Studies on the Syntheses of Heterocyclic Compounds. Part 865.[1] A Novel Synthesis of Indole Derivatives by Intramolecular Nucleophilic Aromatic Substitution

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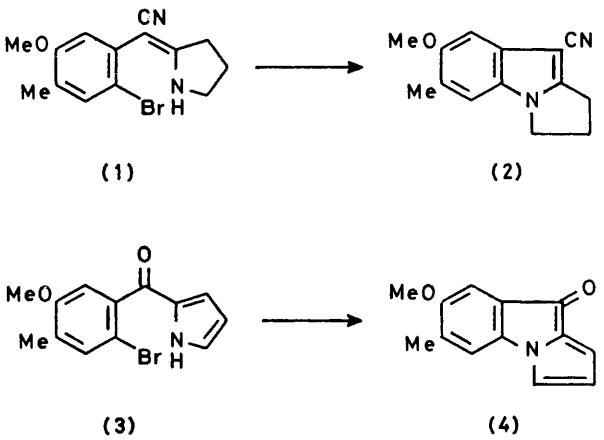
Cyclisation of *N*-(2-bromo-4,5-dimethoxyphenethyl)acetamide (6) afforded 1-acetyl-2,3-dihydro-5,6-dimethoxy-1*H*-indole (13) by intramolecular nucleophilic aromatic substitution using sodium hydride and cuprous halide in dimethylformamide. The dihydroindoles (14), (15), and (16) were also synthesised from the corresponding amides (8) and (10) and the carbamate (12) in a similar manner. The dihydroindoles (13), (14), and (16) were converted into the indoles (20) and (21) in excellent yield by oxidation and subsequent alkaline hydrolysis. The 2-oxindoles (26) and (27) were also prepared under similar reaction conditions from the phenylacetamide (24) and (25).

MANY methods for preparing the indole ring are known [2] and recently there have been reports in which several indoles have been synthesized using reactions catalysed by organometallic compounds such as nickel and palladium complexes.[3] Previously, in an approach to the synthesis of mitomycins, we reported a new intramolecular nucleophilic aromatic substitution using sodium hydride and cuprous bromide in dimethylformamide and converting the aryl bromides (1) and (3) into the pyrrolo[1,2-*a*]indoles (2) [4] and (4) [5] respectively at room temperature in excellent yields. We have further extended this reaction to the facile synthesis of indole derivatives and here report these results.



