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Intramolecular radical additions to pyridines

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Intramolecular 6-*exo*/*endo*-trig and 5-*exo*-trig cyclisations of aryl radical intermediates to the α-, β- and γ-carbons of pyridine have been shown to be facile processes at neutral pH. The tether conjoining the radical donor to the pyridine plays an important role in determining the outcome of the reaction. When a *Z*-alkene is used as a tether, *ortho*-cyclisation proceeds in good yield. A more complex course is followed when a saturated two carbon tether is employed, leading to products derived from hydrogen atom abstraction, *ipso*-cyclisation and *ortho*-cyclisation pathways. All attempts to effect 5-*exo*/*endo*-trig cyclisations failed. Tributyltin hydride, tris(trimethylsilyl)silane, tris(trimethylsilyl)germane and, in part, samarium(II) iodide can each be employed as mediators of the reaction.

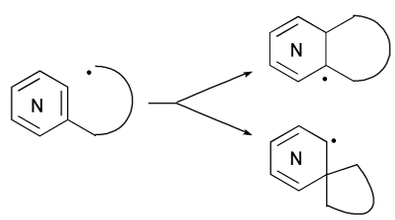
Introduction

The first example of a radical addition to a pyridine was reported in 1893 by Mohlau and Berger. They found that the thermal decomposition of benzene diazonium chloride in pyridine resulted in the formation of 2-phenylpyridine and 4-phenylpyridine in low yield.[1] Later, Overhoff and Tilman attained a similar result when heating dibenzoyl peroxide in pyridine. In this case a 2 : 1 mixture of 2- and 4-phenylpyridine was formed in 18% yield with respect to dibenzoyl peroxide and 4% yield with respect to pyridine.[2] These findings were reassessed by Hey and Walker, using UV spectroscopy to analysed the product mixture.[3] From the data attained they concluded that 2-, 3- and 4-phenylpyridine were all produced in the reaction and estimated the yields for each to be 17%, 10% and 4.4% respectively.

The reaction lay dormant for many years, the low yields and poor selectivity doubtless limiting its appeal to the synthetic community. Interest was rekindled in the 1960's through the seminal work of Dou and Minisci.[4,5] These groups showed that radical additions to pyridines could be effected in good yield when carried out in an acidic medium. Moreover, reactions conducted under such conditions displayed greater selectivity towards addition at C-2, adding further to its synthetic appeal. More recently intramolecular variants of the Minisci reaction have come to the fore.[6–9] Murphy and Sherburn, for example, showed that many *N*-haloalkylpyridinium salts underwent cyclisation to C-2 of the pyridine ring on treatment with tributyltin hydride. Notably, a non-reducing pathway was observed in each of the cases studied – cyclisation being followed by re-aromatisation of the heterocycle.[7]

In contemporaneous work Motherwell showed that *ipso* substitution could outpace *ortho* cyclisation when the radical precursor and pyridine ring were conjoined with an appropriate tether.[8] Latterly, *ortho*-cyclisation to a pyridine featured as a key step in a total synthesis of the alkaloid toddaquinoline.[9,10] Notably, cyclisation of a 2′-bromo-3-azastilbene proceeded in good yield when mediated by tributyltin hydride but gave rise to products derived from radical addition to both the C-2 and C-4 centres of the pyridine. By contrast, cyclisation to C-2 was the only outcome observed when cobalt(I)salophen was employed as a mediator.[10]

Following our completion of the total synthesis of toddaquinoline, we started to consider further extensions of the methodology.[11–14] In particular, we wondered whether radical additions to C-3 of a pyridine would be effective when conducted intramolecularly at neutral pH. We were also keen to gain some insight as to the factors determining whether cyclisation proceeded *via* the 6-*exo*/*endo*-trig mode or the alternative 5-*exo*-trig mode favoured in the majority radical cyclisation reactions involving alkenes (Scheme 1). If examples of the latter could be found, it was unclear whether the resulting radical intermediates would undergo hydrogen atom abstraction from tributyltin hydride leading to a spirocycle or undergo rearrangement so as to facilitate re-aromatisation.



Scheme 1

Results and discussion

Radical cyclisations to C-2, C-3 and C-4 of a pyridine

Our first task was to examine cyclisation reactions involving the addition of aryl radical intermediates to C-3 of a pyridine.[15,16] When *Z*-azastilbene **1** was treated with tributyltin hydride under standard radical forming conditions the expected benzo[*f*]quinoline **2** was formed in low yield with recovered starting material accounting for much of the outstanding mass balance. Indeed, to achieve complete conversion it was found necessary to employ 4.4 equivalents of tributyltin hydride and 30 mol% AIBN. Using these unusual conditions, benzo[*f*]quinoline **2** was given in 47% yield. As with radical additions to C-2 and C-4 of a pyridine, cyclisation followed the non-reducing pathway leading to re-aromatisation (Scheme 2).[9–14]

By way of contrast, the related cyclisation of *Z*-azastilbene **5** to benzo[*h*]isoquinoline **7** was extremely facile, proceeding in 98% yield using the standard radical forming conditions of 1.1 equivalents of tributyltin hydride and 10 mol% AIBN. A striking dichotomy was uncovered when the analogous bromide **6** was exposed to the aforementioned conditions. In this case alkene isomerisation outpaced C–Br bond homolysis as evidenced by the formation of *E*-azastilbene **8** in 97% yield (Scheme 3).

For completeness the tin-mediated radical cyclisation of *Z*-azastilbene **9** was examined. In this case the product mixture

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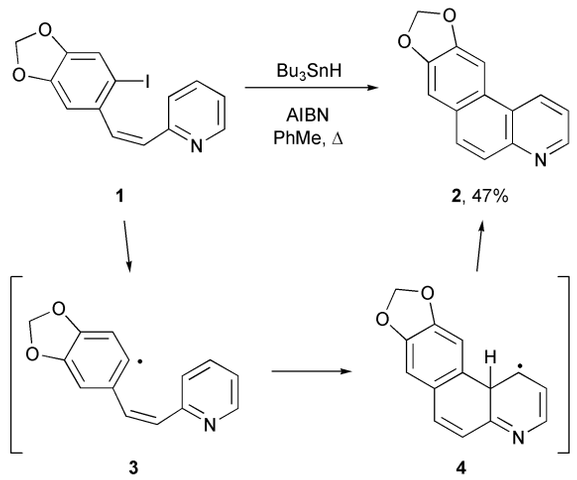
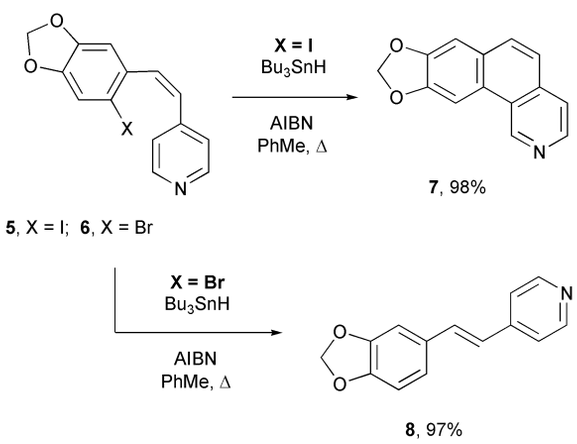
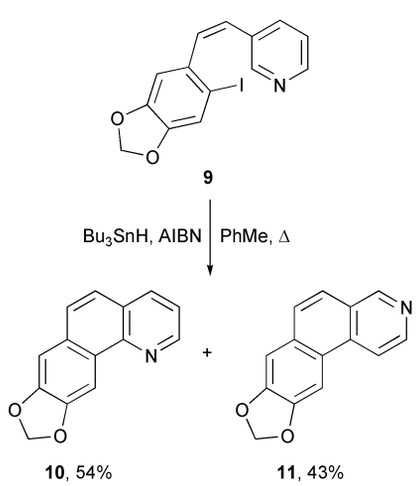


Scheme 2



Scheme 3

attained comprised of a 5 : 4 mixture of benzo[*h*]quinoline **10** and benzo[*f*]isoquinoline **11** (Scheme 4). As expected, cyclisation to C-2 and C-4 occurred with almost equal propensity and in excellent yield. Indeed, no products derived from alkene isomerisation or radical addition to C-3 were observed. Once again, standard radical forming conditions could be used to effect the transformation and just 6 mol% AIBN was needed to achieve complete reaction.

