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SYNTHESIS OF PYRROLO[1,2-a]INDOLES: VILSMEIER FORMYLATION OF SOME 3-METHYLINDOL-2-YL KETONES AND 3(3-METHYLINDOL-2-YL)PROPENOIC ESTER

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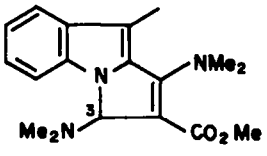
Abstract—3-Methylindol-2-yl methyl ketone reacted with phosphoryl chloride in dimethylformamide to give 3-chloro-3(3-methylindol-2-yl), propenal (4). 2-Carbomethoxy- and 2-carbethoxy-1-chloro- 9H-pyrrolo[1,2-a]indol-9-ylidene acetaldehyde (10a and b) were formed by reaction with the same reagent of 3(3-methylindol-2-yl) propenoate (7) and 3(3-methylindol-2-yl)-3-oxopropanoate (2) respectively. In the latter case, 2-carbethoxy-1-chloro-3-dimethylamino-9-methyl-3H-pyrrolo[1,2-a]indole (9b) was isolated as an intermediate. The structure of the pyrroloindolylidene acetaldehydes was proved by synthesis of the chromophore from 4-acetyl-3-methyl-1-phenyl-pyrrole-2-carboxylate (26). The preparation and behaviour of 1-phenylpyrrole-2,4- and 3,4-dicarboxylates, monomethylated in the pyrrole ring, is described. These compounds were prepared during a search for a satisfactory route to a starting material for the synthesis of compounds related to 10a and b. The saponification of such diesters is remarkably selective, and in the case of the 2,4-dicarboxylates, contradicts accepted generalisations concerning the lability of pyrrole α,β-diesters to selective hydrolysis.

3-Alkylindole-2-acetic esters have been shown to react with two equivalents of phosphoryl chloride in dimethylformamide (the Vilsmeier reagent) to provide, under vigorous conditions, a compound of structure as yet unestablished.[1] During the course of further work on this compound, the determination of the tautomeric properties and UV spectra of 3H - pyrrolo[1,2-a]indole - 2 - carboxylates, and in particular, the 1,3-bisdialkylamino compound 1, became relevant.

Attempted synthesis of 3. The approach adopted for the synthesis of 1 required incorporation of a one-carbon



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unit to provide C-3 of the product in the pyrrole ring-forming step by Vilsmeier reaction on 3-dimethylamino-3-indol-2-yl propenoate (Scheme 1).

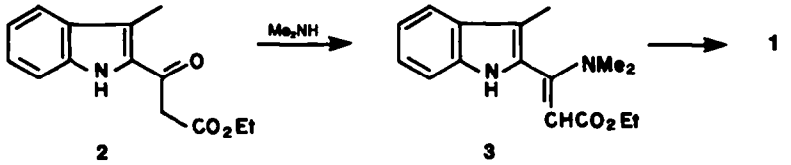
Treatment of 3-methylindole with the half acid chloride of malonic ester gave the indole ketoester 2 in poor yield, but attempted subsequent condensation with dimethylamine, even under forcing conditions,[2,3] failed to provide the aminopropenoate 3. The weak electrophilicity of the CO group of 2-acylindoles, due to mesomeric interaction of the ketone with the indole nitrogen, is well known,[4] although there is a precedent for the condensation of a 2-acylindole with pyrrolidine.[5]

The chloropropenal 4 formed readily on exposure of 3-methylindol-2-yl methyl ketone to phosphoryl chloride in hot dimethylformamide. This Vilsmeier reaction, in which formylation is accompanied by chlorination (Scheme 2) is mechanistically unexceptional[6] but novel in the indole series.† The chloropropenal was converted with KCN/MeOH/MnO_2[8] to the ester 5, but this too failed to provide the methylaminopropenoate corresponding to 3 on treatment with dimethylamine.

Vilsmeier formylation of 7 *and* 2

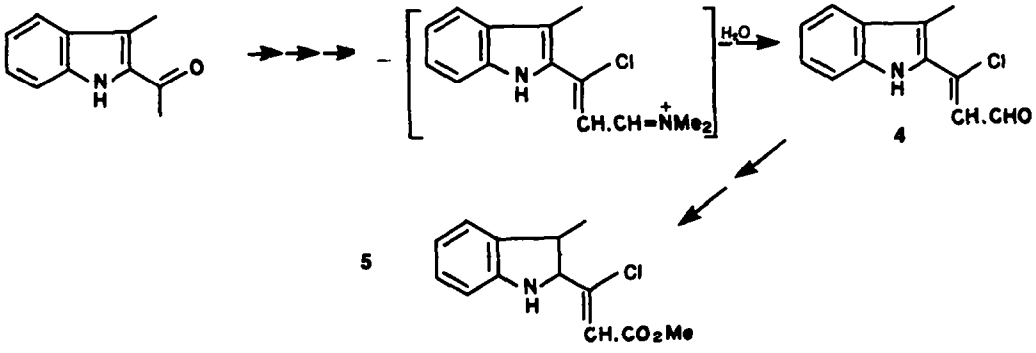
The behaviour of the simple 3-indol-2-yl propenoate 7 under Vilsmeier conditions was next investigated. It was prepared from 3-methylindole-2-carboxylate[9] by reduction with LAH, oxidation of the alcohol with pyridine/CrO_3[10] and Wittig reaction of the aldehyde with methyl phosphonoacetate/NaH.[11] Heating 7 with the Vilsmeier reagent at 60° gave the N-formyl derivative as a minor product, along with two other compounds, one of which slowly converted into the other. The PMR of the stable major product showed that it was not 9a, the expected pyrroloindole analogue of 1 (Scheme 3) but one of the geometric isomers of 10a. Instead of an aromatic Me singlet, there was a doublet at δ 10.30 coupled to a doublet at 6.45, establishing the feature C_2C:CH.CHO as present in the molecule. The compound possessed two CO groups (1664 and 1708 cm^{-1}), and absorbed at 250 (sh), 263 (sh), 270,

†The tricyclic 2-acylindole 6 yields the expected 9-formyl derivative with extreme inefficiency, and formylation at C-2 is not reported.[7]

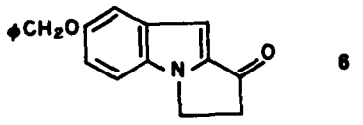


2 3

Scheme 1.



Scheme 2.



