

Electrophilic Substitution in Indoles. Part 18.^{1,2} Cyclisation of *N*-Acyltryptamines

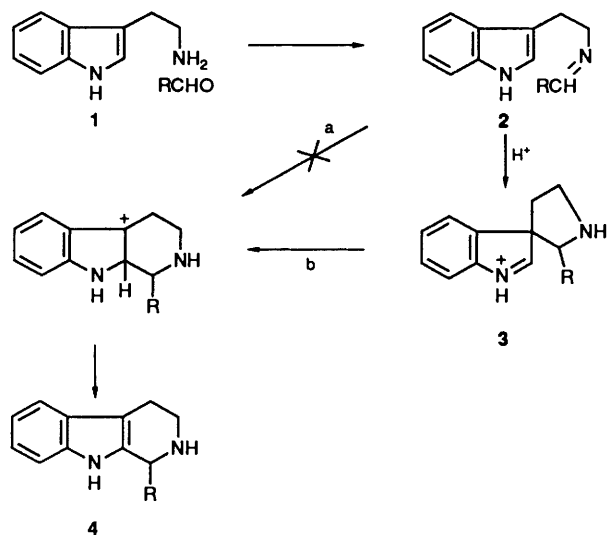
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Cyclisation of *N*₆-acetyltryptamines **8** with trifluoroacetic anhydride, or pentafluoropropionic anhydride, affords spirocyclic indolines of types **14** and **15** in virtually quantitative yields. The mechanism of the reactions involves cyclisation by *ipso*-attack at the 3-position of the indole nucleus, to form spirocyclic 3*H*-indoles **12** and **13**, which subsequently undergo addition of the anhydride to the 1,2-double bond of the 3*H*-indole. The generality of the latter reaction has been established by converting the 3*H*-indole-3-spirocyclopentane **16** and benzylideneaniline **18** into the anhydride adducts **17a** and **19** respectively. The spirocyclic indoline adducts **14a**, **14b**, **15a**, **15b** and **17a** are rapidly hydrolysed by dilute aqueous ammonia to the hydroxy spirocyclic indolines **20a**, **20b**, **21a**, **21b** and **17b** respectively.

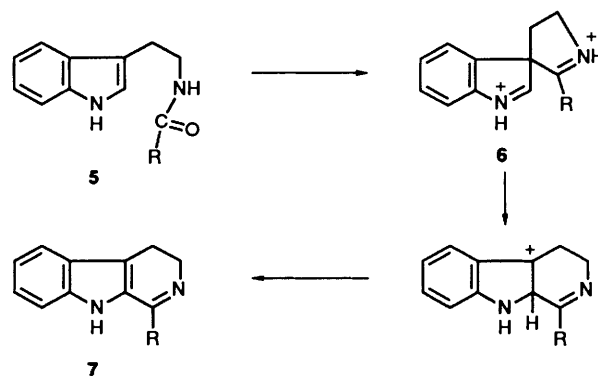
The Pictet–Spengler type cyclisation³ of tryptamines with aldehydes (Scheme 1) is one of the classical methods for the chemical synthesis of tetrahydro-β-carbolines, and it is also the way in which the latter are biosynthesised.⁴ Some years ago, we provided circumstantial evidence⁵ that such reactions do not occur by direct cyclisation at the 2-position of the indole nucleus of the tryptamine **1** (Scheme 1, path a); instead the initially



Scheme 1

formed Schiff's base **2** undergoes cyclisation at the 3-position to afford a spirocyclic 3*H*-indole **3** which then rearranges to the tetrahydro-β-carboline **4** (Scheme 1, path b). Synthetic studies by other workers,⁶ in which the intermediate spirocyclic 3*H*-indole was trapped by a subsequent intramolecular nucleophilic cyclisation, have provided more direct evidence for this view, and in one case an intermediate 3*H*-indole has been trapped by an *in situ* catalytic reduction to the corresponding spirocyclic indoline.⁷

Like the Pictet–Spengler reaction, the related Bischler–Napieralski type cyclisation of *N*-acyltryptamines **5** (e.g. with phosphoryl chloride) is a very useful synthetic procedure³ for preparing β-carboline type intermediates **7** required for the synthesis of indole alkaloids and related compounds. The products



Scheme 2

7 are dihydro- rather than tetrahydro-β-carbolines, and we envisaged that the mechanism of the cyclisation also involved the formation of intermediate 3*H*-indoles **6**, but that the latter would not normally be observed because of the ease with which they would rearrange to the dihydro-β-carbolines **7** under the acidic conditions normally used in the cyclisation (Scheme 2). As with the Pictet–Spengler type cyclisations (Scheme 1), however, the intermediate 3*H*-indoles **6** may also be trapped by a further intramolecular nucleophilic cyclisation, as in the case of the cyclisation of the dimethoxyphenylacetyltryptamine **5** (R = CH₂Ar) described in the preceding paper in this series.¹

Here, we describe studies of the cyclisation of *N*-acetyltryptamines **8**, and initially we investigated the reaction of *N*-acetyltryptamine **8a** itself with phosphoryl chloride in pyridine hoping that the basic conditions used would enable us to isolate a spirocyclic 3*H*-indole type product (cf. **6**) rather than a dihydro-β-carboline (cf. **7**). However, the sole product was a rather insoluble material, the mass spectrum of which was consistent with an oligomer of the free base of the spirocyclic 3*H*-indole **6** (R = Me). In hindsight, the formation of such a polymeric material was not surprising because of the well-known tendency of imines to polymerise, e.g. piperidines readily trimerise and 3,3-disubstituted 3*H*-indoles also form cyclic trimers.⁸

Subsequently, we investigated the use of trifluoroacetic anhydride as a cyclisation reagent for the *N*-acetyltryptamines **8** because of its successful utilisation in the cyclisation of 4-(1,2-dimethylindol-3-yl)butyric acid,⁹ and of the dimethoxyphenyl-

Table 1 ^{13}C NMR spectra* of the spirocyclic indolines **14**, **15**, **17**, **20** and **21b** (δ values)

