Novel heterocycles from 5-methyldibenz[*b*,*f*]azocin-6,12-dione and its derivatives

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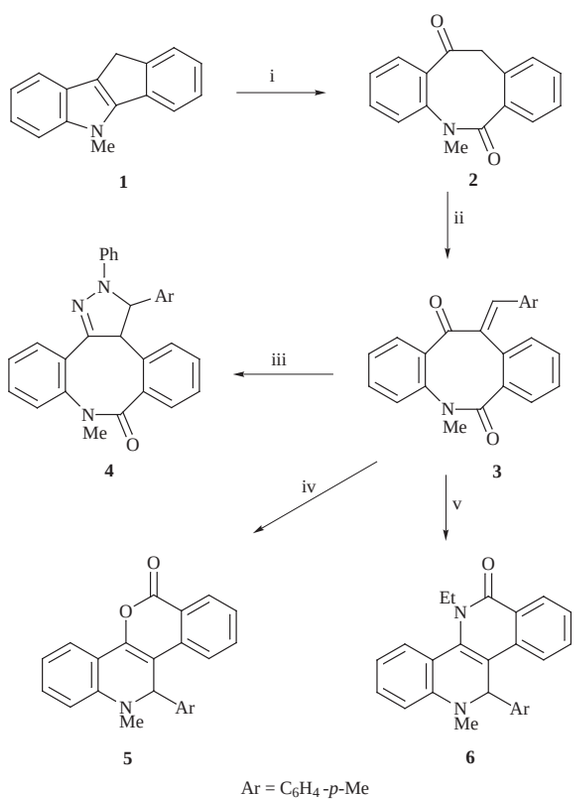
The multifunctional dibenzazocine 2 and its benzylidene derivative 3 have been shown to take part in a variety of rearrangement reactions to produce novel heterocycles. Heterochrysenes 5 and 6 are formed from 3 on treatment with hydroxylamine and ethylamine respectively. The novel spiro-compounds 7 and 9 are obtained from 2 with aniline (at 120 °C) and $NaIO_4$ (or SeO_2) oxidation respectively, and acid and amine treatment of 2 gives the isocoumarin 10 and isoquinolines 8(a–c) respectively. Alkaline hydrolysis of 2 gives the deoxybenzoin 11 from which 5, 7, 8(a–c), 9 and 10 are also obtainable leading to mechanistic suggestions for the formation of these compounds. Treatment of 10 with Lawesson's reagent gives the thionoisocoumarin 13.

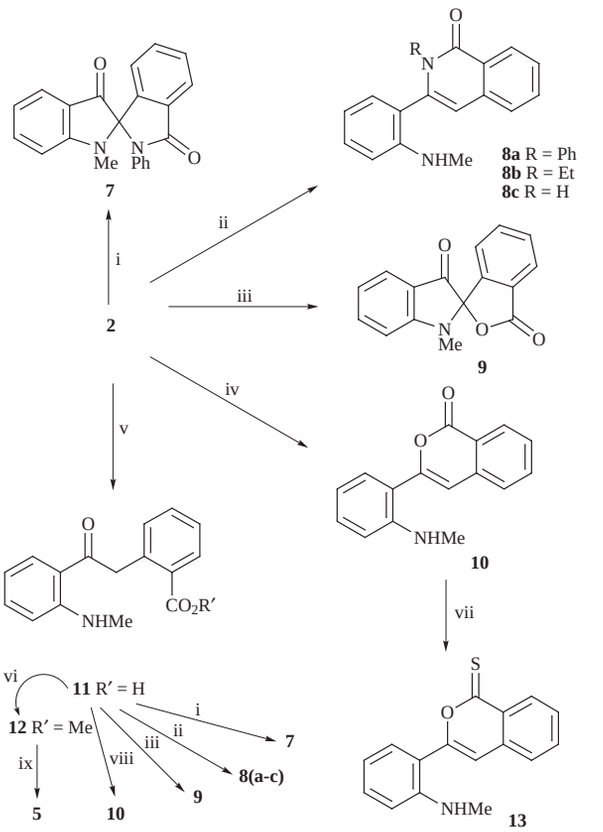
From the hydrogen peroxide oxidation of the known[1] indeno[1,2-*b*]indole **1**, 5-methyldibenz[*b*,*f*]azocin-6,12-dione **2** is readily obtained. Azocine **2**, with its varied functional groups (amide, ketone or rather a vinylogous amide, and an activated methylene group) in close proximity to each other, attracted our attention as a possible readily available candidate for undergoing transannular and tandem reactions to give novel heterocycles. Our earlier experiments on the reactions of **3**, the benzylidene derivative of azocine **2**, have appeared in a communication[2] in which we reported the following three reactions: (i) with phenylhydrazine, **3** reacted as an α,β-unsaturated ketone to give the (*E*)-pyrazolodibenzazocine **4**; (ii) with hydroxylamine no oxime or oxazole was obtained but instead the 5-oxa-12-azachrysene **5** was isolated and its structure confirmed by X-ray crystallography, and (iii) a similar reaction occurred between **3** and ethylamine giving the 5,12-diazachrysene **6**. These reactions are outlined in Scheme 1 and full details appear in the Experimental section. The stereochemistry in **3** was established as (*E*) from an analysis of the vicinal ^{13}C, ^{1}H coupling constants exhibited by the 'ketone' carbonyl carbon atom.[3] Compounds **5** and **6** exhibit strong yellow fluorescence under ultraviolet light.