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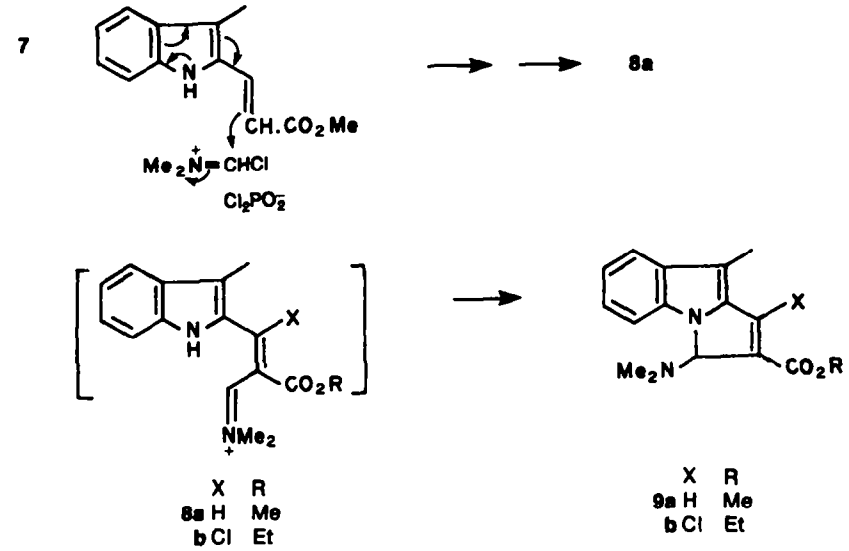
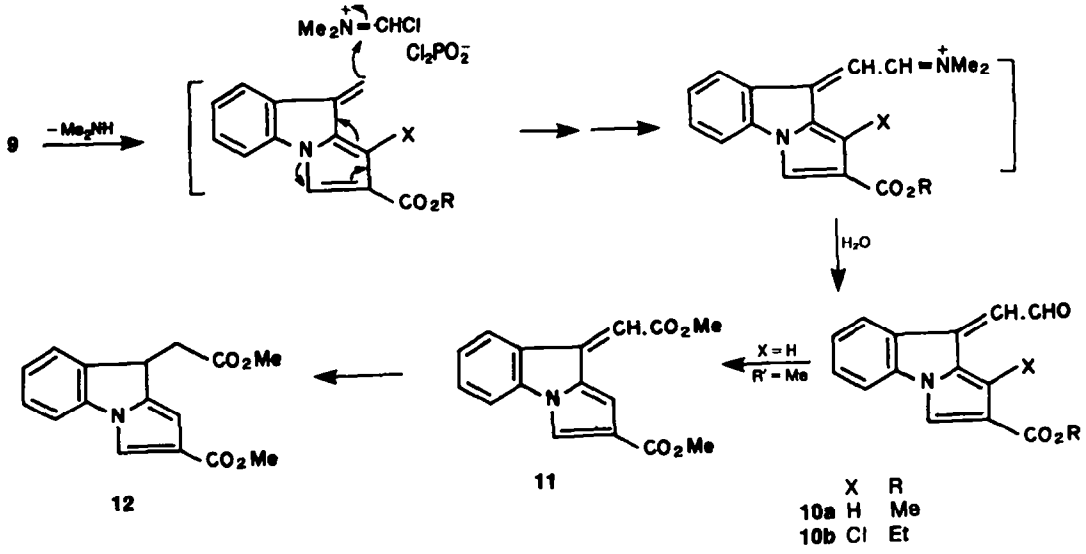
325–40 and 362 nm (log ϵ 4.27, 4.43, 4.51, 4.03, 4.14). The loss of the aromatic Me group can be explained if the expected product of the reaction (**9a** or one of its double bond isomers) eliminates dimethylamine to form a vinylpyrroloindole (Scheme 4). Subsequent formylation



	X	R
8a	H	Me
b	Cl	Et

	X	R
9a	H	Me
b	Cl	Et

Scheme 3.



	X	R
10a	H	Me
10b	Cl	Et

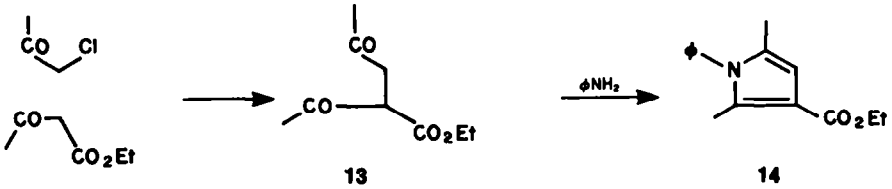
Scheme 4.

of this would give a product which, on hydrolysis, would yield 2 - carbomethoxy - 9H - pyrrolo[1,2-a]indol - 9 - ylidene acetaldehyde (**10a**) as a mixture of geometric isomers.

A similar pyrroloindolylidene acetaldehyde **10b** was obtained on treating the β-ketoester **2** with two equivalents of the Vilsmeier reagent, presumably via the formation of the chloropropenoate **8b** (*cf* Scheme 2). The ketoester **2** was more labile than the propenoate **7** and the reaction could be initiated at room temperature. In that case, the intermediate 3H-pyrroloindole **9b** was isolated. Its UV spectrum closely resembled that of the indolyl propenoate **5**, which observation, together with the absence of a Me doublet in the PMR, confirmed the structure as **9b** rather than either the 1H tautomeric form or, as might have been expected from previous reports[5,12,13] of the ring system, the alternative 9H tautomer.

Conversion of **10** *to* **12**. In an endeavour to establish the structures of the products **10**, catalytic reduction of the exocyclic double bond at C-9 was carried out after conversion of the aldehyde **10a** to the ester **11**. The dihydroester **12** was an oil, absorbing at 225, 273, 282 and 293 nm (log ε 4.18, 4.14, 4.07, 4.01) that crystallised over several months. Ethyl 2,5 - dimethyl - 1 - phenylpyrrole - 3 - carboxylate (**14**) was synthesised (Scheme 5) from ethyl hexa - 2,5 - dione - 3 - carboxylate (**13**)[15] phenylhydroxylamine with ethyl acetoacetate, giving 3,5 - dimethyl - 1 - phenylpyrrole - 2,4 - dicarboxylate in poor yield, with competing side reactions.[18] However, pyrrole - 2,4 - dicarboxylates lacking a 1-phenyl group are described widely, the syntheses being of the Hantzsch or Knorr types, involving the condensation of a C_2N with a C_2 unit to provide the pyrrole ring. The Knorr synthesis has the drawback for the preparation of 1-substituted pyrroles that the usual method of *in situ* generation of the unstable α-aminoketones required, by reduction of α-oximinoketones, is inapplicable.

Using the Hantzsch approach (Scheme 6), ethyl bromopyruvate[19] was condensed with ethyl anilinocrotonate (**15a**).[20a] A major problem with this and subsequent work was the lack of information on PMR shifts of ring protons in comparable pyrroles, and the similarity of the UV spectra of various pyrrole dicarboxylates. This required reliance on chemical methods to solve questions of positional isomerism, and this turned out to be misleading. Thus the product of reaction of pyruvate and crotonate gave a pyrrole diester whose expected structure **16** was apparently confirmed by selective hydrolysis in ethanolic potassium hydroxide, carried out in fair yield to a mono acid, in accord with the claim[21] that in pyrrole polyesters "β-position (esters) can be attacked only by alkali in excess of the amount required to hydrolyse all esters in α-positions". However, the half acid obtained



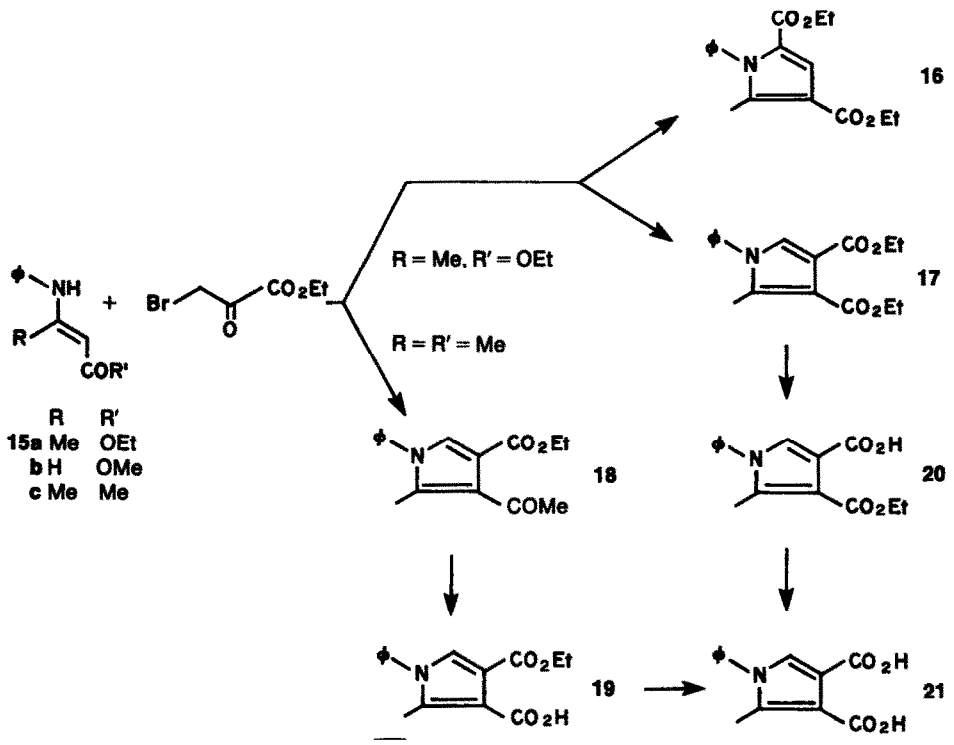
Scheme 5.

and aniline, but the simple confirmation of structure of **12** hoped for was not forthcoming when **14** showed absorption at 237 and 265 (sh) nm (log ε 4.04, 3.68). The UV spectra of 1-phenylpyrroles are dependent upon coplanarity of the aromatic rings[16] and this is ensured in the case of **12** by the C-9 bridge. The 2,5-dimethyl groups in **14** on the other hand force the rings to skew relative to one another. Indeed, atropisomerism has been demonstrated in a similar compound,[14] carboxylated in the phenyl ring.