Carbon No.	14a	14b	15a	15b	17a	17b	20a	20b
2	89.8	90.2	90.1	89.9	92.7	91.0	89.9	90.7
3	59.0	59.1	59.2	58.9	57.5	57.2	60.3	61.0
3a	130.8	132.4	130.8	131.9	137.2	138.6	133.4	129.3
4	127.6	109.5	128.1	109.1	127.0	126.3	127.8	110.8
5	123.5	159.3	123.5	159.1	122.3	122.5	125.1	160.2
6	130.3	114.9	130.6	114.8	128.4	127.9	130.3	115.4
7	118.1	119.5	118.8	119.5	117.8	118.1	118.3	120.1
7a	140.2	133.5	140.7	133.5	138.8	138.6	141.9	135.5
2'	145.1	145.0	145.5	148.7	40.1	39.9	149.7	149.9
3'	59.0	59.1	59.2	58.9	24.8	25.3	60.3	61.0
4'	27.1	27.2	27.4	27.1	24.8	24.7	27.9	28.3
5'	46.4	46.4	46.4	46.1	30.3	29.9	47.9	48.1
=CH ₂	102.7	101.8	102.6	102.3	—	—	99.5	99.8
OCH ₃	—	55.7	—	55.6	—	—	—	56.2
N-CO	154.5	153.7	~156.2	154.8	155.2	153.7	156.3	156.1
	154.8	155.0	~156.2	156.1	—	—	156.3	156.3
O-CO	155.7	156.2	~156.2	157.3	157.3	—	—	—
CF ₃	TW	TW	—	—	TW	TW	TW	TE
CF ₂ CF ₃	—	—	~118	—	—	—	—	—
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* Spectra were measured in deuteriochloroform except for **14b** (deuteriomethanol) and **20a** (deuterioacetonitrile); TW = too weak.

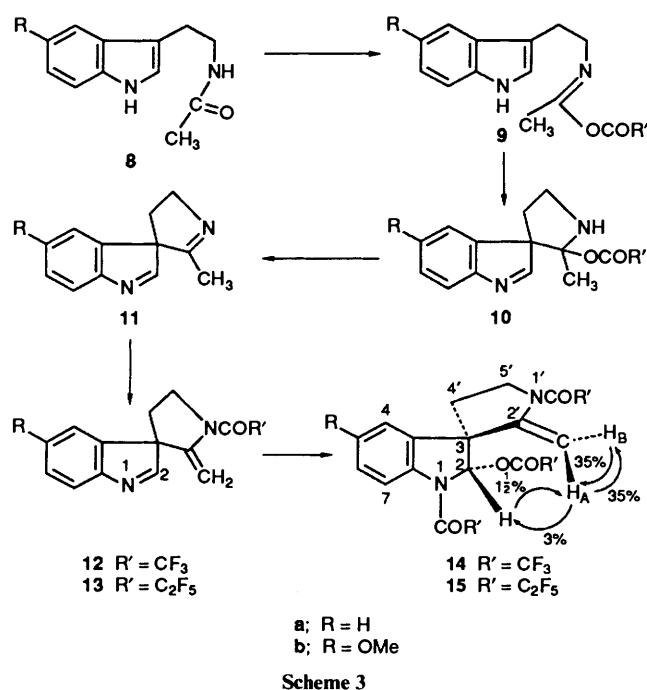
acetyltryptamine **5** ($\text{R} = \text{CH}_2\text{Ar}$) described in the preceding paper.¹ The use of pentafluoropropionic anhydride as a derivatising reagent for GC and GC/MS studies of physiologically active *N*-acetyltryptamines had also been described previously^{10,11} but we had some reservations (*cf.* ref. 2) about the structures assigned¹¹ to the products (see below).

In the event, the product (*ca.* 95% yield) obtained on treatment of *N*-acetyltryptamine **8a** with trifluoroacetic anhydride at 0–5 °C in benzene was a crystalline solid with a UV spectrum ($\lambda_{\text{max}}/\text{nm}$ 252, 277 and 285) much more typical of an indoline than that of an indole or 3*H*-indole.

The ^1H NMR spectrum showed that the *N*-acetyl proton signal of the starting material had been replaced by two vinyl proton signals at δ 4.15 and 6.07. Four aromatic proton signals could also be discerned as well as those of the four aliphatic protons in the aminoethyl side-chain, and a singlet at δ 6.90 was assigned to the 2-proton of the indole nucleus. Both the EI and FD mass spectra (M^+ , m/z 490) corresponded to the incorporation of three trifluoroacetyl residues into the original *N*-acetyltryptamine, and this together with the UV and NMR data led to the novel structure **14a** for the cyclisation product. This was confirmed by elemental analysis and by the ^{19}F NMR spectrum, which clearly showed three signals, as well as by the ^{13}C NMR spectrum (see Experimental section) (and Tables 1 and 2).

This somewhat unexpected result can be explained by the mechanism shown in Scheme 3, in which the initial product of cyclisation **10a** ($\text{R}' = \text{CF}_3$) was assumed to undergo elimination to form the spirocyclic 3*H*-indole **11a** (*cf.* also Scheme 2, structure **6**); subsequent addition of trifluoroacetic anhydride across the 3*H*-indole C=N group of **11a** after trifluoroacetylation of the N_6 nitrogen atom would then afford the observed product **14a**. Evidence for this pathway was obtained by the synthesis of the related 3*H*-indole spirocyclopentane¹² **16** and confirmation that it also underwent an addition reaction with trifluoroacetic anhydride to form the 2-trifluoroacetoxy-*N*-trifluoroacetylindoline **17a** (90%) which was fully characterised by elemental analysis and spectroscopic methods. Moreover, it was shown that benzyldeneaniline **18** reacts similarly to form the adduct **19** in quantitative yield. This type of addition reaction may well be general for the imino group.

These results are of considerable interest in relation to the earlier reports in the literature¹¹ (already referred to above) on the use of pentafluoropropionic anhydride to derivatise mel-



tonin **8b** and various related *N*-acetyltryptamines, for analysis by GC, with electron capture detection, or GC/MS;^{10,11,13} the use of GC with negative chemical ionisation MS was reported to provide an even more sensitive method of detection for melatonin in plasma.¹⁴ Melatonin is produced in the pineal gland of vertebrates and has been shown to lighten the skin colour of certain mammals by reversing the darkening effect of melanocyte stimulating hormone. The general structure previously assigned,¹¹ however, to the products of the reactions of melatonin and its analogues with pentafluoropropionic anhydride corresponded to that of the spirocyclic 3*H*-indole **12a**, considered to be an intermediate in our reactions. We, therefore, prepared melatonin **8b** from 5-methoxytryptamine and investigated its reaction with both trifluoroacetic anhydride and pentafluoropropionic anhydride; the NMR spectra of the products were virtually identical with each other and with the published spectrum¹¹ of the pentafluoropropionic anhydride cyclised

Table 2 ^{19}F NMR chemical shifts* for the spirocyclic indolines **14**, **15**, **17**, **20** and **21** and the benzylideneaniline adduct **19** (δ values)