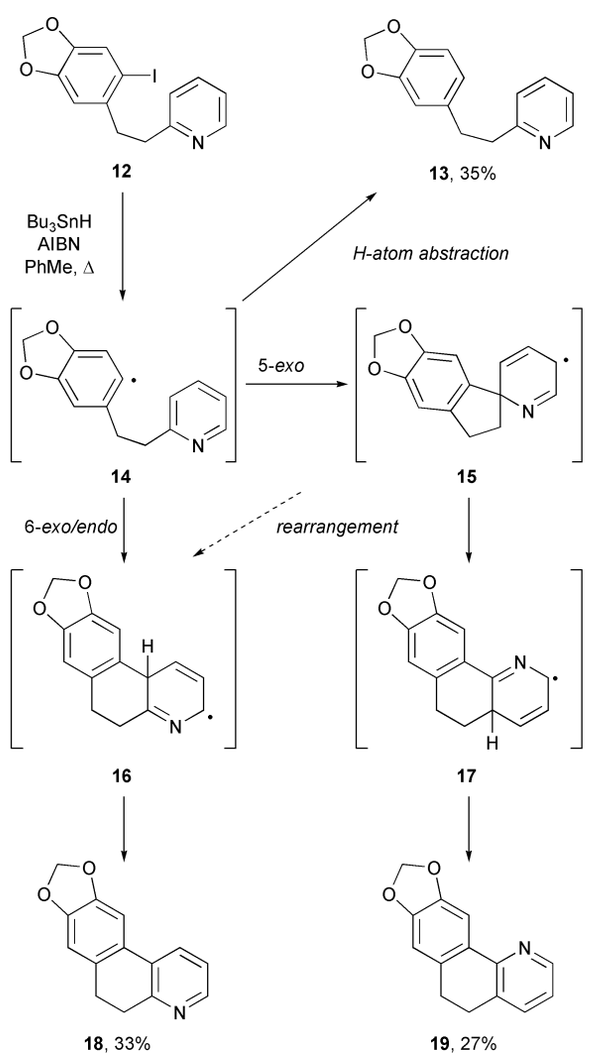


Scheme 4

A new rearrangement

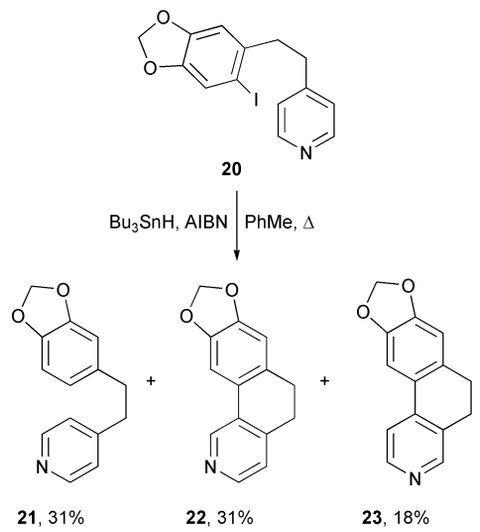
In each of the aforementioned examples we believed that the use of a *cis*-alkene to conjoin the radical donor to the pyridine ring biased reactions in favour of the 6-*exo*/*endo*-trig cyclisation mode over the alternative 5-*exo*-trig pathway. Our reasoning was based on the need to contract bond angles in going to a cyclopentadiene intermediate, a barrier that would be less severe in the formation of cyclohexadiene intermediates akin to **4**. To test this hypothesis, each of the substrates **1**, **5**, **6** and **9** were reduced to the corresponding dihydroazastilbenes with diimide. These materials were then exposed to tributyltin hydride and the resulting product mixtures analysed.

Three products were evident when iodide **12** was treated under standard tin-mediated radical forming conditions, accounting for 95% of the mass balance. The presence of **13**, the product of C–I bond reduction, showed that the 6-*exo*/*endo*-trig cyclisation mode had indeed been slowed by the inclusion of a more flexible tether. This was further evidenced by the production of both dihydrobenzo[*f*]quinoline **18** and dihydrobenzo[*h*]quinoline **19**, formed respectively by 6-*exo*/*endo*-trig and 5-*exo*-trig cyclisation of the aryl radical intermediate **14** (Scheme 5). The formation of **19** can be viewed as a direct rearrangement of spirocycle **15** to tetracycle **17**, or as a stepwise process involving scission of the indane followed by 6-*exo*/*endo*-trig cyclisation of the resultant alkyl radical.[17]



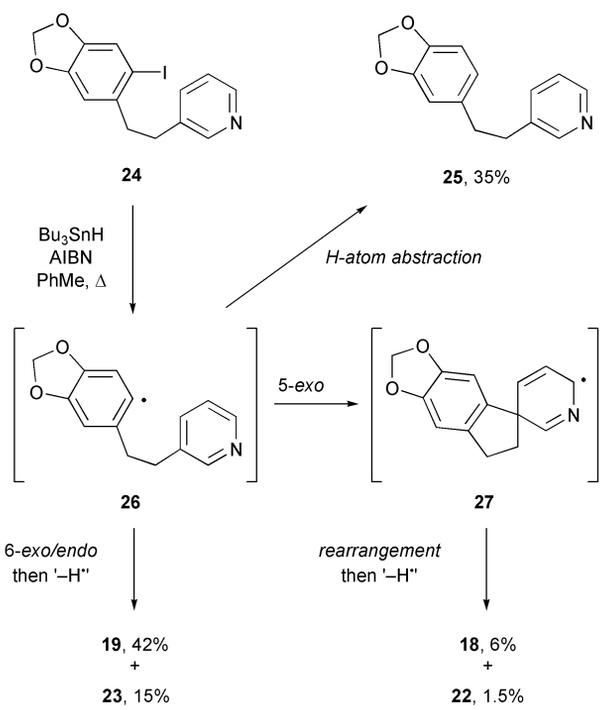
Scheme 5

Irrespective of the nature of that rearrangement, it appears to be quite general within the pyridine series. Thus, aryl iodide **20** gave a similar product mixture when treated with tributyltin hydride, comprising of dihydrostilbene **21**, dihydrobenzo[*h*]isoquinoline **22** and dihydrobenzo[*f*]isoquinoline **23**. These correspond to the products of reduction, *ortho*-cyclisation, and *ipso*-cyclisation and rearrangement, respectively (Scheme 6).



Scheme 6

For aryl iodide **24** the situation was even more complex. With two 6-*exo*/*endo*-trig cyclisation pathways available and two courses by which rearrangement could occur, we envisioned a product mixture comprising at least five components. In the event, all five of the anticipated products were observed, though dihydrobenzo[*h*]quinoline **19** was formed as the major product (Scheme 7).



Scheme 7

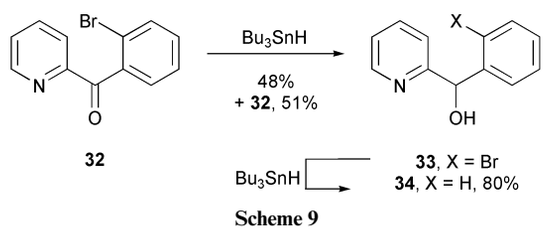
Attempted 5-*exo*/*endo*-trig cyclisations

All attempts to effect the corresponding 5-*exo*/*endo*-trig cyclisation reaction met with failure.[16] In each of the cases studied carbon to halogen bond reduction outpaced cyclisation, indicating that such processes are more akin to 5-*endo*-trig reactions than 5-*exo*-trig reactions (Schemes 8 to 10).[11–14] Unexpectedly, treatment of aryl pyridyl ketone **32** with tributyltin hydride and AIBN led to reduction of the ketone rather than carbon to halogen bond homolysis.

