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# Cobalt-Mediated Aryl Radical Cyclisations: A Formal Synthesis of Physovenine

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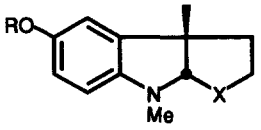
*Key Words:* cobalt, aryl radical cyclisation, physovenine.

***Abstract***: A synthesis of the tetrahydrofuro[2,3-*b*]indole (3) in 6 steps from 4-methoxyaniline involving a key cobalt-mediated aryl radical cyclisation is presented. This heterocycle is a known, late intermediate in the synthesis of the alkaloid physovenine (2).

Radical cyclisation reactions have achieved considerable importance in the formation of carbon/carbon bonds particularly in sterically hindered situations[1]. The majority of publications concerned with radical reactions have involved the use of tributyltin hydride and alkyl, vinyl or aryl halides. Of necessity, this process is overall reductive in nature and leads, in the simple cases, to the loss of two functional groups for the gain of one carbon/carbon bond. The high level of toxicity of organotin compounds in general has also caused some concern. Recent methods such as the use of tristrimethylsilylsilane,[2] triethylsilane/ethanethiol[3] and samarium diiodide[4] have addressed the latter problem, whilst the use of manganese(III) acetate[5] and low-valent cobalt complexes[6] have addressed the former problem. In particular, the work of Pattenden has shown that the cobalt(I) salen complex can react with aryl iodides to give dihydroindoles and dihydrobenzofurans.[7] Our interest in the synthesis of oxidoles via aryl radical cyclisation and their subsequent use in alkaloid synthesis prompted us to explore the use of the cobalt(I) salen-mediated cyclisations of *o*-haloacryloylanilides. Our preliminary results[8] indicated that these reactions proceed via aryl radical intermediates. We now wish to disclose the use of such a cyclisation as the key step in a short synthesis of an advanced synthetic intermediate for the alkaloid physovenine (2).

The calabar bean alkaloids physostigmine (1) and physovenine (2) have attracted considerable synthetic interest in recent years.[9] Both act upon the parasympathetic nervous system by inhibition of acetylcholinesterase.[10] Physovenine was first isolated by Salway in 1911[11] and its structure elucidated by

Robinson in 1964.[12] There have been a number of syntheses of physovenine including a recent one by Kametani[13] which proceeded via the tricyclic furo[2,3-*b*]indole (**3**). This was synthesised from 4-methoxybenzaldehyde in *ca.* 20 steps and was converted to physovenine by cleavage of the methyl ether using boron tribromide followed by reaction of the resulting phenol with methyl isocyanate.

