Intramolecular Reaction of the Hydrazonyl Group with Formyl and Oxo Groups: Preparation of Pyrazolo[1,5-*a*]indoles and Related Pyrazolo Compounds[1]

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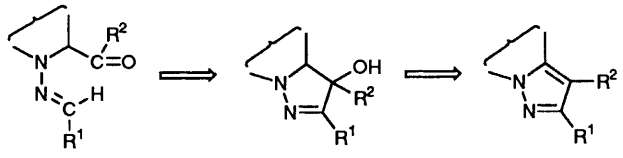
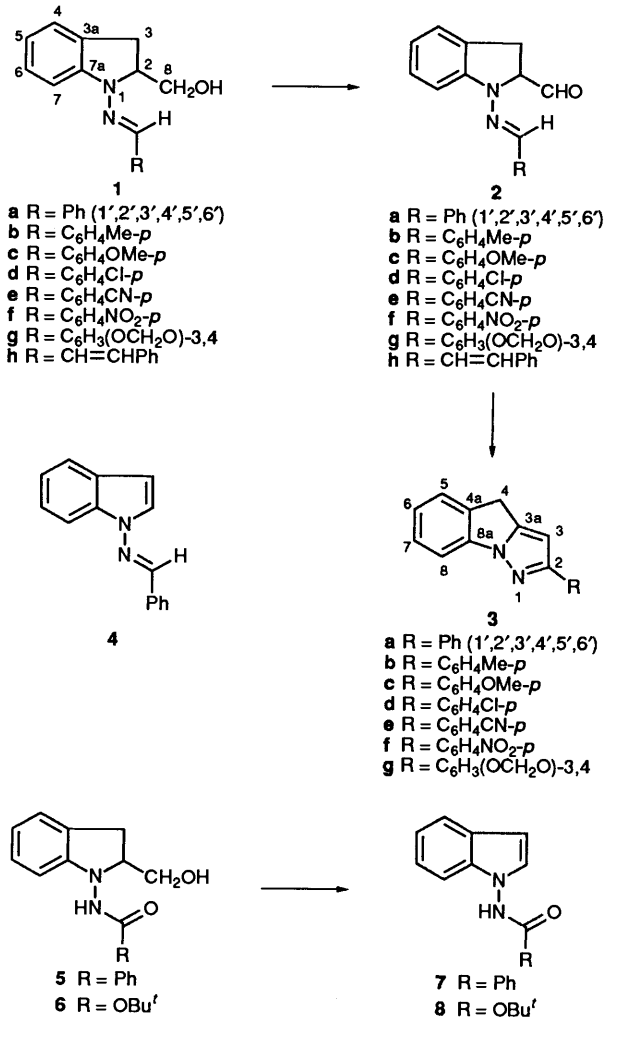
Lewis acid-catalysed intramolecular nucleophilic attack of a hydrazonyl group onto aldehyde and ketone groups gives pyrazoles and dihydropyrazoles. Pyrazolo[1,5-*a*]indoles and related pyrazolo compounds have also been prepared.

We are interested in the chemistry of pyrazolo[1,5-*a*]indoles, three isomers, 1*H*-, 3*H*- and 4*H*- of which are possible.[2] They can be regarded as 3-aza-isosters[3] of pyrrolo[1,2-*a*]indole, the basic skeleton of which occurs in the anticancer agents, the mitomycins.[4] In the expectation of the potential bioactivity of the pyrazolo[1,5-*a*]indoles, we needed a versatile method to construct this skeleton, there being no general method.[5] Inspired by the reductive coupling of an imine with an aldehyde reported by Roskamp and Pedersen,[6] we initiated a study of reductive coupling between hydrazonyl and formyl groups. This reaction when carried out in an intramolecular fashion, proceeded as shown in Scheme 1 to give an effective preparation of pyrazolo[1,5-*a*]indole derivatives; it was also useful for the preparation of a variety of pyrazole and dihydropyrazole derivatives. Here we present the full details of these findings.



Scheme 1

Initially, 1-amino-2-hydroxymethylindoline[7] was selected as a starting material, this masked hydrazine being condensed with aldehyde in 60% acetic acid to give the hydroxy hydrazones **1**; these upon oxidation yielded the formyl hydrazones **2**. Principally, two methods were employed for this oxidation. For aromatic aldehydes which have electron-donating group on the aromatic ring, Swern's procedure (dimethyl sulfoxide/oxalyl chloride/triethylamine/−78 °C)[8] was applied (method a). Whilst with an electron-attracting group present the Parikh–Doering method (dimethyl sulfoxide/sulfur trioxide–pyridine complex)[9] was used (method b). The latter method has the advantages of higher reactivity and the ability to dissolve hydrazones having an electron-withdrawing group present. Oxidation results are shown in Table 1. Hydrazones derived from aliphatic aldehydes such as pivalaldehyde or from electron-rich aromatic aldehydes such as *p*-dimethylaminobenzaldehyde and pyrrole-2-carbaldehyde were insufficiently stable to survive the conditions of oxidation. In the Swern oxidation of **1a**, the hydrazone **4** was obtained in 5% yield as a side-product; it was identified by comparison with an authentic specimen prepared by dehydrogenation of the hydrazone derived from 1-aminoindoline[10] and benzaldehyde. This elimination mechanism was rationalized in terms of Grob fragmentation[11] of the oxidation intermediate and a consideration of stereoelectronic requirements.[12] Further investigation of this elimination revealed that Parikh–Doering oxidation of 1-benzoylaminoindole **5** and both Swern and



Scheme 2

Parikh–Doering oxidation of **6** smoothly eliminated methanol from these alcohols to give as the sole products **7** and **8**. However, no general structural requirements for this elimination were found.* Product **8** was independently prepared by

* No elimination product was detected upon Swern oxidation of the following primary alcohols: 1-benzyl- and 1-benzoyl-2-hydroxymethylindoline, 1-benzoylamino-2-hydroxymethyl-1,2,3,4-tetrahydroquinoline and 2-benzoylamino-3-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline. When *N*-methylmaleimide was added in the Swern oxidation of **8**, no elimination of methanol was observed and a normal aldehyde product was obtained.

Table 1 Yields (%) of the products **1**, **2** and **3**

Compound	R	1	2	3
a	C_6H_5	92	92[a]	64
b	C_6H_4Me-*p*	95	81[a]	69
c	C_6H_4OMe-*p*	85	86[a]	73
d	C_6H_4Cl-*p*	92	90[b]	63
e	C_6H_4CN-*p*	85	96[b]	64
f	$C_6H_4NO_2$-*p*	83	93[b]	63
g	$C_6H_3OCH_2O$-3,4	87	85[a]	61

[a] Swern procedure. [b] Parikh–Doering procedure.

Table 2 Effects of Lewis acids in the transformation of **2a** into **9a**

Entry	Lewis acid	Equiv.	Solvent	*T*/°C[a]	*t*/h[b]	Yield (%)[c]
1	$SnCl_4$	1.2	CH_2Cl_2	0–5	1	97
2	BF_3·OEt_2	1.2	CH_2Cl_2	0–5	1	96
3	$TiCl_4$	1.2	CH_2Cl_2	RT[d]	6	35
4	$ZnBr_2$	1.5	Et_2O	RT[d]	48	30

[a] Reaction temp. [b] Reaction time. [c] Isolated yield. [d] RT = Room temp.

dehydrogenation of 1-*tert*-butoxycarbonylaminoindoline with dichlorodicyano-*p*-benzoquinone (DDQ). The structure of **7** was confirmed by a detailed comparison of its ^{1}H NMR spectrum with the spectra of the 1-aminoindole derivatives **4** and **8**.

The formylhydrazone **2a** when allowed to react with the niobium trichloride–dimethoxyethane complex ($NbCl_3$·DME, 1 equiv.) in tetrahydrofuran (THF) under reflux for 30 min gave the cyclization product **3a** (64%) as the sole product. In the ^{1}H NMR spectrum of the latter, the methylene signal appeared at δ 3.88 (s) and the 3-H at δ 6.59 with small long-range couplings (t, *J* 1.2 Hz); this is characteristic of a pyrazole 4-H.[13] Product **3a**[14] was identified by comparison with a specimen prepared by DDQ oxidation of 3,3a-dihydro-2-phenyl-4*H*-pyrazolo[1,5-*a*]indole.[5] The other formylhydrazones **2b–g** behaved similarly and the products **3b–g** were obtained in the yields listed in Table 1. This reaction was thus found to be quite useful for the construction of 4*H*-pyrazolo[1,5-*a*]indole derivatives.

Since it was difficult to explain the reaction path of this intramolecular coupling in terms of the reported mechanism,[6] this reaction was investigated in detail. The coupling reaction when conducted at lower temperature (room temp., *ca.* 25 °C), was slow and in addition to **3a** (30%) and recovered starting material (35%), a new polar product was obtained in (22%). High resolution mass spectroscopy established that the latter had the same molecular composition as the starting material. However, the absence of formyl and hydrazonyl groups were evident from its IR (no carbonyl absorption) and ^{1}H NMR (no hydrazonyl proton signal) spectra. These observations were consistent with an intramolecular addition reaction for the preparation of **9a**. The presence of an OH group was indicated at 3388 cm^{-1} in its IR spectrum and in its MS spectrum a peak due to the elimination of water from molecular ion was detected at *m*/*z* 232 ($M^+ - 18$). In its ^{1}H NMR spectrum an aromatic signal corresponding to 3-H of **3** was absent, instead a doublet (*J* 2.4 Hz) due to the secondary carbinol proton (3-H) was observed at δ 5.34; this coupled with an adjacent proton (3a-H) at δ 4.52 (td, *J* 2.4, 9.3 Hz). Methylene protons (4-H) was observed at δ 3.27 and 3.02 as a AB part of ABX type couplings (J_{AB} 16.1, J_{AX} 9.8 and J_{BX} 9.0). The X part of ABX type couplings was found to be the signal at δ 4.53 by decoupling experiments. When the X part of signals was saturated by irradiation, the doublet signals of the secondary carbinol proton (δ 5.34) became singlet and ABX-type signals for methylene protons changed into clean AB-type signals. These ^{1}H NMR

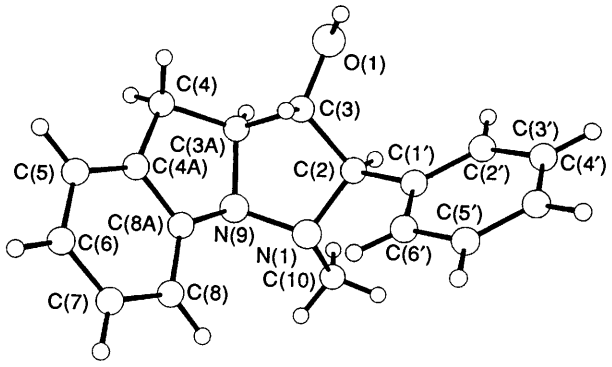
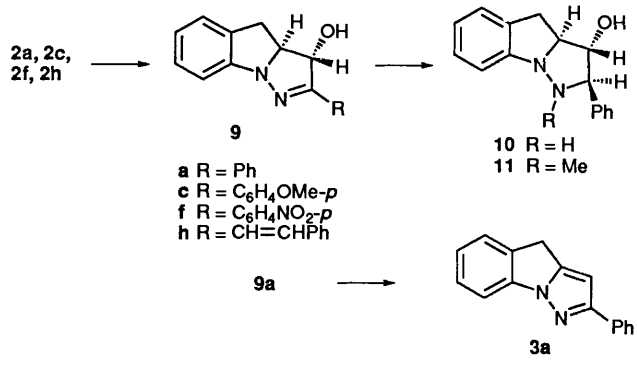


Fig. 1 Perspective view of the molecule **11** with the atom numbering scheme.

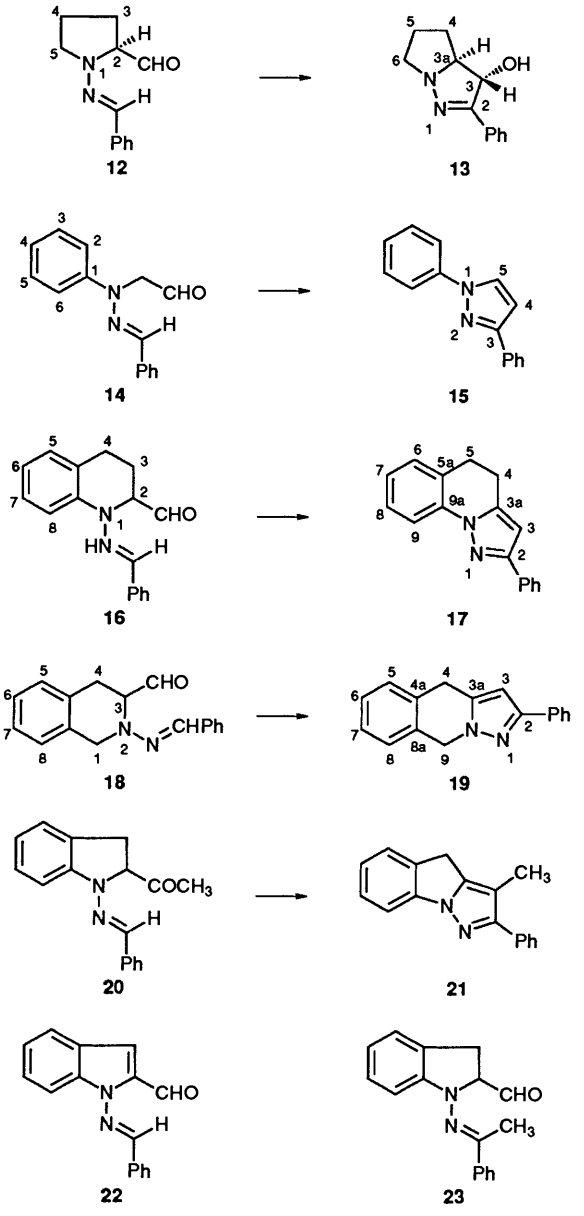


Scheme 3

observations were consistent with the relationship for the protons at C–3, C–3a and C–4 of **9a**. The structure **9a** was also supported by the comparison of its ^{1}H NMR spectrum with that of tetrahydropyrazolo[1,5-*a*]indole derivaties.[5] The relative configuration of 3-H and 3a-H of **9a** was deduced to be *trans* from their coupling constant (*J* 2.4 Hz)[15] and the nuclear Overhauser effect (5.4%) observed between the protons in the same face (δ 5.34 and 3.02 ppm). Definitive conclusion was derived from the X-ray analysis. Since a suitable crystal of **9a** was not available for crystallographic purposes, the following transformation was conducted. The imine **9a** was reduced with lithium aluminium hydride to give **10** which was then methylated with formaldehyde and sodium cyanoborohydride in the presence of acetic acid[16] to give **11**. This was a nicely crystalline compound suitable for single-crystal X-ray diffraction studies; such a study was, therefore, conducted. The result is shown in Fig. 1. As the configuration of C-3 and C-3a of **9a** is reflected in the product **11**, the stereochemistry of **9a** was confirmed. The relative configuration of 2-H indicates that the reduction of C=N bond was directed by an adjacent 3-OH group.

