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1,4-Dihydropyrano[3,4-*b*]indol-3-ones as Precursors to Indole-2,3-quinodimethanes[1]

Edward B. Fray,[a] Christopher J. Moody*[a,b] and Pritom Shah[b]

[a] Department of Chemistry, Loughborough University of Technology, Loughborough, Leicestershire LE11 3TU, U.K.
[b] Department of Chemistry, Imperial College of Science, Technology & Medicine, London, SW7 2AY, U.K.

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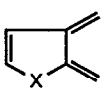
Abstract: The 1,4-dihydropyrano[3,4-*b*]indolones **7**/**8** lose CO_2 on heating to generate the corresponding indole-2,3-quinodimethanes, which can be intercepted in Diels-Alder reactions with a range of dienophiles.

INTRODUCTION

The 5-membered heterocyclic analogues of orthoquinodimethane (*ortho*-xylylene) are of considerable interest both from a theoretical point of view, and for their potential in synthesis. In general, routes to these highly reactive dienes **1** are of two types: 1,4-elimination reactions of suitable 2,3-disubstituted heterocycles **2**, or thermal extrusion of a thermodynamically stable molecule from bicyclic heterocycles **3**. Thus, for example, thiophene-2,3-quinodimethane **1** (X = S) has been generated from 2-chloromethyl-3-methylthiophene **2** (X = S, Y = H, Z = Cl) by flash vacuum pyrolysis,[2] by fluoride induced elimination from **2** (X = S, Y =NMe_3I, Z = $SiMe_3$),[3] or from the thienothiophene dioxide **3** (X = S, Y = SO_2).[4]



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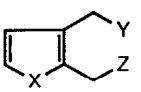

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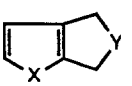

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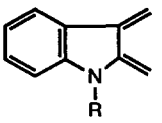
Indole-2,3-quinodimethane **4** is the most widely studied heterocyclic quinodimethane,[5] and intramolecular Diels-Alder reactions of this diene have been used in a number of alkaloid syntheses by Magnus and co-workers.[6] Intermolecular Diels-Alder reactions of this reactive species have, on the other hand, been less successful. The diene has been generated from the 2,3-disubstituted indoles **5** (R =Me or Boc, X = NMe_3I, Y =$SiMe_3$)[7] or (R = COPh or Ac, X = Y= Br),[8-10] or the thieno[3,4-*b*]indole dioxide **6** (R = Ac or Boc)[9] and trapped with reactive dienophiles such as *N*-phenylmaleimide. Although the fact that

SO_2 is so readily extruded from 2,5-dihydrothiophene-1,1-dioxides to generate reactive dienes suggests that other small stable fragments might be similarly lost from appropriate precursors, such extrusions are less commonly used as a preparative route to reactive dienes. As an example of this approach we now report the details of our work on the generation of indole-2,3-quinodimethanes by extrusion of CO_2 from the lactones **7** and **8**, the dihydro versions of pyranoindol-3-ones **9**, compounds much studied by us and others.[5,11]



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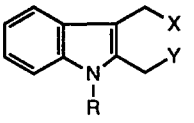

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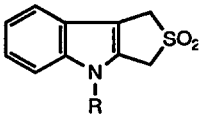

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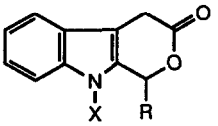
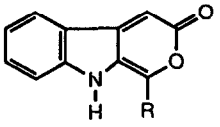


7 X = H
8 X = CO_2Me



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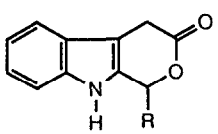
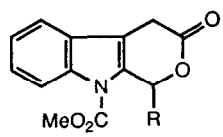
RESULTS AND DISCUSSION

The preparation of dihydropyranoindolones **7** (R = Et and Pr) was first reported by Plieninger and co-workers almost 30 years ago,[12] although only one Diels-Alder reaction of the indole-2,3-quinodimethane generated by elimination of CO_2 from the lactone **7** (R = Et) was described. The reaction involved heating a neat intimate mixture of the lactone **7** (R = Et), prepared by catalytic hydrogenation of the corresponding pyranoindolone **9**, and *N*-phenylmaleimide at 120°C, and gave 6-ethyl-8-phenyl-6,6a,9a,10-tetrahydro-5*H*-pyrrolo[3,4-*b*]carbazole-7,9-dione in 57%. Despite the success of this reaction, and the interest in indole-2,3-quinodimethanes in recent years, the dihydropyranoindolones **7** have not been widely studied since Plieninger's original report.[13] We chose to investigate the scope and limitations of dihydropyranoindolones as precursors to indole-2,3-quinodimethanes using the 'parent' compound **7a** and the 1-alkyl derivatives **7b** and **7c**, together with the *N*-acylated counterparts **8a** and **8b**.

