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Intramolecular radical additions to quinolines

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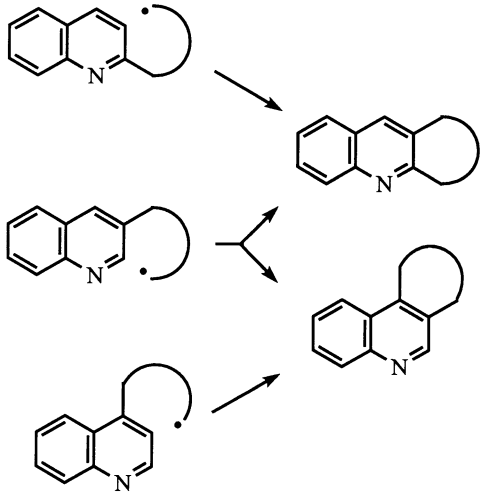
Abstract—The paper is concerned with intramolecular radical additions to quinolines. Radical additions to C-2, C-3 and C-4 of a quinoline have all been shown to proceed under neutral conditions. In each case formation of heteroaromatic products, rather than dihydroquinolines, was observed (implicating the so called oxidative tin hydride pathway).

1. Introduction

Radical additions to quinolines have a long, if chequered, history. First described by Hey and Walker in 1948, the addition of a phenyl radical to quinoline was found to be low yielding and lacking in selectivity.[1] A decade later, Pausacker confirmed that the thermal decomposition of dibenzoyl peroxide in quinoline gave products arising from Ph$^{\cdot}$ additions to each of the C-2 to C-8 carbon centres. Though 8-phenylquinoline was identified as the major component of this mixture, it was produced in such a pitiful yield (ca. 10% yield based on dibenzoyl peroxide; $<1\%$ based on quinoline) that the reaction was of no synthetic value.[2] Thus it remained an academic curiosity until a series of publications appeared showing that radical additions to the C-4 and C-2 carbons of quinoline predominated in acidic media.[3] Several extensions followed leading to a number of high yielding and regioselective methods for the functionalisation of quinolines; the seminal contributions of Minisci being particularly noteworthy.[4] In this paper we report our development of some intramolecular variants of the reaction (Scheme 1).[5] Notably, these studies show that 6-*exo*/*endo*-trig radical cyclisations to C-2, C-3 and C-4 of a quinoline are often efficient processes at neutral pH.



Scheme 1.

2. Results and discussion

All attempts to effect cyclisation reactions leading to five membered rings failed, yielding only the products of halide reduction (Scheme 2). This observation was not entirely unexpected as it confirmed a suspicion that the 5-*exo*/*endo*-trig cyclisation mode is more akin to a 5-*endo*-trig process than a 5-*exo*-trig process.[6]

The incorporation of an additional carbon in the tethering chain gave more encouraging results. Thus, treatment of *cis*-azastilbene **5** with tributyltin hydride under radical forming conditions led to a three component mixture from which the C-2 addition product **7** (24%) and C-4 addition product **8** (46%) were readily separated. Accompanying these materials was *trans*-azastilbene **9** (17%).[7] Its formation, and a need to use a near stoichiometric quantity of the initiator to drive the reaction to completion, suggested an inefficient homolysis of the carbon to bromine bond. Indeed, through the simple expedient of switching the halide from bromine to iodine, a separable 3:2 mixture of the cyclisation products **7** and **8** was given in near quantitative yield and the reaction required only 10 mol% of the initiator (Scheme 3).

The cyclisations of **10** and **11**, where a saturated two carbon chain conjoined the quinoline and aryl halide, were then examined. Treatment of bromide **10** with tributyltin hydride

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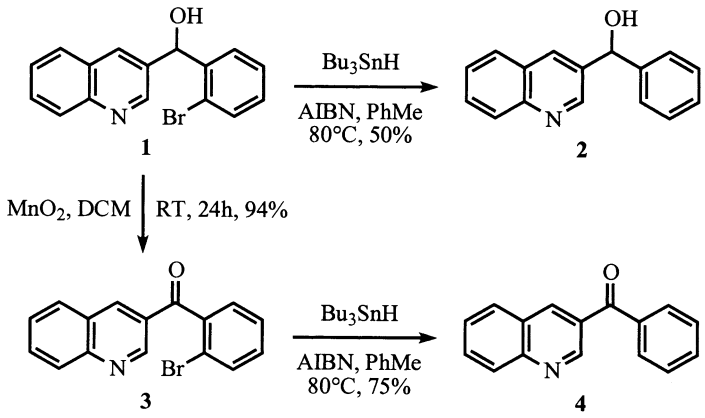
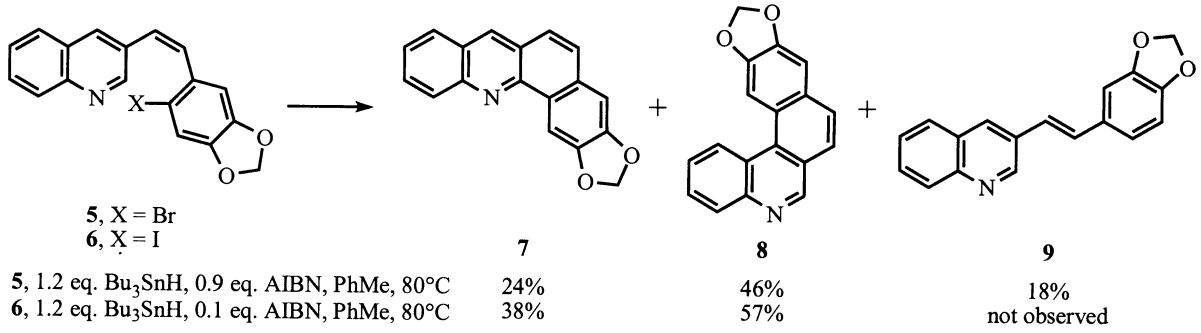
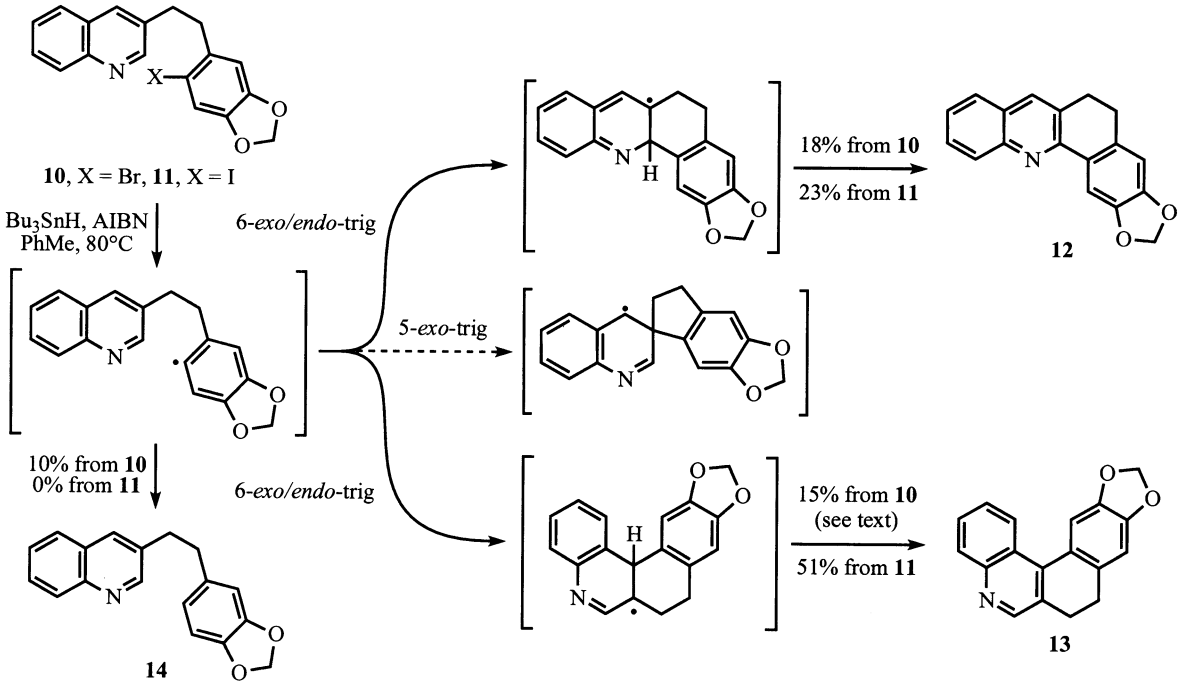


Scheme 2.

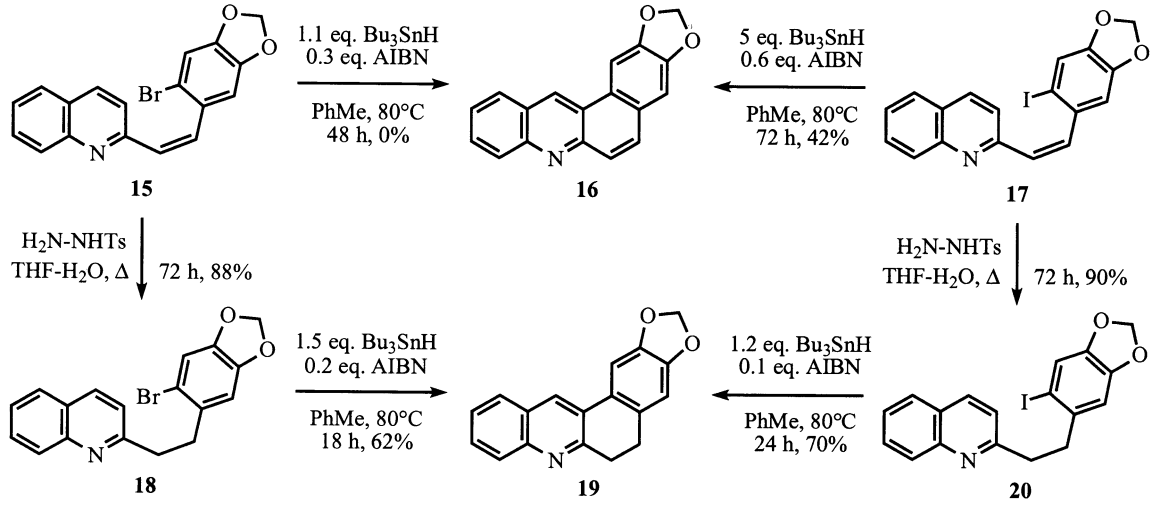


Scheme 3.

under standard radical forming conditions led to a complex product mixture from which the two cyclisation products **12** (18%) and **13** (15%), recovered starting material (27%) and dihydroazastilbene **14** (10%) could be isolated. A mixed fraction, the ^{1}H and ^{13}C NMR spectra of which showed many aliphatic signals, was also given. Attempts to identify the components of this mixture prove intractable. With iodide **11** the reaction proved more efficient, yielding dihydrobenzo[*c*]acridine **12** and dihydrobenzo[*k*]phenanthridine **13** in 23 and 51% yield, respectively (Scheme 4).