We have extended these reactions by firstly treating **3** with aniline: at 130 °C the spiro[indole-2,1′-isoindole] **7** (structure by X-ray crystallography[4]) was obtained in 73% yield, and at 170 °C the isoquinoline **8a** (structure by X-ray crystallography[5]) was isolated in 60% yield. Since the elements of the benzylidine group are not present in **7** and **8a**, it seemed reasonable to presume that azocine **2** would take part in similar reactions. This was found to be the case and **2** reacted with aniline at 120 °C to give **7** and at 170 °C to give isoquinoline **8a**. Other more basic amines gave analogous isoquinolines, *e.g.* **2** reacted with ethylamine to give **8b** and with ammonium acetate to give **8c**. Azocine **2** was also found to react with the oxidising agents $NaIO_4$ or SeO_2, to give the spiro[indole-2,1′-isobenzofuran] **9**, and on treatment with dilute sulfuric acid or trifluoroacetic acid, **2** gave the isocoumarin **10**. The structures of **8**(**b** and **c**) and **9** followed from a comparison of their spectra, especially NMR, with those of the analogous compounds, *viz*. **8a** and **7** respectively. The structure of **10** followed from its spectra including the characteristic isocoumarin carbonyl absorption at 1728 cm^{-1} in the infrared. Alkaline hydrolysis of **2** yielded the deoxybenzoin **11**. Treatment of isocoumarin **10** with Lawesson's reagent gave the thionoisocoumarin **13**. The structures of **11** and **13** followed from an analysis of their spectra, which for compound **13** included a ^{13}C resonance at δ 200.2 which is characteristic of a thionolactone. These reactions are outlined in Scheme 2.

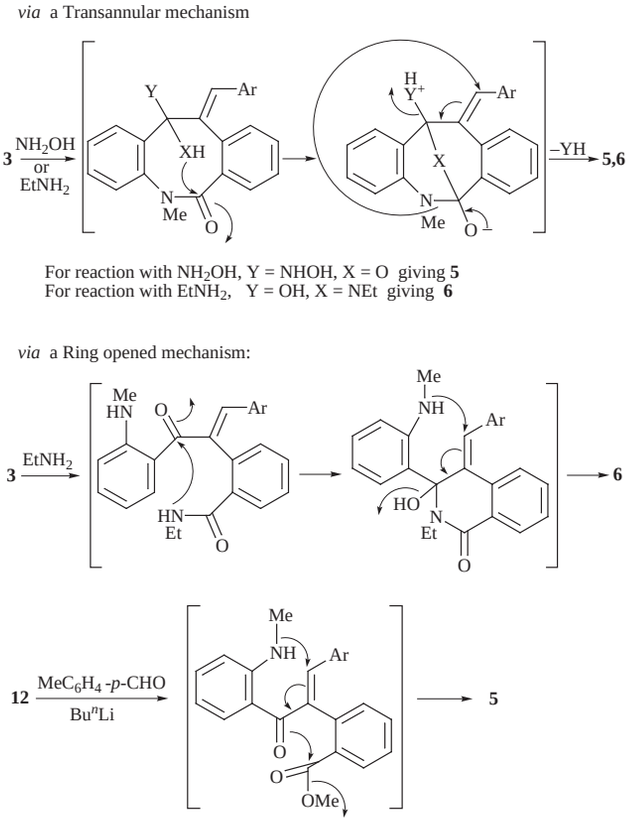


Scheme 1 *Reagents and conditions*: i, H_2O_2, 64%; ii, ArCHO, NaOEt, 92%; iii, $PhNHNH_2$, reflux, 60%; iv, $NH_2OH{\cdot}HCl$, pyridine, reflux, 20%; v, $EtNH_2$, reflux, 50%

In considering mechanisms for the formation of compounds **5**–**10** we have made a number of observations supported by experiments which are detailed below. Firstly, the formation of the heterochrysenes **5** and **6** could have arisen by either (i) initial attack of hydroxylamine or ethylamine at the 12-oxo-group followed by a transannular attack of the resulting C-12 oxygen or nitrogen respectively, at the 6-oxo-group with associated amide cleavage and followed by a tandem ring closure involving Michael addition of the *N*-methyl group to the benzylidene β-carbon, or (ii) the initial step could have been amide cleavage resulting from hydroxylamine or ethylamine attack at the amide carbonyl to give the ring opened deoxybenzoin which could then take part in the various ring closures. In support of the latter we have treated **12**, the methyl ester of the deoxybenzoin **11** (obtained from reaction of **11** with diazomethane)