Compd.	N_aCOF_3	$\text{N}_a\text{COCF}_2\text{CF}_3$	N_bCOCF_3	$\text{N}_b\text{COCF}_2\text{CF}_3$	OCOCF_3	$\text{OCOCF}_2\text{CF}_3$
14a	-71.83	—	-73.00	—	-75.25	—
14b	-71.70	—	-73.10	—	-75.45	—
15a	—	-83.10 -119.60	—	-83.10 -120.20	—	-83.80 -123.60
17a	-72.13	—	—	—	-76.15	—
17b	-67.90	—	—	—	—	—
19	-65.0	—	—	—	-72.58	—
20a	-70.78	—	-72.92	—	—	—
20b	-72.46	—	-74.58	—	—	—
21a	—	-82.62 -123.39	—	-83.19 -123.46	—	—

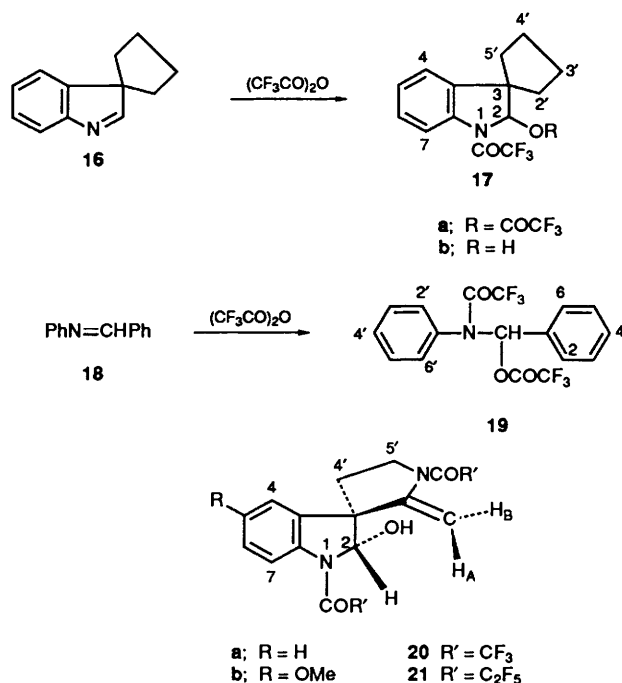
* All spectra were measured in deuteriochloroform except for **20b** which was measured in perdeuteriomethanol.

material but the mass spectra and elemental analyses showed that they were trifluoroacetic anhydride and pentafluoropropionic anhydride adducts **14b** and **15b** of the spirocyclic 3*H*-indoles **12b** and **13b** (cf. Scheme 3). We also confirmed that the pentafluoropropionic anhydride-induced cyclisation of *N*-acetyltryptamine **8a** afforded the indoline adduct **15a**, which was fully characterised by spectroscopic methods. Key features of the ^{13}C and ^{19}F spectra are shown in Tables 1 and 2, respectively.

These results are in complete accord with our findings with *N*-acetyltryptamine itself, and we attributed² the apparent discrepancy between our results and those of the other workers¹¹ to the probability that they had obtained similar adducts with pentafluoropropionic anhydride (to those which we had obtained with trifluoroacetic and pentafluoropropionic anhydrides) but that these products had decomposed in the heated inlet of the gas chromatograph with elimination of the anhydride and formation of the spirocyclic 3*H*-indoles (cf. **12** and **13**). No elemental analyses were reported in the original paper,¹¹ but in contrast to the GC/MS results, we found that direct determination of the mass spectra of our products (both EI and FD—see Experimental section) afforded molecular ions corresponding to the anhydride adducts **14** or **15**. Interestingly, the adduct **17a** formed from the 3*H*-indole spirocyclopropane **16** decomposed back to the 3*H*-indole **16** when heated, or on prolonged treatment with aqueous ammonia; again the mass spectra (EI and CI) showed the formation of a molecular ion corresponding to the adduct **17a**.

The yields of the cyclisation product **14a**, **14b**, **15a** and **15b** obtained from *N*_b-acetyltryptamine **8a** and melatonin **8b** with trifluoroacetic anhydride, or pentafluoropropionic anhydride, were essentially quantitative as shown by TLC and by ^1H and ^{19}F NMR spectroscopy of the crude materials. Direct crystallisation from dry light petroleum, or dry pentane, proved to be the most satisfactory method of purification, but in some early experiments we attempted to purify the semicrystalline reaction products by open column chromatography, or by preparative HPLC on silica. These experiments, however, resulted in partial hydrolysis and, for example, preparative HPLC of the crude product from *N*-acetyltryptamine **8a** and trifluoroacetic anhydride afforded two main fractions; the first fraction proved to be the spirocyclic indoline **14a** (40%) and the more polar second fraction the related 2-hydroxy spirocyclic indoline **20a** (60%). The structure of the latter was deduced from analytical and spectroscopic data; thus the elemental analysis, the mass spectrum and the ^{19}F and ^{13}C NMR spectra showed that only two trifluoroacetyl residues remained, as compared with three in the initial product **14a** (cf. Tables 1 and 2). The ^1H NMR spectrum of **20a** was very similar to that of the spirocyclic indoline **14a** except that the resonance of δ 5.72 attributed to the 2-proton in **20a** was over 1 ppm to higher field than that of the same proton in the original indoline (δ 6.90); an

additional signal at δ 3.3 (removed on shaking the solution with D_2O) was assigned to the hydroxy group. This was confirmed by the IR spectrum which showed a band at 3260 cm^{-1} , and by the prominent $\text{M} - \text{CF}_3\text{CO}_2\text{H}$ ion (at m/z 280) in the mass spectrum. Hydrolysis of the *O*-acyl residue would, moreover, be expected to be faster than that of either of the two *N*-acyl groups.



The same product **20a** was also formed by stirring a solution of the adduct **14a** in benzene, or chloroform solution with dilute aqueous ammonium hydroxide, or with aqueous sodium hydrogen carbonate. Similar products, **20b**, **21a** and **21b** were obtained by partial hydrolysis of the other adducts **14b**, **15a** and **15b** respectively and salient details of their NMR spectra are shown in the Experimental section and in Tables 1 and 2. HPLC of the melatonin derivative **14b** on silica similarly afforded the crystalline hydroxyindoline **20b** in over 80% yield, presumably due to hydrolysis by water adsorbed on the silica gel.

Interestingly, the NMR spectra of the adducts **14a**, **14b**, **15a** and **15b** and the corresponding hydroxyindolines **20a**, **20b**, **21a** and **21b** showed that each was formed as only one diastereoisomer. This was attributed to stereospecific addition of the anhydride to the least hindered side of the 1,2-double bond of the 3*H*-indoles **12** and **13**, i.e. on the opposite face from the *exo*-methylene group as shown in structures **14** and **15** (Scheme 3). This assignment was confirmed by observation of the NOE

enhancements shown between the 2-proton of the indoline ring and the protons of the *exo*-methylene residue in **14a**.

