

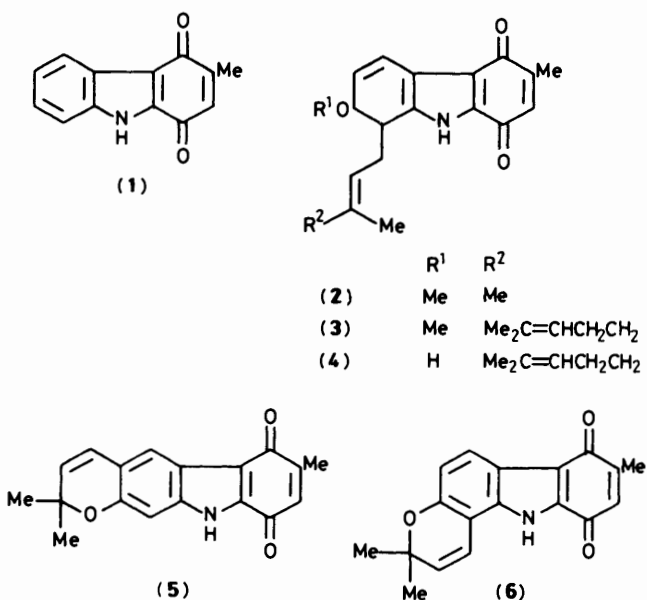
Synthesis of the Carbazole Alkaloid Murrayaquinone-B¹

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A synthesis of the carbazolequinone alkaloid murrayaquinone-B (2) is described. The route to the 1-methoxycarbazole (14a) involves a regioselective Claisen rearrangement to give the 7-(3-methylbut-2-enyl)indole (9a), and formation of the third ring of compound (14a) by cyclisation of the aldehyde (13a), which is prepared from the lactone (11a) (Scheme 1). The methoxycarbazole (14b), which lacks three methyl groups, was prepared by a similar route. Photo-oxidation of the carbazole (14a) gave murrayaquinone-B (2), although a similar photo-oxidation of the pyranocarbazole (21), prepared in an analogous manner (Scheme 2), failed to yield the related carbazolequinone alkaloid, pyrayaquinone-B (6).

Recent studies on the extracts of the root bark of *Murraya euchrestifolia* Hayata have yielded the first examples of naturally occurring carbazolequinones: murrayaquinones-A (1), -B (2), -C (3), and -D (4),^{2,3} and pyrayaquinones-A (5) and -B (6).⁴ In continuation of our interest in heterocyclic quinones from natural sources,⁵ we now report the details of the first synthesis

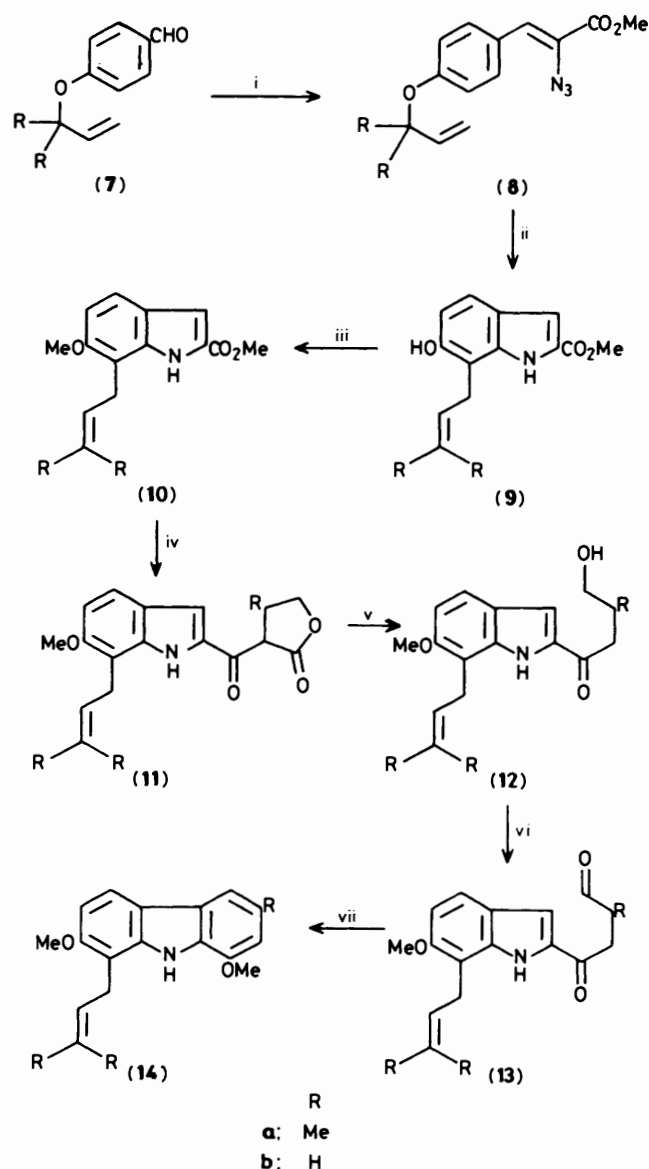


of murrayaquinone-B (2). Since the publication of our preliminary account of this work,¹ other synthetic work in the area has been reported.⁶

Results and Discussion

The overall approach to murrayaquinone-B (2) combines our previous work on the regioselective Claisen rearrangement in indoles⁷ with the new route to 1-oxygenated carbazoles described in the preceding paper.⁸ Thus the key steps in the sequence are the facile formation of the indole (9a) by sequential indolisation and Claisen rearrangement, followed by annelation of the third ring.

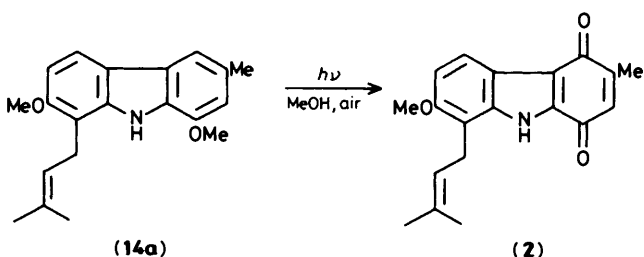
4-(1,1-Dimethylallyloxy)benzaldehyde⁹ (7a) was condensed with methyl azidoacetate under the usual conditions⁵ to give the azide (8a) in 86% yield. When the azide (8a) was heated in toluene for 3 h concomitant indole formation and regio-



Scheme 1. Reagents: i, MeO₂CCH₂N₃, NaOMe, MeOH, -15 °C; ii, toluene (R = Me) or bromobenzene (R = H), reflux; iii, MeI, K₂CO₃, acetone; iv, 4-R-butyrolactone, NaOMe, dioxane; v, H₂O, NaOH, dioxane; vi, PCC, CH₂Cl₂, NaOAc; vii, MeOH-BF₃.