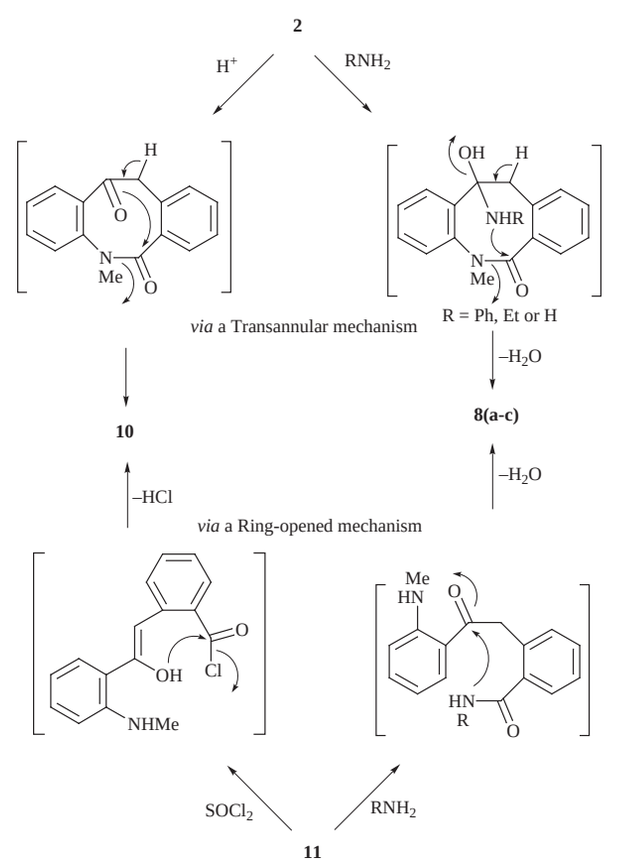


Scheme 2 *Reagents and conditions*: i, $PhNH_2$, 120 °C; ii, $PhNH_2$, 170 °C for **8a**; $EtNH_2$ for **8b**; NH_4Ac for **8c**; iii, SeO_2; or $NaIO_4$; iv, CF_3CO_2H, reflux; v, aq. $NaOH/H^+$; vi, CH_2N_2; vii, $P_2S_4(C_6H_4$-*p*-$OMe)_2$; viii, BF_3–MeOH; ix, MeC_6H_4-*p*-CHO, Bu^nLi

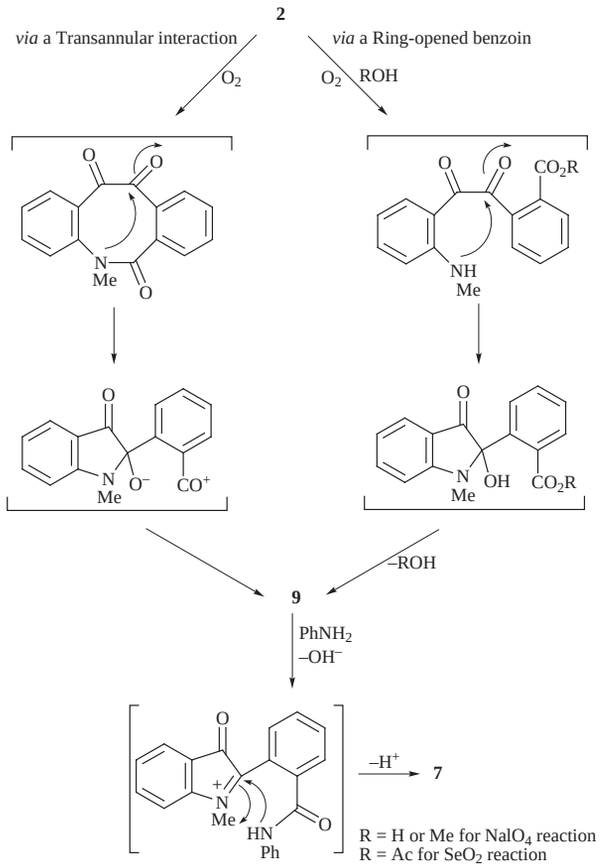


Scheme 3

with *n*-butyllithium and 4-methylbenzaldehyde and obtained chrysene **5**. These mechanisms are all outlined in Scheme 3. The formation of compounds **8**(**a**–**c**) and **10** from **2** may also be considered to involve either a transannular reaction or an initial amide cleavage followed by subsequent formation of the heterocyclic ring from the ring opened deoxybenzoin. The latter process is supported by the fact that treatment of **11** with acidic reagents gives **10**, possibly *via* the enol of the ketone, and treatment of **11** with the appropriate amine gives **8a**, **8b** or **8c**. These mechanisms for **8**(**a**–**c**) and **10** are outlined in Scheme 4. With regard to the mechanism for the formation of the spiro-compounds **7** and **9** from **2**, the way in which functionalisation of the methylene group occurs is clearly important. *A priori* these reactions could go *via* either an initial transannular reaction or *via* the initial formation of a ring opened deoxybenzoin. The latter process is supported by the fact that we have found that the ring opened deoxybenzoin **11** reacts with SeO_2 to give **9**, and with aniline at 120 °C to give **7**. One way in which functionalisation of the methylene group could occur is *via* autoxidation to a ketone, and therefore likely intermediates in these reactions would be 5-methyl-6,11,12-trioxodibenz[*b*,*f*]azocine or the corresponding ring opened benzoin (see Scheme 5). Attempts to prove this by isolating or trapping such intermediates have failed; for example heating **2** and 1,2-phenylenediamine in refluxing toluene into which air was bubbled, gave only the spiro[benzimadazole-2′,12-dibenzazocine] **14**; failure to trap the diketone may be accounted for by the fact that the autoxidation reaction is slow compared with imadazole ring formation. This suggestion that oxidation of the methylene group is necessary in order for the spiro-compounds **7** and **9** to form, is supported by the fact that the formation of **9** requires an oxidant ($NaIO_4$ or SeO_2). Furthermore even more strong support comes from the fact that the reactions of **2** or **11** with aniline at 120 °C both fail to yield any product when the reaction is carried out under oxygen-free nitrogen. A further clue to the possible mechanism of formation of the spiro-compound **7** comes from the fact that on heating **9** with aniline, compound **7**

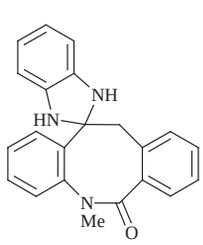


Scheme 4



Scheme 5

was obtained in good yield, strongly suggesting that **7** is formed from **2** (or **11**) *via* initial autoxidation of the methylene group to a ketone, followed by formation of **9**, and finally by attack of aniline on **9** as shown in Scheme 5. These results suggest that the spiro-compound **9**, could itself be formed merely by autoxidation of **2** (or **11**). This has indeed been found to occur since on bubbling air into a solution of **2** in hot dimethylformamide, **9** was obtained. Finally, the temperature dependence of the reactions of **2** (and **11**) with aniline may be explained on the basis of rates of the above reactions: assuming that the α,β-diketone, *i.e.* the autoxidation product, reacts very rapidly in an intramolecular cyclisation to give initially **9**, then the reaction at 120 °C appears to involve an autoxidation to the α,β-diketone which is faster than the intermolecular reaction of aniline with the carbonyls of **2** or **11** to give the isoquinoline **8a**, but at 170 °C this latter reaction would appear to be much faster than the autoxidation. Unfortunately we have not been able to obtain any strong unequivocal evidence on whether the reactions are transannular or go *via* the ring opened azocine, since, apart from the fact that azocine ring opening to the deoxybenzoin occurs easily, the deoxybenzoin **11** has itself been found to transform readily to the azocine **2** in refluxing toluene. Both of these processes could conceivably occur in the reactions in question.



