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CHEMISTRY OF 6H-PYRIDO[4,3-b]CARBAZOLES PART II[1]

SYNTHETIC APPROACHES TO 6H-9-METHOXY-5, 11-DIMETHYLPYRIDO[4,3-b]FLUORENES

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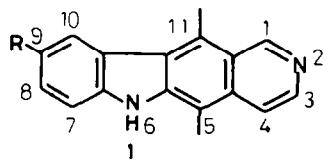
Abstract - Synthetic approaches to 6H-9-methoxy-5, 11-dimethylpyrido[4,3-b] fluorene are described, thus 2-[1-(4-pyridyl)ethyl]6-methoxyindanone has been reacted with vinylmagnesium bromide to yield 2-[1-(4-pyridyl)ethyl]-6 methoxy-1-vinyl-1-indanol. However, on dehydration this compound rearranges to 2-[1-(4-pyridyl)ethyl]-3-ethylidene-5-methoxyindene rather than the required isomer 3-ethylidine-2-[1-(4-pyridyl)ethyl]-5-methoxyindane needed fro pericyclic ring-closure to the pyrido[4,3-b]fluorene system. Reaction of E-2-[1-methyl-1-(4-pyridyl)methylene]-6-methoxyindanone with ethylene triphenylphosphorane similarly gives 6-methoxy-spiro-2-[1-(2,3-dimethyl-3-(4-pyridyl)-cyclopropyl)indanone rather than the desired indane.

It has been established that mammals metabolise the anticancer agent ellipticine (1, R=H), into its 9-hydroxylated derivative (1, R=OH)[2], which may then be further oxidised to the azaquinone (2). It is considered that this last structure is the active form of the drug which then funcions as an alkylating agent and binds covalent -ly to macromolecules such as DNA[3].

Should this hypothesis be correct then it is not surprising that the 6-carbon analogue (3, R=H) of ellipticine is inactive against expermental cancers[4], since it is less likely to be hydroxylated *in vivo* than ellipticine in which the indolic nitrogen atom provides the necessary electronic for electrophilic at position 9. If, however, the pyridofluorene nucleus already bears a hydroxyl function at this site then its conversion into a quinone methide (4) is quite feasible and, in this form, it may well function in a similar manner to the azaquinone (2).

In this paper we discuss some attempts to prepare the pyridofluorene (3, R= OMe) *en route* to the necessary hydroxy compound (3, R=OH) and



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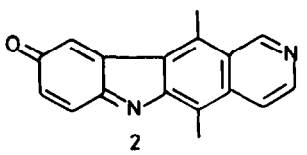

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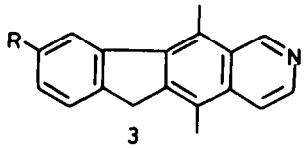

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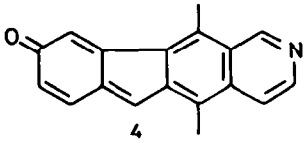