Synthesis and reactions of pyrroles related to **11**

(i) *Phenylpyrrole carboxylic acids.* As there is no simple method of synthesising a 1-phenylpyrrole-3-carboxylate without alkyl substituents at the 2- and/or 5-positions, the synthesis of bridged models was undertaken. 1-Phenylpyrrole-2-carbonyl chlorides bearing a variety of substituents on both rings have been cyclised to 9H - pyrrolo[1,2-a]indol - 9 - ones by Friedel Crafts reaction, establishing a carbonyl bridge between the rings.[12,17] It seemed plausible therefore to use this approach and follow it with a Wittig reaction to complete the synthesis of a pyrroloindolylidene acetate such as **11**. However, there were no examples in which the starting phenylpyrrole-2-carbonyl chloride bore a carboxylic group at position 4 which would be required to provide the carboxylate at C-3 to complete the chromophore present in **11**. The only simple 1 - phenylpyrrole - 2,4 - dicarboxylate so far reported involved the reflux of thereby, after conversion to the half acid chloride, failed to cyclise in the Friedel Crafts reaction. This was initially interpreted as due to steric hindrance to ring coplanarity offered by the pyrrole α-methyl group present in **16**. Although not very convincing, the selectivity of the saponification and the refusal of the diacid obtained by total saponification to form a cyclic anhydride made this conclusion more tenable than the alternative explanation, which was that the product of reaction of pyruvate and crotonate was the β,β-diester **17**. Accordingly, it was decided to synthesise the desmethyl analogue of **16**, using the anilinoacrylate **15b**[22] instead of the crotonate. However, the acrylate reacted with bromopyruvate to give a complex mixture under conditions (reflux in ethanol) which sufficed to produce product cleanly in the case of the crotonate.

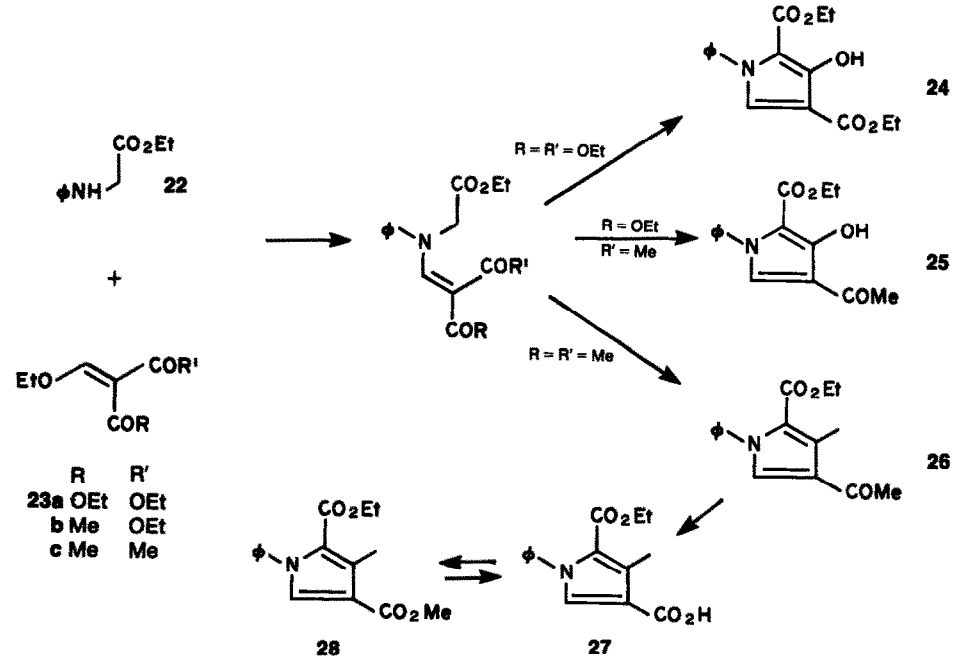
The choice between the isomeric diester structures **16** and **17** was settled in favour of the latter by converting the compound via the diacid **21** to the known[23] dimethyl ester. It remained to show which ester had hydrolysed in the selective saponification undergone by **17**. 3 - Acetyl - 2 - methyl - 1 - phenylpyrrole - 4 - carboxylate (**18**) was synthesised from bromopyruvate and 4 - anilinopent - 3 - en - 2 - one (**15c**).[24] A subsequent haloform reaction at room temperature gave the half acid **19** (m.p. 148°, ν 1625, 1710 cm^{-1}). This was not identical to the half acid obtained by partial saponification of **17**, which therefore must have been **20** (m.p. 122°, ν 1630, 1720 cm^{-1}). Both acids gave the same diacid **21** on complete hydrolysis.



Scheme 6.

The misleading failure of this diacid to undergo internal anhydride formation, in contrast to the behaviour reported for 1 - phenylpyrrole - 3,4 - dicarboxylate,[25] may reflect the fact that the 3-carboxy group is forced out of coplanarity with the ring.[23] This explanation was suggested for the split CO absorption displayed in the IR spectrum by the dimethyl ester of **21**. Equally, though pyrrole β-esters are no doubt, other things being equal, less labile to base hydrolysis than α-esters, an ester function which is adjacent to an unsubstituted position—irrespective of whether that position is α or β in the pyrrole ring—is probably more labile to hydrolysis than one which is not, for purely steric reasons.

These problems dictated another approach: assembly of the pyrrole ring in terms of C_1N+C_3 components. This idea had been used in the synthesis of prodigiosin[26] and employed diethyl ethoxymethylenemalonate (**23a**) as a key material. Similar compounds were employed in the



Scheme 7.

synthesis of some amino and hydroxy 1 - phenylpyrrole - 2,4 - dicarboxylates.[27] Ethyl N-phenylglycinate (**22**)[28] was added to the diester **23a**[20b] to give a product which was immediately treated with base, giving the hydroxypyrrole **24** in excellent yield (Scheme 7). The ketoester **23b**[29] was substituted for **23a** since it was thought likely that the cyclisation of the resulting intermediate would occur at the acetyl CO to give 3 - methyl - 1 - phenylpyrrole - 2,4 - dicarboxylate. However, the compound isolated was again a 3-hydroxypyrrole, **25**, resulting from the alternative mode of closure, onto the ester CO. This regiospecificity could not be altered by changing conditions. It finally became necessary to use the diketone **23c**[29] to obtain an intermediate whose cyclisation to **26** was necessarily unambiguous, but provided the 4-acetyl in place of the 4-carbethoxy pryyole. Bromoform reaction at 60° gave the half acid **27** (ν 1660, 1690 cm^{-1}), methylation with diazomethane yielding the mixed ester **28**. The synthesis of the pyrroloindolone then required the selective hydrolysis of the ethyl ester, formation of the acid chloride and cyclisation. However, in confirmation of our earlier result with the hydrolysis of **17**, hydrolysis cleaved the *methyl* ester to give back **27**.

(ii) *Tricyclic pyrrole and synthesis of* **32**. The ketoacid **29** (Scheme 8) formed by hydrolysing the ester **26** was warmed with a slight excess of freshly-distilled thionyl chloride in chloroform, giving the corresponding crystalline acid chloride. Upon briefly warming the acid chloride in a solution of aluminium chloride in nitrobenzene, the pyrroloindolone **30** was obtained in excellent yield. Stirring with sodium hypobromite in dioxan under carefully controlled conditions gave the corresponding keto acid after acidification. Because of insolubility problems, this was not characterised but immediately esterified to **31** with diazomethane/THF. Notwithstanding that a similar diaryl ketone, fluorenone, condenses with phosphonoacetate anion,[30] attempts to effect such a condensation in the present case failed. This was ascribed to the steric hindrance presented by the peri Me group to the approach to the CO carbon of the bulky anion. However, Reformatsky reaction gave a β-hydroxyester which eliminated water on warming in benzene with a trace of acid, affording the required crystalline ethyl 2 - carbomethoxy - 1 - methyl - 9H - pyrrolo[1,2-a]indol - 9 - ylidene acetate (**32**), the similarity of whose UV spectrum to that of the Vilsmeier-derived adduct **11** confirmed the structure of the latter.

