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Pyrrole-2,3-quinodimethane Analogues in the Synthesis of Indoles. Part 2.[1] Synthesis and Diels-Alder Reactions of 1,6-Dihydropyrano[4,3-*b*]pyrrol-6(1*H*)-ones

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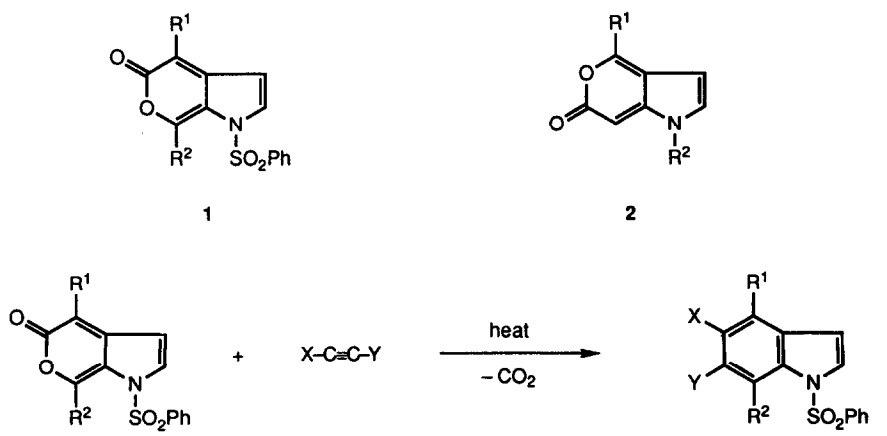
Dedicated to Professor Alan R. Katritzky, FRS on the occasion of his 65th birthday

Abstract: The pyrano[4,3-*b*]pyrrol-6-ones **7-9**, **12** and **13** are stable cyclic analogues of pyrrole-2,3-quinodimethane, and undergo Diels-Alder reaction with a range of alkynes to give, after loss of carbon dioxide, indoles.

In a previous paper,[1] we have described the preparation of a range of 1,5-dihydropyrano[3,4-*b*]pyrrol-5-ones **1**, stable pyrrole-2,3-quinodimethanes, which undergo Diels-Alder reaction with acetylenes to give, after loss of carbon dioxide, indoles (Scheme 1). It was therefore of interest to investigate the preparation and Diels-Alder reactions of the isomeric pyrano[4,3-*b*]pyrrol-6-ones **2** as an extension of this new route to indoles.



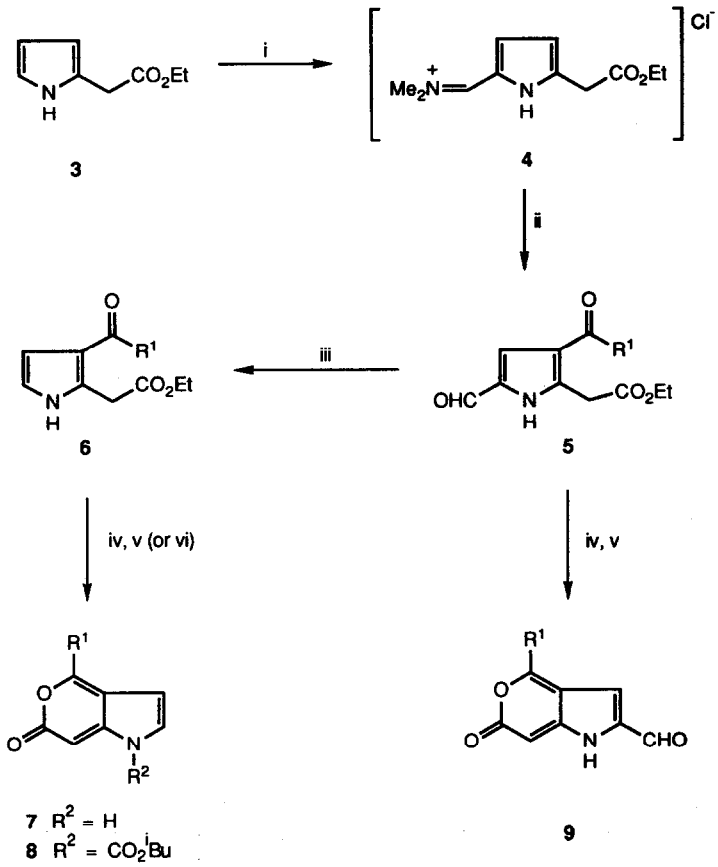
Scheme 1

RESULTS AND DISCUSSION

Preparation of 1,6-Dihydropyrano[4,3-b]pyrrol-6-ones

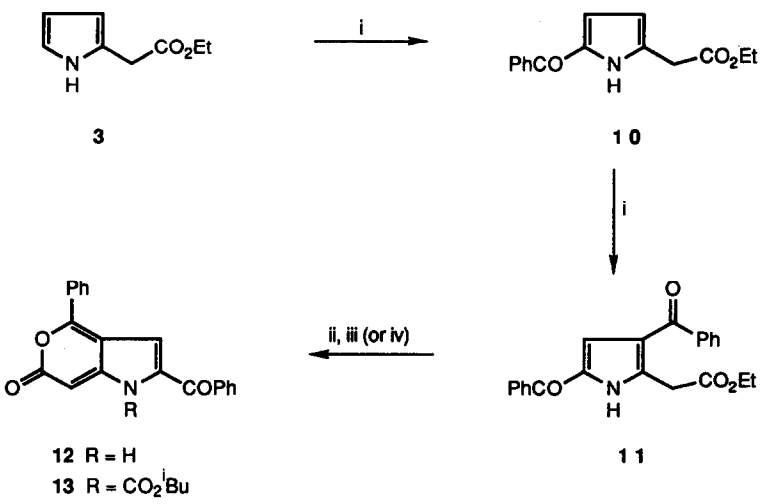
The pyranopyrrolone ring system **1** is readily prepared from pyrrole-3-acetic acid derivatives by treatment with carboxylic acid anhydrides in the presence of boron trifluoride diethyl ether,[1] and therefore the most likely precursors to the isomeric pyranopyrrolone **2** would be the corresponding pyrrole-2-acetic acids. We have used this simple strategy to prepare both the isomeric fused α-pyrone systems of indole (from indole-2- and 3-acetic acids),[2] of benzothiophene (from benzothiophene-2- and 3-acetic acids),[3] and of thiophene (from thiophene-2- and 3-acetic acids).[4] However, there is an inherent problem in starting from a pyrrole-2-acetic acid in that any acylation type reaction is most likely to proceed at the free 5-position rather than the desired 3-position. Thus treatment of pyrrole-2-acetic acid itself with acetic anhydride in the presence of boron trifluoride diethyl ether, not surprisingly, did not result in the formation of the desired pyranopyrrolone. Similar problems were also encountered in the thiophene series, which were only solved when the 5-position was blocked by the introduction of a bromine substituent.[4] In the pyrrole series, however, we adopted a slightly different approach to the 3-acylation of 2-substituted pyrroles, based on the known ability of the pyrrole Vilsmeier complex (at the 5-position) to direct acylation to the 3-position.[5] 3-Acyl-5-formyl pyrroles are obtained on aqueous work-up, and subsequent decarbonylation then gives the desired 3-acylpyrroles.[6] Thus, treatment of ethyl pyrrol-2-ylacetate **3**, prepared by acylation of pyrrole with ethyl oxalyl chloride[7] followed by reduction of the glyoxalate using sodium hypophosphite in the presence of palladium-on-carbon,[8] with the Vilsmeier salt (from oxalyl chloride and dimethylformamide) gave an intermediate pyrrole Vilsmeier complex **4** which could be acylated further in the presence of aluminium chloride (Scheme 2). Reaction with dichloromethyl methyl ether gave, after aqueous work-up, ethyl 3,5-diformylpyrrol-2-yl acetate **5a** in 60% yield; acetylation and benzoylation (with the acid chlorides) proceeded similarly to give the corresponding acetyl and benzoyl pyrroles **5b** and **5c** in 92 and 40% yield respectively. Decarbonylation of the formyl group in pyrroles **5b** and **5c** was readily achieved in high yield by heating in mesitylene containing palladium-on-activated carbon for 10-12 h, and gave the corresponding pyrroles **6**. Decarbonylation of the 3,5-diformylpyrrole **5a** proved more difficult, since the 3-formyl group was also susceptible to decarbonylation; fortunately the 5-formyl group was more reactive, and the desired ethyl 3-formylpyrrol-2-yl acetate **6a** could be obtained in 63% yield if the reaction was stopped after 5 h.

Hydrolysis of the esters **6** gave the corresponding acids, which on treatment with one equivalent of isobutyl chloroformate underwent cyclodehydration to give the pyrano[4,3-*b*]pyrrol-6-ones in good yield. Alternatively, treatment of the acids with *two* equivalents of isobutyl chloroformate resulted in the formation of the *N*-substituted pyranopyrrolones **8** (Scheme 2). The isolation of the crystalline pyrano[4,3-*b*]pyrrolones **7b** and **7c**, unsubstituted on nitrogen, is in direct contrast to the isomeric [3,4-*b*]-series, where *N*-unsubstituted derivatives could not be prepared.[1]



Scheme 2 (**a** R^1 = H; **b** R^1 = Me; **c** R^1 = Ph)
Reagents: i, $(COCl)_2$, DMF, $ClCH_2CH_2Cl$; ii, $MeNO_2$, $AlCl_3$, Cl_2CHOMe (R^1 = H) or R^1COCl (R^1 = Me or Ph); iii, Pd/C, mesitylene, reflux; iv, KOH, H_2O, MeOH, THF; v, $ClCO_2{}^iBu$ (1.05 equiv.), Et_3N, THF; vi, $ClCO_2{}^iBu$ (2.2 equiv.), Et_3N, THF.

As an alternative to the removal of the 5-formyl group by decarbonylation, it can be left in place, and the corresponding 2-formyl pyranopyrrolones **9b** and **9c** can be prepared from the corresponding pyrroles **5** simply by ester hydrolysis and cyclodehydration (Scheme 2). Likewise a benzoyl group may be introduced into the pyrrole-5-position and left in place; hence the 2-benzoyl pyranopyrrolones **12** and **13** can be prepared by a similar sequence (Scheme 3). Attempts to prepare 2-acetylpyranopyrrolones by a similar route were unsuccessful owing to poor regioselectivity and low overall yield in the Friedel Crafts acylation of **3** with acetyl chloride.



Scheme 3

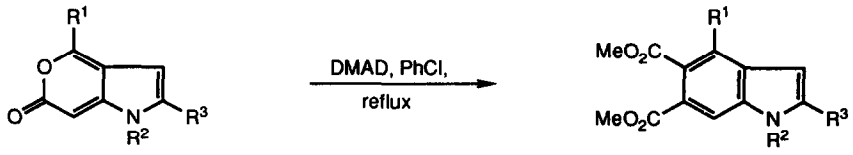
Reagents: i, PhCOCl, $AlCl_3$, $MeNO_2$, $ClCH_2CH_2Cl$; ii, KOH, H_2O, THF, MeOH; iii, $ClCO_2{}^iBu$ (1.05 equiv.), Et_3N, THF; iv, $ClCO_2{}^iBu$ (2.2 equiv.), Et_3N, THF.

Diels-Alder Reactions

On heating with the electron deficient alkyne dimethyl acetylenedicarboxylate (DMAD) in boiling chlorobenzene, the pyranopyrrolones **7** underwent Diels-Alder reactions to give, after loss of carbon dioxide, the indole-5,6-esters **14** (Table 1). Likewise the 1-isobutyloxycarbonyl pyranopyrrolones **8** and the 2-substituted derivatives **12** and **13** also reacted readily with DMAD to give the corresponding indoles **14** (Table 1).