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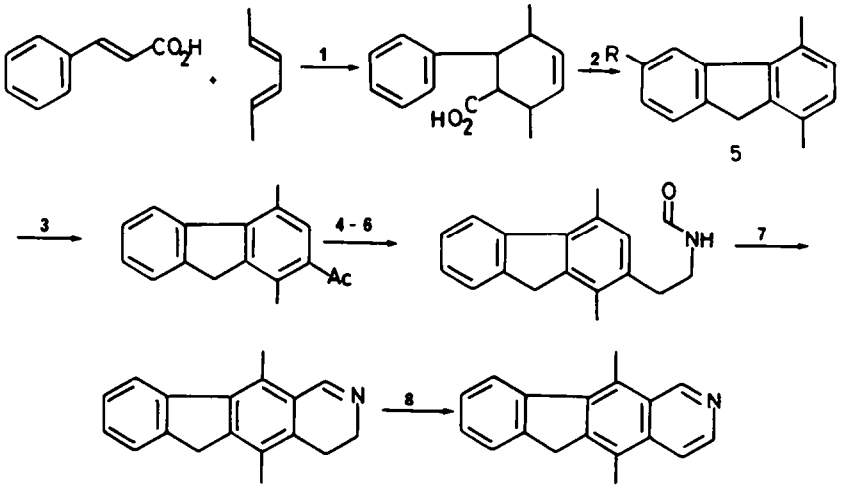
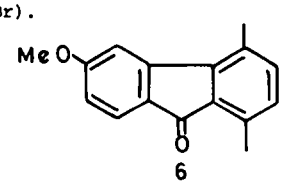
although we have not yet been successful, some interesting new chemistry has emerged. Dixit's synthesis[4] of the parent structure (3, R=H), outlined in scheme 1, is inapplicable to our targets since we have been unable to effect the initial Diels Alder reaction between the 2,4-hexadiene and 4-methoxycinnamic acid, its esters, or related derivatives, despite numerous attempts under many sets of reaction conditions including high pressure experiments. The yield in this reaction was only 12% and so far, we have not been able to improve upon it. Unfortunately, this is insufficient for our purposes, especially since the starting material is relatively inaccessible and this approach was abandoned. Palladium (II) salts have been used to cyclise benzophenones to fluorenones[5], but this technique was unsuccessful when applied to the benzophenone (7, R=H), and to its bromo derivative (7, R=Br).



1. 210°, 10h; 2. P_2O_5; 3. $Ac_2O/AlCl_3/CS_2$; 4. $(NH_4)_2Sx$; 5. LAH; 6. HCO_2Et; 7. PPA, 170°, 8. Pd/C, Δ.

Scheme 1 Synthesis of 5,11-Dimethyl-6H-pyrido[4,3-b]fluorene.

The simple fluorene (5, R=OMe) might be synthesised by base treatment of 3-bromo-4-methoxy-2', 5'-dimethyldiphenylmethane, via an aryne intermediate. In practice such a reaction was unsuccessful, as was a Pschorr cyclisation on the corresponding amine. An alternative procedure is the reduction of the fluorenone (6), and so this compound was prepared by photocyclisation of the bromobenzophenone (7, R=Br). Another approach to the synthesis of the pyrido-fluorene (3, R=OMe) involves the thermal or photochemical ring closure of the diene (8). In order to prepare this compound the lithium enolate of 6-methoxyindanone (9) was reacted with 4-acetylpyridine, affording the hydroxyketone (10) in high yield as a mixture of diastereomers.



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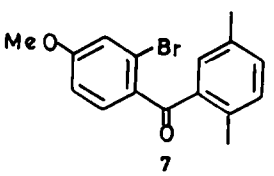

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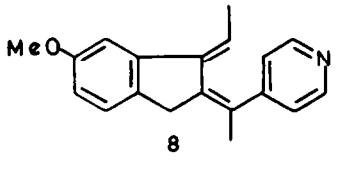

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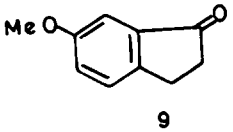

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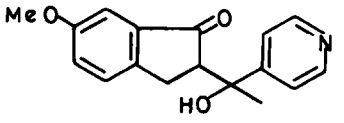

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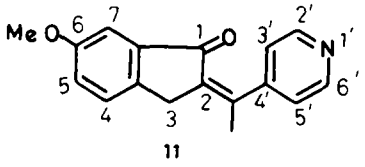
The hydroxyketone is very labile, reverting to starting materials by a retro-aldol reaction. However, when treated with thionyl chloride in pyridine, it gave the enones (11) and (12) in approximately equal amounts. The isomers were separated and the E-isomer (11) reacted with ethylenetriphenylphosphorane to yield the cyclopropane derivative (13), as a mixture of diastereomers, rather than the desired structure (8). Similar results have been observed previously with other hindered ketones[6] and illustrates the difficulty which exists in effecting reagent approach to the carbonyl group of the enone (11). Not surprisingly, attempts to react this compound with ethyl lithium or with ethylmagnesium bromide, also failed. The Z-isomer even failed to react with the phosphorane.