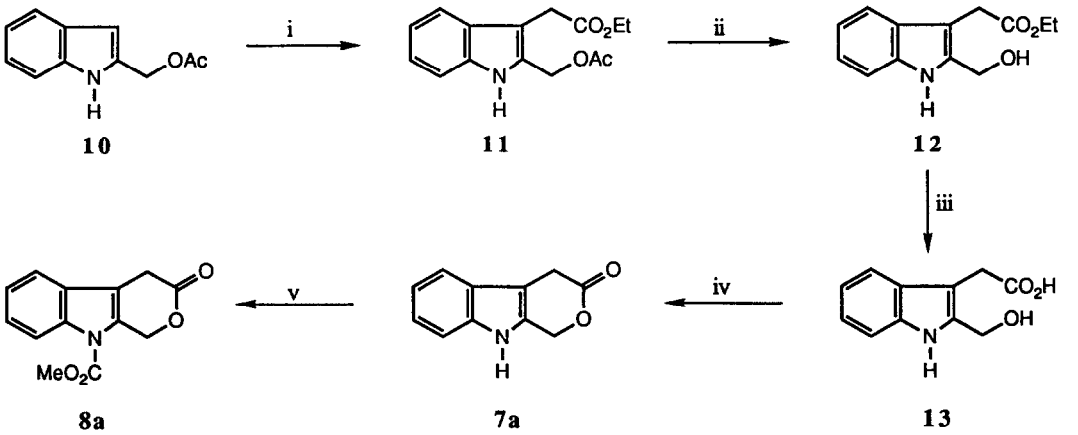


7a R = H
7b R = Me
7c R = C_5H_{11}



8a R = H
8b R = Me

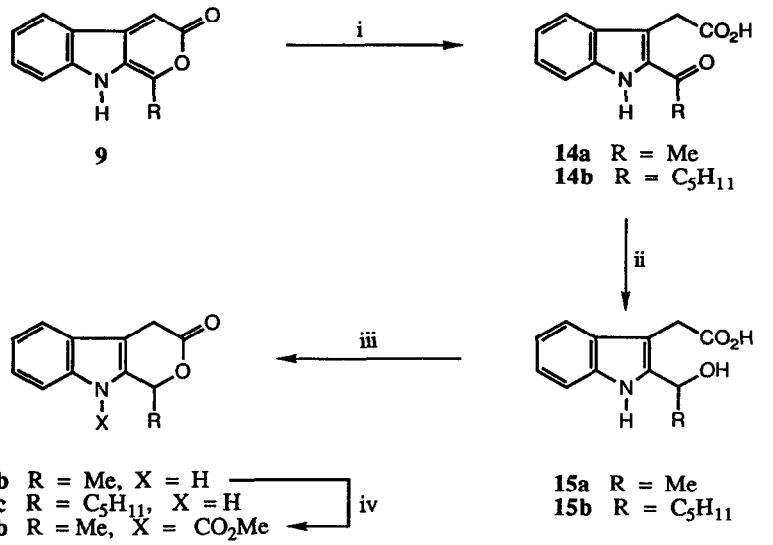
The 'parent' lactone **7a** is in fact a known compound, prepared from 2-acetoxymethylindole **10** (Scheme 1).[14] The compound has also been reported in the patent literature.[15] In our hands the preparation of **7a** was straightforward though poor yielding overall. In particular, the copper catalysed decomposiition of ethyl diazoacetate in the presence of the indole **10** gave at best 35% of the desired indoleacetic ester **11** in a messy reaction. Attempts to improve the reaction by use of rhodium(II) acetate as catalyst were unsuccessful. We also found it more convenient to carry out the hydrolysis of the acetoxy ester **11** in two stages to give the hydroxy acid **13**, which was not purified, but cyclised directly to the desired lactone **7a**. This cyclodehydration could be effected using either isobutyl chloroformate and triethylamine, or dicyclohexyl carbodiimide (DCC). The *N*-substituted compound **8a** was prepared in 91% yield by reaction with dimethyl pyrocarbonate in the presence of 4-dimethylaminopyridine (DMAP). This facile high yielding acylation procedure contrasts sharply with the reported acetylation of **7b** which proceeded in only 5% yield.[9]



Scheme 1. *Reagents*: i, EtO_2CCHN_2, Cu, toluene; ii, K_2CO_3, EtOH; iii, KOH, MeOH, H_2O; iv, i–BuO_2CCl, Et_3N, THF; v, $(MeO_2C)_2O$, DMAP, MeCN.

The preparation of the 1-alkyl derivatives **7b** and **7c** was approached by two routes. Following Plieninger's work,[12] we attempted to hydrogenate the pyranoindole **9** (R = Me). However, this did not give the required dihydro derivative **7b**, but instead resulted in the formation of 2-ethylindole-3-acetic acid. Presumably this derives by further hydrogenolysis of the desired product, a reaction also reported by others.[16] The 1-pentyl pyranoindole **9** ($R = C_5H_{11}$), however, could be reduced to the desired lactone **7c**, albeit in low yield, by hydrogenation over platinum.

The second route (Scheme 2) though longer proved more satisfactory. Thus the pyranoindolone **9** was hydrolysed to the keto acid **14**, which was reduced to the corresponding alcohol **15**, which without purification was cyclodehydrated to the lactones **7** using DCC. The lactone **7b** was acylated under the same conditions as above to give **8b**.



Scheme 2. *Reagents*: i, NaOH, MeOH, H_2O; ii, $NaBH_4$, THF; iii, DCC, pyridine; iv, $(MeO_2C)_2O$, DMAP, MeCN.

Heating the indole lactone **7a** in boiling bromobenzene in the presence of the reactive dienophile *N*-phenylmaleimide (NPM) resulted in the formation of the pyrrolocarbazoledione **16a** in 58% yield. We assume that the reaction proceeds by loss of CO_2 to give the indole-2,3-quinodimethane which is intercepted by the dienophile. The lactones **7b**, **7c**, **8a** and **8b** behave similarly and give the pyrrolocarbazolediones **16b-16e** in varying yield (Table 1). It is interesting to note that the reactions of the *N*-CO_2Me lactones **8** take longer than their *N*-H counterparts. The reactions of the 1-methylpyranoindolones **8b** both gave single isomers of the products **16d**. On the basis of NOE studies, in which pre-irradiation of the H-6 caused enhancement of the signal due to H-6a, the stereochemistry of the adducts was assigned as shown. The stereochemistry of **16c** is assumed to be the same as **16d**. The NMR spectrum of the corresponding pentyl derivative **16e** was complex, and no stereochemical assignment was made.