Scheme 4.



Scheme 5.

The increased yield of **13** relative to **12** when iodide **11** was used suggests that the unidentified products in the reaction with bromide **10** were derived from reduction of **13** or its cyclisation precursor, vide infra. Notably, and in contrast to the related radical cyclisation to a pyridine, no products derived from the 5-*exo*-trig (*ipso*-addition) pathway were detected (Scheme 4).[6]

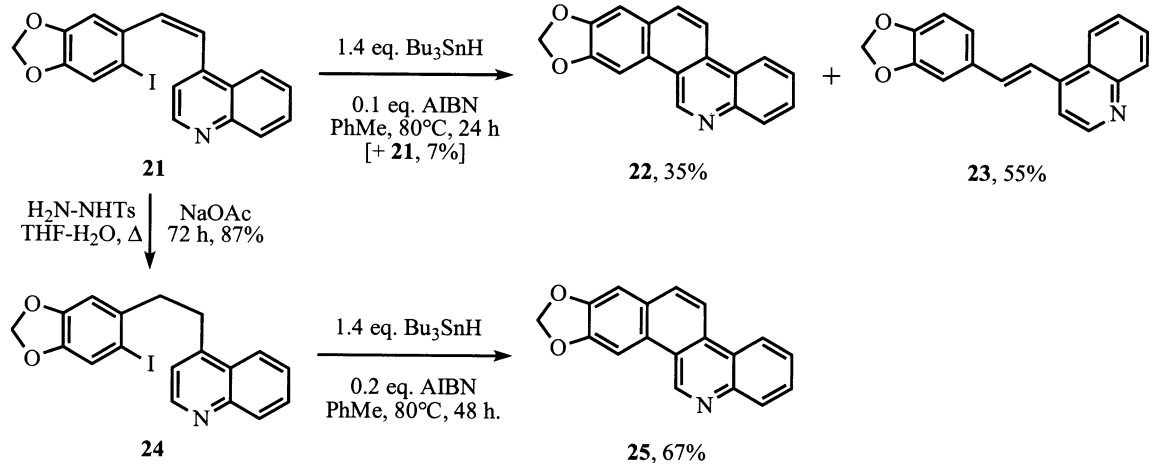
A series of cyclisations to C-3 of a quinoline were also investigated. Thus, while treatment of *cis*-azastilbene **15** with tributyltin hydride under standard radical forming conditions returned a mixture of *cis*- and *trans*-**15**, the corresponding iodide **17** gave benzo[*a*]acridine **16** in 42% yield. Dihydroazastilbenes **18** and **20** also underwent cyclisation leading to **19** in 62 and 70% yield, respectively (Scheme 5).

The cyclisation of aryl iodide **21**, in which the radical precursor was tethered at C-4 of the quinoline by a *cis*-alkene, proved less efficient. In this case alkene isomerisation outpaced homolysis of the carbon to iodine bond/cyclisation, leading to a product mixture comprising of the *trans*-azastilbene **23** (55% yield) and the C-3 addition product **22** (35% yield). With the corresponding dihydroazastilbene **24**, cyclisation again became the dominant course, with dihydrobenzo[*i*]phenanthridine **25** being given in 67% yield (Scheme 6).

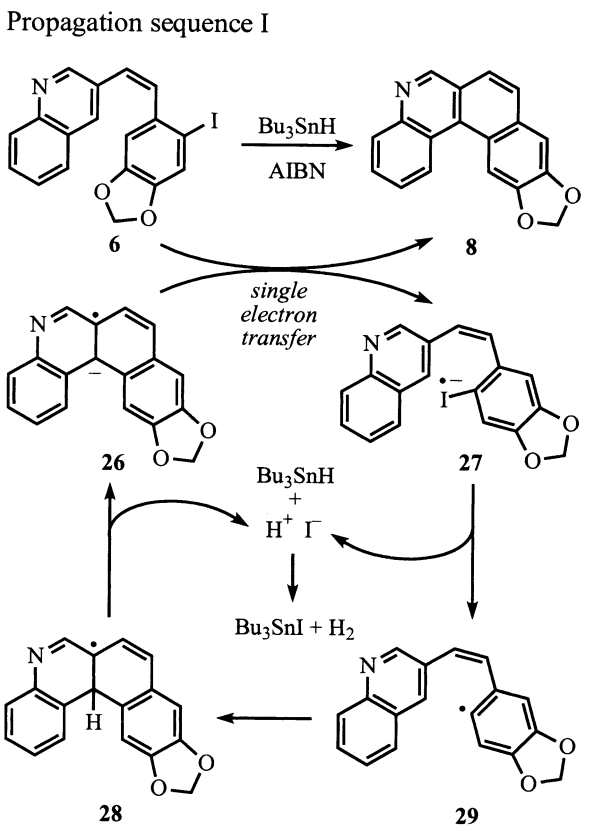
2.1. A note on the mechanism of non-reducing radical reactions mediated by tributyltin hydride

Finally, a referee asked that we comment on an apparent dichotomy between our results and a report by Allin et al.[7] in which it was stated that 'In the Bu_3SnH mediated oxidative cyclisations reported in the literature, greater than 1 equiv. of AIBN is required suggesting that AIBN is involved with a H-abstraction mechanism for this step'.[8] Though this is undoubtedly true for some reactions, many results were overlooked in reaching that conclusion, including our preliminary communication of this work.[5,9] Most notably, non-reducing radical reactions mediated by tributyltin hydride *generally* require ~10 mol% of AIBN when iodides are used as substrates and substantially more when bromides or selenides are used as substrates.[9] This is best illustrated by the cyclisation reactions of **5** and **6** (and **14** and **15** in Ref. 9x).

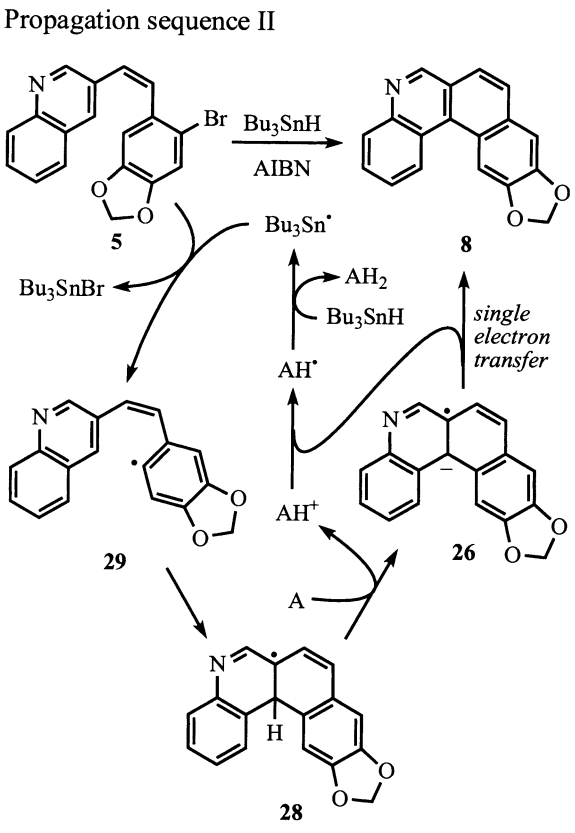
Our rationale is that two propagation sequences are in operation and that the dominant course is dictated by the



Scheme 6.



Scheme 7.



Scheme 8.

nature of the substrate. Thus, for substrates akin to iodide **6**, initiation follows the classical mechanism. However, once the reaction is underway, we suggest that the dominant course followed is that depicted in Scheme 7. Cyclisation of **29** is followed by loss of a proton from intermediate **28**. The resulting radical anion **26** then gives up an electron to **6** yielding the aromatic product **8** and radical anion **27**. Loss of iodide from **27** next gives **29**, thereby propagating the chain reaction. Finally, the hydrogen iodide formed as a by-product (and presumed to be tied up as a salt in this case) reacts with tributyltin hydride to produce tributyltin iodide and a molecule of hydrogen.

Single electron transfer to a bromide (or selenide) is much less facile than to an iodide. Hence, for substrates akin to **5** the sequence outlined in Scheme 7 becomes less significant. After classical initiation and cyclisation, we suggest that intermediate **28** loses a proton to some acceptor (A) in the system (which might be the substrate, the initiator or a product) giving radical anion **26** and AH^+. A single electron transfer from **26** to AH^+ then gives the product **8** and a radical intermediate $AH^{\cdot}$. The chain reaction is then propagated by a hydrogen atom abstraction from tributyltin hydride by $AH^{\cdot}$ (Scheme 8).

Work is ongoing to probe the mechanism in more detail as at this time our thoughts are based more on conjecture than scientific rigour. Nonetheless, the proposal provides a working hypothesis that is consistent with the results disclosed to date. It also provides an explanation as to why iodides usually give superior yields to bromides in such processes and how the halide can influence the product ratio when these materials are good electron acceptors.

3. Conclusions

In conclusion, we have shown that:

- Intramolecular 6-*exo*/*endo*-trig radical cyclisations to C-2, C-3 and C-4 of a quinoline are all facile processes and outpace the alternative *ipso*-cyclisation (5-*exo*-trig) pathways.
- Radical cyclisations to quinolines follow a non-reducing course and can be effected at neutral pH.[8]
- Cyclisation reactions that employ aryl iodides generally proceed more efficiently than the corresponding reaction with an aryl bromide. They also require less AIBN.
- When a *cis*-alkene is used to conjoin the radical precursor and quinoline at C-2 or C-4, isomerisation of the alkene competes with carbon to halogen bond homolysis when tributyltin hydride is used as a mediator.[10]
- 5-*exo*/*endo*-Trig radical cyclisations to quinolines fail and thus appear to be more akin to 5-*endo*-trig processes than 5-*exo*-trig processes.

4. Experimental

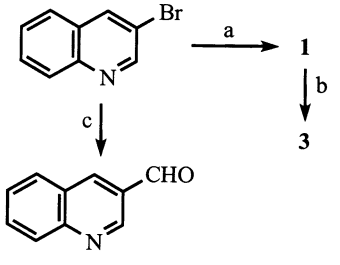
4.1. General remarks

Melting points were recorded on a Reichert melting point apparatus using a Comark digital temperature probe and are

uncorrected. Samples for combustion analysis and melting point determination were freshly recrystallised from the solvent indicated in parentheses after the mp. 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 67.5 MHz for ^{13}C), or a Bruker AC300 (operating at 300 MHz for ^{1}H and at 75 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 attained using atmospheric pressure chemical ionisation (APCI) or electrospray (ES) 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. 5-Bromo-6-(bromomethyl)-1,3-benzodioxole **31**, mp 92–94°C (chloroform) [lit. 88–89°C; 91–92°C],[11,12] was prepared by the method of Padwa et al.[11] [(6-Bromo-1,3-benzodioxole-5-yl)-methyl]-triphenylphosphonium bromide **32**, mp 275–279°C (EtOH) [Lit. 278–280°C (xylene)],[13] was prepared by the method of Harrowven et al.[14]



Scheme 9. *Reagents*: (a) *t*-BuLi then 2-bromobenzaldehyde; (b) MnO_2; (c) *t*-BuLi then DMF.

