Electrophilic Substitution in Indoles. Part 17.[1,2] The Cyclisation of (Dimethoxyphenylacetyl)tryptamines† to Spiropentacyclic Indole Derivatives

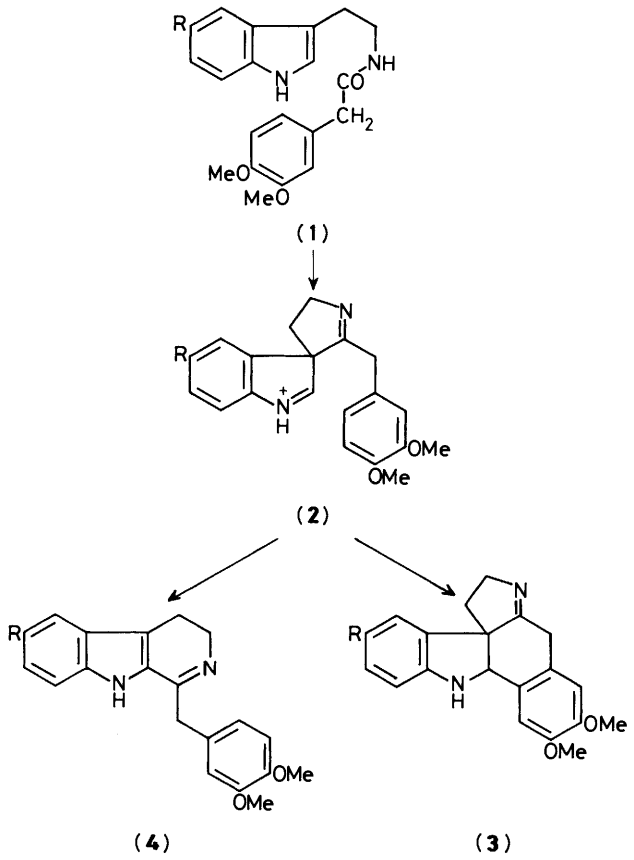
Kshetra M. Biswas
Department of Chemistry, University of Calcutta, Calcutta, 700009, India
Anthony H. Jackson *
School of Chemistry and Applied Chemistry, University of Wales, Cardiff CF1 3TB, Wales

N-(3,4-Dimethoxyphenylacetyl)tryptamine (**1a**) cyclises with either phosphoryl chloride or phosphorus trichloride to afford the oxo spirocyclic indoline (**10a**) in 68% yield together with small amounts of β-carboline derivatives. Trifluoroacetic anhydride-catalysed cyclisation affords a virtually quantitative yield of the bis-*N*-trifluoroacetyl spirocyclic indoline (**12**). The latter undergoes hydrolysis with aqueous ammonia, followed by autoxidation, to afford (**10a**) in 95% yield.

In related studies[3] we showed that intramolecular cyclisation of N_b-acetyltryptamines occurs initially at the 3-position of the indole nucleus to afford spirocyclic indolenines, which subsequently undergo further addition reactions to the 1,2-double bond to form spirocyclic indolines. It has also been shown that 4-(1,2-dimethylindol-3-yl)butyric acid can be cyclised by trifluoroacetic anhydride (TFAA) to form a 3,3-spirocyclic indolenine by *ipso*-substitution at the 3-position:[4] 1,2,3-trimethylindole also reacts with TFAA to give a 3-methyl-3-trifluoroacetylindole derivative.[5] In the present paper, we show how an N_b-acyltryptamine containing a suitable nucleophilic sidechain in the acyl residue will cyclise initially to a spirocyclic indolenine, and that the latter will then undergo a second intramolecular cyclisation by the nucleophilic moiety to form a spirocyclic indoline.[2] Our interest in this possibility was not only concerned with mechanistic aspects of indole chemistry but also with the possibility of utilising such reactions in the synthesis of pentacyclic indole alkaloids, such as those from *Aspidosperma* and *Strychnos* sources.

A suitable derivative on which to test this hypothesis was the dimethoxyphenylacetyl tryptamine (**1a**) which, it was hoped, might undergo acid catalysed cyclisation as shown in Scheme 1; we reasoned that the dimethoxyphenyl residue might act as a nucleophilic trap for the intermediate indolenine (**2a**) giving the spirocyclic indoline (**3a**) rather than rearranging to give the normal Bischler-Napieralski product,[6] the 3,4-dihydrocarboline (**4a**). A precedent for this approach was an observation by Harley-Mason and Waterfield[7] that treatment of the 1-(dihydroxybenzyl)tetrahydro-β-carboline (**5**) with boiling concentrated hydrochloric acid resulted in formation of the spirocyclic indoline (**7**), presumably *via* rearrangement to the corresponding spirocyclic indolenine (**6**) (Scheme 2).