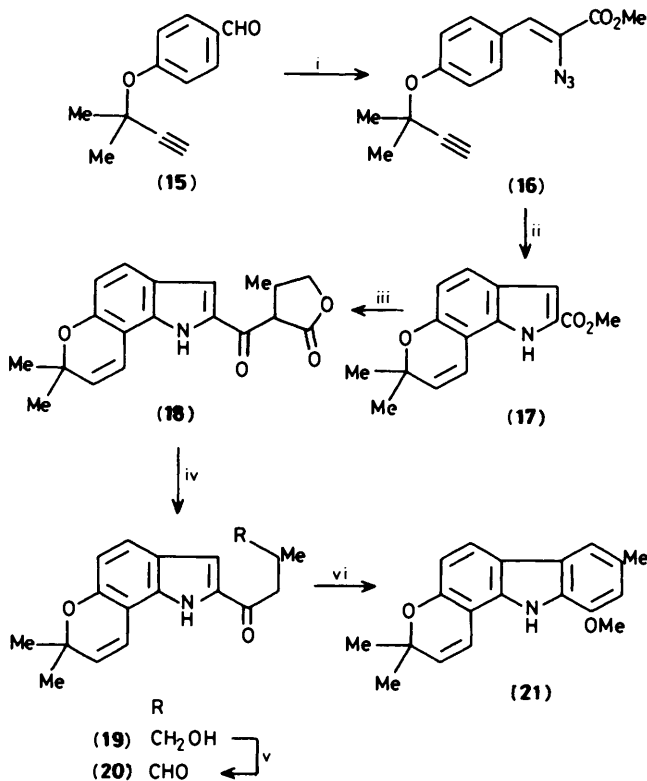
selective Claisen rearrangement occurred to form the 6-hydroxyindole (**9a**) (53%), which was converted into the corresponding 6-methoxyindole (**10a**) by treatment with iodomethane and potassium carbonate in acetone. In an exactly analogous sequence, 4-allyloxybenzaldehyde¹⁰ (**7b**) was converted into the indole (**10b**), although the azide (**8b**) needed to be heated in bromobenzene (156 °C) to effect the Claisen rearrangement part of the sequence.⁷

The remaining carbons required for the third ring were added by a simple Claisen condensation^{8,11} of the indole ester (**10a**) with 4-methylbutyrolactone to give the lactone (**11a**), which when heated in aqueous dioxane containing a trace of sodium hydroxide underwent hydrolysis and decarboxylation to give the alcohol (**12a**) (85%). Oxidation of the alcohol (**12a**) with pyridinium chlorochromate (PCC) gave the corresponding aldehyde (**13a**), which was cyclised into the required carbazole (**14a**) by stirring in a boron trifluoride-methanol complex at



room temperature (Scheme 1). Similarly the indole (**10b**) was converted into the 'tridemethyl' derivative (**14b**).

Since model studies on the carbazole (**14b**), which lacks three methyl groups, suggested that the ring-C methoxy group could

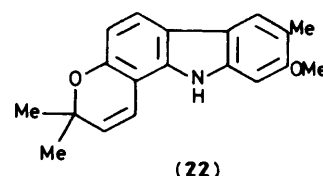


Scheme 2. Reagents: i, $\text{MeO}_2\text{CCH}_2\text{N}_3$, NaOMe, MeOH; ii, toluene, reflux; iii, 4-Me-butylolactone, NaOMe, dioxane; iv, H_2O , NaOH, dioxane; v, PCC, NaOAc, CH_2Cl_2 ; vi, MeOH- BF_3

not be selectively demethylated using boron tribromide, a route to murrayaquinone-B (**2**) from the 1,7-dimethoxy-3-methyl-8-(3-methylbut-2-enyl)carbazole (**14a**) by oxidation of the corresponding 1-hydroxy derivative seemed inappropriate. However, photo-oxidation³ of the 1-methoxycarbazole (**14a**) by irradiation of an aerated methanol solution gave murrayaquinone-B (**2**) directly, albeit in low yield, whose spectral properties were identical with those of the natural product.

A similar regioselective Claisen rearrangement was also used in an approach to the related carbazolequinone alkaloid, pyrayaquinone-B (**6**).⁴ Thus 4-(1,1-dimethylprop-2-ynoxy)benzaldehyde⁹ (**15**) was converted into the pyranindole (**17**) via the azide (**16**) (Scheme 2). It is well known that aryl prop-2-ynyl ethers rearrange to form cyclised products on heating,¹² and as expected, in this indole case, the rearrangement was regioselective. The pyranindole (**17**) was subsequently converted into the pyranocarbazole (**21**) (Scheme 2) by an analogous route to that used for the carbazole (**14a**). Unfortunately photo-oxidation of the methoxycarbazole (**21**) resulted in its complete decomposition, and no pyrayaquinone-B (**6**) was isolated.

Interestingly, since our work was completed, the methoxy-pyranocarbazole (**21**) has been synthesized by other workers,¹³ as one of the possible structures for the new carbazole alkaloid pyrayafoline. The spectral data for synthetic compound (**21**) obtained by both routes are identical. The natural product, pyrayafoline, however, has the isomeric structure (**22**)¹³ with a



different oxygenation pattern to pyrayaquinone-B (**6**), despite the fact that both alkaloids are obtained from the same plant source.

Experimental

For general points see ref. 8.