Treatment of the polar product **9a** with $NbCl_3$·DME in refluxing THF gave the dehydrated product **3a** (93%), *cis* elimination taking place smoothly because of stable pyrazole-ring formation. From these experiments, it is clear that initial formation of **9a** is involved in the transformation of **2a** into **3a**. In the transformation of **2a** into **9a**, it seemed possible that niobium trichloride functioned as a Lewis acid by facilitating the intramolecular nucleophilic attack of the hydrazonyl group[17] onto the formyl group; such an intermolecular reaction of this type has been reported for the preparation of pyrazole compounds.[18] We then looked at a range of Lewis acids to see which was most effective in inducing transformation of **2a** into **3a**; the results are summarized in Table 2. Although all the Lewis acids listed were effective, tin tetrachloride and boron

trifluoride–diethyl ether were found to be the best. The selection of solvent was also important for the reaction. With boron trifluoride in THF or benzene the reaction failed at room temperature; this contrasts with the same reaction in dichloromethane which was complete within 2 h at 0–5 °C. For reasons of convenience and reactivity, the reaction of **2a** with boron trifluoride–diethyl ether in dichloromethane was chosen as presenting optimal reaction conditions. Application of this reaction to the other formylhydrazones **2c**, **2f** and **2h**, gave the intramolecular addition products **9c**, **9f** and **9h** in good yields (Table 3). The dehydration of **9a** into **3a** was also effected either by warming with boron trifluoride–diethyl ether or under mesylating conditions (mesyl chloride and triethylamine). Although there are a number of methods available for the synthesis of 4*H*-pyrazolo[1,5-*a*]indole derivatives,[2,5] our method has the advantage of allowing the synthesis of a variety of 2-substituted 4*H*-pyrazolo[1,5-*a*]indoles and also providing easy access to 3-oxygenated 4*H*-pyrazolo[1,5-*a*]indole derivatives. In order to test the generality of this intramolecular reaction we applied it to other systems having a formyl or oxo group and a hydrazonyl group in the same molecule (Scheme 4).



Scheme 4

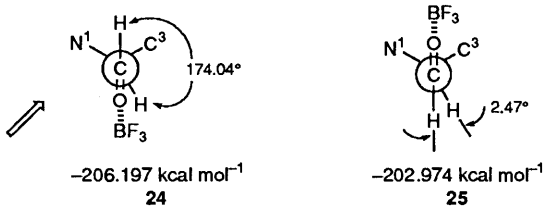
Table 3 Reactions of formyl- or oxo-hydrazones with BF_3·OEt_2

Entry	Compd.	Conditions[a]	Product	Yield (%)
1	**2a**	0–5/1	**9a**	96
2	**2c**	0–5/2	**9c**	83
3	**2f**	0–5/2	**9f**	79
4	**2h**	RT/3	**9h**	69
5	**12**	RT/9	**13**	45
6	**14**	0–5/0.5	**15**	87
7	**16**	0–5/< 0.5	**17**	90
8	**18**	RT/3	**19**	82
9	**20**	RT/16	**21**	84

[a] Reaction temp. (°C)/reaction time (h); RT = room temp. (*ca.* 25 °C).

Our results are summarized in Table 3. The starting materials for these reactions were prepared basically in the similar way as described for **2a** (see Experimental Section). Among the products listed in Table 3, the pyrazole **15**[19] and the pyrazolo[1,5-*b*]quinoline **17**[14] are known compounds. The pyrazoline **13** is a pyrolo[1,2-*b*]pyrazole derivative,[20] and was dehydrated with mesylating agents to give isowithasomnine.[21] Product **19** is a derivative of pyrazolo[1,5-*b*]isoquinoline.[22] Compounds **13** and **19** are novel and methods for their preparation are quite limited. From Tables 1 and 3, the following points are noteworthy. First, pyrazoline derivatives such as **9** and **13** were available only when their dehydrations were slow. Secondly, boron trifluoride–diethyl ether was found to be a more effective Lewis acid than niobium trichloride since it catalyzed the transformation of hydrazones **2h** and **20** into the cyclization products **9h** and **21** respectively, whilst the latter did not. As demonstrated in the transformation of **20** into **21**, the ketone carbonyl is also susceptible to intramolecular nucleophilic attack by a hydrazonyl group when a strong Lewis acid is used. In spite of the success of the intramolecular reaction of a hydrazonyl group with a formyl group a parallel intermolecular reaction failed. Thus, addition of benzaldehyde to a solution of 1-benzylideneaminoindoline and $NbCl_3$·DME gave recovery of hydrazone but consumption of benzaldehyde, probably because of the high susceptibility of the latter to $NbCl_3$·DME.[23] When boron trifluoride–diethyl ether was used instead of $NbCl_3$·DME, the reaction became complex and no product was isolated. These observations rule out the involvement of a reductive coupling and elimination mechanism in the transformation of **2a** into **9a**. Also, the hydrazones **22** and **23** failed to react in the presence of boron trifluoride–diethyl ether. Samarium iodide was reported to catalyze the reductive coupling of imine and ketone[24] but the reaction of **2a** in the presence of samarium iodide resulted in the formation of a intractable mixture.

The high stereoselectivities observed in the formation of compounds **9** and **13** were explained by conformational analysis of the hydrazones in which boron trifluoride complexes with a carbonyl group (Scheme 5). When boron trifluoride coordinates



Scheme 5

with the formyl oxygen atom, the complexed group favours conformer **24** over conformer **25** since it allows the largest group to rest in the least crowded position, *i.e.* a position furthest from the indoline nucleus. Conformer **24** also allows formation of a product in which 3-H and 3a-H are in a *trans* relationship. This

reasoning was supported by an AM1 calculation [25] in which the difference in heat of formation between conformers **24** and **25** was 3.23 kcal mol^{-1}.

Experimental

All m.p.s were determined with Yanaco micro melting point apparatus and are uncorrected. IR spectra (KBr pellet unless stated otherwise) were recorded on Perkin–Elmer FT-IR 1720 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on a JEOL JNM-FT 200 spectrophotometer (δ_H with 200 MHz and δ_C with 50.1 MHz) in $CDCl_3$ containing tetramethylsilane as an internal standard, unless noted otherwise. Low-resolution and high-resolution mass spectra were measured with Hitachi RMU-7MG spectrophotometer. The work-up procedure was as follows. The quenched reaction mixture was extracted thrice either with ether or with dichloromethane. The combined organic extracts were washed with saturated brine, dried over anhydrous magnesium sulfate, filtered and evaporated under reduced pressure to give a crude product which was purified by flash column chromatography (silica gel, ethyl acetate–light petroleum). Tetrahydrofuran (THF) was distilled from potassium/benzophenone ketyl under a nitrogen atmosphere. Dichloromethane and dimethyl sulfoxide (DMSO) were distilled from calcium hydride.

Preparation of Alcoholic Hydrazones **1**: *General Procedure.*— 1-Amino-2-hydroxymethylindoline [7] (2 mmol) was dissolved in 60% acetic acid (20 cm^3) and the solution was kept under a nitrogen atmosphere. The aldehyde (2–3 mmol) was added to the solution which was then stirred overnight at room temperature (RT). The reaction mixture was diluted with water and extracted with diethyl ether. The combined extracts were washed with 1 mol dm^{-3} aqueous sodium carbonate and upon work-up gave the following hydrazones.

1-*Benzylideneamino*-2-*hydroxymethylindoline* **1a**. This compound formed yellow crystals, m.p. 81.0–82.0 °C (from ethyl acetate–pentane) (Found: C, 76.0; H, 6.4; N, 11.09. Calc. for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.11%); ν_{max}/cm^{-1} 3407, 1609, 1588, 1561, 1481, 1465, 1447, 1403, 1217, 1032, 756 and 694; δ_H 1.76 (1 H, t, *J* 6.0, OH), 3.10 (1 H, dd, *J* 16.2, 4.3, 3-H), 3.43 (1 H, dd, *J* 16.2, 9.9, 3-H), 3.85 (2 H, m, 8-H_2), 4.51 (1 H, m, 2-H), 6.84 (1 H, m, 5-H), 7.10–7.40 (6 H, m, ArH), 7.66 (2 H, m, 2′,6′-H) and 7.72 (1 H, s, N=CH); δ_C 31.8 (C-3), 61.3 (C-2), 62.5 (C-8), 110.0 (C-7), 120.9 (C-5), 124.8 (C-4), 126.0 (C-2′,6′), 126.3 (C-3a), 127.8 (C-6), 128.0 (C-4′), 128.6 (C-3′,5′), 134.1 (N=C), 136.2 (C-1′) and 148.5 (C-7a); *m/z* 252 (M^+, 40%), 221 (100), 118 (75), 91 (25), 77 (23) and 61 (38) (Found: M^+, 252.1245. $C_{16}H_{16}N_2O$ requires 252.1261).

2-*Hydroxymethyl*-1-(4-*methylbenzylideneamino*)*indoline* **1b**. This compound formed yellow crystals, m.p. 84.0–85.0 °C (from ethyl acetate–pentane) (Found: C, 76.7; H, 6.8; N, 10.6. Calc. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52%); ν_{max}/cm^{-1} 3421, 3012, 2924, 1609, 1587, 1559, 1483, 1216, 1032, 754 and 669; δ_H 1.72 (1 H, br s, OH), 2.36 (3 H, s, CH_3), 3.10 (1 H, dd, *J* 16.4, 4.3, 3-H), 3.43 (1 H, dd, *J* 16.4, 10.3, 3-H), 3.86 (2 H, m, 8-H_2), 4.54 (1 H, m, 2-H), 6.84 (1 H, m, 5-H), 7.10–7.22 (5 H, m, ArH), 7.56 (2 H, m, 2′,6′-H) and 7.73 (1 H, s, N=CH); δ_C 21.3 (CH_3), 31.8 (C-3), 61.5 (C-2), 62.6 (C-8), 110.0 (C-7), 120.8 (C-5), 124.8 (C-4), 126.0 (C-2′,6′), 126.3 (C-3a), 127.8 (C-6), 129.3 (C-3′,5′), 133.4 (C-1′), 134.9 (C=N), 138.1 (C-4′) and 148.7 (C-7a); *m/z* 266 (M^+, 18%), 235 (100), 118 (98) and 91 (40) (Found: M^+, 266.1434. $C_{17}H_{18}N_2O$ requires 266.1418).

2-*Hydroxymethyl*-1-(4-*methoxybenzylideneamino*)*indoline* **1c**. This compound formed yellow crystals; m.p. 127.0–128.0 °C (from ethyl acetate–pentane) (Found: C, 72.05; H, 6.4; N, 9.8. Calc. for $C_{17}H_{18}N_2O_2$: C, 72.31; H, 6.42; N, 9.92%); ν_{max}/cm^{-1} 3558, 3005, 2961, 1600, 1562, 1485, 1460, 1252, 1157, 1108, 1027, 758 and 747; δ_H 1.90 (1 H, br s, OH), 3.08 (1 H, dd, *J* 16.4, 4.8, 3-H), 3.41 (1 H, dd, *J* 16.4, 9.8, 3-H), 3.82 (3 H, s, OCH_3), 3.85 (2 H, m, 8-H_2), 4.51 (1 H, m, 2-H), 6.82 (1 H, m, 5-H), 6.90 (2 H, m, 3′,5′-H), 7.09–7.18 (3 H, m, 4,6,7-H), 7.60 (2 H, m, 2′,6′-H) and 7.74 (1 H, s, N=CH); δ_C 31.8 (C-3), 55.3 (OCH_3), 61.7 (C-2), 62.7 (C-8), 110.0 (C-7), 114.2 (C-3′,5′), 120.7 (C-5), 124.8 (C-4), 126.3 (C-3a), 127.4 (C-2′,6′), 127.8(C-6), 129.0 (C-1′), 135.2 (N=C), 148.9 (C-7a) and 159.9 (C-4′); *m/z* 282 (M^+, 24%), 251 (100), 118 (89) and 91 (22).

1-(4-*Chlorobenzylideneamino*)-2-*hydroxymethylindoline* **1d**. This compound formed yellow crystals, m.p. 120.0–121.0 °C (from ethanol) (Found: C, 67.1; H, 5.25; N, 9.8. Calc. for $C_{16}H_{15}ClN_2O$: C, 61.01; H, 5.27; N, 9.77%); ν_{max}/cm^{-1} 3387, 3032, 2928, 1611, 1585, 1557, 1487, 1408, 1161, 1089 and 757; δ_H 1.77 (1 H, br s, OH), 3.09 (1 H, dd, *J* 16.6, 3.8, 3-H), 3.43 (1 H, dd, *J* 16.6, 10.1, 3-H), 3.85 (2 H, m, 8-H_2), 4.54 (1 H, m, 2-H), 6.86 (1 H, m, 5-H), 7.12 (1 H, d, *J* 7.3, 4-H), 7.19 (2 H, m, 6,7-H), 7.31 (2 H, m, 3′,5′-H), 7.58 (2 H, m, 2′,6′-H) and 7.66 (1 H, s, N=CH); δ_C 31.8 (C-3), 61.2 (C-2), 62.6 (C-8), 110.0 (C-7), 121.2 (C-5), 124.9 (C-4), 126.3 (C-3a), 127.0 (C-2′,6′), 127.9 (C-6), 128.8 (C-3′,5′), 132.3 (N=C), 133.5 (C-4′), 134.8 (C-1′) and 148.2 (C-7a); *m/z* 286 (M^+, 10%), 255 (100), 149 (15), 118 (97) and 91 (35).

1-(4-*Cyanobenzylideneamino*)-2-*hydroxymethylindoline* **1e**. This compound formed yellow crystals, m.p. 153.0–154.0 °C (from ethanol) (Found: C, 73.7; H, 5.4; N, 15.2. Calc. for $C_{17}H_{15}N_3O$: C, 73.62; H, 5.45; N, 15.15%); ν_{max}/cm^{-1} 3445, 2932, 2227, 1605, 1577, 1546, 1483, 1156 and 750; δ_H 1.77 (1 H, br s, OH), 3.11 (1 H, dd, *J* 16.3, 3.2, 3-H), 3.47 (1 H, dd, *J* 16.3, 9.8, 3-H), 3.86 (2 H, d, *J* 4.9, 8-H_2), 4.60 (1 H, m, 2-H), 6.90 (1 H, m, 5-H), 7.15 (1 H, d, *J* 7.3, 4-H), 7.22 (2 H, m, 6, 7-H), 7.59 (2 H, m, 3′,5′-H), 7.65 (1 H, s, N=CH) and 7.71 (2 H, m, 2′,6′-H); δ_C 31.8 (C-3), 61.0 (C-2), 62.3 (C-8), 110.1 (C-7), 110.3 (C-4′), 119.2 (CN), 121.9 (C-5), 125.1 (C-4′), 125.9 (C-2′,6′), 126.5 (C-3a), 128.0 (C-6), 130.3 (C=N), 132.4 (C-3′, 5′), 140.9 (C-1′) and 147.5 (C-7a); *m/z* 277 (M^+, 14%), 246 (100), 118 (29), 116 (50) and 91 (17).