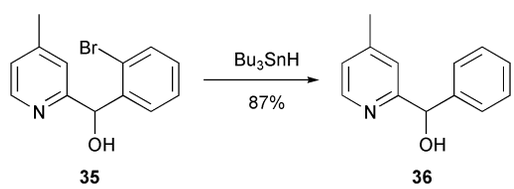
Comparing different methodologies

To conclude our study we decided to explore the use of other mediators as well as 'catalytic' variants of the tributyltin methodology. It also seemed apposite to determine the appropriateness of various commonly employed solvents. The systems chosen for the study were azastilbene **5** and the corresponding dihydroazastilbene **20**.

Scheme 8



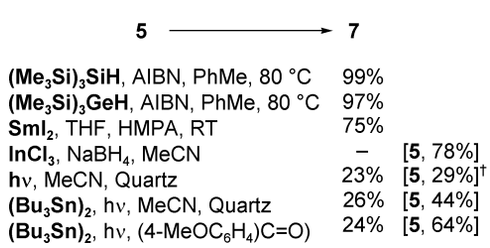
Scheme 9



Scheme 10

Use of other radical mediators

Cyclisation of *Z*-azastilbene **5** to benzo[*h*]isoquinoline **7** proceeded equally well with tris(trimethylsilyl)silane and tris(trimethylsilyl)germane.[18,19] Samarium(II) iodide was also effective but gave a poorer conversion.[20] No reaction was observed with the indium(III) chloride – sodium borohydride reagent.[21] Photoinduced homolysis of the C–I bond was also investigated.[22] Though some cyclisation was observed when an acetonitrile solution of **5** was irradiated with a medium pressure mercury lamp, the reaction was slow and complicated by photo-isomerisation of the alkene. That side reaction was of less significance when hexabutylditin was included in the reaction mixture, though yields remained low (Scheme 11).

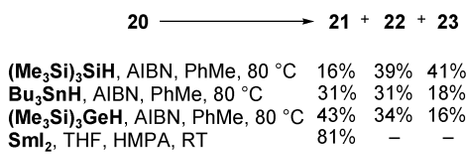


† (*E*)-**8**, 12% and (*Z*)-**8**, 17% were also given

Scheme 11

Dihydroazastilbene **20** likewise reacted smoothly with both tris(trimethylsilyl)silane and tris(trimethylsilyl)germane. Notably, tris(trimethylsilyl)germane gave more of the reduction product **21** while tris(trimethylsilyl)silane gave more of the cyclisation products **22** and **23**. The result was in line with expectation as it reflects the relative strengths of the Si–H, Sn–H and Ge–H bonds and hence the relative rate of hydrogen atom abstraction from the mediator. These experiments also revealed an inconsistency in the distribution of cyclisation products **22** and **23**. At this time we have no satisfactory explanation for the phenomenon as that ratio can display

considerable variation within parallel experiments on the same substrate. In most cases the ratio of products **22** and **23** given falls in the region of 1 : 1 to 2 : 1. Samarium(II) iodide was also examined and in this case gave only the product of reduction, **21** (Scheme 12).

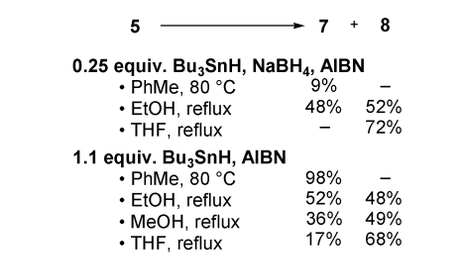


Scheme 12

'Catalytic tin' methodologies

The use of triorganotin hydrides and halides in conjunction with a reducing agent has found widespread use as a means of reducing the quantity of these toxic and relatively expensive reagents to sub-stoichiometric levels.[23] Removal of tin residues from the product mixture is also eased as the residual triorganotin hydride can usually be separated from the product by elution through a silica column. Sodium borohydride and sodium cyanoborohydride are the most commonly employed reducing agents, limiting the range of solvents that may be employed.

Cyclisation of azastilbene **5** was attempted in toluene, THF and ethanol using 0.25 equivalents of tributyltin hydride and 1.5 equivalents of sodium borohydride. Toluene proved to be an unsatisfactory solvent, with only 9% of the substrate converted into benzo[*h*]isoquinoline **7**. The low solubility of sodium borohydride in toluene provides an explanation for the poor conversion in this case. THF also proved to be a poor solvent for the reaction, albeit for a quite different reason. In this case alkene isomerisation outpaced C–I bond homolysis leading to the production of (*E*)-azastilbene **8** in 76% yield. Indeed, benzo[*h*]isoquinoline **7** was only observed in significant quantity (48%) when ethanol was employed. Here too, (*E*)-**8** was observed as a major by-product accounting for 52% of the mass balance (Scheme 13).



Scheme 13

No satisfactory solvent could be found for the cyclisation of **20** to **22** and **23** using the 'catalytic tin' methodology. For example, applying the aforementioned conditions using ethanol resulted in the formation of dihydroazastilbene **21** in 93% yield. The observation suggests that hydrogen atom abstraction is significantly faster in ethanol than in toluene, prompting us to examine the influence of the solvent in greater detail.

Solvent effects

Accordingly, cyclisation of (*Z*)-azastilbene **5** was carried out in toluene, THF, ethanol and methanol. With toluene the sole product of the reaction was benzo[*h*]isoquinoline **7** (98% yield). By contrast, alkene isomerisation competed with C–I bond homolysis when reactions were conducted in ethanol, methanol and THF. Isomerisation was most pronounced in THF and on each occasion was accompanied by reduction of the C–I bond (Scheme 13).

Conclusions

We have shown that intramolecular radical additions to the α-, β- and γ-carbons of a pyridine can be efficient processes, even at neutral pH. The tether conjoining the radical donor to the pyridine plays an important role in determining the outcome of the reaction. When a *Z*-alkene is employed as a tether a 6-*exo*/*endo*-trig cyclisation to an *ortho*-carbon follows. A more complex course is followed when a saturated two-carbon tether is used. In such cases, hydrogen atom abstraction and 5-*exo*-trig (*ipso*-) cyclisation pathways compete with the 6-*exo*/*endo*-trig (*ortho*-) cyclisation mode. Where cyclisation occurs to the *ipso*-carbon, the resulting spirocycle collapses with migration of the alkyl 'tether' leading to a skeletal rearrangement.

5-*exo*/*endo*-trig cyclisations have been attempted but no case has been found where addition of the aryl radical to the pyridine occurs. From this we conclude that such 5-*exo*/*endo*-trig cyclisations are more akin to a 5-*endo*-trig than 5-*exo*-trig process.

While the bulk of this work was carried out using stoichiometric tributyltin hydride as a mediator, catalytic variants of the method were also examined. These proved less rewarding as the requisite change of solvent from toluene to ethanol or THF, led to the promotion of side reactions. Notably, tris(trimethylsilyl)silane, tris(trimethylsilyl)germane and, in part, samarium(II) iodide were found to be useful substitutes for tributyltin hydride.

Experimental

General remarks

Melting points were recorded on a Reichert melting point apparatus using a Comark digital temperature probe and are uncorrected. UV spectra were recorded on a Shimadzu UV-1601 spectrometer. IR spectra were recorded using a Bio-Rad FTS 135 Fourier transform infrared spectrometer equipped with a Golden Gate Single Reflection Diamond ATR (*n.b.* IR data were attained directly from solid samples). NMR spectra were recorded on a Bruker AM250 (operating at 250 MHz for ^{1}H and at 62.9 MHz for ^{13}C), or a Bruker AC300 (operating at 300 MHz for ^{1}H and at 75.5 MHz for ^{13}C), or a Bruker AM400 (operating at 400 MHz for ^{1}H and at 100 MHz for ^{13}C). Chemical shifts (δ_H) are reported as values in parts per million relative to tetramethylsilane (δ_H 0.00, δ_C 0.00), $CDCl_3$ (δ_C 77.2) or residual $CHCl_3$ (δ_H 7.27). Mass spectra were attained using atmospheric pressure chemical ionisation (APCI) or electrospray (ES) and were recorded on a Micromass Platform quadrupole mass analyser with an electrospray ion source. The eluent was distilled acetonitrile and experiments were conducted at a flow rate of 200 μL min^{-1}. Electron impact (EI) mass spectra were recorded on a VG Analytical 70–250-SE normal geometry double focusing mass spectrometer using 70 eV ionisation energy and a 200 °C source temperature. High resolution mass spectra (HRMS) were recorded on the same instrument giving a resolution of 10^4.