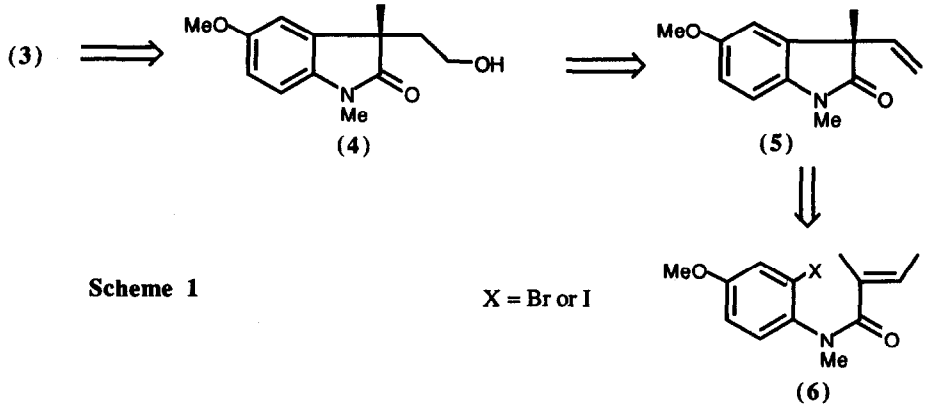



(**1**) X = NMe, R = MeHNCO

(**2**) X = O, R = MeHNCO

(**3**) X = O, R = Me

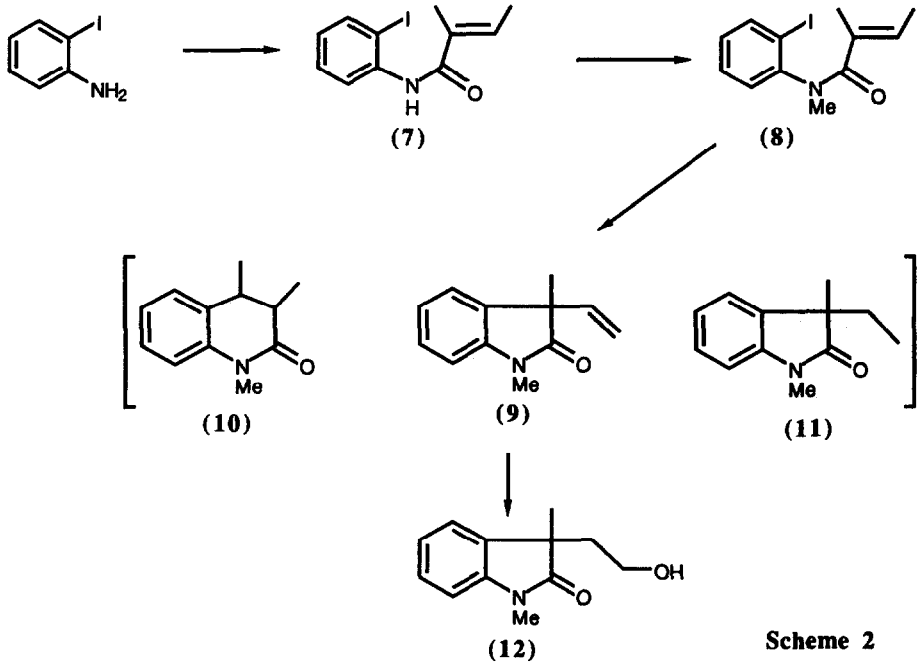
Our approach to (**3**) is summarised retrosynthetically in Scheme 1 and involves synthesis of the 3-vinyloxindole (**5**) by cobalt(I)-mediated radical cyclisation followed by hydroboration/oxidation to give the alcohol (**4**) and finally reductive cyclisation to give the furo[2,3-*b*]indole (**3**).




**Scheme 1**

We decided to explore the cobalt(I)-mediated cyclisation first by treatment of iodoacryloylanilide (**8**) (prepared from *o*-iodoaniline and tigloyl chloride followed by methylation in 51% overall yield) with the cobalt(I) salen complex derived by reduction of (triphenylphosphine), salen cobalt(III) bromide with 1% sodium amalgam (Scheme 2).[14] An inseparable mixture of three products was isolated in 66% yield. The three products were assigned the structures (**9**), (**10**)[15] and (**11**) based on spectroscopic data and hydrogenation of the mixture which proceeded in high yield to give two products, unchanged (**10**) and 1,3-dimethyl-3-ethyloxindole (**11**). The ratio of the products isolated from the cobalt(I)-mediated cyclisation was 76:22:2 respectively for (**9**), (**10**) and (**11**). The ratio of 5-exo to 6-endo cyclisation exactly mirrors that found in the tin hydride-mediated cyclisation.[8] The fact that two reduced products dihydroquinolone (**10**) and oxindole (**11**) are isolated presumably reflects the fact that the radicals obtained after addition of the aryl radical to the double bond can pick up a hydrogen atom from the solvent prior to reacting with the cobalt(II) species.

For the case of the 6-endo cyclisation, the radical formed is stabilised by being adjacent to a carbonyl group and tertiary consequently it reacts rather slowly with the sterically demanding cobalt(II) complex and fails to form an alkyl cobalt(III) complex. Thus β-elimination is not possible and reduced product is obtained. The small amount of (**11**) obtained presumably reflects a minor pathway for the primary radical formed by 5-exo cyclisation. With the vinyloxindole (**9**) in hand (albeit as a mixture), hydroboration was attempted to ensure it was possible to select between reaction at the double bond and reduction of the oxindole. Treatment of the mixture obtained from cobalt(I)-mediated cyclisation with 9-BBN in refluxing tetrahydrofuran (THF) proceeded smoothly to give, after chromatography, the primary alcohol (**12**) in 45% yield.