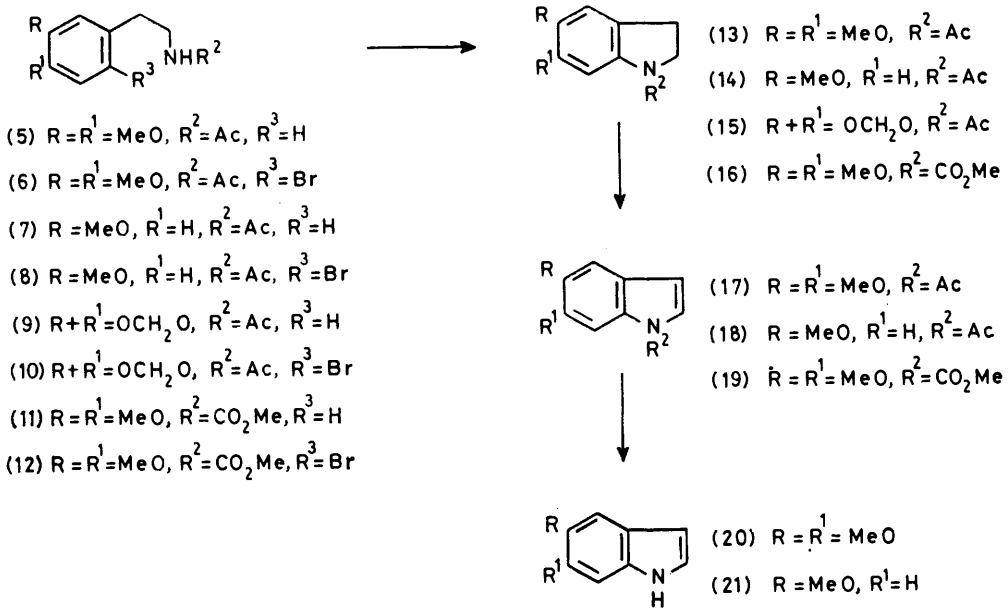
SCHEME 1

To begin with, this cyclisation was applied to *N*-acetyl-2-bromophenethylamines. All starting materials (6), (8), and (10) were prepared in high yield by the bromination of the corresponding acetamides (5),[6] (7),[7] and (9) [8] with bromine in glacial acetic acid or chloroform at room temperature. Treatment of *N*-(2-bromo-4,5-dimethoxyphenethyl)acetamide (6) with sodium hydride and cuprous iodide in dimethylformamide at 80—85 °C for 12 h under nitrogen atmosphere afforded 1-acetyl-2,3-dihydro-5,6-dimethoxy-1*H*-indole (13) in 74.0% yield. Reaction conditions leading to benzyne formation, namely treatment of the bromoacetamide (6) with sodium amide in liquid ammonia and tetrahydrofuran at −33 °C for 1 h, gave the same indoline (13) in only 13.7% yield. This result seemed to support the assumption that the benzyne reaction mechanism did not operate in this substitution. It was, furthermore, ascertained that this cyclisation did not proceed without sodium hydride nor cuprous ion. Other cuprous halides, cuprous bromide and cuprous chloride, were also effective, although lower yields, 58.9% and 57.9% respectively, were observed. Catalytic amounts of the cuprous halide completed the above reaction but the use of a stoicheiometric amount of cuprous ions gave always better yield. As to the base used, sodium hydride seemed to be more efficient and handy than other bases, for instance potassium hydride. Dimethylformamide was found to be a more suitable solvent than dimethyl sulphoxide or dimethylformamide–hexamethylphosphoric triamide [10 : 1 (v/v)].

Subsequently, the conversion of the indole (13) into the indole (20) was examined. In order to remove the acetyl group, the indoline (13) was treated with Claisen's alkali [9] under reflux for 1 h, but gave several products including a small amount of the indole (20) which could be formed by concomitant aerial oxidation. Therefore the indoline (13) was firstly oxidised with manganese dioxide in methylene chloride at room temperature for 2 days affording an *N*-acetylindole (17) in 85.6% yield (based on starting material consumed). The *N*-acetylindole obtained was submitted to alkaline hydrolysis, namely refluxing with Claisen's alkali for 1 h, to give the indole (20) in 72.6% yield.

In a similar manner, the bromoacetamides (8) and (10) were treated under the same reaction conditions to afford the indolines (14) and (15) in 51.6 and 53.0% yields, respectively. The indoline (14) was converted into the indole (21) in 53.0% yield by the same sequence, oxidation with manganese dioxide followed by alkaline hydrolysis of the *N*-acetylindole (18). The utility of the carbamate in place of acetamide was then studied. Methyl 2-bromo-4,5-dimethoxyphenethylcarbamate (12), obtained by bromination of the urethane (11) [10] with

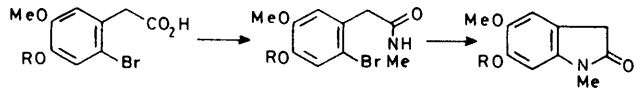
bromine in glacial acetic acid, was subjected to this cyclisation, using sodium hydride and cuprous bromide in dimethylformamide at 80—85 °C for 12 h, to give 2,3-dihydro-5,6-dimethoxy-1-methoxycarbonyl-1*H*-indole



SCHEME 2

(16) in 65.7% yield. In this case, cuprous bromide was more effective than cuprous iodide. Reaction in the presence of cuprous iodide gave the indoline (16) in 51.7% yield. The indoline (16) was also converted into the indole (20) in 63.4% yield by oxidation with manganese dioxide followed by alkaline hydrolysis of the resulting *N*-methoxycarbonylindole (19).