All reactions were magnetically stirred under an inert atmosphere. Reactions were monitored by thin layer chromatography using Macherey-Nagel Alugram Sil G/UV_{254} precoated aluminium foil plates of layer thickness 0.25 mm. Compounds were visualised firstly by UV irradiation, then by exposure to iodine vapour and finally by heating plates exposed to solutions of phosphomolybdic acid in ethanol or basified aqueous potassium permanganate. Column chromatography was performed on Sorbsil 60 silica (230–400 mesh), slurry packed and run under low pressure.

Tetrahydrofuran was dried by distillation over sodium and benzophenone. Toluene was dried by distillation over sodium. Dichloromethane was dried by distillation over calcium hydride. Ether refers to diethyl ether and petrol refers to the

fraction of petroleum ether in the boiling point range 40–60 °C. [(6-Iodo-1,3-benzodioxole-5-yl)-methyl]triphenylphosphonium bromide **37**, mp 268–272 °C (EtOH) [Lit. 268–272 °C (EtOH)],[14] and [(6-bromo-1,3-benzodioxole-5-yl)-methyl]triphenylphosphonium bromide **38**, mp 275–279 °C (EtOH) [Lit. 278–280 °C (xylene)],[10] were prepared by the method of Harrowven *et al*.[14,10]

Preparation of substrates

(*Z*)-2-[2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine 1. NaH (400 mg, 10.0 mmol, 60% dispersion in oil) was washed with THF (10 mL) then cooled to 0 °C and stirred in suspension with THF (40 mL) under argon. Phosphonium salt **37** (5.00 g, 8.29 mmol) was added and the reaction stirred for 30 min whilst warming to RT. The mixture was re-cooled to 0 °C and 2-pyridinecarbaldehyde (0.70 mL, 788 mg, 7.36 mmol) added. After 2 h the precipitated triphenylphosphine oxide was removed by filtration and the liquors concentrated *in vacuo*. Purification by column chromatography (silica, Et_2O) and recrystallisation (EtOH) gave **1** (2.20 g, 6.27 mmol, 85%) as a white crystalline solid; mp 108–110 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1582 w, 1500 w, 1474 s, 1433 w, 1411 w, 1231 m, 1035 s; UV (MeOH, nm) λ_{max} (ε_{max}) 294 (12710); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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*C*H_2O), 87.9 (Ar, *C*); LRMS (APCI) 352 (100%, MH^+); Anal. 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%.

(*Z*)-4-[2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine (*Z*)-5 and (*E*)-4-[2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]-pyridine (*E*)-5. NaH (400 mg, 10.0 mmol, 60% dispersion in oil) was washed with THF (10 mL) then cooled to 0 °C and stirred in suspension with THF (40 mL) under argon. Phosphonium salt **37** (5.00 g, 8.29 mmol) was added and the reaction stirred for 30 min whilst warming to RT. The mixture was re-cooled to 0 °C and 4-pyridinecarbaldehyde (0.70 mL, 785 mg, 7.33 mmol) added. After 2 h the precipitated triphenylphosphine oxide was removed by filtration and the liquors concentrated *in vacuo*. Purification by column chromatography (silica, Et_2O) gave firstly (*Z*)-**5** (1.63 g, 4.65 mmol, 63%) as a pale yellow crystalline solid after recrystallisation from EtOH; mp 100–102 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1741 m, 1593 m, 1489 m, 1473 m, 1429 m, 1365 m, 1235 s, 1032 s; UV (MeOH, nm) λ_{max} (ε_{max}) 298 (13340), 245 (27010); ^{1}H NMR (250 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 149.9 (Ar, 2 × *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 × *C*H), 118.4 (Ar, *C*H), 109.7 (Ar, *C*H), 101.7 (O*C*H_2O), 87.7 (Ar, *C*); LRMS (APCI) 352 (100%, MH^+); Anal. 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. Then (*E*)-**5** (796 mg, 2.27 mmol, 31%) as a pale yellow crystalline solid after recrystallisation from EtOH; mp 115–117 °C; (EtOH); IR (solid, cm^{-1}) υ_{max} 1742 w br., 1591 w, 1498 m, 1469 s, 1407 w, 1232 s, 1111 w, 1032 s; UV (MeOH, nm) λ_{max} (ε_{max}) 346 (18560), 303 (17810), 258 (18540); ^{1}H NMR (250 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) 150.3 (Ar, 2 × *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 × *C*H), 118.8 (Ar, *C*H), 106.0 (Ar, *C*H), 102.0 (O*C*H_2O), 90.1 (Ar, *C*); LRMS (APCI) 352 (100%, MH^+); Anal. 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%.

(*Z*)-4-[2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine (*Z*)-6 and (*E*)-4-[2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]-pyridine (*E*)-6. NaH (84 mg, 3.50 mmol, 60% dispersion in oil) was washed with THF (10 mL) then cooled to 0 °C and stirred in suspension with THF (40 mL) under argon. Phosphonium salt **38** (1.70 g, 3.06 mmol) was added and the reaction warmed to RT and stirred for 18 h. The mixture was re-cooled to 0 °C and 4-pyridinecarbaldehyde (0.24 mL, 269 mg, 2.51 mmol) added. After 2 h the precipitated triphenylphosphine oxide was removed by filtration and the liquors concentrated *in vacuo*. Purification by column chromatography (silica, 2 : 3 – Et_2O : petrol) gave firstly (*Z*)-**6** (471 mg, 1.55 mmol, 51%) as a white soild; mp 93–94 °C (Et_2O); IR (solid, cm^{-1}) 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; UV (MeOH, nm) λ_{max} (ε_{max}) 297 (7560); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.44 (2H, d, *J* 4.4 Hz, Ar*H*), 7.00 (1H, s, Ar*H*), 7.00 (2H, d, *J* 4.4, Ar*H*), 6.66 (1H, d, *J* 12.5 Hz, RC*H*=CHR), 6.54 (1H, s, Ar*H*), 6.46 (1H, d, *J* 12.5 Hz, RCH=C*H*R), 5.93 (2H, s, OCH_2O); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 149.9 (Ar, 2 × *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 × *C*H), 114.7 (Ar, *C*), 112.7 (Ar, *C*H), 109.8 (Ar, *C*), 101.9 (O*C*H_2O); LRMS (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$^+$); Anal. 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%. Then (*E*)-**6** (310 mg, 1.02 mmol, 33%) as a white solid; mp 112–113 °C (Et_2O); IR (solid, cm^{-1}) 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; UV (MeOH, nm) λ_{max} (ε_{max}) 341 (12900), 301 (11700); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, 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, OCH_2O); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 150.2 (Ar, 2 × *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 × *C*H), 116.4 (Ar, *C*), 113.1 (Ar, *C*H), 106.1 (Ar, *C*), 102.2 (O*C*H_2O); LRMS (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%); Anal. 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%.

(*Z*)-3-[2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]pyridine (*Z*)-9 and (*E*)-3-[2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]-pyridine (*E*)-9. NaH (400 mg, 10.0 mmol, 60% dispersion in oil) was washed with THF (10 mL) then cooled to 0 °C and stirred in suspension with THF (40 mL) under argon. Phosphonium salt **37** (5.00 g, 8.29 mmol) was added and the reaction stirred for 1 h whilst warming to RT. The mixture was re-cooled to 0 °C and 3-pyridinecarbaldehyde (0.70 mL, 795 mg, 7.42 mmol) added. After 2 h the precipitated triphenylphosphine oxide was removed by filtration and the liquors concentrated *in vacuo*. Purification by column chromatography (silica, Et_2O) gave firstly (*Z*)-**9** (1.50 g, 4.27 mmol, 58%) as a pale yellow crystalline solid after recrystallisation from EtOH; mp 102–103 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1496 m, 1473 s, 1432 m, 1244 m, 1229 m, 1105 w, 1037 s; UV (MeOH, nm) λ_{max} (ε_{max}) 290 (11180); ^{1}H NMR (250 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz,

$CDCl_3$) δ_C 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*); LRMS (APCI) 352 (100%, MH^+), 225 (62%), 224 (88%); Anal. 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%. Then (*E*)-**9** (1.05 g, 2.98 mmol, 40%) as a pale yellow crystalline solid after recrystallisation from EtOH; mp 132–133 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1500 m, 1475 s, 1407 w, 1285 w, 1248 m br., 1187 m, 1113 m, 1040 m; UV (MeOH, nm) λ_{max} (ε_{max}) 338 (13410), 297 (14720), 250 (15070); ^{1}H NMR (250 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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*); LRMS (APCI) 352 (100%, MH^+), 226 (41%); Anal. 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.