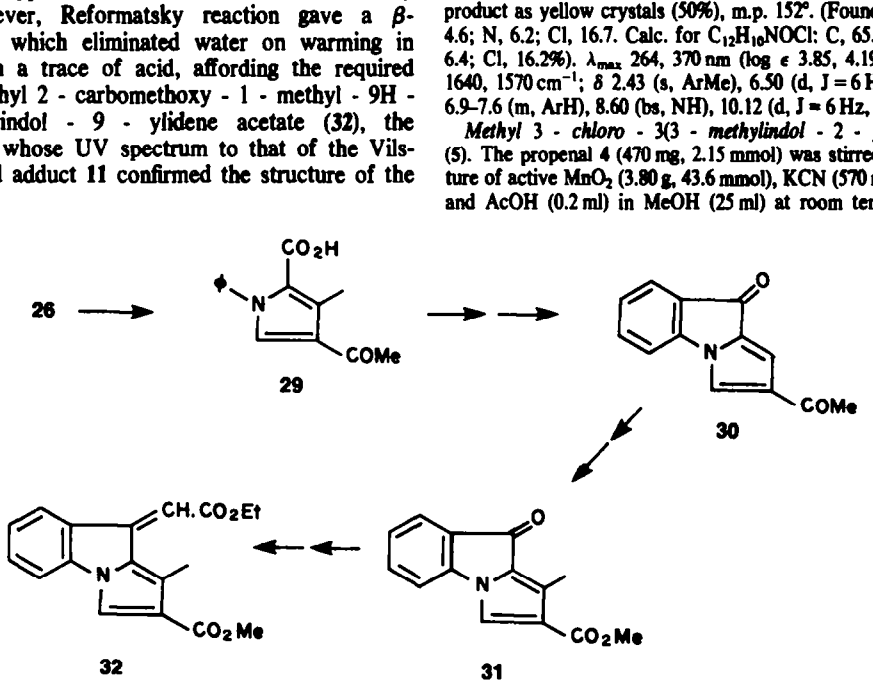
EXPERIMENTAL

Unless otherwise stated: IR spectra were run in KBr on a Unicam SP200 spectrometer; UV spectra were obtained on a Unicam SP800 spectrometer with samples in EtOH; PMR spectra were run at 60 MHz on a Perkin–Elmer R12 spectrometer with samples in $CDCl_3$; ethyl ester methylene/methyl coupling constants were 7 Hz; TLC data refers to silica GF_{254} plates and development in benzene/EtOAc 9/1; solvents were redistilled; Fluka "Practical" Grade reagents were used throughout without further purification; melting points are uncorrected and were determined on a Kofler hot-stage; solvents were removed during workup of reaction by rotary evaporator at water pump vacuum using a waterbath at approximately 60°.

Ethyl 3(3 - *methylindol* - 2 - *yl*) - 3 - *oxopropanoate* (**2**). $ZnCl_2$ (12.0 g, 88 mmol) was added with mechanical stirring to 3-methylindole (4.40 g, 34 mmol) in Na-dried Et_2O (32 ml). The mixture was cooled in ice and ethyl 3 - oxo - 3 - chloropropanoate[35] in Na-dried Et_2O (40 ml) added over 30 min, maintaining stirring. The reaction was stirred for a further 90 min, the icebath being removed 30 min after stirring was complete. The mixture was again cooled in ice, and water (50 ml) added with mechanical stirring. The phases were separated, the Et_2O evaporated and replaced with $CHCl_3$ (40 ml). The aqueous phase from the reaction was extracted with $CHCl_3$ soln, the organic phase washed with water (2 × 50 ml), 5% aq $NaHCO_3$ (50 ml) and water (20 ml), dried ($MgSO_4$), filtered and evaporated to give 8.6 g oil. This was chromatographed on a Grade I Alumina column, eluting with EtOAc/benzene, initially 5/95 and finally 1/9, giving 2.8 g crude crystalline product, which yielded 2.04 g (24%), m.p. 100–1°, on recrystallisation from $CHCl_3/Et_2O$. (Found: C, 68.4; H, 6.0; N, 5.9. Calc. for $C_{14}H_{15}NO_3$: C, 68.6; H, 6.2; N, 5.7%). λ_{max} 239, 317 nm (log ϵ 4.17, 4.32); λ_{max} (EtOH/HO^-) 337 nm (log ϵ 4.41); ν_{max} 3320, 1738, 1638 cm^{-1}; δ 1.30 (t, CH_2CH_3), 2.60 (s, ArMe), 3.99 (s, CH_2), 4.24 (q, CH_2CH_3), 7.0–7.8 (m, ArH), 9.39 (bs, NH).

3 - *Chloro* - 3(3 - *methylindol* - 2 - *yl*)*propenal* (**4**). $POCl_3$ (2.5 ml, 27 mmol), redistilled from Na, was added to ice cold DMF (7 ml) redistilled from CaH_2 and stored over Linde 4A sieve, and the mixture added to 3 - methylindol - 2 - yl methyl ketone[1] (1.38 g, 8 mmol) in pure dry DMF at room temp. The mixture was heated for 5 min at 86° with stirring, allowed to cool to room temp and partitioned between aq 1 M KOH (20 ml) and EtOAc (20 ml). The organic phase was washed with water (4 × 20 ml), dried (Na_2CO_3), filtered and evaporated to give 1.46 g of crude product. Recrystallisation from benzene gave 880 mg of product as yellow crystals (50%), m.p. 152°. (Found: C, 65.9; H, 4.6; N, 6.2; Cl, 16.7. Calc. for $C_{12}H_{10}NOCl$: C, 65.6; H, 4.6; N, 6.4; Cl, 16.2%). λ_{max} 264, 370 nm (log ϵ 3.85, 4.19); ν_{max} 3280, 1640, 1570 cm^{-1}; δ 2.43 (s, ArMe), 6.50 (d, J = 6 Hz, CHCHO), 6.9–7.6 (m, ArH), 8.60 (bs, NH), 10.12 (d, J = 6 Hz, CHO).

Methyl 3 - *chloro* - 3(3 - *methylindol* - 2 - *yl*)*propenoate* (**5**). The propenal **4** (470 mg, 2.15 mmol) was stirred with a mixture of active MnO_2 (3.80 g, 43.6 mmol), KCN (570 mg, 8.8 mmol) and AcOH (0.2 ml) in MeOH (25 ml) at room temperature for



Scheme 8.

12 hr.[8] The MnO_2 was filtered off and triturated with small portions of MeOH until the triturate was clear in the UV. The MeOH phases were combined and evaporated and the residue partitioned between water (15 ml) and Et_2O (15 ml). The aqueous phase was washed with Et_2O (2 × 10 ml), the organic phases combined, dried (Na_2CO_3), filtered and evaporated to give 361 mg gum. This was chromatographed on a plate, developing with $CHCl_3$/hexane 3/7, to give two compounds: the Z product (138 mg, 26%), R_f = 0.32, m.p. 90–103°, and the E product (81 mg, 15%), R_f = 0.54, an oil. The crystalline product was twice recrystallised from benzene/hexane to give yellow needles, m.p. 132–3°. (Found: 63.0; H, 4.4; N, 5.1; Cl, 14.0. Calc. for $C_{13}H_{12}NO_2Cl$: C, 62.5; H, 4.8; N, 5.6; Cl, 14.2%). λ_{max} 254, 340 nm (log ϵ 3.98, 4.25); ν_{max} 3410, 1705, 1603 cm^{-1}; δ 2.49 (s, ArMe), 3.80 (s, OMe), 6.38 (s, vinyl CH), 7.0–7.7 (m, ArH), 8.45 (bs, NH). The E isomer had similar spectroscopic characteristics, the only notable difference being the vinyl singlet, which appeared at δ 6.17.

