Synthesis of 2,3-Dihydro-1*H*-pyrrolo[1,2-*a*]indoles by Intramolecular Nucleophilic Aromatic Substitution

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Condensation of 2-methoxy-Δ^1-pyrroline (3) with 2-bromo-5-methoxy-4-methylphenylacetonitrile (6) [prepared from 3-hydroxy-4-methylbenzaldehyde (17) in four steps] gave α-(2-bromo-5-methoxy-4-methylphenyl)-α-pyrrolidin-2-ylideneacetonitrile (10). Several other α-aryl-α-pyrrolidin-2-ylideneacetonitriles [(8), (9), and (11)] were also synthesised from the corresponding phenylacetonitriles [(4), (5), and (7)]. (*Z*)-α-Aryl-α-pyrrolidin-2-ylideneacetates [(14)—(16)] were prepared by similar condensation reactions or by ethanolysis of the nitriles (8) and (10). Treatment of compounds (9), (10), and (16) with sodium hydride and copper(I) bromide in dimethylformamide gave quantitatively the 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-9-carbonitriles (21)—(23). Heating the nitriles (21) and (22) with nickel–aluminium alloy in aqueous acetic acid yielded the corresponding aldehydes (24) and (25). 2,3-Dihydro-7-methoxy-6-methyl-1*H*-pyrrolo[1,2-*a*]indole-9-carbaldehyde (25) was further converted *via* the 8-nitro-compound (26) into the 5,8-quinone (28).

MITOMYCINS (1), isolated from *Streptomyces* cultures, have been found to be active against bacteria and in cancer chemotherapy. Much work has been done on approaches to the synthesis of mitomycins, mainly involving the formation of the pyrrolo[1,2-*a*]indole system,[1-6] but the reported procedures are inconvenient. In unactivated aromatic rings which have no electron-withdrawing substituents, a direct displacement of a halogen by a nucleophile demands drastic conditions; several modified nucleophilic aromatic substitutions have been reported recently.[7-12] We now describe a simple synthesis of the pyrrolo[1,2-*a*]indolequinone (28) by a route involving an intramolecular nucleophilic aromatic substitution. The conversion of the quinone (28) into 7-methoxymitosene (2), a potential antibacterial agent, has been reported.[1]

Heating 2-methoxy-Δ^1-pyrroline (3) with the arylacetonitriles (4)—(7) in the presence of triethylamine or 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) at 100—120 °C gave the corresponding α-aryl-α-pyrrolidin-2-ylideneacetonitriles (8)—(11) in good yield. Use of DBU always gave better results than that of triethylamine, and required a shorter reaction time. 2-Bromo-5-methoxy-4-methylphenylacetonitrile (6) was prepared as follows.

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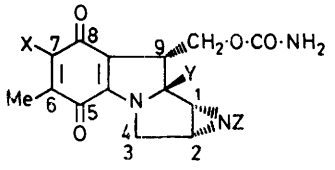
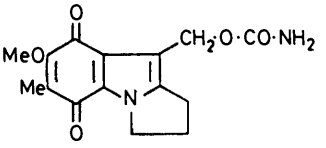
[3] T. Takada and M. Akiba, *Chem. and Pharm. Bull. (Japan)*, 1972, **20**, 1785.
[4] T. Takada, Y. Kosugi, and M. Akiba, *Tetrahedron Letters*, 1974, 3283.
[5] K. Uzu, K. Nakano, M. Shimizu, S. Kinoshita, and M. Matsui, *J. Antibiotics*, 1971, **14**, 181.
[6] G. J. Siuta, R. W. Franck, and R. J. Kempton, *J. Org. Chem.*, 1974, **39**, 3739 and references therein.
[7] R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, 1973, **38**, 1407.
[8] J. F. Bunnett, *J. Chem. Educ.*, 1974, **51**, 312.
[9] R. G. R. Bacon and A. Karim, *J.C.S. Perkin I*, 1973, 272.
[10] A. Bruggink and A. McKillop, *Angew. Chem. Internat. Edn.*, 1974, **13**, 340.
[11] M. F. Semmelhack and H. T. Hall, *J. Amer. Chem. Soc.*, 1974, **96**, 7091.
[12] M. F. Semmelhack, B. P. Chong, R. D. Stauffer, T. D. Rogerson, A. Chong, and L. D. Jones, *J. Amer. Chem. Soc.*, 1975, **97**, 2507.