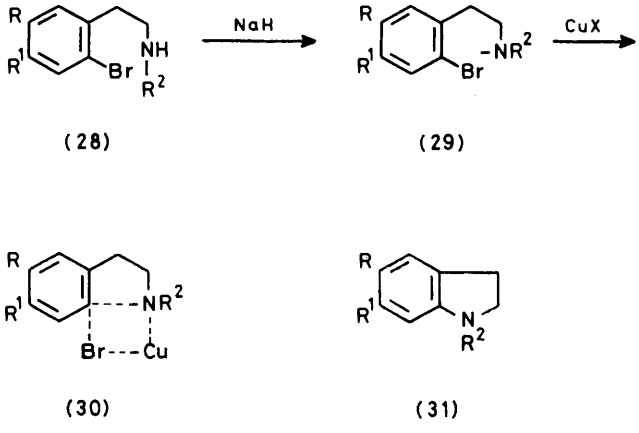
Furthermore, attempts to examine the possibility to synthesise oxindoles using this cyclization was carried out. *N*-Methyl-4-benzyloxy-2-bromo-5-methoxyphenylacetamide (24), prepared in high yield from an acid chloride of a bromocarboxylic acid (22) [11] and methylamine hydrochloride in benzene in the presence of sodium carbonate at room temperature, was treated with sodium hydride and cuprous bromide in dimethylformamide at room temperature for 3 h and at 80—85 °C for 30 min to afford the oxindole (26) in 72.5%



SCHEME 3

yield. Similarly, the 4-methoxy analogue (25), obtained in high yield from the bromocarboxylic acid (23) [12] in the same way, was treated with sodium hydride and cuprous bromide at room temperature for 10 h in dimethylformamide to give the oxindole (27) in 63.4% yield.

This cyclization which is thought to proceed *via* the intermediates (29) and (30) [13] provides a useful and efficient method for the synthesis of indoles, the starting materials being easily prepared from commercially available compounds. Moreover, since as in the present reaction the substitution should take place at a bromine substituent, a number of indoles with electron-donating substituents could be synthesised.



SCHEME 4

EXPERIMENTAL

I.r. spectra were obtained with a Hitachi 215 spectrometer, n.m.r. spectra with a JEOL-PMX-60 spectrometer ($SiMe_4$ as an internal reference), and mass spectra with Hitachi M-52G and JEOL-JMS-01SG-2-spectrometers. M.p.s were determined with a Yanaco micro-melting point apparatus and are uncorrected.

N-(2-*Bromo*-4,5-*dimethoxyphenethyl*)*acetamide* (6).—To a solution of the acetamide (5) (2 g) in glacial acetic acid (20

ml) was added bromine (1 g) in one portion. The resulting mixture was stirred at room temperature for 2 h and then poured into water; it was then extracted with methylene chloride. The extract was washed successively with saturated aqueous sodium hydrogen carbonate, water, 5% aqueous sodium thiosulphate, and water; it was then dried (Na_2SO_4), and evaporated to afford a crystalline mass, recrystallisation of which from benzene–n-hexane gave the *bromoacetamide* (6) (2.6 g, 96.3%) as needles, m.p. 102—103 °C (Found: C, 48.1; H, 5.25; N, 4.65. $C_{12}H_{16}BrNO_3$ requires C, 47.7; H, 5.35; N, 4.65%), $\nu_{max.}$ ($CHCl_3$) 3 480 (NH) and 1 670 (CO) cm^{-1}; δ($CDCl_3$) 1.97 (3 H, s, MeCO), 2.77—3.13 (2 H, m, CH_2CH_2NH), 3.36—3.77 (2 H, m, CH_2CH_2NH), 3.92 (6 H, s, 2 × OMe), 5.67br (1 H, s, NH), and 6.80 and 7.07 (each 1 H, each s, 2 × ArH).