As expected, the unsymmetrical alkyne ethyl propynoate (EP) was not regioselective in its Diels-Alder reactions and gave a mixture of indole-5- **15** and 6-esters **16** (Table 2). In the case of the pyranopyrrolone **7a** there was a slight preference for the formation of the indole 6-ester **16a**, the NMR spectrum of the mixture being assigned by comparison with the published spectra of the known methyl (and ethyl) indole-5-carboxylate.[9] Use of the *N*-acylated pyranopyrrolones **8** did not lead to any increase in regioselectivity, although the 2-benzoyl derivative **12** was significantly more regioselective in its Diels-Alder reaction with EP. Greater regioselectivity was observed, however, when ethyl trimethylsilyl propynoate (ETMSP) was used as dienophile. A single product, the indole-5-ester **15f**, was observed from the reaction with the pyranopyrrolone **7b**, although the yield was low (Table 2), due to competing decomposition of **7b** that occurred on prolonged heating. The *N*-isobutyloxycarbonyl pyrones **8** are more thermally stable and gave good yields of indole-5-esters **15** on heating with ETMSP in a regioselective reaction (Table 2). The structure of indole **15h** was confirmed by protodesilylation, using aqueous trifluoroacetic acid, to give the corresponding 4-methylindole-5-ester. As expected the regioselectivity in the Diels-Alder reactions with ETMSP was opposite to that observed with isomeric pyrano[4,3-*b*]pyrrol-5-ones.[1]

Table 1. *Diels-Alder reactions of pyrano[4,3-b]pyrrol-6-ones with DMAD*

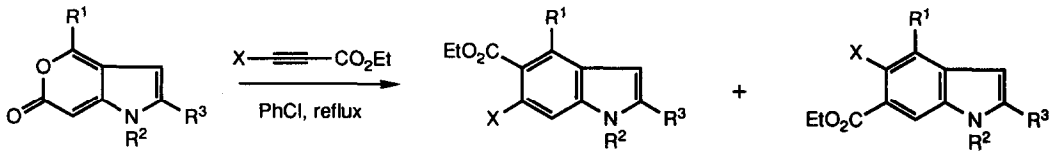


14

Compound	*R¹*	*R²*	*R³*	*Product*	*Yield (%)*
7a	H	H	H	**14a**	82
7b	Me	H	H	**14b**	63
8a	H	$CO_2{}^iBu$	H	**14c**	99
8b	Me	$CO_2{}^iBu$	H	**14d**	88
9b	Me	H	CHO	**14e**	40[a]
9c	Ph	H	CHO	**14f**	52[a]
12	Ph	H	COPh	**14g**	51
13	Ph	$CO_2{}^iBu$	COPh	**14h**	88

[a] overall yield from carboxylic acid (obtained on hydrolysis of **5**).

Table 2. *Diels-Alder reactions of pyrano[4,3-b]pyrrol-6-ones with EP and ETMSP*



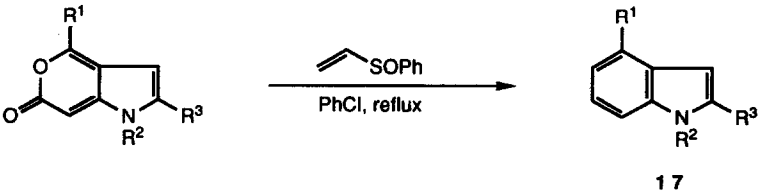
15 **16**

Compound	*R¹*	*R²*	*R³*	*X*	*Product*	*Yield (%)*	*Ratio*
7a	H	H	H	H	**15/16a**	51	1:1.8
7b	Me	H	H	H	**15/16b**	79	1:1
8a	H	$CO_2{}^iBu$	H	H	**15/16c**	81	1:1
8b	Me	$CO_2{}^iBu$	H	H	**15/16d**	75	1.2:1
12	Ph	H	COPh	H	**15/16e**	67	5:1[a]
7b	Me	H	H	$SiMe_3$	**15/16f**	11	>20:1
8a	H	$CO_2{}^iBu$	H	$SiMe_3$	**15/16g**	90	7:1
8b	Me	$CO_2{}^iBu$	H	$SiMe_3$	**15/16h**	64	>20:1[b]
12	Ph	H	COPh	$SiMe_3$	**15/16i**	6	8:1

[a] methyl propiolate used; gives corresponding methyl esters; [b] only one isomer observed by NMR.

The pyrano[4,3-*b*]pyrrol-6-ones also reacted with the acetylene equivalent, phenyl vinyl sulfoxide, to give 5,6-unsubstituted indoles **17** in varying yield (Table 3)

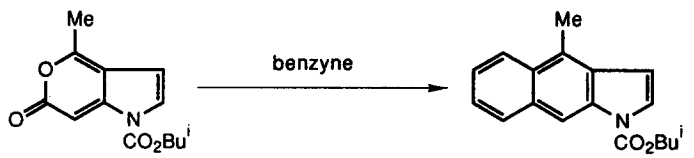
Table 3. *Diels-Alder reactions of pyrano[4,3-b]pyrrolones with phenyl vinyl sulfoxide*



17

Compound	*R1*	*R2*	*R3*	*Product*	*Yield (%)*
7b	Me	H	H	**17a**	32
8b	Me	$CO_2{}^iBu$	H	**17b**	85
8c	Ph	$CO_2{}^iBu$	H	**17c**	91
12	Ph	H	COPh	**17d**	20
13	Ph	$CO_2{}^iBu$	COPh	**17e**	64

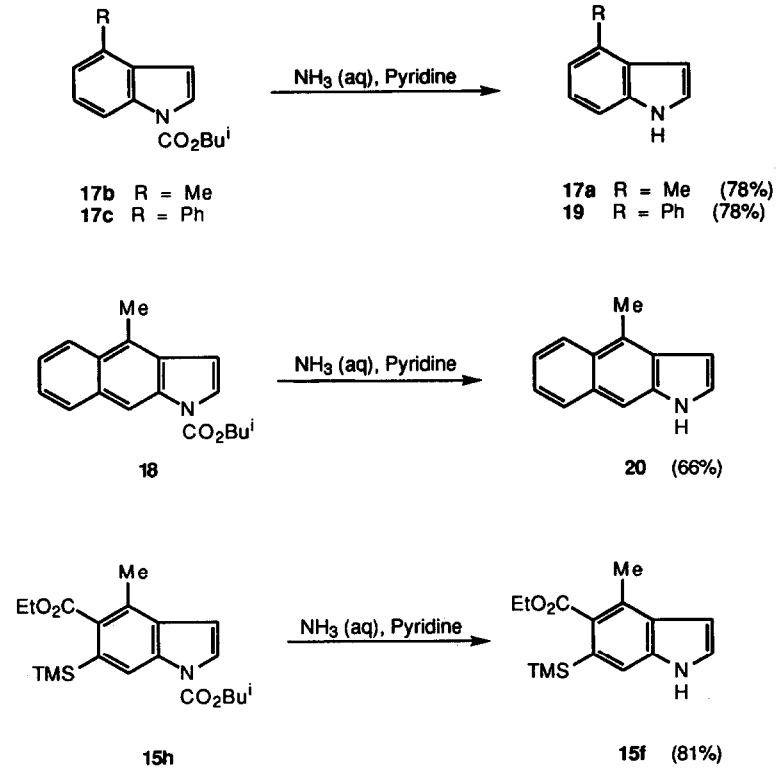
One reaction with benzyne, generated from 2-(3,3-dimethyltriazen-1-yl)benzoic acid, was carried out. Thus the pyranopyrrolone **8b** gave the benz[*f*]indole **18** in 84% yield.



8b **18**

Hydrolysis of the isobutyl carbamate

Isobutyl carbamates are usually readily hydrolysed using a mixture of aqueous ammonia and pyridine.[10] Deprotection of the indoles-1-carboxylates **17b** and **17c** using this method gave the known 4-methylindole **17a**[11] and 4-phenylindole **19**[12] respectively in good yield. Similarly the indole-1-esters **18** and **15h** were readily deprotected to give the corresponding indoles **20** and **15f**.



Conclusion

The Diels-Alder reactions of the pyrano[4,3-*b*]pyrrol-6-ones with alkynes complement those of the [3,4-*b*]isomers, and extend this cycloaddition route to indoles. A variety of 4-substituted, and 4,5,6-trisubstituted indoles can be readily prepared, and the incorporation of an additional substituent in the pyrrole ring leads to the formation of 2-substituted indoles.

EXPERIMENTAL

Commercially available solvents and reagents were used throughout without further purification, except for those detailed below which were purified as described. 'Light petroleum' refers to the fraction of petroleum ether boiling between 40°C and 60°C, and was distilled through a 36 cm Vigreux column before use. 'Ether' refers to diethyl ether; this, together with benzene and toluene, was dried where necessary by standing over sodium wire for several days. THF was distilled from potassium benzophenone ketyl under nitrogen prior to use. Dichloromethane was dried where necessary by distillation from phosphorus pentoxide. DMSO and DMF were stirred for 15 h over barium oxide, decanted, and distilled under reduced pressure before storing over activated 4Å molecular sieves, under nitrogen. Pyridine and triethylamine were each distilled from, and stored over, potassium hydroxide pellets.

Analytical thin layer chromatography was carried out on Merck Kieselgel 60 GF_{254} aluminium-backed plates. Visualisation was achieved using UV light at 254 and 360 nm, iodine, and, in the case of indoles, by lightly spraying the plate with Ehrlich's reagent followed by gentle heating to produce a usually blue-purple colour. Ehrlich's reagent was prepared by adding 1 g of *p*-(dimethylamino)benzaldehyde to 100 ml of a 25% solution of concentrated hydrochloric acid in absolute ethanol. 'Column chromatography' refers to the flash method and was performed on Merck Kieselgel 60 H or Sorsil C60, using medium pressure provided by means of hand-bellows. The sample mixture was applied to the top of the column as a solution in a small amount of the column eluant, or by preadsorption onto silica.

Infra-red spectra ($\nu_{max.}$) were recorded on a Nicolet 205 Fourier transform infra-red spectrometer, the samples being analysed as thin films, KBr discs, Nujol mulls, or in solution, as indicated. Ultra-violet/visible spectra ($\lambda_{max.}$) were obtained using a Shimadzu UV-160 scanning spectrophotometer, the samples being dissolved in spectroscopic grade methanol. Fourier transform proton nuclear magnetic resonance spectra (δ_H) were recorded on a Bruker ACF 250 (250 MHz) spectrometer. Chemical shifts are reported in parts per million downfield of tetramethylsilane by referencing to the residual protons of the respective solvents. Coupling constants (*J*) in Hertz are included where possible. ^{13}C-Spectra (δ_C) were recorded on the Bruker ACF 250 (62.9 MHz) instrument, and referenced to the solvent. Electron impact (EI) ionisation mass spectra (*m/z*) were recorded at 70eV on a Kratos MS80 instrument; CI and FAB spectra were recorded at the S.E.R.C. Service at Swansea. Results are obtained under EI unless otherwise stated.

Preparation of Pyrano[4,3-*b*]pyrrol-6(1*H*)-ones

Ethyl 3,5-*Diformylpyrrol-2-ylacetate* (**5a**)

A solution of dimethylformamide (0.73 ml, 9.42 mmol) in 1,2-dichloroethane (15 ml) was cooled in an ice-salt bath. A solution of oxalyl chloride (0.58 ml, 6.67 mmol) in 1,2-dichloroethane (5 ml) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 15 min. The mixture was cooled in ice and a solution of ethyl pyrrol-2-ylacetate (**3**) (941 mg, 6.14 mmol) in 1,2-dichloroethane (5 ml) added dropwise. The mixture was allowed to warm to room temperature, stirred for 15 min, and then recooled in ice. Aluminium chloride (3.64 g, 27.27 mmol) was added and the mixture warmed to room temperature over 10 min. Nitromethane (1.10 ml, 20.4 mmol) was added, the mixture cooled in ice, and dichloromethyl methyl ether (0.83 ml, 9.22 mmol) added rapidly. The mixture was stirred for 4 h at room temperature, poured into ice-water, and stirred for 5 h. The mixture was extracted with dichloromethane. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed [ether-light petroleum (4:1)] to give the *title compound* (**5a**) (771 mg, 60%), m.p. 74-76°C, (Found: C, 57.2; H, 5.3; N, 6.7. $C_{10}H_{11}NO_4$ requires C, 57.4; H, 5.3; N, 6.7%); $\nu_{max.}$(Nujol) 3212, 1728, 1646 and 1208 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.93 (1 H, br, NH), 9.91 (1 H, s, CHO), 9.56 (1 H, s, CHO), 7.34 (1 H, d, *J* 2.5 Hz, 4-H), 4.22 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.16 (2 H, s, CH_2CO_2Et) and 1.31 (3 H, t, *J* 7.1 Hz, ester CH_3); *m/z* 209 (M^+, 24%), 181 (4), 163 (49) and 136 (100).