Methyl 2-Azido-3-[4-(1,1-dimethylallyloxy)phenyl]propionate (8a).—Sodium (1.23 g, 53 mmol) was added to dry methanol (30 ml) under nitrogen and the solution cooled to -15°C . A solution of 4-(1,1-dimethylallyloxy)benzaldehyde⁹ (**7a**) (2.56 g, 13.5 mmol) and methyl azidoacetate (6.18 g, 54 mmol) in dry methanol (4 ml) was added over 15 min the temperature being maintained at -15°C . The reaction mixture was stirred for 3 h at this temperature and then allowed to warm to room temperature over 3 h. The flask contents were poured into water (50 ml) and extracted with ether (100 ml). The ethereal extracts were washed with water (2×50 ml), dried (MgSO_4), and concentrated under reduced pressure to give the title compound (**8a**) (3.33 g, 86%) as a lemon-yellow oil, ν_{max} (film) 2120, 1710, 1620, and 1600 cm^{-1} ; δ (90 MHz; CDCl_3) 1.50 (6 H, s, Me), 3.92 (3 H, s, OMe), 5.11–5.38 (2 H, m, $\text{CH}=\text{CH}_2$), 6.00–6.40 (1 H, m, $\text{CH}=\text{CH}_2$), 6.90 (1 H, s, 3-H), 7.02 (2 H, d, J 9 Hz, ArH), and 7.72 (2 H, d, J 9 Hz, ArH); m/z (100 °C) 287 (M^+ , 4%), 259 (23), 242 (22), 203 (11), 191 (81), 183 (6), 172 (12), 159 (66), 147 (12), 132 (100), and 69 (89).

Methyl 6-Hydroxy-7-(3-methylbut-2-enyl)indole-2-carboxylate (9a).—A solution of the azide (**8a**) (0.92 g, 3.21 mmol) in dry toluene (40 ml) was refluxed for 3 h under nitrogen, and then

evaporated under reduced pressure to give a red foam. The crude product was chromatographed on silica (14 g), eluting with light petroleum-ether, to give the *title compound* (**9a**) (0.44 g, 53%) as a lemon-yellow crystalline solid, m.p. 129–130 °C (Found: C, 69.3; H, 6.65; N, 5.4. $C_{15}H_{17}NO_3$ requires C, 69.5; H, 6.6; N, 5.4%; ν_{\max} (Nujol) 3 460 (NH), 3 340br (OH), 1 690, and 1 630 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.79 (3 H, d, *J* 1.5 Hz, Me), 1.88 (3 H, s, Me), 3.56 (2 H, d, *J* 6 Hz, $CH_2CH=$), 3.92 (3 H, s, CO_2Me), 5.34 (1 H, m, $CH_2CH=$), 5.38 (1 H, s, OH), 6.73 (1 H, d, *J* 8 Hz, 5-H), 7.15 (1 H, d, *J* 2 Hz, 3-H), 7.41 (1 H, d, *J* 8 Hz, 4-H), and 8.76 (1 H, br s, NH); *m/z* (140 °C) 259 (M^+ , 82%), 226 (8), 212 (18), 203 (73), 199 (9), 184 (19), 172 (100), 157 (7), 143 (7), 128 (7), and 115 (15).

Methyl 6-Methoxy-7-(3-methylbut-2-enyl)indole-2-carboxylate (10a).—A mixture of the hydroxyindole (**9a**) (0.58 g, 2.24 mmol), iodomethane (2.1 ml, 34.00 mmol), and potassium carbonate (0.51 g, 3.70 mmol) in acetone (20 ml) was heated under reflux for 14.5 h. The mixture was cooled, filtered, and evaporated under reduced pressure and the residue extracted with ether (75 ml) and water (10 ml). The ethereal extracts were washed with aqueous sodium hydroxide (1M; 4 × 50 ml) and water (2 × 50 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give a yellow solid that was recrystallised from hexane-chloroform to yield the *title compound* (**10a**) (0.43 g, 70%) as a pale lemon-yellow crystalline solid, m.p. 142–143 °C (Found: C, 70.2; H, 7.0; N, 5.1. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%; ν_{\max} (Nujol) 3 350, 1 620, and 1 255 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.76 (3 H, d, *J* 1.5 Hz, Me), 1.89 (3 H, s, Me), 3.59 (2 H, d, *J* 6 Hz, $CH_2CH=$), 3.90 (3 H, s, OMe), 3.92 (3 H, s, OMe), 5.29 (1 H, m, $CH_2CH=$), 6.90 (1 H, d, *J* 8 Hz, 5-H), 7.15 (1 H, d, *J* 2 Hz, 3-H), 7.49 (1 H, d, *J* 8 Hz, 4-H), and 8.69 (1 H, br s, NH); *m/z* (150 °C) 273 (M^+ , 100%), 258 (10), 242 (7), 226 (34), 218 (24), 213 (17), 205 (8), 198 (14), 186 (39), 182 (6), 173 (6), 156 (9), 128 (6), and 115 (6).

4,5-Dihydro-3-[6-methoxy-7-(3-methylbut-2-enyl)indol-2-ylcarbonyl]-4-methylfuran-2-one (11a).—A mixture of the indole (**10a**) (0.28 g, 1.0 mmol), 4,5-dihydro-4-methylfuran-2-one (0.41 g, 4.1 mmol), and sodium methoxide (0.44 g, 8.15 mmol) in dry dioxane (5 ml) was heated at 110 °C for 45 h under nitrogen. Ice-water (5 ml) was added and the mixture acidified to pH 4–6. The mixture was extracted with chloroform (80 ml) and the extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The crude product was chromatographed on silica (6 g), eluting with light petroleum-ether, to give the *title compound* (**11a**) (0.23 g, 67%) as a lemon-yellow crystalline solid, m.p. 159–160 °C (Found: C, 70.2; H, 6.8; N, 4.1. $C_{20}H_{23}NO_4$ requires C, 70.4; H, 6.7; N, 4.1%; ν_{\max} (Nujol) 3 360, 1 770, 1 645, and 1 620 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.25 (3 H, d, *J* 8 Hz, $CHMe$), 1.76 (3 H, d, *J* 2 Hz, Me), 1.88 (3 H, s, Me), 3.22 (1 H, m, 4-H), 3.57 (2 H, d, *J* 6 Hz, $CH_2CH=$), 3.91 (3 H, s, OMe), 3.98 (2 H, m, 5-H), 4.62 (1 H, dd, *J* 8, 6 Hz, 3-H), 5.26 (1 H, m, $CH_2CH=$), 6.91 (1 H, d, *J* 8 Hz, 5-ArH), 7.29 (1 H, d, *J* 2 Hz, 3-ArH), 7.54 (1 H, d, *J* 8 Hz, 4-ArH), and 8.91 (1 H, br s, NH); *m/z* (180 °C) 341 (M^+ , 100%), 286 (46), 273 (7), 242 (13), 226 (51), 214 (17), 210 (19), 186 (35), 172 (5), and 156 (15).