N-(2-Bromo-5-methoxyphenethyl)acetamide (8).—To a solution of the acetamide (7) (1 g) in chloroform (30 ml) was added bromine (1 g) in one portion and the mixture was stirred at room temperature for 2 h and then worked up as above. Recrystallisation of the resulting solid from benzene–n-hexane afforded the *bromoacetamide* (8) (1.34 g, 95.3%) as needles, m.p. 89—90 °C (Found: C, 48.75; H, 5.15; N, 4.95. $C_{11}H_{14}BrNO_2$ requires C, 48.55; H, 5.2; N, 5.2%), $\nu_{max.}$ ($CHCl_3$) 3 480 (NH) and 1 670 (CO) cm^{-1}; δ ($CDCl_3$) 1.97 (3 H, s, MeCO), 2.80—3.15 (2 H, m, CH_2CH_2-NH), 3.33—3.80 (2 H, m, CH_2CH_2NH), 3.81 (3 H, s, OMe), 5.90br (1 H, s, NH), 6.75 (1 H, dd, *J* 4, 9 Hz, 4-H), 6.83 (1 H, d, *J* 4 Hz, 6-H), and 7.52 (1 H, d, *J* 9 Hz, 3-H).

N-(2-Bromo-4,5-methylenedioxyphenethyl)acetamide (10).—To a solution of the acetamide (9) (1.85 g) in glacial acetic acid (25 ml) was added bromine (1.8 g) in one portion and the mixture was stirred at room temperature for 2 h and then worked up as above. The resulting solid was recrystallised from benzene–n-hexane to afford the *bromoacetamide* (10) (2.45 g, 94.7%) as needles, m.p. 128—129 °C (Found: C, 45.95; H, 4.35; N, 4.8. $C_{11}H_{12}BrNO_3$ requires C, 46.15; H, 4.2; N, 4.9%), $\nu_{max.}$ ($CHCl_3$) 3 480 (NH) and 1 670 (CO) cm^{-1}; δ ($CDCl_3$) 2.0 (3 H, s, MeCO), 2.77—3.10 (2 H, m, CH_2CH_2NH), 3.33—3.77 (2 H, m, CH_2CH_2NH), 5.77br (1 H, s, NH), 6.05 (2 H, s, OCH_2O), and 6.83 and 7.13 (each 1 H, each s, 2 × ArH).

Methyl 2-Bromo-4,5-dimethoxyphenethylcarbamate (12).—To a solution of the urethane (11) (2.1 g) in glacial acetic acid (30 ml) was added bromine (1.8 g) in one portion; the mixture was stirred at room temperature for 2 h and then worked up as above. Recrystallisation of the resulting solid from benzene–n-hexane afforded the *bromocarbamate* (12) (2.67 g, 95.6%) as needles, m.p. 88—89 °C (Found: C, 45.3; H, 5.1; N, 4.3. $C_{12}H_{16}BrNO_4$ requires C, 45.3; H, 5.05; N, 4.4%), $\nu_{max.}$ ($CHCl_3$) 3 480 (NH) and 1 715 (CO_2Me) cm^{-1}; δ ($CDCl_3$) 2.78—3.13 (2 H, m, CH_2CH_2NH), 3.30—3.70 (2 H, m, CH_2CH_2NH), 3.73 (3 H, s, CO_2Me), 3.90 (6 H, s, 2 × OMe), 4.80br (1 H, s, NH), and 6.82 and 7.10 (each 1 H, each s, 2 × ArH).

1-*Acetyl*-2,3-*dihydro*-5,6-*dimethoxy*-1H-*indole* (13).—To a solution of the bromoacetamide (6) (200 mg) in dimethylformamide (8 ml) was added 50% sodium hydride (70 mg). After stirring for 30 min at room temperature, cuprous iodide (126 mg) was added to the above mixture, which was heated at 80—85 °C for 12 h with stirring in a current of nitrogen. An excess of crystalline ammonium chloride was added to the above mixture, to which benzene was added. The mixture was washed with brine, dried (Na_2SO_4), and evaporated to afford the residue, which was applied to chromatography on silica gel. Evaporation of benzene–acetone [97 : 3 (v/v)] eluate gave a powder, which was recrystallised from benzene–n-hexane to afford the indoline (13) (108 mg, 74.0%) as needles, m.p. 173—174 °C (lit.,[14] m.p. 176 °C), i.r. and n.m.r. spectra of which were identical with those reported.[14]

