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Cyclopropamitosenes, Novel Bioreductive Anticancer Agents. Synthesis of 7-Methoxycyclopropamitosene and Related Indolequinones

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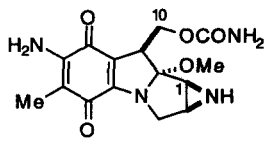
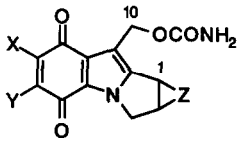
Abstract: *The synthesis of the 7-methoxy-1,2-cyclopropapyrrolo[1,2-a]indoles (cyclopropamitosenes)* **5** *and the related indolequinone* **6** *is described.*

INTRODUCTION

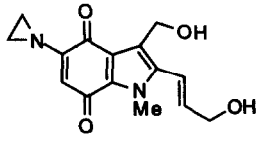
Mitomycin C (MMC) **1**, a clinically useful antitumour antibiotic, is the archetypical quinone bioreductive alkylating agent.[1-4] The understanding of the reductive activation mechanism of MMC and related mitosenes, such as aziridinomitosenes **2** and the indolequinone EO9 **3**,[5] in which quinone reduction sequentially activates electrophilic sites in the drug molecules (C-1 and C-10 for MMC), has increased markedly in recent years due to the efforts of several research groups.[6-25] Our own work in the area was designed to investigate the role of C-10 in alkylation processes by preparing compounds in which electrophilicity at C-1 is much reduced by substituting a cyclopropane for the aziridine ring.[26] The resulting ring system which we term cyclopropamitosene **4**, could on reductive activation, by either 1- or 2-electron processes, followed by elimination of the carbamate, generate a powerful electrophile capable of alkylating DNA (or other nucleophiles) at C-10 (Scheme 1). However, ionic ring opening of the cyclopropane, analogous to that proposed for the corresponding 'natural' aziridine, is very unlikely, although radical induced ring opening of the cyclopropane[27,28] to give a highly reactive radical capable of abstracting the 4'-hydrogen from the deoxyribose ring of DNA (and hence causing strand cleavage),[29,30] is an alternative possibility (Scheme 1).



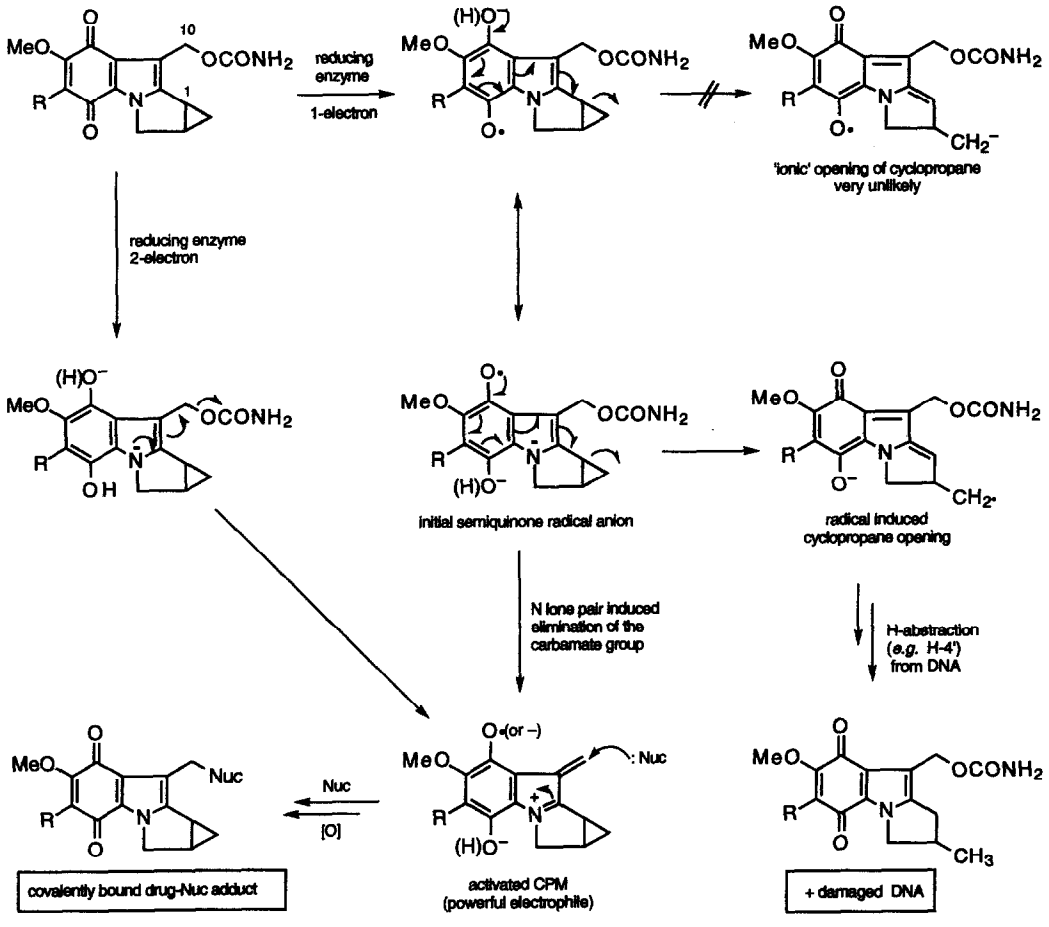
1 mitomycin C (MMC)



2 Z = NR aziridinomitosene
4 Z = CR_2 cyclopropamitosene

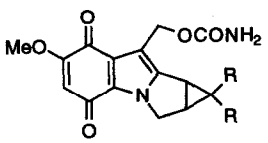


3 EO9



Scheme 1

In order to investigate these mechanistic possibilities, and to evaluate the biological activity of cyclopropamitosenes, a range of compounds was required. In this paper we report the details of the synthesis of the 7-methoxycyclopropamitosenes **5**, and the related indolequinone **6**. The synthesis of the simpler indolequinone **7**, and the conversion of **5**-**7** into other mitosenes, together with their electrochemical and biological properties will be described separately.



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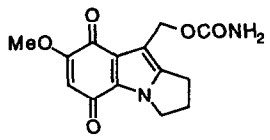

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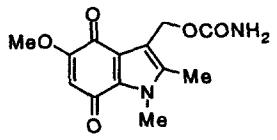

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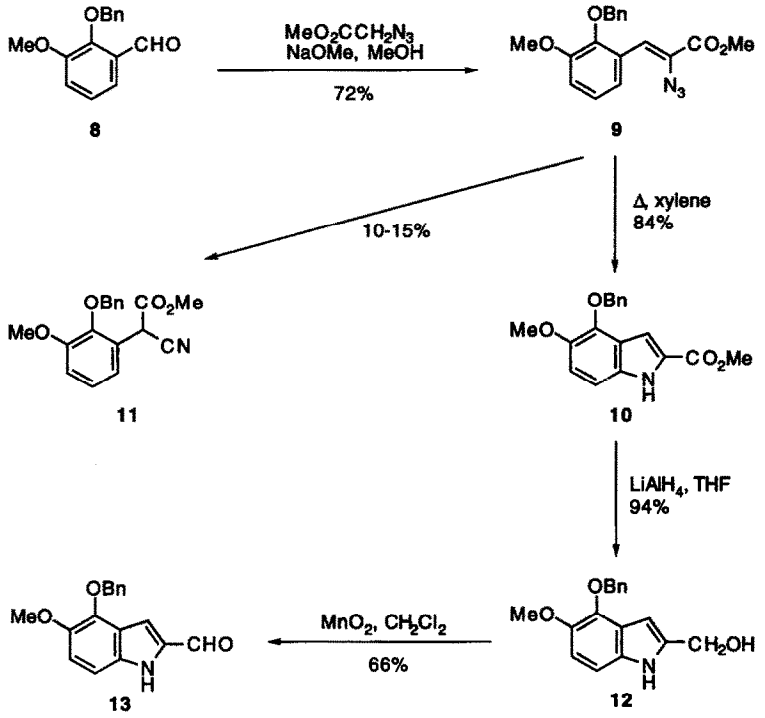
RESULTS AND DISCUSSION

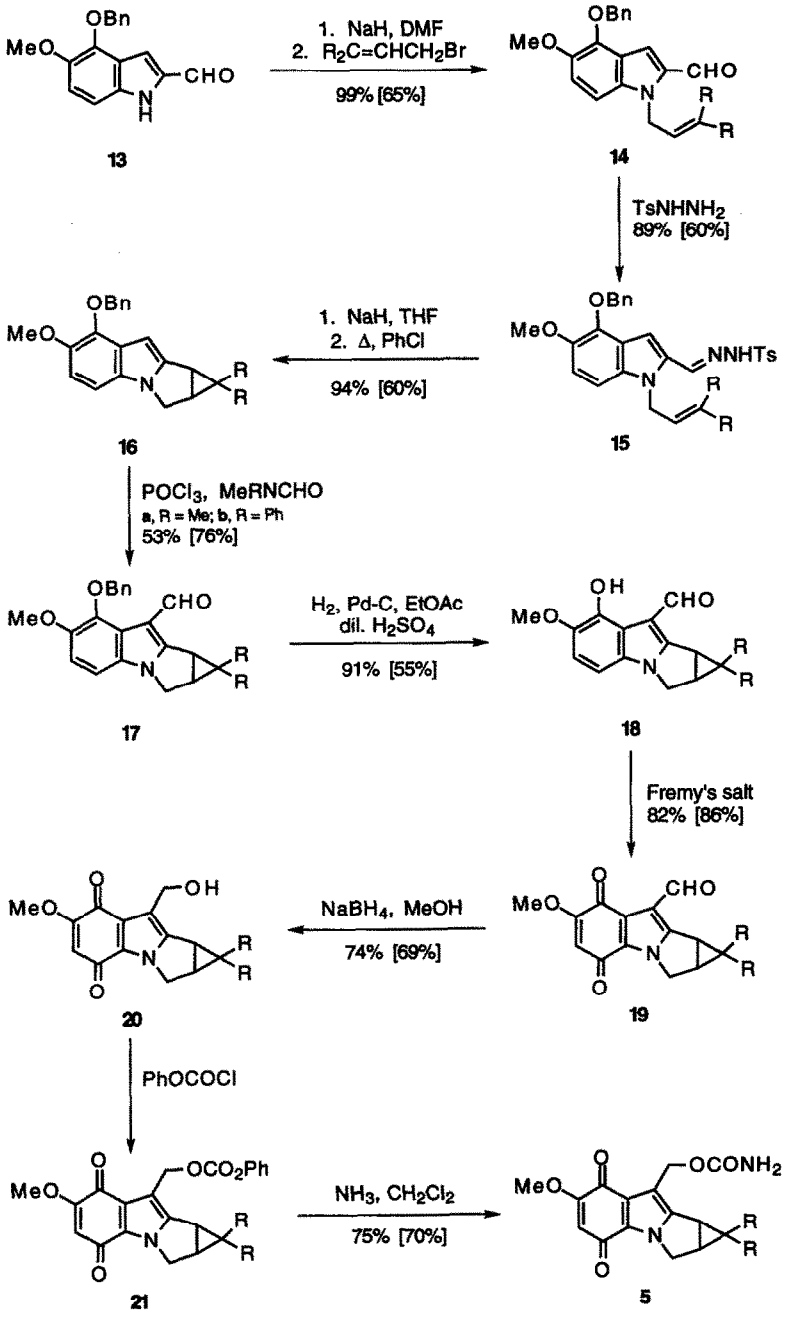
The synthesis of the cyclopropamitosene **5** was based on our previously described route.[26,31] The key intermediate is 4-benzyloxy-5-methoxyindole-2-carboxaldehyde **13**, prepared from 2-benzyloxy-3-methoxybenzaldehyde **8** as shown in Scheme 2. Thus, condensation of the aldehyde with methyl azidoacetate gave the azidocinnamate **9** as a pale yellow solid (72%), thermolysis of which in boiling xylene gave the indole-2-ester **10** (84%). It was important that this thermolysis reaction was carried out in dilute solution; the reaction was considerably less clean when carried out in more concentrated solution. On one occasion a small amount of the nitrile **11** (10-15%) was isolated; the formation of phenylacetonitriles from azidostyrenes is a known process and proceeds by way of the corresponding 2*H*-azirine.[32] Finally the ester **10** was converted into the desired aldehyde **13** by reduction (94%) and re-oxidation (66%) (Scheme 2). The indole-2-aldehyde **13** is not only the key building block for the cyclopropamitosenes **5**, but also for the related indolequinone **6**, and in our recently described synthesis of the naturally occurring thiazoloindolequinone BE 10988, a powerful inhibitor of topoisomerase II.[33]