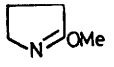
Bromination of 3-hydroxy-4-methylbenzaldehyde (17) [13] yielded the bromide (18) in 80% yield, which was then methylated with dimethyl sulphate to give the aldehyde (19) in 94% yield. Reduction of (19) with sodium borohydride, followed by chlorination of the resulting alcohol (20) with thionyl chloride, and cyanation with potassium cyanide in the presence of sodium iodide in ethyl methyl ketone, gave the nitrile (6) in 69% yield from (19).



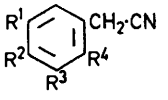


(1)	X	Y	Z
mitomycin A	MeO	MeO	H
mitomycin B	MeO	HO	Me
mitomycin C	NH_2	MeO	H
porfiromycin	NH_2	MeO	Me

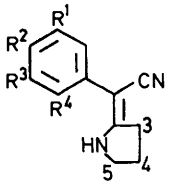
(2)



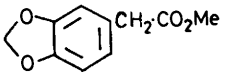
(3)



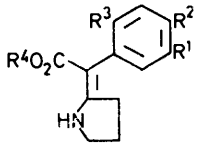
(4) $R^1=R^3=R^4=H$, $R^2=MeO$
(5) $R^1=R^2=MeO$, $R^3=H$, $R^4=Br$
(6) $R^1=MeO$, $R^2=Me$, $R^3=H$, $R^4=Br$
(7) $R^1=R^2=MeO$, $R^3=Br$, $R^4=H$



(8) $R^1=R^3=R^4=H$, $R^2=MeO$
(9) $R^1=R^2=MeO$, $R^3=H$, $R^4=Br$
(10) $R^1=MeO$, $R^2=Me$, $R^3=H$, $R^4=Br$
(11) $R^1=R^2=MeO$, $R^3=Br$, $R^4=H$
(12) $R^1=R^2=MeO$, $R^3=R^4=H$



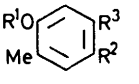
(13)



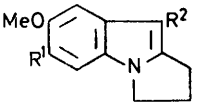
(14) $R^1R^2=O{\cdot}CH_2{\cdot}O$, $R^3=H$, $R^4=Me$
(15) $R^1=R^3=H$, $R^2=MeO$, $R^4=Et$
(16) $R^1=MeO$, $R^2=Me$, $R^3=Br$, $R^4=Et$

Condensation of 2-methoxy-Δ^1-pyrroline (3) with methyl 3,4-methylenedioxyphenylacetate (13) gave a pyrrolidinylideneacetate (14), in 10% yield by heating with DBU or in very low yield by heating with triethylamine Refluxing the pyrrolidinylideneacetonitriles (8) and (10) with ethanol previously saturated with dry hydrogen chloride gas gave the corresponding ethyl pyrrolidinylideneacetates (15) and (16). The α-aryl-α-pyrrolidin-2-ylideneacetates (14)—(16) showed i.r. absorptions due to NH at 3 350 and ester at 1 640 cm^{-1}. Their n.m.r. spectra (solvent $CDCl_3$) showed the NH signals at δ 8.40—8.50 (broad singlet) and the pyrrolidine 3-H_2 signals at δ 2.42—2.46 (triplet, J 6 Hz). The nitriles (8)—(12) showed i.r. absorptions at 3 440—3 450 (NH) and 2 180 cm^{-1} (CN). Their n.m.r. spectra showed the NH signals at δ 4.80—5.50 (broad singlet) and the pyrrolidine 3-H signals at δ 2.95 p.p.m. (triplet, J 6 Hz). In the light of the above observations, a hydrogen bond between the NH and the ester group is expected for the acetates (14)—(16). Therefore these acetates are thought to exist in the Z-form, in which the pyrrolidine 3-protons are shielded by the aryl group. The nitriles (8)—(12), showing no such shielding, may well exist in the E-form.

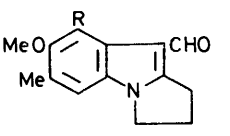
Cyclisation of the nitrile (9) by intramolecular nucleophilic aromatic substitution was examined under various conditions. Refluxing with sodium hydride in dry dimethylformamide, followed by chromatographic purification, gave the desired pyrrolo[1,2-*a*]indole (21) in 60—70% yield. The reaction was catalysed by copper(I) bromide. Thus a treatment of (9) with an equimolar amount of sodium hydride in the presence of copper(I) bromide in dry dimethylformamide at 80 °C for 1 h or at room temperature for 3 h afforded (21) in 90% yield.



