A New Synthetic Route to Pyrrolo[3,2-*b*]carbazoles, 1*H*-Benzofuro[3,2-*f*]indoles and 1*H*-[1]Benzothieno[2,3-*f*]indoles

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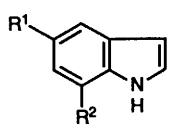
The heterocyclic systems pyrrolo[3,2-*b*]carbazole, 1*H*-benzofuro[3,2-*f*]indole and 1*H*-[1]benzothieno-[2,3-*f*]indole were synthesised by Montmorillonite K10 clay-catalysed condensation of 5-acetoxymethyl-4-acetylpyrroles with various indoles, benzofuran and benzothiophene. Ring closure of the intermediate 3-(pyrrolylmethyl)indoles was achieved with clay, whereas 2-(pyrrolylmethyl)benzofuran and 3-(pyrrolylmethyl)benzothiophene required toluene-*p*-sulfonic acid in ethanol or toluene for cyclisation to the tetracyclic compounds. When an indole and a benzyl pyrrole-2-carboxylate was used, the resultant pyrrolo[3,2-*b*]carbazole benzyl ester could be hydrogenolysed to the corresponding carboxylic acid.

In a previous paper,[1] we described the synthesis of 3-(pyrrolylmethyl)indoles under mild conditions using Montmorillonite K10 clay to catalyse the condensation of 5-(acetoxymethyl)pyrroles with indoles. We have found that under more forcing conditions, when the pyrrole contains a 4-acetyl substituent, cyclisation of the first-formed 3-(pyrrolylmethyl)-indole occurs in a one-pot process to give the corresponding pyrrolo[3,2-*b*]carbazoles in moderate to good yields. Previously, the only other reported synthesis of pyrrolo[3,2-*b*]-carbazoles was by Borsche cyclisation of 1-acetyl-5-indolylhydrazine with cyclohexanone[2] followed by deacetylation and dehydrogenation. Alternatively diazotisation of 2-aminocarbazole, followed by condensation with ethyl pyruvate[3] gave the [2,3-*b*]isomer.

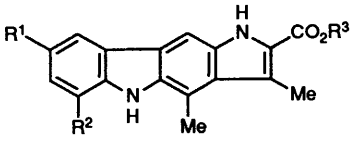
Ethyl 5-acetoxymethyl-4-acetyl-3-methylpyrrole-2-carboxylate[1] **1** was heated under reflux in 1,2-dichloroethane with indole in the presence of an excess of Montmorillonite K10 clay. Work-up gave the solid pyrrolocarbazole **2** in 65% yield after recrystallisation. The EI mass spectrum M^+ 306.1356 and the elemental analysis confirmed the formula $C_{19}H_{18}N_2O_2$. In the ^1H NMR spectrum (in [$^2H_6$]-DMSO) of **2**, of the signals originally due to the starting materials, the 4-acetyl, 3-methyl and 5-acetoxymethyl groups of the pyrrole **1** and the 2- and 3-protons of indole were replaced by a one proton singlet at δ 7.85 and two additional three proton singlets at δ 2.90 and 2.91. These changes indicated a fused system involving the 2- and 3-positions of indole and the 4- and 5-positions of the pyrrole. The fusion of indole and the pyrrole **1** to give uniquely the pyrrolo[3,2-*b*]carbazole **2**, rather than its [2,3-*b*] isomer **3**, was proved by NOE difference spectra as indicated. Only structure **2** would give enhancement of the 9-H doublet. If the mixture of indole and pyrrole **1** was heated for a shorter period, it was possible to isolate the (pyrrolylmethyl)indole **4**[1] and the intermediacy of this compound was shown experimentally by its conversion to **2**. If the conversion of the (pyrrolylmethyl)indole **4** to the pyrrolocarbazole **2** proceeds *via* a spirocyclic intermediate **5**, which would be expected from our earlier work,[4] there must be specific migration of the hydroxyethyl substituent in the spirocycle as shown. The alternative, but perhaps less likely possibility, is a direct electrophilic substitution at the indolyl 2-position by the carbonyl group in **4**.

We next investigated variations in the structure of the indole and pyrrole. In particular we examined the condensation of the pyrrole **1** with the indoles **6**, **7** and **8**. In general the yields of the corresponding pyrrolocarbazoles **9**, **10** and **11** were comparable with that for the parent compound **2**. Variations in the pyrrole component appeared equally successful. When the pyrrole **12**, prepared by acetoxylation of the methyl analogue,[5] was used instead of **1**, the pyrrolo[3,2-*b*]carbazole benzyl esters **13**–**16** were obtained. Hydrogenolysis of the esters **13**, **15** and **16** over palladium-on-charcoal gave the corresponding carboxylic acids **17**–**19** in high yields. Similarly the pyrroles **20**,† and **21** (prepared by acetoxylation of its methyl analogue)[6] gave, with indole, the analogues **13** and **22**. Finally, it was intriguing that fusion of the 5-acetoxymethyl-4-acetylpyrrole unit with hetero analogues of indole might prove a facile route to tetracyclic systems involving oxygen and sulfur. Hitherto, the only reported examples of the 1*H*-benzofuro[2,3-*f*]indole and 1*H*-benzofuro[3,2-*f*]indole[7,8] systems were those described by

† This sample was provided by the late Dr. S. F. MacDonald.