1-*Acetyl*-2,3-*dihydro*-5-*methoxy*-1H-*indole* (14).—After a mixture of the bromoacetamide (8) (900 mg) and 50% sodium hydride (300 mg) in dimethylformamide (15 ml) had been stirred for 30 min at room temperature, cuprous iodide (600 mg) was added and the resulting mixture was heated at 80—85 °C for 15 h under a nitrogen atmosphere; it was then worked up as above. The resulting residue was chromatographed on silica gel. Evaporation of the benzene–acetone [97 : 3 (v/v)] eluate afforded a powder, recrystallisation of which from benzene–n-hexane gave the indoline (14) (326 mg, 51.6%) as needles, m.p. 137—138 °C (lit.,[15] m.p. 135—136 °C), $\nu_{max.}$ ($CHCl_3$) 1 640 (CO) cm^{-1}; δ ($CDCl_3$) 2.25 (3 H, s, MeCO), 3.23 (2 H, t, *J* 8 Hz, CH_2CH_2N), 3.83 (3 H, s, OMe), 4.15 (2 H, t, *J* 8 Hz, CH_2CH_2N), 6.70—6.95 (2 H, m, 4 and 6-H), and 8.25 (1 H, d, *J* 10 Hz, 7-H); *m/e* 191 (M^+).

1-*Acetyl*-2,3-*dihydro*-5,6-*methylenedioxy*-1H-*indole* (15).—To a solution of the bromoacetamide (10) (900 mg) in dimethylformamide (15 ml) was added 50% sodium hydride (300 mg). After the mixture had been stirred for 30 min at room temperature, cuprous iodide (600 mg) was added to it and the whole then heated at 80—85 °C for 15 h under a nitrogen atmosphere; it was then worked up as in the case of compound (13). The resulting residue was chromatographed on silica gel. Evaporation of the benzene–acetone [97 : 3 (v/v)] eluate afforded a powder, which was recrystallised from benzene–n-hexane to give the *indoline* (15) (342 mg, 53.0%) as needles, m.p. 117—118 °C (Found: C, 64.65; H, 5.35; N, 6.55. $C_{11}H_{11}NO_3$ requires C, 64.4; H, 5.4; N, 6.85%), $\nu_{max.}$ ($CHCl_3$) 1 650 (CO) cm^{-1}; δ ($CDCl_3$) 2.33 (3 H, s, MeCO), 3.20 (2 H, t, *J* 8 Hz, CH_2CH_2N), 4.20 (2 H, t, *J* 8 Hz, CH_2CH_2N), 6.10 (2 H, s, OCH_2O), and 6.80 and 8.05 (each 1 H, each s, 2 × ArH); *m/e* 205 (M^+).

2,3-*Dihydro*-5,6-*dimethoxy*-1-*methoxycarbonyl*-1H-*indole* (16).—After a solution of the bromourethane (12) (500 mg) and 50% sodium hydride (150 mg) in dimethylformamide (15 ml) had been stirred for 30 min at room temperature, cuprous bromide was added to the mixture which was then heated at 80—85 °C for 12 h under nitrogen atmosphere and worked up as above. The resulting residue was chromatographed on silica gel. Evaporation of benzene–acetone [97.5 : 2.5 (v/v)] eluate gave a powder, which was recrystallised from benzene–n-hexane to afford the *indoline* (16) (245 mg, 65.7%) as needles, m.p. 134—135 °C (Found: C, 60.65; H, 6.4; N, 5.4. $C_{12}H_{15}NO_4$ requires C, 60.75; H, 6.35; N, 5.9%), $\nu_{max.}$ ($CHCl_3$) 1 700 (CO_2Me) cm^{-1}; δ ($CDCl_3$) 3.17 (2 H, t, *J* 9 Hz, CH_2CH_2N), 3.93 (6 H, s, 2 × OMe), 4.00 (3 H, s, CO_2Me), 4.15 (2 H, t, *J* 9 Hz, CH_2CH_2N), 6.78 (1 H, s, 4-H), and 7.70br (1 H, s, 7-H); *m/e* 237 (M^+).