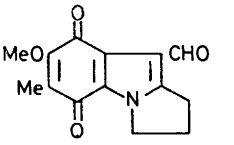
(17) $R^1=R^2=H$, $R^3=CHO$
(18) $R^1=H$, $R^2=Br$, $R^3=CHO$
(19) $R^1=Me$, $R^2=Br$, $R^3=CHO$
(20) $R^1=Me$, $R^2=Br$, $R^3=CH_2{\cdot}OH$



(21) $R^1=MeO$, $R^2=CN$
(22) $R^1=Me$, $R^2=CN$
(23) $R^1=Me$, $R^2=CO_2Et$
(24) $R^1=MeO$, $R^2=CHO$
(25) $R^1=Me$, $R^2=CHO$



(26) $R=NO_2$
(27) $R=NH_2$



(28)

For the above reactions, a benzyne mechanism is not probable because heating the 3-bromo-4,5-dimethoxyphenyl analogue (11) with sodium hydride in dry dimethyl formamide in the presence or in the absence of copper(I) bromide gave no cyclised compound (21), but only the starting material (11) and the debrominated compound (12), from a tarry product. A normal benzyne reaction of the nitrile (9) with sodium amide in

[13] N. V. Sidgwick and E. N. Allott, *J. Chem. Soc.*, 1923, **123**, 2819.

liquid ammonia gave no compound (21). By a photo-induced $S_{RN}1$ reaction,[7] irradiation of (9) and potassium t-butoxide in liquid ammonia afforded (21) in 2% yield together with the debrominated product (12) in 20% yield.

Treatment of the nitrile (10) with sodium hydride and copper(I) bromide in dry dimethylformamide gave in 93% yield the pyrrolo[1,2-*a*]indole (22), the spectral data of which were identical with those reported.[2] When the acetate (16) was treated similarly, the pyrrolo[1,2-*a*]-indole (23) was obtained in 88% yield. Thus the geometry of the pyrrolidine derivative appears not to influence the cyclisation. All the foregoing 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole derivatives were coloured pink by cerium(IV) sulphate in sulphuric acid, which was used as a spray reagent for their detection on t.l.c.

Refluxing the pyrroloindolecarbonitriles (21) and (22) with nickel–aluminium alloy in 50% aqueous acetic acid [14] gave the aldehydes (24) and (25) [2] in 91 and 89% yield, respectively. Replacement of aqueous acetic acid by aqueous formic acid in this reaction gave an unsatisfactory result. Nitration of the aldehyde (25) afforded the nitro-compound (26) in 80% yield, which was reduced with iron and acetic acid. The resulting amino-compound (27) was oxidised to the quinone (28) with Fremy's salt [in 28% yield from (26)].

EXPERIMENTAL

I.r. spectra were measured with a Hitachi EPI-3 recording spectrophotometer, n.m.r. spectra with a JEOL JNM-PMX 60 spectrophotometer, and mass spectra with a Hitachi RMU-7 spectrometer.

2-Bromo-5-methoxy-4-methylphenylacetonitrile (6).—To a solution of the alcohol (20) (23 g) in dry benzene (300 ml), thionyl chloride (11.9 g) was slowly added; the mixture was kept for 30 min at room temperature and then refluxed for 2 h. The excess of reagent and solvent were distilled off and the residue was taken up in benzene. The extract was washed with water and dried (Na_2SO_4). Evaporation left a syrup, which was dissolved in ethyl methyl ketone (200 ml); to this solution potassium cyanide (9.8 g), sodium iodide (3 g), and water (20 ml) were added and the mixture was refluxed for 3 h. After addition of benzene the organic layer was washed with water, dried (Na_2SO_4), and evaporated to leave a solid, recrystallisation of which from benzene–n-hexane gave the nitrile (6) (17.3 g, 72%) as *needles*, m.p. 108—110° (Found: C, 50.25; H, 4.5; N, 5.75. $C_{10}H_{10}BrNO$ requires C, 50.0; H, 4.2; N, 5.8%), $\nu_{max.}$ ($CHCl_3$) 2 250 cm^{-1} (CN); δ($CDCl_3$) 7.25 (1 H, s, ArH), 6.90 (1 H, s, ArH), 3.82 (3 H, s, OMe), 3.76 (2 H, s, CH_2·CN), and 2.20 (3 H, s, ArMe).