2-*Hydroxymethyl*-1-(4-*nitrobenzylideneamino*)*indoline* **1f**. This compound formed yellow crystals, m.p. 166.0–167.0 °C (from ethanol) (Found: C, 64.65; H, 5.1; N, 14.2. Calc. for $C_{16}H_{15}N_3O_3$: C, 64.63; H, 5.08; N, 14.13%); ν_{max}/cm^{-1} 3349, 2933, 1597, 1553, 1507, 1483, 1336, 1108, 750 and 693; δ_H 1.63 (1 H, br s, OH), 3.13 (1 H, dd, *J* 16.5, 3.3, 3-H), 3.49 (1 H, dd, *J* 16.5, 9.8, 3-H), 3.89 (2 H, d, *J* 4.9, 8-H_2), 4.64 (1 H, m, 2-H), 6.93 (1 H, m, 5-H), 7.17 (1 H, d, *J* 7.3, 4-H), 7.26 (2 H, m, 6, 7-H), 7.71 (1 H, s, N=CH), 7.76 (2 H, m, 2′, 6′-H) and 8.21 (2 H, m, 3′, 5′-H); δ_C 31.8 (C-3), 61.1 (C-2), 62.4 (C-8), 110.3 (C-7), 122.1 (C-5), 124.1 (C-3′,5′), 125.1 (C-4), 125.8 (C-2′,6′), 126.7 (C-3a), 128.1 (C-6), 129.7 (C=N), 142.8 (C-1′), 146.7 (C-4′) and 147.3 (C-7a); *m/z* 297 (M^+, 25%), 266 (100), 220 (13), 149 (11), 118 (61), 116 (94) and 91 (33).

2-*Hydroxymethyl*-1-(3,4-*methylenedioxybenzylideneamino*)-*indoline* **1g**. This compound formed yellow crystals, m.p. 103.5–104.5 °C (from ethyl acetate–pentane) (Found: C, 68.9; H, 5.4; N, 9.4. Calc. for $C_{17}H_{16}N_2O_3$: C, 68.90; H, 5.44; N, 9.45%); ν_{max}/cm^{-1} 3587, 3533, 2608, 1608, 1599, 1566, 1501, 1479, 1465, 1446, 1297, 1186, 1120, 952, 889 and 758; δ_H 1.68 (1 H, br s, OH), 3.09 (1 H, dd, *J* 16.1, 4.5, 3-H), 3.42 (1 H, dd, *J* 16.1, 9.8, 3-H), 3.85 (2 H, m, 8-H_2), 4.51 (1 H, m, 2-H), 5.97 (2 H, s, OCH_2O), 6.79 (1 H, d, *J* 8.1, 5′-H), 6.83 (1 H, m, 5-H), 6.98 (1 H, dd, *J* 8.1, 1.5, 6′-H), 7.11 (1 H, d, *J* 7.3, 4-H), 7.17 (2 H, m, 6, 7-H), 7.33 (1 H, d, *J* 1.5, 2′-H) and 7.69 (1 H, s, N=CH); δ_C 31.8 (C-3), 61.5 (C-2), 62.7 (C-8), 101.1 (OCH_2O), 104.9 (C-2′), 108.2 (C-5′), 110.0 (C-7), 120.8 (C-5), 121.4 (C-6′), 124.8 (C-4), 126.2 (C-3a), 127.8 (C-6), 130.9 (C-1′), 134.4 (C=N), 147.8 (C-4′), 148.2 (C-3′) and 148.7 (C-7a); *m/z* 296 (M^+, 30%), 265 (57), 248 (25), 148 (35), 118 (100) and 91 (21) (Found: M^+, 296.1191. $C_{17}H_{16}N_2O_3$ requires 296.1159).

1-*Cinnamylideneamino*-2-*hydroxymethylindoline* **1h**. This compound formed yellow crystals, m.p. 121.0–5–122.5 °C (from ethyl acetate) (Found: C, 77.7; H, 6.6; N, 10.0. Calc. for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.07%); ν_{max}/cm^{-1} 3350, 3053, 2915, 1609, 1538, 1483, 1466, 1405, 1301, 1254, 1195, 1061, 963, 738 and 686; δ_H 1.78 (1 H, br s, OH), 3.07 (1 H, dd, *J* 16.2, 4.0, 3-H), 3.41 (1 H, dd, *J* 16.2, 9.9, 3-H), 3.82 (2 H, m, 8-H_2), 4.50 (1 H, m, 2-H), 6.69 (1 H, d, *J* 16.1, N=CHCH=C*H*Ph), 6.83 (1 H, td, *J* 7.5, 1.5, 5-H), 7.01 (1 H, dd, *J* 16.1, 8.9, N=CHC*H*=CHPh), 7.10 (1 H, d, *J* 7.5, 7-H), 7.15 (1 H, d, *J* 7.5, 4-H), 7.18–7.37 (4 H, m, ArH), 7.44 (2 H, m, 2′, 6′-H) and 7.62 (1 H, d, *J* 8.9, N=CH); δ_C 31.7 (C-3), 61.3 (C-2), 62.5 (C-8), 109.8 (C-7), 121.0 (C-5), 124.8 (C-4), 126.4 (C-2′, 6′, 3a), 127.1 (N=CHC*H*=CHPh), 127.8 (C-6), 127.9 (C-4′), 128.7 (C-3′, 5′), 133.5 (N=CHCH=*C*HPh), 136.9 (C=N), 137.0 (C-1′) and 148.0 (C-7a); *m*/*z* 278 (M^+, 26%), 247 (100), 130 (16), 118 (54), 103 (32), 91 (25) and 77 (16) (Found: M^+, 278.1424. $C_{18}H_{18}N_2O$ requires 278.1418).

Swern Oxidation of **1a**: *Method a*.—Under dry nitrogen, anhydrous DMSO (1.78 cm^3, 25.1 mmol) was added to a solution of oxalyl chloride (1.05 cm^3, 12.1 mmol) and dry dichloromethane (30 cm^3) at −60 °C and the solution was stirred for 10 min at the same temperature. Into this reagent, a solution of the alcohol **1a** (2.64 g, 10.5 mmol) in dry dichloromethane (10 cm^3) was introduced and the mixture was stirred for 20 min at −60 °C. Triethylamine (7.30 cm^3, 52.4 mmol) was then added to the reaction mixture which, after being set aside for 30 min at the same temperature, was quenched with water. The solution was extracted with dichloromethane and the combined extracts were worked-up to give **2a** (2.42 g, 92%) and **4** (116 mg, 5%). A similar procedure was employed for the preparation of the other formylhydrazones **2**.

1-*Benzylideneamino*-2-*formylindoline* **2a**. This compound formed yellow crystals, m.p. 135.0–136.0 °C (from ethyl acetate–pentane) (Found: C, 76.7; H, 5.5; N, 11.2. Calc. for $C_{16}H_{14}N_2O$: C, 76.77; H, 5.64; N, 11.20%); ν_{max}/cm^{-1} 2836, 1725, 1608, 1587, 1562, 1481, 1405, 1192, 762, 749 and 697; δ_H 3.22 (1 H, dd, *J* 16.7, 6.0, 3-H), 3.57 (1 H, dd, *J* 16.7, 10.8, 3-H), 4.74 (1 H, m, 2-H), 6.89 (1 H, td, *J* 7.3, 1.6, 5-H), 7.13 (1 H, d, *J* 7.3, 4-H), 7.20–7.40 (5 H, m, ArH), 7.42 (1 H, s, N=CH), 7.65 (2 H, m, 2′,6′-H) and 9.69 (1 H, d, *J* 4.1, CHO); δ_C 30.2 (C-3), 67.9 (C-2), 110.1 (C-7), 121.3 (C-5), 124.4 (C-3a), 124.7 (C-4), 126.2 (C-2′, 6′), 128.5 (C-4′, 6), 128.6 (C-3′, 5′), 134.5 (C=N), 135.4 (C-1′), 148.2 (C-7a) and 199.4 (CHO); *m*/*z* 250 (M^+, 10%), 221 (100), 118 (60), 91 (28) and 77 (33) (Found: M^+, 250.1072. $C_{16}H_{14}N_2O$ requires 250.1105).

1-*Benzylideneaminoindole* **4**. This formed pale yellow crystals, m.p. 104.0–105.0 °C (from benzene) (Found: C, 82.05; H, 5.2; N, 12.8. Calc. for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72%), ν_{max}/cm^{-1} 3132, 3058, 1615, 1605, 1506, 1475, 1455, 1305, 1294, 1208, 937, 744, 716 and 693; δ_H 6.66 (1 H, d, *J* 3.7, 3-H), 7.17 (1 H, td, *J* 7.6, 1.3, 5-H), 7.31 (1 H, td, *J* 7.6, 1.0, 6-H), 7.40–7.50 (3 H, m, ArH), 7.59 (1 H, d, *J* 7.6, 4-H), 7.67 (1 H, d, *J* 3.7, 2-H), 7.85 (3 H, m, ArH) and 8.38 (1 H, s, N=CH); δ_C 104.2 (C-3), 110.7 (C-7), 116.6 (C-2), 120.9 (C-4), 121.1 (C-5), 123.2 (C-6), 126.8 (C-3a), 127.4 (C-2′, 6′), 128.8 (C-3′, 5′), 130.2 (C-4′), 134.2 (C-1′), 136.4 (C-7a) and 144.2 (C=N); *m*/*z* 220 (M^+, 100%), 117 (47), 89 (33) and 77 (18). DDQ oxidation (1.024 g, 4.5 mmol) of the hydrazone (888 mg, 4.0 mmol) derived from 1-aminoindoline[10] and benzaldehyde in THF (15 cm^3) at RT for 3 h yielded the crystalline product **4** (712 mg, 81%).

2-*Formyl*-1-(4-*methylbenzylideneamino*)*indoline* **2b**. This formed yellow crystals, m.p. 129.0–130.5 °C (from dichloromethane–diisopropyl ether) (Found: C, 77.1; H, 6.0; N, 10.5. Calc. for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.60%); ν_{max}/cm^{-1} 3052, 2943, 2836, 1724, 1610, 1588, 1484, 1464, 1403, 1378, 1297, 1226, 1187, 1164, 862, 817 and 750; δ_H 2.36 (3 H, s, CH_3), 3.21 (1 H, dd, *J* 16.5, 6.4, 3-H), 3.55 (1 H, dd, *J* 16.5, 10.8, 3-H), 4.71 (1 H, m, 2-H), 6.87 (1 H, td, *J* 7.6, 1.6, 5-H), 7.12 (1 H, d, *J* 7.6, 4-H), 7.16 (2 H, m, 3′, 5′-H), 7.25 (1 H, d, *J* 7.6, 7-H), 7.27 (1 H, t, *J* 7.6, 6-H), 7.41 (1 H, s, N=CH), 7.54 (2 H, m, 2′, 6′-H) and 9.69 (1 H, d, *J* 4.1, CHO); δ_C 21.3 (CH_3), 30.3 (C-3), 68.1 (C-2), 110.1 (C-7), 121.2 (C-5), 124.4 (C-3a), 124.7 (C-4), 126.3 (C-2′, 6′), 128.5 (C-6), 129.3 (C-3′, 5′), 132.8 (C-1′), 135.0 (C=N), 138.6 (C-4′), 148.4 (C-7a) and 199.6 (CHO); *m*/*z* 264 (M^+, 10%), 235 (100), 218 (11), 118 (95) and 91 (52) (Found: M^+, 264.1256. $C_{17}H_{16}N_2O$ requires 264.1261).

2-*Formyl*-1-(4-*methoxybenzylideneamino*)*indoline* **2c**. This formed yellow crystals, m.p. 130.5–131.5 °C (from dichloromethane–diisopropyl ether) (Found: C, 72.7; H, 5.7; N, 9.9. Calc. for $C_{17}H_{16}N_2O_2$: C, 72.83; H, 5.75; N, 10.00%); ν_{max}/cm^{-1} 3025, 2937, 2844, 1729, 1607, 1563, 1514, 1484, 1441, 1418, 1402, 1294, 1246, 1214, 1167, 1107, 1024, 891, 833 and 749; δ_H 3.20 (1 H, dd, *J* 16.5, 6.4, 3-H), 3.55 (1 H, dd, *J* 16.5, 10.8, 3-H), 3.82 (3 H, s, OCH_3), 4.70 (1 H, m, 2-H), 6.82–6.94 (3 H, m, 3′,5′,5-H), 7.12 (1 H, d, *J* 7.3, 4-H), 7.18–7.30 (2 H, m, 6, 7-H), 7.41 (1 H, s, N=CH), 7.59 (2 H, m, 2′,6′-H) and 9.61 (1 H, d, *J* 3.8, CHO); δ_C 30.3 (C-3), 55.3 (OCH_3), 68.3 (C-2), 110.1 (C-7), 114.1 (C-3′,5′), 121.1 (C-5), 124.4 (C-3a), 124.7 (C-4), 127.7 (C-2′,6′), 128.4 (C-1′), 128.5 (C-6), 135.0 (C=N), 148.6 (C-7a), 160.2 (C-4′) and 199.8 (CHO); *m*/*z* 280 (M^+, 9%), 251 (77), 134 (43), 118 (100), 107 (17), 91 (33) and 77 (27) (Found: M^+, 280.1205. $C_{17}H_{16}N_2O_2$ requires 280.1210).

2-*Formyl*-1-(3,4-*methylenedioxybenzylideneamino*)*indoline* **2g**. This formed yellow crystals, m.p. 170.0–171.0 °C (from dichloromethane–diisopropyl ether) (Found: C, 69.45; H, 4.8; N, 9.5. Calc. for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.79; N, 9.52%); ν_{max}/cm^{-1} 3058, 2915, 2845, 1714, 1609, 1599, 1576, 1504, 1480, 1450, 1407, 1296, 1257, 1188, 1034, 934, 887 and 752; δ_H 3.21 (1 H, dd, *J* 16.8, 6.4, 3-H), 3.56 (1 H, dd, *J* 16.8, 11.3, 3-H), 4.69 (1 H, m, 2-H), 5.98 (2 H, s, OCH_2O), 6.78 (1 H, d, *J* 7.9, 5′-H), 6.88 (1 H, m, 5-H), 6.95 (1 H, dd, *J* 7.9, 1.6, 6′-H), 7.13 (1 H, d, *J* 7.3, 4-H), 7.19–7.29 (2 H, m, 6, 7-H), 7.33 (1 H, d, *J* 1.6, 2′-H), 7.35 (1 H, s, N=CH) and 9.68 (1 H, d, *J* 4.1, CHO); δ_C 30.3 (C-3), 68.2 (C-2), 101.2 (OCH_2O), 105.1 (C-2′), 108.2 (C-5′), 110.1 (C-7), 121.2 (C-5), 121.8 (C-6′), 124.4 (C-3a), 124.7 (C-4), 128.5 (C-6), 130.2 (C-1′), 134.7 (C=N), 148.2 (C-3′, 4′), 148.4 (C-7a) and 199.5 (CHO); *m*/*z* 294 (M^+, 12%), 265 (40), 248 (12), 148 (32), 118 (100) and 91 (28) (Found: M^+, 294.0993. $C_{17}H_{14}N_2O_3$ requires 294.1003).