Scheme 2

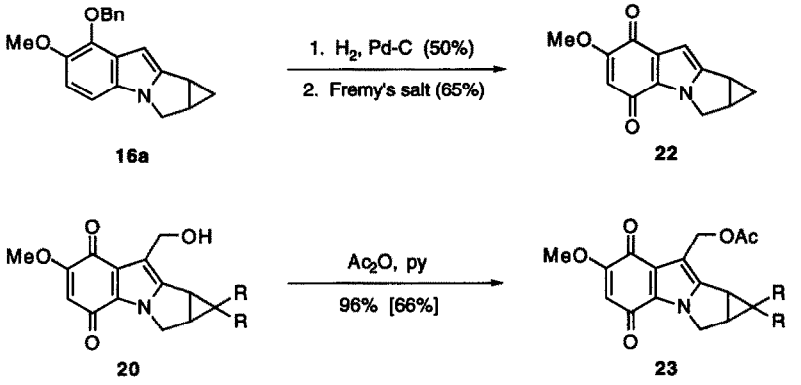
The construction of the tetracyclic cyclopropapyrrolo[1,2-*a*]indole ring system relies on our previously developed intramolecular cycloaddition reaction.[31] Alkylation of the indole nitrogen (99%), followed by reaction of the aldehyde with tosyl hydrazide gave the tosylhydrazone **15a** (89%), decomposition of which gave the desired tetracycle **16a** in 94% yield. In a similar manner the dimethylcyclopropane derivative **16b** was prepared from **13** in 24% overall yield. The C-10 carbon was introduced by Vilsmeier-Haack formylation and the *O*-benzyl group was hydrogenolysed over Pd/C in ethyl acetate in the presence of a small amount of dilute sulfuric acid. In the absence of acid, the hydrogenolysis was considerably slower, and a certain amount of reductive cleavage of the cyclopropane was observed. Oxidation of the phenol with Fremy's salt gave the corresponding indolequinone **19**, the side chain of which was elaborated in the usual way to give the desired

cyclopropapyrroloindoles **5a** and **5b** in overall yields of 18.2 and 4.1% from **13**, respectively (Scheme 3). The reason for the discrepancy in overall yield is that the sequence to give **5a** has been carried out several times on a larger scale with optimisation of as many steps as possible.



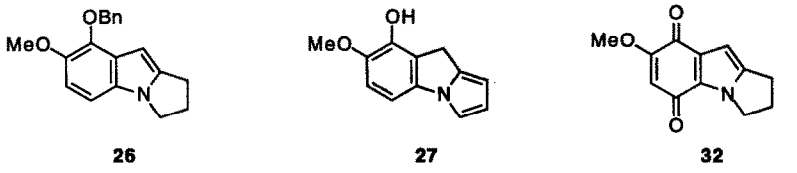
Scheme 3 [**a**, R = H; **b**, R = Me] Yields in [ ] refer to the **b**-series of compounds.

Finally, in the cyclopropamitosene series, the indole **16a** was elaborated into the corresponding quinone **22** lacking the C-10 side chain, and the alcohols **20** were converted into the corresponding acetates **23a** and **23b** by simple acetylation (Scheme 4).

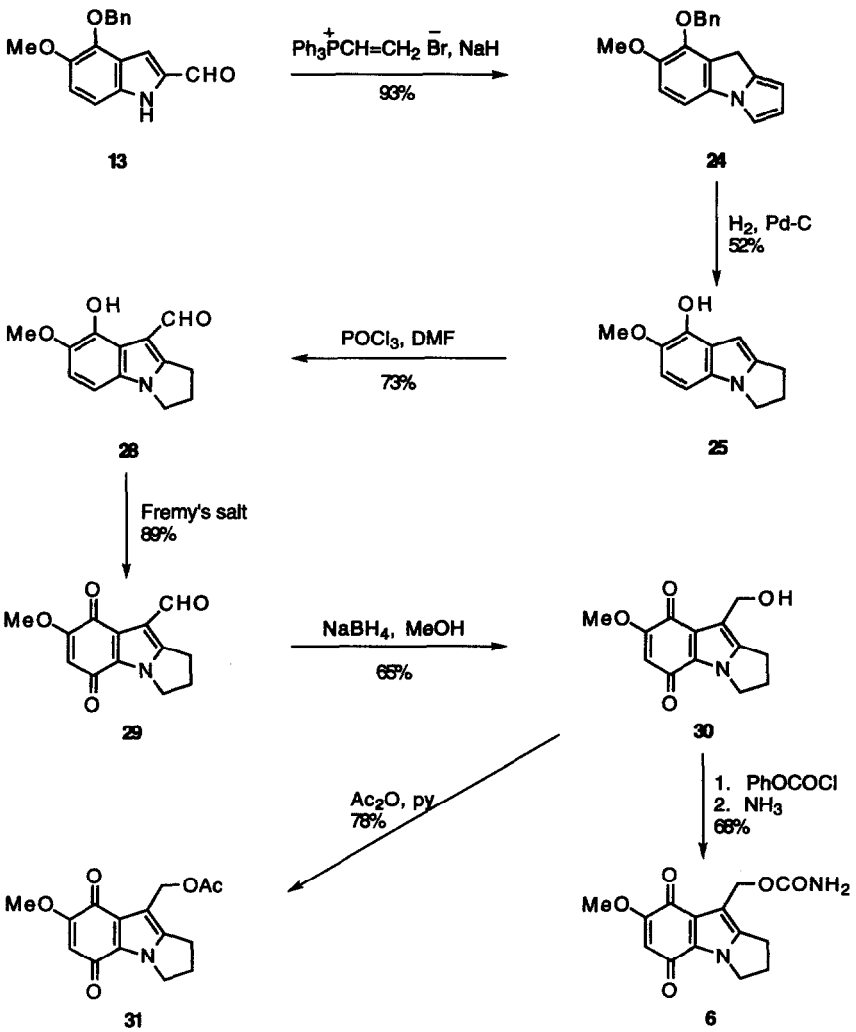


Scheme 4 [for **20** and **23**: **a**, R = H; **b**, R = Me]

In order to compare the properties of cyclopropane containing indolequinones with simpler derivatives, the indolequinone **6** was also prepared. The pyrrolo[1,2-*a*]indoles were prepared from the key indole-2-carboxaldehyde **13** by reaction with vinyltriphenylphosphonium bromide in the presence of sodium hydride. This reagent is known to be useful for the annelation of both pyrrole- and indole-2-carbaldehydes to give pyrrolo-pyrroles and -indoles respectively.[34,35] Reaction of the sodium salt of the indole-2-carbaldehyde **13** with the phosphonium salt gave the 9*H*-pyrrolo[1,2-*a*]indole **24** in excellent yield (93%) (Scheme 5). As expected, the initially formed 3*H*-isomer isomerises to the more stable 9*H*-isomer.[35] Prolonged hydrogenation of **24** over Pd-C at 3 atmospheres pressure resulted in *O*-debenzylation and reduction of one double bond (followed by isomerisation) to give the pyrroloindole **25** in 52% yield together with a small amount of the corresponding *O*-benzyl compound **26** (6%) and the debenzylated starting material **27** (3%). Formylation of **25** proceeded without incident to give the aldehyde **28**, which was oxidised to the corresponding quinone **29**[36] in good yield. Finally, elaboration of the side chain using the usual conditions gave the desired mitosene derivative **6** (Scheme 5). As in the cyclopropane series, the corresponding acetate **31** was also prepared, as was the indolequinone **32** lacking the C-10 side chain.



The further elaboration of the indolequinones into a range of amine substituted derivatives, together with their electrochemical and biological properties will be described elsewhere.



Scheme 5

EXPERIMENTAL

For general experimental details, see ref. 33. Compounds characterised by high resolution mass spectrometry were chromatographically homogeneous. NMR coupling constants are given in Hz.

***2-Benzyloxy-3-methoxybenzaldehyde* 8**

Potassium hydroxide pellets (16.0 g, 286 mmol) were added to a stirred solution of *o*-vanillin (40.0 g, 264 mmol) in ethanol (98%, 240 ml), followed by benzyl chloride (32.8 ml, 286 mmol). The stirred mixture was refluxed for 12 h, then water (200 ml) was added and the mixture extracted with ether (3 x 300 ml). The ethereal extracts were washed with water (2 x 100 ml), potassium hydroxide solution (2M, 5 x 200 ml), water (2 x 200 ml) and brine (200 ml). The organic layer was dried ($MgSO_4$), then condensed *in vacuo*, to give the title compound (60.7 g, 95%) as a colourless solid on trituration with hexane, m.p. 45-47°C (lit.,[37] 45-46°C) (Found: C, 74.6; H, 5.8. Calc. for $C_{15}H_{14}O_3$: C, 74.4; H, 5.8%); υ_{max} (Nujol) 1695, 1584, 1367, 1266,

1247 and 1222 cm^{-1}; δ_H (250 Mz; $CDCl_3$) 10.23 (1 H, s, CHO), 7.40-7.09 (8 H, m, Ar-H), 5.17 (2 H, s, OCH_2Ph) and 3.94 (3 H, s, OMe); δ_C (62.9 MHz; $CDCl_3$) 190.00 (CHO), 153.04, 136.38, 130.28, 128.65, 128.57, 128.50, 124.25, 118.97, 118.00, 76.29 (OCH_2Ph) and 56.05 (OMe); *m/z* 242 (M^+, 33%), 213 (19), 150 (12), 91 (100) and 28 (40).