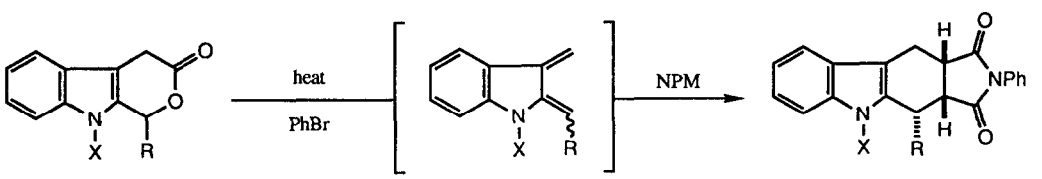


Table 1

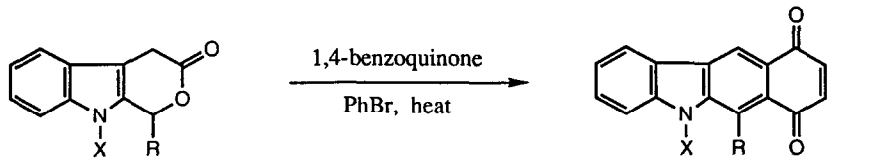
Indole lactone	*X*	*R*	*Time (h)*	*Product*	*Yield (%)*
7a	H	H	5	**16a**	58[a]
8a	CO_2Me	H	26	**16b**	19
7b	H	Me	1	**16c**	50[b]
8b	CO_2Me	Me	6	**16d**	86[b]
7c	H	C_5H_{11}	0.5	**16e**	78[c]

a The corresponding reaction with *N*-methylmaleimide took 4.5 h and gave 50% yield of the product.

b The stereochemistry of the product was assigned by NMR (see text).

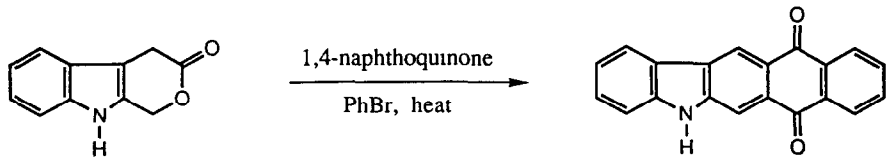
c The stereochemistry of the product was not assigned.

Various other dienophiles were also investigated. When heated in the presence of excess of 1,4-benzoquinone, the lactone **7a** gave the corresponding quinone **17**, presumably formed by dehydrogenation of the initial adduct. Likewise, heating **7a** and 1,4-naphthoquinone gave the quinone **18**. The Diels-Alder reaction was somewhat limited, and, for example, the reaction of the quinodimethane precursor **7a** with dimethyl fumarate, maleic anhydride, dicyanoethylene or dimethyl acetylenedicarboxylate was unsuccessful and resulted in the formation of complex mixtures. However, the use of the *N*-methoxycarbonyl derivative resulted in somewhat cleaner reactions, allowing the isolation of the dimethyl fumarate and dimethyl maleate adducts **19** and **20** (E = CO_2Me) respectively albeit in poor yield. Both of these cycloadditions proceeded stereospecifically with retention to give the *trans*- and *cis*-products. Methyl vinyl ketone (MVK) reacted, also in poor yield, to give a single acetyl tetrahydrocarbazole **21**, although we were unable to assign it as the 2- or 3-isomer. Unfortunately the literature contains conflicting reports on related reactions: the reaction of the *N*-acetyl derivative of **7b** with MVK is reported to give 2,9-diacetyl-1,2,3,4-tetra-hydrocarbazole with 99:1 regioselectivity,[9] whilst the *N*-benzoyl derivative of **7a** is reported to give a 4:1 mixture of the corresponding 3- and 2-acetyl tetrahydrocarbazoles.[10]



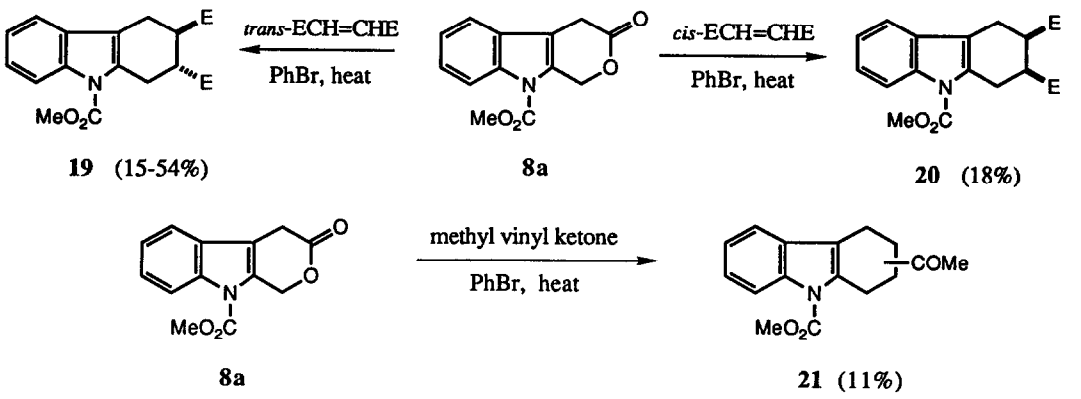
7a R = X = H

17a R = X = H (45%)



7a

18 (31%)



Conclusions

The lactones **7** lose CO_2 on heating and hence are attractive precursors of indole-2,3-quinodimethane. Although incorporation of the electron-withdrawing methoxycarbonyl group often results in a cleaner reaction, the Diels-Alder reactions of the intermediates derived from the lactones **7** and **8** are somewhat limited.

EXPERIMENTAL

Commercially available reagents were used throughout without further purification, except for those detailed below which were purified as described. All solvents were distilled prior to use. 1,4-Benzoquinone and *N*-phenylmaleimide were recrystallised before use. Methyl vinyl ketone, dimethyl maleate and bromobenzene were freshly distilled in a Kugelrohr apparatus prior to use. 'Light petroleum' refers to the fraction of petroleum ether boiling between 40°C and 60°C, and 'ether' refers to diethyl ether. Compounds characterised by high-resolution mass spectrometry were chromatographically homogeneous.

