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# The Fischer indolisation reaction and the synthesis of dihydroindenoindoles

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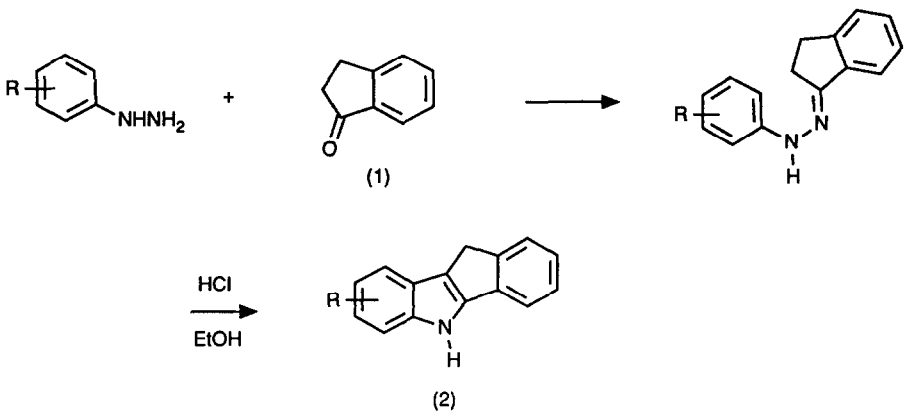
*Abstract*: The Fischer reaction between indanones and certain alkoxyarylhydrazines fails; the indanones are returned unreacted and the arylhydrazines are converted into the corresponding alkoxy-2-chloroarylamines and other products. A new *N*-amination route to arylhydrazines from the arylamines has been developed and it has been demonstrated that problems with the indolisation of alkoxyarylhydrazones can be circumvented by ring closures of their *O*-tosylated analogues. Some results using the Lepke synthesis of indoles are recorded.

Typically the Fischer indolisation[1] procedure involves the reaction between an arylhydrazine and an aldehyde, or ketone, in an acidic medium. An arylhydrazone is formed *in situ* and cyclises to the indole in the presence of the acid. The method can be used to synthesise many 5,10-dihydroindeno[1,2-*b*]indoles (DHIIs) (2), which are of interest as antioxidants,[2] from indanones (1) (see scheme 1).[3]

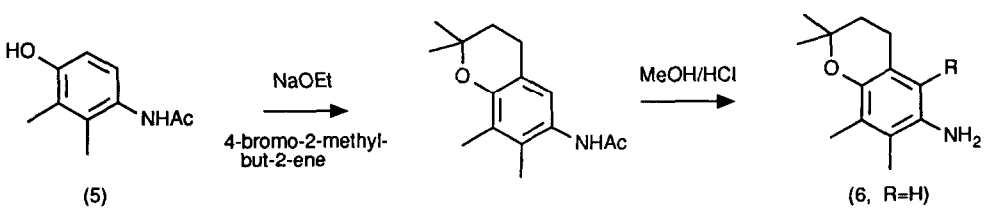
We now record a limitation to the Fischer approach to the construction of the DHIIs (3) and (4) from the arylamines (6, R=H) and (14, R=H) respectively. The arylamine (6, R=H) was obtained from the acetamidophenol (5) (scheme 2) and (14, R=H) was synthesised from the furanocyclohexanone (7)[4] (scheme 3). In each case the arylamine, after diazotisation and reduction, should afford the corresponding arylhydrazine and thence the required DHII.

Whereas the synthesis of the arylamine (6, R=H) is straightforward, that of the arylamine (14, R=H) poses difficulties. The ketone (7) when reacted with methyl lithium (1.25 eq) gives a mixture of the compounds (8), (9), (10), and (11) in the ratio 8:4:1:1. However, if a larger excess (1.43 eq) of methyl lithium is used the alcohol is the sole product. The alcohol (8) when heated with sulphur in boiling xylene gives a mixture of the benzofuran (11) and the dihydrobenzofuran (12), which when treated with triethylsilane in trifluoroacetic acid affords only the dihydrobenzofuran (12). Attempts to aromatise the mixed isomers (9) and (10), by heating them with palladium on charcoal, with chloranil, or with sulphur, gives mainly the benzofuran (11),

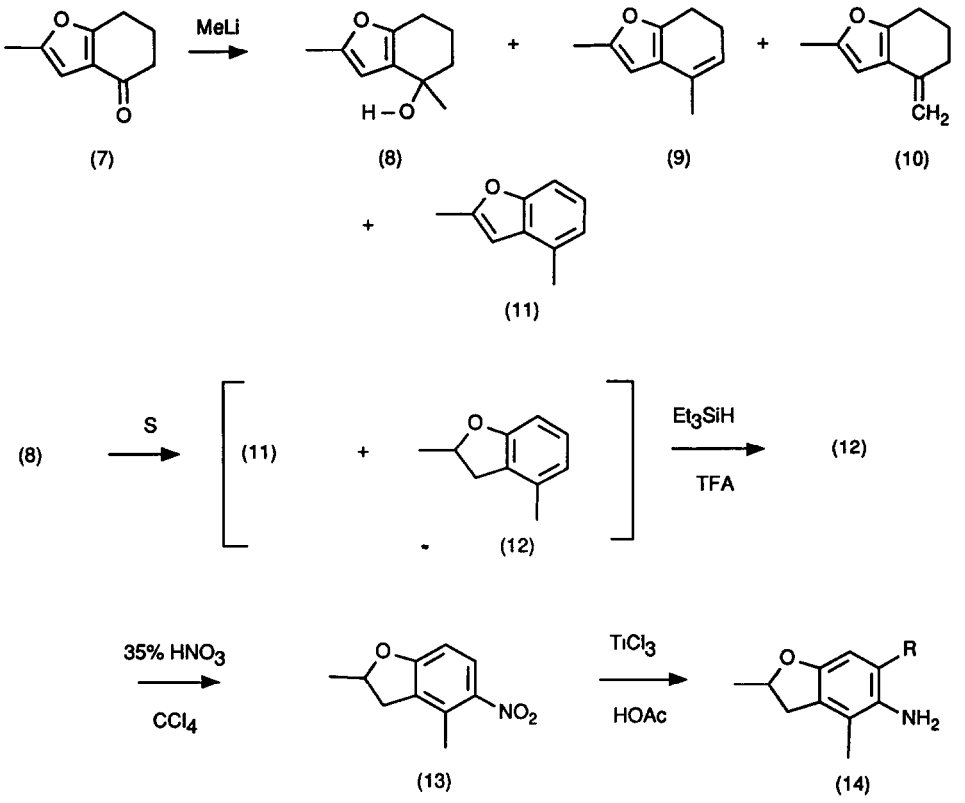
contaminated with its 4,5,6,7-tetrahydro derivative and other compounds. Nitration of the dihydrobenzofuran (12) yields the 5-nitro derivative (13) plus the 7-nitro isomer in a ratio of *ca.* 28:1. These compounds are separated by chromatography, and the 5-nitro isomer when reduced with titanium trichloride affords the arylamine (14, R=H)




Scheme 1


Scheme 2




Scheme 3

In the next stage when the arylamine (14, R=H) is diazotised and the diazonium salt treated with sodium dithionite, under identical conditions to those previously successfully used to form a variety of other arylhydrazines,[3] the starting arylamine is returned together with the chloro compound (14, R=Cl) and the dihydrobenzofuran (12). When sodium dithionite is replaced by tin (II) chloride the only product isolated is the chloro derivative (14, R=Cl). In neither experiment is the expected arylhydrazine detected. A similar result is observed for the other arylamine (6, R=H), which upon diazotisation and reduction with tin (II) chloride affords mainly the chloro derivative (6, R=Cl).