The results described in this paper accord with all the other evidence concerning the mode of electrophilic substitutions in indoles which are already substituted with alkyl groups at the 3-position¹⁵ (*cf.* Schemes 1 and 2). The acylation of 3-alkylindoles to form 2-acyl-3-alkylindoles also follows a similar pathway, and the acylation of 1,2,3-trisubstituted indoles affords 3-acylindole derivatives by *ipso*-attack at the 3-position (*cf.* refs. 9 and 16).

Experimental

M.p.s were determined on a hot-stage apparatus and are uncorrected. UV spectra were measured on a Unicam SP-800 spectrophotometer and NMR spectra with a Perkin-Elmer R32 90 MHz or, when stated, with a Bruker 360 MHz spectrometers. ¹H and ¹³C NMR spectra were measured in CDCl₃ unless otherwise stated, and are given as δ values relative to TMS, and ¹⁹F spectra as δ values relative to CFCl₃. *J* Values are given in Hz. Mass spectra were determined with a Varian CH5D double focussing instrument, EI spectra at 50 μ A and 70 eV, and FD spectra with wire currents in the range 10–20 μ A. Reactions were followed by either TLC or HPLC wherever possible. Light petroleum refers to solvent boiling in the range 60–80 °C.

Tryptamine.—DL-Tryptophan (25 g) and dry redistilled diphenyl ether (330 cm³) were placed in a Dean and Stark apparatus which was protected against moisture with a silica gel guard tube. The system was initially flushed with oxygen-free dry nitrogen. The mixture was boiled under reflux under a slow stream of nitrogen until the evolution of CO₂ ceased (9–10 h). The tryptophan dissolved after *ca.* 2 h. The clear solution was cooled to *ca.* 30 °C and dry hydrogen chloride gas was passed through it until it was saturated. The resulting mixture containing crystalline solids was subjected to distillation under reduced pressure of dry nitrogen to remove the diphenyl ether as completely as possible. The residue was cooled to 20 °C, triturated with sodium-dried ether (250 cm³), filtered and washed with the same solvent. The pale yellow crystalline residue was purified by recrystallisation from a mixture of ethanol and ethyl acetate to give pure tryptamine hydrochloride (12.2 g), m.p. 251–253 °C.

The mother-liquor was evaporated to dryness and the residue was dissolved in CHCl₃ (600 cm³). The solution was washed with 15% aqueous sodium hydroxide (4 \times 100 cm³) and then with cold water. After drying (K₂CO₃), the chloroform was removed on a rotary evaporator and the residue dissolved in absolute ethanol. Dry hydrogen chloride gas was passed into the solution, which was then evaporated to dryness and the residue crystallised from ethanol–ethyl acetate to give further tryptamine hydrochloride (3.1 g) as colourless needles, m.p. 251–253 °C. The combined products (15.3 g, 63.4%) were dissolved in water, and the solution was cooled in ice and rendered strongly alkaline with 20% aqueous sodium hydroxide. The resulting mixture was extracted with chloroform (4 \times 80 cm³), washed with cold water (2 \times 40 cm³), dried (K₂CO₃) and then evaporated to dryness on a rotary evaporator to give tryptamine (12.31 g; 63% based on tryptophan), m.p. 116–117 °C (*lit.*,¹⁷ m.p. 118 °C).

N_b-Acetyltryptamine 8a.—Tryptamine (2.6 g, 16.2 mmol) was added to acetic anhydride (15 cm³) and heated briefly to 75 °C until it dissolved. The solution was allowed to cool to 20–25 °C and was kept at this temperature for a further 15 min before removal of the acetic anhydride by vacuum distillation. The residual oil was distilled to yield the desired *N*-acetyltryptamine (2.3 g, 72%), b.p. 196–200 °C/0.2 mmHg which was recrystal-

lised from benzene–light petroleum to give crystals, m.p. 76–77 °C (*lit.*,¹⁸ m.p. 77 °C); δ_{H} 8.2–8.5 (1 H, br s, exchanged with D₂O, N_aH), 7.60 (1 H, dd, *J* 8 and 2, 4-H), 7.06–7.4 (3 H, m, ArH), 6.99 (1 H, s, 2-H), 5.45–5.75 (1 H, br s, exchanged with D₂O, N_b-H), 3.58 (2 H, q, *J* 8, CH₂NH), 2.94 (2 H, t, *J* 8, CH₂CH₂NH) and 1.88 (3 H, s, COCH₃).

N_b-Acetyl-5-methoxytryptamine (Melatonin) 8b.—5-Methoxytryptamine hydrochloride (1.0 g, 4.75 mmol) was dissolved in pyridine (10 cm³) and acetic anhydride (10 cm³) and kept overnight at 20 °C. The solution was poured onto ice, neutralised with dilute hydrochloric acid and extracted with chloroform (2 \times 25 cm³). The combined extracts were washed with water (25 cm³), dried (MgSO₄), and evaporated to afford a liquid, shown to be the N_bN_b-diacetyltryptamine derivative by spectroscopic means. This was dissolved in methanol (25 cm³) containing concentrated ammonium hydroxide (1 cm³) and the solution was then poured into water (50 cm³) and extracted with chloroform (2 \times 25 cm³). The combined organic layers were washed with water (25 cm³), dried (MgSO₄) and evaporated to dryness. The residual solid crystallised from benzene to afford melatonin (819 mg, 80%), as needles, m.p. 116–117 °C (*lit.*,¹⁹ m.p. 116–118 °C); δ_{H} 8.1–8.4 (1 H, br s, exchanged with D₂O, N_a-H), 7.20 (1 H, d, *J* 8, 7-H), 7.15 (1 H, d, *J* 1.5, 4-H), 7.0 (1 H, s, 2-H), 6.95 (1 H, dd, *J* 8 and 1.5, 6-H), 5.5–5.7 (1 H, s br, exchanged with D₂O, N_b-H), 3.80 (3 H, s, 5-OCH₃), 3.2–3.4 (4 H, m, CH₂CH₂N) and 1.90 (3 H, s, COCH₃).

Cyclisation of N_b-Acetyltryptamine with Phosphoryl Chloride in Pyridine.—A mixture of N_b-acetyltryptamine **8a** (1.0 g, 4.97 mmol) and phosphoryl chloride (1.0 cm³, 2 equiv.) in pyridine (5 cm³) was heated under reflux for 2 h. The pyridine and phosphoryl chloride were evaporated under reduced pressure and the residual oil was treated with aqueous sodium carbonate (5%; 20 cm³) to give a yellowish solid material. This was filtered off and washed with water and then with ethanol to afford an insoluble pale yellow solid (0.7 g), m.p. 290–295 °C (*decomp.*), identified as an oligomer of **11a**: *m/z* (%) (FD) 737 (26, 4 M + 1), 630 (70), 595 (66), 553 (30, 3 M + 1), 552 (27, 3 M), 446 (60), 403 (94), 368 (90, 2 M) and 78 (100): *m/z* (%) (EI) 369 (2, 2 M + 1), 368 (5, 2 M), 327 (2, 2 M – CH₃CN), 325 (2), 185 (7, M + 1), 184 (10, M⁺), 144 (19), 143 (2, M – CH₃CN), 85 (71) and 83 (100).