Preparation of 1,4-Dihydropyrano[3,4-*b*]indol-3-ones

1,4-*Dihydropyrano*[3,4-b]*indol*-3-*one* (**7a**).

Potassium carbonate (3.01 g, 21.82 mmol) was added in one portion to a stirred solution of ethyl 2-acetoxymethylindole-3-acetate (**11**)[14] (2.00 g, 7.27 mmol) in ethanol (50 ml). After stirring at room temperature for 30 min, water (150 ml) was added, and the aqueous mixture extracted with ether (2 x 80 ml). The combined ethereal extracts were washed with water (2 x 50 ml), brine (50 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give *compound* (**12**) (1.61 g, 95%), m.p. 112-113°C, (Found: C, 67.1; H, 6.5; N, 6.0. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%); $\nu_{max.}$ (Nujol) 3472, 3226, 1714, 1031, 1008, 985, 739 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.23 (3 H, t, *J* 7 Hz), 3.35 (1 H, br, OH), 3.74 (2 H, s), 4.12 (2 H, q, *J* 7 Hz), 4.68 (2 H, s), 7.05-7.30 (3 H, m), 7.45-7.68 (1 H, m), 8.82 (1 H, br, NH); *m/z* 233 (M^+, 69%), 216 (3), 204 (8), 187 (5), 160 (100), 158 (14), 146 (42), 142 (31), 130 (28).

A mixture of potassium hydroxide (2 M; 20 ml) and methanol (30 ml) was added to the indole-ester (**12**) (2.16 g, 9.27 mmol) and the reaction stirred at room temperature for 15 min. Ether (100 ml) was added and the mixture acidified with dilute phosphoric acid. The organic phase was separated and aqueous extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated to give 2-hydroxymethylindole-3-acetic acid (**13**) as a pale brown gum (1.72 g, 91%).

The above crude product (1.72 g, 8.4 mmol) was dissolved in THF (100 ml) and the solution cooled to 0°C under nitrogen. Triethylamine (2.12 g, 21 mmol, 2.92 ml) was added followed by dropwise addition of *iso*-butyl chloroformate (1.2 g, 8.8 mmol, 1.14 ml) over a period of 10 min. After stirring for 2 h saturated ammonium chloride (100 ml) was added and the mixture extracted with ethyl acetate. The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated and the residue chromatographed (ethyl acetate-light petroleum) to give the title compound (**7a**) (674 mg, 43%), m.p. 169-171°C (darkens, gas evolution observed on heating above 180°C), (lit.,[14] 170°C), $\nu_{max.}$ (Nujol) 3265, 1713, 1456, 1416, 1209, 1193, 1052, 747 cm^{-1}; δ_H [250 MHz; $(CD_3)_2CO$] 3.80 (2 H, t, *J* 1.7 Hz), 5.59 (2 H, t, *J* 1.7 Hz), 7.05 (1 H, ~ t, *J* 7.6 Hz), 7.14 (1 H, ~ t, *J* 7.6 Hz), 7.41 (1 H, br d, *J* 7.6 Hz), 7.48 (1 H, d, *J* 7.6 Hz), 10.20 (1 H, br, NH); *m/z* 187 (M^+, 35%), 143 (100).

Methyl 1,4-*Dihydro*-3-*oxopyrano*[3,4-b]*indole*-9-*carboxylate* (**8a**).
Dimethyl pyrocarbonate (466 mg, 3.48 mmol) was added to a stirred solution of the dihydropyranoindole (**7a**) (325 mg, 1.74 mmol) in acetonitrile (15 ml) followed by DMAP (25 mg, 0.2 mmol). After 20 min, the precipitate which had formed was filtered to give the *title compound* (**8a**) (388 mg, 91%), m.p. 198-202°C, (Found: M^+ 245.0690. $C_{13}H_{11}NO_4$ requires 245.0688); $\nu_{max.}$ (Nujol) 1736 sh, 1723, 1455, 1408, 1361, 1324, 1260, 1221, 1191, 1165, 1147, 1122, 1055, 760 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.78 (2 H, t, *J* 3 Hz), 4.08 (3 H, s), 5.79 (2 H, t, *J* 3 Hz), 7.27-7.40 (2 H, m), 7.43 (1 H, br d, *J* 8 Hz), 8.11 (1 H, br d, *J* 8 Hz); δ_C (62.5 MHz; $CDCl_3$) 172.5, 163.1, 134.8, 133.0, 132.1, 129.9, 128.3, 123.8, 120.1, 116.2, 72.5, 59.4, 38.4; *m/z* 245 (M^+, 100%), 201 (72).

1-*Methyl*-1,4-*dihydropyrano*[3,4-b]*indol*-3-*one* (**7b**).
1-Methylpyrano[3,4-*b*]indol-3-one (**9**, R = Me) (3 g, 11.76 mmol) and sodium hydroxide (2 M; 28.5 ml) were dissolved in methanol (28.5 ml), and the reaction mixture brought to reflux for 20 min. On cooling, the pH of the reaction mixture was brought to 1 with 2 M hydrochloric acid and the brown solid filtered and recrystallised (methanol-water) to give 2-acetylindole-3-acetic acid (**14a**) (2.9 g, 90%), m.p. 202-203°C (lit.,[12] 214°C) (Found: M^+, 217.074 Calc. for $C_{12}H_{11}NO_3$ 217.0738); $\nu_{max.}$ ($CHCl_3$) 3500-2500, 1691, 1665 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 2.48 (3 H, s), 3.94 (2 H, s), 6.94 (1 H, t, *J* 7.5 Hz), 7.15 (1 H, t, *J* 7.5 Hz), 7.24 (1 H, m), 7.50 (1 H, t, *J* 8.8 Hz), 10.45 (1 H, br); *m/z* 218 (MH^+, 100%), 200 (50), 172 (96), 158 (29), 130 (56).