4-Hydroxy-1-[6-methoxy-7-(3-methylbut-2-enyl)indol-2-yl]-3-methylbutan-1-one (12a).—The indole (**11a**) (0.133 g, 0.39 mmol), dioxane (1.75 ml), and water (1.75 ml) were heated together at 110 °C in the presence of a few drops of dilute aqueous sodium hydroxide for 20 h. The mixture was concentrated under reduced pressure and cooled in ice to give a solid which was filtered off, and dried to give the *title compound* (**12a**) (0.105 g, 85%) as a beige crystalline solid, m.p. 79–80 °C (from hexane-chloroform) (Found: C, 72.3; H, 8.0; N, 4.4. C_{19} -

$H_{25}NO_3$ requires C, 72.4; H, 7.9; N, 4.4%; ν_{\max} (Nujol) 3 340br (NH, OH), 1 645, and 1 620 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.03 (3 H, d, *J* 6 Hz, $CHMe$), 1.74 (3 H, d, *J* 1 Hz, Me), 1.88 (3 H, s, Me), 2.20 (1 H, br s, OH), 2.37 (1 H, m, 3-H), 2.83 (1 H, dd, *J* 14, 6 Hz, 4-H), 3.03 (1 H, dd, *J* 14, 6 Hz, 4-H), 3.47–3.71 (2 H, m, 2-H), 3.57 (2 H, d, *J* 6 Hz, $CH_2CH=$), 3.89 (3 H, s, OMe), 5.26 (1 H, m, $CH_2CH=$), 6.89 (1 H, d, *J* 8 Hz, 5-ArH), 7.18 (1 H, d, *J* 2 Hz, 3-ArH), 7.51 (1 H, d, *J* 8 Hz, 4-ArH), and 8.89 (1 H, br s, NH); *m/z* (140 °C) 315 (M^+ , 100%), 297 (89), 282 (92), 273 (11), 266 (13), 257 (71), 242 (26), 226 (20), 214 (12), 210 (8), 202 (11), 198 (13), 186 (33), 182 (7), 172 (8), 168 (8), 156 (13), 144 (7), 128 (10), and 115 (8).

1-[6-Methoxy-7-(3-methylbut-2-enyl)indol-2-yl]-3-methylbutane-1,4-dione (13a).—A solution of the alcohol (**12a**) (65.2 mg, 0.21 mmol) in dry dichloromethane (1.5 ml) was added to PCC (66.3 mg, 0.31 mmol) and anhydrous sodium acetate (4.95 mg, 0.06 mmol) in dry dichloromethane (3 ml) under nitrogen. The mixture was stirred at room temperature for 2.5 h. Dry ether (6 ml) was added and the liquid decanted off; this procedure was repeated three times. The ethereal product was filtered through a Florisil pad and the filtrate was evaporated under reduced pressure to give the *title compound* (**13a**) (54.2 mg, 84%) as a beige solid, m.p. 114.5–115.5 °C (purified by chromatography) (Found: C, 72.5; H, 7.4; N, 4.4. $C_{19}H_{23}NO_3$ requires C, 72.8; H, 7.35; N, 4.5%; ν_{\max} (Nujol) 3 350, 1 730, 1 700, 1 645, 1 620, and 1 260 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.25 (3 H, d, *J* 8 Hz, $CHMe$), 1.75 (3 H, s, Me), 1.88 (3 H, s, Me), 2.97 (1 H, dd, *J* 15, 6 Hz, 2-H), 3.10 (1 H, m, 3-H), 3.40 (1 H, dd, *J* 15, 6 Hz, 2-H), 3.57 (2 H, d, *J* 6 Hz, $CH_2CH=$), 3.90 (3 H, s, OMe), 5.26 (1 H, m, $CH_2CH=$), 6.90 (1 H, d, *J* 8 Hz, 5-ArH), 7.19 (1 H, d, *J* 2 Hz, 3-ArH), 7.52 (1 H, d, *J* 8 Hz, 4-ArH), 8.82 (1 H, br s, NH), and 9.80 (1 H, s, CHO); *m/z* (150 °C) 313 (M^+ , 100%), 297 (39), 282 (43), 270 (11), 259 (32), 242 (22), 230 (12), 226 (18), 214 (19), 200 (12), 186 (40), 172 (9), 167 (7), 156 (12), 128 (10), and 115 (9).

1,7-Dimethoxy-3-methyl-8-(3-methylbut-2-enyl)-9H-carbazole (14a).—Boron trifluoride-methanol complex (14% w/v; 0.75 ml, 1.54 mmol) was added to a solution of the aldehyde (**13a**) (34.5 mg, 0.11 mmol) in dry methanol (0.5 ml) under nitrogen, and the mixture stirred at room temperature for 17 h. The dark mauve solution was poured into water (4 ml) and extracted with ether (20 ml). The organic extracts were washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was chromatographed on silica (1 g), eluting with light petroleum-dichloromethane, to yield the *title compound* (**14a**) (15.7 mg, 46%) as a colourless solid, m.p. 103–105 °C (Found: C, 78.0; H, 7.6; N, 4.6. $C_{20}H_{23}NO_2$ requires C, 77.7; H, 7.4; N, 4.5%; λ_{\max} (EtOH) 225sh (log ϵ 4.44), 242 (4.58), 252 (4.54), 299 (3.99), 320sh (3.59), and 335sh nm (3.49); ν_{\max} (Nujol) 3 380, 1 630, 1 620, 1 595, and 1 230 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.74 (3 H, d, *J* 1 Hz, Me), 1.90 (3 H, s, Me), 2.51 (3 H, s, ArMe), 3.63 (2 H, d, *J* 6 Hz, $CH_2CH=$), 3.92 (3 H, s, OMe), 4.00 (3 H, s, OMe), 5.32 (1 H, m, $CH_2CH=$), 6.67 (1 H, s, 7-H), 6.86 (1 H, d, *J* 8 Hz, 3-H), 7.38 (1 H, s, 5-H), 7.79 (1 H, d, *J* 8 Hz, 4-H), and 7.98 (1 H, br s, NH); *m/z* (160 °C) 309 (M^+ , 100%), 294 (22), 278 (9), 264 (7), 254 (45), 241 (7), 234 (3), 224 (10), 220 (3), 211 (8), 204 (2), 196 (7), 192 (2), 180 (6), 167 (6), 155 (7), 147 (6), 139 (6), 132 (5), 127 (9), and 41 (20).