3-Methylindole-2-carboxaldehyde. Anhydrous CrO_3 (17.21 g, 0.11 mol) in CH_2Cl_2 (100 ml) was slowly added to pyridine (150 ml, 1.9 mol) with stirring, cooling the flask in an icebath. 3-Methylindole-2-methanol (8.00 g, 50 mmol, prepared from the 2-ester[9] by hydride reduction)[10] was added quickly and stirring continued for a further 5 min. The mixture was allowed to warm to room temp and the solvent evaporated. The residue was partitioned between 2 M HCl (40 ml) and EtOAc (40 ml), the organic phase washed with water (40 ml), dried (Na_2CO_3), filtered and evaporated to give 5.65 g (71%) of yellow product, m.p. 135–9°. A sample recrystallised from benzene gave white rods, m.p. 142–3° (139°).[10]

Methyl 3(3-methylindol-2-yl)propenoate (7). THF was dried by distillation from LAH. Trimethylphosphonoacetate (224 mg, 1.23 mmol) in THF (5 ml) was added dropwise to a slurry of 60% NaH/oil (50 mg, 1.25 mmol) in THF (15 ml) at room temp and stirred 10 min. 3 - Methylindole - 2 - carboxaldehyde (196 mg, 1.23 mmol) in the THF (5 ml) was added dropwise with stirring at room temp, and stirring continued 30 min after addition was complete. The solvent was evaporated and the residue partitioned between water (10 ml) and Et_2O (15 ml), the organic phase washed with water (2 × 10 ml), dried (Na_2CO_3), filtered and evaporated to give 237 mg yellow crystals, m.p. 125°. Recrystallisation from EtOH gave 172 mg (65%), m.p. 182°. (Found: C, 72.0; H, 6.0; N, 6.5. Calc. for $C_{13}H_{13}NO_2$: C, 72.5; H, 6.1; N, 6.5%). λ_{max} 255, 350 nm (log ϵ 4.08, 4.62); ν_{max} 3370, 1690, 1620 cm^{-1}; δ 2.41 (s, ArMe). 3.78 (s, OMe), 6.06 (d, J = 15 Hz, =CHCO–), 7.0–7.5 (m, ArH), 7.80 (d, J = 15 Hz, ArCH=).

2 - Carbethoxy - 1 - chloro - 3 - dimethylamino - 9 - methyl - 3H - pyrrolo[1,2-a]indole (9b). $POCl_3$/DMF mixture (0.35 ml, 1.0 mmol of formylating reagent), prepared as in the synthesis of 4, was added to 2 (203 mg, 0.83 mmol) dissolved in the minimum volume of $(CH_2Cl)_2$. After 1 hr the reaction was partitioned between $CHCl_3$ (15 ml) and sat Na_2CO_3 aq (10 ml). The organic phase was washed with water (10 ml), dried (Na_2CO_3), filtered and evaporated to give 266 mg thick oil. This was chromatographed on a plate, and the crystalline product recrystallised from Et_2O/40–60° petrol, affording 90 mg (34%) of product as pale yellow crystals, m.p. 90–1°. (Found: C, 64.7; H, 5.8; N, 8.5; Cl, 11.1. Calc. for $C_{17}H_{19}N_2O_2Cl$: C, 64.1; H, 6.0; N, 8.8; Cl, 11.2%). λ_{max} 267, 364 nm (log ϵ 3.79, 4.24); ν_{max} 1700, 1565, 1310, 735 cm^{-1}; δ 1.30 (t, CH_2CH_3), 2.20 (s, NMe_2), 2.38 (s, ArMe), 4.26 (q, CH_2CH_3), 5.25 (s, $CHNMe_2$), 6.6–7.4 (m, ArH).

2 - Carbethoxy - 1 - chloro - 9H - pyrrolo[1,2-a]indol - 9 - ylidene acetaldehyde (10b). Reagents were combined as in the preparation of 9b except that 0.70 ml of formylating reagent was employed, and the reaction was heated at 70° for 1 hr. A hard crystalline mass formed, which was triturated with sat Na_2CO_3 aq. Recrystallisation of the residue from aqueous DMF gave 184 mg (73%) of the yellow crystalline product, m.p. 204–5°. The PMR spectrum established that this was a mixture of the two geometric isomers, present in equal amounts. (Found: C, 64.0; H, 4.0; N, 4.5; Cl, 12.0. Calc. for $C_{16}H_{12}O_3NCl$: C, 63.7; H, 4.0; N, 4.6; Cl, 11.8%). λ_{max} 255 (sh), 263 (sh), 270, 325–340, 359 nm (log ϵ 4.21, 4.26, 4.27, 3.87, 3.98). ν_{max} 3100, 1695, 1660, 1625 cm^{-1}; δ 1.43 (t, CH_2CH_3), 4.35 (q, CH_2CH_3), 6.45 (d, J = 9 Hz, 0.5 H approx, =CHCHO), 6.94 (d, J = 8 Hz, 0.5 H approx., =CHCHO), 7.0–8.2 (m, ArH, among which two signals at 7.65 and 7.70 could be singlets due to H-3), 10.75 (d, J = 8 Hz, 0.5 H approx., CHO), 11.21 (d, J = 9 Hz, 0.5 H approx., CHO). Spin–spin decoupling confirmed the coupling of the signals at δ 6.45 and 6.94 with those at 11.21 and 10.75 respectively.

2 - Carbomethoxy - 9H - pyrrolo[1,2-a]idol - 9 - ylidene acetaldehyde (10a). $POCl_3$/DMF mixture (0.84 ml, 2.4 mmol of formylating reagent), prepared as in the synthesis of 4, was added to 7 (165 mg, 0.77 mmol) and the reaction stirred at 60° for 1 hr. After cooling, the mixture was partitioned between $CHCl_3$ (15 ml) and sat Na_2CO_3 aq (10 ml). The aqueous phase was washed with $CHCl_3$ (15 ml), the organic phases combined, washed with water (3 × 15 ml), dried (Na_2CO_3), filtered and evaporated. The residue was chromatographed on a plate, giving, in order of increasing R_f, A (83 mg, m.p. 192–8°), B (71 mg, oil), C (24 mg, m.p. 183–5°). On standing B converted to A, which was identified as the acetaldehyde 10a. Recrystallisation of the combined A and B fractions from MeOH gave 130 mg (67%) of the acetaldehyde as yellow crystals, m.p. 195–8°. (Found: C, 71.8; H, 4.2; N, 5.8. Calc. for $C_{15}H_{11}NO_3$: C, 71.1; H, 4.4; N, 5.5%). λ_{max}—see Discussion; ν_{max} 3100, 1708, 1664, 1618 cm^{-1}; δ 3.85 (s, OMe), 6.45 (d, J = 6 Hz, =CHCHO), 7.1–7.6 (m, H-[5–8]), 7.32 (s, H-3), 7.69 (s, H-1), 10.30 (d, J = 6 Hz, CHO). C was identified as methyl 3(1 - formyl - 3 - methylindol - 2 - yl)propenoate (i.e. the N-formylated starting material) on the basis of the following: λ_{max} 254, 348 nm (log ϵ 3.67, 4.17); ν_{max} 1709, 1625 cm^{-1}; δ 2.40 (s, ArMe), 3.85 (s, OMe), 6.20 (d, J = 16 Hz, =CHCO$_2$Me), 7.3–8.3 (m, ArH), 7.95 (d, J = 16 Hz, ArCH=), 9.35 (s, CHO). The crude yield of C thus represents 13%.

