Bromoquinone–enaminone annulations: syntheses of murrayaquinone-A and (±)-bismurrayaquinone-A

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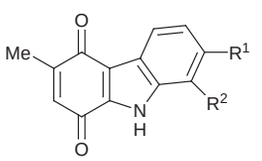
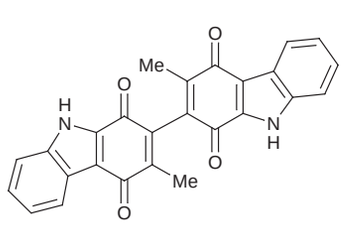
A total synthesis of the carbazolequinone alkaloid, murrayaquinone-A was achieved by an initial annulation of the *N*-benzyl enamine **8** with 2-methyl-5-bromobenzoquinone **6**. Shapiro deoxygenation–olefination followed by heating with DDQ resulted in the exclusive formation of *N*-benzylmurrayaquinone-A **16**. Debenzylation proved very difficult but was finally achieved by heating briefly in trifluoroacetic acid with a catalytic quantity of trifluoromethanesulfonic acid. A single dimeric annulation side product was also formed in the annulation reaction. By using the same synthetic sequence as was employed in the synthesis of **1**, the *N*,*N*-bis-*p*-methoxybenzyl dimer **13** was successfully converted to (±)-bismurrayaquinone-A **5**.

The plants of the genus *Murraya* are indigenous in Southern Asia. Extracts of the leaves of these 4–5 m tall shrubs have been used as a folk medicine for analgesia and local anaesthesia and for the treatment of eczema, rheumatism and dropsy.[1] The physiological effects have not yet been correlated to specific carbazole alkaloids.[2] The plants of this genus are the main source of carbazole alkaloids of which there are now about 60 known.[3] The carbazolequinones, murrayaquinone-A to D **1**–**4**, first isolated from *Murraya euchrestifolia* HAYATA (Rutaceae) collected in Taiwan,[4] form a small group of unique structural type. More recently the first dimeric carbazole alkaloids including biscarbazolequinones have been isolated.[5] (±)-Bismurrayaquinone-A **5** has now been synthesised and its chirotypical properties investigated.[6]



	R^1	R^2
1 A,	H	H
2 B,	OMe	
3 C,	OMe	
4 D,	OH	



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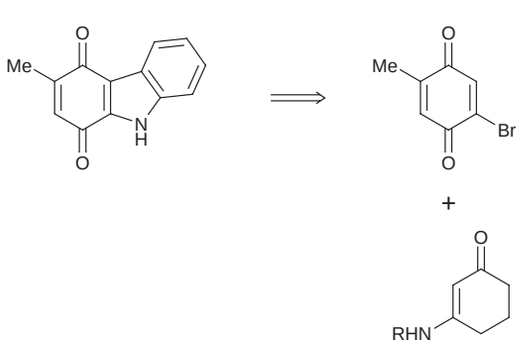
A wide variety of syntheses of these naturally occurring indoloquinones have been reported. Ramesh and Kapil described the one step oxidation of known 1-oxotetrahydrocarbazole into murrayaquinone-A.[7] Martin and Moody devised a BF_3-catalysed intramolecular cyclisation route to 1-methoxycarbazoles which were subsequently converted to the natural product.[8] A concise synthesis involving Pd-assisted cyclisation of arylamino-1,4-benzoquinones to carbazole-1,4-quinones was described by Furukawa *et al.*[9] Both a Diels–Alder[10] and a novel anionic annulation[11] have also been successfully employed in the synthesis of murrayaquinone-A. Matsuo and Ishida cyclised iodarylaminocyclohexenone with NaH–Cu(I) iodide and converted the resulting tetrahydrocarbazole to the natural product.[12] The only synthesis to date of bismurrayaquinone-A was reported by Bringmann and co-workers[6] and was based on a highly efficient regioselective biomimetic oxidative dimerisation of the appropriate phenolic carbazole 'monomer'. The resulting dimer was converted to the natural product by very brief treatment with PCC.

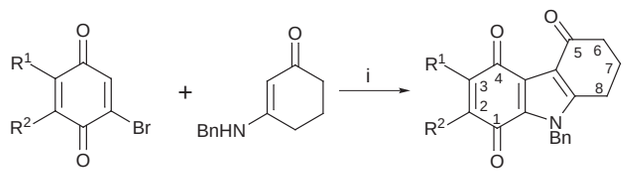
We now report a new approach to the synthesis of murrayaquinone-A **1** and bismurrayaquinone-A **5** which involves the bromoquinone–enamino ketone/enamino ester annulation reaction which we had devised for the regioselective syntheses of mitosenes[13] and the ring framework of the originally proposed structure of kinamycin.[14] We sought to build the murrayaquinone framework in a one-step annulation and complete the synthesis with a judicious selection of functional group interconversions (Scheme 1).