1-*Cinnamylideneamino*-2-*formylindoline* **2h**. This formed yellow crystals, m.p. 160.0–161 °C (from ethyl acetate) (Found: C, 78.35; H, 5.6; N, 10.1. Calc. for $C_{18}H_{16}N_2O$: C, 78.23; H, 5.84; N, 10.14%), ν_{max}/cm^{-1} 3030, 2986, 2844, 1722, 1608, 1556, 1485, 1464, 1403, 1294, 1194, 1165, 910, 749 and 691; δ_H 3.20 (1 H, dd, *J* 16.7, 5.9, 3-H), 3.54 (1 H, dd, *J* 16.7, 10.9, 3-H), 4.68 (1 H, m, 2-H), 6.69 (1 H, d, *J* 15.9, N=CHCH=C*H*Ph), 6.88 (1 H, m, 5-H), 6.99 (1 H, dd, *J* 15.9, 8.9, N=CHC*H*=CHPh), 7.12 (1 H, dd, *J* 7.3, 0.5, 4-H), 7.15–7.37 (6 H, m, ArH and N=CH), 7.44 (2 H, m, 2′, 6′-H) and 9.65 (1 H, d, *J* 4.0, CHO); δ_C 30.1 (C-3), 67.9 (C-2), 109.9 (C-7), 121.3 (C-5), 124.5 (C-3a), 124.7 (C-4), 126.3 (N=CH*C*H=CHPh), 126.5 (C-2′, 6′), 128.0 (C-4′), 128.6 (C-6), 128.7 (C-3′, 5′), 134.8 (N=CHCH=*C*HPh), 136.7 (C-1′), 137.2 (C=N), 147.9 (C-7a) and 199.1 (CHO); *m*/*z* 276 (M^+, 14%), 247 (100), 118 (48), 103 (34), 91 (23) and 77 (22).

Parikh–Doering Oxidation of **1d**: *Method b*.—A solution of sulfur trioxide–pyridine complex (4.85 g, 30.5 mmol) in anhydrous DMSO (15 cm^3) was added to a solution of the alcohol **1d** (2.91 g, 10.2 mmol) and dry triethylamine (8.4 cm^3, 60.9 mmol) in anhydrous DMSO (10 cm^3) under an atmosphere of nitrogen. The resulting solution was stirred for 15 min at RT. The reaction mixture was poured into ice–water (100 cm^3) and work-up of the solution gave **2d** (2.61 g). Other formylhydrazones were prepared similarly.

1-(4-*Chlorobenzylideneamino*)-2-*formylindoline* **2d**. This formed pale yellow crystals, m.p. 136.0–137.0 °C (from ethyl

acetate) (Found: C, 67.7; H, 4.6; N, 9.8. Calc. for $C_{16}H_{13}ClN_2O$: C, 67.49; H, 4.60; N, 9.84%); ν_{max}/cm^{-1} 3059, 2915, 2838, 1720, 1611, 1585, 1484, 1469, 1408, 1295, 1190, 1092, 879, 823 and 754; δ_H 3.23 (1 H, dd, *J* 16.8, 6.2, 3-H), 3.58 (1 H, dd, *J* 16.8, 11.1, 3-H), 4.73 (1 H, m, 2-H), 6.90 (1 H, m, 5-H), 7.14 (1 H, d, *J* 7.3, 4-H), 7.25 (2 H, m, 6, 7-H), 7.32 (2 H, m, 3', 5'-H), 7.34 (1 H, s, N=CH), 7.57 (2 H, m, 2', 6'-H) and 9.67 (1 H, d, *J* 4.1, CHO); δ_C 30.2 (C-3), 67.9 (C-2), 110.1 (C-7), 121.6 (C-5), 124.4 (C-3a), 124.8 (C-4), 127.3 (C-2', 6'), 128.6 (C-6), 128.8 (C-3', 5'), 133.1 (C=N), 134.1 (C-1', 4') 148.0 (C-7a) and 198.9 (CHO); *m*/*z* 286 (M^+ +2, 2.4%), 284 (M^+, 8), 257 (32), 255 (100), 118 (97) and 91 (41) (Found: M^+, 284.0726. $C_{16}H_{13}ClN_2O$ requires 284.0715).

1-(4-*Cyanobenzylideneamino*)-2-*formylindole* **2e**. This formed pale yellow needles, m.p. 171.5–173.0 °C (ethyl acetate) (Found: C, 74.3; H, 4.7; N, 15.25. Calc. for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26%); ν_{max}/cm^{-1} 3533, 2961, 2850, 2219, 1723, 1605, 1582, 1546, 1484, 1465, 1402, 1386, 1295, 1190, 1171, 886, 866, 824 and 747; δ_H 3.28 (1 H, dd, *J* 16.8, 5.4, 3-H), 3.62 (1 H, dd, *J* 16.8, 11.3, 3-H), 4.80 (1 H, m, 2-H), 6.94 (1 H, m, 5-H), 7.17 (1 H, d, *J* 7.3, 4-H), 7.27 (2 H, m, 6, 7-H), 7.34 (1 H, s, N=CH), 7.62 (2 H, m, 3', 5'-H), 7.72 (2 H, m, 2', 6'-H), and 9.66 (1 H, d, *J* 3.8, CHO); δ_C 30.1 (C-3), 67.7 (C-2), 110.3 (C-7), 111.1 (C-4'), 119.0 (CN), 122.2 (C-5), 124.7 (C-3a), 125.0 (C-4), 126.3 (C-2', 6'), 128.7 (C-6), 131.4 (C=N), 132.4 (C-3', 5'), 140.0 (C-1'), 147.3 (C-7a) and 197.9 (CHO); *m*/*z* 275 (M^+, 8%), 246 (100), 116 (75) and 91 (32) (Found: M^+, 275.1057. $C_{17}H_{13}N_3O$ requires 275.1057).

2-*Formyl*-1-(4-*nitrobenzylideneaminoindoline* **2f**. This formed red crystals, m.p. 177.0–178.0 °C (from ethyl acetate) (Found: C, 64.9; H, 4.6; N, 14.2. Calc. for $C_{16}H_{13}N_3O_3$: C, 65.08; H, 4.44; N, 14.23%); ν_{max}/cm^{-1} 3038, 2838, 1729, 1609, 1594, 1554, 1505, 1479, 1465, 1417, 1387, 1338, 1298, 1217, 1192, 1170, 1105, 894, 841, 749 and 693; δ_H 3.30 (1 H, dd, *J* 16.7, 5.6, 3-H), 3.65 (1 H, dd, *J* 16.7, 11.0, 3-H), 4.84 (1 H, m, 2-H), 6.97 (1 H, td, *J* 7.0, 1.6, 5-H), 7.19 (1 H, d, *J* 7.0, 4-H), 7.25–7.37 (2 H, m, 6, 7-H), 7.38 (1 H, s, N=CH), 7.77 (2 H, m, 2', 6'-H), 8.21 (2 H, m, 3', 5'-H) and 9.67 (1 H, d, *J* 3.5, CHO); δ_C 30.0 (C-3), 67.6 (C-2), 110.3 (C-7), 122.4 (C-5), 124.1 (C-3', 5'), 124.8 (C-3a), 125.0 (C-4), 126.3 (C-2', 6'), 128.8 (C-6), 130.9 (C=N), 141.8 (C-1'), 147.1 (C-7a, 4') and 197.6 (CHO); *m*/*z* 295 (M^+, 8%), 266 (70), 220 (12), 145 (9), 116 (100), 91 (46) and 84 (38) (Found: M^+, 295.0978. $C_{16}H_{13}N_3O_3$ requires 295.0956).

1-*Benzoylamino*-2-*hydroxymethylindoline* **5**.—1-Amino-2-hydroxymethylindoline[7] (1.599 g, 9.7 mmol) dissolved in a mixture of dichloromethane (40 cm^3) and water (2 cm^3) was treated with benzoyl chloride (1.13 cm^3, 9.7 mmol) and potassium carbonate (2.000 g, 14.6 mmol) at −5 to 0 °C for 2 h, then at RT for 2 h. 1 mol dm^{-3} Sodium hydroxide (20 cm^3) was added to the reaction mixture which was then vigorously stirred for an additional 2 h. The organic phase was separated and the aqueous phase was extracted with dichloromethane. Work-up of the combined organic extracts gave **5** (2.508 g, 95%), m.p. 170.5–172.0 °C (from dichloromethane–diethyl ether) (Found: C, 71.6; H, 5.8; N, 10.4. Calc. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44%); ν_{max}/cm^{-1} 3498, 3438, 3272, 3051, 2951, 2865, 1635, 1609, 1600, 1578, 1524, 1488, 1294, 1091, 757, 716 and 691; δ_H([$^2H_6$]$_6$-DMSO) 2.84 (1 H, dd, *J* 15.6, 10.6, 3-H), 3.14 (1 H, dd, *J* 15.6, 9.1, 3-H), 3.64 (2 H, m, 8-H_2), 3.95 (1 H, m, 2-H), 4.65 (1 H, t, *J* 5.9, OH), 6.53 (1 H, d, *J* 7.6, 7-H), 6.75 (1 H, t, *J* 7.6, 5-H), 7.04 (1 H, t, *J* 7.6, 6-H), 7.11 (1 H, d, *J* 7.6, 4-H), 7.44–7.64 (3 H, m, ArH), 7.91 (2 H, m, 2', 6'-H), 10.36 (1 H, s, NH); δ_C([$^2H_6$]-DMSO) 30.9 (C-3), 61.8 (C-8), 68.4 (C-2), 108.6 (C-7), 119.7 (C-5), 124.4 (C-4), 126.9 (C-4), 126.9 (C-6, 3a), 127.3 (C-2', 6'), 128.4 (C-3', 5'), 131.7 (C-4'), 132.8 (C-1'), 151.4 (C-7a) and 166.3 (C=O); *m*/*z* 268 (M^+, 15%), 237 (80), 163 (41), 133 (42), 116 (46), 105 (100), 91 (11) and 77 (45) (Found: M^+, 268.1222. $C_{16}H_{16}N_2O_2$ requires 268.1211).

1-tert-*Butoxycarbonylamino*-2-*hydroxymethylindoline* **6**.—A mixture of 1-amino-2-hydroxymethylindoline[7] (2.000 g, 12.2 mmol), di-*tert*-butyl dicarbonate (3.190 g, 14.6 mmol) and sodium hydrogen carbonate (2.046 g, 24.3 mmol) in dioxane (40 cm^3) containing water (4 cm^3) was treated as described for **5** to give **6** (2.336 g, 72%), m.p. 113.5–114.5 °C (from ethyl acetate) (Found: C, 63.5; H, 7.9; N, 10.6. Calc. for $C_{14}H_{20}N_2O_3$: C, 63.61; H, 7.63; N; 10.60%); ν_{max}/cm^{-1} 3510, 3281, 3050, 2985, 1703, 1688, 1515, 1278, 1257, 1157 and 758; δ_H 1.51 (9 H, s, Bu^t), 2.78 (1 H, br s, OH), 2.96 (1 H, dd, *J* 15.4, 8.9, 3-H), 3.15 (1 H, dd, *J* 15.4, 10.7, 3-H), 3.56 (1 H, m, 2-H), 3.58 and 3.65 (2 H, m, 8-H_2), 6.04 (1 H, br s, NH), 6.68 (1 H, d, *J* 7.8, 7-H), 6.85 (1 H, t, *J* 7.5, 5-H) and 7.06–7.18 (2 H, m, 4, 6-H); δ_C 28.2 [C(*C*H$_3$)$_3$], 29.7 (C-3), 60.4 (C-8), 71.2 (C-2), 81.8 [*C*(CH$_3$)$_3$], 109.2 (C-7), 121.3 (C-5), 124.9 (C-4), 127.4 (C-6), 150.6 (C-7a) and 156.6 (C=O); *m*/*z* 264 (M^+, 11%), 208 (42), 177 (74), 163 (41), 133 (89), 117 (32) and 57 (100).

1-*Benzoylaminoindole* **7**.—The oxidation of compound **5** (50 mg, 0.19 mmol) with sulfur trioxide–pyridine complex (90 mg, 0.56 mmol) and triethylamine (0.16 cm^3, 1.11 mmol) in DMSO (4 cm^3) described for method b and work-up yielded **7** (25 mg, 57%), m.p. 182–183.0 °C (from ethyl acetate) (Found: C, 76.3; H, 5.05; N, 11.9. Calc. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86%); ν_{max}/cm^{-1} 3215, 3056, 1666, 1535, 1283, 720 and 692; δ_H 6.55 (1 H, d, *J* 3.3, 3-H), 7.06 (1 H, d, *J* 3.3, 2-H), 7.10–7.27 (3 H, m, 5,6,7-H), 7.45 (2 H, m, 3', 5'-H), 7.60 (1 H, t, *J* 8.1, 4'-H), 7.63 (1 H, d, *J* 7.1, 4-H), 7.84 (2 H, m, 2', 6'-H) and 8.77 (1 H, s, NH); δ_C 101.9 (C-3), 108.6 (C-7), 120.8 (C-5), 121.3 (C-4), 122.9 (C-6), 126.6 (C-3a), 127.5 (C-2', 6'), 128.3 (C-2), 128.9 (C-3', 5'), 132.7 (C-1', 4'), 136.1 (C-7a) and 166.8 (C=O); *m*/*z* 236 (M^+, 18%), 105 (100) and 77 (45).

1-*tert*-*Butoxycarbonylaminoindole* **8**.—The alcohol **6** (264 mg, 1 mmol) in dry dichloromethane (5 cm^3) was added to a solution of oxalyl chloride (0.1 cm^3, 1.1 mmol) and DMSO (0.17 cm^3 187 mg, 2.4 mmol) in dichloromethane (15 cm^3) at −78 °C and the mixture was stirred for a short period. Triethylamine (0.7 cm^3, 5 mmol) was then added to the mixture and the reaction was conducted as described for method a to give **8** (195 mg, 84%) as white crystals, m.p. 113.5–115.0 °C (from benzene) (Found: C, 67.2; H, 7.0; N, 12.0. Calc. for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06%); ν_{max}/cm^{-1} 3280, 3057, 2980, 1727, 1707, 1526, 1275, 1229, 1165 and 743; δ_H 1.47 (9 H, s, Bu^t), 6.48 (1 H, d, *J* 3.4, 3-H), 7.05–7.32 (5 H, m, 2,5,6,7-H and N-H) and 7.59 (1 H, d, *J* 7.6, 4-H); δ_C 28.1 [C(*C*H$_3$)$_3$], 82.4[*C*(CH$_3$)$_3$], 101.3 (C-3), 108.4 (C-7), 120.6 (C-5), 121.2 (C-4), 122.7 (C-6), 126.5 (C-3a), 128.7 (C-2), 136.4 (C-7) and 154.4 (C=O); *m*/*z* 232 (M^+, 12%), 176 (18), 132 (20), 131 (14) and 57 (100). Oxidation of **6** (1.320 g, 5 mmol) with a mixture of sulfur trioxide–pyridine complex (2.38 g, 15 mmol), DMSO (25 cm^3) and triethylamine (4.18 cm^3, 30 mmol) as described for method b afforded **8** (748 mg, 64%) as the sole product. Also, product **8** (1.356 g, 89%) was prepared by DDQ oxidation (1.652 g, 7.2 mmol) in THF at 0 °C for 1 h from 1-*tert*-butoxycarbonylaminoindoline (1.537 g, 6.6 mmol), m.p. 59.0–60.0 °C (from ethyl acetate–pentane) (Found: C, 66.8; H, 7.93; N, 11.99. Calc. for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96%); ν_{max}/cm^{-1} 3253, 3223, 3025, 1720, 1698, 1612, 1529, 1368, 1254, 1168 and 753; δ_H 1.47 [9 H, s, C(CH$_3$)$_3$], 2.98 (2 H, t, *J* 8.1, 3-H_2), 3.57 (2 H, t, *J* 8.1, 2-H_2), 6.04 (1 H, br s, NH), 6.66 (1 H, d, *J* 7.3, 7-H), 6.82 (1 H, td, *J* 7.4, 1.0, 5-H) and 7.06–7.16 (2 H, m, 4,6-H); δ_C27.7 (C-3), 28.3 [C(*C*H$_3$)$_3$], 56.2 (C-2), 80.9 [*C*(CH$_3$)$_3$], 109.3 (C-7), 120.7 (C-5), 124.8 (C-4), 127.3 (C-6), 127.7 (C-3a), 151.4 (C-7a) and 155.0 (C=O); *m*/*z* 234 (M^+, 16%), 178 (78), 133 (100), 118 (44), 91 (13) and 57 (77).