To a stirred solution of the ketoacid (**14a**) (0.3 g, 1.38 mmol) in aqueous THF (5:2) (6.1 ml) was added gradually sodium borohydride (0.157 g, 4.14 mmol) whilst maintaining the temperature at 20°C. After stirring at 20°C for 30 min, ether (30 ml) was added and the mixture acidified with phosphoric acid. The organic layer was removed and the aqueous further extracted with ether (30 ml). The organic fractions were recombined, washed with water, brine and dried (Na_2SO_4), then evaporated under reduced pressure to give the hydroxyacid (**15a**) as an unstable buff oil which was used immediately in the next stage.

The above oil was dissolved in dry pyridine (15 ml) and DCC (0.29 g, 1.40 mmol) added. The reaction was stirred under dry nitrogen at ambient temperature for 18 h. before the pyridine was removed under reduced pressure. The residue was resuspended in dichloromethane and the dicyclohexylurea removed by filtration. The organic liquors were concentrated, passed through a short silica gel column and crystallised (ethyl acetate-dichloromethane) to afford the *title compound* (**7b**) as a crystalline solid (102 mg, 37%). m.p. 150-151°C (decomp. with loss of CO_2), (Found: M^+, 201.0790. $C_{12}H_{11}NO_2$ requires 201.0790); $\nu_{max.}$ (Nujol) 3243, 1709 cm^{-1}; δ_H (250 MHz; d_6-dmso) 1.65 (3 H, d, *J* 6.7 Hz), 3.74 (1 H, dd, *J* 21 Hz, 2.3 Hz), 3.84 (1 H, d, *J* 21 Hz, 2.3 Hz), 5.81 (1 H, m), 7.00 (1 H, dt, *J* 7.8 Hz, 1.2 Hz, 0.9 Hz), 7.11 (1 H, dt, *J* Hz, 1.2 Hz), 7.37 (1 H, dt, *J* 8.5 Hz, 0.9 Hz), 7.45 (1 H, d, *J* 7.7 Hz), 11.20 (1 H, br, s); δ_C (62.5 MHz; $CDCl_3$) 163.2, 141.9, 136.9, 130.1, 126.8, 124.2, 123.2, 116.6, 108.3, 78.6, 38.4, 26.6; *m/z* 202 (MH^+, 100%), 158 (92), 144 (15), 130 (10).

Methyl 1,4-*Dihydro*-1-*methyl*-3-*oxopyrano*[3,4-b]*indole*-9-*carboxylate* (**8b**)
To a mixture of the lactone (**7b**) (0.3 g, 0.15 mmol) and 4-dimethylaminopyridine (23 mg, 0.19 mmol) in acetonitrile (14 ml) was added dropwise dimethyl pyrocarbonate (0.44 g, 0.32 mmol). The mixture was stirred under a calcium chloride drying tube at ambient temperature for 15 min. The precipitate was filtered, the filtrate passed through a short flash silica column (dichloromethane), evaporated, and the residue crystallised (ethyl acetate-dichloromethane) to afford the *title compound* (**8b**) (0.21 g, 53%), m.p. 158.4-158.7°C, (Found: C, 64.9; H, 5.3; N, 5.2. $C_{14}H_{13}NO_4$ requires C, 64.9; H, 5.1; N, 5.4%); (Found: M^+, 259.0845. $C_{14}H_{13}NO_4$ requires 259.0844); $\nu_{max.}$ ($CHCl_3$) 1737 (br) cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.73 (3 H, d, *J* 6.4 Hz), 3.77 (2 H, AB with additional fine splitting, *J* 21.2 Hz), 4.09 (3 H, s), 6.17 (1 H, dt, *J* 8 Hz, 1.7 Hz), 7.26-7.44 (3 H, m), 8.10 (1 H, d, *J* 8 Hz); *m/z* 259 (M^+, 80%), 215 (100), 156 (45), 144 (44), 128 (70).

1,4-*Dihydro*-1-*pentylpyrano*[3,4-b]*indol*-3-*one* (**7c**).
Method A.
Platinum(IV) oxide (6 mg) was added to solution of the pyranoindole (**9**, R = pentyl) (99 mg, 0.39 mmol) in THF (20 ml) and the mixture hydrogenated at atmospheric pressure for 6 h. The reaction mixture was filtered through Celite, the filtrate evaporated and the residue chromatographed to give the *title compound* (**7c**) (14 mg, 14%), m.p. 113-115°C, (Found: C, 74.7; H, 7.5; N, 5.4. $C_{16}H_{19}NO_2$ requires C, 74.7; H, 7.4; N, 5.4%); $\nu_{max.}$ (Nujol) 3255, 1705, 1210, 1028, 741 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 0.87 (3 H, ~ t, *J* 7 Hz) 1.22-1.55 (6 H, m), 1.87-2.19 (2 H, m), 3.87 (2 H, d, *J* 2 Hz), 5.69-5.75 (1 H, m), 7.13-7.28 (2 H, m), 7.40 (1 H, d, *J* 8 Hz), 7.48 (1 H, d, *J* 8 Hz), 8.19 (1 H, br, NH); *m/z* 257 (M^+, 3%), 213 (34), 184 (10), 170 (22), 156 (24), 143 (100), 44 (85).