α-(4-Methoxyphenyl)-α-pyrrolidin-2-ylideneacetonitrile (8).—(*a*) A mixture of 4-methoxyphenylacetonitrile (4) (2.94 g), 2-methoxy-Δ^1-pyrroline (4.0 g) and triethylamine (0.2 g) was heated for 4 days at 120 °C with stirring in a current of nitrogen. After cooling, the precipitate was filtered off and washed with ethanol. The combined filtrate and washing was chromatographed on silica gel in benzene to afford more product. Recrystallisation from ethanol gave the pyrrolidine (8) (2.2 g, 51%) as *prisms*, m.p. 154—155° (Found: C, 72.8; H, 6.55; N, 13.05. $C_{13}H_{14}N_2O$ requires C, 72.85; H, 6.6; N, 13.1%), $\nu_{max.}$ ($CHCl_3$) 3 440 (NH) and 2 180 cm^{-1} (CN); δ($CDCl_3$) 7.22 (2 H, d, *J* 8 Hz, aryl 2- and 6-H), 6.80 (2 H, d, *J* 8 Hz, aryl 3- and 5-H), 5.35br (1 H, s, NH), 3.80 (3 H, s, OMe), 3.50 (2 H, t, *J* 6 Hz, 5-H_2), 2.95 (2 H, t, *J* 6 Hz, 3-H_2), and 2.40—1.90 (2 H, m, 4-H_2).

(*b*) A mixture of 4-methoxyphenylacetonitrile (4) (147 mg), 2-methoxy-Δ^1-pyrroline (200 mg), and 1,5-diazabicyclo[5.4.0]undec-5-ene (15 mg) was heated for 48 h at 100 °C with stirring in a current of nitrogen. The mixture was chromatographed on silica gel in benzene to give a solid, recrystallisation of which from ethanol afforded (8) (140 mg, 65%) as prisms, m.p. 154—155°, identical with that described above (t.l.c. and i.r. and n.m.r. spectra).

α-(2-Bromo-4,5-dimethoxyphenyl)-α-pyrrolidin-2-ylideneacetonitrile (9).—A mixture of 2-bromo-4,5-dimethoxyphenylacetonitrile (5) (5.12 g), 2-methoxy-Δ^1-pyrroline (4 g) and 1,5-diazabicyclo[5.4.0]undec-5-ene (0.5 g) was stirred for 72 h at 120 °C in a current of nitrogen. After cooling, the precipitate (4 g) was filtered off and washed with ethanol. The filtrate was concentrated and the residue was purified by silica gel column chromatography. Elution with benzene gave a powder (1.6 g), which was combined with the precipitate and recrystallised from ethanol to give (9) (5.1 g, 79%) as *prisms*, m.p. 173—174° (Found: C, 52.4; H, 4.6; N, 8.7 $C_{14}H_{15}BrN_2O_2$ requires C, 52.0; H, 4.65; N, 8.65%), $\nu_{max.}$ ($CHCl_3$) 3 450 (NH) and 2 180 cm^{-1} (CN); δ($CDCl_3$) 7.00 (1 H, s, ArH), 6.80 (1 H, s, ArH), 4.80br (1 H, s, NH), 3.82 (6 H, s, 2 × OMe), 3.50 (2 H, t, *J* 6 Hz, 5-H_2), 2.95 (2 H, t, *J* 6 Hz, 3-H_2), and 2.40—1.90 (2 H, m, 4-H_2).

α-(2-Bromo-5-methoxy-4-methylphenyl)-α-pyrrolidin-2-ylideneacetonitrile (10).—A mixture of the nitrile (6) (4.8 g), 2-methoxy-Δ^1-pyrroline (4 g) and 1,5-diazabicyclo[5.4.0]-undec-5-ene (0.8 g) was heated for 72 h at 120 °C with stirring in a current of nitrogen. The mixture was then taken up in chloroform and treated with active charcoal. Evaporation left a residue which was recrystallised from ethanol to afford the pyrrolidine (10) as *needles* (4.0 g, 64%), m.p. 142—143° (Found: C, 54.75; H, 5.05; N, 9.15. $C_{14}H_{15}BrN_2O$ requires C, 54.75; H, 4.95; N, 9.1%), $\nu_{max.}$ ($CHCl_3$) 3 450 (NH) and 2 180 cm^{-1} (CN); δ($CDCl_3$) 7.30 (1 H, s, ArH), 6.75 (1 H, s, ArH), 4.95br (1 H, s, NH), 3.80 (3 H, s, OMe), 3.50 (2 H, t, *J* 6 Hz, 5-H_2), 2.95 (2 H, t, *J* 6 Hz, 3-H_2), and 2.15 (3 H, s, ArMe).