6 R^1 = OMe, R^2 = H
7 R^1 = F, R^2 = H
8 R^1 = H, R^2 = Me



9 R^1 = OMe, R^2 = H, R^3 = Et
10 R^1 = F, R^2 = H, R^3 = Et
11 R^1 = H, R^2 = Me, R^3 = Et
13 R^1 = H, R^2 = H, R^3 = CH_2Ph
14 R^1 = OMe, R^2 = H, R^3 = CH_2Ph
15 R^1 = F, R^2 = H, R^3 = CH_2Ph
16 R^1 = H, R^2 = Me, R^3 = CH_2Ph
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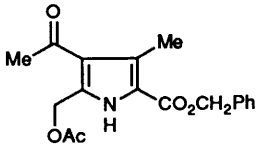
19 R^1 = H, R^2 = Me, R^3 = H



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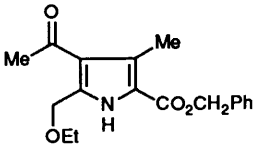

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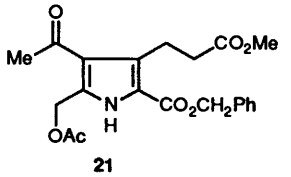
Russian workers who synthesised the monosubstituted systems by indolisation of the hydrazines of dibenzofuran with ethyl pyruvate. The route which we envisaged, not only would be potentially a more convergent synthesis, but by appropriate choice of the benzofuran, benzothiophene and pyrrole would allow of a variety of substituents in the final tetracycles.

In the event, the pyrrole **1**, when heated in refluxing 1,2-dichloroethane for 2 h with an equimolar amount of benzofuran, in the presence of K10 clay, afforded only the 2-(pyrrolylmethyl)benzofuran **24** (39%) and the 2,3-disubstituted derivative **25** as a minor product (9%). The position of substitution in the benzofuran **24** was clear since its 2-proton signal at δ 7.79 had disappeared and the 3-proton signal had moved 0.2 ppm upfield to δ 6.57. The structure was confirmed by NOE difference spectra as indicated.

Treatment of the monosubstituted compound **24** with toluene-*p*-sulfonic acid, however, in refluxing ethanol, or better in toluene, gave an 88% yield of ethyl 3,4-dimethyl-1*H*-benzofuro[3,2-*f*]indole-2-carboxylate **26**. The compound gave a molecular ion at *m/z* 307 (53%) in its EI mass spectrum. Since the ring-closure to the tetracycle **26** occurred from the 2-substituted benzofuran **24**, it was likely, but not certain, that the orientation of **26** was as shown, *i.e.* the [3,2-*f*] system. This was confirmed by the ^1H NMR spectroscopic data. The benzofuran 3-H, the CH_2 bridge singlet and pyrrolyl-4-acetyl signals in **24** at δ 6.57, 4.50 and 2.50 were replaced by the expected singlets due to the 4-Me and 10-H protons in **26** and the NOE difference spectra showed, on saturation of the 4-Me protons, 4.5 and 2.6% enhancements of the 5-H (δ 8.18) and 3-methyl (δ 2.91) signals, respectively.

Finally, the pyrrole **1**, under identical conditions to those described for reaction with benzofuran, but with an equimolar amount of benzothiophene gave the 3-substituted (pyrrolyl methyl)benzothiophene **27** (28%) and 10% of the 2,3-disubsti-



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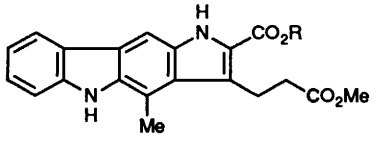
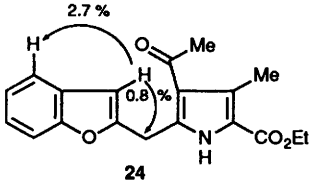


22 R = CH_2Ph
23 R = H



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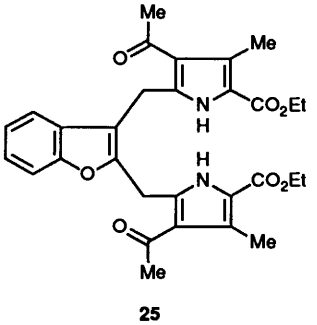

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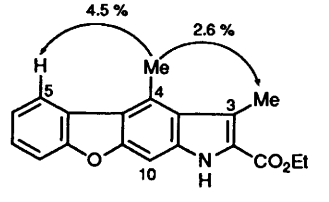

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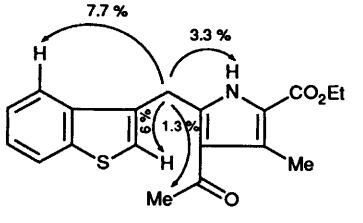

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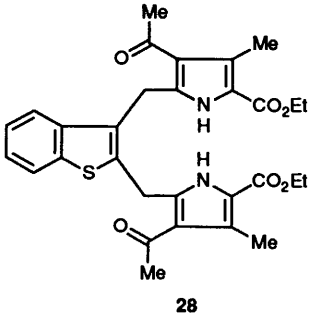

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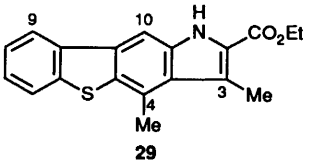

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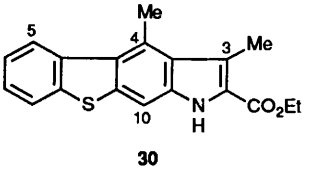

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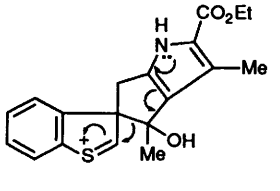

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tuted compound **28**. The monosubstituted compound **27** gave a molecular ion at *m/z* 341. The position of substitution in the benzothiophene could not be determined on the basis of chemical shifts of the benzothiophene 2- and 3-H signals (δ 7.33 and 7.23, respectively). However, the NOE difference spectra proved conclusively the structure **27**, since the uniquely low-field 4-H signal of the benzothiophene moiety was enhanced by 7.7% on saturation of the bridging CH_2 group.