Method B.
Sodium hydroxide solution (2 M, 40 ml) was added to a solution of pyranoindole (**9**, R = pentyl) (4.228 g, 16.58 mmol) in methanol (40 ml) and the mixture heated on a steam bath for 15 min. The reaction mixture was cooled in an ice bath and then acidified with dilute hydrochloric acid. The resulting pale brown precipitate was filtered and washed with water (15 ml) and dried *in vacuo*. The crude acid was recrystallised from methanol-water to give 2-*hexanoylindole*-3-*acetic acid* (**14b**) (3.25 g, 72%), m.p. 163-165°C, (Found: C, 70.2; H, 6.9; N, 5.1. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%); $\nu_{max.}$ (Nujol) 3340, 1710, 1650, 1535, 1345, 1230, 1220, 750 cm^{-1}; δ_H [250 MHz; $(CD_3)_2CO$] 0.90 (3 H, ~ t, *J* 6.4 Hz)

1.27-1.45 (4 H, m), 1.65-1.79 (2 H, m), 3.02 (2 H, t, *J* 7 Hz), 4.18 (2 H, s), 7.10 (1 H, ddd, *J* 8, 8, and 1 Hz), 7.29 (1 H, ddd, *J* 8, 8 and 1 Hz), 7.47 (1 H, d, *J* 8 Hz), 7.74 (1 H, d, *J* 8 Hz), 10.83 (1 H, br, NH); *m/z* 273 (M^+, 57%), 255 (35), 229 (31), 217 (23), 173 (100), 158 (75), 130 (52).

Sodium borohydride (190 mg, 5.0 mmol) was added to a solution of keto-acid (**14b**) (341 mg, 1.25 mmol), in THF:water (2:5; 10 ml) and the reaction mixture stirred for 10 min. Ether (40 ml) was added and the mixture acidified with dilute phosphoric acid. The organic phase was separated and aqueous extracted with ether. The combined organic extracts were washed with brine, dried, and evaporated to give the hydroxy acid (**15b**) as an unstable yellow oil, $\nu_{max.}$ (Nujol) 3350 br, 1710, 745 cm^{-1}; δ_H [250 MHz; $(CD_3)_2CO$] 0.85 (3 H, ~ t, *J* 7 Hz) 1.20-1.55 (6 H, m), 1.80-1.98 (2 H, m), 3.76 (2 H, s), 5.05 (1 H, t, *J* 6.7 Hz), 6.96-7.09 (2 H, m), 7.35 (1 H, d, *J* 7.5 Hz), 7.53 (1 H, d, *J* 7.5 Hz), 10.10 (1 H, br, NH); *m/z* 257 (M^+-H_2O, 17%), 215 (48), 214 (100), 213 (81), 212 (53), 184 (11), 168 (21), 156 (39), 143 (69).

The above crude hydroxy acid (**15b**) was dissolved in pyridine (8 ml) and DCC (309 mg, 1.5 mmol) added and the reaction allowed to stir at room temperature for 18 h. The pyridine was removed *in vacuo* and dichloromethane (50 ml) added. The resulting solid was filtered and washed well with dichloromethane. The filtrate was concentrated and the residue chromatographed (ether-light petroleum) to give the *title compound* (**7c**) (213 mg, 66%) with identical ^1H NMR and TLC properties to the previous sample described above.

Diels-Alder Reactions

8-*Phenyl*-6,6a,9a,10-*tetrahydro*-5H-*pyrrolo*[3,4-b]*carbazole*-7,9-*dione* (**16a**).
A mixture of the lactone (**7a**) (55 mg, 0.29 mmol) and *N*-phenylmaleimide (61 mg, 0.35 mmol) in bromobenzene (5 ml) was heated under reflux under nitrogen for 5 h. The solvent was evaporated and the residue chromatographed (ethyl acetate-hexane) to give the *title compound* (**16a**) (54 mg, 58%), m.p. 200-201°C, (Found: M^+, 316.1215. $C_{20}H_{16}N_2O_2$ requires 316.1212); $\nu_{max.}$ (Nujol) 3393, 1697, 1497, 1392, 1312, 1188, 1142, 742 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 3.05-3.18 (2 H, m), 3.38-3.60 (4 H, m), 7.05-7.18 (4 H, m), 7.25-7.40 (4 H, m), 7.50 (1 H, d, *J* 7.5 Hz), 7.98 (1 H, br, NH); *m/z* 316 (M^+, 100%), 168(36), 143(89).

8-*Methyl*-6,6a,9a,10-*tetrahydro*-5H-*pyrrolo*[3,4-b]*carbazole*-7,9-*dione*.
A mixture of the lactone (**7a**) (97 mg, 0.52 mmol) and *N*-methylmaleimide (115 mg, 1.04 mmol) in bromobenzene (12 ml) was heated under reflux under nitrogen for 4.5 h. The solvent was evaporated and the residue chromatographed (dichloromethane) to give the *title compound* (66 mg, 50%), m.p. 223-227°C, (Found: C, 70.7; H, 5.5; N, 10.9. $C_{15}H_{14}N_2O_2$ requires C, 70.8; H, 5.55; N, 11.0%); $\nu_{max.}$ (Nujol) 3362, 1767, 1695, 1435, 1386, 1324, 1289, 1117, 1102, 1014, 879, 750, 736 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 2.87 (3 H, s), 2.90-3.13 (2 H, m), 3.31-3.48 (4 H, m), 7.07-7.18 (2 H, m), 7.30 (1 H, br d, *J* 8 Hz), 7.50 (1 H, br d, *J* 8 Hz), 7.97 (1 H, br, NH); *m/z* 254 (M^+, 76%), 143 (100).

