employing aryl bromides.

It has been shown that the nature of the tether used to conjoin the radical precursor to the heteroaromatic can have a significant baring on the outcome of a reaction. When a fully saturated two carbon tether is used to conjoin an aryl radial to a pyridine an unprecedented rearrangement by *ipso*-radical cyclisation (5-*exo*-trig) - alkyl migration - aromatisation sequence competes with the 6-*exo*/*endo*-trig cyclisation pathway. When an *E* alkene is used to tether the radical precursor to a pyridine, or if the heteroaromatic is a quinoline or isoquinoline, only the 6-*exo*/*endo*-trig pathway is followed.

Using the methodology developed, approaches to the alkaloid avicine are discussed. A comparison of various techniques commonly employed to generate aryl radicals from aryl iodides is also reported.

A literature review concerning radical additions to nitrogen containing heteroaromatics is presented.

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PREFACE

The research described in this thesis was carried out under the supervision of Dr. D. C. Harrowven at the University of Southampton between October 1999 and October 2002. No part of this thesis has previously been submitted for a degree.

ABBREVIATIONS

ACN	azobis(cyclohexanecarbonitrile)
AIBMe	dimethyl 2,2'-azobis(*iso*butyrate)
AIBN	azobis(*iso*butyronitrile)
amu	atomic mass units
APCI	atmospheric pressure chemical ionisation
aq.	aqueous
Ar	aryl
Bn	benzyl
Bu	butyl
CHN	combustion analysis
CI	chemical ionisation
conc.	concentrated
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL-H	di-*iso*-butylaluminium hydride
DME	ethylene glycol dimethyl ether
DMF	*N*,*N*-dimethylformamide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DMSO	dimethylsulfoxide
EI	electron ionisation
ES	electrospray
eq.	equivalents
Et	ethyl
FT	Fourier Transform
GC	gas chromatography
HMPA	hexamethylphosphoramide
HPLC	high-performance liquid chromatography
HRMS	high resolution mass spectra
IR	infra red
LDA	lithium diisopropylamide

lit.	literature
LRMS	low resolution mass spectra
M	mol dm^{-3}
Me	methyl
min.	minute
M.P.	melting point
n.O.e	nuclear Overhauser effect
NMR	nuclear magnetic resonance
PCC	pyridinium chlorochromate
Ph	phenyl
ppm	parts per million
r.t.	room temperature
sat.	saturated
SET	single electron transfer
THF	tetrahydrofuran
Ts	*p*-toluenesulfonyl
UV	ultra violet

ACKNOWLEDGEMENTS

Dr. David Harrowven, for continual encouragement, ideas and enthusiasm and a not insignificant amount of proof reading.

Dr. Steven Coulton, for putting up with me for three months and running a never ending supply of elemental analyses.

Prof. John Mellor for reading all my reports and providing many helpful suggestions.

Joan Street, John Langley, Mike Hursthouse, Julie Herniman, Neil Wells, Mark Light and Simon Coles for their spectroscopic services.

The Engineering and Physical Sciences Research Council and GlaxoSmithKline for financial support.

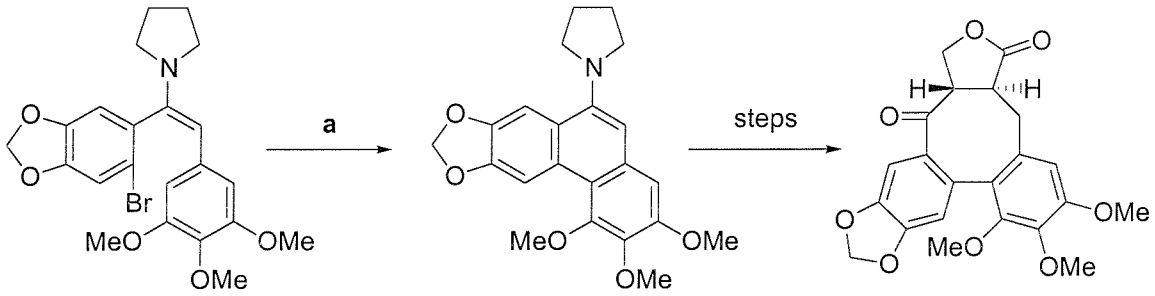
And finally, the Harrowven Group, past and present, and all my friends and family, especially Mum, Dad and Joe.

CHAPTER 1

RADICAL ADDITIONS TO NITROGEN CONTAINING HETEROAROMATICS

1.1 RADICAL CYCLISATIONS

Radical cyclisation reactions proceed under mild, neutral conditions, often with high chemo-, regio- and stereoselectivity and are tolerant of many functional groups.[1] The high reactivity of a carbon centred radical means formation of carbon-carbon bonds through radical additions to alkenes, alkynes and aromatics are commonplace.[2,3] Indeed even sterically hindered carbon-carbon bonds may be formed in this way as radical intermediates have no solvation sphere or counter ion. Nowhere have these attributes of the radical been more widely exploited than in natural product and target orientated synthesis.[3-5] An example of this is Narasimhan's formal total synthesis of steganone **3**,[6,7] an antileukaemic lignan[8,9] isolated from *Steganotaenia araliacea* Hoechst (Scheme 1).[9] The homolysis of the carbon-bromine bond followed by intramolecular attack of the aryl radical onto a second aromatic ring is of great interest.

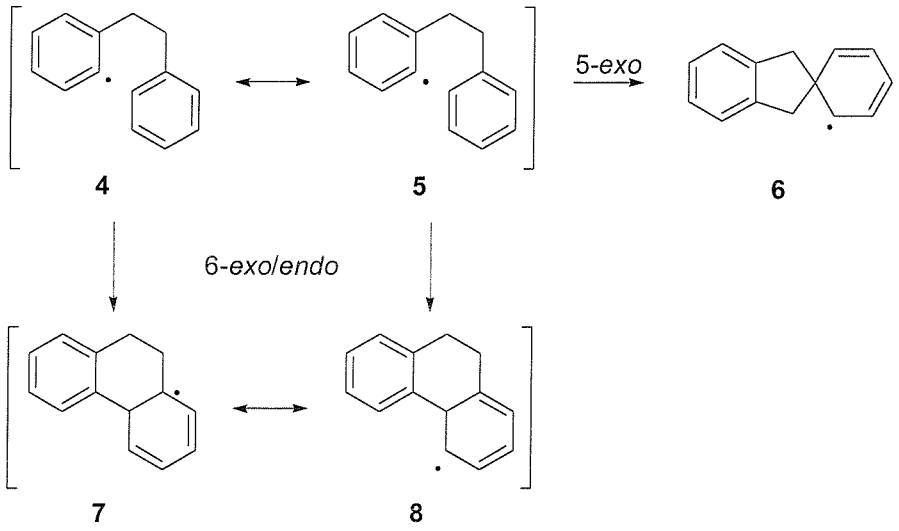


1 **2** **3**

a. Bu_3SnH, AIBN, PhH, 66 %.

Scheme 1

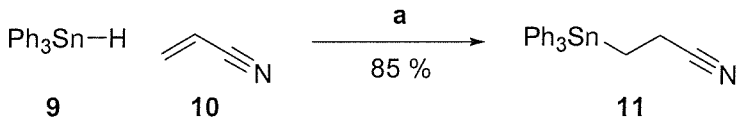
It is the attack of an aryl radical onto a nitrogen containing heteroaromatic that is the basis of this review. The vast majority of radical cyclisations onto a benzene ring involve 5-*exo* (*ipso*) or 6-*exo*/*endo* (*ortho*) ring closure (Scheme 2).



Scheme 2

1.2 ORGANOTIN HYDRIDES

The realisation that organotin hydrides are very efficient mediators of radical reactions led to their widespread adoption in mainstream organic chemistry. First synthesised by van der Kerk in 1957,[10] tri-*n*-butyltin hydride was formed by reduction of tri-*n*-butyltin chloride with lithium aluminium hydride in diethyl ether. In the preceding paper van der Kerk[11] also noted the addition of several organotin hydrides to double bond systems, although he discounted the involvement of free radicals as no peroxides were required to initiate such processes (Scheme 3). However with hindsight it is possible that trace peroxides arising from aerial oxidation were present in the reaction mixture as this would explain the apparent self-initiation of the addition process.



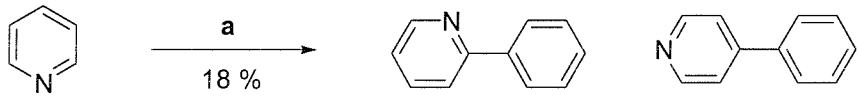
a. 80 °C, neat.

Scheme 3

A review by Kuivila 11 years later highlighted all the major advances in organotin hydride mediated radical reactions that have occurred in modern times,[12] with the reduction of alkyl and aryl halides,[11] hydrostannation,[11] and cyclisation reactions dominating the discussion.

1.3 Early Intermolecular Radical Additions to Pyridines and Quinolines

Interest in radical additions to nitrogen containing heteroaromatics precedes the emergence of organotin mediated pathways. The first radical addition to pyridine reported was by Mohlau and Berger in 1893.[13] They heated benzene diazonium chloride in pyridine to form the phenyl radical and observed the formation of 2-phenylpyridine **13** in 18 % yield together with a trace of 4-phenylpyridine **14**. Overhoff and Tilman confirmed this result in 1929,[14] when they heated dibenzoyl peroxide in pyridine and also observed the formation of **13** and **14** in 18 % yield based on dibenzoyl peroxide, 4 % yield based on pyridine (Scheme 4). Interestingly they noted a 2 : 1 ratio of **13** : **14**, showing the preference for radical addition to C-2 of a pyridine over C-4. Notably, no 3-phenylpyridine was observed in either of these experiments.



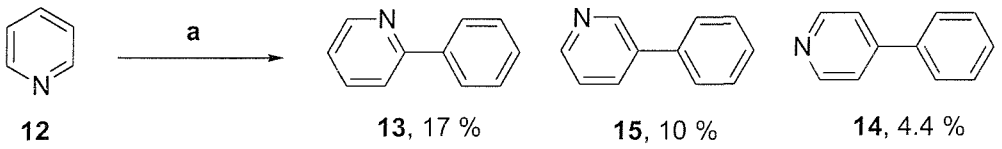
12 **13** **14**

a. dibenzoyl peroxide, Δ

Scheme 4

This work was followed up by Wieland who, in 1934, reported that phenyl radicals could be produced by heating phenylazotriphenylmethane in pyridine.[15] Once again 2- and 4-phenylpyridine, **13** and **14**, were given as products. Next, Hey and Walker examined the reaction of dibenzoyl peroxide and quinoline and observed the formation of 4- and 5-phenylquinoline in a yield of less than 2 % (Scheme 5).[16] Indeed this was so pitiful that they didn't pursue the reaction any further. They did, however, repeat the work of Overhoff and Tilman[14] and using an ultraviolet spectroscopic technique on the

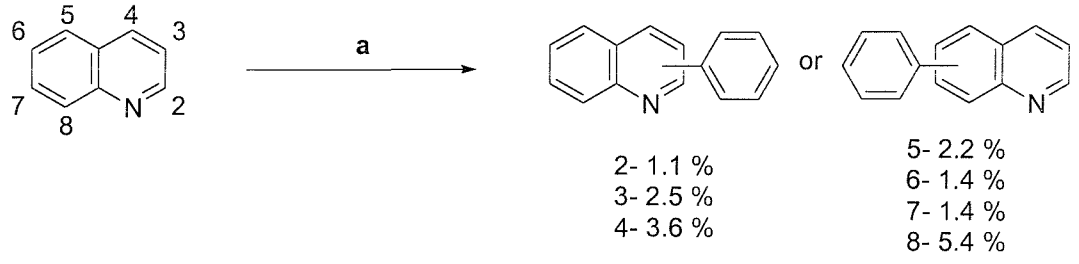
crude mixture of isomers they were able to calculate the ratio of 2-, 3- and 4-phenylpyridine formed in the reaction (Scheme 5).[17]



a. dibenzoyl peroxide, Δ

Scheme 5

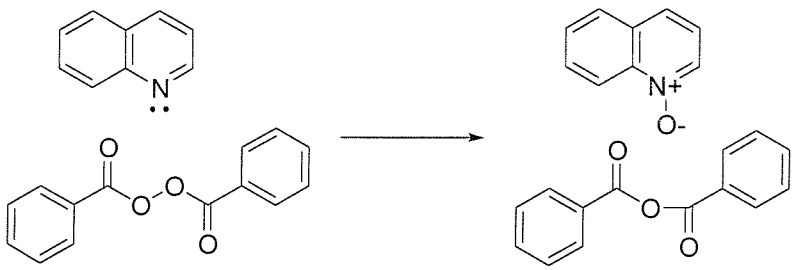
These results show that the 2 position of pyridine is most easily attacked by the phenyl radical with addition to the 3- and 4- positions occurring to a much lesser extent. In 1958 Pausacker[18] re-examined the thermal decomposition of dibenzoyl peroxide in quinoline and observed the addition of the phenyl radical to all 7 carbon centres. 8-Phenylquinoline was the major product of the reaction but the low yield and lack of selectivity limited its synthetic utility (Scheme 6).



a. dibenzoyl peroxide, Δ

Scheme 6

Pausacker made no mention of products containing two or more phenyl groups, possibly because his technique for determining the product ratios by a mixture of chromatography and mixed melting point determination would not allow for this extra complication. He did, however, give a reasoned argument that the low yields observed result from the oxidation of quinoline by dibenzoyl peroxide (Scheme 7).



Scheme 7

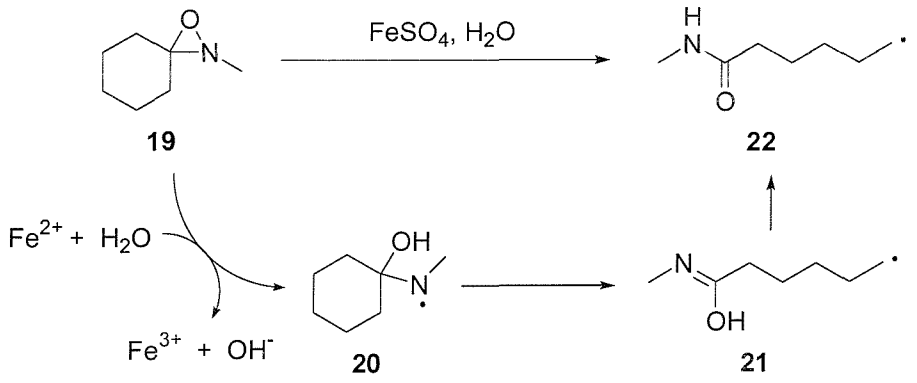
This might explain why 8-phenylquinoline is the major product as the nitrogen lone pair is blocked from oxidation by the phenyl group. As a result it will be more resistant to oxidation in the presence of dibenzoyl peroxide.

At this point interest in radical additions to pyridines and quinolines was starting to waver. They were low yielding, unselective and wasteful, often being carried out in a large excess of neat pyridine or quinoline. A decade passed until Dou and Lynch renewed interest in the field with the publication of results carried out in acidic medium.[19] Their reactions were still carried out in a large excess of pyridine, quinoline and for the first time isoquinoline but the addition of stoichiometric acetic acid meant that dibenzoyl peroxide could not oxidise the ring bound nitrogen. A yield of 35 % of a mixture of 2-, 3- and 4-phenylpyridine was reported with the bulk of the material substituted in the 2 position. Vernin, Dou and Metzger also successfully compared the position of substitution in quinoline under both acidic and neutral conditions.[20] Their neutral results were broadly inline with those of Pausacker and their results from acidic medium showed 88 % of phenyl substitution was in the 2 (35 %), 4 (38 %) and 8 (13 %) positions.[18] This dramatic increase in selectivity allowed an academic curiosity to become an important tool for heteroaromatic substitution.

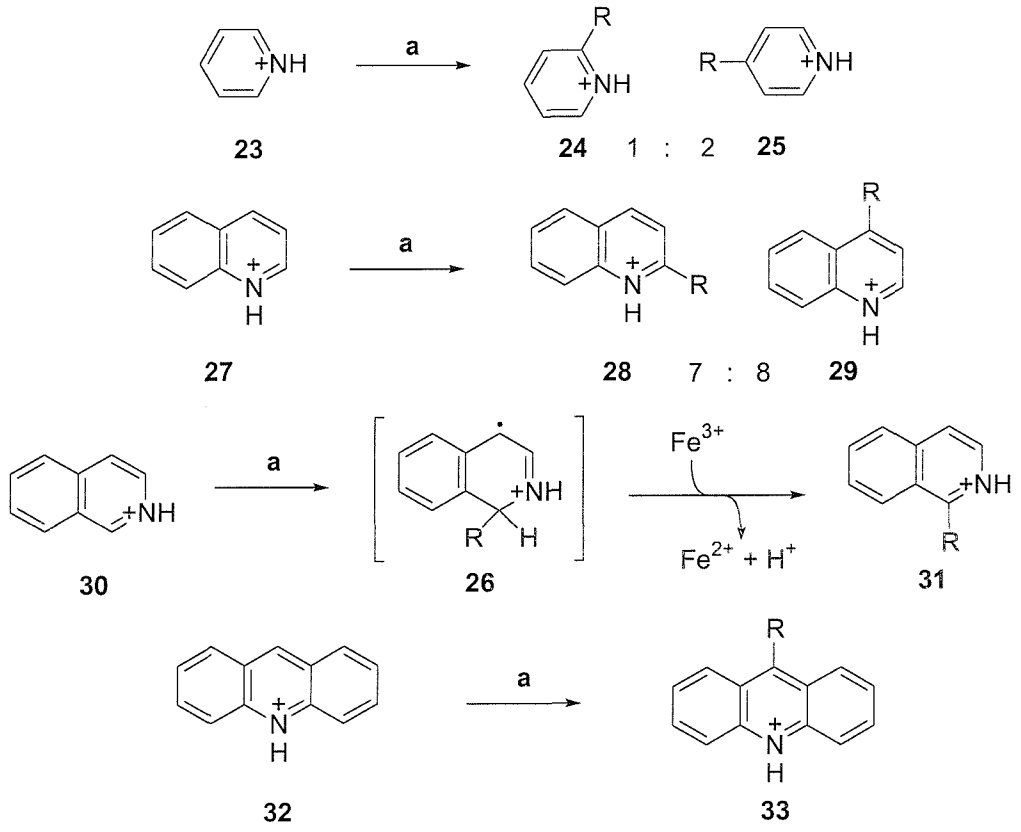
1.4 MINISCI'S CONTRIBUTIONS TO THE AREA[21,22]

It was at this time that Francesco Minisci published his first work in this fledgling area.[23] By protonating his substrates he was able to conduct radical additions in water with the reactions occurring up to 100 times faster than those of the unprotonated heterocycle.[22] The inclusion of a solvent immediately increased the mass balance of products and made the reaction synthetically useful. Also, by choosing to use

'nucleophilic' alkyl radicals rather than aryl radicals, he was able to selectively substitute at electron deficient carbon atoms in a ring system, leading to far fewer products (Schemes 8 and 9).



Scheme 8



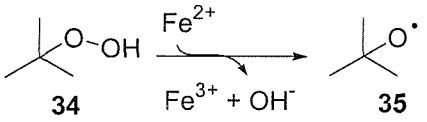
a. **19**, cat. $FeSO_4$, H_2O, R = $(CH_2)_5CONHCH_3$.

Scheme 9

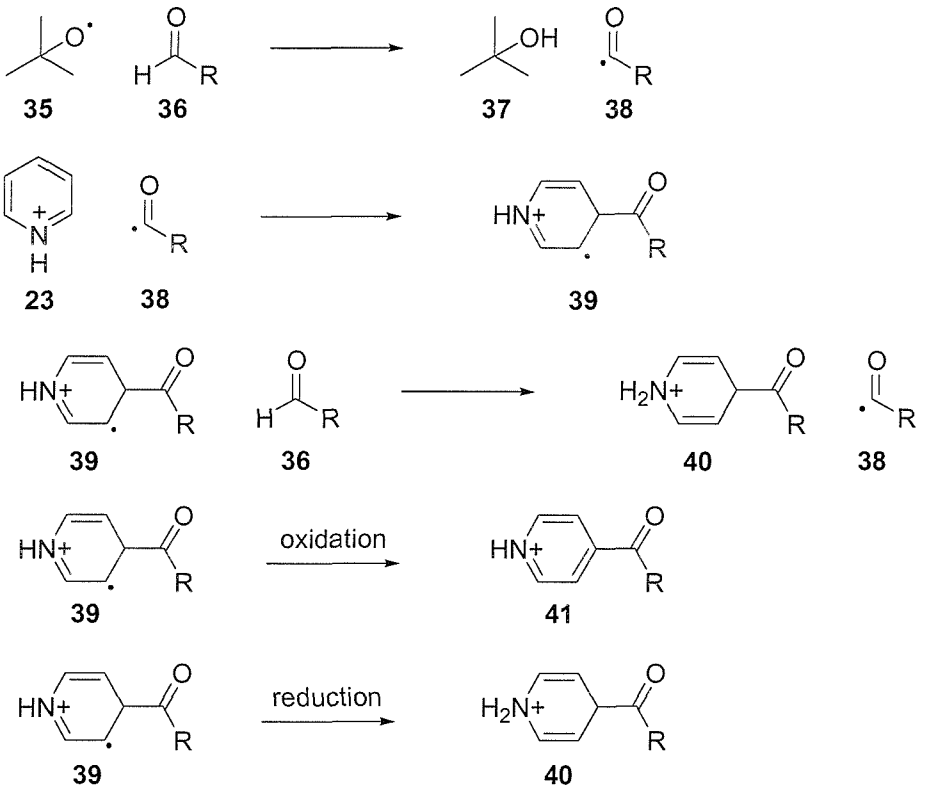
Minisci chose to generate radicals by reduction with ferrous sulfate (Scheme 8). The ferric ion produced then oxidises the addition product **26**, rearomatises the substituted ring and regenerates ferrous sulfate (Scheme 9). By limiting the amount of ferrous sulfate in solution the concentration of radicals was kept low minimising dimerisation and other unwanted side reactions.

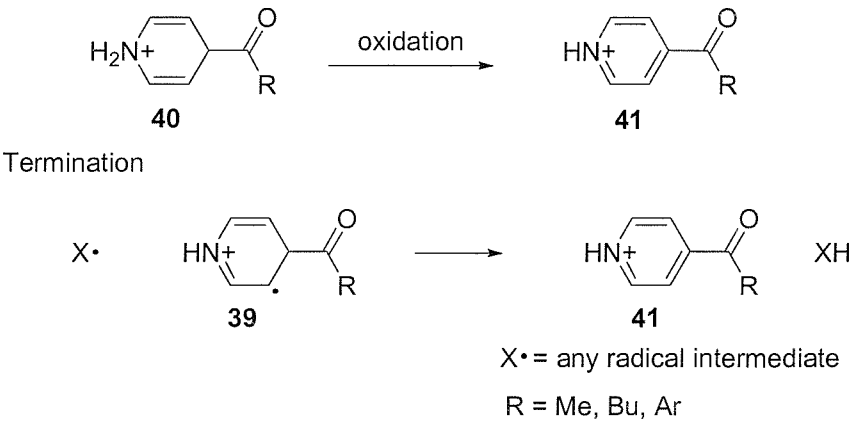
Acyl radical formation by hydrogen atom abstraction from an aldehyde led Minisci to investigate the acylation of pyridines and related heteroaromatics under acidic conditions (Scheme 10).[24-26] This was of synthetic value as high yields were obtained when substrates containing electron-withdrawing substituents were used which is, of course, the converse of Friedel-Crafts chemistry. Once again high selectivity was shown to positions α or γ to the nitrogen atom.

Initiation



Propagation





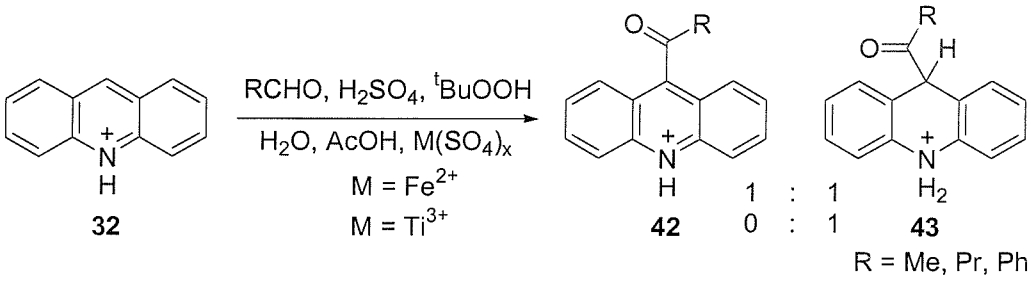
Scheme 10

It is worth noting that the oxidations and reductions could not be classed as termination steps as they involve transitions between ferrous and ferric ions and hence continuation of the chain. The termination step could be disproportionation of two molecules of **39** to **40** and **41**.

The results showed that with a four fold excess of aldehyde, quinoline could be diacetylated in 70 % yield. This highlights the major drawback of the technique. Once a ring system has been acetylated the ring becomes more electron deficient and, if there is another site available α or γ to the nitrogen atom, then the diacetylated product is formed. The monoacetylated product may be formed, but only with a large excess of the heteroaromatic compared to the acyl radical. Minisci concentrated his work on acylation of 2 and 4 substituted quinolines. With the acyl radical blocked from attacking one site by an electron withdrawing group such as chloro, cyano or carboxy function, yields were moderate to high (41 % to 90 %). He did illustrate one way to get around the problem of diacetylation by taking advantage of a change in the pKa of the monoacylated product arising from the acylation of 4-cyanopyridine. Once the ring has been acetylated in the 2 position it loses its proton and precipitates from solution before a second acyl group can be added.

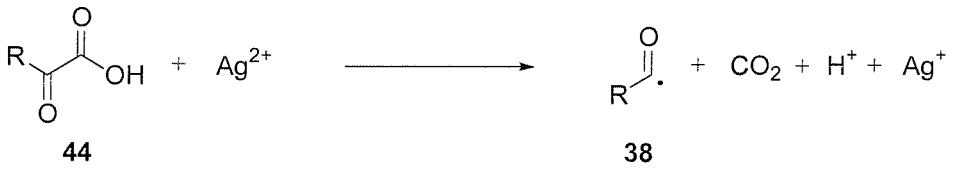
Acridine acetylated in the 9 position, as expected, but both the dihydroacridine **43** and the fully aromatic product **42** were formed in a 1 : 1 ratio. When Minisci switched to Ti^{3+}, a metal more reducing than Fe^{2+}, only the former product **43** was recovered. This

suggests that there is much less of a driving force for the rearomatisation of the middle ring of acridine than for pyridines and quinolines (Scheme 11).



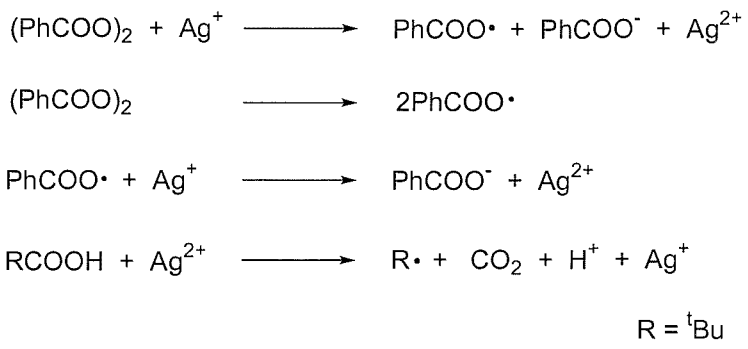
Scheme 11

As well as aldehydes, α-keto-acids can also form acyl radicals *via* silver(II) mediated decarboxylation. These acyl radicals behave in the same manner as those formed from aldehydes (Scheme 12).



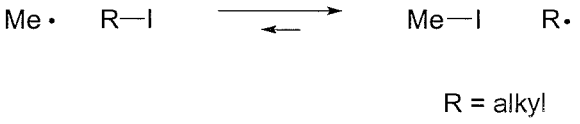
Scheme 12

The use of silver(II) salts as oxidising agents didn't stop here. We have seen that when dibenzoyl peroxide is decomposed in the presence of a heteroaromatic base phenylation occurs (Schemes 4, 5, 6). If catalytic silver nitrate and a carboxylic acid are also present an alkyl radical can be formed by loss of CO_2 and the peroxides role changes from radical source to oxidising agent (Scheme 13).[27] This alkyl radical can now attack the heteroaromatic base and following further oxidation by either peroxide or the silver(II) species the alkylated product is recovered.

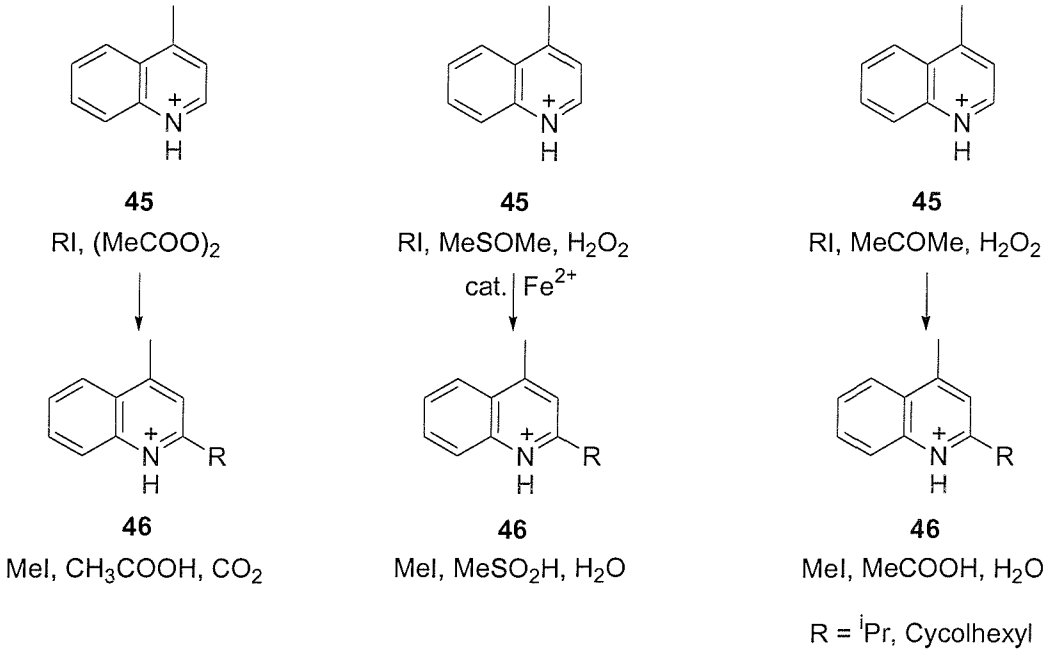


Scheme 13

Minisci's most general method for alkylation was presented in 1984.[28] This neatly used the weakness of the C-I bond to generate alkyl radicals. Initiation was *via* decomposition of an aryl peroxide or diazonium salt and the generated aryl radical abstracts an iodine atom from the alkyl iodide. This had several initial drawbacks such as the reactivity of arylcarboxy radicals ($ArCOO^{\cdot}$) towards substrates and the problem of addition of nucleophilic radicals to the diazonium group.[29] All these were overcome by the use of a methyl radical to abstract the iodine atom from the aryl iodide.[30] Methylcarboxy radicals decarboxylate much more readily than arylcarboxy radicals so addition of this intermediate to the substrate is not observed. The high energy of the methyl radical causes its equilibrium with other alkyl iodides to be far to the right and hence little or no methyl addition to the heteroaromatic base is seen (Scheme 14). Several methods were used by Minisci to generate methyl radicals which all add to the versatility of this procedure (Scheme 15).

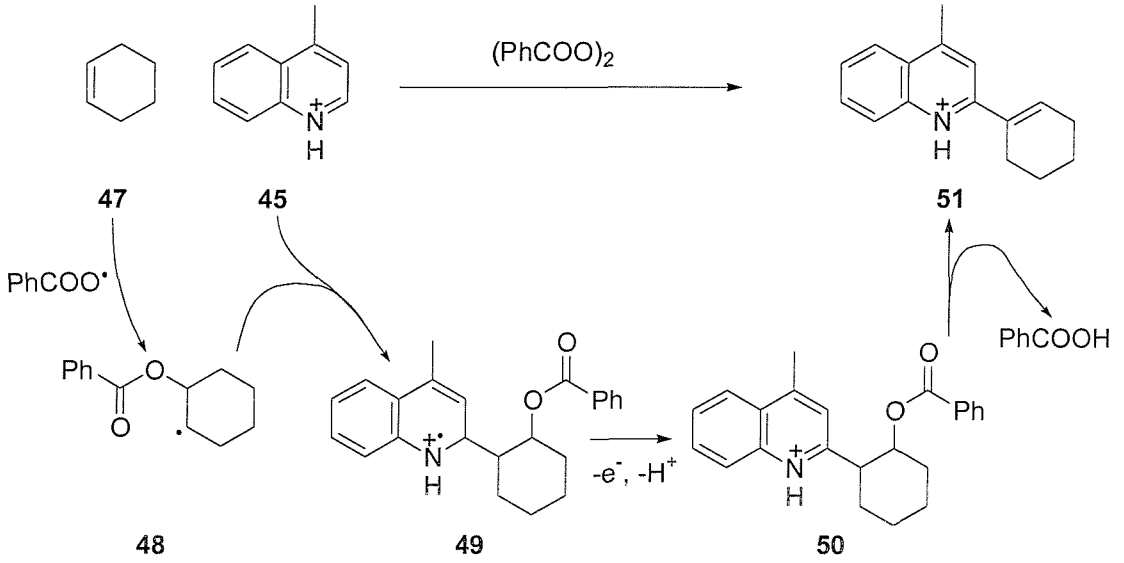


Scheme 14



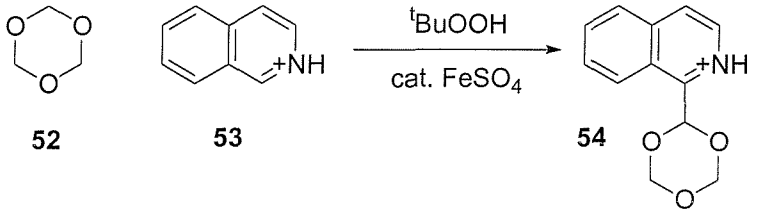
Scheme 14

Vinyl groups can also be added to a heteroaromatic base in radical fashion.[31] Firstly an electrophilic peroxide radical adds to the vinyl group, then the nucleophilic radical thus generated attacks the protonated heteroaromatic base. Further oxidation followed by elimination of the acetyl group reforms the vinyl moiety (Scheme 15).



Scheme 15

The formylation of a heteroaromatic with trioxane provides a further example of the practical uses of Minisci's radical chemsitry.[32] Indeed the example given was used by this author to form an important aldehyde precursor. Hydroxy or butoxy radicals are unselective when abstracting hydrogen atoms from saturated cyclic ethers such as THF. When a system like trioxane is used there is effectively only one type of C-H bond present and hence only one 'nucleophilic' radical is formed. In the presence of catalytic ferric salts these radicals can add to a heteroaromatic base and rearomatise to give a masked aldehyde (Scheme 16).

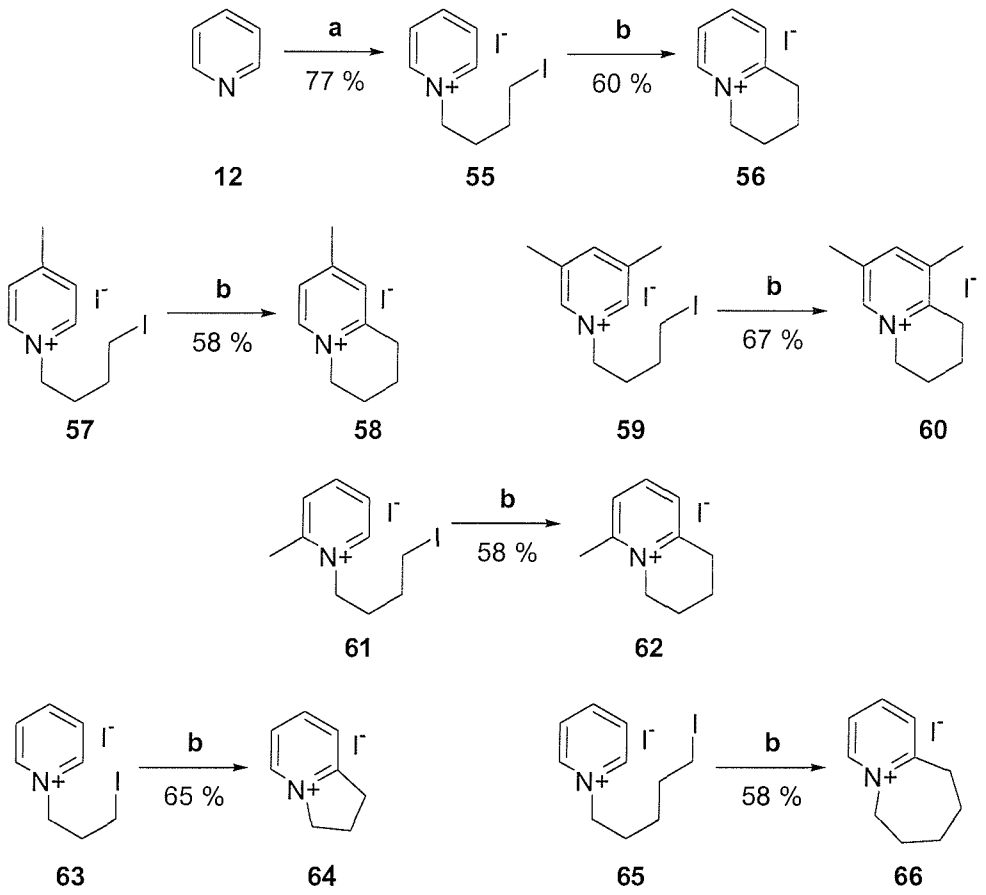


52 53 54

Scheme 16

1.5 MURPHY AND SHERBURN'S INTRAMOLECULAR WORK

It was not until 1989 that an intramolecular radical addition to a pyridine base was carried out.[33,34] This was a logical extension to Minisci's work and had several inherent advantages. Firstly the radical formed was in close proximity to the ring it was required to attack and so intermolecular side reactions like polymerisation, dimerisation and attack of the solvent were less likely to occur. Secondly, and more importantly, the radical can only add to proximal carbon centres thereby controlling the position of attack on the ring. By conducting reactions in an organic solvent, it was also possible to employ the more efficient organotin hydride methodology, rather than rely upon the decomposition of a peroxide, diazonium salt or azide. Formation of the radical precursor was accomplished by condensation of an excess of a diiodoalkane with the desired pyridine. An excess of diiodoalkane was used to minimise the production of bis-pyridine adducts. By using varying chain lengths 5, 6 and 7 membered rings were formed in high yield from radical addition to C-2 or C-6 of the pyridine (Scheme 17).



a. 1,4-diiodobutane, acetonitrile, Δ;

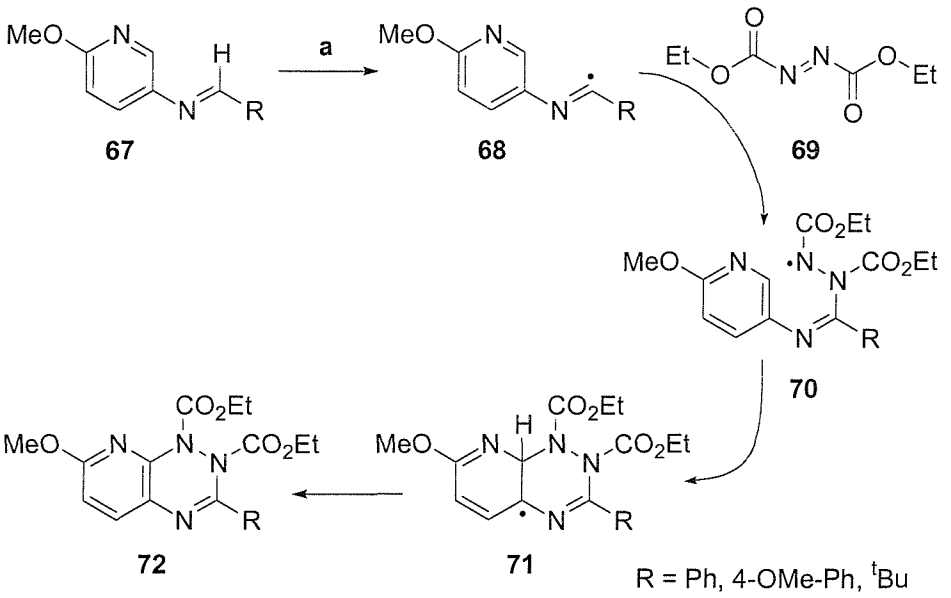
b. tri-*n*-butyltin hydride, AIBN, acetonitrile / THF, Δ.

Scheme 17

However Murphy and Sherburn's radical additions to pyridine bases were not the first intramolecular radical additions to pyridines. One year earlier Nanni and his co-workers had demonstrated that neutral pyridines could also be attacked selectively in an intramolecular fashon.[35]

1.6 Intramolecular Additions to Pyridine Based Heterocycles

Nanni was demonstrating an intermolecular attack of a radical onto an azo moiety. The nitrogen centred radical could then attack a co-joined pyridine in an intramolecular fashion, forming several complex condensed nitrogen heterocyclic derivatives (Scheme 18).[35]



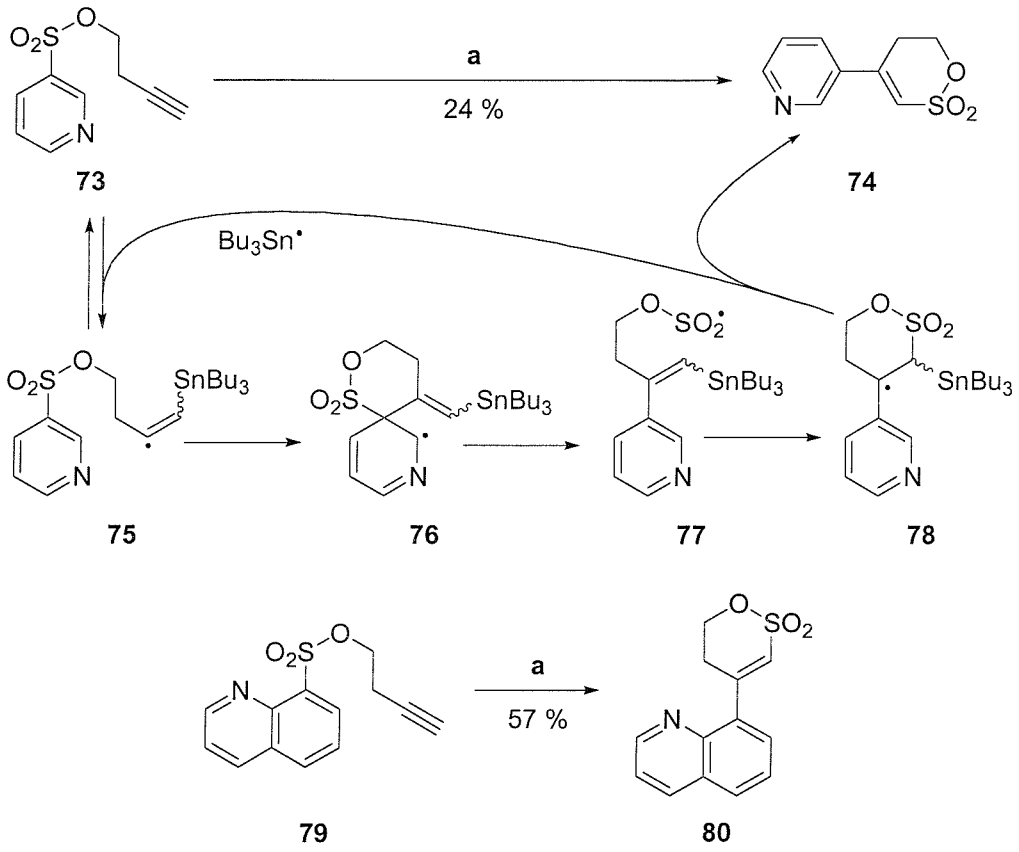
a. di-isopropyl peroxydicarbonate, benzene, **69**, Δ.

Scheme 18

It is worth noticing that the radical centred on nitrogen adds to the pyridine in a 6-*exo*/*endo*-trig fashion rather than following a 5-*exo*-trig cyclisation pathway which is also possible. Again an aromatic product is formed rather than a dihydropyridine.

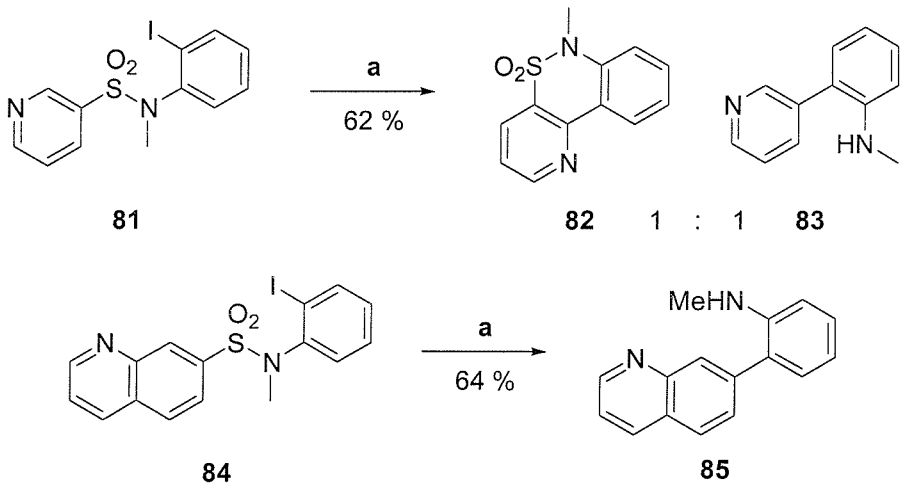
In 1992, Motherwell reported a new method of carbon-carbon bond formation by free radical *ipso* substitution.[36-39] Tethering a radical precursor to a pyridine or a quinoline *via* a sulfonate tether promoted *ipso* substitution and elimination to generate **77**. A second cyclisation and elimination then gave **74** in 24 % yield (Scheme 19).[36]

Motherwell showed that alkynes and aryl iodides were effective as radical precursors.[38] In the latter case, *e.g.* **81**, a mixture of products arising from *ipso* and *ortho* cyclisation were given when pyridine was the heterocyclic radical acceptor, whereas with quinoline, **84**, only the product derived from *ipso* attack, **85**, was recovered (Scheme 20).



a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

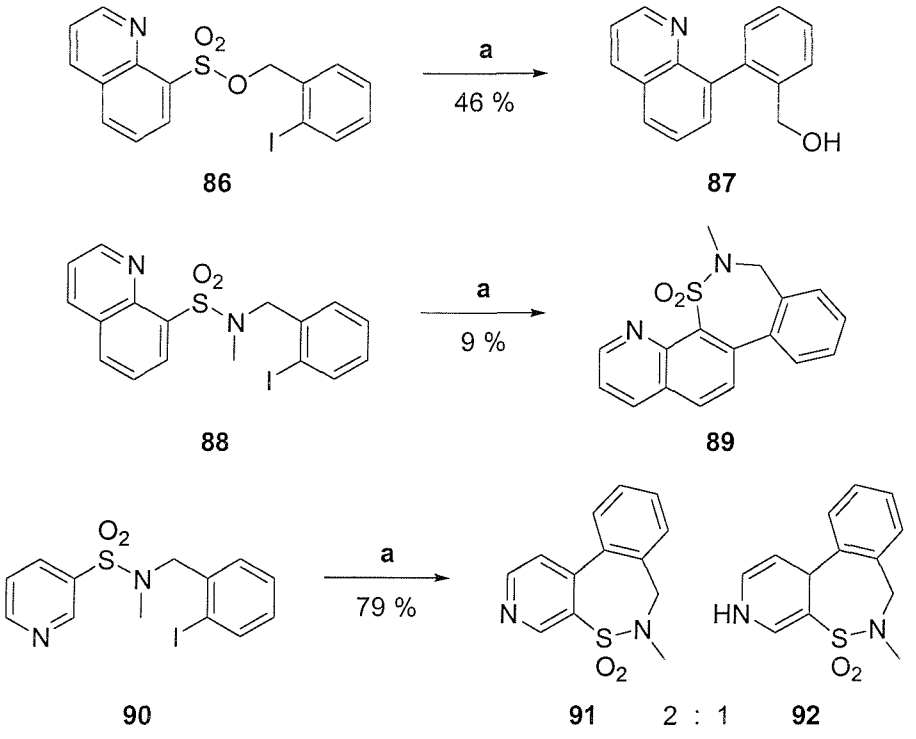
Scheme 19



a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 20

The length and nature of the tether was shown to influence the mode of cyclisation in these systems. Quinoline sulfonate, **86**, underwent *ipso* substitution *via* a 6-*exo*-trig cyclisation. Quinoline sulfonamide, **88**, underwent *ortho* substitution *via* a 7-*exo*-trig cyclisation, albeit in low yield. With pyridyl substituted sulfonamide, **90**, both the dihydropyridine **92** and pyridine **91** were recovered, following *ortho* substitution (Scheme 21).

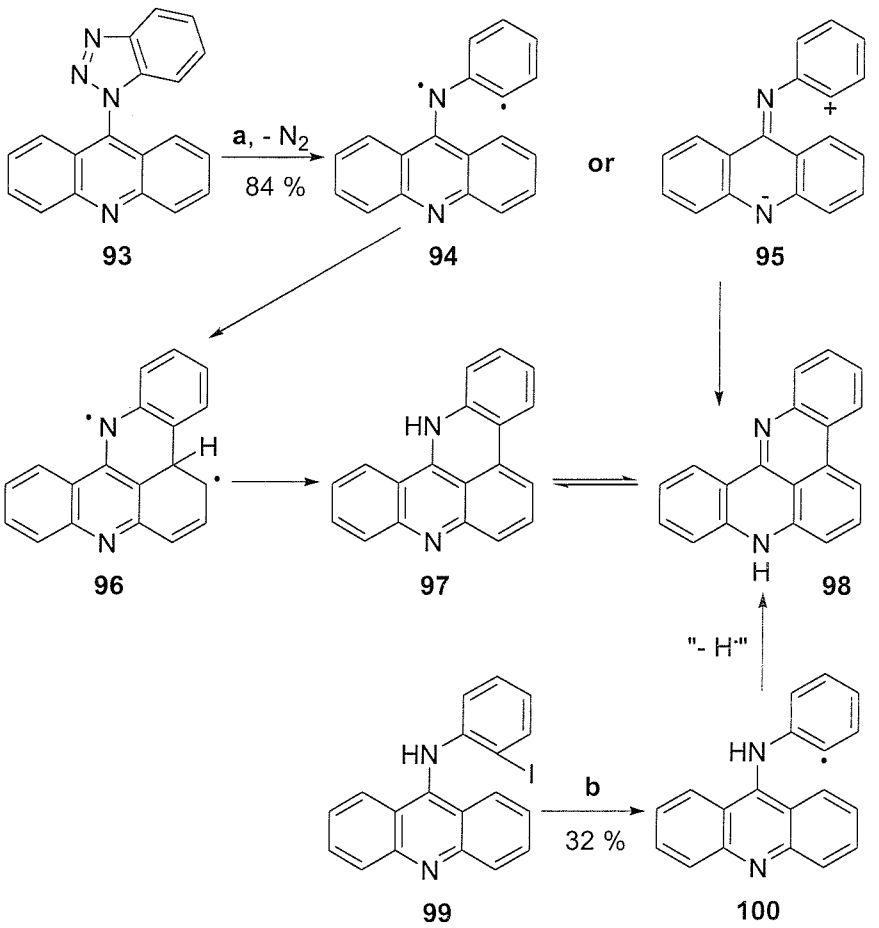


86 **87** **88** **89** **90** **91** **92**

a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 21

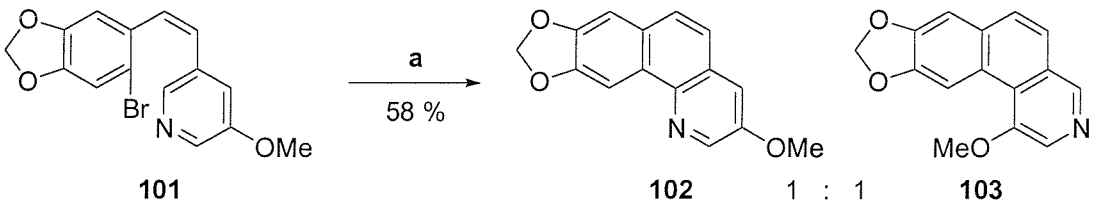
More recently Stevens *et al.*[40] prepared a series of polycyclic acridines using the known thermal rearrangement of **93** to the pentacycle **97** / **98**.[41] Stevens suggested that this too was as result of radical addition, a theory reinforced when aryl iodide **99** was transformed into **97** / **98** on treatment with tributyltin hydride under radical forming conditions (Scheme 22).



a. diphenyl ether, Δ; **b**. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 22

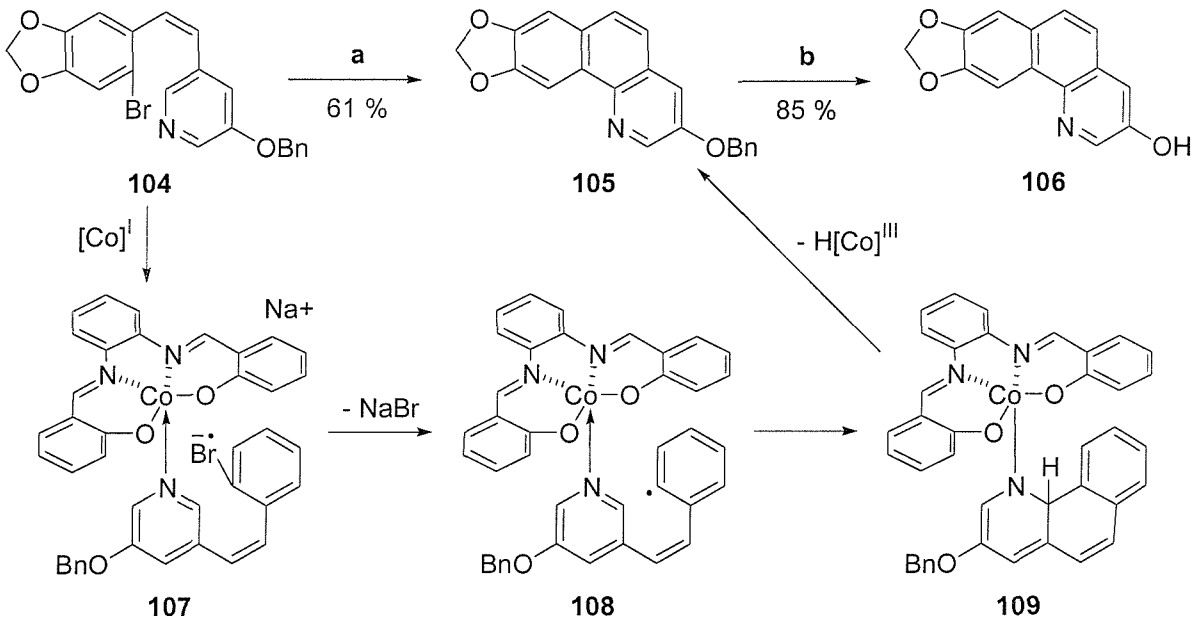
Harrowven and Nunn's total synthesis of toddaquinoline **106**, an alkaloid from the root of Formosan *Toddalia asiatica*, used the addition of an aryl radical to a pyridine as a key step (Scheme 23).[42-44]



a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 23

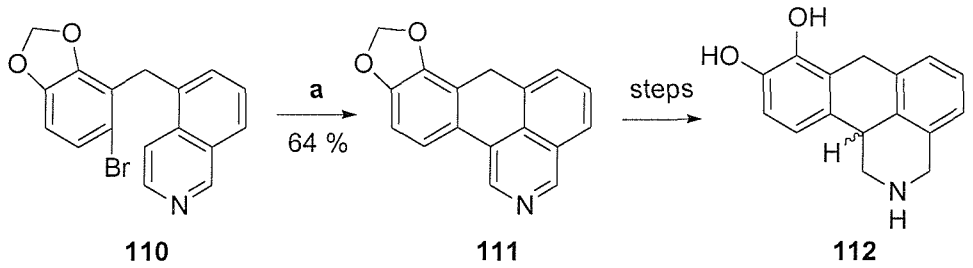
Notably, they found that tin mediated radical cyclisation of **101** gave a 1 : 1 mixture of regioisomeric products **102** and **103**. However conducting the reaction with cobalt(I) salophen gave toddaquinoline benzyl ether **105**, from **104** exclusively (Scheme 24).



a. NaCo(I)salophen, THF; **b**. H_2, Pd-C.

Scheme 24

Most recently Sit and his co-workers at Bristol-Myers Squibb have used a radical addition to an isoquinoline in a large scale synthesis of the dopamine agonist (+)-dinapsoline **112** (Scheme 25).[45]

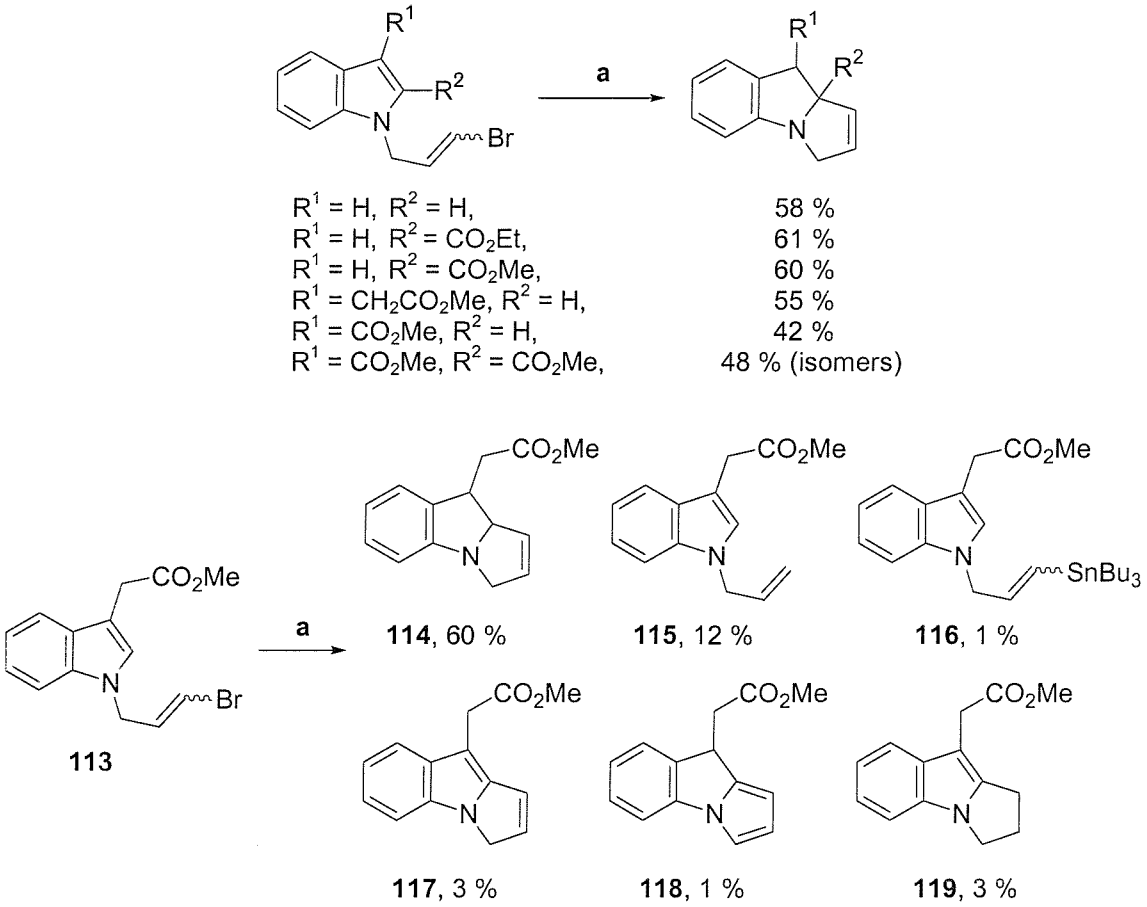


a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 25

1.7 INTRAMOLECULAR ADDITIONS TO INDOLES

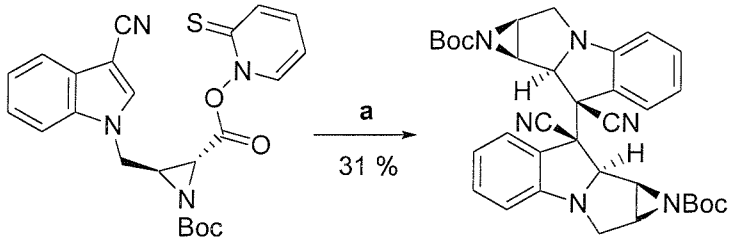
Studies on intramolecular radical additions to indoles are better developed. Zeigler was the first to study the cyclisation of radical intermediates attached to an indole *via* an *N*-linked tether.[46,47] Products arising from 5-*exo*-trig cyclisation to C-2 of the indole, followed by hydrogen atom extraction from tri-*n*-butyltin hydride, were generally formed in modest to good yield (Scheme 26). Zeigler also looked at the trace products formed during the cyclisation of indole **113**. As well as the cyclisation product **114** and reduced product **115** the vinylstannane **116** was recovered together with products arising from oxidation of the dihydropyrroloindole nucleus **117** and **118**. It was not known if oxidation occurred before or after the quenching of any radical intermediates involved. Formation of **119** was unexpected and possibly the result of a rearrangement of **114** (Scheme 26).



a. tri-*n*-butyltin hydride, AIBN, ACN, toluene, Δ.

Scheme 26

Several years later Zeigler looked at forming radical intermediates tethered to indoles from aziridine carboxylates.[47] He was able to effect cyclisation but the major product derived from **120** was **121**, a result of dimerisation of the cyclised radical intermediates (Scheme 27).

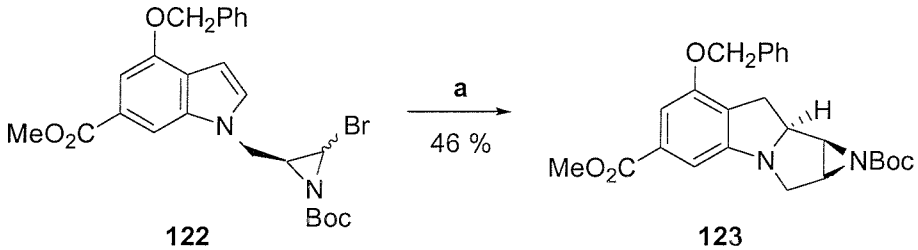


120 **121**

a. dichloromethane, hv.

Scheme 27

This problem was easily overcome by switching from a thiohydroxamate ester to a bromide as the radical precursor.[48] Thus, **122** gave **123** in moderate yield on treatment with tributyltin hydride and AIBN (Scheme 28).

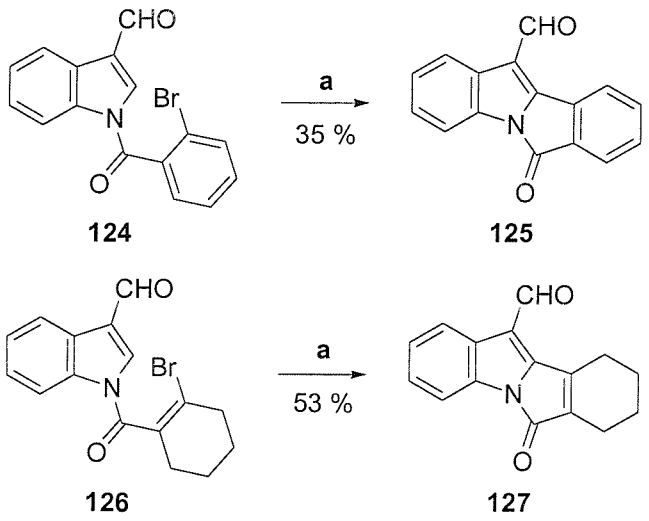


122 **123**

a. tri-*n*-butyltin hydride, AIBN, benzene, hv, Δ.

Scheme 28

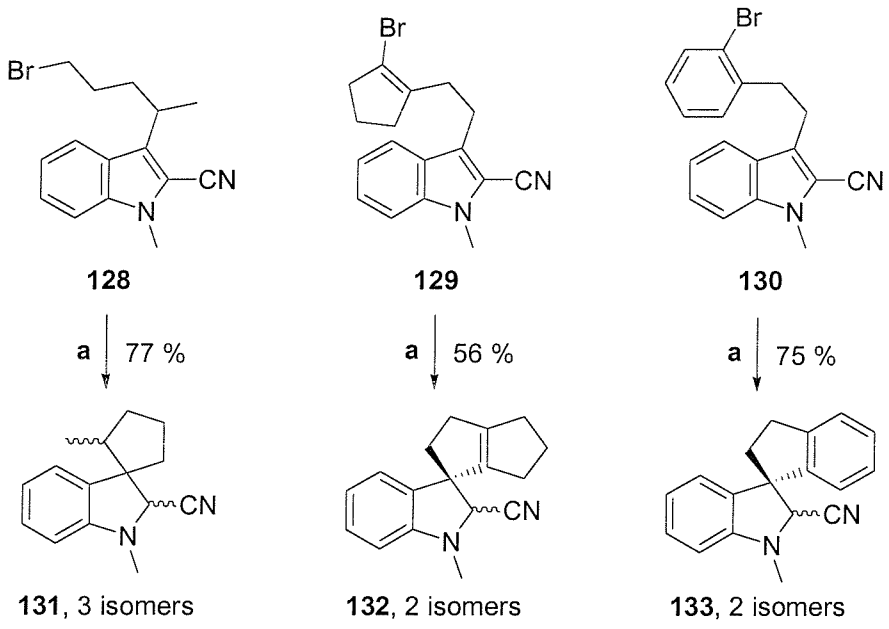
Kraus was next to demonstrate that amides, resulting from *N*-acylation of indoles with 2-bromobenzoic acid, could undergo carbon-bromine bond homolysis and cyclisation. Notably, and in contrast to Zeigler's study, aromatic products were formed rather than the dihydro species. A similar course was also observed with vinyl bromide **126** (Scheme 29).[49]



a. tri-*n*-butyltin hydride, AIBN, benzene, hν, Δ.

Scheme 29

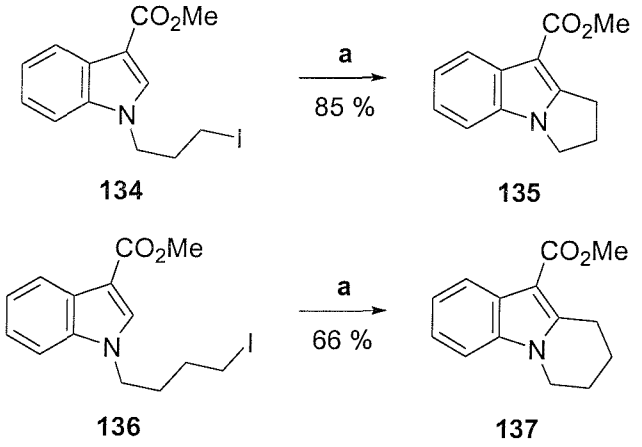
Fang and his co-workers were able to demonstrate intramolecular radical addition to C-3 of an indole *via ipso* attack.[50] By varying the nature of tether a wide range of products were available in high yield by this method (Scheme 30).



a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 30

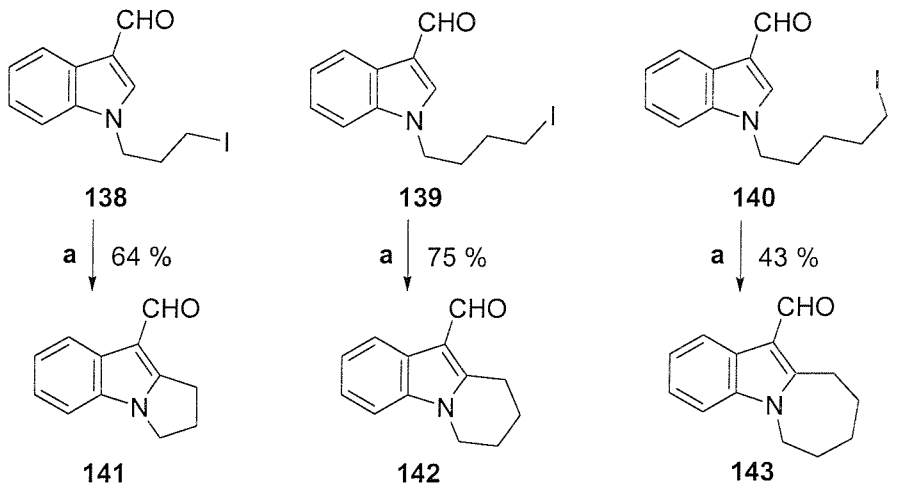
Shortly after Muchowski showed that the addition of alkyl radical intermediates to C-2 of an indole was also facile.[51] Good yields were obtained for 5- and 6-*exo*-trig cyclisations and various groups were tethered in the C-3 position (Scheme 31). Reactions were effected using a catalytic ferric / ferrous sulfate system in which the formation of methyl radicals from DMSO mediates the reaction (Scheme 14).



a. H_2O_2, 0.3 eq. $FeSO_4$, DMSO.

Scheme 31

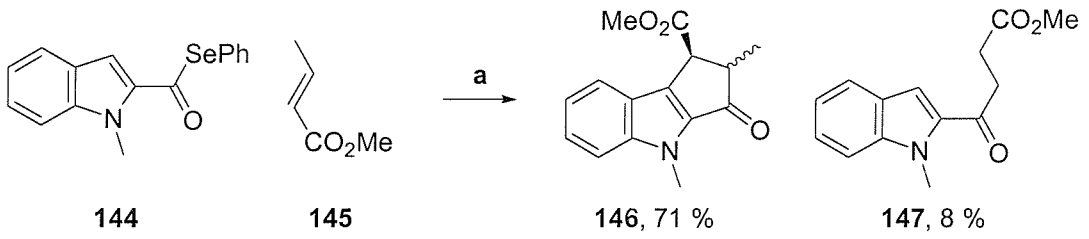
Moody was able to show that in many cases such reactions could be mediated by the tri-*n*-butyltin radical.[52,53] Yields were good for both 5- and 6-*exo*-trig cyclisations and even the more difficult 7-*exo*-trig cyclisation could be achieved, albeit in moderate yield (Scheme 32).



a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 32

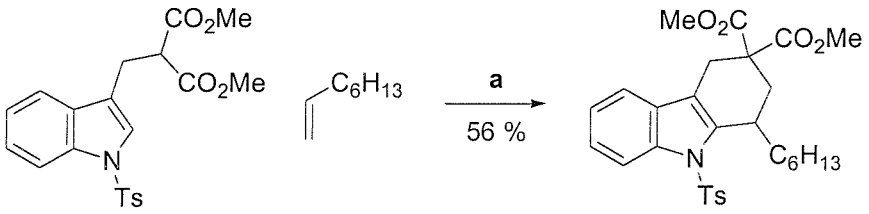
Recently Bennasar *et al.* have reported a cascade sequence in which a radical cyclisation to C-3 of an indole features as a key step.[54] Thus, formation of an acyl radical from selenoester **144** is followed by union with α,β-unsaturated ester **145**. A 5-*endo*-trig cyclisation and loss of a hydrogen atom then gives indole **146**. Yields were high, dependent on the nature of the radical acceptor. With methyl crotonate, **145**, yields obtained were as high as 71 % (Scheme 33).



a. hexa-*n*-butylditin, benzene, hv.

Scheme 33

Earlier Chuang and Wang had effected a similar cascade radical reaction with cyclisation occurring to C-2 of an indole.[55,56] Manganese(III) acetate was used as a mediator in this case and several simple alkenes were employed as acceptors. A typical example is shown in Scheme 34.

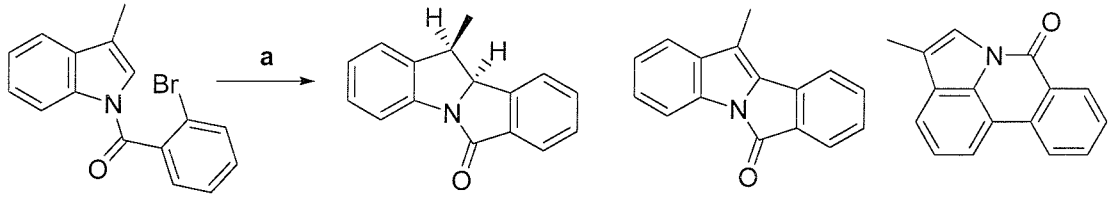


148 **149** **150**

a. $Mn(OAc)_3$, acetic acid.

Scheme 34

An example of radical addition to the arene ring of an indole system was recently reported by Tsuge.[57] Thus, cyclisation of **151** gave **152** as the major product in 83 % yield. Isolation of **154** as a minor by-product confirmed that radical addition to C-7 was also favourable (Scheme 35).