Treatment of the monosubstituted derivative **27** with toluene-*p*-sulfonic acid in refluxing toluene for 3 h gave the 1*H*-[1]benzothieno[2,3-*f*]indole **29** (80%). Its EI mass spectrum gave (M^+ 323, 57%) and its ^1H NMR spectrum showed the replacement of the benzothiophene 2-H signal, the CH_2 bridge singlet and the pyrrolyl 4-acetyl signal in **27** by a new methyl singlet and the 10-H singlet in **29** at δ 8.12. We attempted to confirm the orientation of the structure **29** (rather than the alternative **30**) by NOE difference spectra. The preferred experiment, saturation of the 10-H proton in **29**, to demonstrate enhancement of the 9-H signal proved impossible since the chemical shifts of these proton were too close. However, the 3- and 4-methyl groups were of virtually identical chemical shift at δ 2.85 and 2.87; saturation at δ 2.86 gave no detectable enhancements. In the alternative structure **30**, saturation of the 4-Me group would have been expected to give a significant enhancement of the 5-H signal as was observed in the analogue **26**.

Mechanistic consideration would also favour structure **29**. Thus direct substitution by the acetyl group at the 2-position in the (pyrrolylmethyl)benzothiophene **27** would lead uniquely to isomer **29**. If, however, the cyclisation of **27** took place *via* the spirocyclic intermediate **31**, selective 3 → 2 migration of the higher migratory aptitude hydroxyethyl branch of the spirocyclic ring would again lead to **29**.

As with the pyrrolocarbazole **2** and benzofuroindole **26** our route appears to be potentially a convergent and general synthesis of benzothienoindoles. The only previous mention of this system describes a synthesis[9] by indolisation of dibenzothiophenylhydrazines and ethyl pyruvate.

Experimental

IR spectra were recorded on a Perkin-Elmer 257 grating spectrophotometer; UV spectra were measured in ethanol on a Unicam SP 800 spectrophotometer and ^1H NMR spectra were obtained on a Bruker WM 360-NMR spectrophotometer at 360 MHz. *J*-values are given in Hz. EI mass spectra were run on a Varian CH 5D instrument. Flash column chromatography was carried out with Kieselgel 60, 230–400 mesh Merck silica. Light petroleum was of boiling range 40–60 °C.

Preparation of the 5-Acetoxymethyl-4-acetylpyrroles **1**, **12**, **21**.—*General procedure*. To a cooled (0 °C) and stirred suspension of the 4-acetyl-5-methylpyrrole (0.02 mol) in dry diethyl ether (20 cm^3) was added, dropwise over 15 min, freshly distilled sulfonyl chloride (2.2 cm^3, 1.25 equiv.). The reaction mixture was stirred further and the chloromethyl derivative crystallised out slowly, filtration gave the 5-chloromethyl derivative as colourless crystals. The purity of the chloromethylpyrrole was checked by ^1H NMR spectroscopy (90 MHz) and it was used directly without recrystallisation.

The above chloromethylpyrrole (0.01 mol) was added to a solution of sodium acetate (3 g) in acetic acid (50 cm^3), the mixture stirred for 2 h and poured into ice–water (200 cm^3). The resulting solid was washed well with water until acid-free before drying.

Ethyl 5-acetoxymethyl-4-acetyl-3-methylpyrrole-2-carboxylate **1** crystallised from benzene as colourless needles (1.87 g, 70%) m.p. 135.5–138 °C (Found: C, 58.6; H, 6.45; N, 5.15. $C_{13}H_{17}NO_5$ requires C, 58.4; H, 6.37; N, 5.24%); $\delta_H(CDCl_3)$ 9.57 (1 H, br s, NH), 5.40 (2 H, s, CH_2OAc), 4.35 (2 H, q, OCH_2CH_3), 2.6 (3 H, s, 3-CH_3) 2.5 (3 H, s, $COCH_3$), 2.17 (3 H, s, $OCOCH_3$) and 1.4 (3 H, t, OCH_2CH_3); *m/z* (%) 267 (83, M^+), 224 (46), 207 (27), 178 (100) and 162 (42).

Benzyl 5-acetoxymethyl-4-acetyl-3-methylpyrrole-2-carboxylate **12** crystallised from methanol as colourless needles (2.34 g, 71%) m.p. 138–141 °C (Found: C, 65.8; H, 5.95; N, 4.3. $C_{18}H_{19}NO_5$ requires C, 65.65; H, 5.77; N, 4.25%); $\delta_H(CDCl_3)$ 9.44 (1 H, br s, NH), 7.49–7.32 (5 H, m, ArH), 5.40 (2 H, s, CH_2OAc), 5.35 (2 H, s, CH_2Ph), 2.62 (3 H, s, 3-CH_3), 2.49 (3 H, s, CH_3CO) and 2.14 (3 H, s, $OCOCH_3$); *m/z* (%) 329 (9, M^+), 286 (13), 269 (4), 178 (19) and 91 (100).

In the case of *benzyl 5-acetoxymethyl-4-acetyl-3-(2-methoxycarbonylethyl)-pyrrole-2-carboxylate* **21**, there was no precipitation when the solution was poured into ice–water. Extraction with chloroform (3 × 100 cm^3), drying and removal of solvent under reduced pressure gave an oil which was crystallised from benzene–light petroleum to yield colourless needles (2.69 g, 67%) m.p. 97–100 °C (Found: C, 62.9; H, 5.9; N, 3.45. $C_{21}H_{23}NO_7$ requires C, 62.8; H, 5.74; N, 3.49%); $\delta_H(CDCl_3)$ 9.15 (1 H, br s, NH), 7.50–7.30 (5 H, m, ArH), 5.35 (4 H, s, CH_2 Ph and CH_2OAc), 3.63 (3 H, s, OCH_3), 3.37 (2 H, t, CH_2CH_2CO), 2.58 (2 H, t, CH_2CO), 2.51 (3 H, s, $COCH_3$) and 2.15 (3 H, s, $OCOCH_3$); *m/z* (%) 401 (4, M^+), 341 (8), 268 (6), 250 (60) and 91 (100).