Next the mixed enones were reduced to the ketone (14) and this reacted with vinyl magnesium bromide to yield the alcohol (15). Numerous attempts to dehydrate this product (e.g. heating with silica, alumina, potassium bisulphate, thionyl chloride, hydrogen chloride, sulphuric acid, or dimethyl sulphoxide) invariably gave a yellow glass which when heated strongly in dimethylsulphoxide afforded the diene (16) as the sole product.

This compound was not isomerised by treatment with base, but the fact that it was obtained through a prototropic shift(s) encouraged us to pyrolyse it and the alcohol, in separate experiments, in anticipation that enough of the alternative isomer (8) might be formed to allow cyclisation and aromatisation to the pyridofluorene (3, R=OMe). These reactions were unsuccessful and lead ultimately only to charring. Similarly, photochemical irradiation of the diene (16) served only to fragment the single bond joining the fluorenyl and pyridyl moieties.

Bergman and Carlsson[7] have shown that pyrolysis of the pyridinium salt (17) at 300-500° leads to ellipticine (1, R=H), presumably through a prototropic shift, electrocyclisation and loss of butane. However, when the N-butyl salt (18) was heated under these conditions N-dealkylation, dehydration and rearrangement occurred to afford the diene (16) in low yield.

At the present time we are still seeking alternative routes to the required pyridofluorene (3, R=OMe) and will report on our progress in due course.



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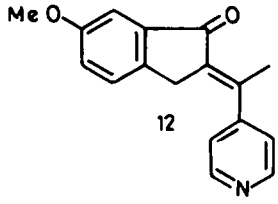

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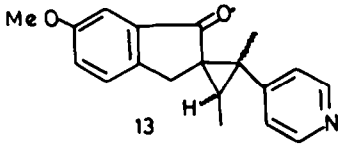

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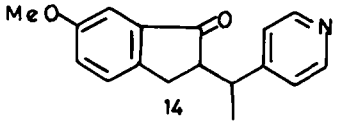

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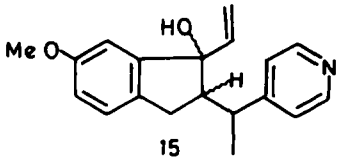

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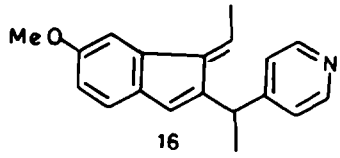

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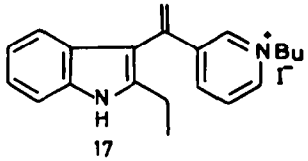

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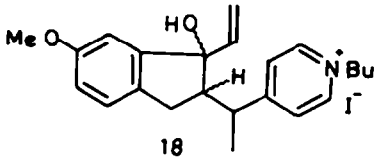

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EXPERIMENTAL

Infrared spectra were recorded as solutions in dichloromethane unless stated otherwise. ^1H n.m.r. data were obtained at 100 MHz and ^{13}C n.m.r. data at 22.5 MHz. Melting points are uncorrected.