***Methyl 2-azido-3-(2-benzyloxy-3-methoxyphenyl)propenoate* 9**

Sodium (7.60 g, 330 mmol) was added to dry methanol (150 ml). The solution was cooled to -15°C and a solution of methyl azidoacetate (38.02 g, 330 mmol) and 2-benzyloxy-3-methoxybenzaldehyde **8** (20.00 g, 82.0 mmol) in dry methanol (15 ml) was added dropwise. The mixture was stirred at -10°C for 3 h then at 4°C for 12 h. Water (50 ml) was cautiously added to the mixture, which was then extracted with ethyl acetate (2 x 250 ml). The combined extracts were washed with water (500 ml), brine (250 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave a pale yellow residue, which was triturated with a small quantity of ether and the resulting precipitate filtered off. The remaining oily residue was purified by column chromatography (50% light petroleum/50% ether) to give the *title compound* (20.35 g, 72%) as pale yellow rhomboids, m.p. 66-67°C (Found: C, 63.7; H, 5.0; N, 12.1. $C_{18}H_{17}N_3O_4$ requires C, 63.7; H, 5.05; N, 12.4%); υ_{max} (film) 2120, 1712, 1457, 1260 and 1218 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.79 (1 H, d, *J* 8, 6'-H), 7.44-7.27 (5 H, m, Ar-H), 7.13 (1 H, s, 3-H), 6.96 (1 H, t, *J* 8, 5'-H), 6.93 (1 H, d, *J* 8, 4'-H), 4.99 (2 H, s, OCH_2Ph), 3.89 (3 H, s, CO_2CH_3) and 3.85 (3 H, s, OMe); δ_C (62.9 MHz; $CDCl_3$) 164.04 (CO_2CH_3), 152.66, 146.77, 137.08, 128.76, 128.68, 128.33, 128.14, 127.85, 125.59, 123.93, 122.05, 120.05, 119.65, 113.52 , 75.86 (OCH_2Ph), 55.88 (OMe) and 52.77 (CO_2CH_3); *m/z* 339 (M^+, 1%), 311 (27), 220 (49), 188 (32), 91 (88) and 28 (100).

***Methyl 4-benzyloxy-5-methoxyindole-2-carboxylate* 10**

A solution of methyl 2-azido-3-(2-benzyloxy-3-methoxyphenyl)propenoate **9** (5.00 g, 14.8 mmol) in dry xylene (200 ml) was introduced, dropwise, by means of a pressure equalising dropping funnel, to refluxing dry xylene (800 ml). After the addition was complete (*ca.* 1 h), the solution was refluxed for a further 45 min. Removal of solvent *in vacuo* gave a yellow solid residue. The residue was triturated with a small quantity of ether and the resulting precipitate was filtered off. The remaining oily residue was purified by column chromatography (dichloromethane) to give the *title compound* (3.14 g, 84%) as pale yellow needles, m.p. 97-100°C, together with the more polar cyano by-product **11** described below (Found: C, 69.5; H, 5.5; N, 4.5. $C_{18}H_{17}NO_4$ requires C, 69.4; H, 5.5; N, 4.5%); υ_{max} (Nujol) 3342, 3031, 1697, 1528, 1453 and 1257 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.82 (1 H, s, NH), 7.53 (2 H, m, Ar-H), 7.52-7.34 (3 H, m, Ar-H), 7.33 (1 H, s, 3-H), 7.08 (2 H, s, 6,7-H), 5.26 (2 H, s, CH_2), 3.92 (3 H, s, CO_2Me) and 3.91 (3 H, s, OMe); δ_C (62.9 MHz; $CDCl_3$) 162.55 (CO_2CH_3), 145.12, 141.78, 137.89, 134.20, 128.35, 128.0, 127.88, 127.31, 123.13, 116.26, 107.21, 106.15, 75.04 (OCH_2Ph), 58.45 (OMe) and 52.03 (CO_2CH_3); *m/z* 311 (M^+, 33%), 220 (100), 188 (86) and 91 (94).

***Methyl 2-(2-benzyloxy-3-methoxyphenyl)-2-cyanoacetate* 11**

The *title compound* was isolated in 10-15% yield as colourless rhomboids, m.p. 88-89°C (ether) (Found: C, 69.5; H, 5.4; N, 4.4. $C_{18}H_{17}NO_4$ requires C, 69.4; H, 5.5; N, 4.5%); υ_{max} (KBr) 3469, 2898, 2234 and 1734 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.36-7.50 (5 H, m, Ar-H), 6.99-7.17 (3 H, m, Ar-H), 5.26 (1 H, d, *J* 12.3, OCH_2Ph), 5.17 (1 H, d, *J* 12.3, OCH_2Ph), 5.04 (1 H, s, 2-H), 3.92 (3 H, s, OMe) and 3.68 (3 H, s, OMe); δ_C (62.9 MHz; $CDCl_3$) 165.53 (CO_2Me), 152.70, 146.00, 137.02, 128.53, 128.25, 113.66, 74.73 (OCH_2Ph), 55.88 (OMe), 53.61 (OMe) and 37.80 (C-2); *m/z* 311 (M^+, 9%) and 91 (100).

***4-Benzyloxy-5-methoxyindole-2-methanol* 12**

A solution of methyl 4-benzyloxy-5-methoxyindole-2-carboxylate **10** (10.0 g, 32.15 mmol) in dry THF (200 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (1.22 g, 32.15 mmol) in dry

THF (100 ml), such that the mixture achieved gentle reflux. After 30 min, water (1.2 ml), sodium hydroxide (15%, 1.2 ml) and water (3.6 ml), were added to the mixture and the resultant precipitate removed by filtration (through a bed of Celite). The filtrate was dried ($MgSO_4$), then condensed *in vacuo* to give the *title compound* (8.55 g, 94%) as a colourless crystalline solid; m.p. 91°C (Found: C, 72.1; H, 6.1; N, 4.8. $C_{17}H_{17}NO_3$ requires C, 72.1; H, 6.1; N, 4.9%); υ_{max} (Nujol) 3479, 3282, 1506, 1324, 1283, 1244, 1091 and 701 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.24 (1 H, s, NH), 7.49 (2 H, m, Ar-H), 7.33-7.29 (3 H, m, Ar-H), 6.97 (2 H, AB, *J* 9, 6,7-H), 6.39 (1 H, s, 3-H), 5.21 (2 H, s, OCH_2Ph), 4.74 (2 H, s, CH_2OH), 3.88 (3 H, s, OMe) and 1.67 (1 H, s, OH); δ_C (62.9 MHz; $CDCl_3$) 144.94, 140.00, 138.36, 138.07, 133.57, 128.33, 128.10, 127.84, 123.10, 111.63, 106.45, 97.56, 75.05 (OCH_2Ph), 58.29 (OMe) and 58.22 (CH_2OH); *m/z* 283 (M^+, 27%), 192 (100), 174 (28) and 91 (38).

***4-Benzyloxy-5-methoxyindole-2-carboxaldehyde* 13**

Manganese dioxide (14.0 g, 160 mmol) was added to a stirred solution of 4-benzyloxy-5-methoxyindole-2-methanol **12** (9.0 g, 32.0 mmol) in dichloromethane (1000 ml). The suspension was refluxed for 12 h, then the mixture was filtered and the residue washed with dichloromethane (3 x 500 ml). The combined filtrate and washings were evaporated to an oil, which was chromatographed (ether) to give the *title compound* (5.96 g, 66%) as a yellow crystalline solid, m.p. 143-145°C (Found: C, 72.5; H, 5.3; N, 4.9. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.4; N, 5.0%); υ_{max} (Nujol) 3188, 1667, 1446, 1148 and 1094 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.75 (1 H, s, CHO), 9.05 (1 H, s, NH), 7.52-7.21 (5 H, m, Ar-H), 7.15 (1 H, d, *J* 8.8, 6/7-H), 7.12 (1 H, d, *J* 8.8, 7/6-H), 5.28 (2 H, s, CH_2) and 3.91 (3 H, s, OMe); δ_C (62.9 MHz; $CDCl_3$) 182.08 (CHO), 145.23, 142.20, 137.78, 136.20, 135.11, 128.42, 128.13, 128.02, 123.43, 118.33, 112.47, 107.61, 75.22 (OCH_2Ph) and 58.42 (OMe); *m/z* 281 (M^+, 15%), 253 (12), 220 (10), 190 (33) and 91 (100).

***1-Allyl-4-benzyloxy-5-methoxyindole-2-carboxaldehyde* 14a**

To a flask charged with sodium hydride (80%; 0.475 g, 15.8 mmol) was added dry light petroleum (10 ml). The mixture was stirred for 10 min, the petroleum removed by syringe and the flask contents dried under reduced pressure. 4-Benzyloxy-5-methoxyindole-2-carboxaldehyde **13** (3.56 g, 12.7 mmol) in DMF (51 ml) was added dropwise and the mixture was stirred at room temperature for 30 min. Allyl bromide (1.36 ml, 15.8 mmol) was added and the mixture was stirred at room temperature. After 1 h, water (150 ml) was cautiously added and the mixture was extracted with ether (4 x 250 ml). The combined ethereal extracts were washed with water (8 x 200 ml), brine (200 ml), dried ($MgSO_4$) and evaporated to give the *title compound* (4.03 g, 99%) as a yellow solid, m.p. 69-70°C (Found: C, 74.8; H, 6.05; N, 4.2. $C_{20}H_{19}NO_3$ requires C, 74.75; H, 6.0; N, 4.4%); υ_{max} (Nujol) 1670, 1490, 1407, 1248 and 1141 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.77 (1 H, s, CHO), 7.51 (2 H, m, Ar-H), 7.25 (3 H, m, Ar-H), 7.20 (1 H, s, 3-H), 7.17 (1 H, d, *J* 9.0, 6/7-H), 7.14 (1 H, d, *J* 9.0, 7/6-H), 5.97 (1 H, m, $CH_2CH{=}CH_2$), 5.28 (2 H, s, OCH_2Ph), 5.16 (3 H, m, $CH_2CH{=}CHH$ and $CH_2CH{=}CHH$), 4.94 (1 H, d, *J* 18.0, $CH_2CH{=}CHH$) and 3.91 (3 H, s, OMe); δ_C (62.9 MHz; $CDCl_3$) 182.00 (CHO), 145.17, 137.83, 137.44, 135.33, 133.45, 128.43, 128.11, 122.00, 118.15, 116.33, 115.23, 105.90, 75.23 (OCH_2Ph), 58.49 (OMe) and 46.98 (NCH_2); *m/z* 321 (M^+, 37%), 293 (14), 230 (100) and 91 (48).