Preparation of 4H-*Pyrazolo*[1,5-a]*indole Derivatives* **3**:

General Procedure.—Under an argon atmosphere $NbCl_3$·DME (579 mg, 2 mmol) was added to anhydrous THF (90 cm^3) and the solution was refluxed. A solution of **2** (2 mmol) in anhydrous THF (10 cm^3) was then introduced into the hot dark-brown solution, and the resulting mixture was heated at reflux for 1.5 h. After being cooled, the reaction mixture was quenched with 10% aqueous sodium hydroxide and worked up to give the cyclization product **3**.

2-*Phenyl*-4H-*pyrazolo*[1,5-a]*indole* **3a**. This formed colourless plates, m.p. 80.0–80.5 °C (from ethyl acetate–pentane) [lit.,[14] m.p. 82–83 °C (from ethanol)] (Found: C, 82.7; H, 5.1; N, 12.0. Calc. for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06%); λ_{max}(MeCN)/nm 204 (log ε/dm^3 mol^{-1} cm^{-1} 4.48) and 295 (4.33); ν_{max}/cm^{-1} 3036, 1625, 1550, 1472, 1455, 1394, 1305, 952, 764, 751 and 692; δ_H 3.88 (2 H, s, 4-H_2), 6.59 (1 H, t, *J* 1.2, 3-H), 7.18 (1 H, td, *J* 7.6, 1.0, 6-H), 7.27–7.47 (5 H, m, ArH), 7.69 (1 H, d, *J* 7.8, 8-H) and 7.90 (2 H, m, 2′,6′-H); δ_C 28.5 (C-4), 98.3 (C-3), 110.7 (C-8), 124.4 (C-6), 125.9 (C-5), 126.0 (C-2′,6′), 128.0 (C-4′), 128.2 (C-7), 128.8 (C-3′,5′), 133.5 (C-4a), 134.0 (C-1′), 140.7 (C-8a), 145.9 (C-3a) and 156.3 (C-2); *m*/*z* 232 (M^+, 100%), 204 (7), 155 (6), 129 (35) and 102 (11).

2-(4-*Methylphenyl*)-4H-*pyrazolo*[1,5-a]*indole* **3b**. This formed colourless crystals, m.p. 137.5–138.5 °C (from ethyl acetate–pentane) (Found: C, 82.8; H, 5.6; N, 11.3. Calc. for $C_{17}H_{14}N_2$: C, 82.89; H, 5.73; N, 11.38%); ν_{max}/cm^{-1} 3055, 2900, 1622, 1593, 1551, 1526, 1470, 1397, 1304, 954, 828, 797 and 748; δ_H 2.39 (3 H, s, CH_3), 3.90 (2 H, s, 4-H_2), 6.57 (1 H, t, *J* 1.2, 3-H), 7.18 (1 H, td, *J* 7.6, 1.0, 6-H), 7.23 (1 H, m, 3′,5′-H), 7.40 (1 H, t, *J* 7.6, 7-H), 7.45 (1 H, d, *J* 7.6, 5-H), 7.69 (1 H, d, *J* 7.6, 8-H) and 7.79 (2 H, m, 2′,6′-H); δ_C 21.3 (CH_3), 28.4 (C-4), 97.9 (C-3), 110.5 (C-8), 124.2 (C-6), 125.7 (C-2′,6′,5), 128.0 (C-7), 129.3 (C-3′,5′), 131.0 (C-1′), 133.3 (C-4a), 137.7 (C-4′), 140.6 (C-8a), 145.7 (C-3a) and 156.3 (C-2); *m*/*z* 246 (M^+, 100%), 155 (7), 129 (46) and 102 (10).

2-(4-*Methoxyphenyl*)-4H-*pyrazolo*[1,5-a]*indole* **3c**. This formed colourless crystals, m.p. 177.0–178.5 °C (from ethyl acetate–pentane) (Found: C, 77.9; H, 5.3; N, 10.7. Calc. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68%); ν_{max}/cm^{-1} 3023, 2903, 1623, 1609, 1592, 1549, 1523, 1480, 1449, 1435, 1303, 1247, 1180, 1031, 838, 795 and 748; δ_H 3.85 (3 H, s, OCH_3), 3.89 (2 H, s, 4-H_2), 6.52 (1 H, s, 3-H), 6.96 (2 H, m, 3′,5′-H), 7.17 (1 H, td, *J* 7.6, 0.7, 6-H), 7.40 (1 H, t, *J* 7.6, 7-H), 7.44 (1 H, d, *J* 7.6, 5-H), 7.68 (1 H, d, *J* 7.6, 8-H) and 7.83 (2 H, m, 2′,6′-H); δ_C 28.4 (C-4), 55.3 (OCH_3), 97.7 (C-3), 110.4 (C-8), 114.1 (C-3′,5′), 124.1 (C-6), 125.8 (C-5), 126.6 (C-1′), 127.1 (C-2′,6′), 128.1 (C-7), 133.3 (C-4a), 140.6 (C-8a), 145.8 (C-3a), 156.0 (C-2) and 159.6 (C-4′); *m*/*z* 262 (M^+, 100%), 247 (81), 219 (23), 129 (43) and 102 (9).

2-(4-*Chlorophenyl*)-4H-*pyrazolo*[1,5-a]*indole* **3d**. This formed pale yellow crystals, m.p. 169.0–170.0 °C (from ethyl acetate–pentane) (Found: C, 72.2; H, 4.1; N, 10.5. Calc. for $C_{16}H_{11}ClN_2$: C, 72.04; H, 4.16; N, 10.51%); ν_{max}/cm^{-1} 3130, 3062, 1625, 1548, 1471, 1434, 1408, 1305, 1089, 953, 832, 804 and 747; δ_H 3.89 (2 H, s, 4-H_2), 6.56 (1 H, s, 3-H), 7.20 (1 H, t, *J* 7.5, 6-H), 7.35–7.49 (4 H, m, ArH), 7.68 (1 H, d, *J* 7.8, 8-H) and 7.82 (2 H, m, 2′,6′-H); δ_C 28.4 (C-4), 98.1 (C-3), 110.6 (C-8), 124.5 (C-6), 125.8 (C-5), 127.0 (C-2′,6′), 128.1 (C-7), 128.8 (C-3′,5′), 132.4 (s), 133.3 (s), 133.6 (s), 140.5 (C-8a), 145.9 (C-3a) and 155.0 (C-2); *m*/*z* 268 (M^+ + 2, 29%), 266 (M^+, 88), 231 (8), 204 (14), 155 (11), 129 (100) and 102 (45).

2-(4-*Cyanophenyl*)-4H-*pyrazolo*[1,5-a]*indole* **3e**. This formed pale yellow crystals, m.p. 180.5–181.5 °C (from ethyl acetate–pentane) (Found: C, 79.6; H, 4.2; N, 16.3. Calc. for $C_{17}H_{11}N_3$: C, 79.36; H, 4.31; N, 16.33%); ν_{max}/cm^{-1} 2224, 1624, 1608, 1471, 1412, 1305, 1269, 1146, 957, 854, 827, 781 and 754; δ_H 3.92 (2 H, s, 4-H_2), 6.65 (1 H, s, 3-H), 7.24 (1 H, td, *J* 7.5, 1.0, 6-H), 7.44 (1 H, t, *J* 7.5, 7-H), 7.49 (1 H, d *J* 7.5, 5-H), 7.69 (3 H, m, ArH) and 7.99 (2 H, m, 2′,6′-H); δ_C 28.4 (C-4), 98.8 (C-3), 110.8 (C-8), 111.0 (C-4′), 119.1 (CN), 125.0 (C-6), 126.0 (C-5), 126.1 (C-2′,6′), 128.2 (C-7), 132.5 (C-3′,5′), 133.4 (C-4a), 138.3 (C-1′), 140.2 (C-8a), 146.1 (C-3a) and 154.0 (C-2); *m*/*z* 257 (M^+, 100%), 229 (14), 155 (9), 129 (75) and 102 (32).

2-(4-*Nitrophenyl*)-4H-*pyrazolo*[1,5-a]*indole* **3f**. This formed orange crystals, m.p. 182.0–183.0 °C (from ethyl acetate) (Found: C, 69.4; H, 4.2; N, 15.2. Calc. for $C_{16}H_{11}N_3O_2$: C, 69.20; H, 4.00; N, 15.15%); ν_{max}/cm^{-1} 1625, 1597, 1509, 1474, 1342, 1305, 1107, 855, 758 and 699; δ_H 3.94 (2 H, s, 4-H_2), 6.69 (1 H, s, 3-H), 7.25 (1 H, td, *J* 7.6, 1.0, 6-H), 7.43 (1 H, d, *J* 7.6, 5-H), 7.48 (1 H, t, *J* 7.6, 7-H), 7.72 (1 H, d, *J* 7.6, 8-H), 8.04 (2 H, m, 2′,6′-H) and 8.27 (2 H, m, 3′,5′-H); δ_C 18.4 (C-4), 99.1 (C-3), 110.9 (C-8), 124.1 (C-3′, 5′), 125.1 (C-6), 126.0 (C-5), 126.1 (C-2′, 6′), 128.3 (C-7), 133.4 (C-4a), 140.2 (C-1′, 8a), 146.2 (C-3a), 147.1 (C-4′) and 153.6 (C-2); *m*/*z* 277 (M^+, 100%), 230 (31), 204 (30), 155 (10), 149 (19), 129 (53), 115 (15) and 102 (28).

2-*Piperonyl*-4H-*pyrazolo*[1,5-a]*indole* **3g**. This formed colourless crystals, m.p. 150.0–151.0 °C (from ethyl acetate–pentane) (Found: C, 73.8; H, 4.3; N, 10.1. Calc. for $C_{17}H_{12}N_2O_2$: C, 73.90; H, 4.38; N, 10.14%); ν_{max}/cm^{-1} 3067, 2886, 1622, 1596, 1557, 1517, 1478, 1456, 1427, 1242, 1044, 886 and 751; δ_H 3.88 (2 H, s, 4-H_2), 5.99 (2 H, s, OCH_2O), 6.49 (1 H, t, *J* 1.1, 3-H), 6.86 (1 H, d, *J* 7.8, 5′-H), 7.17 (1 H, td, *J* 7.5, 1.0, 6-H), 7.34–7.48 (4 H, m, ArH) and 7.66 (1 H, d, *J* 7.8, 8-H); δ_C 28.4 (C-4), 97.8 (C-3), 101.1 (OCH_2O), 106.5 (C-2′), 108.5 (C-5′), 110.4 (C-8), 119.6 (C-6′), 124.2 (C-6), 125.8 (C-5), 128.1 (C-7), 128.3 (C-1′), 133.3 (C-4a), 140.6 (C-8a), 145.7 (C-3a), 147.5 (C-4′), 148.1 (C-3′) and 156.0 (C-2); *m*/*z* 276 (M^+, 100%), 248 (9), 217 (11), 190 (8), 155 (7), 146 (16), 129 (79) and 102 (19).

Reaction of **2a** *with* $NbCl_3$·DME *at RT*.—The reaction of **2a** (250 mg, 1 mmol) with $NbCl_3$·DME (289 mg, 1 mmol) in dry THF (20 cm^3) was carried out under argon at RT for 24 h. The reaction mixture was worked up as described for **3** to give **9a** (55 mg, 22%), **3a** (76 mg, 30%) and starting material **2a** (88 mg, 35%). (3SR,3aSR)-3-*Hydroxy*-2-*phenyl*-3a,4-*dihydro*-3H-*pyrazolo*[1,5-a]*indole* **9a** formed colourless crystals, m.p. 128.0–128.5 °C (from ethyl acetate) (Found: C, 76.6; H, 5.5; N, 11.1. Calc. for $C_{16}H_{14}N_2O$: C, 76.77; H, 5.64; N, 11.20%); ν_{max}/cm^{-1} 3388, 3109, 2947, 1607, 1478, 1461, 1241, 1064, 983, 766 and 691; δ_H 3.18 (1 H, br s, OH), 3.02 (1 H, dd, *J* 16.1, 9.0, 4-H), 3.27 (1 H, dd, *J* 16.1, 9.8, 4-H), 4.52 (1 H, td, *J* 9.3, 2.4, 3a-H), 5.34 (1 H, d, *J* 2.4, 3-H), 7.06 (1 H, td, *J* 7.3, 1.2, 6-H), 7.16 (1 H, d, *J* 7.3, 5-H), 7.22 (1 H, t, *J* 7.3, 7-H), 7.32–7.38 (4 H, m, ArH) and 7.82 (2 H, m, 2′, 6′-H); δ_C 33.6 (C-4), 72.3 (C-3a), 81.0 (C-3), 118.7 (C-8), 125.0 (C-5), 125.5 (C-6), 127.2 (C-2′, 6′), 128.1 (C-7), 128.6 (C-3′, 5′), 129.7 (C-4′), 130.4 (C-4a), 131.9 (C-1′), 148.1 (C-8a) and 157.1 (C-2); *m*/*z* 250 (M^+, 20%), 232 (4), 117 (100), 104 (22), 91 (21) and 77 (20).