Ethyl 3-*Formylpyrrol-2-ylacetate* (**6a**)

A mixture of the dialdehyde (**5a**) (1.04 g, 4.97 mmol) and palladium on activated carbon (10%, 90 mg) in mesitylene (20 ml) was refluxed for 5 h under nitrogen. The mixture was allowed to cool to room temperature, diluted with dichloromethane, and filtered through Celite. The solvent was evaporated and the residue chromatographed [ether-light petroleum (3:1)] to give the *title compound* (**6a**) (563 mg, 63%) as a yellow oil, (Found: M^+, 181.0739. $C_9H_{11}NO_3$ requires *M*, 181.0739); $\nu_{max.}$(film) 3312 (br), 1730 and 1658 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.87 (1 H, s, CHO), 9.85 (1 H, br, NH), 6.74 (1 H, dd, *J* 3.0, 2.5 Hz), 6.60 (1 H, t, *J* 2.9 Hz), 4.22 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.10 (2 H, s, CH_2CO_2Et) and 1.30 (3 H, t, *J* 7.1 Hz, ester CH_3); *m/z* 181 (M^+, 27%), 135 (45), 108 (100) and 80 (20).

3-*Formylpyrrol-2-ylacetic acid*

Potassium hydroxide solution (2 M, 15 ml) was added dropwise to a solution of ethyl 3-formylpyrrol-2-ylacetate (**6a**) (321 mg, 1.77 mmol) in tetrahydrofuran (9 ml) and methanol (1 ml) at 0°C. The mixture was allowed to warm to room temperature and stirred for 2 h. Water was added, the mixture extracted with ether, and this extract discarded. The aqueous phase was acidified with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ethyl acetate. The combined extracts were dried

($MgSO_4$), the solvent evaporated, and the residue recrystallised (ethyl acetate-light petroleum) to give the *title compound* (226 mg, 83%), m.p. 170-175°C (decomp.), (Found: MH^+, 154.0504. $C_7H_7NO_3$ requires MH, 154.0504); $\nu_{max.}$(Nujol) 3356, 1710, 1606, 1544, 1464, 1376 and 1246 cm^{-1}; δ_H [250 MHz; $CDCl_3$+$(CD_3)_2SO$] 11.2 (1 H, br, NH), 9.82 (1 H, s, CHO), 6.69 (1 H, t, *J* 2.7 Hz), 6.51 (1 H, t, *J* 2.7 Hz) and 3.94 (2 H, s, CH_2CO_2H); *m/z* 154 (MH^+, 18%),153 (M^+, 12), 135 (26), 109 (82), 108 (100) and 80 (44).

Pyrano[4,3-b]*pyrrol-6*(1H)*-one* (**7a**)

A mixture of 3-formylpyrrol-2-ylacetic acid (234 mg, 1.53 mmol) and triethylamine (0.64 ml, 4.58 mmol) in dry tetrahydrofuran (25 ml) was stirred at 0°C. Isobutyl chloroformate (219 mg, 1.60 mmol) in dry tetrahydrofuran (5 ml) was added dropwise. The mixture was stirred at room temperature for 3 h, poured into brine, and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed [ether-methanol (9:1)] to give the *title compound* (**7a**) (140 mg, 68%), m.p. ~70°C (darkens), (Found: C, 62.3; H, 3.7; N, 10.5. $C_7H_5NO_2$ requires C, 62.2; H, 3.7; N, 10.4%); $\nu_{max.}$(Nujol) 3104 (br), 1678 and 1588 cm^{-1}; δ_H [250 MHz; $CDCl_3$ + $(CD_3)_2SO$] 10.4 (1 H, br, NH), 7.97 (1 H, s, 4-H), 6.91 (1 H, dd, *J* 3.7, 2.0 Hz, 2-H), 6.12 (1 H, m, 3-H) and 5.73 (1 H, s, 7-H); *m/z* 135 (M^+, 40%), 107 (29), 79 (51) and 52 (100).

Isobutyl 6-*Oxopyrano*[4,3-b]*pyrrole*-1-*carboxylate* (**8a**)

A mixture of 3-formylpyrrol-2-ylacetic acid (153 mg, 1.00 mmol) and triethylamine (0.56 ml, 4.00 mmol) in dry tetrahydrofuran (10 ml) was stirred at 0°C. Isobutyl chloroformate (0.29 ml, 2.20 mmol) in dry tetrahydrofuran (5 ml) was added dropwise. The mixture was allowed to warm to room temperature and stirred overnight. The mixture was poured into brine and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed (ether) to give the *title compound* (**8a**) (198 mg, 84%), m.p. 77-78°C, (Found: C, 61.1; H, 5.5; N, 6.0. $C_{12}H_{13}NO_4$ requires C, 61.3; H, 5.6; N, 6.0%); $\nu_{max.}$(Nujol) 1738 and 1688 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.79 (1 H, s, 4-H), 7.27 (1 H, d, *J* 3.4 Hz, 2-H), 6.74 (1 H, brs, 7-H), 6.23 (1 H, d, *J* 4.1 Hz, 3-H), 4.18 (2 H, d, *J* 6.7 Hz, isobutyl CH_2), 2.10 (1 H, m, isobutyl CH) and 1.02 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 235 (M^+, 12%), 179 (10), 135 (15), 107 (19), 79 (14), 57 (100), 51 (26) and 41 (79).

Ethyl 3-*Acetyl*-5-*formylpyrrol*-2-*ylacetate* (**5b**)

A solution of dimethylformamide (1.71 ml, 22.12 mmol) in 1,2-dichloroethane (30 ml) was cooled in an ice-salt bath. A solution of oxalyl chloride (1.37 ml, 15.66 mmol) in 1,2-dichloroethane (15 ml) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 15 min. The mixture was cooled in ice and a solution of ethyl pyrrol-2-ylacetate (**3**) (2.21 g, 14.43 mmol) in 1,2-dichloroethane (15 ml) added dropwise. The mixture was allowed to warm to room temperature, stirred for 15 min, and then recooled in ice. Aluminium chloride (8.54 g, 64.05 mmol) was added and the mixture warmed to room temperature over 10 min. Nitromethane (2.60 ml, 47.9 mmol) was added, the mixture cooled in ice, and acetyl chloride (1.54 ml, 21.65 mmol) added rapidly. The mixture was stirred for 4 h at room temperature, poured into ice-water (200 ml), and stirred for a further 4 h. The mixture was extracted with dichloromethane. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated. The resulting solid was recrystallised (dichloromethane-light petroleum) to give the *title compound* (**5b**) (2.95 g, 92%), m.p. 109-111°C, (Found: C, 59.1; H, 5.9; N, 6.2. $C_{11}H_{13}NO_4$ requires C, 59.2; H, 5.9; N, 6.3%); $\nu_{max.}$(Nujol) 3228, 1730 and 1642 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.94 (1 H, br, NH), 9.52 (1 H, s, CHO), 7.29 (1 H, s, 4-H), 4.23 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.19 (2 H, s, CH_2CO_2Et), 2.47 (3 H, s, CH_3CO) and 1.30 (3 H, t, *J* 7.1 Hz, ester CH_3); *m/z* 223 (M^+, 32%), 177 (100), 149 (40), 136 (26) and 78 (25).

Ethyl 3-*Acetylpyrrol*-2-*ylacetate* (**6b**)

A mixture of ethyl 3-acetyl-5-formylpyrrol-2-ylacetate (**5b**) (2.548 g, 11.41 mmol) and palladium on activated carbon (5%, 335 mg) in mesitylene (30 ml) was refluxed for 10 h under nitrogen. The mixture was allowed to cool to room temperature, diluted with dichloromethane, and filtered through Celite. The solvent was evaporated and the residue chromatographed [ether-light petroleum (3:1)] to give the *title compound* (**6b**) (2.143 g, 96%) as a yellow oil, (Found: M^+, 195.0892. $C_{10}H_{13}NO_3$ requires M, 195.0895); $\nu_{max.}$(film) 3312, 3120, 1734, 1638 and 1562 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.83 (1 H, br, NH), 6.67

(1 H, m), 6.54 (1 H, t, *J* 2.9 Hz), 4.21 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.16 (2 H, s, CH_2CO_2Et), 2.42 (3 H, s, CH_3CO) and 1.30 (3 H, t, *J* 7.1 Hz, ester CH_3); *m/z* 195 (M^+, 34%), 149 (58) and 122 (100).

3-Acetylpyrrol-2-ylacetic acid

Potassium hydroxide solution (2 M, 15 ml) was added dropwise to a solution of ethyl 3-acetylpyrrol-2-ylacetate (**6b**) (503 mg, 2.58 mmol) in tetrahydrofuran (18 ml) and methanol (2 ml) at 0°C. The mixture was allowed to warm to room temperature and stirred for 4 h. Water was added, the mixture extracted with ethyl acetate, and this extract discarded. The aqueous phase was acidified with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$), the solvent evaporated, and the residue recrystallised (ethyl acetate-light petroleum) to give the *title compound* (380 mg, 88%), m.p. 175-180°C (decomp.), (Found: C, 57.4; H, 5.4; N, 8.25. $C_8H_9NO_3$ requires C, 57.5; H, 5.4; N, 8.4%); $\nu_{max.}$(Nujol) 3344, 1706 and 1632 cm^{-1}; δ_H [250 MHz; $CDCl_3$+$(CD_3)_2SO$] 10.93 (1 H, br, NH), 6.65 (1 H, m), 6.52 (1 H, t, *J* 2.6 Hz), 4.00 (2 H, s, CH_2CO_2H) and 2.44 (3 H, s, CH_3CO); *m/z* 167 (M^+, 27%), 149 (23), 123 (72) and 108 (100).

4-Methylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**7b**)

A mixture of 3-acetylpyrrol-2-ylacetic acid (570 mg, 3.41 mmol) and triethylamine (1.43 ml, 10.23 mmol) in dry tetrahydrofuran (60 ml) was stirred at 0°C. Isobutyl chloroformate (489 mg, 3.58 mmol) in dry tetrahydrofuran (10 ml) was added dropwise. The mixture was stirred at room temperature for 5 h, poured into brine, and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed [ether-methanol (9:1)] to give the *title compound* (**7b**) (433 mg, 85%), m.p. 130°C (decomp.), (Found: M^+, 149.0485. $C_8H_7NO_2$ requires *M*, 149.0477); $\nu_{max.}$(Nujol) 3104, 1698, 1662, 1632, 1610, 1584 and 1534 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.52 (1 H, br, NH), 6.89 (1 H, dd, *J* 3.7, 2.0 Hz, 2-H), 6.15 (1 H, dd, *J* 3.4, 1.6 Hz, 3-H), 5.74 (1 H, s, 7-H) and 2.52 (3 H, s, 4-Me); *m/z* 149 (M^+, 100%), 134 (51) and 121 (37).

Isobutyl 4-Methyl-6-oxopyrano[4,3-b]*pyrrole-1-carboxylate* (**8b**)

A mixture of 3-acetylpyrrol-2-ylacetic acid (606 mg, 3.63 mmol) and triethylamine (2.02 ml, 14.50 mmol) in dry tetrahydrofuran (60 ml) was stirred at 0°C. Isobutyl chloroformate (1.03 ml, 7.98 mmol) in dry tetrahydrofuran (10 ml) was added dropwise. The mixture was allowed to warm to room temperature, stirred overnight, poured into brine, and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed (ether) to give the *title compound* (**8b**) (779 mg, 86%), m.p. 109-110°C, (Found: C, 62.6; H, 6.0; N, 5.5. $C_{13}H_{15}NO_4$ requires C, 62.6; H, 6.1; N, 5.6%); $\nu_{max.}$(Nujol) 1734, 1702, 1658 and 1584 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.22 (1 H, d, *J* 4.1 Hz, 2-H), 6.59 (1 H, brs, 7-H), 6.22 (1 H, dd, *J* 4.2, 0.8 Hz, 3-H), 4.18 (2 H, d, *J* 6.7 Hz, isobutyl CH_2), 2.46 (3 H, s, 4-Me), 2.11 (1 H, m, isobutyl CH) and 1.03 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 249 (M^+, 24%), 149 (36), 121 (21), 57 (100), 41 (71) and 29 (69).