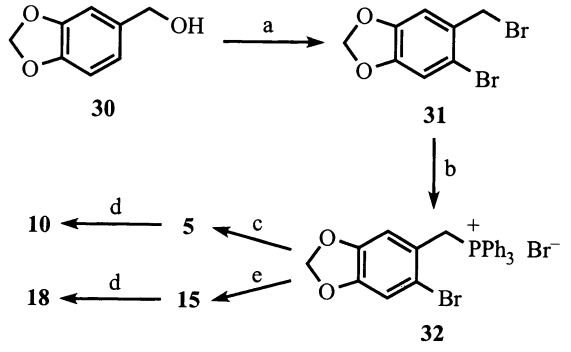
4.2. Preparation of substrates (Schemes 9–11)

4.2.1. α-(2-Bromophenyl)-3-quinolinemethanol 1. *t*-Butyllithium (1.25 M in hexane, 5.9 mL, 7.38 mmol) was added dropwise over 10 min to a solution of 3-bromoquinoline (1.0 mL, 1.53 g, 7.35 mmol) in Et_2O (20 mL) at −100°C. After 2 h a solution of 2-bromobenzaldehyde (0.87 mL, 1.38 g, 7.45 mmol) in Et_2O (20 mL) was added. After warming to −60°C over 2 h, brine (90 mL) and THF (50 mL) were added. The organic phase was separated, dried ($MgSO_4$), filtered and concentrated in vacuo. The residues were purified by column chromatography (silica, chloroform) to give the title product **1** (1.78 g, 5.65 mmol, 77%) as a white solid; mp 153–155°C (Et_2O/petrol); IR (solid, cm^{-1}) ν_{max} 3061 br. w, 2831 w, 2701 w, 1579 w, 1496 m, 1464 m, 1380 w, 1284 w, 1162 m, 1071 m, 1008 w; UV (MeOH, nm) λ_{max} (ε_{max}) 318 (3770), 304 (3330), 290 (3200); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.74 (1H, d, *J*=2.2 Hz, Ar*H*), 8.11 (1H, br. s, Ar*H*), 7.99 (1H, d, *J*=8.1 Hz, Ar*H*), 7.74–7.47 (5H, m, 5×Ar*H*), 7.33 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.14 (1H, app. td, *J*=8.1, 1.5 Hz, Ar*H*), 6.35 (1H, s, C*H*OH), 5.44 (1H, s, O*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 150.3 (*C*H), 147.0 (*C*), 142.1 (*C*), 135.8 (*C*), 134.3 (*C*H), 133.0 (*C*H), 129.8 (*C*H), 129.5 (*C*H), 128.7 (*C*H), 128.7 (*C*H), 128.2 (*C*H), 128.1 (*C*H), 127.9 (*C*), 127.0 (*C*H), 122.8 (*C*), 72.6 (*C*HOH); LRMS (APCI) 316 (83%, [MH(^{81}Br)]$^+$), 314 (100%, [MH(^{79}Br)]$^+$), 298 (12%, [MH(^{81}Br)−H_2O]$^+$), 296 (12%, [MH(^{79}Br)−H_2O]$^+$), 234 (18%, [MH−HBr]$^+$); HRMS (EI) *m/z* Found: M$^+$: 313.0096, $C_{16}H_{12}{}^{79}BrNO$ requires 313.0102; Anal. 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.

4.2.2. (2-Bromophenyl)-3-quinolinyl-methanone 3. The alcohol **1** (500 mg, 1.59 mmol) and activated manganese dioxide (4.00 g, 46 mmol) were stirred in dichloromethane (50 mL) at ambient temperature under an argon atmosphere for 24 h. After filtration through celite and concentration in vacuo, the organic residues were recrystallised from ether to give **3** (468 mg, 1.50 mmol, 94%) as a white solid; mp 129–131°C (Et_2O); IR (solid, cm^{-1}) ν_{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; UV (MeOH, nm) λ_{max} (ε_{max}) 292 (9930), 251 (38,000); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.37 (1H, d, *J*=1.8 Hz, Ar*H*), 8.50 (1H, d, *J*=1.8 Hz, Ar*H*), 8.21 (1H, d, *J*=8.8 Hz, Ar*H*), 7.93–7.86 (2H, m, 2×Ar*H*), 7.72 (1H, d, *J*=7.4 Hz, Ar*H*), 7.64 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.54–7.42 (3H, m, 3×Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 194.6 (*C*=O), 150.0 (*C*H), 149.8 (*C*), 139.8 (*C*H), 139.7 (*C*), 133.5 (*C*H), 132.5 (*C*H), 131.9 (*C*H), 129.6 (*C*H), 129.5 (*C*H), 129.3 (*C*H), 128.6 (*C*), 127.7 (*C*H), 127.6 (*C*H), 126.8 (*C*), 119.7 (*C*); LRMS (APCI) 355 (24%, [MH(^{81}Br)+MeCN]$^+$), 353 (20%, [MH(^{79}Br)+MeCN]$^+$), 314 (100%, [MH(^{81}Br)]$^+$), 312 (95%, [MH(^{79}Br)]$^+$), 259 (10%); HRMS (EI) *m/z* Found M$^+$: 310.9950, $C_{16}H_{10}{}^{79}BrNO$ requires 310.9946; Anal. Found: C, 61.65; H, 3.23; N, 4.49; $C_{16}H_{10}BrNO$ requires C, 61.56; H, 3.23; N, 4.49.

4.2.3. 3-Quinolinecarbaldehyde. *t*-Butyllithium (1.25 M in hexane, 5.9 mL, 7.38 mmol) was added dropwise over 5 min to a cooled (−100°C) solution of 3-bromoquinoline (1.0 mL, 1.53 g, 7.35 mmol) in Et_2O (20 mL). After 2 h, DMF (2 mL, 1.89 g, 25.8 mmol) was added, dropwise

over 5 min. The solution was warmed to −60°C over 4 h then brine (50 mL) and THF (20 mL) were added. After warming to ambient temperature the aqueous phase was separated and extracted with Et_2O (20 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The resulting residues were recrystallised from ether to give the title compound (704 mg, 4.48 mmol, 61%) as a white crystalline solid; mp 70–72°C (ether/petrol) [Lit. 71°C (EtOH); 70°C (H_2O)];[15,16] IR (DCM, cm^{-1}) ν_{max} 3047 w, 2835 w, 1700 s, 1618 s, 1596 m, 1572 m, 1498 m, 1372 m, 1272 s, 1210 m, 1165 m, 1125 m; UV (MeOH, nm) λ_{max} (ε_{max}) 315 (250), 282 (410), 246 (1330), 227 (2680); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 10.27 (1H, s, C*H*O), 9.38 (1H, br. s, Ar*H*), 8.65 (1H, d, *J*=1.5 Hz, Ar*H*), 8.21 (1H, d, *J*=8.1 Hz, Ar*H*), 8.01 (1H, d, *J*=8.1 Hz, Ar*H*), 7.90 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.68 (1H, app. t, *J*=7.7 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 190.8 (*C*HO), 150.6 (*C*), 149.1 (*C*H), 140.2 (*C*H), 132.7 (*C*H), 129.7 (*C*H), 129.4 (*C*H), 128.6 (*C*), 127.9 (*C*H), 127.0 (*C*); LRMS (CI) 158 (100%, $[MH]^+$), 157 (42%, $[M]^+$), 129 (26%, $[MH-CHO]^+$). These data were consistent with reported literature values.



Scheme 10. *Reagents*: (a) Br_2, AcOH; (b) PPh_3; (c) NaH, 3-quinolinecarboxaldehyde; (d) NH_2NHTs, NaOAc; (e) NaH, 2-quinolinecarboxaldehyde.

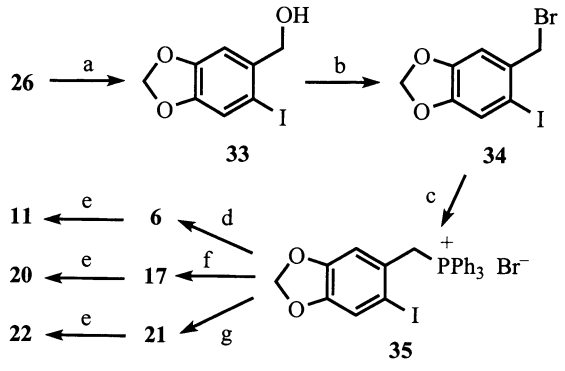
4.2.4. 3-[(*Z*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline, *cis*-5, and 3-[(*E*)-2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline, *trans*-5. NaH (176 mg, 4.40 mmol, 60% dispersion in oil) was washed with THF (10 mL) then suspended in THF (25 mL) at 0°C. The phosphonium salt **32** (2.04 g, 3.66 mmol) was added and the reaction warmed to room temperature over 18 h then re-cooled to 0°C. 3-Quinolinecarbaldehyde (500 mg, 3.02 mmol) was then added and after 3 h precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated in vacuo and purified by column chromatography (silica, 30:70, Et_2O/petrol) to give firstly *cis*-**5** (638 mg, 1.80 mmol, 60%) as a white crystalline solid; mp 115–117°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3012 w, 2896 w, 1616 w, 1567 w, 1500 m, 1475 s, 1423 m, 1230 m, 1037 m; UV (MeOH, nm) λ_{max} (ε_{max}) 300 (12,200), 275 (13,800); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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×Ar*H*), 7.52 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.10 (1H, s, Ar*H*), 6.75 (2H, s, C*H*=C*H*), 6.59 (1H, s, Ar*H*), 5.92 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 151.0 (*C*H), 148.2 (*C*), 147.4 (*C*), 146.7 (*C*), 135.4 (*C*H), 131.9 (*C*H), 130.1 (*C*), 129.7 (*C*), 129.5 (*C*H), 129.1 (*C*H), 127.8 (*C*H), 127.2 (*C*H), 126.9 (*C*H), 114.9 (*C*), 112.9 (*C*H), 109.9 (*C*H), 101.9 (OCH_2O) with one quaternary *C* obscured; LRMS (ES) 356 (16%, $[MH(^{81}Br)]^+$), 354 (16%, $[MH(^{79}Br)]^+$); Anal. 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; then *trans*-**5** (252 mg, 0.71 mmol, 24%) as a white solid; mp 175–177°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3065 w, 2897 w, 1501 m, 1475 s, 1411 w, 1240 m, 1115 w, 1038 m; UV (MeOH, nm) λ_{max} (ε_{max}) 337 (19,100), 309 (20,200), 281 (23,600); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, app. t, *J*=7.4 Hz, Ar*H*), 7.62 (1H, d, *J*=16.2 Hz, C*H*=C*H*), 7.57 (1H, app. 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, C*H*=C*H*), 6.03 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 149.4 (*C*H), 148.4 (*C*), 147.9 (*C*), 147.3 (*C*), 132.5 (*C*H), 130.2 (*C*), 129.9 (*C*), 129.5 (*C*H), 129.4 (*C*H), 129.1 (*C*H), 128.1 (*C*), 127.9 (*C*H), 127.1 (*C*H), 126.1 (*C*H), 115.8 (*C*), 112.9 (*C*H), 105.8 (*C*H), 102.0 (OCH_2O); LRMS (ES) 397 (13%, $[MH(^{81}Br)+CH_3CN]^+$), 395 ($MH(^{79}Br)+CH_3CN]^+$), 356 (100%, $[MH(^{81}Br)]^+$), 354 (96%, $[MH(^{79}Br)]^+$); Anal. Found: C, 60.71; H, 3.40; N, 3.83; $C_{18}H_{12}BrNO_2$ requires C, 61.04; H, 3.41; N, 3.95.