Synthesis of the 3-(Pyrrolylmethyl)indole **4**, *2-(Pyrrolylmethyl)benzofuran* **24** *and 3-(Pyrrolylmethyl)benzothiophene* **27**.—*General procedure*. A solution of the 5-acetoxymethyl 4-acetylpyrrole **1** (1.0 mmol) and indole (1.0 mmol) in 1,2-dichloroethane (10 cm^3) was heated at gentle reflux and stirred with Montmorillonite clay (1 g) for 1.5–2 h. After filtration from clay and washing well with 1,2-dichloroethane, evaporation of the combined filtrates under reduced pressure gave an oil. This oil was submitted to flash chromatography on silica eluting with ethyl acetate in light petroleum to give *3-(3′-acetyl-5′-ethoxycarbonyl-4′-methylpyrrol-2′-ylmethyl)indole* **4**. It gave colourless crystals from ethyl acetate–light petroleum (0.1465 g, 45%), m.p. 180–182 °C (Found: C, 70.5; H, 6.25; N, 8.65. $C_{19}H_{20}N_2O_3$ requires C, 70.4; H, 6.17; N, 8.64%); $\delta_H(CDCl_3)$ 8.78 (1 H, s, pyr-NH), 8.27 (1 H, s, ind-NH), 7.45 (1 H, d, *J* 7, 4-H) 7.42 (1 H, d, *J* 7, 7-H), 7.25 (1 H, t, *J* 7, 6-H), 7.14 (1 H, t, *J* 7, 5-H), 7.10 (1 H, s, 2-H), 4.45 (2 H, s, 3-CH_2), 4.22 (2 H, q, OCH_2CH_3), 2.63 (3 H, s, 4′-CH_3), 2.53 (3 H, s, CH_3CO) and 1.25 (3 H, t, OCH_2CH_3); *m/z* (%) 324 (100, M^+) 309 (48), 277 (25), 263 (54), 250 (38), 235 (30), 207 (48), 139 (24), 130 (30), 117 (67) and 90 (16); $\nu_{max}(CHCl_3)/cm^{-1}$ 3490, 3430, 1680 and 1650.

Benzofuran (1.0 mmol) when used instead of indole after chromatography gave *2-(3′-acetyl-5′-ethoxycarbonyl-4′-methylpyrrol-2′-ylmethyl)benzofuran* **24** (0.106 g, 38.4%), m.p. 124–127 °C (Found: C, 70.1; H, 6.1; N, 4.15. $C_{19}H_{19}NO_4$ requires C, 70.15; H, 5.85; N, 4.31%); $\delta_H(CDCl_3)$ 9.25 (1 H, s, NH), 7.50 (1 H, d, *J* 7.3, 4-H), 7.44 (1 H, d, *J* 7.3, 7-H), 7.28–7.18 (2 H, m, 6-H and 5-H), 6.57 (1 H, s, 3-H), 4.50 (2 H, s, 2-CH_2), 4.31 (2 H, q, OCH_2CH_3) 2.62 (3 H, s, 4′-CH_3), 2.50 (3 H, s, CH_3CO) and 1.35 (3 H, t, OCH_2CH_3); saturation of the singlet 3-H at δ 6.57 enhanced the signals due to 4-H at δ 7.50 (2.7%) and 2-CH_2 at δ 4.50 (0.8%); *m/z* (%) 325 (100, M^+), 310 (4), 279 (29), 264 (17), 251 (59), 236 (27), 208 (19), 193 (9), 131 (7) and 118 (7); and the *2,3-bis(3′-acetyl-5′-ethoxycarbonyl-4′-methylpyrrol-2′-ylmethyl)benzofuran* **25** (0.0238 g, 8.94%) m.p. 255–257 °C; $\delta_H(CDCl_3)$ 10.09 (1 H, s, NH) 9.95 (1 H, s, NH), 7.32 (1 H, d, *J* 7.7, 4-H), 7.27 (1 H, d, *J* 7.7, 7-H), 7.17 (1 H, t, *J* 7.7, 6-H), 7.08 (1 H, t, *J* 7.7, 5-H) 4.45 (2 H, s, 2-CH_2), 4.40 (2 H, s, 3-CH_2), 4.36 (2 H, q, OCH_2CH_3), 4.27 (2 H, q, OCH_2CH_3), 2.64 (3 H, s, 4′-CH_3), 2.63 (3 H, s, 4′-CH_3), 2.58 (3 H, s, CH_3CO), 2.54 (3 H, s, CH_3CO), 1.39 (3 H, t, OCH_2CH_3) and 1.31 (3 H, t,

OCH_2CH_3); *m/z* (%) 532 (11, M^+), 490 (24), 444 (9), 397 (6), 324 (100), 282 (18), 278 (27), 236 (20), 209 (28) and 162 (28) (Found: M^+, 532.2210. $C_{30}H_{32}N_2O_7$ requires *M*, 532.2209).