2-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]pyridine 12. Azastilbene **1** (300 mg, 0.854 mmol), tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) in THF (15 mL) and water (15 mL) were heated at reflux for 72 h. After cooling to RT, potassium carbonate solution (2M, 100 mL) was added. The reaction mixture was extracted with Et_2O (4 × 50 mL) and the combined organic phases were dried ($MgSO_4$), concentrated *in vacuo*, then purified by column chromatography (silica, Et_2O) to give **10** (278 mg, 0.787 mmol, 92%) as a white crystalline solid; mp 69–70 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1589 w, 1498 m, 1473 s, 1432 w, 1224 s, 1112 w, 1032 s; UV (MeOH, nm) λ_{max} (ε_{max}) 295 (4650), 269 (4620), 262 (5760), 224 (8860); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O), 3.09–2.99 (4H, m, RCH_2CH_2R); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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_2O), 87.7 (Ar, *C*), 40.9 (Ar*C*H_2), 38.9 (Ar*C*H_2); LRMS (APCI) 354 (96%, MH^+), 227 (100%); Anal. 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-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]pyridine 20. A mixture of azastilbenes (*Z*)-**5** and (*E*)-**5** (500 mg, 1.42 mmol), tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) in THF (15 mL) and water (15 mL) were heated at reflux for 72 h. After cooling to RT, potassium carbonate solution (2M, 100 mL) was added. The reaction mixture was extracted with Et_2O (4 × 50 mL) and the combined organic phases were dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to give **20** (460 mg, 1.30 mmol, 91%) as a white crystalline solid; mp 49–51 °C (Et_2O); IR (solid, cm^{-1}) υ_{max} 1601 m, 1501 m, 1475 s, 1228 s, 1039 s; UV (MeOH, nm) λ_{max} (ε_{max}) 295 (4190), 244 (8170); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.97–2.91 (2H, m, RCH_2CH_2R), 2.87–2.81 (2H, m, RCH_2CH_2R); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 150.0 (Ar, *C*), 149.7 (Ar, 2 × *C*H), 148.5 (Ar, *C*), 147.0 (Ar, *C*), 136.4 (Ar, *C*), 124.0 (Ar, 2 × *C*H), 118.7 (Ar, *C*H), 109.3 (Ar, *C*H), 101.6 (O*C*H_2O), 87.7 (Ar, *C*), 41.6 (Ar*C*H_2), 35.9 (Ar*C*H_2); LRMS (ES) 395 (28%, [MH + MeCN]$^+$), 354 (100%, MH^+); Anal. 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-[2-(6-Iodo-1,3-benzodioxol-5-yl)ethyl]pyridine 24. A mixture of the azastilbenes (*Z*)-**9** and (*E*)-**9** (1.05 g, 2.99 mmol), tosyl hydrazine (2.90 g, 15.6 mmol) and sodium acetate (1.28 g, 15.6 mmol) in THF (15 mL) and water (15 mL) were heated at reflux for 72 h. After cooling to RT, potassium carbonate solution (2M, 100 mL) was added. The reaction mixture was extracted with Et_2O (4 × 50 mL) and the combined organic phases were dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to give **24** (1.00 g, 2.83 mmol, 95%) as a white crystalline solid; mp 86–87 °C (Et_2O); IR (solid, cm^{-1}) υ_{max} 1501 m, 1478 s, 1226 s, 1135 m, 1044 s, 1028 m; UV (MeOH, nm) λ_{max} (ε_{max}) 295 (2550), 269 (2030), 263 (2490), 244 (4770); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.95–2.90 (2H, m, RCH_2CH_2R), 2.87–2.82 (2H, m, RCH_2CH_2R); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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_2O), 87.7 (Ar, *C*), 42.4 (Ar*C*H_2), 33.8 (Ar*C*H_2); LRMS (APCI) 354 (100%, MH^+), 228 (35%), 226 (50%); Anal. 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%.

(2-Bromophenyl)(3-pyridyl)methanol 29. *tert*-Butyllithium (1.25 M in hexane, 8.30 mL, 10.38 mmol) was added dropwise over 10 min to a cooled (−100 °C) solution of 3-bromopyridine (1.0 mL, 1.64 g, 10.38 mmol) in Et_2O (20 mL). After 1 h, 2-bromobenzaldehyde (1.25 mL, 1.98 g, 10.71 mmol) in Et_2O (20 mL) was added, dropwise over 5 min. The solution was warmed to −60 °C over a period of 2 h and saturated sodium chloride solution (90 mL) added along with THF (50 mL). The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 50 : 50, Et_2O : petrol) to give **29** (2.27 g, 8.59 mmol, 83%) as a white solid; mp 125–126 °C ($CHCl_3$) [Lit. 125–126 °C (ethyl acetate)];[24] IR (solid, cm^{-1}) υ_{max} 3091 br. m, 2826 w, 1589 w, 1564 w, 1434 m, 1315 w, 1178 w, 1108 w, 1055 m, 1018 w; UV (MeOH, nm) λ_{max} (ε_{max}) 262 (1930); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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 × Ar*H*), 6.17 (1H, s, C*H*OH), 4.99 (1H, s, CHO*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 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); LRMS (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%); Anal. 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 28. To a suspension of MnO_2 (4.00 g, 46 mmol, activated by azeotropic distillation of toluene (15 mL)) in DCM (50 mL) was added alcohol **29** (500 mg, 1.89 mmol). After 18 h the residual solid was removed by filtration through celite. Concentration *in vacuo* and purification by column chromatography (silica, chloroform) gave **28** (485 mg, 1.85 mmol, 98%) as a colourless oil; IR (oil, cm^{-1}) υ_{max} 3051 m, 2851 w, 1671 s, 1583 s, 1466 m, 1430 w, 1417 s, 1289 s, 1253 m, 1024 m; UV (MeOH, nm) λ_{max} (ε_{max}) 267 (5100), 235 (10100); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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 × Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 194.7 (Ar_2*C*O), 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*); LRMS (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.[24,25]

(2-Bromophenyl)(2-pyridyl)methanol 33. *n*-Butyllithium (1.44 M in hexane, 2.19 mL, 3.15 mmol) was added dropwise over 2 min to a cooled (−90 °C) solution of 2-bromopyridine (0.3 mL, 497 mg, 3.15 mmol) in THF (20 mL). The solution turned dark brown immediately. 2-Bromobenzaldehyde (0.37 mL, 586 mg, 3.17 mmol) was then added dropwise over 1 min causing the solution to turn light yellow. After 5 min saturated ammonium chloride (50 mL) was added and the solution was allowed to warm to RT over 30 min. The organic phase was separated, washed with water (30 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 1 : 4 – Et_2O : petrol) and recrystallisation from petrol to give **33** (626 mg, 2.37 mmol, 75%) as a white solid; mp 77–79 °C (petrol); IR (solid, cm^{-1}) 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; UV (MeOH, nm) λ_{max} (ε_{max}) 260 (4800); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.58 (1H, d, *J* 5.2 Hz, Ar*H*), 7.66–7.57 (2H, m, 2 × Ar*H*), 7.40–7.12 (5H, m, 5 × Ar*H*), 6.27 (1H, s, Ar_2CHOH), 5.64 (1H, s, Ar_2CHOH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 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_2CHOH); LRMS (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; Anal. 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 32. To a suspension of MnO_2 (2.00 g, 23.0 mmol, activated by azeotropic distillation of toluene (15 mL)) in DCM (50 mL) was added alcohol **33** (200 mg, 0.76 mmol). After 24 h the residual solid was removed by filtration through celite. Concentration *in vacuo* and recrystallisation from ethanol yielded **32** (167 mg, 0.673 mmol, 84%) as a colourless solid; mp 72–73 °C (EtOH/petrol) [Lit. 63–63.5];[26] IR (solid, cm^{-1}) υ_{max} 3056 w, 2925 w, 2853 w, 1682 s, 1583 m, 1467 w, 1434 m, 1310 s, 1243 m, 1043 m, 1026 m; UV (MeOH, nm) λ_{max} (ε_{max}) 269 (5400), 235 (7300); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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 × Ar*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 196.0 (Ar_2CO), 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*); LRMS (CI) 264 (27%, M(^{81}Br)H^+), 262 (26%, M(^{79}Br)H^+), 170 (100%), 168 (37%), 94 (19%), 80 (19%); Anal. Found: C, 54.90; H, 3.02; N, 5.23. $C_{12}H_8BrNO$ requires C, 54.99; H, 3.08; N, 5.34%.