We note the report[5] that hydrazones of the type (15) do not undergo the typical [3,3]-sigmatropic change which is considered to be the first step in the Fischer indolisation reaction. Instead, the N-N bond is cleaved and the iminoquinone (16) then formed traps chloride ion and affords the chloroaniline (17) (scheme 4). We consider that a similar reaction occurs with our substrates, thus, for example, when the diazonium salt (18) is

reduced with sodium dithionite the arylhydrazine (19) is produced. This compound now undergoes acid promoted decomposition to the iminoquinone (20). As well as entrapment of chloride ion to give (14, R=Cl), the iminoquinone can also react with excess dithionite ion to give an intermediate (21), which may eliminate two molecules of sulphur dioxide to afford the arylamine (14, R=H) (scheme 5). The origin of the dihydrobenzofuran (12) is uncertain, but it may arise from reductive decomposition of the intermediate diazonium salt.

It is possible that side reactions such as these are commonly experienced when arylhydrazines (or their precursors) bearing electron donating groups orientated *ortho-* or *para-* to the hydrazine unit are treated with acids. Indeed, it may be an inherent problem in Fischer indolisation reactions utilising such arylhydrazines, for yields are often low and, as the workups normally involve the filtration of the solid indoles from the acidic reaction mixtures, any amino compounds which are formed could be easily lost.

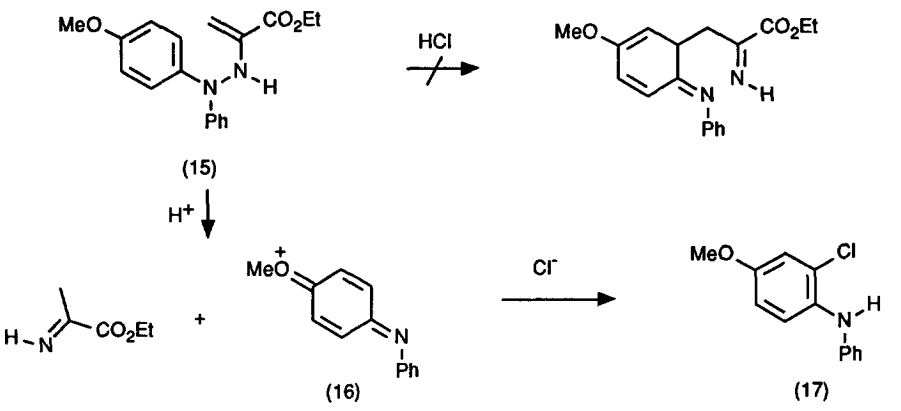
In order to overcome this difficulty, three improvements are needed (a) a method of preparing arylhydrazines which avoids acidic conditions, (b) the use of arylhydrazines in which powerful electron donating groups are moderated by suitable derivatisation, and (c) the avoidance of potential nucleophiles in the Fischer reaction, *i.e.* the use of acids having weakly nucleophilic conjugate anions.

We have found that arylhydrazinium mesitylene sulphonates are very readily synthesised by treating arylamines with *O*-mesitylenesulphonyl hydroxylamine (MSH).[6] Thus, when the *O*-4-toluenesulphonate (22) is reacted with MSH the hydrazinium salt (23) is obtained in 68% yield. This product reacts with 1-indanone in ethanolic hydrochloric acid to form the corresponding hydrazone (24), and this gives the DHII (25, R=Ts) when it is heated in ethanol. More efficiently, the hydrazone can be cyclised to the DHII by heating it with 2-carboxy-4-hydroxybenzenesulphonic acid[7] in glacial acetic acid. The most expeditious route, however, avoids the prior isolation of the hydrazone, thus the hydrazinium mesitylate (23), 1-indanone and a catalytic amount of 4-toluenesulphonic acid afford the DHII(25, R=Ts) in an overall yield of 69% when heated in toluene in a Dean-Stark apparatus. The 5-benzyl derivative of this compound is reduced with triethylsilane to give the *O*-tosyltetrahydroindenoindole (26, R=Ts) Reaction of this tosylate with lithium aluminium hydride in THF solution gives the corresponding phenol (26, R=H).

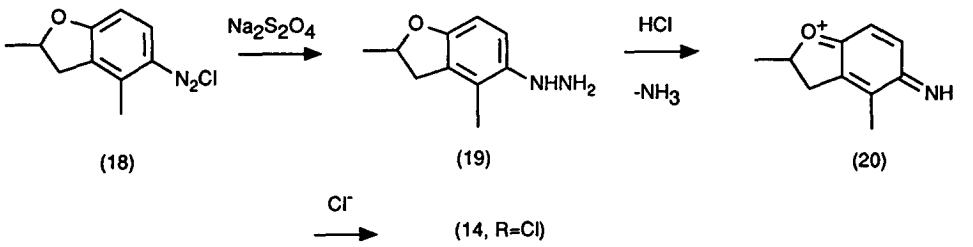
Since the phenol (5) is readily converted into the dihydrobenzopyran (6, R=H), treatment of the phenate salt (26, R=Na) with 4-bromo-2-methylbut-2-ene should lead to the desired dihydropyranotetrahydroindenoindole (27) *via* the appropriate *C*-allyl intermediate. However, in practice the only compound isolated is the *O*-allyl ether (28) (Scheme 7). The reason for this undesirable reaction is probably increased steric congestion in the *cis*-fused pentacycle compared with that in the simple substrate (5), but since steric congestion in this molecule would be less than in its planar dihydro analogue a similar reaction in the DHII series should also not succeed and we discontinued the investigation.