When benzothiophene (1.0 mmol) was used in the same way as indole, chromatography using ethyl acetate in dichloromethane as eluent gave colourless crystals of 3-(*4'-acetyl-5'-ethoxycarbonyl-3'-methylpyrrol-2'-ylmethyl)benzothiophene* **27** (0.0963 g, 28.2%) m.p. 125–128 °C (Found: C, 66.75; H, 5.8; N, 4.1. $C_{19}H_{19}NO_3S$ requires C, 66.9; H, 5.57; N, 4.11%); δ_H($CDCl_3$) 8.72 (1 H, br s, NH), 7.88 (1 H, m, 4-H), 7.63 (1 H, m, 7-H), 7.37 (2 H, m, 6-H and 5-H), 7.20 (1 H, s, 2-H), 4.54 (2 H, s, 3-CH_2), 4.23 (2 H, q, OCH_2CH_3), 2.62 (3 H, s, 4'-CH_3), 2.53 (3 H, s, CH_3CO) and 1.28 (3 H, t, OCH_2CH_3); saturation of the 3-CH_2 protons at δ 4.54 enhanced the signals due to NH at δ 8.72 (3.3%) 4-H at δ 7.88 (7.7%), 2-H at δ 7.20 (6%) and CH_3CO at δ 2.53 (1.3%); *m/z* (%) 341 (100, M^+), 326 (9), 298 (6), 295 (20), 230 (39), 267 (46), 252 (32), 224 (27), 194 (26) and 148 (22); and the 2,3-*bis*(*3'-acetyl-5'-ethoxycarbonyl-4'-methylpyrrol-2'-ylmethyl)benzothiophene* **28** as a pale yellow solid (0.0264 g, 9.6%), m.p. 206–209 °C (Found: C, 65.6; H, 5.8; N, 5.1. $C_{30}H_{32}N_2O_6S$ requires C, 65.7; H, 5.80; N, 5.11%); δ_H($CDCl_3$) 9.77 (1 H, br s, NH), 9.43 (1 H, br s, NH), 7.70 (1 H, m, 4-H), 7.49 (1 H, m, 7-H), 7.26 (2 H, m, 6-H and 5-H), 4.55 (2 H, s, CH_2), 4.53 (2 H, s, CH_2), 4.32 (2 H, q, OCH_2CH_3), 4.24 (2 H, q, OCH_2CH_3), 2.61 (3 H, s, 4'-CH_3), 2.60 (3 H, s, 4'-CH_3), 2.57 (3 H, s, CH_3CO) 2.49 (3 H, s, CH_3CO), 1.35 (3 H, t, OCH_2CH_3) and 1.28 (3 H, t, OCH_2CH_3); *m/z* (%) 548 (5, M^+), 530 (11), 340 (100), 294 (27) and 162 (10).

Ethyl 3,4-*Dimethylpyrrolo*[3,2-b]*carbazole-2-carboxylate* **2**.—A solution of the 3-(pyrrolylmethyl)indole **4** (0.108 g, 0.33 mmol) was heated at gentle reflux in 1,2-dichloroethane (10 cm^3) and stirred with Montmorillonite clay (1 g) for 2 h, TLC then showed a single compound had been formed and that reaction was complete. After filtration from clay and washing well with 1,2-dichloroethane, evaporation of the combined filtrates under reduced pressure gave a yellow solid which crystallised from ethyl acetate to give the *pyrrolo*[3,2-b]*carbazole* **2** as yellow crystals (0.076 g; 75%), m.p. 209.5–211 °C (Found: C, 74.6; H, 6.14; N, 9.03. $C_{19}H_{18}N_2O_2$ requires C, 74.5; H, 5.88; N, 9.15%); δ_H([$^2H_6$]-DMSO) 11.22 (1 H, s, 1-NH), 10.7 (1 H, s, 5-H), 8.06 (1 H, d, *J* 7, 9-H), 7.85 (1 H, s, 10-H), 7.40 (1 H, d, *J* 7, 6-H), 7.35 (1 H, t, *J* 7, 7-H), 7.08 (1 H, t, *J* 7, 8-H), 4.35 (2 H, q, OCH_2CH_3), 2.91 (3 H, s, CH_3), 2.90 (3 H, s, CH_3) and 1.35 (3 H, t, OCH_2CH_3). Saturation of the 10-H at δ 7.85 enhanced the singlets due to 1-NH at δ 11.22 (3%) and 9-H at δ 8.06 (4%); *m/z* (%) 306 (56, M^+), 260 (100), 323 (39), 205 (15), 140 (18) and 130 (26); ν_{max}($CHCl_3$)/cm^{-1} 3480, and 1700; λ_{max}(EtOH)/nm 226, 268, 310sh, 327sh, 340, 390, 410sh.

Ethyl 3,4-*Dimethyl*-1*H*-*benzofuro*[3,2-f]*indole-2-carboxylate* **26**.—Toluene-*p*-sulfonic acid (50 mg) was added to a solution of the 2-(pyrrolylmethyl)benzofuran **24** (0.100 g, 0.3 mmol) in toluene (10 cm^3), the reaction mixture was heated under reflux for 3 h. On cooling, the product crystallised out, and after filtration and washing with ethanol gave the *title compound* **26** as pale yellow crystals (0.084 g, 88.8%), m.p. 262–265 °C (Found: C, 74.25; H, 5.55; N, 4.6. $C_{19}H_{17}NO_3$ requires C, 74.3; H, 5.54; N, 4.56%); δ_H([$^2H_6$]-DMSO) 11.52 (1 H, s, NH), 8.18 (1 H, d, *J* 7.5, 5-H), 7.62 (1 H, d, *J* 7.5, 8-H), 7.46 (1 H, t, *J* 7.5, 7-H), 7.38 (1 H, t, *J* 7.5, 6-H), 7.38 (1 H, s, 10-H), 4.37 (2 H, q, OCH_2CH_3), 3.14 (3 H, s, 4-CH_3), 2.91 (3 H, s, 3-CH_3) and 1.39 (3 H, t, OCH_2CH_3); saturation of the 4-CH_3 at δ 3.14 enhanced the signals due to 5-H at δ 8.18 (4.5%) and 3-CH_3 at δ 2.91 (2.6%); *m/z* (%) 307 (53, M^+), 261 (100), 233 (31) and 205 (9); ν_{max}(Nujol)/cm^{-1} 3350 and 1686; λ_{max}(EtOH)/nm 240, 269, 293, 330 and 344.