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Experimental

General

All melting points were determined with a Kofler hotstage microscope apparatus and are uncorrected. ^{1}H NMR (90, 270 MHz) and ^{13}C NMR (22.6 and 67.9 MHz) spectra were recorded on JEOL spectrometers, in $CDCl_3$ and were referenced against tetramethylsilane; chemical shifts are reported in ppm on the δ scale, coupling constants (J) are given in Hz, and multiplicity was determined from off-resonance decoupled or DEPT spectra. Mass spectra and accurate mass measurements were recorded on a Finnigan MAT-95 instrument using the EI mode with a direct inlet system and operating at 70 eV. Infrared spectra were recorded for Nujol mulls and ultraviolet spectra were recorded in 95% ethanol. Column chromatography was carried out using Merck Kieselgel 60 (70–230 mesh) and thin layer chromatography was performed on precoated silica gel 60 GF_{254} (Merck 5729) plates (20 cm^2) which had been activated at 120 °C for 3 hours. All compounds reported were found to be homogeneous on TLC analysis, and their NMR spectra revealed no spurious signals.

5-Methyl-5,6,11,12-tetrahydrodibenz[*b*,*f*]azocin-6,12-dione 2

A mixture of 5-methyl-5,10-dihydroindeno[1,2-*b*]indole **1**[1] (15.00 g, 78 mmol) in chloroform (200 cm^3) and 50% aqueous hydrogen peroxide (45 cm^3) was heated under reflux for 15 h. Water (100 cm^3) was added and the organic layer separated and washed with saturated aqueous sodium sulfite solution, followed by water, before being dried ($MgSO_4$) and concentrated under reduced pressure to give a brown solid which on recrystallisation gave **2** (11.00 g, 64%) as pale brown plates mp 177.5–178.5 °C (chloroform–ethanol) (Found: C, 76.7; H, 4.9; N, 5.3. $C_{16}H_{13}NO_2$ requires C, 76.45; H, 5.2; N, 5.55%); λ_{max}/nm 260 (log ε 4.267); ν_{max}/cm^{-1} 1650; δ_H 3.40 (3 H, s, NCH_3), 3.82 (1 H, d, J 16.4, H-11), 4.32 (1 H, d, J 16.4, H-11), 6.98–7.54 (8 H, m); δ_C 37.4 (q, NCH_3), 49.8 (t, CH_2), 127.0 (d), 127.5 (d), 128.0 (d), 128.4 (d), 129.0 (d), 129.6 (d), 130.2 (d), 132.6 (s), 133.0 (d), 134.5 (s), 136.6 (s), 142.1 (s), 170.0 (s, NCO), 199.3 (s, CO); *m*/*z* 251 (M$^+$, 100%), 223 (20), 206 (20), 194 (22), 180 (15). Compound **2** (75%) was also obtained by heating **11** (540 mg, 2 mmol) in refluxing toluene with a Dean–Stark trap for 4 days, followed by evaporation of the solvent and column chromatography (using chloroform).

(*E*)-11-(4-Methylbenzylidene)-5-methyl-5,6,11,12-tetrahydrodibenz[*b*,*f*]azocin-6,12-dione 3

To a solution of **2** (4.00 g, 16 mmol) dissolved in warm absolute ethanol (125 cm^3) was added 4-methylbenzaldehyde (1.92 g, 16 mmol) and sodium ethoxide (1.10 g, 16 mmol). After standing for 2 days the resulting solid was filtered giving **3** (5.20 g, 92%) as large pale yellow prisms mp 218–219 °C (ethanol) (Found: C, 81.5; H, 5.45; N, 3.9. $C_{24}H_{19}NO_2$ requires C, 81.55; H, 5.4; N, 3.95%); λ_{max}/nm 234 infl. (log ε 4.540) and 330 (4.387); ν_{max}/cm^{-1} 1662, 1647; δ_H 2.25 (3 H, s, $ArCH_3$), 3.33 (3 H, s, NCH_3), 6.89–7.55 (12 H, m), 7.96 (1 H, s, ArCH=); δ_C 21.4 (q, $ArCH_3$), 36.9 (q, NCH_3), 126.5 (d), 127.3 (d), 128.7 (d), 128.7 (d), 129.0 (d), 129.0 (d), 129.3 (d), 129.3 (d), 130.4 (d), 131.0 (s), 131.2 (d), 131.2 (d), 131.9 (d), 135.1 (s), 136.5 (s), 136.8 (s), 137.8 (s), 140.5 (s), 140.9 (d), 141.3 (s), 169.7 (s, NCO), 194.0 (s, CO); *m*/*z* 353 (M$^+$, 100%), 324 (65), 308 (30), 262 (85).