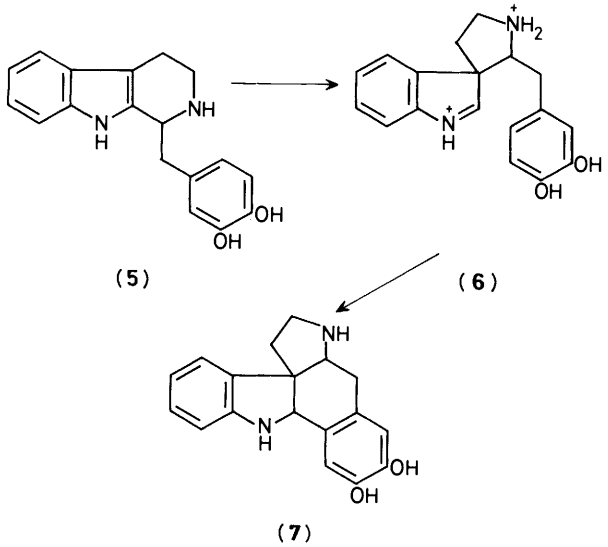
N-(3,4-Dimethoxyphenylacetyl)tryptamine (**1a**) has been prepared previously,[8,9] and its cyclisation with phosphorus trichloride was reported to afford the 3,4-dihydro-β-carboline (**4**) as the major product.[8] On the other hand, the cyclisation of the 5-methoxy analogue (**1b**) with phosphoryl chloride, followed by borohydride reduction of the crude product[10] was reported to give a mixture of the tetrahydrocarboline (**8**) and two diastereoisomeric spirocyclic indolines (**9**); these products were presumably formed by the pathway shown in Scheme 1, followed by reduction of the imino groups in (**3b**) and (**4b**). However, when we repeated the reaction of (**1a**) with phosphorus trichloride a mixture of products was obtained



Scheme 1. a, R = H; b, R = OMe

which was separated by column chromatography and preparative t.l.c. into five products (**10a, b, c**) and (**11a, b**), none of which was the 3,4-dihydro-β-carboline (**4a**). A similar cyclisation using phosphoryl chloride in benzene as catalyst afforded four of the same products (Table 1). In both the phosphorus trichloride and the phosphoryl chloride catalysed cyclisations, the major product proved to be the spirocyclic indoline (**10a**), presumably formed by autoxidation of the initially formed spirocyclic indoline (**3a**). The use of phosphoryl chloride in presence of pyridine, which it was hoped might suppress rearrangement and consequent formation of the β-carboline derivatives (**11a**) and (**11b**), led to slightly lower

† Tryptamine is 3-(2-aminoethyl)indole.



(5) (6) (7)

Scheme 2.

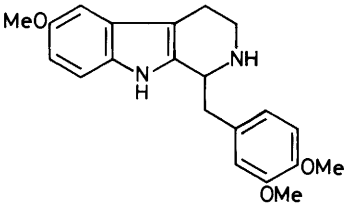
yields of the spirocyclic indoline (**10a**) but (**11a**) and (**11b**) were still formed in low yields (Table 1).

The structure assigned to the major product (**10a**) was supported by its u.v. spectrum ($\lambda_{max.}$ 240, 303, and 344 nm), the appearance of a carbonyl band in the i.r. spectrum (1 665 cm^{-1}), and the ^1H and ^{13}C n.m.r. spectra; the ^1H n.m.r. spectrum in particular showed a singlet resonance at δ 4.79 corresponding to the 2-proton in the indoline nucleus (*i.e.* 12b-H) and two singlets at δ 6.94 and 7.50 corresponding to the aromatic protons of the dimethoxybenzene residue. The elemental analysis and mass spectrum were also in accord with structure (**10a**).

The n.m.r. spectrum of the hydroperoxide (**10b**) was very similar to that of the ketone (**10a**) and mass spectral determination of molecular weight confirmed the presence of the peroxide residue; an intense $M - 18$ peak in the mass spectrum was also consistent with the hydroperoxide formulation [*i.e.* $>CH(OOH) \longrightarrow >C{=}O + H_2O$]. A minor spirocyclic indoline byproduct, obtained in very low yield in only one of the cyclisations (see Table 1) was tentatively assigned the N_a-hydroxy indoline structure (**10c**); accurate mass determination showed the presence of one extra oxygen compared with the spirocyclic indoline (**10a**). This was assigned to an *N*-hydroxy group, as the n.m.r. spectrum was very similar to that of the spirocyclic indoline (**10a**) except that the 11a-H resonance (*i.e.* that due to the hydrogen at the 2-position of the indoline nucleus) at δ 5.80 was *ca.* 1 p.p.m. to lower field than that of the corresponding proton resonance (δ 4.79) of the indoline (**10a**) (Table 2).

Small amounts of the two β-carboline derivatives (**11a**) and (**11b**) were also formed in the reactions; these were readily identified by spectroscopy. The formation of these oxo derivatives and the further oxidation to the β-carboline (**11b**) were again attributed to autoxidation of the crude cyclisation product during work-up, as their formation was not suppressed by conducting the reactions under nitrogen.

Because of our successful experience of using trifluoroacetic anhydride as a cyclisation reagent in other experiments,[3,4] we investigated its use for the cyclisation of the dimethoxyphenylacetyltryptamine (**1a**). The spirocyclic indoline (**12**) was formed in quantitative yield under very mild conditions (0 °C in benzene) and its structure proved by elemental analysis and spectroscopy. Thus the ^1H n.m.r. spectrum was similar to that of the oxo spirocyclic indoline (**10a**) but showed a singlet olefinic resonance at δ 7.38, and the ^{19}F n.m.r. spectrum exhibited two



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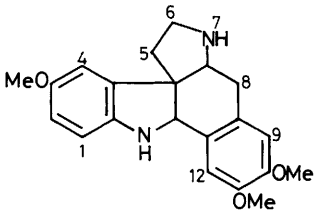

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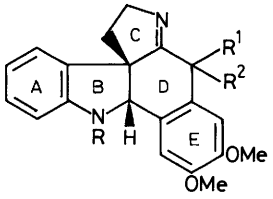