1,4-Dihydro-7-methoxy-3-methyl-8-(3-methylbut-2-enyl)carbazole-1,4-dione (Murrayquinone-B) (2).—A solution of the carbazole (**14a**) (15.7 mg, 0.05 mmol) in methanol (20 ml), contained in a quartz tube was irradiated with two 125 W mercury lamps for 1.5 h, whilst air was passed through the solution. The methanol was evaporated under reduced pressure and the crude product chromatographed on silica (1 g), eluting with light petroleum-dichloromethane, to give the *title com-*

pound (**2**) (2 mg, 13%) as a dark mauve solid, m.p. 220–221 °C (lit.,³ m.p. 221–223 °C) (Found: M^+ , 309.1363. $C_{19}H_{19}NO_3$ requires M , 309.1365); λ_{max} (EtOH) 229 (log ϵ 4.31), 261 (4.18), 288sh (3.49), and 401 nm (3.38); ν_{max} (KBr) 3 293, 1 638, 1 616, and 1 260; ν_{max} (Nujol) 3 300, 1 645, 1 620, and 1 260 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.77 (3 H, s, Me), 1.87 (3 H, s, Me), 2.16 (3 H, d, J 1.5 Hz, Me), 3.58 (2 H, d, J 6 Hz, $CH_2CH=$), 3.92 (3 H, s, OMe), 5.26 (1 H, m, $CH_2CH=$), 6.46 (1 H, q, J 1.5 Hz, 2-H), 7.04 (1 H, d, J 8 Hz, 6-ArH), 8.02 (1 H, d, J 8 Hz, 5-ArH), and 8.90 (1 H, br s, NH); m/z (200 °C) 309 (M^+ , 100%), 294 (37), 279 (26), 266 (10), 254 (55), 250 (3), 241 (13), 224 (14), 210 (2), 196 (3), 184 (3), 167 (3), 154 (3), 140 (6), 127 (4), and 115 (3).

Methyl 3-(4-Allyloxyphenyl)-2-azidopropenoate (8b).—Sodium (6.80 g, 0.296 mol) was added to dry methanol (160 ml) under nitrogen and the solution cooled to -15 °C. A solution of 4-allyloxybenzaldehyde¹⁰ (**7b**) (12.00 g, 0.074 mol) and methyl azidoacetate (34.07 g, 0.296 mol) in dry methanol (10 ml) was added over 45 min the temperature being maintained at -15 °C. The reaction mixture was stirred for 3 h at this temperature and then allowed to warm to room temperature over 2.5 h. The flask contents were poured into water (300 ml) and extracted with ether (300 ml). The ethereal extracts were washed with water (600 ml), dried ($MgSO_4$), and evaporated under reduced pressure to yield the *title compound* (**8b**) (15.85 g, 83%) as a lemon-yellow solid, m.p. 45–46 °C (from hexane) (Found: C, 60.1; H, 5.15; N, 16.0. $C_{13}H_{13}N_3O_3$ requires C, 60.2; H, 5.0; N, 16.2%); ν_{max} (Nujol) 2 110, 1 690, and 1 600 cm^{-1} ; δ (60 MHz; $CDCl_3$) 3.84 (3 H, s, CO_2Me), 4.54 (2 H, m, OCH_2), 5.01–5.59 (2 H, m, $CH=CH_2$), 5.69–6.40 (1 H, m, $CH=CH_2$), 6.84 (1 H, s, 3-H), 6.90 (2 H, d, J 8 Hz, ArH), and 7.76 (2 H, d, J 8 Hz, ArH); m/z (110 °C) 259 (M^+ , 1%), 231 (43), 190 (100), 172 (8), 158 (52), and 130 (26).

Methyl 7-Allyl-6-hydroxyindole-2-carboxylate (9b).—A solution of the azide (**8b**) (7.93 g, 30.62 mmol) in bromobenzene (600 ml) was refluxed for 23.5 h under nitrogen and then concentrated to provide a solid precipitate which was filtered off and dried. A further crop of the indole was obtained on complete evaporation of the bromobenzene under reduced pressure. The *title compound* (**9b**) (5.58 g, 79%) was obtained as a lemon-yellow crystalline solid, m.p. 165–166 °C (from hexane–chloroform) (Found: C, 67.4; H, 5.6; N, 6.05. $C_{13}H_{13}NO_3$ requires C, 67.5; H, 5.6; N, 6.1%); ν_{max} (Nujol) 3 340br (OH), 3 315 (NH), 1 680, 1 620, and 1 600 cm^{-1} ; δ [90 MHz; $CDCl_3$ –(CD_3)₂SO] 3.62 (2 H, m, $CH_2CH=$), 3.85 (3 H, s, CO_2Me), 4.94–5.26 (2 H, m, $CH=CH_2$), 5.78–6.27 (1 H, m, $CH=CH_2$), 6.75 (1 H, d, J 8 Hz, 5-H), 7.05 (1 H, d, J 2 Hz, 3-H), 7.27 (1 H, d, J 8 Hz, 4-H), 8.14 (1 H, s, CHO), and 8.92 (1 H, br s, NH); m/z (200 °C) 231 (M^+ , 100%), 199 (34), 171 (90), 131 (13), and 115 (17).

Methyl 7-Allyl-6-methoxyindole-2-carboxylate (10b).—A mixture of the hydroxyindole (**9b**) (2.77 g, 0.012 mol), iodomethane (25.54 g, 0.180 mol), and potassium carbonate (9.93 g, 0.072 mol) in acetone (110 ml) was heated under reflux for 42 h. The mixture was cooled, filtered and evaporated under reduced pressure to yield a pale lemon-yellow solid which was extracted with ether (300 ml). The organic extracts were washed with aqueous sodium hydroxide (1M; 4 × 100 ml) and water (200 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the *title compound* (**10b**) (2.82 g, 96%) as a pale lemon-yellow solid, m.p. 127–128 °C (from hexane–chloroform) (Found: C, 68.6; H, 6.2; N, 5.8. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.1; N, 5.7%); ν_{max} (Nujol) 3 360, 1 700, 1 640, 1 620, and 1 260 cm^{-1} ; δ (250 MHz; $CDCl_3$) 3.66 (2 H, d, J 6 Hz, $CH_2CH=$), 3.90 (3 H, s, OMe), 3.93 (3 H, s, OMe), 5.06–5.19 (2 H, m, $CH=CH_2$), 6.02 (1 H, m, $CH=CH_2$), 6.91 (1 H, d, J 8 Hz, 5-H), 7.16 (1 H, d, J

2 Hz, 3-H), 7.53 (1 H, d, J 8 Hz, 4-H), and 8.73 (1 H, br s, NH); m/z (140 °C) 245 (M^+ , 100%), 212 (10), 198 (25), 185 (47), 170 (22), 156 (6), 142 (6), and 115 (18).