(2RS,3SR,3aSR)-3-*Hydroxy*-1-*methyl*-2-*phenyl*-2,3,3a,4-*tetrahydro*-1H-*pyrazolo*[1,5-a]*indole* **11**.—A solution of **9a** (2.50 g, 10.0 mmol) in dry ether (100 cm^3) was added to a suspension of lithium aluminium hydride (569 mg, 15.0 mmol) in dry ether (200 cm^3) under a nitrogen atmosphere and cooled in an ice bath. After completion of addition, the reaction mixture was stirred at RT for 3 h after which sodium fluoride (2.52 g, 60.0 mmol) and water (2.2 cm^3) were carefully added to it. After the heterogeneous mixture had been stirred for 30 min, it was filtered and the filtrate dried ($MgSO_4$) and worked up to give 3-*hydroxy*-2-*phenyl*-2,3,3a,4-*tetrahydro*-1H-*pyrazolo*[1,5-a]*indole* **10** in quantitative yield; this was immediately used for the following reaction without purification. The reduction product **10**, sodium cyanoborohydride (1.01 g, 16.0 mmol) and 37% aqueous formaldehyde (4.0 cm^3, 50 mmol) were dissolved in acetonitrile (45 cm^3) and to this solution was added acetic acid at such rate as to keep its pH neutral at ice-bath temperature. The reaction mixture was stirred at RT for 1.5 h after which it was evaporated under reduced pressure and the residue was basified with 2 mol dm^{-3} aqueous potassium hydroxide. Work-

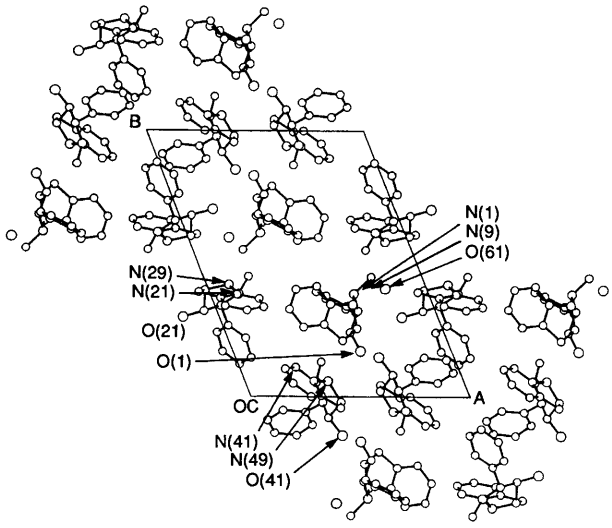


Fig. 2 [001] Projections of the crystal structure of **11**

up gave compound **11** (2.63 g, 99%), as colourless plates, m.p. 80.0–81.0 °C (from ethyl acetate–pentane) (Found: C, 75.05; H, 6.9; N, 10.3. Calc. for $C_{17}H_{18}N_2O\cdot1/3H_2O$: C, 74.97; H, 6.91; N, 10.29%); ν_{max}/cm^{-1} 3371, 3203, 3031, 2920, 1603, 1474, 1461, 1251, 1120, 1096, 768 and 701; δ_H 2.07 (1 H, br s, OH), 2.83 (3 H, s, NCH_3), 3.06 (1 H, d, *J* 15.6, 4-H), 3.13 (1 H, dd, *J* 15.6, 6.4, 4-H), 3.63–3.74 (2 H, m, 2,3-H), 4.08 (1 H, m, 3a-H), 6.92 (1 H, td, *J* 7.6, 1.0, 6-H), 7.05 (1 H, d, *J* 7.6, 8-H), 7.12 (1 H, d, *J* 7.6, 5-H), 7.22 (1 H, t, *J* 7.6, 7-H) and 7.23–7.35 (5 H, m, ArH); δ_C 30.9 (C-4), 47.2 (NCH_3), 67.5 (C-3a), 80.2 (C-2), 82.1 (C-3), 113.8 (C-8), 121.9 (C-6), 125.1 (C-5), 126.1 (C-4a), 127.1 (C-2′, 6′), 127.4 (C-7), 127.6 (C-4′), 128.5 (C-3′, 5′), 139.7 (C-1′) and 155.0 (C-8a); *m/z* 266 (M^+, 30%), 251 (5), 145 (100), 118 (45), 103 (40), 91 (25) and 77 (21) (Found M^+, 266.1387. $C_{17}H_{18}N_2O$ requires 266.1417).

Single-crystal X-Ray Analysis of Compound **11**.—Suitable crystals of compound **11** for an X-ray diffraction study were grown from ethyl acetate. A crystal of approximate dimensions, 0.400 × 0.400 × 0.200 mm was used for data collection. All measurements were made on Rigaku AFC5R diffractometer with graphite monochromated Cu-Kα radiation. The unit cell dimensions were obtained by least squares of 25 reflections with the range $77.35 < 2\theta < 79.70°$. The crystal data are as follows: $C_{17}H_{18}N_2O\cdot1/3H_2O$, M_r = 272.30, colourless plate, triclinic space group $P\bar{1}$(No 2), lattice parameters: a = 13.175(3), b = 17.418(4), c = 10.697(2) Å; α = 91.87(2), β = 95.02(2), γ = 112.20(2)°, V = 2258.4(9) Å^3, Z = 6, D_c 1.202 g cm^{-3}. The ω-2θ scan technique to a maximum 2θ value of 120.1° was used. Scans of (1.63 + 0.30 tan θ)° were made at a speed of 16.0° min^{-1} (in omega). The ratio of peak counting time to background counting time was 2:1. Of the collected 6967 reflections, 6708 were unique (R_{int} = 0.047). The data were corrected for Lorenz and polarization effects. A correction for secondary extinction was applied.

The structure was solved by direct methods. Three crystallographically independent molecules and one water molecule are in an asymmetric unit. The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinements was based on 4558 observed reflections [$I > 3.00\sigma(I)$] and 551 variable parameters. The final R, R_w and S (goodness of fit) were 0.053, 0.072 and 1.71, respectively. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.20 and −0.16 e/A3 respectively. All calculations were performed using the program of TEXSAN.[26] The final values of positional parameters, bond distances and bond angles are available from the Cambridge Crystallographic Data Centre.*

Perspective view of one of the three molecules, along with the atom-numbering system, is shown in Fig. 1. The atoms of the other two are represented by the corresponding numbers of the 20 and 40 levels, respectively. The water molecule is named O(61). The conformations of the molecules are very similar. The crystal structure viewed down the *c* axis is presented in Fig. 2. The intermolecular hydrogen bonds of OH···N and OH···O are formed: O(1)···N(49) = 2.905(3); N(9)···O(61) = 2.973(3); O(21)···O(61) [$x-1$, y, $z-1$] = 2.719(3); O(21)···O(41)[$-x$, $-y$, $-z$] = 2.757(3); N(29)···O(61) [$1-x$, $1-y$, $1-z$] = 2.949(3) Å.

General Procedure for the Preparation of Compounds **9**.—Under an atmosphere of dry nitrogen boron trifluoride–diethyl ether (1.2 mmol) was added to a solution of the hydrazone **2** (1.0 mmol) in dry dichloromethane (20 cm^3) at 0 °C and the resulting solution was stirred at RT for 30 min. The reaction mixture was then basified with 1 mol dm^{-3} aqueous sodium hydroxide and worked up to give the results summarized in Table 3.

(3SR,3aSR)-3-*Hydroxy*-2-(4-*methoxyphenyl*)-3a,4-*dihydro*-3H-*pyrazolo*[1,5-a]*indole* **9c**. This formed colourless crystals (83%), m.p. 168.0–169.0 °C (from ethyl acetate) (Found: C, 72.75; H, 5.6; N, 9.9. Calc. for $C_{17}H_{16}N_2O_2$: C, 72.83; H, 5.75; N, 10.00%); ν_{max}/cm^{-1} 3401, 3054, 2958, 1609, 1516, 1480, 1461, 1422, 1311, 1251, 1179, 1046 and 759; δ_H 3.03 (1 H, dd, *J* 16.1, 9.3, 4-H), 3.28 (1 H, dd, *J* 16.1, 9.8, 4-H), 3.45 (1 H, br s, OH), 3.81 (3 H, s, OCH_3), 4.51 (1 H, td, *J* 9.3, 2.4, 3a-H), 5.30 (1 H, br s, 3-H), 6.86 (2 H, m, 3′, 5′-H), 7.05 (1 H, td, *J* 7.6, 1.0, 6-H), 7.16 (1 H, d, *J* 7.6, 5-H), 7.22 (1 H, t, *J* 7.6, 7-H), 7.35 (1 H, d, *J* 7.6, 8-H) and 7.75 (2 H, m, 2′, 6′-H); δ_C 33.7 (C-4), 55.3 (OCH_3), 72.2 (C-3a), 81.3 (C-3), 114.1 (C-3′, 5′), 118.7 (C-8), 123.1 (C-1′), 125.0 (C-5), 125.3 (C-6), 128.1 (C-7), 128.8 (C-2′, 6′), 132.0 (C-4a), 148.6 (C-8a), 156.7 (C-2) and 160.9 (C-4′); *m/z* 280 (M^+, 26%), 134 (100), 118 (59) and 91 (12).

(3SR,3aSR)-3-*Hydroxy*-2-(4-*nitrophenyl*)-3a,4-*dihydro*-3H-*pyrazolo*[1,5-a]*indole* **9f**. This formed orange crystals (79%), m.p. 188.0–189.0 °C (from methylacetate) (Found: C, 65.2; H, 4.6; N, 14.2. Calc. for $C_{16}H_{13}N_3O_3$: C, 65.08; H, 4.44; N, 14.23%); ν_{max}/cm^{-1} 3369, 3078, 2944, 1599, 1572, 1516, 1476, 1460, 1314, 1226, 1105, 1064, 1028, 965, 848, 772 and 696; δ_H 2.75 (1 H, br s, OH), 3.09 (1 H, dd, *J* 16.1, 9.0, 4-H), 3.39 (1 H, dd, *J* 16.1, 9.8, 4-H), 4.59 (1 H, td, *J* 9.4, 2.4, 3a-H), 5.38 (1 H, br s, 3-H), 7.11 (1 H, td, *J* 7.4, 1.2, 6-H), 7.21 (1 H, d, *J* 7.4, 5-H), 7.28 (1 H, t, *J* 7.4, 7-H), 7.41 (1 H, d, *J* 7.4, 8-H), 7.99 (2 H, m, 2′, 6′-H) and 8.21 (2 H, m, 3′, 5′-H); δ_C 33.5 (C-4), 73.0 (C-3a), 80.6 (C-3), 118.2 (C-8), 123.9 (C-3′, 5′), 125.3 (C-5), 125.8 (C-6), 127.6 (C-2′, 6′), 128.3 (C-7), 131.5 (C-4a), 136.8 (C-1′), 147.1 (s), 148.1 (s) and 154.3 (C-2); *m/z* 295 (M^+, 14%), 117 (100) and 91 (10).

(3SR,3aSR)-2-(E)- *cinnamyl*-3-*hydroxy*-3a,4-*dihydro*-3H-*pyrazolo*[1,5-a]*indole* **9h**. This formed pale yellow crystals (69%) m.p. 167–168 °C (from ethyl acetate) (Found: C, 78.5; H, 5.7; N, 10.1. Calc. for $C_{18}H_{16}N_2O$: C, 78.23; H, 5.84; N, 10.14%); ν_{max}/cm^{-1} 3294, 3032, 2950, 1629, 1606, 1551, 1494, 1479, 1462, 1232, 1075, 1049, 966, 762, 751 and 695; δ_H 3.02 (1 H, dd, *J* 16.1, 9.3, 4-H), 3.28 (1 H, dd, *J* 16.1, 9.8, 4-H), 3.30 (1 H, d, *J* 9.3, OH), 4.49 (1 H, td, *J* 9.4, 2.2, 3a-H), 5.23 (1 H, dd, *J* 9.3, 2.2, 3-H), 6.99 (1 H, d, *J* 16.5, C*H*=CHPh), 7.14 (1 H, d, *J* 16.5, CH=C*H*Ph), 7.05–7.31 (6 H, m, ArH), 7.35 (1 H, d, *J* 7.8, 8-H) and 7.43 (2 H, m, 2′, 6′-H); δ_C 33.6 (C-4), 72.6 (C-3a), 80.3 (C-3), 118.3 (C-8), 119.4 (*C*H=CHPh), 125.1 (C-5), 125.4 (C-6), 127.0 (C-2′, 6′), 128.2 (C-7), 128.7 (C-4′), 128.8 (C-3′, 5′), 131.8 (C-4a), 136.2 (C-

* For details see 'Instructions for Authors (1993)', *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

1'), 136.3 (CH=*C*HPh), 148.0 (C-8a) and 157.7 (C-2); *m/z* 276 (M^+, 36%), 158 (17), 130 (57), 118 (100), 91 (18) and 77 (9).

Dehydration of **9a** *into* **3a**.—(*a*) A solution of **9a** (125 mg, 0.50 mmol) in dry THF (10 cm^3) was added into a solution of $NbCl_3$·DME (145 mg, 0.5 mmol) in dry THF (20 cm^3) and the mixture was refluxed for 10 min. Work-up as described above gave **3a** (108 mg, 93%) as colourless crystals.

(*b*) Mesyl chloride (1.5 cm^3, 19.6 mmol) was added to a solution of **9a** (3.28 g, 13.1 mmol) and triethylamine (3.65 cm^3, 26.2 mmol) in dry dichloromethane (40 cm^3) at 0 °C and the reaction mixture was stirred at the same temperature for 2 h. It was then diluted with ether and worked up to give **3a** (2.94 g, 97%).

1-*Benzylideneamino*-2-*formylpyrrolidine* **12**.—Benzaldehyde (780 mg, 7.4 mmol) was condensed, as described for **1**, with 1-aminoprolinol[27] [prepared from prolinol (743 mg, 7.3 mmol by *N*-nitrosoation and subsequent lithium aluminium hydride reduction of the *N*-nitrosoprolinol] to give 1-*benzylideneamino*-2-*hydroxymethylproline* (796 mg, 53% overall) as an oil; ν_{max}(neat)/cm^{-1} 3429, 3058, 2949, 2875, 1587, 1558, 1446, 1377, 1343, 1327, 1241, 1199, 1153, 1040, 755 and 695; δ_H 1.48–1.69 and 1.83–2.14 (4 H, m, 3,4-H_2), 3.03–3.18 and 3.39–3.53 (2 H, m, 5-H_2), 3.58–3.95 (4 H, m, 6-H_2, 2-H and OH), 7.21 (1 H, s, N=CH), 7.30 (3 H, m, 3',4',5'-H) and 7.49 (2 H, m, 2',6'-H); δ_C 22.1 (C-4), 25.9 (C-3), 48.5 (C-5), 64.0 (C-2), 66.6 (C-6), 125.4 (C-2',6'), 127.5 (C-4'), 128.6 (C-3',5'), 133.4 (C=N) and 136.4 (C-1'); *m/z* 204 (M^+, 9%), 173 (100), 104 (9), 77 (17) and 70 (44) (Found: M^+, 204.1269. $C_{12}H_{16}N_2O$ requires 204.1262). Swern oxidation of this alcohol yielded **12** (70%) as a colourless oil (rapidly turning red in air); ν_{max}(neat)/cm^{-1} 3058, 2975, 2714, 1733, 1590, 1560, 1447, 1377, 1197, 757 and 695; δ_H 2.07 (4 H, m, 3,4-H_2), 3.21 and 3.61 (2 H, m, 5-H_2), 4.05 (1 H, m, 2-H), 7.17–7.37 (4 H, m, 3',4',5'-H and N=CH), 7.54 (2 H, m, 2',6'-H) and 9.73 (1 H, d, *J* 2.9, CHO); δ_C 23.0 (C-4), 25.0 (C-3), 49.3 (C-5), 71.1 (C-2), 125.6 (C-2',6'), 127.7 (C-4'), 128.5 (C-3',5'), 134.8 (C=N), 136.4 (C-1') and 202.3 (CHO); *m/z* 202 (M^+, 10%), 173 (100), 104 (15), 77 (35) and 70 (90) (Found: M^+, 202.1090. $C_{12}H_{14}N_2O$ requires 202.1105).