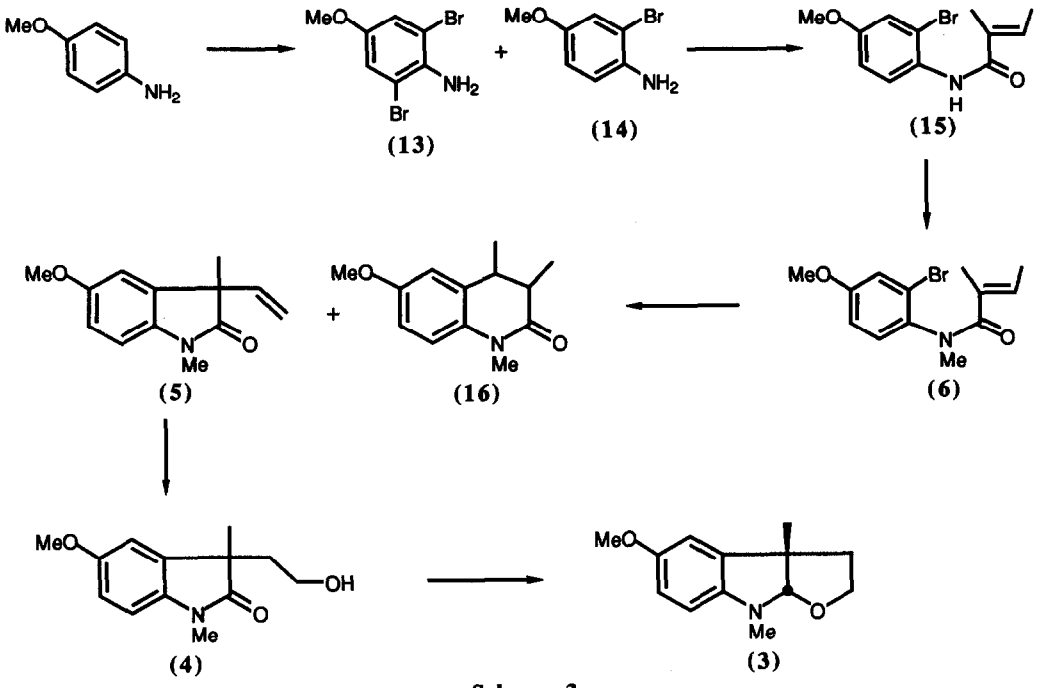



**Scheme 2**

With these encouraging results in hand, we turned our attention to the synthesis of (**4**) carrying the methoxy group. The required 2-iodo-4-methoxyaniline proved rather elusive and we were forced to consider using the 2-bromo-4-methoxyaniline (**14**). Aryl bromides are known to be inferior to aryl iodides in the reaction with cobalt(I) species[16] and hence there were doubts about the viability of the radical cyclisation reaction.

2-Bromo-4-methoxyaniline (**14**) has previously been prepared via a three step route from 3-bromophenol in an overall yield of 33%.[17] A more convenient procedure was found to involve the reaction of *p*-anisidine with 1 molar equivalent of bromine in acetic acid. This gave a separable mixture of the desired 2-bromo-4-methoxyaniline (**14**) and the 2,5-dibromo derivative (**13**). Optimisation of the desired monobrominated product was achieved by careful manipulation of the conditions to give (**14**) in 40 % yield. Acylation of (**14**) with tigloyl chloride in the presence of triethylamine gave the *N*-unsubstituted acryloylanilide (**15**) in 59% yield. *N*-Methylation gave the cyclisation precursor (**6**) in 85% yield.