2 - Carbomethoxy - 9H - pyrrolo[1,2-a]idol - 9 - ylidene acetic acid methyl ester (11). A mixture of 10a (133 mg, 0.53 mmol), KCN (141 mg, 2.16 mmol), active MnO_2 (935 mg, 10.75 mmol), AcOH (2 drops) and MeOH (6 ml) was stirred at room temp for 15 hr. The MnO_2 was filtered off and triturated with small portions of MeOH until the triturate was clear in the UV. The MeOH phases were combined and evaporated, and the residue partitioned between water (15 ml) and Et_2O (15 ml). The organic phase was dried Na_2CO_3), filtered and evaporated to give a crystalline product which on recrystallisation from MeOH afforded 116 mg (77%) of the yellow product, m.p. 190–2°. (Found: C, 67.5; H, 4.2; N, 5.0. Calc. for $C_{16}H_{13}NO_4$: C, 67.8; H, 4.6; N, 5.0%). λ_{max} 243, 265, 303, 316, 344 nm (log ϵ 4.32, 4.62, 4.11, 4.15, 4.15); ν_{max} 1707, 1624, 1160 cm^{-1}; δ 3.89 (s, 2 × OMe), 6.38 (s, =CHCO$_2$Me), 7.2–8.2 (m, ArH).

2 - Carbomethoxy - 9H - pyrrolo[1,2-a]indol - 9 - yl acetic acid methyl ester (12). The ester 11 (187 mg, 0.66 mmol) in EtOAc (25 ml) was stirred with PtO_2 (10 mg) under 1 atm H_2 for 30 min. The soln was filtered through Celite and evaporated to give an oil (137 mg). This was chromatographed on an alumina plate, developing with benzene/EtOAc 9/1, to give 98 mg (52%) of the product as a yellow oil which crystallised over several months. λ_{max}—see Discussion; ν_{max} 1738, 1708, 1240, 1212, 755 cm^{-1}; δ $CHCl_3$ 2.6–2.8 (m, CH_2), 3.71 (s, OMe), 3.78 (s, OMe), 4.1–4.5 (m, benzylic CH), 6.47 (d, J = 1 Hz, H-1), 7.0–7.5 (m, H-[5–8]), 7.62 (d, J = 1 Hz, H-3).

Ethyl 2,5 - dimethyl - 1 - phenylpyrrole - 3 - carboxylate (14). The ester 13 (3.72 g, 20 mmol)[15] was stirred with aniline (1.86 g, 20 mmol) at 70° for 30 min and allowed to cool. The oil was chromatographed on a column, developing with benzene, to give 3.43 g (71%) of the product as a reddish syrup which slowly crystallised on refrigeration, affording plates m.p. 39–43°. A sample was recrystallised with difficulty from MeOH aq, raising the m.p. to 45–6°. (Found: C, 73.8; H, 6.8; N, 5.6. Calc. for $C_{15}H_{17}NO_2$: C, 74.1; H, 7.0; N, 5.8%). λ_{max}—see Discussion; $\nu_{max(film)}$ 1700, 1605, 1585, 1220, 1080, 770, 690 cm^{-1}; δ 1.35 (t, CH_2CH_3), 1.97 (s, ArMe), 2.32 (s, ArMe), 4.25 (q, CH_2CH_3), 6.39 (s, H-4), 7.0–7.6 (m, phenyl H).

Diethyl 2 - methyl - 1 - phenylpyrrole - 3,4 - dicarboxylate (17). Ethyl bromopyruvate (488 mg, 2.5 mmol)[19] was added to 15a (512 mg, 2.5 mmol)[20a] in abs EtOH (2 ml). The mixture was refluxed for 20 min, evaporated, and the residue partitioned between water (20 ml) and Et_2O (20 ml). The organic phase was dried ($MgSO_4$), filtered and evaporated, ultimately under high vacuum, to yield 544 mg brown syrup (72%), pure enough for

subsequent reaction. Chromatography of 200 mg on a plate yielded 140 mg (70% recovery) as a brown syrup. (Found: C, 67.4; H, 6.5; N, 4.2. Calc. for $C_{17}H_{19}NO_4$: C, 67.8; H, 6.4; N, 4.6%). λ_{max} 229, 256 (sh) nm (log ϵ 4.22, 3.97); $\nu_{max(film)}$ 1730–10, 1240 cm^{-1}; δ (CCl_4) 1.30 (t, CH_2CH_3), 1.33 (t, CH_2CH_3), 2.26 (s, ArMe), 4.17 (q, CH_2CH_3), 4.20 (q, CH_2CH_3), 7.09 (s, pyrrole H), 7.2–7.5 (m, phenyl H).

2 - *Methyl* - 1 - *phenylpyrrole* - 3,4 - *dicarboxylic acid* 3 - *ethyl ester* (**20**). The diester **17** (1.25 g, 4.2 mmol) was stirred with ethanolic KOH (8.2 ml of a soln containing 55 mg ml^{-1}) at room temp overnight. The mixture was evaporated and partitioned between water (20 ml) and Et_2O (20 ml). The aqueous phase was acidified with 2 M HCl, and extracted with Et_2O (2 × 10 ml). The organic phases were combined, dried ($MgSO_4$), filtered and evaporated, giving 635 mg (55%) of the product as a syrup which slowly crystallised. A sample recrystallised from EtOH gave m.p. 122–3°. (Found: C, 65.3; H, 5.2; N, 5.1. Calc. for $C_{15}H_{15}NO_4$: C, 65.9; H, 5.5; N, 5.1%). λ_{max} 226, 256–68 nm (log ϵ 4.22, 3.90); ν_{max} 3500–2500, 1720, 1630, 1248 cm^{-1}; δ 1.43 (t, CH_2CH_3), 2.40 (s, ArMe), 4.42 (q, CH_2CH_3), 7.1–7.6 (m, ArH), 11–13 (bs, OH).

2 - *Methyl* - 1 - *phenylpyrrole* - 3,4 - *dicarboxylic acid* (**21**). The diester **17** (1.25 g, 4.2 mmol) was stirred under reflux with ethanolic KOH (40 ml of a soln containing 55 mg ml^{-1}) for 1 hr. The mixture was evaporated and the residue partitioned between water (10 ml) and Et_2O (10 ml). The aqueous phase was acidified with 2 M HCl and the product collected by filtration to give, after drying over P_2O_5 *in vacuo*, 740 mg (72%) d.p. 240–5°. (Found: C, 64.2; H, 4.8; N, 5.3. Calc. for $C_{13}H_{11}NO_4$: C, 63.7; H, 4.5; N, 5.7%). λ_{max} 229, 260 (sh) nm (log ϵ 4.30, 3.95); ν_{max} 3500–2500, 1672, 1598, 1300 cm^{-1}; δ (d_6-DMSO) 2.22 (s, ArMe), 7.29 (s, phenyl H), 7.40 (s, pyrrole H), 8.6 (bs, 2 × OH).

Dimethyl 2 - *methyl* - 1 - *phenylpyrrole* - 3,4 - *dicarboxylate*. The diacid **21** (300 mg, 1.22 mmol) was dissolved in dry THF (40 ml) and ethereal diazomethane added with stirring until gas evolution ceased. The solvent was evaporated and the residue partitioned between sat Na_2CO_3 aq (10 ml) and Et_2O (15 ml). The organic phase was dried (Na_2CO_3), filtered and evaporated to give a yellow oil. This was chromatographed on a plate, affording 280 mg (84%) of the product which slowly crystallised (m.p. 50–5°) on standing. Recrystallisation from MeOH gave material m.p. 67–9° (70°).[23]

Ethyl 3 - *acetyl* - 2 - *methyl* - 1 - *phenylpyrrole* - 4 - *carboxylate* (**18**). This was prepared in the same manner as **17** substituting the amide **15c** (437 mg, 2.5 mol)[24] for **15a** and refluxing for 40 min. This gave 448 mg brown syrup (66%), pure enough for further reaction. 190 mg yielded 110 mg (58% recovery) as a brown syrup after chromatography on a plate. (Found: C, 70.2; H, 6.5; N, 5.7. Calc. for $C_{16}H_{17}NO_3$: C, 70.8; H, 6.4; N, 5.2%). λ_{max} 234, 270 (broad sh) nm (log ϵ 4.21, 3.84); $\nu_{max(film)}$ 1710, 1665 cm^{-1}; δ (CCl_4) 1.32 (t, CH_2CH_3), 2.19 (s, ArMe), 2.49 (s, Ac), 4.20 (q, CH_2CH_3), 7.14 (s, pyrrole H), 7.1–7.5 (m, phenyl H).