***1-Allyl-4-benzyloxy-5-methoxyindole-2-carboxaldehyde tosylhydrazone* 15a**

1-Allyl-4-benzyloxy-5-methoxyindole-2-carboxaldehyde **14a** (2.43 g, 7.57 mmol) was added to a stirred solution of 4-toluenesulfonyl hydrazide (1.69 g, 9.08 mmol) in methanol (20 ml). The mixture was stirred at 40°C for 45 min. Removal of the solvent *in vacuo*, gave a dark green residue which was recrystallised from ether and the resulting precipitate filtered off. The remaining mother liquors were purified by column chromatography (50% light petroleum/50% ether) to give the *title compound* (3.29 g, 89%) as a colourless solid, m.p. 49-50°C (dec.) (Found: C, 66.2; H, 5.6; N, 8.6. $C_{27}H_{27}N_3O_4S$ requires C, 66.3; H, 5.5; N, 8.3%); υ_{max} (Nujol) 2956, 1718, 1492, 1456, 1358 and 1166 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.83 (2 H, m, Ar-H), 7.81 (2 H, m, NH and $CH{=}N$), 7.47 (2 H, m, Ar-H), 7.38-7.30 (5 H, m, Ar-H), 7.04 (1 H, d, *J* 7.5,

6/7-H), 6.95 (1 H, d, *J* 7.5, 7/6-H), 6.67 (1 H, s, 3-H), 5.85 (1 H, m, C*H*=CH_2), 5.20 (2 H, s, OCH_2Ph), 5.04 (3 H, m, CH_2CH=CH_2 and CH_2CH=C*H*H), 4.85 (1 H, d, *J* 17.5, CH_2CH=CH*H*), 3.87 (3 H, s, OMe) and 2.42 (3 H, s, Ts-Me); δ_C (62.9 MHz; $CDCl_3$) 144.33, 141.15, 138.08, 136.78, 135.25, 133.68, 131.74, 129.86, 129.68, 128.36, 128.09, 128.05, 127.89, 116.14, 114.79, 107.34, 105.23, 75.10 (OCH_2Ph), 58.38 (OMe), 47.41 (NCH_2) and 21.58 (Ts-CH_3); *m/z* (FAB, 3-NBA Matrix) 490 (*M*+H^+, 19%), 489 (*M*$^+$, 13), 398 (52) and 91 (100).

***8-Benzyloxy-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-a]indole* 16a**

Sodium hydride (50%, 0.291 g, 6.07 mmol) was added to a stirred solution of the tosylhydrazone **15a** (1.98 g, 4.05 mmol) in dry THF (60 ml). After 10 min the solution was filtered and the filtrate evaporated. The residue was dissolved in dry chlorobenzene (600 ml) and the solution refluxed for 3 h. The solvent was evaporated and the residue purified by column chromatography (50% light petroleum/50% ether) to give the *title compound* (1.16 g, 94%) as a pale yellow oil (Found: *M*$^+$, 305.1420. $C_{20}H_{19}NO_2$ requires *M* 305.1415); υ_{max} (film) 1500, 1495, 1288, 1234 and 750 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.53 (2 H, m, Ar-H), 7.41-7.23 (3 H, m, Ar-H), 6.82 (1 H, d, *J* 7.5, 5/6-H) 6.78 (1 H, d, *J* 7.5, 6/5-H), 5.27 (2 H, s, OCH_2Ph), 4.06 (2 H, m, 3-H), 3.86 (3 H, s, OMe), 2.37 (2 H, m, 1,2-H), 1.25 and 0.65 (each 1 H, m, 1a-H); *m/z* 305 (*M*$^+$, 20%), 215 (25), 214 (100) and 91 (36).

***8-Benzyloxy-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-a]indole-9-carboxaldehyde* 17a**

DMF (10 ml) and phosphorus oxychloride (0.15 ml, 1.61 mmol) were stirred under nitrogen for 30 min. The resulting yellow solution was cooled to 0°C and 8-benzyloxy-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole **16a** (0.250 g, 0.819 mmol) in DMF (2 ml) was added and the mixture stirred for 45 min. Sodium acetate (1M, 6 ml) was added and the mixture was extracted with ether (6 x 20 ml). The combined ethereal extracts were washed with brine (6 x 50 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave a green oily residue which was recrystallised with a small quantity of ether and the resulting precipitate filtered off. The mother liquors were purified by column chromatography (ether) to give the *title compound* as a colourless solid (0.145 g, 53%), m.p. 128-130°C (Found: C, 75.6; H, 5.8; N, 4.1. $C_{21}H_{19}NO_3$ requires C, 75.65; H, 5.7; N, 4.2%); υ_{max} (Nujol) 1648, 1536, 757 and 702 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.32 (1 H, s, CHO), 7.49 (2 H, m, Ar-H), 7.40-7.26 (3 H, m, Ar-H), 6.90 and 6.85 (each 1 H, d, *J* 8.7, 5,6-H), 5.18 (2 H, s, OCH_2Ph), 4.10 (2 H, m, 3-H), 4.03 (3 H, s, OMe), 2.99 (1 H, m, 1-H), 2.46 (1 H, m, 2-H), 1.48 and 0.72 (each 1 H, m, 1a-H); δ_C (62.9 MHz; $CDCl_3$) 186.57 (CHO), 154.56, 147.97 (4a-C), 141.49, 137.50 (8-C), 129.49 (8a/9a-C), 125.28 (9a/8a-C), 110 49 (5/6-C), 110.06 (9-C), 105.31 (6/5-C), 74.86 (OCH_2Ph), 57.72 (OMe), 47.57 (3-C), 21.59 (1-C), 18.06 (2-C) and 17.50 (1a-C); *m/z* 333 (*M*$^+$, 26%), 305 (8), 242 (100), 277 (24) and 91 (15).

***8-Hydroxy-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-a]indole-9-carboxaldehyde* 18a**

To a solution of 8-benzyloxy-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole-9-carboxaldehyde **17a** (0.200 g, 0.601 mmol) in ethyl acetate (100 ml) was added 10% palladium on carbon (0.04 g) and dilute sulfuric acid (4 drops). The mixture was stirred under an atmosphere of hydrogen for 12 h. After this time, the suspension was filtered and washed with dichloromethane. The combined filtrate and washings were washed with water (3 x 50 ml), brine (40 ml) and dried ($MgSO_4$). The organic layer was evaporated to dryness to give a brown solid. Purification of the residue by column chromatography (ethyl acetate) gave the *title compound* (0.133 g, 91%) as a colourless solid, m.p. 146-147°C (ethyl acetate-hexane) (Found: *M*$^+$, 243.0901. $C_{14}H_{13}NO_3$ requires *M*, 243.0895); υ_{max} (Nujol) 1606, 1304, 1252 and 825 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.87 (1 H, s, OH), 9.58 (1 H, s, CHO), 6.82 (1 H, d, *J* 8.5, 6/5-H), 6.46 (1 H, d, *J* 8.5, 5/6-H), 4.04 (2 H, m, 3-H), 3.88 (3 H, s, OMe), 2.56 (2 H, m, 1,2-H), 1.45 and 0.72 (each 1 H, m, 1a-H); δ_C (62.9 MHz; $CDCl_3$) 183.20 (CHO), 159.64, 142.62, 141.15 129.70, 118.84, 111.95 (5/6-C), 110.69,

99.94 (6/5-C), 57.55 (OMe), 47.91 (3-C), 21.88 (1-C), 17.28 (1a-C) and 15.93 (2-C); *m/z* 243 (M^+, 100%), 230 (41), 228 (87) and 135 (25).

***9-Formyl-7-methoxy-1,2-dihydro-3H-1,2-cyclopropapyrrolo[1,2-a]indole-5,8-dione* 19a**

Potassium nitrosodisulfonate (0.607 g, 2.26 mmol) was added to a solution of the phenol **18a** (0.250g, 1.03 mmol) in acetone (100 ml), sodium dihydrogen phosphate solution (0.167M, 30 ml) and water (30 ml) and the resulting suspension stirred at room temperature for 12 h. The mixture was extracted with dichloromethane (3 x 50 ml) and the combined organic extracts were dried (Na_2SO_4) and evaporated. Purification of the residue by column chromatography (ethyl acetate) gave the *title compound* (0.232 g, 82%) as orange needles, m.p. 217-218°C (Found: C, 61.3; H, 4.1; N, 4.9. $C_{14}H_{11}NO_4.H_2O$ requires C, 61.1; H, 4.0; N, 5.1%); λ_{max} (MeOH) 447 (log ε 3.75), 329 (4.42), 280 (4.99) and 219 nm (5.03); υ_{max} (Nujol) 1684, 1666, 1637, 1588, 1502, 1242 and 1212 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.37 (1 H, s, CHO), 5.68 (1 H, s, 6-H), 4.32 (2 H, m, 3-H), 3.85 (3 H, s, OMe), 2.86 (1 H, m, 1-H), 2.47 (1 H, m, 2-H), 1.47 and 0.65 (each 1 H, m, 1a-H); δ_C (62.9 MHz; $CDCl_3$) 187.84, 186.58 (CHO), 177.98, 160.64, 150.77, 115.78, 106.47, 105.29 (6-C), 56.65 (OMe), 50.46 (3-C), 22.07 (1-C), 16.74 (2-C) and 16.53 (1a-C); *m/z* 259 (M^++H_2, 54%), 258 (M^++H, 21), 257 (M^+, 100), 256 (68) and 228 (12).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-3H-1,2-cyclopropapyrrolo[1,2-a]indole-5,8-dione* 20a**