Cyclisation of (6) using the cobalt(I) salen complex as before gave an inseparable mixture of vinyloxindole (5) and dihydroquinolone (16) in a ratio of 3:1 and a combined yield of 40%. As anticipated, the yield was not as good as for the cyclisation of the iodoarene (8). Hydroboration/oxidation of the mixture using the same procedure as described above, gave the alcohol (4) in 60% yield. The final step involved the reductive cyclisation of (4) to the furo[2,3-*b*]indole. Treatment of (4) with one molar equivalent of diisobutylaluminium hydride in toluene at -78°C gave a 4:1 mixture of the desired product (3) and dihydroindole from reduction of the oxindole carbonyl in 92% yield based on recovered starting material. The furo[2,3-*b*]indole (3) was isolated by chromatography over alumina and displayed identical spectral data to those reported.[13]




**Scheme 3**

In summary, we have prepared the advanced physovenine intermediate (3) by a short, 6 step route beginning from *p*-anisidine.

**Acknowledgements**

We should like to thank the SERC for a Research Studentship to AJC.

**Experimental**

Solutions were dried over anhydrous magnesium sulphate and THF was distilled from potassium benzophenone ketyl immediately before use. Purification was carried out by column chromatography using the flash chromatography technique. Nmr were obtained on a Bruker AM360 operating at 360 MHz for $^{1}H$ and 90 MHz for $^{13}C$ and all spectra were recorded as solutions in $CDCl_3$. Mass spectra were run at the SERC

Mass Spectrometry Centre, University College Swansea. Melting points are uncorrected.

**N-(2'-Iodophenyl)-2-methyl-2-butenamide (7)**

To a solution of 2-iodoaniline (1.85 g, 8.5 mmol) and triethylamine (3.44 g, 34 mmol) in dry ether (20 ml) at 0°C under argon was added dropwise 2-methyl-2-butenoyl chloride (1.0 g, 8.5 mmol). The mixture was warmed to room temperature and stirred for 2 hours. The resultant mixture was diluted with ether (30 ml) washed with aqueous HCl (1M, 2 x 20 ml), aqueous NaOH (1M, 2 x 15 ml), dried and the solvent evaporated to give a crude solid This was purified by flash chromatography to give the product (7) as a white crystalline solid (1.81 g, 70%), m.p. 47-48°C (Found: C, 43.75; H, 3.83; N, 4.71; $M^+$, 301.0003. $C_{11}H_{12}INO$ requires C, 43.85; H, 3.99; N, 4.65%; $M^+$ 300.9965.); $\delta_H$ 1.86 (3H, dq, *J*7 and 1.1 Hz, $CHC\underline{H}_3$), 2.02 (3H, q, *J*1.2 Hz, $CC\underline{H}_3$), 6.72 (1H, m, $C\underline{H}CH_3$), 6.83 (1H, td, *J*7.7 and 1.4 Hz, H-4'), 7.35 (1H, td, *J*8.6 and 1.5 Hz, H-5'), 7.78 (1H, dd, *J*8 and 1.5 Hz, H-3'), 7.87 (1H, br.s, NH), 8.35 (1H, dd, *J*8.3 and 1.6 Hz, H-6'); $\nu_{max}$ 3399 (s, NH), 1687 (s, C=O), 1640 (m, C=C), 1581 (s, C=C aromatic); **m/z** 301 ($M^+$, 16%), 219 (27%), 174 (77%), 134 (79%), 83 (100%).

**N-(2'-Iodophenyl)-N-methyl-2-methyl-2-butenamide (8)**

*N*-(2'-Iodophenyl)-2-methyl-2-butenamide (7) (0.55 g, 1.8 mmol) in dry THF (10 ml) was added to a stirred suspension of sodium hydride (48 mg, 1.98 mmol) in dry THF (5 ml) at 0°C under argon. After hydrogen evolution had ceased (about 15 minutes) methyl iodide (767 mg, 5.4 mmol) was added. The reaction mixture was stirred overnight at room temperature and then quenched with water (1 ml). The solvent was evaporated and the residue dissolved in ether (30 ml). This was washed with water (2 x 10 ml), dried and the solvent evaporated to give a crude solid. This was purified by flash chromatography to give (8) as a white crystalline solid (423 mg, 70%), m.p. 79-80°C (Found: C, 46.07; H, 4.42; N, 4.42; $M^+$, 315.0125. $C_{10}H_{19}NO_3$ requires C, 45.71; H, 4.44; N, 4.42%; $M^+$ 315.0122.); $\delta_H$ 1.45 (3H, br. d, *J*4.1 Hz, $CHC\underline{H}_3$), 1.62 (3H, br. s, $CC\underline{H}_3$), 3.23 (3H, s, $NCH_3$), 5.79 (1H, br. s, $C\underline{H}CH_3$), 6.98 (1H, td, *J*6.4, 1.4 Hz, H-4'), 7.14 (1H, d, *J*7.3 Hz, H-6'), 7.34 (1H, t, *J*7 Hz, H-5'), 7.87 (1H, dd, *J*7, 1.4 Hz, H-3'); $\nu_{max}$ 1659 (s, C=O), 1580 (s, C=C aromatic); **m/z** 315 ($M^+$, 1.5%), 188 (100%), 83 (96%), 55 (82%).