Accepting that Fischer indolisations are inapplicable to the synthesis of the required dihydrofurano- and dihydropyrano- DHIIs, we have examined a Wender type reaction[8] between the dianion (29) and 2-bromoindanone (scheme 8). This fails to give indanylamide (30) and thence the pyrano-DHII (3),[9] and as an alternative approach we considered a Lepke reaction[10] between the arylamine (14, R=H) and 2-hydroxyindanone (31). Unfortunately, a preliminary experiment using aniline such a reaction gives five

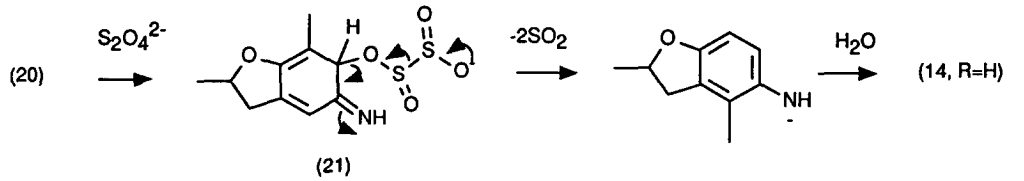
products DHII (32), iso-DHII (33), the pentacycles (34) and (35) plus the diketopentacycle (36).




Scheme 4




Scheme 5

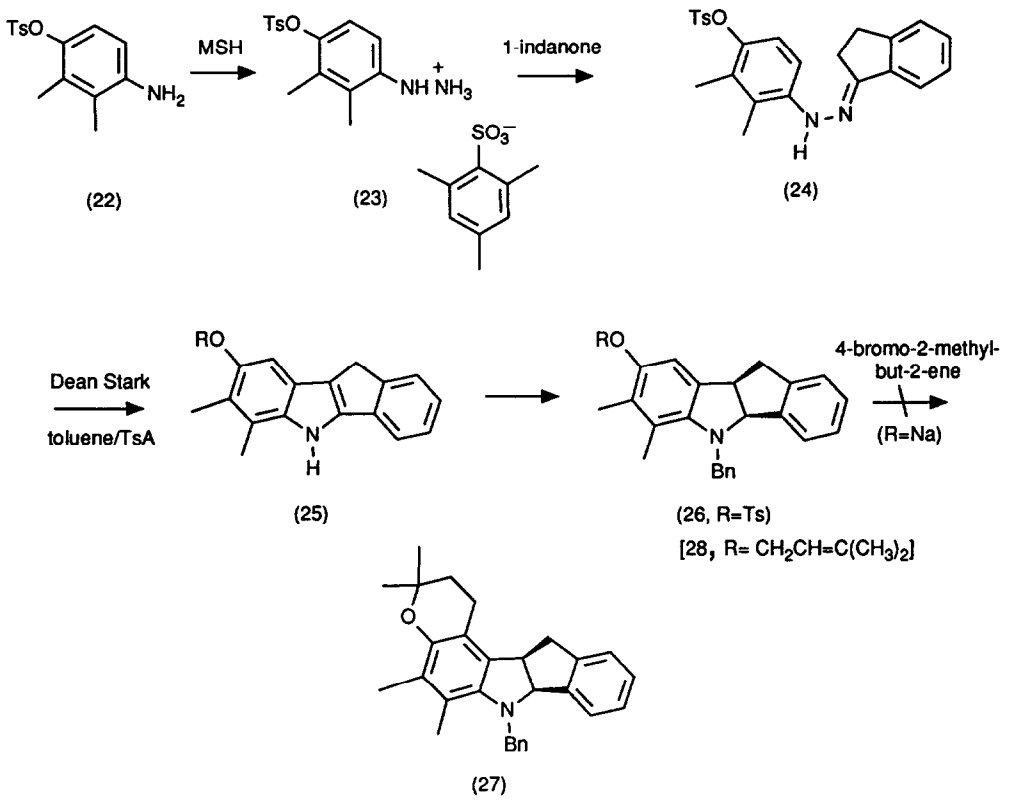



Scheme 6

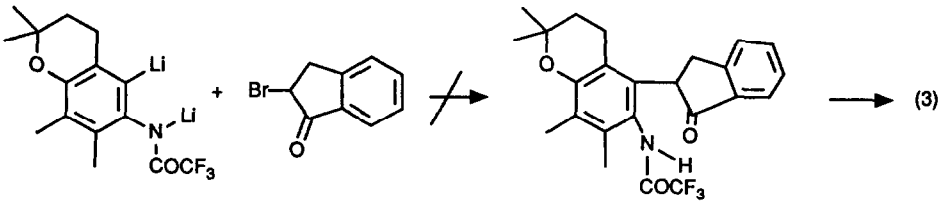
The formation of both DHII and iso-DHII indicates that either 2-hydroxyindanone is in tautomeric equilibrium with 1-hydroxy-2-indanone, or that a similar tautomerism occurs in the imine formed by reaction

of 2-hydroxyindanone with aniline. It is conceivable that the diketopentacycle (36) might be generated as follows, utilising the enamine tautomer (37) as a nucleophile to attack a second molecule of 2-hydroxyindanone (scheme 9). The structure of the final product is confirmed by X-ray crystallography, and the stereochemistry observed lends support to the mechanism. Thus, the preferred intermediate (38) should adopt the conformation shown, but it can only cyclise from the corresponding staggered representation. This determines the stereochemistry of the hydrogen atoms at the bridging positions in (39) and, since only *cis* fusions for the five-membered rings can be accommodated, also ensures the all *cis*- orientation for the final product (36).

Unfortunately, the lack of specificity in the Lepke reaction compares with that we have previous noted[9] in the related Bischler procedure [11]and neither can be used as a route to the desired targets.

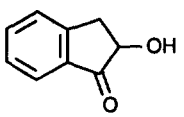



Scheme 7 (Ts = 4-toluenesulphonyl)




(29) (30)

Scheme 8

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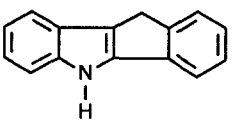


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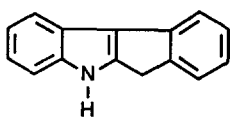


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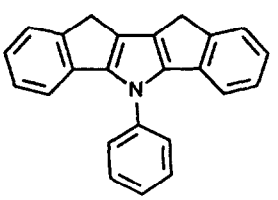


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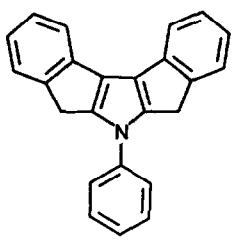


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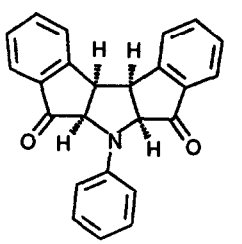


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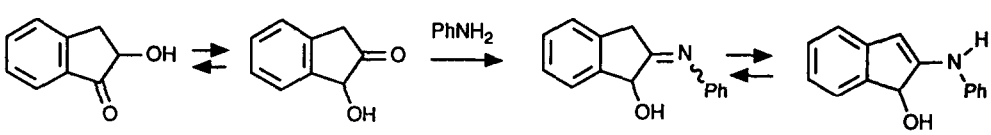