4.2.5. 3-[2-(6-Bromo-1,3-benzodioxol-5-yl)-ethyl]-quinoline 10. A solution of *cis*- and *trans*-azastilbenes **5** (12:5, 901 mg, 2.54 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) was heated at reflux for 72 h then cooled to ambient temperature and partitioned between saturated potassium carbonate (30 mL) and ether (15 mL). The aqueous phase was extracted with ether (3×20 mL) then the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residues were recrystallised from ether to give dihydroazastilbene **10** (532 mg, 1.49 mmol, 59%) as a white crystalline solid; mp 115–117°C (EtOH); IR (solid, cm^{-1}) ν_{max} 2899 w, 1501 m, 1475 s, 1236 m, 1119 w, 1038 m; UV (MeOH, nm) λ_{max} (ε_{max}) 318 (6820), 304 (10,100), 292 (11,900); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.77 (1H, d, *J*=2.2 Hz, Ar*H*), 8.09 (1H, d, *J*=8.8 Hz, Ar*H*), 7.92 (1H, br. s, Ar*H*), 7.76 (1H, d, *J*=8.1 Hz, Ar*H*), 7.67 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.52 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.01 (1H, s, Ar*H*), 6.64 (1H, s, Ar*H*), 5.93 (2H, s, OCH_2O), 3.03 (4H, s, CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 152.1 (*C*H), 147.5 (*C*), 147.1 (*C*), 147.1 (*C*), 134.6 (*C*H), 134.0 (*C*), 133.2 (*C*), 129.4 (*C*H), 128.9 (*C*H), 128.2 (*C*), 127.5 (*C*H), 126.8 (*C*H), 114.6 (*C*), 113.0 (*C*H), 110.2 (*C*H), 101.8 (OCH_2O), 38.0 (CH_2), 33.8 (CH_2); LRMS (ES) 358 (100%, $[MH(^{81}Br)]^+$), 356 (98%, $[MH(^{79}Br)]^+$), 140 (20%), 127 (25%); Anal. Found: C, 60.36; H, 3.96; N, 3.82; $C_{18}H_{14}BrNO_2$ requires C, 60.69; H, 3.96; N, 3.93.

4.2.6. 2-[(*Z*)-2-(6-Bromo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline 15. NaH (176 mg, 4.40 mmol, 60% dispersion in oil) was washed with THF (10 mL) then suspended in THF (25 mL) at 0°C. The phosphonium salt **32** (2.04 g, 3.66 mmol) was added followed after 2 h by 2-quinolinecarbaldehyde (500 mg, 3.02 mmol). After a further 3 h the precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated in vacuo and purified by column chromatography (silica, 20:80, ethyl acetate/petrol) to give **15** (1.01 g, 2.84 mmol, 88%) as a white

solid; mp 96–98°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3055 w, 2897 w, 1614 w, 1594 m, 1554 w, 1500 s, 1474 s, 1416 m, 1232 m, 1036 m; UV (MeOH, nm) λ_{max} (ε_{max}) 331 (10,100), 235 (23,700); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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×Ar*H*), 7.50 (1H, app. 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, =C*H*), 6.66 (1H, s, Ar*H*), 5.92 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 156.1 (*C*), 148.3 (*C*), 148.1 (*C*), 147.1 (*C*), 135.5 (*C*H), 133.6 (*C*H), 131.6 (*C*H), 130.1 (*C*), 129.6 (*C*H), 129.2 (*C*H), 127.5 (*C*H), 126.9 (*C*), 126.5 (*C*H), 122.0 (*C*H), 115.0 (*C*), 112.7 (*C*H), 110.6 (*C*H), 101.8 (OCH_2O); LRMS (ES) 356 (100%, $[MH(^{81}Br)]^+$), 354 (98%, $[MH(^{79}Br)]^+$), 144 (41%, $[C_{10}H_9NH]^+$); Anal. Found: C, 60.86; H, 3.42; N, 3.94; $C_{18}H_{12}BrNO_2$ requires C, 61.04; H, 3.41; N, 3.95.

4.2.7. 2-[2-(6-Bromo-1,3-benzodioxol-5-yl)ethyl]quinoline 18. A solution of *cis*-azastilbene **15** (667 mg, 1.88 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) was heated at reflux for 72 h then cooled to ambient temperature. The reaction was partitioned between saturated potassium carbonate (30 mL) and ether (30 mL). The aqueous phase was extracted with ether (3×30 mL) then the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residues were purified by column chromatography (silica, 30:70, Et_2O/petrol) to give dihydroazastilbene **18** (590 mg, 1.66 mmol, 88%) as a white crystalline solid; mp 108–110°C (Et_2O/petrol); IR (solid, cm^{-1}) ν_{max} 3050 w, 2892 w, 1600 w, 1502 m, 1475 s, 1233 m, 1113 m, 1038 m; UV (MeOH, nm) λ_{max} (ε_{max}) 316 (4550), 302 (6420), 290 (6610); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, app. t, J=7.7 Hz, Ar*H*), 7.51 (1H, app. 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, OCH_2O), 3.25–3.18 (4H, m, CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 161.5 (*C*), 148.1 (*C*), 147.5 (*C*), 146.9 (*C*), 136.5 (*C*H), 133.9 (*C*), 129.6 (*C*H), 129.0 (*C*H), 127.7 (*C*H), 127.0 (*C*), 126.0 (*C*H), 121.7 (*C*H), 114.6 (*C*), 112.9 (*C*H), 110.4 (*C*H), 101.7 (OCH_2O), 39.5 (CH_2), 36.3 (CH_2); LRMS (ES) 358 (97%, $[MH(^{81}Br)]^+$), 356 (100%, $[MH(^{79}Br)]^+$), 153 (32%), 146 (32%), 143 (45%), 127 (60%); Anal. 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.



Scheme 11. *Reagents*: (a) I_2, AgO_2CCF_3; (b) HBr; (c) PPh_3; (d) NaH, 3-quinolinecarboxaldehyde; (e) NH_2NHTs, NaOAc; (f) NaH, 2-quinolinecarboxaldehyde; (g) NaH, 4-quinolinecarboxaldehyde.

4.2.8. (6-Iodo-1,3-benzodioxol-5-yl)-methanol 33. To a cooled (−5°C) solution of piperonyl alcohol **30** (9.3 g, 61.1 mmol) in $CHCl_3$ (130 mL) were added iodine (17.3 g, 68.0 mmol) and silver trifluroacetate (15.0 g, 67.9 mmol). After stirring for 30 min the reaction was filtered through Celite®. The filtrate was washed with saturated $Na_2S_2O_3$ (100 mL), dried ($MgSO_4$) and concentrated in vacuo to a light yellow solid. Recrystallisation from $CHCl_3$ gave iodide **33** (14.7 g, 52.8 mmol, 87%) as a white crystalline solid; mp 110–112°C ($CHCl_3$) [Lit. 108–109°C ($CHCl_3$)].[17]

4.2.9. 5-(Bromomethyl)-6-iodo-1,3-benzodioxole 34. Concentrated HBr (48%, 40 mL) was slowly added to the alcohol **33** (10.1 g, 36.3 mmol) and the resulting suspension stirred for 2 h at rt then extracted with DCM (3×100 mL). The combined organic phases were washed with Na_2CO_3 (2 M, 50 mL), dried ($MgSO_4$) and concentrated in vacuo to give benzyl bromide **34** (11.2 g, 32.9 mmol, 90%) as a white solid; mp 72–73°C (EtOH) [lit. 72°C].[17]

4.2.10. Bromo-[(6-iodo-1,3-benzodioxol-5-yl)-methyl]-triphenylphosphorane 35. A solution of bromide **34** (11.0 g, 32.3 mmol) and triphenylphosphine (8.7 g, 33.0 mmol) in xylene (50 mL) was heated at 100°C for 24 h. The resultant white precipitate was collected by filtration, washed with cold xylene (2×20 mL) and cold petrol (2×20 mL), then recrystallised from EtOH/Et_2O to give the phosphonium salt **35** (18.6 g, 30.8 mmol, 95%) as a white crystalline solid; mp 268–272°C (EtOH); IR (solid, cm^{-1}) ν_{max} 2848 w, 1584 w, 1498 m, 1480 m, 1470 m, 1432 w, 1246 s, 1236 s, 1109 s, 1036 s; UV (MeOH, nm) λ_{max} (ε_{max}) 302 (4420), 275 (4830), 268 (5430); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.81–7.61 (15H, m, 15×Ar*H*), 7.02 (1H, s, Ar*H*), 6.92 (1H, d, J=2.2 Hz, Ar*H*), 5.92 (2H, s, OCH_2O), 5.45 (2H, d, J=13.2 Hz, ArCH_2PPh_3Br); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 148.9 (*C*), 148.8 (*C*), 135.3 (J_{C-P}=3.4 Hz, 3×*C*H), 134.4 (J_{C-P}=10.2 Hz, 6×*C*H), 130.3 (J_{C-P}=12.4 Hz, 6×*C*H), 123.4 (J_{C-P}=10.2 Hz, *C*), 118.5 (J_{C-P}=3.4 Hz, *C*H), 117.1 (J_{C-P}=84.8 Hz, 3×*C*), 111.5 (J_{C-P}=3.4 Hz, *C*H), 102.3 (OCH_2O), 93.4 (J_{C-P}=7.9 Hz, *C*), 35.7 (J_{C-P}=48.6 Hz, CH_2); LRMS (ES) 524 (28%), 523 (100%; $[M-Br]^+$).