Sodium borohydride (0.200 g, 5.26 mmol) was added to a stirred solution of 9-formyl-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole-5,8-dione **19a** (0.200 g, 0.778 mmol) in methanol (150 ml). After stirring for 1 h at room temperature, air was blown rapidly through the solution and the mixture was extracted with dichloromethane (3 x 200 ml). The combined extracts were washed with water (2 x 200 ml), brine (2 x 200 ml) and dried (Na_2SO_4). The solvent was evaporated and the residue purified by column chromatography (ethyl acetate) to give the *title compound* (0.149 g, 74%) as an orange solid, m.p. 150-151°C (Found: C, 65.0; H, 5.3; N, 5.1. $C_{14}H_{13}NO_4$ requires C, 64.9; H, 5.1; N, 5.4%); λ_{max} (MeOH) 471 (log ε 3.95), 348 (4.30), 290 (4.96) and 238 nm (4.99); υ_{max} (Nujol) 3312, 1668, 1630, 1586 and 722 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 5.61 (1 H, s, 6-H), 4.68 (2 H, m, 10-H), 4.26 (2 H, m, 3-H), 3.89 (1 H, t, *J* 7.1, OH), 3.82 (3 H, s, OMe), 2.36 (2 H, m, 1,2-H), 1.30 and 0.60 (each 1 H, m, 1a-H); δ_C (62.9 MHz; $CDCl_3$) 177.65, 160.85 143.81, 121.08, 117.36 (6-C), 56.63 (OMe), 56.52 (10-C), 50.04 (3-C), 26.90 (1-C), 16.42 (1a-C) and 14.23 (2-C); *m/z* 261 (M^++H_2, 48%), 260 (M^++H, 15), 259 (M^+, 59), 258 (100), 246 (17), 245 (7), 244 (21), 243 (33), 242 (22) and 241 (6).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-3H-1,2-cyclopropapyrrolo[1,2-a]indole-5,8-dione phenyl carbonate* 21a**

Phenyl chloroformate (0.03 ml, 0.232 mmol) was added dropwise to a stirred, ice cold solution of the alcohol **20a** (0.040g, 0.153 mmol) in dry pyridine (10 ml). The mixture was stirred at room temperature for 2 h, then water (4 ml) was added. The mixture was extracted with ether (3 x 25 ml) and the combined organic extracts were washed with brine (6 x 25 ml), water (2 x 25 ml), saturated aqueous copper sulfate solution (2 x 25 ml), water (2 x 25 ml) and dried (Na_2SO_4). The solvent was evaporated and the residue purified by column chromatography (ethyl acetate) to give the *title compound* (0.054g, 92%) as an orange solid, m.p. 40-43°C (dec.) (Found: M^++H, 380.1134. $C_{21}H_{18}NO_6$ requires *M*, 380.1133); λ_{max} (MeOH) 475 (log ε 3.00), 348 (3.29), 271 (4.61) and 213 nm (4.68); υ_{max} (Nujol) 1785, 1758 and 1592 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.27 (5 H, m, Ar-H), 5.60 (1 H, s, 6-H), 5.28 (2 H, m, 10-H), 4.28 (2 H, m, 3-H), 3.80 (3 H, s, OMe), 2.35 (1 H, m, 1-H), 2.17 (1 H, m, 2-H), 1.26 and 0.57 (each 1 H, m, 1a-H); *m/z* (FAB, 3-NBA matrix) 380 (M^++H, 8%), 244 (61), 243 (32) and 242 (64).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-3H-1,2-cyclopropyrrolo[1,2-a]indole-5,8-dione carbamate* 5a**

A solution of phenyl carbonate **21a** (0.110 g, 0.290 mmol) in dry dichloromethane (80 ml) was cooled to -78°C. Ammonia gas was bubbled into the solution for approximately 45 min, after which time the contents were allowed to warm to room temperature and the solvent removed *in vacuo*. Trituration of the residue with hot dichloromethane gave the *title compound* (0.071 g, 81%) as red needles, m.p. 175-177°C (Found: M^+, 302.0909. $C_{15}H_{14}N_2O_5$ requires M, 302.0903); λ_{max} (MeOH, qualitative) 234, 293, 346 and 459 nm; υ_{max} (Nujol) 3408, 3212, 1764, 1668, 1620, 1584, 1350, 1306 and 1242 cm^{-1}; δ_H (250 MHz; $CDCl_3$/DMSO) 5.56 (1 H, s, 6-H), 4.92 (2 H, m, 10-H), 4.42 (2 H, br s, NH_2), 3.55 (2 H, m, 3-H), 3.06 (3 H, s, OMe), 1.83 (1 H, m, 1-H), 1.65 (1 H, m, 2-H), 0.58 and 0.03 (each 1 H, m, 1a-H); δ_C (62.9 MHz; $CDCl_3$) 177.68 (8-C), 177.20 (5-C), 160.44 (7-C/*C*ONH_2), 156.77 (*C*ONH_2/7-C), 146.31 (4a-C), 129.24 (8a/9a-C), 123.90 (9a/8a-C), 111.33 (9-C), 105.35 (6-C), 57.87 (10-H), 56.38 (OMe), 50.00 (3-C), 20.63 (1-C), 16.17 (1a-C) and 14.69 (2-C); *m/z* 302 (M^+, 13%), 264 (32), 260 (20), 259 (77), 258 (94), 244 (51), 243 (100), 242 (54), 241 (23), 240 (26) and 198 (14).

***9-Acetoxymethyl-7-methoxy-1,2-dihydro-3H-1,2-cyclopropapyrrolo[1,2-a]indole-5,8-dione* 23a**

To a solution of 9-hydroxymethyl-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole-5,8-dione **20a** (0.080 g, 0.309 mmol), in distilled pyridine (8.0 ml), was added acetic anhydride (1.5 ml) and the resulting solution was stirred at room temperature under nitrogen for 15 h. Water (2 ml) was added and the mixture extracted with dichloromethane (3 x 25 ml). The combined organic extracts were washed with water (3 x 20 ml), brine (30 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave an orange residue which was purified by column chromatography (ethyl acetate) to give an orange solid. Recrystallisation from dichloromethane-light petroleum gave the *title compound* (0.089 g, 96%) as an orange solid, m.p. 164-166°C (Found: M^+, 301.0954. $C_{16}H_{15}NO_5$ requires M, 301.0950); λ_{max} (MeOH) 236 (log ε 4.29), 291 (4.23), 348 (3.53) and 467 nm (3.17); ν_{max} ($CHCl_3$) 2956, 2924, 1730, 1672, 1636, 1594 and 1230 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 5.59 (1 H, s, 6-H), 5.28 (2 H, m, 10-H), 4.27 (2 H, m, 3-H), 3.80 (3 H, s, OMe), 2.45 (1 H, m, 1-H), 2.35 (1 H, m, 2-H), 2.08 (3 H, s, Me), 1.31 and 0.57 (each 1 H, m, 1a-H); δ_C (100.6 MHz; $CDCl_3$) 177.76 (8-C), 177.20 (5-C), 170.87 (*C*OCH_3), 160.52 (7-C), 146.17 (4a-C), 126.52 (9a/8a-C), 124.04 (8a/9a-C), 110.73 (9-C), 105.36 (6-C), 57.49 (10-C), 56.40 (OMe), 50.00 (3-C), 20.88 (1-C/CO*C*H_3), 20.67 (CO*C*H_3/1-C), 16.14 (1a-C) and 14.61 (2-C); *m/z* 301 (M^+, 10%), 258 (100), 242 (39), 226 (6), 212 (12), 198 (12), 43 (37) and 28 (13).

7-Methoxy-1,2-dihydro-3H-1,2-cyclopropapyrrolo[1,2-a]indol-8-ol

To a solution of 8-benzyloxy-7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole **16a** (0.500 g, 1.656 mmol) in ethyl acetate (250 ml) was added 10% palladium on carbon (0.100 g) and dilute sulfuric acid (5 drops). The mixture was stirred under an atmosphere of hydrogen for 5 h. After this time the suspension was filtered and washed with dichloromethane (3 x 75 ml). The filtrate and washings were washed with water (3 x 50 ml), brine (50 ml) and dried ($MgSO_4$). The organic layer was condensed *in vacuo* to give an oil. Purification of the residue by column chromatography (gradient elution: 100% light petroleum - 20% ethyl acetate/80% light petroleum) gave the *title compound* as a colourless oil (0.179 g, 50%) (Found: M^+, 215.0942. $C_{13}H_{13}NO_2$ requires M, 215.0946); ν_{max} ($CHCl_3$) 3537 (sharp), 1510, 1458, 1255 and 1241 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 6.78 (1 H, d, *J* 8.6, 5/6-H), 6.59 (1 H, d, *J* 8.6, 6/5-H), 6.23 (1 H, s, 9-H), 5.83 (1 H, s, OH), 4.04 (2 H, m, 3-H), 3.87 (3 H, s, OMe), 2.45-2.27 (2 H, m, 1,2-H), 1.24 and 0.62 (each 1 H, m, 1a-H), δ_C (62.9 MHz; $CDCl_3$) 146.66 (8-C), 138.83 (7-C), 138.02, 130.48, 121.97, 107.78 (5/6-C), 100.05 (6/5-C), 88.71 (9-C), 58.39 (OMe), 46.58 (3-C), 21.44 (1-C), 17.22 (1a-C) and 15.82 (2-C); *m/z* 215 (M^+, 96%), 200 (100) and 172 (23).

***7-Methoxy-1,2-dihydro-3H-1,2-cyclopropapyrrolo[1,2-a]indole-5,8-dione* 22**

Potassium nitrosodisulfonate (0.491 g, 1.832 mmol) in water (24 ml) was added to a stirred solution of 7-methoxy-1,2-dihydro-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indol-8-ol (0.179 g, 0.833 mmol) in acetone (81 ml). The mixture was buffered with sodium dihydrogen phosphate solution (0.167 M, 24 ml). After stirring at room temperature for 15 h the acetone was removed *in vacuo*. The aqueous residue was extracted with dichloromethane (3 x 75 ml) and the combined organic extracts were washed with water (3 x 75 ml), brine (100 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave an orange residue which was purified by column chromatography (ether) to give an orange solid. Recrystallisation of this orange residue from dichloromethane-light petroleum gave the *title compound* (0.125 g, 65%) as an orange solid, m.p. 185-186°C (Found: M^+, 229.0740. $C_{13}H_{11}NO_3$ requires M, 229.0739); λ_{max} (MeOH) 235 (log ε 4.44), 289 (4.40), 345 (3.65) and 463 nm (3.26); ν_{max} ($CHCl_3$) 1676, 1641, 1596, 1499, 1476 and 1237 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 6.30 (1 H, s, 9-H), 5.57 (1 H, s, 6-H), 4.27 (2 H, m, 3-H), 3.60 (3 H, s, OMe), 2.36 (2 H, m, 1,2-H), 1.29 and 0.59 (each 1 H, m, 1a-H); δ_C (62.9 MHz; $CDCl_3$) 177.77 (8-C), 177.09 (5-C), 160.70 (7-C), 146.75 (4a-C), 127.39 (9a/8a-C), 126.70 (8a/9a-C), 105.65 (6-C), 99.19 (9-C), 56.50 (OMe), 49.92 (3-C), 21.05 (1-C), 16.36 (1a-C) and 15.23 (2-C); *m/z* 229 (M^+, 100%), 200 (34), 186 (33) and 51 (33).

