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NEW SYNTHESIS OF MURRAYAQUINONE-A AND PYRAYAQUINONES A AND B[1]

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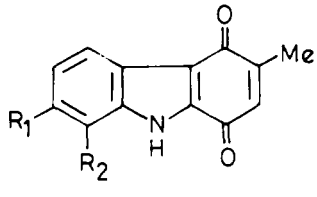
Recent chemical investigations on *Murraya euchrestifolia* Hayata (Rutaceae) (1-3) have revealed the presence of novel carbazolequinones, a subgroup of the well known carbazole alkaloids. Since their isolation, some efforts on their synthesis have also been reported (2,4-6). In continuation of our studies on the synthesis of carbazolequinones (5,6), we now wish to report a convenient synthesis of these alkaloids by DDQ transformation of 1-oxotetrahydrocarbazoles **6-8**, **11**, and **12** to the corresponding quinones 1-5.

The 1-oxo-1,2,3,4-tetrahydro-3-methylcarbazoles 6-9 were prepared in 3 steps from 3-methylcyclohexanone by known procedures (5,7,8). Initial attempts to convert 6, 7, and 8 to the corresponding carbazolequinones **1**, **2**, and **3** by DDQ oxidation in dioxan gave the products in 45%, 35%, and 28% yield, respectively. This observation encouraged us to undertake the synthesis of **4** and **5**.

The required 1-oxotetrahydrocarbazoles **11** and **12** were prepared from 1-oxo-1,2,3,4-tetrahydro-3-methyl-7-hydroxycarbazole [**9**]. Condensation of **9** with 2-methyl-3-buten-2-ol in the presence of BF_3 etherate gave a mixture from which 10-oxo-3,3,8-trimethyl-1,2,3,7,8,9,10-heptahydropyrano[3,2-*a*]carbazole [**11**] (15%), 10-oxo-2,2,8-trimethyl-2,3,4,5,6,7,8-heptahydropyrano[2,3-*b*]carbazole [**12**] (16%), and 1-oxo-1,2,3,4-tetrahydro-3-methyl-6,8-bis(3,3-dimethylallyl)-7-hydroxycarbazole [**10**] (20%) could be isolated by column chromatography over florisil. The compounds **11** and **12** were refluxed with DDQ in dioxan to afford pyrayaquinone-A [**4**] (18%) and pyrayaquinone-B [**5**] (19%), respectively. All the synthetic compounds [1-5] were spectroscopically (uv, ir, nmr, ms) found to be identical with the corresponding natural products.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All the melting points were taken on an electrically heated block (Toshniwal Bros. Ltd.) and are uncorrected. Ir spectra were recorded on a Beckman Acculab-1 and uv spectra on a Hitachi model 3200 spectrophotometer. ^{1}H-nmr spectra were taken either on CFT-20 (80 MHz) or on Bruker WM-400 (400 MHz) spectrometers using TMS as an internal reference, and chemical shift values are expressed in δ units. Mass spectra were measured on a Jeol D-300 mass spectrometer.



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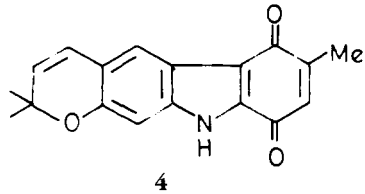
2 $R_1=OMe$, $R_2=H$
3 $R_1=OAc$, $R_2=H$



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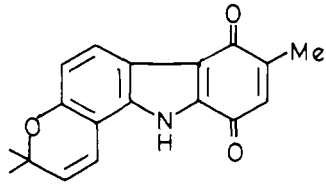
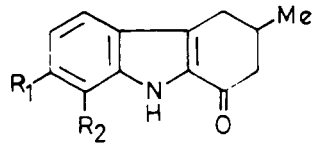
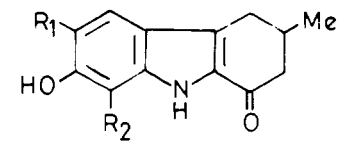


5

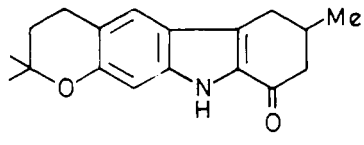
[1]CDRI Communication No. 4006.