4.2.11. 3-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline *cis*-6 and 3-[(*E*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline *trans*-6. NaH (176 mg, 4.40 mmol, 60% dispersion in oil) was washed with THF (10 mL) then suspended in THF (30 mL) at 0°C. Phosphonium salt **35** (2.00 g, 3.32 mmol) was added and the reaction mixture was allowed to warm to rt over 2 h then re-cooled to 0°C. 3-Quinolinecarbaldehyde (500 mg, 3.02 mmol) was then added and after 2 h precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated in vacuo and purified by column chromatography (silica, 50:50, Et_2O/petrol) and fractional crystallisation from aqueous ethanol to give firstly *cis*-**6** (610 mg, 1.52 mmol, 48%) as a yellow crystalline solid; mp 118–120°C (EtOH/H_2O); IR (solid, cm^{-1}) ν_{max} 1493 m, 1473 s, 1426 w, 1257 m, 1222 m, 1230 m, 1038 m; UV (MeOH, nm) λ_{max} (ε_{max}) 291 (9130); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, =C*H*), 6.64 (1H, d, J=11.8 Hz, =C*H*), 6.59 (1H, s, Ar*H*), 5.91 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 151.1 (*C*H), 148.5 (*C*), 148.2 (*C*), 146.8 (*C*), 135.9 (*C*H), 135.3 (*C*H), 134.2 (*C*), 129.5 (*C*), 129.4 (*C*H), 129.2 (*C*H), 127.8 (*C*H), 127.8 (*C*), 127.1 (*C*H), 126.8 (*C*H), 118.6 (*C*H), 109.7 (*C*H), 101.7 (O*C*H_2O), 88.1 (*C*); LRMS (ES) 443 (20%, $[MH+MeCN]^+$), 402 (83%, $[MH]^+$), 127 (100%); Anal. Found: C, 53.60; H, 3.02; N, 3.44; $C_{18}H_{12}INO_2$ requires C, 53.89; H, 3.01; N, 3.49; then *trans*-**6** (610 mg, 1.52 mmol, 48%) as a yellow crystalline solid; mp 177–179°C (EtOH/H_2O); IR (solid, cm^{-1}) ν_{max} 2897 w, 1500 m, 1473 s, 1406 w, 1231 s, 1114 w, 1038 m; UV (MeOH, nm) λ_{max} (ε_{max}) 346 (25,880), 317 (23,090), 283 (28,130), 256 (29,490); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 9.12 (1H, s, Ar*H*), 8.17 (1H, s, Ar*H*), 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, =C*H*), 7.32 (1H, s, Ar*H*), 7.19 (1H, s, Ar*H*), 6.95 (1H, d, J=16.2 Hz, =C*H*), 6.02 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 149.6 (*C*H), 148.9 (*C*), 148.5 (*C*), 147.5 (*C*), 134.4 (*C*H), 133.2 (*C*), 132.3 (*C*H), 130.0 (*C*), 129.3 (*C*H), 129.3 (*C*H), 128.1 (*C*), 127.9 (*C*H), 127.1 (*C*H), 126.5 (*C*H), 118.8 (*C*H), 105.7 (*C*H), 101.9 (O*C*H_2O), 89.7 (*C*); LRMS (ES) 443 (10%, $[MH+MeCN]^+$), 402 (34%, $[MH]^+$), 127 (100%); Anal. 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.

4.2.12. 3-[2-(6-Iodo-1,3-benzodioxol-5-yl)-ethyl]-quinoline 11. A solution of *cis*- and *trans*-azastilbenes **6** (1:1, 400 mg, 0.997 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) was heated at reflux for 24 h then cooled to ambient temperature. The reaction mixture was partitioned between saturated potassium carbonate (60 mL) and ether (30 mL) and separated. The aqueous phase was extracted with ether (4×30 mL) then the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, Et_2O) to give dihydroazastilbene **11** (398 mg, 0.987 mmol, 99%) as a white crystalline solid; mp 115–117°C (EtOH/H_2O); IR (solid, cm^{-1}) ν_{max} 1498 m, 1471 s, 1235 m, 1121 w, 1039 m; UV (MeOH, nm) λ_{max} (ε_{max}) 318 (4800), 304 (7340), 297 (7460); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, OCH_2O), 3.01 (4H, s, CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 152.1 (*C*H), 148.7 (*C*), 147.2 (*C*), 147.1 (*C*), 136.7 (*C*), 134.6 (*C*H), 133.8 (*C*), 129.4 (*C*H), 128.9 (*C*H), 128.2 (*C*), 127.5 (*C*H), 126.8 (*C*H), 118.8 (*C*H), 109.6 (*C*H), 101.7 (O*C*H_2O), 87.9 (*C*I), 42.5 (*C*H_2), 34.1 (*C*H_2); LRMS (ES) 445 (15%, $[MH+MeCN]^+$), 405 (18%, $[MH(^{13}C)]^+$), 404 (100%, $[MH]^+$), 127 (71%); Anal. 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.

4.2.13. 2-[(*Z*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline 17. NaH (154 mg, 3.85 mmol, 60% dispersion in oil) was washed with THF (10 mL) then suspended in THF (25 mL) at 0°C. Phosphonium salt **35** (1.80 g, 2.98 mmol) was added, followed after 2 h by 2-quinolinecarbaldehyde (500 mg, 3.18 mmol). After a further 2 h precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated in vacuo and purified by column chromatography (silica, ether) to give **17** (1.10 g, 2.74 mmol, 92%) as a white crystalline solid; mp 129–131°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3057 w, 2915 w, 1614 w, 1596 m, 1556 w, 1499 s, 1477 s, 1434 m, 1241 s, 1036 s; UV (MeOH, nm) λ_{max} (ε_{max}) 330 (12,400), 302 (12,200), 243 (33,400); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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×Ar*H*), 7.52 (1H, app. 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, =C*H*), 6.83 (1H, d, J=12.5 Hz, =C*H*), 6.66 (1H, s, Ar*H*), 5.94 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 156.2 (*C*), 148.4 (*C*), 148.4 (*C*), 137.9 (*C*H), 135.6 (*C*H), 134.3 (*C*), 131.6 (*C*H), 129.7 (*C*H), 129.3 (*C*H), 127.7 (*C*H), 127.0 (*C*), 126.7 (*C*H), 122.2 (*C*H), 118.6 (*C*H), 110.6 (*C*H), 101.9 (O*C*H_2O), 88.2 (*C*) with one quaternary *C* obscured; LRMS (ES) 402 (100%, $[MH]^+$), 127 (43%); Anal. 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.

4.2.14. 2[-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethyl]quinoline 20. A solution of azastilbene **17** (1.10 g, 2.74 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) was heated at reflux for 72 h then cooled to ambient temperature. The reaction was partitioned between saturated potassium carbonate (60 mL) and ether (30 mL) then separated. The aqueous phase was extracted with ether (2×30 mL) then the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by recrystallisation from ethanol to give dihydroazastilbene **20** (993 mg, 2.46 mmol, 90%) as a white crystalline solid; mp 139–141°C (EtOH); IR (solid, cm^{-1}) ν_{max} 2896 w, 1621 w, 1598 w, 1499 m, 1473 s, 1226 s, 1116 m, 1041 m; UV (MeOH, nm) λ_{max} (ε_{max}) 316 (5620), 303 (7590), 293 (7160); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, app. t, J=7.4 Hz, Ar*H*), 7.52 (1H, app. 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, OCH_2O), 3.27–3.14 (4H, m, CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 161.4 (*C*), 148.6 (*C*), 148.1 (*C*), 147.0 (*C*), 137.4 (*C*), 136.5 (*C*H), 129.6 (*C*H), 129.0 (*C*H), 127.7 (*C*H), 127.0 (*C*), 126.0 (*C*H), 121.7 (*C*H), 118.7 (*C*H), 109.7 (*C*H), 101.7 (O*C*H_2O), 88.0 (*C*), 40.9 (*C*H_2), 39.8 (*C*H_2); LRMS (ES) 404 (100%, $[MH]^+$), 127 (24%); Anal. 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.

4.2.15. 4-[(*E*)-2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline *trans*-21 and 4-[(*Z*)-2-(6-iodo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline *cis*-21. NaH (176 mg, 4.40 mmol, 60% dispersion in oil) was washed with THF (10 mL) then suspended in THF (25 mL) at 0°C. Phosphonium salt **35** (2.00 g, 3.32 mmol) was added, followed after 2 h by 4-quinolinecarbaldehyde (500 mg, 3.18 mmol). After a further 2 h precipitated triphenylphosphine oxide was removed by filtration. The filtrate was concentrated in vacuo and purified by column chromatography (silica, ether) to give a 1:1 mixture of *cis*- and *trans*-**21** (1.07 g,

2.67 mmol, 84%). Fractional crystallisation from methanol yielded firstly *trans*-**21** as a pale orange solid (510 mg, 1.27 mmol, 40%); mp 175–176°C (MeOH); IR (solid, cm^{-1}) ν_{max} 2896 w, 1621 w, 1598 w, 1499 m, 1473 s, 1226 s, 1116 m, 1041 m; UV (MeOH, nm) λ_{max} (ε_{max}) 356 (19,430), 232 (39,860); ^{1}H NMR (250 MHz, d_6-DMSO) δ_H 8.91 (1H, d, J=4.6 Hz, Ar*H*), 8.53 (1H, d, J=7.6 Hz, Ar*H*), 8.05 (1H, dd, J=7.9, 0.9 Hz, Ar*H*), 7.94 (1H, d, J=15.9 Hz, =C*H*), 7.80 (1H, app. td, J=7.6, 1.3 Hz, ArH), 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, =C*H*R), 7.50 (1H, s, Ar*H*), 6.14 (2H, s, OCH_2O); ^{13}C NMR (63 MHz, d_6-DMSO) δ_C 150.7 (*C*H), 149.2 (*C*), 149.1 (*C*), 148.7 (*C*), 142.4 (*C*), 138.1 (*C*H), 132.7 (*C*), 129.9 (*C*H), 129.9 (*C*H), 126.9 (*C*H), 126.1 (*C*), 124.7 (*C*H), 124.5 (*C*H), 118.6 (*C*H), 117.0 (*C*H), 107.2 (*C*H), 102.5 (O*C*H_2O), 91.5 (*C*); LRMS (APCI) 403 (19%, [MH (^{13}C)]$^+$), 402 (100%, [MH]$^+$), 279 (14%); Anal. 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; then from the mother liquor *cis*-**21** (500 mg, 1.25 mmol, 39%) as a pale yellow solid; mp 112–113°C (EtOH); IR (solid, cm^{-1}) ν_{max} 1496 m, 1471 s, 1427 w, 1240 s, 1223 m, 1192 w, 1140 w, 1112 w, 1034 s; UV (MeOH, nm) λ_{max} (ε_{max}) 303 (7910); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 8.74 (1H, d, J=4.4 Hz, Ar*H*), 8.14 (1H, d, J=8.1 Hz, Ar*H*), 8.05 (1H, d, J=8.1 Hz, Ar*H*), 7.75 (1H, t, J=7.0 Hz, Ar*H*), 7.58 (1H, t, J=7.0 Hz, Ar*H*), 7.28 (1H, s, Ar*H*), 7.10 (1H, d, J=4.4 Hz, Ar*H*), 7.03 (1H, d, J=11.8 Hz, =C*H*), 6.89 (1H, d, J=11.8 Hz, =C*H*), 6.28 (1H, s, Ar*H*), 5.84 (2H, s, OCH_2O); ^{13}C NMR (63 MHz, $CDCl_3$) δ_C 149.8 (*C*H), 148.2 (*C*), 148.1 (*C*), 142.9 (*C*), 138.4 (*C*H), 133.2 (*C*), 129.9 (*C*H), 129.7 (*C*H), 126.8 (*C*H), 126.8 (*C*), 126.0 (*C*H), 124.4 (*C*H), 121.2 (*C*H), 118.3 (*C*H), 118.3 (*C*), 109.8 (*C*H), 101.6 (*C*H_2), 88.4 (Ar, *C*); LRMS (APCI) 403 (18%, [MH (^{13}C)]$^+$), 402 (86%, [MH]$^+$), 153 (85%), 127 (100%); Anal. 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.