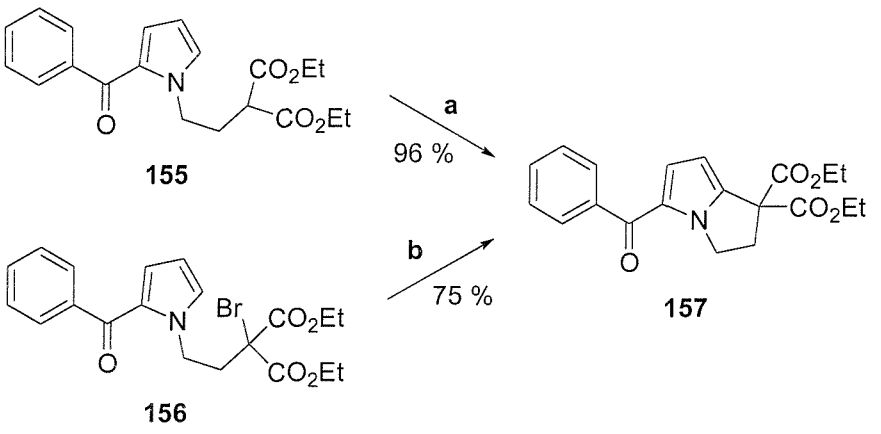
151 **152**, 83 % **153**, 3 % **154**, 8 %

a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 35

1.8 INTRAMOLECULAR ADDITIONS TO PYRROLES

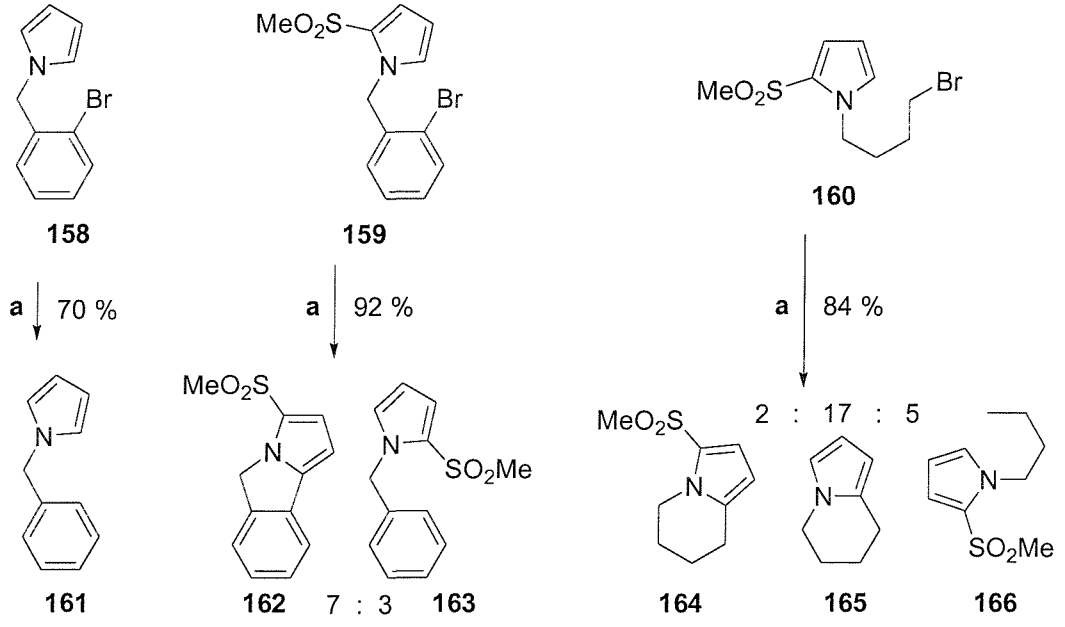
Intramolecular radical additions to pyrroles have received significant attention over the last decade. In 1992, Muchowski and his co-workers showed that pyrroles tethered through nitrogen to a malonate group, *e.g.* **155**, underwent cyclisation when subjected to manganese(III) acetate induced radical formation.[51,58,59] Cyclisation could also be effected by treatment of the analogous bromomalonates, *e.g.* **156**, with triethylborane and molecular oxygen (Scheme 36).



a. $KMnO_4$, NaOAc, $Mn(OAc)_2$, AcOH, Ac_2O; **b**. Et_3B, O_2, hexane.

Scheme 36

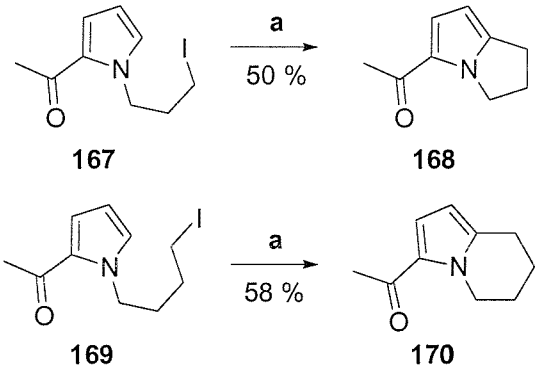
Cyclisation of aryl and alkyl radicals to C-2 were equally effective. In each case C-Br bond homolysis was achieved using the tributyltin radical. Importantly, it was found necessary to include an electron withdrawing substituent on the pyrrole in order to attain satisfactory yields (Scheme 37).



a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 37

Muchowski also explored the use of carbon-iodine bond homolysis by *in situ* generation of methyl radicals. This technique enabled 5- and 6-*exo*-trig cyclisations to be achieved with a flexible alkane tether. Notably the yield of cyclised product attained from the 5-*exo*-trig cyclisation was lower than that attained in the homologous 6-*exo*-trig cyclisation (Scheme 38).

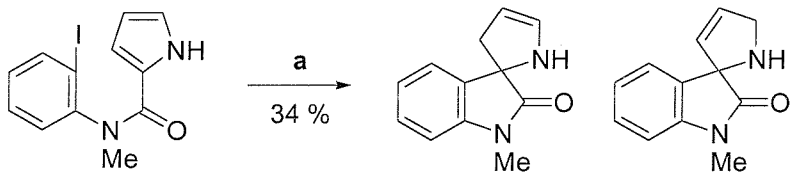


167 **168** **169** **170**

a. H_2O_2, 0.3 eq. $FeSO_4$, DMSO.

Scheme 38

Jones and his group went on to effect spiro cyclisation reactions to C-2 of a pyrrole. The products formed from **171** resulted from radical cyclisation and hydrogen atom quench by tri-*n*-butyltin hydride at C-3 (**172**) or C-5 (**173**) (Scheme 39).[60-62]



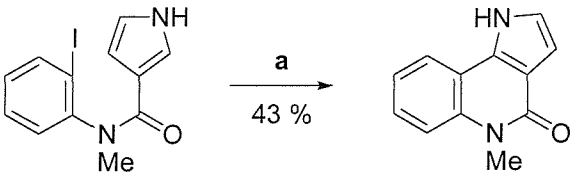
171 **172** **173**

a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 39

Interestingly the analogous C-3 substituted pyrrole, **174**, underwent 6-*endo*-trig cyclisation to C-2 with rearomatisation in moderate yield. This highlights the preference of radical attack to C-2 over C-3 of pyrrole (Scheme 40). Though several

examples of cyclisation to C-3 were reported, yields were low and products that occurred from addition to C-2 were always dominant.

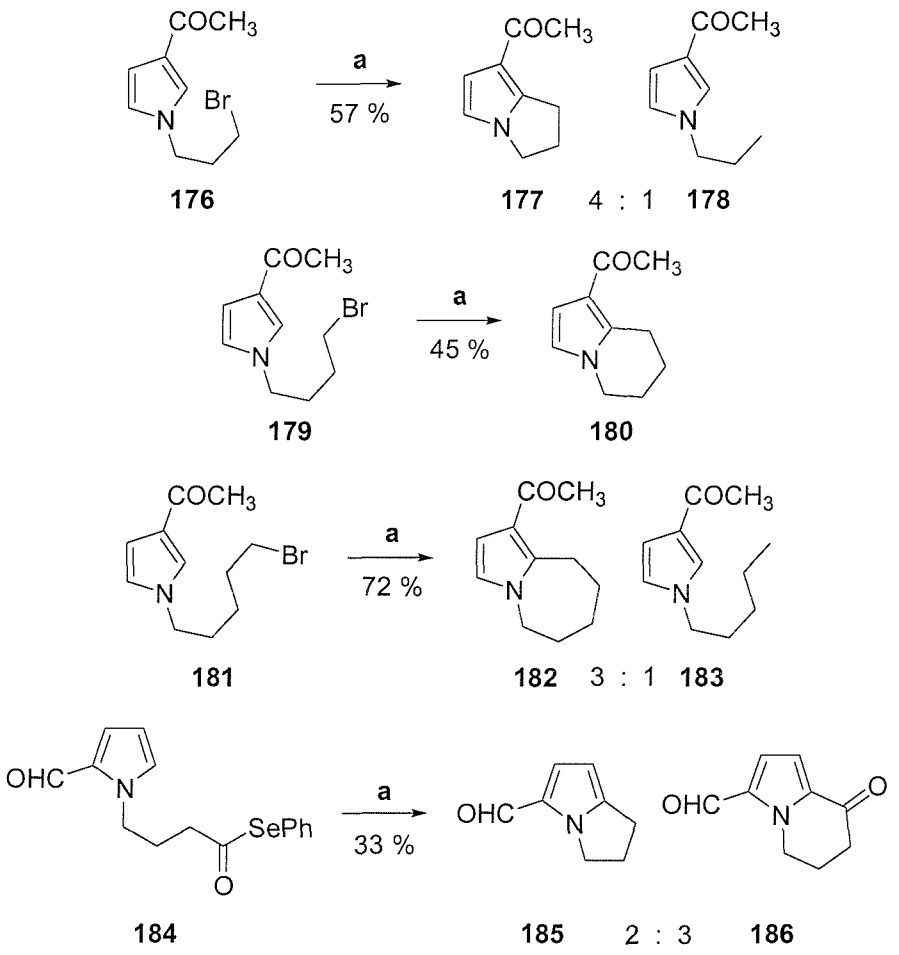


174 **175**

a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 40

Most recently Bowman *et al.* have shown that 5-, 6- and 7-*exo*-trig cyclisations to C-2 of a pyrrole are all facile processes.[63-65] Radicals were formed by carbon-bromine bond homolysis and no products arising from radical addition to C-3 were observed. Acyl radicals formed from selenoesters also underwent cyclisation to C-2 of pyrrole, albeit in low yield. Decarbonylation of the acyl radical competed with cyclisation rendering such processes less useful synthetically (Scheme 41).

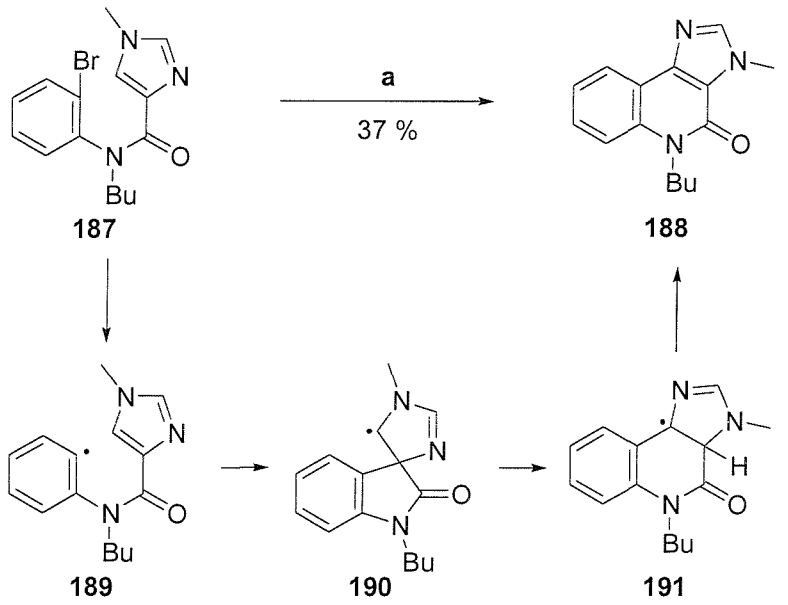


a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 41

1.9 Intramolecular Additions to Pyrazoles, Imidazoles and Benzimidazoles

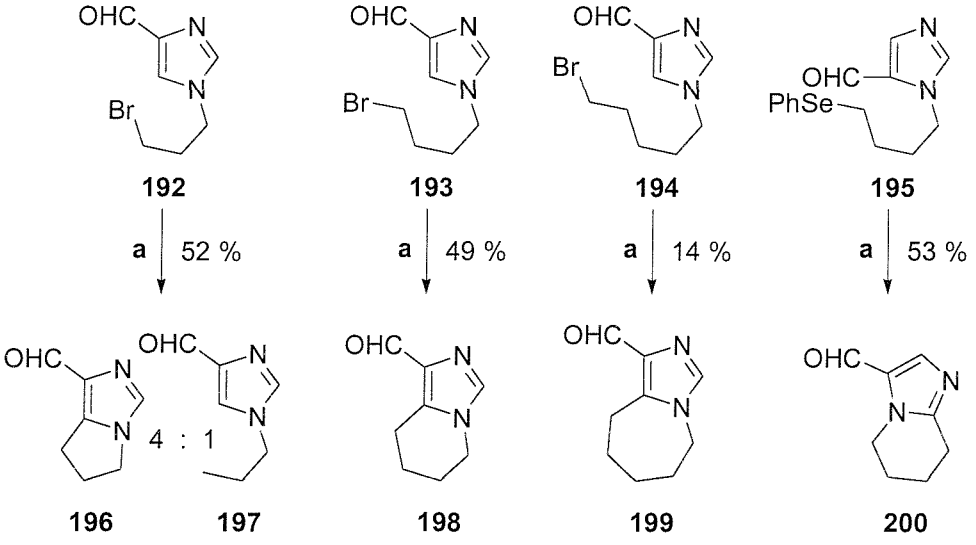
Bowman later reported a comprehensive study of intramolecular radical additions to pyrazoles, imidazoles and benzimidazoles.[64] This field had been opened by Suzuki *et al.* who used a 5-*exo*-trig radical cyclisation to C-4 of an imidazole in the synthesis of a potential antiasthmatic drug **188**.[66] It is worth noting that the product obtained, **188**, results from an acyl shift of the intermediate spirocycle **190** (Scheme 42).



a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 42

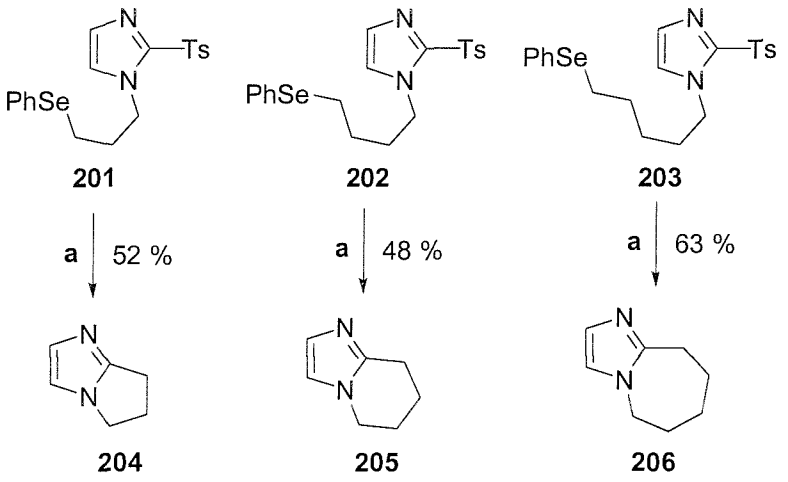
Bowman then published work demonstrating that a radical tethered to N-1 on imidazole undergoes cyclisation to C-5.[63] Cyclisation to C-2 could be forced by blocking the C-5 position with an aldehyde function (Scheme 43).



a. tri-*n*-butyltin hydride, AIBN, acetonitrile, Δ.

Scheme 43

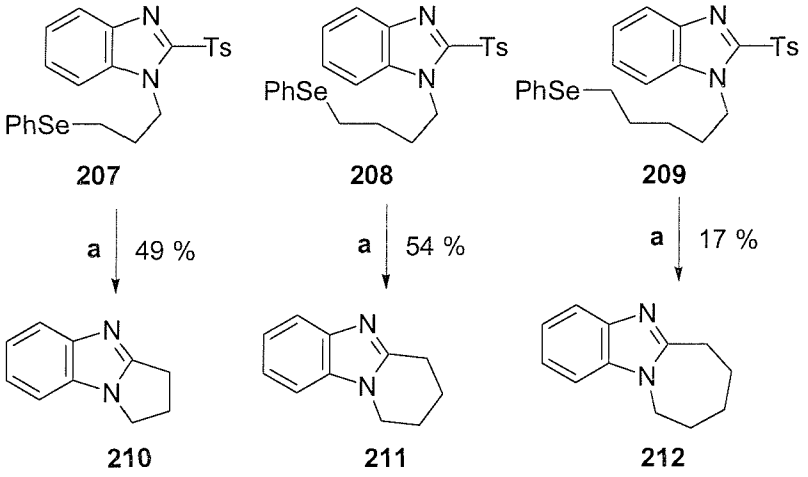
Cyclisation onto C-2 was also possible if a radical leaving group, such as tosyl, was attached to that centre. In such instances a blocking group was not needed on C-5. Yields for the 5-, 6- and 7-*exo*-trig cyclisation pathways were all good and compared favourably to those observed for C-5 addition (Scheme 44).[67]



a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 44

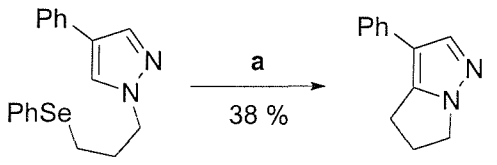
The same was true for benzimidazoles, though 7-*exo*-trig cyclisation reactions were somewhat less efficient (Scheme 45).[67]



a. tri-*n*-butyltin hydride, AIBN, toluene, Δ.

Scheme 45

Allin, Bowman and McInally have recently adapted this methodology to effect the first intramolecular radical cyclisation onto a pyrazole. The reaction was used in a short synthesis of withasomnine **214** (Scheme 46).[68]



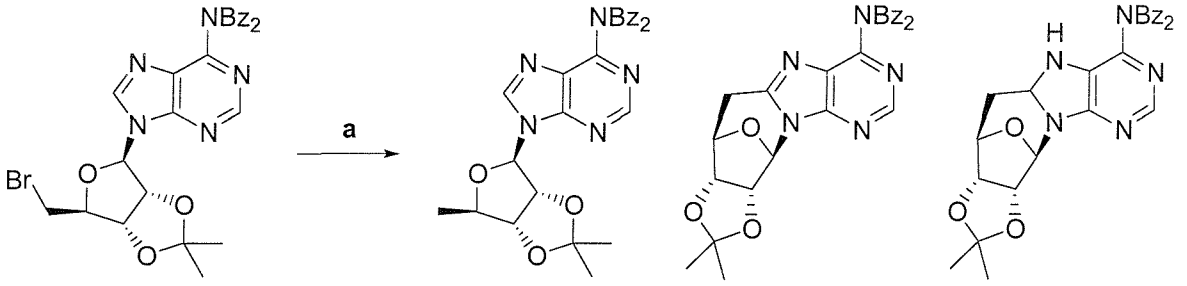
213 **214**

a. tri-*n*-butyltin hydride, 2 eq. ACN, toluene, Δ.

Scheme 46

1.10 Intramolecular Additions to other Nitrogen Containing Heterocycles

There are two further intramolecular radical additions to be discussed. The first is the addition to the purine core of an adenosine derivative. Such an intramolecular radical addition was described by Duong *et al.* in 1975,[69] who found that **215** gave the dihydro purine derivative **218** in 52 % yield. This was accompanied by the product of reduction, **216**, and cyclisation - aromatisation, **217** (Scheme 47).

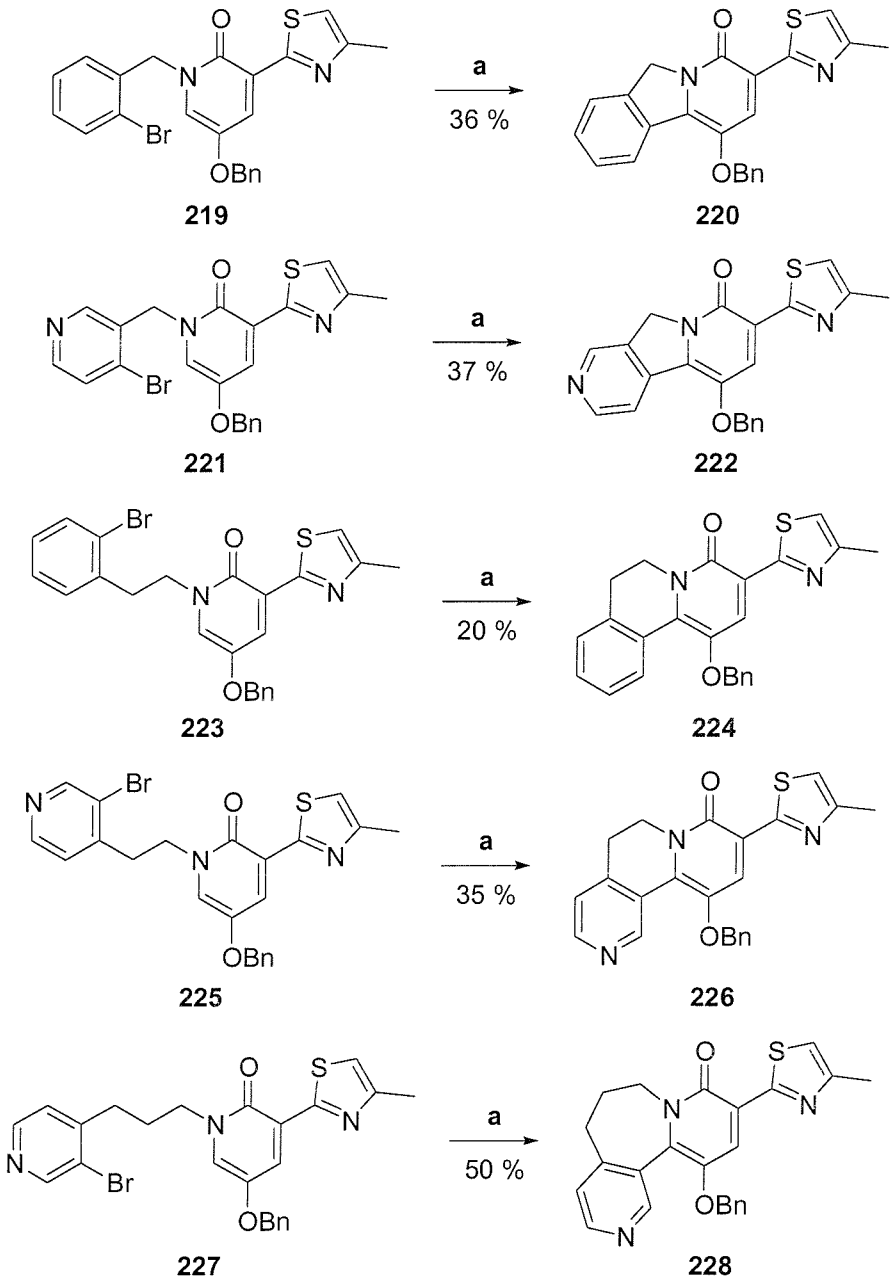


215 **216**, 24 % **217**, 16 % **218**, 52 %

a. tri-*n*-butyltin hydride, AIBN, Δ.

Scheme 47

A second example is more recent and involves radical additions to pyridones. Nadin *et al.* have shown that 5-, 6- and 7-*exo*-trig cyclisations by intramolecular addition of an aryl radical to C-6 are all possible.[70] The products were all achieved by cyclisation and loss of a hydrogen atom and interestingly cyclisation leading to a 7-membered ring was the highest yielding (Scheme 48).

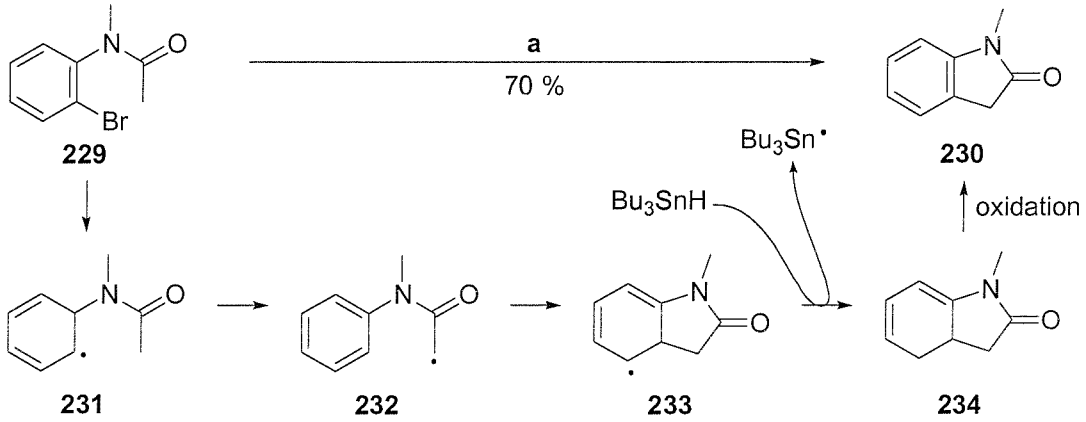


a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 48

1.11 A NOTE ON OXIDATION

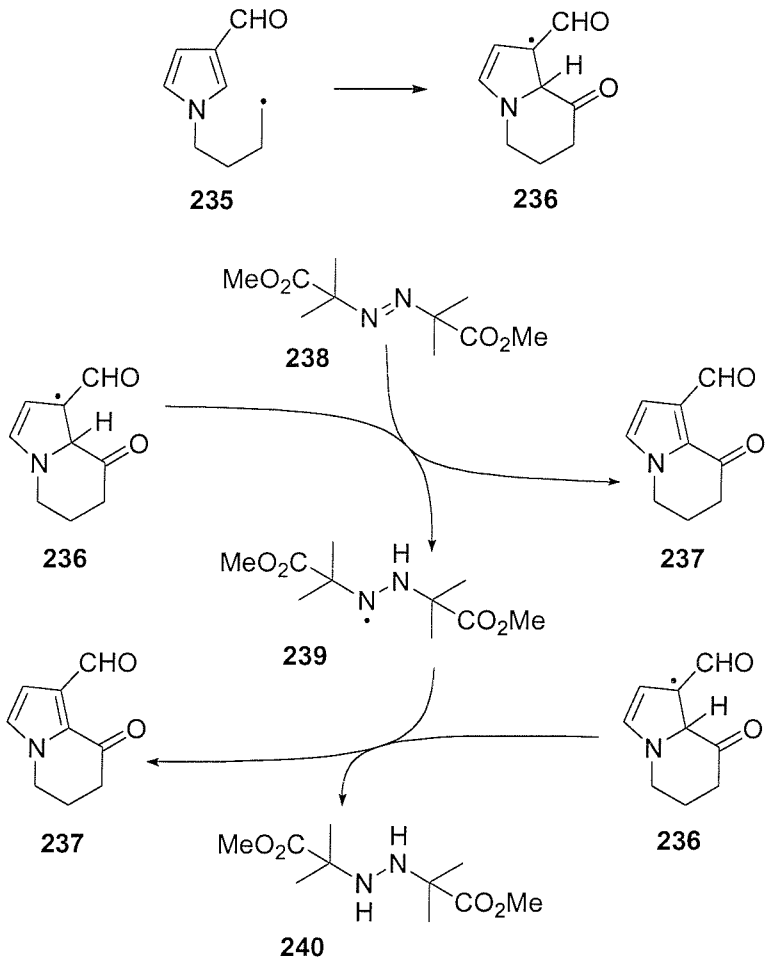
In the preceding discussion, propagation frequently involves the loss of a hydrogen atom. The course of that rearomatisation step is the subject of much conjecture and little evidence. A number of plausible pathways have been suggested. Firstly, Beckwith suggested that the dihydro-species, **234**, is formed as the product of the radical chain reaction. Oxidation during work-up yields the rearomatised product **230**.[71] However when tri-*n*-butyltin deuteride was used as a mediator, no deuterium was incorporated into the cyclised products, precluding this as a possibility (Scheme 49).



a. tri-*n*-butyltin hydride, AIBN, benzene, Δ.

Scheme 49

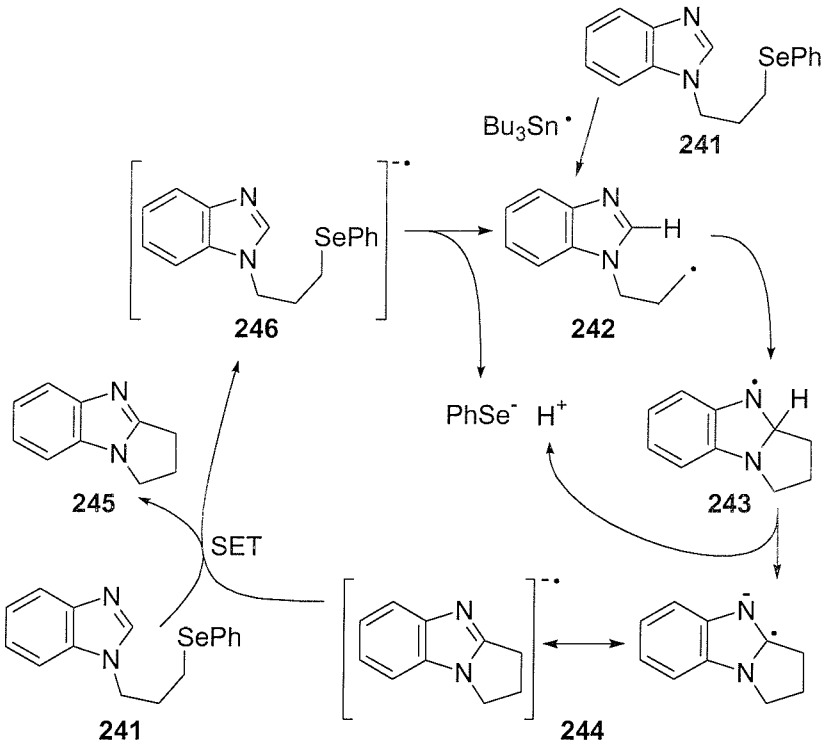
The initiator has also been implicated in the 'oxidative' step. Curran first suggested that an initiator such as AIBN could undergo reduction in order to oxidise the cyclised product back to an aromatic species.[72] In order for this to occur the initiator must be present in stoichiometric quantities which is frequently, but not always, the case in such radical cyclisation reactions.



Scheme 50

Bowman *et al.*[65] have recently shown that AIBMe **238** can be reduced during such cyclisation reactions and have proposed a mechanism to account for this finding. Thus AIBMe removes a hydrogen atom from an intermediate such as **236** leading to nitrogen centred radical **239** and the heteroaromatic product **237**. This also abstracts a hydrogen atom from **236** to give **237** and AIBMe-H_2 **240** (Scheme 50). When large quantities of initiator are used this may be a significant pathway. Bennasar has suggested that 2-cyano-2-propyl radicals formed from initiation of AIBN abstract a hydrogen atom[54] but this was already disproved in the literature by Lobo *et al.*[73] who were working with deuterated substrates and saw no deuterated products derived from the initiator.

The most widely accepted mechanism involves a SET from a radical anion, such as **244**, to the radical precursor, *e.g.* **241**, normally an aryl bromide, iodide or selenide species. Bowman was first to propose this in 1991 (Scheme 51)[64,67,74] and recently Harrowven has refined the hypothesis to account for differences observed with bromides and selenides, which are much less activated towards a SET than iodides. This will be discussed in Chapter 3.[75]



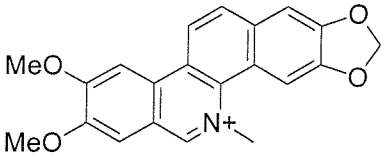
Scheme 51

CHAPTER 2

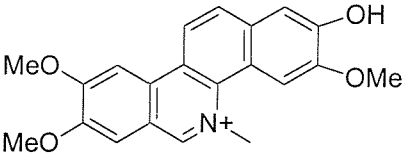
INTRAMOLECULAR RADICAL ADDITIONS TO PYRIDINES

2.1 ROUTES TO CONJUGATED PYRIDINES, QUINOLINES AND ISOQUINOLINES

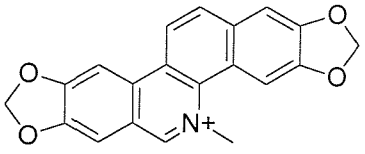
Condensed pyridines, quinolines and isoquinolines are prolific in nature. Benzo[*c*]quinoline and benzo[*h*]quinoline are known to be cytotoxic in nepatoma PLHC-1 fish cell lines[76] and acridine, phenanthridine, benzo[*f*]quinoline, benzo[*h*]quinoline, benzo[*a*]acridine and benzo[*c*]acridine are acutely toxic to larvae of the midge *Chironomus riparius*.[77] Many plants produce these alkaloids and derivatives based upon them. Examples include nitidine **300** from *Xanthoxylum integrifoliolum*,[78] *Xanthoxylum nitidum*[79] and *Toddalia asiatica*,[80] fagaronine **301** from *Xanthoxylum integrifoliolum*,[78] avicine **302** from *Zanthoxylum avicennae*[81] and *Toddalia asiatica*[80] and toddaquinoline **106** from *Toddalia asiatica*.[80]



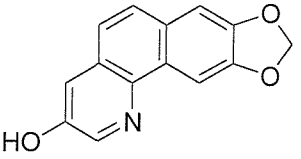
300



301

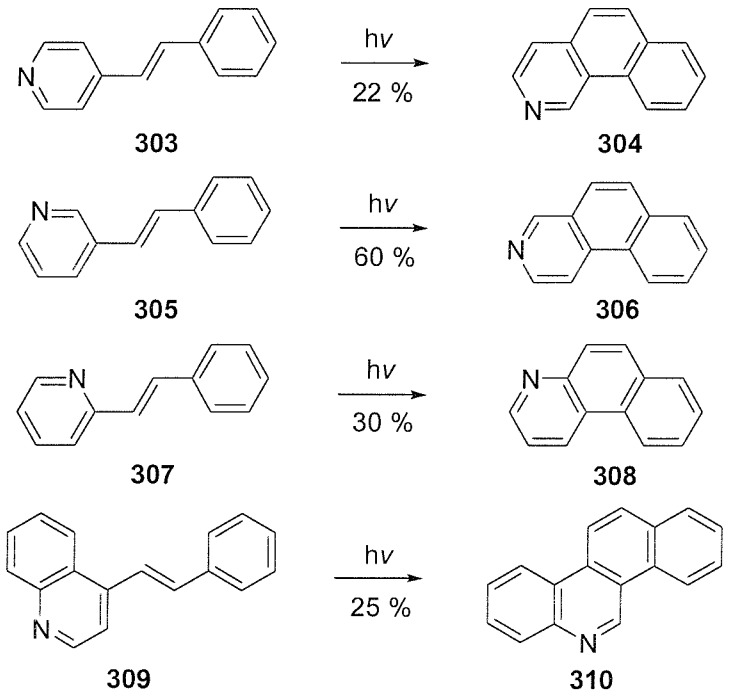


302



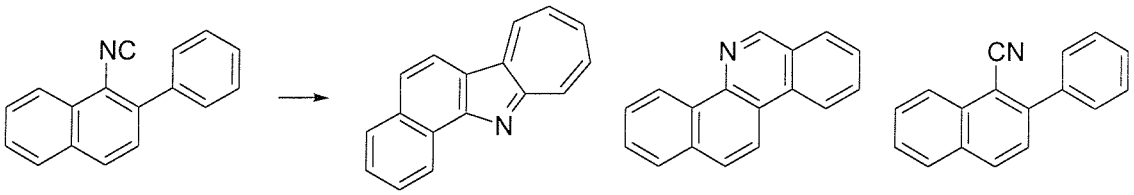
106

It is not surprising then to find that many methods have been devised to synthesize these ring systems. By far the most widely exploited is the photochemical cyclisation of azastilbene derivatives to give condensed polyaromatic systems. Loader, Sargent and Timmons were the first to extend earlier work on the cyclisation of stilbenes[82] to demonstrate that 2-, 3- and 4-azastilbenes also undergo photocyclisation (Scheme 52).[83]



Scheme 52

The high yield and selectivity observed when the 3-substituted azastilbene **305** is cyclised, indicates that the C-4 position is highly activated towards photocyclisation. Timmons also started to target more complex ring systems, developing many selective and higher yielding routes to condensed aromatic and heteroaromatic systems.[84-88] Boyer and Patel extended the methodology to isonitriles, the cyclisation of which could be induced both photochemically and thermally (Scheme 53).[89,90]

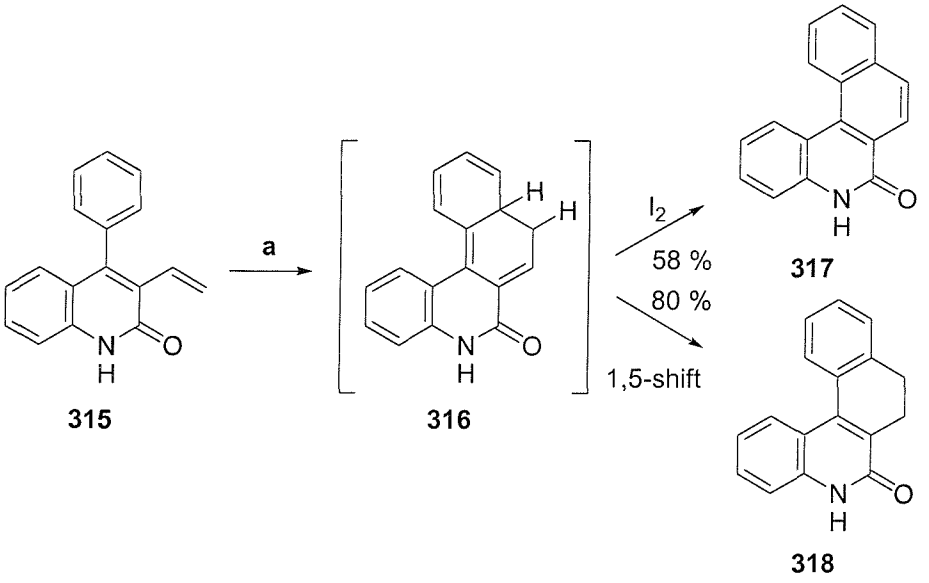


	311	312	313	314
a		27 %	0 %	0 %
b		3 %	31 %	35 %

a. methanol, hv; **b**. 253 °C, *n*-tetradecane.

Scheme 53

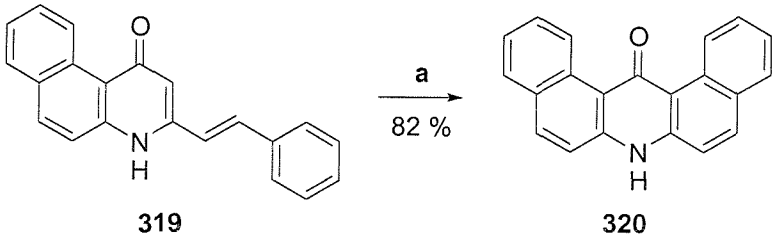
Shanmugam *et al.* reported the high yielding photocyclisation of vinylquinolinone derivatives[91] and was able to bias the reaction to give the dihydro products, *e.g.* **318**, or fully aromatic species, *e.g.* **317** (addition of iodine catalysed the oxidation reaction). The only down side was the complexity of the synthesis leading to the photocyclisation precursors used (Scheme 54).



a. benzene, hv; **b**. benzene, methanol, hv, iodine.

Scheme 54

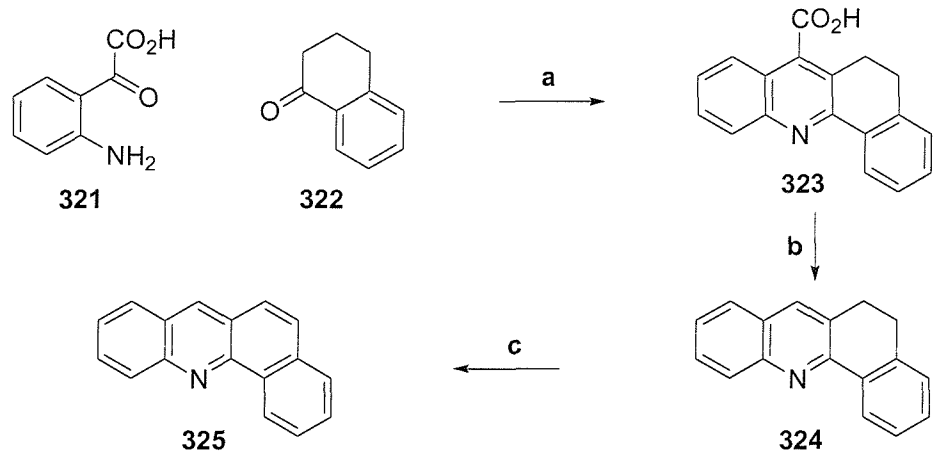
The same group also showed that styrylquinolines such as **319** could be cyclised to condensed styrylquinolones, *e.g.* **320** (Scheme 55).[92-94]



a. benzene, methanol, hv, iodine.

Scheme 55

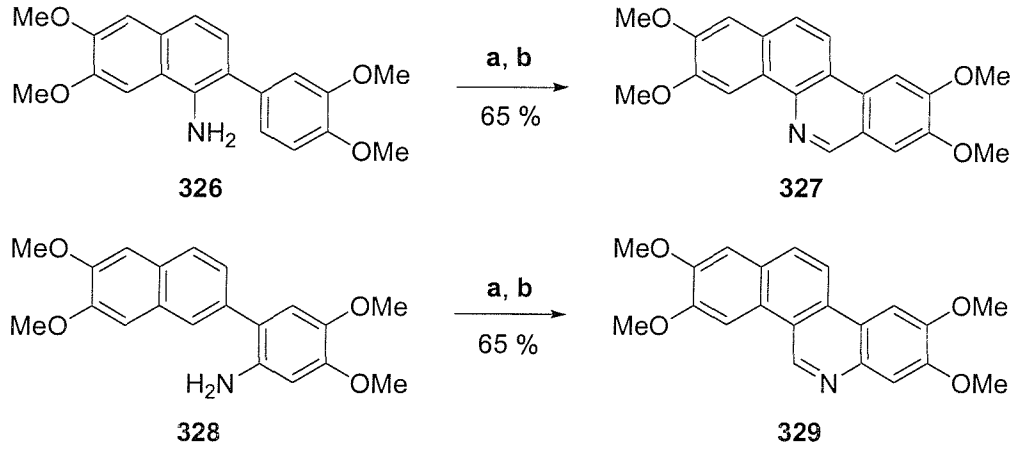
von Braun *et al.* exploited the Pfitzinger - Borsche reaction to prepare condensed quinolines.[95,96] This involves condensation of an isatin **321** with 1-tetralone **322** followed by decarboxylation and dehydrogenation to **325**. Buu-Hoi *et al.* used a similar sequence to produce a formidable series of benzo[*c*]acridines (Scheme 56).[97]



a. KOH, ethanol, water, Δ; **b**. *in vacuo*, Δ; **c**. chloranil, xylene, Δ.

Scheme 56

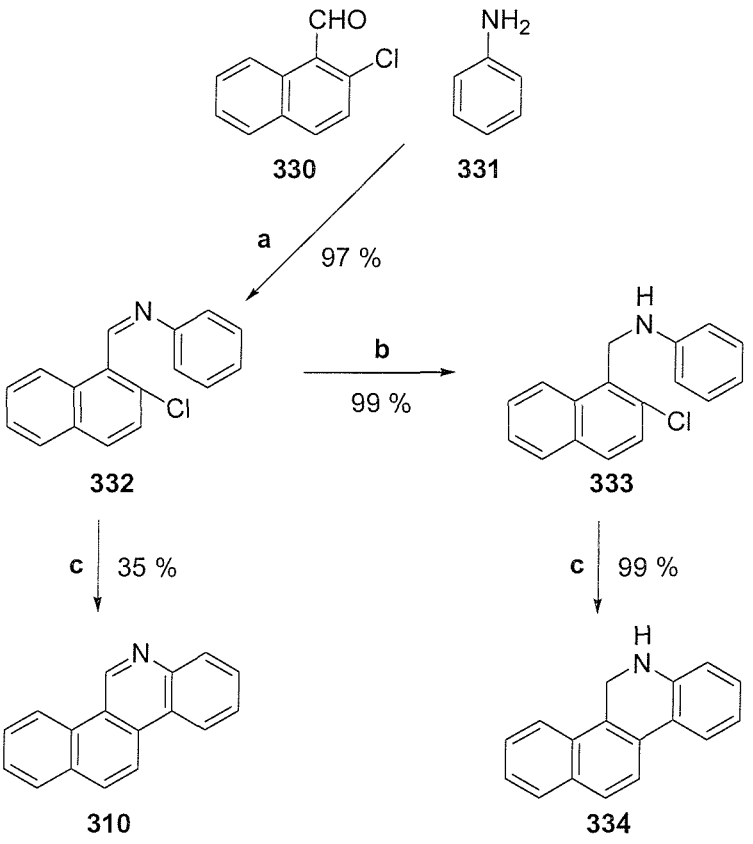
Gopinath *et al.* showed that benzo[*c*]phenanthridines and benzo[*i*]phenanthridines could be made by a classical condensation route, albeit from more complex naphthalene type derivatives *viz.* **326** **327** and **328** **329** (Scheme 57).[98]



a. formic acid; **b**. $POCl_3$, Δ.

Scheme 57

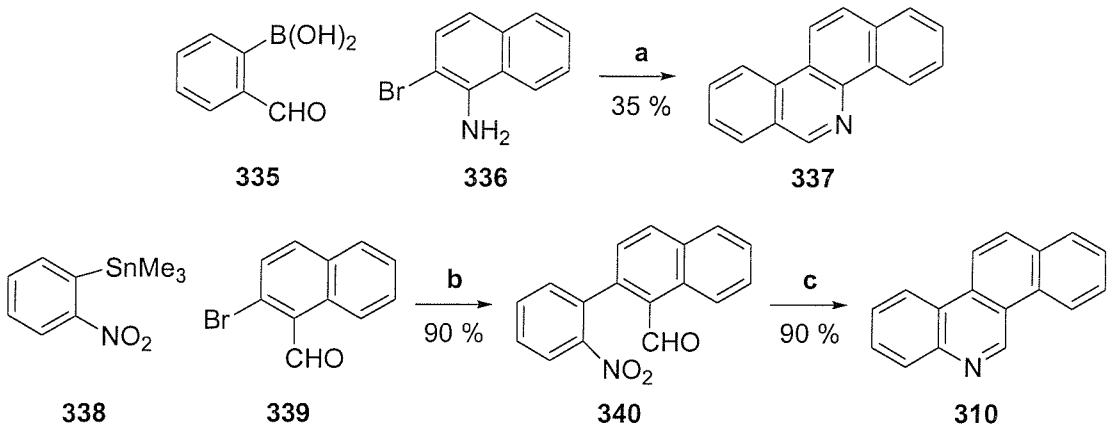
Simpler precursors, readily formed by condensing an aniline with an *ortho*-chloroarylaldehyde to form a chloroanil. These were used by Kessar *et al.* to form benzo[*i*]phenanthridine by treatment with potassium amide (Scheme 58).[99,100]



a. ethanol, Δ; **b**. ethanol, $NaBH_4$, Δ; **c**. KNH_2, $NH_{3(l)}$, diethyl ether.

Scheme 58

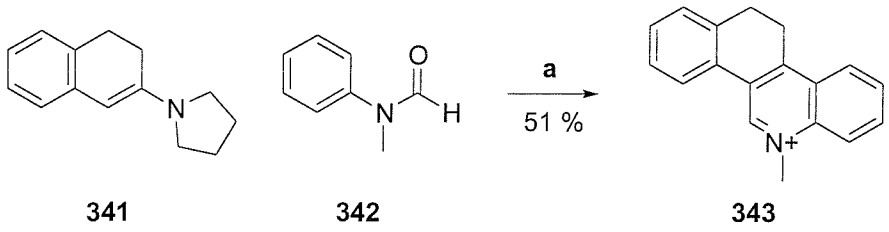
Independently Geen[101] and LaVoie[102] showed that biaryls formed by a Suzuki or Stille coupling respectively could be readily transformed into benzo[*c*]phenanthridines and benzo[*i*]phenanthridines (Scheme 59).



a. $Pd(OAc)_2$, PPh_3, DME, $Na_2CO_{3(aq)}$; **b**. $Pd(PPh_3)_4$, CuBr, THF, Δ; **c**. AcOH, Zn, Δ.

Scheme 59

More recently Mackay approached the synthesis of dihydrobenzo[*i*]phenanthridines in a more traditional way. He employed a reverse-Vilsmeier synthesis to prepare several quinolinium salts by cyclocondensation, *e.g.* Scheme 60.[103]

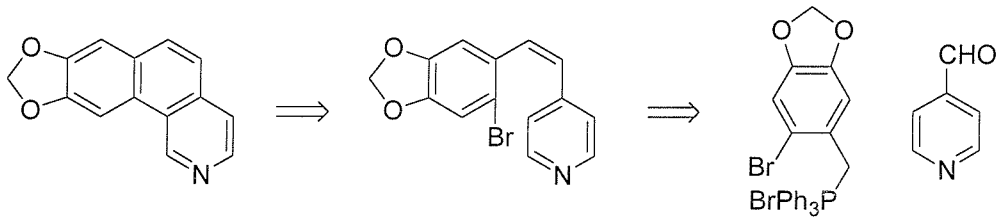


a. $POCl_3$, Δ.

Scheme 60

2.2 INTRODUCTION

The total synthesis of the alkaloid toddaquinoline **106** within our laboratories led us to consider whether other intramolecular radical additions to the pyridine ring system might be facile. If so, the methodology would afford a rapid entry to an array of condensed heteroaromatics, hopefully in a reliable, high yielding and cost effective manner. From our retrosynthetic analysis it immediately became clear that our radical precursors would be most effectively formed *via* a Wittig reaction from two simple substituted aromatics (Scheme 61).



345 **346** **347** **348**

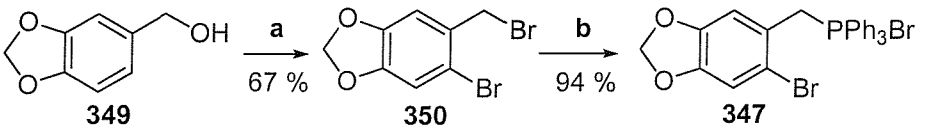
Scheme 61

Only the *Z*-alkene **346** can undergo radical cyclisation as the double bond will bring the radical centre into close proximity with the heteroaromatic ring. By contrast, with the *E* isomer the radical cannot undergo cyclisation as it is positioned too far from the pyridine ring to interact with it.

The inclusion of a methylenedioxy group in our systems was not accidental. As well as occurring in many natural product ring systems it also serves to activate the aromatic ring towards electrophilic substitution allowing easy and selective insertion of the halide radical precursor. Moreover, product analysis by NMR is greatly simplified, there being a characteristic 2H signal in the ^{1}H NMR at $\delta \sim 6$ ppm along with two singlets for the aromatic protons.

2.3 6-MEMBERED RING FORMATION

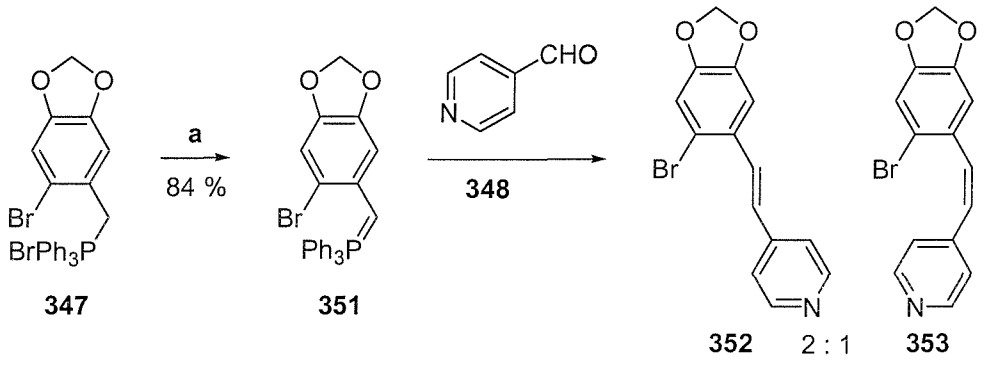
The system chosen to test whether radical additions to C-3 of a pyridine could be effected was **346**. The procedure of Barthel and Alexander[104] was used to convert piperonol **349** to the dibromide **350** which was then transformed into phosphonium salt **347** by the procedure of Jaegfeldt[105] and Ghera[106] (Scheme 62).



a. Br_2, AcOH, 0 °C; **b**. PPh_3, xylene, Δ.

Scheme 62

Pleasingly, upon deprotonation of the phosphonium salt **347** with sodium hydride, the Wittig reaction with 4-pyridinecarboxaldehyde **348** was high yielding and gave a 2 : 1 mixture in favour of the desired *Z* isomer **353** indicating that the ylid **351** was only moderately stable (Scheme 63).

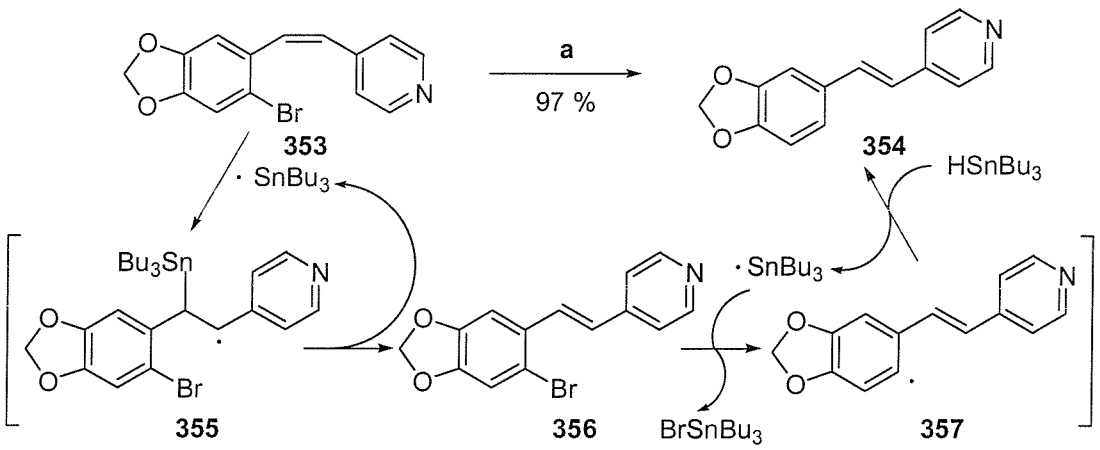


a. NaH, THF, 0 °C.

Scheme 63

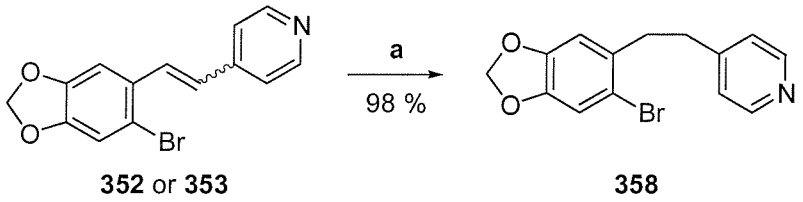
Upon exposing the *Z* alkene **353** to tributyltin hydride in the presence of substoichiometric AIBN the reduced *E* isomer **354** was formed in 97 % yield. We concluded that attack by the tributyltin radical onto the double bond was faster in this case than homolysis of the C-Br bond (Scheme 64). The identity of **354** was

established by spectroscopic methods and further confirmed when the *E* isomer **352** was subjected to the same reaction conditions to give a spectroscopically identical product.



a. Bu_3SnH, AIBN, toluene, Δ.

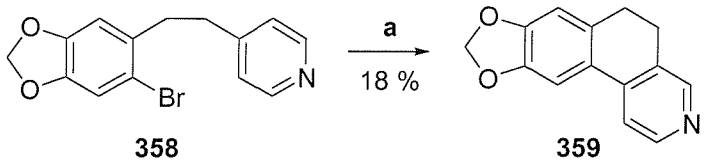
Scheme 64



a. tosyl hydrazine, NaOAc, THF, H_2O, Δ.

Scheme 65

To alleviate the isomerisation problem the double bond was reduced with diimide to give dihydroazastilbene **358** (Scheme 65). Treatment of **358** under standard radical forming conditions gave cyclised product **359** along with two unidentified products. *Importantly the cyclised compound recovered was the product of rearrangement rather than of direct attack at the C-3 of the pyridine* (Scheme 66).[37,38]



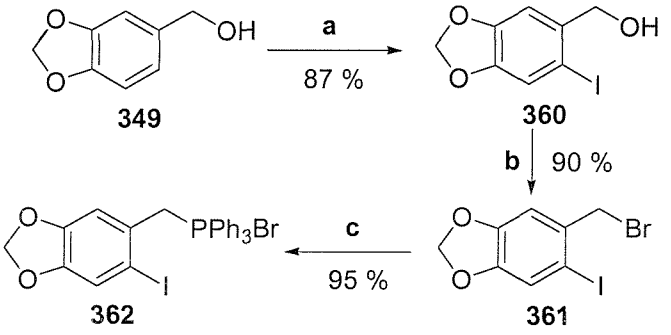
a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 66

It was clear that for certain substrates homolysis of the C-Br bond by tributyltin radicals was slow. This led us to look at using iodides as radical precursors as the C-I bond is much weaker than the C-Br bond.

2.4 CYCLISATIONS OF A SERIES OF AZASTILBENES

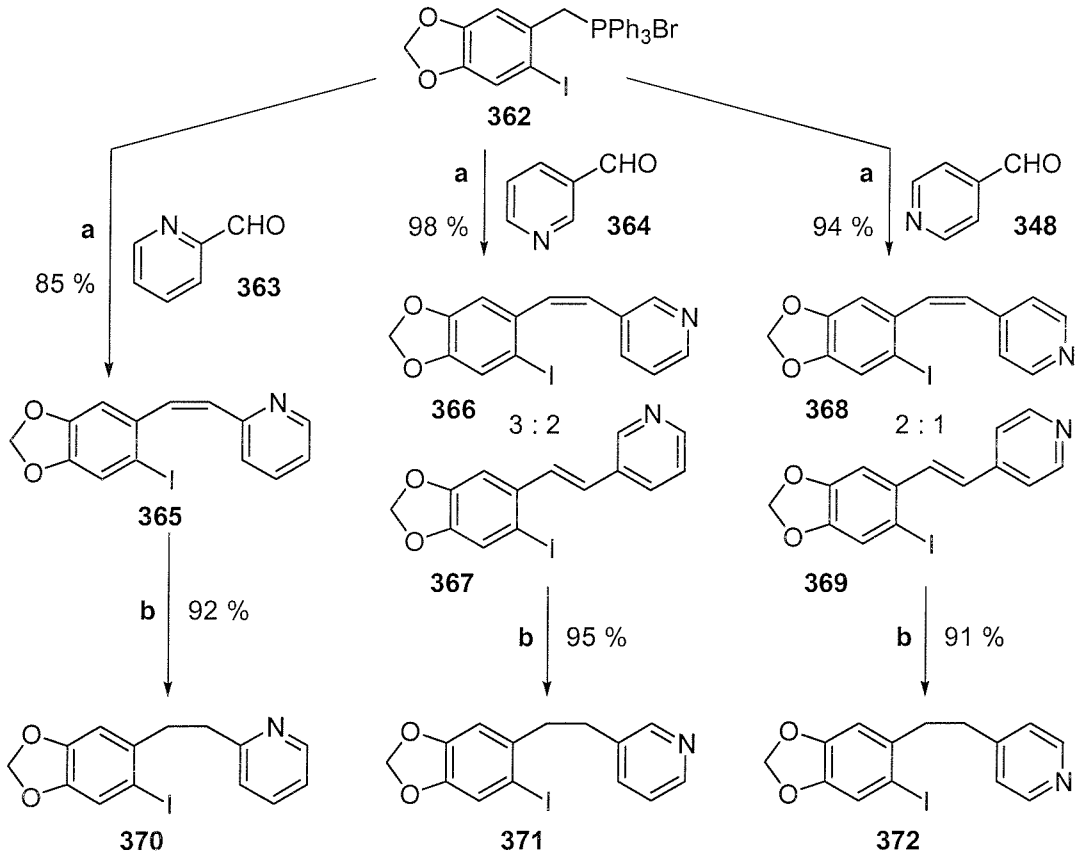
The phosphonium salt **362** was formed in high yield from piperonol **349** in three steps. Following the procedure of Overman[107] piperonol was iodinated using iodine and stoichiometric silver trifluroacetate as a Lewis acid. Bromination with concentrated hydrobromic acid quickly afforded the benzylic bromide **361** in high yield and addition of triphenylphosphine completed the synthesis (Scheme 67).[105]



a. I_2, AgO_2CCF_3, $CHCl_3$, 0 °C, 5 min.; **b**. conc. HBr; **c**. PPh_3, xylene, Δ.

Scheme 67

With **362** in hand we were in a position to study a range of radical cyclisation reactions to pyridines. Accordingly precursors **365**, **366**, **368**, **370**, **371** and **372** were synthesized from the ylid and 2-, 3- and 4-pyridinecarboxaldehydes. Pleasingly the Wittig reaction carried out with the 2-pyridinecarbaldehyde **363** yielded only the desired *Z* alkene **365**. Reaction with the 3- and 4-pyridinecarboxaldehydes yielded both geometric isomers, but favoured the *Z* alkene (Scheme 68).

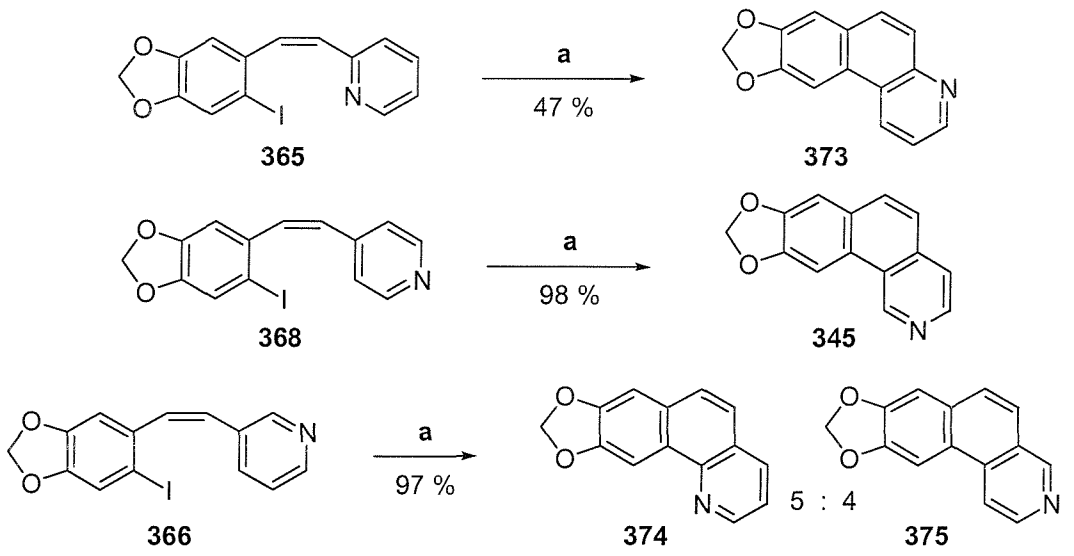


a. NaH, THF, 0 °C; **b**. tosyl hydrazine, NaOAc, THF, H_2O, Δ.

Scheme 68

To achieve complete cyclisation azastilbene **365** required forcing conditions. 4.4 Equivalents of tributyltin hydride were needed to consume all the starting material and the mass balance of the reaction was low. Thankfully azastilbene **368** underwent cyclisation to C-3 of the pyridine in very high yield. This difference in behaviour was unexpected as the position of the tether was not expected to influence the rate of cyclisation to C-3 of the pyridine. This led us to believe that the lower yield might be as a result of cyclisation to nitrogen as this would have given rise to a salt. Cyclisation

to C-2 and C-4 of pyridine each occurred when the radical precursor was tethered at C-3 by a *Z*-alkene. With a choice of two positions to attack it was hoped to see good discrimination between addition to C-2 and C-4. In the event, these processes occurred with almost equal propensity giving a 5 : 4 mixture of **374** and **375** (Scheme 69).



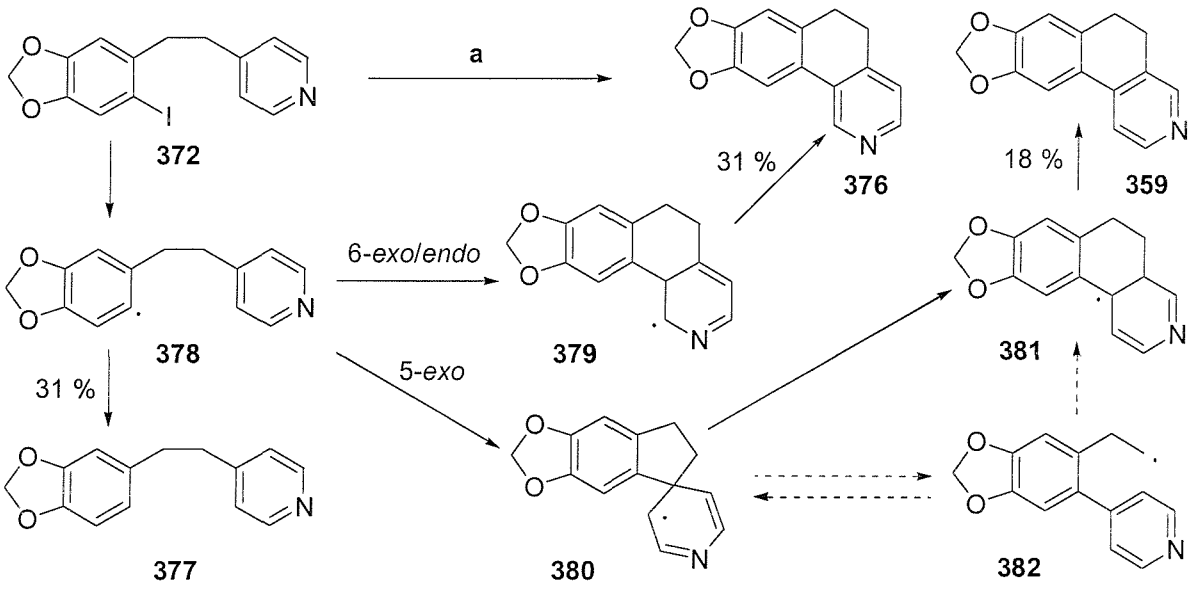
a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 69

With these cyclisations completed we had readily accessed substituted benzo[*f*]quinoline **373**, benzo[*h*]isoquinoline **345**, benzo[*h*]quinoline **374** and benzo[*f*]isoquinoline **375** with good overall yields. Also of note is that all the products recovered have undergone rearomatisation rather than quenching with a hydrogen atom, the nature of which will be discussed in Chapter 3.

2.5 CYCLISATIONS OF A SERIES OF DIHYDROAZASTILBENES

High yielding diimide reduction of the azastilbenes led to the corresponding dihydroazastilbenes (Scheme 68). We were eager to see if these iodides would give cleaner product mixtures than we had observed with bromide **358**. Accordingly the iodide **372** was subjected to standard radical forming conditions and from the resulting product mixture **376, 359** and **377** were recovered (Scheme 70).

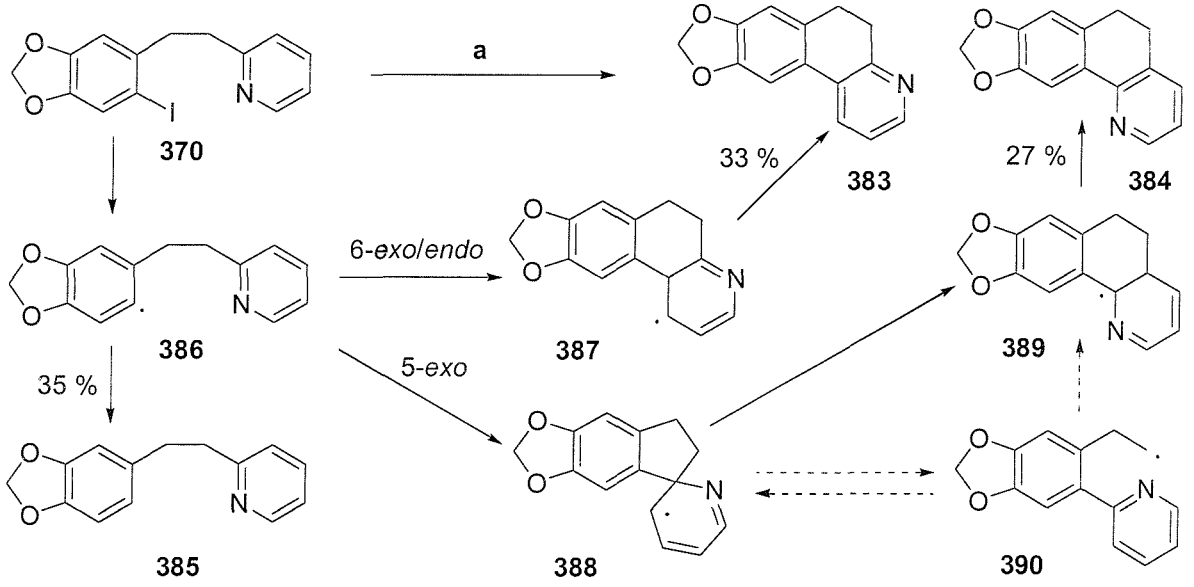


a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 70

Clearly the greater flexibility of the tethering chain has had a significant impact on the course of the reaction. Firstly, cyclisation by the 6-*exo*/*endo*-trig mode has been slowed allowing other processes to compete. Most notably, hydrogen atom abstraction from tributyltin hydride is now a significant process leading to **377**. Also the radical can now add to the pyridine ring through the alternative 5-*exo*-trig cyclisation mode, leading to the spirocyclic intermediate **380**. Rearrangement to **381** and re-aromatisation gives **359**.

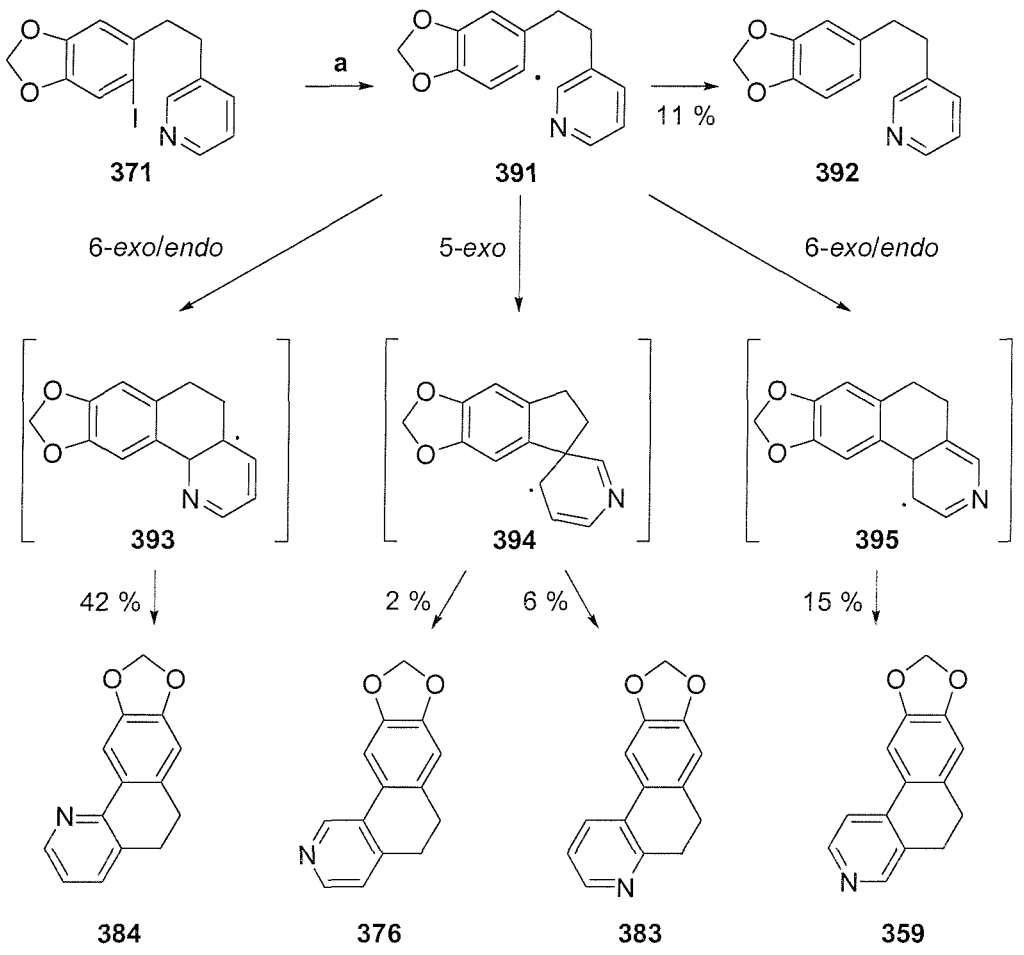
The product arising from the 5-*exo*-trig pathway **384** was also seen when the pyridine was tethered at C-2 to the aryl iodide. Thus, when **370** was subjected to tributyltin hydride and AIBN a 1 : 1 ratio of **383** and **384** was formed. In this case spirocyclisation was even more favourable. Again, much of the remaining mass was accounted for with the reduction product **385** (Scheme 71).



a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 71

Although of great interest from an academic perspective this novel rearrangement is not helpful when aiming for a selective synthesis. With this in mind we were pleased to see that one product dominated when dihydroazastilbene **371** was cyclised. Together with the reduction product **392** we had expected to observe, two cyclisation products arising from the 6-*exo*/*endo*-trig cyclisation, **384** and **359**, as well as two products arising from the rearrangement of the spirocyclic intermediate, **376** and **383**, were isolated. After protracted separation of the product mixture by column chromatography the major product isolated was **384** in 42 % yield (Scheme 72). This was as expected given the affinity for α attack in related intermolecular radical additions to pyridines.

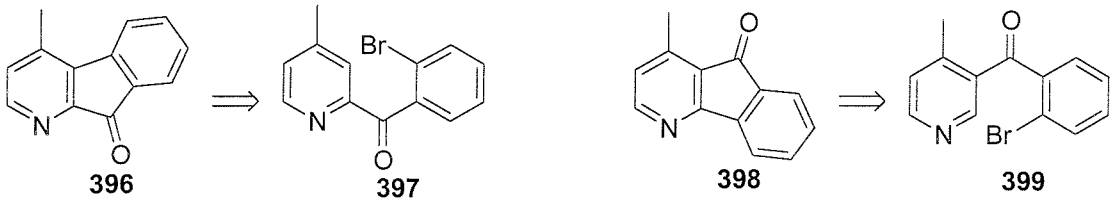


a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 72

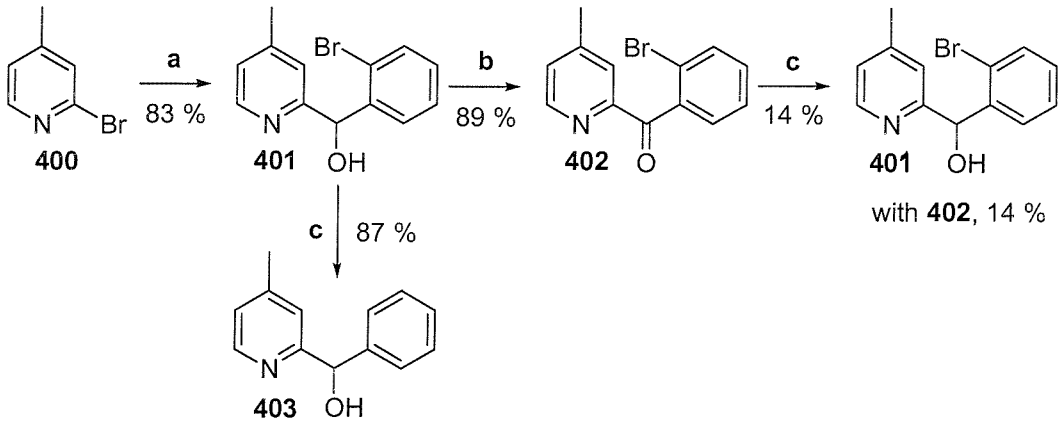
2.6 ATTEMPTED 5-MEMBERED RING FORMATION

Our success with the formation of 6 membered rings led us to consider whether 5-*exo*/*endo*-trig cyclisations onto pyridines were facile processes. The natural product onychine **396** (or **398**) was targeted in the first instance to demonstrate 5-membered ring closures to the α and β positions of a pyridine. This synthesis was of interest as there has been much debate in the literature over the structure of this natural product (Scheme 73).[108-113]



Scheme 73

Several attempts were made to synthesise the two reported structures of onychine **396** and **398**. Initially pyridine **400** was lithiated[114] and coupled with 2-bromobenzaldehyde to form alcohol **401**. A tin mediated radical cyclisation was then attempted on both the alcohol **401** and the corresponding ketone **402** (Scheme 74).