Ethyl 3-Benzoyl-5-formylpyrrol-2-ylacetate (**5c**)

A solution of dimethylformamide (1.66 ml, 21.45 mmol) in 1,2-dichloroethane (20 ml) was cooled in an ice-salt bath. A solution of oxalyl chloride (1.37 ml, 15.7 mmol) in 1,2-dichloroethane (20 ml) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 15 min. The mixture was cooled in ice and a solution of ethyl pyrrol-2-ylacetate (**3**) (2.19 g, 14.30 mmol) in 1,2-dichloroethane (20 ml) added dropwise. The mixture was allowed to warm to room temperature, stirred for 15 min, and then recooled in ice. Aluminium chloride (8.47 g, 63.48 mmol) was added and the mixture warmed to room temperature over 10 min. Nitromethane (2.57 ml, 47.5 mmol) was added, the mixture cooled in ice, and benzoyl chloride (2.49 ml, 21.45 mmol) added rapidly. The mixture was stirred for 6 h at room temperature, poured into ice-water (200 ml), and stirred overnight. The mixture was extracted with dichloromethane. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated. The resulting oil was chromatographed [ether-light petroleum (4:1)] to give the *title compound* (**5c**) (1.64 g, 40%), m.p. 112-113°C, (Found: C, 67.3; H, 5.2; N, 4.85. $C_{16}H_{15}NO_4$ requires C, 67.4; H, 5.3; N, 4.9%); $\nu_{max.}$(Nujol) 3228, 1730, 1644 and 1630 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.87 (1 H, br, NH), 9.52 (1 H, s, CHO), 7.80 (2 H, d, *J* 8 Hz), 7.61-7.46 (3 H, m), 7.17 (1 H, d, *J* 2.5 Hz, 4-H), 4.26 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.25 (2 H, s, CH_2CO_2Et) and 1.31 (3 H, t, *J* 7.1 Hz, ester CH_3); *m/z* 285 (M^+, 57%), 239 (94), 211 (100), 183 (48) and 77 (46).

Ethyl 3-*Benzoylpyrrol-2-ylacetate* (**6c**)

A mixture of ethyl-3-benzoyl-5-formylpyrrol-2-ylacetate (**5c**) (1.06 g, 3.72 mmol) and palladium on activated carbon (5%, 110 mg) in mesitylene (15 ml) was refluxed for 12 h under nitrogen. The mixture was allowed to cool to room temperature, diluted with dichloromethane, and filtered through Celite. The solvent was evaporated and the residue chromatographed [ether-light petroleum (3:1)] to give the *title compound* (**6c**) (860 mg, 90%), m.p. 84-85°C, (Found: C, 70.0; H, 5.9; N, 5.4. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.45%); $\nu_{max.}$(Nujol) 3208, 1738, 1598 and 1560 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.9 (1 H, br, NH), 7.81 (2 H, d, *J* 8 Hz), 7.52-7.41 (3 H, m), 6.70 (1 H, t, *J* 2.7 Hz), 6.44 (1 H, t, *J* 2.8 Hz), 4.24 (2 H, q, *J* 7.1 Hz, ester CH_2), 4.22 (2 H, s, CH_2CO_2Et) and 1.31 (3 H, t, *J* 7.1 Hz, ester CH_3); *m/z* 257 (M^+, 60%), 211 (85), 184 (93), 183 (100) and 77 (41).

3-*Benzoylpyrrol-2-ylacetic acid*

Potassium hydroxide solution (2 M, 12 ml) was added dropwise to a solution of ethyl 3-benzoylpyrrol-2-ylacetate (**6c**) (612 mg, 2.38 mmol) in tetrahydrofuran (18 ml) and methanol (2 ml) at 0°C. The mixture was allowed to warm to room temperature and stirred for 4 h. Water was added, the mixture extracted with ether, and this extract discarded. The aqueous phase was acidified with dilute hydrochloric acid and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$), the solvent evaporated, and the residue recrystallised (ether-light petroleum) to give the *title compound* (513 mg, 94%), m.p. 151-152°C (decomp.), (Found: M^+, 229.0739. $C_{13}H_{11}NO_3$ requires *M*, 229.0739.); $\nu_{max.}$(Nujol) 3260, 1768 and 1594 cm^{-1}; δ_H [250 MHz; $CDCl_3$ + $(CD_3)_2SO$] 11.04 (1 H, br, NH), 7.68 (2 H, d, *J* 8 Hz), 7.43-7.27 (3 H, m), 6.53 (1 H, t, *J* 2.7 Hz), 6.24 (1 H, t, *J* 2.7 Hz) and 3.85 (2 H, s, CH_2CO_2H); *m/z* 229 (M^+, 5%), 211 (9), 184 (100), 108 (91) and 77 (30).

Isobutyl 6-*Oxo*-4-*phenylpyrano*[4,3-b]*pyrrole*-1-*carboxylate* (**8c**)

A mixture of 3-benzoylpyrrol-2-ylacetic acid (411 mg, 1.79 mmol) and triethylamine (1.00 ml, 7.17 mmol) in dry tetrahydrofuran (40 ml) was stirred at 0°C under nitrogen. Isobutyl chloroformate (539 mg, 3.94 mmol) in dry tetrahydrofuran (10 ml) was added dropwise. The mixture was allowed to warm to room temperature, stirred overnight, poured into brine, and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed [ether-light petroleum (3:1)] to give the *title compound* (**8c**) (512 mg, 92%), m.p. 109-110°C, (Found: C, 69.3; H, 5.3; N, 4.4. $C_{18}H_{17}NO_4$ requires C, 69.4; H, 5.5; N, 4.5%); $\nu_{max.}$ (Nujol) 1748, 1700, 1638 and 1558 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.85 (2 H, m), 7.56-7.50 (3 H, m), 7.35 (1 H, d, *J* 4.2 Hz, 2-H), 6.79 (1 H, brs, 7-H), 6.59 (1 H, d, *J* 4.2 Hz, 3-H), 4.21 (2 H, d, *J* 6.7 Hz, isobutyl CH_2), 2.13 (1 H, m, isobutyl CH) and 1.04 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 311 (M^+, 13%), 255 (17), 211 (15), 77 (46), 57 (78) and 41 (100).

3-Acetyl-5-formylpyrrol-2-ylacetic acid

A solution of ethyl 3-acetyl-5-formylpyrrol-2-ylacetate (**5b**) (3.5 g, 15.7 mmol) in a mixture of THF (227 ml) and methanol (26 ml) was treated with aqueous potassium hydroxide (2 M; 92 ml) and stirred at room temperature overnight. After this period the reaction mixture was diluted with water and extracted with ethyl acetate (x 3). The aqueous phase was then acidified with hydrochloric acid, saturated with sodium chloride, extracted with ethyl acetate (x 3) and concentrated *in vacuo* to give the *title compound* as a yellow-brown solid (2.6 g, 88%) which was not purified further, m.p. 194-196°C (decomp.), (Found: MH^+, 196.0610. $C_9H_{10}NO_4$ requires *M*H, 196.0610); $\nu_{max.}$ (KBr) 1725 and 1646 cm^{-1}; δ_H [250 MHz; $CDCl_3$ + $(CD_3)_2SO$] 11.86 (1 H, br s, CO_2H), 9.41 (1 H, s, CHO), 7.17 (1 H, d, *J* 2.35 Hz, pyrrole C*H*), 3.98 (2 H, s, CH_2CO_2H) and 2.35 (3 H, s, *Me*CO); δ_C (62.9 MHz; $CDCl_3$) 32.6, 37.8, 126.8, 127.9, 135.7, 143.2, 175.9, 183.9, 199.0; *m/z* (CI) 196 (MH^+, 70%), 178 (28), 152 (100) and 136 (20).

2-Formyl-4-methylpyrano[4,3-b]pyrrol-6(1H)-one (**9b**)

A solution of 3-acetyl-5-formylpyrrol-2-yl acetic acid (133 mg, 0.68 mmol) in THF (3.0 ml) was treated with acetic anhydride (3.0 ml) and stirred at room temperature for 2 h. After this period TLC analysis of the reaction mixture shows the presence of the desired fluorescent yellow α-pyrone together with base line material and some non-polar impurities. Attempts to purify this material by chromatography on silica gel or by recrystallisation proved unsuccessful. It was therefore used crude in subsequent Diels-Alder reactions and the purified yield for its formation was not calculated. Crude yield: 162 mg.

3-Benzoyl-5-formylpyrrol-2-ylacetic acid

Ethyl 3-benzoyl-5-formylpyrrol-2-ylacetate (**5c**) was hydrolysed as above to give the title compound (100% yield on 0.74 mmol scale), m.p. 195-197°C (decomp.), (Found: MH^+, 258.0766. $C_{14}H_{12}NO_4$ requires MH, 258.0766); $\nu_{max.}$ (KBr) 1700, 1666 and 1638 cm^{-1}; δ_H [250 MHz; $CDCl_3$ + $(CD_3)_2SO$] 12.13 (1 H, br s, CO_2H), 9.33 (1 H, s, CHO), 7.64 (2 H, m, ArH), 7.35 (3 H, m, ArH), 6.98, (1 H, s, pyrrole CH) and 3.94 (2 H, s, CH_2CO_2H); δ_C (62.9 MHz; $CDCl_3$) 33.2, 122.1, 123.6, 128.2, 128.9, 131.1, 131.8, 138.3, 140.0, 171.1, 179.3 and 191.3 (2 carbons unobserved); *m/z* 258 (MH^+, 55%), 240 (42), 214 (100), 183 (36), 154 (18), 136 (70), 105 (25), 77(20) and 51 (12).

2-Formyl-4-phenylpyrano[4,3-b]pyrrol-6(1H)-one (**9c**)

A solution of 3-benzoyl-5-formylpyrrol-2-yl acetic acid was treated with acetic anhydride (3.0 ml) to give the α-pyrone (**9c**) (100% crude yield) which was not purified further.

Ethyl 5-Benzoylpyrrol-2-ylacetate (**10**)

A flame-dried flask was charged with anhydrous aluminium chloride (7.7 g, 57.5 mmol, 4.4 eq), 1,2–dichloroethane (20 ml), nitromethane (2.3 ml, 43.1 mmol, 3.3 eq) and benzoyl chloride (0.83 ml, 7.18 mmol, 1.5 eq) at 0°C. Ethyl pyrrol-2-ylacetate (**3**) (2.0 g, 13.1 mmol, 1.0 eq) was dissolved in a minimum of 1,2-dichloroethane (approx. 15 ml) and cannulated onto the $PhCOCl{\bullet}AlCl_3$ addition complex at 0°C. The ice bath was removed after 10 min, and the reaction mixture stirred at room temperature for 2 h and then poured into a mixture of ice and dilute hydrochloric acid. Extraction (chloroform x 3), washing, (water, 3 dimethylaminopropylamine, dilute hydrochloric acid, saturated brine), drying ($MgSO_4$) and concentration *in vacuo* yielded a brown solid. The crude product could be purified by precipitation from ether to give the *title compound* (**10**) as a beige solid (1.07 g, 32%), m.p. 158-159°C, (Found: C, 69.7; H, 5.8; N, 5.45. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.4%); (Found: M^+ 257.105. $C_{15}H_{15}NO_3$ requires M, 257.105) $\nu_{max.}$ (KBr) 1742 and 1731 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.38 (1 H, br s, NH), 7.88 (2 H, m, ArH), 7.5 (3 H, m, ArH), 6.82 (1 H, dd, *J* 2.6, 3.7 Hz, pyrrole 4-H), 6.19 (1 H, t, *J* 3.2 Hz, pyrrole 3-H), 4.2 (2 H, q, *J* 7.1 Hz, $CO_2CH_2CH_3$), 3.78 (2 H, s, CH_2CO_2Et) and 1.28 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$); δ_C (62.9 MHz; $CDCl_3$) 14.1, 33.6, 61.4, 110.75, 120.4, 128.3, 128.4, 128.6, 129.0, 131.0. 131.7, 132.5, 138.5, 169.7 and 184.2; *m/z* 257 (M^+, 40%), 184 (100), 106 (32) and 77 (31).