***4-Benzyloxy-5-methoxy-1-(2-methyl-2-butenyl)indole-2-carboxaldehyde* 14b**

4-Benzyloxy-5-methoxyindole-2-carboxaldehyde **13** (2.34 g, 8.33 mmol) in DMF (170 ml) was added dropwise to pre-washed sodium hydride (80%, 0.30 g, 10.0 mmol), and the mixture was stirred at room temperature for 45 min. 4-Bromo-2-methyl-2-butene (1.15 ml, 10.0 mmol) was added and the mixture was stirred at room temperature. After 15 h, water (20 ml) was cautiously added and the mixture was extracted with ethyl acetate (3 x 150 ml). The combined extracts were washed with water (8 x 150 ml), brine (150 ml), dried ($MgSO_4$) and evaporated to dryness. The residue was purified by column chromatography (50% ether/50% light petroleum) to give the *title compound* (1.89 g, 65%) as a pale yellow solid, m.p. 55-57°C (Found: C, 75.4; H, 6.6; N, 3.9. $C_{22}H_{23}NO_3$ requires C, 75.6; H, 6.6; N, 4.0%); ν_{max} ($CHCl_3$) 1666, 1516, 1488, 1460, 1290, 1248 and 1140 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.79 (1 H, s, CHO), 7.50 (2 H, m, Ar-H), 7.35 (3 H, m, Ar-H), 7.22 (1 H, s, 3-H), 7.19 (1 H, d, *J* 9.0, 6/7-H), 7.04 (1 H, d, *J* 9.0, 7/6-H), 5.27 (2 H, s, OCH_2Ph), 5.18 (3 H, m, 3',4'-H), 3.91 (3 H, s, OMe), 1.85 and 1.69 (each 3 H, s, Me); *m/z* 350 (M+H^+, 7%), 349 (M^+, 28), 258 (41), 190 (100), 91 (60), 69 (93) and 41 (71).

***4-Benzyloxy-5-methoxy-1-(2-methyl-2-butenyl)indole-2-carboxaldehyde tosylhydrazone* 15b**

4-Toluenesulfonyl hydrazide (1.516 g, 8.141 mmol) in dry methanol (20 ml) was added to a stirred solution of 4-benzyloxy-5-methoxy-1-(2-methyl-2-butenyl)indole-2-carboxaldehyde **14b** (1.894 g, 5.427 mmol) in dry methanol (30 ml). After stirring at 40°C for 15 h, the solvent was removed *in vacuo* and the residue was purified by chromatography (70% ether/30% light petroleum) to give a cream foam. Recrystallisation from dichloromethane-light petroleum gave the *title compound* (1.681 g, 60%) as a colourless solid, m.p. 77-79°C (Found: C, 67.0; H, 6.0; N, 8.2. $C_{29}H_{31}N_3O_4S$ requires C, 67.3; H, 6.0; N, 8.1%); ν_{max} ($CHCl_3$) 3184, 1608, 1598, 1516, 1490, 1454, 1344 and 1166 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.21 (1 H, br s, NH), 7.80 (2 H, d, *J* 8.7, Ts-H), 7.68 (1 H, s, HC=N), 7.44 (2 H, m, Ar-H), 7.33 (3 H, m, Ar-H), 7.24 (2 H, d, *J* 8.7, Ts-H), 7.00 (1 H, d, *J* 8.8, 7/6-H), 6.91 (1 H, d, *J* 8.8, 6/7-H), 6.62 (1 H, s, 3-H), 5.18 (2 H, s, OCH_2Ph), 5.05 (3 H, m, 3',4'-H), 3.86 (3 H, s, OMe), 2.36 (3 H, s, Ts-Me), 1.82 and 1.66 (each, 3 H, s, Me); *m/z* (FAB, 3-NBA Matrix) 518 (M+H^+, 55%), 426 (100) and 242 (20).

***8-Benzyloxy-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo-[1,2-a]indole* 16b**

Sodium hydride (80%, 0.032 g, 1.066 mmol) was added to a stirred solution of the tosylhydrazone **15b** (0.369 g, 0.714 mmol) in dry THF (11 ml). After 20 min, the solution was filtered and the filtrate evaporated. The residue was dissolved in dry chlorobenzene (105 ml) and the solution refluxed for 3.5 h. The solvent was

evaporated and the residue purified by chromatography (5% gradient elution: 100% light petroleum - 60% light petroleum/40% ether) to give the *title compound* (0.143 g, 60%) as a brown oil (Found: M^+, 333.1729. $C_{22}H_{23}NO_2$ requires *M*, 333.1729); ν_{max} ($CHCl_3$) 1570, 1490, 1452, 1432, 1262 and 1232 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.55 (2 H, m, Ar-H), 7.33 (3 H, m, Ar-H), 6.84 (1 H, d, *J* 8.6, 5/6-H), 6.80 (1 H, d, *J* 8.6, 6/5-H), 6.21 (1 H, br s, 9-H), 5.22 (2 H, s, OCH_2Ph), 4.13 (1 H, dd, *J* 10.8 and 6.1, 3-H), 3.88 (3 H, s, OMe), 3.84 (1 H, m, 3-H), 2.28 (1 H, dd, *J* 6.8 and 0.5, 1-H), 2.09 (1 H, m, 2-H), 1.19 and 0.67 (each 3 H, s, Me); *m/z* 334 (M+H^+, 8%), 333 (M^+, 31), 242 (100), 200 (13) and 91 (17).

***8-Benzyloxy-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo-[1,2a]indole-9-carboxaldehyde* 17b**

To *N*-methylformanilide (0.070 g, 0.515 mmol) and phosphorus oxychloride (0.080 g, 0.0515 mmol) was added 8-benzyloxy-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole **16b** (0.143 g, 0.429 mmol) in 1,2-dichloroethane (2 ml). The mixture was refluxed for 1.25 h. Sodium acetate (1 M, 9 ml) was added and the mixture extracted with ethyl acetate (3 x 50 ml). The combined organic extracts were washed with water (2 x 50 ml), brine (50 ml), dried ($MgSO_4$) and evaporated. Purification of the residue by column chromatography (ether) gave the *title compound* (0.118 g, 76%) as a yellow oil (Found: M^+, 361.1678. $C_{23}H_{23}NO_3$ requires *M*, 361.1678); ν_{max} ($CHCl_3$) 1666, 1596, 1526, 1492, 1452 and 696 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.28 (1 H, s, CHO), 7.49-7.15 (5 H, m, Ar-H), 6.87 (2 H, AB, *J* 8.6, 5,6-H), 5.18 (2 H, s, OCH_2Ph), 4.13 (1 H, dd, *J* 11.8 and 6.3, 3-H), 3.91 (3 H, s, OMe), 3.86 (1 H, m, 3-H), 2.86 (1 H, d, *J* 6.3, 1-H), 2.20 (1 H, t, *J* 6.3, 2-H), 1.26 (3 H, s, Me) and 0.68 (3 H, s, Me); *m/z* 362 (M+H^+, 12%), 361 (M^+, 28), 270 (100), 228 (32) and 91 (45).

***8-Hydroxy-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo-[1,2-a]indole-9-carboxaldehyde* 18b**

To a solution of 8-benzyloxy-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole-9-carboxaldehyde **17b** (0.300 g, 0.831 mmol) in ethyl acetate (160 ml) was added 10% palladium on carbon (0.065 g), dilute sulfuric acid (10 drops) and the mixture was stirred under an atmosphere of hydrogen. After 2.5 h the suspension was filtered and washed with dichloromethane (~150 ml). The organic layer was extracted with water (3 x 50 ml), brine (50 ml), dried ($MgSO_4$) and evaporated. Purification of the residue by column chromatography (10% gradient elution: 50% light petroleum/50% ether- 100% ether) gave the *title compound* (0.123 g, 55%) as a colourless solid, m.p. 119-121°C (Found: M^+, 271.1208. $C_{16}H_{17}NO_3$ requires *M*, 271.1208); ν_{max} ($CHCl_3$) 1606 br, 1298 and 1252 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.90 (1 H, s, CHO), 9.54 (1 H, s, OH), 6.89 (1 H, d, *J* 8.5, 6/5-H), 6.55 (1 H, d, *J* 8.5, 5/6-H), 4.18 (1 H, dd, *J* 12.1 and 6.4, 3-H), 3.91 (3 H, s, OMe), 3.86 (1 H, m, 3-H), 2.60 (1 H, dd, *J* 6.5 and 1.4, 1-H), 2.34 (1 H, m, 2-H), 1.29 and 0.77 (each 3 H, s, Me); *m/z* 273 (M+H_2^+, 17%), 272 (M+H^+, 57) and 271 (M^+, 100).

***9-Formyl-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo[1,2-a]indole-5,8-dione* 19b**

Potassium nitrosodisulfonate (0.268 g, 1.000 mmol) in water (13 ml) was added to a stirred solution of 8-hydroxy-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole-9-carboxaldehyde **18b** (0.123 g, 0.454 mmol) in acetone (44 ml). The mixture was buffered with sodium dihydrogen phosphate solution (0.167 M, 13 ml). After stirring at room temperature for 12 h, the mixture was concentrated *in vacuo*, filtered and the residue recrystallised from dichloromethane-light petroleum to give the *title compound* (0.111 g, 86%) as orange crystals, m.p. 246-248°C (Found: M^+, 285.0999. $C_{16}H_{15}NO_4$ requires *M*, 285.1001); ν_{max} ($CHCl_3$) 1678, 1640, 1596, 1506, 1238 and 1136 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.37 (1 H, s, CHO), 5.69 (1 H, s, 6-H), 4.32 (1 H, dd, *J* 14.1 and 6.4, 3-H), 4.18 (1 H, m, 3-H), 3.85 (3 H, s, OMe), 2.71 (1 H, dd, *J* 6.5 and 1.5, 1-H), 2.22 (1 H, m, 2-H), 1.26 and 0.72 (each 3 H, s, Me); *m/z* 285 (M^+, 100) and 270 (69).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo-[1,2-a]indole-5,8-dione* 20b**

Sodium borohydride (0.071 g, 1.887 mmol) was added to a stirred solution of 9-formyl-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3*H*-1,2-cyclopropapyrrolo[1,2-*a*]indole-5,8-dione **19b** (0.078 g, 0.274 mmol) in methanol (53 ml). After stirring for 4 h at room temperature under nitrogen, air was blown rapidly through the solution for 5 min. The mixture was extracted with dichloromethane (3 x 100 ml). The organic extracts were washed with water (3 x 100 ml), brine (100 ml), dried ($MgSO_4$) and evaporated. Purification of the residue by column chromatography (gradient elution: 50% ethyl acetate/50% light petroleum - 100% ethyl acetate) gave the *title compound* (0.054 g, 69%) as a red solid, m.p. 162-164°C (Found: M^+, 287.1158. $C_{16}H_{17}NO_4$ requires M, 287.1158); ν_{max} ($CHCl_3$) 3468, 1658, 1636 and 1594 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 5.61 (1 H, s, 6-H), 4.64 (2 H, m, 10-H), 4.28 (1 H, dd, *J* 14.0 and 6.3, 3-H), 4.08 (1 H, m, 3-H), 3.82 (3 H, s, OMe), 2.20 (1 H, dd, *J* 6.9 and 1.0, 1-H), 2.08 (1 H, m, 2-H), 1.19 and 0.72 (each 3 H, s, Me); *m/z* 289 ($M+H_2^+$, 8%), 288 ($M+H^+$, 19) and 287 (M^+, 100).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo-[1,2-a]indole-5,8-dione carbamate* 5b**

Phenyl chloroformate (0.04 ml, 0.28 mmol) was added dropwise to a stirred, ice cold solution of alcohol **20b** (0.050 g, 0.174 mmol) in pyridine (11 ml). The mixture was stirred at room temperature for 2 h then water (5 ml) was added. The mixture was extracted with dichloromethane (3 x 50 ml). The combined organic extracts were washed with water (3 x 50 ml), brine (100 ml) and dried ($MgSO_4$). The solvent was evaporated and the residue purified by column chromatography (ether) to give the phenylcarbonate **21b** as an orange gummy solid.