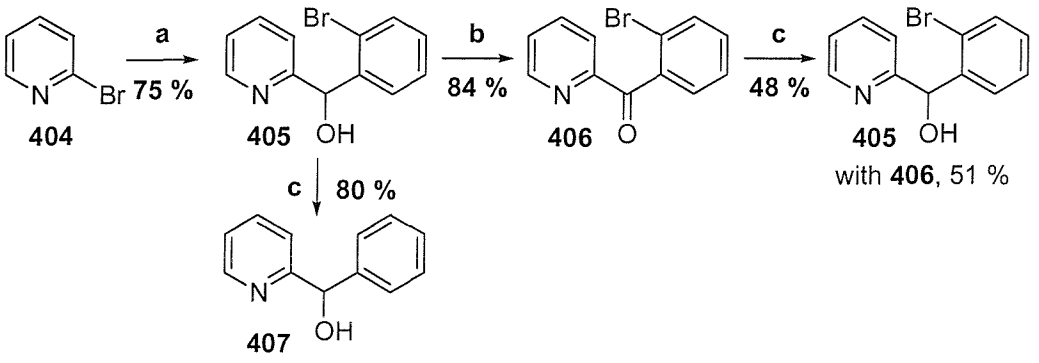


a. 1) ^{n}BuLi, THF, -90 °C, 2) 2-bromobenzaldehyde; **b**. MnO_2, DCM;

c. Bu_3SnH, AIBN, toluene, Δ.

Scheme 74

The ketone **402** was reduced under standard radical forming conditions to give the alcohol **401** in low yield. The same conditions were then used to effect homolysis of the carbon-bromine bond of the alcohol **401**. This was achieved but we were disappointed to find that the radical formed abstracted a hydrogen atom from tributyltin hydride leading to the reduced product **403** in high yield, rather than undergoing cyclisation to the pyridine (Scheme 74). We therefore decided to try a simpler system, without the methyl group in the 4 position of the pyridine (Scheme 75).



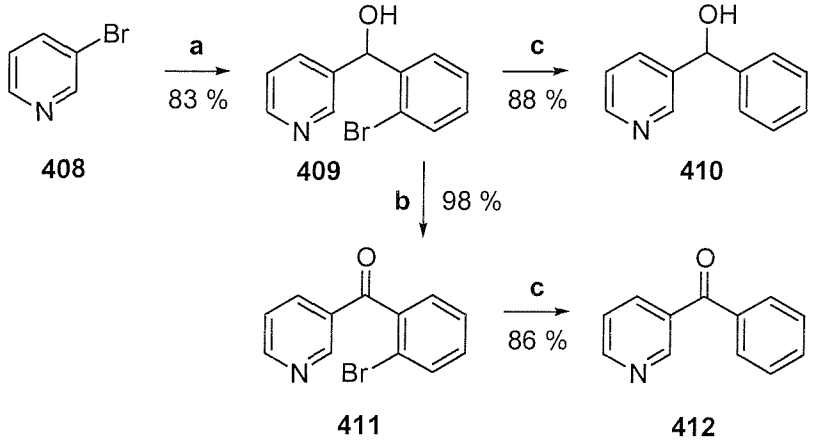
a. 1) ^{n}BuLi, THF, -90 °C, 2) 2-bromobenzaldehyde; **b**. MnO_2, DCM;

c. Bu_3SnH, AIBN, toluene, Δ.

Scheme 75

Formation of alcohol **405** and ketone **406** was easily accomplished. However attempted cyclisation of ketone **406** again caused reduction to alcohol **405** which turn was reduced to **407** on exposure to tributyltin hydride under standard radical forming conditions.

Attempts were also made to form desmethylonychine. Although no reduction of the ketone was observed with **411**, cyclisation still did not occur (Scheme 76).



a. 1) ^{t}BuLi, Et_2O, -100 °C, 2) 2-bromobenzaldehyde; **b**. MnO_2, DCM;

c. Bu_3SnH, AIBN, toluene, Δ.

Scheme 76

2.7 CONCLUSIONS

We have shown that intramolecular radical additions to the α, β and γ carbons of a pyridine are all facile processes. The tether plays an important role in determining the outcome of the reaction. When a *Z* alkene conjoins the pyridine to the aryl radical a 6-*exo*/*endo*-trig course is followed. When a saturated two carbon tether is used, hydrogen atom extraction and 5-*exo*-trig cyclisation compete with the 6-*exo*/*endo*-trig cyclisation mode. That the spirocyclic intermediate underwent rearrangement with alkyl migration is noteworthy.

5-*exo*/*endo*-trig cyclisations were also attempted but no intramolecular addition of an aryl radical to the pyridine was observed in such cases. Indeed, cyclisation was much slower than radical quenching in this case. Our failure to effect these 5-*exo*/*endo*-trig cyclisations has led us to conclude that the process is more akin to a 5-*endo*-trig than a 5-*exo*-trig reaction.

CHAPTER 3

INTRAMOLECULAR RADICAL ADDITIONS TO QUINOLINES[75,115]

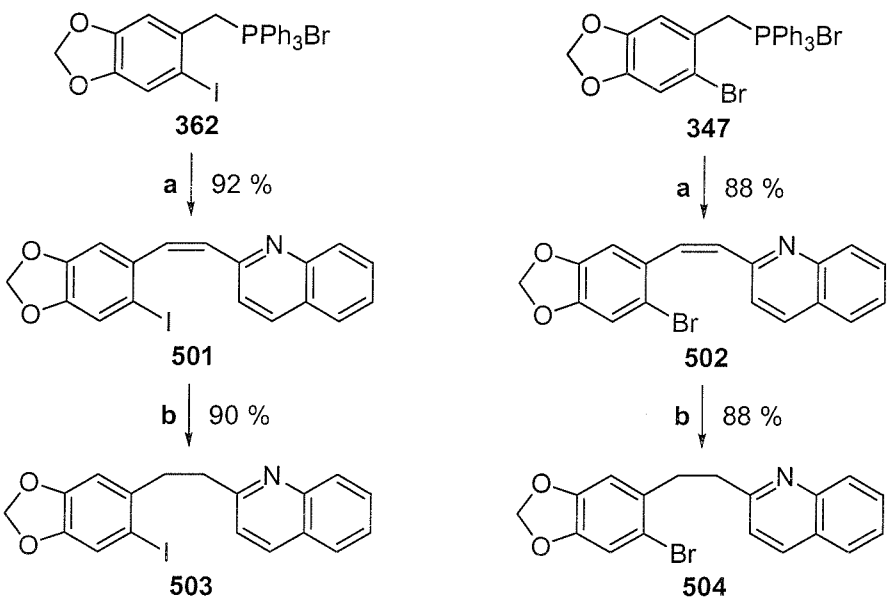
3.1 INTRODUCTION

Following our success at effecting intramolecular radical additions to pyridines, we felt that a logical extension to this work would be to demonstrate intramolecular radical additions to quinolines. This serves two purposes. Firstly tolerance of an extra ring will give the reaction more versatility, leading to a greater number of possible targets. Secondly the heterocyclic ring of quinoline has significantly less aromatic character than that of pyridine and so there was a possibility that reactions would lead to dihydroquinolines as products, rather than undergoing rearomatisation.

As an additional point of interest we felt it was important to compare the performance of aryl bromides and aryl iodides as radical precursors. Accordingly quinolines tethered to each aryl halide at both C-2 and C-3 were synthesised.

3.2 PRECURSOR FORMATION

As with the pyridine series, the precursors were synthesised using a Wittig reaction. Formation of the 2-substituted quinolines **501** and **502** was high yielding and gave only the desired *Z*-diastereoisomers. Diimide reduction to **503** and **504** was once again a clean and high yielding reaction (Scheme 77).

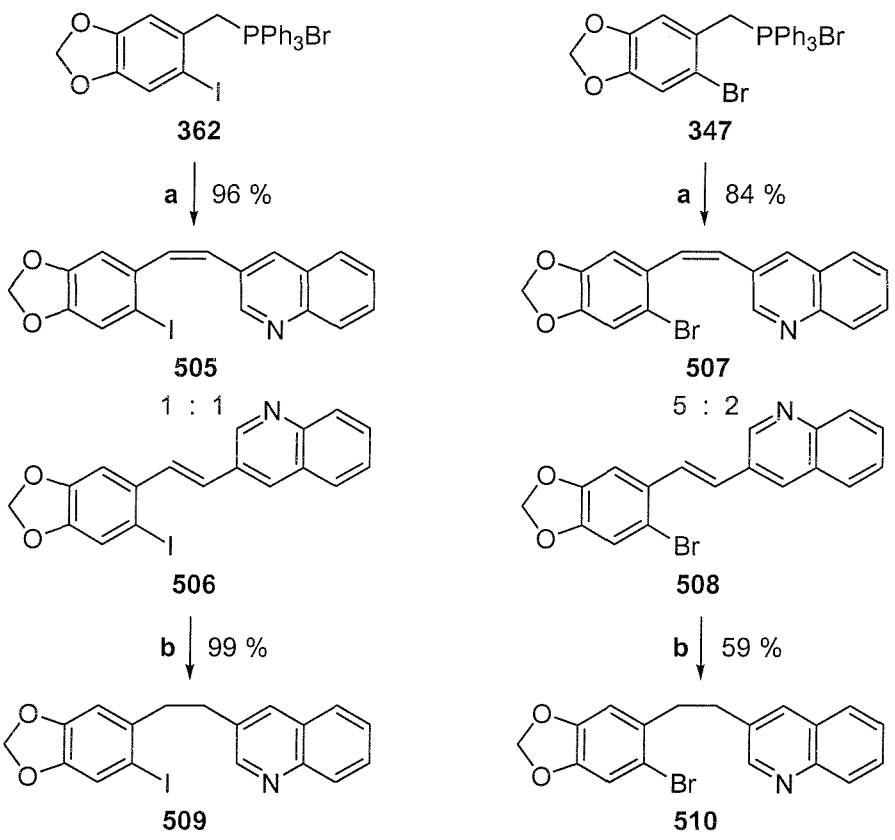


a. 1) NaH, THF, 0 °C, 2) 2-quinolinecarboxaldehyde;

b. tosyl hydrazine, NaOAc, THF, H_2O, Δ.

Scheme 77

Formation of the analogous 3-substituted quinolines gave different results for the iodide and bromide precursors. Thus, while union of 3-quinolinecarboxaldehyde with **362** gave a 1 : 1 mixture of **505** and **506**, with **347** a 5 : 2 ratio of **507** and **508** was observed. This difference in the *E* : *Z* ratio is difficult to explain by conventional arguments. Conceivably traces of iodine may be formed in the reaction of **362** and 3-quinolinecarboxaldehyde. This could then catalyse *E* / *Z* isomerisation biasing the product ratio in favour of the thermodynamic alkene (Scheme 78).

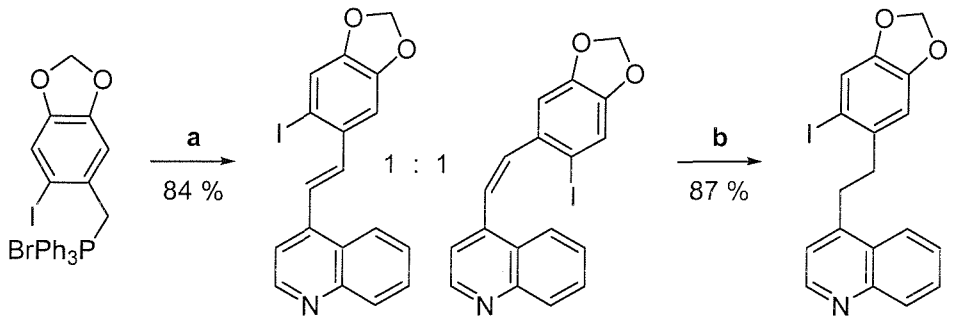


a. 1) NaH, THF, 0 °C, 2) 3-quinolinecarboxaldehyde;

b. tosyl hydrazine, NaOAc, THF, H_2O, Δ.

Scheme 78

In the reaction of **362** with 4-quinolinecarboxaldehyde an equal ratio of *E* and *Z* isomers, **511** and **512**, was given. Thus it seems that the high selectivity observed with 2-quinolinecarboxaldehyde is the exceptional result. Diimide reduction of the alkene tether gave **513** to complete the synthesis of our radical precursors (Scheme 79).



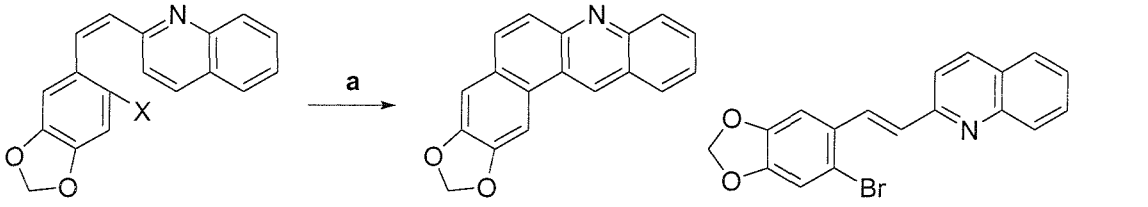
a. 1) NaH, THF, 0 °C, 2) 4-quinolinecarboxaldehyde;

b. tosyl hydrazine, NaOAc, THF, H_2O, Δ;

Scheme 79

3.3 RADICAL CYCLISATION REACTIONS

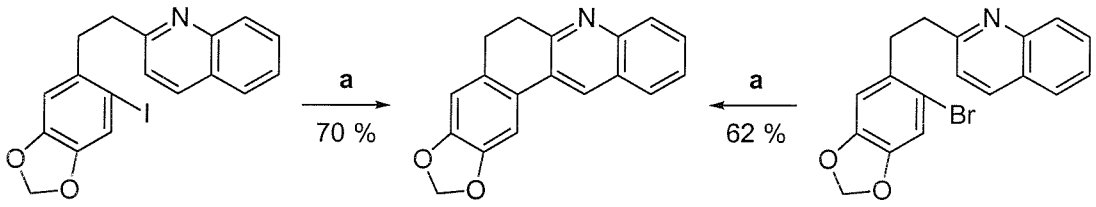
Treatment of the bromo-azastilbene **502** with tributyltin hydride in the presence of a radical initiator led to a disappointing result. After a prolonged reaction time the starting material was recovered together with *E*-azastilbene **515**. Switching to the iodide **501** and using more forcing conditions (5 equivalents of tributyltin hydride) the cyclised product was recovered in moderate yield (Scheme 80).



a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 80

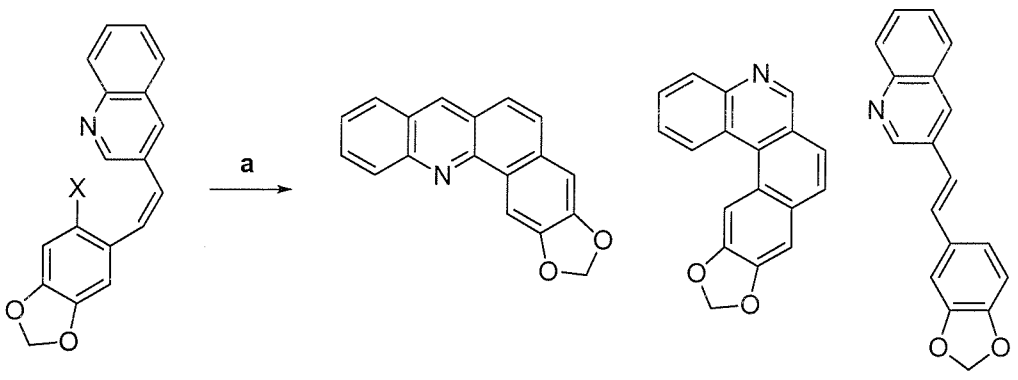
When the analogous dihydroazastilbenes **503** and **504** were subjected to standard radical forming conditions, cyclisation to C-3 became the dominant reaction. Notably only the product **516**, arising from a direct 6-*exo*/*endo*-trig (*ortho*) cyclisation was observed (Scheme 81).



a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 81

The 3-substituted azastilbene was next to be investigated. Once again the bromide precursor **507** was shown to be less efficient than the iodide **505**, requiring near stoichiometric amounts of initiator and giving inferior yields of cyclised products. Both substrates gave the same ratio of α to γ attack, 1 : 2, demonstrating that the same intermediate is produced in both cases (Scheme 82).

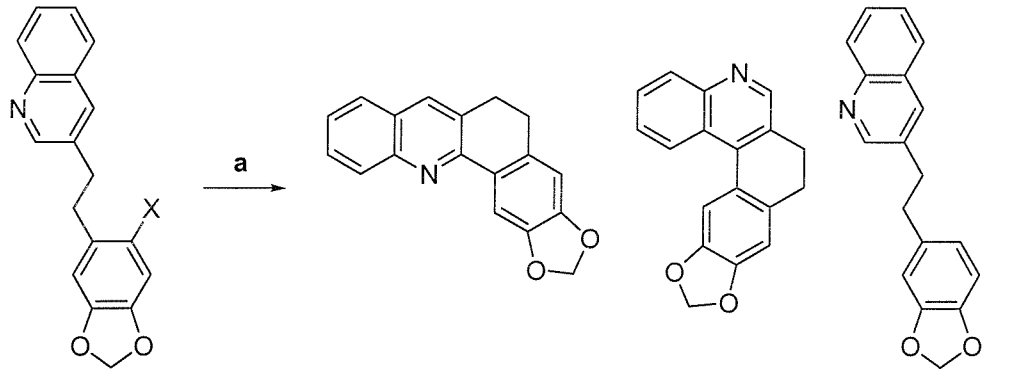


	517	**518**	**519**
505, X = I	38 %	57 %	0 %
507, X = Br	24 %	46 %	18 %

a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 82

The 3-substituted dihydroazastilbenes **509** and **510** also cyclised to both C-2 and C-4 of the quinoline. The iodide precursor **509** gave superior results to the bromide **510**, the latter giving rise to a complex product mixture and poor isolated yields. The ratio of the two cyclised products in the case of the bromide is meaningless as much of the mass balance was lost in workup. Notably, for iodide **509** the reaction favoured cyclisation to C-4 and the ratio of C-2 to C-4 addition was similar to that observed with azastilbenes **505** and **507** (Scheme 83).

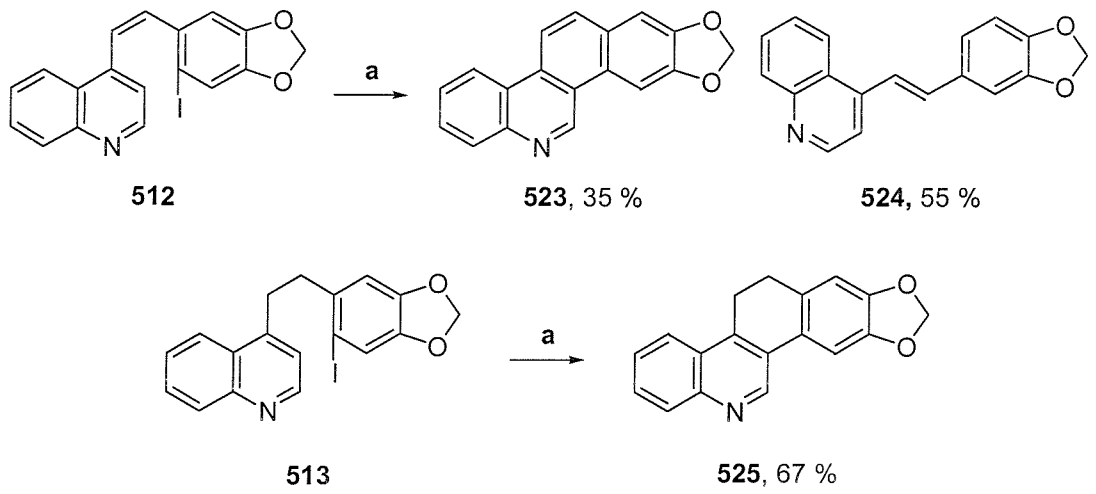


	520	**521**	**522**	with
509, X = I	23 %	51 %	0 %	**509**, 0 %
510, X = Br	18 %	15 %	10 %	**510**, 27 %

a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 83

Cyclisations to C-3 of quinoline from a radical precursor tethered at C-4 were also investigated. Aryl iodide **512**, with an unsaturated tether, proved to be a poor substrate for cyclisation as alkene isomerisation outpaced homolysis of the C-I bond. For aryl iodide **513** no such side reaction can occur and this is reflected in the greater efficiency of the intramolecular radical addition reaction, leading to **525** (Scheme 84).



512 **523**, 35 % **524,** 55 %

513 **525**, 67 %

a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 84

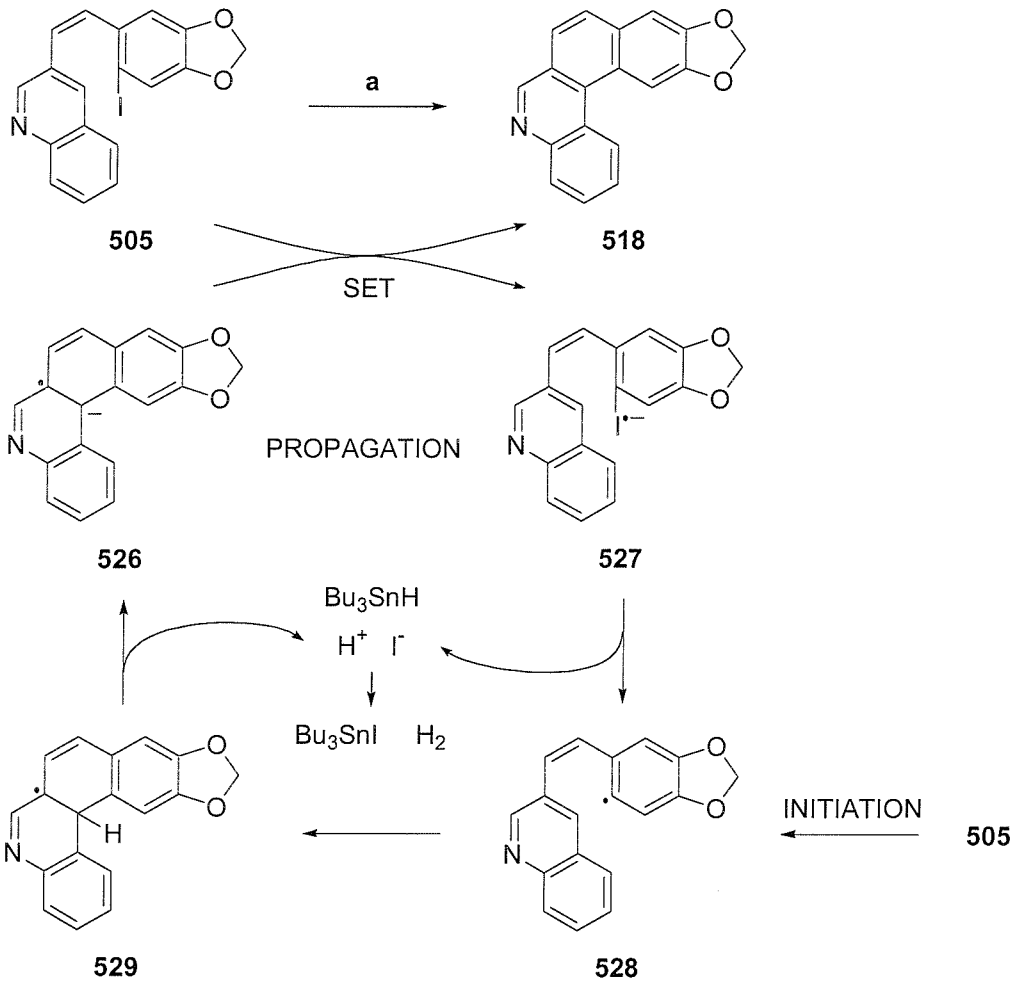
Thus, intramolecular radical additions to quinoline provide a short entry to benzo[*a*]acridines, benzo[*c*]acridines, benzo[*k*]phenanthridines and benzo[*i*]phenanthridines. Importantly, and in contrast to the related cyclisations to pyridines, no products derived from *ipso* attack were observed, only those arising from the 6-*exo*/*endo*-trig pathway were detected. Another important observation is that in all cases studied radical cyclisation is followed by rearomatisation rather than hydrogen atom extraction from tributyltin hydride.

3.4 A NOTE ON THE MECHANISM OF REAROMATISATION

On many occasions during the course of this work we have thought about the nature of the rearomatisation step that occurs in many of the radical cyclisations reported in the literature and in all of the cyclisations reported in this thesis. The observation that iodides require substantially less initiator than bromides in many analogous reactions is an important one. Several research groups have implied that the initiator must be used stoichiometrically and that it is therefore involved in the rearomatisation step. Clearly this cannot be true for many of the cyclisations discussed in this thesis as the initiator is used at sub-stoichiometric levels and the mass balance of the reactions is frequently high. Our rationale is that two propagation sequences occur and that the course followed is dictated by the nature of the radical precursor. That initiation is *via* the

classical mechanism is not in doubt. Once the reaction is underway we suspect that a single electron transfer process may be facile in some cases and not in others.

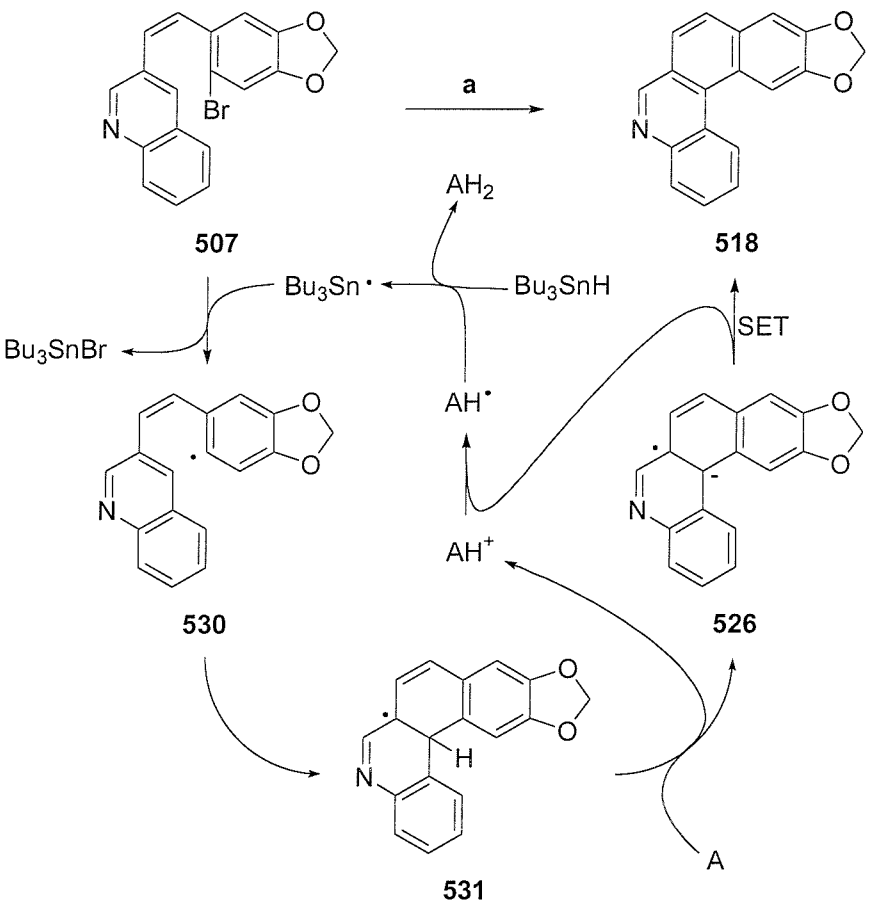
When an iodide such as **505** is used as a radical precursor cyclisation of **528** to **529** may be followed by loss of a proton resulting in radical anion **526**. This then donates an electron to the starting material **505** giving the product **518** and the radical anion **527**. Loss of iodide generates the radical **528**, which can then undergo cyclisation to **529**, propagating the chain reaction. The hydrogen iodide formed as a by-product will react with the tributyltin hydride producing hydrogen and tributyltin iodide (Scheme 85).



a. Bu_3SnH, AIBN.

Scheme 85

When a bromide or selenide is employed as a radical precursor the sequence outlined in Scheme 85 becomes less significant. The cyclised radical intermediate **531** may again lose a proton to an acceptor (A). Candidates for the proton acceptor include the substrate, initiator, product or, in some cases, the solvent. A single electron transfer (SET) to the protonated acceptor leads to the radical intermediate AH˙, which may abstract a hydrogen atom from tributyltin hydride to propagate the sequence (Scheme 86).

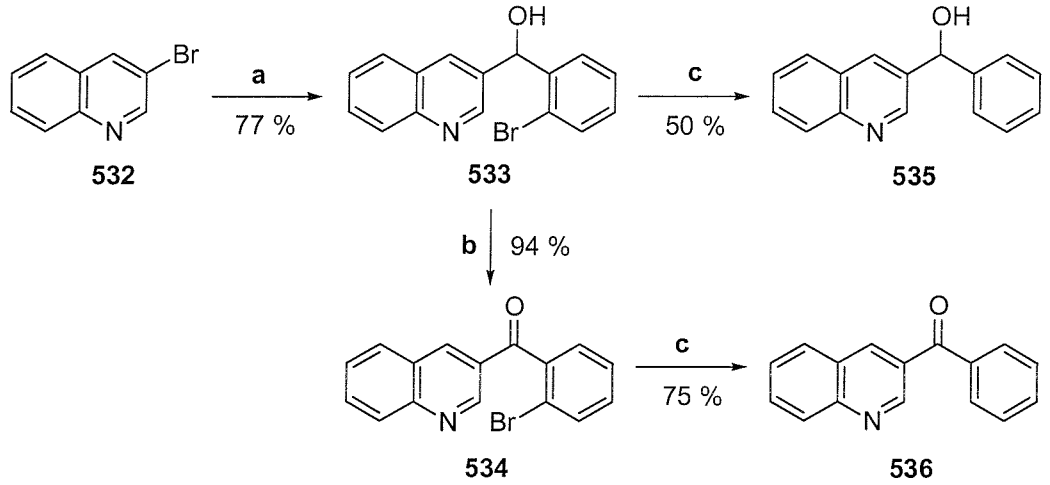


a. Bu_3SnH, AIBN.

Scheme 86

3.5 ATTEMPTED 5 MEMBERED RADICAL CYCLISATIONS

Two attempts were made to effect 5-*exo*/*endo*-trig radical cyclisations to quinolines. As was seen in the pyridine series, only products derived from hydrogen atom abstraction were observed. This confirmed our belief that such 5-*exo*/*endo*-trig cyclisation reactions are more akin to 5-*endo*-trig processes than 5-*exo*-trig processes (Scheme 87).



a. 1) ^{t}BuLi, Et_2O, -100 °C. 2) 2-bromobenzaldehyde; **b**. MnO_2, DCM;
c. Bu_3SnH, AIBN, toluene, Δ.

Scheme 87

3.6 CONCLUSIONS

We have shown that intramolecular 6-*exo*/*endo*-trig (*ortho*) radical cyclisations to C-2, C-3 and C-4 of a quinoline are all facile processes at neutral *p*H and outpace any *ipso* cyclisation pathways. When a *Z*-alkene is used to tether a radical precursor to quinoline at C-2 or C-4, isomerisation of the alkene competes with carbon halide bond homolysis. Cyclisations that employ aryl iodides as radical precursors are more efficient than those which employ aryl bromides. All the cyclisation reactions follow non-reducing pathways. 5-*exo*/*endo*-trig cyclisations to quinolines fail and appear to be more akin to 5-*endo*-trig processes.

CHAPTER 4

INTRAMOLECULAR RADICAL ADDITIONS TO ISOQUINOLINES

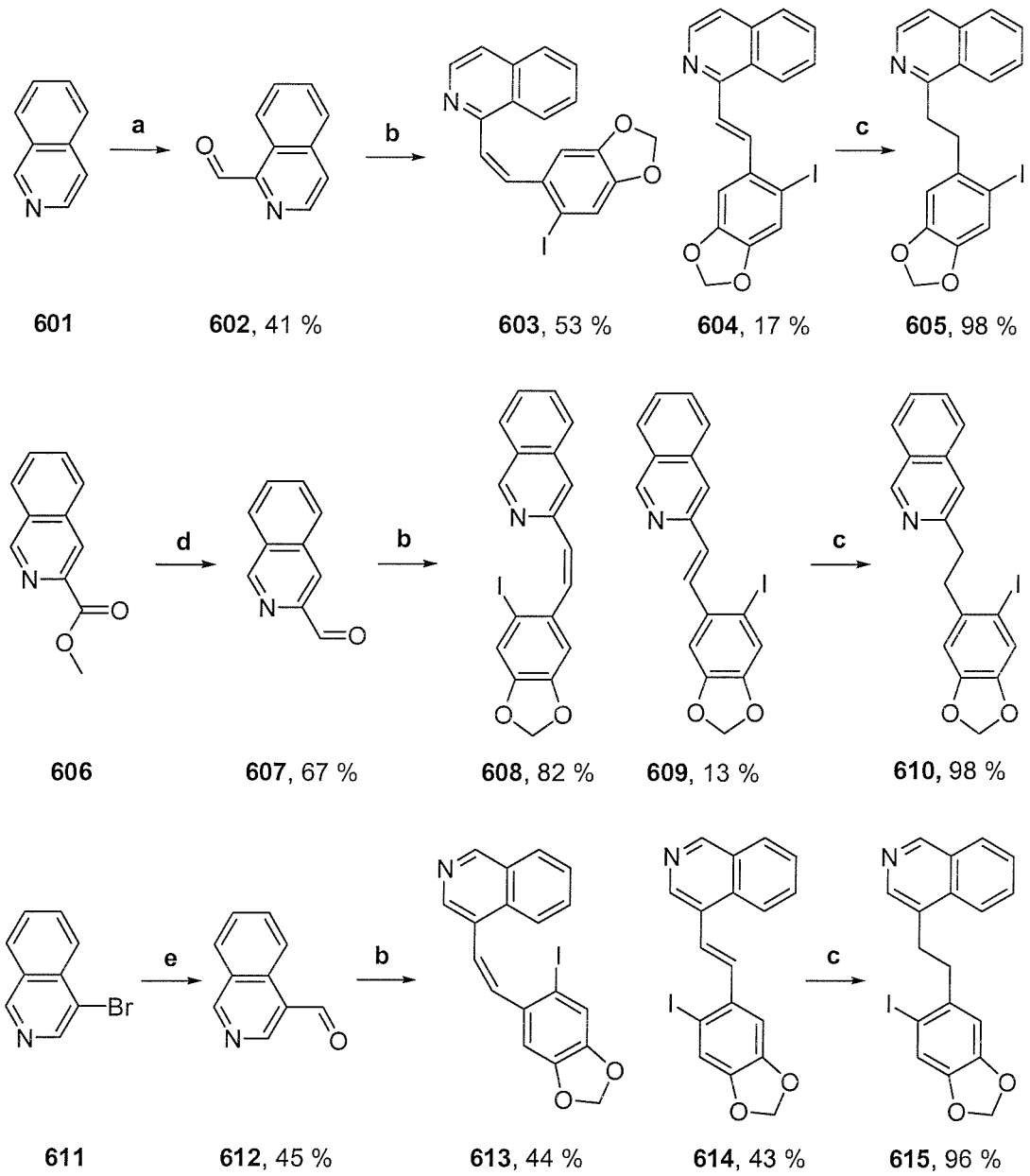
4.1 INTRODUCTION

Following our successful realisation of intramolecular radical cyclisation reactions to pyridines and quinolines, the next logical step was to extend the methodology to isoquinolines. Also documented in this Chapter is work directed towards the synthesis of the natural product avicine.

4.2 PRECURSOR FORMATION

As we have seen with the series of pyridine and quinoline substrates discussed in the preceding chapters, radical precursors are most easily formed *via* a Wittig reaction between commercially available aldehydes and an appropriate phosphonium salt. In the case of the isoquinoline series the aldehydes were not available commercially and had to be synthesised. 1-Isoquinolinecarboxaldehyde was formed from isoquinoline itself using Minisci's radical addition of trioxane, discussed in Chapter 1.[32] 3-Isoquinolinecarboxaldehyde was formed by reduction of the corresponding methyl ester according to Tiffin's procedure[116] and 4-isoquinolinecarboxaldehyde was prepared by Knochel's metallation of 4-bromoisoquinoline followed by quenching with DMF.[117]

Pleasingly, Wittig reaction with all the aldehydes and **362** preceded in high yield. 1-Isoquinolinecarboxaldehyde produced the desired *Z*-alkene **603** and the *E*-alkene **604** in a 3 : 1 ratio in high yield. Likewise, 3-isoquinolinecarboxaldehyde gave a 6 : 1 ratio of the *Z*-alkene **608** and *E*-alkene **609**, while 4-isoquinolinecarboxaldehyde produced an equimolar amount of both isomers **613** and **614**. In each case diimide reduction of these azastilbenes, to **605**, **610** and **615** respectively, proceeded in excellent yield (Scheme 88).



601 **602**, 41 % **603**, 53 % **604**, 17 % **605**, 98 %

606 **607**, 67 % **608**, 82 % **609**, 13 % **610**, 98 %

611 **612**, 45 % **613**, 44 % **614**, 43 % **615**, 96 %

a. 1) TFA, H_2O_2, *s*-trioxane, $FeSO_4$, MeCN, Δ, 2) H_2SO_4, H_2O, Δ;

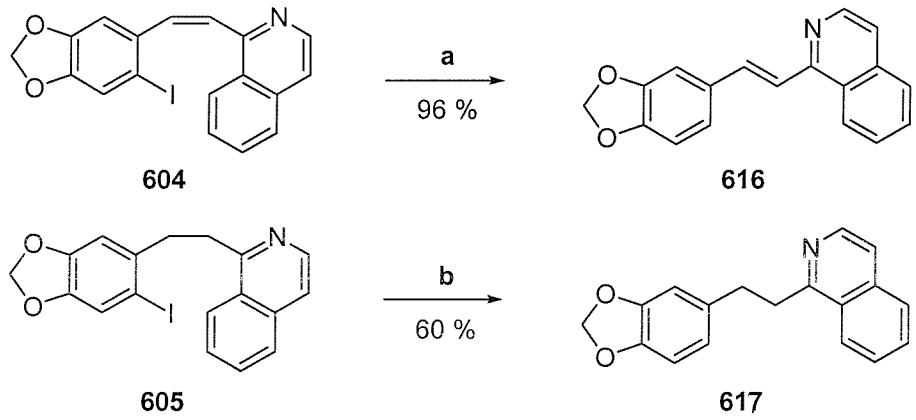
b. NaH, THF, 0 °C, **362**; **c**. tosyl hydrazine, NaOAc, THF, H_2O, Δ;

d. -100 °C, DIBAL-H, DCM; e. 1) Et_2O, -90 °C, ^tBuLi, 2) DMF, -60 °C.

Scheme 88

4.3 RADICAL CYCLISATIONS

We chose first to study an isoquinoline with a radical precursor attached at C-1. It was hoped that we might be able to observe some *ipso* attack, as in the pyridine series, or perhaps attack onto nitrogen. However this was not the case, as with both **604** and **605** simple reduction of the C-I bond was observed. Notably, the alkene tether in **604** was isomerised from *Z* to *E* indicating that addition of the tributyltin radical to the alkene was facile in this case. The yield of recovered product was much lower for isoquinoline **605** suggesting that some competitive side reactions occur. These may involve addition of the radical intermediate to the nitrogen atom or *ipso* attack followed by fragmentation and / or rearrangement. Alas, no evidence for these suggestions was forthcoming (Scheme 89).



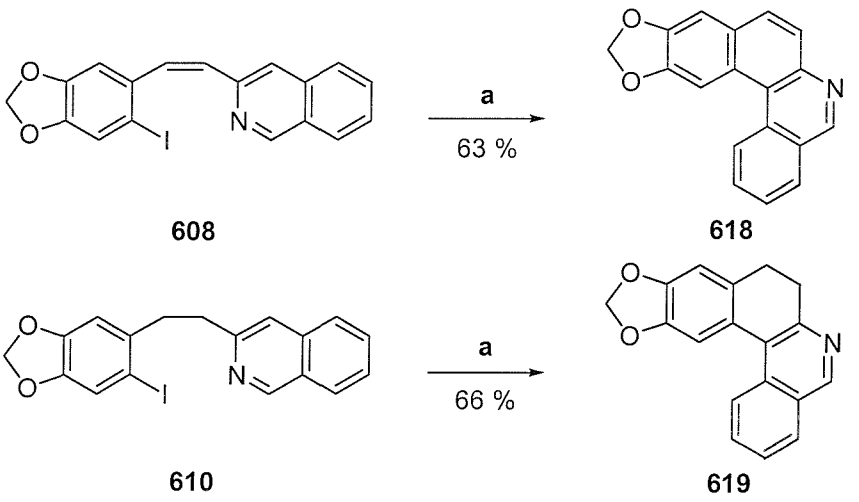
604 **616**

605 **617**

a. Bu_3SnH, AIBN, toluene, Δ; **b**. Bu_3SnH, AIBN, THF, Δ.

Scheme 89

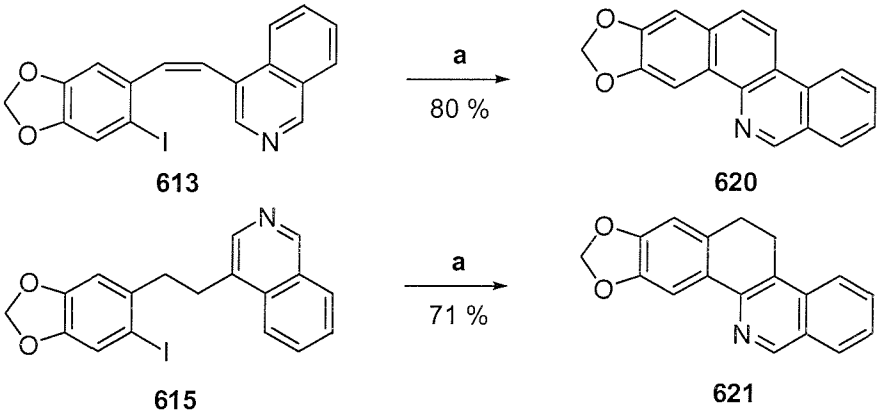
Pleasingly cyclisation of the C-3 substituted isoquinoline precursors **608** and **610**, with both alkane and alkene tethers, proved clean and high yielding. Crucially no rearranged products were observed nor products derived from cyclisation to nitrogen (Scheme 90).



a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 90

Cyclisation to the C-3 position of isoquinoline was also found to be favourable. Thus **613** and **615** were converted into **620** and **621** respectively, and in high yield, on treatment with tributyltin hydride and AIBN. Noteworthy is the higher yield of the substrate with the unsaturated tether compared to the substrate with the saturated tether. This provides a further illustration that the cyclisation of the conformationally restricted substrate is generally more efficient than those substrates with a flexible tether provided *E* / *Z* isomerisation is slow. The ability to form the radical in close proximity to the acceptor ring is why the chemistry we have developed is important as a tool to form such condensed heteroaromatic ring systems (Scheme 91).



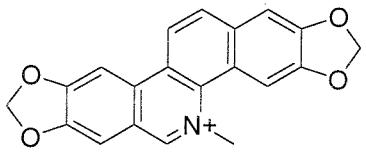
a. Bu_3SnH, AIBN, toluene, Δ.

Scheme 91

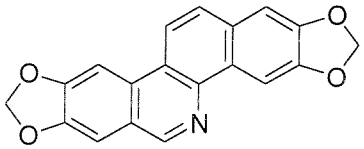
4.4 AVICINE AND NORAVICINE

4.41 BACKGROUND

Avicine **302** is a benzo[*c*]phenanthridine based alkaloid first isolated from the root bark of *Zanthoxylum avicennae* by Arthur *et al.* in Hong Kong, 1959.[81] This plant has attracted much interest because of its medicinal values, Arthur having described it as 'an erect shrub with white flower ... used in the Colony against sore throat and jaundice'.[81] Noravicine **622** is the des-*N*-methyl derivative of avicine and has only been isolated from the Japanese rutaceous plant *Xanthoxylum cuspidatum*.[118]



302



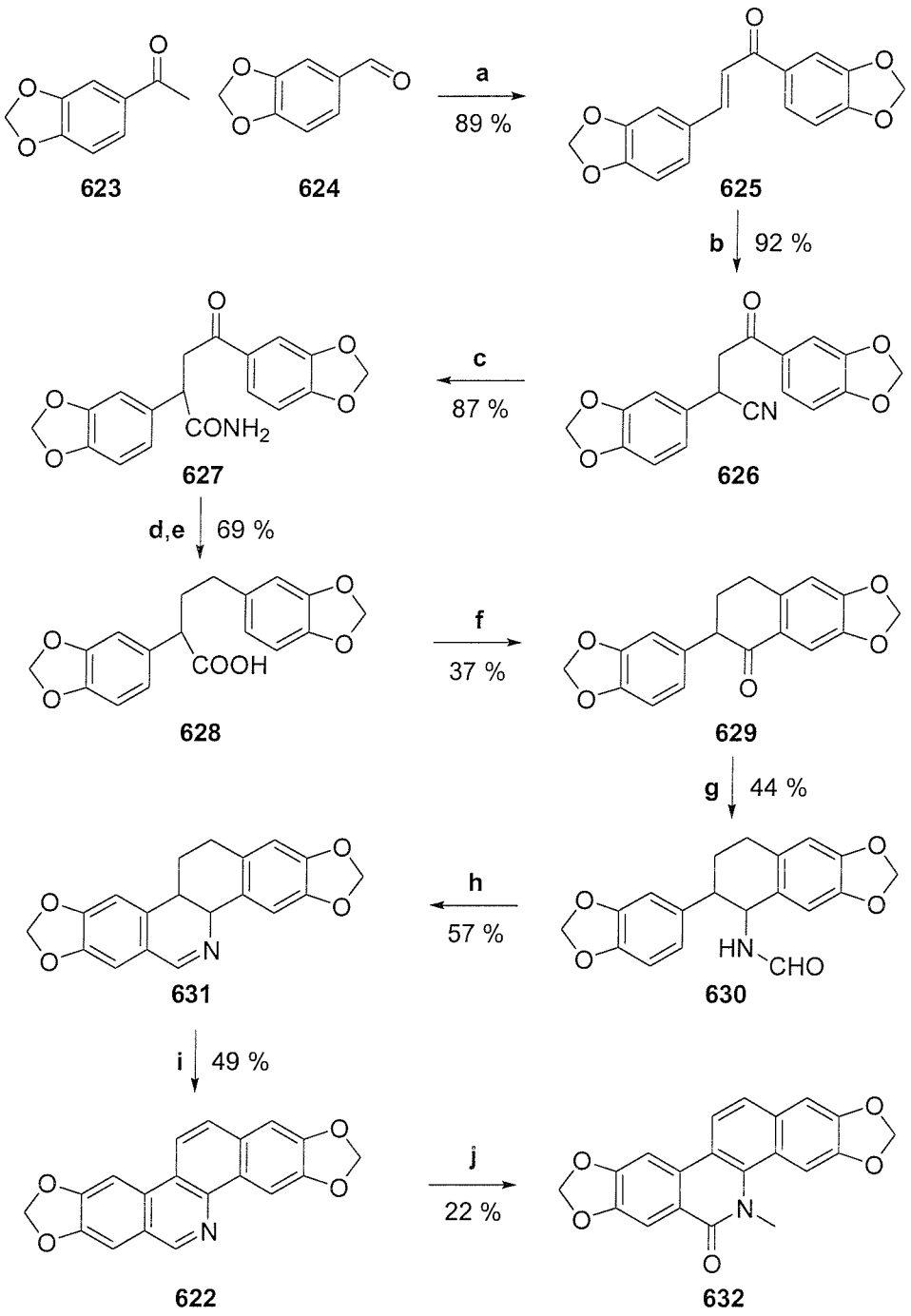
622

Avicine is isolated from the bark of *Xanthoxylum inerme*,[119] the wood and root bark of *Toddalia asiatica*,[80,120,121] the bark of *Zanthoxylum integrifoliolum*[122] and the root bark and wood of *Zanthoxylum simulans*.[123] Recently it has been isolated from the root bark of *Zanthoxylum nitidum*, a scandent shrub found in Moluccas, New Guinea, China and Taiwan, which is used in folk medicine to relieve pain and to detoxify snake-bites.[124]

Avicine has also been the subject of more mainstream biological testing, showing modest antitumour activity against the Sarcoma 180 tumour cell line[125] and significant inhibition of the avian myeloblastosis virus reverse transcriptase.[126,127] More importantly it inhibits ADP induced platelet aggregation and was the lead compound in a successful study into the activity of its derivatives.[122]

4.42 PREVIOUS SYNTHETIC STRATEGIES

Avicine has been prepared using a variety of synthetic strategies. As it disproportionates readily its structure was confirmed in 1961 by Gopinath's synthesis, *via* noravicine, of oxyavicine **632** (Scheme 92).[128]

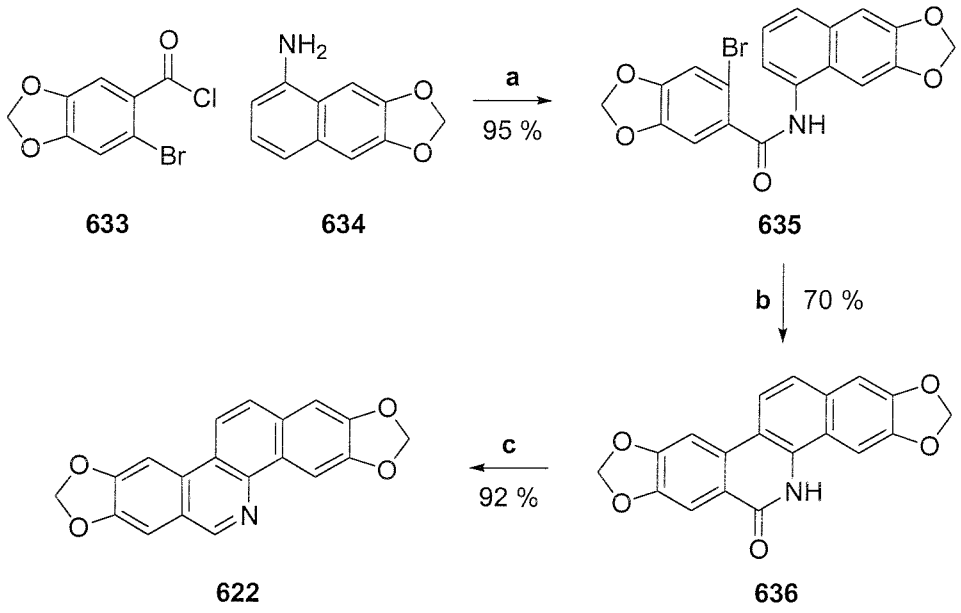


a. EtOH, $NaOH_{(aq)}$; **b**. $EtO(CH_2)_2OH$, AcOH, $KCN_{(aq)}$, Δ; **c**. AcOH, conc. $H_2SO_{4(aq)}$;
d. EtOH, $NaOH_{(aq)}$, Δ; **e**. AcOH, $HClO_{4(aq)}$, Pd/C, H_2, Δ; **f**. $POCl_3$, Δ;
g. $HCONH_2$, HCO_2H, $(NH_4)_2SO_4$, Δ; **h**. $POCl_3$, toluene, Δ; **i**. Pd/C, Δ;
j. 1) xylene, nitrobenzene, Δ, Me_2SO_4, 2) $KOH_{(aq)}$, $K_3Fe(CN)_{6(aq)}$, Δ.

Scheme 92

This ten step pathway has an overall yield of 2.2 % for noravicine and 0.5 % for oxyavicine. The first three steps are all high yielding but the classic tetralone synthesis followed by a Leuckart - Pictet - Hubert amidation, to form the core of the benzo[*c*]phenanthridine, is carried out under such harsh conditions that more than 90 % of the material is lost.

Kessar published a much shorter and more efficient synthesis of noravicine in 1974, relying upon the photocyclisation of an aromatic bromide as the key step. Interestingly the photocyclisation of the debromo species failed to effect any cyclisation (Scheme 93).[129]

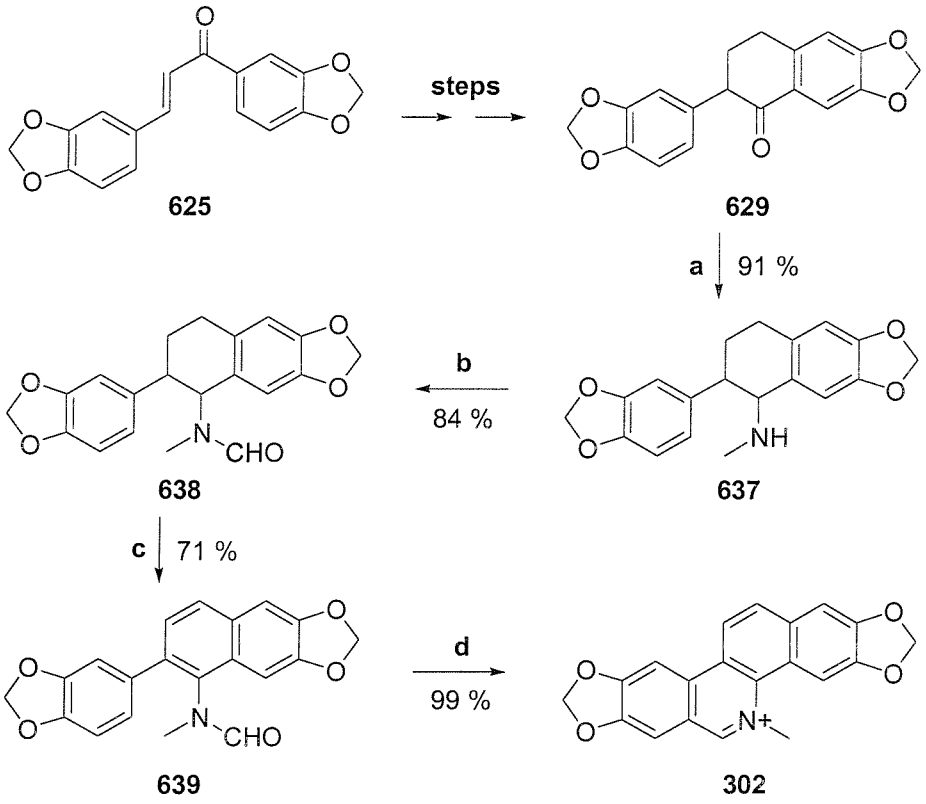


a. no conditions given; **b**. benzene, MeOH, hυ; **c**. $LiAlH_4$.

Scheme 93

Ishhi was next to publish a synthesis of avicine, based on Gopinath's synthesis of the tetralone **629**, with the overall yield increased to 10 % (Scheme 94).[125,130,131] This time avicine itself was the target, being formed directly in a high yielding Bischler - Napieralski reaction. Interestingly, Ishhi has recently published a report on the use of triphosgene [$(Cl_3CO)_2CO$] as an alternative to $POCl_3$ in this step. The resulting workup is reported to be much cleaner, although with a yield of 99 % from $POCl_3$ I think most

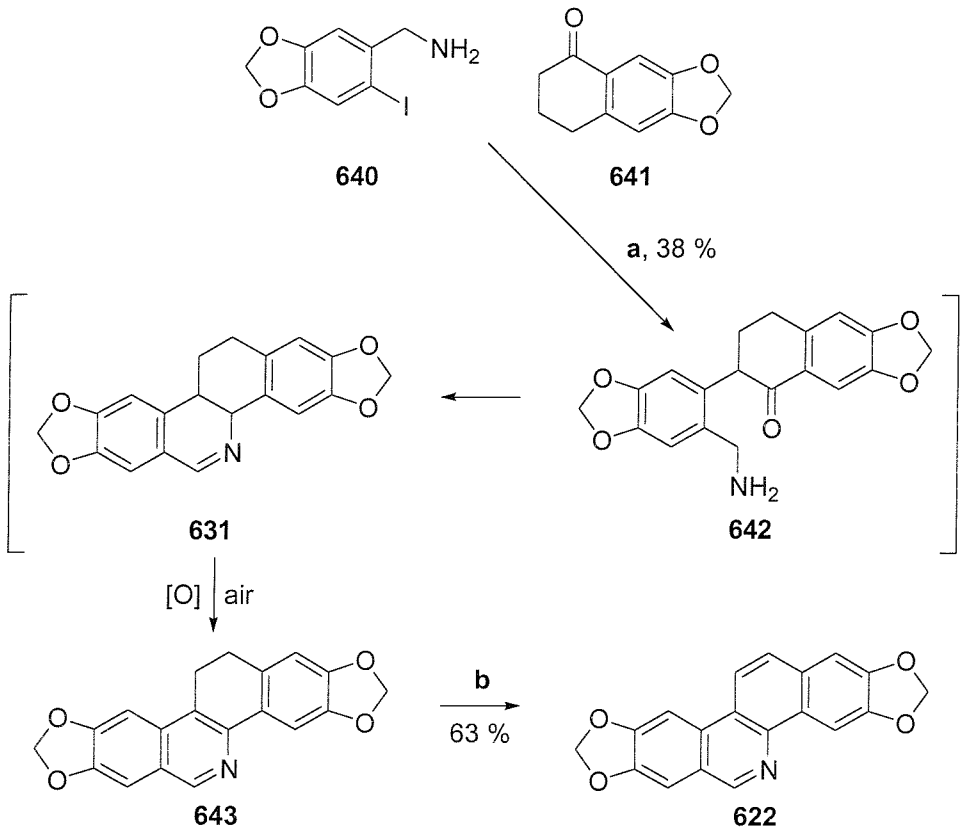
researchers would choose the original procedure to avoid the use of a potential nerve agent![132]



a. 1) $MeNH_2$, $TiCl_4$, $CHCl_3$, Δ, 2) $NaBH_4$, MeOH, DMF; **b**. Cl_3CCHO, $CHCl_3$, Δ; **c**. DDQ, benzene, Δ; **d**. $POCl_3$, MeCN, Δ.

Scheme 94

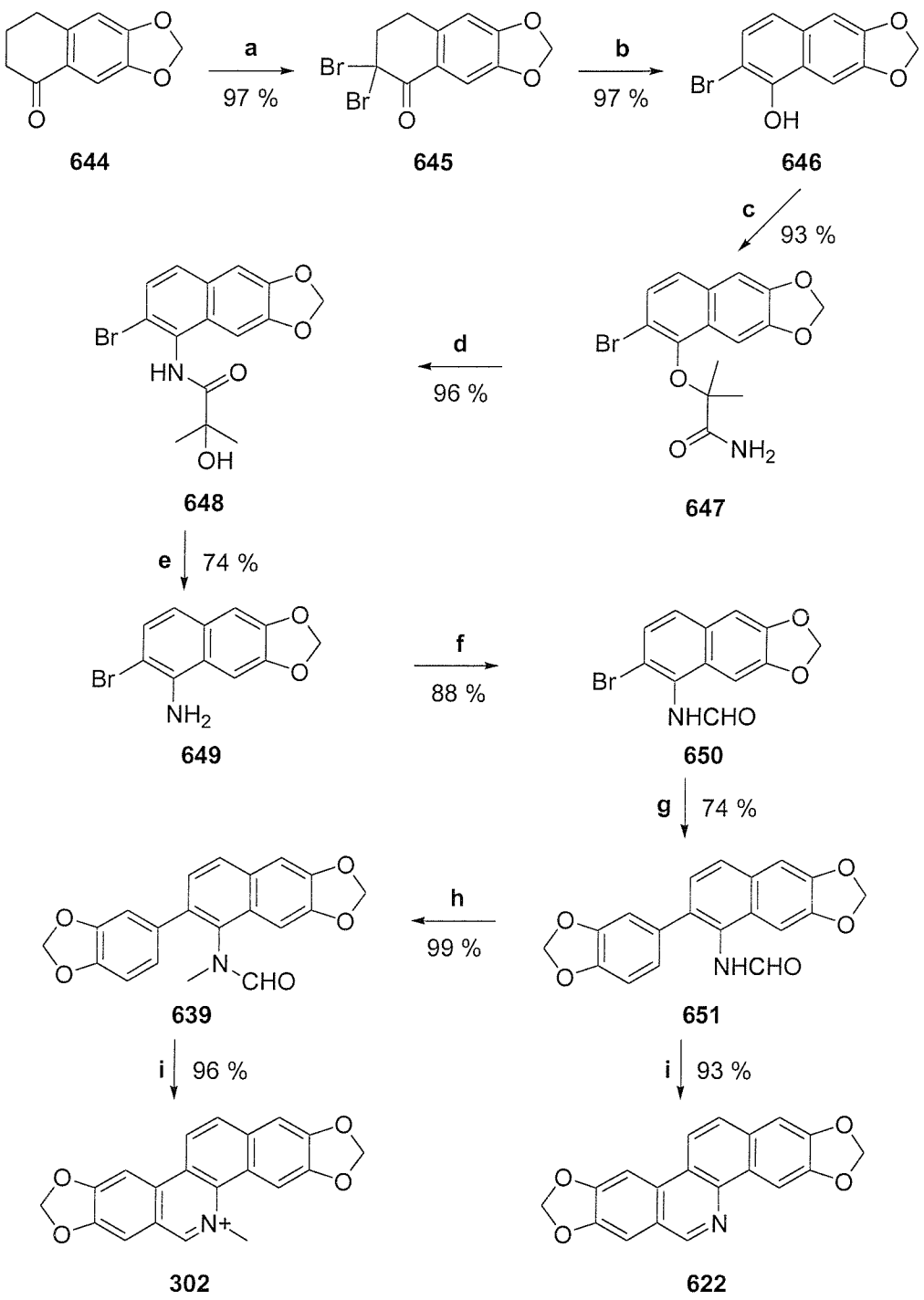
Roussi was next to report an approach to noravicine.[133] Starting from the known iodinated benzylamine **640** and substituted tetralone **641**, his extended $S_{RN}1$ reaction featured as a key step. Aerial oxidation of the tetrahydro species **631** to the dihydro species **643** was followed by dehydrogenation over Pd / C to complete the synthesis (Scheme 95).



a. $NH_{3(l)}$, $^{t}BuOK$, $CHCl_3$, hυ; **b**. Pd/C, Δ.

Scheme 95

Geen and co-workers were first to exploit a Suzuki coupling in the synthesis of avicine and noravicine.[101,134] A Smiles rearrangement neatly formed the required napthylamine **649** from napthol **646** and the latter stages of Ishhi's synthesis finished this high yielding approach (Scheme 96).

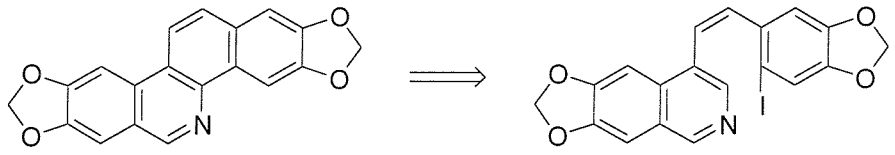


a. Br_2, $CHCl_3$; **b**. DBU, MeCN, Δ; **c**. $(Me)_2CBrCONH_2$, NaOH, DMPU;
d. NaH, DMF, DMPU, Δ; **e**. $NaOH_{(aq)}$, MeOH, Δ; **f**. HCO_2H, $(CH_3CO)_2O$;
g. piperonyl-boronic acid, $Pd(OCOCH_3)_2$, PPh_3, DME, $Na_2CO_{3(aq)}$;
h. MeI, NaH, THF; **i**. $POCl_3$, MeCN, Δ.

Scheme 96

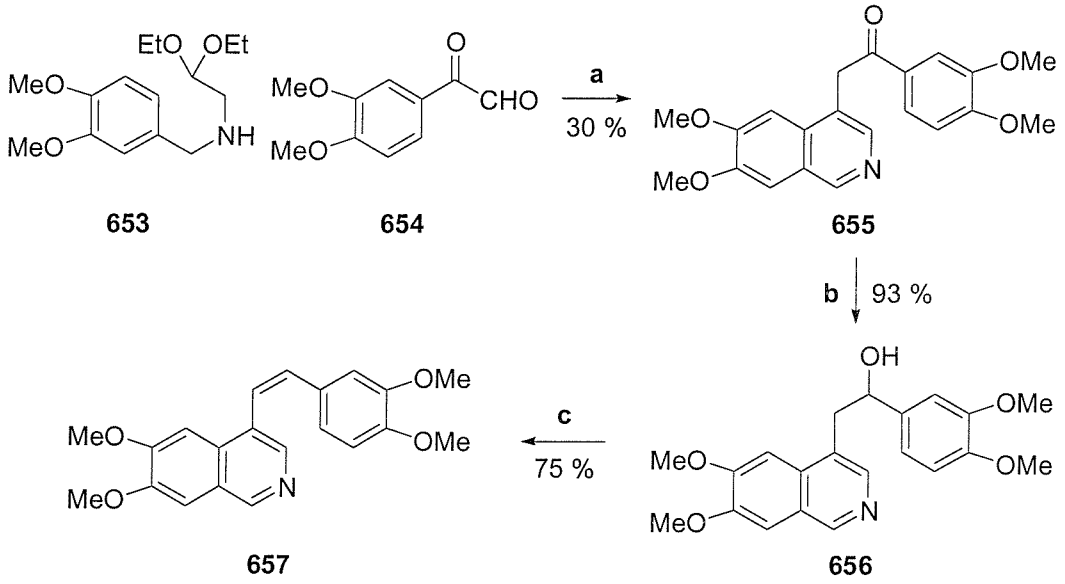
4.43 Our First Approach to Avicine

Once again our key disconnection led back to an isoquinoline tethered in the 4 position to an iodopiperonyl group (Scheme 97). On this occasion we sought to form the radical precursor using a modification of Dyke and Sainsbury's synthesis of the similar compound **657** rather than use the Wittig reaction (Scheme 98).[135] This synthesis was a modification of Bobbitt's tetrahydroisoquinoline formation from **653**.[136,137]



622 **652**

Scheme 97



653 **654** **655** **656** **657**

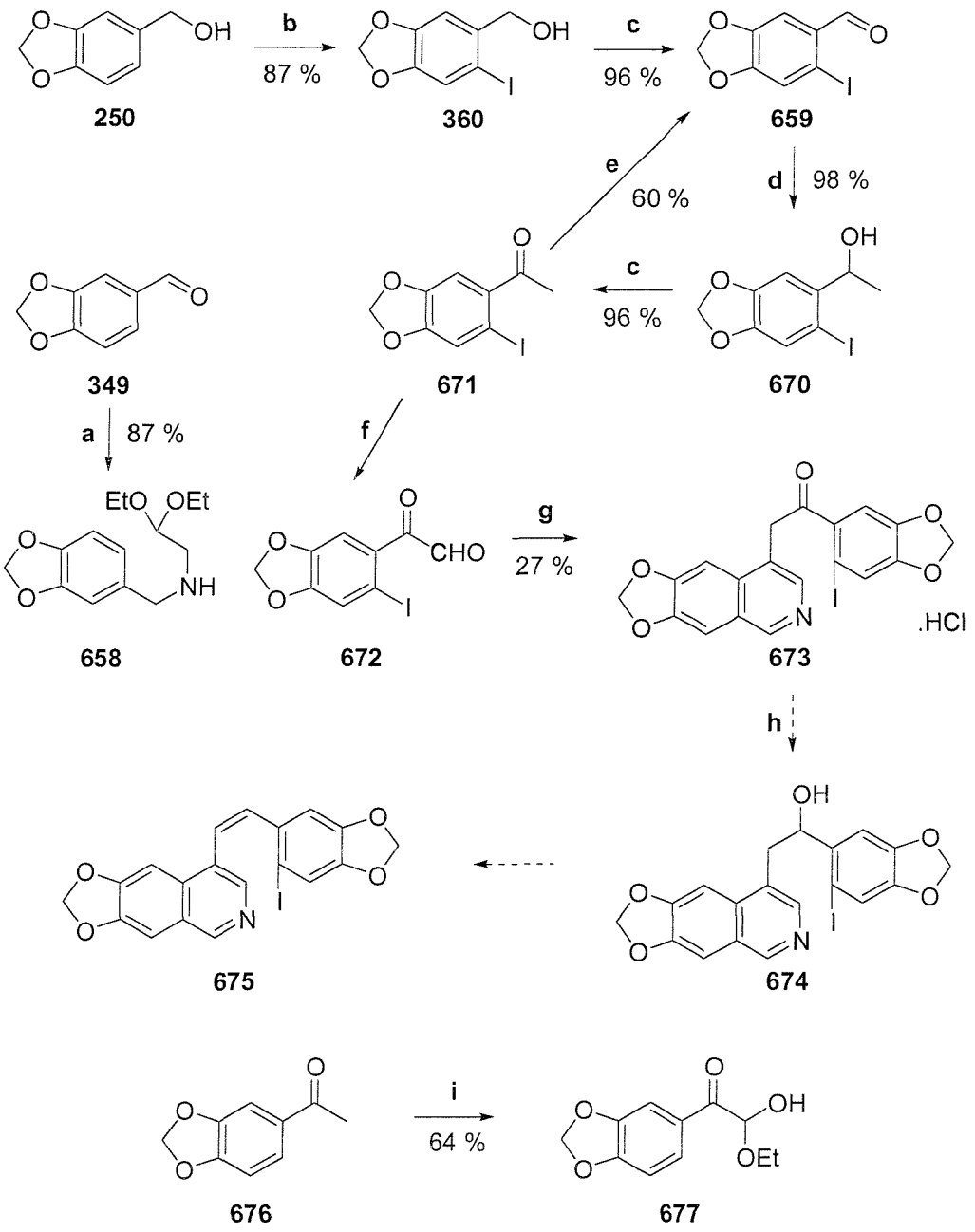
a. conc. $HCl_{(aq)}$, EtOH, Δ; **b**. EtOH, $NaBH_4$, Δ; **c**. $CHCl_3$, $HCl_{(g)}$.

Scheme 98

The advantage of this route was that cyclisation could be attempted on the ketone **673**, the alcohol **674** or the azastilbene **675**. Accordingly the acetal was prepared by a modification of Bobbitt's reductive amination to form **658**.[136,138] The arylglyoxal **672** was more of a synthetic challenge but a recent paper by Floyd[139] gave several excellent

examples of arylglyoxal formation from the corresponding acetophenones *via* bromination and then oxidation by DMSO. The acetophenone **671** was formed in three steps from iodinated piperonol **360**.[140,141] Our first attempt to oxidise the acetophenone **671** resulted in isolation of 6-iodopiperonal **659**. As the crude ^{1}H NMR showed two distinct aldehyde peaks, one of which was assigned to **659**, we felt that **672** might be prone to decarbonylation. Lachman was first to report this thermal extrusion of CO in 1922 when benzil was converted to benzoic acid.[142] After many attempts to purify the glyoxal by column chromatography or recrystallisation we decided to embark on a different method of synthesis. Classically selenium dioxide has been used for the oxidation of an acetophenone to a glyoxal but these reactions tend to suffer from poor yields and the persistence of selenium residues in the product.[143] This is exactly what we found when the method was applied to acetophenone **671**. The crude reaction mixture still contained a mixture of the aldehyde **659** and the glyoxal **672**. We returned to Floyd's[139] synthesis and carried out a trial reaction on the commercially available acetophenone **676**. This resulted in formation of the expected glyoxal, isolated as the hemiacetal **677**, which was thermally stable (Scheme 99).

As we were unable to purify the glyoxal **672** we decided to use it crude. Acid induced cyclisation of the acetal **658** produced the unstable 1,2-dihydroisoquinoline which then added to glyoxal **672**. Pleasingly the yield, based upon the acetal **658**, was similar to that achieved by Dyke and Sainsbury,[135] showing that the use of the crude glyoxal hadn't had any significant impact the outcome of the reaction. The isolated HCl salt **673** was not as easy to handle as we might have expected. Dependent on *p*H, a mixture of the keto and enol forms as well as the free base and isoquinoline salt were all present in the mixture. Reduction of this mixture with sodium borohydride led to an intractable mixture of compounds (Scheme 99). Attempts to optimise this reaction met with failure so a new route to avicine was sought.



a. $NH_2CH_2CH(OEt)_2$, $NaBH_3CN$, $HCl_{(aq)}$, MeOH; **b**. I_2, AgO_2CCF_3, $CHCl_3$, 0 °C;

c. PCC, DCM; **d**. MeMgCl, Et_2O, 0 °C;[141] **e**. 1) HBr, DMSO, 55 °C, 2) EtOAc, 77 °C;

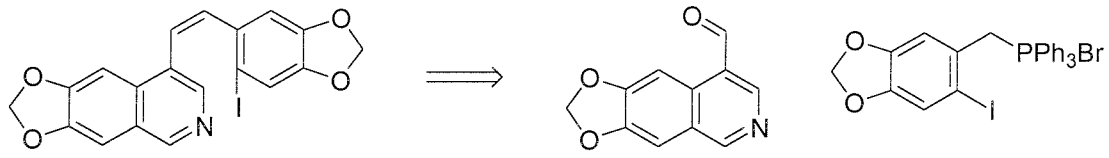
f. HBr, DMSO, 55 °C, crude; **g**. HCl, EtOH, Δ; **h**. $NaBH_4$, EtOH, Δ;

i. 1) HBr, DMSO, 55 °C, 2) EtOH, Δ.