3-Bromo-4-methoxy-2', 5'-dimethylbenzophenone. Method 1. To an ice-cooled suspension of imidazole (3.06 g) in trifluoroacetic acid (5 cm^3) was added trifluoroacetic anhydride 6.35 cm^3, dropwise, during five minutes. When addition was complete stirring was continued at room temperature before adding a solution of 2,5-dimethylbenzoic acid (6.75 g and 2-bromoanisole (7.01 g) in trifluoroacetic acid (30 cm^3). The reaction mixture was heated under reflux for 18 h, cooled, poured into water and basified with aqueous sodium hydroxide. The aqueous mixture was extracted with ether (3 x 150 cm^3) and the combined extracts dried ($MgSO_4$) and evaporated under reduced pressure to a yellow solid (10.7 g). Flash chromatography on silica eluting with petroleum ether (b.p. 60 80°) and then diethyl ether afforded the pure benzophenone as a very pale yellow solid (7g, 58.5%) m.p. 89° (diethyl ether ν_{max}1650 cm^{-1} (Nujol); λ_{max} 216, 233, 281 nm (etnanol); ^1H n.m.r. ($CDCl_3$) 2.21 (3H, s, Ar-CH_3), 2.30 (3H, s, Ar-CH_3), 3.91 (3H, s, Ar-O-CH_3), 6.86 (1H, d, J^1 = 8.5 Hz, Ar-H-5), 7.04 (1H, s, Ar-H-5'), 7.12 (2H, s, Ar-H-3' and H-4'), 7.70 (1H, dd, J^1 = 8.5 Hz, J^2 = 2Hz, Ar-H-6), 8.00 (1H, d, J^2 = 2 Hz, Ar-H-2), ^{13}C n.m.r. ($CDCl_3$) 19.3 (q, Ar-CH_3), 20.9 (q, Ar-CH_3), 56.5 (q, Ar-O-CH_3), 111.2 (d, Ar-C-5), 112.1 (s, Ar-C-3), 128.4 (d, Ar-C-2), 130.9 (d, Ar-C-6), 131.5 (d, Ar-C-6'), 131.9 (s, Ar-C-1), 133.1 (s, Ar-C-1'), 134.9 (d, Ar-C-3'), 135.2 (d, Ar-C-4'), 138.6 (s, Ar-C-2' and C-5'), 159.8 (s, Ar-C-4), 196.2 (s, C=O); m/z (M+) 318.0262, 320.0232, $C_{16}H_{15}BrO_2$ requires: 318.0256, 320.0236.

3-Bromo-4-methoxy-2', 5'-dimethylbenzophenone. Method 2. To a vigorously stirred mixture of 2,5-dimethyl-4'-methoxybenzophenone (6 g, 0.025 mol) and thallium(III)acetate sesquihydrate (30.6 g, 0.075 mol) in carbon tetrachloride (250 cm^3) was added bromine (1.29 cm^3, 0.025 mol) in carbon tetrachloride (150 cm^3) during 1 h. The mixture was heated under reflux for 0.5 h, cooled filtered and washed with aqueous sodium metabisulphate (300 cm^3), aqueous sodium bicarbonate (300 cm^3) and finally with water (300 cm^3). The non-aqueous phase was dried ($MgSO_4$) and evaporated under reduced pressure to yield a yellow solid. Traces of thallium were removed by elution through a short alumina column with chloroform. Evaporation of the chloroform afforded the title benzophenone as a pale yellow solid identical in all respects to the material produced in the previous procedure (4.86 g, 61%).

3-Bromo-4-hydroxy-2', 5'-dimethyldiphenylmethane. To a mixture of 3-bromo-4-methoxy-2', 5'-dimethylbenzophenone (4.3 g, potassium hydroxide (4.6 g), and hydrazine hydrate (4.75 cm^3) was added digol (8 cm^3) and the mixture was heated under reflux for 2 h. After this time the temperature of the heating bath was raised to 190° and the condenser removed from the reaction vessel. After 1 h, the reaction mixture was poured into water and extracted with diethyl ether (3 x 50 cm^3). The combined ether extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a brown oil which was purified by flash chromatography on silica, eluting with dichloromethane, to afford a colourless gum (2.65 g, 65%). ^1H n.m.r. ($CDCl_3$) 2.16 (3H, s, Ar-CH_3), 2.29 (3H, s, Ar-CH_3), 3.83 (2H, s, Ar-CH_2-Ar), 5.41 (1H, bs, Ar-OH), 6.9 - 7.3 (6H, m, Ar-H). [Found: C, 62.7; H, 5.1; Br, 27.9 $C_{15}H_{15}BrO$ requires: C, 61.9; H, 5.2; Br, 27.4%].

3-Bromo-4-methoxy-2', 5'-dimethyldiphenylmethane. A solution of 3-bromo-2', 5'-dimethyl-4-hydroxydiphenyl-methane (1.2 g) in acetone (30 cm^3) was treated with potassium carbonate (1.14 g) and methyl iodide (2.5 cm^3), 8 equiv.) and the mixture heated under reflux for 2.5 h. The cooled mixture was filtered and evaporated under reduced pressure to yield a white solid (1.07 g, 85%), m.p. 55-58% (ethanol/water) ^1H n.m.r. ($CDCl_3$) 2.16 (3H, s, Ar-CH_3), 2.27 (3H, s, Ar-CH_3), 3.80 (5H, s, Ar-OCH_3 and Ar-CH_2-Ar), 6.74 (1H, d, J = 9Hz, Ar-H-5), 6.80 - 7.04 (4H, m, Ar-H-3', H-4', H-6', H-6), 7.27 (1H, d, J = 2 Hz, Ar-H-2) [Found: C, 62.9; H, 5.75; Br, 26.6 $C_{16}H_{17}BrO$ requires: C, 63.0; H, 5.6; Br, 26.2%.