**Cobalt-mediated Cyclisation of (8)**

To a solution of the (triphenylphosphine), *N, N'*-bis salicylidene cobalt (III) bromide (254 mg, 0.38 mmol) in dry deoxygenated THF (40 ml) under argon was added 1% sodium/mercury amalgam (10 g). The solution was stirred for 3 hours until the initial black solution became emerald green. The air sensitive solution was transferred by cannula under a positive pressure of argon into a solution of *N*-(2'-Iodophenyl)-N-methyl-2-methyl-2-butenamide (9) 60 mg, 0.19 mmol) dissolved in dry deoxygenated THF (5 ml) and the solution as alowed to stir overnight. The solvent was evaporated and the solid residue dissolved in dichloromethane (10 ml) and methanol (0.5 ml). The solution was passed through a small plug of silica gel and the solvents evaporated. Purification of the crude solid obtained was carried out by flash chromatography (5:1 petrol:ethyl acetate) to give a clear oil (24 mg, 66%) which was an inseparable mixture of (**9**), (**10**) and (**11**) in a ratio of 76:22:2 as judged by nmr. product (Found $M^+$, 187.0099. $C_{12}H_{13}NO$ requires $M^+$, 187.0097; $M^+$, 189.1151 $C_{12}H_{15}NO$ requires $M^+$, 189.1154); Data for vinyloxindole (**9**): $\delta_H$ 1.50 (3H, s, $CH_3$), 3.22 (3H, s, $NCH_3$), 5.13 (1H, dd, *J*17.3, 0.6 Hz, $C{=}CH\underline{H}_{cis}$), 5.16 (1H, dd, *J*9.8, 0.6 Hz, $C{=}CH\underline{H}_{trans}$), 5.95 (1H, dd, *J*17.3, 10.5 Hz, $\underline{H}C{=}CH_2$), 6.87 (1H, d, *J*7.8 Hz, H-7), 7.11 (1H, td, *J*7.6, 0.9 Hz, H-5), 7.19 (1H, dd, *J*7, 1.2 Hz, H-6), 7.29 (1H, td, *J*7.7, 1.3 Hz, H-6); **m/z** 187 ($M^+$, 100%), 172 (39%), 158 (34%). Data for dihydroquinolone (**10**): $\delta_H$ 1.11 (3H, d, *J*7 Hz, C-4methyl), 1.18 (3H, d, *J*7 Hz, C-

3methyl), 2.75 (1H, qd, *J*7, 5 Hz, H-3), 2.96 (1H, qd, *J*7, 5 Hz, H-4), 3.36 (3H, s, $NCH_3$) 6.96-7.03 (2H, m, H-5, H-6), 7.20 (1H, br. d, *J*7 Hz, H-8), 7.25 (1H, td, *J*7, 1.5 Hz, H-7); **m/z** 189 ($M^+$, 100%), 174 (79%), 160 (24%), 56 (98%). Data for oxindole (): $\delta_H$ 0.58 (3H, t, *J*7.4 Hz, $CH_2\underline{CH_3}$), 1.35 (3H, s, C-3methyl), 1.74-1.93 (2H, m, $\underline{CH_2}CH_3$), 3.23 (3H, s, Nmethyl), 6.84 (1H, d, *J*7.8 Hz, H-7), 7.09 (1H, td, *J*7.4, 0.9 Hz, H-5), 7.16 (1H, dd, *J*7.2, 0.9 Hz, H-4), 7.26 (1H, td, *J*7.4, 1.4 Hz, H-6). Data for mixture: $\nu_{max}$ 1716 (s, C=O oxindole) 1676 (s, C=O dihydroquinolone).