Scheme 99

4.44 Our Second Approach to Avicine

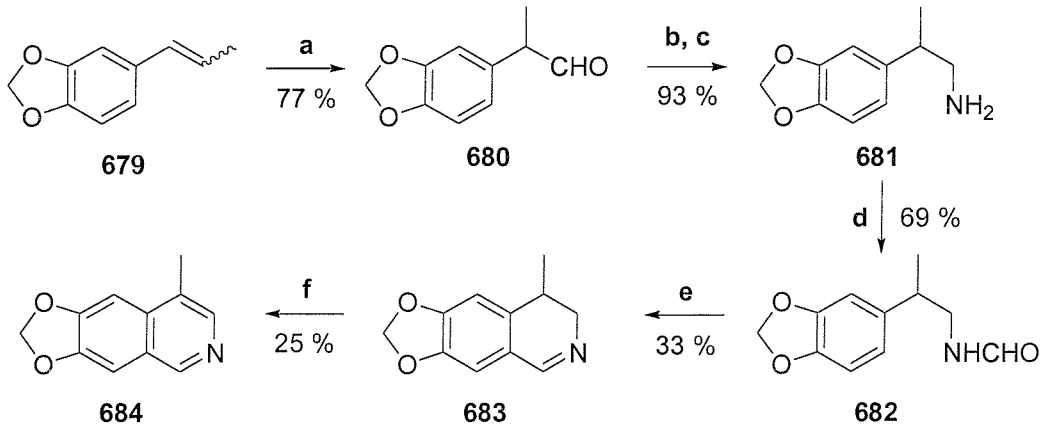
Our new approach to **652** was based on a Wittig reaction between phosphonium salt **362** and the unknown isoquinolinecarboxaldehyde **678** (Scheme 100).



652 **678** **362**

Scheme 100

It was hoped that **678** might be prepared by oxidation of the known isoquinoline **684**. Takagi's synthesis of **684** started with a rearrangement of isosafrol **679** to aldehyde **680** and concluded with a Bischler - Napieralski cyclisation **682** **683** (Scheme 101).[144]

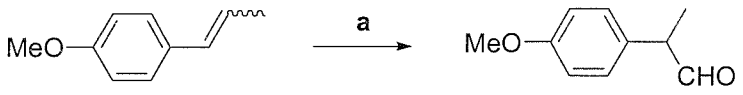


679 **680** **681** **682** **683** **684**

a. I_2, HgO, Et_2O, H_2O; **b**. NH_2OH, pyridine, MeOH; **c**. $LiAlH_4$, Et_2O, Δ;
d. $HCO_2H_{(aq)}$, Δ; **e**. $POCl_3$, xylene, Δ; **f**. *p*-cymene, Pd/C, Δ.

Scheme 101

A more recent paper by Kikuchi had shown that the rearrangement of arylpropenes *e.g.* **685** could be carried out in the presence of many different bases, with the optimal being silver nitrate (Scheme 102).[145]



685

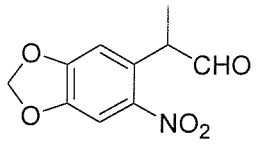
686

$AgNO_3$	95 %
Ag_2O	95 %
CuO	95 %
Cu_2O	86 %
Na_2CO_3	31 %

a. I_2, base, dioxane, H_2O, (Δ for CuO, Cu_2O, Na_2CO_3).

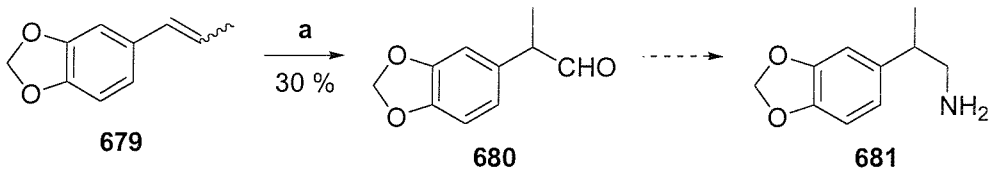
Scheme 102

Keen to avoid the use of toxic mercuric salts we decided to carry out the rearrangement with silver nitrate. The reaction mixture was unexpectedly complex and the only product isolated in significant quantity was the rearranged and nitrated product **687**.



687

The rearrangement was attempted using silver(I) oxide and then copper(II) oxide both at room temperature and under reflux. Perplexingly, no significant products could be isolated. As we had had some success with effecting the rearrangement using silver nitrate we decided to try the reaction with silver trifluroacetate. This proved successful although we were disappointed by the low yield. It was felt that optimisation could be left until we had evaluated the rest of our route. This was fortunate because although formation of the oxime was easily accomplished the reduction to the amine was not (Scheme 103).



679 680 681

a. AgO_2CCF_3, I_2, dioxane, H_2O.

Scheme 103

At this juncture we decided to abandon avicine. Although it should be possible to achieve it's synthesis using our radical cyclisation methodology our approach to the syntheses of the precursor **652** was becoming long and low yielding. If a convenient synthesis of aldehyde **678** could be devised then I believe that our methodology will be a key part of an efficient synthesis of avicine.

4.5 CONCLUSIONS

We have shown that intramolecular 6-*exo*/*endo*-trig radical cyclisations to C-3 and C-4 of an isoquinoline are facile processes at neutral *p*H and outpace any *ipso* cyclisation pathways. No 5-*exo*-trig, *ipso* attack onto C-1 of an isoquinoline was observed when a radical precursor was attached to that carbon. Indeed only hydrogen atom abstraction from tributyltin hydride was noted. All the cyclisation reactions follow non-reducing pathways and no cyclisation onto nitrogen was observed. In addition to this we attempted to synthesise the alkaloid avicine using a disconnection designed to show the versatility of our methodology.

CHAPTER 5

A COMPARISON OF RADICAL MEDIATORS

5.1 BACKGROUND

Organotin hydrides have widespread use in modern organic chemistry.[146] Being tolerant of many carbonyl, hydroxyl and amino groups, its primary use is as a mediator of radical reactions. It does, however, have some drawbacks. In 1886 White did the first meaningful tests on the toxicity of organotin compounds in an assortment of mammalian species.[147] Since then it has been well documented that organotin compounds are neurotoxins.[148] Hence, any pharmaceuticals that are prepared using an organotin mediated cyclisation must be rigorously purified to ensure no tin residues remain. The cost of the reagent and stoichiometric production of waste organotin residues, which are notoriously difficult to remove, provide further barriers to its widespread use. Several methods are available for the removal of tin residues including the conversion of triorganotin halides to fluorides through a vigorous wash with aqueous potassium fluoride solution, followed by precipitation of polymerised triorganotin fluoride.[44] $Ph_2PO_2Bu_4N$ can also be used during work-up as a triorganotin scavenger.[149,150] Hydrolysis of triorganotin halides using wet DBU has also been effective, the tin hydroxides formed being retained at the head of a silica column along with the DBU hydrohalide whilst the cyclised product is chromatographed free of tin.[151] Another protocol involves reaction of the spent reagent with a reducing agent to convert the triorganotin halide to the hydride. This non-polar compound can then be separated by elution through a silica column and, if desired, recyclied.[152] There has been much interest in the development of non-toxic, cheap, easily handleable and easily separable radical mediators to replace tributyltin hydride.

Many researchers have looked to modify organotin hydrides by including groups that simplify the removal of its unwanted by-products. These include the very polar pyridylstannanes,[153] fluorous tin hydrides which can be selectively extracted into fluorinated solvents,[146] water soluble tin hydrides and polymer supported tin hydrides.[148,153] All of these methods fail to tackle the main issues with organotin hydride use. They undoubtedly help the synthetic organic chemist purify his

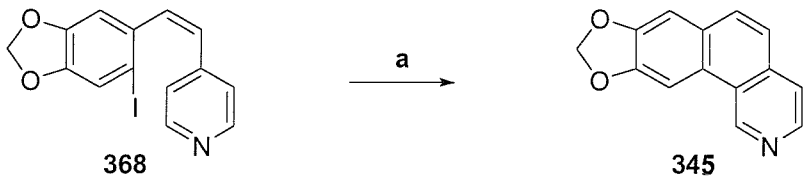
compounds but they do not stop the production of waste tin compounds and serve to increase the cost of the reactions they mediate. With this in mind we were keen to look at other methods of radical generation which reduced the environmental impact of tin.

5.2 SILICON AND GERMANIUM HYDRIDES

Lying above tin in the periodic table, silicon and germanium were immediate contenders in the search for alternative radical mediators. Tris(trimethylsilyl)silane is the best mimic of tributyltin hydride.[154] With a bond strength of about 5 kcal mol^{-1} more than that of a Sn-H bond, the Si-H bond undergoes hydrogen atom abstraction less readily but at a useful rate. In a cyclisation reaction this means that reduction will be slower allowing radical intermediates more time to form cyclic products. On the other hand, tris(trimethylsilyl)germanium hydride has a weaker metal to hydrogen bond and undergoes hydrogen atom extraction much more readily than tributyltin hydride.[155] Criticism of these reagents stems from their very high cost and air sensitivity. In addition to this tris(trimethylsilyl)germanium residues are almost as difficult to remove from reaction mixtures as tributyltin resides.

Keen to see if these reagents would give the outcomes expected with our system we set up a direct comparison. Pyridines tethered by both a saturated and an unsaturated two carbon chain at C-4, **368** and **372**, were chosen as our test substrates. It was hoped that these would allow us to see the effect of the mediators on the course of reactions where reduction occurs along with both 6-*exo*/*endo*-trig and 5-*exo*-trig cyclisations.

Accordingly the substrates were heated under identical reaction conditions with tris(trimethylsilyl)silane, tributyltin hydride and tris(trimethylsilyl)germanium hydride. Pleasingly with azastilbene **368** all 3 mediators gave very high yields of **345** (99, 98 and 97 % respectively). It should be noted that the trend we appear to see is not to be trusted as essentially all three reactions were quantitative and mechanical losses would cause the results to fluctuate by a few percent (Scheme 104).

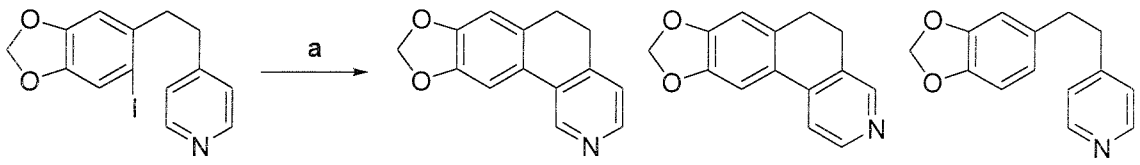


$(Me_3Si)_3SiH$	99 %
Bu_3SnH	98 %
$(Me_3Si)_3GeH$	97 %

a. AIBN, PhMe, Δ.

Scheme 104

Cyclisation of the dihydroazastilbene led to an unexpected set of results. Mass recovery for both the silane and germane based reagents was higher than that for the tin mediated cyclisation. This is due in part to the more extensive purification process involved in removing tin residues from the reaction mixtures. We can still see the trends we are expecting, with the yield of cyclised products being far higher for $(Me_3Si)_3SiH$ than for either Bu_3SnH or $(Me_3Si)_3GeH$. Recovery of the reduced product **377**, formed by hydrogen atom extraction, is much higher with $(Me_3Si)_3GeH$ than with Bu_3SnH which is in turn much higher than that for $(Me_3Si)_3SiH$. This trend clearly shows that the Ge-H bond is weaker than the Sn-H bond which in turn is weaker than the Si-H bond. We can also see a new trend that is noticeable throughout this Chapter. The ratio of the 6-*exo*/*endo*-trig cyclisation product to the 5-*exo*-trig cyclisation product has some variability. Here we can see the two extremes, from a 1 : 1 to a 2 :1 ratio in favour of direct cyclisation (Scheme 105).



$(Me_3Si)_3SiH$	39 %	41 %	16 %
Bu_3SnH	31 %	18 %	31 %
$(Me_3Si)_3GeH$	34 %	19 %	43 %

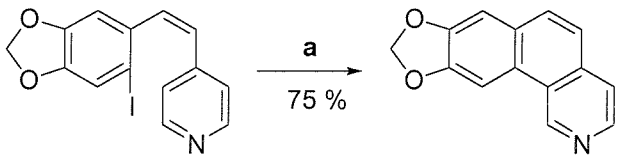
a. AIBN, PhMe, Δ.

Scheme 105

5.3 ALTERNATIVES TO GROUP 14 METAL HYDRIDES

Several non-group 14 metals are able to mediate radical reactions including samarium, cobalt and indium based reagents. In each case a single electron transfer from the metal to the organic halide occurs resulting in a change in oxidation state. The use of samarium diiodide was first reported by Molander in 1990.[156] Carbon halide bonds are homolytically cleaved by the reagent to give a carbon centred radical and samarium trihalide. Cyclisation can then occur with the resultant radical being reduced to an organosamarium species. Another possible pathway is that of the initial radical formed is reduced to an organosamarium species. In turn this species may add to an electrophilic centre. This will only occur if cyclisation of the radical intermediate is slow. In both cases the resultant organosamarium is hydrolysed on workup.

Exposure of azastilbene **368** to samarium diiodide in the presence of HMPA resulted in high yielding cyclisation and formation of the fully aromatic product **345**. It is not clear whether reduction to an organosamarium intermediate occurs, but if it does an oxidative step must follow (Scheme 106).

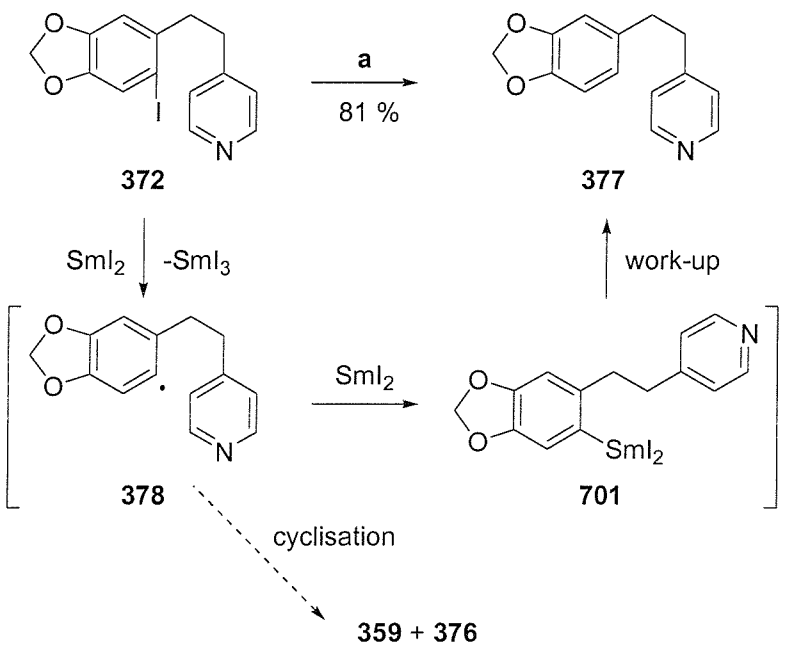


368 **345**

a. SmI_2, HMPA, THF, 0 °C.

Scheme 106

By contrast, the dihydroazastilbene **372** did not undergo cyclisation to **359** and / or **376**. In this case only **377**, the product arising from reduction, was recovered. This result suggests that the aryl radical formed is readily trapped by SmI_2 and that this outpaces both the 5-*exo*-trig and the 6-*exo*/*endo*-trig cyclisation pathways (Scheme 107).



a. SmI_2, HMPA, THF, 0 °C.

Scheme 107

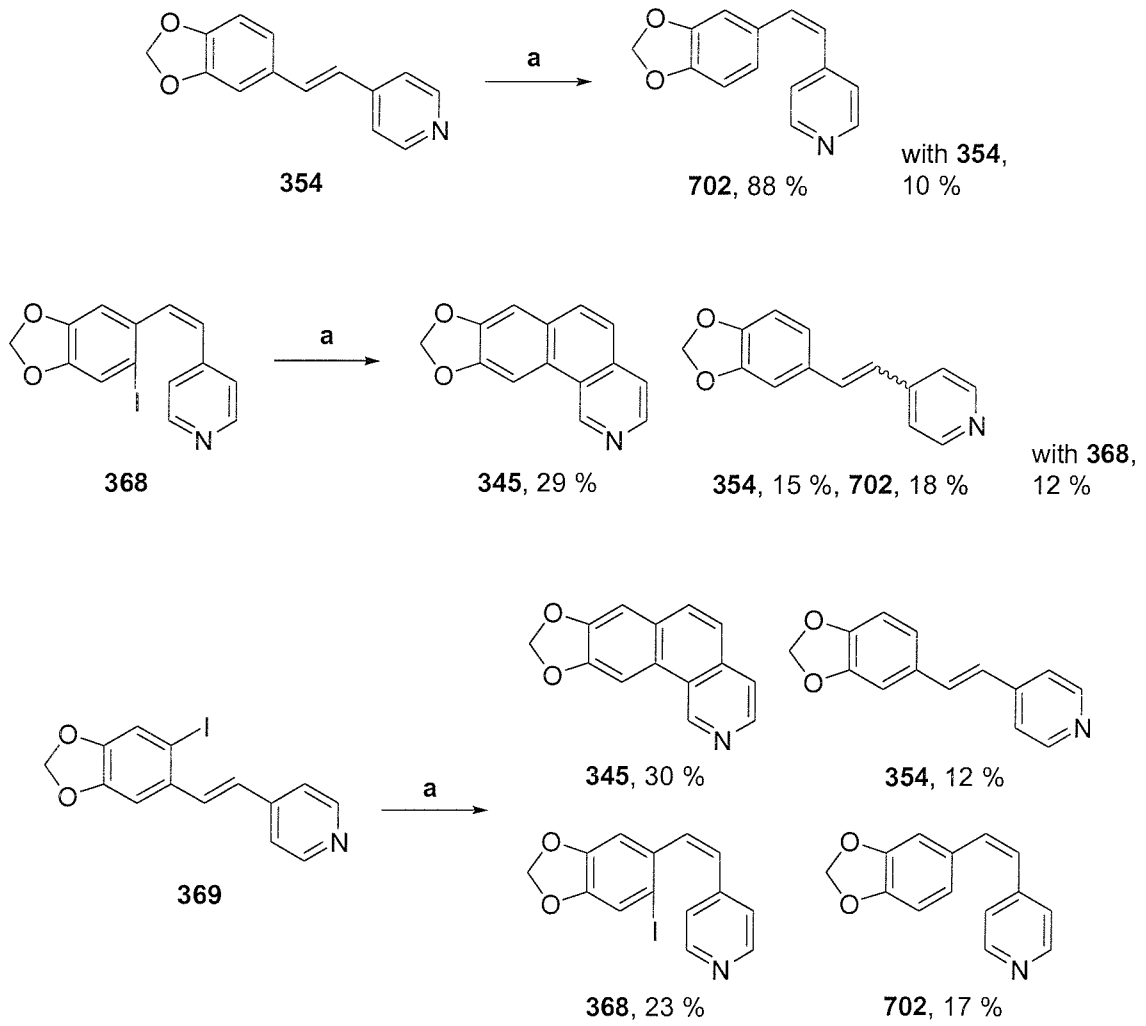
The use of sodium cobalt(I)salophen to effect intramolecular cyclisations to C-2 and C-4 of pyridines has already been demonstrated within our research group in the total synthesis of the alkaloid toddaquinoline.[44] When both the azastilbene **368** and the dihydroazastilbene **372** were exposed to these conditions homolysis of the carbon-iodine bond could not be effected, resulting in recovery of starting material in both cases. At this juncture it is not clear why radical formation failed as the cobalt(I) salophen complex was generated, as evidenced by its distinctive deep green colour.

Not perturbed we were excited to see a recent series of papers by Baba *et al.* entitled 'Indium(III) Chloride-Sodium Borohydride System: A Convenient Radical Reagent for an Alternative to Tributyltin Hydride System'.[157,158] Indium(III) chloride is reduced, typically by sodium borohydride, to $HInCl_2$. In turn this reduces alkyl halides to the corresponding hydrocarbon. A radical mechanism was shown to operate by the inclusion of a radical acceptor group in the substrates. Products derived from a radical cyclisation were duly formed. The 'convenient' reaction procedure includes heating the catalytic indium(III) chloride at 150 °C *in vacuo* for 60 minutes followed by the addition of acetonitrile and sodium borohydride. After cooling to -78 °C, the solution is

allowed to warm to room temperature to thaw and the substrate added. Following this procedure we were not able to cause carbon-iodine bond homolysis and recovered starting material from each attempt. It might be that our procedure did not reproduce the conditions established by Baba. Alternatively, these conditions may be limited to the homolysis of alkyl iodide bonds and are not useful for the homolysis of the stronger aryl iodide bond. On the basis of our results this is certainly not 'a convenient radical reagent'.

5.4 INITIATION BY LIGHT

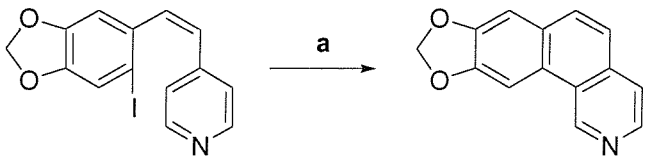
The seminal work of Timmons *et al.* in the 1960's showed how benzo[*c*]phenanthrenes can be formed by photocyclisation of azastilbenes without the need for an aryl halide as a radical precursor.[82-88] Any chemist who has worked with iodides for a period of time knows that in daylight the carbon-iodine bond can be broken. We felt that this could be used to effect a radical cyclisation. Having a Quartz photocell and sodium vapour lamp available to us we attempted the photocyclisation of a series of azastilbene substrates. We found that the *E*-azastilbene **354** readily isomerised to the *Z*-azastilbene **702** but did not undergo any cyclisation to **345**. The iodinated *Z*-azastilbene **368** does cyclise in moderate yield under the aforementioned conditions, the reaction also giving rise to products derived from isomerisation of the alkene and reduction of the carbon-iodine bond (**354** and **702**). From these studies we were keen to see if the iodinated *E*-azastilbene **369** could be isomerised and then cyclised through the action of light. Pleasingly, cyclisation to **345** occurs in a similar yield to that encountered with the *Z*-azastilbene **368**. Also recovered was a significant amount of the iodinated *Z*-azastilbene **368**, indicating that this technique could be used to transform the *E*-azastilbene by-product of the Wittig reaction **369**, into **368** (Scheme 108).



a. UV (sodium vapour lamp), MeCN.

Scheme 108

At this juncture we also examined the use of $(Bu_3Sn)_2$ as a mediator of the photocyclisation reaction of **368**. Unexpectedly this lowered the yield of the cyclised product **345**, possibly because the Sn-Sn bond needs high energy UV irradiation to cause cleavage and under such harsh conditions the Sn-C bonds may also be homolysed. The plethora of unwanted species formed are likely to cause many side reactions which consume the substrate and product and serve to complicate any purification procedure (Scheme 109).[159]

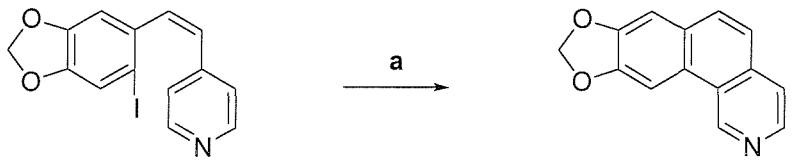


368 **345**, 26 % with **368**, 44 %

a. UV (sodium vapour lamp), MeCN, $(Bu_3Sn)_2$.

Scheme 109

The use of triplet sensitizers was also of interest. These molecules posses a chromophore that absorbs daylight and transmits this energy to the triplet state of $(Bu_3Sn)_2$ which gives selective Sn-Sn bond splitting. Neumann has found that 4-methoxyacetophenone is very efficient at causing Sn-Sn bond splitting under the action of a daylight lamp rather than harsher UV irradiation.[160] We carried out our photocyclisation using the sodium vapour lamp and $(Bu_3Sn)_2$ as before but with the addition of 2 equivalents of the triplet sensitizer. We found no significant difference between these results and those obtained without the triplet sensitizer. Attempting the photocyclisation using a daylight lamp led only to recovery of starting material both with and without the inclusion of a triplet sensitizer (Scheme 110).



368	**345**	with **368**
UV (sodium vapour lamp), 4-methoxyacetophenone	24 %	64 %
UV (daylight lamp)	0 %	86 %
UV (daylight lamp), 4-methoxyacetophenone	0 %	96 %

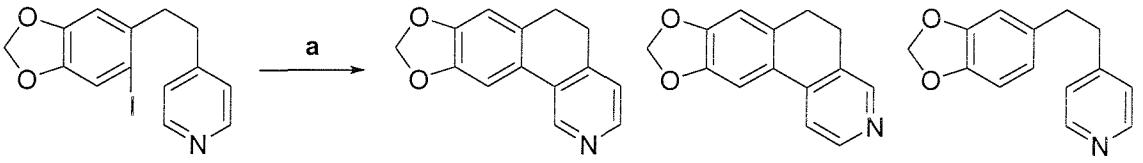
a. MeCN, $(Bu_3Sn)_2$.

Scheme 110

5.5 THE EFFECT OF TRIBUTYLTIN HYDRIDE CONCENTRATION

As we had had only modest success with these common alternatives to tributyltin hydride we decided to investigate the effect of reagent concentration on the course of these radical reactions. With this in mind we carried out a series of eight reactions at differing concentrations using the same ratio of reactants to substrate. The dihydroazastilbene **372** was chosen as the substrate as there was a significant quantity of the reduced product **377** recovered when standard conditions were applied. Logically, if the concentration of the tributyltin hydride is increased then the rate of the second order hydrogen atom abstraction will increase relative to the rate of intramolecular cyclisation, which is unimolecular.

The results of this study are summarised in Scheme 111. Once again we see some variance in the ratio of the 6-*exo*/*endo*-trig cyclisation product compared to the 5-*exo*-trig - rearrangement product, which is difficult to explain. However, importantly the expected trend, allowing for experimental variations, is observed. At low concentrations significantly greater quantities of cyclised products **376** and **359** are recovered, compared to those reactions run at high concentrations, where hydrogen atom abstraction to form **377** dominates (Scheme 111).



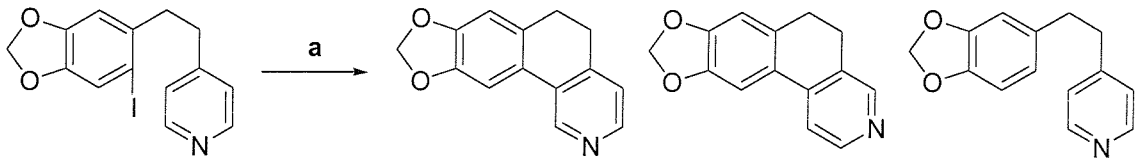
372, concentration:	**376**	**359**	**377**
0.590 $mmol^{-1}$ dm^{-3}	60 %	37 %	0 %
1.18 $mmol^{-1}$ dm^{-3}	46 %	37 %	16 %
2.37 $mmol^{-1}$ dm^{-3}	37 %	13 %	39 %
4.72 $mmol^{-1}$ dm^{-3}	41 %	19 %	39 %
9.43 $mmol^{-1}$ dm^{-3}	40 %	11 %	45 %
18.9 $mmol^{-1}$ dm^{-3}	32 %	0 %	54 %
37.7 $mmol^{-1}$ dm^{-3}	27 %	21 %	41 %
75.5 $mmol^{-1}$ dm^{-3}	23 %	17 %	53 %

a. Bu_3SnH, AIBN, PhMe, Δ.

Scheme 111

5.6 SOLVENT EFFECTS

The choice of toluene as a solvent for most of the radical reactions described in this thesis is not accidental. Toluene is a poor radical acceptor compared to pyridines, quinolines and isoquinolines and so does not compete for radical addition with them. It is also a poor hydrogen atom donor and so quenching of intermediates by the solvent is slow. Radical reactions have been conducted in many other solvents and so it was pertinent for us to test the effect of different solvents on our systems.[1-5] Accordingly, cyclisation of dihydroazastilbene **372** was carried out in benzene, toluene and THF. As we might expect the yield of cyclised products **376** and **359** was highest for benzene, the least likely to donate a hydrogen atom, and lowest for THF. In the latter case hydrogen atoms are α to ethereal oxygen's and are more readily abstracted than the benzylic and aryl hydrogen atoms found in toluene and benzene (Scheme 112).

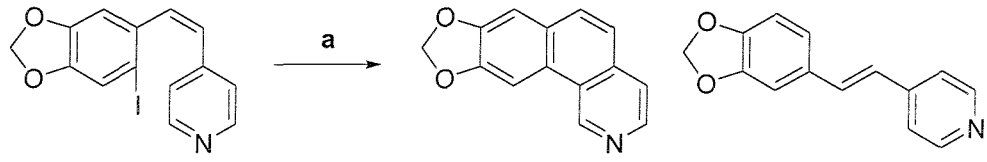


372		**376**	**359**	**377**
	benzene	53 %	11 %	35 %
	toluene	40 %	11 %	45 %
	THF	0 %	0 %	90 %

a. Bu_3SnH, AIBN, Δ.

Scheme 112

Azastilbene **368**, with the *Z*-alkene conjoining the aryl iodide to the pyridine, was also examined in this way. Comparison between toluene, THF, ethanol and methanol showed some interesting trends. Using toluene as the solvent the sole product was the heterocycle **345**. When THF was used, some cyclisation occurred but a majority of the substrate was converted into **354** by isomerisation and C-I bond reduction. Ethanol allowed **345** to be recovered along with an equal amount of **354** while in methanol just over a third of the substrate underwent cyclisation. This shows us again that THF is the worst solvent for such radical reactions with hydrogen atom extraction and alkene isomerisation occurring very readily. The alcohols promote this side reaction, albeit to a lesser extent (Scheme 113).



368		345	354
	toluene	98 %	0 %
	THF	17 %	68 %
	ethanol	52 %	48 %
	methanol	36 %	49 %

a. Bu_3SnH, AIBN, Δ.

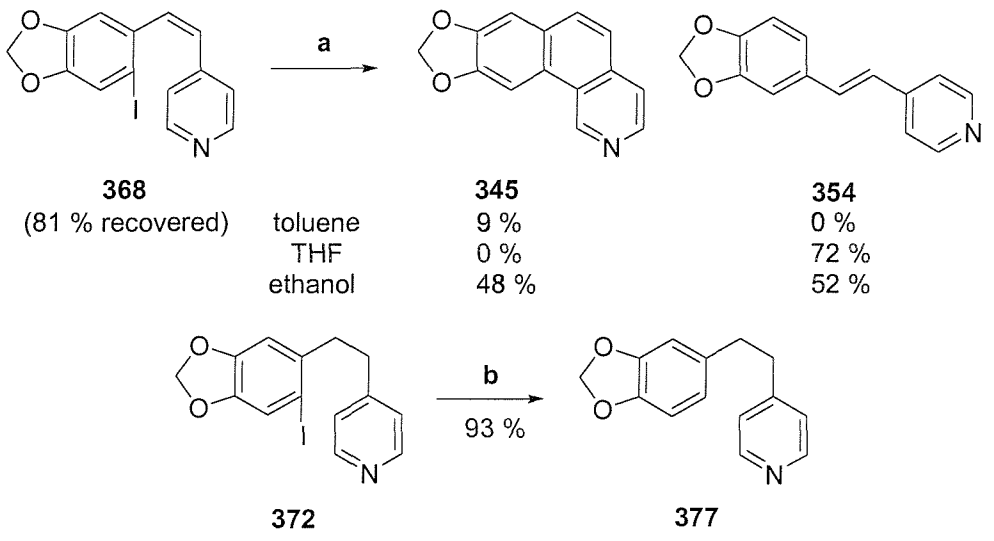
Scheme 113

5.7 Catalytic Tin Systems

The use of catalytic triorganotin halides, in conjunction with a reducing agent to regenerate the hydride, is widespread.[161-163] By using only a small quantity of the triorganotin reagent the cost is minimised, making it ideal for large scale reactions. The triorganotin hydride remaining at the end of the reaction is easily separated from the products by elution through a silica column. Sodium cyanoborohydride or sodium borohydride are typically used as the reducing agents, presenting solubility issues with typical solvents.

We attempted cyclisation of our azastilbene **368** in toluene, THF and ethanol using 0.25 equivalents of tributyltin hydride and 1.5 equivalents of sodium borohydride. Toluene proved to be the worst solvent with only 9 % of the substrate converted into benzo[*h*]isoquinoline **345**, even less than would be expected if the tributyltin hydride was not regenerated. It is likely that the cause of this is the insolubility of sodium borohydride in toluene. When THF was used as the solvent, carbon-iodine bond homolysis was facile and tributyltin hydride was indeed regenerated. However, alkene isomerisation and hydrogen atom abstraction occurred in this case leading to *E*-azastilbene **354**. Ethanol proved to be the best solvent for the catalytic variant with around half of our substrate **368** cyclising to **345** and half undergoing alkene isomerisation and carbon-iodine bond reduction to **354**. This shows again that tributyltin hydride is regenerated *in situ* but that the conditions allow for easier alkene isomerisation and / or hydrogen atom abstraction.

Interesting this is almost exactly the same result as we obtained from our stoichiometric tributyltin hydride mediated cyclisation carried out in ethanol (Scheme 113) showing us that the sodium borohydride - catalytic tributyltin hydride system works effectively when the reagents are homogeneous. The real challenge is to optimise the system for the new solvent. We also applied this methodology to dihydroazastilbene **372** but, as we have seen previously, it did not undergo cyclisation and only the reduced product **377** was recovered (Scheme 114).



a. 0.25 eq. Bu_3SnH, $NaBH_4$, AIBN, Δ; **b**. 0.25 eq. Bu_3SnH, $NaBH_4$, AIBN, EtOH, Δ.

Scheme 114

5.8 CONCLUSIONS

We have shown that tris(trimethylsilyl)silane is an excellent, if expensive, alternative to tributyltin hydride in our systems. If carbon-halide bond reduction is desired over cyclisation then tris(trimethylsilyl)germane is the reagent of choice being the best hydrogen atom donor of the group 14 hydrides. Samarium diiodide mediated cyclisations can be successful when applied to azastilbenes but fail with dihydroazastilbenes. We suspect that reductive addition of samarium diiodide to the uncyclised radical intermediate is faster than cyclisation in this case. Sodium cobalt(I)salophen mediated cyclisations failed to cleave the carbon-iodine bond, as did indium hydride. Iodides **368** and **369** underwent cyclisation to some extent under the action of hard UV irradiation from a sodium vapour lamp but not when a daylight lamp was employed. The addition of $(Bu_3Sn)_2$ or a triplet sensitizer did not increase the yield of the cyclised product. One major advantage of photocyclisation over chemically mediated cyclisations is that under the reaction conditions the *E* alkene tether is isomerised to the *Z* alkene allowing for the cyclisation of such substrates. Azastilbene **702** did not undergo photocyclisation.

Concentration had a pronounced effect on the course of these reactions. Under conditions of high dilution cyclisation is promoted while hydrogen atom extraction is slowed. At high concentrations abstraction of a hydrogen atom from tributyltin hydride outpaces cyclisation. The choice of solvent is also critical to the success of a cyclisation reaction. Benzene and toluene are poor hydrogen atom donors and do not appear to promote alkene isomerisation. Ethanol and methanol give lower yields of cyclised products while THF enhanced alkene isomerisation and C-I bond reduction. Ethanol was found to be the solvent of choice for radical cyclisations employing catalytic tributyltin hydride.

CHAPTER 6

EXPERIMENTAL SECTION

6.1 GENERAL REMARKS

Melting points were recorded on Reichert melting point apparatus using a Comark digital temperature probe and are given uncorrected in °C. Infrared spectra were recorded on either a Perkin Elmer 1600 series Fourier transform spectrometer, using a solution in dichloromethane held between two NaCl plates, or a Bio-Rad FTS 135 Fourier transformed spectrometer equipped with a Golden Gate Single Reflection Diamond. Maxima are reported as υ_{max} in units of cm^{-1} followed by the relative signal intensity using the abbreviations s, strong; m, medium; w, weak; br., broad. UV spectra were recorded on a Pye Unicam SP8-400 spectrometer between 190 and 450 nm using methanol as the solvent. Maxima are reported as λ_{max} in units of nm followed by ε, the extinction coefficient, in units of mol^{-1} dm^3 cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on either a Bruker AM300 spectrometer at 300 MHz and 75.5 MHz respectively or a Bruker AM400 spectrometer at 400 MHz and 100 MHz respectively. Where d-chloroform is used as the solvent, chloroform is the lock signal, where d6-DMSO is used as the solvent, DMSO is the lock signal and where d4-methanol is used as the solvent, methanol is the lock signal. Chemical shifts are given on the δ scale in ppm relative to tetramethylsilane, where δ_H = 0 ppm and δ_C = 0 ppm. Multiplets in ^1H NMR spectra are reported using the abbreviations s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and are followed by the *J* value in Hz and an assignment of the signal to an atom or atoms within the molecule. Signals observed in ^{13}C NMR spectra are followed by an assignment to an atom or atoms within the molecule based partially upon the DEPT 135 experiment. Atmospheric pressure chemical ionisation (APCI) mass spectra and electrospray (ES) mass spectra were recorded on a Micromass Platform quadrupole mass analyser with an electrospray ion source. The eluent was distilled acetonitrile with a flow rate of 200 μL min^{-1}. Electron impact (EI) mass spectra and chemical ionisation (CI) mass spectra were recorded on a Thermoquest Trace GC-MS with a 15 meter Rtx-5MS column. The source is a combined EI/CI source with a quadrupole analyser. Signals are reported in atomic mass units divided by charge ($^m/_z$) followed by the relative intensity of the peak. High

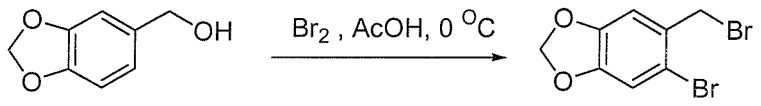
resolution mass spectra (HRMS) were recorded on either a VG Analytical 70-250-SE normal geometry double focusing mass spectrometer giving a resolution of 10^4, a Bruker Apex 3 FT ion cyclotron resonance MS with flow injection analysis *via* a HP1100 HPLC or at the EPSRC national mass spectrometry centre, Swansea. Combustion analyses (CHN) were carried out by GlaxoSmithKline, Harlow. X-ray crystal structures were collected and solved by the EPSRC National Crystallography Service, Southampton.

Unless otherwise stated all reactions were carried out under an inert atmosphere of nitrogen. All reactions were magnetically stirred and monitored by thin layer chromatography using aluminium backed 0.25 mm thick Silica Gel 60. Visualization was by short wave (254 nm) UV light and phosphomolybdic acid (PMA) in ethanol. Reactions that required anhydrous conditions were carried out in apparatus that had been flame dried under argon. Acetonitrile was dried by distillation over calcium hydride. Benzene was dried by distillation over sodium. Dichloromethane was dried by distillation over calcium hydride. Diethyl ether was dried by distillation over sodium. *N*,*N*-Dimethylformamide was dried by distillation over magnesium sulfate at reduced pressure. Tetrahydrofuran was dried by distillation over sodium and benzophenone. Toluene was dried by distillation over sodium. Petrol refers to petroleum ether (boiling point 40 – 60 °C). Column chromatography was run under a slight positive pressure with slurry packed flash silica (0.04 – 0.06 mm particle size). Yields refer too chromatographically and spectroscopically (^{1}H and ^{13}C NMR) pure materials.

6.2 EXPERIMENTAL FOR CHAPTER 2

6.21 CYCLISATIONS USING BROMIDES

5-Bromo-6-(bromomethyl)-1,3-benzodioxole **350**



$C_8H_8O_3$ (152.15) $C_8H_6Br_2O_2$ (293.94)

Following the procedure of Barthel and Alexander.[104] Piperanol **349** (10.0 g, 65.7 mmol) was dissolved in acetic acid (20 mL) at 0 °C. Bromine (4.0 mL, 12.4 g, 77.6 mmol) in acetic acid (12 mL) was added dropwise to this solution over a period of 15 minutes and the reaction stirred for a further 2 hours. The resultant solid was filtered, washed with water (2 x 20 mL) and recrystallised from hot EtOH to give **350** (13.0 g, 44.3 mmol, 67 %) as a white crystalline solid.

Spectral and physical data were in accord with the literature.[104,164,165]

M.P. 92 - 94 °C ($CHCl_3$). Lit. 94 °C (petrol).[164]

FT-IR (solid) υ_{max} 3108 w, 3044 w, 2898 w, 1619 w, 1501 s, 1483 s, 1409 m, 1388 m, 1359 m, 1249 s, 1213 m, 1124 m, 1035 s cm^{-1}.

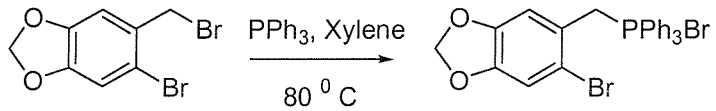
UV (MeOH) λ_{max} (ε) 293 (4580), 243 (4350) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 7.01 (1H, s, Ar**H**), 6.92 (1H, s, Ar**H**), 6.00 (2H, s, O**CH_2**O), 4.56 (2H, s, Ar**CH_2**Br).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 148.8 (Ar, **C**OR), 147.6 (Ar, **C**OR), 129.9 (Ar, **C**), 115.6 (Ar, **C**), 113.1 (Ar, **C**H), 110.5 (Ar, **C**H), 102.1 (O**C**H_2O), 34.2 (Ar**C**H_2Br).

MS $^m/_z$ (APCI) 215 (10 %; [M(^{81}Br)-Br]$^+$), 213 (9 %; [M(^{79}Br)-Br]$^+$), 186 (9 %), 165 (100 %).

[(6-Bromo-1,3-benzodioxole-5-yl)methyl]triphenylphosphonium bromide **347**



$C_8H_6Br_2O_2$ (293.94) $C_{26}H_{21}Br_2O_2P$ (556.23)

Following the procedure of Jaegfeldt *et al.*[105] The dibromide **350** (12.0 g, 40.8 mmol) was dissolved in xylene (50 mL) containing triphenylphosphine (12.0 g, 45.8 mmol) and heated at 80 °C for 5 hours. The resultant white precipitate was filtered, washed with cold xylene (2 x 20 mL) and cold petrol (2 x 20 mL) then dried *in vacuo* to give **347** (21.3 g, 38.3 mmol, 94 %) as a white solid.

Spectral and physical data were in accord with the literature.[106,165]

M.P. 275 - 279 °C (EtOH). Lit. 278 - 280 °C (methanol / ether).[106]

FT-IR (solid) υ_{max} 3050 w, 3007 w, 2844 w, 2777 w, 1502 m, 1477 s, 1438 s, 1392 w, 1245 m, 1111 s, 1033 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 300 (3690), 268 (4130) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 7.82 - 7.60 (15H, m, 15 x Ar**H**), 6.97 (1H, s, Ar**H**), 5.93 (2H, s, O**CH_2**O), 5.49 (2H, d, *J* 13.2 Hz, Ar**CH_2**PPh_3Br).

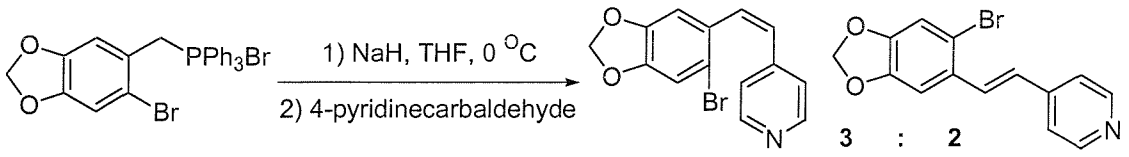
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 149.0 (*J* 4.5 Hz, Ar, **C**), 148.0 (Ar, **C**), 135.2 (*J* 3.4 Hz, Ar, 3 x **C**H), 134.3 (*J* 9.0 Hz, Ar, 6 x **C**H), 130.3 (*J* 12.4 Hz, Ar, 6 x **C**H), 119.9 (*J* 9.0 Hz, Ar, **C**), 118.2 (*J* 7.9 Hz, Ar, **C**), 117.4 (*J* 85.9 Hz, Ar, 3 x **C**), 112.6 (*J* 3.4 Hz, Ar, **C**H), 112.1 (*J* 4.5 Hz, Ar, **C**H), 102.3 (O**C**H_2O), 31.1 (*J* 48.6 Hz, Ar**C**H_2PPh_3Br).

MS $^m/_z$ (APCI) 477 (30 %; $[M(^{81}Br)]^+$), 475 (32 %; $[M(^{79}Br)]^+$), 279 (27 %), 263 (28 %), 165 (100 %; $[M\text{-}3Ph\text{-}Br]^+$).

CHN Found: C, 55.88; H, 3.88. $C_{26}H_{21}Br_2O_2P$ requires C, 56.14; H, 3.81.

4[(*Z*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **353** and

4[(*E*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **352**



$C_{26}H_{21}Br_2O_2P$ (556.23)

$C_{14}H_{10}BrNO_2$ (304.14)

NaH (84 mg, 3.50 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The bromide **347** (1.70 g, 3.06 mmol) was added and the reaction warmed to room temperature over a period of 18 hours. The mixture was cooled to 0 °C again and the aldehyde **348** (0.24 mL, 269 mg, 2.51 mmol) added dropwise. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (40 : 60, Et_2O : petrol) to give firstly the *Z*-azastilbene **353** (471 mg, 1.55 mmol, 51 %) followed by the *E*-azastilbene **352** (310 mg, 1.02 mmol, 33 %) each as a white solid.

Data for 4[(*Z*)-2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **353**

M.P. 93 - 94 °C (Et_2O).

FT-IR (solid) υ_{max} 3111 w, 3036 w, 2911 w, 1629 m, 1544 m, 1491 s, 1470 m, 1385 m, 1318 m, 1276 m, 1155 m, 1106 s, 1030 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 297 (7560) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.40 (2H, d, *J* 4.4 Hz, Ar**H**), 7.00 (1H, s, Ar**H**), 6.99 (2H, d, *J* 4.4 Hz, Ar**H**), 6.66 (1H, d, *J* 12.5 Hz, RC**H**=CHR), 6.48 (1H, s, Ar**H**), 6.46 (1H, d, *J* 12.5 Hz, RCH=C**H**R), 5.87 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	149.9 (Ar, 2 x **C**H), 148.3 (Ar, **C**), 147.2 (Ar, **C**), 143.9 (Ar, **C**), 133.3 (**C**H=CH), 129.6 (Ar, **C**), 128.2 (CH=**C**H), 123.4 (Ar, 2 x **C**H), 114.7 (Ar, **C**), 112.7 (Ar, **C**H), 109.8 (Ar, **C**H), 101.9 (O**C**H_2O).
MS $^m/_z$ (APCI)	347 (12 %; [M(^{81}Br)+MeCN]$^+$), 345 (13 %; [M(^{79}Br)+ MeCN]$^+$), 306 (85 %; M(^{81}Br)H$^+$), 304 (100 %; M(^{79}Br)H$^+$).
CHN	Found: C, 55.30; H, 3.33; N, 4.60. $C_{14}H_{10}BrNO_2$ requires C, 55.29; H, 3.31; N, 4.61.

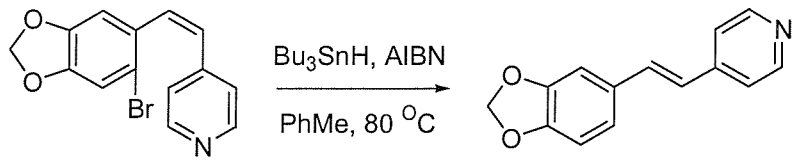
Data for 4[(*E*)-2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **352**

M.P.	112 - 113 °C (Et_2O).
FT-IR (solid) υ_{max}	3066 w, 3011 w, 2976 w, 2631 w, 1629 m, 1591 w, 1548 m, 1501 s, 1476 m, 1315 m, 1275 s, 1252 m, 1198 m, 1160 m, 1118 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	341 (12900), 301 (11700) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	8.58 (2H, br. s, Ar**H**), 7.58 (1H, d, *J* 16.2 Hz, RC**H**=CHR), 7.35 (2H, d, *J* 4.4 Hz, Ar**H**), 7.12 (1H, s, Ar**H**), 7.04 (1H, s, Ar**H**), 6.77 (1H, d, *J* 16.2 Hz, RCH=C**H**R), 6.00 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	150.2 (Ar, 2 x **C**H), 149.0 (Ar, **C**), 148.1 (Ar, **C**), 144.8 (Ar, **C**), 132.0 (**C**H=CH), 129.4 (Ar, **C**), 127.0 (CH=**C**H), 121.1 (Ar, 2 x **C**H), 116.4 (Ar, **C**), 113.1 (Ar, **C**H), 106.1 (Ar, **C**H), 102.2 (O**C**H_2O).

MS $^{m}/_{z}$ (APCI) 347 (15 %; $[M(^{81}Br)+MeCN]^{+}$), 345 (15 %; $[M(^{79}Br)+ MeCN]^{+}$), 306 (95 %; $M(^{81}Br)H^{+}$), 304 (100 %; $M(^{79}Br)H^{+}$), 251 (22 %), 165 (18 %), 163 (9 %).

CHN Found: C, 55.14; H, 3.29; N, 4.59. $C_{14}H_{10}BrNO_2$ requires C, 55.29; H, 3.31; N, 4.61.

4[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **354**



$C_{14}H_{10}BrNO_2$ (304.14) $C_{14}H_{11}NO_2$ (225.24)

The *Z* azastilbene **353** (347 mg, 1.14 mmol) in toluene (80 mL) was stirred under argon at 80 °C with Bu_3SnH (0.38 mL, 411 mg, 1.41 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 48 hours with $KF_{(aq)}$ (2M, 40 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (30 : 70, Et_2O : petrol) to give **354** (250 mg, 1.11 mmol, 97 %) as a white solid.

Spectral and physical data were in accord with the literature.[166-168]

M.P. 102 - 103 °C (Et_2O / petrol). Lit. 98 °C (EtOH).[166]

FT-IR (CH_2Cl_2) υ_{max} 3072 w, 3031 w, 2892 w, 1635 w, 1594 s, 1549 w, 1504 s, 1488 m, 1441 m, 1416 w, 1361 w, 1245 s, 1096 w, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 336 (12700), 306 (8280), 239 (9500) nm (mol^{-1} dm^3 cm^{-1}).

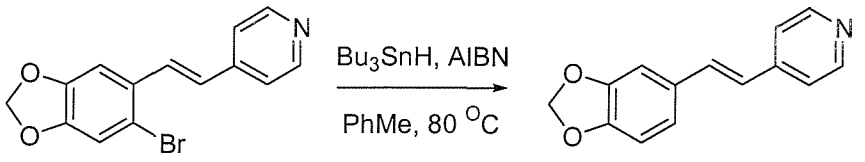
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.56 (2H, s, Ar**H**), 7.32 (2H, d, *J* 4.4 Hz, Ar**H**), 7.21 (1H, d, *J* 15.4 Hz, ArC**H**=CHAr), 7.08 (1H, s, Ar**H**), 6.98 (1H, d, *J* 7.0 Hz, Ar**H**), 6.84 (1H, d, *J* 7.0 Hz, Ar**H**), 6.83 (1H, d, *J* 15.4 Hz, ArCH=C**H**Ar), 6.00 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 150.1 (Ar, 2 x **C**H), 148.3 (Ar, **C**), 148.3 (Ar, **C**), 144.8 (Ar, **C**), 132.8 (**C**H=CH), 130.6 (Ar, **C**), 124.1 (CH=**C**H), 122.6 (Ar, 2 x **C**H), 120.7 (Ar, **C**H), 108.5 (Ar, **C**H), 105.8 (Ar, **C**H), 101.4 (O**C**H$_2$O).

MS $^{m}/_{z}$ (APCI) 227 (10 %), 226 (100 %; MH^{+}).

CHN Found: C, 74.62; H, 4.92; N, 6.16. $C_{14}H_{11}NO_2$ requires C, 74.65; H, 4.92; N, 6.22.

4[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **354**

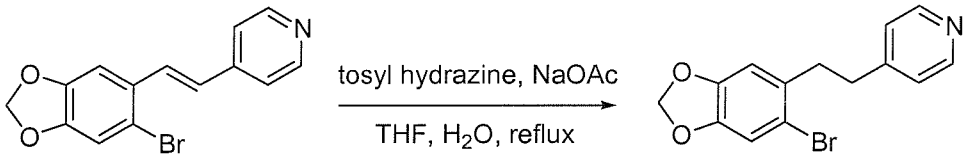


$C_{14}H_{10}BrNO_2$ (304.14) $C_{14}H_{11}NO_2$ (225.24)

The *E*-azastilbene **352** (150 mg, 0.49 mmol) in toluene (40 mL) was stirred under argon at 80 °C with Bu_3SnH (0.16 mL, 173 mg, 0.59 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 40 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (40 : 60, Et_2O : petrol) to give **354** (104 mg, 0.46 mmol, 94 %) as a white solid.

Data identical to those described previously.

4[-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethyl]pyridine **358**



$C_{14}H_{10}BrNO_2$ (304.14) $C_{14}H_{12}BrNO_2$ (306.16)

The azastilbene **352** (1.01 g, 3.32 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 48 hours. The solution was cooled to room temperature and potassium carbonate solution (15 mL) added along with Et_2O (15 mL). The aqueous phase was separated and washed with Et_2O (3 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **358** (1.00 g, 3.27 mmol, 98 %) as a colourless oil.

FT-IR (CH_2Cl_2) υ_{max} 3070 w, 3024 w, 2897 m, 1600 m, 1559 w, 1501 m, 1475 s, 1413 m, 1229 s, 1113 m, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 294 (4290), 241 (5510) nm (mol^{-1} dm^3 cm^{-1}).

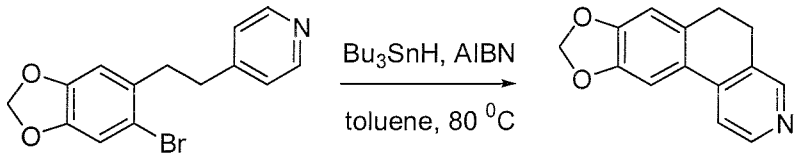
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.49 (2H, d, *J* 5.2 Hz, Ar**H**), 7.11 (2H, d, *J* 5.2 Hz Ar**H**), 6.99 (1H, s, Ar**H**), 6.60 (1H, s, Ar**H**), 5.93 (2H, s, O**CH$_2$**O), 2.95 - 2.90 (2H, m, 2 x Ar**CH$_2$**), 2.86 - 2.82 (2H, m, 2 x Ar**CH$_2$**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 150.0 (Ar, **C**), 149.8 (Ar, 2 x **C**H), 147.3 (Ar, **C**), 146.9 (Ar, **C**), 132.9 (Ar, **C**), 123.9 (Ar, 2 x **C**H), 114.3 (Ar, **C**), 112.8 (Ar, **C**H), 110.0 (Ar, **C**H), 101.7 (O**C**H$_2$O), 37.0 (Ar**C**H$_2$), 35.5 (Ar**C**H$_2$).

MS $^m/_z$ (APCI) 349 (42 %; [M(^{81}Br)H+MeCN]$^+$), 347 (41 %; [M(^{79}Br)H+MeCN]$^+$), 308 (100 %; M(^{81}Br)H$^+$), 306 (99 %; M(^{79}Br)H$^+$).

HRMS (CI) Found: MH$^+$, 306.0132. $C_{14}H_{13}NO_2{}^{79}Br$ requires 306.0129.

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**



$C_{14}H_{12}BrNO_2$ (306.15) $C_{14}H_{11}NO_2$ (225.24)

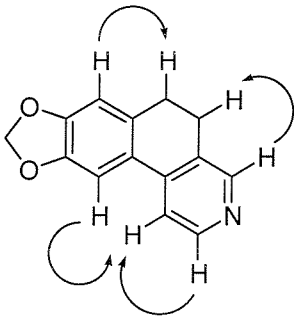
The bromide **358** (187 mg, 0.611 mmol) in toluene (80 mL) was stirred under argon at 80 °C with Bu_3SnH (0.22 mL, 238 mg, 0.816 mmol) and AIBN (100 mg, 0.609 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 8 hours with $KF_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50 Et_2O : petrol → 80 : 20 Et_2O : petrol) to yield firstly two unidentified products followed by **359** (25 mg, 0.111 mmol, 18 %) as a white solid.

M.P. 144 - 148 °C (Et_2O).

FT-IR (solid) υ_{max} 2909 s, 1593 m, 1552 w, 1504 m, 1481 s, 1415 m, 1369 w, 1282 w, 1235 s, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 326 (33500), 287 (17800) nm (mol^{-1} dm^3 cm^{-1}).

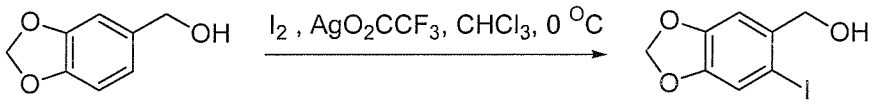
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.39 (1H, d, *J* 5.0 Hz, Ar**H**), 8.37 (1H, s, Ar**H**), 7.36 (1H, d, *J* 5.0 Hz, Ar**H**), 7.19 (1H, s, Ar**H**), 6.68 (1H, s, Ar**H**), 5.93 (2H, s, O**CH_2**O), 2.76 (4H, s, RC**H_2CH_2**R).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 8.39 (1H, d, *J* 5.0 Hz, Ar**H**) caused an n.O.e. enhancement at δ_H 7.36 (1H, d, *J* 5.0 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 8.37 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.76 (4H, s, RC**H$_2$**C**H$_2$**R). n.O.e Irradiation of the signal at δ_H 7.36 (1H, d, *J* 5.0 Hz, Ar**H**) caused an n.O.e. enhancement at δ_H 8.39 (1H, d, *J* 5.0 Hz, Ar**H**) and δ_H 7.19 (1H, s, Ar**H**). n.O.e Irradiation of the signal at δ_H 2.76 (4H, s, RC**H$_2$**C**H$_2$**R) caused an n.O.e. enhancement at δ_H 8.37 (1H, s, Ar**H**) and δ_H 6.68 (1H, s, Ar**H**).
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	149.0 (Ar, **C**), 148.7 (Ar, **C**H), 148.6 (Ar, **C**H), 147.5 (Ar, **C**), 142.4 (Ar, **C**), 133.4 (Ar, **C**), 131.4 (Ar, **C**), 125.8 (Ar, **C**), 117.4 (Ar, **C**H), 109.2 (Ar, **C**H), 104.9 (Ar, **C**H), 101.6 (O**C**H$_2$O), 28.9 (Ar**C**H$_2$), 25.8 (Ar**C**H$_2$).
MS $^{m}/_{z}$ (ES)	267 (13 %; $[MH+MeCN]^+$), 227 (16 %; $M(^{13}C)H^+$), 226 (16 %; MH^+).
CHN	Found: C, 74.50; H, 4.92; N, 6.19. $C_{14}H_{11}NO_2$ requires C, 74.65; H, 4.92; N, 6.22.

6.22 IODIDE PRECURSOR FORMATION

(6-Iodo-1,3-benzodioxol-5-yl)methanol **360**



$C_8H_8O_3$ (152.15) $C_8H_7IO_3$ (278.04)

Following the procedure of Overman *et al.*[107] The alcohol **349** (9.3 g, 61.1 mmol) was dissolved in $CHCl_3$ (130 mL) at - 5 °C. Iodine (17.3 g, 68.0 mmol) and silver trifluoroacetate (15.0 g, 67.9 mmol) were added sequentially and the heterogeneous mixture stirred for 30 minutes. The reaction was filtered through celite and the filtrate washed with saturated $Na_2S_2O_{3(aq)}$ (100 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The light yellow solid was recrystallised from hot $CHCl_3$ to give **360** (14.7 g, 52.8 mmol, 87 %) as a white crystalline solid.

Spectral and physical data were in accord with the literature.[169-171]

M.P. 110 - 112 °C ($CHCl_3$). Lit. 111 °C (EtOH / water).[169]

FT-IR (solid) υ_{max} 3255 br. w, 2911 w, 1498 m, 1474 s, 1449 m, 1236 s, 1100 m, 1038 s cm^{-1}.

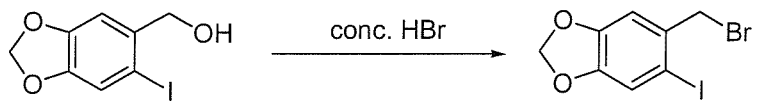
UV (MeOH) λ_{max} (ε) 293 (3740), 243 (6540) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, DMSO) 7.30 (1H, s, Ar**H**), 7.04 (1H, s, Ar**H**), 6.04 (2H, s, OC**H$_2$**O), 5.10 (1H, s, O**H**), 4.35 (2H, s, ArC**H$_2$**OH).

^{13}C NMR δ_C ppm (75.5 MHz, DMSO) 148.0 (Ar, **C**OR), 146.9 (Ar, **C**OR), 137.3 (Ar, **C**), 117.5 (Ar, **C**H), 108.0 (Ar, **C**H), 101.5 (O**C**H$_2$O), 84.4 (Ar, **C**), 67.2 (Ar**C**H$_2$OH).

MS $^m/_z$ (ES) 168 (15 %; $[M+NH_4\text{-}HI]^+$), 153 (45 %), 128 (28 %; HI^+), 127 (100 %; I^+).

5-(Bromomethyl)-6-iodo-1,3-benzodioxole **361**



$C_8H_7IO_3$ (278.04) $C_8H_6BrIO_2$ (340.94)

An adaptation of the procedure of Robinson and Robinson was employed.[172] Concentrated $HBr_{(aq)}$ (48 %, 40 mL) was slowly added to the alcohol **360** (10.1 g, 36.3 mmol) and the suspension stirred for 2 hours at room temperature. The aqueous layer was extracted with DCM (3 x 100 mL) and the organic phases combined, washed with $Na_2CO_{3(aq)}$ (2M, 50 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* to give **361** (11.2 g, 32.9 mmol, 90 %) as a white solid.

Spectral and physical data were in accord with the literature.[171]

M.P. 72 - 73 °C (EtOH). Lit. 72 °C (EtOAc / hexane).

FT-IR (solid) υ_{max} 2968 w, 2893 w, 1613 w, 1500 m, 1477 s, 1403 w, 1382 m, 1353 w, 1234 s, 1209 m, 1120 m, 1035 s cm^{-1}.

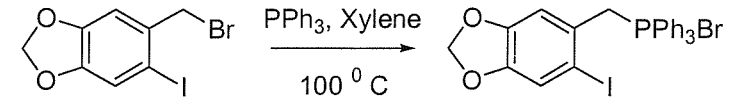
UV (MeOH) λ_{max} (ε) 298 (5290), 258 (6710) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 7.25 (1H, s, Ar**H**), 6.96 (1H, s, Ar**H**), 5.99 (2H, s, O**CH_2**O), 4.56 (2H, s, Ar**CH_2**Br).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 148.7 (Ar, **C**OR), 148.7 (Ar, **C**OR), 133.3 (Ar, **C**), 119.0 (Ar, **C**H), 110.1 (Ar, **C**H), 102.1 (O**C**H_2O), 88.9 (Ar, **C**), 39.6 (Ar**C**H_2Br).

MS $^m/_z$ (ES) 363 (12 %), 362 (100 %), 153 (13 %).

Bromo[(6-iodo-1,3-benzodioxol-5-yl)methyl]triphenylphosphorane **362**



$C_8H_6BrIO_2$ (340.94) $C_{26}H_{21}BrIO_2P$ (603.23)

An adaptation of the procedure of Jaegfeldt *et al.* was employed.[105] The iodide **361** (11.0 g, 32.3 mmol) was dissolved in xylene (50 mL) containing triphenylphosphine (8.7 g, 33.0 mmol) and heated at 100 °C for 24 hours. The resultant white precipitate was filtered and washed with cold xylene (2 x 20 mL) and cold petrol (2 x 20 mL) and recrystallised from EtOH / Et_2O to give **362** (18.6 g, 30.8 mmol, 95 %) as a white crystalline solid.

M.P. 268 - 272 °C (EtOH).

FT-IR (solid) υ_{max} 2848 w, 1584 w, 1498 m, 1480 m, 1470 m, 1432 w, 1246 s, 1236 s, 1109 s, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 302 (4420), 275 (4830), 268 (5430) nm (mol^{-1} dm^3 cm^{-1}).

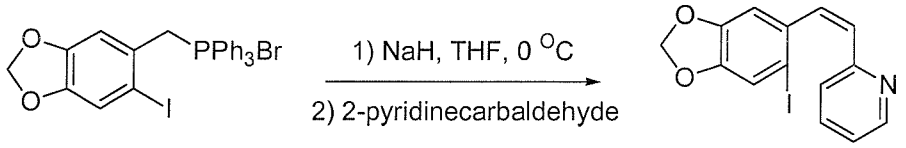
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 7.81 - 7.61 (15H, m, 15 x Ar**H**), 7.02 (1H, s, Ar**H**), 6.92 (1H, d, *J* 2.2 Hz, Ar**H**), 5.92 (2H, s, OC**H$_2$**O), 5.45 (2H, d, *J* 13.2 Hz, ArC**H$_2$**PPh_3Br).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 148.9 (Ar, **C**), 148.9 (Ar, **C**), 135.3 (*J* 3.4 Hz, Ar, 3 x **C**H), 134.4 (*J* 10.2 Hz, Ar, 6 x **C**H), 130.3 (*J* 12.4 Hz, Ar, 6 x **C**H), 123.4 (*J* 10.2 Hz, Ar, **C**), 118.5 (*J* 3.4 Hz, Ar, **C**H), 117.1 (*J* 84.8 Hz, Ar, 3 x **C**), 111.5 (*J* 3.4 Hz, Ar, **C**H), 102.3 (O**C**H$_2$O), 93.4 (*J* 7.9 Hz, Ar, **C**), 35.7 (*J* 48.6 Hz, Ar**C**H$_2$$PPh_3Br$).

MS $^m/_z$ (ES) 524 (28 %), 523 (100 %; $[M-Br]^+$).

HRMS (ES) Found: $[M-Br]^+$, 523.0323. $C_{26}H_{21}IO_2P$ requires 523.0324.

2-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **365**



$C_{26}H_{21}BrIO_2P$ (603.23) $C_{14}H_{10}INO_2$ (351.14)

NaH (400 mg, 10.0 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (40 mL) at 0 °C. The iodide **362** (5.00 g, 8.29 mmol) was added and the reaction stirred for 30 minutes under argon. The mixture was cooled to 0 °C again and 2-pyridinecarbaldehyde **363** (0.70 mL, 788 mg, 7.36 mmol) added. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (Et_2O) to give **365** (2.20 g, 6.27 mmol, 85 %), recrystallised from EtOH as a white crystalline solid.

M.P. 108 - 110 °C (EtOH).

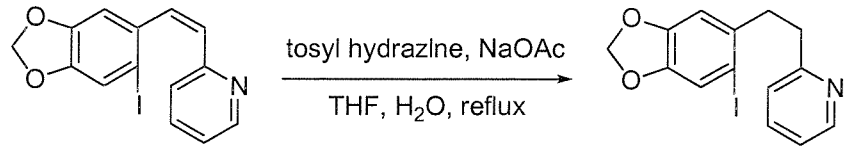
FT-IR (solid) υ_{max} 1582 w, 1500 w, 1474 s, 1433 w, 1411 w, 1231 m, 1035 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 294 (12710) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)
8.57 (1H, ddd, *J* 4.8, 1.6, 0.8 Hz, Ar**H**),
7.45 (1H, app. td, *J* 7.7, 1.8 Hz, Ar**H**), 7.31 (1H, s, Ar**H**),
7.07 (1H, ddd, *J* 7.5, 4.9, 1.0 Hz, Ar**H**),
7.01 (1H, d, *J* 8.0 Hz, Ar**H**),
6.69 (1H, d, *J* 12.2 Hz, RCH=C**H**R),
6.65 (1H, d, *J* 12.1 Hz, RC**H**=CHR), 6.64 (1H, s, Ar**H**),
5.93 (2H, s, OC**H$_2$**O).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	155.5 (Ar, **C**), 149.6 (Ar, **C**H), 148.2 (Ar, **C**), 148.0 (Ar, **C**), 136.3 (Ar, **C**H), 135.7 (**C**H=CH), 134.3 (Ar, **C**), 131.1 (CH=**C**H), 123.9 (Ar, **C**H), 121.8 (Ar, **C**H), 118.4 (Ar, **C**H), 110.0 (Ar, **C**H), 101.7 (**O**$\mathbf{C}$$H_2$**O**), 87.9 (Ar, **C**).
MS $^m/_z$ (APCI)	353 (15 %; M(^{13}C)H^+), 352 (100 %; MH^+).
CHN	Found: C, 47.78; H, 2.74; N, 3.90. $C_{14}H_{10}INO_2$ requires C, 47.89; H, 2.87; N, 3.99.

2-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **370**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{12}INO_2$ (353.16)

The azastilbene **365** (300 mg, 0.854 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and potassium carbonate solution (2M, 100 mL) added. The reaction mixture was washed with Et_2O (4 x 50 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **370** (278 mg, 0.787 mmol, 92 %) as a white crystalline solid.

M.P. 69 - 70 °C (EtOH).

FT-IR (solid) υ_{max} 1589 w, 1498 m, 1473 s, 1432 w, 1224 s, 1112 w, 1032 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 295 (4650), 269 (4620), 262 (5760), 224 (8860) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.57 (1H, d, *J* 4.6 Hz, Ar**H**), 7.59 (1H, app. td, *J* 7.7, 1.8 Hz, Ar**H**), 7.24 (1H, s, Ar**H**), 7.14 (1H, d, *J* 7.7 Hz, Ar**H**), 7.13 (1H, app. t, *J* 5.2 Hz, Ar**H**), 6.70 (1H, s, Ar**H**), 5.93 (2H, s, OC**H**$_2$O), 3.09-2.99 (4H, m, RC**H**$_2$C**H**$_2$R).

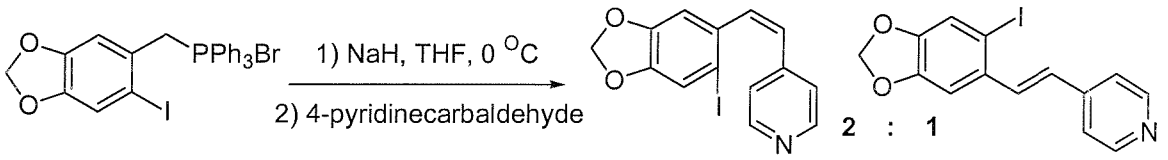
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$) 160.7 (Ar, **C**), 149.4 (Ar, **C**H), 148.4 (Ar, **C**), 146.8 (Ar, **C**), 137.3 (Ar, **C**), 136.4 (Ar, **C**H), 123.1 (Ar, **C**H), 121.3 (Ar, **C**H), 118.6 (Ar, **C**H), 109.5 (Ar, **C**H), 101.5 (O**C**H$_2$O), 87.7 (Ar, **C**), 40.9 (Ar**C**H$_2$), 38.9 (Ar**C**H$_2$).

MS $^{m}/_{z}$ (APCI) 355 (18 %; M(^{13}C)H^{+}), 354 (96 %; MH^{+}), 227 (100 %).

CHN Found: C, 47.64; H, 3.41; N, 3.79. $C_{14}H_{12}INO_2$ requires C, 47.61; H, 3.42; N, 3.97.

4-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** and

4-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **369**



$C_{26}H_{21}BrIO_2P$ (603.23)

$C_{14}H_{10}INO_2$ (351.14)

NaH (400 mg, 10.0 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (40 mL) at 0 °C. The iodide **362** (5.00 g, 8.29 mmol) was added and the reaction stirred for 30 minutes under argon. The mixture was cooled to 0 °C again and 4-pyridinecarbaldehyde **348** (0.70 mL, 785 mg, 7.33 mmol) added. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (Et_2O) to give to give firstly the *Z*-azastilbene **368** (1.63 g, 4.65 mmol, 63 %) which was recrystallised from EtOH as a pale yellow crystalline solid followed by the *E*-azastilbene **369** (796 mg, 2.27 mmol, 31 %) which was also recrystallised from EtOH as a pale yellow crystalline solid.

Data for 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**

M.P. 100 - 102 °C (EtOH).

FT-IR (solid) υ_{max} 1741 m br., 1593 m, 1489 m, 1473 m, 1429 m, 1365 m br., 1235 s, 1032 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 298 (13340), 245 (27010) nm (mol^{-1} dm^3 cm^{-1}).

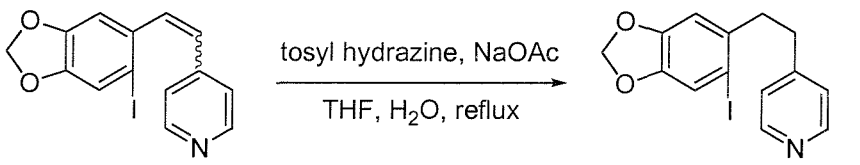
^{1}H NMR δ_H ppm (250 MHz, $CDCl_3$) 8.44 (2H, dd, *J* 4.6, 1.6 Hz, Ar**H**), 7.30 (1H, s, Ar**H**), 7.00 (2H, dd, *J* 4.6, 1.5 Hz, Ar**H**), 6.62 (1H, d, *J* 11.9 Hz, RC**H**=CHR), 6.54 (1H, s, Ar**H**), 6.46 (1H, d, *J* 11.9 Hz, RCH=C**H**R), 5.93 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	149.9 (Ar, 2 x **C**H), 148.3 (Ar, **C**), 148.2 (Ar, **C**), 143.7 (Ar, **C**), 137.4 (**C**H=CH), 133.7 (Ar, **C**), 128.0 (CH=**C**H), 123.4 (Ar, 2 x **C**H), 118.4 (Ar, **C**H), 109.7 (Ar, **C**H), 101.7 (OCH_2O), 87.7 (Ar, **C**).
MS $^m/_z$ (APCI)	353 (40 %; M(^{13}C)H$^+$), 352 (100 %; MH$^+$).
CHN	Found: C, 47.84; H, 2.85; N, 3.92. $C_{14}H_{10}INO_2$ requires C, 47.89; H, 2.87; N, 3.99.