6-Methoxy-1, 4-dimethylflurenone (6). 2-Bromo-6-methoxy-2'5'-dimethylbenzophenone (1.2 g, 0.0038 mol) was dissolved in absolute methanol (500 cm^3) and the solution degassed with nitrogen for 2 h. Subsequent irradiation with ultraviolet light from a medium pressure Hanovia source for 96 h afforded a yellow solution which, on thin layer chromatographic analysis, was shown to contain starting material and a product. The methanol was evaporated to give a green solid which was purified by flash chromatography on silica eluting with 10% ethyl acetate in petroleum ether (b.p. 60-80°). 6-Methoxy-1, 4-dimethylfluorenone was obtained as a yellow solid (0.11 g, 12%), m.p. 125-6° (ethylacetate) ν_{max} 1760 cm^{-1}; ^1H n.m.r. ($CDCl_3$) 2.39 (3H, s, Ar-CH_3), 2.53 (3H, s, Ar-CH_3), 3.86 (3H, s, Ar-O-CH_3), 6.70 (1H, dd, J^1 = 8 Hz, J^2-2 Hz, Ar-H-7), 6.80 - 7.30 (3H, m, Ar-H-2, H-3, H-5), 7.56 (1H, d, J-8 Hz, Ar-H-8), [Found: C, 80.5; H, 6.1 $C_{16}H_{14}O_2$ requires: C, 80.65; H, 5.9%].

2-Bromo-4-methoxy-2', 5'-dimethylbenzophenone (7, R=Br). To an ice-cooled suspension of imidazole (3.06 g) in trifluoracetic acid (5 cm^3) was added trifluoroacetic anhydride (6.35 cm^3) dropwise, during five minutes. When addition was complete stirring was continued at room temperature for 10 minutes before a solution of 2,5-dimethylbenzoic acid (6.75 g) and 3-bromoanisole (7.01 g) in trifluoroacetic acid (30 cm^3) were added. The reaction mixture was heated under reflux for 20 h, cooled, poured into water and basified with aqueous sodium hydroxide. The aqueous mixture was extracted with dichloromethane (3 x 100 cm^3) and the combined extracts dried ($MgSO_4$) and evaporated to a yellow oil (9.4 g). Thin layer chromatography showed this to be a mixture of 2,5-dimethylbenzoic acid and three products having similar polarity. Flash chromatography on silica eluting with petroleum ether (b.p. 60-80°) afforded pure 2-bromo-2', 5'-dimethyl-4-methoxybenzophenone (7, R=Br) as a yellow viscous oil (4.1 g, 35%). ν_{max} 1650 cm^{-1}, ^1H n.m.r. ($CDCl_3$) 2.32 (3H, s, Ar-CH_3), 2.49 (3H, s, Ar-CH_3), 3.92 (3H, s, Ar-O-CH_3), 6.94 (1H, dd, J^1 = 9 Hz, J^2 = 8 Hz, Ar-H-5), 7.1 - 7.35 (4H, m. Ar-H-3', H-4', H-6', H-3), 7.48 (1H, d, J = 9 Hz, Ar-H-6) [Found: C, 59.9; H, 4.8; Br, 25.4 $C_{16}H_{15}BrO$ requires: C, 60.2; H, 4.7; Br, 25.0%].