3-(7-Allyl-6-methoxyindol-2-ylcarbonyl)-4,5-dihydrofuran-2-one (11b).—A mixture of the indole (**10b**) (1.00 g, 4.08 mmol), 4,5-dihydrofuran-2-one (1.41 g, 16.40 mmol), and sodium methoxide (1.76 g, 32.59 mmol) in dry dioxane (18 ml) was heated at 110 °C for 45 h under nitrogen. Ice–water (20 ml) was added, and the mixture was cooled and acidified to pH 4–6. The mixture was then extracted with chloroform (200 ml) and the extracts were washed with water, dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was chromatographed on silica (2 × 15 g), eluting with light petroleum and ether–ethyl acetate to give the *title compound* (**11b**) (0.79 g, 65%) as a fluffy lemon-yellow solid, m.p. 138.5–139.5 °C (from hexane–chloroform) (Found: C, 67.9; H, 5.7; N, 4.6. $C_{17}H_{17}NO_4$ requires C, 68.2; H, 5.7; N, 4.7%); ν_{max} (Nujol) 3 300, 1 755, 1 640, 1 615, and 1 250 cm^{-1} ; δ (250 MHz; $CDCl_3$) 2.54 (1 H, m, 4-H), 2.89 (1 H, m, 4-H), 3.63 (2 H, dt, J 6, 1.5 Hz, $CH_2CH=$), 3.91 (3 H, s, OMe), 4.40 (2 H, m, 5-H), 4.55 (1 H, m, 3-H), 5.03–5.20 (2 H, m, $CH=CH_2$), 6.00 (1 H, m, $CH=CH_2$), 6.93 (1 H, d, J 8 Hz, 5-ArH), 7.38 (1 H, d, J 2 Hz, 3-ArH), 7.59 (1 H, d, J 8 Hz, 4-ArH), and 8.94 (1 H, br s, NH); m/z (120 °C) 299 (M^+ , 100%), 214 (36), 198 (19), 186 (9), 170 (8), and 115 (7).

1-(7-Allyl-6-methoxyindol-2-yl)-4-hydroxybutan-1-one (12b).—The lactone (**11b**) (63.2 mg, 0.21 mmol), dioxane (1.3 ml), and water (1.3 ml) were heated together at 110 °C in the presence of a few drops of dilute aqueous sodium hydroxide for 17 h. The mixture was concentrated under reduced pressure to provide a solid precipitate which was filtered off and dried to give the *title compound* (**12b**) (48 mg, 83%) as a beige crystalline solid, m.p. 114–115 °C (from hexane–chloroform) (Found: C, 70.4; H, 7.0; N, 5.2. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%); ν_{max} (Nujol) 3 470 (NH), 3 300 (OH), 1 630, and 1 250 cm^{-1} ; δ (250 MHz; $CDCl_3$) 1.75 (1 H, br s, OH), 2.05 (2 H, m, 3-H), 3.06 (2 H, t, J 6 Hz, 4-H), 3.63 (2 H, dt, J 6, 2 Hz, $CH_2CH=$), 3.76 (2 H, m, 2-H), 3.90 (3 H, s, OMe), 5.05–5.18 (2 H, m, $CH=CH_2$), 6.00 (1 H, m, $CH=CH_2$), 6.91 (1 H, d, J 8 Hz, 5-ArH), 7.20 (1 H, d, J 2 Hz, 3-ArH), 7.55 (1 H, d, J 8 Hz, 4-ArH), and 8.91 (1 H, br s, NH); m/z (130 °C) 273 (M^+ , 95%), 255 (98), 240 (40), 229 (100), 214 (43), 198 (23), 186 (19), 170 (18), 154 (8), 144 (8), 128 (7), and 115 (12).

1-(7-Allyl-6-methoxyindol-2-yl)butane-1,4-dione (13b).—A solution of the alcohol (**12b**) (38 mg, 0.14 mmol) in dry dichloromethane (1 ml) was added to PCC (45 mg, 0.21 mmol) and anhydrous sodium acetate (3.4 mg, 0.04 mmol) in dry dichloromethane (2 ml) under nitrogen. The mixture was stirred at room temperature for 2 h. Dry ether (3 ml) was added and the liquid decanted off; this procedure was repeated three times. The ethereal product was filtered through a Florisil pad and the filtrate was evaporated under reduced pressure to yield the *title compound* (**13b**) (25.3 mg, 67%) as a beige solid, m.p. 110.5–112.5 °C (from hexane–chloroform) (Found: C, 70.65; H, 6.2; N, 5.05. $C_{16}H_{17}NO_3$ requires C, 70.85; H, 6.3; N, 5.2%); ν_{max} (Nujol) 3 370, 1 710, 1 650, and 1 615 cm^{-1} ; δ (90 MHz; $CDCl_3$) 2.89 (2 H, t, J 6 Hz, 3-H), 3.25 (2 H, t, J 6 Hz, 2-H), 3.60 (2 H, m, $CH_2CH=$), 3.88 (3 H, s, OMe), 4.94–5.32 (2 H, m, $CH=CH_2$), 5.74–6.23 (1 H, m, $CH=CH_2$), 6.85 (1 H, d, J 8 Hz, 5-ArH), 7.20 (1 H, m, 3-ArH), 7.49 (1 H, d, J 8 Hz, 4-ArH), 8.81 (1 H, br s, NH), and 9.78 (1 H, s, CHO); m/z (130 °C) 271 (M^+ , 100%), 243 (50), 228 (8), 214 (50), 200 (8), 187 (18), 170 (17), 154 (7), 144 (10), 128 (7), and 115 (17).