Ethyl 3,4-*Dimethyl*-1H-[1]*benzothieno*[2,3-f]*indole-2-carboxylate* **29**.—Toluene-*p*-sulfonic acid (45 mg) was added to the solution of the 3-(pyrrolylmethyl)benzothiophene **27** (0.100 g, 0.29 mmol) in toluene (10 cm^3) and the reaction mixture was heated under reflux for 3 h. Evaporation of the solvent and washing the resulting solid with ethanol gave the *title compound* **29** as a pale yellow solid (0.0758 g, 80%), m.p. 191–193 °C (Found: C, 70.3; H, 5.5; N, 4.2. $C_{19}H_{17}NO_2S$ requires C, 70.6; H, 5.26; N, 4.33%); δ_H([$^2H_6$]-DMSO) 11.64 (1 H, s, NH), 8.25 (1 H, m, 9-H), 8.12 (1 H, s, 10-H), 7.95 (1 H, m, 6-H), 7.48 (2 H, m, 7-H and 8-H), 4.38 (2 H, q, OCH_2CH_3), 2.87 (3 H, s, CH_3), 2.85 (3 H, s, CH_3) and 1.37 (3 H, t, OCH_2CH_3); *m/z* (%) 323 (53, M^+), 277 (100), 249 (33), 221 (15), 139 (7) and 111 (11); ν_{max}(Nujol)/cm^{-1} 3350 and 1686; λ_{max}(EtOH)/nm 240, 269, 293, 330 and 344.

One-pot Synthesis of the Pyrrolo[3,2-b]*carbazoles* **2**, **9–11** *and* **13–19**.—*General procedure.* A solution of indole **6–8** (1.0 mmol) and the 5-acetoxymethyl-4-acetylpyrrole **1**, **12**, **20** and **21** (1.0 mmol) in 1,2-dichloroethane (10 cm^3) was heated under gentle reflux and stirred with Montomorillonite clay (1 g) for 3–4h. The colour of clay turned light brown and the reaction was followed to completion by TLC. After filtration from clay and washing well with 1,2-dichloroethane, evaporation of the combined filtrates gave the pyrrolo[3,2-*b*]carbazoles which were obtained as yellow crystals after crystallisation from dichloromethane or ethyl acetate.

Ethyl 3,4-*Dimethylpyrrolo*[3,2-b]*carbazole-2-carboxylate* **2** (0.199 g, 65%) was obtained from the reaction of indole and the 5-acetoxymethyl-4-acetylpyrrole **1**, it was identical in all respects to the pyrrolo[3,2-*b*]carbazole **2** in the previous experiment.

Benzyl 3,4-*dimethylpyrrolo*[3,2-b]*carbazole-2-carboxylate* **13** (0.179 g, 48.8%) was obtained from the reaction between indole and the 5-acetoxymethyl-4-acetylpyrrole **12**, it had m.p. 229–232 °C (Found: C, 78.2; H, 5.65; N, 7.8. $C_{24}H_{20}N_2O_2$ requires C, 78.3; H, 5.43; N, 7.61%); δ_H([$^2H_6$]-DMSO-d_6) 11.29 (1 H, s, 1-NH), 10.65 (1 H, s, 5-NH), 8.08 (1 H, d, *J* 8, 9-H), 7.89 (1 H, s, 10-H), 7.56–7.34 (7 H, m, ArH, 6-H and 7-H), 7.08 (1 H, t, *J* 7, 8-H), 5.42 (2 H, s, CH_2Ph) and 2.92 (6 H, s, 2 × CH_3); *m/z* (%) 368 (74, M^+), 354 (10), 260 (100), 246 (13), 231 (20) and 91 (31).

The *pyrrolo*[3,2-b]*carbazole* **13** (0.166 g, 45%) was also obtained from the reaction of indole and the 4-acetyl-5-(ethoxymethyl)pyrrole **20**.

Ethyl 8-*methoxy*-3,4-*dimethylpyrrolo*[3,2-b]*carbazole-2-carboxylate* **9** was obtained from the reaction of 5-methoxyindole **6** and the 5-acetoxymethyl-4-acetyl pyrrole **1**, it had m.p. 119–122 °C (Found: C, 71.6; H, 6.0; N, 8.05. $C_{20}H_{20}N_2O_3$ requires C, 71.4; H, 5.95; N, 8.33%); δ_H([$^2H_6$]-DMSO) 11.20 (1 H, s, 1-NH), 10.38 (1 H, s, 5-NH), 7.85 (1 H, s, 10-H), 7.62 (1 H, d, *J* 2.5, 9-H), 7.31 (1 H, d, *J* 9, 6-H), 7.01 (1 H, dd, *J* 9 and 2.5, 7-H), 4.38 (2 H, q, OCH_2CH_3), 3.88 (3 H, s, OCH_3), 2.89 (3 H, s, CH_3), 2.87 (3 H, s, CH_3) and 1.39 (3 H, t, OCH_2CH_3); *m/z* (%) 336 (60, M^+), 290 (100), 275 (5), 262 (4), 247 (23), 219 (8) and 145 (9).

Benzyl 8-*methoxy*-3,4-*dimethylpyrrolo*[3,2-b]*carbazole-2-carboxylate* **14** (0.139 g, 35%) was obtained from the reaction of 5-methoxyindole **6** and the 5-acetoxymethyl-4-acetylpyrrole **12**, it had m.p. 212–215 °C (Found: C, 75.4; H, 5.55; N, 6.95. $C_{25}H_{22}N_2O_3$ requires C, 75.4; H, 5.53; N, 7.03%); δ_H([$^2H_6$]-DMSO) 11.29 (1 H, s, 1-NH), 10.38 (1 H, s, 5-NH), 7.88 (1 H, s, 10-H), 7.65 (1 H, d, *J* 2.5, 9-H), 7.32 (1 H, d, *J* 9, 6-H), 7.02 (1 H, dd, *J* 9 and 2.5, 7-H), 5.43 (2 H, s, CH_2Ph), 3.88 (3 H, s, OCH_3), 2.92 (3 H, s, 4-CH_3) and 2.89 (3 H, s, 3-CH_3); *m/z* (%) 3.98 (73, M^+), 290 (100), 262 (10), 247 (15), 219 (7) and 91 (17).