Cyclisation of N_b-Acetyltryptamine 8a with Trifluoroacetic Anhydride.—(a) N_b-Acetyltryptamine (750 mg, 3.57 mmol) in dry benzene (60 cm³) was added to a solution of freshly distilled trifluoroacetic anhydride (10 cm³) in dry benzene (430 cm³) at 5 °C, and the mixture stirred at 5 °C for 10 min, before removal of the solvent on a rotary evaporator at 20 °C. The pale yellow crystalline product (1.82 g, 100%), m.p. 115–120 °C, was shown to be essentially homogeneous by TLC and by NMR spectroscopy. Recrystallisation from dry light petroleum afforded the *spirocyclic indoline 14a* (1.68 g, 92%) as needles, m.p. 124–126 °C. On sublimation at 70–80 °C/0.07 mmHg the product formed shining needles, m.p. 127–129 °C (Found: C, 44.1; H, 2.4; N, 5.5. C₁₈H₁₁F₉N₂O₄ requires C, 44.1; H, 2.3; N, 5.7%); λ_{max} (EtOH)/nm (log ϵ_{max} /dm³ mol⁻¹ cm⁻¹) 252 (4.24), 277sh (3.87), 285sh (3.73); no change in the spectrum was observed on addition of a few drops of hydrochloric acid; ν_{max} (CHCl₃)/cm⁻¹ 1778 (2 – OCOCF₃) and 1700 (2 \times N-COCF₃); δ_{H} (360 MHz) 8.2 (1 H, d, br, 7-H), 7.53 (1 H, t, *J* 8, 6-H), 7.39 (1 H, t, *J* 8, 5-H), 7.29 (1 H, t, *J* 8, 4-H), 6.9 (1 H, s, 2-H), 6.07 (1 H, s, br, =CH *anti*), 4.25 (1 H, m, 5' α or β H), 4.15 (1 H, s, =CH *syn*), 4.00 (1 H, m, 5 β or α H), 2.65 (1 H, m, 4 α or β H) and 2.22 (1 H, m, 4' β or α H). We are indebted for this spectrum and to the NOE difference spectra enhancements quoted to Miss F. McKay; *m/z* (%) (EI) 491 (12), 490 (41, M⁺), 394 (5, M – COCF₃ + H), 3.77 (21,

M – OCOCF₃), 376 (26, M – CF₃CO₂H), 281 (19), 280 (100, M – CF₃CO and CF₃CO₂), 279 (60), 239 (21), 238 (48), 211 (19, M – CF₃COCF₃ and CF₃CO₂), 183 (62, M – CF₃CO, CF₃CO and CF₃CO₂), 155 (50), 143 (41), 130 (50), 115 (62) and 97 (76, COCF₃⁺); *m/z* (%) (FD) 491 (17), 490 (100, M⁺), 395 (17), 394 (79, M – COCF₃ + H) and 280 (5, M – CF₃CO and CF₃CO₂).

(b) In some early experiments on the cyclisations of *N*-acetyltryptamine, TLC showed that the main product was contaminated by other products, and it was subjected to preparative HPLC on silica gel using ether–cyclohexane in varying proportions as eluent. The product formed from *N*_b-acetyltryptamine (0.92 g) and trifluoroacetic anhydride in benzene as in (a) above afforded two main fractions on HPLC: A [with ether–cyclohexane (1:3, v/v as eluent) (890 mg, 40%) and B (with ether–cyclohexane (1:1) (1.07 g, 60%)].

Fraction A proved to be identical with the spirocyclic indoline **14a** obtained in preparation (a) above, as shown by m.p., mixed m.p., TLC and NMR spectroscopy. Fraction B was recrystallised from chloroform–light petroleum to afford a new product, m.p. 148–149 °C, identified by its spectral characteristics as the *hydroxyspirocyclic indoline 20a* (Found: C, 48.6; H, 3.0; N, 7.3. C₁₆H₁₂F₆N₂O₃ requires C, 48.7; H, 3.1; N, 7.1%; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 3530w and 3260m (OH), 1690s (2 × N–COCF₃); $\lambda_{\max}(\text{EtOH})/\text{cm}^{-1}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 252 (4.18), 277sh (3.81) and 285sh (3.67); the spectrum did not change on addition of acid; δ_{H} 8.08 (1 H, m, 7-H), 7.2–7.5 (3 H, m, 4, 5, 6-H), 5.94 (1 H, d, *J* 2, =CH), 5.72 (1 H, s, 2-H), 4.03 (1 H, d, *J* 2, =CH), 3.75–4.3 (2 H, m) and 2.1–2.9 (2 H, m) (CH₂CH₂N), 3.3 (1 H, br, OH, exchanged with D₂O); δ_{H} -(CF₃CO₂H) 8.3 (1 H, d, *J* 8, 7-H), 7.45–7.7 (3 H, m, 4, 5, 6-H), 6.39 (1 H, s, 2-H), 4.51 (2 H, t, *J* 8, CH₂CH₂N), 2.6–3.6 (2 H, m, CH₂CH₂N) and 2.3 (2 H, br s, CH₂D); *m/z* (%) (FD) 395 (66), 394 (100, M⁺); *m/z* (%) (EI) 395 (13), 394 (100, M⁺), 298 (7, M – COCF₃ + H), 281 (8), 280 (7, M – CF₃CO and OH), 253 (19), 240 (28), 184 (8), 183 (9, M – CF₃CO, CF₃CO and OH), 130 (10), 115 (9) and 69 (17, CF₃⁺).