9-Methyl-3-(4-methylphenyl)-2-phenyl-3,3a,8,9-tetrahydro-2*H*-dibenz[*b*,*f*]pyrazolo[3,4-*d*]azocin-8-one 4

A mixture of benzylidene **3** (350 mg, 1 mmol), phenylhydrazine (220 mg, 2 mmol) and glacial acetic acid (0.2 cm^3) in ethanol (10 cm^3) was heated under reflux for 2 h. After evaporating the ethanol under reduced pressure, a solid formed which was filtered and recrystallised from ethanol to give small yellow crystals of **4** (260 mg, 60%), mp 223–225 °C (Found: C, 81.2; H, 5.9; N, 9.3. $C_{30}H_{25}N_3O$ requires C, 81.25; H, 5.7; N, 9.5%); λ_{max}/nm 268 (log ε 5.110) and 366 (4.270); ν_{max}/cm^{-1} 1650; δ_H 2.30

(3 H, s, $ArCH_3$), 3.33 (3 H, s, NCH_3), 4.85 (1 H, d, *J* 8.8, H-3a), 5.72 (1 H, d, *J* 8.8, H-3), 6.85–7.91 (17 H, m); δ_C 21.1 (q, $ArCH_3$), 38.3 (q, NCH_3), 61.1 (d, C-3a), 69.0 (d, C-3), 114.1 (d), 114.1 (d), 120.2 (d), 123.4 (d), 125.7 (d), 125.7 (d), 127.3 (d), 127.8 (d), 127.8 (d), 128.0 (d), 128.4 (s), 129.0 (d), 129.0 (d), 129.3 (d), 129.8 (d), 130.0 (d), 130.0 (d), 130.5 (d), 133.8 (s), 136.3 (s), 137.7 (s), 138.3 (s), 140.8 (s), 144.8 (s), 147.2 (s), 170.5 (s, CO); *m*/*z* 443 (M^+, 100%), 414 (100).

12-Methyl-11-(4-methylphenyl)-11,12-dihydro-6*H*-isochromeno-[4,3-*c*]quinolin-6-one 5

A mixture of benzylidene **3** (700 mg, 2 mmol), hydroxylamine hydrochloride (350 mg, 5 mmol) and pyridine (10 cm^3) was heated under reflux for 8 h before evaporating the solvent and crystallising the product from ethanol to give **5** (140 mg, 20%) as intense bright yellow flat prisms mp 174–175 °C (HRMS: found M^+, 353.1410. $C_{24}H_{19}NO_2$ requires *M*, 353.1416); *m*/*z* 353 (M^+, 10%), 262 (100); λ_{max}/nm 272 (log ε 4.89) and 416 (3.94); ν_{max}/cm^{-1} 1733, 1712, 1642; δ_H 2.25 (3 H, s, $ArCH_3$), 2.86 (3 H, s, NCH_3), 5.60 (1 H, s, H-11), 6.43–8.33 (12 H, m); δ_C 21.1 (q, $ArCH_3$), 36.3 (q, NCH_3), 63.9 (d, C-11), 107.4 (s), 111.6 (d), 115.5 (s), 117.3 (d), 121.0 (s), 122.0 (d), 123.1 (d), 126.8 (d), 126.8 (d), 127.2 (d), 129.5 (d), 129.5 (d), 130.3 (d), 131.5 (d), 134.7 (d), 135.4 (s), 135.6 (s), 138.4 (s), 144.5 (s), 146.7 (s), 161.8 (s, CO). Compound **5** was also obtained by treating a solution of the deoxybenzoin **12** (700 mg, 2.5 mmol) in dry tetrahydrofuran (20 cm^3) at −90 °C with *n*-butyllithium (1.8 cm^3 of a 15% solution in hexane) and stirring the solution at −90 °C for 2 h before adding 4-methylbenzaldehyde (300 mg, 2.5 mmol) and standing at room temperature for 8 h; a saturated solution of ammonium chloride (30 cm^3) was added to the mixture which was extracted with diethyl ether (3 × 30 cm^3) and evaporation of the combined ethereal extracts gave an orange gum which on column chromatography [eluted with (1:1) ethyl acetate–hexane] gave **5** as bright yellow crystals (130 mg, 15%).

5-Ethyl-12-methyl-11-(4-methylphenyl)-5,6,11,12-tetrahydro-dibenzo[*c*,*h*][1,6]naphthyridin-6-one 6

The benzylidine **3** (350 mg, 1 mmol) and a 70% solution of ethylamine in ethanol (30 cm^3) was heated to reflux for 2 days, after which the solvent was evaporated and the resulting product crystallised from ethanol giving **6** (175 mg, 50%) as yellow rhombic crystals mp 222–223 °C (Found: C, 81.9; H, 6.3; N, 7.1. $C_{26}H_{24}N_2O$ requires C, 82.05; H, 6.35; N, 7.35%); λ_{max}/nm 274 (log ε 4.56) and 384 (3.88); ν_{max}/cm^{-1} 1640; δ_H 1.52 (3 H, t, *J* 7, CH_2CH_3), 2.18 (3 H, s, $ArCH_3$), 2.88 (3 H, s, NCH_3), 4.45 (2 H, m, CH_2), 5.41 (1 H, s, H-11), 6.55–8.5 (12 H, m, ArH); δ_C 14.9 (q, CH_2CH_3), 21.0 (q, $ArCH_3$), 36.6 (q, NCH_3), 44.1 (t, CH_2), 64.6 (d, C-11), 114.6 (d), 118.2 (d), 118.5 (s), 120.4 (s), 122.1 (d), 125.4 (s), 125.7 (d), 126.5 (d), 127.6 (d), 127.6 (d), 128.3 (d), 129.1 (d), 129.1 (d), 129.7 (d), 132.3 (d), 133.0 (s), 133.3 (s), 135.5 (s), 137.8 (s), 146.3 (s), 164.4 (s, CO); *m*/*z* 380 (M^+, 14%), 289 (100).