α-(3-Bromo-4,5-dimethoxyphenyl)-α-pyrrolidin-2-ylideneacetonitrile (11).—A mixture of 3-bromo-4,5-dimethoxyphenylacetonitrile (7) (1.28 g), 2-methoxy-Δ^1-pyrroline (1.0 g), and 1,5-diazabicyclo[5.4.0]undec-5-ene (150 mg) was heated for 48 h at 110 °C with stirring in a current of nitrogen. The mixture was chromatographed on silica gel with benzene to give a solid, recrystallisation of which from ethanol afforded (11) as *needles* (1.20 g, 75%), m.p. 144—145° (Found: C, 51.95; H, 4.8; N, 8.75. $C_{14}H_{15}BrN_2O_2$ requires C, 52.0; H, 4.65; N, 8.65%), $\nu_{max.}$ ($CHCl_3$) 3 450 (NH) and 2 180 (CN); δ ($CDCl_3$) 7.02 and 6.78 (each 1 H, d, *J* 2 Hz, aryl 2- and 6-H), 5.50br (1 H, s, NH), 3.86 and 3.82 (each 3 H, each s, 2 × OMe), 3.50 (2 H, t, *J* 6 Hz, 5-H_2), 2.95 (2 H, t, *J* 6 Hz, 3-H_2), and 2.40—1.90 (2 H, m, 4-H_2).

Attempted Cyclisation of the Nitrile (11).—A mixture of the nitrile (11) (323 mg), 50% sodium hydride (50 mg), copper(I) bromide (140 mg), and dry dimethylformamide (20 ml) was heated for 1.5 h at 80 °C with stirring in a current of nitrogen and then refluxed for 15 h. An excess of ammonium chloride was then added and the mixture was stirred for 20 min at

[14] T. van Es and B. Staskun, *J. Chem. Soc.*, 1965, 5775.

room temperature. Chloroform was added and the organic mixture was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on alumina (Woelm, grade III) in benzene to give the starting material (11) (60 mg) and the debrominated compound (12) (30 mg, 12%), identical (i.r. and n.m.r. spectra and t.l.c.) with the compound described later.

Methyl (Z)-α-(3,4-*Methylenedioxyphenyl*)-α-*pyrrolidin*-2-*ylideneacetate* (14).—A mixture of methyl 3,4-methylenedioxyphenylacetate (13) (194 mg), 2-methoxy-Δ^1-pyrroline (99 mg), and 1,5-diazabicyclo[5.4.0]undec-5-ene (15 mg) was heated for 4 days at 100 °C with stirring in a current of nitrogen. The mixture was then chromatographed on silica gel with benzene to give a solid, recrystallisation of which from ether afforded (14) as *prisms* (25 mg, 10%), m.p. 126—126.5° (Found: C, 64.25; H, 5.85; N, 5.35. $C_{14}H_{15}NO_4$ requires C, 64.35; H, 5.8; N, 5.35%), $\nu_{max.}$ ($CHCl_3$) 3 350 (NH) and 1 640 cm^{-1} (C=O); δ($CDCl_3$) 6.45 (3 H, s, 3 × ArH), 5.85 (2 H, s, OCH_2O), 3.58 (2 H, t, *J* 6 Hz, 5-H_2), 3.50 (3 H, s, OMe), 2.46 (2 H, t, *J* 6 Hz, 3-H_2), and 2.20—1.70 (2 H, m, 4-H_2).

Ethyl (Z)-α-(4-*Methoxyphenyl*)-α-*pyrrolidin*-2-*ylideneacetate* (15).—A mixture of the nitrile (8) (100 mg) and ethanol (10 ml), previously saturated with hydrogen chloride gas, was refluxed for 3 h and evaporated. The residue was taken up in chloroform, washed with saturated aqueous sodium hydrogen carbonate, and dried (K_2CO_3). Evaporation, followed by column chromatography on silica gel with benzene, gave (15) as a syrup (60 mg, 46%), $\nu_{max.}$ ($CHCl_3$) 3 350 (NH) and 1 640 cm^{-1} (C=O); δ($CDCl_3$) 8.40br (1 H, s, NH), 6.82 (2 H, d, *J* 8 Hz, aryl 2- and 6-H), 6.64 (2 H, d, *J* 8 Hz, aryl 3- and 5-H), 4.00 (2 H, q, *J* 7 Hz, O·CH_2·CH_3), 3.74 (3 H, s, OMe), 3.58 (2 H, t, *J* 6 Hz, 5-H_2), 2.42 (2 H, t, *J* 6 Hz, 3-H_2), 2.15—1.75 (2 H, m, 4-H_2), and 1.15 (3 H, t, *J* 7 Hz, O·CH_2·CH_3); *m/e* 261 (M^+). All attempts at crystallisation failed.