Scheme 1

Results and discussion

The annulation reaction between bromo-1,4-benzoquinone **6** and the *N*-benzylenamino ketone **8** occurs smoothly at room



6 R^1 = Me ; R^2= H **8** **9** R^1 = Me ; R^2= H

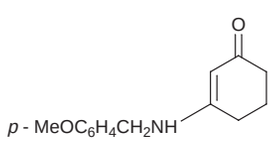
7 R^1 = H; R^2= Me **10** R^1 = H ; R^2= Me

Scheme 2 *Reagents and conditions:* i, $CuCl_2$, $NaHCO_3$, CH_3CN, 40 °C, 48 h.

temperature, using the one-pot procedure previously reported,[14] to give the hexahydrocarbazoletrione **9** (Scheme 2). The reaction was extremely slow. In an effort to optimise the reaction, most parameters such as the N-protecting group, leaving group, solvent, base, reaction time and temperature were investigated in detail, but without major improvement. Employment of the anion of **8** at −78 °C led to many side products. The most effective conditions were $NaHCO_3$ with Cu(II) chloride and 3 Å molecular sieves at 40 °C, 48 h in dry acetonitrile in dry air. The yield was 30%.

The annulation was regioselective. There was no evidence for the formation of the regioisomeric annulation product, **10**. The two regioisomers, **9** and **10**, prepared separately from the bromoquinones **6** and **7**, have distinct melting points and ^{1}H NMR spectra.[15] This result is consistent with the mechanism (Michael addition, followed by *in situ* re-oxidation and subsequent dehalocyclisation) proposed in the original report.[12] Therefore, there was no involvement of an azetidine type intermediate, as proposed by Echavarren in a similar case.[16]

The dimeric side-product **12** was formed, though not reproducibly, in low yield, during the annulation reaction. The dimeric structure was proved by means of ^{1}H NMR and FAB MS spectrometry. This dimer was also formed, albeit in very low yield, when the carbazole **9** was treated with $FeCl_3$. The dimer **13** was similarly prepared when the *p*-methoxybenzyl protected enamino ketone **11** was employed in the annulation step. It seems probable that the dimer is formed by free radical dimerisation of the first formed annulation product. This dimerisation reaction has not been optimised.



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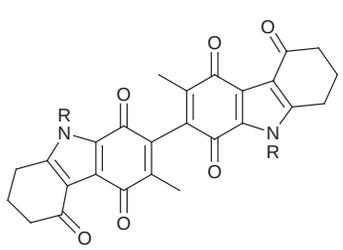
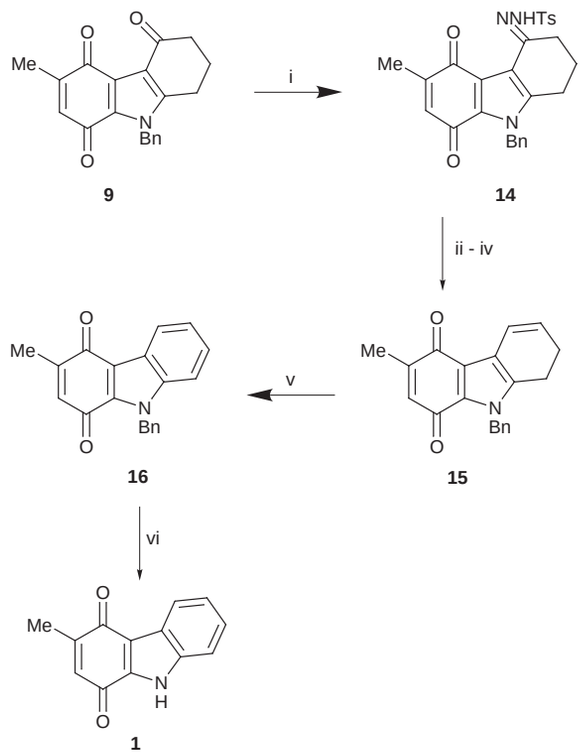


R

12 $C_6H_5CH_2$
13 *p* - $MeOC_6H_4CH_2$

Synthesis of murrayaquinone-A

The carbazolequinone ring framework of **9** represents an advanced intermediate in the synthesis of the *Murraya euchrestifolia* alkaloids.[5] We successfully completed the synthesis of murrayaquinone-A **1** from **9** in three steps (Scheme 3).