1-Methyl-2′-phenyl-2,2′,3,3′-tetrahydrospiro[(1*H*)-indole-2,1′-(1*H*)-isoindole]-3,3′-dione 7

Azocine **2** (500 mg, 2 mmol) was dissolved in aniline (5 cm^3) and the solution heated to 120 °C for 5 days before cooling, adding 1 M hydrochloric acid (20 cm^3) and extracting with diethyl ether (3 × 30 cm^3). After drying ($MgSO_4$), the combined ethereal extracts were concentrated to give **7** (480 mg, 70%) as dark yellow lathes mp 209–209.5 °C, [chloroform–light petroleum (bp 40–60 °C)] (HRMS: found M^+, 340.1208. $C_{22}H_{16}N_2O_2$ requires *M*, 340.1212); *m*/*z* 340 (M^+, 30%), 311 (100), 235 (20); λ_{max}/nm 238 (log ε 4.840) and 263 (4.631); ν_{max}/cm^{-1} 1718, 1609; δ_H 2.70 (3 H, s, CH_3), 6.73–8.07 (13 H, m, ArH); δ_C 28.1 (q, NCH_3), 87.6 (s, spiro-C), 109.1 (d), 118.7 (d), 119.45 (s), 120.8 (d), 125.0 (d), 125.65 (d), 126.2 (d), 126.2 (d), 127.2 (d), 129.1 (d), 129.1 (d), 130.25 (d), 132.7 (d), 132.9 (s), 135.6 (s), 138.9 (d), 139.6 (s), 160.8 (s), 168.1 (s, NCO), 194.9 (s, CO). Compound **7** was also obtained by using the above procedure but replacing **2** in the following reactions: (i) heating deoxybenzoin **11** with aniline for 4 days at 120 °C gave **7** (56% yield) and (ii) heating the spiro-compound **9** with aniline at 120 °C for 24 h gave **7** (86%).

When the above reactions involving either **2** or **11** were carried out in an oxygen free nitrogen atmosphere for 7 days, no evidence of the formation of **7** could be found from NMR or TLC analysis.

2-Phenyl-3-(2-methylaminophenyl)-1,2-dihydroisoquinolin-1-one 8a

Azocine **2** (500 mg, 2 mmol) was heated at 170 °C in aniline (20 cm^3) for 24 h before evaporating the mixture to dryness under reduced pressure and separating the resulting residue by column chromatography (eluted with diethyl ether) to give **8a** (210 mg, 33%) as fine colourless needles mp 215–217 °C (ethanol–chloroform) (Found: C, 80.9; H, 5.7; N, 8.4. $C_{22}H_{18}N_2O$ requires C, 80.95; H, 5.55; N, 8.6%); λ_{max}/nm 230 (log ε 4.838), 284 (4.480) and 320 (4.150); ν_{max}/cm^{-1} 1651, 1623; δ_H 2.71 (3 H, s, NCH_3), 6.45 (2 H, m, ArH), 6.57 (1 H, s, H-4), 6.86–8.43 (11 H, m, ArH); δ_C 30.4 (q, CH_3), 108.1 (d), 109.9 (d), 116.1 (d), 121.4 (s), 125.8 (s), 125.9 (d), 127.0 (d), 127.8 (d), 127.8 (d), 128.1 (d), 128.1 (d), 128.3 (d), 128.3 (d), 130.0 (d), 130.8 (d), 132.7 (d), 136.8 (s), 138.5 (s), 140.8 (s), 146.2 (s), 163.4 (s, CO); *m*/*z* 326 (M^+, 100%), 234 (67), 233 (94). Compound **8a** (26%) was also obtained by replacing **2** by carboxydeoxybenzoin **11** and following the above procedure.

2-Ethyl-3-(2-methylaminophenyl)-1,2-dihydroisoquinoline-1-one 8b

The azocine **2** (250 mg, 1 mmol) and a 70% solution of ethylamine in ethanol (20 cm^3) were heated under reflux for 24 h before evaporating the solvent and crystallising the residue from ethanol–chloroform to give **8b** (100 mg, 65%) as pale cream prisms mp 199–201 °C (Found: C, 77.4; H, 6.3; N, 10.1. $C_{18}H_{18}N_2O$ requires C, 77.65; H, 6.5; N, 10.05%); λ_{max}/nm 227 (log ε 4.750), 292 (4.335) and 315 (4.243); ν_{max}/cm^{-1} 1652, 1621; δ_H 1.1 (3 H, t, *J* 7.0, CH_2CH_3), 2.81 (3 H, s, NCH_3), 3.45–3.68 (2 H, m, CH_2), 4.24 (1 H, br m, NH), 6.44 (1 H, s, H-4), 6.44–8.45 (8 H, m); δ_C 14.2 (q, CH_2CH_3), 30.5 (q, NCH_3), 40.5 (t, CH_2), 108.3 (d), 110.1 (d), 116.7 (d), 121.2 (s), 125.7 (s), 125.8 (d), 126.7 (d), 128.0 (d), 130.2 (d), 130.7 (d), 132.2 (d), 136.6 (s), 140.7 (s), 146.8 (s), 163.0 (s, CO); *m*/*z* 278 (M^+, 100%), 263 (14), 249 (38), 233 (40). Following the procedure above but replacing **2** by carboxydeoxybenzoin **11** also gave **8b** (65%).