Ethyl (Z)-α-(2-*Bromo*-5-*methoxy*-4-*methylphenyl*)-α-*pyrrolidine*-2-*ylideneacetate* (16).—Under the same conditions as above, the nitrile (10) (614 mg) afforded (16) as a syrup (200 mg, 28%), $\nu_{max.}$ ($CHCl_3$) 3 350 (NH) and 1 640 cm^{-1} (C=O); δ (CCl_4) 8.40br (1 H, s, NH), 7.22 and 6.55 (each 1 H, s, 2 × ArH), 3.76 (3 H, s, OMe), 2.16 (3 H, s, ArMe), and 1.14 (3 H, t, *J* 7 Hz, O·CH_2CH_3); *m/e* 355 and 353 (M^+) and 274 (M^+ − Br). All attempts at crystallisation failed.

2-*Bromo*-5-*hydroxy*-4-*methylbenzaldehyde* (18).—To a stirred solution of 3-hydroxy-4-methylbenzaldehyde (17)[13] (47 g) in chloroform (500 ml), bromine (55.4 g) was added dropwise during 30 min. The precipitate was collected and recrystallised from chloroform to give the bromide (18) as *needles* (60.0 g, 80%), m.p. 159—161° (Found: C, 44.9; H, 3.4. $C_8H_7BrO_2$ requires C, 44.6; H, 3.3%), $\nu_{max.}$ ($CHCl_3$) 1 680 cm^{-1} (C=O); δ($CDCl_3$) 10.25 (1 H, s, CHO), 7.35 (1 H, s, ArH), 7.37 (1 H, s, ArH), and 2.30 (3 H, s, ArMe).

2-*Bromo*-5-*methoxy*-4-*methylbenzaldehyde* (19). Aqueous 33% (w/w) potassium hydroxide (30 ml) and dimethyl sulphate (26 ml) were added to the bromide (18) (30 g) and the mixture was stirred vigorously. After 20 min, more aqueous 33% (w/w) potassium hydroxide (10 ml) and dimethyl sulphate (9 ml) were added. After vigorous stirring for 10 min, a further addition of aqueous 33% (w/w) potassium hydroxide (10 ml) and dimethyl sulphate (9 ml) was made and the mixture was stirred for 30 min. Aqueous 33% (w/w) potassium hydroxide (40 ml) was added again and stirring was continued for 1 h. Extraction with benzene followed by washing with water, drying (Na_2SO_4), and evaporation gave a powder, recrystallisation of which from ether–n-hexane afforded the aldehyde (19) as *needles* (30 g, 94%), m.p. 95—96° (Found: C, 47.3; H, 4.15. $C_9H_9BrO_2$ requires C, 47.2; H, 3.95%), $\nu_{max.}$ ($CHCl_3$) 1 680 cm^{-1} (C=O); δ($CDCl_3$) 10.25 (1 H, s, CHO), 7.35 (1 H, s, ArH), 7.40 (1 H, s, ArH), 3.90 (3 H, s, OMe), and 2.30 (3 H, s, ArMe).

2-*Bromo*-5-*methoxy*-4-*methylbenzyl Alcohol* (20).—To a solution of the aldehyde (19) (23 g) in methanol (500 ml), sodium borohydride (8 g) was added in small portions at 0—5 °C with stirring. Stirring was continued for 15 h at room temperature and the solvent was evaporated off. The residue was taken up in chloroform, washed with water, and dried (Na_2SO_4). Evaporation left a residue, recrystallisation of which from ether–n-hexane afforded the alcohol (20) as *needles* (23 g, 95%), m.p. 94° (Found: C, 46.85; H, 4.9. $C_9H_{11}BrO_2$ requires C, 46.75; H, 4.8%), $\nu_{max.}$ ($CHCl_3$) 3 580 cm^{-1} (OH); δ($CDCl_3$) 7.15 (1 H, s, ArH), 6.90 (1 H, s, ArH), 4.60 (2 H, s, CH_2·OH), 3.80 (3 H, s, OMe), and 2.15 (3 H, s, ArMe).