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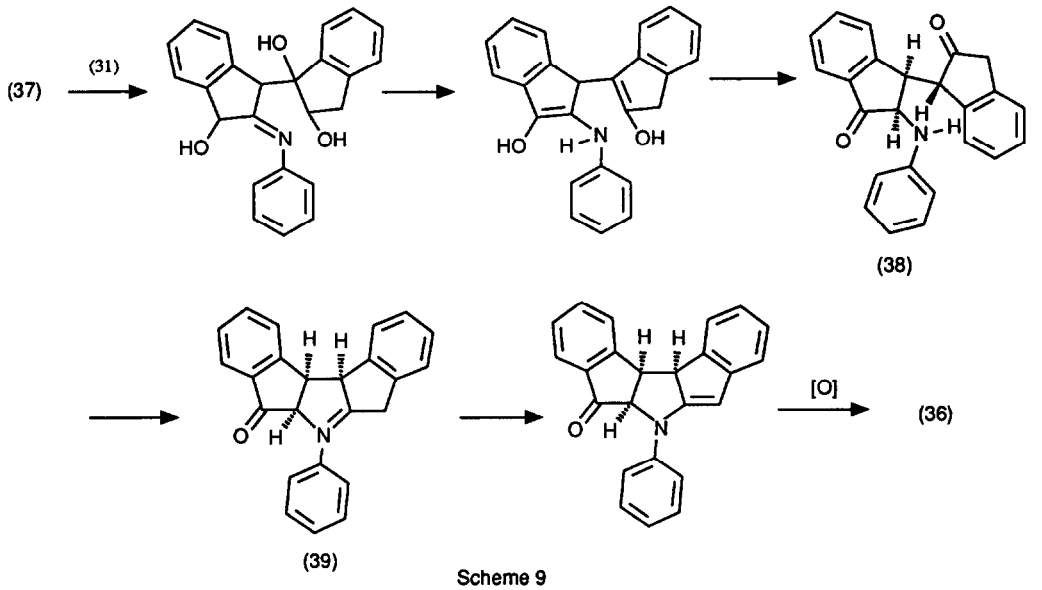


Scheme 9

## EXPERIMENTAL

All solvents, other than ethanol and methanol, were distilled prior to use and, where necessary, dried and purified by standard methods. Petrol refers to 60-80°C petroleum ether. Medium pressure (flash) column chromatography was used for the purification of reaction mixtures. "Silica" refers to Amicon 84072 silica gel (230-400 mesh), or Merck 9385 silica gel. Thin layer chromatography was performed on aluminium plates coated with Kieselgel 600 $F_{254}$. Electronic spectra were recorded in 95% ethanol with a Perkin Lambda 3 spectrometer, and infra red spectra were recorded as liquid films or Nujol mulls, using a Perkin Elmer 938G instrument. N.M.R. spectra were obtained with either JEOL GX FT 400 or 270 instruments, or with a Bruker AM 200 spectrometer; the solvent was deuteriochloroform, unless stated otherwise, and the internal reference was tetramethylsilane. Mass spectra were measured with a VG 7070E spectrometer linked to a 2000 data system.

6-Amino-3,4-dihydro-2,2,7,8-tetramethyl-2*H*-benzopyran (6, R=H)

A mixture of 4-amino-2,3-dimethyl-1-hydroxybenzene hydrochloride (8.3 g) and imidazole (4.9 g) in dry *N,N*-dimethylformamide (10 $cm^3$) was stirred under nitrogen and $^t$butyldimethylsilyl chloride (3.3 g, 1.1 equiv.) in *N,N*-dimethylformamide (3 $cm^3$) was added slowly with stirring at room temperature. After 4h, the solvent was removed under reduced pressure and the residue was partitioned between water and chloroform. The aqueous phase was separated and extracted with chloroform (3 x 5 $cm^3$) and the combined organic phases were then dried and evaporated to give 4-($^t$butyldimethylsilyloxy)-2,3-dimethylacetaniline as a colourless oil. This was stirred with acetic anhydride (25 $cm^3$) for 1h and the excess reagent was then removed under reduced pressure. The residue was heated under reflux with methanol (50 $cm^3$) containing concentrated hydrochloric acid (0.5 $cm^3$) for 2h. After this time, the solvent was removed and the residue was chromatographed on silica, eluting with chloroform : methanol (95:5) to give 4-hydroxy-2,3-dimethyl-acetanilide (8.0 g, 93.4%), $R_f$ = 0.33 ($CHCl_3$: MeOH 19:1). The acetanilide (4.08 g, 0.023 mol) was dissolved in ethanol and treated with a solution of sodium ethoxide, prepared by dissolving sodium (0.6 g, 1.1 equiv.) in

ethanol. The mixture was evaporated to dryness giving the corresponding sodium phenate, which was mixed with benzene (50 $cm^3$) and 4-bromo-2-methylbut-2-ene (5 $cm^3$) and heated under reflux for 20h under an atmosphere of nitrogen. The solvent and excess reagent were removed and the residue was partitioned between 2M hydrochloric acid (50 $cm^3$) and chloroform (50 $cm^3$). The aqueous layer was removed and extracted with chloroform (3 x 25 $cm^3$) and the combined organic phases were then dried and evaporated to give an oily residue. This was chromatographed eluting with dichloromethane:methanol (98:2) to give 6-acetamido-3,4-dihydro-2,2,7,8-tetramethyl-2*H*-benzopyran as colourless prisms (3.15 g, 56%); $R_f$ 0.42 ( chloroform: methanol 19:1); m.p. 123-125°; $\upsilon_{max}$ 3260, 1650 $cm^{-1}$; $\delta_H$ [$(CD_3)_2SO$] 1.26 (6H, s), 1.71 (2H, t, $J$ = 6.8 Hz), 1.98 (6H, s), 2.02 (3H, s), 2.65 (2H, t, $J$ = 6.8 Hz), 6.75 (1H, s), 9.14 (1H, s, exchanged by $D_2O$) [Found: C,72.65; H,8.7; N,5,7 $C_{15}H_{21}NO_2$ requires: C,72.8; H,8.6; N,5.7%]. This product (2.5 g) was heated under reflux with a mixture of methanol and concentrated hydrochloric acid (25 $cm^3$) (2:1) for 24h, and then the reaction mixture was cooled to 0°C overnight. During this time crystals of the title amine, as its hydrochloride salt, separated. These were collected (2.35 g, 96%), m.p. 246-250°C (dec.); $\upsilon_{max}$ 3360, 2600 $cm^{-1}$; $\delta_H$ [$(CD_3)_2SO$] 1.27 (6H, s), 1.74 (2H, t, $J$=6.8 Hz), 2.1 (3H, s), 2.2 (3H, s), 2.7 (2H, t, $J$=6.8 Hz), 7.04 (1H, s), 10.1 (3H, br.s, exchanged by $D_2O$); *m/z* (%) 205 (60, $M^+$), 149 (95, $M^+$-$C_4H_8$).