Data for 4-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **369**

M.P.	115 - 117 °C (EtOH).
FT-IR (solid) υ_{max}	1742 w br., 1591 w, 1498 m, 1469 s, 1407 w, 1232 s, 1111 w, 1032 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	346 (18560), 303 (17810), 258 (18540) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (250 MHz, $CDCl_3$)	8.58 (2H, dd, *J* 4.6, 1.6 Hz, Ar**H**), 7.45 (1H, d, *J* 16.0 Hz, RC**H**=CHR), 7.35 (2H, dd, *J* 4.6, 1.6 Hz, Ar**H**), 7.30 (1H, s, Ar**H**), 7.12 (1H, s, Ar**H**), 6.72 (1H, d, *J* 16.0 Hz, RCH=C**H**R), 6.00 (2H, s, O**CH$_2$**O).
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	150.3 (Ar, 2 x **C**H), 149.0 (Ar, **C**), 148.9 (Ar, **C**), 144.2 (Ar, **C**), 136.6 (Ar, **C**H), 132.6 (Ar, **C**), 127.2 (Ar, **C**H), 120.9 (Ar, 2 x **C**H), 118.8 (Ar, **C**H), 106.0 (Ar, **C**H), 102.0 (O**C**H$_2$O), 90.1 (Ar, **C**).
MS $^m/_z$ (APCI)	353 (24 %; M(^{13}C)H$^+$), 352 (100 %; MH$^+$).
CHN	Found: C, 47.97; H, 2.82; N, 3.93. $C_{14}H_{10}INO_2$ requires C, 47.89; H, 2.87; N, 3.99.

4-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{12}INO_2$ (353.16)

A mixture of the azastilbenes **368** and **369** (500 mg, 1.42 mmol) were refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and potassium carbonate solution (2M, 100 mL) added. The reaction mixture was washed with Et_2O (4 x 100 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **372** (460 mg, 1.30 mmol, 91 %) as a white crystalline solid.

M.P. 49 - 51 °C (Et_2O).

FT-IR (solid) υ_{max} 1601 m, 1501 m, 1475 s, 1228 s, 1039 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 295 (4190), 244 (8170) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.52 (2H, d, *J* 5.2 Hz, Ar**H**), 7.26 (1H, s, Ar**H**), 7.16 (2H, d, *J* 5.9 Hz, Ar**H**), 6.66 (1H, s, Ar**H**), 5.96 (2H, s, $OC\mathbf{H_2}O$), 2.97 - 2.91 (2H, m, $RCH_2C\mathbf{H_2}R$), 2.87 - 2.81 (2H, m, $RC\mathbf{H_2}CH_2R$).

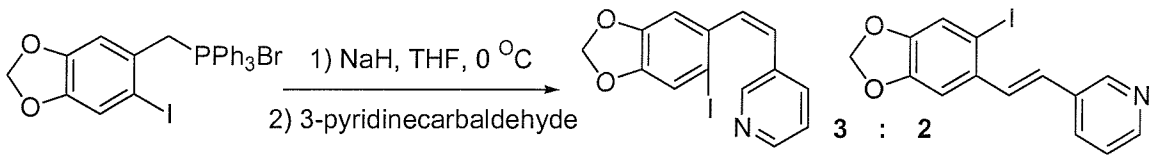
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 150.0 (Ar, **C**), 149.7 (Ar, 2 x **C**H), 148.5 (Ar, **C**), 147.0 (Ar, **C**), 136.4 (Ar, **C**), 124.0 (Ar, 2 x **C**H), 118.7 (Ar, **C**H), 109.3 (Ar, **C**H), 101.6 ($O\mathbf{C}H_2O$), 87.7 (Ar, **C**), 41.6 ($Ar\mathbf{C}H_2$), 35.9 ($Ar\mathbf{C}H_2$).

MS $^m/_z$ (ES) 395 (28 %; $[MH+MeCN]^+$), 355 (19 %; $M(^{13}C)H^+$), 354 (100 %; MH^+).

CHN Found: C, 47.79; H, 3.43; N, 3.96. $C_{14}H_{12}INO_2$ requires C, 47.61; H, 3.42; N, 3.97.

3-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **366** and

3-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **367**



$C_{26}H_{21}BrIO_2P$ (603.23)

$C_{14}H_{10}INO_2$ (351.14)

NaH (400 mg, 10.0 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (40 mL) at 0 °C. The iodide **362** (5.00 g, 8.29 mmol) was added and the reaction stirred for 1 hour under argon. The mixture was cooled to 0 °C again and 3-pyridinecarbaldehyde **364** (0.70 mL, 795 mg, 7.42 mmol) added. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (Et_2O) to give to give firstly the *Z*-azastilbene **366** (1.50 g, 4.27 mmol, 58 %) which was recrystallised from EtOH as a pale yellow crystalline solid followed by the *E*-azastilbene **367** (1.05 g, 2.98 mmol, 40 %) which was also recrystallised from EtOH as a pale yellow crystalline solid.

Data for 3-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **366**

M.P. 102 - 103 °C (EtOH).

FT-IR (solid) υ_{max} 1496 m, 1473 s, 1432 m, 1244 m, 1229 m, 1105 w, 1037 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 290 (11180) nm (mol^{-1} dm^3 cm^{-1}).

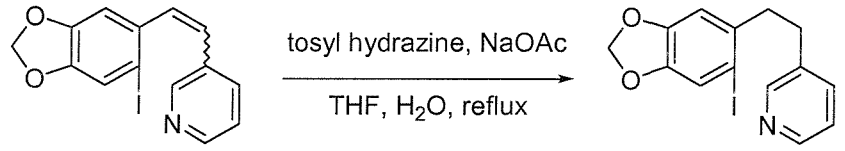
^{1}H NMR δ_H ppm (250 MHz, $CDCl_3$)
8.40 (2H, app. dd, *J* 4.8, 1.8 Hz, Ar**H**),
7.40 (1H, dt, *J* 8.0, 1.9 Hz Ar**H**), 7.30 (1H, s, Ar**H**),
7.12 (1H, ddd, *J* 7.9, 4.8, 0.8 Hz, Ar**H**),
6.57 (1H, d, *J* 11.8 Hz, RC**H**=CHR), 6.56 (1H, s, Ar**H**),
6.51 (1H, d, *J* 12.0 Hz, RCH=C**H**R), 5.92 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	150.2 (Ar, **C**H), 148.4 (Ar, **C**), 148.2 (Ar, **C**), 148.1 (Ar, **C**H), 135.8 (Ar, **C**H), 135.8 (**C**H=CH), 134.1 (Ar, **C**), 132.0 (Ar, **C**), 127.0 (CH=**C**H), 123.1 (Ar, **C**H), 118.5 (Ar, **C**H), 109.6 (Ar, **C**H), 101.7 (O**C**H_2O), 87.9 (Ar, **C**).
MS $^m/_z$ (APCI)	353 (65 %; M(^{13}C)H^+), 352 (100 %; MH^+), 225 (62 %), 224 (88 %).
CHN	Found: C, 47.87; H, 2.87; N, 3.95. $C_{14}H_{10}INO_2$ requires C, 47.89; H, 2.87; N, 3.99.

Data for 3-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **367**

M.P.	132 - 133 °C (EtOH).
FT-IR (solid) υ_{max}	1500 m, 1475 s, 1407 w, 1285 w, 1248 m br., 1187 m, 1113 m, 1040 m cm^{-1}.
UV (MeOH) λ_{max} (ε)	338 (13410), 297 (14720), 250 (15070) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (250 MHz, $CDCl_3$)	8.71 (1H, d, *J* 4.6, 2.2 Hz, Ar**H**), 8.50 (1H, dd, *J* 4.8, 1.6 Hz, Ar**H**), 7.84 (1H, dt, *J* 8.0, 1.8 Hz, Ar**H**), 7.31 (1H, d, *J* 16.0 Hz, RC**H**=CHR), 7.31 (1H, d, *J* 5.1 Hz, Ar**H**), 7.30 (1H, s, Ar**H**), 7.14 (1H, s, Ar**H**), 6.79 (1H, d, *J* 16.1 Hz, RCH=C**H**R), 6.00 (2H, s, OC**H**$_2$O).
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	149.0 (Ar, **C**H), 148.8 (Ar, **C**H), 148.7 (Ar, **C**), 148.5 (Ar, **C**), 134.3 (**C**H=CH), 133.2 (Ar, **C**), 132.7 (Ar, **C**H), 132.7 (Ar, **C**), 126.2 (CH=**C**H), 123.6 (Ar, **C**H), 118.8 (Ar, **C**H), 105.8 (Ar, **C**H), 101.9 (O**C**H_2O), 89.5 (Ar, **C**).
MS $^m/_z$ (APCI)	353 (42 %; M(^{13}C)H^+), 352 (100 %; MH^+), 226 (41 %).
CHN	Found: C, 47.82; H, 2.83; N, 3.92. $C_{14}H_{10}INO_2$ requires C, 47.89; H, 2.87; N, 3.99.

3-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **371**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{12}INO_2$ (353.16)

A mixture of the azastilbenes **366** and **367** (1.05 g, 2.99 mmol) were refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and potassium carbonate solution (2M, 100 mL) added. The reaction mixture was washed with Et_2O (4 x 50 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **371** (1.00 g, 2.83 mmol, 95 %) as a white crystalline solid.

M.P. 86 - 87 °C (Et_2O).

FT-IR (solid) υ_{max} 1501 m, 1478 s, 1226 s, 1135 m, 1044 s, 1028 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 295 (2550), 269 (2030), 263 (2490), 244 (4770) nm (mol^{-1} dm^3 cm^{-1}).

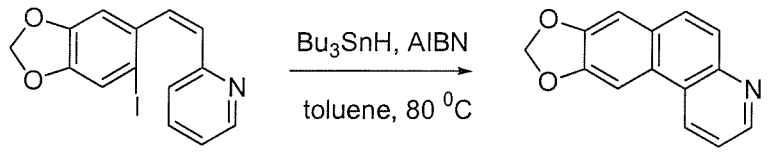
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.47 (2H, d, *J* 2.8 Hz, Ar**H**), 7.52 (1H, app. dt, *J* 7.8, 1.8 Hz, Ar**H**), 7.24 (1H, s, Ar**H**), 7.22 (1H, dd, *J* 7.7, 4.8 Hz, Ar**H**), 6.65 (1H, s, Ar**H**), 5.93 (2H, s, O**C**$\mathbf{H_2}$O), 2.95 - 2.90 (2H, m, RCH$_2$C$\mathbf{H_2}$R), 2.87 - 2.82 (2H, m, RC$\mathbf{H_2}$CH$_2$R).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$) 150.1 (Ar, **C**H), 148.5 (Ar, **C**), 147.7 (Ar, **C**H), 147.0 (Ar, **C**), 136.6 (Ar, **C**), 136.3 (Ar, **C**), 136.0 (Ar, **C**H), 123.3 (Ar, **C**H), 118.7 (Ar, **C**H), 109.4 (Ar, **C**H), 101.6 (O**C**H$_2$O), 87.7 (Ar, **C**), 42.4 (Ar**C**H$_2$), 33.8 (Ar**C**H$_2$).

MS $^{m}/_{z}$ (APCI)	355 (50 %; M(^{13}C)H^{+}), 354 (100 %; MH^{+}), 228 (35 %), 226 (50 %).
CHN	Found: C, 47.80; H, 3.43; N, 3.96. $C_{14}H_{12}INO_2$ requires C, 47.61; H, 3.42; N, 3.97.

6.23 IODIDE RADICAL CYCLISATIONS

[1,3]Dioxolo[4'5':4,5]benzo[*f*]quinoline **373**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

The azastilbene **365** (600 mg, 1.71 mmol) in toluene (140 mL) was stirred under argon at 80 °C with Bu_3SnH (0.6 mL, 649 mg, 2.23 mmol) and AIBN (20 mg, 0.122 mmol) for 18 hours. A further portion of Bu_3SnH (1.4 mL, 1.51 g, 5.20 mmol) and AIBN (60 mg, 0.365 mmol) were added and the reaction stirred for another 24 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 200 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield the cyclised product **373** (180 mg, 0.81 mmol, 47 %) as a pale yellow crystalline solid.

Data for [1,3]dioxolo[4'5':4,5]benzo[*f*]quinoline **373**

M.P. 200 - 201 °C (EtOH).

FT-IR (solid) υ_{max} 1497 m, 1478 s, 1374 w, 1257 s, 1195 s, 1084 w, 1030 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 286 (19400), 256 (12870), 237 (22130) nm (mol^{-1} dm^3 cm^{-1}).

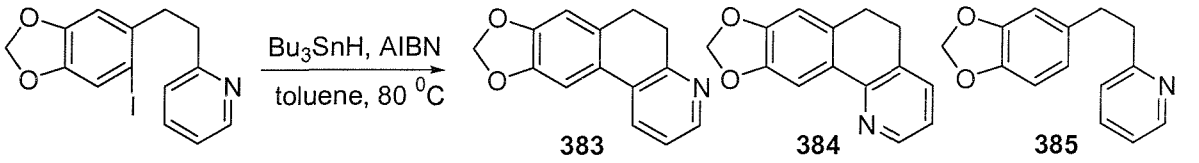
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.91 (1H, dd, *J* 4.3, 1.5 Hz, Ar**H**), 8.75 (1H, d, *J* 8.4 Hz, Ar**H**), 7.95 (1H, s, Ar**H**), 7.90 (1H, d, *J* 9.1 Hz, Ar**H**), 7.86 (1H, d, *J* 9.1 Hz, Ar**H**), 7.51 (1H, dd, *J* 8.4, 4.3 Hz, Ar**H**), 7.26 (1H, s, Ar**H**), 6.14 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	149.1 (Ar, **C**H), 148.7 (Ar, **C**), 148.2 (Ar, **C**), 147.3 (Ar, **C**), 130.5 (Ar, **C**H), 130.2 (Ar, **C**H), 128.3 (Ar, **C**), 126.5 (Ar, **C**H), 125.9 (Ar, **C**), 125.2 (Ar, **C**), 121.0 (Ar, **C**H), 105.9 (Ar, **C**H), 101.6 (O**C**H_2O), 100.7 (Ar, **C**H).
MS $^m/_z$ (APCI)	225 (32 %; M(^{13}C)H^+), 224 (100 %; MH^+).
CHN	Found: C, 75.07; H, 4.06; N, 6.25. $C_{14}H_9NO_2$ requires C, 75.33; H, 4.06; N, 6.27.

2-[2-(1,3-Benzodioxol-5-yl)ethyl]pyridine **385**,

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]quinoline **384** and

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]quinoline **383**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **370** (900 mg, 2.55 mmol) in toluene (200 mL) was stirred under argon at 80 °C with Bu_3SnH (0.82 mL, 887 mg, 3.05 mmol) and AIBN (20 mg, 0.122 mmol) for 40 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield firstly **384** (156 mg, 0.69 mmol, 27 %) as a light yellow solid, then **385** (200 mg, 0.88 mmol, 35 %) as a white solid and then **383** (187 mg, 0.83 mmol, 33 %) as a white solid.

Data for 2-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **385**

M.P. 26 - 27 °C (Et_2O).

FT-IR (solid) υ_{max} 1592 w, 1502 m, 1488 s, 1441 m, 1245 s, 1039 s cm^{-1}.

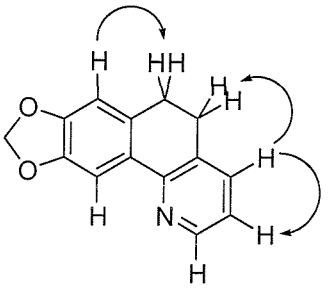
UV (MeOH) λ_{max} (ε) 287 (3670), 269 (3730), 263 (4140), 236 (4270) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.54 (1H, d, *J* 5.1 Hz, Ar**H**), 7.56 (1H, td, *J* 7.6, 1.8 Hz, Ar**H**), 7.11 (1H, dd, *J* 7.2, 4.9 Hz, Ar**H**), 7.07 (1H, d, *J* 7.7 Hz, Ar**H**), 6.70 (1H, d, *J* 8.0 Hz, Ar**H**), 6.69 (1H, s, Ar**H**), 6.63 (1H, dd, *J* 7.8, 1.7 Hz, Ar**H**), 5.91 (2H, s, OCH_2O), 3.09 - 3.02 (2H, m, RCH_2CH_2R), 3.00 - 2.93 (2H, m, RCH_2CH_2R).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	161.1 (Ar, **C**), 149.4 (Ar, **C**H), 147.5 (Ar, **C**), 145.7 (Ar, **C**), 136.3 (Ar, **C**H), 135.4 (Ar, **C**), 123.0 (Ar, **C**H), 121.2 (Ar, **C**H), 121.2 (Ar, **C**H), 109.0 (Ar, **C**H), 108.1 (Ar, **C**H), 100.8 (O**C**H_2O), 40.5 (Ar**C**H_2), 35.7 (Ar**C**H_2).
MS $^m/_z$ (APCI)	229 (15 %; M(^{13}C)H^+), 228 (100 %; MH^+).
HRMS (ES)	Found: MH^+, 228.1028. $C_{14}H_{14}NO_2$ requires 228.1024.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]quinoline **384**

M.P.	73 - 75 °C (EtOH / petrol).
FT-IR (solid) υ_{max}	1568 w, 1495 m, 1483 m, 1450 s, 1416 w, 1374 w, 1326 w, 1288 w, 1234 s, 1037 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	329 (10840), 290 (5070), 280 (4700) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	8.45 (1H, dd, *J* 4.8, 1.8 Hz, Ar**H**), 7.80 (1H, s, Ar**H**), 7.41 (1H, ddt, *J* 7.6, 1.8, 0.8 Hz, Ar**H**), 7.03 (1H, dd, *J* 7.6, 4.8 Hz, Ar**H**), 6.66 (1H, s, Ar**H**), 5.93 (2H, s, OC**H**$_2$O), 2.92 - 2.77 (4H, m, RC**H**$_2$C**H**$_2$R).

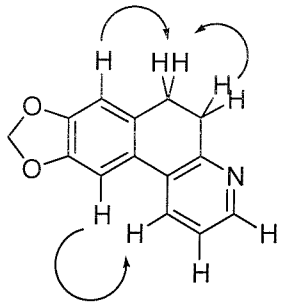


^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 7.80 (1H, s, Ar**H**) caused no n.O.e. enhancement. n.O.e Irradiation of the signal at δ_H 7.41 (1H, ddt, *J* 7.6, 1.8, 0.8 Hz, Ar**H**) caused an n.O.e. enhancement at δ_H 7.03 (1H, dd, *J* 7.6, 4.8 Hz, Ar**H**) and δ_H 2.92 - 2.77 (4H, m, RC**H$_2$**C**H$_2$**R). n.O.e Irradiation of the signal at δ_H 6.66 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.92 - 2.77 (4H, m, RC**H$_2$**C**H$_2$**R).
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	152.9 (Ar, **C**), 148.7 (Ar, **C**), 148.0 (Ar, **C**H), 147.5 (Ar, **C**), 135.6 (Ar, **C**H), 133.2 (Ar, **C**), 131.3 (Ar, **C**), 129.2 (Ar, **C**), 121.9 (Ar, **C**H), 108.4 (Ar, **C**H), 105.8 (Ar, **C**H), 101.4 (O**C**H$_2$O), 28.7 (Ar**C**H$_2$), 28.6 (Ar**C**H$_2$).
MS $^m/_z$ (APCI)	227 (30 %; M(^{13}C)H$^+$), 226 (100 %; MH$^+$).
CHN	Found: C, 74.53; H, 4.87; N, 6.21. $C_{14}H_{11}NO_2$ requires C, 74.65; H, 4.92; N, 6.22.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]quinoline **383**

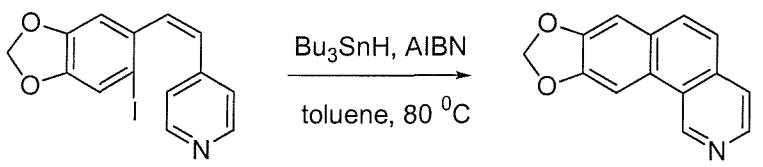
M.P.	143 - 145 °C (EtOH).
FT-IR (solid) υ_{max}	1744 m, 1712 m, 1502 s, 1457 m, 1365 m, 1237 s, 1114 m, 1030 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	326 (18220), 285 (13810) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	8.37 (1H, dd, *J* 5.1, 1.8 Hz, Ar**H**), 7.82 (1H, dd, *J* 7.8, 1.5 Hz, Ar**H**), 7.20 (1H, dd, *J* 7.8, 4.8 Hz, Ar**H**), 7.17 (1H, s, Ar**H**), 6.75 (1H, s, Ar**H**), 5.98 (2H, s, O**CH_2**O), 3.09 - 3.02 (2H, m, RCH_2C**H_2**R), 2.94 - 2.87 (2H, m, RC**H_2**CH_2R).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 7.82 (1H, dd, *J* 7.8, 1.5 Hz, Ar**H**) caused an n.O.e. enhancement at δ_H 7.20 (1H, dd, *J* 7.8, 4.8 Hz, Ar**H**) and δ_H 7.17 (1H, s, Ar**H**). n.O.e Irradiation of the signal at δ_H 6.75 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.94 - 2.87 (2H, m, RC**H_2**CH_2R). n.O.e Irradiation of the signal at δ_H 3.09 - 3.02 (2H, m, RCH_2C**H_2**R) caused no n.O.e. enhancement. n.O.e Irradiation of the signal at δ_H 2.94 - 2.87 (2H, m, RC**H_2**CH_2R) caused an n.O.e. enhancement at δ_H 6.75 (1H, s, Ar**H**) and δ_H 3.09 - 3.02 (2H, m, RCH_2C**H_2**R).
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	157.1 (Ar, **C**), 147.6 (Ar, **C**), 147.2 (Ar, **C**H), 147.1 (Ar, **C**), 131.3 (Ar, **C**), 129.9 (Ar, **C**H), 129.8 (Ar, **C**), 126.6 (Ar, **C**), 122.2 (Ar, **C**H), 108.7 (Ar, **C**H), 104.2 (Ar, **C**H), 101.2 (O**C**H_2O), 31.8 (Ar**C**H_2), 28.7 (Ar**C**H_2).
MS $^m/_z$ (APCI)	227 (19 %; M(^{13}C)H^+), 226 (100 %; MH^+).
CHN	Found: C, 74.48; H, 4.85; N, 6.17. $C_{14}H_{11}NO_2$ requires C, 74.65; H, 4.92; N, 6.22.

[1,3]Dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

The azastilbene **368** (450 mg, 1.28 mmol) in toluene (110 mL) was stirred under argon at 80 °C with Bu_3SnH (0.45 mL, 487 mg, 1.67 mmol) and AIBN (20 mg, 0.122 mmol) for 72 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield **345** (280 mg, 1.25 mmol, 98 %) recrystallised from EtOH as a yellow solid.

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

M.P. 182 - 183 °C (EtOH).

FT-IR (solid) υ_{max} 1739 m br., 1501 m, 1468 s, 1431 m, 1375 m, 1241 m, 1226 s, 1038 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 354 (7090), 338 (5670), 322 (3670), 280 (17590), 259 (32690), 237 (34190) nm (mol^{-1} dm^3 cm^{-1}).

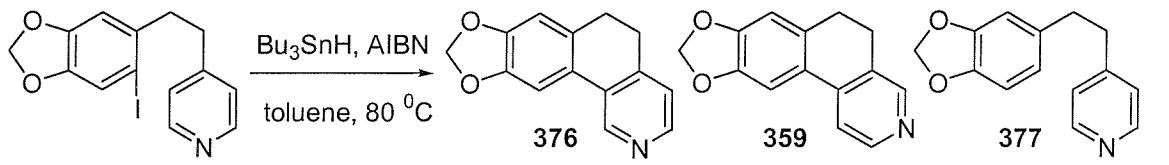
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 9.84 (1H, s, Ar**H**), 8.62 (1H, d, *J* 5.5 Hz, Ar**H**), 8.11 (1H, s, Ar**H**), 7.80 (1H, d, *J* 8.8 Hz, Ar**H**), 7.66 (1H, d, *J* 5.4 Hz, Ar**H**), 7.58 (1H, d, *J* 8.8 Hz, Ar**H**), 7.25 (1H, s, Ar**H**), 6.14 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	149.1 (Ar, **C**), 148.2 (Ar, **C**), 146.7 (Ar, **C**H), 144.0 (Ar, **C**H), 135.0 (Ar, **C**), 131.0 (Ar, **C**H), 128.9 (Ar, **C**), 125.8 (Ar, **C**), 125.0 (Ar, **C**), 123.2 (Ar, **C**H), 121.1 (Ar, **C**H), 106.1 (Ar, **C**H), 101.7 (O**C**H_2O), 100.1 (Ar, **C**H).
MS $^m/_z$ (APCI)	225 (52 %; M(^{13}C)H^+), 224 (100 %; MH^+).
CHN	Found: C, 75.14; H, 4.06; N, 6.25. $C_{14}H_9NO_2$ requires C, 75.33; H, 4.06; N, 6.27.

4-[2-(1,3-Benzodioxol-5-yl)ethyl]pyridine **377**,

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **376** and

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **372** (500 mg, 1.42 mmol) in toluene (200 mL) was stirred under argon at 80 °C with Bu_3SnH (0.48 mL, 519 mg, 1.78 mmol) and AIBN (20 mg, 0.122 mmol) for 40 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield firstly a 1:1 mixture of **376** (100 mg, 0.44 mmol, 31 %) and **377** (100 mg, 0.44 mmol, 31 %) and then **359** (58 mg, 0.26 mmol, 18 %) as a pale yellow solid. The mixture of **376** and **377** was separated by fractional recrystallisation from EtOH, with **376** crystallising first as a white crystalline solid.

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

M.P. 56 - 58 °C (pentane).

FT-IR (solid) υ_{max} 1600 m, 1489 s, 1443 m, 1416 m, 1243 s, 1191 m, 1037 s cm^{-1}.

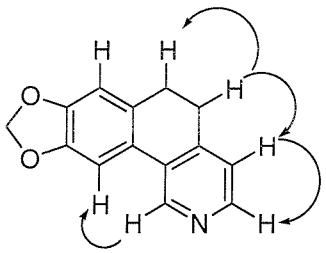
UV (MeOH) λ_{max} (ε) 287 (4640), 263 (2700), 237 (6150) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (250 MHz, $CDCl_3$) 8.48 (2H, dd, *J* 4.5, 1.6 Hz, Ar**H**), 7.06 (2H, dd, *J* 4.5, 1.6 Hz, Ar**H**), 6.71 (1H, d, *J* 7.9 Hz, Ar**H**), 6.64 (1H, d, *J* 1.7 Hz, Ar**H**), 6.57 (1H, dd, *J* 7.9, 1.6 Hz, Ar**H**), 5.92 (2H, s, OC**H**$_2$O), 2.86 (4H, s, RC**H**$_2$C**H**$_2$R).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	150.3 (Ar, **C**), 149.7 (Ar, 2 x **C**H), 147.7 (Ar, **C**), 145.9 (Ar, **C**), 134.5 (Ar, **C**), 123.9 (Ar, 2 x **C**H), 121.2 (Ar, **C**H), 108.8 (Ar, **C**H), 108.2 (Ar, **C**H), 100.9 (O**C**H_2O), 37.3 (Ar**C**H_2), 36.3 (Ar**C**H_2).
MS $^m/_z$ (APCI)	229 (18 %; M(^{13}C)H^+), 228 (100 %; MH^+).
CHN	Found: C, 74.02; H, 5.79; N, 6.11. $C_{14}H_{13}NO_2$ requires C, 73.99; H, 5.77; N, 6.16.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **376**

M.P.	208 - 210 °C (EtOH).
FT-IR (solid) υ_{max}	1640 m br., 1483 s, 1415 m, 1393 w, 1226 s, 1193 m, 1161 s, 1134 m, 1031 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	322 (17320), 276 (12710), 238 (24460) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (400 MHz, MeOH)	8.89 (1H, s, Ar**H**), 8.46 (1H, d, *J* 5.3 Hz, Ar**H**), 7.60 (1H, d, *J* 5.3 Hz, Ar**H**), 7.22 (1H, s, Ar**H**), 6.68 (1H, s, Ar**H**), 6.05 (2H, s, O**CH$_2$**O), 3.13 - 3.07 (2H, m, RCH$_2$C**H$_2$**R), 2.93 - 2.87 (2H, m, RC**H$_2$**CH$_2$R).



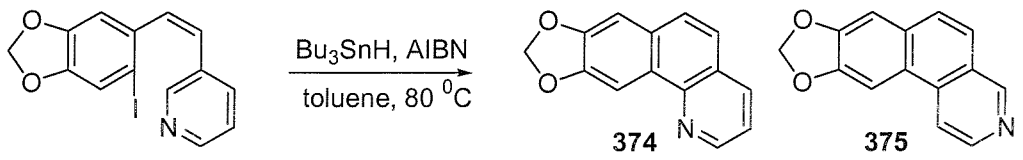
^{1}H NMR δ_H ppm (400 MHz, MeOH)	n.O.e Irradiation of the signal at δ_H 8.89 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.22 (1H, s, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.60 (1H, d, *J* 5.3 Hz, Ar**H**) caused an n.O.e. enhancement at δ_H 8.46 (1H, d, *J* 5.3 Hz, Ar**H**) and δ_H 3.13 - 3.07 (2H, m, $RCH_2C\mathbf{H_2}R$). n.O.e Irradiation of the signal at δ_H 3.13 - 3.07 (2H, m, $RCH_2C\mathbf{H_2}R$) caused an n.O.e. enhancement at δ_H 7.60 (1H, d, *J* 5.3 Hz, Ar**H**) and δ_H 2.93 - 2.87 (2H, m, $RC\mathbf{H_2}CH_2R$).
^{13}C NMR δ_C ppm (62.9 MHz, MeOH)	163.7 (Ar, **C**), 157.4 (Ar, **C**), 151.5 (Ar, **C**), 140.9 (Ar, **C**H), 137.9 (Ar, **C**H), 136.3 (Ar, **C**), 134.4 (Ar, **C**), 127.4 (Ar, **C**H), 123.6 (Ar, **C**), 110.3 (Ar, **C**H), 105.8 (Ar, **C**H), 103.6 ($O\mathbf{C}H_2O$), 30.4 ($Ar\mathbf{C}H_2$), 28.2 ($Ar\mathbf{C}H_2$).
MS $^{m}/_{z}$ (APCI)	226 (100 %; MH^+), 186 (22 %).
CHN	Found: C, 74.50; H, 4.89; N, 6.41. $C_{14}H_{11}NO_2$ requires C, 74.65; H, 4.92; N, 6.22.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**

Data identical to those described previously.

[1,3]Dioxolo[4'5':4,5]benzo[*h*]quinoline **374** and

[1,3]Dioxolo[4'5':4,5]benzo[*f*]isoquinoline **375**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

The azastilbene **366** (735 mg, 2.09 mmol) in toluene (150 mL) was stirred under argon at 80 °C with Bu_3SnH (0.70 mL, 757 mg, 2.60 mmol) and AIBN (20 mg, 0.122 mmol) for 90 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield **374** (250 mg, 1.12 mmol, 54 %), recrystallised from EtOH as a yellow solid, and then **375** (200 mg, 0.90 mmol, 43 %), also recrystallised from EtOH as a yellow solid.

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]quinoline **374**

M.P. 121 - 122 °C (EtOH).

FT-IR (solid) υ_{max} 1497 m, 1462 s, 1401 w, 1249 s, 1235 w, 1215 w, 1035 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 334 (2590), 283 (36440), 254 (25800), 235 (44870) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.93 (1H, dd, *J* 4.3, 1.7 Hz, Ar**H**), 8.64 (1H, s, Ar**H**), 8.12 (1H, dd, *J* 8.0, 1.7 Hz, Ar**H**), 7.67 (1H, d, *J* 8.8 Hz, Ar**H**), 7.56 (1H, d, *J* 8.8 Hz, Ar**H**), 7.44 (1H, dd, *J* 8.0, 4.3 Hz, Ar**H**), 7.22 (1H, s, Ar**H**), 6.12 (2H, s, O**CH$_2$**O).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	148.9 (Ar, **C**), 148.6 (Ar, **C**H), 148.3 (Ar, **C**), 146.1 (Ar, **C**), 135.8 (Ar, **C**H), 130.3 (Ar, **C**), 128.2 (Ar, **C**), 127.1 (Ar, **C**H), 125.7 (Ar, **C**), 123.7 (Ar, **C**H), 121.0 (Ar, **C**H), 105.0 (Ar, **C**H), 102.4 (Ar, **C**H), 101.4 (O**C**H_2O).
MS $^m/_z$ (APCI)	225 (32 %; M(^{13}C)H^+), 224 (100 %; MH^+).
CHN	Found: C, 75.03; H, 4.06; N, 6.18. $C_{14}H_9NO_2$ requires C, 75.33; H, 4.06; N, 6.27.

Data for [1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **375**

M.P.	182 - 183 °C (EtOH).
FT-IR (solid) υ_{max}	1740 br. w, 1602 w, 1482 s, 1271 w, 1240 m, 1196 m, 1032 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	356 (4210), 339 (4450), 324 (3470), 277 (35870), 256 (39540) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	9.20 (1H, s, Ar**H**), 8.67 (1H, d, *J* 5.8 Hz, Ar**H**), 8.19 (1H, d, *J* 5.8 Hz, Ar**H**), 7.98 (1H, s, Ar**H**), 7.73 (2H, s, Ar**H**), 7.26 (1H, s, Ar**H**), 6.15 (2H, s, O**CH$_2$**O).
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	152.0 (Ar, **C**H), 149.3 (Ar, **C**), 148.6 (Ar, **C**), 144.5 (Ar, **C**H), 134.2 (Ar, **C**), 130.6 (Ar, **C**), 127.8 (Ar, **C**H), 126.5 (Ar, **C**), 124.7 (Ar, **C**), 123.3 (Ar, **C**H), 115.8 (Ar, **C**H), 106.0 (Ar, **C**H), 101.8 (O**C**H_2O), 101.2 (Ar, **C**H).
MS $^m/_z$ (APCI)	225 (15 %; M(^{13}C)H^+), 224 (100 %; MH^+).
CHN	Found: C, 75.06; H, 4.06; N, 6.21. $C_{14}H_9NO_2$ requires C, 75.33; H, 4.06; N, 6.27.

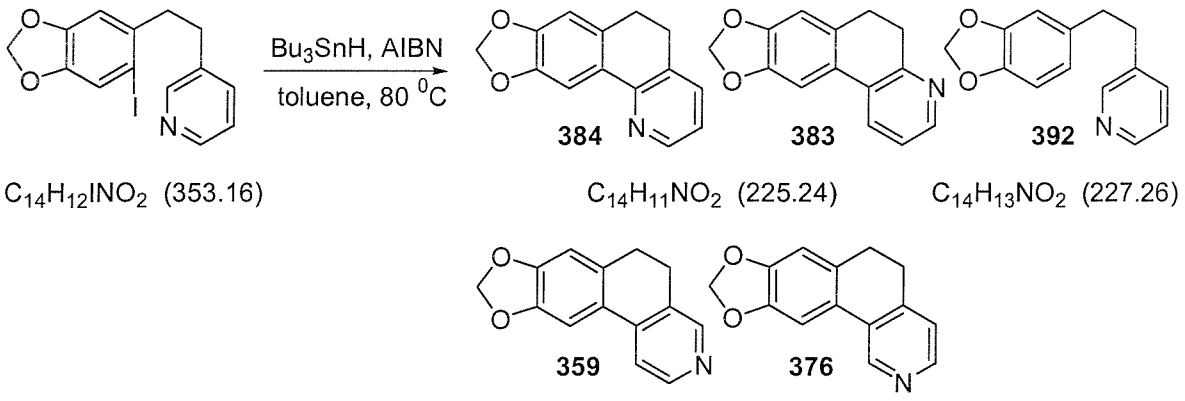
5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]quinoline **384**,

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]quinoline **383**,

3-[2-(1,3-Benzodioxol-5-yl)ethyl]pyridine **392**,

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **376** and

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **359**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **371** (200 mg, 0.566 mmol) in toluene (150 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.20 mL, 216 mg, 0.744 mmol) and AIBN (20 mg, 0.122 mmol) for 48 hours. The mixture was cooled to room temperature and stirred for 48 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield firstly **384** (70 mg, 0.311 mmol, 42 %), then a mixture of **392** (19 mg, 0.084 mmol, 11 %) and **383** (9.5 mg, 0.042 mmol, 6 %) and finally followed by a mixture of **359** (26 mg, 0.115 mmol, 15 %) **376** (2.4 mg, 0.011 mmol, 1.5 %).

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]quinoline **384**

Data identical to those described previously.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]quinoline **383**

Data identical to those described previously.

Data for 3-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **392**

Spectral and physical data were in accord with the literature.[173]

M.P. 37 - 39 °C (Et_2O).

FT-IR (solid) υ_{max} 1503 m, 1490 s, 1443 m, 1246 s, 1191 m, 1039 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 287 (4420), 270 (4010), 263 (4280), 235 (5780) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (250 MHz, $CDCl_3$) 8.44 (1H, dd, *J* 4.8, 1.6 Hz, Ar**H**), 8.40 (1H, d, *J* 2.0 Hz, Ar**H**), 7.42 (1H, dt, *J* 7.8, 2.0 Hz, Ar**H**), 7.18 (1H, ddd, *J* 7.8, 4.8, 0.8 Hz, Ar**H**), 6.70 (1H, d, *J* 7.9 Hz, Ar**H**), 6.64 (1H, d, *J* 1.6 Hz, Ar**H**), 6.56 (1H, dd, *J* 7.9, 1.7 Hz, Ar**H**), 5.92 (2H, s, OC**H$_2$**O), 2.92 - 2.79 (4H, m, RC**H$_2$**C**H$_2$**R).

^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$) 150.0 (Ar, **C**H), 147.6 (Ar, **C**H), 147.5 (Ar, **C**), 145.9 (Ar, **C**), 136.7 (Ar, **C**), 135.9 (Ar, **C**H), 134.6 (Ar, **C**), 123.2 (Ar, **C**H), 121.3 (Ar, **C**H), 108.9 (Ar, **C**H), 108.2 (Ar, **C**H), 100.8 (O**C**H$_2$O), 37.2 (Ar**C**H$_2$), 35.2 (Ar**C**H$_2$).

MS $^m/_z$ (APCI) 229 (20 %; M(^{13}C)H$^+$), 228 (100 %; MH$^+$).

CHN Found: C, 73.94; H, 5.79; N, 6.20. $C_{14}H_{13}NO_2$ requires C, 73.99; H, 5.77; N, 6.16.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **376**

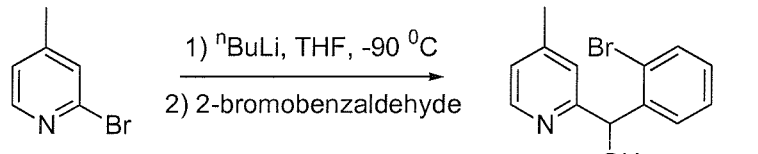
Data identical to those described previously.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **359**

Data identical to those described previously.

6.24 ATTEMPTED 5-MEMBERED RING FORMATION

(2-Bromophenyl)(4-methyl-2-pyridyl)methanol **401**



C_6H_6BrN (172.03) $C_{13}H_{12}BrNO$ (278.15)

^{n}Butyllithium (1.6 M in hexane; 3.7 mL, 5.92 mmol) was added dropwise to 2-bromo-4-methylpyridine **400** (1.00 g, 5.81 mmol) in THF (20 mL) at - 90 °C and the solution stirred for 30 minutes. 2-Bromobenzaldehyde (1.08 g, 5.84 mmol) in THF (5 mL) was then added dropwise to the solution, which was stirred for a further 2 hours at - 90 °C. The reaction mixture was then warmed to room temperature over 2 hours and saturated ammonium chloride (50 mL) added. The organic phase was separated, washed with water (50 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (40 : 60, Et_2O : petrol) to give **401** (1.34 g, 4.83 mmol, 83 %) as a beige solid.

M.P. 78 - 80 °C (ethanol / petrol).

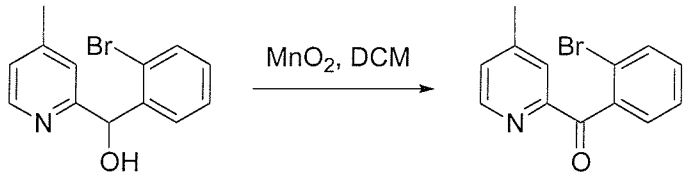
FT-IR (CH_2Cl_2) υ_{max} 3588 w, 3358 br. m, 3060 w, 2925 w, 1608 s, 1564 m, 1470 m, 1438 m, 1389 m, 1024 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 257 (830) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.44 (1H, d, *J* 4.4 Hz, Ar**H**), 7.59 (1H, dd, *J* 8.1, 1.5 Hz, Ar**H**), 7.38-7.04 (5H, m, 5 x Ar**H**), 6.21 (1H, s, Ar_2CHOH), 5.62 (1H, s, Ar_2CHOH), 2.31 (3H, s, $ArCH_3$).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	159.7 (Ar, **C**), 148.6 (Ar, **C**), 147.6 (Ar, **C**H), 142.6 (Ar, **C**) 132.9 (Ar, **C**H), 129.3 (Ar, **C**H), 129.3 (Ar, **C**H), 128.0 (Ar, **C**H), 124.0 (Ar, **C**H), 123.3 (Ar, **C**), 122.2 (Ar, **C**H), 73.0 (Ar_2**C**HOH), 21.3 (Ar**C**H_3).
MS $^m/_z$ (CI)	280 (22 %; M(^{81}Br)H^+), 278 (24 %; M(^{79}Br)H^+), 184 (59 %), 119 (24 %), 109 (55 %), 94 (100 %).
HRMS (EI)	Found: M^+, 277.0113. $C_{13}H_{12}NO^{79}Br$ requires 277.0102.
CHN	Found: C, 56.03; H, 4.31; N, 4.93. $C_{13}H_{12}BrNO$ requires C, 56.14; H, 4.35; N, 5.04.

(2-Bromophenyl)(4-methyl-2-pyridyl)methanone **402**



$C_{13}H_{12}BrNO$ (278.15) $C_{13}H_{10}BrNO$ (276.13)

MnO_2 (4.70 g, 54.1 mmol) was activated by azeotroping with toluene (15 mL). The alcohol **401** (500 mg, 1.80 mmol) in DCM (50 mL) was then added and the reaction mixture stirred under argon for 18 hours. The MnO_2 residues were removed by filtration through celite and the solvent removed *in vacuo* to yield **402** (443 mg, 1.60 mmol, 89 %) as a white crystalline solid.

M.P. 76 - 78 °C (ethanol).

FT-IR (CH_2Cl_2) υ_{max} 3048 m, 2926 m, 2853 m, 1884 s, 1600 s, 1589 m, 1565 w, 1470 w, 1434 m, 1300 s, 1216 m, 1050 m, 1027 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 266 (6600), 242 (8700) nm (mol^{-1} dm^3 cm^{-1}).

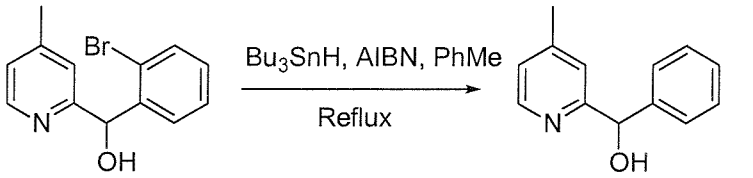
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.55 (1H, d, *J* 4.4 Hz, Ar**H**), 8.00 (1H, s, Ar**H**), 7.64 (1H, d, *J* 8.1 Hz, Ar**H**), 7.49 - 7.30 (4H, m, 4 x Ar**H**), 2.48 (3H, s, Ar**CH**$_3$).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 196.3 (Ar_2**C**O), 153.5 (Ar, **C**), 149.3 (Ar, **C**H), 148.6 (Ar, **C**), 140.6 (Ar, **C**), 133.2 (Ar, **C**H), 131.6 (Ar, **C**H), 130.0 (Ar, **C**H), 128.0 (Ar, **C**H), 127.2 (Ar, **C**H), 124.9 (Ar, **C**H), 120.2 (Ar, **C**), 21.3 (Ar**C**H_3).

MS $^m/_z$ (EI) 278 (54 %; M(^{81}Br)H^+), 276 (55 %; M(^{79}Br)H^+), 199 (36 %), 184 (100 %), 182 (49 %).

CHN Found: C, 56.38; H, 3.67; N, 4.99. $C_{13}H_{10}BrNO$ requires C, 56.55; H, 3.65; N, 5.07.

(4-Methyl-2-pyridyl)(phenyl)methanol **403**



$C_{13}H_{12}BrNO$ (278.14) $C_{13}H_{13}NO$ (199.25)

The alcohol **401** (100 mg, 0.360 mmol) in toluene (25 mL) was stirred under argon at reflux with Bu_3SnH (0.19 mL, 206 mg, 0.706 mmol) and AIBN (20 mg, 0.122 mmol) for 5 hours. The mixture was cooled to room temperature and stirred for 65 hours with $KF_{(aq)}$ (2M, 25 mL). The mixture was then extracted into diethyl ether (2 x 50 mL) and the organic phases combined, washed with water (2 x 50 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give **403** (62 mg, 0.311 mmol, 87 %) as a beige solid.

Spectral and physical data were in accord with the literature.[174,175]

M.P. 84 - 86 °C (petrol). Lit. 89 - 90 °C (distilled).[175]

FT-IR (CH_2Cl_2) υ_{max} 3595 w, 3373 br. m, 3063 w, 3030 w, 2959 w, 2926 m, 2855 w, 1721 m, 1609 s, 1562 m, 1389 m, 1295 m, 1055 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 257 (4000) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.43 (1H, d, *J* 5.2 Hz, Ar**H**), 7.42 - 7.27 (5H, m, 5 x Ar**H**), 7.03 (1H, d, *J* 4.4 Hz, Ar**H**), 6.97 (1H, s, Ar**H**), 5.72 (1H, s, Ar_2CHOH), 5.32 (1H, s, Ar_2CHOH), 2.30 (3H, s, $ArCH_3$).

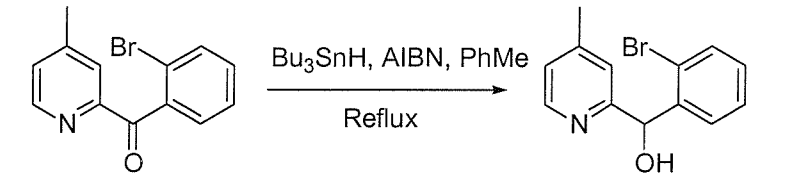
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 160.8 (Ar, **C**), 148.3 (Ar, **C**), 147.6 (Ar, **CH**), 143.6 (Ar, **C**) 128.7 (Ar, 2 x **CH**), 127.9 (Ar, **CH**), 127.2 (Ar, 2 x **CH**), 123.8 (Ar, **CH**), 122.2 (Ar, **CH**), 75.0 (Ar_2CHOH), 21.3 ($ArCH_3$).

MS $^{m}/_{z}$ (CI) 200 (58 %; MH^+), 199 (30 %; M^+), 184 (100 %; $[M\text{-}CH_3]^+$), 94 (38 %).

HRMS (CI) Found: M^+, 199.1002. $C_{13}H_{13}NO$ requires 199.0997.

CHN Found: C, 78.47; H, 6.64; N, 7.04. $C_{13}H_{13}NO$ requires C, 78.36; H, 6.58; N, 7.03.

(2-Bromophenyl)(4-methyl-2-pyridyl)methanol **401**

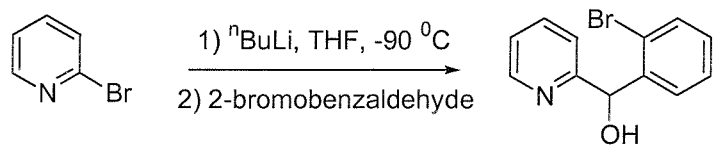


$C_{13}H_{10}BrNO$ (276.13) $C_{13}H_{12}BrNO$ (278.15)

The ketone **402** (196 mg, 0.710 mmol) in toluene (20 mL) was stirred under nitrogen at reflux with Bu_3SnH (0.19 mL, 206 mg, 0.706 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 30 mL). The mixture was then extracted into diethyl ether (2 x 30 mL) and the organic phases combined, washed with brine (30 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give firstly recovered starting material **402** (28 mg, 0.101 mmol, 14 %) and then the alcohol **401** (28 mg, 0.101 mmol, 14 %) as a white crystalline solid.

Data identical to those described previously.

(2-Bromophenyl)(2-pyridyl)methanol **405**



C_5H_4BrN (158.00) $C_{12}H_{10}BrNO$ (264.12)

^{n}Butyllithium (1.44 M in hexane, 2.19 mL, 3.15 mmol) was added dropwise to 2-bromopyridine **404** (0.3 mL, 497 mg, 3.15 mmol) in THF (20 mL) at - 90 °C. The solution immediately turned dark brown and 2-bromobenzaldehyde (0.37 mL, 586 mg, 3.17 mmol) was then added dropwise. The solution immediately turned to a clear, light yellow. Saturated ammonium chloride (50 mL) was then added and the solution warmed to room temperature over 30 minutes. The organic phase was separated, washed with water (30 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (20 : 80, Et_2O : petrol) and further purified by recrystallisation from hot petrol to give **405** (626 mg, 2.37 mmol, 75 %) as a white solid.

M.P. 77 - 79 °C (petrol).

FT-IR (CH_2Cl_2) υ_{max} 3371 br. m, 3070 w, 3018 w, 2927 w, 1594 s, 1571 m, 1472 s, 1438 s, 1402 s, 1191 m, 1062 m, 1022 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 260 (4800) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.58 (1H, d, *J* 5.2 Hz, Ar**H**), 7.66 - 7.57 (2H, m, 2 x Ar**H**), 7.40 - 7.12 (5H, m, 5 x Ar**H**), 6.27 (1H, s, Ar_2C**H**OH), 5.64 (1H, s, Ar_2CHO**H**).

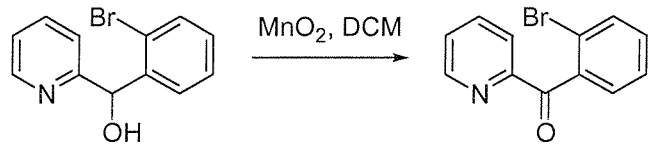
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 159.9 (Ar, **C**), 148.0 (Ar, **C**H), 142.4 (Ar, **C**), 137.2 (Ar, **C**H), 133.0 (Ar, **C**H), 129.4 (Ar, **C**H), 129.3 (Ar, **C**H), 128.1 (Ar, **C**H), 123.3 (Ar, **C**), 122.9 (Ar, **C**H), 121.6 (Ar, **C**H), 73.2 (Ar_2**C**HOH).

MS $^{m}/_{z}$ (CI) 266 (9 %; M(^{81}Br)H^{+}), 264 (11 %; M(^{79}Br)H^{+}), 170 (100 %), 168 (38 %), 94 (23 %), 80 (21 %).

HRMS (ES) Found: MH^{+}, 264.0023. $C_{12}H_{11}NO^{79}Br$ requires 264.0024.

CHN Found: C, 54.47; H, 3.82; N, 5.23. $C_{12}H_{10}BrNO$ requires C, 54.57; H, 3.82; N, 5.30.

(2-Bromophenyl)(2-pyridyl)methanone **406**



$C_{12}H_{10}BrNO$ (264.12) $C_{12}H_8BrNO$ (262.11)

MnO_2 (2 g, 23.0 mmol) was activated by azeotroping with toluene (15 mL). The alcohol **405** (200 mg, 0.757 mmol) in DCM (50 mL) was then added and the reaction mixture stirred under argon for 24 hours. The MnO_2 residues were removed by filtration through celite and the solvent removed *in vacuo* to yield **406** (167 mg, 0.673 mmol, 84 %) as a colourless semi-solid.

Spectral and physical data were in accord with the literature.[176-178]

M.P. 72 - 73 °C (EtOH / petrol). Lit. 63 - 63.5 (no solvent given).[177]

FT-IR (CH_2Cl_2) υ_{max} 3056 w, 2925 w, 2853 w, 1682 s, 1583 m, 1467 w, 1434 m, 1310 s, 1243 m, 1043 m, 1026 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 269 (5400), 235 (7300) nm (mol^{-1} dm^3 cm^{-1}).

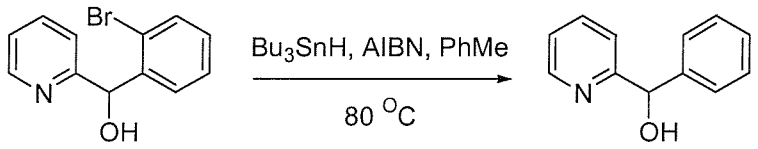
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.69 (1H, d, *J* 4.4 Hz, Ar**H**), 8.17 (1H, d, *J* 8.1 Hz, Ar**H**), 7.92 (1H, td, *J* 8.1, 1.5 Hz, Ar**H**), 7.64 (1H, d, *J* 7.4 Hz, Ar**H**), 7.51 - 7.34 (4H, m, 4 x Ar**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 196.0 (Ar_2**C**O), 153.6 (Ar, **C**), 149.5 (Ar, **C**H), 140.4 (Ar, **C**), 137.2 (Ar, **C**H), 133.2 (Ar, **C**H), 131.7 (Ar, **C**H), 130.0 (Ar, **C**H), 127.3 (Ar, **C**H), 127.2 (Ar, **C**H), 124.1 (Ar, **C**H), 120.2 (Ar, **C**).

MS $^m/_z$ (CI) 264 (27 %; M(^{81}Br)H^+), 262 (26 %; M(^{79}Br)H^+), 170 (100 %), 168 (37 %), 94 (19 %), 80 (19 %).

CHN Found: C, 54.90; H, 3.02; N, 5.23. $C_{12}H_8BrNO$ requires C, 54.99; H, 3.08; N, 5.34.

(Phenyl)(2-pyridyl)methanol **407**



$C_{12}H_{10}BrNO$ (264.12) $C_{12}H_{11}NO$ (185.22)

The alcohol **405** (300 mg, 1.14 mmol) in toluene (80 mL) was stirred under argon at 80 °C with Bu_3SnH (0.37 mL, 400 mg, 1.37 mmol) and AIBN (20 mg, 0.122 mmol) for 100 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 80 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (40 : 60, Et_2O : petrol) to give **407** (200 mg, 1.08 mmol, 95 %) as a white solid.

Spectral and physical data were in accord with the literature.[179-181]

M.P. 73 - 74 °C (Et_2O). Lit. 76 - 78 °C (distilled).[179]

FT-IR (solid) υ_{max} 3090 br. m, 2895 w, 1593 m, 1476 m, 1453 m, 1434 m, 1311 m, 1050 m, 1005 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 261 (3370) nm (mol^{-1} dm^3 cm^{-1}).

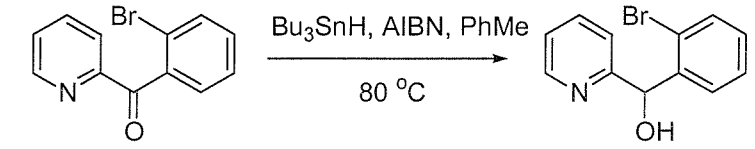
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.57 (1H, d, *J* 4.4 Hz, Ar**H**), 7.63 (1H, td, *J* 8.1, 1.5 Hz, Ar**H**), 7.41 - 7.16 (7H, m, 7 x Ar**H**), 5.77 (1H, s, Ar_2C**H**OH), 5.38 (1H, br. s, Ar_2CHO**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 161.1 (Ar, **C**), 148.0 (Ar, **C**H), 143.4 (Ar, **C**), 137.0 (Ar, **C**H), 128.7 (Ar, 2 x **C**H), 128.0 (Ar, **C**H), 127.2 (Ar, 2 x **C**H), 122.6 (Ar, **C**H), 121.5 (Ar, **C**H), 75.2 (Ar_2**C**HOH).

MS $^m/_z$ (ES) 187 (12 %), 186 (100 %; MH^+).

CHN Found: C, 77.64; H, 6.05; N, 7.59. $C_{12}H_{11}NO$ requires C, 77.81; H, 5.99; N, 7.56.

(2-Bromophenyl)(2-pyridyl)methanol **405**

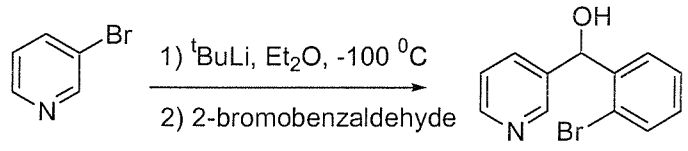


$C_{12}H_8BrNO$ (262.11) $C_{12}H_{10}BrNO$ (264.13)

The ketone **406** (434 mg, 1.66 mmol) in toluene (150 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.67 mL, 725 mg, 2.49 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 8 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (20 : 80, Et_2O : petrol) to give firstly recovered starting material **406** (223 mg, 0.851 mmol, 51 %) and then the alcohol **405** (210 mg, 0.795 mmol, 48 %) as a white crystalline solid.

Data identical to those described previously.

(2-Bromophenyl)(3-pyridyl)methanol **409**



C_5H_4BrN (158.00) $C_{12}H_{10}BrNO$ (264.12)

^{t}Butyllithium (1.25 M in hexane, 8.30 mL, 10.38 mmol) was added dropwise to 3-bromopyridine **408** (1.0 mL, 1.64 g, 10.38 mmol) in Et_2O (20 mL) at - 100 °C. After 1 hour, 2-bromobenzaldehyde (1.25 mL, 1.98 g, 10.71 mmol) in Et_2O (20 mL) was added dropwise. The solution was warmed to - 60 °C over a period of 2 hours and saturated sodium chloride solution (90 mL) added along with THF (50 mL) to aid product solubility. The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give **409** (2.27 g, 8.59 mmol, 83 %) as a white solid.

Spectral and physical data were in accord with the literature.[182-184]

M.P. 125 - 126 °C ($CHCl_3$). Lit. 125 - 126 °C (ethyl acetate).[182]

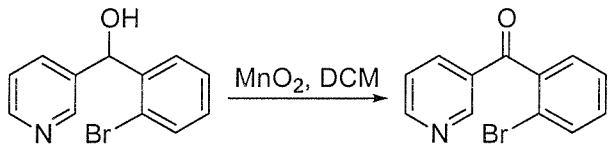
FT-IR (solid) υ_{max} 3091 br. m, 2826 w, 1589 w, 1564 w, 1434 m, 1315 w, 1178 w, 1108 w, 1055 m, 1018 w cm^{-1}.

UV (MeOH) λ_{max} (ε) 262 (1930) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.48 (1H, d, *J* 2.1 Hz, Ar**H**), 8.30 (1H, dd, *J* 4.4, 1.4 Hz, Ar**H**), 7.69 (1H, dt, *J* 7.4, 1.5 Hz, Ar**H**), 7.64 (1H, dd, *J* 8.1, 2.2 Hz, Ar**H**), 7.51 (1H, dd, *J* 8.1, 1.5 Hz, Ar**H**), 7.35 (1H, td, *J* 7.4, 1.5 Hz, Ar**H**), 7.23 - 7.12 (2H, m, 2 x Ar**H**), 6.17 (1H, s, C**H**OH), 4.99 (1H, s, CHO**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	148.6 (Ar, **C**H), 148.2 (Ar, **C**H), 142.3 (Ar, **C**), 138.7 (Ar, **C**), 135.3 (Ar, **C**H), 133.0 (Ar, **C**H), 129.5 (Ar, **C**H), 128.5 (Ar, **C**H), 128.1 (Ar, **C**H), 123.7 (Ar, **C**H), 122.6 (Ar, **C**), 72.4 (Ar_2**C**HOH).
MS $^m/_z$ (CI)	266 (4 %; M(^{81}Br)H^+), 264 (4 %; M(^{79}Br)H^+), 184 (10 %; $[M-Br]^+$), 170 (100 %), 169 (98 %), 168 (82 %), 167 (36 %).
HRMS (EI)	Found: M^+, 264.9934. $C_{12}H_{10}NO^{81}Br$ requires 264.9925.
CHN	Found: C, 54.53; H, 3.75; N, 5.14. $C_{12}H_{10}BrNO$ requires C, 54.57; H, 3.82; N, 5.30.

(2-Bromophenyl)(3-pyridyl)methanone **411**



$C_{12}H_{10}BrNO$ (264.12) $C_{12}H_8BrNO$ (262.10)

MnO_2 (4.00 g, 46 mmol) was activated by azeotroping with toluene (15 mL). The alcohol **409** (500 mg, 1.89 mmol) in DCM (50 mL) was then added and the reaction mixture stirred under argon for 18 hours. The MnO_2 residues were removed by filtration through celite and the solvent removed *in vacuo*. The residues were eluted through a silica column (chloroform) to give **411** (485 mg, 1.85 mmol, 98 %) as a colourless oil.

Spectral and physical data were in accord with the literature.[182-185]

FT-IR (solid) υ_{max} 3051 m, 2851 w, 1671 s, 1583 s, 1466 m, 1430 w, 1417 s, 1289 s, 1253 m, 1024 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 267 (5100), 235 (10100) nm (mol^{-1} dm^3 cm^{-1}).

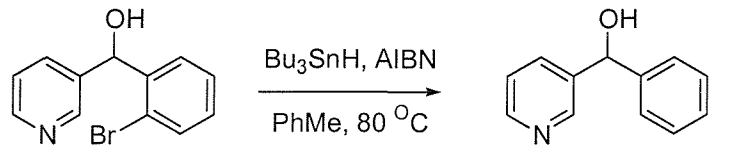
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.89 (1H, s, Ar**H**), 8.75 (1H, d, *J* 3.7 Hz, Ar**H**), 8.08 (1H, d, *J* 8.1 Hz, Ar**H**), 7.61 (1H, d, *J* 7.4 Hz, Ar**H**), 7.43 - 7.27 (4H, m, 4 x Ar**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 194.7 (Ar_2CO), 154.0 (Ar, **C**H), 151.7 (Ar, **C**H), 139.6 (Ar, **C**), 137.1 (Ar, **C**H), 133.6 (Ar, **C**H), 132.0 (Ar, **C**H), 131.7 (Ar, **C**), 129.4 (Ar, **C**H), 127.7 (Ar, **C**H), 123.8 (Ar, **C**H), 119.6 (Ar, **C**).

MS $^m/_z$ (APCI) 305 (65 %; $[M(^{81}Br)+MeCN]^+$), 303 (60 %; $[M(^{79}Br)+ MeCN]^+$), 264 (100 %; $M(^{81}Br)H^+$), 262 (79 %; $M(^{79}Br)H^+$), 209 (22 %).

HRMS (ES) Found: MNa^+, 283.9680. $C_{12}H_8{}^{79}BrNNaO$ requires 283.9681.

(Phenyl)(3-pyridyl)methanol **410**



$C_{12}H_{10}BrNO$ (264.12) $C_{12}H_{11}NO$ (185.22)

The alcohol **409** (200 mg, 0.757 mmol) in toluene (50 mL) was stirred under nitrogen at 100 °C with Bu_3SnH (0.4 mL, 433 mg, 1.484 mmol) and AIBN (12 mg, 0.073 mmol) for 30 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **410** (124 mg, 0.669 mmol, 88 %) as a white solid.

Spectral and physical data were in accord with the literature.[186]

M.P. 65 - 66 °C (Et_2O). Lit. 67.5 - 69 °C (no solvent given).[186]

FT-IR (solid) υ_{max} 3160 br. s, 2844 w, 2667 w, 1593 m, 1579 m, 1477 m, 1451 m, 1423 m, 1185 m, 1023 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 261 (1080) nm (mol^{-1} dm^3 cm^{-1}).

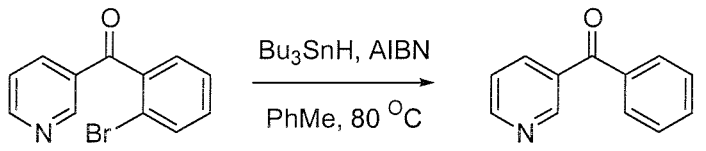
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.36 (1H, br. s, Ar**H**), 8.20 (1H, br. s, Ar**H**), 7.68 (1H, d, *J* 7.4 Hz, Ar**H**), 7.32 - 7.16 (6H, m, 6 x Ar**H**), 5.75 (2H, s, Ar_2C**H**OH and Ar_2CHO**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 147.8 (Ar, **C**H), 147.7 (Ar, **C**H), 143.4 (Ar, **C**), 140.2 (Ar, **C**), 134.7 (Ar, **C**H), 128.6 (Ar, 2 x **C**H), 127.7 (Ar, **C**H), 126.6 (Ar, 2 x **C**H), 123.6 (Ar, **C**H), 73.6 (Ar_2**C**HOH).

MS $^m/_z$ (APCI) 227 (17 %; $[MH+MeCN]^+$), 187 (11 %), 186 (100 %; MH^+).

CHN Found: C, 77.65; H, 5.99; N, 7.51. $C_{12}H_{11}NO$ requires C, 77.81; H, 5.99; N, 7.56.

(Phenyl)(3-pyridyl)methanone **412**



$C_{12}H_8BrNO$ (262.10) $C_{12}H_9NO$ (183.21)

The ketone **411** (200 mg, 0.763 mmol) in toluene (50 mL) was stirred under nitrogen at 100 °C with Bu_3SnH (0.40 mL, 433 mg, 1.484 mmol) and AIBN (12 mg, 0.073 mmol) for 30 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (80 : 20, Et_2O : petrol) to give **412** (120 mg, 0.655 mmol, 86 %) as a white solid.

Spectral and physical data were in accord with the literature.[177,187-191]

M.P. 40 - 41 °C (petrol). Lit. 32 - 34 °C (no solvent given).[187]

FT-IR (solid) υ_{max} 3047 w, 1658 s, 1584 m, 1448 w, 1415 w, 1316 w, 1282 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 257 (10500) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.95 (1H, d, *J* 1.5 Hz, Ar**H**), 8.77 (1H, dd, *J* 4.4, 1.5 Hz, Ar**H**), 8.07 (1H, d, *J* 8.1 Hz, Ar**H**), 7.77 (2H, d, *J* 7.4 Hz, Ar**H**), 7.59 (1H, t, *J* 7.4 Hz, Ar**H**), 7.47 (2H, t, *J* 7.4 Hz, Ar**H**), 7.41 (1H, dd, *J* 8.1, 5.2 Hz, Ar**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 195.0 (Ar_2CO), 153.0 (Ar, **C**H), 151.1 (Ar, **C**H), 137.3 (Ar, **C**H), 136.8 (Ar, **C**), 133.3 (Ar, **C**H), 130.1 (Ar, 2 x **C**H), 128.7 (Ar, 2 x **C**H), 123.5 (Ar, **C**H). One Ar **C** signal is obscured.

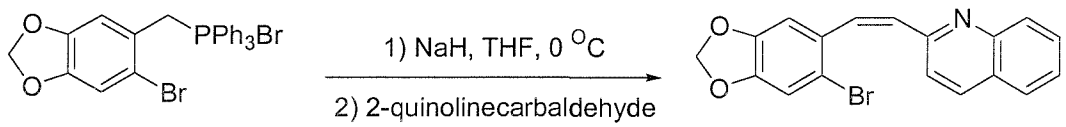
MS $^m/_z$ (APCI) 225 (28 %; $[MH+MeCN]^+$), 213 (10 %), 184 (100 %; MH^+).

CHN Found: C, 78.56; H, 4.98; N, 7.60. $C_{12}H_9NO$ requires C, 78.67; H, 4.95; N, 7.65.

6.3 EXPERIMENTAL FOR CHAPTER 3

6.31 BROMIDE PRECURSOR FORMATION

2[(*Z*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **502**



$C_{26}H_{21}Br_2O_2P$ (556.23) $C_{18}H_{12}BrNO_2$ (354.20)

NaH (176 mg, 4.40 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The bromide **347** (2.04 g, 3.67 mmol) was added and the reaction stirred for 2 hours. The aldehyde (510 mg, 3.24 mmol) was then added and the mixture was stirred for a further 2 hours at 0 °C. The mixture was filtered to remove triphenylphosphine oxide and the solvent removed *in vacuo*. The residues were eluted through a silica column (20 : 80, ethyl acetate : petrol) to give **502** (1.01 g, 2.84 mmol, 88 %) as a white crystalline solid.

M.P. 96 - 98 °C (EtOH).

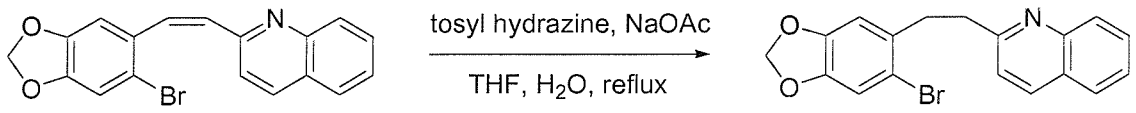
FT-IR (solid) υ_{max} 3055 w, 2897 w, 1614 w, 1594 m, 1554 w, 1500 s, 1474 s, 1416 m, 1232 m, 1036 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 331 (10100), 235 (23700) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.06 (1H, d, *J* 8.1 Hz, Ar**H**), 7.90 (1H, d, *J* 8.1 Hz, Ar**H**), 7.77 - 7.68 (2H, m, 2 x Ar**H**), 7.50 (1H, t, *J* 7.4 Hz, Ar**H**), 7.17 (1H, d, *J* 8.1 Hz, Ar**H**), 7.09 (1H, s, Ar**H**), 6.93 (2H, s, RC**H**=C**H**R), 6.66 (1H, s, Ar**H**), 5.92 (2H, s, OC$\mathbf{H}_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	156.1 (Ar, **C**), 148.3 (Ar, **C**), 148.1 (Ar, **C**), 147.1 (Ar, **C**), 135.5 (Ar, **C**H), 133.6 (**C**H=CH), 131.6 (CH=**C**H), 130.1 (Ar, **C**), 129.6 (Ar, **C**H), 129.2 (Ar, **C**H), 127.5 (Ar, **C**H), 126.9 (Ar, **C**), 126.5 (Ar, **C**H), 122.0 (Ar, **C**H), 115.0 (Ar, **C**), 112.7 (Ar, **C**H), 110.6 (Ar, **C**H), 101.8 (O**C**H_2O).
MS $^m/_z$ (ES)	356 (100 %; $[M(^{81}Br)+H]^+$), 354 (98 %; $[M(^{79}Br)+H]^+$), 144 (41 %; $[C_{10}H_9NH]^+$).
CHN	Found : C, 55.30; H, 3.33; N, 4.60; $C_{18}H_{12}BrNO_2$ requires C, 55.29; H, 3.31; N, 4.61.

2-[2-(6-Bromo-1,3-benzodioxol-5-yl)ethyl]quinoline **504**



$C_{18}H_{12}BrNO_2$ (354.20) $C_{18}H_{14}BrNO_2$ (356.22)

The bromide **502** (667 mg, 1.88 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and potassium carbonate solution (30 mL) added along with Et_2O (30 mL). The aqueous phase was separated and washed with Et_2O (3 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (30 : 70, Et_2O : petrol) to give **504** (590 mg, 1.66 mmol, 88 %) as a white crystalline solid.

M.P. 108 - 110 °C (Et_2O / petrol).

FT-IR (solid) υ_{max} 3050 w, 2892 w, 1600 w, 1502 m, 1475 s, 1233 m, 1113 m, 1038 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 316 (4550), 302 (6420), 290 (6610) nm (mol^{-1} dm^3 cm^{-1}).

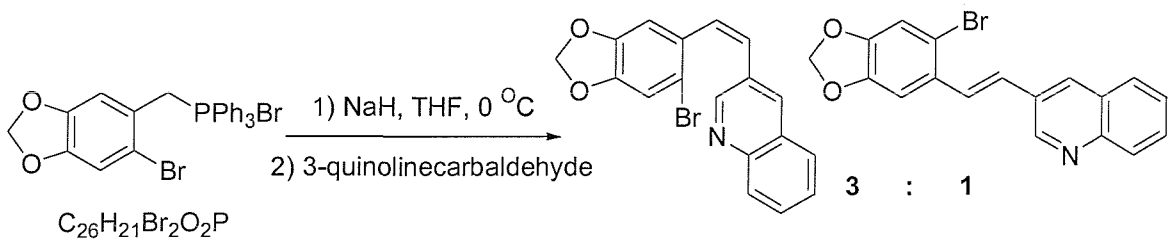
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.09 (1H, d, *J* 8.1 Hz, Ar**H**), 8.06 (1H, d, *J* 8.1 Hz, Ar**H**), 7.80 (1H, d, *J* 8.1 Hz, Ar**H**), 7.71 (1H, t, *J* 7.7 Hz, Ar**H**), 7.51 (1H, t, *J* 7.4 Hz, Ar**H**), 7.29 (1H, d, *J* 8.1 Hz, Ar**H**), 7.02 (1H, s, Ar**H**), 6.75 (1H, s, Ar**H**), 5.93 (2H, s, OC**H**$_2$O), 3.25 - 3.18 (4H, m, RC**H**$_2$C**H**$_2$R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 161.5 (Ar, **C**), 148.1 (Ar, **C**), 147.5 (Ar, **C**), 146.9 (Ar, **C**), 136.5 (Ar, **C**H), 133.9 (Ar, **C**), 129.6 (Ar, **C**H), 129.0 (Ar, **C**H), 127.7 (Ar, **C**H), 127.0 (Ar, **C**), 126.0 (Ar, **C**H), 121.7 (Ar, **C**H), 114.6 (Ar, **C**), 112.9 (Ar, **C**H), 110.4 (Ar, **C**H), 101.7 (O**C**H$_2$O), 39.5 (Ar**C**H$_2$), 36.3 (Ar**C**H$_2$).

MS $^{m}/_{z}$ (ES)	358 (97 %; $[M(^{81}Br)+H]^+$), 356 (100 %; $[M(^{79}Br)+H]^+$), 153 (32 %), 146 (32 %), 143 (45 %), 127 (60 %).
CHN	Found : C, 60.52; H, 3.97; N, 3.82; $C_{18}H_{14}BrNO_2$ requires C, 60.69; H, 3.96; N, 3.93.

3[(*Z*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **507** and

3[(*E*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **508**



$C_{26}H_{21}Br_2O_2P$
(556.23)

$C_{18}H_{12}BrNO_2$ (354.20)

NaH (176 mg, 4.40 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The bromide **347** (2.04 g, 3.66 mmol) was added and the reaction warmed to room temperature over a period of 18 hours. The mixture was recooled to 0 °C and the aldehyde (500 mg, 3.02 mmol) added. The mixture was stirred for a further 3 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (30 : 70, Et_2O : petrol) to give firstly the *Z*-azastilbene **507** (638 mg, 1.80 mmol, 60 %) followed by the *E*-azastilbene **508** (252 mg, 0.71 mmol, 24 %) each as a white solid.