2,3-*Dihydro*-6,7-*dimethoxy*-1H-*pyrrolo*[1,2-a]*indole*-9-*carbonitrile* (21).—(*a*) A mixture of the nitrile (9) (323 mg), 50% sodium hydride (96 mg), and dry dimethylformamide (25 ml) was refluxed for 30 min in a current of nitrogen. After cooling, an excess of ammonium chloride was added, and the mixture was stirred for 20 min at room temperature. After addition of water, the mixture was extracted several times with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated and the residue was chromatographed on silica gel. Elution with benzene afforded a pale green solid which was recrystallised from ethanol to yield (21) as *needles* (170 mg, 70%), m.p. 203—203.5° (Found: C, 69.4; H, 5.6; N, 11.6. $C_{14}H_{14}N_2O_2$ requires C, 69.4; H, 5.85; N, 11.55%), $\nu_{max.}$ ($CHCl_3$) 2 210 cm^{-1} (CN); δ($CDCl_3$) 7.00 (1 H, s, ArH), 6.62 (1 H, s, ArH), 4.02 (2 H, t, *J* 7 Hz, 3-H_2), 3.85 (6 H, s, 2 × OMe), and 3.20—2.40 (4 H, m, 1- and 2-H_2), *m/e* 242 (M^+).

(*b*) A mixture of (9) (1.615 g), 50% sodium hydride (0.5 g), copper(I) bromide (150 mg), and dry dimethylformamide (100 ml) was stirred for 1 h at 80 °C in a current of nitrogen. After cooling, any excess of ammonium chloride was added and the mixture was stirred for 20 min at room temperature. Water was then added and the product was extracted several times with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a solid, recrystallisation of which from ethanol afforded needles (1.1 g, 90%), m.p. 203—203.5°, identical with the above sample of (21) (i.r., n.m.r., and t.l.c.).

(*c*) Potassium t-butoxide (1.12 g) was placed in a photoreactor equipped with a condenser cooled in solid CO_2–acetone. Dry liquid ammonia (1 l) was distilled into the apparatus and the nitrile (9) (323 mg) was added (with protection from moisture). The mixture was irradiated for 30 min with a high-pressure mercury lamp (400 W; Pyrex filter) with stirring in a current of nitrogen. Addition of an excess of ammonium chloride was followed by evaporation of ammonia, and the residue was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated and the residue was chromatographed on silica gel. Benzene eluted the product (21) (5 mg, 2%), m.p. 203—203.5° (from ethanol). Chloroform eluted a reddish solid, which was recrystallised from ethanol to afford α-(4,5-*dimethoxyphenyl*)-α-*pyrrolidin*-2-*ylideneacetonitrile* (12) as prisms (50 mg, 20%), m.p. 161—162° (Found: C, 68.8; H, 6.65; N, 11.5. $C_{14}H_{16}N_2O_2$ requires C, 68.85; H, 6.6; N, 11.45%), $\nu_{max.}$ ($CHCl_3$) 3 450 (NH) and 2 180 cm^{-1} (CN); δ($CDCl_3$) 6.84 (3 H, s, 3 × ArH), 5.50br

(1 H, s, NH), 3.86 (6 H, s, 2 × OMe), 3.50 (2 H, t, *J* 6 Hz, 5-H_2), 2.95 (2 H, t, *J* 6 Hz, 3-H_2), and 2.40—1.80 (2 H, m, 4-H_2); *m/e* 244 (M^+).

2,3-*Dihydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*[1,2-a]*indole*-9-*carbonitrile* (22).—A mixture of the pyrrolidine (10) (307 mg), 50% sodium hydride (50 mg), copper(I) bromide (50 mg), and dry dimethylformamide (20 ml) was heated for 1 h at 80 °C with stirring in a current of nitrogen. An excess of ammonium chloride was added, and the mixture was stirred for 20 min at room temperature. After addition of chloroform, the mixture was washed with water, dried (Na_2SO_4), and evaporated to give a solid, recrystallisation of which from ethanol afforded the nitrile (22) as needles (210 mg, 93%), m.p. 174—174.5° (lit.,[2] 173.5°); *m/e* 226 (M^+), identical [i.r. ($CHCl_3$), u.v. (MeOH), and n.m.r. ($CDCl_3$)] with the material described in the literature.[2]

Ethyl 2,3-*Dihydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*[1,2-a]-*indole*-9-*carboxylate* (23).—A mixture of the ester (16) (106 mg), 50% sodium hydride (15 mg), and copper(I) bromide (45 mg) in dry dimethylformamide (3 ml) was stirred for 1.5 h at room temperature in a current of nitrogen. An excess of ammonium chloride was added and the mixture was stirred for a further 20 min at the same temperature. After addition of chloroform, the organic layer was washed with water, dried (Na_2SO_4), and evaporated and the residue was chromatographed on silica gel in benzene to afford a solid; recrystallisation from ether gave (23) as *needles* (72 mg, 88%), m.p. 118—119° (Found: C, 70.15; H, 7.05; N, 5.05. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.15%), $\nu_{max.}$ ($CHCl_3$) 1 662 cm^{-1} (C=O); δ (CCl_4) 7.52 and 6.92 (each 1 H, each s, 2 × ArH), 4.35 (2 H, q, *J* 7 Hz, O·CH_2·CH_3), 3.92 (3 H, s, OMe), 2.34 (3 H, s, ArMe), and 1.40 (3 H, t, *J* 7 Hz, O·CH_2·CH_3); *m/e* 273 (M^+).