6-Amino-5-chloro-3,4-dihydro-2,2,7,8-tetramethyl-2*H*-benzopyran (6, R=Cl)

The amine hydrochloride (1g), from the previous experiment, suspended in 10M hydrochloric acid (5$cm^3$) was cooled to 0°C and treated with sodium nitrite (0.4g) in water (1$cm^3$). A blue coloured solution formed and this was reacted with a solution of freshly purified stannous chloride (3.5g) in conc. hydrochloric acid (3.5$cm^3$). A precipitate formed and this was collected, suspended in water (2$cm^3$), and sodium acetate (0.5g) added. This mixture was heated, then cooled and the solid which remained was dissolved in diethyl ether (5$cm^3$). This solution was added to the top of a short column of basic alumina and eluted with diethyl ether. The eluant upon evaporation gave a gum, which on chromatography afforded the title compound as an oil [Found: *m/z* 239.10857 $C_{13}H_{18}NO^{35}Cl$ requires: 239.10769]

4,5,6,7-Tetrahydro-4-hydroxy-2-methylbenzo[*b*]furan (8)

The ketone (7) (45.0 g, 0.30 M) was dissolved in dry diethyl ether (160 $cm^3$) and stirred at room temperature under nitrogen. To this was added methyl lithium (1.5 M in diethyl ether, 250 $cm^3$) *via* a cannula at about 100 drops/min. The rise in temperature was controlled using an ice bath and the rate of addition was increased in the later stages of the reaction, the addition taking 3.45h. After stirring the reaction mixture at room temperature for 4h, a sample (2.0 $cm^3$) of the reaction mixture was removed, poured onto saturated aqueous ammonium chloride solution, and extracted with diethyl ether. Evaporation of the solvent gave a colourless oil. The $^1H$ N.M.R. spectrum of this product suggested that some starting compound remained and a mixture of compounds (8), (9), (10), and (11) had been produced in a ratio of approximately 28:8:4:1.

A further addition (35 $cm^3$) of 1.5M methyl lithium in diethyl ether was made to the original reaction mixture in order to remove the remaining starting material. The reaction mixture was then stirred for a further 3h, and left overnight. Next day it was cooled in an ice bath and saturated ammonium chloride solution (20 $cm^3$) was added cautiously over a period of 3h, followed by the rapid addition of water (150 $cm^3$). The upper layer was separated and the aqueous phase was extracted with diethyl ether (3 x 50 $cm^3$). The organic phases were

combined, dried, and evaporated to give a light coloured mobile oil (38.5 g, 75%). Which was mainly the required alcohol. This oil was then fractionally distilled to give the title compound, b.p.113-115°C/0.7mm: $\upsilon_{max}$cm$^{-1}$(liquid film) 3380 (broad, s) 1630; $\delta_H$ 1.45 (3H, s), 1.60-2.00 (4H, m), 2.24 (3H, s), 2.42-2.57 (2H, m), 5.98 (1H, s) [Found: C, 72.6; H, 8.3, $C_{10}H_{14}O_2$ requires: C, 72.3; H, 8.5%].

2,4-Dimethylbenzofuran (11)

(a) The alcohol (8)(6.4 g, 38.6 mmol) was heated with stirring under Dean-Stark conditions in boiling *p*-xylene (100 cm$^3$) containing a few crystals of 4-toluenesulphonic acid for 1h. The reaction mixture was then cooled, decanted from a few oily drops and the solvent evaporated to leave a light coloured oil (5.6 g). This consisted of a mixture of the isomers (10) [$\delta_H$ 1.84 (2H, pent, $J$ = 6.5 Hz), 2.21 (3H, s), 2.35 (2H, m), 2.59 (2H, t, $J$ = 6.5 Hz), 4.69 (1H, s), 4.89 (1H, s), 6.01 (1H, s)] and (9) [$\delta_H$ 1.85 (3H, d, $J$ = 1.5 Hz), 2.23 (3H, s), 2.42 (2H, m), 2.66 (2H, t, $J$ = 9.0 Hz), 5.20 (1H, sex, $J$ = 1.5 Hz), 5.86 (1H, s)], together with the corresponding benzofuran (12) in the ratio 5:2:1.

Without separation, the mixture was heated under reflux in xylene with 10% Pd/C (1.0 g) for 1h. On cooling, the mixture was filtered and the filtrate evaporated giving a pale mobile oil (5.1 g) which contained the required benzofuran (12) and 2,4-dimethyl-4,5,6,7-tetrahydrobenzo[*b*]furan [$\delta_H$ 1.10 (3H, d, $J$ = 7.0 Hz), 1.15-1.30 (1H, m), 1.60-1.72 (1H, m), 1.76-1.93 (2H, m), 2.22 (3H, s), 2.49 (2H, br t, $J$ = 8.5 Hz), 2.57 (1H, m), 5.82 (1H, s)] in the ratio 9:5.

(b) The alcohol (8) (10.2 g) was heated and stirred at 165°C with sulphur (2.4 g). After 1h, a further addition of sulphur (2.4 g,) was made and the mixture was heated for 1.5h. The cooled mixture was treated with dichloromethane (50 cm$^3$) and unreacted sulphur (2.1 g) was removed by filtration. The filtrate was washed with 1M sodium hydroxide (3 x 20 cm$^3$), and with brine (1 x 20 cm$^3$). It was then dried and evaporated to yield a dark oil (10.3 g). This was extracted with hot petrol (5 x 12 cm$^3$). Evaporation of the combined extracts gave a straw coloured oil (8.1 g,), which was shown to be the benzofuran (11) containing the corresponding 2,3-dihydrobenzofuran (12) as a minor impurity.

The benzofuran was purified by column chromatography to give a colourless oil [$\delta_H$ 2.24 (3H, d, $J$ = 1.0 Hz), 2.33 (3H, s), 6.13 (1H, dd, $J$ = 1.0, 0.5 Hz), 6.86 (1H, dd, $J$ = 7.5, 0.5 Hz), 6.96 (1H, t, $J$ = 7.5 Hz), 7.18 (1H, dd, $J$ = 7.5, 0.5 Hz)], which was characterised as its picrate, m.p. 75-76°C [Found: C, 50.8; H, 3.2; N, 11.1 $C_{16}H_{13}N_3O_8$ requires: C, 51.2; H, 3.5; N, 11.2%].