Ethyl 8-*fluoro*-3,4-*dimethylpyrrolo*[3,2-b]*carbazole-2-carboxylate* **10** (0.131 g, 40.5%) was obtained from the reaction of 5-fluoroindole **7** and the 5-acetoxymethyl-4-acetylpyrrole **1**, it had

m.p. 231–234 °C (Found: C, 70.5; H, 5.3; N, 8.4. $C_{19}H_{17}FN_2O_2$ requires C, 70.4; H, 5.25; N, 8.64%); $\delta_H([^2H_6]$-DMSO) 11.27 (1 H, s, 1-NH), 10.64 (1 H, s, 5-NH), 7.93 (1 H, dd, *J* 9 and 2.5, 9-H), 7.88 (1 H, s, 10-H), 7.36 (1 H, dd, *J* 9 and 6, 6-H), 7.19 (1 H, dt, *J* 9 and 2.5, 7-H), 4.36 (2 H, q, OCH_2CH_3), 2.88 (6 H, s, 2 × CH_3) and 1.37 (3 H, t, OCH_2CH_3); *m/z* (%) 324 (50, M^+) 278 (100), 250 (31), 220 (10), 139 (8), 125 (7) and 111 (8).

Benzyl 8-*fluoro*-3,4-*dimethylpyrrolo*[3,2-b]*carbazole*-2-*carboxylate* **15** (0.155 g, 40%) was obtained from 5-fluoroindole **7** and the 5-acetoxymethyl-4-acetylpyrrole **12**; it had m.p. 217–219 °C (Found: C, 74.6; H, 4.95; N, 7.3. $C_{24}H_{19}FN_2O_2$ requires C, 74.6; H, 4.92; N, 7.25); $\delta_H([^2H_6]$-DMSO) 11.36 (1 H, s, 1-NH), 10.68 (1 H, s, 5-NH), 7.94 (1 H, dd, *J* 9 and 2.5, 9-H), 7.89 (1 H, s, 10-H), 7.56–7.38 (5 H, m, ArH), 7.39 (1 H, dd, *J* 9 and 4, 6-H), 7.21 (1 H, dt, *J* 9 and 2.5, 7-H), 5.42 (2 H, s, CH_2Ph), 2.90 (3 H, s, CH_3) and 2.91 (3 H, s, CH_3); *m/z* (%) 386 (68, M^+), 278 (100), 249 (22) and 91 (43).

Ethyl 3,4,6-*trimethylpyrrolo*[3,2-b]*carbazole*-2-*carboxylate* **11** (0.206 g, 64.4%) was obtained from the reaction of 7-methylindole **8** and the 5-acetoxymethyl-4-acetylpyrrole **1**, it had m.p. 230 °C (decomp.) (Found: C, 74.9; H, 6.25; N, 8.65. $C_{20}H_{20}N_2O_2$ requires C, 75.0; H, 6.25; N, 8.75%); $\delta_H([^2H_6]$-DMSO) 11.20 (1 H, s, 1-NH), 10.11 (1 H, s, 5-NH), 7.89 (1 H, d, *J* 7.5, 9-H), 7.84 (1 H, s, 10-H), 7.18 (1 H, d, *J* 7.5, 7-H), 7.01 (1 H, t, *J* 7.5, 8-H), 4.37 (2 H, q, OCH_2CH_3), 2.98 (3 H, s, 4-CH_3), 2.91 (3 H, s, 3-CH_3), 2.58 (3 H, s, 6-CH_3) and 1.34 (3 H, t, OCH_2CH_3); *m/z* (%) 320 (54, M^+), 274 (100), 246 (30), 230 (5), 137 (9), 123 (7) and 109 (6).

Benzyl 3,4,6-*trimethylpyrrolo*[3,2-b]*carbazole*-2-*carboxylate* **16** (0.167 g, 43.7%) was obtained from the reaction of 7-methylindole **8** and the 5-acetoxymethyl-4-acetylpyrrole **12**, it had m.p. 222 °C (decomp.) (Found: C, 78.5; H, 5.9; N, 7.25. $C_{25}H_{22}N_2O_2$ requires C, 78.5; H, 5.76; N, 7.33%); $\delta_H([^2H_6]$-DMSO) 11.27 (1 H, s, 1-NH), 10.11 (1 H, s, 5-NH), 7.89 (1 H, d, *J* 7, 9-H), 7.85 (1 H, s, 10-H), 7.56–7.35 (5 H, m, ArH), 7.18 (1 H, d, *J* 7, 7-H), 7.08 (1 H, t, *J*, 8-H), 5.43 (2 H, s, CH_2Ph), 2.99 (3 H, s, 4-CH_3), 2.93 (3 H, s, 3-CH_3) and 2.59 (3 H, s, 6-CH_3); *m/z* (%) 382 (71, M^+) 274 (100), 246 (19) and 91 (22).