1-*Acetyl*-5,6-*dimethoxy*-1H-*indole* (17)—A mixture of the indoline (13) (340 mg) and activated manganese dioxide (1.28 g) in methylene chloride (40 ml) was stirred at room temperature for 2 days. Manganese dioxide was then filtered off and the filtrate was evaporated to leave a residue, which was chromatographed on silica gel. Evaporation of the benzene–acetone [98 : 2 (v/v)] eluate afforded a powder, which was recrystallised from benzene–n-hexane to give the N-*acetylindole* (17) (218 mg, 64.7%) as needles, m.p. 95.5—96.5 °C (Found: C, 65.95; H, 6.05; N, 6.55. $C_{12}H_{13}NO_3$ requires C, 65.75; H, 6.0; N, 6.4%), $\nu_{max.}$ ($CHCl_3$) 1 700 (CO) cm^{-1}; δ ($CDCl_3$) 2.62 (3 H, s, MeCO), 3.97 and 4.00 (each

3 H, each s, 2 × OMe), 6.57 (1 H, d, *J* 4 Hz, 2-H), 7.10 (1 H, s, 4-H), 7.41 (1 H, d, *J* 4 Hz, 3-H), and 8.20 (1 H, s, 7-H); *m/e* 219 (M^+). Evaporation of benzene–acetone [97 : 3 (v/v)] eluate gave the starting material (83 mg).

1-*Acetyl*-5-*methoxy*-1H-*indole* (18).—To a solution of the indoline (14) (250 mg) in methylene chloride (30 ml) was added activated manganese dioxide (2 g) and the mixture was stirred at room temperature for 3 days. Manganese dioxide was filtered off and the filtrate was evaporated to give a solid, which was recrystallised from n-hexane to afford the *N*-acetylindole (18) (203 mg, 82.1%) as needles, m.p. 80—81 °C (lit.,[16] m.p. 82 °C), $\nu_{max.}$ ($CHCl_3$) 1 700 (CO) cm^{-1}; δ ($CDCl_3$) 2.53 (3 H, s, MeCO), 3.83 (3 H, s, OMe), 6.57 (1 H, d, *J* 4 Hz, 2-H), 6.97 (1 H, dd, *J* 10, 2.5 Hz, 6-H), 7.07 (1 H, d, *J* 2.5 Hz, 4-H), 7.40 (1 H, d, *J* 4 Hz, 3-H), and 8.42 (1 H, d, *J* 10 Hz, 7-H); *m/e* 189 (M^+).

5,6-*Dimethoxy*-1-*methoxycarbonyl*-1H-*indole* (19).—To a solution of the indoline (16) (55 mg) in methylene chloride (10 ml) was added activated manganese dioxide (300 mg); the mixture was stirred at room temperature for 3 days and worked up as in the case of compound (17). The resulting solid was recrystallised from n-hexane to give the 1-*methoxycarbonylindole* (19) (48 mg, 88.1%) as needles, m.p. 106—107 °C (Found: C, 61.05; H, 5.5; N, 5.7. $C_{12}H_{13}NO_4$ requires C, 61.25; H, 5.55; N, 5.7%), $\nu_{max.}$ ($CHCl_3$) 1 730 (CO_2Me) cm^{-1}; δ ($CDCl_3$) 3.95 and 4.0 (each 3 H, each s, 2 × OMe), 4.05 (3 H, s, CO_2Me), 6.55 (1 H, d, *J* 4 Hz, 2-H), 7.08 (1 H, s, 4-H), 7.53 (1 H, d, *J* 4 Hz, 3-H), and 7.88 (1 H, s, 7-H); *m/e* 235 (M^+).