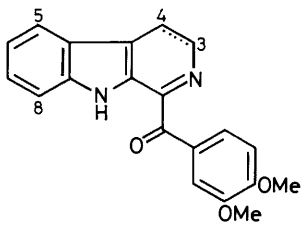
(10)

a; R = H, R^1,R^2 = O

b; R = H, R^1,R^2 = H, OOH

c; R = OH, R^1,R^2 = O

d; R = Ac, R^1,R^2 = O



(11)

a; 3,4-dihydro

b; 3,4-dehydro

$NCOCF_3$ resonances at δ −70.39 and −72.59, whilst the f.d. mass spectrum showed the molecular ion at *m/z* 512 (100%). Interestingly, the e.i. mass spectrum showed relatively intense $(M + 1)^+$ and $(M + 2)^+$ ions, but a very weak M^+ ion, and the ammonia chemical ionisation mass spectrum showed a base peak at *m/z* 529 ($M + NH_3$) as well as the molecular ion at 512 (70%).

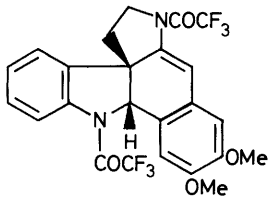
Treatment of a solution of the bis(trifluoroacetyl) spirocyclic indoline (**12**) in a mixture of ethanol and tetrahydrofuran with concentrated aqueous ammonia for a few hours at 20 °C afforded the oxo derivative (**10a**) (95%). The latter was presumably formed by hydrolysis of both trifluoroacetyl

Table 1. Products formed from the cyclisations of *N*-(3,4-dimethoxyphenylacetyl)tryptamine (**1a**) with phosphorus trichloride or phosphoryl chloride

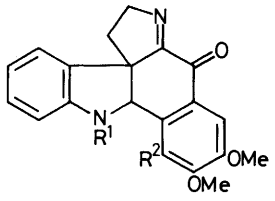
Expt.	Concentration of (1) mmol	Cyclising agent (mmol)	Solvent (ml)	Reaction conditions	Method of isolation of products	Products	Yield (%)
1	20.1	PCl_3 (155)	Benzene (300)	Reflux 1 h	Open column cromatography and prep. t.l.c.	(**10a**)	46
						(**10b**)	1
						(**10c**)	0.2
						(**11a**)	1
						(**11b**)	3
2	5.7	$POCl_3$ (44)	Benzene (15)	Reflux 1.5 h	Prep. h.p.l.c. and prep. t.l.c.	(**10a**)	68
						(**10b**)	2
						(**11a**)	5
						(**11b**)	5
3	0.8	$POCl_3$ (1.2) pyridine (1.2)		22 °C/24 h and 100 °C/8 h	Semi-prep h.p.l.c.	(**10a**)	43
						(**11a**)	3
						(**11b**)	3
4	0.5	$POCl_3$ (1.0) pyridine (1.0)	Benzene (17)	22 °C/17 h reflux 3.5 h	Semi-prep h.p.l.c.	(**10a**)	45
						(**11a**)	4
						(**11b**)	5
5	0.3	$POCl_3$ (0.6) pyridine (0.6)	Chloroform (15)	Reflux 5 h	Semi-prep. h.p.l.c.	(**10a**)	39
						(**11a**)	5
						(**11b**)	6

Table 2. Key proton n.m.r. chemical shift assignments of the spiropentacyclic indolines (δ values)

Compound	12-H	9-H	8-H	12b-H
(**10a**)	6.94s	7.50s		4.79s
(**10b**)	6.81s	6.94s	5.01s	4.21s
(**10c**)	7.11s	7.57s		5.80br s
(**10d**)	6.96s	7.50s		6.13s
(**12**)	6.54s	6.68s	7.38s	5.73s
(**13a**)	6.88s	7.54s		6.17s
(**13b**)		7.61s		5.65s



(**12**)



(**13**)

a; $R^1 = COCF_3$, $R^2 = H$

b; $R^1 = H$, $R^2 = COCF_3$

residues followed by autoxidation of the imine-enamine system of the primary product (**3a**). The hydroperoxy derivative (**10b**) is presumably an intermediate in this autoxidation process, and there are ample precedents for this type of reaction.[11–14] Attempted acidic hydrolysis of the bis(trifluoroacetyl)indoline (**12**) in concentrated sulphuric acid, or with 4M hydrochloric acid, was unsuccessful and starting material was recovered.

The stereochemistry of the spirocyclic indoline system is presumed to be that shown in the structural formulae (**10**) and (**12**) with *cis*-fusion of rings B and D; the benzene ring and the *N*-trifluoroacetyl group in ring D ensure that the D ring is essentially planar, and thus ring B cannot be joined to it in a *trans* fashion. The stereochemistry of the hydroperoxy group in (**10b**) is not known, but only one isomer was isolated as shown by the 360 MHz n.m.r. spectrum.

Attempts to reduce the enamine double bond of the bis(trifluoroacetyl)indoline (**12**) were not successful, *e.g.* with hydrogen over platinum oxide a mixture of two products (**13a**) and (**13b**) was obtained. The same product mixture was also formed on trifluoroacetylation of the oxo spirocyclic indoline (**10a**), and it would thus appear that in the attempted hydrogenation reaction, the N_a-trifluoroacetyl group had partly migrated to the neighbouring aromatic ring, and that hydrolysis of the N_b-trifluoroacetyl group had been followed by autoxidation during work-up.