(2-Bromophenyl)(4-methyl-2-pyridyl)methanol 35. *n*-Butyllithium (1.6 M in hexane; 3.7 mL, 5.92 mmol) was added dropwise over 3 min to a cooled (−90 °C) solution of 2-bromo-4-methylpyridine (1.00 g, 5.81 mmol) in THF (20 mL). After 30 min, a solution of 2-bromobenzaldehyde (1.08 g, 5.84 mmol) in THF (5 mL) was added, dropwise over 3 min. After 2 h the cooling bath was removed and the reaction was allowed to warm to RT. After 2 h, saturated ammonium chloride (50 mL) was added and the organic phase was separated, washed with water (50 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 2 : 3 – Et_2O : petrol) to give **35** (1.34 g, 4.83 mmol, 83%) as a beige solid; mp 78–80 °C (ethanol/petrol); IR (solid, cm^{-1}) υ_{max} 3588 w, 3358 br. m, 3060 w, 2925 w, 1608 s, 1564 m, 1470 m, 1438 m, 1389 m, 1024 m; UV (MeOH, nm) λ_{max} (ε_{max}) 257 (830); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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 × Ar*H*), 6.21 (1H, s, Ar_2CHOH), 5.62 (1H, s, Ar_2CHOH), 2.31 (3H, s, $ArCH_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 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_2CHOH), 21.3 ($ArCH_3$); LRMS (CI) 280 (22%, M(^{81}Br)H^+), 278 (24%, M(^{79}Br)H^+), 184 (59%), 119 (24%), 109 (55%), 94 (100%); Anal. 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%.

Radical reactions mediated by Bu_3SnH

[1,3]Dioxolo[4′5′:4,5]benzo[*f*]quinoline 2. A solution of azastilbene **1** (600 mg, 1.71 mmol), Bu_3SnH (0.6 mL, 649 mg, 2.23 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (140 mL) was heated at 80 °C under argon for 18 h. Further portions of Bu_3SnH (1.4 mL, 1.51 g, 5.20 mmol) and AIBN (60 mg, 0.365 mmol) were then added and heating was continued for 24 h. After cooling to RT, a 2M KF solution (200 mL) was added and the biphasic mixture was stirred vigorously for 24 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to yield **2** (180 mg, 0.81 mmol, 47%) as a pale yellow crystalline solid; mp 200–201 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1497 m, 1478 s, 1374 w, 1257 s, 1195 s, 1084 w, 1030 s; UV (MeOH, nm) λ_{max} (ε_{max}) 286 (19400), 256 (12870), 237 (22130); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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 (OCH_2O), 100.7 (Ar, *C*H); LRMS (APCI) 224 (100%, MH^+); Anal. 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%.

[1,3]Dioxolo[4′5′:4,5]benzo[*h*]isoquinoline 7. A solution of azastilbene **5** (450 mg, 1.28 mmol), Bu_3SnH (0.45 mL, 487 mg, 1.67 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (110 mL) was heated at 80 °C under argon for 72 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 18 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) and recrystallisation from ethanol to yield **7** (280 mg, 1.25 mmol, 98%) as a yellow solid; mp 182–183 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1739 m br., 1501 m, 1468 s, 1431 m, 1375 m, 1241 m, 1226 s, 1038 s; UV (MeOH, nm) λ_{max} (ε_{max}) 354 (7090), 338 (5670), 322 (3670), 280 (17590), 259 (32690), 237 (34190); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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 (OCH_2O), 100.1 (Ar, *C*H); LRMS (APCI) 224 (100%, MH^+); Anal. 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%.

(*E*)-4-[2-(1,3-Benzodioxol-5-yl)-1-ethenyl]pyridine 8. A solution of azastilbene **6** (347 mg, 1.14 mmol), Bu_3SnH (0.38 mL, 411 mg, 1.41 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (80 mL) was heated at 80 °C under argon for 24 h. After cooling to RT, a 2M KF solution (40 mL) was added and the biphasic mixture was stirred vigorously for 24 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 3 : 7 – Et_2O : petrol) to give **8** (250 mg, 1.11 mmol, 97%) as a white solid; mp 102–103 °C (Et_2O/petrol) [Lit. 98 °C (EtOH/water)];[27] IR (solid, cm^{-1}) 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; UV (MeOH, nm) λ_{max} (ε_{max}) 336 (12700), 306 (8280), 239 (9500); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.56 (2H, s, Ar*H*), 7.32 (2H, d, *J* 4.4 Hz, Ar*H*), 7.21 (1H, d, *J* 15.4 Hz, RC*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, RCH=C*H*R), 6.00 (2H, s, OCH_2O); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 150.1 (Ar, 2 × *C*H), 148.3 (Ar, *C*), 148.3 (Ar, *C*), 144.8 (Ar, *C*), 132.8 (=*C*H), 130.6 (Ar, *C*), 124.1 (=*C*H), 122.6 (Ar, 2 × *C*H), 120.7 (Ar, *C*H), 108.5 (Ar, *C*H), 105.8 (Ar, *C*H), 101.4 (O*C*H_2O); LRMS (APCI) 226 (100%, MH^+); Anal. 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%.

[1,3]Dioxolo[4′5′:4,5]benzo[*h*]quinoline 10 and [1,3]dioxolo-[4′5′:4,5]benzo[*f*]isoquinoline 11. A solution of azastilbene **9** (735 mg, 2.09 mmol), Bu_3SnH (0.70 mL, 757 mg, 2.60 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (150 mL) was heated at 80 °C under argon for 90 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 18 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) and recrystallisation from ethanol to yield **10** (250 mg, 1.12 mmol, 54%) as a yellow solid; mp 121–122 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1497 m, 1462 s, 1401 w, 1249 s, 1235 w, 1215 w, 1035 s; UV (MeOH, nm) λ_{max} (ε_{max}) 334 (2590), 283 (36440), 254 (25800), 235 (44870); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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); LRMS (APCI) 224 (100%, MH^+); Anal. 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%. A second fraction **11** (200 mg, 0.90 mmol, 43%) was also recrystallised from EtOH, as a yellow solid; mp 182–183 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1740 br. w, 1602 w, 1482 s, 1271 w, 1240 m, 1196 m, 1032 s; UV (MeOH, nm) λ_{max} (ε_{max}) 356 (4210), 339 (4450), 324 (3470), 277 (35870), 256 (39540); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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); LRMS (APCI) 224 (100%, MH^+); Anal. 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%.