Ethyl 3,5-Dibenzoylpyrrol-2-ylacetate (**11**)

The method used was as for (**10**) but after the ice bath was removed, the reaction mixture was heated to reflux until TLC showed that no starting material remained (approx. 3 h). The work up and purification procedure is the same as for (**10**). A small sample was purified by flash chromatography for analytical purposes. On a 6 mmol scale the title compound (**11**) was obtained as a beige solid (91% crude yield; 78% after crystallisation from ether), m.p. 172-173°C, (Found: C, 72.7; H, 5.3; N, 3.8. $C_{22}H_{19}NO_4$ requires C, 73.1; H, 5.3; N, 3.9%); (Found: M^+, 361.1314. $C_{22}H_{19}NO_4$ requires M, 361.1314); $\nu_{max.}$ (KBr) 1747, 1641 and 1611 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 11.82 (1H, br s, NH), 7.84 (4 H, m, ArH), 7.52 (6 H, m, ArH), 7.06 (1 H, s, pyrrole CH), 4.27 (2 H, s, CH_2CO_2Et), 4.24 (2 H, q, *J* 7.2 Hz, $CO_2CH_2CH_3$) and 1.30 (3 H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$); δ_C (62.9 MHz; $CDCl_3$) 14.0, 32.85, 61.3, 122.2, 122.5, 128.2, 128.3, 128.4, 128.9, 129.0, 129.2, 131.8, 132.3, 137.5, 138.5, 139.2, 169.7, 185.1 and 190.2 (3 carbons unobserved); *m/z* 361 (M^+, 20%), 315 (28), 287 (22), 105 (100), 77 (61) and 51 (20).

3,5-Dibenzoylpyrrol-2-ylacetic acid

Ethyl 3,5-dibenzoylpyrrol-2-ylacetate (**11**) was hydrolysed as above to give the *title compound* (73% yield on 3.7 mmol scale), m.p. 194.5-195.5°C, (Found: C, 71.6; H, 4.6; N, 4.2. $C_{20}H_{15}NO_4$ requires C, 72.1; H, 4.5; N, 4.2%); (Found: MH^+, 334.1079. $C_{20}H_{15}NO_4$ requires MH 334.1001); $\nu_{max.}$ (KBr) 1698, 1636 and 1607 cm^{-1}; δ_H [250 MHz; $CDCl_3$ + $(CD_3)_2SO$] 11.95 (1 H, br s, CO_2H), 7.69 (4 H, m, ArH), 7.35 (6 H, m, ArH), 6.87 (1 H, d, *J* 2.4 Hz, pyrrole CH) and 4.04 (2 H, s, CH_2CO_2H); δ_C (62.9 MHz, $CDCl_3$) 33.2, 121.9, 122.1, 128.2, 128.3, 128.4, 128.8, 129.1, 129.4, 131.9, 132.0, 138.0, 139.16, 139.2, 171.5, 185.0 and 192.1 (3 carbons unobserved); *m/z* (CI) 334 (MH^+, 10%), 290 (100) and 105 (10).

2-Benzoyl-4-phenylpyrano[4,3-b]pyrrol-6(1H)-one (12)

3,5-Dibenzoylpyrrol-2-ylacetic acid (0.7 g, 2.1 mmol) was treated with isobutyl chloroformate (1 equiv.) as above to give the α-pyrone (12) (561 mg, 85%) after flash chromatography on silica gel, eluting with ethyl acetate:light petroleum(1:1), m.p. 104-105°C, (Found: M^+, 315.0895. $C_{20}H_{13}NO_3$ requires M, 315.0895); $\nu_{max.}$ (KBr) 1686 and 1693 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.99 (1 H, br s, N*H*), 7.74 (4 H, m, ArH), 7.39 (6 H, m, ArH), 6.83 (1 H, s, 7-*H*) and 5.72 (1 H, d, *J* 0.85 Hz, 3-*H*); *m/z* 315 (M^+, 80%), 105 (85) and 77 (100).

Isobutyl 2-Benzoyl-6-oxo-4-phenylpyrano[4,3-b]pyrrole-1-carboxylate (13)

3,5-Dibenzoylpyrrol-2-ylacetic acid (125 mg, 0.38 mmol) was treated with isobutyl chloroformate (2 equiv.) as above to give the *title compound* (13) (71 mg, 46%), m.p. 160-164°C, (decomp.), (Found: MH^+ 416.1498. $C_{25}H_{22}NO_5$ requires MH 416.1498); $\nu_{max.}$ (KBr) 1752 and 1673 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 7.95 (2 H, m, ArH), 7.85 (2 H, m, ArH), 7.64 (1 H, m, ArH), 7.52 (5 H, m, ArH), 6.9 (1 H, d, *J* 0.8 Hz, 7-*H*), 6.8 (1 H, d, *J* 0.8 Hz, 3-H), 3.99 (2 H, d, *J* 6.7 Hz, CO_2CH_2), 1.82 (1 H, tq, *J* 6.7 Hz, $CHMe_2$) and 0.82 (6 H, d, *J* 6.7 Hz, $CHMe_2$); δ_C (62.9 MHz; $CDCl_3$) 18.8 (2C), 27.5, 74.65, 92.6, 111.9, 112.8, 124.7, 127.9, 128.7, 128.9, 129.0, 129.2, 129.4, 129.6, 131.3, 131.6, 134.1, 136.1, 140.8, 149.8, 151.9, 156.65, 162.8 and 185.8; *m/z* (CI) 416 (MH^+, 52%), 180 (100), 174 (100), 163 (72), 134 (33), 118 (21), 102 (24) and 58 (18).

Diels-Alder Reactions of Pyrano[4,3-*b*]pyrrol-6(1*H*)-ones

1. Dimethyl acetylenedicarboxylate

With pyrano[4,3-b]*pyrrol*-6(1H)-*one* (7a)

A mixture of the pyranopyrrolone (7a) (36 mg, 0.27 mmol) and dimethyl acetylenedicarboxylate (76 mg, 0.53 mmol) in chlorobenzene (10 ml) was refluxed under nitrogen for 1.5 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (3:1)] to give *dimethyl indole*-5,6-*dicarboxylate* (14a) (51 mg, 82%), m.p. 82-86°C, (Found: C, 61.6; H, 4.7; N, 5.9. $C_{12}H_{11}NO_4$ requires C, 61.8; H, 4.75; N, 6.0%); $\nu_{max.}$(Nujol) 3352, 1712, 1328 and 1254 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.79 (1 H, br, NH), 8.06 (1 H, s), 7.77 (1 H, s), 7.37 (1 H, t, *J* 2.8 Hz, 2-H), 6.64 (1 H, m, 3-H) and 3.91 (6 H, s, CO_2Me); *m/z* 233 (M^+, 36%) and 202 (100).

With 4-*methylpyrano*[4,3-b]*pyrrol*-6(1H)-*one* (7b)

A mixture of the pyranopyrrolone (7b) (49 mg, 0.33 mmol) and dimethyl acetylenedicarboxylate (93 mg, 0.66 mmol) in chlorobenzene (5 ml) was refluxed under nitrogen for 4 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (3:1)] to give *dimethyl* 4-*methylindole*-5,6-*dicarboxylate* (14b) (51 mg, 63%), m.p. 156-161°C, (Found: C, 63.1; H, 5.3; N, 5.65. $C_{13}H_{13}NO_4$ requires C, 63.15; H, 5.3; N, 5.7%); $\nu_{max.}$(Nujol) 3388 and 1706 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.65 (1 H, br, NH), 7.95 (1 H, s, 7-H), 7.38 (1 H, t, *J* 2.9 Hz, 2-H), 6.63 (1 H, m, 3-H), 3.96 (3 H, s, CO_2Me), 3.89 (3 H, s, CO_2Me) and 2.54 (3 H, s, 4-Me); *m/z* 247 (M^+, 48%), 216 (100), 215 (94), 157 (70) and 129 (34).

With isobutyl 6-*oxopyrano*[4,3-b]*pyrrole*-1-*carboxylate* (8a)

A mixture of the pyranopyrrolone (8a) (65 mg, 0.28 mmol) and dimethyl acetylenedicarboxylate (78 mg, 0.53 mmol) in chlorobenzene (10 ml) was refluxed for 2 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (2:1)] to give 1-*isobutyl* 5,6-*dimethylindole*-1,5,6-*tricarboxylate* (14c) (91 mg, 99%) as a colourless oil, (Found: C, 61.2; H, 5.7; N, 4.1. $C_{17}H_{19}NO_6$ requires C, 61.3; H, 5.75; N, 4.2%); $\nu_{max.}$(film) 1726 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.60 (1 H, brs, 7-H), 7.96 (1 H, s, 4-H), 7.79 (1 H, d, *J* 3.7 Hz, 2-H), 6.69 (1 H, d, *J* 3.7 Hz, 3-H), 4.27 (2 H, d, isobutyl CH_2), 3.93 (6 H, s, CO_2Me), 2.17 (1 H, m, *J* 6.6 Hz, isobutyl CH) and 1.08 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 333 (M^+, 54%), 302 (32), 246 (25), 233 (19), 201 (85), 57 (100) and 41 (25).

With isobutyl 4-methyl-6-oxopyrano[4,3-b]*pyrrole-1-carboxylate* (**8b**)

A mixture of the pyranopyrrolone (**8b**) (40 mg, 0.16 mmol) and dimethyl acetylenedicarboxylate (46 mg, 0.32 mmol) in chlorobenzene (5 ml) was refluxed for 18 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (2:1)] to give *1-isobutyl 5,6-dimethyl 4-methylindole-1,5,6-tricarboxylate* (**14d**) (49 mg, 88%) as a colourless oil, (Found: C, 62.2; H, 6.3; N, 3.8. $C_{18}H_{21}NO_6$ requires C, 62.2; H, 6.1; N, 4.0%); $\nu_{max.}$(film) 1734, 1424, 1352 and 1292 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.73 (1 H, brs, 7-H), 7.81 (1 H, d, *J* 3.8 Hz, 2-H), 6.71 (1 H, dd, *J* 3.7, 0.7 Hz, 3-H), 4.27 (2 H, d, *J* 6.5 Hz, isobutyl CH_2), 3.97 (3 H, s, CO_2Me), 3.91 (3 H, s, CO_2Me), 2.51 (3 H, s, 4-Me), 2.18 (1 H, m, isobutyl CH) and 1.09 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 347 (M^+, 28%), 315 (64), 259 (17), 215 (80), 57 (100), 41 (63) and 29 (68).

With 2-formyl-4-methylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**9b**)

3-Acetyl-5-formylpyrrol-2-ylacetic acid (200 mg, 1.05 mmol) was converted into the pyranopyrrolone (**9b**), which without purification was heated under reflux with dimethyl acetylenedicarboxylate (0.25 ml, 2.05 mmol) in chlorobenzene for 7 h to give, after chromatography (45% ethyl acetate in light petroleum), *dimethyl 2-formyl-4-methylindole-5,6-dicarboxylate* (**14e**) (114 mg, 40% over 2 steps), m.p. 195-197°C, (Found: M^+ 275.0794. $C_{14}H_{13}NO_5$ requires *M*, 275.0794); $\nu_{max.}$ (KBr) 1725 and 1662 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.03 (1 H, br s, NH), 9.90 (1 H, s, CHO), 7.99 (1 H, s, 7-H), 7.34 (1 H, dd, *J* 0.9, 2.0 Hz, 3-H), 3.96 (3 H, s, CO_2Me), 3.91 (3 H, s, CO_2Me) and 2.57 (3 H, s, ArMe); δ_C (62.9 MHz; $CDCl_3$) 15.9, 52.5 (2C), 112.9, 113.6, 126.6, 126.9, 130.1, 131.2, 136.7, 138.3, 166.8, 170.2 and 182.2; *m/z* 275 (M^+, 30%), 243 (84), 185 (100), 157 (48) and 77(20).