Further work is in progress to explore the possibility of extending the basic hypothesis outlined in this paper, and some success has already been achieved [15] in the synthesis of alicyclic analogues of the pentacyclic indoline (**12**).

Experimental

Melting points were determined on a hot-stage apparatus and are uncorrected. I.r. spectra were determined in chloroform solutions and u.v. spectra in ethanol. ^1H N.m.r. spectra were determined in deuteriochloroform with a Perkin-Elmer R32 90 MHz or Bruker 360 MHz instruments, and ^{19}F n.m.r. spectra in chloroform on a Perkin-Elmer R32 instrument operating at 84.6 MHz. ^{13}C N.m.r. spectra were run in deuteriochloroform on Varian XL 100 or Bruker 360 MHz instruments. The ^{13}C chemical shifts are in p.p.m. from TMS, and ^{19}F spectra in p.p.m. from $CFCl_3$ using $CFCl_2CFCl_2$ as external standard. Mass spectra were run on Varian CH5D or VG 70/70 spectrometers operating at 70 eV and 25 A for e.i. spectra, or with wire currents in the range 10—20 A for f.d. spectra. Neutral grade III alumina and silica gel (60—100 mesh) were used for column chromatography.

N-(3,4-Dimethoxyphenylacetyl)tryptamine (**1a**) was prepared from tryptamine and 3,4-dimethoxyphenylacetic acid following the previously published method,[8] and purified by column chromatography on alumina with benzene–chloroform (85:15) as eluant. It was obtained in 93% yield as a colourless, viscous mass which sublimed at 174 °C, 0.15 mmHg to give a colourless

glass, m.p. 56—58 °C (lit.,[8,9] m.p. 65—66 °C); $\nu_{max.}$ 3 700, 3 150 (NH), and 1 660 (C=O) cm^{-1}; $\lambda_{max.}$ (log $\varepsilon_{max.}$) 223 (4.63), 281 (3.94), and 290 (3.89) nm; δ_H 2.85 (2 H, t, *J* 8 Hz, $NHCH_2CH_2$), 3.39 (2 H, s, $ArCH_2$), 3.50 (2 H, m, $NHCH_2$), 3.68 and 3.80 (3 H, each, 2 s, 3′- and 4′-OCH_3), 5.40 (1 H, br s, exch. with D_2O, CONH), 6.57 (1 H, d, *J* 2 Hz, 2′-H), 6.70 (1 H, d, *J* 7 Hz, 5′-H), 6.72 (1 H, dd, *J* 7 and 2 Hz, 6′-H), 7.00—7.55 (5 H, m, 2-, 4-, 5-, 6-, and 7-H), and 8.10 (1 H, br s, exch. with D_2O, NH). The picrate formed dark red needles, m.p. 142—143 °C (from abs. EtOH); δ_H 9.0 (2 H, s, 3- and 5-H of picric acid), 8.20 (1 H, br s, exch. with D_2O, NH), 6.95—7.52 (5 H, m, 2-, 4-, 5-, 6-, and 7-H), 6.6—6.75 (3 H, dd, *J* 8 and 2 Hz, 2′-, 5′-, and 6′-H), 5.5 (1 H, br s, CONH), 3.70 and 3.83 (3 H each, 2 s, 3′- and 4′-OCH_3), 3.50 (2 H, q, *J* 7 Hz, $NHCH_2$), 3.4 (2 H, s, $COCH_2$), and 2.85 (2 H, t, *J* 7 Hz, $NHCH_2CH_2$); *m/z* (e.i.) 229 (96%), 230 (17), 199 (15), and 91 (100).

The same amide (**1a**) was also obtained[9] from methyl 3,4-dimethoxyphenylacetate and tryptamine and after chromatography furnished the pure product as a viscous mass in 92% yield.

Cyclisation of N-(3,4-*Dimethoxyphenylacetyl*)*tryptamine* (**1a**).—In a typical experiment, freshly distilled phosphorus trichloride (13.6 ml) was added slowly to a well-stirred solution of the amide (**1a**) (6.8 g) in dry benzene (300 ml) under nitrogen at 20 °C. The mixture was heated under reflux for 1 h and then evaporated to dryness under reduced pressure. The residue was treated with hot 50% aqueous acetic acid until a clear solution was obtained, and then cooled and extracted with benzene (3 × 40 ml). The combined extracts were washed with water (3 × 20 ml) and the washings combined with the aqueous acetic acid. The benzene solution was dried ($MgSO_4$) and evaporated to dryness to afford recovered starting material (0.84 g, 10%), identified by t.l.c. and n.m.r. spectroscopy.

The combined aqueous acidic solution was cooled to 0 °C and made alkaline with ammonium hydroxide (*d* 0.880). The mixture was extracted with chloroform (3 × 75 ml) and the combined extracts washed with water (3 × 15 ml), dried ($MgSO_4$) and evaporated to dryness. The semi-solid residue was chromatographed on alumina in benzene and then benzene–dichloromethane which afforded the major product (**8a**); further chromatography of the mother liquors, followed by thick-layer chromatography on silica gel using ethyl acetate–methanol (95:5 v/v) afforded the other four products shown in Table 1 (Entry 1).

Similar preparations were carried out with phosphoryl chloride as cyclising reagent, or with phosphoryl chloride in pyridine and the results are also summarised in Table 1. The physical and spectral characteristics of the five products obtained are reported below.