**Hydrogenation of Cyclisation mixture**

To a solution of the mixture of (**9**), (**10**) and (**11**) (12 mg, 0.064 mmol) obtained from the above cyclisation reaction in methanol (5 ml) was added palladium on charcoal (5%, 20 mg) and the mixture was stirred under atmospheric pressure of hydrogen until uptake ceased. The mixture was filtered and the solvent evaporated to give a clear oil (12 mg, 99%) which proved to be an inseparable 78:22 mixture of (**11**) and (**10**) with spectral data as reported above.

**1,3-Dimethyl-3-(2'-hydroxyethyl-indol-2(3H)-one (12)**

To a solution of a mixture of vinyloxindole (**9**) and dihydroquinolone (**10**) (2.6:1 mixture, 23 mg i.e. 16.6 mg, 0.088 mmol in vinyloxindole (**9**))in dry THF (5 ml) under argon was added a solution of 9-BBN in THF (0.5 M, 0.27 ml, 0.13 mmol). The mixture was heated under reflux for 2 hours and allowed to cool to room temerature. Water (1 ml) and a mixture of hydrogen peroxide (30%, 0.5 ml) and aqueous NaOH (1M, 0.5 ml) was added and the mixture heated under reflux for a further hour. The THF was evaporated and the reidue dissolved in ether. The ether solution was washed with water (2 x 10 ml), dried and the solvent removed by evaporation to give a yellow oil. This was purified by flash chromatography (gradient elution starting with 5:1 petrol: ethyl acetate and ending with ethyl acetate) to give alcohol (**12**) as a clear oil (8 mg, 45%); (Found: $M^+$, 205.1095. $C_{12}H_{15}NO_2$ requires $M^+$, 205.1103); $\delta_H$ 1.41 (3H, s, $CH_3$), 1.97 (1H, m, $\underline{CH_2}CH_2OH$), 2.15 (1H, m, $\underline{CH_2}CH_2OH$), 2.38 (1H, br.s, OH), 3.22 (3H, s, $NCH_3$), 3.46 (1H, dt, *J*10.5, 6 Hz, $CH_2\underline{CH_2}OH$), 3.67 (1H, dt, *J*10.5, 6 Hz, $CH_2\underline{CH_2}OH$), 6.86 (1H, d, *J*7.8 Hz, H-7), 7.08 (1H, td, *J*7.4, 0.9 Hz, H-5), 7.18 (1H, dd, *J*7.3, 1.1 Hz, H-4), 7.28 (1H, td, *J*7.7, 1.3 Hz, H-6); $\nu_{max}$ 3600-3200 (s, OH), 1700 (s, C=O), 1610 (s, C=C aromatic); **m/z** 205 ($M^+$, 37%), 161 (100%), 77 (10%).

**2-Bromo-4-methoxyaniline (14)**

To a solution of 4-methoxyaniline (21.96 g, 16 mmol) in acetic acid (30 ml) was added bromine (10% in acetic acid, 8.34 ml, 16.1 mmol) and the mixture was stirred at room temperature. After 5 minutes the reaction was quenched with water (10 ml) and the solvents evaporated. The residue was dissolved in ether (150 ml) and washed with water (5 x 50 ml), dried and concentrated to give a crude black solid. This was purified by flash chromatogrophy to give the required product (**14**) as a dark oil (1.046 g, 51% based on recovered starting material); $\delta_H$ 3.73 (5H, s, $OCH_3$, $NH_2$), 6.73 (2H, m, H-5, H-6), 7.00 (1H, m, H-3).[17]