A solution of the phenyl carbonate **21b** in dry dichloromethane (30 ml) was cooled to -78°C. Ammonia gas was bubbled into the solution for 30 min (~100 ml), after which the contents were allowed to warm to room temperature and the solvent was evaporated. Recrystallisation of the residue from dichloromethane-light petroleum gave the *title compound* (0.040 g, 70%) as an orange crystalline solid, m.p. 204-206°C (Found: M^+, 330.1216. $C_{17}H_{18}N_2O_5$ requires M, 330.1216); λ_{max} (MeOH) 240 (log ε 4.32), 292 (4.21), 348 (3.57) and 474 nm (3.24); ν_{max} ($CHCl_3$) 3540, 3428, 1724, 1670, 1636, 1594, 1496 and 1232 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 5.59 (1 H, s, 6-H), 5.28 (2 H, m, 10-H), 4.59 (2 H, br s, NH_2), 4.28 (1 H, dd, *J* 14.0 and 6.3, 3-H), 4.08 (1 H, m, 3-H), 3.80 (3 H, s, OMe), 2.37 (1 H, br d, *J* 6.9, 1-H), 2.09 (1 H, m, 2-H), 1.19 and 0.69 (each 3 H, s, Me); *m/z* 330 (M^+, 15%), 287 (100), 273 (83), 254 (33), 228 (18) and 51 (14).

***9-Acetoxymethyl-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3H-1,2-cyclopropapyrrolo-[1,2-a]indole-5,8-dione* 23b**

To a solution of 9-hydroxymethyl-7-methoxy-1,2-dihydro-1a,1a-dimethyl-3*H*-1,2-cyclopropapyrrolo-[1,2-*a*]indole-5,8-dione **20b** (0.005 g, 0.017 mmol) in pyridine (2 ml) was added acetic anhydride (0.5 ml). The mixture was stirred at room temperature for 15 h. The mixture was then extracted with dichloromethane (3 x 25 ml). The combined organic extracts were washed with water (3 x 50 ml), brine (50 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave an orange residue which was purified by column chromatography (ether), to give an orange solid. Recrystallisation of this solid from dichloromethane-light petroleum gave the *title compound* (0.004 g, 66%) as an orange solid, m.p. 167-169°C (Found: M^+, 329.1245. $C_{18}H_{19}NO_5$ requires M 329.1263); ν_{max} ($CHCl_3$) 3008, 1730, 1670, 1636, 1594 and 1228 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 5.60 (1 H, s, 6-H), 5.26 (2 H, m, 10-H), 4.29 (1 H, dd, *J* 14.0 and 6.3, 3-H); 4.08 (1 H, m, 3-H), 3.80 (3 H, s, OMe), 2.31 (1 H, dd, *J* 7.0 and 1.2, 1-H), 2.08 (1 H, m, 2-H), 2.07 (3 H, s, COMe), 1.20 and 0.68 (each 3 H, s, Me); *m/z* 329 (M^+, 27%), 287 (100) and 254 (35).

***8-Benzyloxy-7-methoxy-9H-pyrrolo[1,2-a]indole* 24**

To a flask charged with sodium hydride (80%, 9.980 mmol, 0.299 g) was added light petroleum (10 ml). The mixture was stirred for 10 min, the light petroleum removed by syringe and the flask contents dried *in vacuo*. 4-Benzyloxy-5-methoxyindole-2-carboxaldehyde **13** (2.337 g, 8.317 mmol) in dry THF (47 ml) was added dropwise and the mixture stirred at room temperature for 30 min (the mixture turned yellow-green in colour). Vinyltriphenylphosphonium bromide (3.685 g, 9.980 mmol) was added and the solution was stirred under reflux for 15 h. The salts were removed by filtration through a bed of Celite. The combined filtrate and washings were condensed *in vacuo* to give a brown solid residue which was purified by column chromatography (dichloromethane) to give the *title compound* (2.261 g, 93%) as a colourless solid, m.p. 87-89°C (Found: C, 78.2; H, 5.8; N, 4.6. $C_{19}H_{17}NO_2$ requires C, 78.3; H, 5.9; N, 4.8%); ν_{max} ($CHCl_3$) 2996, 2936, 1482, 1288 and 1264 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 7.46-7.31 (5 H, m, Ar-H), 7.02 (1 H, dd, *J* 2.7 and 0.8, 3-H), 6.93 (1 H, d, *J* 8.4, 5/6-H), 6.86 (1 H, d, *J* 8.4, 5/6-H), 6.35 (1 H, t, *J* 3.1, 2-H), 6.05 (1 H, m, 1-H), 5.17 (2 H, s, OCH_2Ph), 3.91 (3 H, s, OMe) and 3.66 (2 H, s, 9-H); δ_C (62.9 MHz; $CDCl_3$) 149.30 (7/8-C), 145.27 (8/7-C), 137.64, 135.86, 135.51, 128.62, 128.45, 128.35, 128.17, 112.63, 111.67, 109.53, 104.40, 101.46, 74.57 (OCH_2Ph), 56.59 (OMe) and 27.15 (9-C); *m/z* 292 (M+H^+, 9%), 291 (M^+, 41), 200 (36) and 91 (100)

***7-Methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indol-8-ol* 25**

To a solution of 8-benzyloxy-7-methoxy-9*H*-pyrrolo[1,2-*a*]indole **24** (0.500 g, 1.718 mmol) in ethyl acetate (150 ml) was added 10% palladium on carbon (0.040 g) and the mixture was shaken under an atmosphere of hydrogen (60 psi) for 168 h. (Noting, at least once during the course of the 168 h the catalyst must be filtered off and new catalyst must be added to the reaction mixture). After this time the suspension was filtered and the filtrate condensed *in vacuo* to give a colourless oil. Purification of the residue by column chromatography (gradient elution: 100% light petroleum - 80% light petroleum/20% ether) gave the following products: **25** (0.349 g, 52%), **26** (0.030 g, 6%) and **27** (0.010 g, 3%), all as colourless solids [NB. hydrogenolysis using ethanol as solvent at atmospheric pressure gave **25** in 64% yield with only a minor amount of **27**].

***7-Methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indol-8-ol* 25**

m.p. 123-124°C (Found: M^+, 203.0946. $C_{12}H_{13}NO_2$ requires *M*, 203.0946); ν_{max} ($CHCl_3$) 3528 (sharp), 2952, 1494, 1452 and 1254 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 6.82 (1 H, d, *J* 8.6, 5/6-H), 6.70 (1 H, d, *J* 8.6, 6/5-H), 6.21 (1 H, br s, 9-H), 5.82 (1 H, s, OH), 3.98 (2 H, t, *J* 7.3, 3-H), 3.89 (3 H, s, OMe), 2.98 (2 H, t, *J* 7.3, 1-H) and 2.59 (2 H, p, *J* 7.3, 2-H); δ_C (62.9 MHz; $CDCl_3$) 144.66 (8-C), 138.68, 138.00, 130.40, 122.38, 107.73 (5/6-C), 100.56 (6/5-C), 88.92 (9-C), 58.43 (OMe), 43.72 (3-C), 27.93 (1-C) and 24.38 (2-C); *m/z* 204 (M+H^+, 9%), 203 (M^+, 62) and 188 (100).

***8-Benzyloxy-7-methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole* 26**

ν_{max} ($CHCl_3$) 2992, 1490, 1432 and 1262 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.56-7.53 (2 H, m, Ar-H), 7.41-7.27 (3 H, m, Ar-H), 6.91 (1 H, d, *J* 8.6, 5/6-H), 6.85 (1 H, d, *J* 8.6, 6/5-H), 6.20 (1 H, br s, 9-H), 5.21 (2 H, s, OCH_2Ph), 4.00 (2 H, t, *J* 7.2, 3-H), 3.88 (3 H, s, OMe), 2.98 (2 H, t, *J* 7.2, 1-H) and 2.58 (2 H, p, *J* 7.2, 2-H); δ_C (62.9 MHz; $CDCl_3$) 145.08 (7/8-C), 145.02 (8/7-C), 140.80, 138.57, 130.24, 128.38, 128.30, 128.01, 127.93, 127.67, 110.14 (5/6-C), 104.68 (6/5-C), 89.63 (9-C), 74.91 (OCH_2Ph), 58.60 (OMe), 43.83 (3-C), 27.88 (1-C) and 24.43 (2-C).

***7-Methoxy-9H-pyrrolo[1,2-a]indol-8-ol* 27**

m.p. 122-123°C (ether) (Found: M^+ 201.0796. $C_{12}H_{11}NO_2$ requires *M* 201.0790); ν_{max} ($CHCl_3$) 3532 (sharp), 1486 and 1266 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.05 (1 H, m, 3-H), 6.80 (1 H, d, *J* 8.3, 5/6-H), 6.75 (1 H, d, *J* 8.3, 6/5-H), 6.37 (1 H, t, *J* 3.0, 2-H), 6.10 (1 H, m, 1-H), 3.90 (3 H, s, OMe) and 3.83 (2 H, s,

9-H); δ_C (62.9 MHz; $CDCl_3$) 143.45, 142.38, 136.22, 135.68, 120.13, 112.57, 109.55, 109.23, 101.46, 100.30, 56.55 (OMe) and 26.23 (C-9); *m/z* 201 (M^+, 100%), 186 (97) and 158 (21).