1-Allyl-2,8-dimethoxy-9H-carbazole (14b).—Boron trifluoride–methanol complex (14% w/v; 0.8 ml, 1.65 mmol) was added

to a solution of the aldehyde (**13b**) (29.6 mg, 0.11 mmol) in dry methanol (0.6 ml) under nitrogen, and the mixture stirred at room temperature for 17 h. The dark mauve solution was poured into water (6 ml) and extracted with ether (25 ml). The ethereal extracts were washed with water, dried (MgSO₄), and concentrated under reduced pressure. The crude product was chromatographed on silica (1 g), eluting with light petroleum-ether, to yield the *title compound* (**14b**) (11.6 mg, 40%) as a pale lemon-yellow crystalline solid, m.p. 119–120 °C (Found: C, 76.1; H, 6.4; N, 5.1. C₁₇H₁₇NO₂ requires C, 76.4; H, 6.4; N, 5.2%); λ_{max}(EtOH) 224sh (log ε 4.39), 240 (4.61), 250 (4.57), 296 (4.00), 318sh (3.58), and 329 nm (3.49); ν_{max}(Nujol) 3 450, 3 410, 1 620, 1 580, and 1 260 cm⁻¹; δ(250 MHz; CDCl₃) 3.72 (2 H, dt, *J* 6, 1.5 Hz, CH₂CH=), 3.91 (3 H, s, OMe), 4.01 (3 H, s, OMe), 5.06–5.20 (2 H, m, CH=CH₂), 6.07 (1 H, m, CH=CH₂), 6.84 (1 H, d, *J* 8 Hz, 7-H), 6.89 (1 H, d, *J* 8 Hz, 3-H), 7.12 (1 H, t, *J* 8 Hz, 6-H), 7.59 (1 H, d, *J* 8 Hz, 5-H), 7.86 (1 H, d, *J* 8 Hz, 4-H), and 8.10 (1 H, br s, NH); *m/z* (150 °C) 267 (*M*⁺, 100%), 252 (26), 240 (3), 236 (12), 224 (4), 221 (8), 209 (5), 195 (2), 192 (3), 180 (2), 154 (3), 133 (6), and 126 (7).

Methyl 2-Azido-3-[4-(1,1-dimethylprop-2-ynyloxy)phenyl]-propenoate (**16**).—Sodium (0.23 g, 10.0 mmol) was added to dry methanol (6 ml) under nitrogen and the solution cooled to –15 °C. A solution of 4-(1,1-dimethylprop-2-ynyloxy)benzaldehyde⁹ (**15**) (0.48 g, 2.55 mmol) and methyl azidoacetate (1.17 g, 10.17 mmol) in dry methanol (1 ml) was added over 15 min the temperature being maintained at –15 °C. The reaction mixture was stirred for 3 h at this temperature and then allowed to warm to room temperature over 3 h. The flask contents were poured into water (10 ml) and extracted with ether (20 ml). The ethereal extracts were washed with water, dried (MgSO₄), and evaporated under reduced pressure to yield the *title compound* (**16**) (0.57 g, 78%) as a lemon-yellow oil (purified by chromatography) (Found: *M*⁺, 285.1117. C₁₅H₁₅N₃O₃ requires *M*, 285.1113); ν_{max}(film) 3 300, 2 130, 1 715, 1 620, and 1 600 cm⁻¹; δ(90 MHz; CDCl₃) 1.65 (6 H, s, Me), 2.61 (1 H, s, ≡CH), 3.87 (3 H, s, CO₂Me), 6.91 (1 H, s, 3-H), 7.23 (2 H, d, *J* 9 Hz, ArH), and 7.77 (2 H, d, *J* 9 Hz, ArH); *m/z* (160 °C) 285 (*M*⁺, 1%), 257 (4), 242 (2), 234 (7), 219 (5), 210 (2), 203 (18), 191 (19), 168 (9), 159 (9), and 137 (100).

Methyl 7,7-Dimethyl-1H,7H-pyrano[2,3-g]indole-2-carboxylate (**17**).—The azide (**16**) (0.57 g, 2 mmol) in dry toluene (30 ml) was refluxed under nitrogen for 3 h and then concentrated under reduced pressure to give a colourless crystalline solid which was filtered off and dried. The toluene filtrate was evaporated under reduced pressure to give a lemon-yellow, oily solid which was recrystallised from hexane-chloroform to give a further yield of the *title compound* (**17**) (0.33 g, 65%), m.p. 191–192 °C (Found: C, 70.05; H, 5.85; N, 5.4. C₁₅H₁₅NO₃ requires C, 70.0; H, 5.8; N, 5.45%); ν_{max}(Nujol) 3 340, 1 695, 1 645, 1 610, 1 270, and 1 200 cm⁻¹; δ(250 MHz; CDCl₃) 1.48 (6 H, s, Me), 3.95 (3 H, s, CO₂Me), 5.66 (1 H, d, *J* 9 Hz, 2-H), 6.67 (1 H, d, *J* 9 Hz, 1-H), 6.72 (1 H, d, *J* 8 Hz, 5-H), 7.15 (1 H, d, *J* 2 Hz, 7-H), 7.42 (1 H, d, *J* 8 Hz, 6-H), and 9.05 (1 H, br s, NH); *m/z* (160 °C) 257 (*M*⁺, 34%), 242 (55), 210 (100), 182 (11), 127 (7), and 105 (22).

2-(4,5-Dihydro-4-methylfuran-2-on-3-ylcarbonyl)-7,7-dimethyl-1H,7H-pyrano[2,3-g]indole (**18**).—A mixture of the indole (**17**) (0.20 g, 0.78 mmol), 4,5-dihydro-4-methylfuran-2-one (0.31 g, 3.10 mmol), and sodium methoxide (0.34 g, 6.30 mmol) in dry dioxane (5 ml) was heated at 110 °C for 5 h under nitrogen. Ice-water (6 ml) was added and the mixture acidified to pH 4–6. The mixture was then extracted with ether (50 ml) and the extracts were washed with water, dried (Na₂SO₄), and evaporated under reduced pressure. The crude product was

chromatographed on silica (7 g), eluting with light petroleum (b.p. 60–80 °C)-ether, to give (i) the starting indole (**17**) (102 mg, 51%), and (ii) the *title compound* (**18**) (83.8 mg, 33%) as a lemon-yellow crystalline solid, m.p. 225–226 °C (from hexane-chloroform) (Found: C, 70.3; H, 5.7; N, 4.3. C₁₉H₁₉NO₄ requires C, 70.15; H, 5.85; N, 4.3%); ν_{max}(Nujol) 3 330, 1 775, 1 640, 1 620, and 1 600 cm⁻¹; δ(250 MHz; CDCl₃) 1.25 (3 H, d, *J* 7 Hz, CHMe), 1.48 (6 H, s, Me), 3.23 (1 H, m, CHMe), 3.98 (2 H, m, CHCO, CH₂O), 4.62 (1 H, dd, *J* 8, 6 Hz, CH₂O), 5.67 (1 H, d, *J* 8 Hz, 2-H), 6.62 (1 H, d, *J* 8 Hz, 1-H), 6.72 (1 H, d, *J* 8 Hz, 5-H), 7.27 (1 H, d, *J* 2 Hz, 7-H), 7.46 (1 H, d, *J* 8 Hz, 6-H), and 9.30 (1 H, br s, NH); *m/z* (170 °C) 325 (*M*⁺, 24%), 310 (100), and 183 (10).