4.2.16. 4-[2-(6-Iodo-1,3-benzodioxol-5-yl)-1-ethyl]quinoline 24. A solution of *cis*- and *trans*-azastilbenes **21** (ratio 1:1, 780 mg, 1.94 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) was heated at reflux for 72 h then cooled to ambient temperature. The reaction was partitioned between 2 M potassium carbonate (30 mL) and ether (50 mL). The aqueous phase was extracted with ether (2×50 mL) then the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, ether) to give dihydroazastilbene **24** (678 mg, 1.68 mmol, 87%) as a white crystalline solid; mp 98–100°C (ether/petrol); IR (solid, cm^{-1}) ν_{max} 2896 w, 1592 w, 1502 m, 1474 s, 1227 s, 1110 m, 1038 s; UV (MeOH, nm) λ_{max} (ε_{max}) 314 (2990), 300 (7870), 290 (8880); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, app. t, J=7.7 Hz, Ar*H*), 7.57 (1H, app. 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, OCH_2O), 3.30–3.25 (2H, app. dd, J=9.9, 6.3 Hz, CH_2), 3.07–3.02 (2H, app. dd, J=9.6, 5.9 Hz CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 150.4 (*C*H), 148.6 (*C*), 148.3 (*C*), 147.1 (*C*), 146.9 (*C*), 136.8 (*C*), 130.3 (*C*H), 129.2 (*C*H), 127.5 (*C*), 126.5 (*C*H), 123.6 (*C*H), 121.0 (*C*H), 118.7 (*C*H), 109.4 (*C*H), 101.6 (O*C*H_2O), 87.6 (*C*), 41.2 (*C*H_2), 32.9 (*C*H_2); LRMS (ES) 445 (15%, [MH+MeCN]$^+$), 404 (100%, [MH]$^+$), 153 (15%), 144 (16%); Anal. 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.

4.3. Radical reactions

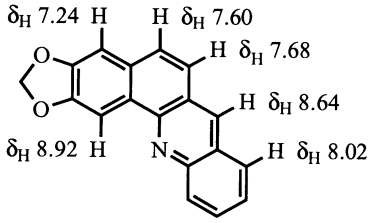
4.3.1. α-Phenyl-3-quinolinemethanol 2. A stirred solution of aryl bromide **1** (300 mg, 0.95 mmol), Bu_3SnH (0.25 mL, 280 mg, 0.96 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (30 mL) was heated at 80°C under nitrogen for 5 h then cooled to rt. Saturated KF (25 mL) and water (25 mL) were added and the two phase mixture was stirred vigorously for 18 h. The organic phase was separated, dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, 97:3, $CHCl_3$/MeOH) to yield the title compound **2** (112 mg, 0.48 mmol, 50%) as a white solid; mp 136–138°C ($CHCl_3$); IR (solid, cm^{-1}) ν_{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; UV (MeOH, nm) λ_{max} (ε_{max}) 318 (2700), 304 (2350), 291 (2240), 269 (2630); ^{1}H NMR (300 MHz, d_6-DMSO) δ_H 8.91 (1H, s, Ar*H*), 8.34–8.33 (2H, m, 2×Ar*H*), 7.99 (2H, app. t, J=7.4 Hz, Ar*H*), 7.71 (1H, app. t, J=7.7 Hz, Ar*H*), 7.58 (1H, app. t, J=7.7 Hz, Ar*H*), 7.50–7.21 (4H, m, 4×Ar*H*), 6.29 (1H, d, J=3.7 Hz, C*H*OH), 6.01 (1H, d, J=3.7 Hz, O*H*); ^{13}C NMR (75 MHz, d_6-DMSO) δ_C 150.2 (*C*H), 146.8 (*C*), 144.8 (*C*), 138.5 (*C*), 132.2 (*C*H), 129.2 (*C*H), 128.7 (*C*H), 128.4 (2×*C*H), 128.2 (*C*H), 127.5 (*C*), 127.2 (*C*H), 126.8 (*C*H), 126.5 (2×*C*H), 72.5 (*C*HOH); LRMS (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; Anal. 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.

4.3.2. Phenyl-3-quinolinyl-methanone 4. A stirred solution of aryl bromide **3** (129 mg, 0.413 mmol), Bu_3SnH (0.14 mL, 151 mg, 0.519 mmol) and AIBN (10 mg, 0.061 mmol) in toluene (40 mL) was heated at 80°C under nitrogen for 48 h then cooled to rt. Saturated KF (20 mL) and water (20 mL) were added and the two phase mixture was stirred vigorously for 48 h. The organic phase was separated, dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, 1:1, Et_2O/petrol) to yield the title compound **4** (72 mg, 0.31 mmol, 75%) as a white solid; mp 75–76°C (petrol) [Lit. 76–78°C];[18] Anal. Found: C, 82.11; H, 4.79; N, 6.02; $C_{16}H_{11}NO$ requires C, 82.38; H, 4.75; N, 6.00. Spectral data were in accord with literature values.

4.3.3. [1,3]Dioxolo[4′,5′:4,5]benzo[*c*]acridine 7, [1,3]-dioxolo[4′,5′:4,5]benzo[*k*]phenanthridine 8 and 3-[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline 9. A stirred solution of aryl bromide **5** (250 mg, 0.706 mmol), Bu_3SnH (0.23 mL, 249 mg, 0.853 mmol) and AIBN (100 mg, 0.609 mmol) in toluene (80 mL) was heated at 80°C under nitrogen for 18 h then cooled to rt. Saturated KF (25 mL) and water (25 mL) were added and the two phase mixture was stirred vigorously for 8 h. The organic phase was separated, dried ($MgSO_4$), concentrated in vacuo and

purified by column chromatography (silica, 1:1 Et_2O/petrol) to yield firstly [1,3]dioxolo[4′,5′:4,5]benzo[*c*]acridine **7** (47 mg, 0.172 mmol, 24%), then 3-[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]quinoline **9** (35 mg, 0.127 mmol, 18%) as a white solid; mp 117–119°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3032 w, 2894 w, 1502 s, 1490 s, 1445 m, 1253 s, 1039 m; UV (MeOH, nm) λ_{max} (ε_{max}) 336 (28,900), 308 (19,000), 282 (25,200); ^1H NMR (400 MHz, $CDCl_3$) δ_H 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, =C*H*), 7.06 (1H, d, *J*=1.5 Hz, Ar*H*), 7.02 (1H, d, *J*=16.1 Hz, =C*H*), 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, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 148.0 (*C*H), 146.9 (*C*), 146.5 (*C*), 146.0 (*C*), 130.4 (*C*H), 129.9 (*C*), 129.2 (*C*H), 129.0 (*C*), 127.9 (*C*H), 127.6 (*C*H), 126.7 (*C*), 126.3 (*C*H), 125.6 (*C*H), 122.1 (*C*H), 120.5 (*C*H), 107.1 (*C*H), 104.2 (*C*H), 99.9 (OCH_2O); LRMS (ES) 317 (9%, $[MH+MeCN]^+$), 276 (100%, $[MH]^+$), 140 (17%), 127 (22%); HRMS (ES+) Found MH^+: 276.1009, $C_{18}H_{14}NO_2$ requires 276.1019; and finally [1,3]dioxolo[4′,5′:4,5]benzo[*k*]phenanthridine **8** (89 mg, 0.326 mmol, 46%).

Alternatively, a stirred solution of aryl iodide **6** (100 mg, 0.249 mmol), Bu_3SnH (0.08 mL, 87 mg, 0.297 mmol) and AIBN (4 mg, 0.024 mmol) in toluene (20 mL) was heated at 80°C under nitrogen for 18 h then cooled to rt. Saturated KF (25 mL) and water (25 mL) were added and the two phase mixture was stirred vigorously for 24 h. The organic phase was separated, dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, 1:1 Et_2O/petrol) to yield firstly [1,3]dioxolo[4′,5′:4,5]benzo[*c*]acridine **7** (26 mg, 0.095 mmol, 38%) as a white solid; mp 180–182°C (Et_2O/petrol); IR (solid, cm^{-1}) ν_{max} 1487 m, 1464 s, 1405 m, 1278 m, 1232 m, 1039 m; UV (MeOH, nm) λ_{max} (ε_{max}) 385 (7620), 366 (8340), 350 (6290), 307 (59,500), 282 (59,600); ^1H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O); nOe (400 MHz, $CDCl_3$) irradiation of the signal at δ_H 8.92 caused no nOe enhancement. Irradiation of the signal at δ_H 8.64 led to nOe enhancement at δ_H 8.02 and δ_H 7.68. Irradiation of the signal at δ_H 7.24 led to nOe enhancement at δ_H 7.60; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 149.3 (*C*), 148.2 (*C*), 147.7 (*C*), 147.2 (*C*), 135.1 (*C*H), 130.4 (*C*), 129.6 (*C*H), 129.6 (*C*H), 127.8 (*C*H), 127.1 (*C*H), 126.6 (*C*), 125.5 (*C*H), 124.6 (*C*), 124.1 (*C*H), 105.7 (*C*H), 103.9 (*C*H), 101.6 (OCH_2O) with one quaternary *C* obscured; LRMS (ES) 275 (17%, $[MH(^{13}C)]^+$), 274 (100%, $[MH]^+$), 153 (41%), 127 (48%); HRMS (ES+) Found MH^+: 274.0865, $C_{18}H_{12}NO_2$ requires 274.0868; then [1,3]dioxolo[4′,5′:4,5]benzo[*k*]phenanthridine **8** (39 mg, 0.143 mmol, 57%) as a white solid; mp 200–202°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3062 w, 2903 w, 1578 w, 1501 m, 1476 s, 1450 m, 1385 w, 1365 w, 1249 s, 1037 m; UV (MeOH, nm) λ_{max} (ε_{max}) 382 (2430), 363 (2320), 332 (5730), 303 (10,200), 282 (31,200); ^1H NMR (400 MHz, $CDCl_3$) δ_H 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×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, OCH_2O); nOe (400 MHz, $CDCl_3$) irradiation of the signal at δ_H 9.29 led to nOe enhancement at δ_H 7.86–7.79. Irradiation of the signal at δ_H 8.50 led to nOe enhancement at δ_H 8.96. Irradiation of the signal at δ_H 7.34 led to nOe enhancement at δ_H 7.86–7.79; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 153.2 (*C*H), 149.2 (*C*), 148.9 (*C*), 146.7 (*C*), 133.1 (*C*), 130.9 (*C*), 130.6 (*C*H), 128.4 (*C*H), 128.4 (*C*H), 126.9 (*C*H), 126.7 (*C*H), 125.6 (*C*), 125.0 (*C*), 125.0 (*C*), 124.2 (*C*H), 106.1 (*C*H), 105.8 (*C*H), 102.2 (OCH_2O); LRMS (ES) 275 (17%, $[MH(^{13}C)]^+$), 274 (100%, $[MH]^+$); Anal. Found: C, 78.63; H, 4.04; N, 5.10; $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.