Cyclisation of N_b-Acetyltryptamine with Pentafluoropropionic Anhydride.—Pentafluoropropionic anhydride was prepared immediately prior to use in 80% yield from pentafluoropropionic acid by refluxing for several hours over an excess of phosphorus pentoxide, followed by fractional distillation over phosphorus pentoxide; the fraction boiling at 71–72 °C (lit.²⁰ b.p. 71.5–72 °C) was collected; δ_{F} – 84.70 (3 F, s, CF₃) and – 126.19 (2 F, s, CF₂CO). CF₃CF₂CO₂H showed δ_{F} – 84.68 (3 F, s, CF₃) and – 127.12 (2 F, s, CF₂CO). *N_b*-Acetyltryptamine (120 mg, 0.59 mmol) was added to a magnetically stirred solution of freshly prepared pentafluoropropionic anhydride (1.91 cm³) in redistilled sodium-dried benzene (96 cm³) at 0–5 °C. Stirring at 0–5 °C was continued for a further 10 min after the addition, and then the reaction mixture was evaporated to dryness on a rotary evaporator at 20 °C. Dry benzene (100 cm³) was added to the residue and again evaporated to dryness at 20 °C. The residue was finally dried *in vacuo* to give a slightly yellowish crystalline product (380 mg, 100%). NMR spectroscopy and TLC indicated that this product was essentially homogeneous and recrystallisation from dry light petroleum afforded the *spirocyclic indoline 15a* (304 mg, 80%) as plates, m.p. 105–106 °C (Found: C, 39.4; H, 1.7; N, 4.5. C₂₁H₁₁F₁₅N₂O₄ requires C, 39.4; H, 1.7; N, 4.4%; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 1770 (s, 2 – OCOCF₃), 1700 (br s, N_a- and N_b-COCF₃); $\lambda_{\max}(\text{EtOH})/\text{cm}^{-1}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 254 (4.21), 278sh (3.92) and 286sh (3.81); the spectrum did not show any appreciable change on addition of acid; δ_{H} 8.15 (1 H, dd, *J* 8, 1.5, 7-H), 7.54 (1 H, dd, *J* 8, 1.5, 4-H), 7.2–7.45 (2 H, m, 5, 6-H), 6.96 (1 H, s, 2-H), 6.08 (1 H, d, *J* 1.5, =CH), 4.10 (1 H, d, *J* 1.5, =CH), 3.95–4.35 (2 H, m) and 2.0–2.75 (2 H, m) (CH₂CH₂N). Irradiation at δ 8.16, 8.19 or 8.22

changed the aromatic multiplet to a much simpler pattern showing two *ortho* couplings (*J* 9 Hz each) and two *meta* coupling (*J* 1.5 Hz each). Irradiation at δ 6.10 turned the doublet at δ 4.10 to a sharp singlet and irradiation at δ 4.13 changed the doublet at δ 6.08 also to a sharp singlet. These irradiations had no effect on the singlet at δ 6.96. Similarly, irradiation at δ 7.02 had no effect on the two doublets at δ 6.08 and 4.10 or on the signals in the aromatic region; *m/z* (%) (FD) 641 (18) and 640 (100, M⁺); *m/z* (%) (EI) 640 (10, M⁺), 639 (44), 621 (6), 493 (5, M – COC₂F₅), 478 (9), 477 (46, M – CO₂C₂F₅), 476 (34), 463 (17), 330 (38), 329 (100, M – C₂F₅CO, C₂F₅CO₂ and H), 290 (17), 183 (14, M – C₂F₅CO₂ and 2 × C₂F₅CO), 182 (10), 154 (18), 143 (39), 142 (11), 119 (51, C₂F₅⁺), 115 (19) and 69 (19, CF₃⁺).

Cyclisation of Melatonin 8b with Trifluoroacetic Anhydride.—

(a) Melatonin (1.0 g, 4.3 mmol) was added to a stirred solution of freshly prepared trifluoroacetic anhydride (14 cm³) in dry benzene (680 cm³) at 5 °C. After 10 min, the solvent was removed under reduced pressure on a rotary evaporator to afford the crude product (2.24 g, 100%), as a yellow crystalline mass. Recrystallisation of this from dry light petroleum gave the *spirocyclic indoline 14b* (2.0 g, 89%) as colourless plates, m.p. 126–128 °C (Found: C, 43.6; H, 2.6; N, 5.2. C₁₉H₁₃F₉N₂O₅ requires C, 43.9; H, 2.5; N, 5.4%; $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 1775s (2 – OCOCF₃) and 1700br (2 × N–COCF₃); $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 263 (4.21), 292s (3.91) and 303sh (3.74); the spectrum did not change on addition of acid; δ_{H} 8.09 (1 H, d, *J* 9, 7-H), 6.96 (1 H, dd, *J* 9, 2, 6-H), 6.86 (1 H, s, 2-H), 6.73 (1 H, d, *J* 2, 4-H), 6.08 (1 H, br s, =CH), 4.16 (1 H, d, *J* 1.5, =CH), 3.80 (3 H, s, OCH₃), 3.5–4.3 (2 H, m) and 1.9–2.7 (2 H, m) (CH₂CH₂N). Irradiation of the signal at δ 6.08 caused the signal at δ 4.16 to become a sharp singlet; irradiation at δ 4.16 collapsed the signal at δ 6.08 to a singlet; *m/z* (%) (FD) 521 (24), 520 (100, M⁺), 442 (8) and 424 (3, M – CF₃CO + H); *m/z* (%) (EI) 521 (24), 520 (100, M⁺), 407 (54, M – CF₃CO₂), 310 (30, M – CF₃CO₂ and CF₃CO), 309 (55, M – CF₃CO₂, CF₃CO and H), 213 (8, M – CF₃CO₂ and 2 × CF₃CO), 204 (12), 202 (20), 201 (26), 200 (34), 199 (35), 198 (18), 173 (12), 158 (10) and 69 (36, CF₃⁺).

(b) In a similar experiment to that described in (a) above, the crude product (2.34 g) was subjected to preparative HPLC on silica eluting with chloroform–cyclohexane (3:7, v/v). The eluates afforded the *spirocyclic indoline 14b* (181 mg, 8%) identical in all respects with the compound characterised above.

The main fraction (1.46 g, 80%) (obtained by elution with chloroform–cyclohexane (1:1, v/v) crystallised from methanol or benzene as prisms, m.p. 159–160 °C and was characterised as the *hydroxyspirocyclic indoline 20b* by analysis and spectroscopic studies (Found: C, 48.3; H, 3.4; N, 6.4. C₁₇H₁₄F₆N₂O₄ requires C, 48.1; H, 3.3; N, 6.6%; $\nu_{\max}(\text{Nujol})/\text{cm}^{-1}$ 3400w (OH), 1704m and 1694s (N_a- and N_b-COCF₃); $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 264 (4.11), 292sh (3.81) and 303sh (3.66); $\delta_{\text{H}}(\text{CD}_3\text{OD}, 360 \text{ MHz})$ 8.2 (1 H, d, *J* 9, 7-H), 7.02 (1 H, d, *J* 9, 6-H), 7.0 (1 H, s, 4-H), 6.0 (1 H, br s, =CH_A), 4.3 (1 H, s, br, =CH_B), 5.8 (1 H, s, 2-H), 4.05 (2 H, q, *J* 6, –CH₂N), 3.80 (3 H, s, OCH₃), 2.60 (1 H, m) and 2.80 (1 H, m) (CH₂CH₂N). It was established by spin decoupling experiments that the signals at δ 6.0 and 4.3 were coupled to each other; *m/z* (%) (FD) 425 (67) and 424 (100, M⁺); *m/z* (%) (EI) 425 (8), 424 (51, M⁺), 395 (17), 394 (20), 327 (22, M – COCF₃), 311 (24), 310 (41, M – COCF₃ and OH), 309 (29), 299 (31), 298 (27), 284 (29), 283 (58), 270 (59), 269 (25), 230 (15), 229 (25), 215 (17), 214 (32), 213 (41, M – 2 × CF₃CO and OH), 202 (25), 187 (42), 160 (44), 158 (44), 130 (42) and 115 (59).