2,3-*Dihydro*-6,7-*dimethoxy*-1H-*pyrrolo*[1,2-a]*indole*-9-*carbaldehyde* (24).—A mixture of the nitrile (21) (97 mg), nickel–aluminium alloy (200 mg), and 50% aqueous acetic acid (20 ml) was heated under reflux for 2 h. After removal of the catalyst, the product was extracted with chloroform and the extract was washed with water, saturated aqueous sodium hydrogen carbonate, and saturated aqueous sodium chloride, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from ethanol gave the *aldehyde* (24) as needles (95 mg, 91%), m.p. 210—211° (Found: C, 68.5; H, 6.0; N, 5.55. $C_{14}H_{15}NO_3$ requires C, 68.55; H, 6.15; N, 5.7%), $\nu_{max.}$ ($CHCl_3$) 1 640 cm^{-1} (C=O); δ($CDCl_3$) 9.75 (1 H, s, CHO), 7.60 (1 H, s, ArH), 6.72 (1 H, s, ArH), and 3.85 (3 H, s, OMe), *m/e* 245 (M^+).

2,3-*Dihydro*-7-*methoxy*-6-*methyl*-1H-*pyrrolo*[1,2-a]*indole*-9-*carbaldehyde* (25).—Under the same conditions as above, the nitrile (22) (113 mg) afforded the aldehyde (25) as needles (100 mg, 89%), m.p. 187—188° (lit.,[2] 190°), *m/e* 229 (M^+), with i.r. ($CHCl_3$), u.v. (MeOH), and n.m.r. ($CDCl_3$) spectral data identical with those reported.[2]

2,3-*Dihydro*-7-*methoxy*-6-*methyl*-8-*nitro*-1H-*pyrrolo*[1,2-a]-*indole*-9-*carbaldehyde* (26).—To a solution of the aldehyde (25) (230 mg) in glacial acetic acid (10 ml), 70% nitric acid (0.2 ml) was added and the mixture was stirred for 3 min at room temperature. After addition of water, the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a powder, recrystallisation of which from chloroform–benzene gave the nitro-compound (26) (220 mg, 80%) as pale orange *prisms* (Found: C, 58.95; H, 5.0. $C_{14}H_{14}N_2O_4$,0.5H_2O requires C, 59.35; H, 5.35%), $\nu_{max.}$ ($CHCl_3$) 1 650 cm^{-1} (C=O); δ($CDCl_3$) 9.74 (1 H, s, CHO), 7.15 (1 H, s, ArH), 4.14 (2 H, t, *J* 7 Hz, 3-H_2), 3.88 (3 H, s, OMe), 3.55—2.55 (4 H, m, 1- and 2-H_2), 2.42 (3 H, s, ArMe), and 1.52 (1 H, s, 0.5H_2O, disappeared with D_2O); *m/e* 274 (M^+).

2,3-*Dihydro*-7-*methoxy*-6-*methyl*-5,8-*dioxo*-1H-*pyrrolo*[1,2-a]*indole*-9-*carbaldehyde* (28).—A mixture of the nitro-compound (26) (135 mg) and iron (230 mg) in 50% aqueous acetic acid (10 ml) was stirred for 2 h at 80—85 °C. After addition of water, the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give an amino-compound (27) as a solid, which was used without purification. To a solution of the amino-compound (27) in acetone (20 ml) and 0.167M-potassium dihydrogen phosphate (10 ml), potassium nitrosodisulphonate (0.8 g) and water (20 ml) were added. The mixture was stirred for 16 h at room temperature and then diluted with water and extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4), and evaporated to leave a gum which was chromatographed on alumina (Woelm, grade III). Benzene eluted an orange solid, recrystallisation of which from chloroform–n-hexane afforded (28) (35 mg, 28%) as orange needles, m.p. 222—224° (lit.,[1] 224—227°), showing i.r. and n.m.r. spectra consistent with those reported.[1]

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