Data for 3[(*Z*)-2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **507**

M.P. 115 - 117 °C (EtOH).

FT-IR (solid) υ_{max} 3012 w, 2896 w, 1616 w, 1567 w, 1500 m, 1475 s, 1423 m, 1230 m, 1037 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 300 (12200), 275 (13800) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.69 (1H, s, Ar**H**), 8.04 (1H, d, *J* 8.8 Hz, Ar**H**), 7.96 (1H, s, Ar**H**), 7.74 - 7.66 (2H, m, 2 x Ar**H**), 7.52 (1H, t, *J* 7.4 Hz, Ar**H**), 7.10 (1H, s, Ar**H**), 6.75 (2H, s, RC**H**=C**H**R), 6.59 (1H, s, Ar**H**), 5.92 (2H, s, OC$\mathbf{H_2}$O).

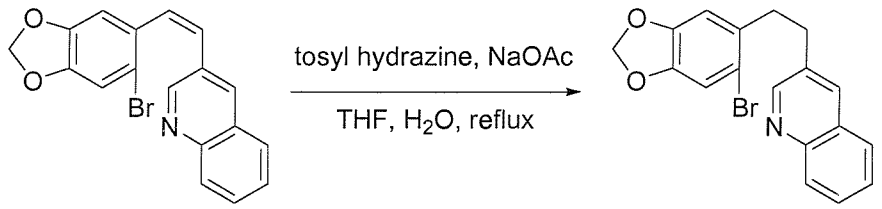
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	151.0 (Ar, **C**H), 148.2 (Ar, **C**), 147.4 (Ar, **C**), 146.7 (Ar, **C**), 135.4 (Ar, **C**H), 131.9 (**C**H=CH), 130.1 (Ar, **C**), 129.7 (Ar, **C**), 129.5 (Ar, **C**H), 129.1 (Ar, **C**H), 127.8 (Ar, **C**H), 127.2 (CH=**C**H), 126.9 (Ar, **C**H), 114.9 (Ar, **C**), 112.9 (Ar, **C**H), 109.9 (Ar, **C**H), 101.9 (O**C**H_2O). One Ar, **C** signal is obscured.
MS $^m/_z$ (ES)	369 (13 %; $[M(^{81}Br)+CH_3]^+$), 367 (12 %; $[M(^{79}Br)+ CH_3]^+$), 356 (3 %; $[M(^{81}Br)+H]^+$), 354 (3 %; $[M(^{79}Br)+H]^+$), 144 (100 %; $[C_{10}H_9NH]^+$).
CHN	Found : C, 60.85; H, 3.41; N, 3.85; $C_{18}H_{12}BrNO_2$ requires C, 61.04; H, 3.41; N, 3.95.

Data for 3[(*E*)-2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **508**

M.P.	175 - 177 °C (EtOH).
FT-IR (solid) υ_{max}	3065 w, 2897 w, 1501 m, 1475 s, 1411 w, 1240 m, 1115 w, 1038 m cm^{-1}.
UV (MeOH) λ_{max} (ε)	337 (19100), 309 (20200), 281 (23600) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	9.11 (1H, s, Ar**H**), 8.20 (1H, s, Ar**H**), 8.12 (1H, d, *J* 8.8 Hz, Ar**H**), 7.85 (1H, d, *J* 8.1 Hz, Ar**H**), 7.70 (1H, t, *J* 7.4 Hz, Ar**H**), 7.62 (1H, d, *J* 16.2 Hz, RC**H**=C**H**R), 7.57 (1H, t, *J* 7.4 Hz, Ar**H**), 7.20 (1H, s, Ar**H**), 7.07 (1H, s, Ar**H**), 7.02 (1H, d, *J* 16.2 Hz, RC**H**=C**H**R), 6.03 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	149.4 (Ar, **C**H), 148.4 (Ar, **C**), 147.9 (Ar, **C**), 147.3 (Ar, **C**), 132.5 (Ar, **C**H), 130.2 (Ar, **C**), 129.9 (Ar, **C**), 129.5 (Ar, **C**H), 129.4 (**C**H=CH), 129.1 (Ar, **C**H), 128.1 (Ar, **C**), 127.9 (Ar, **C**H), 127.1 (CH=**C**H), 126.1 (Ar, **C**H), 115.8 (Ar, **C**), 112.9 (Ar, **C**H), 105.8 (Ar, **C**H), 102.0 (O**C**H_2O).
MS $^m/_z$ (ES)	369 (10 %; $[M(^{81}Br)+CH_3]^+$), 367 (9 %; $[M(^{79}Br)+ CH_3]^+$), 356 (9 %; $[M(^{81}Br)+H]^+$), 354 (10 %; $[M(^{79}Br)+H]^+$), 144 (100 %; $[C_{10}H_9NH]^+$).
CHN	Found : C, 60.93; H, 3.37; N, 3.84; $C_{18}H_{12}BrNO_2$ requires C, 61.04; H, 3.41; N, 3.95.

3-[2-(6-Bromo-1,3-benzodioxol-5-yl)ethyl]quinoline **510**



$C_{18}H_{12}BrNO_2$ (354.20) $C_{18}H_{14}BrNO_2$ (356.22)

The bromide **507** (901 mg, 2.54 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and potassium carbonate solution (30 mL) added along with Et_2O (15 mL). The aqueous phase was separated and washed with Et_2O (3 x 20 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were recrystallised from hot Et_2O to give **510** (532 mg, 1.49 mmol, 59 %) as a white crystalline solid.

M.P. 115 - 117 °C (EtOH).

FT-IR (solid) υ_{max} 2899 w, 1501 m, 1475 s, 1236 m, 1119 w, 1038 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 318 (6820), 304 (10100), 292 (11900) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.77 (1H, d, *J* 2.2 Hz, Ar**H**), 8.09 (1H, d, *J* 8.8 Hz, Ar**H**), 7.92 (1H, s, Ar**H**), 7.76 (1H, d, *J* 8.1 Hz, Ar**H**), 7.67 (1H, t, *J* 7.4 Hz, Ar**H**), 7.52 (1H, t, *J* 7.4 Hz, Ar**H**), 7.01 (1H, s, Ar**H**), 6.64 (1H, s, Ar**H**), 5.93 (2H, s, OC**H**$_2$O), 3.03 (4H, s, RC**H**$_2$C**H**$_2$R).

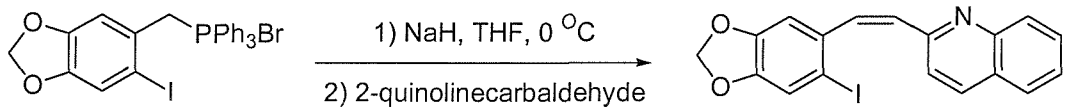
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 152.1 (Ar, **C**H), 147.5 (Ar, **C**), 147.1 (Ar, **C**), 147.1 (Ar, **C**), 134.6 (Ar, **C**H), 134.0 (Ar, **C**), 133.2 (Ar, **C**), 129.4 (Ar, **C**H), 128.9 (Ar, **C**H), 128.2 (Ar, **C**), 127.5 (Ar, **C**H), 126.8 (Ar, **C**H), 114.6 (Ar, **C**), 113.0 (Ar, **C**H), 110.2 (Ar, **C**H), 101.8 (O**C**H$_2$O), 38.0 (Ar**C**H$_2$), 33.8 (Ar**C**H$_2$).

MS $^{m}/_{z}$ (ES) 358 (100 %; $[M(^{81}Br)+H]^{+}$), 356 (98 %; $[M(^{79}Br)+H]^{+}$), 140 (20 %), 127 (25 %).

CHN Found : C, 60.64; H, 4.01; N, 3.80; $C_{18}H_{14}BrNO_2$ requires C, 61.69; H, 3.96; N, 3.93.

6.32 IODIDE PRECURSOR FORMATION

2-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **501**



$C_{26}H_{21}BrIO_2P$ (603.23) $C_{18}H_{12}INO_2$ (401.20)

NaH (154 mg, 3.85 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The iodide **362** (1.80 g, 2.98 mmol) was added and the reaction stirred for 2 hours. The aldehyde (500 mg, 3.18 mmol) was then added and the mixture was stirred for a further 2 hours at 0 °C. The mixture was filtered to remove triphenylphosphine oxide and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **501** (1.10 g, 2.74 mmol, 92 %) as a white crystalline solid.

M.P. 129 - 131 °C (EtOH).

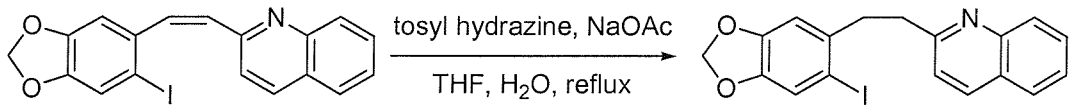
FT-IR (solid) υ_{max} 3057 w, 2915 w, 1614 w, 1596 m, 1556 w, 1499 s, 1477 s, 1434 m, 1241 s, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 330 (12400), 302 (12200), 243 (33400) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.06 (1H, d, *J* 8.1 Hz, Ar**H**), 7.90 (1H, d, *J* 8.8 Hz, Ar**H**), 7.76 - 7.69 (2H, m, 2 x Ar**H**), 7.52 (1H, t, *J* 7.4 Hz, Ar**H**), 7.35 (1H, s, Ar**H**), 7.11 (1H, d, *J* 8.8 Hz, Ar**H**), 6.90 (1H, d, *J* 12.5 Hz, RC**H**=CHR), 6.83 (1H, d, *J* 12.5 Hz, RCH=C**H**R), 6.66 (1H, s, Ar**H**), 5.94 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	156.2 (Ar, **C**), 148.4 (Ar, **C**), 148.4 (Ar, **C**), 137.9 (Ar, **C**H), 135.6 (**C**H=CH), 134.3 (Ar, **C**), 131.6 (CH=**C**H), 129.7 (Ar, **C**H), 129.3 (Ar, **C**H), 127.7 (Ar, **C**H), 127.0 (Ar, **C**), 126.7 (Ar, **C**H), 122.2 (Ar, **C**H), 118.6 (Ar, **C**H), 110.6 (Ar, **C**H), 101.9 (O**C**H_2O), 88.2 (Ar, **C**), One Ar, **C** signal is obscured.
MS $^m/_z$ (ES)	402 (100 %; MH^+), 127 (43 %).
CHN	Found: C, 53.91; H, 3.02; N, 3.39. $C_{18}H_{12}INO_2$ requires C, 53.89; H, 3.01; N, 3.49.

2[-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethyl]quinoline **503**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{14}INO_2$ (403.21)

The iodide **501** (1.10 g, 2.74 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and $K_2CO_{3(aq)}$ (2M, 30 mL) added along with Et_2O (15 mL). The aqueous phase was separated and extracted with Et_2O (3 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were recrystallised from hot EtOH / petrol to give **503** (993 mg, 2.46 mmol, 90 %) as a white crystalline solid.

M.P. 139 - 141 °C (EtOH / petrol).

FT-IR (solid) υ_{max} 2896 w, 1621 w, 1598 w, 1499 m, 1473 s, 1226 s, 1116 m, 1041 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 316 (5620), 303 (7590), 293 (7160) nm (mol^{-1} dm^3 cm^{-1}).

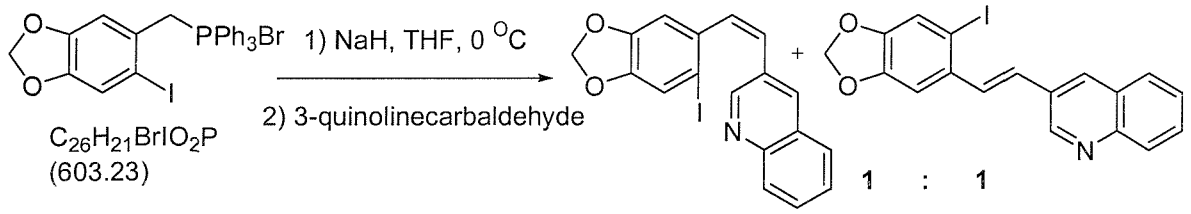
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.09 (1H, d, *J* 8.1 Hz, Ar**H**), 8.09 (1H, d, *J* 8.8 Hz, Ar**H**), 7.81 (1H, d, *J* 8.1 Hz, Ar**H**), 7.72 (1H, t, *J* 7.4 Hz, Ar**H**), 7.52 (1H, t, *J* 7.4 Hz, Ar**H**), 7.34 (1H, d, *J* 8.8 Hz, Ar**H**), 7.27 (1H, s, Ar**H**), 6.80 (1H, s, Ar**H**), 5.95 (2H, s, OC**H$_2$**O), 3.27 - 3.14 (4H, m, RC**H$_2$**C**H$_2$**R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 161.4 (Ar, **C**), 148.6 (Ar, **C**), 148.1 (Ar, **C**), 147.0 (Ar, **C**), 137.4 (Ar, **C**), 136.5 (Ar, **C**H), 129.6 (Ar, **C**H), 129.0 (Ar, **C**H), 127.7 (Ar, **C**H), 127.0 (Ar, **C**), 126.0 (Ar, **C**H), 121.7 (Ar, **C**H), 118.7 (Ar, **C**H), 109.7 (Ar, **C**H), 101.7 (O**C**H$_2$O), 88.0 (Ar, **C**), 40.9 (Ar**C**H$_2$), 39.8 (Ar**C**H$_2$).

MS $^{m}/_{z}$ (ES)	404 (100 %; MH^{+}), 127 (24 %).
CHN	Found: C, 53.65; H, 3.48; N, 3.45. $C_{18}H_{14}INO_2$ requires C, 53.62; H, 3.50; N, 3.47.

3[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **505** and

3[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **506**



NaH (176 mg, 4.40 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (30 mL) at 0 °C. The iodide **362** (2.00 g, 3.32 mmol) was added and the reaction stirred for 2 hours. The mixture was cooled to 0 °C again and 3-quinolinecarbaldehyde (500 mg, 3.18 mmol) added. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (50 : 50, Et_2O : petrol) to give firstly the *Z*-azastilbene **505** (610 mg, 1.52 mmol, 48 %) which was recrystallised form EtOH / H_2O as a yellow crystalline solid followed by the *E*-azastilbene **506** (610 mg, 1.52 mmol, 48 %) which was recrystallised form EtOH / H_2O as a yellow crystalline solid.

Data for 3[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **505**

M.P. 118 - 120 °C (EtOH / H_2O).

FT-IR (solid) υ_{max} 2898 w, 1493 m, 1473 s, 1426 w, 1257 m, 1222 m, 1230 m, 1038 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 291 (9130) nm (mol^{-1} dm^3 cm^{-1}).

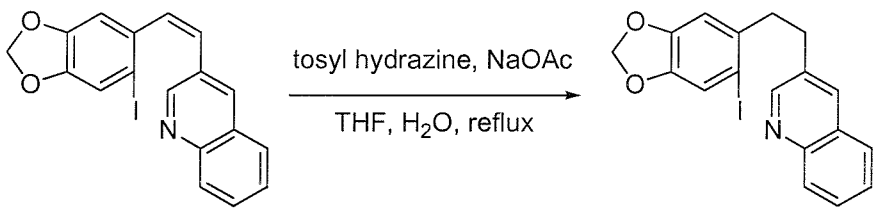
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	8.65 (1H, s, Ar**H**), 8.02 (1H, d, *J* 8.8 Hz, Ar**H**), 7.91 (1H, s, Ar**H**), 7.69 (1H, app. t, *J* 7.7 Hz, Ar**H**), 7.66 (1H, d, *J* 8.1 Hz, Ar**H**), 7.50 (1H, app. t, *J* 7.4 Hz, Ar**H**), 7.33 (1H, s, Ar**H**), 6.70 (1H, d, *J* 11.8 Hz, RCH=C**H**R), 6.64 (1H, d, *J* 11.8 Hz, RC**H**=CHR), 6.59 (1H, s, Ar**H**), 5.91 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	151.1 (Ar, **C**H), 148.5 (Ar, **C**), 148.2 (Ar, **C**), 146.8 (Ar, **C**), 135.9 (Ar, **C**H), 135.3 (**C**H=CH), 134.2 (Ar, **C**), 129.5 (Ar, **C**), 129.4 (Ar, **C**H), 129.2 (Ar, **C**H), 127.8 (Ar, **C**H), 127.8 (Ar, **C**), 127.1 (CH=**C**H), 126.8 (Ar, **C**H), 118.6 (Ar, **C**H), 109.7 (Ar, **C**H), 101.7 (O**C**H$_2$O), 88.1 (Ar, **C**).
MS $^m/_z$ (ES)	443 (20 %; $[MH+MeCN]^+$), 403 (14 %; $M(^{13}C)H^+$), 402 (83 %; MH^+), 127 (100 %).
CHN	Found: C, 53.65; H, 3.05; N, 3.43. $C_{18}H_{12}INO_2$ requires C, 53.89; H, 3.01; N, 3.49.

Data for 3[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **506**

M.P.	177 - 179 °C (EtOH / H_2O).
FT-IR (solid) υ_{max}	2897 w, 1500 m, 1473 s, 1406 w, 1231 s, 1114 w, 1038 m cm^{-1}.
UV (MeOH) λ_{max} (ε)	346 (25880), 317 (23090), 283 (28130), 256 (29490) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm	9.12 (1H, s, Ar**H**), 8.17 (1H, s, Ar**H**),
(300 MHz, $CDCl_3$)	8.10 (1H, d, *J* 8.1 Hz, Ar**H**), 7.84 (1H, d, *J* 8.1 Hz, Ar**H**),
	7.69 (1H, app. t, *J* 7.4 Hz, Ar**H**),
	7.56 (1H, app. t, *J* 7.4 Hz, Ar**H**),
	7.48 (1H, d, *J* 16.2 Hz, RC**H**=C**H**R), 7.32 (1H, s, Ar**H**),
	7.19 (1H, s, Ar**H**), 6.95 (1H, d, *J* 16.2 Hz, RC**H**=C**H**R),
	6.02 (2H, s, OC$\mathbf{H_2}$O).
^{13}C NMR δ_C ppm	149.6 (Ar, **C**H), 148.9 (Ar, **C**), 148.5 (Ar, **C**), 147.5 (Ar, **C**),
(75.5 MHz, $CDCl_3$)	134.4 (Ar, **C**H), 133.2 (Ar, **C**), 132.3 (**C**H=CH), 130.0 (Ar, **C**),
	129.3 (Ar, **C**H), 129.3 (Ar, **C**H), 128.1 (Ar, **C**), 127.9 (Ar, **C**H),
	127.1 (CH=**C**H), 126.5 (Ar, **C**H), 118.8 (Ar, **C**H),
	105.7 (Ar, **C**H), 101.9 (O**C**H_2O), 89.7 (Ar, **C**).
MS $^{m}/_{z}$ (ES)	443 (10 %; $[MH+MeCN]^+$), 403 (8 %; $M(^{13}C)H^+$),
	402 (34 %; MH^+), 127 (100 %).
CHN	Found: C, 53.60; H, 2.95; N, 3.31. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

3-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]quinoline **509**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{14}INO_2$ (403.21)

The iodide **505** (400 mg, 0.997 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 24 hours. The solution was cooled to room temperature and potassium carbonate solution (60 mL) added. The reaction mixture was washed with Et_2O (5 x 30 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **509** (398 mg, 0.987 mmol, 99 %) as a white crystalline solid.

M.P. 115 - 117 °C (EtOH / H_2O).

FT-IR (solid) υ_{max} 1498 m, 1471 s, 1235 m, 1121 w, 1039 m cm^{-1}.

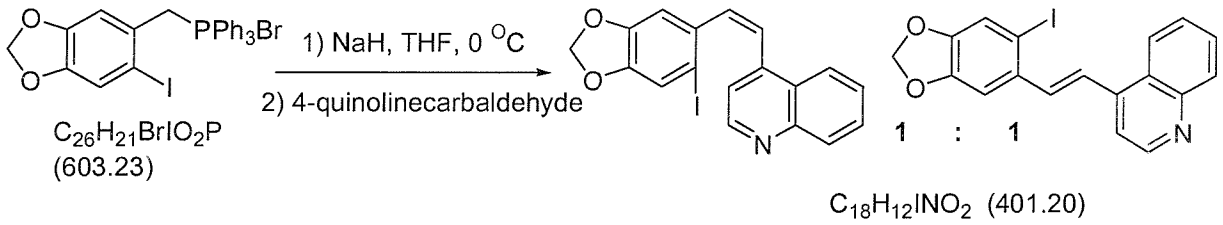
UV (MeOH) λ_{max} (ε) 318 (4800), 304 (7340), 297 (7460) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.80 (1H, s, Ar**H**), 8.09 (1H, d, *J* 8.8 Hz, Ar**H**), 7.93 (1H, s, Ar**H**), 7.76 (1H, d, *J* 7.4 Hz, Ar**H**), 7.67 (1H, app. t, *J* 7.7 Hz, Ar**H**), 7.52 (1H, app. t, *J* 7.4 Hz, Ar**H**), 7.24 (1H, s, Ar**H**), 6.68 (1H, s, Ar**H**), 5.92 (2H, s, O**C**$\mathbf{H_2}$O), 3.01 (4H, s, R**C**$\mathbf{H_2}$**C**$\mathbf{H_2}$R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	152.1 (Ar, **C**H), 148.7 (Ar, **C**), 147.2 (Ar, **C**), 147.1 (Ar, **C**), 136.7 (Ar, **C**), 134.6 (Ar, **C**H), 133.8 (Ar, **C**), 129.4 (Ar, **C**H), 128.9 (Ar, **C**H), 128.2 (Ar, **C**), 127.5 (Ar, **C**H), 126.8 (Ar, **C**H), 118.8 (Ar, **C**H), 109.6 (Ar, **C**H), 101.7 (O**C**H_2O), 87.9 (Ar, **C**), 42.5 (Ar**C**H_2), 34.1 (Ar**C**H_2).
MS $^m/_z$ (ES)	445 (15 %; $[MH+MeCN]^+$), 405 (18 %; $M(^{13}C)H^+$), 404 (100 %; MH^+), 127 (71 %).
CHN	Found: C, 53.78; H, 3.52; N, 3.33. $C_{18}H_{14}INO_2$ requires C, 53.62; H, 3.50; N, 3.47.

4-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **511** and

4-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **512**



NaH (176 mg, 4.40 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The iodide **362** (2.00 g, 3.32 mmol) was added and the reaction stirred for 2 hours under argon. The mixture was cooled to 0 °C again and 4-quinolinecarbaldehyde (500 mg, 3.18 mmol) added. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (Et_2O) to give a 1:1 mixture of the *Z*- and *E*-azastilbenes (1.07 g, 2.67 mmol, 84 %). Fractional recrystallisation from methanol yielded firstly the *E*-azastilbene **511** as a pale orange solid. The *Z*-azastilbene **512** was then recovered from the mother liquor as a pale yellow solid.

Data for 4-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **511**

M.P. 175 - 176 °C (MeOH).

FT-IR (solid) υ_{max} 1577 m, 1496 m, 1471 s, 1390 w, 1283 w, 1245 m, 1228 s, 1113 m, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 356 (19430), 232 (39860) nm (mol^{-1} dm^3 cm^{-1}).

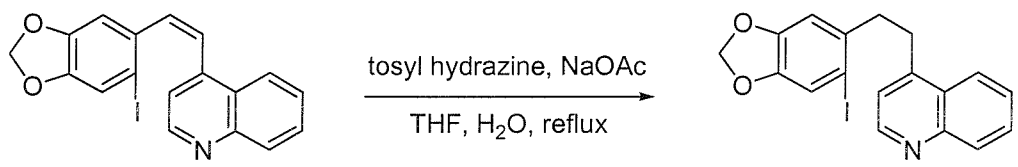
^{1}H NMR δ_H ppm	8.91 (1H, d, *J* 4.6 Hz, Ar**H**), 8.53 (1H, d, *J* 7.6 Hz, Ar**H**),
(250 MHz, DMSO)	8.05 (1H, dd, *J* 7.9, 0.9 Hz, Ar**H**),
	7.94 (1H, d, *J* 15.9 Hz, RC**H**=CHR),
	7.80 (1H, app. td, *J* 15.2, 1.3 Hz, Ar**H**), 7.80 (1H, s, Ar**H**),
	7.73 (1H, d, *J* 4.4 Hz, Ar**H**),
	7.66 (1H, app. td, *J* 7.6, 1.3 Hz, Ar**H**),
	7.51 (1H, d, *J* 15.8 Hz, RCH=C**H**R), 7.50 (1H, s, Ar**H**),
	6.14 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm	150.7 (Ar, **C**H), 149.2 (Ar, **C**), 149.1 (Ar, **C**), 148.7 (Ar, **C**),
(62.9 MHz, DMSO)	142.4 (Ar, **C**), 138.1 (**C**H=CH), 132.7 (Ar, **C**), 129.9 (Ar, **C**H),
	129.9 (Ar, **C**H), 126.9 (Ar, **C**H), 126.1 (Ar, **C**), 124.7 (CH=**C**H),
	124.5 (Ar, **C**H), 118.6 (Ar, **C**H), 117.0 (Ar, **C**H),
	107.2 (Ar, **C**H), 102.5 (O**C**H$_2$O), 91.5 (Ar, **C**).
MS $^m/_z$ (APCI)	403 (19 %; M(^{13}C)H$^+$), 402 (100 %; MH$^+$),
	279 (14 %).
CHN	Found: C, 53.75; H, 2.98; N, 3.39. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

Data for 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **512**

M.P.	175 - 176 °C (MeOH / DMSO).
FT-IR (solid) υ_{max}	1576 m, 1561 w, 1491 s, 1466 m, 1247 s, 1230 s, 1115 m,
	1032 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	358 (20150), 232 (34170) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm	8.92 (1H, d, *J* 4.6 Hz, Ar**H**), 8.19 (1H, d, *J* 8.0 Hz, Ar**H**),
(400 MHz, $CDCl_3$)	8.14 (1H, d, *J* 8.1 Hz, Ar**H**),
	7.74 (1H, app. td, *J* 7.7, 1.3 Hz, Ar**H**),
	7.62 (1H, d, *J* 4.6 Hz, Ar**H**),
	7.59 (1H, app. td, *J* 7.6, 1.2 Hz, Ar**H**),
	7.53 (1H, d, *J* 15.9 Hz, RC**H**=CHR),
	7.48 (1H, d, *J* 15.8 Hz, RCH=C**H**R), 7.34 (1H, s, Ar**H**),
	7.26 (1H, s, Ar**H**), 6.04 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm	150.3 (Ar, **C**H), 149.0 (Ar, **C**), 148.9 (Ar, **C**), 148.7 (Ar, **C**),
(62.9 MHz, $CDCl_3$)	142.5 (Ar, **C**), 138.5 (**C**H=CH), 133.2 (Ar, **C**), 130.2 (Ar, **C**H),
	129.3 (Ar, **C**H), 126.6 (Ar, **C**H), 126.3 (Ar, **C**), 124.3 (Ar, **C**H),
	123.4 (CH=**C**H), 118.9 (Ar, **C**H), 117.4 (Ar, **C**H),
	106.3 (Ar, **C**H), 102.0 (O**C**H$_2$O), 90.0 (Ar, **C**).
MS $^{m}/_{z}$ (APCI)	403 (18 %; M(^{13}C)H$^+$), 402 (100 %; MH$^+$).
CHN	Found: C, 53.74; H, 2.94; N, 3.45. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

4-[2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethyl]quinoline **513**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{14}INO_2$ (403.21)

A mixture of *E*- and *Z*-azastilbene, **511** and **512** (780 mg, 1.94 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and $K_2CO_{3(aq)}$ (2M, 30 mL) added along with Et_2O (50 mL). The aqueous phase was separated and washed with Et_2O (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **513** (678 mg, 1.68 mmol, 87 %) as a white crystalline solid.

M.P. 98 - 100 °C (Et_2O / petrol).

FT-IR (solid) υ_{max} 2896 w, 1592 w, 1502 m, 1474 s, 1227 s, 1110 m, 1038 s cm^{-1}.

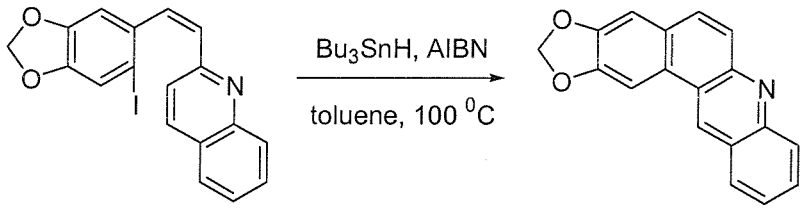
UV (MeOH) λ_{max} (ε) 314 (2990), 300 (7870), 290 (8880) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)
8.81 (1H, d, *J* 4.4 Hz, Ar**H**), 8.14 (1H, d, *J* 8.8 Hz, Ar**H**),
8.14 (1H, d, *J* 8.8 Hz, Ar**H**), 7.71 (1H, t, *J* 7.7 Hz, Ar**H**),
7.57 (1H, t, *J* 7.4 Hz, Ar**H**), 7.27 (1H, s, Ar**H**),
7.23 (1H, d, *J* 4.4 Hz, Ar**H**), 6.75 (1H, s, Ar**H**),
5.93 (2H, s, OC**H$_2$**O),
3.30 - 3.25 (2H, dd, *J* 9.9, 6.3 Hz, RC**H$_2$**CH$_2$R),
3.07 - 3.02 (2H, dd, *J* 9.6, 5.9 Hz RCH$_2$C**H$_2$**R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	150.4 (Ar, **C**H), 148.6 (Ar, **C**), 148.3 (Ar, **C**), 147.1 (Ar, **C**), 146.9 (Ar, **C**), 136.8 (Ar, **C**), 130.3 (Ar, **C**H), 129.2 (Ar, **C**H), 127.5 (Ar, **C**), 126.5 (Ar, **C**H), 123.6 (Ar, **C**H), 121.0 (Ar, **C**H), 118.7 (Ar, **C**H), 109.4 (Ar, **C**H), 101.6 (O**C**H_2O), 87.6 (Ar, **C**), 41.2 (Ar**C**H_2), 32.9 (Ar**C**H_2).
MS $^m/_z$ (ES)	445 (15 %; $[MH+MeCN]^+$), 404 (100 %; MH^+), 153 (15 %), 144 (16 %).
CHN	Found: C, 53.70; H, 3.51; N, 3.41. $C_{18}H_{14}INO_2$ requires C, 53.62; H, 3.50; N, 3.47.

6.33 RADICAL CYCLISATIONS

[1,3]Dioxolo[4',5':4,5]benzo[*a*]acridine **514**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{11}NO_2$ (273.29)

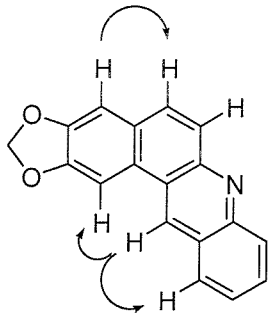
The iodide **501** (500 mg, 1.25 mmol) in toluene (100 mL) was stirred under nitrogen at 100 °C with Bu_3SnH (1.62 mL, 1.75 g, 6.01 mmol) and AIBN (120 mg, 0.73 mmol) for 72 hours. The mixture was cooled to room temperature and stirred for 36 hours with $KF_{(aq)}$ (2M, 80 mL). The aqueous phase was separated and extracted with Et_2O (2 x 100 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **514** (142 mg, 0.52 mmol, 42 %) as a yellow crystalline solid.

M.P. 215 - 217 °C (Et_2O / petrol).

FT-IR (solid) υ_{max} 3045 w, 2946 w, 1737 w, 1633 w, 1618 w, 1504 m, 1470 s, 1394 w, 1371 m, 1271 m, 1252 s, 1039 s cm^{-1}.

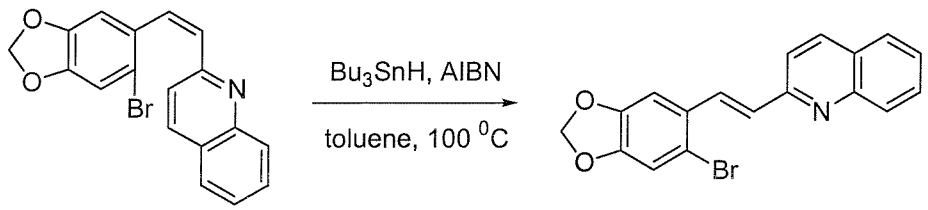
UV (MeOH) λ_{max} (ε) 385 (10740), 366 (10190), 309 (7172), 295 (53370) 284 (63090), 242 (60200) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 9.13 (1H, s, Ar**H**), 8.17 (1H, d, *J* 8.5 Hz, Ar**H**), 8.02 (1H, s, Ar**H**), 7.98 (1H, d, *J* 8.0 Hz, Ar**H**), 7.87 (1H, d, *J* 9.0 Hz, Ar**H**), 7.77 (1H, d, *J* 9.5 Hz, Ar**H**), 7.72 (1H, t, *J* 8.3 Hz, Ar**H**), 7.51 (1H, t, *J* 7.5 Hz, Ar**H**), 7.17 (1H, s, Ar**H**), 6.06 (2H, s, O**CH$_2$**O).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 9.13 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.02 (1H, s, Ar**H**) and δ_H 7.98 (1H, d, *J* 8.0 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.17 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.77 (1H, d, *J* 9.5 Hz, Ar**H**).
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	149.2 (Ar, **C**), 149.1 (Ar, **C**), 148.7 (Ar, **C**), 148.3 (Ar, **C**), 132.4 (Ar, **C**H), 130.5 (Ar, **C**H), 130.2 (Ar, **C**H), 129.4 (Ar, **C**H), 128.6 (Ar, **C**H), 127.8 (Ar, **C**), 127.1 (Ar, **C**H), 126.8 (Ar, **C**), 126.3 (Ar, **C**H), 124.4 (Ar, **C**), 107.1 (Ar, **C**H), 102.1 (Ar, **C**H), 102.1 (O**C**H_2O), One Ar, **C** signal is obscured.
MS $^m/_z$ (ES)	274 (8 %; MH^+), 123 (100 %).
HRMS (EI)	Found: MH^+, 274.0864. $C_{18}H_{12}NO_2$ requires 274.0863.
CHN	Found: C, 78.79; H, 4.09; N, 5.09. $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.

2[(*E*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **515**



$C_{18}H_{12}BrNO_2$ (354.20) $C_{18}H_{12}BrNO_2$ (354.20)

The bromide **502** (116 mg, 0.327 mmol) in toluene (80 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.10 mL, 108 mg, 0.371 mmol) and AIBN (15 mg, 0.091 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 50 mL). The aqueous phase was separated and extracted with Et_2O (2 x 100 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give a mixture of **515** and **502**. **515** (16 mg, 0.045 mmol, 14 %) was fractionally recrystallised from EtOH as a white crystalline solid. The resulting mother liquor furnished starting material **502** (95 mg, 0.268 mmol, 82 %).

M.P. 198 - 200 °C (EtOH).

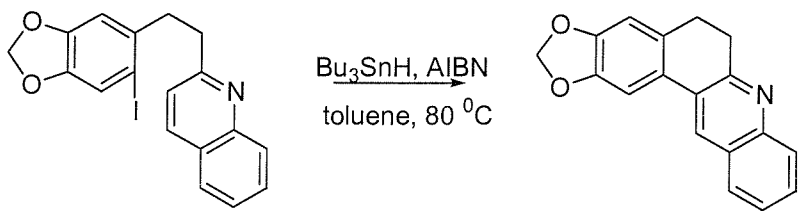
FT-IR (solid) υ_{max} 1597 m, 1486 s, 1412 w, 1308 w, 1265 m, 1242 m, 1232, m, 1119 m, 1034 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 351 (18460), 252 (19900) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.14 (1H, d, *J* 8.8 Hz, Ar**H**), 8.09 (1H, d, *J* 8.8 Hz, Ar**H**), 7.93 (1H, d, *J* 16.2 Hz, RC**H**=CHR), 7.80 (1H, d, *J* 8.1 Hz, Ar**H**), 7.75 (1H, d, *J* 8.8 Hz, Ar**H**), 7.72 (1H, t, *J* 7.4 Hz, Ar**H**), 7.51 (1H, t, *J* 7.4 Hz, Ar**H**), 7.29 (1H, s, Ar**H**), 7.23 (1H, d, *J* 16.2 Hz, RCH=C**H**R), 7.08 (1H, s, Ar**H**), 6.03 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	155.9 (Ar, **C**), 148.8 (Ar, **C**), 148.2 (Ar, **C**), 147.9 (Ar, **C**), 136.4 (Ar, **C**H), 132.8 (**C**H=CH), 130.2 (CH=**C**H), 129.8 (Ar, **C**H), 129.7 (Ar, **C**), 129.2 (Ar, **C**H), 127.5 (Ar, **C**H), 127.3 (Ar, **C**), 126.3 (Ar, **C**H), 118.8 (Ar, **C**H), 116.4 (Ar, **C**), 112.9 (Ar, **C**H), 106.1 (Ar, **C**H), 102.0 (O**C**H_2O).
MS $^m/_z$ (ES)	356 (86 %; $[M(^{81}Br)+H]^+$), 356 (15 %; $[M(^{81}Br, ^{13}C)+H]^+$), 354 (80 %; $[M(^{79}Br)+H]^+$), 354 (21 %; $[M(^{79}Br, ^{13}C)+H]^+$), 276 (17 %), 152 (100 %).
CHN	Found : C, 60.90; H, 3.41; N, 3.77; $C_{18}H_{12}BrNO_2$ requires C, 61.04; H, 3.41; N, 3.95.

5,6-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*a*]acridine **516**



$C_{18}H_{14}INO_2$ (403.21) $C_{18}H_{13}NO_2$ (275.30)

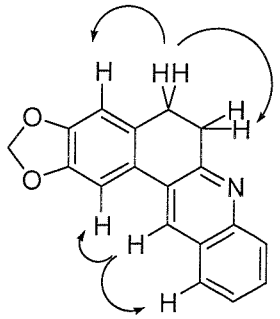
The iodide **503** (570 mg, 1.41 mmol) in toluene (80 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.46 mL, 498 mg, 1.71 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 50 mL). The aqueous phase was separated and washed with Et_2O (50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give **516** (270 mg, 0.98 mmol, 70 %) as a white solid.

M.P. 168 - 170 °C (EtOH).

FT-IR (solid) υ_{max} 3042 w, 2948 w, 2891 w, 1619 w, 1502 m, 1482 s, 1383 m, 1363 m, 1250 m, 1222 m, 1038 s cm^{-1}.

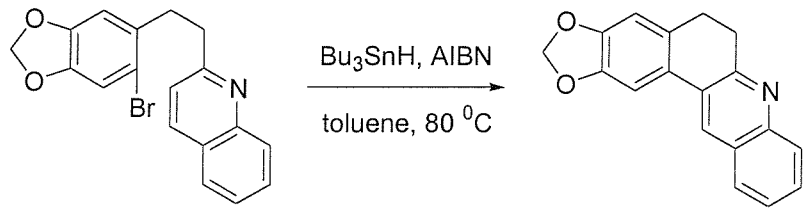
UV (MeOH) λ_{max} (ε) 357 (13500), 322 (10700), 309 (7970), 278 (17400) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.19 (1H, s, Ar**H**), 8.02 (1H, d, *J* 8.1 Hz, Ar**H**), 7.81 (1H, d, *J* 8.1 Hz, Ar**H**), 7.64 (1H, t, *J* 7.4 Hz, Ar**H**), 7.48 (1H, t, *J* 7.4 Hz, Ar**H**), 7.33 (1H, s, Ar**H**), 6.77 (1H, s, Ar**H**), 6.00 (2H, s, OC**H**$_2$O), 3.24 (2H, t, *J* 7.0 Hz, ArC**H**$_2$), 2.97 (2H, t, *J* 7.0 Hz, ArC**H**$_2$).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 8.19 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.81 (1H, d, *J* 8.1 Hz, Ar**H**) and δ_H 7.33 (1H, s, Ar**H**). n.O.e lrradiation of the signal at δ_H 3.24 (2H, t, *J* 7.0 Hz, ArC**H$_2$**) caused an n.O.e. enhancement at δ_H 2.97 (2H, t, *J* 7.0 Hz, ArC**H$_2$**). n.O.e Irradiation of the signal at δ_H 2.97 (2H, t, *J* 7.0 Hz, ArC**H$_2$**) caused an n.O.e. enhancement at δ_H 6.77 (1H, s, Ar**H**) and δ_H 3.24 (2H, t, *J* 7.0 Hz, ArC**H$_2$**).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	159.1 (Ar, **C**), 148.0 (Ar, **C**), 147.5 (Ar, **C**), 146.7 (Ar, **C**), 132.1 (Ar, **C**), 129.1 (Ar, **C**H), 128.6 (Ar, **C**H), 128.5 (Ar, **C**H), 128.4 (Ar, **C**), 128.2 (Ar, **C**), 127.8 (Ar, **C**H), 126.8 (Ar, **C**), 126.2 (Ar, **C**H), 108.8 (Ar, **C**H), 104.6 (Ar, **C**H), 101.4 (OCH_2O), 33.2 (Ar**C**H_2), 28.9 (Ar**C**H_2).
MS $^{m}/_{z}$ (ES)	276 (100 %; MH^+), 153 (35 %), 130 (22 %).
CHN	Found: C, 78.47; H, 4.77; N, 5.04. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

5,6-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*a*]acridine **516**



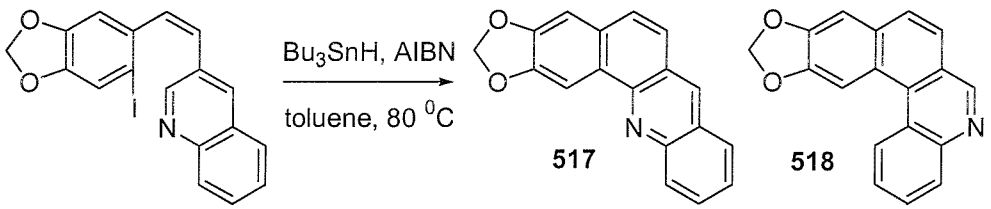
$C_{18}H_{14}BrNO_2$ (356.22) $C_{18}H_{13}NO_2$ (275.30)

The bromide **504** (91 mg, 0.255 mmol) in toluene (80 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.10 mL, 108 mg, 0.371 mmol) and AIBN (10 mg, 0.061 mmol) for 18 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 50 mL). The aqueous phase was separated and washed with Et_2O (50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give **516** (43 mg, 0.156 mmol, 62 %) as a white solid.

Data identical to those described previously.

[1,3]Dioxolo[4',5':4,5]benzo[*c*]acridine **517** and

[1,3]Dioxolo[4',5':4,5]benzo[*k*]phenanthridine **518**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{11}NO_2$ (273.29)

The iodide **505** (100 mg, 0.249 mmol) in toluene (20 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.08 mL, 87 mg, 0.297 mmol) and AIBN (4 mg, 0.024 mmol) for 18 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 20 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50 Et_2O : petrol) to yield firstly **517** (26 mg, 0.095 mmol, 38 %) as a pale yellow solid and then **518** (39 mg, 0.143 mmol, 57 %) as a pale yellow solid.

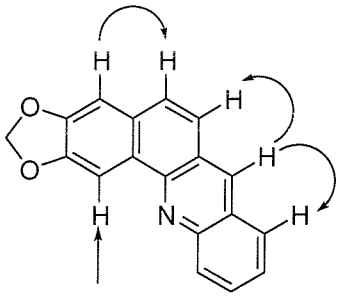
Data for [1,3]dioxolo[4',5':4,5]benzo[*c*]acridine **517**

M.P. 180 - 182 °C (Et_2O / petrol).

FT-IR (solid) υ_{max} 2893 w, 1487 m, 1464 s, 1405 m, 1278 m, 1232 m, 1039 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 385 (7620), 366 (8340), 350 (6290), 307 (59500), 282 (59600) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.92 (1H, s, Ar**H**), 8.64 (1H, s, Ar**H**), 8.34 (1H, d, *J* 8.8 Hz, Ar**H**), 8.02 (1H, d, *J* 8.0 Hz, Ar**H**), 7.81 (1H, app. t, *J* 7.7 Hz, Ar**H**), 7.68 (1H, d, *J* 8.8 Hz, Ar**H**), 7.60 (1H, d, *J* 8.8 Hz, Ar**H**), 7.57 (1H, app. t, *J* 7.7 Hz, Ar**H**), 7.24 (1H, s, Ar**H**), 6.17 (2H, s, O**CH$_2$**O).



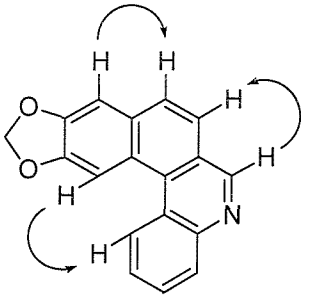
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 8.92 (1H, s, Ar**H**) caused no n.O.e. enhancement. n.O.e Irradiation of the signal at δ_H 8.64 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.02 (1H, d, *J* 8.0 Hz, Ar**H**) and δ_H 7.68 (1H, d, *J* 8.8 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.24 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.60 (1H, d, *J* 8.8 Hz, Ar**H**).
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	149.3 (Ar, **C**), 148.2 (Ar, **C**), 147.7 (Ar, **C**), 147.2 (Ar, **C**), 135.1 (Ar, **C**H), 130.4 (Ar, **C**), 129.6 (Ar, **C**H), 129.6 (Ar, **C**H), 127.8 (Ar, **C**H), 127.1 (Ar, **C**H), 126.6 (Ar, **C**), 125.5 (Ar, **C**H), 124.6 (Ar, **C**), 124.1 (Ar, **C**H), 105.7 (Ar, **C**H), 103.9 (Ar, **C**H), 101.6 (O**C**H_2O). One Ar, **C** signal is obscured.
MS $^m/_z$ (ES)	275 (17 %; M(^{13}C)H^+), 274 (100 %; MH^+), 153 (41 %), 127 (48 %).
CHN	Found: C, 78.90; H, 4.15; N, 5.04. $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.

Data for [1,3]dioxolo[4',5':4,5]benzo[*k*]phenanthridine **518**

M.P.	200 - 202 °C (EtOH).
FT-IR (solid) υ_{max}	3062 w, 2903 w, 1578 w, 1501 m, 1476 s, 1450 m, 1385 w, 1365 w, 1249 s, 1037 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 382 (2430), 363 (2320), 332 (5730), 303 (10200), 282 (31200) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 9.29 (1H, s, Ar**H**), 8.96 (1H, d, *J* 8.5 Hz, Ar**H**), 8.50 (1H, s, Ar**H**), 8.32 (1H, dd, *J* 8.0, 1.0 Hz, Ar**H**), 7.86 - 7.79 (3H, m, 3 x Ar**H**), 7.72 (1H, ddd, *J* 8.5, 7.0, 1.5 Hz, Ar**H**), 7.34 (1H, s, Ar**H**), 6.19 (2H, s, O**C**$\mathbf{H_2}$O).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) n.O.e Irradiation of the signal at δ_H 9.29 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.86 - 7.79 (3H, m, Ar**H**). n.O.e Irradiation of the signal at δ_H 8.50 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.96 (1H, d, *J* 8.5 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.34 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.86 - 7.79 (3H, m, Ar**H**).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$) 153.2 (Ar, **C**H), 149.2 (Ar, **C**), 148.9 (Ar, **C**), 146.7 (Ar, **C**), 133.1 (Ar, **C**), 130.9 (Ar, **C**), 130.6 (Ar, **C**H), 128.4 (Ar, **C**H), 128.4 (Ar, **C**H), 126.9 (Ar, **C**H), 126.7 (Ar, **C**H), 125.6 (Ar, **C**), 125.0 (Ar, **C**), 125.0 (Ar, **C**), 124.2 (Ar, **C**H), 106.1 (Ar, **C**H), 105.8 (Ar, **C**H), 102.2 (O**C**$\mathbf{H_2}$O).

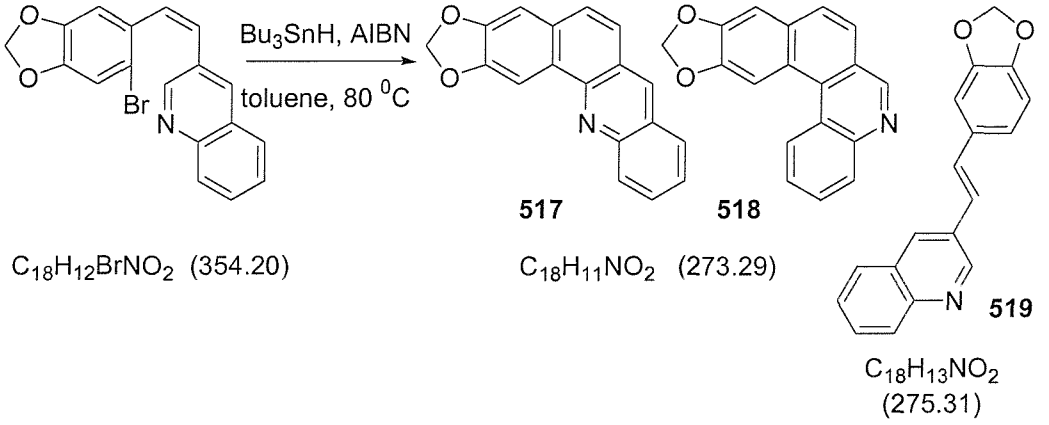
MS $^m/_z$ (ES) 275 (17 %; M(^{13}C)H$^+$), 274 (100 %; MH$^+$).

CHN Found: C, 78.87; H, 4.10; N, 5.07. $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.

[1,3]Dioxolo[4',5':4,5]benzo[*c*]acridine **517**,

[1,3]Dioxolo[4',5':4,5]benzo[*k*]phenanthridine **518** and

4-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **519**



$C_{18}H_{12}BrNO_2$ (354.20)

$C_{18}H_{11}NO_2$ (273.29)

$C_{18}H_{13}NO_2$
(275.31)

The bromide **507** (250 mg, 0.706 mmol) in toluene (80 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.23 mL, 249 mg, 0.853 mmol) and AIBN (100 mg, 0.609 mmol) for 18 hours. The mixture was cooled to room temperature and stirred for 8 hours with $KF_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50 Et_2O : petrol) to yield firstly **517** (47 mg, 0.172 mmol, 24 %) as a pale yellow solid, then **518** (35 mg, 0.127 mmol, 18 %) as a white solid and finally **519** (89 mg, 0.326 mmol, 46 %) as a white solid.

Data for [1,3]dioxolo[4',5':4,5]benzo[*c*]acridine **517**

Data identical to those described previously.

Data for [1,3]dioxolo[4',5':4,5]benzo[*k*]phenanthridine **518**

Data identical to those described previously.

Data for 3[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **519**

M.P. 117 - 119 °C (EtOH).

FT-IR (solid) υ_{max} 3032 w, 2894 w, 1502 s, 1490 s, 1445 m, 1253 s, 1039 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 336 (28900), 308 (19000), 282 (25200) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 9.02 (1H, d, *J* 2.0 Hz, Ar**H**), 8.06 (1H, d, *J* 2.0 Hz, Ar**H**), 8.01 (1H, d, *J* 8.5 Hz, Ar**H**), 7.74 (1H, d, *J* 8.0 Hz, Ar**H**), 7.60 (1H, ddd, *J* 8.5, 7.0, 1.5 Hz, Ar**H**), 7.47 (1H, ddd, *J* 8.0, 7.0, 1.0 Hz, Ar**H**), 7.18 (1H, d, *J* 16.6 Hz, RC**H**=C**H**R), 7.06 (1H, d, *J* 1.5 Hz, Ar**H**), 7.02 (1H, d, *J* 16.1 Hz, RC**H**=C**H**R), 6.95 (1H, dd, *J* 8.0, 1.5 Hz, Ar**H**), 6.77 (1H, d, *J* 8.0 Hz, Ar**H**), 5.94 (2H, s, OC**H**$_2$O).

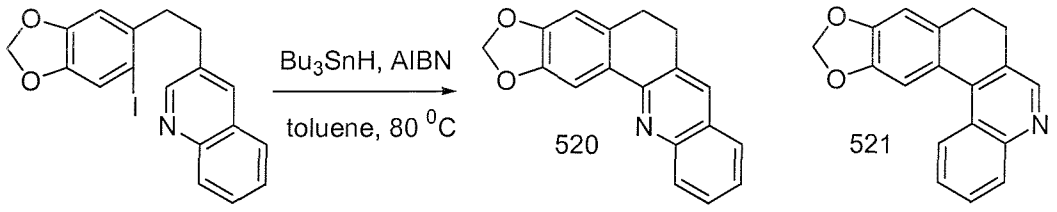
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$) 148.0 (Ar, **C**H), 146.9 (Ar, **C**), 146.5 (Ar, **C**), 146.0 (Ar, **C**), 130.4 (Ar, **C**H), 129.9 (Ar, **C**), 129.2 (**C**H=CH), 129.0 (Ar, **C**), 127.9 (Ar, **C**H), 127.6 (Ar, **C**H), 126.7 (Ar, **C**), 126.3 (Ar, **C**H), 125.6 (Ar, **C**H), 122.1 (CH=**C**H), 120.5 (Ar, **C**H), 107.1 (Ar, **C**H), 104.2 (Ar, **C**H), 99.9 (O**C**H$_2$O).

MS $^m/_z$ (ES) 317 (9 %; $[M+H+MeCN]^+$), 277 (18 %; $[M(^{13}C)+H]^+$), 276 (100 %; $[M+H]^+$), 140 (17 %), 127 (22 %).

CHN Found : C, 78.42; H, 4.80; N, 5.14; $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

5,6-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*c*]acridine **520** and

7,8-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*k*]phenanthridine **521**



$C_{18}H_{14}INO_2$ (403.21) $C_{18}H_{13}NO_2$ (275.30)

The iodide **509** (750 mg, 1.86 mmol) in toluene (170 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.70 mL, 757 mg, 2.60 mmol) and AIBN (30 mg, 0.183 mmol) for 36 hours. The mixture was cooled to room temperature and stirred for 16 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give firstly **520** (116 mg, 0.421 mmol, 23 %) as a white crystalline solid and then **521** (260 mg, 0.944 mmol, 51 %) as a white crystalline solid.

Data for 5,6-dihydro[1,3]dioxolo[4',5':4,5]benzo[*c*]acridine **520**

M.P. 138 - 140 °C (Et_2O / petrol).

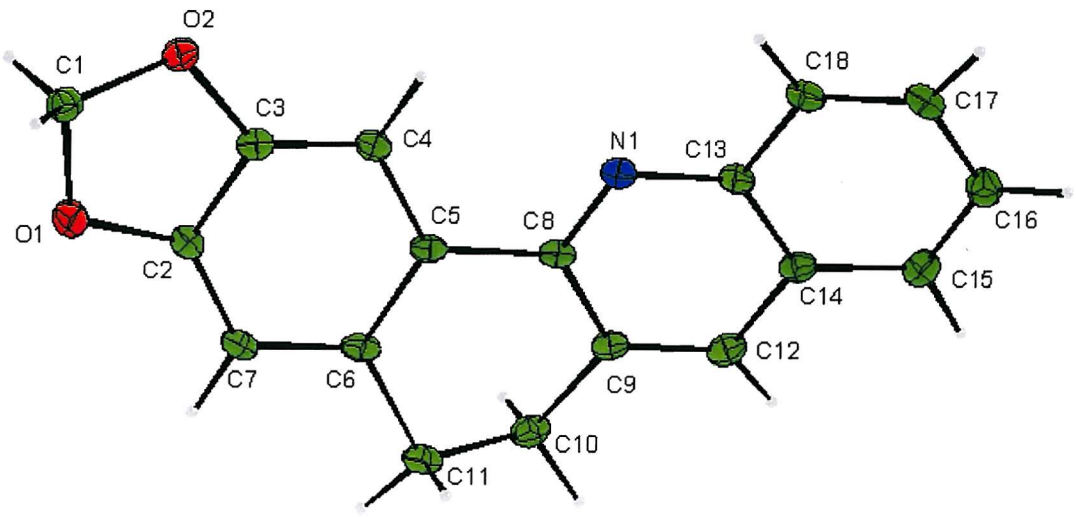
FT-IR (solid) υ_{max} 2894 w, 2835 w, 1612 w, 1484 s, 1449 m, 1405 m, 1376 m, 1268 s, 1226 m, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 359 (30200), 320 (10100), 275 (19700) 252 (29900) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.10 (1H, d, *J* 8.1 Hz, Ar**H**), 8.08 (1H, s, Ar**H**), 7.86 (1H, s, Ar**H**), 7.72 (1H, d, *J* 8.1 Hz, Ar**H**), 7.64 (1H, app. t, *J* 7.4 Hz, Ar**H**), 7.46 (1H, app. t, *J* 7.4 Hz, Ar**H**), 6.74 (1H, s, Ar**H**), 6.01 (2H, s, OC**H$_2$**O), 3.08 (2H, app. t, *J* 7.0 Hz, C**H$_2$**), 2.91 (2H, app. t, *J* 6.6 Hz, C**H$_2$**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	153.2 (Ar, **C**), 148.9 (Ar, **C**), 147.5 (Ar, **C**), 147.3 (Ar, **C**), 134.5 (Ar, **C**), 133.4 (Ar, **C**H), 130.0 (Ar, **C**), 129.1 (Ar, **C**H), 128.9 (Ar, **C**), 128.6 (Ar, **C**H), 127.6 (Ar, **C**), 126.9 (Ar, **C**H), 125.7 (Ar, **C**H), 108.0 (Ar, **C**H), 106.2 (Ar, **C**H), 101.2 (O**C**H_2O), 28.9 (Ar**C**H_2), 28.5 (Ar**C**H_2).
MS $^m/_z$ (ES)	277 (18 %; M(^{13}C)H^+), 276 (100 %; MH^+).
CHN	Found: C, 78.39; H, 4.74; N, 5.03. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

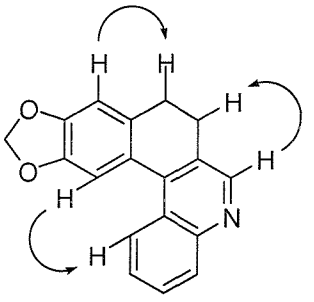
X-RAY



Data for 7,8-dihydro[1,3]dioxolo[4',5':4,5]benzo[*k*]phenanthridine **521**

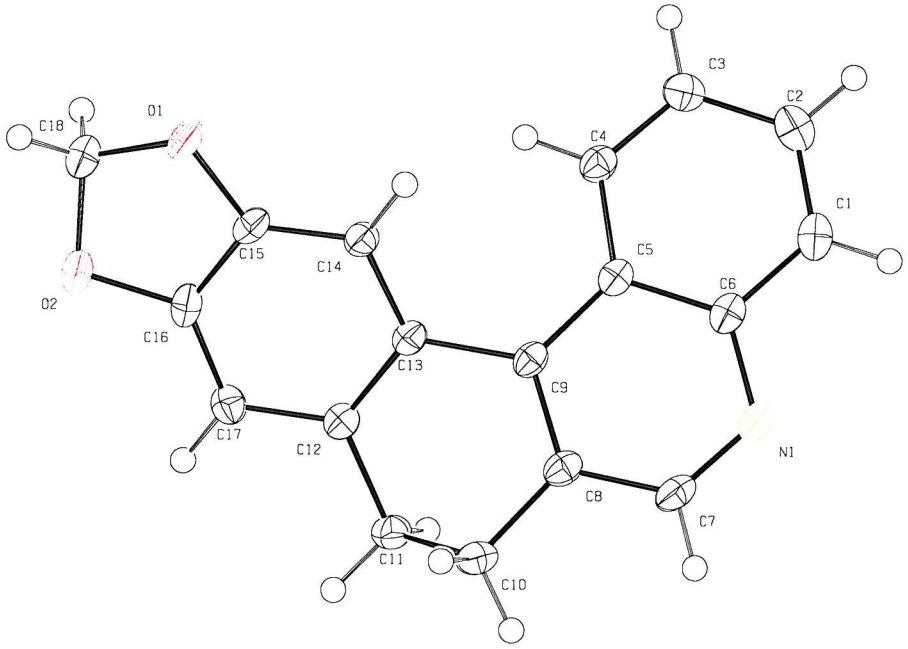
M.P.	144 - 146 °C (CH_2Cl_2 / petrol)
FT-IR (solid) υ_{max}	2898 w, 1618 w, 1562 m, 1501 s, 1485 s, 1419 w, 1389 m, 1283 m, 1224 s, 1167 m, 1041 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	353 (7880), 327 (5060), 243 (15800) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	8.84 (1H, s, Ar**H**), 8.47 (1H, d, *J* 8.5 Hz, Ar**H**), 8.17 (1H, d, *J* 8.0 Hz, Ar**H**), 7.72 (1H, app. t, *J* 7.3 Hz, Ar**H**), 7.59 (1H, app. t, *J* 7.5 Hz, Ar**H**), 7.53 (1H, s, Ar**H**), 6.95 (1H, s, Ar**H**), 6.09 (2H, s, O**CH_2**O), 2.94 - 2.91 (2H, m, **CH_2**), 2.86 - 2.82 (2H, m, **CH_2**).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 8.84 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.94 - 2.91 (2H, m, **CH_2**). n.O.e Irradiation of the signal at δ_H 7.53 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.47 (1H, d, *J* 8.5 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 6.95 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.86 - 2.82 (2H, m, **CH_2**).
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	151.1 (Ar, **C**H), 150.0 (Ar, **C**), 148.7 (Ar, **C**), 147.4 (Ar, **C**), 140.4 (Ar, **C**), 136.1 (Ar, **C**), 131.3 (Ar, **C**H), 131.0 (Ar, **C**), 129.1 (Ar, **C**H), 127.5 (Ar, **C**H), 126.6 (Ar, **C**), 126.1 (Ar, **C**H), 125.4 (Ar, **C**), 110.7 (Ar, **C**H), 109.9 (Ar, **C**H), 102.4 (O**C**H_2O), 30.3 (Ar**C**H_2), 27.7 (Ar**C**H_2).
MS $^m/_z$ (ES)	277 (18 %; M(^{13}C)H$^+$), 276 (100 %; MH$^+$), 242 (16 %).
CHN	Found: C, 78.38; H, 4.78; N, 5.04. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

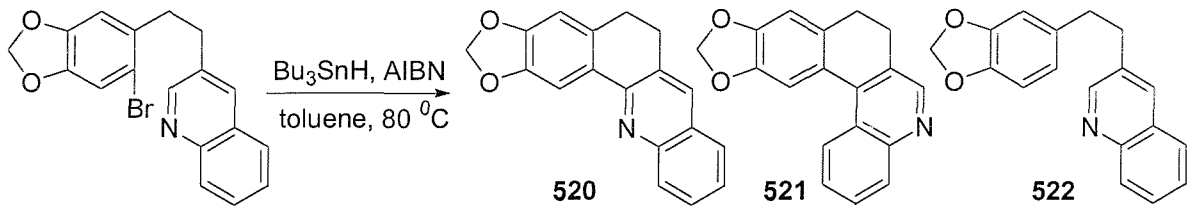
X-RAY


C3
C2
C18
O1
C4
C1
C15
C14
C5
O2
C6
C16
C13
C9
C17
C12
N1
C8
C7
C11
C10

5,6-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*c*]acridine **520** and

7,8-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*k*]phenanthridine **521** and

3-[2-(1,3-Benzodioxol-5-yl)-1-ethyl]quinoline **522**



$C_{18}H_{14}BrNO_2$ (356.21) $C_{18}H_{13}NO_2$ (275.30) $C_{18}H_{15}NO_2$ (277.32)

The bromide **510** (286 mg, 0.803 mmol) in toluene (120 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.30 mL, 325 mg, 1.11 mmol) and AIBN (10 mg, 0.061 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 50 mL). The aqueous phase was separated and washed with Et_2O (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (petrol 80 : 20 Et_2O : petrol) to give firstly **520** (40 mg, 0.145 mmol, 18 %), then recovered starting material (71 mg, 0.194 mmol, 27 %), then **522** (33 mg, 0.120 mmol, 15 %) as a white crystalline solid and finally **521** (22 mg, 0.079 mmol, 10 %).

Data for 5,6-dihydro[1,3]dioxolo[4',5':4,5]benzo[*c*]acridine **520**

Data identical to those described previously.

Data for 7,8-dihydro[1,3]dioxolo[4',5':4,5]benzo[*k*]phenanthridine **521**

Data identical to those described previously.

Data for 3-[2-(1,3-benzodioxol-5-yl)-1-ethyl]quinoline **522**

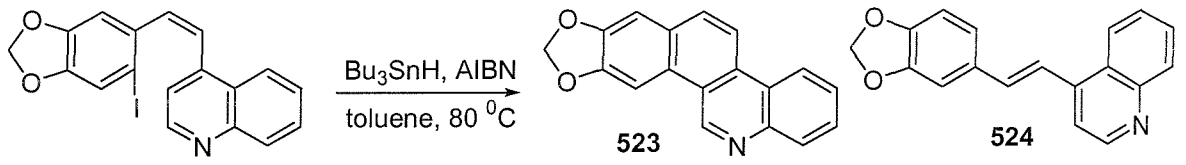
M.P. 91 - 93 °C (EtOH).

FT-IR (solid) υ_{max} 1500 m, 1483 s, 1440 m, 1360 w, 1241 s, 1190 w, 1038 s cm^{-1}.

UV (MeOH) λ_{max} (ε)	318 (4510), 304 (4210), 285 (7310), 233 (37410) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	8.73 (1H, d, *J* 2.2 Hz, Ar**H**), 8.09 (1H, d, *J* 8.1 Hz, Ar**H**), 7.88 (1H, s, Ar**H**), 7.76 (1H, d, *J* 8.1 Hz, Ar**H**), 7.68 (1H, t, *J* 7.4 Hz, Ar**H**), 7.53 (1H, t, *J* 7.7 Hz, Ar**H**), 6.72 (1H, d, *J* 8.1 Hz, Ar**H**), 6.71 (1H, s, Ar**H**), 6.60 (1H, d, *J* 8.1 Hz, Ar**H**), 5.93 (2H, s, O**C**$\mathbf{H_2}$O), 3.10 - 3.05 (2H, m, $RCH_2C\mathbf{H_2}R$), 2.97 - 2.92 (2H, m, $R\mathbf{C}H_2CH_2R$).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	151.9 (Ar, **C**H), 147.7 (Ar, **C**), 146.8 (Ar, **C**), 145.9 (Ar, **C**), 134.5 (Ar, **C**H), 134.1 (Ar, **C**), 129.1 (Ar, **C**H), 128.7 (Ar, **C**H), 128.1 (Ar, **C**), 127.4 (Ar, **C**H), 126.6 (Ar, **C**H), 121.4 (Ar, **C**H), 108.9 (Ar, **C**H), 108.2 (Ar, **C**H), 100.9 (O**C**H_2O), 37.2 (RCH_2CH_2R), 35.3 ($R\mathbf{C}H_2CH_2R$), one Ar**H** obscured.
MS $^m/_z$ (ES)	279 (19 %; $[M(^{13}C)+H]^+$), 278 (100 %; $[M+H]^+$).
CHN	Found: C, 77.95; H, 5.47; N, 4.99. $C_{18}H_{15}NO_2$ requires C, 77.96; H, 5.45; N, 5.05.

[1,3]Dioxolo[4'5':4,5]benzo[*i*]phenanthridine **523** and

4-[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]quinoline **524**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{11}NO_2$ (273.29) $C_{18}H_{13}NO_2$ (275.30)

The iodide **512** (600 mg, 1.50 mmol) in toluene (120 mL) was stirred under argon at 80 °C with Bu_3SnH (0.55 mL, 595 mg, 2.04 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield firstly recovered starting material **512** (40 mg, 0.10 mmol, 7 %) and then a mixture of **523** (142 mg, 0.52 mmol, 35 %) and **524** (226 mg, 0.82 mmol, 55 %). This mixture was separated by fractional recrystallisation from EtOH, with the **523** crystallising out first as a white solid.

Data for [1,3]dioxolo[4'5':4,5]benzo[*i*]phenanthridine **523**

M.P. 237 - 239 °C (EtOH).

FT-IR (solid) υ_{max} 1744 m, 1701 m, 1470 s, 1370 m, 1356 m, 1230 s, 1190 m, 1030 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 372 (10340), 354 (8740), 329 (11250), 307 (14690), 254 (39010) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	10.02 (1H, s, Ar**H**), 8.64 (1H, dd, *J* 8.0, 1.0 Hz, Ar**H**), 8.50 (1H, d, *J* 9.0 Hz, Ar**H**), 8.25 (1H, dd, *J* 8.0, 1.5 Hz, Ar**H**), 8.23 (1H, s, Ar**H**), 8.05 (1H, d, *J* 8.5 Hz, Ar**H**), 7.77 (1H, td, *J* 7.5, 1.5 Hz, Ar**H**), 7.71 (1H, td, *J* 7.5, 1.0 Hz, Ar**H**), 7.33 (1H, s, Ar**H**), 6.17 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	148.2 (Ar, **C**), 146.9 (Ar, **C**), 146.8 (Ar, **C**H), 143.5 (Ar, **C**), 130.0 (Ar, **C**H), 129.8 (Ar, **C**), 128.8 (Ar, **C**H), 127.9 (Ar, **C**), 127.2 (Ar, **C**H), 125.8 (Ar, **C**H), 125.7 (Ar, **C**), 123.1 (Ar, **C**), 121.3 (Ar, **C**H), 120.4 (Ar, **C**), 117.0 (Ar, **C**H), 104.4 (Ar, **C**H), 100.5 (O**C**H$_2$O), 98.6 (Ar, **C**H).
MS $^m/_z$ (APCI)	275 (20 %; M(^{13}C)H$^+$), 274 (100 %; MH$^+$).
HRMS (EI)	Found: MH$^+$, 274.0863. $C_{18}H_{12}NO_2$ requires 274.0863.

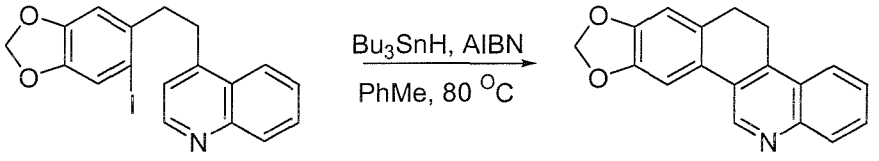
Data for 4-[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **524**

Spectral and physical data were in accord with the literature.[192]

M.P.	117 - 118 °C (EtOH). Lit. 129 °C (EtOH).[192]
FT-IR (solid) υ_{max}	1575 w, 1501 m, 1489 w, 1446 m, 1253 s, 1197 m, 1038 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	316 (7430), 304 (7430), 227 (27020) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	8.88 (1H, d, *J* 4.5 Hz, Ar**H**), 8.20 (1H, d, *J* 8.4 Hz, Ar**H**), 8.12 (1H, d, *J* 8.4 Hz, Ar**H**), 7.73 (1H, app. t, *J* 7.6 Hz, Ar**H**), 7.64 (1H, d, *J* 16.0 Hz, RCH=C**H**R), 7.58 (1H, app. t, *J* 7.4 Hz, Ar**H**), 7.56 (1H, d, *J* 4.2 Hz, Ar**H**), 7.26 (1H, d, *J* 16.0 Hz, RC**H**=CHR), 7.19 (1H, s, Ar**H**), 7.05 (1H, d, *J* 7.9 Hz, Ar**H**), 6.86 (1H, d, *J* 8.0 Hz, Ar**H**), 6.02 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm (62.9 MHz, $CDCl_3$)	150.2 (Ar, **C**H), 148.8 (Ar, **C**), 148.4 (Ar, **C**), 148.3 (Ar, **C**), 143.0 (Ar, **C**), 134.7 (Ar, **C**H), 131.1 (Ar, **C**), 130.2 (Ar, **C**H), 129.3 (Ar, **C**H), 126.4 (Ar, **C**H), 126.4 (Ar, **C**), 123.4 (Ar, **C**H), 122.6 (**C**H=CH), 121.0 (CH=**C**H), 116.8 (Ar, **C**H), 108.6 (Ar, **C**H), 105.9 (Ar, **C**H), 101.4 (O**C**H$_2$O).
MS $^m/_z$ (APCI)	277 (19 %; M(^{13}C)H$^+$), 276 (100 %; MH$^+$), 158 (32 %).
CHN	Found: C, 78.42; H, 4.81; N, 5.09. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

5,6-Dihydro[1,3]dioxolo[4',5':4,5]benzo[*i*]phenanthridine **525**



$C_{18}H_{14}INO_2$ (403.21) $C_{18}H_{13}NO_2$ (275.30)

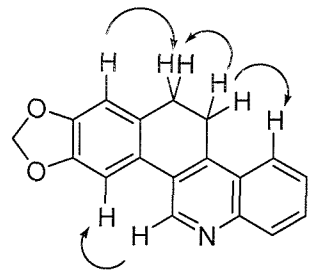
The iodide **513** (415 mg, 1.03 mmol) in toluene (80 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.40 mL, 433 mg, 1.48 mmol) and AIBN (40 mg, 0.24 mmol) for 48 hours. The mixture was cooled to room temperature and stirred for 24 hours with $KF_{(aq)}$ (2M, 80 mL). The aqueous phase was separated and washed with Et_2O (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **525** (190 mg, 0.690 mmol, 67 %) as a white solid.

M.P. 138 - 140 °C (DCM / petrol).

FT-IR (solid) υ_{max} 2900 w, 1687 w, 1502 m, 1486 s, 1471 s, 1366 m, 1267 m, 1232 s, 1038 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 357 (7910), 269 (18140), 239 (16620) nm (mol^{-1} dm^3 cm^{-1}).