With 2-formyl-4-phenylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**9c**)

3-Benzoyl-5-formylpyrrol-2-ylacetic acid was converted into the pyranopyrrolone (**9c**), which without purification was heated under reflux with dimethyl acetylenedicarboxylate (0.08 ml, 0.63 mmol) as described above to give, after chromatography (40% ethyl acetate in light petroleum), *dimethyl 2-formyl-4-phenylindole-5,6-dicarboxylate* (**14f**) (52% over 2 steps), m.p. 269-271°C, (Found: M^+, 337.0950. $C_{19}H_{15}NO_5$ requires *M*, 337.0950); $\nu_{max.}$ (KBr) 1721 and 1660 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 11.30 (1 H, br s, NH), 9.78 (1 H, s, CHO), 8.15 (1 H, s, 7-H), 7.41 (5 H, m, ArH), 7.03 (1 H, d, *J* 2.0 Hz, 3-H), 3.89 (3 H, s, CO_2Me) and 3.6 (3 H, s, CO_2Me); δ_C (62.9 MHz; $CDCl_3$) 52.1, 52.5, 113.9, 115.3, 126.15, 126.18, 128.0, 128.2, 128.8, 129.1, 129.5, 131.6, 135.4, 137.0, 137.3, 139.1, 166.7, 169.6 and 182.4; *m/z* 337 (M^+, 40%), 306 (73), 212 (100), 184 (38), 136 (87), 105 (20), 77 (36) and 51 (22).

With 2-benzoyl-4-phenylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**12**)

A mixture of the pyranopyrrolone (**12**) (70 mg, 0.22 mmol) and dimethyl acetylenedicarboxylate (0.05 ml, 0.44 mmol) in chlorobenzene (6 ml) was refluxed under nitrogen for 4 h. The solvent was evaporated and the residue chromatographed [ethyl acetate-light petroleum (1:3)] to give *dimethyl 2-benzoyl-4-phenylindole-5,6-dicarboxylate* (**14 g**) (47 mg, 51%), m.p. 193-194°C, (Found: M^+, 413.1263. $C_{25}H_{19}NO_5$ requires *M*, 413.1263); $\nu_{max.}$ (KBr) 1726, 1707 and 1635 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.85 (1 H, br s, NH), 8.14 (1 H, s, 7-H), 7.84 (2 H, m, ArH), 7.46 (8 H, m, ArH), 6.87 (1 H, d, *J* 1.2 Hz, 3-H), 3.87 (3 H, s, CO_2Me) and 3.57 (3 H, s, CO_2Me); δ_C (62.9 MHz; $CDCl_3$) 52.3, 52.7, 112.0, 114.4, 126.1, 127.1, 128.1, 128.3, 128.7, 129.2, 130.2, 133.0, 135.8, 136.1, 136.9, 137.2, 137.3, 166.6, 169.7 and 187.0 (5 carbons unobserved); *m/z* 413 (M^+, 72%), 382 (100), 105 (100) and 77 (52).

With isobutyl 2-benzoyl-6-oxo-4-phenylpyrano[4,3-b]*pyrrole-1-carboxylate* (**13**)

A mixture of the pyranopyrrolone (**13**) (32 mg, 0.08 mmol) and dimethyl acetylenedicarboxylate (0.02 ml, 0.16 mmol) in chlorobenzene (5 ml) was refluxed under nitrogen for 2 days. Extra dimethyl acetylenedicarboxylate (0.02 ml, 0.16 mmol) was added and the heating continued for 2 days. The solvent was evaporated and the residue chromatographed to give *1-isobutyl-5,6-dimethyl 2-benzoyl-4-phenylindole-1,5,6-tricarboxylate* (**14h**) (35 mg, 88%) as an oil, (Found: M^+, 513.1788; $C_{30}H_{27}NO_7$ requires *M*, 513.1788); $\nu_{max.}$ ($CHCl_3$) 1729 and 1668 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.9 (1 H, d, *J* 0.6 Hz, 7-H), 7.86 (3H, m, ArH), 7.61 (1H, m, ArH), 7.44 (6 H, m, ArH), 6.73 (1 H, d, *J* 0.6 Hz, 3-H), 4.00 (2 H, d, *J* 6.53 Hz, CO_2CH_2), 3.96 (3 H, s, CO_2Me), 3.66 (3 H, s, CO_2Me), 1.86 (1 H, tq, *J* 6.7 Hz, $CHMe_2$) and 0.86 (6 H, d, *J* 6.7 Hz, $CHMe_2$); δ_C (62.9

MHz; $CDCl_3$) 18.8 (2C) 27.5, 52.3, 52.6, 74.6, 112.8, 116.8, 126.2, 128.3, 128.35, 128.7, 129.3, 129.4, 130.4, 131.0, 133.8, 134.5, 135.9, 136.1, 136.6, 139.8, 150.3, 166.3, 169.1 and 187.3 (4 carbons unobserved); *m/z* 513 (M^+, 20%), 413 (35), 382 (54), 105 (63), 77 (30), 57 (100) and 41 (82).

2. Ethyl (or methyl) propiolate

With pyrano[4,3-b]*pyrrol*-6(1H)-*one* (**7a**)

A mixture of the pyranopyrrolone (**7a**) (42 mg, 0.31 mmol) and ethyl propiolate (152 mg, 1.55 mmol) in chlorobenzene (8 ml) was refluxed under nitrogen for 4 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (2:1)] to give *ethyl indole*-5-*carboxylate* (**15a**) and *ethyl indole*-6-*carboxylate* (**16a**) (30 mg, 51%) in the ratio 1 to 1.8, m.p. 57-63°C, (Found: C, 69.6; H, 5.85; N, 7.3. $C_{11}H_{11}NO_2$ requires C, 69.8; H, 5.9; N, 7.4%); $\nu_{max.}$(Nujol) 3300, 1684 and 1296 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.56 (1 H, br, NH, 6-ester), 8.50 (1 H, br, NH, 5-ester), 8.43 (1 H, s, 4-H, 5-ester), 8.18 (1 H, s, 7-H, 6-ester), 7.92 (1 H, dd, *J* 8.6, 1.6 Hz, 6-H, 5-ester), 7.83 (1 H, dd, *J* 8.5, 1.2 Hz, 5-H, 6-ester), 7.66 (1 H, d, *J* 8.3 Hz, 4-H, 6-ester), 7.40 (1 H, d, *J* 8.7 Hz, 7-H, 5-ester), 7.36 (1 H, m, 2-H, 6-ester), 7.27 (1 H, m, 2-H, 5-ester), 6.65 (1 H, m, 3-H, 5-ester), 6.61 (1 H, m, 3-H, 6-ester), 4.40 (q, *J* 7.1 Hz, ester CH_2, both isomers) and 1.41 (t, *J* 7.1 Hz, ester CH_3, both isomers); *m/z* 189 (M^+, 85%), 144 (100) and 116 (24).

With 4-*methylpyrano*[4,3-b]*pyrrol*-6(1H)-*one* (**7b**)

A mixture of the pyranopyrrolone (**7b**) (83 mg, 0.56 mmol) and ethyl propiolate (273 mg, 2.78 mmol) in chlorobenzene (12 ml) was refluxed under nitrogen for 24 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (2:1)] to give *ethyl* 4-*methylindole*-5-*carboxylate* (**15b**) and *ethyl* 4-*methylindole*-6-*carboxylate* (**16b**) (89 mg, 79%) in the ratio 1 to 1, m.p. 70-89°C, (Found: C, 70.7; H, 6.5; N, 6.8. $C_{12}H_{13}NO_2$ requires C, 70.9; H, 6.45; N, 6.9%); $\nu_{max.}$(Nujol) 3300 and 1686 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.47 (1 H, br, NH), 8.38 (1 H, br, NH), 8.02 (1 H, s, 7-H, 6-ester), 7.84 (1 H, d, *J* 8.6 Hz, 6-H, 5-ester), 7.62 (1 H, s, 5-H, 6-ester), 7.34 (1 H, t, *J* 2.8 Hz, 2-H), 7.23 (2 H, m), 6.70 (1 H, m, 3-H), 6.60 (1 H, m, 3-H), 4.37 (4 H, m, ester CH_2, both isomers), 2.85 (3 H, s, 4-Me, 5-ester), 2.59 (3 H, s, 4-Me, 6-ester) and 1.41 (6 H, t, *J* 7.1 Hz, ester CH_3, both isomers); *m/z* 203 (M^+, 87%), 174 (20), 158 (100) and 130 (60).

With isobutyl 6-*oxopyrano*[4,3-b]*pyrrole*-1-*carboxylate* (**8a**)

A mixture of the pyranopyrrolone (**8a**) (71 mg, 0.30 mmol) and ethyl propiolate (148 mg, 1.51 mmol) in chlorobenzene (10 ml) was refluxed for 4 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:3)] to give 5-*ethyl* 1-*isobutyl indole*-1,5-*dicarboxylate* (**15c**) and 6-*ethyl* 1-*isobutyl indole*-1,6-*dicarboxylate* (**16c**) (71 mg, 81%) in the ratio 1 to 1, m.p. 40-52°C, (Found: C, 66.5; H, 6.65; N, 4.95. $C_{16}H_{19}NO_4$ requires C, 66.4; H, 6.6; N, 4.8%); $\nu_{max.}$(Nujol) 1740, 1708, 1230 and 762 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.86 (1 H, brs, 7-H, 6-ester), 8.31 (1 H, d, *J* 1.7 Hz, 4-H, 5-ester), 8.22 (1 H, d, *J* 8.7 Hz, 7-H, 5-ester), 8.04 (1 H, dd, *J* 8.7, 1.7 Hz, 6-H, 5-ester), 7.97 (1 H, dd, *J* 8.2, 1.5 Hz, 5-H, 6-ester), 7.79 (1 H, d, *J* 3.7 Hz, 2-H, 6-ester), 7.68 (1 H, d, *J* 3.7 Hz, 2-H, 5-ester), 7.60 (1 H, d, *J* 8.2 Hz, 4-H, 6-ester), 6.68 (1 H, d, *J* 3.8 Hz, 3-H, 5-ester), 6.65 (1 H, d, *J* 3.7 Hz, 3-H, 6-ester), 4.41 (4 H, q, *J* 6.9 Hz, ethyl CH_2, both isomers), 4.28 (2 H, d, *J* 6.5 Hz, isobutyl CH_2, 6-ester), 4.25 (2 H, d, *J* 6.7 Hz, isobutyl CH_2, 5-ester), 2.22-2.13 (2 H, m, isobutyl CH, both isomers), 1.42 (6 H, t, *J* 7.1 Hz, ethyl CH_3, both isomers), 1.11 (6 H, d, *J* 6.7 Hz, isobutyl CH_3, 6-ester) and 1.07 (6 H, d, *J* 6.7 Hz, isobutyl CH_3, 5-ester); *m/z* 289 (M^+, 60%), 189 (68), 161 (46), 144 (70), 116 (43), 57 (100) and 41 (77).

With isobutyl 4-*methyl*-6-*oxopyrano*[4,3-b]*pyrrole*-1-*carboxylate* (**8b**)

A mixture of the pyranopyrrolone (**8b**) (79 mg, 0.32 mmol) and ethyl propiolate (155 mg, 1.58 mmol) in chlorobenzene (10 ml) was refluxed for 20 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:3)] to give 5-*ethyl* 1-*isobutyl* 4-*methylindole*-1,5-*dicarboxylate* (**15d**) and 6-*ethyl* 1-*isobutyl* 4-*methylindole*-1,6-*dicarboxylate* (**16d**) (72 mg, 75%) in the ratio 1.2 to 1 as a colourless oil, (Found: C, 67.25; H, 7.1; N, 4.4. $C_{17}H_{21}NO_4$ requires C, 67.3; H, 7.0; N, 4.6%); $\nu_{max.}$(film) 1738, 1712, 1598 and 1522 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.71 (1 H, brs, 7-H, 6-ester), 8.04 (1 H, d, *J* 8.8

Hz, 7-H, 5-ester), 7.93 (1 H, d, *J* 8.8 Hz, 6-H, 5-ester), 7.78 (2 H, m, 2-H + 5-H, 6-ester), 7.66 (1 H, d, *J* 3.8 Hz, 2-H, 5-ester), 6.76 (1 H, d, *J* 3.8 Hz, 3-H, 5-ester), 6.67 (1 H, d, *J* 3.7 Hz, 3-H, 6-ester), 4.44 (m, ethyl CH_2, both isomers), 4.27 (2 H, d, *J* 6.5 Hz, isobutyl CH_2, 6-ester), 4.24 (2 H, d, *J* 6.6 Hz, isobutyl CH_2, 5-ester), 2.79 (3 H, s, 4-Me, 5-ester), 2.56 (3 H, s, 4-Me, 6-ester), 2.24-2.11 (m, isobutyl CH, both isomers), 1.42 (t, *J* 7.1 Hz, ethyl CH_3, both isomers), 1.10 (6 H, d, *J* 6.7 Hz, isobutyl CH_3, 6-ester) and 1.07 (6 H, d, *J* 6.7 Hz, isobutyl CH_3, 5-ester); *m/z* 303 (M^+, 39%), 203 (27), 158 (22), 57 (100), 41 (49) and 29 (60).