Methyl 7,9-*Dioxo*-8-*phenyl*-6,6a,9a,10-*tetrahydropyrrolo*[3,4-b]*carbazole*-5-*carboxylate* (**16b**)
A mixture of the lactone (**8a**) (50 mg, 0.21 mmol) and *N*-phenylmaleimide (38.8 mg, 0.22 mmol) was dissolved in bromobenzene (5 ml) and heated to reflux under dry nitrogen for 26 h. The solvent was

evaporated under reduced pressure and the residue subjected to silica gel flash chromatography (ether-light petroleum) to afford the *title compound* (**16b**) (14.5 mg, 19%) as a buff oil, (Found: M^+, 374.1267. $C_{22}H_{18}N_2O_4$ requires 374.1266); $\nu_{max.}$ ($CHCl_3$) 3422, 1709 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 3.31-3.59 (6 H, m), 4.04 (3 H, s), 7.06-7.40 (8 H, m), 8.05 (1 H, d); *m/z* 374 (M^+, 100%), 316 (40), 201 (23), 168 (28), 167 (45).

6-*Methyl*-8-*phenyl*-6,6a,9a,10-*tetrahydropyrrolo*[3,4,b]*carbazole*-7,9-*dione* (**16c**)
The lactone (**7b**) (50 mg, 0.249 mmol) and *N*-phenylmaleimide (0.116 g, 0.675 mmol) in bromobenzene (6 ml) was brought to reflux for 1 h. On cooling the residual solvent was removed under reduced pressure and the residue subjected to silica gel flash chromatography (ether-light petroleum) to afford the *title compound* (**16c**) (41.1 mg, 50%) as a pale brown oil, (Found:M^+ 330.1368. $C_{21}H_{18}N_2O_2$ requires 330.1368); $\nu_{max.}$ ($CHCl_3$) 3400 (br), 1702 (br) cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.97 (3 H, d, *J* 7.1 Hz), 3.56 (1 H, m), 3.78 (1 H, m), 4.02 (2 H, m), 4.15 (1 H, m), 7.48 (2 H, m), 7.54 (2 H, m), 7.83 (4 H, m), 7.93 (1 H, m), 10.64 (1 H, br, s); *m/z* 330 (M^+, 50%), 167 (63), 157 (100).

Methyl 7,9-*Dioxo*-6-*methyl*-8-*phenyl*-6,6a,9a,10-*tetrahydropyrrolo*[3,4-b]*carbazole*-5-*carboxylate* (**16d**)
A mixture of the lactone (**8b**) (50 mg, 0.25 mmol) and *N*-phenylmaleimide (117 mg, 0.68 mmol) in bromobenzene (6 ml) was heated under reflux for 6 h. On cooling the solvent was removed under reduced pressure and the residue subjected to flash chromatography on silica gel (ether-light petroleum) to give a crude product. Trituration of the crude with ether at 0°C afforded the *title compound* (**16d**) as a white solid (70.6 mg, 86%), m.p. 181-182°C, (Found: M^+, 388.1423. $C_{23}H_{20}N_2O_4$ requires 388.1423); $\nu_{max.}$ ($CHCl_3$) 1736, 1715, 1713 cm^{-1}; δ_H (250 MHz; d_8-toluene) 1.06 (3 H, d, *J* 6.9 Hz), 2.63-2.70 (1 H, m), 2.82-2.86 (1 H, m), 2.88-3.05 (2 H, m), 3.40 (3 H, s), 4.41 (1 H, quint. *J* 6.9 Hz), 7.13-7.25 (6 H, m), 7.39-7.42 (2 H, m), 8.24 (1 H, d, *J* 8.2 Hz); δ_C (62.5 MHz; $CDCl_3$) 178.9, 176.6, 152.1, 138.3, 135.9, 131.6, 129.3, 128.7, 128.5, 126.4, 124.6, 123.3, 117.8, 115.9, 115.0, 53.7, 45.4, 38.7, 30.0, 17.8, 15.5; *m/z* 388 (M^+, 100%), 373 (20), 328 (15), 215 (56), 194 (53), 18) (58), 166 (78).

6-*Pentyl*-8-*phenyl*-6,6a,9a,10-*tetrahydro*-5H-*pyrrolo*[3,4-b]*carbazole*-7,9-*dione* (**16e**).
A mixture of the lactone (**7c**) (54 mg, 0.21 mmol) and *N*-phenylmaleimide (99 mg, 0.57 mmol) in bromobenzene (6 ml) was heated under reflux under nitrogen for 0.5 h. The solvent was evaporated and the residue chromatographed (dichloromethane-light petroleum-dichloromethane-ether) to give the *title compound* (**16e**) (63 mg, 78%), m.p. 187-189°C, then resolidifies and melts again at 213-215°C, (Found: C, 77.9; H, 6.85; N, 7.3. $C_{25}H_{26}N_2O_2$ requires C, 77.7; H, 6.8; N, 7.25%); $\nu_{max.}$ (Nujol) 3385, 1698, 743 cm^{-1}; δ_H [250 MHz; $(CD_3)_2CO$] 0.85 (3 H, ~ t, *J* 7.5 Hz), 1.20-1.70 (6 H, m), 1.73-1.92 (2 H, m), 3.12-3.30 (2 H, m), 3.35-3.47 (1 H, m), 3.59-3.75 (2 H, m), 6.96-7.52 (9 H, m), 10.30 (1 H, br); *m/z* 386 (M^+, 100%), 315 (40), 168 (80).

5H-*Benzo*[b]*carbazole*-7,10-*dione* (**17**).
A mixture of the lactone (**7a**) (114 mg, 0.61 mmol) and 1,4-benzoquinone (197 mg, 1.82 mmol) in bromobenzene (15 ml) was heated under reflux under nitrogen for 2.5 h. The solvent was evaporated and the residue chromatographed (ether-dichloromethane) to give the *title compound* (**17**) (65 mg, 45%), m.p. darkens ~ 260°C, (Found: M^+, 247.0636. $C_{16}H_9NO_2$ requires 247.0633); $\nu_{max.}$ (Nujol) 3313, 1658,

1622, 1593, 1357, 835, 751, 728 cm^{-1}; δ_H [270 MHz; $(CD_3)_2CO$] 7.01 (2 H, s), 7.34 (1 H, ~ t, *J* 8 Hz), 7.56 (1 H, ~ t, *J* 8 Hz), 7.66 (1 H, d, *J* 8 Hz), 8.15 (1 H, s), 8.39 (1 H, d, *J* 8 Hz), 8.82 (1 H, s), 11.13 (1 H, br, NH); *m/z* 247 (M^+, 100%), 219 (18), 191 (20), 165 (20).