8-(4-Hydroxy-3-methylbutyryl)-7,7-dimethyl-1H,7H-pyrano[2,3-g]indole (**19**).—The indole (**18**) (20 mg, 0.062 mmol), dioxane (0.7 ml), and water (0.7 ml) were heated together at 110 °C in the presence of a few drops of dilute aqueous sodium hydroxide for 1.5 h under nitrogen. The reaction mixture was cooled in ice and a few drops of water were added to provide a crystalline solid which was filtered off and dried. Saturated brine was added to the filtrate and this was extracted with ether, washed with water, dried (Na₂SO₄), and evaporated under reduced pressure to yield a lemon-yellow oil. The oil was chromatographed on silica (1 g), eluting with light petroleum-ether, to give a further 4.6 mg of the desired product. The *title compound* (**19**) (13.6 mg, 74%) was obtained as a beige crystalline solid, m.p. 135.5–136.5 °C (from hexane-chloroform) (Found: C, 72.1; H, 7.15; N, 4.5. C₁₈H₂₁NO₃ requires C, 72.2; H, 7.0; N, 4.7%); ν_{max}(Nujol) 3 390br, 3 230br, 1 630, and 1 610 cm⁻¹; δ(250 MHz; CDCl₃) 1.04 (3 H, d, *J* 6 Hz, CHMe), 1.48 (6 H, s, Me), 2.12 (1 H, br s, OH), 2.38 (1 H, m, CHMe), 2.82 (1 H, dd, *J* 14, 6 Hz, CH₂OH), 3.05 (1 H, dd, *J* 14, 6 Hz, CH₂OH), 3.48–3.70 (2 H, m, CH₂CH), 5.66 (1 H, d, *J* 8 Hz, 2-H), 6.62 (1 H, d, *J* 8 Hz, 1-H), 6.72 (1 H, d, *J* 8 Hz, 5-H), 7.18 (1 H, d, *J* 2 Hz, 7-H), 7.45 (1 H, d, *J* 8 Hz, 6-H), and 9.15 (1 H, br s, NH); *m/z* (180 °C) 299 (*M*⁺, 46%), 284 (86), 266 (100), 226 (15), 210 (17), and 184 (28).

7,7-Dimethyl-2-(3-methylsuccinyl)-1H,7H-pyrano[2,3-g]indole (**20**).—A solution of the alcohol (**19**) (18.0 mg, 0.06 mmol) in dry dichloromethane (0.4 ml) was added to a stirred suspension of PCC (19.2 mg, 0.09 mmol) and anhydrous sodium acetate (1.4 mg, 0.02 mmol) in dry dichloromethane (0.8 ml) at room temperature under nitrogen. The mixture was stirred for 3 h, dry ether (3 ml) added, and the liquid decanted off; this ether addition procedure was repeated three times. The ethereal product was filtered through a Florisil pad and the filtrate evaporated under reduced pressure. The crude product was chromatographed on silica (1 g), eluting with light petroleum (b.p. 60–80 °C)-ether to give the *title compound* (**20**) (4.2 mg, 23%) as a lemon-yellow solid, m.p. 169–172 °C (Found: *M*⁺, 297.1369. C₁₈H₁₉NO₃ requires *M*, 297.1365); ν_{max}(Nujol) 3 320, 1 720, 1 640, and 1 605 cm⁻¹; δ(250 MHz; CDCl₃) 1.23 (3 H, d, *J* 6 Hz, CHMe), 1.48 (6 H, s, Me), 2.96 (1 H, dd, *J* 16, 6 Hz, CH₂CH), 3.11 (1 H, m, CHMe), 3.38 (1 H, dd, *J* 16, 6 Hz, CH₂CH), 5.66 (1 H, d, *J* 8 Hz, 2-H), 6.58 (1 H, d, *J* 8 Hz, 1-H), 6.71 (1 H, d, *J* 8 Hz, 5-H), 7.18 (1 H, d, *J* 2 Hz, 7-H), 7.45 (1 H, d, *J* 8 Hz, 6-H), 8.96 (1 H, br s, NH), and 9.80 (1 H, s, CHO); *m/z* (150 °C) 297 (*M*⁺, 29%), 282 (100), 264 (4), 254 (6), 238 (2), 226 (4), 210 (5), 197 (3), 184 (22), and 105 (12).

10-Methoxy-3,3,8-trimethyl-3H,11H-pyrano[3,2-a]carbazole (**21**).—Boron trifluoride-methanol complex (14% w/v; 0.23 ml, 0.47 mmol) was added to a solution of the aldehyde (**20**) (10 mg, 0.034 mmol) in dry methanol (0.16 ml) at room temperature under nitrogen. The solution was stirred at room temperature for 17 h and then poured into water (2 ml) and extracted with

ether (20 ml). The ethereal extracts were washed with water, dried (MgSO_4), and concentrated under reduced pressure. The crude product was chromatographed on silica (0.5 g), eluting with light petroleum (b.p. 60–80 °C)–dichloromethane, to give the *title compound* (**21**) (3.5 mg, 35%) as a pale lemon-yellow solid, m.p. 143–145 °C (Found: M^+ , 293.1406. $\text{C}_{19}\text{H}_{19}\text{NO}_2$ requires M , 293.1416); λ_{max} (EtOH) 238 (log ϵ 4.36), 274 (4.08), 285 (4.20), 341 (3.64), and 355 nm (3.63); ν_{max} (Nujol) 3 410, 1 640, and 1 610 cm^{-1} ; δ (250 MHz; CDCl_3) 1.50 (6 H, s, Me), 2.52 (3 H, s, ArMe), 4.00 (3 H, s, OMe), 5.69 (1 H, d, J 10 Hz, 2-H), 6.62–6.74 (3 H, m, 1-, 5-, and 9-H), 7.35 (1 H, m, 7-H), 7.72 (1 H, d, J 8 Hz, 6-H), and 8.04 (1 H, br s, NH); m/z (160 °C) 293 (M^+ , 35%), 278 (100), 263 (25), and 139 (20).

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