***N*-(2'-Bromo-4'-methoxyphenyl)-2-methyl-2-butenamide (15)**

Procedure as for (**7**). 2-Bromo-4-methoxyaniline (500 mg, 2.47 mmol), tigloyl chloride (300 mg, 2.53 mmol) and triethylamine (760 mg, 7.5 mmol) gave, after purification by flash chromatography, (**15**) as a white crystalline solid (413 mg, 59%), m.p. 73-74°C (Found: C, 50.51; H, 4.89; N, 4.78; $M^+$, 285.0198/283.0216. $C_{12}H_{14}NO_2Br$ requires C, 50.70; H, 4.92; N, 4.92%; $M^+$ 285.0188/283.0208); $\delta_H$ 1.84 (3H, dq, *J*7 and 1.1 Hz, $CHC\underline{H_3}$), 1.98 (3H, q, *J*0.9 Hz, $C\underline{CH_3}$), 3.79 (3H, s, $OCH_3$), 6.65 (1H, qd,

*J*6.8 and 1.1 Hz, C<u>H</u>CH$_3$), 6.89 (1H, dd, *J*9 and 2.9 Hz, H-5'), 7.10 (1H, d, *J*2.8 Hz, H-3'), 7.82 (1H, br.s, NH), 8.27 (1H, d, *J*9.1 Hz, H-6'); $\nu_{max}$ 3430 (w, NH), 1680 (s, C=O), 1645 (m, C=C); **m/z** 285/283 ($M^+$, 69%), 204 (83%), 83 (100%).

***N*-(2'-Bromo-4'-methoxyphenyl)-*N*-(methyl)-2-methyl-2-butenamide (6)**

Procedure as for (**8**). N-(2'-Bromo-4'-methoxyphenyl)-2-methyl-2-butenamide (**15**) (310 mg, 1.1 mmol), sodium hydride (39 mg, 1.65 mmol) and methyl iodide (780 mg, 5.5 mmol) gave, after purification by flash chromatography, (**6**) as a clear oil (305 mg, 93%) (Found: $M^+$, 299.0346/297.0364. $C_{13}H_{16}NO_2Br$ requires $M^+$ 299.0345/297.0365); $\delta_H$ 1.46 (3H, br.d, *J*6 Hz, CHC<u>H</u>$_3$), 1.60 (3H, br.s, CC<u>H</u>$_3$), 3.20 (3H, s, NCH$_3$) 3.80 (3H, s, OCH$_3$), 5.78 (1H, br.m, C<u>H</u>CH$_3$), 6.81 (1H, dd, *J*8.8 and 2.6 Hz, H-5'), 7.04 (1H, d, *J*7.3 Hz, H-6'), 7.12 (1H, d, *J*2.8 Hz, H-3'); $\nu_{max}$ 1659 (s, C=O), 1639 (m, C=C), 1598 (m, C=C aromatic); **m/z** 299/297 ($M^+$, 6%), 218 (100%), 83 (68%).

**1,3-Dimethyl-5-methoxy-3-vinylindol-2(3H)-one (5)**

Procedure as for (**9**). *N*-(2'-Bromo-4'-methoxyphenyl)-*N*-(methyl)-2-methyl-2-butenamide (**6**) (300 mg, 0.99 mmol) and (triphenylphosphine), *N, N'*-bis salicylidene cobalt (III) bromide (1.334 g, 2.0 mmol) in THF (50 ml) gave a inseparable 3:1 mixture of the desired product (**5**) along with the dihydroquinolone (**16**) (85 mg, 40%) Data for vinyloxindole (**5**) (Found: $M^+$, 217.1103. $C_{13}H_{15}NO_2$ requires $M^+$, 217.1103); $\delta_H$ 1.48 (3H, s, CH$_3$), 3.80 (3H, s O CH$_3$), 3.19 (3H, s, NCH$_3$), 3.80 (3H, s O CH$_3$), 5.13 (1H, dd, *J*17.2, 0.7 Hz, C=CH<u>H</u>$_{cis}$), 5.16 (1H, dd, *J*10.6, 0.7 Hz, C=CH<u>H</u>$_{trans}$), 5.94 (1H, dd, *J*17.2, 10.6 Hz, <u>H</u>C=CH$_2$), 6.73-6.80 (3H, m, H-aromatics); **m/z** 217 ($M^+$, 100%), 202 (64%), 188 (13%). Data for dihydroquinolone (**16**) (Found: $M^+$, 219.1255. $C_{13}H_{17}NO_2$ requires $M^+$, 219.1260); $\delta_H$ 1.12 (3H, d, *J*7 Hz, C-4methyl), 1.16 (3H, d, *J*7 Hz, C-3methyl), 2.72 (1H, qd, *J*7, 5 Hz, H-3), 2.92 (1H, qd, *J*7, 5 Hz, H-4), 3.34 (3H, s, NCH$_3$), 3.80 (3H, s, OCH$_3$), 6.73-6.80 (3H, m, H-aromatics); **m/z** 219 ($M^+$, 100%), 204 (45%), 190 (13%). Data for mixture: $\nu_{max}$ 1713 (s, C=O oxindole) 1670 (s, C=O dihydroquinolone), 1599 (m, C=C aromatic).