2,3-Dihydro-2,4-dimethylbenzo[*b*]furan (12)

The benzofuran (11)(5.3 g) in trifluoroacetic acid (20 cm$^3$) at room temperature was treated with triethylsilane (6.0 cm$^3$) dropwise over 10m. The reaction mixture was allowed to stand for 7h at room temperature, and then the excess solvent and reagent were removed. The residue was distilled to give the title compound as a clear mobile oil (2.4 g, 45%), b.p. 135-140°C/1 mm; $\delta_H$ 1.51 (3H, d, $J$ = 6.0 Hz), 2.27 (3H, s), 2.75 (1H, dd, $J$ = 7.5, 16.0 Hz), 3.27 (1H, dd, $J$ = 16.0, 9.0 Hz), 4.95 (1H, br sex, $J \approx 7$ Hz), 6.64 (1H, d, $J$ = 8.0 Hz), 6.69 (1H, d, $J$ = 8.0 Hz), 7.05 (1H, t, $J$ = 8.0 Hz) [Found: C, 80.9; H, 8.1, $C_{10}H_{12}O$ requires: C, 81.0; H, 8.2%].

2,3-Dihydro-2,4-dimethyl-5-nitrobenzo[*b*]furan (13)

The dihydrobenzofuran (3.6 g) in carbon tetrachloride (25 cm$^3$) was stirred and treated with a solution of

conc. nitric acid (6 $cm^3$) in water (9 $cm^3$) in one portion, maintaining the temperature at 18-20°C. The reaction mixture was stirred rapidly for 3h, and then left overnight without stirring. Water (20 $cm^3$) was then added and the organic phase separated and dried ($Na_4SO_4/K_2CO_3$). Removal of the solvent gave an oil which was absorbed onto silica (4 g) and added to the top of a column of silica (15 g). Chromatographic separation was effected eluting with 60-80°C petrol containing increasing amounts of ethyl acetate (0-3%). Early fractions contained the required product (13) as pale yellow crystals (0.67 g, 14%, m.p. 78°C, from ethanol): $\upsilon_{max}cm^{-1}$ 1575 (s), 1490 (s), 1370 (s): $\delta_H$ 1.50 (3H, d, $J$ = 6.0 Hz), 2.47 (3H, s), 2.83 (1H, dd, $J$ = 15.5, 7.0 Hz), 3.34 (1H, dd, $J$ = 15.5, 9.0 Hz), 5.09 (1H, br sex, $J \approx$ 7Hz), 6.70 (1H, d, $J$ = 9.0 Hz), 7.92 (1H, d, $J$ = 9.0 Hz) [Found: C, 62.3; H,5.8; N,7.2 $C_{10}H_{11}NO_3$ requires: C, 62.2; H, 5.7; N, 7.25%].

Later fractions afforded the 7-nitro isomer as bright yellow crystals; $\delta_H$ 1.56 (3H, d, $J$ = 5.5 Hz), 2.29 (3H, s), 3.34 (1H, dd, $J$ = 15.5, 7.0 Hz), 3.32 (1H, dd, $J$ = 15.5, 9.0 Hz), 5.21 (1H, br sex, $J$ = 8 Hz), 6.70 (1H, d, $J$ = 9.0 Hz), 7.79 (1H, d, $J$ = 9.0 Hz) [Found: C, 62.0; H, 5.6; N, 7.05 $C_{10}H_{11}NO_3$ requires: C,62.2; H, 5.7; N, 7.25%].

5-Amino-2,3-dihydro-2,4-dimethylbenzo[*b*]furan (14, R=H)

The nitro-compound (13)(0.91 g) was dissolved in glacial acetic acid (8 $cm^3$) and titanium trichloride (30% w/v, in conc. hydrochloric acid) (18 $cm^3$) was added in portions (3 $cm^3$) over 0.75h, the reaction mixture being stirred continuously and maintained at room temperature. After a further 2h, the reaction mixture was extracted with chloroform (1x60$cm^3$, then 9 x 10 $cm^3$). The combined extracts were filtered through phase separation paper and evaporated to give the amine (17), as its hydrochloride, as a colourless oil, which crystallised upon trituration with diethyl ether (0.80 g, 85%), m.p. 232-234°C, darkens *ca* 210°C): $\delta_H$ 1.37 (3H, d, $J$ = 7.0 Hz), 2.20 (3H, s), 2.75 (1H, dd, $J$ = 16.0, 7.0 Hz), 3.30 (1H, dd, $J$ = 16.0, 9.0 Hz), 4.95 (1H, br sex, $J \approx$ 7 Hz), 6.62 (1H, d, $J$ = 8.5 Hz), 7.18 (1H, d, $J$ = 8.5 Hz), 10.09 (3H, br s) [Found: C, 59.7; H, 7.0; N, 7.0 $C_{10}H_{14}NOCl$ requires: C, 60.15; H, 7.0; N, 7.0%].

5-Amino-6-chloro-2,3-dihydro-2,4-dimethylbenzo[*b*]furan (14, R=Cl)

The amine hydrochloride (0.68 g), from the previous reaction, in 6M hydrochloric acid (5 $cm^3$), was cooled to 0°C, and protected under a nitrogen atmosphere. A solution of sodium nitrite [0.30 g in water (1.5 $cm^3$)] was added dropwise over 0.75 h, causing the solution to become deep blue in colour. The reaction mixture was stirred a for a further 0.5h at 0°C, before it was added to an ice-cold solution of sodium dithionite (3.2 g in water (15 $cm^3$). A brown solution was produced together with some oily material, but after stirring for 20m at 0°C the colour faded and the solution became almost colourless. After stirring for another 20m at this temperature, the oily product was extracted into diethyl ether (2x5$cm^3$), and the extracts were then combined, dried and evaporated to give a brown oil, which was shown to be a 1:1 mixture of 2,3-dihydro-2,4-dimethyl-benzo[b]furan (12) and 5-amino-6-chloro-2,3-dihydro-2,4-dimethylbenzo[b]furan (14, R=Cl). The oil was subjected to column chromatography which afforded the pure chloro compound (25mg) as a colourless oil: $\upsilon_{max}cm^{-1}$ 3420 (m), 3340 (m), 1590 (s), 1430 (s); $\delta_H$ 1.45 (3H, d, $J$ = 6.0 Hz), 2.07 (3H, s), 2.67 (1H, dd, $J$ = 15.5, 8.0 Hz), 3.18 (1H, $J$ = 15.5, 9.0 Hz), 3.62 (2H, br s), 4.83 (1H, br sex, $J$ = 8 Hz), 6.58(1H, s) [Found: *m/z* 199.05800 $C_{10}H_{12}NO^{37}Cl$ requires: 199.05779].