Benzyl 3(2-*methoxycarbonylethyl*)-4-*methylpyrrolo*[3,2-b]-*carbazole*-2-*carboxylate* **22** (0.230 g, 52.3%) was obtained from indole and the 5-acetoxymethyl-4-acetylpyrrole **21**, it had m.p. 211–213 °C (Found: C, 73.7; H, 5.6; N, 6.2. $C_{27}H_{24}N_2O_4$ requires C, 73.6; H, 5.45; N, 6.36%); $\delta_H([^2H_6]$-DMSO) 11.51 (1 H, s, 1-NH), 10.71 (1 H, s, 5-NH), 8.75 (1 H, d, *J* 7.5, 9-H), 7.92 (1 H, s, 10-H), 7.57–7.44 (7 H, m, ArH, 6-H and 7-H), 7.18 (1 H, t, *J* 7.5, 8-H), 5.43 (2 H, s, CH_2Ph), 3.63 (3 H, s, OCH_3), 3.59 (2 H, partially obscured, t, CH_2CH_2CO), 2.88 (3 H, s, 4-CH_3) and 2.65 (2 H, t, CH_2CO); *m/z* (%) 440 (100, M^+), 332 (20), 290 (47) and 91 (57).

Pyrrolo[3,2-b]*carbazole*-2-*carboxylic Acids* **17–19** *and* **23**.—*General procedure.* To a solution of the benzyl pyrrolo[3,2-*b*]carbazole-2-carboxylate **13–15** and **22** in dry tetrahydrofuran (THF) (10 cm^3) was added 10% Pd-on-C (50 mg). The reaction mixture was hydrogenated at one atmos. pressure and room temperature. After uptake of H_2 had ceased, the catalyst was filtered through Celite and washed well with THF, and the combined filtrates were evaporated under reduced pressure. Crystallisation of the resulting solid from acetone or aqueous methanol gave the pyrrolo[3,2-*b*]carbazole-2-carboxylic acids **17–19** and **23** as yellow crystals.

3,4-*Dimethylpyrrolo*[3,2-b]*carbazole*-2-*carboxylic acid* **17** (0.234 g, 84.3%) had m.p. 237 °C (decomp.); $\delta_H([^2H_6]$-DMSO) 12.74 (1 H, br s, CO_2H), 11.13 (1 H, s, 1-NH), 10.60 (1 H, s, 5-NH), 8.05 (1 H, d, *J* 7.5, 9-H), 7.87 (1 H, s, 10-H), 7.42 (1 H, d, *J* 7.5, 6-H), 7.36 (1 H, t, *J* 7.5, 7-H), 7.08 (1 H, t, *J* 7.5, 8-H), 2.92 (3 H, s, CH_3) and 2.91 (3 H, s, CH_3); *m/z* (%) 278 (30, M^+), 260 (39), 234 (100), 218 (19), 204 (8), 167 (8), 149 (16), 130 (10) and 117 (25) (Found: M^+, 278.1060. $C_{17}H_{14}N_2O_2$ requires *M*, 278.1055).

8-*Fluoro*-3,4-*dimethylpyrrolo*[3,2-b]*carbazole*-2-*carboxylic acid* **18** (0.0845 g, 85.6%) m.p. 236–239 °C; $\delta_H([^2H_6]$-DMSO) 12.80 (1 H, br s, CO_2H), 11.19 (1 H, s, 1-NH), 10.6 (1 H, s, 5-NH), 7.91 (1 H, dd, *J* 9 and 2.5, 9-H), 7.86 (1 H, s, 10-H), 7.37 (1 H, dd, *J* 9 and 4, 6-H), 7.20 (1 H, dt, *J* 9 and 2.5, 7-H) and 2.89 (6 H, s, 2 × CH_3); *m/z* (%) 296 (51, M^+), 278 (71), 252 (100), 250 (37), 236 (19), 222 (13), 139 (22), 125 (36) and 111 (28) (Found: M^+, 296.0960. $C_{17}H_{13}FN_2O_2$ requires *M*, 296.0961).

3,4,6-*Trimethylpyrrolo*[3,2-b]*carbazole*-2-*carboxylic acid* **19** (0.065 g, 85%) m.p. 230 °C (decomp.) (Found: C, 74.2; H, 5.55; N, 9.4. $C_{18}H_{16}N_2O_2$ requires C, 74.0; H, 5.48; N, 9.59%); $\delta_H([^2H_6]$-DMSO) 12.80 (1 H, br s, CO_2H), 11.01 (1 H, s, 1-NH), 10.08 (1 H, s, 5-NH), 7.90 (1 H, d, *J* 7.5, 9-H), 7.82 (1 H, s, 10-H), 7.16 (1 H, d, *J* 7.5, 7-H), 7.01 (1 H, t, *J* 7.5, 8-H), 2.97 (3 H, s, 4-CH_3), 2.92 (3 H, s, 3-CH_3) and 2.58 (3 H, s, 6-CH_3); *m/z* (%) 292 (72, M^+), 274 (100), 246 (50), 230 (11), 137 (25), 122 (24) and 109 (30).

3-(2-*Methoxycarbonylethyl*)-4-*methylpyrrolo*[3,2-b]*carbazole*-2-*carboxylic acid* **23** (0.0673 g, 84.6%) m.p. 255 °C (decomp.) (Found: C, 68.4; H, 5.3; N, 7.75. $C_{20}H_{18}N_2O_4$ requires C, 68.6; H, 5.14; N, 8.00%); $\delta_H([^2H_6]$-DMSO) 12.88 (1 H, br s, CO_2H), 11.34 (1 H, s, 1-NH), 10.65 (1 H, s, 5-NH), 8.06 (1 H, d, *J* 7.5, 9-H), 7.88 (1 H, s, 10-H), 7.42 (1 H, d, *J* 7.5, 6-H), 7.36 (1 H, t, *J* 7.5, 7-H), 7.07 (1 H, t, *J* 7.5, 8-H), 3.66 (3 H, s, OCH_3), 3.63 (2 H, partially obscured t, CH_2CH_2CO), 2.89 (3 H, s, CH_3), 2.66 (2 H, t, CH_2CO); *m/z* (%) 350 (100, M^+), 332 (17), 306 (30), 290 (63), 272 (22), 259 (32) and 233 (47).

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