With 2-*benzoyl*-4-*phenylpyrano*[4,3-b]*pyrrol*-6(1H)-*one* (**12**)

A mixture of the pyranopyrrolone (**12**) (96 mg, 0.32 mmol) and methyl propiolate (0.13 ml, 1.6 mmol) in chlorobenzene (8 ml) was refluxed under nitrogen for 16 h. The solvent was evaporated and the residue chromatographed [30% ethyl acetate, 70% light petroleum] to give *methyl* 2-*benzoyl*-4-*phenylindole*-5-*carboxylate* (**15e**) and *methyl* 2-*benzoyl*-4-*phenylindole*-6-*carboxylate* (**16e**) (72 mg, 67%) in the ratio 5 to 1, (data recorded on 5:1 isomeric mixture), m.p. (range for 2 regioisomers) 184-194°C, (Found: M^+, 355.1208. $C_{23}H_{17}NO_3$ requires *M*, 355.1208); $\nu_{max.}$ (KBr) 1701 and 1641 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 10.02 (1 H, br s, NH), 7.95 (3 H, m, ArH), 7.48 (9 H, m, ArH), 6.95 (1 H, d, 5-ester, d, 6-ester, *J* 0.8 Hz, 3-H's), 3.99 (0.5 H, s, CO_2Me 6-ester) and 3.65 (2.5 H, s, CO_2Me 5 ester); δ_C (62.9 MHz; $CDCl_3$) 51.8, 52.3, 114.1, 111.7, 113.6, 113.9, 121.2, 121.9, 122.5, 127.5, 127.8, 128.1, 128.3, 128.4, 128.6, 128.69, 128.75, 128.9, 129.0, 129.1, 129.3, 129.4, 132.0, 132.2, 132.4, 132.7, 132.8, 134.6, 135.5, 136.86, 136.91, 137.56, 137.63, 139.0, 139.1, 139.7, 139.8, 167.5, 168.9, 187.3 and 187.4 (5 carbons unobserved); *m/z* 355 (M^+, 100%), 324 (55), 105 (68) and 77 (52).

3. Ethyl 3-trimethylsilylpropynoate

With 4-*methylpyrano*[4,3-b]*pyrrol*-6(1H)-*one* (**7b**)

A mixture of the pyranopyrrolone (**7b**) (50 mg, 0.34 mmol) and ethyl 3-trimethylsilylpropynoate (171 mg, 1.01 mmol) in chlorobenzene (10 ml) was refluxed under nitrogen for 96 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:1)] to give *ethyl* 4-*methyl*-6-*trimethylsilylindole*-5-*carboxylate* (**15f**) (10 mg, 11%), m.p. 55-56°C, (Found: M^+, 275.1342. $C_{15}H_{21}NO_2Si$ requires *M*, 275.1342); $\nu_{max.}$($CHCl_3$) 3476, 1706, 1282, 1252, 856 and 840 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.26 (1 H, br, NH), 7.49 (1 H, s, 7-H), 7.24 (1 H, dd, *J* 3.2, 2.5 Hz, 2-H), 6.60 (1 H, m, 3-H), 4.40 (2 H, q, *J* 7.1 Hz, ester CH_2), 2.60 (3 H, s, 4-Me), 1.41 (3 H, t, *J* 7.1 Hz, ester CH_3) and 0.32 (9 H, s, Me_3Si); *m/z* 275 (M^+, 4%), 260 (82) and 232 (100).

With isobutyl 6-*oxopyrano*[4,3-b]*pyrrole*-1-*carboxylate* (**8a**)

A mixture of the pyranopyrrolone (**8a**) (80 mg, 0.34 mmol) and ethyl 3-trimethylsilylpropynoate (173 mg, 1.02 mmol) in chlorobenzene (10 ml) was refluxed for 20 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:7)] to give 5-*ethyl* 1-*isobutyl* 6-*trimethylsilylindole*-1,5-*dicarboxylate* (**15g**) and 6-*ethyl* 1-*isobutyl* 5-*trimethylsilylindole*-1,6-*dicarboxylate* (**16g**) (111 mg, 90%) in the ratio 7 to 1, m.p. 32-50°C, (Found: C, 63.3; H, 7.7; N, 3.9. $C_{19}H_{27}NO_4Si$ requires C, 63.1; H, 7.5; N, 3.9%); $\nu_{max.}$(Nujol) 1742, 1718, 1336, 1234, 844 and 766 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.86 (1 H, s, 7-H, minor), 8.52 (1 H, s, 7-H, major), 8.32 (1 H, s, 4-H, major), 7.89 (1 H, s, 4-H, minor), 7.76 (1 H, d, *J* 4 Hz, 2-H, minor), 7.70 (1 H, d, *J* 3.7 Hz, 2-H, major), 6.66 (d, *J* 3.7 Hz, 3-H, both isomers), 4.40 (q, *J* 7.1 Hz, ethyl CH_2, both isomers), 4.28 (2 H, d, *J* 6.8 Hz, isobutyl CH_2, minor), 4.25 (2 H, d, *J* 6.8 Hz, isobutyl CH_2, major), 2.19 (m, isobutyl CH, both isomers), 1.43 (t, *J* 7.1 Hz, ethyl CH_3, both isomers), 1.11 (6 H, d, *J* 6.8 Hz, isobutyl CH_3, minor), 1.07 (6 H, d, *J* 6.7 Hz, isobutyl CH_3, major), 0.38 (9 H, s, Me_3Si, major) and 0.35 (9 H, s, Me_3Si, minor); *m/z* 361 (M^+, 1%), 346 (100), 318 (20), 262 (28) and 218 (28).

Protodesilylation of 5-*ethyl* 1-*isobutyl* 6-*trimethylsilylindole*-1,5-*dicarboxylate* (**15g**) and 6-*ethyl* 1-*isobutyl* 5-*trimethylsilylindole*-1,6-*dicarboxylate* (**16g**)

A mixture of the silylated indoles (**15g**) and (**16g**) (58 mg, 0.16 mmol) was dissolved in trifluoroacetic acid (2 ml) and water (1 ml) and the mixture refluxed under nitrogen for 2 h. The mixture was allowed to cool to room temperature, diluted with water and

extracted with ether. The combined ether extracts were washed with saturated sodium hydrogen carbonate solution (until the washings remained basic), water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:3)] to give *5-ethyl 1-isobutyl indole-1,5-dicarboxylate* (**15c**) and *6-ethyl 1-isobutyl indole-1,6-dicarboxylate* (**16c**) (24 mg, 52%) in the ratio 7 to 1, m.p. 48-60°C, spectral data given above.

Hydrolysis of 5-ethyl 1-isobutyl indole-1,5-dicarboxylate (**15c**) and *6-ethyl 1-isobutyl indole-1,6-dicarboxylate* (**16c**)
A mixture of the isobutyl indole-1-esters (**15c**) and (**16c**) (18 mg, 0.06 mmol) in 0.88 ammonia (3 ml) and pyridine (1 ml) was stirred at room temperature for 36 h. Water was added and the mixture extracted with ether. The combined ether extracts were washed with saturated aqueous copper (II) sulfate solution, water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (2:1)] to give *ethyl indole-5-carboxylate* (**15a**) and *ethyl indole-6-carboxylate* (**16a**) (9.4 mg, 80%) in the ratio 7 to 1, m.p. 76-85°C, spectral data given above.

With isobutyl 4-methyl-6-oxopyrano[4,3-b]*pyrrole-1-carboxylate* (**8b**) *with ethyl 3-trimethylsilylpropynoate*
A mixture of the pyranopyrrolone (**8b**) (100 mg, 0.40 mmol) and ethyl 3-trimethylsilylpropynoate (206 mg, 1.21 mmol) in chlorobenzene (10 ml) was refluxed for 168 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:5)] to give *5-ethyl 1-isobutyl 4-methyl-6-trimethylsilylindole-1,5-dicarboxylate* (**15h**) (97 mg, 64%), m.p. 51-52°C, (Found: C, 64.2; H, 8.0; N, 3.7. $C_{20}H_{29}NO_4Si$ requires C, 64.0; H, 7.8; N, 3.7%); $\nu_{max.}$(Nujol) 1738, 1334, 1284, 1142 and 840 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.30 (1 H, brs, 7-H), 7.67 (1 H, d, *J* 3.8 Hz, 2-H), 6.66 (1 H, d, *J* 3.9 Hz, 3-H), 4.40 (2 H, q, *J* 7.1 Hz, ethyl CH_2), 4.23 (2 H, d, *J* 6.7 Hz, isobutyl CH_2), 2.54 (3 H, s, 4-Me), 2.17 (1 H, m, isobutyl CH), 1.41 (3 H, t, *J* 7.1 Hz, ethyl CH_3), 1.07 (6 H, d, *J* 6.7 Hz, isobutyl CH_3) and 0.33 (9 H, s, Me_3Si); *m/z* 375 (M^+, 1%), 360 (100), 332 (20), 276 (26), 232 (19), 57 (24), 41 (34) and 29 (43).

Protodesilylation of 5-ethyl 1-isobutyl 4-methyl-6-trimethylsilylindole-1,5-dicarboxylate (**15h**)
The 6-trimethylsilylindole (**15h**) (40 mg, 0.11 mmol) was dissolved in trifluoroacetic acid (2 ml) and water (1 ml) and the mixture refluxed under nitrogen for 2 h. The mixture was allowed to cool to room temperature, diluted with water, and extracted with ether. The combined ether extracts were washed with saturated sodium hydrogen carbonate solution (until the washings remained basic), water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:3)] to give *5-ethyl 1-isobutyl 4-methylindole-1,5-dicarboxylate* (**15d**) (14 mg, 43%) as a colourless oil, spectral data given above.

With 2-benzoyl-4-phenylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**12**)
The pyranopyrrole (**12**) (100 mg, 0.32 mmol) was heated with ethyl-3-trimethylsilylpropynoate (0.18 ml, 0.95 mmol) to give, after chromatography (20% ethyl acetate in light petroleum), *ethyl 2-benzoyl-4-phenyl-6-trimethylsilylindole-5-carboxylate* (**15i**) and *ethyl 2-benzoyl-4-phenyl-5-trimethylsilylindole-6-carboxylate* (**16i**) (9 mg, 6%) as an 8 to 1 mixture, m.p. 207-210°C, (Found: MH^+, 442.1838. $C_{27}H_{28}NO_3Si$ requires *M*H, 442.1838); $\nu_{max.}$ (KBr) 1714 and 1614 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.69 (1 H, br s, NH, both isomers), 7.96 (2 H, m, ArH, both isomers), 7.79 (1 H, 2s, 7-H, both isomers), 7.53 (8 H, m, ArH, both isomers), 7.0 (1 H, 2d, *J* 0.9 Hz, 3-H, both isomers), 4.27 (0.22 H, q, *J* 7.1 Hz, $CO_2CH_2CH_3$, 6-ester), 3.98 (1.77 H, q, *J* 7.1 Hz, $CO_2CH_2CH_3$, 5-ester), 1.35 (2.66 H, t, *J* 7.1 Hz, $CO_2CH_2CH_3$, 6-ester), 0.87 (0.33 H, t, *J* 7.1 Hz, $CO_2CH_2CH_3$, 5-ester), 0.42 (8 H, s, Me_3Si, 5-ester) and 0.30 (1 H, s, Me_3Si, 6-ester); δ_C (62.9 MHz; $CDCl_3$) **15i** only: 0.2 (3 C's) 13.4, 60.8, 112.3, 118.0, 127.5, 127.7, 128.2, 128.5, 129.0, 129.2, 130.7, 132.5, 135.3, 135.9, 137.2, 137.4, 137.6, 138.9, 171.2 and 187.0 (4 carbons unobserved); *m/z* (CI) 442 (MH^+, 100), 426 (55) and 398 (22).