2-[2-(1,3-Benzodioxol-5-yl)ethyl]pyridine 13, 5,6-dihydro-[1,3]dioxolo[4′5′:4,5]benzo[*f*]quinoline 18 and 5,6-dihydro-[1,3]dioxolo[4′5′:4,5]benzo[*h*]quinoline 19. A solution of iodide **12** (900 mg, 2.55 mmol), Bu_3SnH (0.82 mL, 887 mg, 3.05 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (200 mL) was heated at 80 °C under argon for 40 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 18 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to yield firstly **19** (156 mg, 0.69 mmol, 27%) as a pale yellow solid; mp 73–75 °C (EtOH/petrol); IR (solid, cm^{-1}) υ_{max} 1568 w, 1495 m, 1483 m, 1450 s, 1416 w, 1374 w, 1326 w, 1288 w, 1234 s, 1037 s; UV (MeOH, nm) λ_{max} (ε_{max}) 329 (10840), 290 (5070), 280 (4700); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.92–2.77 (4H, m, RCH_2CH_2R); NOE (400 MHz, $CDCl_3$) Irradiation at δ_H 7.80 led to no discernable enhancement; irradiation at δ_H 7.41 led to enhancement at δ_H 7.03 and δ_H 2.92–2.77; irradiation at δ_H 6.66 led to enhancement at δ_H 2.92–2.77; ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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_2O), 28.7 (Ar*C*H_2), 28.6 (Ar*C*H_2); LRMS (APCI) 226 (100%, MH^+); Anal. 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%. Then **13** (200 mg, 0.88 mmol, 35%) as a white solid; mp 26–27 °C (Et_2O); IR (solid, cm^{-1}) υ_{max} 1592 w, 1502 m, 1488 s, 1441 m, 1245 s, 1039 s; UV (MeOH, nm) λ_{max} (ε_{max}) 287 (3670), 269 (3730), 263 (4140), 236 (4270); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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 (62.9 MHz, $CDCl_3$) δ_C 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); LRMS (APCI) 228 (100%, MH^+); HRMS (ES) Found: MH^+, 228.1028. $C_{14}H_{14}NO_2$ requires 228.1024. And finally **18** (187 mg, 0.83 mmol, 33%) as a white solid; mp 143–145 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1744 m, 1712 m, 1502 s, 1457 m, 1365 m, 1237 s, 1114 m, 1030 s; UV (MeOH, nm) λ_{max} (ε_{max}) 326 (18220), 285 (13810); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O), 3.09–3.02 (2H, m, RCH_2CH_2R), 2.94–2.87 (2H, m, RCH_2CH_2R); NOE (400 MHz, $CDCl_3$) Irradiation at δ_H 7.82 led to enhancement at δ_H 7.20 and δ_H 7.17; irradiation at δ_H 6.75 led to enhancement at δ_H 2.94–2.87; irradiation at δ_H 3.09–3.02 led to no discernable enhancement; irradiation at δ_H 2.94–2.87 led to enhancement at δ_H 6.75 and δ_H 3.09–3.02; ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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); LRMS (APCI) 226 (100%, MH^+); Anal. 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%.

4-[2-(1,3-Benzodioxol-5-yl)ethyl]pyridine 21, 5,6-dihydro-[1,3]dioxolo[4′5′:4,5]benzo[*h*]isoquinoline 22 and 5,6-dihydro-[1,3]dioxolo[4′5′:4,5]benzo[*f*]isoquinoline 23. A solution of iodide **20** (500 mg, 1.42 mmol), Bu_3SnH (0.48 mL, 519 mg, 1.78 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (200 mL) was heated at 80 °C under argon for 40 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 18 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to yield firstly a mixture of **21** and **22**. Fractional crystallisation of that mixture from EtOH gave firstly **22** (100 mg, 0.44 mmol, 31%) as a white crystalline solid; mp 208–210 °C (EtOH); IR (solid, cm^{-1}) υ_{max} 1640 m br., 1483 s, 1415 m, 1393 w, 1226 s, 1193 m, 1161 s, 1134 m, 1031 s; UV (MeOH, nm) λ_{max} (ε_{max}) 322 (17320), 276 (12710), 238 (24460); ^{1}H NMR (400 MHz, MeOH) δ_H 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, OCH_2O), 3.13–3.07 (2H, m, RCH_2CH_2R), 2.93–2.87 (2H, m, RCH_2CH_2R); NOE (400 MHz, MeOH) Irradiation at δ_H 8.89 led to enhancement at δ_H 7.22; irradiation at δ_H 7.60 led to enhancement at δ_H 8.46 and δ_H 3.13–3.07; irradiation at δ_H 3.13–3.07 led to enhancement at δ_H 7.60 and δ_H 2.93–2.87; ^{13}C NMR (62.9 MHz, MeOH) δ_C 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*C*H_2O), 30.4 (Ar*C*H_2), 28.2 (Ar*C*H_2); LRMS (APCI) 226 (100%, MH^+), 186 (22%); Anal. 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. Then **21** (100 mg, 0.44 mmol, 31%) as a white crystalline solid; mp 56–58 °C (pentane); IR (solid, cm^{-1}) υ_{max} 1600 m, 1489 s, 1443 m, 1416 m, 1243 s, 1191 m, 1037 s; UV (MeOH, nm) λ_{max} (ε_{max}) 287 (4640), 263 (2700), 237 (6150); ^{1}H NMR (250 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.86 (4H, s, RCH_2CH_2R); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 150.3 (Ar, *C*), 149.7 (Ar, 2 × *C*H), 147.7 (Ar, *C*), 145.9 (Ar, *C*), 134.5 (Ar, *C*), 123.9 (Ar, 2 × *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); LRMS (APCI) 228 (100%, MH^+); Anal. 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%. Further elution of the column led to **23** (58 mg, 0.26 mmol, 18%) as a pale yellow solid; mp 144–148 °C (Et_2O); IR (solid, cm^{-1}) υ_{max} 2909 s, 1593 m, 1552 w, 1504 m, 1481 s, 1415 m, 1369 w, 1282 w, 1235 s, 1036 s; UV (MeOH, nm) λ_{max} (ε_{max}) 326 (33500), 287 (17800); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.76 (4H, s, RCH_2CH_2R); NOE (400 MHz, $CDCl_3$) Irradiation at δ_H 8.39 led to enhancement at δ_H 7.36; irradiation at δ_H 8.37 led to enhancement at δ_H 2.76; irradiation at δ_H 7.36 led to enhancement at δ_H 8.39 and δ_H 7.19; irradiation at δ_H 2.76 led to enhancement at δ_H 8.37 and δ_H 6.68; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 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_2O), 28.9 (Ar*C*H_2), 25.8 (Ar*C*H_2); LRMS (ES) 267 (13%, [MH + MeCN]$^+$), 226 (16%, MH^+); Anal. 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%.

5,6-Dihydro[1,3]dioxolo[4′5′:4,5]benzo[*f*]quinoline 18, 5,6-dihydro[1,3]dioxolo[4′5′:4,5]benzo[*h*]quinoline 19, 5,6-dihydro-[1,3]dioxolo[4′5′:4,5]benzo[*f*]isoquinoline 22, 5,6-dihydro[1,3]-dioxolo[4′5′:4,5]benzo[*h*]isoquinoline 22 and 3-[2-(1,3-benzo-dioxol-5-yl)ethyl]pyridine 25. A solution of iodide **24** (200 mg, 0.566 mmol), Bu_3SnH (0.20 mL, 216 mg, 0.744 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (150 mL) was heated at 80 °C under argon for 48 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 48 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to yield firstly **19** (70 mg, 0.31 mmol, 42%); then **25** (58 mg, 0.26 mmol, 35%); mp 37–39 °C (Et_2O); IR (solid, cm^{-1}) υ_{max} 1503 m, 1490 s, 1443 m, 1246 s, 1191 m, 1039 s; UV (MeOH, nm) λ_{max} (ε_{max}) 287 (4420), 270 (4010), 263 (4280), 235 (5780); ^{1}H NMR (250 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.92–2.79 (4H, m, RCH_2CH_2R); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C 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_2O), 37.2 (Ar*C*H_2), 35.2 (Ar*C*H_2); LRMS (APCI) 228 (100%, MH^+); Anal. 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%; then **18** (9.5 mg, 0.042 mmol, 6%); and finally a 10 : 1 mixture of **23** and **22** (28 mg, 0.13 mmol, 17%).