5,6-*Dimethoxy*-1H-*indole* (20).—(*a*) A solution of *N*-acetylindole (17) (31 mg) in Claisen's alkali (5 ml) was refluxed for 1 h and then poured into water; the mixture was then extracted with methylene chloride. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a solid residue, recrystallisation of which from benzene–n-hexane afforded the indole (20) (18 mg, 72.6%) as needles, m.p. 155—156 °C (lit.,[17] m.p. 154—155 °C), $\nu_{max.}$ ($CHCl_3$) 3 490 (NH) cm^{-1}; δ ($CDCl_3$) 3.90 and 3.97 (each 3 H, each s, 2 × OMe), 6.50 (1 H, dd, *J* 3, 3 Hz, 2-H), 6.93 (1 H, s, 4-H), 7.15 (1 H, d, *J* 3 Hz, 3-H), 7.20 (1 H, s, 7-H), and 8.28br (1 H, s, NH); *m/e* 177 (M^+).

(*b*) A mixture of the *N*-methoxycarbonylindole (19) (37 mg) and Claisen's alkali (5 ml) was refluxed for 30 min and then worked up as above. The solid obtained was recrystallised from benzene–n-hexane to afford the indole (20) (20 mg, 71.9%) as needles, m.p. 155—156 °C (lit.,[17] 154—155 °C), i.r. and n.m.r. spectra of which were identical with those of the above compound prepared by the method (*a*).

5-*Methoxy*-1H-*indole* (21).—A solution of the *N*-acetylindole (18) (40 mg) and Claisen's alkali (5 ml) was refluxed for 30 min and then worked up as above. The resulting residue was chromatographed on silica gel. Evaporation of benzene eluate gave a powder, which was recrystallised from benzene–n-hexane to give the 5-methoxyindole (21) (20 mg, 64.5%) as needles, m.p. 52.5—53.5 °C (lit.,[15] m.p. 52—53 °C), $\nu_{max.}$ ($CHCl_3$) 3 490 (NH) cm^{-1}; δ ($CDCl_3$) 3.83 (3 H, s, OMe), 6.50 (1 H, dd, *J* 3, 3 Hz, 2-H), 6.87 (1 H, dd, *J* 2.5, 10 Hz, 5-H), 7.07—7.40 (3 H, m, 3, 4 and 7-H), and 8.03br (1 H, s, NH); *m/e* 147 (M^+).

N-*Methyl*-4-*benzyloxy*-2-*bromo*-5-*methoxyphenylacetamide* (24).—To a solution of the bromocarboxylic acid (22) (3 g) in benzene (50 ml) was added thionyl chloride (1.5 g) and the mixture was refluxed for 3 h. After evaporation of the excess of reagent and solvent, the residue was dissolved in benzene (60 ml). To this solution was added crystalline methylamine hydrochloride (2.4 g) and then a solution of sodium carbonate (3.8 g) in water (40 ml) whilst the whole was cooled with ice–water. The mixture was stirred at room temperature for 15 min and then extracted with benzene. The extract was washed successively with saturated aqueous sodium hydrogen carbonate, brine, 10% aqueous hydrochloric acid, and brine; it was then dried (Na_2SO_4) and evaporated to afford the crystalline solid, which was recrystallised from benzene–n-hexane to give the *bromophenylacetamide* (24) (2.8 g, 90.3%) as needles, m.p. 186—187 °C (Found: C, 56.25; H, 5.05; N, 3.65. $C_{17}H_{18}BrNO_3$ requires C, 56.05; H, 5.0; N, 3.85%), $\nu_{max.}$ ($CHCl_3$) 3 480 (NH), 1 665 (CO) cm^{-1}; δ($CDCl_3$) 2.83 (3 H, d, *J* 5 Hz, NMe), 3.68 (2 H, s, CH_2CO), 3.90 (3 H, s, OMe), 5.18 (2 H, s, OCH_2Ph), 5.55br (1 H, s, NH), 6.97 and 7.20 (each 1 H, each s, 2 × Ar*H*), and 7.50br (5 H, s, OCH_2Ph).