5,6,12b,13-*Tetrahydro*-10,11-*dimethoxybenzo*[a]*pyrrolo*[2,3-d]*carbazol*-8-*one* (**10a**) crystallised as light orange plates (3.12 g, 46%), m.p. 241—242 °C (from ethyl acetate) (Found: C, 71.4; H, 5.4; N, 8.4. $C_{20}H_{18}N_2O_3$ requires C, 71.8; H, 5.4; N, 8.4%); $\nu_{max.}$ 3 395 (NH), 1 665 (C=O), and 1 620 cm^{-1} (C=N); $\lambda_{max.}$ (log $\varepsilon_{max.}$) 210 (4.51), 240 (4.34), 303 (4.06), and 344 nm (3.99); δ_H 2.40 (2 H, t, *J* 8 Hz, NCH_2CH_2), 3.84 and 3.97 (3 H each, 2 s, 10- and 11-OCH_3), 4.25 (2 H, m, NCH_2), 4.71 (1 H, s, exch. with D_2O, NH), 4.79 (1 H, s, NHCH), 6.94 (1 H, s, 12-H), 7.50 (1 H, s, 9-H), and 6.5—7.2 (4 H, m, ArH); δ_C 106.50 (C-12), 154.72 (C-11), 147.05 (C-10), 109.06 (C-9), 129.23 (C-8a), 139.01 (C-12b), 181.23 (C=O), 169.33 (C-7a), 62.12 (C-4b), 126.04 (C-4a), 121.32 (C-4), 117.67 (C-3), 128.32 (C-2), 109.65 (C-1), 148.22 (C-13a), 66.44 (C-12b), 40.00 (C-5), 58.01 (C-6), 55.44 (11-OCH_3), and 54.91 (10-OCH_3); *m/z* (f.d.) 335 (25%) and 334 (M^+, 100); *m/z* (e.i.) 334 (M^+, 100%), 333 (47), 317 (33), 306 (33), and 305 (26); *picrate* brown micro-needles, m.p. 185 °C (from EtOH); *m/z* (e.i.) 334 (40%), 333 (17), 332 (38), 331 (23), 317 (15), 303 (23), 229 (72), 165 (21), and 91 (36); 2,4-*dinitrophenylhydrazone dihydrochloride*, greyish brown needles, m.p. above 360 °C with softening and blackening at 229 °C (from EtOH) (Found: C, 53.6; H, 4.3; N, 14.3. $C_{26}H_{24}Cl_2N_6O_6$ requires C, 53.2; H, 4.1; N, 14.3%); $\lambda_{max.}$(log $\varepsilon_{max.}$) 238 (4.76), 290 (4.39), and 428 nm (4.79).

5,6,12b,13-*Tetrahydro*-13-*hydroxy*-10,11-*dimethoxybenzo*[a]*pyrrolo*[2,3-d]*carbazol*-8-*one* (**10c**) crystallised as cream coloured micro-needles (13 mg, 0.2%), m.p. 330 °C (from ethanol); $\nu_{max.}$ 3 400, 1 655, and 1 615 cm^{-1}; $\lambda_{max.}$(log $\varepsilon_{max.}$) 225 (4.40), 244 (4.41), 278 (sh) (4.20), 295 (4.34), and 372 (3.87) nm; δ_H (360 MHz; $CDCl_3$ + CD_3CN) 9.62 (1 H, s, OH), 7.58 (2 H, m, 1- and 4-H), 7.57 (1 H, s, 9-H), 7.11 (1 H, s, 12-H), 7.15 (1 H, dd, *J* 8 and 1 Hz, 3-H), 7.25 (1 H, dd, *J* 8 and 1 Hz, 2-H), 5.80 (1 H, br s, 12b-H), 2.4—3.4 (2 H, m $NCHCH_2$), 3.5—4.2 (2 H, m, NCH_2), 3.99 and 4.00 (3 H each, 2 s, 10- and 11-OCH_3); *m/z* (e.i.) 351.8 (2%), 350.8 (22), 349.8 (M^+, 100), 293.8 (26), 292.8 (16), 291.8 (9), 279.8 (30), and 264.7 (20) (Found: *m/z* 350.1290. $C_{20}H_{18}N_2O_4$ requires *m/z* 350.126 63).