3-(2-Methylaminophenyl)-1,2-dihydroisoquinoline-1-one 8c

After heating a mixture of the azocine **2** (540 mg, 2.15 mmol) and ammonium acetate (1 g, 13 mmol) in glacial acetic acid (10 cm^3) at 95 °C for 16 h, water (30 cm^3) was added and the solution extracted with diethyl ether (3 × 25 cm^3). The ethereal extracts were washed with aqueous saturated sodium hydrogen carbonate solution, dried ($MgSO_4$) and evaporated to give **8c** (240 mg, 45%) as fine colourless needles mp 178–179.5 °C (benzene) (Found: C, 76.6; H, 5.7; N, 11.2. $C_{16}H_{14}N_2O$ requires C, 76.8; H, 5.65; N, 11.2%); λ_{max}/nm 230 (log ε 4.845), 290 (4.447) and 332 (4.318); ν_{max}/cm^{-1} 1651, 1634; δ_H 2.83 (3 H, s, NCH_3), 4.21 (1 H, br s, NH), 6.61 (1 H, s, H-4), 6.72–8.39 (8 H, m, ArH), 9.08 (1 H, br s, NH); δ_C 30.7 (q, NCH_3), 106.2 (d), 110.9 (d), 117.4 (d), 120.1 (d), 125.1 (s), 126.3 (d), 126.8 (d), 129.5 (d), 131.0 (d), 132.8 (d), 137.9 (s), 138.2 (s), 146.4 (s), 163.4 (s, CO); *m*/*z* 250 (M^+, 100%), 233 (60). Treatment of the deoxybenzoin **11** with ammonium acetate and following the procedure for **2** described above also gave **8c** (60%).

1-Methyl-1′,2,3,3′-tetrahydrospiro[(1*H*)-indole-2,1′-benzo[*c*]-furan]-3,3′-dione 9

A mixture of azocine **2** (520 mg, 2.07 mmol), selenium dioxide (250 mg, 2.25 mmol) and glacial acetic acid (25 cm^3) was heated

under reflux for 3 h before cooling and filtering. The resulting black solid was then washed with methylene dichloride (3 × 15 cm^3). The combined filtrates were washed with water (2 × 40 cm^3), dried ($MgSO_4$) and concentrated giving **9** (390 mg, 71%) as dark yellow prisms mp 215–216 °C (benzene) (Found: C, 72.3; H, 4.2; N, 5.2. $C_{16}H_{11}NO_3$ requires C, 72.45; H, 4.2; N, 5.3%); λ_{max}/nm 236 (log ε 4.845) and 272 (4.182); ν_{max}/cm^{-1} 1776, 1732, 1615; δ_H 2.73 (3 H, s, CH_3), 6.80–8.04 (8 H, m, ArH); δ_C 27.7 (q, CH_3), 96.6 (s, spiro-C), 109.1 (d), 118.5 (s), 119.7 (d), 122.3 (d), 126.0 (d), 126.1 (d), 128.8 (s), 131.2 (d), 134.7 (d), 138.9 (d), 142.5 (s), 161.2 (s), 168.0 (s, NCO), 192.8 (s, CO); *m*/*z* 265 (M^+, 55%), 236 (100). Compound **9** was also obtained from the following reactions. (i) A mixture of azocine **2** (510 mg, 2 mmol) and sodium metaperiodate (520 mg, 2.4 mmol) was heated in boiling 50% aqueous methanol (10 cm^3) for 24 h before evaporating to dryness under reduced pressure, acidifying with 1 M hydrochloric acid (1 cm^3) and extracting with methylene dichloride (3 × 10 cm^3). Evaporation of the dried methylene dichloride extracts gave **9** (210 mg, 40%). (ii) Following the selenium dioxide procedure above but replacing **2** by the deoxybenzoin **11** gave **9** (75%). (iii) Refluxing a solution of azocine **2** (250 mg, 1 mmol) in dimethylformamide (10 cm^3) for 2 weeks, followed by evaporation of the solvent and column chromatography, yielded **9** (160 mg, 60%).

3-(2-Methylaminophenyl)-1*H*-benzopyran-1-one 10

Azocine **2** (550 mg, 2.19 mmol) was heated to reflux with trifluoroacetic acid (5 cm^3) for 48 h, before neutralising the mixture with aqueous 2 M sodium hydrogen carbonate solution and extracting with methylene dichloride (3 × 20 cm^3). Evaporation of the combined dried methylene dichloride extracts give **10** (260 mg, 47%) as pale cream needles mp 150.5–152.5 °C (ethanol) (Found: C, 76.6; H, 5.3; N, 5.4. $C_{16}H_{13}NO_2$ requires C, 76.45; H, 5.2; N, 5.55%); λ_{max}/nm 236 (log ε 4.697), 286 (4.370) and 362 (4.107); ν_{max}/cm^{-1} 1728, 1686, 1634; δ_H 2.86 (3 H, s, NCH_3), 5.08 (1 H, br s, N-H), 6.70–8.31 (9 H, m); δ_C 30.6 (q, NCH_3), 104.8 (d), 111.0 (d), 116.7 (d), 117.6 (s), 120.0 (s), 125.8 (d), 128.0 (d), 129.5 (d), 129.5 (d), 131.5 (d), 134.9 (d), 137.8 (s), 147.3 (s), 155.5 (s), 162.3 (s, CO); *m*/*z* 251 (M^+, 100%), 223 (15), 206 (18), 194 (21). Compound **10** (in 55% yield) was also obtained by (i) treating **2** with 70% aqueous sulfuric acid at 100 °C for 1 day; (ii) from carboxydeoxybenzoin **11** by treatment with BF_3–MeOH complex in refluxing methanol for 2 days (75% yield), and (iii) by refluxing **11** with thionyl chloride for 0.5 hr (65% yield).