Cyclisation of Melatonin 8b with Pentafluoropropionic Anhydride.—Pentafluoropropionic acid anhydride (2 cm³) in dry

benzene (30 cm³) was added to a suspension of melatonin (140 mg, 0.503 mmol) in dry benzene (60 cm³) and the mixture stirred at 5 °C for 10 min. Removal of solvent on a rotary evaporator at 20 °C gave a yellow residue which was crystallised from cooled light petroleum to give the *spirocyclic indoline 15b* (300 mg, 75%) as colourless crystals, m.p. 97–99 °C (Found: C, 39.3; H, 2.1; N, 4.65. C₂₂H₁₃F₁₅N₂O₅ requires C, 39.4; H, 1.95; N, 4.2%); $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 1165 (C–O), 1700 and 1780; $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 254 (4.23), 292sh (3.90) and 303sh (3.74); $\delta_{\text{H}}(360 \text{ MHz})$ 8.12 (1 H, d, br, 7-H), 7.0 (1 H, dd, J 8, 2, 6-H), 6.89 (1 H, s, 4-H), 6.76 (1 H, d, J 2, 2-H), 6.12 (1 H, s, br, =CH *anti*), 4.32 (1 H, m, 5' α or β H), 4.2 (1 H, d, J 1.8, =CH *syn*), 4.03 (1 H, m, 5' β or α H), 3.86 (3 H, s, OMe), 2.16 (1 H, m, 4 α or β H) and 2.16 (1 H, m, 4 β or α H); m/z (%) (FD) 670 (M⁺, 100%); m/z (%) (EI) 670 (M⁺, 100%), 507 (44), 493 (16), 360 (46), 345 (29), 320 (23), 213 (37), 197 (22), 186 (27), 173 (40), 159 (24), 147 (39), 130 (21), 115 (21) and 103 (13).

Hydrolysis of the Spirocyclic Indolines.—(a) A solution of the indoline **14a** (1.95 g, 3.98 mmol) in chloroform (50 cm³) was stirred with ammonium hydroxide (5%; 50 cm³) for 1 h. The organic layer was separated and the aqueous layer extracted with chloroform (2 × 50 cm³). The combined organic extracts were washed with water (50 cm³), dried (MgSO₄) and evaporated to dryness. The semi-crystalline residue (1.57 g) crystallised from benzene–light petroleum to afford the hydroxy spirocyclic indoline **20a** (1.23 g, 78%) as plates, m.p. 147–148 °C. This material proved to be identical in all respects with the same compound obtained by silica gel chromatography of the spirocyclic indoline **14a**. The same product **20a** was also obtained in 70% yield by stirring a benzene solution of the spirocyclic indoline **14a** with aqueous sodium hydrogen carbonate (5%) for 24 h.

(b) Treatment of the indoline **14b** in chloroform with aqueous ammonia (5%) for 15 min as described for the analogue above afforded the hydroxy spirocyclic indoline **20b** (75%) which crystallised from benzene as plates, m.p. 159–160 °C.

(c) Hydrolysis of the indoline **15a** (65 mg, 1.01 mmol) in benzene (35 cm³) with ammonium hydroxide (1%; 15 cm³) at 30 °C for 30 min as described in (a) and (b) for the analogues **14a** and **14b** above furnished a colourless homogeneous oil (53 mg). This was chromatographed on a silica gel column in light petroleum–ether (4:1, v/v) to give the *hydroxyspirocyclic indoline 21a* (45 mg, 90%) as a colourless glass, which could not be crystallised (Found: C, 44.0; H, 2.2; N, 5.9. C₁₈H₁₂F₁₀N₂O₃ requires C, 43.7; H, 2.45; N, 5.7%); $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 3400 (OH), 1660–1680 (N_{α} - and N_{β} -COC₂F₅); $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 255 (4.13), 275sh (3.89) and 285sh (3.70); no change in the spectrum was observed on addition of a few drops of hydrochloric acid; $\delta_{\text{H}}(\text{CD}_3\text{OD})$ 8.2 (1 H, d, br, J 8, 7-H), 7.45 (3 H, m, 4, 5, 6-H), 5.98 (1 H, s, br, =CH_A), 5.81 (1 H, s, 2-H), 3.99 (1 H, s, br, =CH_B), 4.2–4.6 (2 H, m) and 2.1–2.8 (2 H, m, NCH₂CH₂); m/z (%) (EI) 495 (13), 494 (68, M⁺), 476 (15), 466 (22), 465 (19), 347 (19, M – COC₂F₅), 331 (16), 330 (33, M – COC₂F₅ and OH), 329 (26), 319 (29), 318 (16), 304 (19), 303 (51), 290 (39), 200 (19, M – 2 × COC₂F₅), 199 (19), 184 (29), 183 (36, M – 2 × COC₂F₅ and OH), 156 (64), 144 (23), 143 (26), 130 (39), 129 (23), 128 (19), 119 (35, C₂F₅⁺), 115 (32), 78 (98) and 77 (100).

(d) **Hydrolysis of the spirocyclic indoline 15b.** The indoline **15b** (100 mg, 0.149 mmol) was stirred at 20 °C for 15 min in chloroform–5% ammonium hydroxide (1:1; 25 cm³). The product was isolated by ether extraction and flash chromatography giving the corresponding *hydroxyspirocyclic indoline 21b* (63 mg, 81%) (Found: M, 524.07771. C₁₉H₁₄F₁₀N₂O₄ requires 524.07935); $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$ 1700, 1790 and 3300; $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 255 (4.12), 275sh (3.89) and 285sh (3.71); $\delta_{\text{H}}(360 \text{ MHz, in CD}_3\text{OD})$ 8.09 (1 H, d, J 8, 7-H),

6.9 (1 H, dd, J 8, 2, 6-H), 6.74 (1 H, d, J 2, 4-H), 6.0 (1 H, s, =CH_A), 5.8 (1 H, s, br, 2-H), 4.09 (1 H, s, br, =CH_B), 4.14 (1 H, m, 5' β or α H), 4.0 (1 H, m, 5' β or α H), 3.84 (3 H, s, OMe), 2.85 (1 H, m, 4' α or β H) and 2.18 (1 H, m, 4' β or α H); m/z (%) (FD) 525 (21), 524 (100), 494 (8), 492 (7) and 474 (12); m/z (%) (EI) 523 (M⁺ – 1, 2%), 507 (31), 493 (5), 360 (27), 359 (35), 320 (10), 213 (9), 182 (4), 173 (25), 158 (18), 156 (5), 143 (5), 130 (2), 119 (100), 116 (7), 115 (9), 103 (6) and 77 (7).