5,6,12b,13-*Tetrahydro*-8-*hydroperoxy*-10,11-*dimethoxy*-8H-*benzo*[a]*pyrrolo*[2,3-d]*carbazole* (**10b**) crystallised as colourless plates (85 mg, 1%), m.p. 273—274 °C (from ethanol) (Found: C, 67.5; H, 5.6; N, 7.7. $C_{20}H_{20}N_2O_4$ requires C, 68.2; H, 5.7; N, 7.9%); $\nu_{max.}$(Nujol) 3 315, 3 390 (NH, OH), 1 645, 1 640, and 1 632 cm^{-1}; $\lambda_{max.}$(log $\varepsilon_{max.}$) 211 (4.61), 239 (4.12), 284 (3.81), 287.5 (3.84), and 292sh nm (3.81); δ_H 2.20 (1 H, dd, *J* 14 and 2 Hz, $CHHCH_2N$), 2.43 (1 H, m, $CHHCH_2N$), 3.33 (1 H, dd, *J* 10 and 2 Hz, $CHHN$), 3.30 (1 H, dd, *J* 10 Hz and 2 Hz, $CHHN$), 4.21 (1 H, s, 12b-H), 4.31 (1 H, br s, OOH), 5.01 (1 H, s, 8-H), 5.97 (1 H, br s, 13-H), 6.81 (1 H, s, 12-H), 6.94 (1 H, s, 9-H), 6.61 (1 H, td, $J_{1,2}$ 7, $J_{1,3}$ 1, and $J_{1,4}$ 0.2 Hz, 1-H), 6.80 (1 H, td, $J_{3,4}$ 7, $J_{3,2}$ 7, and $J_{3,1}$ 1 Hz, 3-H), 7.08 (1 H, td, $J_{2,1}$ 7, $J_{2,3}$ 7 Hz, and $J_{2,4}$ 1 Hz, 2-H), 7.29 (1 H, td, $J_{4,3}$ 7, $J_{4,2}$ 1, and $J_{4,1}$ 0.2 Hz, 4-H), and 3.83 and 3.90 (3 H each, 2 s, 10- and 11-OCH_3); *m/z* (c.i., NH_3), 352 (M^+, 100%); *m/z* (f.d.) 354 (21%), 353 (59), 352 (M^+, 100), and 350 (20); *m/z* (e.i.) 353 (37%), 352 (M^+, 100), 334 ($M - H_2O$, 62), 323 (14), 308 (18), 295 (27), 294 (32), 281 (36), 280 (45), 278 (18), 266 (27), 264 (55), 250 (15), 235 (15), and 151 (14); *picrate*, greenish yellow prisms, m.p. above 323 °C (from ethanol) (Found: C, 53.9; H, 3.8; N, 11.5. $C_{26}H_{23}N_5O_{11}$ requires C, 53.7; H, 4.1; N, 11.9%); *m/z* (e.i.) 352 (M^+, 100%); δ_H(DMSO-d_6) 1.85—2.15 (2 H, m, CH_2CH_2N), 3.1—3.45 (2 H, m, CH_2N), 3.69 and 3.78 (3 H each, 2 s, 10- and 11-OCH_3), 4.1—4.5 (17 H, br s, 12b-H, OOH, HDO), 5.22 (1 H, s, 8-H), 7.0 (1 H, s, 12-H), 7.10 (1 H, s, 9-H), 6.9—7.2 (3 H, m, ArH), 7.48 (1 H, br s, 4-H), 7.88 (1 H, br s, NH), and 8.58 (2 H, s, 3- and 5-H or picric acid).

3,4-*Dihydro*-1-(3,4-*dimethoxybenzoyl*)-9H-*pyrido*[3,4-b]*indole* (**11a**) crystallised as light orange plates (62 mg, 1%), m.p. 142—144 °C (from cyclohexane) (Found: C, 71.7; H, 5.8; N, 8.7. $C_{20}H_{18}N_2O_3$ requires C, 71.8; H, 5.4; N, 8.4%); $\nu_{max.}$ 3 570 (NH) and 1 635 cm^{-1} (C=O); $\lambda_{max.}$(log $\varepsilon_{max.}$) 224 (4.69), 298 (4.28), and 315 nm (4.25); δ_H 2.98 (2 H, t, *J* 8 Hz, 4-H_2), 4.14 (2 H, t, *J* 8 Hz, 3-H_2), 3.92 (6 H, s, 3′- and 4′-OCH_3), 6.87 (1 H, d, *J* 9 Hz, 5′-H), 7.74 (1 H, d, *J* 2 Hz, 2′-H), 7.98 (1 H, dd, *J* 9 and 2 Hz, 6′-H), 7.05—7.66 (4 H, m, ArH), and 9.35 (1 H, br s, exch. with D_2O, 9-H); *m/z* (f.d.) 334 (M^+, 100%); *m/z* (e.i.) 333.9 (M^+, 8%), 332.9 (22), 331.9 (100), 330.9 (58), 316.8 (27), 303 (38), 171 (61), and 165 (28); *picrate*, pale yellow needles, m.p. 238—240 °C (from benzene); *m/z* (e.i.) 334 (27%), 332 (63), 331 (46), 303 (41), and 229 (48).

1-(3,4-*Dimethoxybenzoyl*)-9H-*pyrido*[3,4-b]*indole* (**11b**) crystallised as pale yellow hair-like needles (212 mg, 3%), m.p. 169—171 °C (from cyclohexane) (Found: C, 71.9; H, 4.5; N, 8.7. $C_{20}H_{16}N_2O_3$ requires C, 72.2; H, 4.8; N, 8.4%); $\nu_{max.}$ 3 580 (NH) and 1 630 (C=O) cm^{-1}; $\lambda_{max.}$(log $\varepsilon_{max.}$) 222 (4.65), 298 (4.29), and 389 (4.03) nm; δ_H 10.45 (1 H, br s, exch. with D_2O, NH), 8.58 (1 H, d, *J* 5 Hz, 3-H), 8.10 (1 H, d, *J* 5 Hz, 4-H), 8.26 (1 H, dd, *J* 9 and 2 Hz, 6′-H), 7.99 (1 H, d, *J* 2 Hz, 2′-H), 6.95 (1 H, d, *J* 9 Hz, 5′-H), 7.2—7.6 (4 H, m, ArH), 3.94 (6 H, s, 3′- and 4′-OCH_3; δ_C 152.77 (C-1), 137.37 (C-3), 128.76 (C-4), 120.53 (C-4a), 129.96