**1,3-Dimethyl-3-(2'-hydroxyethyl)-5-methoxyindol-2(3H)-one (4)**

Procedure as for (**12**). Vinyloxindole (**5**) (59 mg of the above mixture containing 43 mg, 0.2 mmol of vinyloxindole) and 9-BBN (0.5M, 1.2 ml, 0.6 mmol) gave (**4**) as a clear oil (28 mg, 61%); (Found: $M^+$, 235.1202. $C_{13}H_{17}NO_3$ requires $M^+$, 235.1208); $\delta_H$ 1.40 (3H, s, CH$_3$), 1.98 (1H, m, C<u>H</u>$_2$CH$_2$OH), 2.11 (1H, m, C<u>H</u>$_2$CH$_2$OH), 2.55 (1H, br.s, OH), 3.20 (3H, s, NCH$_3$), 3.47 (1H, dt, *J*11, 6 Hz, CH$_2$C<u>H</u>$_2$OH), 3.68 (1H, dt, *J*11, 6 Hz, CH$_2$C<u>H</u>$_2$OH), 3.80 (3H, s, OCH$_3$), 6.75-6.81 (3H, m, H-aromatics); $\nu_{max}$ 3600-3200 (br.s, OH), 1708 (s, C=O), 1598 (s, C=C aromatic); **m/z** 235 ($M^+$, 98%), 217 (2%), 191 (100%).

**8-Methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-*b*]indole (3)**

To a solution of 1,3-dimethyl-3-(2'-hydroxyethyl)-5-methoxyindol-2(3H)-one (**4**) (22.8 mg, 0.1 mmol) in toluene (2 ml) at -78°C was added diisobutylaluminium hydride (1M in hexanes, 0.1 ml, 0.1 mmol). The mixture was stirred for 15 minutes and a saturated solution of potassium sodium tartrate (5 ml) added. The solution was stirred for 30 minutes and extracted with ether (3 x 30 ml), dried and evaporated. The crude product was purified by column chromatography on neutral alumina (3:2 petrol:ethyl acetate) to give the starting material (**4**) (13.2 mg), dihydroindole (1.07 mg, 12%) and the desired product (**3**) (7.1 mg, 80% based on recovered starting material) as a clear oil; (Found: $M^+$, 219.1249. $C_{13}H_{17}NO_2$ requires $M^+$,

219.1258); $\delta_H$ 1.44 (3H, s, $CH_3$), 1.99-2.15 (2H, m, $C\underline{H}_2CH_2O$), 2.88 (3H, s, $NCH_3$), 3.43-3.50 (1H, m, $CH_2C\underline{H}_2O$), 3.75 (3H, s, $OCH_3$), 3.90-3.96 (1H, m, $CH_2C\underline{H}_2O$), 5.02 (1H, s, H-8a), 6.28 (1H, d, *J*8.2 Hz, H-7), 6.66 (1H, dd, *J*8.2, 2.5 Hz, H-6), 6.69 (1H, d, *J*2.5 Hz, H-4); $\nu_{max}$ 1598 (s, C=C aromatic); **m/z** 219 ($M^+$, 100%).

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