2,3-Dimethyl-4-tosyloxyphenylhydrazinium mesitylate (23)

To a solution of 2,3-dimethyl-4-tosyloxyaniline (22) (5.5 g, 19 mM) in dichloromethane (75 $cm^3$) was added slowly a solution of *O*-mesitylenesulphonylhydroxylamine (7.5 g, 35 mM) in dichloromethane (25 $cm^3$). The reaction mixture was kept at 15-20°C and the title compound precipitated as a thick white solid within minutes. The mixture was stirred for further 1h, before the product was collected, washed with dichloromethane and dried (8.7 g, 91%); m.p. = 222-224°C; $\upsilon_{max}$ 3400-3540, 1180 (br), 1100 $cm^{-1}$; $\delta_H$ [$(CH_3)_2SO$] 2.28 (3H, s), 2.37 (3H, s), 2.51 (3H, s), 2.78 (3H, s), 2.83 (6H, s), 7.04 (1H, d, $J$ = 8.8 Hz), 7.09 (2H, s), 7.12 (1H, d, $J$ = 8.8 Hz), 7.83 (2H, d, $J$ = 8.4 Hz), 8.02 (2H, d, $J$ = 8.4 Hz), 8.16 (1H, s, $D_2O$ exchangable), 10.31 (3H, br.s, $D_2O$ exchangable); *m/z* (C.I. %) 307 (70), 138 (100).

5,10-Dihydro-6,7-dimethyl-8-tosyloxyindeno[1,2-*b*]indole (25, R=Ts)

The hydrazinium mesitylate (23) (6.0 g, 12 mM) in toluene (100 $cm^3$) was heated under reflux with 1-indanone (1.56 g, 12 mM, 1 equiv) and a few crystals of 4-toluenesulphonic acid, under Dean-Stark conditions for 4h. After this time the reaction mixture was concentrated and kept at 0°C overnight. The off-white solid formed was then collected to give the indenoindole (25, R=Ts) (2.9 g). The filtrate was evaporated and purified by column chromatography to give a further 0.4 g of the product. Total yield = 3.3 g, 69.1 %; m.p. 208-209°C (ethanol); $\upsilon_{max}$ 3400 (NH); $\delta_H$ ($CDCl_3$) 2.09, 2.34 and 2.47 (3 x 3H, 3 x s), 3.60 (2H, s, -$CH_2$-), 7.15 (1H, s), 7.20 (2H, d, $J$ = 6.9 Hz), 7.32 (2H, d, $J$ = 8.1 Hz), 7.49 (2H, t, $J$ = 7.1 Hz), 7.79 (2H, d, $J$ = 8.2 Hz), 8.27 (1H, s, NH); *m/z* (%) 403 (93), 248 (100); [Found: C, 71.1; H, 5.18; N, 3.53; $C_{24}H_{21}NSO_3$ requires: C, 71.4; H, 5.25; N, 3.47].

5-Benzyl-5,10-dihydro-6,7-dimethyl-8-tosyloxyindeno[1,2-*b*]indole

5,10-Dihydro-6,7-dimethyl-8-tosyloxyindeno[1,2-*b*]indole (25, R=Ts) (2.02 g, 5 mM) in dry tetrahydrofuran (25 $cm^3$) was stirred under nitrogen and sodium hydride (0.3 g, 60% suspension in oil) was added portionwise over a period of 30 min. The mixture was then stirred for a further 30m, cooled to 0°C and benzyl bromide (1.0 $cm^3$, 8 mM) was added dropwise. The mixture was warmed slowly to room temperature and stirred for 15h. It was then treated with saturated ammonium chloride solution to destroy the excess sodium hydride and diluted with water. The precipitated solid was collected and the filtrate was extracted with ethyl acetate (2x20$cm^3$), the combined extracts were dried and evaporated to afford more solid product. The solids were combined and crystallised from ethyl acetate to give crystals of the title compound (1.4 g, 56.7%); m.p. = 205-206°C; $\delta_H$ ($CDCl_3$) 2.05 (3H, s), 2.39 (3H, s), 2.47 (3H, s), 3.66 (2H, s), 5.83 (2H, s), 7.1-7.8 (14H, m); *m/z* (%) 247 (100), 149 (90), 192 (50).

5-Benzyl-6,7-dimethyl-8-tosyloxy-4b,5,9b,10-tetrahydroindeno[1,2-*b*]indole (26, R=Ts))

A solution of 5-benzyl-6,7-dimethyl-8-tosyloxy-5,10-dihydroindeno[1,2-*b*]indole (0.78 g, 1.6 mM) in trifluoroacetic acid (10 $cm^3$) was stirred rapidly and triethylsilane (0.3 g, 1.5 mM.) was added in one portion. The mixture was stirred for 4h and the solvent was then removed. The residue was treated with water (10 $cm^3$), neutralised with aqueous sodium hydroxide, extracted with diethyl ether, dried and evaporated to give a gum. This was purified by column chromatography eluting with 20% ethyl acetate in petrol to give the title compound (0.77 g, 98%); $\upsilon_{max}$ 1650, 1590, 1360, 1170 $cm^{-1}$; $\delta_H$ ($CDCl_3$) 1.92 (3H, s), 2.31 (3H, s), 2.48 (3H, s), 2.89 (1H, d, $J$ = 16.3 Hz), 3.22 (1H, dd, $J$ = 16.1, 7.9 Hz), 3.43 (1H, br.t, $J$ = 7.1 Hz), 4.47 (1H, d, $J$ = 13.6

Hz), 4.84 (1H, d, *J* = 13.7 Hz), 5.40 (1H, d, *J* = 6.8 Hz), 6.82 (1H, s), 7.1-7.9 (13H, m); *m/z* (C.I.) (%) 217 (100), 247 (20), 301 (20).

5-Benzyl-6,7-dimethyl-8-hydroxy-4b,5,9b,10-tetrahydroindeno[1,2-*b*] indole (26, R=H)

5-Benzyl-6,7-dimethyl-8-tosyloxy-4b,5 9b,10-tetrahydroindeno[1,2-*b*]indole (26,R=Ts) (0.74 g, 1.5 mM) in dry tetrahydrofuran (40 $cm^3$) was treated with lithium aluminium hydride (0.6 g) at 50°C in small portions over a period of 6h. During this time the reaction mixture was protected by an atmosphere of $N_2$. It was then left at 50°C for another 14h. After this time the reaction mixture was cooled and treated with saturated aqueous ammonium chloride, and extracted with ethyl acetate (3x15$cm^3$). The extracts were combined, dried, and evaporated to afford a gum which crystallised from ethyl acetate to give the title compound as colourless prisms (0.49 g, 96%); m.p. = 154-156°C; $\delta_H((CD_3)_2SO)$ 1.96 (3H, s), 2. 18 (3H, s), 2.93 (1H, d, *J* = 16.1 Hz), 3.24 (1H, dd, *J* = 16.1, 7.6 Hz), 3.84 (1H, d, *J* = 3.9 Hz), 4.09 (1H, q, *J* = 7.1, 7.9 Hz), 4.19 (1H, d, *J* = 13.9 Hz), 4.63 (1H, d, *J* = 6.8 Hz), 6.53 (1H, s), 7.01-7.61 (9H, m), 8.76 (1H, br.s); *m/z* (%) 250 (100), 341 (60, $M^+$) [Found: C, 84.0; H, 6.9; N, 3.9; $C_{24}H_{23}NO$ requires : C, 84.4; H, 6.8; N, 4.1]. Acc. mass 341.1786, $C_{24}H_{23}NO$ requires 341.1780.