(C-4b), 117.76 (C-5), 121.35 (C-6), 120.24 (3-7), 111.69 (C-8), 136.96 (C-8a), 136.73 (C-9a), 131.19 (C-1′), 113.41 (C-2′), 140.70 (C-3′), 148.29 (C-4′), 109.71 (C-5′), 126.70 (C-6′), 192.59 (C=O), and 55.65 (3′- and 4′-OCH_3); *m/z* (e.i.) 333 (22%), 332 (M^+, 100), 331 (59), 317 (21), 303 (31), 289 (14), 167 (13), 166 (17), and 165 (18) (Found: *m/z* 332.1152. $C_{20}H_{16}N_2O_3$ requires *m/z* 332.116 084); *m/z* (f.d.) 332 (M^+, 100%); *picrate*, light orange needles, m.p. 244—245 °C (decomp.) (from ethanol) (Found: C, 55.6; H, 3.4; N, 12.6. $C_{26}H_{19}N_5O_{10}$ requires C, 55.6; H, 3.4; N, 12.5%); δ_H[$CDCl_3$ + $(CD_3)_2SO$] 12.25 (1 H, s, exch. with D_2O, OH), 8.60 (1 H, d, *J* 8 Hz, 3-H), 8.35 (1 H, d, *J* 8 Hz, 4-H), 8.62 (2 H, s, 3- and 5-H of picric acid), 7.65 (1 H, d, *J* 2 Hz, 2′-H), 7.42 (1 H, dd, *J* 8 and 2 Hz, 6′-H), 7.00 (1 H, d, *J* 8 Hz, 5′-H), 7.55—7.85 (4 H, m, ArH), and 3.90 (6 H, s, 3′- and 4′-OCH_3).

13-*Acetyl*-5,6,12b,13-*tetrahydro*-10,11-*dimethoxybenzo*[a]*pyrrolo* [2,3-d]*carbazol*-8-*one* (**10d**).—The amide (**1a**) (180 mg) was cyclised following the general method and the crude product acetylated with acetic anhydride (0.9 ml) for 24 h. After work-up, the basic material was isolated by the usual acid-base treatment and purified by h.p.l.c. to give the *acetyl derivative* (**10d**) (20 mg, 10%) as cream coloured plates, m.p. 228—229 °C (from ethyl acetate–light petroleum) (Found: C, 69.7; H, 5.5; N, 7.4. $C_{22}H_{20}N_2O_4$ requires C, 70.2; H, 5.4; N, 7.4%); $\nu_{max.}$ 1 665 (C=O), 1 640 (N–C=O), and 1 620 (C=N) cm^{-1}; $\lambda_{max.}$(log $\varepsilon_{max.}$) 217 (4.55), 245 (4.34), 290 (4.02), and 345 nm (4.00); δ_H 7.50 (1 H, s, 9-H), 6.96 (1 H, s, 12-H), 6.99—7.16 (4 H, m, ArH), 7.31 (1 H, d, *J* 9 Hz, 1-H), 6.13 (1 H, s, 12b-H), 4.1—4.4 (2 H, m, CH_2N), 3.86 and 3.91 (3 H each, 2 s, 10- and 11-OCH_3), 2.52 (3 H, s, 13-$COCH_3$), and 2.3— 2.5 (2 H, m, CH_2CH_2N); *m/z* (e.i.) 377 (25%), 376 (M^+, 100), 334 (M − CH_2=C=O), 333 (33), 306 (22), 305 (42), and 294 (18).

6,7,12b,13-*Tetrahydro*-10,11-*dimethoxy*-7,13-*bis*(*trifluoroacetyl*)-5H-*benzo*[a]*pyrrolo*[2,3-d]*carbazole* (**12**).—A solution of the amide (**1a**) (920 mg, 2.72 mmol) and freshly prepared TFAA (8.77 ml, 62.1 mmol) in dry benzene (440 ml) was stirred under nitrogen at 0 °C for 3 h and then at 20 °C for 1 h; it was then evaporated to dryness under reduced pressure. The crystalline residue was purified by preparative h.p.l.c. on silica gel, using chloroform–light petroleum (9:1) as eluant, and crystallisation to furnish *compound* (**12**) (1.32 g, 95%) as colourless needles, m.p. 271 °C (from chloroform–light petroleum) (Found: C, 56.5; H, 3.6; N, 5.3. $C_{24}H_{18}F_6N_2O_4$ requires C, 56.2; H, 3.5; N, 5.5%); $\nu_{max.}$ 1 690 and 1 680 cm^{-1} (C=O); $\lambda_{max.}$(log $\varepsilon_{max.}$) 224sh (4.37), 247 (4.34), 286sh (3.91), and 330 nm (4.10); δ_F −70.37 and −73.59 (3 F each, 2 s, 7- and 13-$COCF_3$); δ_H 8.0 (1 H, d, *J* 8 Hz, 1-H), 7.33 (1 H, t, *J* 8 Hz, 2-H), 7.22 (1 H, t, *J* 8 Hz, 3-H), 7.08 (1 H, d, *J* 8 Hz, 4-H), 7.38 (1 H, s, 8-H), 6.68 (1 H, s, 9-H), 6.54 (1 H, s, 12-H), 5.73 (1 H, s, 12b-H), 4.01 and 4.25 (1 H each, m, and t, *J* 10 Hz, CH_2N), 2.1 and 2.5 (1 H each, dd and q, *J* 8 and 10 Hz, CH_2CH_2N), and 3.75 (6 H, s, 10- and 11-OCH_3); *m/z* (e.i.) 515 (18%), 514 (77), 513 (100), 512 (M^+, 3), 498 (18), 481 (14), 415 (M − $COCF_3$, 17), 400 (18), 384 (17), 383 (34), 256 (16), and 69 (CF_3, 12); *m/z* (c.i., NH_3) 529 (M + NH_3, 100%), 512 (M^+, 70), and 417 (20); *m/z* (f.d.) 513 (14%) and 512 (M^+, 100).