***8-Hydroxy-7-methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole-9-carboxyaldehyde* 28**

DMF (0.64 ml, 8.250 mmol) and phosphorus oxychloride (0.17 ml, 1.815 mmol) were stirred in an ice salt bath for 30 min. 7-Methoxy-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-8-ol **25** (0.335 g, 1.650 mmol) in DMF (0.19 ml, 2.475 mmol) were added to the DMF / phosphorus oxychloride mixture and the temperature was kept below 0°C. The reaction mixture was stirred at 35°C for 1 h. After this time, ice water followed by a solution of sodium hydroxide (9.25 M, 8 ml) were added and the mixture extracted with dichloromethane (3 x 100 ml). The organic layers were washed with water (3 x 75 ml), brine (100 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave a residue, which was purified by column chromatography (ethyl acetate) to give the *title compound* (0.277 g, 73%) as a pale yellow solid, m.p. 161-162°C (Found: M^+, 231.0895. $C_{13}H_{13}NO_3$ requires *M*, 231.0895); ν_{max} ($CHCl_3$) 1606, 1296 and 1252 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.76 (1 H, s, CHO), 9.14 (1 H, s, OH), 6.76 (1 H, d, *J* 8.5, 5/6-H), 6.45 (1 H, d, *J* 8.5, 6/5-H), 3.90 (2 H, t, *J* 7.4, 3-H), 3.82 (3 H, s, OMe), 3.03 (2 H, t, *J* 7.4, 1-H) and 2.60 (2 H, p, *J* 7.4, 2-H); δ_C (62.9 MHz; $CDCl_3$) 182.88 (CHO), 158.00 (8/7-C), 142.81 (7/8-C), 140.92, 130.04, 119.58, 111.75 (5/6-C), 110.39, 100.60 (6/5-C), 57.58 (OMe), 44.94 (3-C), 26.24 (1-C) and 24.40 (2-C); *m/z* 232 (M+H^+, 10%), 231 (M^+, 65), 216 (80), 188 (19) and 86 (100).

***9-Formyl-7-methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole-5,8-dione* 29**

Potassium nitrosodisulfonate (1.117 g, 4.167 mmol) in water (56 ml) was added to a stirred solution of 8-hydroxy-7-methoxy-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indole-9-carboxyaldehyde **28** (0.437 g, 1.892 mmol) in acetone (185 ml). The mixture was buffered with sodium dihydrogen phosphate solution (0.167 M, 56 ml). After stirring at room temperature for 15 h, the acetone was removed *in vacuo*. The aqueous layer was extracted with dichloromethane (3 x 75 ml). The organic extracts were washed with water (3 x 50 ml), brine (50 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave an orange residue which was recrystallised from dichloromethane-light petroleum to give the title compound (0.415 g, 89%) as an orange solid, m.p. 224-225°C (lit.,[36] 247-248°C) (Found: M^+, 245.0689. Calc. for $C_{13}H_{11}NO_4$:*M*, 245.0689); ν_{max} ($CHCl_3$) 1668, 1638, 1596, 1506 and 1124 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.28 (1 H, s, CHO), 5.63 (1 H, s, 6-H), 4.22 (2 H, t, *J* 7.5, 3-H), 3.78 (3 H, s, OMe), 3.07 (2 H, t, *J* 7.5, 1-H) and 2.54 (2 H, p, *J* 7.5, 2-H); δ_C (62.9 MHz; $CDCl_3$) 186.86 (CHO), 178.20 (8-C), 177.41 (5-C), 160.65 (7-C), 149.41 (4a-C), 127.06 (9a/8a-C), 125.22 (8a/9a-C), 116.07 (9-C), 105.55 (6-C), 56.74 (OMe), 47.40 (3-C), 26.89 (1-C) and 25.16 (2-C); *m/z* 245 (M^+, 100%).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole-5,8-dione* 30**

Sodium borohydride (0.454 g, 12.001 mmol) was added to a stirred solution of 9-formyl-7-methoxy-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indole-5,8-dione **29** (0.421 g, 1.718 mmol) in distilled methanol (443 ml) which was rigorously degassed with nitrogen. After stirring for 4 h at room temperature, air was rapidly blown through the solution. The solution was extracted with dichloromethane (3 x 300 ml). The combined extracts were washed with water (3 x 200 ml), brine (200 ml) and dried ($MgSO_4$). The solvent was then removed *in vacuo*. Purification of the residue by column chromatography (ethyl acetate) gave the *title compound* (0.274 g, 65%) as a red solid, m.p. 154-156°C (Found: M^+, 247.0839. $C_{13}H_{13}NO_4$ requires *M*, 247.0844); ν_{max} ($CHCl_3$) 3528, 1636 and 1594 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 5.63 (1 H, s, 6-H), 4.61 (2 H, d, *J* 6.8, 10-H), 4.22 (2 H, m, 3-H), 3.97 (1 H, br t, *J* 6.8, OH), 3.83 (3 H, s, OMe), 2.85 (2 H, t, *J* 7.3, 1-H) and 2.56 (2 H, p, *J* 7.3, 2-H); δ_C (62.9 MHz; $CDCl_3$) 179.00 (8-C), 177.83 (5-C), 160.54 (7-C), 141.82 (4a-C), 127.03 (9a/8a-C), 125.18 (8a/9a-C), 117.95 (9-C), 105.99 (6-C), 56.63 (10-C/OMe), 56.54 (OMe/10-C), 46.97 (3-C), 27.40 (1-C) and 22.52 (2-C); *m/z* 247 (M^+, 100), 232 (51) and 51 (36).

***9-Hydroxymethyl-7-methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole-5,8-dione carbamate* 6**

To a stirred cooled solution 9-hydroxymethyl-7-methoxy-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indole-5,8-dione **30** (0.120 g, 0.486 mmol) in anhydrous pyridine (31 ml) at 0°C was added phenyl chloroformate (0.09 ml, 0.729 mmol) dropwise. The solution was allowed to warm to room temperature and stirred for a further 2 h. The solution was extracted with dichloromethane (3 x 75 ml). The combined extracts were washed with water (3 x 75 ml), brine (100 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave an orange residue which was purified by column chromatography (ethyl acetate) to give an orange gummy solid; δ_H (250 MHz; $CDCl_3$) 7.37-7.19 (5 H, m, Ar-H), 5.63 (1 H, s, 6-H), 5.41 (2 H, s, 10-H), 4.23 (2 H, m, 3-H), 3.80 (3 H, s, OMe), 2.94 (2 H, t, *J* 7.3, 1-H) and 2.59 (2 H, p, *J* 7.3, 2-H).

Ammonia gas was bubbled through a solution of the phenyl carbonate in dichloromethane (60 ml) at -78 °C and the reaction was monitored by TLC. After approximately 40 min all the starting material had been consumed and the ammonia was allowed to evaporate at room temperature. The contents were condensed *in vacuo*. Recrystallisation of the residue from dichloromethane-light petroleum gave the *title compound* (0.096 g, 68%) as an orange solid, m.p. 221-223°C (Found: M^+, 290.0901. $C_{14}H_{14}N_2O_5$ requires *M*, 290.0903); λ_{max} (MeOH) (qualitative) 228, 289, 348 and 452 nm; ν_{max} (Nujol) 3368, 3222, 1773, 1670, 1625, 1585, 1499, 1399 and 1084 cm^{-1}; δ_H (250 MHz; DMSO) 6.51 (2 H, br s, NH_2), 5.75 (1 H, s, 6-H), 5.01 (2 H, s, 10-H), 4.13 (2 H, t, *J* 7.3, 3-H), 3.75 (3 H, s, OMe), 2.83 (2 H, t, *J* 7.3, 1-H) and 2.52-2.40 (2 H, m, 2-H); *m/z* 290 (M^+, 17%), 247 (100) and 229 (92).

***9-Acetoxymethyl-7-methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole-5,8-dione* 31**

Distilled acetic anhydride (0.5 ml) was added to a stirred solution of 9-hydroxymethyl-7-methoxy-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indole-5,8-dione **30** (0.015 g, 0.061 mmol) in anhydrous pyridine (3 ml). After 2.5 h, water (5 ml) was added and extracted with dichloromethane (3 x 50 ml). The organic extracts were washed with water (3 x 50 ml), brine (75 ml) and dried ($MgSO_4$). Removal of solvent *in vacuo* gave an orange residue which was recrystallised from dichloromethane-light petroleum to give the *title compound* (0.014 g, 78%) as an orange solid, m.p. 216-218°C (Found: M^+, 289.095. $C_{15}H_{15}NO_5$ requires *M*, 289.095); λ_{max} (MeOH) 227 (log ε 4.57), 286 (4.58), 348 (3.85) and 456 nm (3.52); ν_{max} ($CHCl_3$) 3023, 1739, 1673, 1639, 1597, 1501 and 1233 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 5.61 (1 H, s, 6-H), 5.22 (2 H, s, 10-H), 4.23 (2 H, m, 3-H), 3.80 (3 H, s, OMe), 2.89 (2 H, t, *J* 7.4, 1-H), 2.56 (2 H, p, *J* 7.4, 2-H) and 2.06 (3 H, s, COMe); *m/z* 289 (M^+, 11%), 247 (100), 230 (46) and 43 (39).

***7-Methoxy-1,2-dihydro-3H-pyrrolo[1,2-a]indole-5,8-dione* 32**

Potassium nitrosodisulfonate (0.311 g, 1.160 mmol) in water (15 ml) was added to a stirred solution of 7-methoxy-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-8-ol **25** (0.107 g, 0.527 mmol) in acetone (50 ml). The mixture was buffered with sodium dihydrogen phosphate solution (0.167 M, 15 ml). After stirring at room temperature for 15 h, the acetone was removed *in vacuo*. The aqueous layer was then extracted with dichloromethane (3 x 75 ml). The organic extracts were washed with water (3 x 50 ml), brine (75 ml) and dried ($MgSO_4$). Removal of the solvent *in vacuo* gave an orange residue which was purified by column chromatography (ethyl acetate) to give an orange solid. The orange residue was recrystallised from dichloromethane-light petroleum to give the *title compound* (0.065 g, 57%) as an orange solid, m.p. 186.5°C (dec.) (Found: M^+, 217.0735. $C_{12}H_{11}NO_3$ requires *M*, 217.0739); λ_{max} (MeOH) 226 (log ε 4.33), 288 (4.24) and 445 nm (3.09); ν_{max} ($CHCl_3$) 3024, 1673, 1642, 1596, 1476, 1239, 1154 and 1083 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 6.29 (1 H, s, 9-H), 5.61 (1 H, s, 6-H), 4.23 (2 H, t, *J* 7.3, 3-H), 3.84 (3 H, s, OMe), 2.86 (2 H, t, *J* 7.3, 1-H) and 2.58 (2 H, p, *J* 7.3, 2-H); δ_C (62.9 MHz; $CDCl_3$) 178.00 (8-C), 177.35 (5-C), 160.67 (7-C), 144.81 (4a-C), 127.84 (9a/8a-C), 126.68 (8a/9a-C), 105.79 (6-C), 99.98 (9-C), 56.52 (OMe), 46.86 (3-C), 27.61 (1-C) and 23.61 (2-C); *m/z* 217 (M^+, 100%).

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