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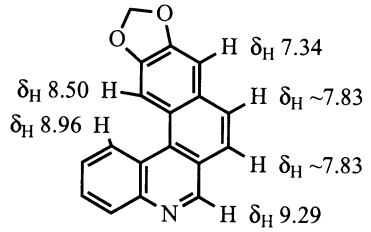

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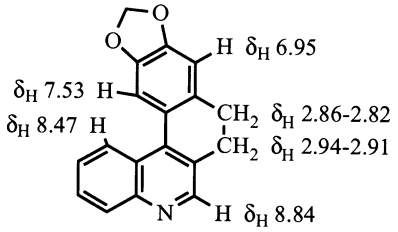
4.3.4. 5,6-Dihydro[1,3]dioxolo[4′,5′:4,5]benzo[*c*]acridine 12, 7,8-dihydro[1,3]dioxolo[4′,5′:4,5]benzo[*k*]phenanthridine 13 and 3-[2-(1,3-benzodioxol-5-yl)-1-ethyl]quinoline 14. A stirred solution of aryl iodide **11** (750 mg, 1.86 mmol), Bu_3SnH (0.70 mL, 757 mg, 2.60 mmol) and AIBN (30 mg, 0.183 mmol) in toluene (170 mL) was heated at 80°C under nitrogen for 36 h then cooled to rt. Saturated KF (50 mL) and water (50 mL) were added and the two phase mixture was stirred vigorously for 36 h. The organic phase was separated, dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, Et_2O) to yield firstly **12** as a white crystalline solid (116 mg, 0.421 mmol, 23%); mp 138–140°C (Et_2O/petrol); IR (solid, cm^{-1}) ν_{max} 2894 w, 2835 w, 1612 w, 1484 s, 1449 m, 1405 m, 1376 m, 1268 s, 1226 m, 1036 s; UV (MeOH, nm) λ_{max} (ε_{max}) 359 (30,200), 320 (10,100), 275 (19,700), 252 (29,900); ^1H NMR (300 MHz, $CDCl_3$) δ_H 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, OCH_2O), 3.08 (2H, app. t, *J*=7.0 Hz, CH_2), 2.91 (2H, app. t, *J*=6.6 Hz, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.2 (*C*), 148.9 (*C*), 147.5 (*C*), 147.3 (*C*), 134.5 (*C*), 133.4 (*C*H), 130.0 (*C*), 129.1 (*C*H), 128.9 (*C*), 128.6 (*C*H), 127.6 (*C*), 126.9 (*C*H), 125.7 (*C*H), 108.0 (*C*H), 106.2 (*C*H), 101.2 (OCH_2O), 28.9 (*C*H_2), 28.5 (*C*H_2); LRMS (ES) 277 (18%, $[MH(^{13}C)]^+$), 276 (100%, $[MH]^+$); Anal. 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; then **13** (260 mg, 0.944 mmol, 51%) as a white crystalline solid; mp 144–146°C (CH_2Cl_2/petrol); IR (solid, cm^{-1}) ν_{max} 2898 w, 1618 w, 1562 m, 1501 s, 1485 s, 1419 w, 1389 m, 1283 m, 1224 s, 1167 m, 1041 s; UV (MeOH, nm) λ_{max} (ε_{max}) 353 (7880), 327 (5060), 243 (15,800); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, OCH_2O), 2.94–2.91 (2H, m, CH_2), 2.86–2.82 (2H, m, CH_2); nOe (400 MHz, $CDCl_3$) irradiation of the signal at δ_H 8.84 led to nOe enhancement at δ_H 2.94–2.91. Irradiation of the signal at δ_H 7.53 led to nOe enhancement at δ_H 8.47. Irradiation of the signal at δ_H 6.95 led to nOe enhancement at δ_H 2.86–2.82; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 151.1 (*C*H), 150.0 (*C*), 148.7 (*C*), 147.4 (*C*), 140.4 (*C*), 136.1 (*C*), 131.3 (*C*H), 131.0 (*C*), 129.1 (*C*H), 127.5 (*C*H), 126.6 (*C*), 126.1 (*C*H), 125.4 (*C*), 110.7 (*C*H), 109.9 (*C*H), 102.4 (O*C*H_2O), 30.3 (*C*H_2), 27.7 (*C*H_2); LRMS (ES) 277 (18%, [MH(^{13}C)]$^+$), 276 (100%, [MH]$^+$), 242 (16%); Anal. Found: C, 78.22; H, 4.76; N, 5.00; $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.



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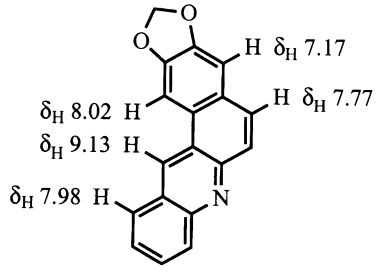
Alternatively, a stirred solution of aryl bromide **10** (286 mg, 0.803 mmol), Bu_3SnH (0.30 mL, 325 mg, 1.11 mmol) and AIBN (10 mg, 0.061 mmol) in toluene (120 mL) was heated at 80°C under nitrogen for 24 h then cooled to rt. Saturated KF (25 mL) and water (25 mL) were added and the two phase mixture was stirred vigorously for 24 h. The phases were separated and the aqueous phase extracted with ether (2×50 mL). The combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, gradient elution 0:100→80:20 ether/petrol) to yield firstly **12** (40 mg, 0.15 mmol, 18%); then an inseparable mixed fraction (38 mg); then recovered **10** (71 mg, 27%) and finally a mixed fraction comprising of **13** and **14**. Fractional crystallisation from ethanol gave **13** (33 mg, 0.12 mmol, 15%). Finally, **14** (22 mg, 0.08 mmol, 10%) was isolated from the mother liquor; mp 91–93°C (EtOH); IR (solid, cm^{-1}) ν_{max} 1500 m, 1483 s, 1440 m, 1360 w, 1241 s, 1190 w, 1038 s; UV (MeOH, nm) λ_{max} (ε_{max}) 318 (4510), 304 (4210), 285 (7310), 233 (37,410); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, OCH_2O), 3.10–3.05 (2H, m, CH_2CH$_2$), 2.97–2.92 (2H, m, CH$_2$CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 151.9 (*C*H), 147.7 (*C*), 146.8 (*C*), 145.9 (*C*), 134.5 (*C*H), 134.1 (*C*), 129.1 (*C*H), 128.7 (*C*H), 128.1 (*C*), 127.4 (*C*H), 126.6 (*C*H), 121.4 (*C*H), 108.9 (*C*H), 108.2 (*C*H), 100.9 (*C*H_2), 37.2 (*C*H_2), 35.3 (*C*H_2), with one *C*H obscured; LRMS (ES) 279 (19%, [MH(^{13}C)]$^+$), 278 (100%, [MH]$^+$); HRMS (ES+) Found MH$^+$: 278.1176, $C_{18}H_{16}NO_2$ requires 278.1167.

4.3.5. Attempted radical cyclisation of 2[(*Z*)-2-(6-bromo-1,3-benzodioxol-5-yl)-1-ethenyl]quinoline 15. The alkene **15** (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 48 h. The resulting mixture was cooled to room temperature, stirred for 18 h with saturated KF (50 mL) then separated. The organic phase was dried ($MgSO_4$), concentrated and purified by column chromatography (silica, 50:50, ether/petrol) to yield a mixture of *cis*-**15** and *trans*-**15**. Fractional crystallisation from ethanol gave *trans*-**15** (16 mg, 0.0451 mmol, 14%) as a white crystalline solid; mp 198–200°C (EtOH); IR (solid, cm^{-1}) ν_{max} 1597 m, 1486 s, 1412 w, 1308 w, 1265 m, 1242 m, 1232, m, 1119 m, 1034 s; UV (MeOH, nm) λ_{max} (ε_{max}) 351 (18,460), 252 (19,900); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, =C*H*), 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, =C*H*), 7.08 (1H, s, Ar*H*), 6.03 (2H, s, OCH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 155.9 (*C*), 148.8 (*C*), 148.2 (*C*), 147.9 (*C*), 136.4 (*C*H), 132.8 (*C*H), 130.2 (*C*H), 129.8 (*C*H), 129.7 (*C*), 129.2 (*C*H), 127.5 (*C*H), 127.3 (*C*), 126.3 (*C*H), 118.8 (*C*H), 116.4 (*C*), 112.9 (*C*H), 106.1 (*C*H), 102.0 (*C*H_2); LRMS (ES) 356 (86%, [M(^{81}Br)+H]$^+$), 354 (80%, [M(^{79}Br)+H]$^+$), 276 (17%), 152 (100%); HRMS (ES+) Found MH$^+$: 354.0124, $C_{18}H_{13}NO_2{}^{79}Br$ requires 354.0116; concentration of the mother liquor furnished *cis*-**15** (95 mg, 0.268 mmol, 82%).

4.3.6. [1,3]Dioxolo[4′,5′:4,5]benzo[*a*]acridine 16. A stirred solution of aryl iodide **17** (500 mg, 1.25 mmol), Bu_3SnH (1.62 mL, 1.75 g, 6.01 mmol) and AIBN (120 mg, 0.73 mmol) in toluene (100 mL) was heated at 80°C under nitrogen for 72 h then cooled to rt. Saturated KF (40 mL) and water (40 mL) were added and the two phase mixture was stirred vigorously for 36 h then separated. The aqueous phase was extracted with ether (2×100 mL) then the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, Et_2O) to give **16** (142 mg, 0.52 mmol, 42%) as a yellow crystalline solid; mp 215–217°C (Et_2O/petrol); IR (solid, cm^{-1}) ν_{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; UV (MeOH, nm) λ_{max} (ε_{max}) 385 (10,740), 366 (10,190), 309 (7172), 295



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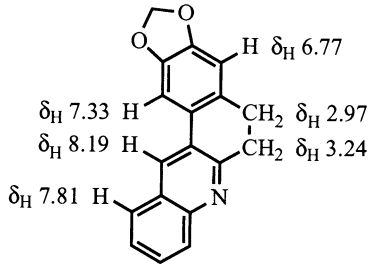
(53,370), 284 (63,090), 242 (60,200); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 9.13 (1H, s, Ar*H*), 8.17 (1H, d, *J*=8.5 Hz, Ar*H*), 8.02 (1H, s, Ar*H*), 7.98 (1H, d, *J*=8.0 Hz, Ar*H*), 7.87 (1H, d, *J*=9.0 Hz, Ar*H*), 7.77 (1H, d, *J*=9.5 Hz, Ar*H*), 7.72 (1H, app. t, *J*=8.3 Hz, Ar*H*), 7.51 (1H, app. t, *J*=7.5 Hz, Ar*H*), 7.17 (1H, s, Ar*H*), 6.06 (2H, s, OCH_2O); nOe (400 MHz, $CDCl_3$) irradiation of the signal at δ_H 9.13 led to nOe enhancement at δ_H 8.02 and δ_H 7.98. Irradiation of the signal at δ_H 7.17 led to nOe enhancement at δ_H 7.77; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 149.2 (*C*), 149.1 (*C*), 148.7 (*C*), 148.3 (*C*), 132.4 (*C*H), 130.5 (*C*H), 130.2 (*C*H), 129.4 (*C*H), 128.6 (*C*H), 127.8 (*C*), 127.1 (*C*H), 126.8 (*C*), 126.3 (*C*H), 124.4 (*C*), 107.1 (*C*H), 102.1 (*C*H), 102.1 (O*C*H$_2$O), with one quaternary *C* obscured; LRMS (ES) 274 (8%, $[MH]^+$), 123 (100%); Anal. Found: C, 78.79; H, 4.07; N, 5.09; $C_{18}H_{11}NO_2$ requires C, 79.11; H, 4.06; N, 5.13.