(Phenyl)(3-pyridyl)methanone 30. A solution of bromide **28** (200 mg, 0.763 mmol), Bu_3SnH (0.40 mL, 433 mg, 1.484 mmol) and AIBN (12 mg, 0.073 mmol) in toluene (50 mL) was heated at 100 °C under nitrogen for 30 h. After cooling to RT, a 2M KF solution (50 mL) was added and the biphasic mixture was stirred vigorously for 24 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 4 : 1 – Et_2O : petrol) to give **30** (120 mg, 0.655 mmol, 86%) as a white solid; mp 40–41 °C (petrol) [Lit. 32–34 °C];[28] Anal. Found: C, 78.56; H, 4.98; N, 7.60. $C_{12}H_9NO$ requires C, 78.67; H, 4.95; N, 7.65%; other spectral and physical data were in accord with the literature values.[28]

(Phenyl)(3-pyridyl)methanol 31. A solution of bromide **29** (200 mg, 0.757 mmol), Bu_3SnH (0.4 mL, 433 mg, 1.484 mmol) and AIBN (12 mg, 0.073 mmol) in toluene (50 mL) was heated at 100 °C under nitrogen for 30 h. After cooling to RT, a 2M KF solution (50 mL) was added and the biphasic mixture was stirred vigorously for 24 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to give **31** (124 mg, 0.669 mmol, 88%) as a white solid; mp 65–66 °C (Et_2O) [Lit. 67.5–69 °C];[28] Anal. 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; other spectral and physical data were in accord with the literature values.[28]

(2-Bromophenyl)(2-pyridyl)methanol 33. A solution of bromide **32** (434 mg, 1.66 mmol), Bu_3SnH (0.67 mL, 725 mg, 2.49 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (150 mL) was heated at 80 °C under argon for 24 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 8 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 1 : 4 – Et_2O : petrol) to give firstly recovered starting material **32** (223 mg, 0.851 mmol, 51%), then alcohol **33** (210 mg, 0.795 mmol, 48%) as a white crystalline solid. Data as described previously.

(Phenyl)(2-pyridyl)methanol 34. A solution of bromide **33** (300 mg, 1.14 mmol), Bu_3SnH (0.37 mL, 400 mg, 1.37 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (80 mL) was heated at reflux under argon for 100 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 24 h. The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, 2 : 3 – Et_2O : petrol) to give **34** (200 mg, 1.08 mmol, 95%) as a white solid; mp 73–74 °C (Et_2O) [Lit. 76–78 °C (distilled)];[29] Anal. 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%. Other spectral data were in accord with the literature values.[29]

(4-Methyl-2-pyridyl)(phenyl)methanol 36. A solution of bromide **35** (100 mg, 0.360 mmol), Bu_3SnH (0.19 mL, 206 mg, 0.706 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (25 mL) was heated at reflux under argon for 5 h. After cooling to RT, a 2M KF solution (100 mL) was added and the biphasic mixture was stirred vigorously for 65 h. The aqueous phase was extracted with ether (2 × 50 mL) and the combined organic phases were washed with water (2 × 50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica, 1 : 1 – Et_2O : petrol) gave **36** (62 mg, 0.311 mmol, 87%) as a beige solid; mp 84–86 °C (petrol) [Lit. 89–90 °C (distilled)];[30] IR (solid, cm^{-1}) 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; UV (MeOH, nm) λ_{max} (ε_{max}) 257 (4000); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.43 (1H, d, *J* 5.2 Hz, Ar*H*), 7.42–7.27 (5H, m, 5 × Ar*H*), 7.03 (1H, d, *J* 4.4 Hz, Ar*H*), 6.97 (1H, s, Ar*H*), 5.72 (1H, s, Ar_2C*H*OH), 5.32 (1H, s, Ar_2CHO*H*), 2.30 (3H, s, ArCH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ_C 160.8 (Ar, *C*), 148.3 (Ar, *C*), 147.6 (Ar, *C*H), 143.6 (Ar, *C*), 128.7 (Ar, 2 × *C*H), 127.9 (Ar, *C*H), 127.2 (Ar, 2 × *C*H), 123.8 (Ar, *C*H), 122.2 (Ar, *C*H), 75.0 (Ar_2*C*HOH), 21.3 (Ar*C*H_3); LRMS (CI) 200 (58%, MH^+), 199 (30%, M^+), 184 (100%, [M − CH_3]$^+$), 94 (38%);

Anal. 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%.

Radical cyclisation reactions of 5 and 20 using other methodologies

$(Me_3Si)_3SiH$. A solution of iodide **5** (100 mg, 0.28 mmol), $(Me_3Si)_3SiH$ (0.132 mL, 106 mg, 0.428 mmol) and AIBN (10 mg, 0.061 mmol) in toluene (30 mL) was heated at 80 °C under nitrogen for 12 h. After cooling to RT, 2M NaOH (50 mL) was added. The aqueous phase was extracted with ether (2 × 50 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica, Et_2O) gave **7** (63 mg, 0.28 mmol, 99%).

The aforementioned procedure was also applied to iodide **20** (100 mg, 0.28 mmol) giving **22** (25 mg, 0.11 mmol, 39%), **21** (10 mg, 0.045 mmol, 16%) and **23** (26 mg, 0.12 mmol, 41%).

$(Me_3Si)_3GeH$. A solution of iodide **5** (100 mg, 0.28 mmol), $(Me_3Si)_3GeH$ (0.133 mL, 125 mg, 0.426 mmol) and AIBN (10 mg, 0.061 mmol) in toluene (30 mL) was heated at 80 °C under nitrogen for 12 h. After cooling to RT, 2M NaOH (30 mL) was added. The aqueous phase was extracted with ether (2 × 50 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica, Et_2O) gave **7** (62 mg, 0.28 mmol, 97%).

The aforementioned procedure was also applied to iodide **20** (100 mg, 0.285 mmol) giving **22** (22 mg, 0.096 mmol, 34%), **21** (28 mg, 0.12 mmol, 16%) and **23** (12 mg, 0.053 mmol, 43%).

SmI_2. To a cooled (0 °C) solution of iodide **5** (100 mg, 0.285 mmol) and HMPA (1 mL, 1.03 g, 5.75 mmol) in degassed THF (20 mL) and under argon was added SmI_2 in THF (0.1M, 10 mL, 1.00 mmol) dropwise over 5 min. The intense blue colour of the SmI_2 turned deep purple. The cooling bath was removed and after 18 h at RT, 2M K_2CO_3 (30 mL) was added. The aqueous phase was extracted with diethyl ether (2 × 30 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then diluted with chloroform (30 mL), washed with water (5 × 30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography (silica, Et_2O) gave **7** (48 mg, 0.22 mmol, 75%).

The aforementioned procedure was also applied to iodide **20** (100 mg, 0.28 mmol) giving **21** (52 mg, 0.23 mmol, 81%) as the only isolated product.

$(Bu_3Sn)_2$, UV light and a triplet sensitiser. A solution of iodide **5** (100 mg, 0.285 mmol), $(Bu_3Sn)_2$ (0.15 mL, 172 mg, 0.296 mmol) and 4-methoxyacetophenone (80 mg, 0.533 mmol) in acetonitrile (100 mL), under nitrogen in a water cooled Quartz photocell, was irradiated for 24 h using a sodium vapour lamp. The reaction mixture was concentrated *in vacuo* and partitioned between 2M NaOH (100 mL) and DCM (100 mL). The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to give **7** (15 mg, 0.068 mmol, 24%) and recovered starting material **5** (64 mg, 64%).

'Catalytic' Bu_3SnH. A THF (30 mL) solution of iodide **5** (100 mg, 0.285 mmol), 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) was heated at reflux under nitrogen for 12 h then cooled to RT. 2M NaOH (30 mL) was added and after 10 min the aqueous phase was separated and extracted with DCM (2 × 30 mL). The combined organic phases were then dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, Et_2O) to give **8** (46 mg, 0.204 mmol, 72%) as a pale yellow solid.

The aforementioned procedure was conducted using ethanol (30 mL) as solvent and gave **7** (30 mg, 0.136 mmol, 48%) and **8** (33 mg, 0.147 mmol, 52%).

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References and notes

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16 Two practical considerations led us to employ aryl iodides rather than aryl bromides in the *ortho*- and *ipso*-cyclisation reactions described herein. Firstly, the dichotomy outlined in Scheme 3 showed that side reactions were more significant when aryl bromides were employed. Secondly, with aryl bromides it was often necessary to add substantial quantities of the initiator AIBN in order to bring about complete conversion (on occasions, greater than a full equivalent!). By contrast, with aryl iodides it was usually possible to bring about complete conversion using 5–20 mol% AIBN. The switch was made after the experiments described in Schemes 8–10 had been conducted.
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