2 - *Methyl* - 1 - *phenylpyrrole* - 3,4 - *dicarboxylic acid* 4 - *ethyl ester* (**19**). Aqueous sodium hypobromite soln, containing 1.5 mmol ml^{-1}, was made by cooling a soln of NaOH (4.0 g) in water (20 ml), and adding Br_2 (4.80 g, 30 mmol) dropwise with stirring, keeping the temp below 10°. The ketoester **18** (284 mg, 1.05 mmol) in dioxan (0.8 ml) was stirred vigorously at room temp and the cold hypobromite soln (1 ml) added dropwise, followed by 0.5 ml aliquots at 15 min intervals until the absorption maximum had shifted to 226 nm and no longer altered. The mixture was partitioned between water (10 ml) and Et_2O (10 ml), the aqueous phase cooled in ice, acidified with 2 M HCl, extracted with Et_2O (2 × 10 ml), the organic phases combined, dried ($MgSO_4$), filtered and evaporated to give 100 mg of crystalline product. This was chromatographed on a plate, developing with MeOH/$CHCl_3$ 1/9, to give 50 mg (17%), m.p. 148–50°. The UV spectrum closely resembled that of **20**. (Found: C, 65.5; H, 5.4; N, 5.0%—isomeric with **20**). ν_{max} 3500–2500, 1710, 1625, 1225 cm^{-1}. This material, on reflux with ethanolic KOH (5 equivs of a soln containing 35 mg ml^{-1}) gave after workup as in the preparation of **21** (*v. supra*), material identical to **21**.

Diethyl 3 - *hydroxy* - 1 - *phenylpyrrole* - 2,4 - *dicarboxylate* (**24**). The diester **23a** (4.32 g, 20 mmol)[20b] was stirred with **22** (3.58 g, 20 mmol)[28] at 130° for 2 hr. The reaction was partitioned between 2 M HCl (30 ml) and Et_2O (50 ml). The organic phase was washed with water (30 ml), dried ($MgSO_4$), filtered and evaporated to give 7.0 g of a gum. This was added in portions to abs EtOH (25 ml), pretreated with 60% NaH/oil (800 mg, 20 mmol). The mixture was stirred 15 min after the exothermic reaction ceased, and the solvent was then evaporated. The remaining oil was partitioned between 2 M HCl (30 ml) and Et_2O (50 ml), and worked up to give 5.0 g of product as yellow crystals. Recrystallisation from MeOH afforded 3.16 g (52%), m.p. 83–8°. (Found: C, 63.8; H, 6.0; N, 4.2. Calc. for $C_{16}H_{17}NO_5$: C, 63.4; H, 5.7; N, 4.6%). λ_{max} 230, 262 nm (log ϵ 4.44, 4.07). λ_{max} (EtOH/HO^-) 233, 250 (sh), 283 (sh), 330 nm (log ϵ 4.41, 4.26, 3.87, 3.97); ν_{max} 3700–2500, 1720, 1645, 1582, 1238 cm^{-1}. δ (CCl_4) 0.90 (t, CH_2CH_3), 1.17 (t, CH_2CH_3), 3.88 (q, CH_2CH_3), 4.05 (q, CH_2CH_3), 6.92 (s, pyrrole H), 7.09 (s, phenyl H), 8.50 (bs, OH).

Ethyl 4 - *acetyl* - 3 - *hedroxy* - 1 - *phenylpyrrole* - 2 - *carboxylate* (**25**). The ketoester **23b** (1.86 g, 10 mmol)[29] was stirred with **22** (1.79 g, 10 mmol) at 130° for 1 hr. The reaction was partitioned as in the preparation of **24**, giving 3.2 g of a gum. An aliquot of this (590 mg) was added to EtOH (10 ml) pretreated with 60% NaH/oil (80 mg, 2 mmol). Workup after 15 min as before gave 402 mg of product as white crystals. Recrystallisation from MeOH gave 251 mg (50%), m.p. 109–15°. A second recrystallisation from benzene/hexane raised this to 116–8°. (Found: C, 65.7; H, 5.5; N, 5.3%—isomeric with **20**). λ_{max} 246 nm (log ϵ 4.23), λ_{max} (EtOH/HO^-) 245, 268, 358 nm (log ϵ 4.12, 4.10, 3.59); ν_{max} 3300, 3130, 1658, 1672, 1260–30 cm^{-1}; δ (CCl_4) 1.05 (t, CH_2CH_3), 2.35 (s, Ac), 4.04 (q, CH_2CH_3), 7.10 (s, pyrrole H), 7.24 (s, phenyl H), 9.27 (bs, OH).

Ethyl 4 - *acetyl* - 3 - *methyl* - 1 - *phenylpyrrole* - 2 - *carboxylate* (**26**). The diketone **23c** (5.22 g, 33.5 mmol)[29] was stirred with **22** (6.00 g, 33.5 mmol) at 110–20° for 2 hr. The reaction was partitioned as in preparation of **24** giving 9.5 g of a gum. This, dissolved in minimum volume of abs EtOH, was added to abs EtOH (50 ml) pretreated with 60% NaH/oil (1.34 g, 33.5 mmol). Crystallisation occurred, and after 5 min, the product was filtered and washed with ice-cold EtOH, giving 5.57 g (61%) m.p. 142–4°. Recrystallisation from aqueous DMF raised this to 144°. (Found: C, 71.1; H, 6.2; N, 5.2%—isomeric with **18**). λ_{max} 238, 272 (broad sh) nm (log ϵ 4.40, 3.88); ν_{max} 1701, 1658, 1248, 1129 cm^{-1}; δ (d_6-DMSO) 0.88 (t, CH_2CH_3), 2.23 (s, Ac), 2.40 (s, ArMe), 3.84 (q, CH_2CH_3), 7.19 (s, phenyl H), 7.75 (s, pyrrole H).

3 - *Methyl* - 1 - *phenylpyrrole* - 2,4 - *dicarboxylic acid* 2 - *ethyl ester* (**27**). The ketoester **26** (271 mg, 1 mmol) suspended in dioxan (1 ml) was stirred vigorously at 60°. sodium hypobromite soln (2 ml, 1 eq) prepared as in the synthesis of **19**, was added. At 2 min intervals, further 1 ml aliquots of hypobromite were added until the absorption maximum had shifted to below 230 nm and no longer altered. The mixture was cooled and partitioned between water (20 ml) and Et_2O (3 × 10 ml). The aqueous phase was ice-cooled, acidified with conc HCl and extracted with Et_2O (2 × 20 ml). The two organic phases were combined, dried ($MgSO_4$), filtered and evaporated to give 243 mg (89%) of product, d.p. 190–200°. Recrystallisation from aqueous MeOH raised this to 200–2°. (Found: C, 65.9; H, 5.7; N, 5.2%—isomeric with **20**). λ_{max} 226, 250–60 nm (log ϵ 4.45, 4.12). λ_{max} (EtOH/HO^-) 226, 266 nm (log ϵ 4.38, 4.17); ν_{max} 3400–3200, 1690, 1660, 1260 cm^{-1}); δ 1.12 (t, CH_2CH_3), 2.69 (s, ArMe), 4.11 (q, CH_2CH_3), 7.2–7.5 (m, phenyl H), 7.52 (s, pyrrole H), 10.0 (bs, OH).

3 - *Methyl* - 1 - *phenylpyrrole* - 2,4 - *dicarboxylic acid* 2 - *ethyl* - 4 - *methyl* - *ester* (**28**). The half acid **27** (127 mg, 0.47 mmol) was dissolved in Et_2O (10 ml) and ethereal diazomethane added with stirring until gas evolution ceased. The mixture was washed with sat Na_2CO_3 aq (5 ml), dried (Na_2CO_3), filtered and evaporated, giving 93 mg (70%) of product as a syrup clean on tlc, λ_{max} 228, 270 (broad sh) nm; ν_{max} 1715–05, 1230–20 cm^{-1}; δ 1.10 (t, CH_2CH_3), 2.65 (s, ArMe), 3.80 (s, OMe), 4.08 (q, CH_2CH_3), 7.1–7.5 (m, phenyl H), 7.39 (s, pyrrole H). This material, on treatment with 1 eq ethanolic KOH as in the preparation of **20**, gave **27** in 70% yield.