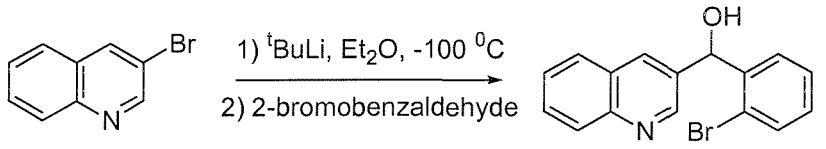
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 9.15 (1H, s, Ar**H**), 8.08 (1H, d, *J* 8.8 Hz, Ar**H**), 8.03 (1H, d, *J* 8.1 Hz, Ar**H**), 7.64 (1H, t, *J* 7.4 Hz, Ar**H**), 7.54 (1H, t, *J* 7.7 Hz, Ar**H**), 7.35 (1H, s, Ar**H**), 6.77 (1H, s, Ar**H**), 5.97 (2H, s, O**CH$_2$**O), 3.21 (2H, t, *J* 7.7 Hz, Ar**CH$_2$**), 2.87 (2H, t, *J* 7.4 Hz, Ar**CH$_2$**).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 9.15 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.35 (1H, s, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.35 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 9.15 (1H, s, Ar**H**). n.O.e Irradiation of the signal at δ_H 3.21 (2H, t, *J* 7.7 Hz, Ar**CH$_2$**) caused an n.O.e. enhancement at δ_H 8.03 (1H, d, *J* 8.1 Hz, Ar**H**) and δ_H 2.87 (2H, t, *J* 7.4 Hz, Ar**CH$_2$**). n.O.e Irradiation of the signal at δ_H 2.87 (2H, t, *J* 7.4 Hz, Ar**CH$_2$**) caused an n.O.e. enhancement at δ_H 6.77 (1H, s, Ar**H**).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	147.3 (Ar, **C**), 147.2 (Ar, **C**), 146.9 (Ar, **C**), 146.5 (Ar, **C**H), 140.6 (Ar, **C**), 130.9 (Ar, **C**), 129.9 (Ar, **C**H), 128.6 (Ar, **C**H), 126.9 (Ar, **C**), 126.7 (Ar, **C**H), 126.4 (Ar, **C**), 125.8 (Ar, **C**), 123.4 (Ar, **C**H), 108.7 (Ar, **C**H), 104.2 (Ar, **C**H), 101.2 (O**C**H$_2$O), 27.9 (Ar**C**H$_2$), 23.3 (Ar**C**H$_2$).
MS $^m/_z$ (ES)	317 (22 %; $[MH+MeCN]^+$), 276 (100 %; MH^+), 168 (22 %), 153 (64 %), 144 (33 %).
CHN	Found: C, 78.56; H, 4.79; N, 5.19. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

6.34 ATTEMPTED 5-MEMBERED RING FORMATION

(2-Bromophenyl)(3-quinolyl)methanol **533**



C_9H_6NBr (208.07) $C_{16}H_{12}NOBr$ (314.18)

^{t}Butyllithium (1.25 M in hexane, 5.9 mL, 7.38 mmol) was added dropwise to 3-bromoquinoline **532** (1.0 mL, 1.53 g, 7.35 mmol) in Et_2O (20 mL) at - 100 °C. After 2 hours 2-bromobenzaldehyde (0.87 mL, 1.38 g, 7.45 mmol) in Et_2O (20 mL) was added dropwise. The solution was warmed to - 60 °C over a period of 2 hours and brine (90 mL) added along with THF (50 mL) to aid product solubility. The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (chloroform) to give **533** (1.78 g, 5.65 mmol, 77 %) as a white solid.

M.P. 153 - 155 °C (Et_2O / petrol).

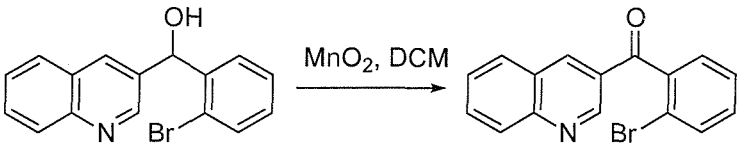
FT-IR (solid) υ_{max} 3061 br. w, 2831 w, 2701 w, 1579 w, 1496 m, 1464 m, 1380 w, 1284 w, 1162 m, 1071 m, 1008 w cm^{-1}.

UV (MeOH) λ_{max} (ε) 318 (3770), 304 (3330), 290 (3200) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.74 (1H, d, *J* 2.2 Hz, Ar**H**), 8.11 (1H, s, Ar**H**), 7.99 (1H, d, *J* 8.1 Hz, Ar**H**), 7.74 - 7.47 (5H, m, 5 x Ar**H**), 7.33 (1H, t, *J* 7.4 Hz, Ar**H**), 7.14 (1H, td, *J* 8.1, 1.5 Hz, Ar**H**), 6.35 (1H, s, Ar_2C**H**OH), 5.44 (1H, s, Ar_2CHO**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	150.3 (Ar, **C**H), 147.0 (Ar, **C**), 142.1 (Ar, **C**), 135.8 (Ar, **C**), 134.3 (Ar, **C**H), 133.0 (Ar, **C**H), 129.8 (Ar, **C**H), 129.5 (Ar, **C**H), 128.7 (Ar, **C**H), 128.7 (Ar, **C**H), 128.2 (Ar, **C**H), 128.1 (Ar, **C**H), 127.9 (Ar, **C**), 127.0 (Ar, **C**H), 122.8 (Ar, **C**), 72.6 (Ar_2**C**HOH).
MS $^m/_z$ (APCI)	316 (83 %; M(^{81}Br)H^+), 314 (100 %; M(^{79}Br)H^+), 298 (12 %; [M(^{81}Br)H-H_2O]$^+$), 296 (12 %; [M(^{79}Br)H-H_2O]$^+$), 234 (18 %; [M-Br]$^+$).
HRMS (EI)	Found: M^+, 313.0096. $C_{16}H_{12}{}^{79}BrNO$ requires 313.0102.
CHN	Found: C, 61.13; H, 3.87; N, 4.35. $C_{16}H_{12}BrNO$ requires C, 61.17; H, 3.85; N, 4.46.

(2-Bromophenyl)(3-quinolyl)methanone **534**



$C_{16}H_{12}NOBr$ (314.18) $C_{16}H_{10}NOBr$ (312.16)

MnO_2 (4.00 g, 46 mmol) was activated by azeotroping with toluene (15 mL). The alcohol **533** (500 mg, 1.59 mmol) in DCM (50 mL) was then added and the reaction mixture stirred under argon for 24 hours. The MnO_2 residues were removed by filtration through celite and the solvent removed *in vacuo*. The residues were recrystallised from Et_2O to give **534** (468 mg, 1.50 mmol, 94 %) as a white solid.

M.P. 129 - 131 °C (Et_2O).

FT-IR (solid) υ_{max} 3031 w, 2926 w, 1665 s, 1614 m, 1594 w, 1566 m, 1489 w, 1459 w, 1365 s, 1290 s, 1240 m, 1152 w, 1117 w, 1018 w cm^{-1}.

UV (MeOH) λ_{max} (ε) 292 (9930), 251 (38000) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 9.37 (1H, d, *J* 2.2 Hz, Ar**H**), 8.50 (1H, d, *J* 1.5 Hz, Ar**H**), 8.21 (1H, d, *J* 8.8 Hz, Ar**H**), 7.93 - 7.86 (2H, m, 2 x Ar**H**), 7.72 (1H, d, *J* 7.4 Hz, Ar**H**), 7.64 (1H, t, *J* 7.4 Hz, Ar**H**), 7.54 - 7.42 (3H, m, 3 x Ar**H**).

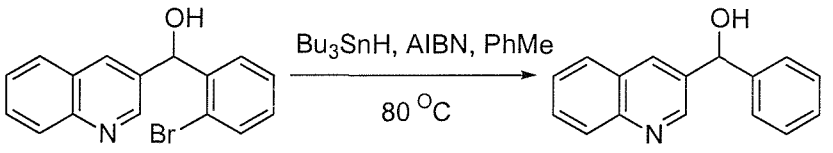
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 194.6 (Ar_2**C**O), 150.0 (Ar, **C**H), 149.8 (Ar, **C**), 139.8 (Ar, **C**H), 139.7 (Ar, **C**), 133.5 (Ar, **C**H), 132.5 (Ar, **C**H), 131.9 (Ar, **C**H), 129.6 (Ar, **C**H), 129.5 (Ar, **C**H), 129.3 (Ar, **C**H), 128.6 (Ar, **C**), 127.7 (Ar, **C**H), 127.6 (Ar, **C**H), 126.8 (Ar, **C**), 119.7 (Ar, **C**).

MS $^{m}/_{z}$ (APCI) 355 (24 %; [M(^{81}Br)+ MeCN]$^{+}$), 353 (20 %; [M(^{79}Br)+ MeCN]$^{+}$), 315 (11 %), 314 (100 %; M(^{81}Br)H^{+}), 312 (85 %; M(^{79}Br)H^{+}), 259 (10 %).

HRMS (EI) Found: M^{+}, 310.9950. $C_{16}H_{10}NO^{79}Br$ requires 310.9946.

CHN Found: C, 61.65; H, 3.23; N, 4.49. $C_{16}H_{10}NOBr$ requires C, 61.56; H, 3.23; N, 4.49.

Phenyl(3-quinolyl)methanol **535**



$C_{16}H_{12}NOBr$ (314.18) $C_{16}H_{13}NO$ (235.28)

The alcohol **533** (300 mg, 0.95 mmol) in toluene (30 mL) was stirred under argon at 80 °C with Bu_3SnH (0.25 mL, 281 mg, 0.96 mmol) and AIBN (20 mg, 0.122 mmol) for 5 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (97 : 3, $CHCl_3$: MeOH) to give **535** (112 mg, 0.48 mmol, 50 %) as a white solid.

M.P. 136 - 138 °C ($CHCl_3$).

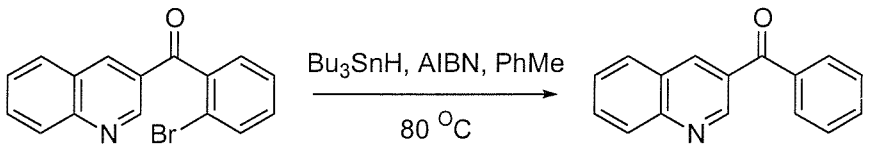
FT-IR (solid) υ_{max} 3146 br. m, 3001 w, 2846 w, 1619 w, 1579 w, 1495 m, 1439 w, 1374 w, 1329 m, 1307 w, 1230 m, 1124 m, 1081 w, 1052 w cm^{-1}.

UV (MeOH) λ_{max} (ε) 318 (2700), 304 (2350), 291 (2240), 269 (2630) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, DMSO) 8.91 (1H, s, Ar**H**), 8.34 - 8.33 (2H, m, 2 x Ar**H**), 7.99 (2H, t, *J* 7.4 Hz, Ar**H**), 7.71 (1H, t, *J* 7.7 Hz, Ar**H**), 7.58 (1H, t, *J* 7.7 Hz, Ar**H**), 7.50 - 7.21 (4H, m, 4 x Ar**H**), 6.29 (1H, d, *J* 3.7 Hz, Ar_2CHOH), 6.01 (1H, d, *J* 3.7 Hz, Ar_2CHOH).

^{13}C NMR δ_C ppm (75.5 MHz, DMSO)	150.2 (Ar, **C**H), 146.8 (Ar, **C**), 144.8 (Ar, **C**), 138.5 (Ar, **C**), 132.2 (Ar, **C**H), 129.2 (Ar, **C**H), 128.7 (Ar, **C**H), 128.4 (Ar, 2 x **C**H), 128.2 (Ar, **C**H), 127.5 (Ar, **C**), 127.2 (Ar, **C**H), 126.8 (Ar, **C**H), 126.5 (Ar, 2 x **C**H), 72.5 (Ar_2**C**HOH).
MS $^m/_z$ (CI)	277 (8 %; $[MH+MeCN]^+$), 275 (6 %; $[MH-H_2+MeCN]^+$), 237 (15 %), 236 (100 %; MH^+), 234 (16 %; $[MH-H_2]^+$), 218 (18 %; $[MH-H_2O]^+$).
HRMS (EI)	Found: M^+, 235.0994. $C_{16}H_{13}NO$ requires 235.0997.
CHN	Found: C, 81.69; H, 5.57; N, 5.96. $C_{16}H_{13}NO$ requires C, 81.68; H, 5.57; N, 5.95.

Phenyl(3-quinolyl)methanone **536**



$C_{16}H_{10}BrNO$ (312.16) $C_{16}H_{11}NO$ (233.26)

The ketone **534** (129 mg, 0.413 mmol) in toluene (40 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.14 mL, 151 mg, 0.519 mmol) and AIBN (10 mg, 0.061 mmol) for 48 hours. The mixture was cooled to room temperature and stirred for 48 hours with $KF_{(aq)}$ (2M, 40 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (50 : 50, Et_2O : petrol) to give **536** (72 mg, 0.309 mmol, 75 %) as a white solid.

Spectral and physical data were in accord with the literature.[188,191,193-195]

M.P. 75 - 76 °C (petrol). Lit. 76 - 78 °C (hexane).[191]

FT-IR (solid) υ_{max} 3063 w, 1653 s, 1617 m, 1597 m, 1569 m, 1493 m, 1446 m, 1366 m, 1286 s, 1242 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 248 (49300) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 9.34 (1H, s, Ar**H**), 8.56 (1H, s, Ar**H**), 8.20 (1H, d, *J* 8.8 Hz, Ar**H**), 7.93 - 7.83 (4H, m, 4 x Ar**H**), 7.69 - 7.52 (4H, m, 4 x Ar**H**).

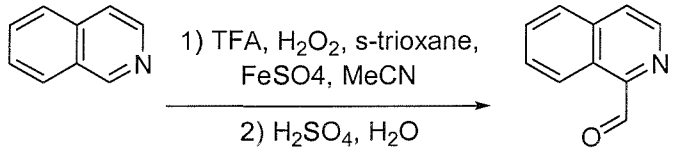
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 194.9 (Ar_2CO), 150.4 (Ar, **C**H), 149.5 (Ar, **C**), 138.9 (Ar, **C**H), 137.0 (Ar, **C**), 133.1 (Ar, **C**H), 131.9 (Ar, **C**H), 130.1 (Ar, 2 x **C**H), 129.5 (Ar, **C**H), 129.2 (Ar, **C**H), 128.7 (Ar, 2 x **C**H), 127.6 (Ar, **C**H), 126.6 (Ar, **C**). One Ar **C** signal is obscured.

MS $^{m}/_{z}$ (APCI)	275 (5 %; $[MH+MeCN]^+$), 234 (8 %; MH^+), 168 (23 %), 153 (100 %), 127 (92 %).
CHN	Found: C, 82.11; H, 4.79; N, 6.03. $C_{16}H_{11}NO$ requires C, 82.38; H, 4.75; N, 6.00.

6.4 EXPERIMENTAL FOR CHAPTER 4

6.41 PRECURSOR FORMATION

1-Isoquinolinecarboxaldehyde **602**



C_9H_7N (129.16) $C_{10}H_7NO$ (157.17)

Following the procedure of Minisci *et al.*[32] Isoquinoline **601** (1.82 mL, 2.0 g, 15.5 mmol), TFA (1.2 mL, 1.78 g, 15.6 mmol), H_2O_2 (4 mL, 30 % w/v in H_2O, 1.2 g, 35.3 mmol), *s*-trioxane (100 g, 1.11 mol) and $FeSO_4.7H_2O$ (60 mg, 0.22 mmol) were refluxed in MeCN (200 mL) for 18 hours. The solution was concentrated under vacuum and basified with $NaOH_{(aq)}$ (2M, 50 mL). The mixture was extracted with Et_2O (3 x 100 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield the masked aldehyde **54** (1.38 g, 6.33 mmol, 41 %) as a pale yellow solid, which was refluxed in $H_2SO_{4(aq)}$ (10 %, 50 mL) for 10 hours. The mixture was basified with $NaOH_{(aq)}$ (2M, 100 mL) and extracted with Et_2O (3 x 100 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo* to yield the aldehyde **602** (995 mg, 6.33 mmol, 41 %) as a white solid.

Data For 1-(1,3,5-trioxan-2-yl)isoquinoline **54**

M.P. 92 - 94 °C (Et_2O).

FT-IR (solid) υ_{max} 1410 w, 1193 m, 1163 s, 1154 m, 1099 s, 1074 m, 1066 m, 1052 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 321 (3110), 308 (2650), 272 (3650) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	8.89 (1H, d, *J* 7.4 Hz, Ar**H**), 8.50 (1H, d, *J* 5.9 Hz, Ar**H**), 7.84 (1H, d, *J* 7.4 Hz, Ar**H**), 7.70 (1H, t, *J* 6.2 Hz, Ar**H**), 7.69 (1H, d, *J* 5.9 Hz, Ar**H**), 7.66 (1H, t, *J* 6.6 Hz, Ar**H**), 6.44 (1H, s, Ar**H**), 5.49 (2H, d, *J* 6.6 Hz, 2 x OC**H**HO), 5.44 (2H, d, *J* 6.6 Hz, 2 x OC**H**HO).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	153.2 (Ar, **C**), 141.1 (Ar, **C**H), 137.2 (Ar, **C**), 130.3 (Ar, **C**H), 127.5 (Ar, **C**H), 127.0 (Ar, **C**H), 126.6 (Ar, **C**H), 126.1 (Ar, **C**), 122.7 (Ar, **C**H), 105.0 (Ar, **C**H), 94.1 (2 x OCH_2O).
MS $^m/_z$ (APCI)	219 (15 %; $M(^{13}C)H^+$), 218 (100 %; MH^+).

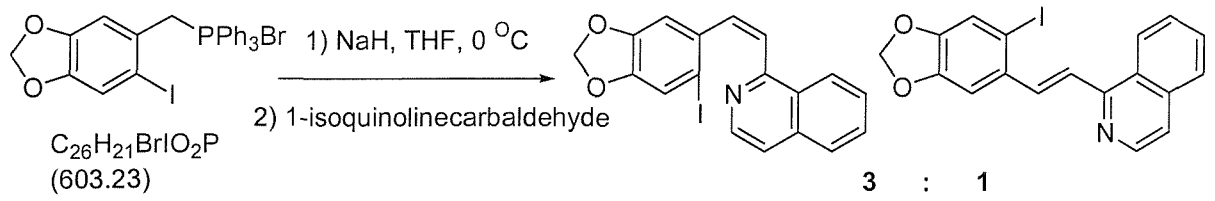
Data For 1-isoquinolinecarboxaldehyde **602**

Spectral and physical data were in accord with the literature.[196,197]

M.P.	54 - 55 °C (Et_2O). Lit. 55 - 55.5 °C (dioxane).[196]
FT-IR (solid) υ_{max}	3053 w, 2824 m, 1705 s, 1623 w, 1580 m, 1498 w, 1454 w, 1388 w, 1321 w, 1230 w, 1207 m, 1057 m cm^{-1}.
UV (MeOH) λ_{max} (ε)	312 (2110), 266 (2830) nm (mol^{-1} dm^3 cm^{-1}).
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	10.40 (1H, s, C**H**O), 9.33 (1H, dd, *J* 7.7, 3.7 Hz, Ar**H**), 8.77 (1H, d, *J* 5.9 Hz, Ar**H**), 7.94 - 7.89 (2H, m, Ar**H**), 7.80 - 7.76 (2H, m, Ar**H**).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	195.7 (Ar**C**HO), 149.8 (Ar, **C**), 142.6 (Ar, **C**H), 136.9 (Ar, **C**), 130.8 (Ar, **C**H), 130.1 (Ar, **C**H), 127.0 (Ar, **C**H), 126.3 (Ar, **C**), 125.7 (Ar, **C**H), 125.5 (Ar, **C**H).
MS $^m/_z$ (APCI)	158 (48 %; MH^+), 153 (30 %).

1-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **603** and

1-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **604**



NaH (140 mg, 3.5 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The iodide **362** (1.3 g, 2.16 mmol) was added and the reaction stirred for 2 hours. The mixture was cooled to 0 °C again and 1-isoquinolinecarbaldehyde **602** (320 mg, 2.04 mmol) added. The mixture was stirred for a further 2 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (1 : 1, Et_2O : petrol) to yield firstly the *E*-azastilbene **604** (164 mg, 0.41 mmol, 20 %) as a pale yellow solid, followed by the *Z*-azastilbene **603** (525 mg, 1.31 mmol, 64 %) as a pale yellow solid.

Data For 1-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **604**

M.P. 142 - 143 °C (EtOH).

FT-IR (solid) υ_{max} 3047 w, 2905 w, 1625 w, 1581 w, 1550 w, 1501 m, 1471 s, 1405 w, 1386 w, 1319 m, 1240 s, 1114 m, 1028 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 308 (3120) nm (mol^{-1} dm^3 cm^{-1}).

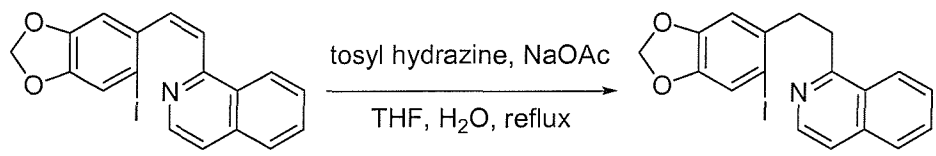
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)	8.60 (1H, d, *J* 5.9 Hz, Ar**H**), 8.35 (1H, d, *J* 8.1 Hz, Ar**H**), 8.09 (1H, d, *J* 14.7 Hz, RC**H**=CHR), 7.85 (1H, d, *J* 8.1 Hz, Ar**H**), 7.72 (1H, d, *J* 14.7 Hz, RCH=C**H**R), 7.70 (1H, t, *J* 7.4 Hz, Ar**H**), 7.63 (1H, t, *J* 8.1 Hz, Ar**H**), 7.60 (1H, d, *J* 5.9 Hz, Ar**H**), 7.36 (1H, s, Ar**H**), 7.32 (1H, s, Ar**H**), 6.04 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	154.2 (Ar, **C**), 148.8 (Ar, **C**), 142.6 (Ar, **C**H), 139.3 (**C**H=CH), 136.7 (Ar, **C**), 133.9 (Ar, **C**), 129.9 (Ar, **C**H), 127.3 (Ar, **C**H), 127.3 (Ar, **C**H), 126.7 (Ar, **C**), 124.7 (Ar, **C**H), 124.5 (CH=**C**H), 120.1 (Ar, **C**H), 119.0 (Ar, **C**H), 106.4 (Ar, **C**H), 101.9 (O**C**H$_2$O), 90.4 (Ar, **C**), one Ar **C** obscured.
MS $^m/_z$ (ES)	403 (16 %; M(^{13}C)H$^+$), 402 (85 %; MH$^+$), 153 (34 %), 127 (100 %).
CHN	Found: C, 54.06; H, 3.00; N, 3.40. $C_{18}H_{12}INO_2$ requires C, 53.89; H, 3.01; N, 3.49.

Data For 1-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **603**

M.P.	120 - 122 °C (EtOH).
FT-IR (solid) υ_{max}	3043 w, 2893 w, 1618 w, 1583 w, 1556 m, 1500 m, 1471 s, 1417 m, 1317 w, 1254 m, 1221 m, 1103 w, 1035 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	314 (8250), 261 (11930) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm	8.52 (1H, d, *J* 5.9 Hz, Ar**H**), 8.01 (1H, d, *J* 8.1 Hz, Ar**H**),
(300 MHz, $CDCl_3$)	7.78 (1H, d, *J* 8.1 Hz, Ar**H**), 7.61 (1H, t, *J* 7.7 Hz, Ar**H**),
	7.56 (1H, d, *J* 5.9 Hz, Ar**H**), 7.47 (1H, t, *J* 7.7 Hz, Ar**H**),
	7.21 (1H, s, Ar**H**), 7.06 (1H, d, *J* 11.8 Hz, RCH=C**H**R),
	6.98 (1H, d, *J* 12.5 Hz, RCH=C**H**R), 6.28 (1H, s, Ar**H**),
	5.75 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm	156.8 (Ar, **C**), 147.7 (Ar, **C**), 147.6 (Ar, **C**), 142.3 (Ar, **C**H),
(75.5 MHz, $CDCl_3$)	138.2 (**C**H=CH), 136.3 (Ar, **C**), 133.4 (Ar, **C**), 130.1 (Ar, **C**H),
	127.6 (Ar, **C**H), 127.2 (Ar, **C**H), 126.9 (Ar, **C**H), 126.7 (Ar, **C**),
	126.4 (CH=**C**H), 120.1 (Ar, **C**H), 118.2 (Ar, **C**H),
	109.9 (Ar, **C**H), 101.4 (O**C**H$_2$O), 88.9 (Ar, **C**).
MS $^m/_z$ (ES)	403 (21 %; M(^{13}C)H$^+$), 402 (100 %; MH$^+$), 127 (38 %).
CHN	Found: C, 54.11; H, 2.98; N, 3.45. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

1-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]isoquinoline **605**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{14}INO_2$ (403.21)

The iodide **603** (310 mg, 0.773 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 48 hours. The solution was cooled to room temperature and washed with Et_2O (2 x 100 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (1 : 1, Et_2O : petrol) to give **605** (306 mg, 0.759 mmol, 98 %) as a white crystalline solid.

M.P. 138 - 139 °C (EtOH).

FT-IR (solid) υ_{max} 3048 w, 2912 w, 1619 w, 1586 w, 1560 w, 1498 m, 1473 s, 1385 m, 1357 m, 1229 s, 1108 m, 1035 s cm^{-1}.

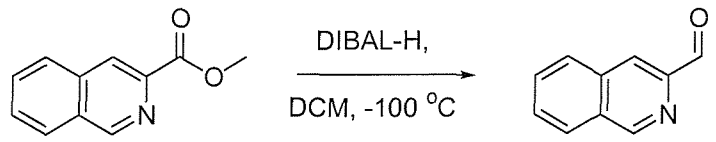
UV (MeOH) λ_{max} (ε) 277 (3800) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.49 (1H, d, *J* 5.9 Hz, Ar**H**), 8.28 (1H, d, *J* 8.8 Hz, Ar**H**), 7.84 (1H, d, *J* 8.1 Hz, Ar**H**), 7.69 (1H, t, *J* 7.4 Hz, Ar**H**), 7.60 (1H, t, *J* 8.5 Hz, Ar**H**), 7.56 (1H, d, *J* 5.9 Hz, Ar**H**), 7.27 (1H, s, Ar**H**), 6.82 (1H, s, Ar**H**), 5.94 (2H, s, OC**H**$_2$O), 3.53 (2H, dd, *J* 9.9, 6.3 Hz, RC**H**$_2$CH$_2$R), 3.23 (2H, dd, *J* 9.9, 6.3 Hz, RCH$_2$C**H**$_2$R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 160.5 (Ar, **C**), 148.5 (Ar, **C**), 146.9 (Ar, **C**), 141.9 (Ar, **C**H), 137.8 (Ar, **C**), 136.2 (Ar, **C**), 129.9 (Ar, **C**H), 127.4 (Ar, **C**H), 127.1 (Ar, **C**H), 125.4 (Ar, **C**H), 119.5 (Ar, **C**H), 118.6 (Ar, **C**H), 109.6 (Ar, **C**H), 101.5 (O**C**H$_2$O), 87.6 (Ar, **C**), 40.3 (Ar**C**H$_2$), 35.9 (Ar**C**H$_2$), one Ar, **C** obscured.

MS $^{m}/_{z}$ (ES)	405 (19 %; M(^{13}C)H^{+}), 404 (100 %; MH^{+}), 127 (17 %).
CHN	Found: C, 53.66; H, 3.48; N, 3.34. $C_{18}H_{14}INO_2$ requires C, 53.62; H, 3.50; N, 3.47.

3-Isoquinolinecarboxaldehyde **607**



$C_{11}H_9NO_2$ (187.19) $C_{10}H_7NO$ (157.17)

Following the procedure of Jones *et al.*[116] The ester **606** (1.00 g, 5.34 mmol) was dissolved in DCM (100 mL) and cooled to –100 °C. DIBAL-H (1M in hexane, 5.34 mL, 5.34 mmol) was added dropwise over a period of 10 minutes and the mixture stirred for a further 6 hours. Rochelle salt ($NaKC_4H_4O_{6(aq)}$, sat., 100 mL) was added and the mixture warmed to room temperature over a period of 18 hours. The organic phase was separated and the aqueous phase extracted with DCM (3 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield the aldehyde **607** (565 mg, 3.60 mmol, 67 %) as a white solid.

Spectral and physical data were in accord with the literature.[197,198]

M.P. 48 - 49 °C (Et_2O). Lit. 41 - 42 °C (ethanol).[198]

FT-IR (solid) υ_{max} 3062 w, 3026 w, 2794 s, 2714 m, 1702 s, 1621 m, 1577 m, 1497 m, 1447 m, 1387 m, 1367 m, 1320 m, 1264 m, 1157 m cm^{-1}.

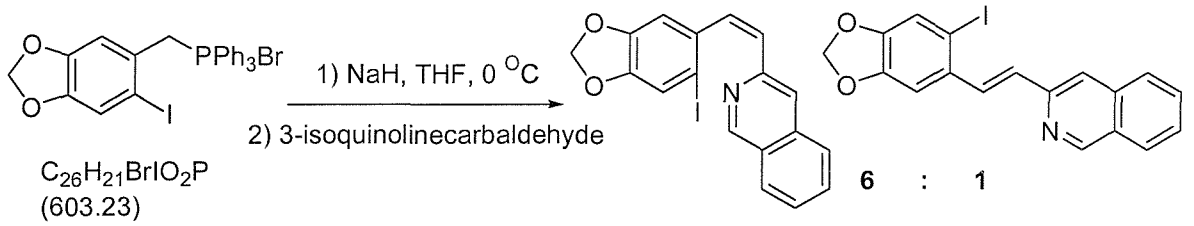
UV (MeOH) λ_{max} (ε) 300 (2810), 271 (3820) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 10.19 (1H, s, C**H**O), 9.28 (1H, s, Ar**H**), 8.27 (1H, s, Ar**H**), 7.98 (1H, d, *J* 5.9 Hz, Ar**H**), 7.92 (1H, d, *J* 6.3 Hz, Ar**H**), 7.73 (1H, t, *J* 5.5 Hz, Ar**H**), 7.71 (1H, t, *J* 5.5 Hz, Ar**H**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	193.2 (Ar**C**HO), 153.2 (Ar, **C**H), 146.8 (Ar, **C**), 135.1 (Ar, **C**), 131.4 (Ar, **C**H), 130.4 (Ar, **C**), 130.1 (Ar, **C**H), 128.5 (Ar, **C**H), 127.7 (Ar, **C**H), 121.7 (Ar, **C**H).
MS $^m/_z$ (APCI)	159 (11 %; M(^{13}C)H$^+$), 158 (100 %; MH$^+$).

3-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **608** and

3-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **609**



$C_{26}H_{21}BrIO_2P$
(603.23)

$C_{18}H_{12}INO_2$ (401.20)

NaH (176 mg, 4.4 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (25 mL) at 0 °C. The iodide **362** (2.0 g, 3.32 mmol) was added and the reaction stirred for 2 hours. The mixture was cooled to 0 °C again and 3-isoquinolinecarbaldehyde **607** (500 mg, 3.18 mmol) added. The mixture was stirred for a further 4 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (1 : 1 : 1 , Et_2O : petrol : DCM) to give a mixture of the *E*- and *Z*-azastilbenes. Recrystallisation from EtOH yielded the *E*-azastilbene **609** (165 mg, 0.41 mmol, 13 %) as pale yellow needles and concentration of the mother liquor afforded the *Z*-azastilbene **608** (1.05 g, 2.62 mmol, 82 %) as white prisms.

Data For 3-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **609**

M.P. 185 - 186 °C (EtOH).

FT-IR (solid) υ_{max} 2975 w, 2898 w, 1619 m, 1570 w, 1562 w, 1499 m, 1461 s, 1436 w, 1388 w, 1267 w, 1251 m, 1226 s, 1170 w, 1112 m, 1035 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 345 (26950), 312 (24370), 246 (25290) nm (mol^{-1} dm^3 cm^{-1}).

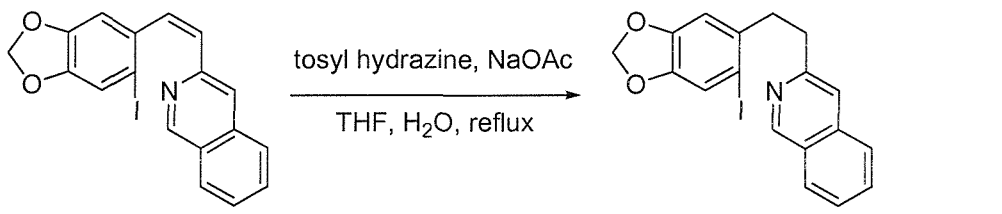
^{1}H NMR δ_H ppm	9.33 (1H, s, Ar**H**), 8.10 (1H, d, *J* 8.1 Hz, Ar**H**),
(300 MHz, DMSO)	7.95 (1H, d, *J* 8.1 Hz, Ar**H**),
	7.94 (1H, d, *J* 15.4 Hz, RC**H**=CHR), 7.77 (1H, s, Ar**H**),
	7.77 (1H, t, *J* 7.0 Hz, Ar**H**), 7.64 (1H, t, *J* 7.4 Hz, Ar**H**),
	7.53 (1H, s, Ar**H**), 7.46 (1H, s, Ar**H**),
	7.33 (1H, d, *J* 15.4 Hz, RC**H**=CHR), 6.11 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm	152.7 (Ar, **C**H), 148.7 (Ar, **C**), 148.5 (Ar, **C**), 148.3 (Ar, **C**),
(75.5 MHz, DMSO)	135.8 (Ar, **C**), 134.0 (**C**H=CH), 132.7 (Ar, **C**), 130.9 (Ar, **C**H),
	129.5 (Ar, **C**H), 127.8 (Ar, **C**H), 127.5 (Ar, **C**), 127.3 (CH=**C**H),
	126.6 (Ar, **C**H), 119.1 (Ar, **C**H), 118.2 (Ar, **C**H),
	105.8 (Ar, **C**H), 102.0 (O**C**H$_2$O), 90.7 (Ar, **C**).
MS $^m/_z$ (ES)	403 (5 %; M(^{13}C)H$^+$), 402 (19 %; MH$^+$), 126 (100 %).
CHN	Found: C, 53.95; H, 3.01; N, 3.49. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

Data For 3-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **608**

M.P.	87 - 88 °C (DCM / petrol).
FT-IR (solid) υ_{max}	3018 w, 2902 w, 1622 w, 1571 w, 1493 w, 1469 s, 1415 m,
	1383 w, 1321 w, 1250 m, 1226 s, 1190 w, 1122 m, 1097 w,
	1028 s cm^{-1}.
UV (MeOH) λ_{max} (ε)	300 (13370) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, DMSO)	9.19 (1H, s, Ar**H**), 8.05 (1H, d, *J* 8.1 Hz, Ar**H**), 7.78 (1H, d, *J* 8.1 Hz, Ar**H**), 7.70 (1H, t, *J* 7.4 Hz, Ar**H**), 7.62 (1H, t, *J* 7.4 Hz, Ar**H**), 7.55 (1H, s, Ar**H**), 7.44(1H, s, Ar**H**), 6.79 (1H, d, *J* 12.5 Hz, RC**H**=CHR), 6.74 (1H, s, Ar**H**), 6.57 (1H, d, *J* 11.8 Hz, RC**H**=CHR), 6.00 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm (75.5 MHz, DMSO)	151.9 (Ar, **C**H), 148.4 (Ar, **C**), 147.6 (Ar, **C**), 147.5 (Ar, **C**), 135.2 (Ar, **C**), 135.1 (**C**H=CH), 134.1 (Ar, **C**), 130.7 (CH=**C**H), 130.2 (Ar, **C**H), 127.5 (Ar, **C**H), 127.5 (Ar, **C**H), 127.0 (Ar, **C**), 126.6 (Ar, **C**H), 119.9 (Ar, **C**H), 117.6 (Ar, **C**H), 109.7 (Ar, **C**H), 101.7 (O**C**H$_2$O), 88.8 (Ar, **C**).
MS $^{m}/_{z}$ (ES)	403 (17 %; M(^{13}C)H$^+$), 402 (84 %; MH$^+$), 126 (100 %).
CHN	Found: C, 53.90; H, 3.01; N, 3.44. $C_{18}H_{12}INO_2$ requires C, 53.89; H, 3.01; N, 3.49.

3-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]isoquinoline **610**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{14}INO_2$ (403.21)

The iodide **608** (610 mg, 1.52 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 48 hours. The solution was cooled to room temperature and stirred with $K_2CO_{3(aq)}$ (2M, 15 mL) for a further 12 hours. The mixture was washed with DCM (3 x 30 mL) and the organic phases combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The resultant white solid was recrystallised from DCM / petrol to give **610** (603 mg, 1.50 mmol, 98 %) as a white crystalline solid.

M.P. 106 - 107 °C (DCM / petrol).

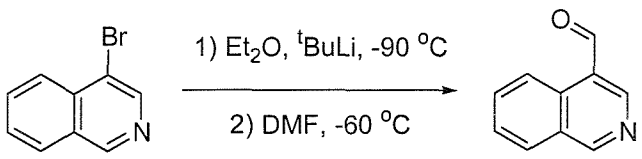
FT-IR (solid) υ_{max} 3055 w, 2926 w, 1629 m, 1590 m, 1579 m, 1497 m, 1468 s, 1401 w, 1384 w, 1348 w, 1268 m, 1224 s, 1106 m, 1032 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 293 (5600) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 9.26 (1H, s, Ar**H**), 7.97 (1H, d, *J* 8.1 Hz, Ar**H**), 7.77 (1H, d, *J* 8.1 Hz, Ar**H**), 7.67 (1H, t, *J* 7.0 Hz, Ar**H**), 7.56 (1H, t, *J* 7.0 Hz, Ar**H**), 7.49 (1H, s, Ar**H**), 7.26 (1H, s, Ar**H**), 6.75 (1H, s, Ar**H**), 5.93 (2H, s, O**CH$_2$**O), 3.17 (4H, s, R**CH$_2$CH$_2$**R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	154.0 (Ar, **C**), 152.3 (Ar, **C**H), 148.4 (Ar, **C**), 146.8 (Ar, **C**), 137.5 (Ar, **C**), 136.5 (Ar, **C**), 130.3 (Ar, **C**H), 127.5 (Ar, **C**H), 127.2 (Ar, **C**), 126.5 (Ar, **C**H), 126.2 (Ar, **C**H), 118.6 (Ar, **C**H), 118.5 (Ar, **C**H), 109.5 (Ar, **C**H), 101.4 (O**C**H_2O), 87.8 (Ar, **C**), 41.0 (Ar**C**H_2), 38.7 (Ar**C**H_2).
MS $^m/_z$ (ES)	405 (18 %; M(^{13}C)H^+), 404 (100 %; MH^+), 152 (24 %), 127 (62 %).
CHN	Found: C, 53.57; H, 3.50; N, 3.43. $C_{18}H_{14}INO_2$ requires C, 53.62; H, 3.50; N, 3.47.

4-Isoquinolinecarboxaldehyde **612**



C_9H_6BrN (208.05) $C_{10}H_7NO$ (157.17)

Following the procedure of Lutz *et al.*[117] The bromide **611** (1.80 g, 8.65 mmol) was dissolved in THF (40 mL) and cooled to – 90 °C. ^{t}BuLi (0.93 M in pentane, 10 mL, 9.3 mmol) was added dropwise over a period of 5 minutes and the mixture stirred for 40 minutes. DMF (4 mL, 3.77 g, 51.7 mmol) was added dropwise to the solution over a period of 5 minutes and the mixture warmed to – 60 °C over the next 3 hours. Brine ($NaCl_{(aq)}$, sat., 30 mL) was added and the mixture warmed to room temperature. The organic phase was separated and the aqueous phase extracted with Et_2O (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield the aldehyde **612** (423 mg, 2.69 mmol, 31 %) as a white solid.

Spectral and physical data were in accord with the literature.[117,199,200]

M.P. 105 - 106 °C (Et_2O). Lit. 103.5 - 104.5 °C (benzene).[199]

FT-IR (solid) υ_{max} 1693 s, 1620 w, 1568 w, 1502 m, 1463 w, 1374 w, 1232 w, 1151 w, 1068 w cm^{-1}.

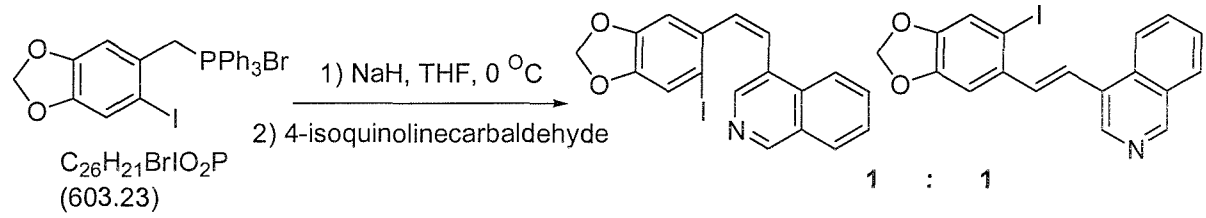
UV (MeOH) λ_{max} (ε) 316 (2730), 273 (2450) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 10.41 (1H, s, C**H**O), 9.45 (1H, s, Ar**H**), 9.22 (1H, d, *J* 8.8 Hz, Ar**H**), 8.96 (1H, s, Ar**H**), 8.10 (1H, d, *J* 8.1 Hz, Ar**H**), 7.94 (1H, t, *J* 7.7 Hz, Ar**H**), 7.76 (1H, t, *J* 7.7 Hz, Ar**H**).

^{13}C NMR δ_C ppm	192.9 (Ar**C**HO), 158.4 (Ar, **C**H), 153.0 (Ar, **C**H),
(75.5 MHz, $CDCl_3$)	133.6 (Ar, **C**), 132.4 (Ar, **C**), 128.5 (Ar, **C**H), 128.4 (Ar, **C**H),
	124.9 (Ar, **C**), 124.5 (Ar, **C**H), one Ar, **C** obscured.
MS $^m/_z$ (APCI)	199 (23 %; $[MH+MeCN]^+$), 158 (41 %; MH^+), 153 (27 %),
	127 (100 %).

4-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **613** and

4-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **614**



NaH (84 mg, 3.50 mmol, 60 % dispersion in oil) was washed with THF (10 mL) to remove the oil and stirred in suspension with THF (30 mL) at 0 °C. The iodide **362** (1.40 g, 2.32 mmol) was added and the reaction stirred for 2 hours. The mixture was cooled to 0 °C again and 4-isoquinolinecarbaldehyde **612** (350 mg, 2.23 mmol) added. The mixture was stirred for a further 3 hours and filtered to remove triphenylphosphine oxide. The solvent was removed *in vacuo* and the residues eluted through a silica column (1 :1, Et_2O : petrol → Et_2O) to give a mixture of the *E*- and *Z*-azastilbenes. Recrystallisation from EtOH yielded the *E*-azastilbene **614** (386 mg, 0.962 mmol, 43 %) as pale yellow crystals and concentration of the mother liquor afforded the *Z*-azastilbene **613** (391 g, 0.975 mmol, 44 %) as small pale yellow crystals.

Data For 4-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **614**

M.P. 176 - 177 °C (EtOH).

FT-IR (solid) υ_{max} 3002 w, 2895 w, 1618 m, 1571 m, 1499 s, 1468 s, 1385 m, 1236 w, 1224 s, 1164 w, 1108 m, 1097 w, 1034 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 342 (14680) nm (mol^{-1} dm^3 cm^{-1}).

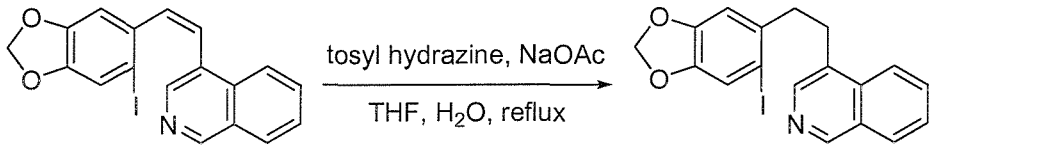
^{1}H NMR δ_H ppm	9.20 (1H, s, Ar**H**), 8.79 (1H, s, Ar**H**),
(300 MHz, $CDCl_3$)	8.17 (1H, d, *J* 8.8 Hz, Ar**H**), 8.02 (1H, d, *J* 8.1 Hz, Ar**H**),
	7.77 (1H, t, *J* 7.0 Hz, Ar**H**), 7.65 (1H, t, *J* 7.4 Hz, Ar**H**),
	7.44 (1H, d, *J* 16.2 Hz, RC**H**=CHR),
	7.36 (1H, d, *J* 15.4 Hz, RC**H**=CHR), 7.34 (1H, s, Ar**H**),
	7.26 (1H, s, Ar**H**), 6.04 (2H, s, OC$\mathbf{H_2}$O).
^{13}C NMR δ_C ppm	151.9 (Ar, **C**H), 148.7 (Ar, **C**), 148.4 (Ar, **C**), 139.8 (Ar, **C**H),
(75.5 MHz, DMSO)	135.5 (**C**H=CH), 132.9 (Ar, **C**), 132.9 (Ar, **C**), 130.8 (Ar, **C**H),
	128.0 (Ar, **C**H), 127.9 (Ar, **C**), 127.8 (Ar, **C**), 127.6 (Ar, **C**H),
	124.0 (Ar, **C**H), 123.3 (CH=**C**H), 118.1 (Ar, **C**H),
	106.5 (Ar, **C**H), 102.0 (O**C**H_2O), 90.3 (Ar, **C**).
MS $^m/_z$ (ES)	443 (9 %; $[MH+MeCN]^+$), 403 (10 %; $M(^{13}C)H^+$),
	402 (41 %; MH^+), 153 (33 %), 126 (100 %).
CHN	Found: C, 53.99; H, 3.01; N, 3.38. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

Data For 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]isoquinoline **613**

M.P.	112 - 113 °C (Et_2O / petrol).
FT-IR (solid) υ_{max}	3008 w, 2897 w, 1621 w, 1574 w, 1500 m, 1472 s, 1422 m,
	1377 w, 1248 w, 1225 m, 1160 w, 1112 m, 1037 m cm^{-1}.
UV (MeOH) λ_{max} (ε)	323 (3700) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm	9.16 (1H, s, Ar**H**), 8.29 (1H, s, Ar**H**),
(400 MHz, $CDCl_3$)	8.04 (1H, d, *J* 7.0 Hz, Ar**H**), 8.02 (1H, d, *J* 7.0 Hz, Ar**H**),
	7.77 (1H, t, *J* 7.5 Hz, Ar**H**), 7.67 (1H, t, *J* 7.8 Hz, Ar**H**),
	7.30 (1H, s, Ar**H**), 7.02 (1H, d, *J* 12.0 Hz, RC**H**=CHR),
	6.89 (1H, d, *J* 11.5 Hz, RC**H**=CHR), 6.33 (1H, s, Ar**H**),
	5.84 (2H, s, OC**H$_2$**O).
^{13}C NMR δ_C ppm	152.1 (Ar, **C**H), 148.4 (Ar, **C**), 148.2 (Ar, **C**), 143.7 (Ar, **C**H),
(100 MHz, $CDCl_3$)	137.9 (**C**H=CH), 134.6 (Ar, **C**), 134.1 (Ar, **C**), 131.0 (Ar, **C**H),
	128.6 (Ar, **C**), 128.6 (Ar, **C**H), 127.8 (Ar, **C**), 127.7 (Ar, **C**H),
	125.4 (Ar, **C**H), 124.0 (CH=**C**H), 118.7 (Ar, **C**H),
	110.2 (Ar, **C**H), 101.9 (O**C**H$_2$O), 89.0 (Ar, **C**).
MS $^{m}/_{z}$ (ES)	443 (15 %; $[MH+MeCN]^+$), 403 (19 %; $M(^{13}C)H^+$),
	402 (100 %; MH^+), 126 (98 %).
CHN	Found: C, 53.94; H, 3.02; N, 3.35. $C_{18}H_{12}INO_2$ requires
	C, 53.89; H, 3.01; N, 3.49.

3-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]isoquinoline **615**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{14}INO_2$ (403.21)

The iodide **613** (523 mg, 1.30 mmol) was refluxed in THF (15 mL) and water (15 mL) with tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) for 72 hours. The solution was cooled to room temperature and shaken with $K_2CO_{3(aq)}$ (2M, 100 mL) and Et_2O (100 mL). The organic phase was separated and the aqueous phase washed with Et_2O (4 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **615** (503 mg, 1.25 mmol, 96 %) as a white crystalline solid.

M.P. 110 - 111 °C (EtOH).

FT-IR (solid) υ_{max} 3064 w, 3036 w, 2929 w, 2862 w, 1622 w, 1566 w, 1506 m, 1475 s, 1385 m, 1275 m, 1222 s, 1128 m, 1110 m, 1028 s cm^{-1}.

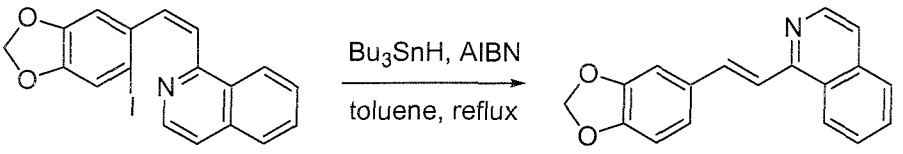
UV (MeOH) λ_{max} (ε) 314 (4960), 282 (7240) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$)
9.16 (1H, s, Ar**H**), 8.38 (1H, s, Ar**H**),
8.14 (1H, d, *J* 8.8 Hz, Ar**H**), 8.00 (1H, d, *J* 8.1 Hz, Ar**H**),
7.76 (1H, t, *J* 7.0 Hz, Ar**H**), 7.63 (1H, t, *J* 7.4 Hz, Ar**H**),
7.26 (1H, s, Ar**H**), 6.67 (1H, s, Ar**H**), 5.95 (2H, s, O**CH$_2$**O),
3.25 (2H, dd, *J* 9.6, 5.9 Hz, RC**H$_2$**CH$_2$R),
3.06 (2H, dd, *J* 9.6, 5.9 Hz, RCH$_2$C**H$_2$**R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	151.5 (Ar, **C**H), 148.5 (Ar, **C**), 147.0 (Ar, **C**), 143.0 (Ar, **C**H), 137.1 (Ar, **C**), 134.7 (Ar, **C**), 130.3 (Ar, **C**H), 130.2 (Ar, **C**), 128.4 (Ar, **C**), 128.4 (Ar, **C**H), 126.9 (Ar, **C**H), 122.9 (Ar, **C**H), 118.7 (Ar, **C**H), 109.4 (Ar, **C**H), 101.6 (O**C**H_2O), 87.6 (Ar, **C**), 41.8 (Ar**C**H_2), 30.9 (Ar**C**H_2).
MS $^m/_z$ (ES)	445 (17 %; $[MH+MeCN]^+$), 405 (21 %; $M(^{13}C)H^+$), 404 (100 %; MH^+), 152 (17 %), 127 (88 %).
CHN	Found: C, 53.76; H, 3.47; N, 3.46. $C_{18}H_{14}INO_2$ requires C, 53.62; H, 3.50; N, 3.47.

6.42 RADICAL CYCLISATIONS

1-[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]isoquinoline **616**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{13}NO_2$ (275.30)

The iodide **604** (142 mg, 0.354 mmol) was refluxed in toluene (150 mL) with Bu_3SnH (0.25 mL, 271 mg, 0.929 mmol) and AIBN (20 mg, 0.122 mmol) for 36 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (1 : 1, Et_2O : petrol) to yield isoquinoline **616** (96 mg, 0.341 mmol, 96 %) as a yellow crystalline solid.

M.P. 120 - 122 °C (EtOH).

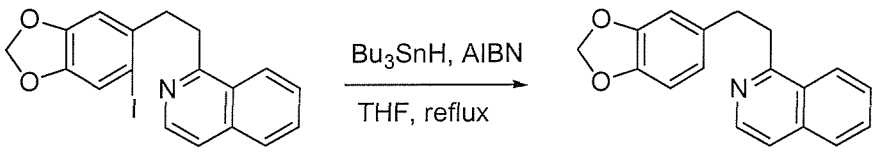
FT-IR (solid) υ_{max} 3047 w, 2914 w, 1625 w, 1601 w, 1582 w, 1551 m, 1499 w, 1489 s, 1442 s, 1392 w, 1336 m, 1248 s, 1095 w, 1036 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 359 (21730), 306 (9920), nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 8.55 (1H, d, *J* 5.0 Hz, Ar**H**), 8.11 (1H, d, *J* 8.5 Hz, Ar**H**), 7.84 (1H, d, *J* 8.0 Hz, Ar**H**), 7.67 (1H, t, *J* 7.3 Hz, Ar**H**), 7.61 (1H, d, *J* 5.5 Hz, Ar**H**), 7.51 (1H, t, *J* 7.5 Hz, Ar**H**), 6.96 (1H, d, *J* 12.6 Hz, RCH=C**H**R), 6.91 (1H, d, *J* 12.6 Hz, RC**H**=CHR), 6.62 (1H, d, *J* 8.0 Hz, Ar**H**), 6.57 (1H, d, *J* 8.0 Hz, Ar**H**), 6.44 (1H, s, Ar**H**), 5.82 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	158.2 (Ar, **C**), 147.6 (Ar, **C**), 147.5 (Ar, **C**), 142.7 (Ar, **C**H), 136.7 (Ar, **C**), 134.7 (**C**H=CH), 130.8 (Ar, **C**), 130.7 (Ar, **C**H), 127.7 (Ar, **C**H), 127.5 (Ar, **C**H), 126.9 (Ar, **C**H), 125.9 (CH=**C**H), 124.4 (Ar, **C**H), 120.5 (Ar, **C**H), 109.2 (Ar, **C**H), 108.4 (Ar, **C**H), 101.3 (O**C**H_2O). One Ar, **C** obscured.
MS $^m/_z$ (ES)	277 (19 %; M(^{13}C)H^+), 276 (100 %; MH^+), 127 (29 %).
CHN	Found: C, 78.32; H, 4.75; N, 4.98. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

1-[2-(1,3-Benzodioxol-5-yl)ethyl]isoquinoline **617**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{15}NO_2$ (277.32)

The iodide **605** (262 mg, 0.650 mmol) was refluxed in THF (150 mL) with Bu_3SnH (0.22 mL, 238 mg, 0.818 mmol) and AIBN (20 mg, 0.122 mmol) for 18 hours. The solvent was removed *in vacuo* and the residues were eluted through a silica column (1 : 9 : 490, NH_3 : MeOH : Et_2O) to yield isoquinoline **617** (109 mg, 0.393 mmol, 60 %) as a white crystalline solid.

M.P. 67 - 68 °C (Et_2O / petrol).

FT-IR (solid) υ_{max} 3050 w, 2889 w, 1622 w, 1586 w, 1561 m, 1500 m, 1487 s, 1440 m, 1387 w, 1356 m, 1241 s, 1186 m, 1036 s cm^{-1}.

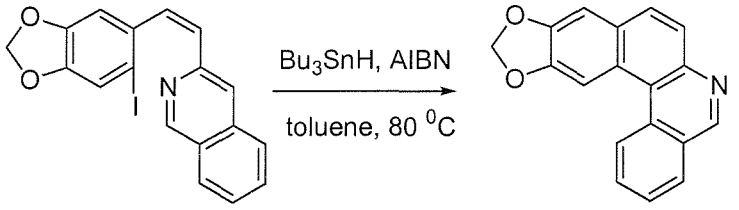
UV (MeOH) λ_{max} (ε) 317 (3590), 279 (7530) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.48 (1H, d, *J* 5.9 Hz, Ar**H**), 8.14 (1H, d, *J* 8.1 Hz, Ar**H**), 7.83 (1H, d, *J* 8.1 Hz, Ar**H**), 7.67 (1H, t, *J* 7.7 Hz, Ar**H**), 7.59 (1H, t, *J* 7.0 Hz, Ar**H**), 7.54 (1H, d, *J* 5.9 Hz, Ar**H**), 6.82 (1H, s, Ar**H**), 6.76 (2H, s, Ar**H**), 5.93 (2H, s, O**CH_2**O), 3.59 - 3.54 (2H, m, RC**H_2**CH_2R), 3.17 - 3.10 (2H, m, RCH_2C**H_2**R).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 160.9 (Ar, **C**), 147.6 (Ar, **C**), 145.8 (Ar, **C**), 141.9 (Ar, **C**H), 136.2 (Ar, **C**), 135.7 (Ar, **C**), 129.8 (Ar, **C**H), 127.4 (Ar, **C**H), 127.1 (Ar, **C**H), 126.9 (Ar, **C**), 125.0 (Ar, **C**H), 121.2 (Ar, **C**H), 119.5 (Ar, **C**H), 109.0 (Ar, **C**H), 108.3 (Ar, **C**H), 100.8 (O**C**H_2O), 37.5 (Ar**C**H_2), 35.2 (Ar**C**H_2).

MS $^{m}/_{z}$ (ES)	279 (19 %; M(^{13}C)H^{+}), 278 (100 %; MH^{+}), 127 (40 %).
CHN	Found: C, 77.78; H, 5.50; N, 5.05. $C_{18}H_{15}NO_2$ requires C, 77.96; H, 5.45; N, 5.05.

[1,3]Dioxolo[4'5':4,5]benzo[*a*]phenanthridine **618**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{11}NO_2$ (273.29)

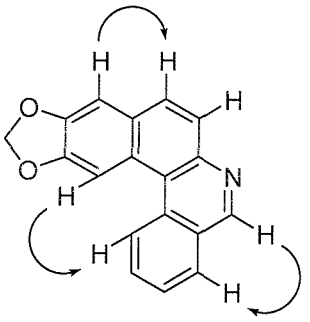
The iodide **608** (200 mg, 0.498 mmol) in toluene (150 mL) was stirred at 80 °C with Bu_3SnH (0.16 mL, 173 mg, 0.595 mmol) and AIBN (30 mg, 0.183 mmol) for 72 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 80 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield **618** (86 mg, 0.315 mmol, 63 %) which was recrystallised from Et_2O as a white crystalline solid.

M.P. 211 - 212 °C (Et_2O).

FT-IR (solid) υ_{max} 3055 w, 2987 w, 2914 w, 1637 w, 1610 w, 1590 w, 1500 w, 1488 w, 1468 m, 1438 s, 1349 w, 1247 s, 1168 m, 1141 m, 1034 s cm^{-1}.

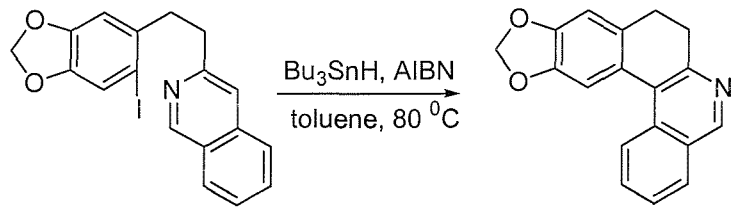
UV (MeOH) λ_{max} (ε) 300 (28150), 278 (31670), 256 (28600) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, DMSO) 9.51 (1H, s, Ar**H**), 9.15 (1H, d, *J* 8.5 Hz, Ar**H**), 8.58 (1H, s, Ar**H**), 8.44 (1H, d, *J* 8.0 Hz, Ar**H**), 8.17 (1H, d, *J* 8.5 Hz, Ar**H**), 8.11 (1H, t, *J* 7.6 Hz, Ar**H**), 8.05 (1H, d, *J* 8.5 Hz, Ar**H**), 7.94 (1H, t, *J* 7.3 Hz, Ar**H**), 7.74 (1H, s, Ar**H**), 6.38 (2H, s, O**CH$_2$**O).



^{1}H NMR δ_H ppm (400 MHz, DMSO)	n.O.e Irradiation of the signal at δ_H 9.51 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.44 (1H, d, *J* 8.0 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 8.58 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 9.15 (1H, d, *J* 8.5 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.74 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.17 (1H, d, *J* 8.5 Hz, Ar**H**).
^{13}C NMR δ_C ppm (100 MHz, DMSO)	152.7 (Ar, **C**H), 149.2 (Ar, **C**), 147.8 (Ar, **C**), 143.6 (Ar, **C**), 132.0 (Ar, **C**), 131.7 (Ar, **C**H), 130.4 (Ar, **C**), 129.4 (Ar, **C**H), 129.4 (Ar, **C**H), 127.6 (Ar, **C**), 127.5 (Ar, **C**H), 126.8 (Ar, **C**H), 126.1 (Ar, **C**H), 125.8 (Ar, **C**), 120.0 (Ar, **C**), 106.0 (Ar, **C**H), 104.9 (Ar, **C**H), 102.4 (O**C**H$_2$O).
MS $^{m}/_{z}$ (ES)	275 (4 %; M(^{13}C)H$^+$), 274 (32 %; MH$^+$), 169 (48 %), 126 (100 %).
CHN	Found: C, 78.84; H, 4.06; N, 5.08. $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.

7,8-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*a*]phenanthridine **619**



$C_{18}H_{14}INO_2$ (403.21) $C_{18}H_{13}NO_2$ (275.30)

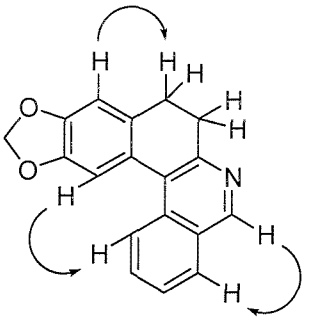
The iodide **610** (280 mg, 0.694 mmol) in toluene (150 mL) was stirred at 80 °C with Bu_3SnH (0.25 mL, 271 mg, 0.929 mmol) and AIBN (30 mg, 0.183 mmol) for 36 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 80 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (1 :1, Et_2O : petrol → Et_2O) to yield **619** (126 mg, 0.458 mmol, 66 %) as a yellow solid.

M.P. 105 - 110 °C (Et_2O, poor crystals).

FT-IR (solid) υ_{max} 2948 w, 2893 w, 1620 w, 1568 w, 1502 m, 1484 s, 1425 w, 1371 m, 1275 m, 1266 m, 1216 m, 1162 w, 1040 s cm^{-1}.

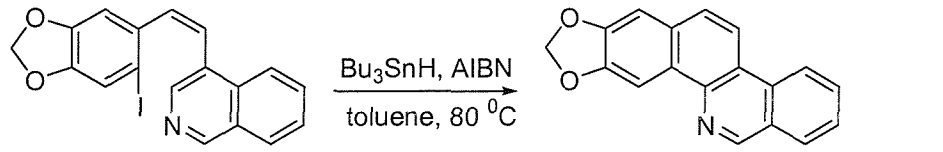
UV (MeOH) λ_{max} (ε) 351 (19870), 304 (18580), 252 (29510) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, DMSO) 9.04 (1H, s, Ar**H**), 8.41 (1H, d, *J* 8.1 Hz, Ar**H**), 7.97 (1H, d, *J* 8.1 Hz, Ar**H**), 7.69 (1H, t, *J* 7.7 Hz, Ar**H**), 7.55 (1H, t, *J* 7.4 Hz, Ar**H**), 7.39 (1H, s, Ar**H**), 6.88 (1H, s, Ar**H**), 6.04 (2H, s, O**CH$_2$**O), 3.12 (2H, t, *J* 6.6 Hz RC**H$_2$**CH$_2$R), 2.83 (2H, t, *J* 7.0 Hz RCH$_2$C**H$_2$**R).



^{1}H NMR δ_H ppm (400 MHz, DMSO)	n.O.e Irradiation of the signal at δ_H 9.04 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.97 (1H, d, *J* 8.1 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.39 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.41 (1H, d, *J* 8.1 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 6.88 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.83 (2H, t, *J* 7.0 Hz $RCH_2C\mathbf{H_2}R$).
^{13}C NMR δ_C ppm (100 MHz, DMSO)	152.1 (Ar, **C**), 150.0 (Ar, **C**H), 146.7 (Ar, **C**), 146.1 (Ar, **C**), 133.6 (Ar, **C**), 132.3 (Ar, **C**), 130.4 (Ar, **C**H), 128.6 (Ar, **C**), 128.4 (Ar, **C**H), 126.3 (Ar, **C**), 126.0 (Ar, **C**H), 124.6 (Ar, **C**), 124.1 (Ar, **C**H), 109.1 (Ar, **C**H), 108.7 (Ar, **C**H), 101.2 ($O\mathbf{C}H_2O$), 32.5 ($Ar\mathbf{C}H_2$), 29.3 ($Ar\mathbf{C}H_2$).
MS $^{m}/_{z}$ (ES)	277 (19 %; M(^{13}C)H$^+$), 276 (100 %; MH$^+$), 127 (24 %).
CHN	Found: C, 78.30; H, 4.86; N, 5.04. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

[1,3]Dioxolo[4'5':4,5]benzo[*c*]phenanthridine **620**



$C_{18}H_{12}INO_2$ (401.20) $C_{18}H_{11}NO_2$ (273.29)

The iodide **613** (300 mg, 0.748 mmol) in toluene (150 mL) was stirred at 80 °C with Bu_3SnH (0.26 mL, 281 mg, 0.967 mmol) and AIBN (20 mg, 0.122 mmol) for 24 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (1 :1, Et_2O : petrol) to yield **620** (163 mg, 0.596 mmol, 80 %) as a yellow crystalline solid.

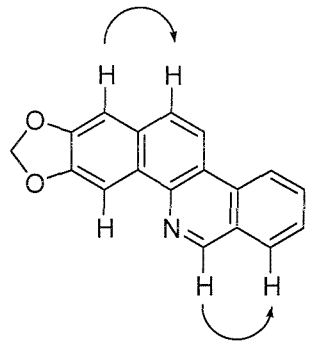
Spectral and physical data were in accord with the literature.[133]

M.P. 195 - 196 °C (DCM / petrol).
Lit. 201 - 204 °C (no solvent given).[133]

FT-IR (solid) υ_{max} 2958 w, 2902 w, 1637 w, 1614 w, 1580 w, 1522 w, 1496 w, 1475 w, 1460 s, 1280 w, 1255 s, 1193 s, 1133 m, 1037 s cm^{-1}.

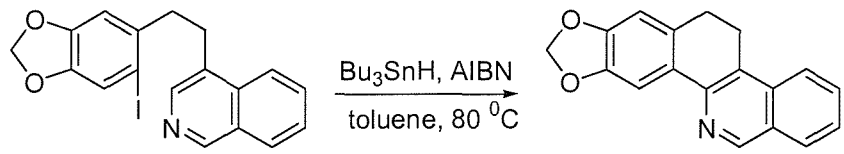
UV (MeOH) λ_{max} (ε) 305 (20080), 265 (57040), 234 (39480) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, D_3COD) 9.51 (1H, s, Ar**H**), 8.87 (1H, d, *J* 8.8 Hz, Ar**H**), 8.65 (1H, d, *J* 8.8 Hz, Ar**H**), 8.58 (1H, s, Ar**H**), 8.29 (1H, d, *J* 7.4 Hz, Ar**H**), 8.03 (1H, d, *J* 8.8 Hz, Ar**H**), 7.97 (1H, t, *J* 7.7 Hz, Ar**H**), 7.81 (1H, t, *J* 7.4 Hz, Ar**H**), 7.56 (1H, s, Ar**H**), 6.23 (2H, s, O**CH$_2$**O).



^{1}H NMR δ_H ppm (300 MHz, D_3COD)	n.O.e Irradiation of the signal at δ_H 9.51 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.29 (1H, d, *J* 7.4 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 8.58 (1H, s, Ar**H**) caused no n.O.e. enhancement. n.O.e Irradiation of the signal at δ_H 7.56 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 8.03 (1H, d, *J* 8.8 Hz, Ar**H**).
^{13}C NMR δ_C ppm (75.5 MHz, D_3COD)	151.9 (Ar, **C**H), 148.2 (Ar, **C**), 148.2 (Ar, **C**), 140.1 (Ar, **C**), 132.2 (Ar, **C**), 131.3 (Ar, **C**H), 129.9 (Ar, **C**), 128.7 (Ar, **C**H), 128.2 (Ar, **C**), 127.3 (Ar, **C**H), 127.0 (Ar, **C**H), 126.1 (Ar, **C**), 122.4 (Ar, **C**H), 119.8 (Ar, **C**), 118.8 (Ar, **C**H), 104.5 (Ar, **C**H), 101.5 (O**C**H_2O), 101.1 (Ar, **C**H).
MS $^{m}/_{z}$ (ES)	275 (3 %; M(^{13}C)H^+), 274 (17 %; MH^+), 153 (56 %), 112 (95 %), 105 (100 %).
CHN	Found: C, 78.97; H, 4.07; N, 5.09. $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.

5,6-Dihydro[1,3]dioxolo[4'5':4,5]benzo[*c*]phenanthridine **621**



$C_{18}H_{14}INO_2$ (403.21) $C_{18}H_{13}NO_2$ (275.30)

The iodide **615** (300 mg, 0.744 mmol) in toluene (150 mL) was stirred at 80 °C with Bu_3SnH (0.24 mL, 260 mg, 0.892 mmol) and AIBN (20 mg, 0.122 mmol) for 48 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (1 :1, Et_2O : petrol) to yield **621** (145 mg, 0.527 mmol, 71 %) as a yellow crystalline solid.

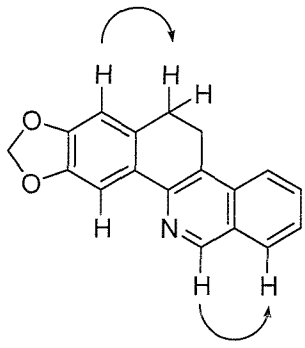
Spectral and physical data were in accord with the literature.[133]

M.P. 111 - 113 °C (EtOH). Lit. 119 °C (no solvent given).[133]

FT-IR (solid) υ_{max} 2954 w, 2896 w, 1615 m, 1570 m, 1370 m, 1478 s, 1458 m, 1430 m, 1362 m, 1286 m, 1258 w, 1244 w, 1229 s, 1166 w, 1035 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 326 (23650), 259 (26520), 232 (40780) nm (mol^{-1} dm^3 cm^{-1}).

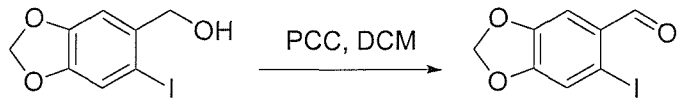
^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$) 9.18 (1H, s, Ar**H**), 8.02 (1H, d, *J* 8.5 Hz, Ar**H**), 7.96 (1H, d, *J* 8.0 Hz, Ar**H**), 7.94 (1H, s, Ar**H**), 7.70 (1H, t, *J* 7.5 Hz, Ar**H**), 7.53 (1H, t, *J* 7.5 Hz, Ar**H**), 6.76 (1H, s, Ar**H**), 5.99 (2H, s, O**CH$_2$**O), 3.27 (2H, t, *J* 7.5 Hz R**CH$_2$**CH_2R), 2.96 (2H, t, *J* 7.5 Hz RCH_2**CH$_2$**R).



^{1}H NMR δ_H ppm (400 MHz, $CDCl_3$)	n.O.e Irradiation of the signal at δ_H 9.18 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 7.96 (1H, d, *J* 8.0 Hz, Ar**H**). n.O.e Irradiation of the signal at δ_H 7.94 (1H, s, Ar**H**) caused no n.O.e. enhancement. n.O.e Irradiation of the signal at δ_H 6.76 (1H, s, Ar**H**) caused an n.O.e. enhancement at δ_H 2.96 (2H, t, *J* 7.5 Hz $RCH_2C\mathbf{H_2}R$).
^{13}C NMR δ_C ppm (100 MHz, $CDCl_3$)	151.2 (Ar, **C**H), 148.1 (Ar, **C**), 147.5 (Ar, **C**), 146.3 (Ar, **C**), 135.0 (Ar, **C**), 131.9 (Ar, **C**), 130.7 (Ar, **C**H), 130.0 (Ar, **C**), 128.8 (Ar, **C**H), 128.0 (Ar, **C**), 126.4 (Ar, **C**H), 124.0 (Ar, **C**), 123.0 (Ar, **C**H), 108.3 (Ar, **C**H), 106.3 (Ar, **C**H), 101.4 ($O\mathbf{C}H_2O$), 28.3 ($Ar\mathbf{C}H_2$), 23.5 ($Ar\mathbf{C}H_2$).
MS $^m/_z$ (ES)	277 (15 %; $M(^{13}C)H^+$), 276 (80 %; MH^+), 127 (100 %).
CHN	Found: C, 78.40; H, 4.87; N, 5.08. $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

6.43 AVICINE AND NORAVICINE

6-Iodo-1,3-benzodioxole-5-carbaldehyde **659**



$C_8H_7IO_3$ (278.04) $C_8H_5IO_3$ (276.03)

Following the procedure of Padwa *et al.*[140] The alcohol **360** (13.6 g, 48.9 mmol) in DCM (500 mL) was stirred at 0 °C and PCC (21.3 g, 98.8 mmol) added. The suspension was warmed to room temperature and stirred for 2 hours before being filtered through a plug of silica. The plug was then washed with DCM (500 mL) and the organic phases combined and the solvent removed *in vacuo*. The residues were recrystallised from Et_2O to yield **659** (13.0 g, 47.1 mmol, 96 %) as a white crystalline solid.

Spectral and physical data were in accord with the literature.[140,201,202]

M.P. 110 - 111 °C (Et_2O). Lit. 108.5 - 110.5 °C (methanol).[201]

FT-IR (solid) υ_{max} 2908 w, 2859 w, 1663 s, 1610 m, 1594 w, 1501 m, 1491 s, 1407 m, 1386 m, 1343 w, 1265 s, 1113 s, 1041 m cm^{-1}.

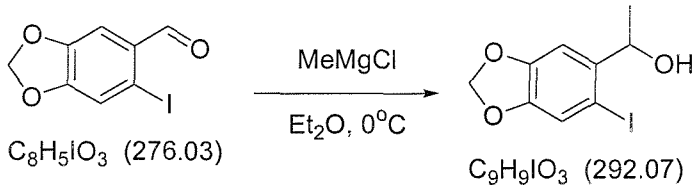
UV (MeOH) λ_{max} (ε) 327 (4880), 276 (6750), 239 (18750) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 9.89 (1H, s, C**H**O), 7.38 (1H, s, Ar**H**), 7.34 (1H, s, Ar**H**), 6.09 (2H, s, OC**H**$_2$O).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 194.5 (ArCHO), 153.6 (Ar, **C**), 149.2 (Ar, **C**), 129.6 (Ar, **C**), 119.4 (Ar, **C**H), 108.9 (Ar, **C**H), 102.7 (O**C**H$_2$O), 93.4 (Ar, **C**).

MS $^m/_z$ (CI) 277 (41 %; MH^+), 276 (67 %; M^+), 150 (100 %; $[MH\text{-}I]^+$).

1-(6-Iodo-1,3-benzodioxol-5-yl)ethanol **670**



$C_8H_5IO_3$ (276.03) $C_9H_9IO_3$ (292.07)

The aldehyde **659** (13.3 g, 48.2 mmol) in Et_2O (500 mL) was stirred at 0 °C and MeMgCl (3M in THF, 17 mL, 51.0 mmol) added. The mixture was stirred for 3 hours and $HCl_{(aq)}$ (2M, 100 mL) slowly added. The reaction was warmed to room temperature and the aqueous phase separated and washed with ethyl acetate (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were recrystallised from Et_2O to yield **670** (13.8 g, 47.2 mmol, 98 %) as a white crystalline solid.