2′-Methylaminodeoxybenzoin-2-carboxylic acid 11

To azocine **2** (4.2 g, 16.7 mmol) dissolved in ethanol (40 cm^3) was added 20% aqueous sodium hydroxide (10 cm^3), and the solution stirred at room temperature for 0.5 h before neutralising with 3 M hydrochloric acid and extracting with diethyl ether (3 × 30 cm^3). Evaporation of the combined dried ethereal extracts gave a solid product which on crystallisation from ethanol yielded **11** (3.60 g, 80%) as yellow plates mp 179–180 °C (Found: C, 71.3; H, 5.7; N, 4.9. $C_{16}H_{15}NO_3$ requires C, 71.35; H, 5.6; N, 5.2%); λ_{max}/nm 232 (log ε 4.702), 266 (4.790) and 382 (4.012); ν_{max}/cm^{-1} 3300–2500, 1717, 1686, 1625; δ_H 2.79 (3 H, d, *J* 2.0, NCH_3), 4.75 (2 H, s, CH_2), 6.54–8.07 (8 H, m, ArH), 8.52 (1 H, br s, NH), 12.66 (1 H, br s, COOH); δ_C 28.9 (q, NCH_3), 44.6 (t, CH_2), 111.1 (d), 113.7 (d), 116.9 (s), 126.6 (d), 130.2 (d), 130.9 (s), 131.6 (d), 131.7 (d), 132.6 (d), 134.7 (d), 137.5 (s), 151.3 (s), 168.2 (s, COOH), 199.16 (s, CO); *m*/*z* 269 (M^+, 100%), 134 (87).

Methyl 2′-methylaminodeoxybenzoin-2-carboxylate 12

Treatment of **11** with excess ethereal diazomethane for 2 h, followed by evaporation to dryness gave **12** (95%) as pale yellow needles mp 72–73 °C (ethanol) (HRMS: found M^+, 283.1203, $C_{17}H_{17}NO_3$ requires *M*, 283.1208); *m*/*z* 283 (M^+, 22%), 134 (100); λ_{max}/nm 234 (log ε 4.720), 266 (4.972) and 384 (4.061); ν_{max}/cm^{-1} 1715, 1638; δ_H 2.84 (3 H, s, NCH_3), 3.75 (3 H, s, OCH_3), 4.73 (2 H, s, CH_2), 6.54–8.10 (8 H, m); δ_C 29.3 (q, NCH_3), 45.1 (t, CH_2), 51.8 (q, OCH_3), 111.4 (d), 114.0 (d), 127.0 (d), 128.1 (s), 129.9 (s), 130.9 (d), 131.6 (d), 132.2 (d), 132.5 (d), 135.0 (d), 137.6 (s), 152.2 (s), 167.6 (s, COO), 199.5 (s, CO).

5-Methyl-2′,3′,5,6,11,12-hexahydrospiro[(1*H*)-benzo[*d*]-imidazole-2′,12-dibenz[*b*,*f*]azocin]-6-one 14

A mixture of azocine **2** (530 mg, 2.1 mmol) and 1,2-phenylenediamine (1.02 g, 9.44 mmol) in toluene (10 cm^3) was heated under reflux for 2 days with air bubbled through the solution. After cooling, 1 M aqueous hydrochloric acid was added and the solution extracted with methylene dichloride (2 × 30 cm^3) which was combined, washed with water, dried ($MgSO_4$) and evaporated to give a solid product which showed only one component on TLC analysis. Crystallisation of the product from ethanol gave yellow plates of **13** (510 mg, 70%) with mp 223–227 °C (Found: C, 77.35; H, 5.8; N, 12.2. $C_{22}H_{19}N_3O$ requires C, 77.4; H, 5.6; N, 12.3%); λ_{max}/nm 242 (log ε 4.938); ν_{max}/cm^{-1} 1649; δ_H 2.87 (3 H, s, NCH_3), 3.48 (1 H, d, *J* 15.1, H-11), 4.12 (1 H, d, *J* 15.1, H-11), 4.58 (1 H, br s, NH), 5.47 (1 H, br s, NH), 6.37–8.25 (12 H, m, ArH); δ_C 30.74 (q, NCH_3), 37.95 (t, C-11), 82.83 (s, spiro-C), 111.9 (d), 115.6 (d), 116.7 (d), 117.1 (d), 123.8 (d), 124.0 (s), 124.6 (d), 126.6 (d), 127.5 (d), 127.9 (d), 128.2 (d), 128.8 (s), 129.2 (d), 132.4 (d), 134.3 (s), 135.1 (s), 139.0 (s), 146.7 (s), 161.9 (s, CO); *m*/*z* 341 (M^+, 100%), 235 (82), 223 (100).

3-(2-Methylaminophenyl)-1*H*-benzopyran-1-thione 13

A mixture of isocoumarin **10** (500 mg, 2.0 mmol) and Lawesson's reagent (660 mg, 2.0 mmol) in dry benzene (10 cm^3) was heated to reflux for 24 h before concentrating, and separating the residue using column chromatography (elution with hexane–diethyl ether 1 : 1). The least polar fraction yielded pale orange needles (330 mg, 50%) of **14** mp 140–140.5 °C (ethanol–chloroform) (HRMS: found M^+, 267.0719. $C_{16}H_{13}NOS$ requires *M*, 267.0718); λ_{max}/nm 230 (log ε 4.705), 294 (4.422) and 366 (4.153); *m*/*z* 267 (M^+, 100%); δ_H 2.92 (3 H, s, NCH_3), 6.72–8.70 (9 H, m); δ_C 30.7 (q, NCH_3), 107.2 (d), 111.2 (d), 116.6 (s), 116.7 (d), 126.3 (d), 129.0 (d), 129.3 (d), 129.6 (s), 131.9 (d), 132.6 (s), 132.7 (d), 135.2 (d), 147.4 (s), 158.6 (s), 200.2 (s, C=S).

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