A small sample of 2-bromo-6-methoxy-2'5'-dimethyl-benzophenone was isolated pure from late column fractions as a yellow oil (0.11 g, 0.9%). ν_{max} 1650 cm^{-1} ^1H n.m.r. ($CDCl_3$) 2.22 (3H, s, Ar-CH_3), 2.62 (3H, s, Ar-CH_3), 3.69 (3H, s, Ar-O-CH_3), 6.87 (1H, dd, J^1 = 8Hz, J^2 = 3 Hz, Ar-H-5), 7.05 - 7.30 (5H, m, Ar-H) [Found: C, 60.0; H, 4.9; Br, 25.5 $C_{16}H_{15}BrO_2$ requires: C, 60.2; H, 4.7; Br, 25.0%].

2-[1-Hydroxy-1-(4-pyridyl)ethyl]-6-methoxyindanone (10). To a solution of distilled diisopropylamine (8.4 cm^3, 0.06 mol) in dry tetrahydrofuran (120 cm^3) protected by a nitrogen atmosphere and cooled to -78° was added a 1.54 M hexane solution of n-butyllithium (39 cm^3), 0.06 mol). The reaction mixture was stirred for a further one hour whereupon the lithium enolate of the 6-methoxyindanone precipitated as a white solid. 4-acetylpyridine (7.26 g, 0.06 mol) was added dropwise to the reaction mixture and the mixture stirred for 1.25 h at -78°. The reaction mixture was then poured into cold saturated aqueous chloride and extracted with diethyl ether. The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to yield a white solid. This was shown by ^1H N.M.R. spectroscopy to be a mixture of starting material and product. Since the product was thermally unstable undergoing a facile retro-aldol reaction, and also unstable in the pressure of silica and alumina. Thus it was used directly for the next stage as a mixture of the three compounds. ^1H n.m.r. ($CDCl_3$) 1.54 (1.5H, s, CH_3), 1.84 (1.5H, s, CH_3), 2.62 - 3.2 (3H, m, Ar-CH_2-CH), 3.78 (1.5H, s, Ar-OCH_3), 3.82, (1.5H, s, Ar-OCH_3), 7.05 - 7.5 (5H, m, Ar-OH), Py-H-3, Py-H-5), 8.42 - 8.58 (Py-H-2' and H-6'); m/z (M+) 283. 1211 $C_{17}H_{17}NO_3$ requires: 283.1214.

Z- and E-6-methoxy-2-[1-methyl-1-(4-pyridyl) methylene]-indanones (11) and (12). Crude 2-[1-hydroxy-1-(4-pyridyl)ethyl]-6-methoxyindanone (10) (13.4 g) in dry pyridine (55 cm^3) maintained at -40° was treated with thionyl chloride (4 cm^3). After a further 1 hour the reaction mixture was allowed to warm to room-temperature, poured into saturated aqueous ammonium chloride solution (750 cm^3) and then extracted with diethyl ether (3 x 250 cm^3). The combined extracts were re-extracted with 2N hydrochloric acid (2 x 150 cm^3), the acid layers basified with sodium carbonate (solid) and again extracted with diethyl ether (3 x 100 cm^3). Evaporation of the solvents afforded the mixed enones (11) and (12) as a yellow solid 6.1 g). Crystallisation from dichloromethane/ethylacetate gave the E-isomer as yellow prisms m.p. 170-1° (ethyl acetate). ν_{max} 1690 cm^{-1} (CH_2Cl_2); ^1H n.m.r. ($CDCl_3$) 2.70 (3H, s, C-CH_3), 3.44 (2H, s, Ar CH_2) 3.84 (3H, s, OCH_3), 7.02 -7.30 (5H, m, 3xAr H, Py-H-3', Py-H-5'), 8.66 (2H, d, J=6 Hz Py-H-2', Py-H-6'); ^{13}C ($CDCl_3$) 19.6 (q C-CH_3), 32.2 (t, Ar CH_2), 55.6 (q, OCH_3), 105.7 (d, C-4), 121.7 (d, C-5), 123.7 (d, C-3', C-5'), 126.7 (d, C-7), 133.4 s, C-3a), 140.9 (s, C-(CH_3)), 141.3 (s, C-4a), 146.7 (s, C-7a) 150.2 (a, C-2' and C-6'), 151.3 (s-C-2), 159.6 (s, C-6), 194.3 (s, C-1). [Found: C, 77.0; H, 5.7; N, 5.4 $C_{17}H_{15}NO_2$ requires: C, 77.0, H, 5.7; N, 5.3%] m/z (M+) 265.1108 $C_{17}H_{15}NO_2$ requires: 265.114. A pure sample of the Z-isomer was obtained by chromatographic purification of the mother liquor from the above crystallisation experiment using silica gel as the column packing and dichloromethane/ethylacetate mixtures as the eluting solvents. It has m.p. 103° (ethylacetate). ν_{max} 1690 cm^{-1}; ^1H n.m.r. ($CDCl_3$) 2.24 (3H, s, C-CH_3), 3.75 (2H, s, ArCH_2), 3.79 (3H, s, OCH_3), 7.1 - 7.48 (5H, m, 3xAr H, Py-H, Py-H-3', Py-H-5'), 8.61 (2H, d, J=6 Hz, Py-H-2' and Py-H-6'); ^{13}C n.m.r. ($CDCl_3$) 23.9 (q, C-CH_3), 3.17 (t, Ar-CH_2), 55.5 (q, OCH_3), 105.7 (d, C-4), 122.3 (d, C-5), 123.7 (d, C-3' and C-5'), 126.7 (d, C-7), 133.5 (s-C-3a), 140.4 (s, C-4'), 140.6 (s, C-CH_3), 149.6 (C-2' and C-6'), 149.8 (s, C-2), 153.0 (s, C-7a), 159.7 (s, C-6), 191.0 (s, C-1). [Found: C, 76.9; H, 5.9; N, 5.2 $C_{17}H_{15}NO_2$ requires: C, 77.0; H, 5.7; N, 5.3%].