Spectral and physical data were in accord with the literature.[141]

M.P. 184 - 185 °C (MeCN). Lit. 72 - 73 °C (diethyl ether / hexane).[141]

FT-IR (solid) υ_{max} 2974 w, 2902 w, 1500 w, 1472 s, 1402 w, 1384 w, 1368 w, 1232 s, 1078 m, 1039 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 290 (3030), 236 (5340) nm (mol^{-1} dm^3 cm^{-1}).

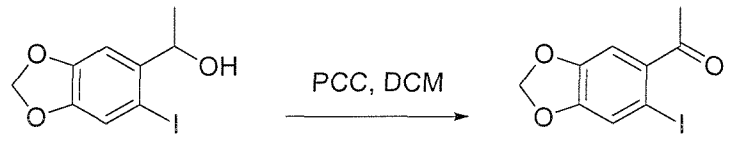
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 7.20 (1H, s, Ar**H**), 7.06 (1H, s, Ar**H**), 6.04 (1H, s, OC**H**HO), 6.00 (1H, s, OCH**H**O), 4.35 (1H, q, *J* 6.4 Hz, ArC**H**OHCH$_3$), 1.28 (3H, d, *J* 6.6 Hz, ArCHOHC**H$_3$**).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 149.1 (Ar, **C**), 147.9 (Ar, **C**), 139.2 (Ar, **C**), 118.2 (Ar, **C**H), 106.7 (Ar, **C**H), 101.6 (O**C**H$_2$O), 86.2 (Ar, **C**), 78.4 (Ar, Ar**C**HOHCH$_3$), 23.2 (ArCHOH**C**H$_3$).

MS $^{m}/_{z}$ (CI) 275 (59 %; $[MH\text{-}H_2O]^+$), 165 (39 %; $[M\text{-}I]^+$), 149 (100 %; $[MH\text{-}OH\text{-}I]^+$).

HRMS (EI) Found: $[MH\text{-}H_2O]^+$, 274.9563. $C_9H_8IO_2$ requires 274.9569.

1-(6-Iodo-1,3-benzodioxol-5-yl)ethanone **671**



$C_9H_9IO_3$ (292.07) $C_9H_7IO_3$ (290.05)

The alcohol **670** (13.8 g, 47.2 mmol) in DCM (500 mL) was stirred at 0 °C and PCC (21.0 g, 97.4 mmol) added. The suspension was warmed to room temperature and stirred for 72 hours before being filtered through a plug of silica and the solvent removed *in vacuo*. The residues were recrystallised from EtOH to yield the acetophenone **671** (13.2 g, 45.5 mmol, 96 %) as a white crystalline solid.

Spectral and physical data were in accord with the literature.[141]

M.P. 79 - 80 °C (EtOH). Lit. 84.5 - 85.5 °C (diethyl ether / hexane).[141]

FT-IR (solid) υ_{max} 3047 w, 2911 w, 1691 s, 1608 m, 1505 m, 1486 s, 1381 m, 1356 m, 1334 m, 1250 s, 1135 m, 1034 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 301 (5200), 270 (6590) nm (mol^{-1} dm^3 cm^{-1}).

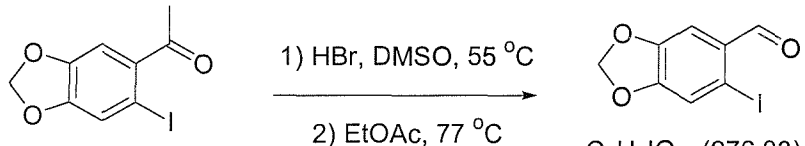
^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 7.37 (1H, s, Ar**H**), 7.06 (1H, s, Ar**H**), 6.06 (2H, s, O**C**$\mathbf{H_2}$O), 2.58 (3H, s, ArCOC$\mathbf{H_3}$).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 199.6 (Ar**C**OCH_3), 150.4 (Ar, **C**), 148.2 (Ar, **C**), 136.5 (Ar, **C**), 120.7 (Ar, **C**H), 109.2 (Ar, **C**H), 102.4 (O**C**H_2O), 81.4 (Ar, **C**), 29.3 (ArCO**C**H_3).

MS $^m/_z$ (CI) 290 (29 %; M^+), 275 (22 %; $[M\text{-}Me]^+$), 165 (100 %; $[MH\text{-}I+H]^+$), 164 (80 %; $[MH\text{-}I]^+$), 149 (73 %; $[MH\text{-}I\text{-}Me]^+$).

CHN Found: C, 37.17; H, 2.40. $C_9H_7IO_3$ requires C, 37.27; H, 2.43.

6-Iodo-1,3-benzodioxole-5-carbaldehyde **659**



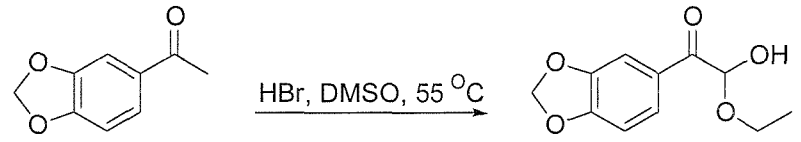
$C_9H_7IO_3$ (290.05)

$C_8H_5IO_3$ (276.03)

The acetophenone **671** (5.5 g, 18.8 mmol) in DMSO (40 mL, 44.0 g, 564 mmol) and $HBr_{(aq)}$ (8.8M, 10 mL, 88 mmol) was warmed to 55 °C and stirred for 18 hours. The mixture was cooled, poured onto water (400 mL) and washed with ethyl acetate (4 x 200 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were recrystallised from ethyl acetate to yield **659** (3.1 g, 11.2 mmol, 60 %) as a white crystalline solid, resulting from oxidation followed by loss of CO.

Data identical to those described previously.

1-(1,3-Benzodioxol-5-yl)-2-ethoxy-2-hydroxy-1-ethanone **677**



$C_9H_8O_3$ (164.16) $C_{11}H_{12}O_5$ (224.21)

Following the procedure of Floyd *et al.*[139] The acetophenone **676** (8.2 g, 50.0 mmol) in DMSO (85 mL, 93.6 g, 1.2 mol) and $HBr_{(aq)}$ (8.8M, 17 mL, 150 mmol) was warmed to 55 °C and stirred for 24 hours. The mixture was cooled, poured onto water (400 mL) and the resultant white precipitate separated by filtration and recrystallised from ethanol to yield **677** (7.2 g, 32.2 mmol, 64 %) as a white crystalline solid.

Spectral and physical data were in accord with the literature.[203]

M.P. 101 - 102 °C (EtOH).

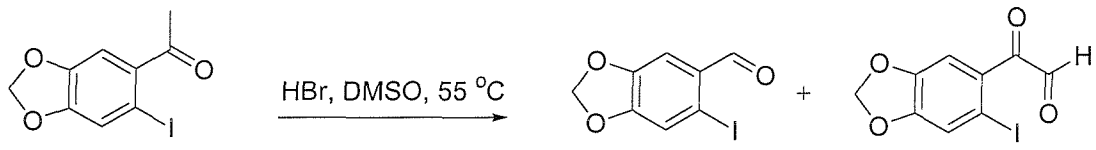
FT-IR (solid) υ_{max} 3363 br. m, 2979 w, 2905 w, 1681 s, 1624 w, 1599 m, 1503 m, 1491 m, 1435 s, 1313 m, 1253 s, 1114 w, 1034 m cm^{-1}.

UV (MeOH) λ_{max} (ε) 310 (6600), 273 (5360) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, DMSO)
7.72 (1H, dd, *J* 8.1, 1.5 Hz, ArCOC**H**(OH)(OEt)),
7.49 (1H, s, Ar**H**), 7.06 (1H, d, *J* 8.1 Hz, Ar**H**),
6.91 (1H, d, *J* 8.8 Hz, Ar**H**), 6.15 (2H, s, OC**H$_2$**O),
5.44 (1H, d, *J* 8.1 Hz, O**H**),
3.78 (1H, dq, *J* 8.1, 7.0 Hz, OC**H**HCH$_3$),
3.59 (1H, dq, *J* 8.1, 7.0 Hz, OCH**H**CH$_3$),
2.51 (1H, t, *J* 7.1 Hz, OCH$_2$C**H$_3$**).

^{13}C NMR δ_C ppm (75.5 MHz, DMSO)	197.8 (Ar**C**OCH(OH)(OEt)), 156.9 (Ar, **C**), 152.7 (Ar, **C**), 133.1 (Ar, **C**), 131.3 (Ar, **C**H), 113.7 (Ar, **C**H), 113.3 (Ar, **C**H), 107.2 (O**C**H$_2$O), 100.3 (ArCO**C**H(OH)(OEt)), 67.4 (O**C**H$_2$CH$_3$), 20.4 (OCH$_2$**C**H$_3$).
MS $^m/_z$ (CI)	248 (12 %; [M(^{13}C)+Na]$^+$), 247 (100 %; [M+Na]$^+$), 179 (14 %).
CHN	Found: C, 58.83; H, 5.40. $C_{11}H_{12}O_5$ requires C, 58.93; H, 5.39.

6-Iodo-1,3-benzodioxol-5-yl(oxo)acetaldehyde **672**



$C_9H_7IO_3$ (290.05) $C_8H_5IO_3$ (276.03) $C_9H_5IO_4$ (304.04)

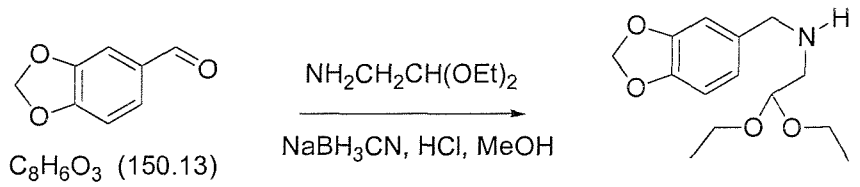
Following the procedure of Floyd *et al.*[139] The acetophenone **671** (12.0 g, 41.1 mmol) was dissolved in DMSO (85 mL, 93.6 g, 1.2 mol) and $HBr_{(aq)}$ (8.8M, 20 mL, 176 mmol) added dropwise over a period of 5 minutes. The reaction was warmed to 55 °C and stirred for 18 hours. The mixture was cooled, poured onto water (400 mL) and washed with ethyl acetate (5 x 200 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude residues (13.6 g) were analysed by NMR and used without further purification in the formation of **673**.

KEY SIGNALS:

^{1}H NMR δ_H ppm	9.88 (1H, s, ArC**H**O) - **659**,
(300 MHz, $CDCl_3$)	9.83 (1H, s, ArCOC**H**O) - **672**.

^{13}C NMR δ_C ppm	194.6 (Ar**C**HO) - **659**,
(75.5 MHz, $CDCl_3$)	187.0 (ArCOCHO), 171.3 (Ar**C**OCHO) - **672**.

N-(1,3-Benzodioxol-5-ylmethyl)-*N*-(2,2-diethoxyethyl)amine **658**



$C_8H_6O_3$ (150.13)

$C_{14}H_{21}NO_4$ (267.32)

The aldehyde **250** (5.0 g, 33.3 mmol), amine (4.85 mL, 4.44 g, 33.4 mmol) and $HCl_{(aq)}$ (10M, 1 mL, 10 mmol) were stirred for 36 hours at room temperature in methanol (200 mL) with $NaBH_3CN$ (2.1 g, 33.4 mmol). The solvent was removed *in vacuo* and the residues taken up into ethyl acetate (50 mL). The solution was washed with $NaOH_{(aq)}$ (2M, 50 mL), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (1 : 5, Et_2O : petrol → Et_2O) to yield **658** (7.74 g, 28.9 mmol, 87 %) as a colourless oil.

Spectral and physical data were in accord with the literature.[204]

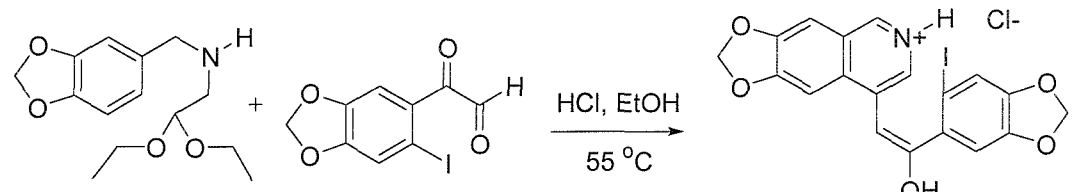
FT-IR (solid) υ_{max} 2975 m, 2883 br. m, 1608 w, 1504 m, 1489 s, 1442 m, 1373 w, 1246 s, 1128 m, 1060 m, 1040 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 283 (3220), 232 (3490) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 6.85 (1H, s, Ar**H**), 6.77 (2H, s, 2 x Ar**H**), 5.95 (2H, s, $OC\mathbf{H}_2O$), 4.62 (1H, t, *J* 5.5 Hz, $RNHCH_2C\mathbf{H}(OEt)_2$), 3.72 (2H, s, $ArC\mathbf{H}_2NHR$), 3.75 - 3.65 (2H, m, 2 x $OC\mathbf{H}HCH_3$), 3.59 - 3.49 (2H, m, 2 x $OCH\mathbf{H}CH_3$), 2.73 (2H, d, *J* 5.2 Hz, $RNHC\mathbf{H}_2CH(OEt)_2$), 1.51 (1H, s, $R_2N\mathbf{H}$), 1.22 (6H, t, *J* 7.0 Hz, 2 x $OCH_2C\mathbf{H}_3$).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$)	147.7 (Ar, **C**), 146.5 (Ar, **C**), 134.2 (Ar, **C**), 121.2 (Ar, **C**H), 108.7 (Ar, **C**H), 108.1 (Ar, **C**H), 102.2 ($RNHCH_2\mathbf{C}H(OEt)_2$), 100.9 ($O\mathbf{C}H_2O$), 62.4 ($O\mathbf{C}H_2CH_3$), 53.7 ($Ar\mathbf{C}H_2NHR$), 51.4 ($RNH\mathbf{C}H_2CH(OEt)_2$), 15.4 ($OCH_2\mathbf{C}H_3$).
MS $^m/_z$ (CI)	269 (12 %; $M(^{13}C)H^+$), 268 (100 %; MH^+), 221 (12 %), 176 (19 %), 127 (17 %).
HRMS (EI)	Found: $[M+Na]^+$, 290.1361. $NaC_{14}H_{21}NO_4$ requires 290.1363.

8-[2-(6-Iodo-1,3-benzodioxol-5-yl)-2-oxoethyl][1,3]dioxolo[4,5-*g*]isoquinolin-6-ium chloride **674**



$C_{14}H_{21}NO_4$ (267.32) $C_9H_5IO_4$ (304.04) $C_{19}H_{13}ClINO_5$ (497.67)

Following the procedure of Dyke and Sainsbury.[135] The amine **658** (1.0 g, 3.74 mmol), glyoxal **672** (3.0 g, crude) and $HCl_{(aq)}$ (6M, 50 mL) were stirred for 2 hours at 55 °C in ethanol (20 mL). The solvents were removed *in vacuo* and the residues recrystallised from ethanol to yield **674** (506 mg, 1.02 mmol, 27 %) as pale yellow cubes.

M.P. 271 - 279 °C (EtOH).

FT-IR (solid) υ_{max} 2908 w, 1655 m, 1624 w, 1611 m, 1519 w, 1497 m, 1473 s, 1399 m, 1380 m, 1241 s, 1126 m, 1030 s cm^{-1}.

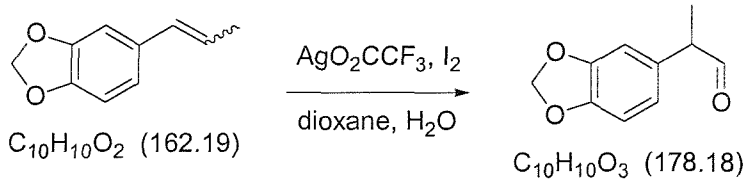
UV (MeOH+HCl, pH 1) λ_{max} (ε) 421 (2400), 310 (29280) nm (mol^{-1} dm^3 cm^{-1}).

UV (MeOH+NH_3, pH 14) λ_{max} (ε) 422 (42210), 290 (23920) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (400 MHz, DMSO) 9.70 (1H, s, Ar**H**), 8.68 (1H, d, *J* 6.8 Hz, ArC**H**=COHAr), 8.50 (1H, d, *J* 6.8 Hz, ArCH=CO**H**Ar), 7.98 (2H, d, *J* 4.8 Hz, 2 x Ar**H**), 7.91 (1H, s, Ar**H**), 6.58 (2H, s, OC**H**$_2$O), 6.55 (2H, s, 2 x Ar**H**), 6.36 (2H, s, OC**H**$_2$O).
Note that peaks have been assigned to the enol form.

^{13}C NMR δ_C ppm (100 MHz, DMSO)	191.5 (Ar**C**OCH$_2$Ar / Ar**C**OH=CHAr), 157.1 (Ar, **C**), 152.1 (Ar, **C**), 151.9 (Ar, **C**), 148.5 (Ar, **C**), 147.3 (Ar, **C**H), 138.4 (Ar, **C**), 135.8 (Ar, **C**H), 130.3 (Ar, **C**), 125.6 (Ar, **C**), 124.1 (Ar, **C**H), 121.6 (Ar, **C**H), 111.1 (Ar, **C**H), 104.9 (Ar, **C**H), 104.7 (O**C**H$_2$O), 103.7 (Ar**C**H=COHAr), 103.6 (O**C**H$_2$O), 85.9 (Ar, **C**), 66.5 (ArCO**C**H$_2$Ar). One Ar **C** signal is obscured. Note that several peaks can only be assigned to either the enol or keto form.
MS $^m/_z$ (CI)	463 (23 %; [M(^{13}C)-Cl]$^+$), 462 (100 %; [M-Cl]$^+$), 148 (19 %).
HRMS (EI)	Found: [M-Cl]$^+$, 461.9823. $C_{19}H_{13}INO_5$ requires 461.9833.

2-(1,3-Benzodioxol-5-yl)propanal **680**



$C_{10}H_{10}O_2$ (162.19) → $C_{10}H_{10}O_3$ (178.18)

Following the procedure of Kikuchi *et al.*[145] Isosafrole **679** (5.0 g, 30.8 mmol), iodine (12.0 g, 47.3 mmol) and silver trifluoroacetate (12.0 g, 54.3 mmol) were stirred in a mixture of dioxane (150 mL) and water (5 mL) for 1 hour at room temperature. The mixture was filtered through celite and the solvent removed *in vacuo*. The residues taken up into diethyl ether (100 mL) and stirred with $NaHSO_3$ (70 g) and KI (8 g) in water (120 mL) for 24 hours. The resultant precipitate was filtered and washed with diethyl ether (50 mL) and then dissolved in water (50 mL). The mixture was basified with $NaOH_{(aq)}$ (6M, 10 mL) and extracted into diethyl ether (6 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo* to yield **680** (1.62 g, 9.09 mmol, 30 %) as a colourless oil.

Spectral and physical data were in accord with the literature.[144,145]

FT-IR (solid) υ_{max} 2977 w, 2896 w, 1726 s, 1608 w, 1504 s, 1488 s, 1441 m, 1247 s, 1040 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 280 (1860) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 9.64 (1H, d, *J* 1.5 Hz, RC**H**O), 6.82 (1H, d, *J* 8.0 Hz, Ar**H**), 6.69 (1H, s, Ar**H**), 6.68 (1H, d, *J* 7.9 Hz, Ar**H**), 5.97 (2H, s, OC**H$_2$**O), 3.56 (1H, q, *J* 6.8 Hz, ArC(CH_3)**H**CHO), 1.41 (3H, d, *J* 7.0 Hz, ArC(C**H$_3$**)HCHO).

^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 200.9 (R**C**HO), 148.3 (Ar, **C**), 147.0 (Ar, **C**), 131.3 (Ar, **C**), 121.6 (Ar, **C**H), 108.8 (Ar, **C**H), 108.5 (Ar, **C**H), 101.2 (O**C**H_2O), 52.6 (Ar**C**H(CH_3)CHO), 14.7 (ArCH(**C**H_3)CHO).

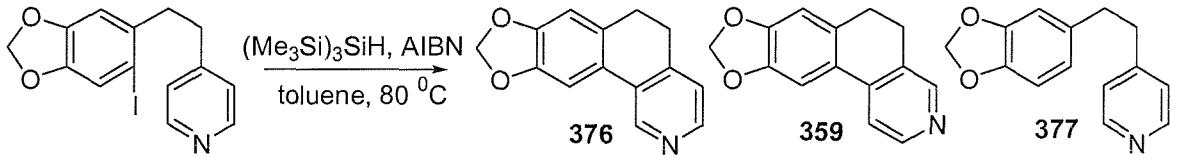
MS $^{m}/_{z}$ (CI) 196 (76 %; $[M+H_2O]^+$), 178 (90 %; M^+), 165 (47 %), 149 (100 %; $[M-CHO]^+$), 91 (56 %).

HRMS (ES) Found: $[3M+Na]^+$, 557.1787. $NaC_{30}H_{30}O_9$ requires 557.1782.

6.5 EXPERIMENTAL FOR CHAPTER 5

6.52 SILICON AND GERMANIUM HYDRIDES

The $(Me_3Si)_3SiH$ mediated cyclisation of
4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **372** (100 mg, 0.283 mmol) in toluene (30 mL) was stirred under nitrogen at 80 °C with $(Me_3Si)_3SiH$ (0.132 mL, 106 mg, 0.428 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The mixture was cooled to room temperature and $NaOH_{(aq)}$ (2M, 30 mL). The aqueous phase was separated and washed with diethyl ether (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (61 mg) of **376** (unisolated, 25 mg, 111 μmol, 39 %), **359** (unisolated, 26 mg, 115 μmol, 41 %) and **377** (unisolated, 10 mg, 45.4 μmol, 16 %).

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

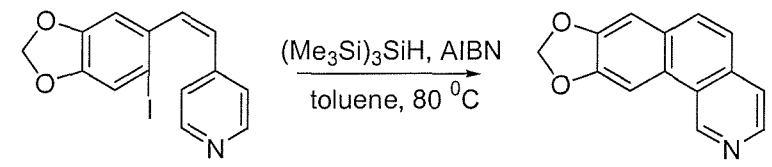
Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **376**

Data For 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**

Data identical to those described previously.

The $(Me_3Si)_3SiH$ mediated cyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



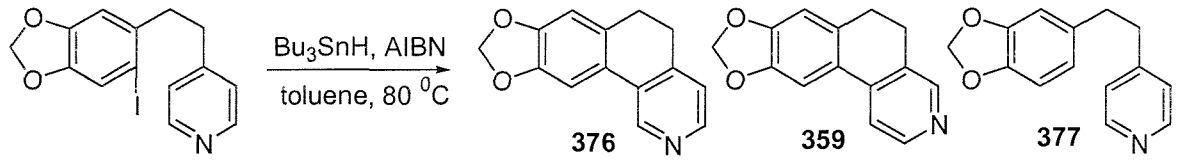
$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

The azastilbene **368** (100 mg, 0.285 mmol) in toluene (30 mL) was stirred under nitrogen at 80 °C with $(Me_3Si)_3SiH$ (0.132 mL, 106 mg, 0.428 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The mixture was cooled to room temperature and $NaOH_{(aq)}$ (2M, 30 mL). The aqueous phase was separated and washed with diethyl ether (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **345** (isolated, 63 mg, 282 μmol, 99 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

The Bu_3SnH mediated cyclisation of 4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **372** (500 mg, 1.42 mmol) in toluene (200 mL) was stirred under argon at 80 °C with Bu_3SnH (0.48 mL, 519 mg, 1.78 mmol) and AIBN (20 mg, 0.122 mmol) for 40 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield firstly a 1:1 mixture of **376** (100 mg, 0.44 mmol, 31 %) and **377** (100 mg, 0.44 mmol, 31 %) followed by **359** (58 mg, 0.26 mmol, 18 %). The mixture of **376** and **377** was separated by fractional recrystallisation from EtOH, with **376** crystallising first.

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

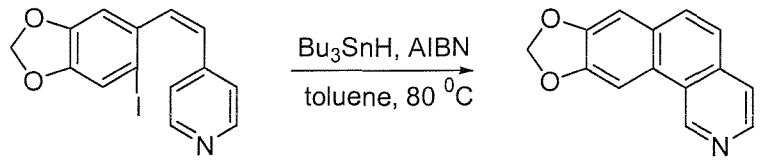
Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **376**

Data For 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**

Data identical to those described previously.

The Bu_3SnH mediated cyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

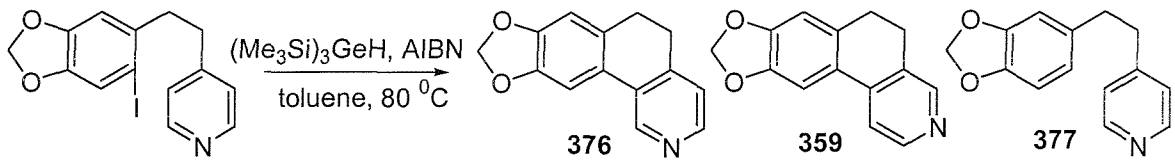
The azastilbene **368** (450 mg, 1.28 mmol) in toluene (110 mL) was stirred under argon at 80 °C with Bu_3SnH (0.45 mL, 487 mg, 1.67 mmol) and AIBN (20 mg, 0.122 mmol) for 72 hours. The mixture was cooled to room temperature and stirred for 18 hours with $KF_{(aq)}$ (2M, 100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to yield **345** (280 mg, 1.25 mmol, 98 %), recrystallised from EtOH as a yellow solid.

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

The $(Me_3Si)_3GeH$ mediated cyclisation of

4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **372** (100 mg, 0.283 mmol) in toluene (30 mL) was stirred under nitrogen at 80 °C with $(Me_3Si)_3GeH$ (0.133 mL, 125 mg, 0.426 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The mixture was cooled to room temperature and $NaOH_{(aq)}$ (2M, 30 mL). The aqueous phase was separated and washed with diethyl ether (3 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (62 mg) of **376** (unisolated, 22 mg, 95.7 μmol, 34 %), **359** (unisolated, 12 mg, 53.0 μmol, 19 %) and **377** (unisolated, 28 mg, 121 μmol, 43 %).

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

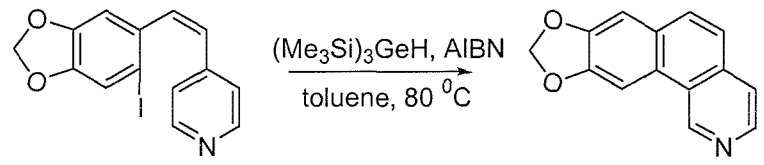
Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **376**

Data For 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**

Data identical to those described previously.

The $(Me_3Si)_3GeH$ mediated cyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

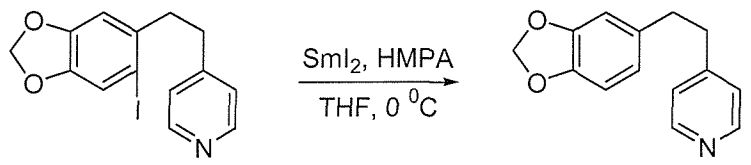
The azastilbene **368** (100 mg, 0.285 mmol) in toluene (30 mL) was stirred under nitrogen at 80 °C with $(Me_3Si)_3GeH$ (0.133 mL, 125 mg, 0.426 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The mixture was cooled to room temperature and $NaOH_{(aq)}$ (2M, 30 mL). The aqueous phase was separated and washed with diethyl ether (2 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **345** (isolated, 62 mg, 278 μmol, 97 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

6.53 ALTERNATIVES TO GROUP 14 METAL HYDRIDES

The attempted SmI_2 mediated cyclisation of
4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372**



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{13}NO_2$ (227.26)

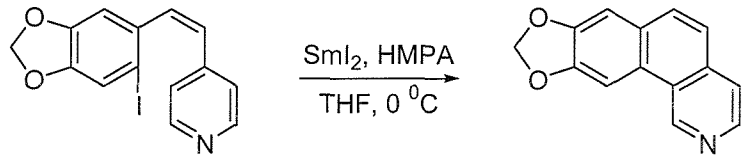
The iodide **372** (100 mg, 0.283 mmol) and HMPA (1 mL, 1.03 g, 5.75 mmol) in degassed THF (20 mL) was stirred under argon at 0 °C. SmI_2 in THF (0.1M, 10 mL, 1.00 mmol) was added dropwise over a period of 5 minutes and the deep blue colour of the SmI_2 turned deep purple (complexation with HMPA). The reaction was stirred for a further 18 hours at room temperature. $K_2CO_{3(aq)}$ (2M, 30 mL) was added to quench the reaction and the aqueous phase washed with diethyl ether (2 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were then taken up in chloroform (30 mL), washed with water (5 x 30 mL, to remove most of the HMPA), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR and then eluted through a silica column (Et_2O) to give **377** (isolated, 52 mg, 229 μmol, 81 %) as the only product.

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

Data identical to those described previously.

The SmI_2 mediated cyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{11}NO_2$ (223.23)

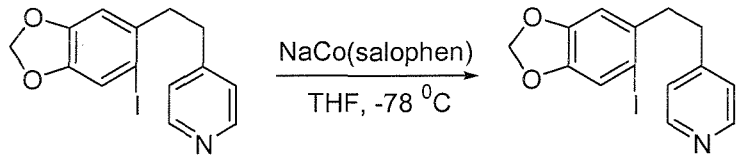
The azastilbene **368** (100 mg, 0.285 mmol) and HMPA (1 mL, 1.03 g, 5.75 mmol) in degassed THF (20 mL) was stirred under argon at 0 °C. SmI_2 in THF (0.1M, 10 mL, 1.00 mmol) was added dropwise over a period of 5 minutes and the deep blue colour of the SmI_2 turned deep purple (complexation with HMPA). The reaction was stirred for a further 18 hours at room temperature. $K_2CO_{3(aq)}$ (2M, 30 mL) was added to quench the reaction and the aqueous phase washed with diethyl ether (2 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were then taken up in chloroform (30 mL), washed with water (5 x 30 mL, to remove most of the HMPA), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR and then eluted through a silica column (Et_2O) to give **345** (isolated, 48 mg, 215 μmol, 75 %) as the only product.

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

The attempted cobalt mediated cyclisation of

4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372**

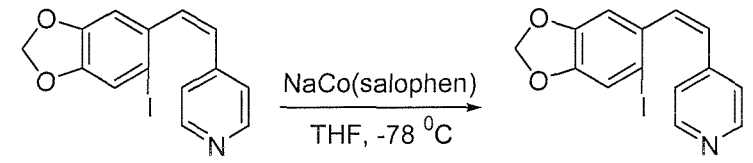


$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{12}INO_2$ (353.16)

Sodium (75 mg, 3.26 mmol) was slowly added to mercury (7.5 g, 37.4 mmol) under argon to form an amalgam. THF (25 mL) was then added along with Co(II)(salophen) complex (250 mg, 0.670 mmol). The mixture was stirred for 2 hours and the dull green solution of Co(I)Na(salophen) decanted away from the amalgam. The mixture was cooled to - 78 °C and the iodide **372** (100 mg, 0.283 mmol) in THF (5 mL) added. The reaction was stirred at - 78 °C for a further 2 hours and then warmed to room temperature over a period of 1 hour. The reaction was filtered through flurosil along with diethyl ether (50 mL) and the solvent removed *in vacuo*. The residues were analysed crude by NMR and then eluted through a silica column (Et_2O) to give starting material **372** (isolated, 82 mg, 232 μmol, 82 %) as the only compound recovered.

The attempted cobalt mediated cyclisation of

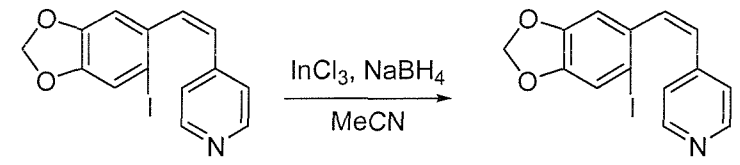
4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{10}INO_2$ (351.14)

Sodium (75 mg, 3.26 mmol) was slowly added to mercury (7.5 g, 37.4 mmol) under argon to form an amalgam. THF (25 mL) was then added along with Co(II)(salophen) complex (250 mg, 0.670 mmol). The mixture was stirred for 2 hours and the dull green solution of Co(I)Na(salophen) decanted away from the amalgam. The mixture was cooled to - 78 °C and the azastilbene **368** (100 mg, 0.285 mmol) in THF (5 mL) added. The reaction was stirred at - 78 °C for a further 2 hours and then warmed to room temperature over a period of 1 hour. The reaction was filtered through flurosil along with diethyl ether (50 mL) and the solvent removed *in vacuo*. The residues were analysed crude by NMR and then eluted through a silica column (Et_2O) to give starting material **368** (isolated, 64 mg, 182 μmol, 64 %) as the only compound recovered.

The attempted indium(III) hydride mediated cyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**

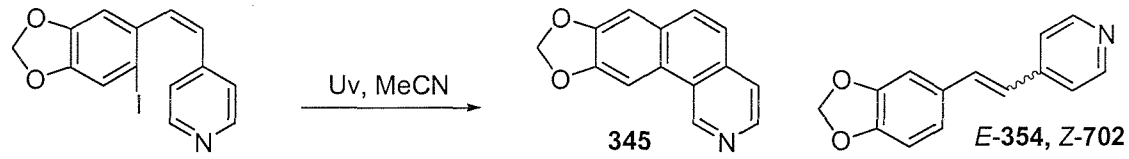


$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{10}INO_2$ (351.14)

$InCl_3$ (22 mg, 0.010 mmol) was heated at 150 °C under high vacuum for 1.5 hours. MeCN (5 mL) was added and the mixture cooled to - 78 °C under argon. $NaBH_4$ (38 mg, 1.00 mmol) was added and the reaction warmed to room temperature over a period of 5 minutes. The azastilbene **368** (100 mg, 0.285 mmol) was added and the reaction was stirred for a further 2 hours. The black heterogeneous solution was diluted with $NaOH_{(aq)}$ (2M, 30 mL) and DCM (30 mL). The aqueous phase was separated and washed with DCM (2 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR and then eluted through a silica column (Et_2O) to give starting material **368** (isolated, 78 mg, 222 μmol, 78 %) as the only compound recovered.

6.54 INITIATION BY LIGHT

The photocyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23) $C_{14}H_{11}NO_2$ (225.24)

The azastilbene **368** (100 mg, 0.285 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a sodium vapour lamp for 48 hours. The solvent was removed *in vacuo* and the residues were dissolved in $NaOH_{(aq)}$ (2M, 30 mL) and ethyl acetate (30 mL). The aqueous phase was separated and washed with ethyl acetate (30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (50.7 mg) of **345** (unisolated, 18 mg, 81.7 μmol, 29 %), **354** (unisolated, 9.7 mg, 43.1 μmol, 15 %), **702** (unisolated, 11 mg, 50.6 μmol, 18 %) and recovered starting material **368** (unisolated, 12 mg, 34.6 μmol, 12 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

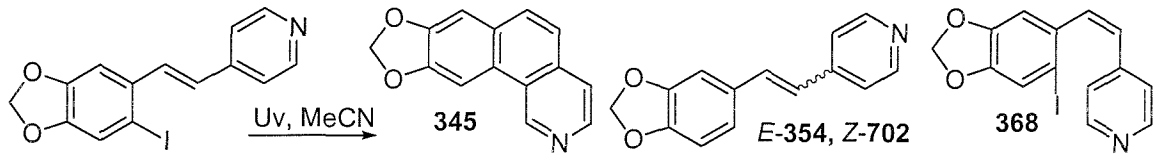
Data for 4-[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **354**

Data identical to those described previously.

Data for 4-[(*Z*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **702**

Data identical to those described previously.

The photocyclisation of 4-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **369**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{10}INO_2$ (351.14)

The azastilbene **369** (100 mg, 0.285 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a sodium vapour lamp for 12 hours. The solvent was removed *in vacuo* and the residues were dissolved in $NaOH_{(aq)}$ (2M, 30 mL) and DCM (30 mL). The aqueous phase was separated and washed with DCM (30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (61 mg) of **345** (unisolated, 19 mg, 84.1 μmol, 30 %), **354** (unisolated, 8.0 mg, 35.5 μmol, 12 %), **702** (unisolated, 11 mg, 49.9 μmol, 17 %) and **368** (unisolated, 23 mg, 66.1 μmol, 23 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

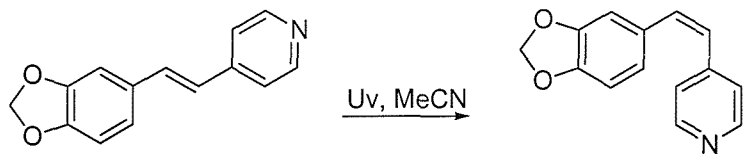
Data for 4-[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **354**

Data for 4-[(*Z*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **702**

Data for 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**

Data identical to those described previously.

The attempted photocyclisation of 4[(*E*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **354**



$C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{11}NO_2$ (225.24)

The azastilbene **354** (100 mg, 0.444 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a sodium vapour lamp for 24 hours. The solvent was removed *in vacuo* and the residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give **702** (isolated, 88 mg, 0.390 mmol, 88 %) as a pale yellow viscose oil and recovered starting material **354** (isolated, 10 mg, 0.045 mmol, 10 %).

Data for 4-[(*Z*)-2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine **702**

FT-IR (CH_2Cl_2) υ_{max} 3019 w, 2891 w, 1593 s, 1540 w, 1502 m, 1484 s, 1440 s, 1411 w, 1352 w, 1237 s, 1117 w, 1090 w, 1035 s cm^{-1}.

UV (MeOH) λ_{max} (ε) 310 (1340) nm (mol^{-1} dm^3 cm^{-1}).

^{1}H NMR δ_H ppm (300 MHz, $CDCl_3$) 8.44 (2H, d, *J* 5.2 Hz, Ar**H**), 7.11 (2H, d, *J* 5.1 Hz, Ar**H**), 6.68 (2H, s, 2 x Ar**H**), 6.64 (1H, s, Ar**H**), 6.63 (1H, d, *J* 12.5 Hz, ArC**H**=CHAr), 6.36 (1H, d, *J* 12.5 Hz, ArCH=C**H**Ar), 5.89 (2H, s, OC$\mathbf{H_2}$O).

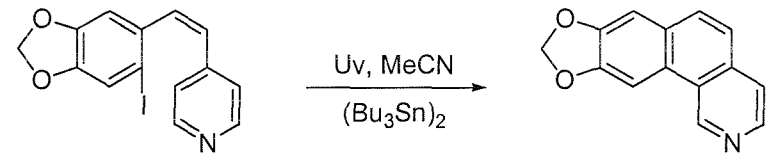
^{13}C NMR δ_C ppm (75.5 MHz, $CDCl_3$) 149.9 (Ar, 2 x **C**H), 147.6 (Ar, **C**), 147.3 (Ar, **C**), 145.1 (Ar, **C**), 133.5 (**C**H=CH), 129.9 (Ar, **C**), 126.4 (CH=**C**H), 123.5 (Ar, 2 x **C**H), 123.0 (Ar, **C**H), 108.7 (Ar, **C**H), 108.4 (Ar, **C**H), 101.1 (O**C**H_2O).

MS $^m/_z$ (APCl) 227 (14 %), 226 (100 %; MH^+).

HRMS (ES) Found: MH^+, 226.0862. $C_{14}H_{12}NO_2$ requires 226.0863.

The $(Bu_3Sn)_2$ mediated photocyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

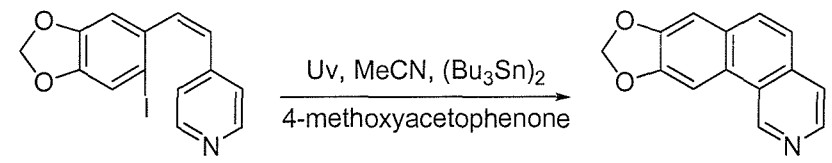
The azastilbene **368** (100 mg, 0.285 mmol) with $(Bu_3Sn)_2$ (0.15 mL, 172 mg, 0.296 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a sodium vapour lamp for 24 hours. The solvent was removed *in vacuo* and the residues were dissolved in $NaOH_{(aq)}$ (2M, 50 mL) and DCM (100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (61 mg) of **345** (unisolated, 17 mg, 74.5 μmol, 26 %) and recovered starting material **368** (unisolated, 44 mg, 125 μmol, 44 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

The $(Bu_3Sn)_2$ mediated photocyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** with a triplet sensitizer



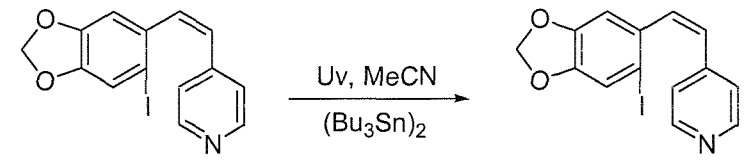
$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

The azastilbene **368** (100 mg, 0.285 mmol) with $(Bu_3Sn)_2$ (0.15 mL, 172 mg, 0.296 mmol) and 4-methoxyacetophenone (80 mg, 0.533 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a sodium vapour lamp for 24 hours. The solvent was removed *in vacuo* and the residues were dissolved in $NaOH_{(aq)}$ (2M, 100 mL) and DCM (100 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (79 mg) of **345** (unisolated, 15 mg, 68.2 μmol, 24 %) and recovered starting material **368** (unisolated, 64 mg, 182 μmol, 64 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

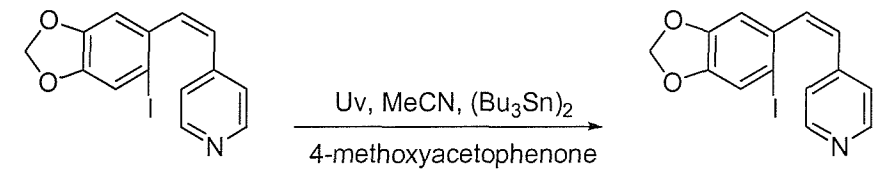
The attempted $(Bu_3Sn)_2$ mediated photocyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368**



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{10}INO_2$ (351.14)

The azastilbene **368** (100 mg, 0.285 mmol) with $(Bu_3Sn)_2$ (0.15 mL, 172 mg, 0.296 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a daylight lamp for 12 hours. The solvent was removed *in vacuo* and the residues were dissolved in ethyl acetate (50 mL). This was stirred for 12 hours with $KF_{(aq)}$ (2M, 50 mL) and basified with $NaOH_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give recovered starting material **368** (isolated, 86 mg, 245 μmol, 86 %).

The attempted $(Bu_3Sn)_2$ mediated photocyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** with a triplet sensitizer

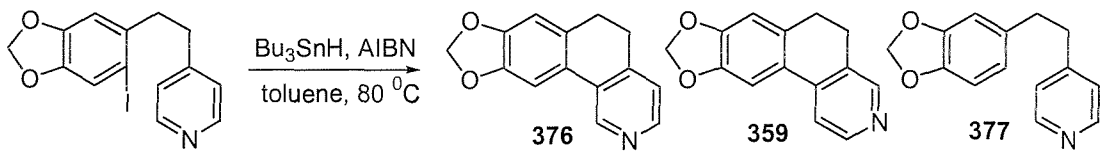


$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{10}INO_2$ (351.14)

The azastilbene **368** (100 mg, 0.285 mmol) with $(Bu_3Sn)_2$ (0.15 mL, 172 mg, 0.296 mmol) and 4-methoxyacetophenone (80 mg, 0.533 mmol) in acetonitrile (100 mL) was stirred under nitrogen in a quartz photocell. The reaction was irradiated using a daylight lamp for 12 hours. The solvent was removed *in vacuo* and the residues were dissolved in ethyl acetate (30 mL). This was stirred for 12 hours with $KF_{(aq)}$ (2M, 30 mL) and basified with $NaOH_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give recovered starting material **368** (isolated, 96 mg, 273 μmol, 96 %).

6.55 The Effect of Tributyltin Hydride Concentration

General procedure for the cyclisation of
4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372** at different concentrations



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

The iodide **372** in toluene was stirred under nitrogen at 80 °C with Bu_3SnH and AIBN for 12 hours. The mixture was cooled to room temperature and stirred for a further 12 hours with $KF_{(aq)}$. The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture of **376, 377** and **359** upon which the individual unisolated yields are based (Table 1).

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

Data identical to those described previously.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **376**

Data identical to those described previously.

Data for 5,6-dihydro[1,3]dioxolo[4'5':4,5]benzo[*f*]isoquinoline **359**

Data identical to those described previously.

Table 1 Reaction conditions and yields

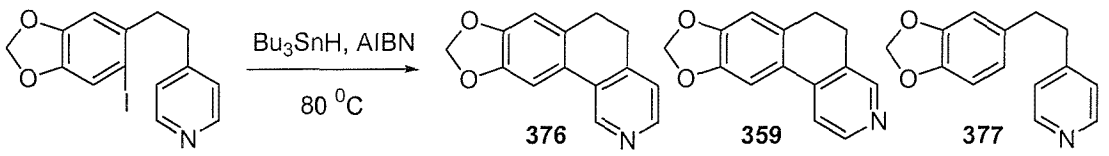
Iodide concentration	Reagents and solvents	Unisolated product yields
0.590 mmol dm^{-3}	Iodide (12.5 mg, 35.4 μmol) Bu_3SnH (13 μL, 14 mg, 48.3 μmol) AIBN (2.0 mg, 12.2 μmol) PhMe (60 mL) $KF_{(aq)}$ (2M, 30 mL)	7.8 mg total mass; **376** (4.8 mg, 21.3 μmol, 60 %) **359** (3.0 mg, 13.2 μmol, 37 %)
1.18 mmol dm^{-3}	Iodide (25 mg, 70.8 μmol) Bu_3SnH (25 μL, 27 mg, 92.8 μmol) AIBN (3.0 mg, 18.3 μmol) PhMe (60 mL) $KF_{(aq)}$ (2M, 30 mL)	15.8 mg total mass; **376** (7.3 mg, 32.5 μmol, 46 %) **359** (5.9 mg, 26.0 μmol, 37 %) **377** (2.5 mg, 11.1 μmol, 16 %)
2.37 mmol dm^{-3}	Iodide (50 mg, 142 μmol) Bu_3SnH (50 μL, 56 mg, 186 μmol) AIBN (5.0 mg, 30.4 μmol) PhMe (60 mL) $KF_{(aq)}$ (2M, 30 mL)	30.4 mg total mass; **376** (12.0 mg, 52.4 μmol, 37 %) **359** (5.4 mg, 24.1 μmol, 13 %) **377** (13.0 mg, 56.0 μmol, 39 %)
4.72 mmol dm^{-3}	Iodide (100 mg, 283 μmol) Bu_3SnH (100 μL, 108 mg, 371 μmol) AIBN (10 mg, 61 μmol) PhMe (60 mL) $KF_{(aq)}$ (2M, 50 mL)	62 mg total mass; **376** (25 mg, 115 μmol, 41 %) **359** (12 mg, 54.3 μmol, 19 %) **377** (25 mg, 110 μmol, 39 %)

Table 1 Reaction conditions and yields

Iodide concentration	Reagents and solvents	Unisolated product yields
9.43 mmol dm^{-3}	Iodide (100 mg, 283 μmol) Bu_3SnH (100 μL, 108 mg, 371 μmol) AIBN (10 mg, 61 μmol) PhMe (30 mL) $KF_{(aq)}$ (2M, 30 mL)	60.8 mg total mass; **376** (25 mg, 113 μmol, 40 %) **359** (6.8 mg, 30.4 μmol, 11 %) **377** (29 mg, 126 μmol, 45 %)
18.9 mmol dm^{-3}	Iodide (100 mg, 283 μmol) Bu_3SnH (100 μL, 108 mg, 371 μmol) AIBN (10 mg, 61 μmol) PhMe (15 mL) $KF_{(aq)}$ (2M, 50 mL)	55 mg total mass; **376** (20 mg, 89.3 μmol, 32 %) **377** (35 mg, 153 μmol, 54 %)
37.7 mmol dm^{-3}	Iodide (100 mg, 283 μmol) Bu_3SnH (100 μL, 108 mg, 371 μmol) AIBN (10 mg, 61 μmol) PhMe (7.5 mL) $KF_{(aq)}$ (2M, 50 mL)	57 mg total mass; **376** (18 mg, 77.8 μmol, 27 %) **359** (13 mg, 59.9 μmol, 21 %) **377** (26 mg, 115 μmol, 41 %)
75.5 mmol dm^{-3}	Iodide (100 mg, 283 μmol) Bu_3SnH (100 μL, 108 mg, 371 μmol) AIBN (10 mg, 61 μmol) PhMe (3.75 mL) $KF_{(aq)}$ (2M, 50 mL)	58.7 mg total mass; **376** (14 mg, 63.8 μmol, 23 %) **359** (10.7 mg, 47.7 μmol, 17 %) **377** (34 mg, 149 μmol, 53 %)

6.56 SOLVENT EFFECTS

General procedure for the cyclisation of
4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372** in different solvents



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{11}NO_2$ (225.24) $C_{14}H_{13}NO_2$ (227.26)

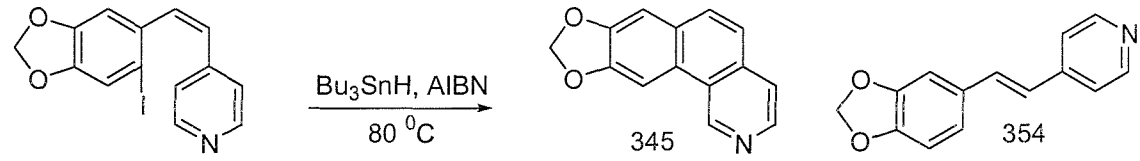
The iodide **372** (100 mg, 0.283 mmol) in solvent (30 mL) was stirred under nitrogen at 80 °C (or reflux for solvents with a lower boiling point) with Bu_3SnH (0.1 mL, 108 mg, 0.371 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The mixture was cooled to room temperature and stirred for a further 12 hours with $KF_{(aq)}$ (2M, 30 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture of **376, 377** and **359** upon which the individual unisolated yields are based (Table 2).

Table 2 Reaction conditions and yields

Solvent	Unisolated product yields
Benzene	63 mg total mass; **376** (34 mg, 150 μmol, 53 %) **359** (7.1 mg, 31.7 μmol, 11 %) **377** (22 mg, 98.8 μmol, 35 %)
Toluene	60.8 mg total mass; **376** (25 mg, 113 μmol, 40 %) **359** (6.8 mg, 30.4 μmol, 11 %) **377** (29 mg, 126 μmol, 45 %)
THF	58 mg total mass; **377** (58 mg, 255 μmol, 90 %)

General procedure for the cyclisation of

4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** in different solvents



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23) $C_{14}H_{11}NO_2$ (225.24)

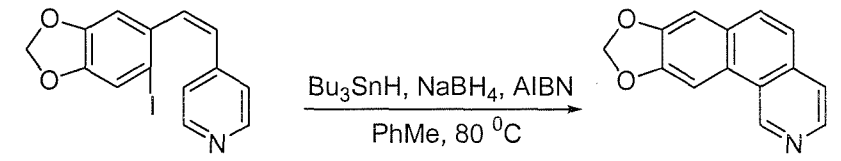
The azastilbene **368** (100 mg, 0.285 mmol) in solvent (30 mL) was stirred under nitrogen at 80 °C (or reflux for solvents with a lower boiling point) with Bu_3SnH (0.1 mL, 108 mg, 0.371 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The mixture was cooled to room temperature and stirred for a further 12 hours with $KF_{(aq)}$ (2M, 30 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture of **345** and **354** upon which the individual unisolated yields are based (Table 3).

Table 3 Reaction conditions and yields

Solvent	Unisolated product yields
Toluene (isolated product yield scaled down by 4.5 as the reaction was carried out on x 4.5 scale)	62 mg total mass; **345** (62 mg, 278 μmol, 98 %) (isolated)
THF	54 mg total mass; **345** (11 mg, 47.2 μmol, 17 %) **354** (43 mg, 193 μmol, 68 %)
Ethanol	58 mg total mass; **345** (33 mg, 147 μmol, 52 %) **354** (31 mg, 136 μmol, 48 %)
Methanol (unisolated product yields scaled up by 4 as the reaction was carried out on one quarter scale)	54 mg total mass; **345** (23 mg, 103 μmol, 36 %) **354** (31 mg, 138 μmol, 49 %)

6.57 CATALYTIC TIN SYSTEMS

Cyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** with catalytic tin and sodium borohydride in toluene



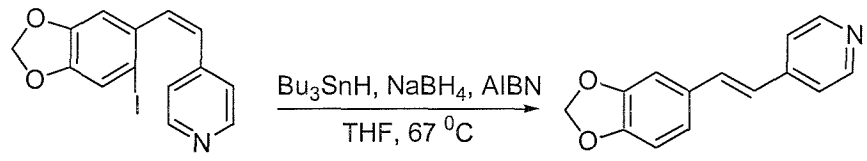
$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23)

The azastilbene **368** (100 mg, 0.285 mmol) in toluene (30 mL) was stirred under nitrogen at 80 °C with Bu_3SnH (0.02 mL, 21.6 mg, 0.074 mmol), sodium borohydride (15 mg, 0.397 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The reaction was cooled to room temperature and stirred for a further 12 hours with $KF_{(aq)}$ (2M, 50 mL). The organic phase was separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (67 mg) of **345** (unisolated, 6 mg, 0.027 mmol, 9 %) and recovered starting material **368** (unisolated, 81 mg, 0.230 mmol, 81 %).

Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

Attempts at cyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** with catalytic tin and sodium borohydride in THF



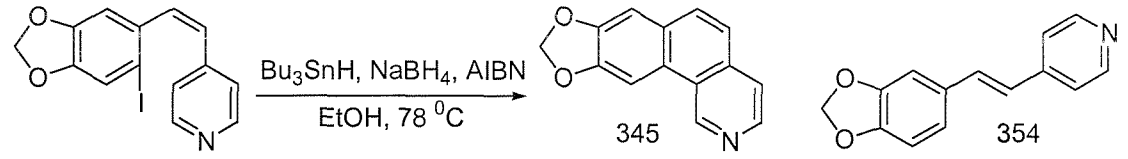
$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_{11}NO_2$ (225.24)

The azastilbene **368** (100 mg, 0.285 mmol) in THF (30 mL) was stirred under nitrogen at 67 °C with Bu_3SnH (0.02 mL, 21.6 mg, 0.074 mmol), sodium borohydride (15 mg, 0.397 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The reaction was cooled to room temperature and $NaOH_{(aq)}$ (2M, 30 mL) added. The aqueous phase was separated and washed with DCM (2 x 30 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were eluted through a silica column (Et_2O) to give **354** (46 mg, 0.204 mmol, 72 %) as a pale yellow solid.

Data for 4-[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **354**

Data identical to those described previously.

Cyclisation of 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **368** with catalytic tin and sodium borohydride in ethanol



$C_{14}H_{10}INO_2$ (351.14) $C_{14}H_9NO_2$ (223.23) $C_{14}H_{11}NO_2$ (225.24)

The azastilbene **368** (100 mg, 0.285 mmol) in ethanol (30 mL) was stirred under nitrogen at 78 °C with Bu_3SnH (0.02 mL, 21.6 mg, 0.074 mmol), sodium borohydride (15 mg, 0.397 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The reaction was cooled to room temperature and the solvent removed *in vacuo*. The residues were dissolved in $NaOH_{(aq)}$ (2M, 50 mL) and washed with diethyl ether (3 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give a mixture (63 mg) of **345** (unisolated, 30 mg, 0.136 mmol, 48 %) and **354** (unisolated, 33 mg, 0.147 mmol, 52 %).

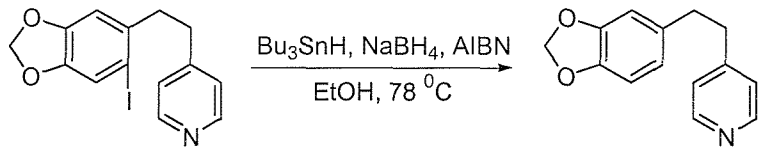
Data for [1,3]dioxolo[4'5':4,5]benzo[*h*]isoquinoline **345**

Data identical to those described previously.

Data for 4-[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]pyridine **354**

Data identical to those described previously.

Attempts at cyclisation of 4-[2-(6-iodo-1,3-benzodioxol-5-yl)ethyl]pyridine **372** with catalytic tin and sodium borohydride in ethanol



$C_{14}H_{12}INO_2$ (353.16) $C_{14}H_{13}NO_2$ (227.26)

The iodide **372** (100 mg, 0.283 mmol) in ethanol (30 mL) was stirred under nitrogen at 78 °C with Bu_3SnH (0.02 mL, 21.6 mg, 0.074 mmol), sodium borohydride (15 mg, 0.397 mmol) and AIBN (10 mg, 0.061 mmol) for 12 hours. The reaction was cooled to room temperature and the solvent removed *in vacuo*. The residues were dissolved in $NaOH_{(aq)}$ (2M, 50 mL) and washed with diethyl ether (3 x 50 mL). The organic phases were combined, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residues were analysed crude by NMR to obtain product ratios and then eluted through a silica column (Et_2O) to give **377** (60 mg, 0.264 mmol, 93 %) as the only product.

Data for 4-[2-(1,3-benzodioxol-5-yl)ethyl]pyridine **377**

Data identical to those described previously.

APPENDIX 1

X-RAY DATA FOR 521 - SOLVED BY DR. S. J. COLES

Table 1. Crystal data and structure refinement.

Identification code	**01sot022**	
Empirical formula	$C_{18}H_{13}NO_2$	
Formula weight	275.29	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*–1	
Unit cell dimensions	$a = 7.9936(16)$ Å	$\alpha = 102.51(3)°$
	$b = 9.1171(18)$ Å	$\beta = 104.74(3)°$
	$c = 9.3710(19)$ Å	$\gamma = 93.63(3)°$
Volume	639.7(2) $Å^3$	
Z	2	
Density (calculated)	1.429 Mg / m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	288	
Crystal	Prism; colourless	
Crystal size	0.28 × 0.10 × 0.10 mm^3	
θ range for data collection	3.01 – 27.50°	
Index ranges	$-10 \le h \le 10, -11 \le k \le 11, -12 \le l \le 12$	
Reflections collected	10400	
Independent reflections	2900 [$R_{int} = 0.0629$]	
Completeness to $\theta = 27.50°$	98.9 %	
Absorption correction	Semi–empirical from equivalents	
Max. and min. transmission	0.9907 and 0.9742	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2900 / 0 / 191	
Goodness-of-fit on F^2	1.013	
Final *R* indices [$F^2 > 2\sigma(F^2)$]	*R1* = 0.0469, *wR2* = 0.1251	
R indices (all data)	*R1* = 0.0577, *wR2* = 0.1342	
Extinction coefficient	0.059(16)	
Largest diff. peak and hole	0.279 and –0.268 e $Å^{-3}$	

Diffractometer: *Enraf Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *Ewald* sphere). **Data collection and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: *SORTAV* (R. H. Blessing, Acta Cryst. **A51** (1995) 33–37; R. H. Blessing, J. Appl. Cryst. **30** (1997) 421–426). **Program used to solve structure**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). **Program used to refine structure**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany).

Further information: http://www.soton.ac.uk/~xservice/strat.htm

Table 2. Atomic coordinates [$\times 10^4$], equivalent isotropic displacement parameters [$Å^2 \times 10^3$] and site occupancy factors. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
C1	156(2)	−3233(2)	9096(2)	26(1)	1
C2	1888(2)	−3366(2)	9306(2)	28(1)	1
C3	2966(2)	−2266(2)	8983(2)	25(1)	1
C4	2300(2)	−1069(2)	8480(1)	21(1)	1
C5	506(2)	−883(1)	8250(1)	18(1)	1
C6	−578(2)	−2015(2)	8565(1)	21(1)	1
C7	−3031(2)	−938(2)	7746(2)	24(1)	1
C8	−2114(2)	214(2)	7359(1)	21(1)	1
C9	−317(2)	296(1)	7650(1)	18(1)	1
C10	−3054(2)	1324(2)	6585(2)	24(1)	1
C11	−2270(2)	1490(2)	5295(1)	23(1)	1
C12	−351(2)	2053(1)	5970(1)	20(1)	1
C13	590(2)	1536(1)	7218(1)	19(1)	1
C14	2314(2)	2206(1)	7999(1)	19(1)	1
C15	3048(2)	3257(1)	7419(1)	20(1)	1
C16	2151(2)	3684(1)	6132(2)	22(1)	1
C17	443(2)	3129(1)	5402(1)	22(1)	1
C18	4891(2)	4776(2)	6811(2)	29(1)	1
N1	−2338(1)	−2012(1)	8337(1)	25(1)	1
O1	4669(1)	4112(1)	8014(1)	26(1)	1
O2	3183(1)	4798(1)	5847(1)	28(1)	1

Table 3. Bond lengths [Å] and angles [°].

C1–C2	1.365(2)
C1–C6	1.4135(19)
C2–C3	1.412(2)
C3–C4	1.3659(19)
C4–C5	1.4220(18)
C5–C6	1.4324(18)
C5–C9	1.4372(18)
C6–N1	1.3687(17)
C7–N1	1.3115(19)
C7–C8	1.4054(18)
C8–C9	1.3862(17)
C8–C10	1.5009(19)
C9–C13	1.4870(17)
C10–C11	1.5258(18)
C11–C12	1.5109(18)
C12–C17	1.4027(18)

C12–C13	1.4117(18)
C13–C14	1.4128(18)
C14–C15	1.3693(17)
C15–O1	1.3830(15)
C15–C16	1.3844(19)
C16–C17	1.3697(19)
C16–O2	1.3810(15)
C18–O1	1.4324(16)
C18–O2	1.4367(18)

C2–C1–C6	121.28(13)
C1–C2–C3	119.30(13)
C4–C3–C2	120.85(13)
C3–C4–C5	121.76(12)
C4–C5–C6	116.84(12)
C4–C5–C9	125.31(11)
C6–C5–C9	117.76(12)
N1–C6–C1	116.90(12)
N1–C6–C5	123.11(12)
C1–C6–C5	119.96(12)
N1–C7–C8	125.45(12)
C9–C8–C7	119.49(12)
C9–C8–C10	119.39(11)
C7–C8–C10	121.08(11)
C8–C9–C5	117.37(11)
C8–C9–C13	117.31(11)
C5–C9–C13	125.18(11)
C8–C10–C11	107.79(11)
C12–C11–C10	108.29(10)
C17–C12–C13	121.19(11)
C17–C12–C11	119.88(11)
C13–C12–C11	118.86(11)
C12–C13–C14	119.63(11)
C12–C13–C9	117.22(11)
C14–C13–C9	123.14(11)
C15–C14–C13	117.47(11)
C14–C15–O1	128.07(11)
C14–C15–C16	122.29(11)
O1–C15–C16	109.52(11)
C17–C16–O2	128.23(12)
C17–C16–C15	121.84(12)
O2–C16–C15	109.66(11)
C16–C17–C12	117.29(12)
O1–C18–O2	107.34(10)
C7–N1–C6	116.68(11)
C15–O1–C18	103.94(10)
C16–O2–C18	104.02(10)

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$]. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + \cdots + 2\,h\,k\,a^*\,b^*\,U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C1	33(1)	22(1)	26(1)	7(1)	10(1)	−1(1)
C2	36(1)	23(1)	25(1)	8(1)	9(1)	7(1)
C3	24(1)	29(1)	23(1)	7(1)	7(1)	6(1)
C4	20(1)	25(1)	20(1)	5(1)	7(1)	1(1)
C5	19(1)	20(1)	15(1)	2(1)	5(1)	−1(1)
C6	22(1)	21(1)	19(1)	3(1)	7(1)	−2(1)
C7	16(1)	31(1)	25(1)	6(1)	7(1)	−2(1)
C8	18(1)	25(1)	18(1)	3(1)	6(1)	1(1)
C9	17(1)	20(1)	16(1)	2(1)	6(1)	−1(1)
C10	16(1)	29(1)	25(1)	6(1)	5(1)	3(1)
C11	18(1)	26(1)	22(1)	7(1)	3(1)	2(1)
C12	19(1)	20(1)	19(1)	3(1)	6(1)	1(1)
C13	17(1)	19(1)	20(1)	4(1)	7(1)	1(1)
C14	18(1)	22(1)	19(1)	6(1)	5(1)	1(1)
C15	16(1)	19(1)	24(1)	2(1)	6(1)	−2(1)
C16	26(1)	17(1)	25(1)	6(1)	12(1)	−1(1)
C17	25(1)	21(1)	20(1)	7(1)	5(1)	3(1)
C18	25(1)	27(1)	38(1)	14(1)	12(1)	−1(1)
N1	21(1)	27(1)	26(1)	6(1)	7(1)	−4(1)
O1	20(1)	27(1)	30(1)	9(1)	6(1)	−6(1)
O2	27(1)	26(1)	35(1)	14(1)	10(1)	−3(1)

Table 5. Hydrogen coordinates [$\times 10^4$] and isotropic displacement parameters [$Å^2 \times 10^3$].

Atom	x	y	z	U_{eq}	*S.o.f.*
H1	−571	−3973	9312	32	1
H2	2363	−4190	9665	33	1
H3	4169	−2360	9118	30	1
H4	3056	−342	8278	26	1
H7	−4256	−939	7565	29	1
H10A	−2913	2316	7317	28	1
H10B	−4314	952	6176	28	1
H11A	−2429	500	4555	27	1
H11B	−2860	2217	4757	27	1
H14	2940	1938	8893	23	1
H17	−179	3460	4546	26	1
H18A	5588	4171	6225	35	1
H18B	5504	5819	7233	35	1

APPENDIX 2

X-RAY DATA FOR 520 - SOLVED BY DR. M. E. LIGHT

Table 1. Crystal data and structure refinement.

Identification code	**00SOT093**
Empirical formula	$C_{18}H_{13}NO_2$
Formula weight	275.29
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	*Cc*
Unit cell dimensions	$a = 11.394(2)$ Å
	$b = 13.119(3)$ Å $\quad \beta = 117.00(3)°$
	$c = 9.5885(19)$ Å
Volume	1277.1(4) Å^3
Z	4
Density (calculated)	1.432 Mg / m^3
Absorption coefficient	0.094 mm^{-1}
F(000)	576
Crystal	Colourless plate
Crystal size	0.30 × 0.15 × 0.07 mm^3
θ range for data collection	3.92 – 25.02°
Index ranges	$-13 \le h \le 13, -13 \le k \le 15, -8 \le l \le 11$
Reflections collected	2149
Independent reflections	1620 [$R_{int} = 0.0542$]
Completeness to $\theta = 25.02°$	95.0 %
Absorption correction	Empirical
Max. and min. transmission	0.9935 and 0.9724
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1620 / 2 / 243
Goodness-of-fit on F^2	1.045
Final *R* indices [$F^2 > 2\sigma(F^2)$]	*R1* = 0.0464, *wR2* = 0.1167
R indices (all data)	*R1* = 0.0494, *wR2* = 0.1204
Absolute structure parameter	not reliably determined
Extinction coefficient	0.022(6)
Largest diff. peak and hole	0.230 and –0.248 e Å^{-3}

Diffractometer: *Enraf Nonius KappaCCD* area detector (ϕ scans and ω scans to fill *Ewald* sphere). **Data collection and cell refinement**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction**: *SORTAV* (R. H. Blessing, Acta Cryst. A**51** (1995) 33–37; R. H. Blessing, J. Appl. Cryst. **30** (1997) 421–426). **Program used to solve structure**: *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A**46** 467–473). **Program used to refine structure**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany).

Further information: http://www.soton.ac.uk/~xservice/strat.htm
Special details: All hydrogen atoms were located from the difference map and fully refined.

Table 2. Atomic coordinates [$\times 10^4$], equivalent isotropic displacement parameters [$Å^2 \times 10^3$] and site occupancy factors. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
C1	−3922(3)	−570(2)	−3129(4)	30(1)	1
C2	−2773(3)	590(2)	−1307(3)	24(1)	1
C3	−2405(3)	−369(2)	−621(4)	25(1)	1
C4	−1445(3)	−488(2)	861(3)	24(1)	1
C5	−820(3)	387(2)	1723(4)	23(1)	1
C6	−1182(3)	1357(2)	1025(4)	26(1)	1
C7	−2176(3)	1462(2)	−497(4)	26(1)	1
C8	235(3)	296(2)	3338(4)	24(1)	1
C9	605(3)	1184(2)	4333(4)	24(1)	1
C10	−131(3)	2164(2)	3668(4)	30(1)	1
C11	−446(3)	2283(2)	1956(4)	29(1)	1
C12	1564(3)	1090(2)	5803(4)	28(1)	1
C13	1778(3)	−686(2)	5301(4)	25(1)	1
C14	2221(3)	145(2)	6367(4)	26(1)	1
C15	3252(3)	5(2)	7884(4)	30(1)	1
C16	3868(3)	−922(2)	8338(4)	32(1)	1
C17	3447(3)	−1744(2)	7281(4)	32(1)	1
C18	2433(3)	−1642(2)	5820(4)	28(1)	1
N1	791(2)	−605(2)	3822(3)	25(1)	1
O1	−3789(2)	516(2)	−2782(3)	32(1)	1
O2	−3188(2)	−1091(2)	−1678(3)	31(1)	1

Table 3. Bond lengths [Å] and angles [°].

C1–O2	1.431(4)
C1–O1	1.454(4)
C2–O1	1.366(4)
C2–C7	1.376(5)
C2–C3	1.394(4)
C3–C4	1.352(4)
C3–O2	1.378(4)
C4–C5	1.404(4)
C5–C6	1.411(4)
C5–C8	1.472(4)
C6–C7	1.389(4)
C6–C11	1.515(4)
C8–N1	1.322(4)
C8–C9	1.442(4)
C9–C12	1.341(4)
C9–C10	1.509(4)

C10–C11	1.521(5)
C12–C14	1.422(4)
C13–N1	1.356(4)
C13–C14	1.422(4)
C13–C18	1.428(4)
C14–C15	1.406(5)
C15–C16	1.372(4)
C16–C17	1.407(5)
C17–C18	1.359(4)

O2–C1–O1	106.9(2)
O1–C2–C7	127.9(3)
O1–C2–C3	110.9(2)
C7–C2–C3	121.2(3)
C4–C3–O2	129.7(3)
C4–C3–C2	121.8(3)
O2–C3–C2	108.5(3)
C3–C4–C5	118.4(3)
C4–C5–C6	119.9(3)
C4–C5–C8	120.4(2)
C6–C5–C8	119.7(2)
C7–C6–C5	120.7(3)
C7–C6–C11	120.6(2)
C5–C6–C11	118.7(3)
C2–C7–C6	118.0(3)
N1–C8–C9	122.7(3)
N1–C8–C5	118.3(2)
C9–C8–C5	119.0(2)
C12–C9–C8	118.4(3)
C12–C9–C10	123.6(3)
C8–C9–C10	118.0(3)
C9–C10–C11	110.9(2)
C6–C11–C10	110.5(2)
C9–C12–C14	121.1(3)
N1–C13–C14	123.2(3)
N1–C13–C18	119.2(3)
C14–C13–C18	117.7(3)
C15–C14–C12	123.8(3)
C15–C14–C13	120.0(3)
C12–C14–C13	116.2(3)
C16–C15–C14	120.7(3)
C15–C16–C17	119.5(3)
C18–C17–C16	121.3(3)
C17–C18–C13	120.7(3)
C8–N1–C13	118.3(2)
C2–O1–C1	105.0(2)
C3–O2–C1	106.6(2)

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$]. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + \cdots + 2\,h\,k\,a^*\,b^*\,U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C1	32(2)	28(2)	29(2)	−2(1)	14(2)	−2(1)
C2	25(1)	24(2)	24(2)	3(1)	13(1)	3(1)
C3	26(1)	22(2)	32(2)	−2(1)	17(1)	0(1)
C4	27(2)	21(2)	28(2)	1(1)	15(2)	2(1)
C5	24(2)	18(2)	32(2)	0(1)	16(1)	1(1)
C6	26(2)	20(2)	38(2)	3(1)	21(1)	−2(1)
C7	26(2)	21(2)	32(2)	7(1)	16(2)	3(1)
C8	26(2)	18(2)	31(2)	0(1)	17(1)	−1(1)
C9	26(2)	20(2)	29(2)	−4(1)	16(2)	−2(1)
C10	30(2)	21(2)	38(2)	−6(1)	15(2)	−2(1)
C11	32(2)	20(2)	39(2)	3(1)	18(2)	0(1)
C12	30(2)	25(2)	32(2)	−7(1)	17(2)	−5(1)
C13	29(2)	23(2)	28(2)	2(1)	17(2)	−2(1)
C14	31(2)	25(2)	29(2)	−2(1)	18(1)	−4(1)
C15	29(2)	34(2)	30(2)	−4(1)	15(2)	−4(1)
C16	32(2)	36(2)	28(2)	2(1)	14(2)	1(1)
C17	38(2)	27(2)	36(2)	9(1)	20(2)	3(1)
C18	36(2)	22(2)	31(2)	2(1)	20(2)	−1(1)
N1	28(1)	21(1)	28(2)	0(1)	14(1)	0(1)
O1	33(1)	26(1)	32(1)	1(1)	10(1)	4(1)
O2	36(1)	23(1)	29(1)	−4(1)	10(1)	−1(1)

Table 5. Hydrogen coordinates [$\times 10^4$] and isotropic displacement parameters [$Å^2 \times 10^3$].

Atom	*x*	*y*	*z*	U_{eq}	*S.o.f.*
H7	−2460(30)	2150(20)	−940(40)	25(7)	1
H10A	−930(40)	2160(20)	3720(40)	34(9)	1
H10B	450(30)	2740(30)	4360(40)	39(9)	1
H11A	380(30)	2320(20)	1880(40)	28(8)	1
H11B	−1040(30)	2890(30)	1430(40)	34(9)	1
H12	1850(30)	1610(30)	6610(50)	42(10)	1
H15	3540(40)	640(30)	8620(40)	46(10)	1
H16	4650(30)	−1010(20)	9350(40)	21(7)	1
H17	4020(40)	−2360(30)	7730(50)	60(12)	1
H18	2110(40)	−2170(30)	5050(50)	42(10)	1
H1A	−4860(30)	−730(30)	−3560(40)	27(8)	1
H1B	−3490(30)	−680(20)	−3960(40)	36(9)	1
H4	−1190(30)	−1150(30)	1380(50)	39(10)	1

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