(3SR,3aSR)-3-*Hydroxy*-2-*phenyl*-3,3a,4,5-*tetrahydro*-6H-*pyrrolo*[1,2-b]*pyrazole* **13**. This formed colourless crystals (45%), m.p. 139.0–140.0 °C (from ethyl acetate) (Found: C, 71.0; H, 6.9; N, 13.7. Calc. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85%); ν_{max}/cm^{-1} 3235, 1584, 1558, 1447, 1301, 1111, 1072, 1061, 772 and 694; δ_H 1.33–1.73 and 1.86–2.06 (4 H, m, 4,5-H_2), 3.06–3.22 and 3.53–3.67 (2 H, m, 6-H_2), 3.77 (1 H, dd, *J* 9.3, 6.8, 3a-H), 3.28–4.39 (1 H, br s, OH), 5.09 (1 H, s, 3-H), 7.35 (3 H, m, 3',4',5'-H) and 7.74 (2 H, m, 2',6'-H); δ_C 24.0 (C-5), 27.1 (C-4), 53.5 (C-6), 73.2 (C-3a), 80.6 (C-3), 126.8 (C-2',6'), 128.6 (C-3',5'), 129.2 (C-4'), 131.1 (C-1') and 155.2 (C-2); *m/z* 202 (M^+, 9%), 184 (2), 104 (14) and 70 (100).

Dehydration of **13**.—The alcohol **13** (30 mg, 0.15 mmol) was treated with mesyl chloride (0.02 cm^3, 0.26 mmol) and triethylamine (0.07 cm^3, 0.50 mmol) in dry dichloromethane (2 cm^3) at 0 °C for 2 h. Dilution of the reaction mixture with diethyl ether and work-up gave 2-*phenyl*-4,5-*dihydro*-6H-*pyrrolo*[1,2-b]*pyrazole* (isowithasomnine) (26 mg, 96%) as colourless needles, m.p. 82.5–83.0 °C (from benzene–hexane) (lit.,[21] 80–81 °C); ν_{max}/cm^{-1} 3064, 2956, 1605, 1539, 1511, 1451, 1427, 1361, 1322, 1298, 1079, 1029, 963, 797, 762 and 686; δ_H 2.59 (2 H, m, 5-H_2), 2.91 (2 H, t, *J* 7.3, 4-H_2), 4.18 (2 H, t, *J* 7.2, 6-H_2), 6.27 (1 H, s, 3-H), 7.26 (1 H, tt, *J* 7.2, 1.4, 4'-H), 7.37 (2 H, m, 3',5'-H) and 7.77 (2 H, m, 2',6'-H); δ_C 23.2 (C-5), 26.1 (C-4), 47.8 (C-6), 95.9 (C-3), 125.4 (C-2',6'), 127.4 (C-4'), 128.5 (C-3',5'), 134.4 (C-1'), 146.9 (C-3a) and 156.2 (C-2); *m/z* 184 (M^+, 100%), 128 (16) and 77 (17).

Benzaldehyde Formylmethyl(phenyl)hydrazone **14**.—Condensation of *N*-(2-hydroxyethyl)-*N*-phenylhydrazine (841 mg, 5.5 mmol)[28] with benzaldehyde (587 mg, 5.5 mmol) in 60% acetic acid (20 cm^3) as described above yielded the *title compound* (945 mg, 71%) as a white powder, m.p. 71.5–72.0 °C (from ethyl acetate) (Found: C, 75.0; H, 6.6; N, 11.7. Calc. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66%); ν_{max}/cm^{-1} 3270, 3029, 2941, 1591, 1565, 1497, 1445, 1393, 1150, 756 and 695; δ_H 2.06 (1 H, t, *J* 6.5, OH), 3.93 (2 H, m, NCH_2CH_2O), 4.07 (2 H, t, *J* 5.7, NCH_2CH_2O), 6.98 (1 H, tt, *J* 7.0, 1.5, 4-H), 7.21–7.45 (7 H, ArH), 7.61 (1 H, s, N=CH) and 7.66 (2 H, m, 2',6'-H); δ_C 49.8 (NCH_2CH_2O), 59.1 (NCH_2CH_2O), 116.7 (C-2,6), 121.7 (C-4), 126.2 (C-2',6'), 128.1 (C-4'), 128.6 (C-3',5'), 129.2 (C-3,5), 133.4 (C=N), 136.3 (C-1') and 147.4 (C-1); *m/z* 240 (M^+, 42%), 209 (100), 106 (80) and 77 (59) (Found: M^+, 240.1259. $C_{15}H_{16}N_2O$ requires 240.1261). Swern oxidation of this alcohol as described above afforded **14** (86%), m.p. 116.0–117.0 °C (from dichloromethane–ethyl ether) (Found: C, 75.65; H, 5.9; N, 11.8. Calc. for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.76%); ν_{max}/cm^{-1} 3057, 2847, 1713, 1593, 1568, 1498, 1392, 1331, 1170, 1160, 747 and 693; δ_H 4.64 (2 H, d, *J* 1.3, CH_2), 7.02 (1 H, m, 4-H), 7.28–7.41 (8 H, m, ArH and N=CH), 7.66 (2 H, m, 2',6'-H) and 9.78 (1 H, t, *J* 1.3, CHO); δ_C 56.9 (CH_2), 116.2 (C-2,6), 122.1 (C-4), 126.4 (C-2',6'), 128.4 (C-4'), 128.6 (C-3',5'), 129.4 (C-3,5), 133.4 (C=N), 135.7 (C-1'), 147.0 (C-1) and 199.5 (CHO); *m/z* 238 (M^+, 24%), 209 (100), 117 (12), 106 (84) and 77 (88).

1-*Benzylideneamino*-2-*formyl*-1,2,3,4-*tetrahydroquinoline* **16**.—Benzaldehyde (400 mg, 3.7 mmol) in 60% acetic acid was condensed with 1-amino-2-hydroxymethyl-1,2,3,4-tetrahydroquinoline [prepared by lithium aluminium hydride reduction of the *N*-nitroso derivative of 2-hydroxymethyl-1,2,3,4-tetrahydroquinoline (650 mg, 3.9 mmol)[29]]. Chromatographic purification of the crude product yielded 1-*benzylideneamino*-2-*hydroxymethyl*-1,2,3,4-*tetrahydroquinoline* (556 mg, 52% overall) as a yellow syrup; ν_{max}(neat)/cm^{-1} 3418, 3060, 1600, 1581, 1563, 1489, 1448, 1392, 1261, 1153, 1049, 752 and 694; δ_H 1.63 (1 H, br s, OH), 1.98 and 2.32 (2 H, m, 3-H_2), 2.73 and 2.94 (2 H, m, 4-H_2), 3.71 and 3.85 (2 H, m, 9-H_2), 4.48 (1 H, m, 2-H), 6.82 (1 H, td, *J* 7.6, 1.2, 6-H), 7.06 (1 H, d, *J* 7.6, 5-H), 7.20 (1 H, t, *J* 7.6, 7-H), 7.26 (1 H, tt, *J* 7.1, 1.5, 4'-H), 7.37 (2 H, m, 3',5'-H), 7.71 (2 H, m, 2',6'-H) and 7.80 (2 H, m, 8-H and N=CH); δ_C 22.0 (C-3), 22.9 (C-4), 52.9 (C-2), 59.8 (C-9), 114.8 (C-8), 119.7 (C-6), 122.1 (C-4a), 126.1 (C-2',6'), 127.3 (C-7), 127.9 (C-4'), 128.6 (C-3',5'), 128.9 (C-5), 131.4 (C=N), 136.7 (C-1') and 142.3 (C-8a); *m/z* 266 (M^+, 33%), 235 (100), 132 (43), 130 (52), 117 (35), 104 (18), 91 (14) and 77 (39) (Found: M^+, 266.1424. $C_{17}H_{18}N_2O$ requires 266.1418). Swern oxidation of this alcohol yielded the title compound **16** (36%), m.p. 152.0–153.0 °C (from ethyl acetate) (Found: C, 77.5; H, 6.1; N, 10.7. Calc. for $C_{17}H_{16}N_2O$: C, 77.24, H, 6.10; N, 10.60%); ν_{max}/cm^{-1} 2938, 2838, 1726, 1605, 1581, 1563, 1487, 1460, 1447, 1164, 1149, 764, 753 and 696; δ_H 2.04–2.28 and 2.43–2.56 (2 H, m, 3-H_2), 2.72 (2 H, m, 4-H_2), 4.69 (1 H, m, 2-H), 6.87 (1 H, td, *J* 7.8, 1.3, 7-H), 7.05 (1 H, d, *J* 7.8, 5-H), 7.21–7.43 (5 H, ArH and N=CH), 7.68 (2 H, 2',6'-H), 7.89 (1 H, d, *J* 7.8, 8-H) and 9.70 (1 H, d, *J* 1.9, CHO); δ_C 23.1 (C-3), 24.2 (C-4), 61.9 (C-2), 114.9 (C-8), 120.4 (C-6), 122.4 (C-4a), 126.3 (C-2',6'), 127.8 (C-7), 128.3 (C-5), 128.5 (C-4'), 128.6 (C-3',5'), 131.9 (C=N), 136.0 (C-1'), 142.1 (C-8a) and 201.8 (CHO); *m/z* 264 (M^+, 15%), 235 (100), 132 (34), 130 (35), 117 (32), 104 (17), 91 (8) and 77 (31).

2-*Phenyl*-4,5-*dihydropyrazolo*[1,5-a]*quinoline* **17**. This formed colourless crystals (90%), m.p. 80.0–81.0 °C (from ethanol) (lit.,[14] b.p. 180 °C/0.2 mmHg, m.p. 80–84 °C (from ethanol)); ν_{max}/cm^{-1} 3051, 2963, 1613, 1589, 1491, 1473, 1458, 1366, 768, 761 and 695; δ_H 2.91–3.10 (4 H, m, 4,5-H_2), 6.47 (1 H, s, 3-H), 7.12 (1 H, td, *J* 7.4, 1.2, 7-H), 7.23 (1 H, d, *J* 7.4, 6-H), 7.27–7.46 (4 H, m, ArH), 7.90 (2 H, m, 2',6'-H) and 8.00 (1 H,

dd, *J* 8.1, 1.0, 9-H); δ_C 21.5 (C-4), 25.7 (C-5), 101.5 (C-3), 116.0 (C-9), 124.9 (C-7), 125.8 (C-2',6'), 126.4 (C-5a), 127.8 (C-4'), 127.9 (C-8), 128.2 (C-6), 128.6 (C-3',5'), 133.4 (s), 136.7 (s), 139.8 (s) and 152.1 (C-2); *m/z* 246 (M^+, 100%), 142 (17), 115 (12) and 77 (7).

1-*Benzylideneamino*-3-*formyl*-1,2,3,4-*tetrahydroisoquinoline* **18**.—Methyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate[30] was treated with nitrous acid to give methyl 1-nitroso-1,2,3,4-tetrahydroisoquinoline-3-carboxylate, m.p. 98.5–99.5 °C (from methanol) (Found: C, 60.0; H, 5.55; N, 12.8. Calc. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72%); ν_{max}/cm^{-1} 2956, 2934, 1737, 1501, 1459, 1427, 1360, 1346, 1317, 1280, 1247, 1215, 1185, 1166 and 755; δ_H 3.43 (2 H, d, *J* 4.0, 4H_2), 3.56 (3 H, s, CH_3), 4.55 (1 H, AB type, *J* 19.3, 1-H), 4.97 (1 H, AB type, *J* 19.3, 1-H), 6.15 (1 H, t, *J* 4.0, 3-H) and 7.25 (4 H, m, ArH); δ_C 31.1 (C-4), 44.1 (C-1), 52.6 (CH_3), 59.0 (C-3), 127.0 (d), 127.1 (d × 2), 128.4 (d), 129.5 (s), 131.3 (s) and 170.1 (C=O); *m/z* 190 (M^+ − NO, 84%), 161 (34), 130 (94), 104 (100), 59 (14) and 45 (21). This *N*-nitroso compound was reduced with lithium aluminium hydride to give 2-*amino*-3-*hydroxymethyl*-1,2,3,4-*tetrahydroisoquinoline* (98% overall yield) which was used immediately without purification. This *N*-amino alcohol (498 mg, 2.8 mmol) was condensed with benzaldehyde (318 mg, 3.0 mmol) in 60% acetic acid to give 2-*benzylideneamino*-3-*hydroxymethyl*-1,2,3,4-*tetrahydroisoquinoline* (580 cm^3, 78%) as a colourless oil; ν_{max}/cm^{-1}(neat) 3419, 3026, 2942, 1590, 1564, 1496, 1455, 1373, 1142, 1071, 1039, 993, 746 and 694; δ_H 2.84 (1 H, dd, *J* 16.1, 4.4, 4-H), 2.98 (1 H, dd, *J* 16.1, 9.7, 4-H), 3.58 (1 H, m, 3-H), 3.92–4.14 (3H, 9-H_2 and OH), 4.20 (1 H, AB type, *J* 15.6, 1-H), 4.73 (1 H, AB type, *J* 15.6, 1-H), 7.13–7.41 (7 H, m, ArH), 7.47 (2 H, m, 2',6'-H) and 7.64 (1 H, s, N=CH); δ_C 32.1 (C-4), 50.5 (C-1), 61.3 (C-3), 65.8 (C-9), 125.9 (C-2',6'), 126.3 (d), 126.6 (d), 126.8 (d), 128.3 (d), 128.6 (d), 128.7 (C-3',5'), 131.5 (s), 133.5 (s), 135.3 (C=N) and 136.0 (s); *m/z* 266 (M^+, 86%), 235 (100), 132 (16), 130 (30), 104 (17) and 77 (21) (Found: M^+, 266.1406. $C_{17}H_{18}N_2O$ requires 266.1417). Swern oxidation of this alcohol as described above afforded the title compound **18** (52%), colourless oil; ν_{max}(neat)/cm^{-1} 3063, 3027, 2916, 2829, 1733, 1636, 1564, 1497, 1455, 1223, 1138, 1106, 748 and 695; δ_H 3.14 (1 H, dd, *J* 15.9, 5.1, 4-H), 3.26 (1 H, dd, *J* 15.9, 7.9, 4-H), 4.14 (1 H, m, 3-H), 4.36 (1 H, AB type, *J* 15.6, 1-H), 4.74 (1 H, AB type, *J* 15.6, 1-H), 7.18–7.40 (7 H, m, ArH), 7.59 (2 H, m, 2',6'-H), 7.67 (1 H, s, N=CH) and 9.87 (1 H, d, *J* 1.9, CHO); δ_C 29.5 (C-4), 49.8 (C-1), 68.1 (C-3), 126.1 (C-2',6'), 126.7 (d), 126.8 (d), 127.0 (d), 128.3 (d), 128.5 (C-3',5'), 128.8 (d), 131.4 (s), 131.8 (s), 135.9 (C=N and s) and 201.2 (CHO); *m/z* 264 (M^+, 9%), 235 (100), 130 (40), 103 (34) and 77 (25) (Found: M^+, 264.1303. $C_{17}H_{16}N_2O$ requires 264.1262).