4 - *Acetyl* - 3 - *methyl* - 1 - *phenylpyrrole* - 2 - *carboxylic acid* (**29**). The ketoester **26** (5.32 g, 19.6 mmol) was stirred under reflux in 50% EtOH (70 ml) containing KOH (5.50 g, 98 mmol) for 90 min when the mixture was homogeneous. The solvent was

evaporated, the residue dissolved in water (30 ml) and washed with Et_2O (15 ml). The aqueous phase was cooled in ice, and acidified with conc H_2SO_4. The ppt was filtered off, washed with a little ice-cold water and dried over P_2O_5 *in vacuo*, giving 3.70 g (77%) of crystalline material, d.p. 195–200°. Recrystallisation from EtOH raised this to 215–8°. (Found: C, 69.1; H, 5.2; N, 5.7. Calc. for $C_{14}H_{13}NO_3$: C, 69.1; H, 5.4; N, 5.8%). λ_{max} 239, 271 (sh) nm (log ϵ 4.31, 4.02), λ_{max} (EtOH/HO$^-$) 248, 271 (sh) nm (log ϵ 4.31, 4.14); ν_{max} 3500–2400, 1700, 1627, 1240 cm^{-1}; δ (d_6-DMSO) 2.30 (s, Ac), 2.49 (s, ArMe), 7.32 (s, phenyl H), 7.78 (s, pyrrole H).

2 - *Acetyl* - 1 - *methyl* - 9 - *oxo* - 9*H* - *pyrrolo*[1,2-*a*]*indole* (**30**). The ketoacid **29** (1.21 g, 5 mmol) in $CHCl_3$ (35 ml) was stirred at 40–50° with excess freshly-distilled $SOCl_2$ (5 ml) until soln was complete (75 min). The solvent and excess reagent were carefully evaporated, giving the crystalline acid chloride, m.p. 140–5°, ν_{max} 1730, 1650 cm^{-1}, quantitatively. This was dissolved in nitrobenzene (4 ml), a soln of resublimed $AlCl_3$ (1.50 g, 11 mmol) in nitrobenzene (6 ml) added, and the mixture stirred at room temp for 2 min, then at 70° for 8 min.[12] The mixture was partitioned between $CHCl_3$ (30 ml) and 2 M HCl (15 ml), the organic phase (containing some suspended solid) washed with water (15 ml) and evaporated. Water (100 ml) was added to the residue and the nitrobenzene steam-distilled off. The residue consisted of a suspension of crystalline product, which was filtered off and dried at 120° to give 930 mg (83%) of pale yellow crystalline product, m.p. 197–206°. This material was used in subsequent reactions. An analysis sample was recrystallised from EtOHaq, raising the m.p. to 209–11°. (Found: C, 74.7; H, 4.8; N, 6.4. Calc. for $C_{14}H_{11}NO_2$: C, 74.7, H, 4.9; N, 6.2%). λ_{max} 247, 269, 277, 286, 332 nm (log ϵ 4.17, 4.39, 4.48, 4.48, 3.81); ν_{max} 1685, 1665 (sh) cm^{-1}; δ 2.43 (s, Ac), 2.57 (s, ArMe), 7.1–7.7 (m, H-[5–8]), 7.55 (s, H-3).

2 - *Carbomethoxy* - 1 - *methyl* - 9 - *oxo* - 9*H* - *pyrrolo*[1,2-*a*]*indole* (**31**). The diketone **30** (600 mg, 2.67 mmol) in dioxan (2.5 ml) was stirred vigorously at 60°. Sodium hypobromite (5.3 ml, 1 eq) prepared as in the synthesis of **19**, was added. At 2 min intervals, further 2.7 ml aliquots of hypobromite were added until the absorption maximum had shifted to 255 nm and no longer altered. The mixture was cooled and washed with Et_2O (10 ml), cooled in ice and acidified with aq 2 M HCl, whereupon precipitation occurred. Filtration proved difficult, but an aliquot was worked up in this way to give a poor sample of the acid corresponding to the ester **31**. [This acid showed λ_{max} 255, 267, 282, 332 nm, λ_{max} (EtOH/HO$^-$) 255, 278, 288, 337 nm; ν_{max} 1680, 1660 (sh) cm^{-1}.] The rest of the mixture was partitioned between sat NaCl aq (15 ml) and enough THF to take all the poorly-soluble solid into soln. The organic phase was separated, dried ($MgSO_4$), filtered and ethereal diazomethane added with stirring until gas evolution ceased. The mixture was evaporated and the residue partitioned between Et_2O (20 ml) and sat Na_2CO_3 aq (10 ml). The organic phase was separated, dried (Na_2CO_3), filtered and evaporated giving 440 mg (68%) of crystalline ester. Recrystallisation from MeOH gave 200 mg (31%), m.p. 136–7°. (Found: C, 70.0; H, 4.4; N, 5.9. Calc. for $C_{14}H_{11}NO_3$: C, 69.7; H, 4.6; N, 5.8%). λ_{max} 256, 272, 282, 332 nm (log ϵ 4.53, 4.40, 4.33, 3.95); ν_{max} 1715, 1685, 1200 cm^{-1}; δ 2.52 (s, ArMe), 3.80 (s, OMe), 7.1–7.7 (m, H-[5–8]), 7.59 (s, H-3).

2 - *Carbomethoxy* - 1 - *methyl* - 9*H* - *pyrrolo*[1,2-*a*]*indol* - 9 - *ylidene acetic acid ethyl ester* (**32**). Compound **31** (289 mg, 1.2 mmol) was mixed intimately with excess Zn dust (200 mg), and a soln of ethyl bromoacetate (171 μl, 1.5 mmol) in dry benzene (7 ml) added. A small crystal of iodine was added and the mixture brought to reflux, stirring vigorously. Reflux was continued until the absorption maximum had shifted to 288 nm and no longer altered. The mixture was cooled and partitioned between $CHCl_3$ (20 ml) and 2 M HCl (10 ml). The organic phase was washed with water (2 × 10 ml), dried (Na_2CO_3), filtered and evaporated to give 320 mg (81%) of the intermediate β-hydroxy ester as a yellow oil which slowly crystallised (m.p. 110–7°). λ_{max} 249, 288, 296 nm (log ϵ 4.12, 4.04, 3.98); ν_{max} 3450, 1740, 1678, 1518, 1215, 1180 cm^{-1}; δ 1.20 (t, CH_2CH_3), 2.47 (s, ArMe), 3.81 (s, OMe), 4.12 (q, CH_2CH_3), 7.1–7.4 (m, H-[5–8]), 7.52 (s, H-3). This material in dry benzene (1.5 ml) containing a trace of *p*-toluenesulphonic acid was refluxed for 1 min. The mixture was partitioned between sat Na_2CO_3 aq (5 ml) and Et_2O (10 ml), and the organic phase dried (Na_2CO_3), filtered and evaporated giving 272 mg (73%) of the product as yellow crystals, m.p. 140–50°. Recrystallisation from MeOH raised this to 156–7°. (Found: C, 69.2; H, 5.4; N, 4.5. Calc. for $C_{18}H_{17}NO_4$: C, 69.4; H, 5.5; N, 4.5%). λ_{max} 247, 267, 308, 357 nm (log ϵ 4.40, 4.61, 4.09, 4.17); ν_{max} 1690 (broad), 1620, 1160 cm^{-1}; δ 2.38 (t, CH_2CH_3), 2.45 (s, ArMe), 3.80 (s, OMe), 4.25 (q, CH_2CH_3), 6.22 (s, =$CHCO_2Et$), 6.9–7.3 (m, H-[5–8]), 7.45 (s, H-3).

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