N-*Methyl*-2-*bromo*-4,5-*dimethoxyphenylacetamide* (25).—To a solution of the acid chloride [prepared from the bromophenylacetic acid (23) (5 g) and thionyl chloride (4 g) in benzene (80 ml) under reflux for 3 h] in benzene (60 ml) was added crystalline methylamine hydrochloride (2.4 g) and then a solution of sodium carbonate (3.8 g) in water (40 ml) the whole being cooled with ice–water. The mixture was stirred at room temperature for 15 min and then worked up as above. The resulting crystalline mass was recrystallised from benzene–n-hexane to give the *bromophenylacetamide* (25) (4.6 g, 88.5%) as needles, m.p. 150—151 °C (Found: C, 45.8; H, 4.8; N, 4.65. $C_{11}H_{14}BrNO_3$ requires C, 45.85; H, 4.9; N, 4.85%), $\nu_{max.}$ ($CHCl_3$) 3 480 (NH) and 1 665 (CO) cm^{-1}; δ ($CDCl_3$) 2.87 (3 H, d, *J* 5 Hz, NMe), 3.72 (2 H, s, CH_2CO), 3.93 (6 H, s, 2 × OMe), 5.58br (1 H, s, NH), and 6.97 and 7.17 (each 1 H, each s, 2 × Ar*H*).

6-*Benzyloxy*-2,3-*dihydro*-5-*methoxy*-1-*methyl*-2-*oxo*-1H-*indole* (26).—To a solution of the bromophenylacetamide (24) (1 g) in dimethylformamide (20 ml) was added 50% sodium hydride (238 mg). After the mixture had been stirred at room temperature for 30 min, cuprous bromide (200 mg) was added to the mixture, which was further stirred for 3 h at room temperature and heated at 80—85 °C for 30 min. After addition of crystalline ammonium chloride, evaporation of the solvent afforded a residue, which was extracted with methylene chloride. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a residue, which was chromatographed on silica gel. Evaporation of benzene–acetone [96 : 4 (v/v)] eluate afforded a powder, which was recrystallised from benzene–n-hexane to give the *oxindole* (26) (566 mg, 72.5%) as needles, m.p. 129—130 °C (Found: C, 72.0; H, 6.0; N, 4.8. $C_{17}H_{17}NO_3$ requires C, 72.05; H, 6.05; N, 4.95%), $\nu_{max.}$ ($CHCl_3$) 1 695 (CO) cm^{-1}; δ ($CDCl_3$) 3.17 (3 H, s, NMe), 3.47 (2 H, s, CH_2CO), 3.90 (3 H, s, OMe), 5.23 (2 H, s, OCH_2Ph), 6.55 and 7.00 (each 1 H, each s, 2 × Ar*H*), and 7.23—7.70 (5 H, m, OCH_2Ph); *m/e* 283 (M^+).

2,3-*Dihydro*-5,6-*dimethoxy*-1-*methyl*-2-*oxo*-1H-*indole* (27).—After a mixture of the bromophenylacetamide (25) (1 g) and 50% sodium hydride (320 mg) had been stirred for 30 min at room temperature, cuprous bromide (240 mg) was added to the above mixture. The resulting mixture was stirred at room temperature for 10 h and worked up as above. The residue obtained was chromatographed on silica gel. Evaporation of benzene–acetone [96 : 4 (v/v)] eluate gave a powder, which was recrystallised from benzene–n-hexane to afford the oxindole (27) (456 mg, 63.4%) as needles, m.p. 111—112 °C (Found: M^+ 207.085 2. $C_{11}H_{13}NO_3$ requires M^+ 207.089 4), $\nu_{max.}$ ($CHCl_3$) 1 695 (CO) cm^{-1};

δ ($CDCl_3$) 3.25 (3 H, s, NMe), 3.50 (2 H, s, CH_2CO), 3.93 and 3.98 (each 3 H, each s, 2 × OMe), 6.53 and 6.93 (each 1 H, each s, 2 × Ar*H*); *m/e* 207 (M^+).

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