2-*Phenyl*-4,9-*dihydropyrazolo*[1,5-b]*isoquinoline* **19**. This formed white crystals (82%), m.p. 188.0–189.0 °C (from benzene) (Found: C, 82.9; H, 5.9; N, 11.4. Calc. for $C_{17}H_{14}N_2$: C, 82.89; H, 5.73; N, 11.38%); ν_{max}/cm^{-1} 3058, 3031, 2916, 1603, 1589, 1548, 1503, 1493, 1456, 1437, 1420, 1350, 1318, 1079, 960, 765, 745 and 692; δ_H 4.17 (2 H, t, *J* 2.3, 4-H_2), 5.39 (2 H, t, *J* 2.3, 9-H_2), 6.46 (1 H, s, 3-H), 7.27–7.45 (7 H, m, ArH) and 7.82 (2 H, m, 2',6'-H); δ_C 27.9 (C-4), 50.0 (C-9), 99.5 (C-3), 125.6 (C-2',6'), 126.6 (d), 126.8 (d), 127.5 (d × 2), 128.5 (d), 128.6 (C-3',5'), 130.6 (s), 130.8 (s), 133.7 (C-1'), 138.1 (C-3a) and 151.5 (C-2); *m/z* 246 (M^+, 94%), 245 (100) and 142 (44).

2-*Acetyl*-1-*benzylideneaminoindoline* **20**.—A diastereoisomeric mixture of 1-amino-2-(1-hydroxyethyl)indoline[31] was condensed with benzaldehyde in 60% acetic acid to give a isomeric mixture of 1-*benzylideneamino*-2-(1-*hydroxyethyl*)-*indoline*. This mixture was separated by flash column chromatography to give isomers A (12%) and B (68%). A mixture of isomers A (67%) and B (12%) with reversed ratio was obtained by the reaction of **2a** (2.50 g, 10 mmol) with methylmagnesium bromide (3 mol dm^{-3} solution in ether; 4 cm^3, 12 mmol) at −78 °C in dry THF (50 cm^3) and subsequent work-up. The reduction of isomer A with Raney Ni in ethanol afforded *threo*-2-(1-hydroxyethyl)indoline (82%).[31] Isomer A, threo-1-*benzylideneamino*-2-(1-*hydroxyethyl*)*indoline*, yellow needles, m.p. 116.0–117.0 °C (from ethyl acetate–pentane) (Found: C,76.7; H, 6.7; N, 10.5. Calc. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N 10.52%); ν_{max}/cm^{-1} 3306, 3056, 2963, 2923, 1608, 1587, 1559, 1484, 1463, 1446, 1398, 1375, 1308, 1292, 1246, 1176, 1156, 1072, 915, 885, 763 and 693; δ_H 1.26 (3 H, d, *J* 6.4, CHCH_3), 1.78 (1 H, d, *J* 2.2, OH), 3.27 (2 H, d, *J* 7.8, 3-H_2), 4.31–4.52 (2 H, m, 2-H and MeC*H*OH), 6.85 (1 H, td, *J* 7.1, 1.7, 5-H), 7.08–7.42 (6 H, m, ArH) and 7.62–7.70 (3 H, m, 2',6'-H and N=CH); δ_C 18.1 (CH_3), 28.0 (C-3), 65.5 (C-2), 65.8 (Me*C*HOH), 110.1 (C-7), 121.1 (C-5), 124.6 (C-4), 126.0 (C-2',6'), 126.7 (C-3a), 127.7 (C-6), 128.2 (C-4'), 128.6 (C-3',5'), 134.5 (C=N), 136.1 (C-1') and 149.1 (C-7a); *m/z* 266 (M^+, 10%), 221 (100), 118 (51), 91 (19) and 77 (15). Isomer B, erythro-1-*benzylideneamino*-2-(1-*hydroxyethyl*)*indoline* formed yellow needles, m.p. 96.5–97.5 °C (from ethyl acetate–pentane) (Found: C, 76.9: H, 7.1; N, 10.4. Calc. for $C_{17}H_{18}N_2O$: 76.66; H, 6.81; N, 10.52%); ν_{max}/cm^{-1} 3429, 3051, 2974, 1604, 1588, 1561, 1486, 1462, 1445, 1387, 1266, 1230, 1146, 1066, 925, 754 and 697; δ_H 1.22 (3 H, d, *J* 6.1, CHCH_3), 3.00 (1 H, dd, *J* 16.4, 4.2, 3-H), 3.35 (1 H, dd, *J* 16.4, 9.8, 3-H), 4.19 (1 H, m, Me*C*HOH), 4.39 (1 H, m, 2-H), 6.87 (1 H, td, *J* 7.3, 2.0, 5-H), 7.11 (1 H, d, *J* 7.3, 4-H), 7.14–7.40 (5 H, m, ArH), 7.66 (2 H, m, 2',6'-H) and 7.89 (1 H, s, N=CH); δ_C 18.0 (CH_3), 30.5 (C-3), 65.6 (C-2), 68.7 (Me*C*HOH), 110.8 (C-7), 121.3 (C-5), 124.6 (C-4), 126.0 (C-2',6'), 126.8 (C-3a), 127.8 (C-6), 128.1 (C-4'), 128.6 (C-3',5'), 135.0 (C=N), 136.1 (C-1') and 148.6 (C-7a); *m/z* 266 (M^+, 10%), 221 (100), 118 (62), 91 (22) and 77 (21). This diastereoisomeric mixture was oxidized by the Swern procedure to give **20** (95%) as yellow crystals, m.p. 107.0–108.0 °C (from ethyl acetate–pentane) (Found: C, 77.5; H, 6.05; N, 10.7. Calc. for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.60%); ν_{max}/cm^{-1} 3030, 2931, 1711, 1609, 1588, 1564, 1484, 1464, 1448, 1404, 1295, 1190, 1172, 1164, 757, 745 and 694; δ_H 2.13 (3 H, s, CH_3), 3.07 (1 H, dd, *J* 16.6, 5.9, 3-H), 3.63 (1 H, dd, *J* 16.6, 11.2, 3-H), 4.69 (1 H, dd, *J* 11.2, 5.9, 2-H), 6.88 (1 H, td, *J* 7.3, 2.0, 5-H), 7.13 (1 H, d, *J* 7.3, 4-H), 7.20–7.41 (6 H, m, ArH and N=CH) and 7.65 (2 H, m, 2',6'-H); δ_C 24.9 (CH_3), 32.5 (C-3), 68.9 (C-2), 109.7 (C-7), 121.1 (C-5), 124.6 (C-3a), 124.8 (C-4), 126.1 (C-2',6'), 128.4 (C-6), 128.6 (C-3',4',5'), 133.6 (C=N), 135.6 (C-1'), 148.0 (C-7a) and 208.4 (C=O); *m/z* 264 (M^+, 15%), 221 (100), 204 (8), 118 (63), 104 (11), 91 (29) and 77 (37).

3-*Methyl*-2-*phenyl*-4H-*pyrazolo*[1,5-a]*indole* **21**. This formed pale yellow crystals (84%), m.p. 102.0–103.0 °C (from ethanol) (Found: C, 83.2; H, 5.6; N, 11.4. Calc. for $C_{17}H_{14}N_2$: C, 82.89; H, 5.73; N, 11.38%); ν_{max}/cm^{-1} 3058, 2942, 2858, 1625, 1602, 1573, 1473, 1459, 1385, 1278, 1236, 1196, 1074, 1016, 818, 777, 756 and 702; δ_H 2.30 (3 H, s, CH_3), 3.82 (2 H, s, 4-H_2), 7.16 (1 H, td, *J* 7.7, 1.0, 6-H), 7.21–7.50 (5 H, m, ArH), 7.67 (1 H, d, *J* 7.7, 8-H) and 7.76 (2 H, m, 2',6'-H); δ_C 9.8 (CH_3), 27.5 (C-4), 108.6 (C-3), 110.3 (C-8), 123.9 (C-6), 125.9 (C-5), 127.5 (C-4'), 127.8 (C-2',6'), 128.0 (C-7), 128.2 (C-3',5'), 133.2 (s), 134.4 (s), 140.7 (C-8a), 143.9 (C-3a) and 154.7 (C-2); *m/z* 246 (M^+, 100%), 231 (7), 143 (37) and 115 (12).

1-*Benzylideneamino*-2-*formylindole* **22**.—A mixture of the hydrazone **1a** (709 mg, 14.2 mmol) and triethylamine (2.20 cm^3, 15.8 mmol) in dry dichloromethane (10 cm^3) was treated with trimethylchlorosilane (1.8 cm^3, 14.2 mmol) and the resulting mixture was stirred overnight at RT. The reaction mixture was diluted with ether and worked up. The crude product was dissolved in THF (20 cm^3) and oxidized with DDQ (702 mg, 3.1 mmol) at RT for 4 h. The reaction mixture was mixed with ether

and 10% aqueous NaOH and then worked up. The product was stirred with potassium carbonate (399 mg, 2.8 mmol) in absolute methanol (20 cm^3) at 0 °C for 1 h to remove the protecting group.[32] Purification of the crude product afforded *1-benzylideneamino-2-hydroxymethylindole* (436 mg, 62% overall) as pale yellow crystals, m.p. 95.0–95.5 °C (from ethyl acetate–pentane) (Found: C, 76.9; H, 5.6; N, 11.2. Calc. for $C_{16}H_{14}N_2O$: C, 76.77; H, 5.64; N, 11.20%); ν_{max}/cm^{-1} 3235, 3044, 1616, 1587, 1448, 1411, 1341, 1286, 1235, 1100, 1073, 1060, 1020, 950, 753, 742, 729 and 691; δ_H 2.90 (1 H, t, *J* 6.6, OH), 4.91 (2 H, d, *J* 6.6, 8-H_2), 6.51 (1 H, s, 3-H), 7.17 (1 H, td, *J* 7.7, 1.1, 5-H), 7.27 (1 H, td, *J* 7.7, 1.4, 6-H), 7.48 (3 H, m, ArH), 7.61 (1 H, d, *J* 7.7, 4-H), 7.73 (1 H, d, *J* 7.7, 7-H), 7.83 (2 H, m, 2′,6′-H) and 8.98 (1 H, s, N=CH); δ_C 57.7 (C-8), 101.6 (C-3), 111.0 (C-7), 121.4 (C-5), 121.6 (-4), 123.2 (C-6), 127.5 (C-2′,6′), 127.7 (C-3a), 129.0 (C-3′,5′), 131.0 (C-4′), 133.0 (C-1′), 133.9 (C-2), 138.9 (C-7a) and 150.9 (C=N); *m/z* 250 (M^+, 100%), 219 (11), 145 (92), 106 (65), 91 (36) and 77 (38). Swern oxidation of this alcohol yielded the title compound **22** (88%), as yellow crystals, m.p. 71.5–72.5 °C (from ethyl acetate–pentane) (Found: C, 77.45; H, 4.6; N, 11.3. Calc. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.29%); ν_{max}/cm^{-1} 3025, 1663, 1617, 1512, 1478, 1448, 1386, 1360, 1312, 1128, 728 and 687; δ_H 7.23 (1 H, td, *J* 7.6, 0.6, 5-H), 7.41 (1 H, s, 3-H), 7.44–7.54 (4 H, ArH), 7.74 (2 H, m, 4,7-H), 7.96 (2 H, m, 2′,6′-H), 8.89 (1 H, s, N=CH) and 10.04 (1 H, s, CHO); δ_C 112.1 (C-7), 116.9 (C-3), 122.2 (C-5), 123.4 (C-4), 124.9 (C-3a), 127.7 (C-6), 128.3 (C-2′,6′), 128.9 (C-3′,5′), 131.4 (C-4′), 133.5 (s), 133.6 (s), 138.1 (C-7a), 157.7 (C=N) and 181.3 (CHO); *m/z* 248 (M^+, 49%), 219 (9), 145 (100), 115 (26), 89 (46) and 77 (37).

2-Formyl-1-methylphenyliminoindoline **23**.—Condensation of 1-amino-2-hydroxymethylindoline[7] with acetophenone in 60% acetic acid gave *2-hydroxymethyl-1-methylphenyliminoindoline* as a yellow syrup (84%); ν_{max}(neat)/cm^{-1} 3392, 3050, 2922, 2873, 1605, 1474, 1460, 1446, 1365, 1300, 1240, 1040, 1026, 751 and 694; δ_H 2.24 (1 H, br s, OH), 2.45 (3 H, s, CH_3), 3.03 (1 H, dd, *J* 15.4, 9.8, 3-H), 3.16 (1 H, dd, *J* 15.4, 8.3, 3-H), 3.82 (2 H, m, 8-H_2), 4.24 (1 H, m, 2-H), 6.30 (1 H, d, *J* 7.5, 7-H), 6.84 (1 H, td, *J* 7.5, 1.0, 5-H), 7.06 (1 H, t, *J* 7.5, 6-H), 7.18 (1 H, d, *J* 7.5, 4-H), 7.42 (3 H, m, ArH) and 7.88 (2 H, m, 2′,6′-H); δ_C 17.1 (CH_3), 30.5 (C-3), 63.7 (C-8), 70.4 (C-2), 109.9 (C-7), 120.8 (C-5), 124.8 (C-4), 126.8 (C-2′,6′), 126.9 (C-6), 128.5 (C-3′,5′), 129.3 (C-3a), 130.3 (C-4′), 137.6 (C-1′), 149.4 (C-7a) and 168.7 (C=N); *m/z* 266 (M^+, 9%), 235 (54), 118 (100), 91 (7) and 77 (40) (Found: M^+, 266.1419. $C_{17}H_{18}N_2O$ requires 266.1418). Swern oxidation of this alcohol afforded the title compound **23** (70%) as yellow crystals, m.p. 98.0–99.0 °C (from ethyl acetate) (Found: C, 77.4; H, 6.0; N, 10.6. Calc. for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.60%); ν_{max}/cm^{-1} 3027, 2962, 2827, 1730, 1601, 1476, 1458, 1240, 754 and 694; δ_H 2.51 (3 H, s, CH_3), 3.16 (1 H, dd, *J* 15.6, 9.1, 3-H), 3.40 (1 H, dd, *J* 15.6, 9.4, 3-H), 4.53 (1 H, td, *J* 9.3, 3.2, 2-H), 6.47 (1 H, d, *J* 7.7, 7-H), 6.90 (1 H, t, *J* 7.7, 5-H), 7.13 (1 H, t, *J* 7.7, 6-H), 7.20 (1 H, d, *J* 7.7, 4-H), 7.38–7.46 (3 H, m, ArH), 7.89 (2 H, m, 2′,6′-H) and 9.82 (1 H, d, *J* 3.2, CHO); δ_C 17.4 (CH_3), 30.1 (C-3), 75.8 (C-2), 110.7 (C-7), 121.4 (C-5), 124.9 (C-4), 126.9 (C-2′,6′), 127.3 (C-3a), 127.6 (C-6), 128.4 (C-3′,5′), 130.4 (C-4′), 137.4 (C-1′), 149.6 (C-7a), 168.8 (C=N) and 201.7 (CHO); *m/z* 264 (M^+, 6%), 235 (54), 118 (100), 91 (4) and 77 (58).

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1 This paper constitutes Part 4 of the series entitled Pyrazolo[1,5-*a*]-indole derivatives. For part 3, see H. Katayama, N. Takatsu, M. Sakurada and Y. Kawada, *Heterocycles*, 1993, **35**, 453. Part of this work has been published in preliminary form: J.-K. Shen and H. Katayama, *Chem. Lett.*, 1992, 451.

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