6-Methoxy-spiro-2-[1- 2,3-dimethyl-3-(4-pyridyl) -cyclopropyl] indanone (13). To a solution of E-2-[1-methyl-1-(4-pyridyl)methylene]-6-methoxy indanone (0.132 g, 0.5 mmol) in tetrahydrofuran (10 cm^3) was added one equivalent of ethylene-triphenylphosphorane in THF (2.5 cm^3). After one hour at room temperature, a second equivalent of phosphorane was added and the orange-brown solution heated under reflux for a further hour. Thin layer chromatographic analysis showed some starting material still present, thus a further two equivalents of phosphorane were added and the heating continued. After a further one hour, the starting material has been totally consumed and the reaction mixture was then worked up for bases. The crude product was repeatedly chromatographed on silica eluting with ethyl acetate to give an amorphous fawn solid (0.097 g, 66.2%), m.p. 125-130°. ν_{max} 1710 cm^{-1}; ^1H, n.m.r. (6d-DMSO) 1.0 - 1.5 (6H, m, C-CH_3 and CH-CH_3), 2.7 - 3.4 (3H, m, CH-CH_3 and Ar-CH_2), 3.80 (3H, s, Ar-OCH_3), 7.0 -7.5 (5H, m, Ar-H and Py-H-3' and Py-H-5'), 8.3 (2H, bs, Py-H-2' and Py-H-6'); m/z (M+) 293/1415, $C_{19}H_{19}NO_2$ requires: 293.1414 [Found: C, 77.8; H, 6.5; N, 4.7 $C_{19}H_{19}NO_2$ requires: C, 77.8; H, 6.5; N, 4.8%]. The Z-isomer failed to react with the phosphorane.

6-Methoxy-2-[1-(4-pyridyl)ethyl]indanone (14). To a slurry of 6-methoxy-2-[1-methyl-1-(4-pyridyl)methylene]indanone (1.25 g) in 95% ethanol (100 cm^3) was added 10% palladium on charcoal (10 mg). The slurry was stirred under a hydrogen atmosphere for twenty-four hours during which time the starting material gradually disappeared. The reaction mixture was filtered through celite and then the solvent was evaporated under reduced pressure to afford a colourless oil which crystallised only after standing several weeks (1.2 g, 95.6%). ν_{max} 17.5 cm^{-1} (liquid film); ^1H n.m.r. ($CDCl_3$) 1.14 (1.5H, J=7Hz, CH_3), 1.56 (1.5H, d, J= 7 Hz, d, J = 7Hz, CH_3), 2.69 3.60 (4H, m, CH_2, COCH, $CHCH_3$), 3.85 (3H, s, Ar-OCH_3), 7.02 - 7.40 (5H, m, Ar-H, Py-H-3 and Py-H-5), 8.38 - 8.58 (2H, m, Py-H-2 and Py-H-6); m/z (M+) 267.1271, $C_{17}H_{17}NO_2$ requires M+ 267.1283.