5H-*Naptho*[2,3-b]*carbazole*-7,12-*dione* (**18**).
A mixture of the lactone (**7a**) (74 mg, 0.4 mmol) and 1,4-naphthoquinone (120 mg, 0.76 mmol) in bromobenzene (10 ml) was heated under reflux under nitrogen for 3 h. The solvent was evaporated and the residue chromatographed (dichloromethane) to give the *title compound* (**18**) (36 mg, 31%), m.p. > 290°C sublimes ~ 230°C, (Found: M^+, 277.0792. $C_{20}H_{11}NO_2$ requires *M*, 297.0790); $\nu_{max.}$ (Nujol) 3297, 1665, 1622, 1593, 1357, 1281, 706 cm^{-1}; δ_H [270 MHz; $(CD_3)_2CO$] 7.36 (1 H, ~ t, *J* 8 Hz), 7.58 (1 H, ~ t, *J* 8 Hz), 7.68 (1 H, d, *J* 8 Hz), 7.83-7.96 (2 H, m), 8.27-8.37 (2 H, m), 8.41 (1 H, s), 8.43 (1 H, d, *J* 7.7 Hz), 9.08 (1 H, s), 11.15 (1 H, br, NH); *m/z* 297 (M^+, 100%), 269 (11), 241 (13), 240 (14).

trans-*Trimethyl* 1,2,3,4-*tetrahydrocarbazole*-2,3,9-*tricarboxylate* (**19**).
A mixture of the lactone (**8a**) (75 mg, 0.31 mmol) and dimethyl fumarate (104 mg, 0.72 mmol) in bromobenzene (8 ml) was heated under reflux under nitrogen for 26 h. The solvent was evaporated and the residue chromatographed (ether) to give the *title compound* (**19**) (263) (57 mg, 54%), m.p. 88-88.5°C, (Found: C, 62.5; H, 5.5; N,4.0. $C_{18}H_{19}NO_6$ requires C, 62.5; H, 5.6; N, 4.1%); $\nu_{max.}$ ($CHCl_3$) 1735 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.78-2.86 (1 H, m), 3.08-3.23 (4 H, m), 3.50-3.55 (1 H, m), 3.75 (6 H, s), 3.86 (3 H, s), 7.20-7.36 (2 H, m), 7.39 (1 H, m), 8.11 (1 H, d, *J* 6.9 Hz); δ_C (100 MHz; $CDCl_3$), 174.6, 174.4, 152.2, 135.8, 132.3, 128.7, 124.2, 123.0, 117.6, 115.4, 115.0, 53.4, 52.1, 52.0, 42.3, 41.1, 27.5, 23.5; *m/z* 345 (M^+, 48%), 285 (47), 226 (54), 194 (50), 167 (44), 47 (100).
In a subsequent experiment carried out a smaller scale, the yield was 15%.

cis-*Trimethyl* 1,2,3,4-*tetrahydrocarbazole*-2,3,9-*tricarboxylate* (**20**)
The lactone (**8a**) (50 mg, 0.21 mmol) was dissolved in dimethyl maleate (2 ml) and the mixture heated to reflux under dry nitrogen for 26 h. The excess dimethyl maleate was removed under reduced pressure and the residue subjected to preparative thin layer chromatography on silica gel (ether-light petroleum) to afford the *title compound* (**20**) (13 mg, 18%), m.p. 88-89°C, (Found: C, 62.6; H, 5.6; N,4.0. $C_{18}H_{19}NO_6$ requires C, 62.5; H, 5.6; N, 4.1%); $\nu_{max.}$ ($CHCl_3$) 1735 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.96-3.03 (1 H, m) 3.15-3.37 (4 H, m) 3.57-3.62 (1 H, m), 3.70 (3 H, s), 3.71 (3 H, s), 4.02 (3 H, s), 7.23-7.29 (2 H, m), 7.40-7.44 (1 H, m), 8.10 (1 H, d, *J* 7.1 Hz); δ_C (100 MHz; $CDCl_3$), 173.1, 172.9, 152.2, 135.9, 132.7, 129.0, 124.0, 122.8, 117.7, 115.4, 115.2, 53.4, 52 0, 51.9, 40.9, 39.9, 26.1, 21.6.

Methyl 2-*Acetyl*-1,2,3,4-*tetrahydrocarbazole*-9-*carboxylate or methyl* 3-*acetyl*-1,2,3,4 *tetrahydrocarbazole*-9-*carboxylate*
The lactone (**8a**) (50 mg, 0.21 mmol) and methyl vinyl ketone (21.4 mg, 0.31 mmol) were dissolved in bromobenzene (5 ml) and heated to reflux for 16 h. On cooling the excess solvent and methyl vinyl ketone were removed under reduced pressure and the residue subjected to flash chromatography on silica gel (ether light petroleum) to afford a brown oil (6 mg, 11%), (Found. M^+, 271.1208. $C_{16}H_{17}NO_3$ requires 271.1208); ν_{max} ($CHCl_3$) 1707, 1702, 1655, 1648, 1643, 1632 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 1.74-1.90 (1 H, m), 2.14-2.25 (2 H, m), 2.27 (3 H, s), 2.57-3.33 (4 H, m), 4.03 (3 H, s), 7.23-7.38 (3 H, m), 8.10-8.13 (1 H, m); *m/z* 271 (M^+, 53%), 228 (100), 167 (40).

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