5-Benzyl-6,7-dimethyl-8-(3-methyl-2-butenyloxy)-4b,5,9b,10-tetrahydroinden o[1,2-*b*] indole (28)

5-Benzyl-6,7-dimethyl-8-hydroxy-4b,5,9b,10-tetrahydroindeno[1,2-*b*]indole (26, R=H) (40 mg, 0.12 mM) dissolved in absolute ethanol was evaporated with sodium ethoxide (1 eq) in ethanol. The resultant sodium salt was heated under reflux with benzene (5 $cm^3$) and 4-bromo-2-methylbut-2-ene (0.14 g, *ca* 10 mM) under an atmosphere of nitrogen for 15 min. The volatiles were removed under reduced pressure and the residue was partitioned between chloroform and 2M hydrochloric acid. The chloroform layer was collected, washed, dried and evaporated giving a gum. This was purified by preparative thin layer chromatography to give the title compound as colourless needles (30 mg, 62.5%); $\delta_H$ ($(CD_3)_2SO$) 1.70 (3H, s), 1.74 (3H, s), 1.98 (3H, s), 2.18 (3H, s), 3.07 (1H, d, *J* = 16.1 Hz), 3.2 (1H, dd, *J* = 16.1, 7.5 Hz), 3.4 (1H, m), 3.88 (1H, d, *J* = 13.8 Hz), 4.21 (1H, d, *J* = 5.8 Hz), 4.23 (1H, d, *J* = 13.8 Hz), 4.44 (1H, t, *J* = 5.8 Hz), 4.67 (1H, d, *J* = 6.8 Hz), 5.42 (1H, m), 6.76 (1H, s), 7.06-7.62 (9H, m); *m/z* (%) (C.I.) 340 (45), 409 (80), 410 (40, M + 1).

5,10-DihydroIndeno[1,2-*b*]indole (DHII)(32), 5,6-dihydroindeno[2,1-*b*]indole (iso-DHII)(33), 11,12-dihydro--5-phenyldiindeno[1,2-*b*,*d*]pyrrole (34), 5,7-dihydro-6-phenyldiindeno[2,1-*b*,*d*]pyrrole (35), and (±)-5β(α),-6a(α),11b(α),11c(α)-tetrahydro-6phenyldiindan-5,7-diono[2,1-b,d]pyrrole (36)

A mixture of 2-hydroxy-1-indanone (4.0g), aniline (7.5g, 3 mol excess), and anilinium chloride (3.5g) was heated at 120-130°C for 2h, under an atmosphere of nitrogen. After cooling, the mixture was neutralised with 2M hydrochloric acid, and extracted with diethyl ether (3x75$cm^3$). The combined extracts were then washed with hydrochloric acid and then with water, dried and evaporated to give a black residue. This was chromatographed on silica, eluting with petrol-ethyl acetate mixtures (10-30% ethyl acetate). Eighty 25$cm^3$ fractions were collected. As the first three evaporated yellow crystals separated these were shown to be the pentacycle (35) (100mg, 1.2%), m.p. 164-168°C; $\delta_H$ 3.59 (4H, s), 6.94-7.67 (13H, m); *m/z* (%) 319.

The remaining fractions were grouped by tlc analysis and each set evaporated yielding in terms of increasing polarity: the pentacycle (34), as yellow plates (80 mg, 1%), m.p. 210-212°C; $\delta_H$ 3.88 (4H, s), 7.14-7.73 (13H, m) *m/z* (%) 319 (12, $M^+$), DHII (32), m.p. and mixed m.p. 258-259°C (lit.,[1] m.p. 258-259°C), iso-DHII (33),

m.p. and mixed m.p. 204-205°C (lit.,[1] 205°C dec.], and finally the diketopentacycle (36) as bright yellow needles (120mg 1.3%), m.p. 236-238°C; $\mu_{max}cm^{-1}$ 1700, 1580; $\delta_H$ 4.47 (2H, dd, $J$ = 4.8, 2.4Hz), 4.86 (2H, dd, $J$ = 4.8, 2.4Hz), 6.91 (1H, p, $J$ = 4.0Hz), 7.08 (2H, d, $J$ = 7.7Hz), 7.28-7.39 (5H, m), 7.43 (3H, ddd, $J$ = 7.5, 7.5, 1.5Hz), 7.57 (2H, d, $J$ = 7.5Hz); $\delta_C$ 46.6(d), 71.7(d), 113.4(d), 124.8(d), 127.2(d), 128.5(d), 128.7(d), 129.1(d), 134.6 (s), 136.1 (s), 149.2 (s), 201.7(s); *m/z*(%) 351(100, $M^+$) [Found: C, 82.0; H, 4.9; N, 4.0 $C_{24}H_{17}NO_2$ requires: C, 82.05; H, 4.8; N, 4.0%]. *Crystal data* for (36) $C_{24}H_{17}NO_2$, $M$=351.4 $a$=10.799(1), $b$=12.871(2), $c$=13.032(1) Å, β=104.43(1)°, $U$=1754.2 $Å^3$, space group $P2_1/n$, $Z$=4, $D_c$=1.23 $gcm^{-3}$, $\upsilon$(Mo-$K_\alpha$)=0.47 $cm^{-1}$, $F$(000)=736. Data were recorded at room temperature on a Hilger and Watts Y290 four-circle diffractometer in the range $2 \leq \theta \leq 22°$. 2421 reflections were collected of which 939 were unique with $I \geq 3\sigma(I)$. Data were corrected for Lorentz and polarisation effects, but not for absorption. The structure was solved by direct methods and refined using the SHELX suite of programmes (Sheldrick G.M., SHELX 76; SHELX86, University of Göttingen, 1976;1986). In the final least squares cycles the oxygen and nitrogen atoms were allowed to vibrate anisotropically. All other atoms were treated isotropically. Hydrogen atoms were included at calculated positions. Final residuals, after 10 cycles of least squares were $R$=$R_w$=0.0839 for unit weights. Max. final shift/esd was 0.005. The max. and min. residual densities were 0.15 and -0.13e$A^{-3}$ respectively. Fractional atomic coordinates and isotropic thermal parameters, bond distances and angles are deposited at the Cambridge crystallography data bank, together with anisotropic temperature factors.

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