Hydrolysis of 6,7,12b,13-*Tetrahydro*-10,11-*dimethoxy*-7,13-*bis*(*trifluoroacetyl*)-5H-*benzo*[a]*pyrrolo*[2,3-d]*carbazole* (**12**).—(*a*) A solution of the bis(trifluoroacetyl) indole (**12**) (100 mg, 0.195 mmol) in a mixture of ethanol (45 ml) and tetrahydrofuran (15 ml) was stirred with conc. aqueous ammonia (5 ml) for 3 h at 20 °C and at 35—40 °C for 3.5 h. It was evaporated to dryness and the residue was recrystallised from ethanol to give the 8-oxo indoline (**10a**) (62 mg, 95%) as light orange plates, m.p. 241—242 °C, identical with material obtained earlier.

(*b*) A suspension of the bis(trifluoroacetyl) indoline (**12**) (100 mg, 0.195 mmol) in aqueous sulphuric acid (15 ml; 75% w/v) was stirred at 20 °C for 24 h and then boiled under reflux for 3 h. After cooling, the mixture was filtered and the precipitate was crystallised from chloroform–light petroleum to afford starting material (53 mg, 53%), m.p. 271 °C. The filtrate, on basification with ammonium hydroxide and extraction with chloroform, furnished the oxo indoline (**10a**) (25 mg, 38%), m.p. 241—242 °C (from methanol).

Catalytic Hydrogenation of 6,7,12b,13-*Tetrahydro*-10,11-*dimethoxy*-7,13-*bis*(*trifluoroacetyl*)-5H-*benzo*[a]*pyrrolo*[2,3-d]*carbazole* (**12**).—(*a*) A solution of the bis(trifluoroacetyl) indoline (**12**) (60 mg, 0.117 mmol) in methanol (15 ml) and tetrahydrofuran (10 ml) was hydrogenated over platinum oxide (30 mg) at 4 atm for 72 h to give a mixture (1:1) of (**13a**) and (**13b**) (14 mg, 28%) as pale yellow prisms, m.p. 229—232 °C (from ethyl acetate) (Found: C, 62.2; H, 4.5; N, 6.4. $C_{22}H_{17}F_3N_2O_4$ requires C, 61.4; H, 4.0; N, 6.5%); $\nu_{max.}$(KBr) 1 705, 1 690, 1 680, and 1 625 cm^{-1}; $\lambda_{max.}$(log $\varepsilon_{max.}$) 242 (4.32), 299 (3.92), and 346 (3.90) nm; δ_F(360 MHz) −69.05 and −69.49 [1.5 F each, 2 s, 13-$COCF_3$ of (**13a**) and 12-$COCF_3$ of (**13b**)]; δ_H(360 MHz): (**13a**) 7.92 (1 H, d, *J* 8 Hz, 1-H), 7.54 (1 H, s, 9-H), 7.33 (1 H, t, *J* 8 Hz, 2-H), 7.15 (1 H, t, *J* 8 Hz, 3-H), 6.99 (1 H, d, *J* 8 Hz, 4-H), 6.88 (1 H, s, 12-H), 6.17 (1 H, s, 12b-H), 4.15 and 4.45 (1 H each, q, *J* 10 Hz, and m, CH_2N), 3.92 and 3.95 (3 H each, 2 s, 10- and 11-OCH_3), and 2.33 and 2.43 (1 H each, m, and q, *J* 10 Hz, CH_2CH_2N): (**13b**) 7.61 (1 H, s, 9-H), 7.35 (1 H, d, *J* 8 Hz, 1-H), 7.33 (1 H, t, *J* 8 Hz, 2-H), 7.15 (1 H, t, *J* 8 Hz, 3-H), 6.99 (1 H, d, *J* 8 Hz, 4-H), 5.65 (1 H, s, 12b-H), 4.15 and 4.45 (1 H each, q, *J* 10 Hz, and m, CH_2N), 3.92 and 3.95 (3 H each, 2 s, 10- and 11-OCH_3), 2.58 (1 H, s, NH), and 2.33 and 2.43 (1 H, each, m and q, *J* 10 Hz, CH_2CH_2N); *m/z* (e.i.· 4315 (25%), 430 (M^+, 100), 399 (10), 361 (M − CF_3, 25), 333 (M −$COCF_3$, 17), 306 (36), 290 (12), and 57 (12); *m/z* (f.d.) 431 (22%) and 430 (M^+, 100).

(*b*) To a cold solution of the indoline (**10a**) (100 mg, 0.299 mmol) in dry benzene (100 ml) was added 2% trifluoroacetic anhydride in dry benzene (20 ml) and the mixture stirred at 5—10 °C for 5 h. The crystalline residue, obtained after evaporation of the reaction mixture to dryness under reduced pressure, was purified by chromatography over a silica gel column to give a mixture (1:1) of (**13a**) and (**13b**) (15 mg, 12%) as pale yellow prisms, m.p. 229—232 °C (from ethyl acetate).

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