6 $R_1=R_2=H$
7 $R_1=OMe$, $R_2=H$
8 $R_1=OAc$, $R_2=H$



9 $R_1=R_2=H$
10 $R_1=R_2=CH_2CHCMe_2$



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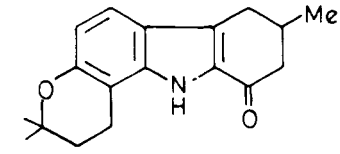

12

Homogenity (purity) of the all compounds was routinely checked by tlc, mp, ms, and ^1H nmr.

MURRAYAQUINONE-A [**1**].—A mixture of 1-oxo-1,2,3,4-tetrahydro-3-methylcarbazole [**6**] (100 mg) and DDQ (200 mg) in dioxan (25 ml) was stirred and heated under reflux for 24 h. The reaction mixture was concentrated. The residue on column chromatography over a short column of florisil using $CHCl_3$ as eluent afforded **1** (48 mg), mp 240-241° [lit. (1), mp 246-247°]; uv λ max (MeOH) 225, 258, 293 (sh), 398 nm; ir (KBr) ν max 3200, 1670, 1650 cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.15 (3H, d, J=2 Hz, -CH_3), 6.45 (1H, q, J=2 Hz, H-2), 7.30-7.45 (3H, m, H-6, -7, -8), 8.23 (1H, m, H-5); eims *m/z* 211 (M^+), 183.

3-METHYL-7-METHOXYCARBAZOLE-1,4-QUINONE [**2**].—1-Oxo-1,2,3,4-tetrahydro-3-methyl-7-methoxycarbazole [**7**] (50 mg) was converted to compound **2** (20 mg) by the procedure as described above, mp 240° (dec); uv λ max (MeOH) 225, 240, 254, 293 (sh), 328, 344, 395 (br) nm; ir (KBr) ν max 3200, 1655, 1630 cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.14 (1H, d, J=2 Hz, -CH_3), 3.85 (3H, s, -OCH_3), 6.45 (1H, q, J=2 Hz, H-2), 6.85 (1H, d, J=2 Hz, H-8), 6.97 (1H, dd, J=8 and 2 Hz, H-6), 7.56 (1H, d, J=8 Hz, H-5); eims *m/z* 241 (M^+), 226, 198.

3-METHYL-7-ACETOXYCARBAZOLE-1,4-QUINONE [**3**].—1-Oxo-1,2,3,4-tetrahydro-3-methyl-7-acetoxycarbazole [**8**] (50 mg) was treated with DDQ to give **3** (16 mg), mp 228-230° (dec); uv λ max (MeOH) 226, 260, 390 (br) nm; ir (KBr) ν max 3300, 1750, 1660, 1630 cm^{-1}; ^1H nmr (DMSO-d_6) δ 2.10 (1H, d, J=2 Hz, -CH_3), 2.30 (3H, s, $OCOCH_3$), 6.65 (1H, q, J=2 Hz, H-2), 7.10 (1H, dd, J=8 and 2 Hz, H-6), 7.30 (1H, d, J=2 Hz, H-8), 8.05 (1H, d, J=8 Hz, H-5); eims *m/z* 269 (M^+), 227, 199.