4.3.7. 5,6-Dihydro[1,3]dioxolo[4′,5′:4,5]benzo[*a*]acridine 19. A stirred solution of aryl bromide **18** (91 mg, 0.255 mmol), Bu_3SnH (0.10 mL, 108 mg, 0.371 mmol) and AIBN (10 mg, 0.06 mmol) in toluene (80 mL) was heated at 80°C under nitrogen for 18 h then cooled to rt. Saturated KF (25 mL) and water (25 mL) were added and the two phase mixture was stirred vigorously for 24 h then separated. The aqueous phase was extracted with ether (50 mL) and the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, 1:1 Et_2O/petrol) to give the title compound **19** (43 mg, 0.156 mmol, 62%) as a white solid.

Alternatively, a stirred solution of aryl iodide **20** (570 mg, 1.41 mmol), Bu_3SnH (0.46 mL, 498 mg, 1.71 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (80 mL) was heated at 80°C under nitrogen for 24 h then cooled to rt. Saturated KF (25 mL) and water (25 mL) were added and the two phase mixture was stirred vigorously for 36 h then separated. The aqueous phase was extracted with ether (50 mL), then the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, 1:1, Et_2O/petrol) to yield **19** (270 mg, 0.98 mmol, 70%) as a white crystalline solid; mp 168–170°C (EtOH); IR (solid, cm^{-1}) ν_{max} 3042 w, 2948 w, 2891 w, 1619 w, 1502 m, 1482 s, 1383 m, 1363 m, 1250 m, 1222 m, 1038 s; UV (MeOH, nm) λ_{max} (ε_{max}) 357 (13,500), 322 (10,700), 309 (7970), 278 (17,400); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 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, app. t, *J*=7.4 Hz, Ar*H*), 7.48 (1H, app. t, *J*=7.4 Hz, Ar*H*), 7.33 (1H, s, Ar*H*), 6.77 (1H, s, Ar*H*), 6.00 (2H, s, OCH_2O), 3.24 (2H, app. t, *J*=7.0 Hz, ArCH_2), 2.97 (2H, app. t, *J*=7.0 Hz, ArCH_2); nOe (400 MHz, $CDCl_3$) irradiation of the signal at δ_H 8.19 led to nOe enhancement at δ_H 7.81 and δ_H 7.33. Irradiation of the signal at δ_H 3.24 led to nOe enhancement at δ_H 2.97. Irradiation of the signal at δ_H 2.97 led to nOe enhancement at δ_H 6.77 and δ_H 3.24; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 159.1 (*C*), 148.0 (*C*), 147.5 (*C*), 146.7 (*C*), 132.1 (*C*), 129.1 (*C*H), 128.6 (*C*H), 128.5 (*C*H), 128.4 (*C*), 128.2 (*C*), 127.8 (*C*H), 126.8 (*C*), 126.2 (*C*H), 108.8 (*C*H), 104.6 (*C*H), 101.4 (O*C*H$_2$O), 33.2 (Ar*C*H$_2$), 28.9 (Ar*C*H$_2$); LRMS (ES) 276 (100%, $[MH]^+$), 153 (35%), 130 (22%); Anal. Found: C, 78.10; H, 4.83; N, 5.03; $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.



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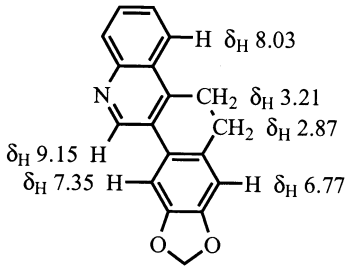
4.3.8. [1,3]Dioxolo[4′5′:4,5]benzo[*i*]phenanthridine 22 and 4-[(*E*)-2-(1,3-benzodioxol-5-yl)-1-ethenyl]-quinoline 23. A stirred solution of aryl iodide **21** (600 mg, 1.50 mmol), Bu_3SnH (0.55 mL, 595 mg, 2.04 mmol) and AIBN (20 mg, 0.122 mmol) in toluene (120 mL) was heated at 80°C under nitrogen for 24 h then cooled to rt. Saturated KF (50 mL) and water (50 mL) were added and the two phase mixture was stirred vigorously for 18 h then separated. The organic phase was dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, Et_2O) to yield firstly recovered starting material **21** (40 mg, 0.10 mmol, 7%) then a mixture of the cyclised product **22** and the reduced product **23**. These materials were separated by fractional crystallisation from EtOH to yield firstly **22** (142 mg, 0.52 mmol, 35%) as a white solid; mp 237–239°C (EtOH); IR (solid, cm^{-1}) ν_{max} 1744 m, 1701 m, 1470 s, 1370 m, 1356 m, 1230 s, 1190 m, 1030 m; UV (MeOH, nm) λ_{max} (ε_{max}) 372 (10,340), 354 (8740), 329 (11,250), 307 (14,690), 254 (39,010); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, app. td, *J*=7.5, 1.5 Hz, Ar*H*), 7.71 (1H, app. td, *J*=7.5, 1.0 Hz, Ar*H*), 7.33 (1H, s, Ar*H*), 6.17 (2H, s, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 148.2 (*C*), 146.9 (*C*), 146.8 (*C*H), 143.5 (*C*), 130.0 (*C*H), 129.8 (*C*), 128.8 (*C*H), 127.9 (*C*), 127.2 (*C*H), 125.8 (*C*H), 125.7 (*C*), 123.1 (*C*), 121.3 (*C*H), 120.4 (*C*), 117.0 (*C*H), 104.4 (*C*H), 100.5 (O*C*H$_2$O), 98.6 (*C*H); LRMS (APCI) 275 (20%, $[MH(^{13}C)]^+$), 274 (100%, $[MH]^+$); HRMS (ES+) Found MH^+: 274.0863, $C_{18}H_{12}NO_2$ requires 274.0867; then **23** (226 mg, 0.82 mmol, 55%) as a white solid; mp 117–118°C (EtOH); IR (solid, cm^{-1}) ν_{max} 1575 w, 1501 m, 1489 w, 1446 m, 1253 s, 1197 m, 1038 s; UV (MeOH, nm) λ_{max} (ε_{max}) 316 (7430), 304 (7430), 227 (27,020); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 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, =C*H*), 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, =C*H*), 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, OCH_2O); ^{13}C NMR (63 MHz, $CDCl_3$) δ_C 150.2 (*C*H), 148.8 (*C*), 148.4 (*C*), 148.3 (*C*), 143.0 (*C*), 134.7 (*C*H), 131.1 (*C*), 130.2 (*C*H), 129.3 (*C*H), 126.4 (*C*H), 126.4 (*C*), 123.4 (*C*H), 122.6 (*C*H), 121.0 (*C*H), 116.8 (*C*H), 108.6 (*C*H), 105.9 (*C*H), 101.4 (O*C*H$_2$O); LRMS (APCI) 277 (19%, $[MH(^{13}C)]^+$), 276 (100%, $[MH]^+$), 158 (32%); Anal. Found: C, 78.13; H, 4.70; N, 5.08; $C_{18}H_{13}NO_2$ requires C, 78.53; H, 4.76; N, 5.09.

4.3.9. 5,6-Dihydro-[1,3]dioxolo[4′,5′:4,5]benzo[*i*]phenanthridine 25. A stirred solution of aryl iodide **24** (415 mg, 1.03 mmol), Bu_3SnH (0.40 mL, 433 mg, 1.48 mmol) and AIBN (40 mg, 0.24 mmol) in toluene (80 mL) was heated at 80°C under nitrogen for 48 h then cooled to rt. Saturated KF (40 mL) and water (40 mL) were added and the two phase mixture was stirred vigorously for 24 h then separated. The aqueous phase was extracted with ether (2×50 mL) then the combined organic phases were dried ($MgSO_4$), concentrated in vacuo and purified by column chromatography (silica, Et_2O) to yield the title compound **25** (190 mg, 0.69 mmol, 67%) as a white solid; mp 138–140°C (DCM/petrol); IR (solid, cm^{-1}) ν_{max} 2900 w, 1687 w, 1502 m, 1486 s, 1471 s, 1366 m, 1267 m, 1232 s, 1038 s; UV (MeOH, nm) λ_{max} (ε_{max}) 357 (7910), 269 (18,140), 239 (16,620); ^1H NMR (300 MHz, $CDCl_3$) δ_H 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, app. t, *J*=7.4 Hz, Ar*H*), 7.54 (1H, app. t, *J*=7.7 Hz, Ar*H*), 7.35 (1H, s, Ar*H*), 6.77 (1H, s, Ar*H*), 5.97 (2H, s, OCH_2O), 3.21 (2H, t, *J*=7.6 Hz, $ArCH_2$), 2.87 (2H, t, *J*=7.6 Hz, $ArCH_2$); nOe (400 MHz, $CDCl_3$) irradiation of the signal at δ_H 9.15 led to nOe enhancement at δ_H 7.35. Irradiation of the signal at δ_H 7.35 led to nOe enhancement at δ_H 9.15. Irradiation of the signal at δ_H 3.21 led to nOe enhancement at δ_H 8.03 and δ_H 2.87. Irradiation of the signal at δ_H 2.87 led to nOe enhancement at δ_H 6.77 and δ_H 3.21; ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 147.3 (*C*), 147.2 (*C*), 146.9 (*C*), 146.5 (*C*H), 140.6 (*C*), 130.9 (*C*), 129.9 (*C*H), 128.6 (*C*H), 126.9 (*C*), 126.7 (*C*H), 126.4 (*C*), 125.8 (*C*), 123.4 (*C*H), 108.7 (*C*H), 104.2 (*C*H), 101.2 (OCH_2O), 27.9 ($ArCH_2$), 23.3 ($ArCH_2$); LRMS (ES) 317 (22%, $[MH+MeCN]^+$), 276 (100%, $[MH]^+$), 168 (22%), 153 (64%), 144 (33%); HRMS (ES) Found MH^+: 276.1026, $C_{18}H_{14}NO_2$ requires 276.1024.



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