4. Phenyl vinyl sulfoxide

With 4-methylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**7b**)
A mixture of the pyranopyrrolone (**7b**) (46 mg, 0.31 mmol) and phenyl vinyl sulfoxide (141 mg, 0.93 mmol) in chlorobenzene (5 ml) was refluxed under nitrogen for 24 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum

(1:1)] to give *4-methylindole* (**17a**) (13 mg, 32%) as a colourless oil, picrate m.p. 187-188°C (lit.,[11b] 188°C); $\nu_{max.}$($CHCl_3$) 3480 and 1342 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.1 (1 H, br, NH), 7.24-7.19 (2 H, m, 2-H + 7-H), 7.11 (1 H, t, *J* 7 Hz, 6-H), 6.92 (1 H, d, *J* 7 Hz, 5-H), 6.57 (1 H, m, 3-H) and 2.57 (3 H, s, 4-Me); δ_C (62.9 MHz; $CDCl_3$) 18.8, 101.1, 108.6, 119.9, 122.1, 123.5, 127.8, 130.2 and 135.4; *m/z* 131 (M^+, 77%), 130 (100), 103 (11) and 77 (20).

With isobutyl 4-methyl-6-oxopyrano[4,3-b]*pyrrole-1-carboxylate* (**8b**)

A mixture of the pyranopyrrolone (**8b**) (90 mg, 0.36 mmol) and phenyl vinyl sulfoxide (165 mg, 1.08 mmol) in chlorobenzene (10 ml) was refluxed for 144 h. The solvent was evaporated and the residue chromatographed [dichloromethane-light petroleum (1:2)] to give *isobutyl 4-methylindole-1-carboxylate* (**17b**) (71 mg, 85%) as a colourless oil, (Found: C, 72.5; H, 7.35; N, 5.9. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4; N, 6.1%); $\nu_{max.}$(film) 1734, 1424, 1348, 1276 and 1132 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.02 (1 H, d, *J* 8.3 Hz, 7-H), 7.62 (1 H, d, *J* 3.8 Hz, 2-H), 7.20 (1 H, m, 6-H), 7.05 (1 H, dd, *J* 7.3, 0.8 Hz, 5-H), 6.64 (1 H, d, *J* 3.8 Hz, 3-H), 4.22 (2 H, d, *J* 6.6 Hz, isobutyl CH_2), 2.53 (3 H, s, 4-Me), 2.15 (1 H, m, isobutyl CH) and 1.06 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 231 (M^+, 37%), 175 (27), 158 (16), 131 (98), 130 (69), 57 (100) and 41 (66).

With isobutyl 6-oxo-4-phenylpyrano[4,3-b]*pyrrole-1-carboxylate* (**8c**)

A mixture of the pyranopyrrolone (**8c**) (204 mg, 0.66 mmol) and phenyl vinyl sulfoxide (499 mg, 3.28 mmol) in chlorobenzene (5 ml) was refluxed under nitrogen for 192 h. The solvent was evaporated and the residue chromatographed [dichloromethane-light petroleum (3:1)] to give *isobutyl 4-phenylindole-1-carboxylate* (**17c**) (175 mg, 91%) as a colourless oil, (Found: C, 77.5; H, 6.6; N, 4.5. $C_{19}H_{19}NO_2$ requires C, 77.8; H, 6.5; N, 4.8%); $\nu_{max.}$(film) 1736, 1418, 1348, 1268 and 1166 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.20 (1 H, d, *J* 8 Hz, 7-H), 7.66 (1 H, d, *J* 3.8 Hz, 2-H), 7.60 (2 H, d, *J* 8 Hz), 7.48-7.41 (4 H, m), 7.31(1 H, d, *J* 8 Hz, 5-H), 6.76 (1 H, d, *J* 3.8 Hz, 3-H), 4.25 (2 H, d, *J* 6.6 Hz, isobutyl CH_2), 2.17 (1 H, m, isobutyl CH) and 1.07 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 293 (M^+, 88%), 237 (38), 193 (100), 165 (39) and 57 (40).

With 2-benzoyl-4-phenylpyrano[4,3-b]*pyrrol-6*(1H)*-one* (**12**)

The pyranopyrrolone (**12**) (98 mg, 0.31 mmol) and phenyl vinyl sulfoxide (0.125ml, 0.93 mmol) were heated together in chlorobenzene (3 ml) for 16 h to give, after chromatography (15% ethyl acetate in light petroleum), *2-benzoyl-4-phenylindole* (**17d**) (18 mg, 20%), m.p. 174-176°C, (Found: M^+, 297.1154. $C_{21}H_{15}NO$ requires *M*, 294.1154); $\nu_{max.}$ (KBr) 1623 and 1579 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 9.50 (1 H, br s, NH), 7.98 (1 H, m, ArH), 7.95 (1 H, m, ArH) and 7.68-7.21 (12 H, series of m's, ArH); δ_C (62.9 MHz; $CDCl_3$) 111.2, 112.1, 120.8, 126.3, 126.8, 127.5, 128.5, 128.7, 129.2, 129.4, 132.4, 134.6, 136.6, 137.2, 137.9, 138.0, 140.3 and 187.1 (3 carbons unobserved); *m/z* 297 (M^+, 100%), 280 (15), 220 (21), 190 (16), 165 (38), 105 (29), 77 (46), 51 (14) and 43 (12).

With isobutyl 2-benzoyl-6-oxo-4-phenylpyrano[4,3-b]*pyrrole-1-carboxylate* (**13**)

The pyranopyrrolone (**13**) (18 mg, 0.04 mmol) and phenyl vinyl sulfoxide (0.03 ml, 0.13 mmol) were heated together in chlorobenzene (5 ml) for 7 days to give, after chromatography (5% ethyl acetate in light petroleum), *isobutyl 2-benzoyl-4-phenylindole-1-carboxylate* (**17e**) (11 mg, 64%) as an oil, (Found: M^+, 397.1678; $C_{26}H_{23}NO_3$ requires *M*, 397.1678); $\nu_{max.}$ ($CHCl_3$) 1741 and 1662 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.15 (1 H, d, *J* 8.4 Hz, ArH), 7.84 (2 H, m, ArH), 7.53-7.03 (10 H, series of m's, ArH), 7.03 (1 H, s, 3-*H*), 3.92 (2 H, d, *J* 6.6 Hz, CH_2O), 1.76 (1 H, tq, *J* 6.7, 6.6 Hz, $CHMe_2$) and 0.76 (6 H, d, *J* 6.7 Hz $CHMe_2$); δ_C (62.9 MHz; $CDCl_3$) 18.9 (2 C's), 27.6, 74.0, 114.2, 114.3, 123.7, 126.4, 127.1, 127.2, 127.5, 127.6, 128.6, 128.7, 128.8, 129.1, 129.5, 133.3, 136.4, 137.1, 137.3, 137.5, 139.6, 150.9 and 187.6 (1 carbon unobserved); *m/z* 397 (M^+, 75%), 297 (100), 105 (42), 84 (40), 57 (45) and 49 (65).

5. Benzyne

With isobutyl 4-methyl-6-oxopyrano[4,3-b]*pyrrole-1-carboxylate* (**8b**)

A mixture of the pyranopyrrolone (**8b**) (73 mg, 0.29 mmol), 2-(3,3-dimethyltriazen-1-yl)benzoic acid (113 mg, 0.59 mmol), and

trifluoroacetic acid (1 drop) in acetonitrile (10 ml) was refluxed for 6 h. The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:3)] to give *isobutyl 4-methylbenz*[f]*indole-1-carboxylate* (**18**) (69 mg, 84%), m.p. 41-45°C, (Found: C, 76.6; H, 6.8; N, 4.9. $C_{18}H_{19}NO_2$ requires C, 76.8; H, 6.8; N, 5.0%); $\nu_{max.}$(Nujol) 1734 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.53 (1 H, brs, 9-H), 8.10 (1 H, m), 7.97 (1 H, m), 7.73 (1 H, d, *J* 4.0 Hz, 2-H), 7.50-7.42 (2 H,m), 6.80 (1 H, d, *J* 4.0 Hz, 3-H), 4.26 (2 H, d, *J* 6.6 Hz, isobutyl CH_2), 2.86 (3 H, s, 4-Me), 2.19 (1 H, m, isobutyl CH) and 1.09 (6 H, d, *J* 6.7 Hz, isobutyl CH_3); *m/z* 281 (M^+, 66%), 225 (65), 181 (100), 57 (69) and 41 (48).

Deprotection of Indoles

4-Methylindole (**17a**)

A solution of the isobutyl indole-1-ester (**17b**) (25 mg, 0.11 mmol) in 0.88 ammonia (3 ml) and pyridine (1 ml) was stirred at room temperature for 24 h. Water was added and the mixture extracted with ether. The combined ether extracts were washed with water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:1)] to give the *title compound* (**17a**) (11 mg, 78%), spectral data given above.

4-Phenylindole (**19**)

A solution of the indole-1-ester (**17c**) (123 mg, 0.42 mmol) in pyridine (2 ml) and 0.88 ammonia (6 ml) was stirred at room temperature for 72 h. The mixture was diluted with water and extracted with ether. The combined extracts were washed with saturated copper (II) sulfate solution, water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:1)] to give the *title compound* (**19**) (63 mg, 78%), m.p. 76-77°C, (lit.,[12] 58-60°C), (Found: C, 86.8; H, 5.6; N, 7.2. $C_{14}H_{11}N$ requires C, 87.0; H, 5.7; N, 7.25%); $\nu_{max.}$(Nujol) 3412 and 750 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.23 (1 H, br, NH), 7.73-7.68 (2 H, m), 7.51-7.44 (2 H, m), 7.41-7.33 (2 H, m), 7.31-7.18 (3 H, m) and 6.74 (1 H, m, 3-H); δ_C (62.9 MHz; $CDCl_3$) 102.2, 110.2, 119.8, 122.3, 124.4, 126.2, 126.9, 128.5, 128.8, 134.5, 136.3 and 141.2; *m/z* 193 (M^+, 100%) and 165 (34).

4-Methylbenz[f]*indole* (**20**)

A solution of the indole-1-ester (**18**) (26 mg, 0.09 mmol) in 0.88 ammonia (1.5 ml) and pyridine (0.5 ml) was stirred at room temperature for 30 h. Water was added and the mixture extracted with ether. The combined ether extracts were washed with water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:1)] to give the *title compound* (**20**) (11 mg, 66%), m.p. 96-98°C, (Found: M^+, 181.0891. $C_{13}H_{11}N$ requires M, 181.0891); $\nu_{max.}$($CHCl_3$) 3480, 1406 and 1320 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 8.15-8.11 (1 H, m), 8.02 (1 H, br, NH), 7.91-7.86 (1 H, m), 7.70 (1 H, s, 9-H), 7.41-7.34 (3 H, m), 6.74 (1 H, m, 3-H) and 2.93 (3 H, s, 4-Me); *m/z* 181 (M^+, 100%), 180 (92), 152 (22), 91 (11) and 77 (14).

Ethyl 4-methyl-6-trimethylsilylindole-5-carboxylate (**15f**)

A solution of the indole-1-ester (**15h**) (27 mg, 0.07 mmol) in 0.88 ammonia (3 ml) and pyridine (1 ml) was stirred at room temperature for 48 h. Water was added and the mixture extracted with ether. The combined ether extracts were washed with saturated aqueous copper (II) sulfate solution, water, brine, and dried ($MgSO_4$). The solvent was evaporated and the residue chromatographed [ether-light petroleum (1:2)] to give the *title compound* (**15f**) (16 mg, 81%), spectral data given above.

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