6-Methoxy-2-[1-(4-pyridyl)ethyl]-1-vinyl-1-indanol (15). A solution of 6-methoxy-2-[1-(4-pyridyl)ethyl]indanone (1.14 g, 4.3 mmol) in dry tetrahydrofuran (20 cm^3) was added dropwise during five minutes to a solution of excess vinyl magnesium bromide (7 mmol) in tetrahydrofuran (20 cm^3). The yellow solution was heated under reflux for one hour and excess reagent was then quenched by adding the reaction mixture to saturated ammonium chloride solution. The aqueous was extracted with ether and the combined extracts dried ($MgSO_4$) and evaporated under reduced pressure to yield a yellow foam which was purified by chromatography on silica

eluting with chloroform containing 3% methanol. Yield 0.67 g (52.8%). ν_{max} 1600 cm^{-1} (Nujol); ^1H n.m.r. ($CDCl_3$) 1.30 (1.5H, d, J = 6Hz, CH_3), 2.3 - 3.4 (4H, m, CH_2, CH_2-CH, CH_3-CH, 3.70 (3H, s, Ar-OCH_3), 4.55 - 6.50 (3H, m, vinyl CH), 6.6 - 7.3 (5H, m, 3xAr-H, Py-H-3' and Py-H-5), 8.2 - 8.4 (2H, m, Py-H-2' and Py-H-6'); m/z (M+) 295.1571; $C_{19}H_{21}NO_2$ requires: 295.1570.

5-Methoxy-3-ethylidine-2-[1-(4-pyridyl)ethyl]indene (16). A solution of 6-methoxy-2-[1-(4-pyridyl)ethyl]-1-vinyl-1-indanol (0.085 g in dimethylsulphoxide (1 cm^3) was heated under reflux for 1h. Evaporation of the solvent in vacuo afforded the title compound as a yellow glass. (0.81 g, 99%). ν_{max} 1600 cm^{-1} ($CHCl_2$); ^1H n.m.r. (d^6-DMSO) 1.50 (3H, d, J = 8Hz, Py-CH-CH_3), 2.18 (3H, d, J = 8Hz, = CH-CH_3, 3.80 (3H, s, Ar-OCH_3), 4.14 (1H, q, J = 8Hz, Py-CH--CH_3), 6.38 (1H, q, J = 8Hz, =8Hz, =CH-CH_3), 6.65 (1H, unresolved doublet, Ar-H-4), 6.82 (1H, dd, J^1 = 3Hz, Ar-H-6), 7.1 - 7.4 (3H, m, Ar-H-7, Py-H-3' and Py-H-5'), 8.45 (2H, m, Py-H-2' and Py-H-6'); m/z (M+) 277.1454 $C_{19}H_{19}NO$ requires: 277.1467.

Pyrolysis of the salt (18). 6-Methoxy-2-[1-(4-pyridyl)ethyl]-1-vinyl-1-indanol (1 g) in diethyl ether: acetone (1:1) (15 cm^3) was treated with n-butyl bromide (1 cm^3), the mixture stirred at room temperature for 24h, and then heated at reflux for a further 2h. Partial evaporation of the solvent gave a gum, this was separated and washed several times with ethyl acetate to remove any unchanged starting material. The gum was then taken up in acetone containing 2% water and the solution evaporated onto basic alumina (15 g), prior to pyrolysis at 350° for 10 minutes in a small electrical furnace. The product still on alumina was added to the top of an alumina column and eluted with ethylacetate. 5-Methoxy-3-ethylidine-2-[1-(4-pyridyl)-ethyl]indene (16) (0.65 g) was obtained identical in all respects with the compound obtained in previous experiments.

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