Reaction of 3H-Indole-3-spirocyclopentane 16 with Trifluoroacetic Anhydride.—3H-Indole-3-spirocyclopentane **16** (70 mg, 0.409 mmol) (prepared from indol-3-ylbutoxy tosylate by treatment with alkaline alumina or potassium *tert*-butoxide¹²) in benzene (5 cm³) was added to a cooled solution of freshly distilled trifluoroacetic anhydride (1.2 cm³) in dry benzene (40 cm³). The mixture was kept at 5 °C for 15 min and then evaporated to dryness under reduced pressure at 30 °C. The oily residue was taken up in dry pentane, filtered, and the filtrate evaporated to dryness on a rotary evaporator at 20 °C and then *in vacuo* (ca. 0.1 mmHg). The oily residue slowly crystallised with time under nitrogen, and was then recrystallised from dry pentane to afford the *trifluoroacetic anhydride adduct 17a* (140 mg, 90%) as prisms, m.p. 72 °C (Found: C, 60.5; H, 3.5; N, 3.6. C₁₆H₁₃F₆NO₃ requires C, 60.4; H, 3.4; N, 3.7%); $\nu_{\max}(\text{in CHCl}_3)/\text{cm}^{-1}$ 1800s (2 – CO₂CF₃) and 1712 (N–COCF₃); $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 227 (4.56), 255 (4.16) and 281 (4.03); δ_{H} 8.04 (1 H, d, br, J 8, 7-H), 7.1–7.4 (3 H, m, ArH), 6.81 (1 H, s, 2-H) and 1.5–2.1 (8 H, m, 4 × CH₂); m/z (%) (EI) 381 (11, M⁺), 268 (41, M – OCOCF₃), 226 (31), 171 (51, M – OCOCF₃ and COCF₃), 170 (40), 143 (100, M – OCOCF₃, COCF₃ and CH₂=CH₂), 97 (34, COCF₃⁺) and 69 (92, CF₃⁺); m/z (%) (CI): 382 (11, M + 1), 269 (17, M + 1 – OCOCF₃), 268 (100, M – OCOCF₃) and 172 [32, M + 1 – (CF₃CO)₂O].

Hydrolysis of the Trifluoroacetic Anhydride Adduct 17a.—(a) The adduct **17a** (125 mg, 0.328 mmol) in chloroform (10 cm³) was stirred with ammonium hydroxide (5%; 15 cm³) for 40 min, at 20 °C. The organic phase was separated, the aqueous phase re-extracted with chloroform (3 × 5 cm³) and the combined extracts were dried (MgSO₄) and evaporated. The residual oil was taken up in dry pentane, filtered and re-evaporated to dryness at 0.1 mmHg/20 °C. The oily residue slowly crystallised with time at 0 °C and was then recrystallised from dry pentane to afford the *hydroxyindoline 17b* (84 mg, 90%) as shining prisms, m.p. 86 °C (Found: C, 59.2; H, 4.95; N, 4.8. C₁₄H₁₄F₃NO₂ requires C, 58.9; H, 4.95; N, 4.9%); $\nu_{\max}(\text{Nujol})/\text{cm}^{-1}$ 3340 (m, NH) and 1690 (NCOCF₃); $\lambda_{\max}(\text{EtOH})/\text{nm}$ (log $\epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) 253 (4.02), 281 (3.57) and 286 (3.57); δ_{H} 8.04 (1 H, d, br, J 7, 7-H), 7.15–7.44 (3 H, m, 4, 5 and 6-H), 5.54 (1 H, s, 2-H), 4.10 (1 H, s, br, OH, exchanged with D₂O), 1.5–2.1 (8 H, m, 4 × CH₂); m/z (%) (EI): 285 (68, M⁺), 268 (11, M – OH), 256 (18), 238 (40), 216 (44, M – CF₃), 188 (100, M – COCF₃), 170 (42), 169 (18), 130 (26), 69 (20, CF₃⁺) and 67 (25); m/z (%) (CI) 286 (100, M + 1), 268 (49, M – OH), 266 (19), 238 (6), 216 (2), 188 (2) and 172 (5).

(b) The trifluoroacetic anhydride adduct **17a** (87 mg, 0.228 mmol) in benzene (10 cm³) was stirred with ammonium hydroxide (5%; 15 cm³) at 20 °C for 4 days, the reaction being followed by TLC. After work-up in the usual manner, the crude product (49 mg, 100%) was identified by TLC and spectral analyses as the indolespirocyclopentane **16**, and a sample on crystallisation from dry benzene afforded the pure indole trimer as prisms, m.p. 142–143 °C (lit.²¹ m.p. 136–137 °C), which proved to be identical with the starting material **16**.

Addition of Trifluoroacetic Anhydride to Benzyldeneaniline 18.—A solution of freshly distilled trifluoroacetic anhydride (6.7

cm³) in dry benzene (670 cm³) was cooled to 5 °C and stirred during the addition of benzyldeneaniline (2.0 g, 11.17 mmol) in dry benzene (10 cm³) via a syringe. The mixture was stirred under dry nitrogen for 10 min at 5 °C and then evaporated to dryness under reduced pressure at 25 °C. The yellow oily residue was taken up in dry pentane and re-evaporated to dryness at 0.1 mmHg pressure and 25 °C. The colourless oily product **19** (4.3 g, 99%) was unstable and did not crystallise; on distillation under reduced pressure it decomposed mainly to starting material; ν_{\max} (film)/cm⁻¹ 1800s (OCOCF₃) and 1725s (NCOCF₃); δ_{H} 8.28 (1 H, s, CHOCO) and 7.1–7.4 (10 H, m, ArH); δ_{C} 82.5 (COCOCF₃), 132.9 (C-1), 126.5 (C-2 and C-6), 128.6 (C-3, C-4' and C-5), 130.6 (C-4), 132.3 (C-1'), 129.9 (C-2', C-3', C-5' and C-6'), 155.6 (q, *J* 43.9, N-COCF₃), and 158.0 (q, *J* 37.6, COCOCF₃) and 96.28–134.81 (m, 2 × CF₃, low intensity); *m/z* (%) (EI) (a) 278 (27, M – OCOCF₃), 190 (22), 189 (30), 182 (58), 181 (100, M – OCOCF₃ and COCF₃), 180 (55), 172 (16), 135 (54), 125 (24), 107 (10), 92 (16), 77 (37), 69 (15, CF₃⁺) and 51 (13).

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