PREPARATION OF **10**, **11**, AND **12**.—To a stirred solution of 1-oxo-1,2,3,4-tetrahydro-3-methyl-7-hydroxycarbazole [**9**] (5) (500 mg) and BF_3 etherate (0.5 ml) in dioxan (50 ml), 2-methyl-3-buten-2-ol was added, and the solution heated under reflux for 1 h. The reaction mixture was cooled, diluted with H_2O (100 ml), and extracted with EtOAc (3×50 ml). The organic layer was concentrated and the residue chromatographed over a florisil column using $CHCl_3$ with increasing amounts of $CHCl_3$-EtOAc (99:1) as eluent yielded **10** (150 mg), mp 205-206° ($CHCl_3$); uv λ max (MeOH) 213, 258, 345 nm; ir (KBr) ν max 3300, 3020, 1665, 1645 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.10 (3H, brd, -CH_3), 1.60, 1.73, and 1.83 [12H, each s, 2×=$C(CH_3)_2$], 2.20-3.00 [5H, m, -CH_2-CH(Me)CH_2-], 3.40 (4H, d, J=7 Hz, -CH_2-CH=C-Me_2), 5.17 (2H, m, 2×CH=CMe_2), 7.10 (1H, s, H-5), 8.50 (1H, brs, NH ; eims *m/z* 352 (M^+), 351, 296, 280, 240.

Elution with $CHCl_3$-EtOAc (98.5:1.5) gave **11** (110 mg), mp 260-262°, uv λ max (MeOH), 215, 257, 337 nm; ir (KBr) ν max 3300, 1655, 1625; ^1H nmr ($CDCl_3$) δ 1.20 (3H, brd, -CH_3), 1.36 [2×3H, s, -$C(CH_3)_2$], 1.81-3.03 (9H, m, -CH_2-CH(Me)-CH_2- and -CH_2-CH_2-O], 6.67 (1H, d, J=8 Hz, H-6), 7.35 (1H, d, J=8 Hz, H-5), 8.02 (1H, brs, NH); eims *m/z* 283 (M^+). Elution with $CHCl_3$-EtOAc (98:2) afforded **12** (120 mg), mp 228-230°; uv λ max (MeOH), 216, 244, 258, 294, 342 nm; ir (KBr) ν max 3250, 1630, 1615 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.20 (3H, brd, -CH_3), 1.36 [6H, s, -$C(CH_3)_2$], 1.58-3.00 [9H, m, -CH_2-CH(Me)-CH_2- and -CH_2-CH_2-CMe_2-O], 6.73 (1H, s, H-8), 7.30 (1H, s, H-5), 8.35 (1H, brs, NH); eims *m/z* 283 (M^+).

PYRAYAQUINONE-A [**4**].—A mixture of **11** (50 mg) and DDQ (170 mg) in dioxan (10 ml) was stirred and refluxed for 12 h. Solvent was removed, and the residue on plc over Si gel gave **4** (10 mg), mp 220-222° [lit. (2), mp 220°]; uv

max (MeOH) 222, 250, 310, 450 (br) nm; ir (KBr) ν max 1660, 1640, 1630, 1605 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.46 [6H, s, $=C(CH_3)_2$], 2.14 (3H, d, J=2 Hz, -CH3), 5.76 (1H, d, J=10 Hz, H-2′), 6.42 (1H, q, J=2 Hz, H-2), 6.48 (1H, d, J=10 Hz, H-1′), 6.82 (1H, s, H-8), 7.79 (1H, s, H-5), 9.01 (1H, brs, NH); eims *m/z* 293 (M^+), 273 (M^+-CH_3, 100%).

PYRAYAQUINONE-B [**5**].—A solution of **12** (50 mg) in dioxan (10 ml) and DDQ (170 mg) was stirred and refluxed for 12 h. Usual work up furnished **5** (9.5 mg), mp 242° [lit. (2), mp 245°]; uv λ max (MeOH) 248, 295 (sh), 320, 405 (br) nm; ir (KBr) ν max 1650, 1640, 1635, 1605 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.48 [6H, s, $=C(CH_3)_2$], 2.16 (3H, d, J=2 Hz, -CH_3), 5.74 (1H, d, J=10 Hz, H-2′), 6.46 (1H, q, J=2 Hz, H-2), 6.64 (1H, d, J=10 Hz, H-1′), 6.86 (1H, d, J=8 Hz, H-6), 7.96 (1H, d, J=8 Hz, H-5), 9.52 (1H, s, brs, NH); eims *m/z* 293 (M^+), 278 (M^+-CH_3, 100%).

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