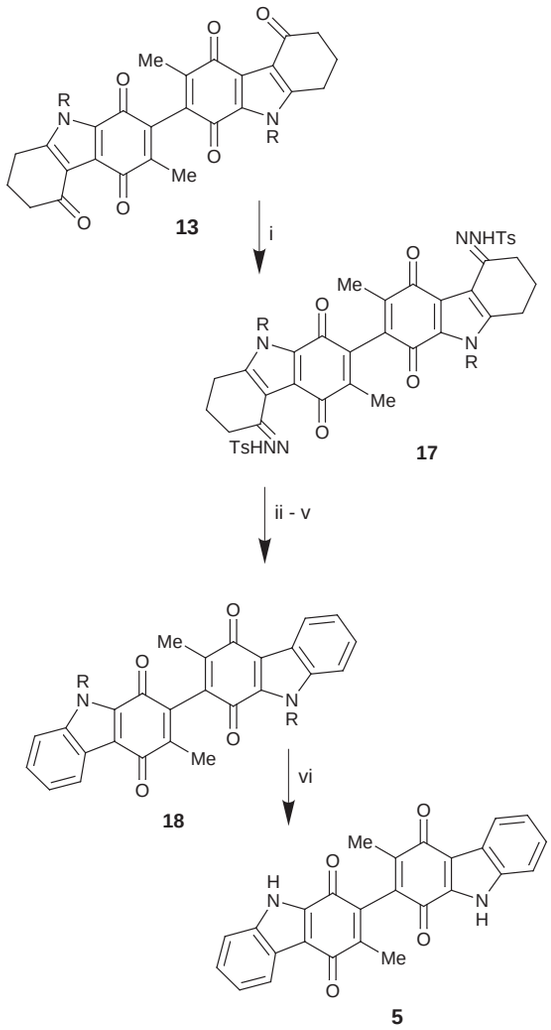
Scheme 3 *Reagents and conditions:* i, $TsNHNH_2$, AcOH, RT; ii, aq. $Na_2S_2O_4$; iii, BuLi (6 equiv.), THF, RT; iv, air oxidation; v, DDQ, dioxane, Δ, 1 h; vi, TFA, TfOH (cat.), Δ, 15 min.

The first step involved the Shapiro reaction.[17] Formation of the requisite tosylhydrazone **14** occurred rapidly at room temperature. The quinone carbonyl groups were unreactive under these conditions. Since the next step of the Shapiro reaction involved the use of butyllithium, protection of the quinone functionality was necessary. However, we found that the formal involvement of protecting groups could be avoided by converting the quinone to the corresponding hydroquinone. As such, the quinone carbonyl functional groups were rendered impervious to butyllithium. The quinone tosylhydrazone **14** was reduced with sodium dithionite. This intermediate was then treated *in situ* without purification, with a large excess of butyllithium: neither methyllithium nor *tert*-butyllithium were as effective. Rapid air oxidation occurred during workup. The product **15** was readily isolable from the polar baseline products. Aromatization to *N*-benzylmurrayaquinone-A **16** was readily achieved by heating with DDQ in dioxane.

Deprotection of the nitrogen proved extremely problematical. A wide range of both oxidative[18] and reductive methods[19,20] were investigated without success. Finally, deprotection was successfully accomplished by heating to reflux *N*-benylmurrayaquinone-A **16** in TFA with traces of TfOH for 15–20 min. The reaction required careful monitoring, since longer reaction times resulted in the destruction of the reactants and products.

Synthesis of (±)-bismurrayaquinone-A

Conversion of the biscarbazole **13** to the natural product was effected by employing the same procedures as for the synthesis of murrayaquinone-A (Scheme 4). No difficulties were encountered regarding reactivities or solubilities. In the final step it was noted that hydrogenolysis of the *p*-methoxy-



Scheme 4 (R = *p*-$MeOC_6H_4CH_2$) *Reagents and conditions:* i, $TsNHNH_2$, AcOH, RT; ii, aq. $Na_2S_2O_4$; iii, BuLi (24 equiv.), THF, RT; iv, air oxidation; v, DDQ, dioxane, Δ, 2 h; vi, TFA, TfOH (cat.), RT, 20 min.

benzyl groups occurred more readily than benzyl groups. Thus, deprotection occurred cleanly even at room temperature, within 10 min at 40–60 °C in trifluoroacetic acid with traces of trifluoromethanesulfonic acid. Deprotection also occurred in pure trifluoroacetic acid, although more slowly. Deprotection occurred stepwise (TLC). (±)-Bismurrayaquinone-A **5** was quite stable towards these acidic conditions. The structure of the orange coloured natural product was confirmed by ^{1}H NMR and CIHRMS spectrometry.

Experimental

Melting points were determined on a Reichert microscope hot stage melting point apparatus. FT-IR spectra (KBr discs) were recorded on a Perkin-Elmer Paragon 1000 and on Nicolet 205 FT-IR spectrophotometers. UV spectra were recorded on a Perkin-Elmer Lambda 5 UV–visible spectrometer in $CHCl_3$ solution. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL GSX 270 MHz and on a Bruker WP250 instrument in $CDCl_3$ with TMS as internal marker, at 270 and 67.8 MHz respectively, unless otherwise stated. Chemical shifts are expressed in ppm (δ) downfield from TMS. ^{1}H splitting patterns are designated as s, singlet; t, triplet; q, quartet; quin, quintet; and m, multiplet. Multiplicity of carbon signals was determined using ^{13}C DEPT experiments. EIMS and EIHRMS were recorded on a Kratos HV5 spectrometer at 70 eV, CIMS (isobutane) were recorded on a AEI MS-9 spectrometer, FABMS (LSIMS) and CIHRMS (methane) were recorded on a Kratos MS80 RF spectrometer. Elemental analyses were performed at the UCC Microanalytical Laboratory, Cork, Ireland and at the Service de microanalyse, Institut de Chimie des Substances Naturelles, CNRS, Gif-sur-Yvette, France.

Thin layer chromatography and preparative dry column chromatography were performed on silica gel 60 PF254 (E. Merck). Acetonitrile was distilled from phosphorus pentoxide, then potassium carbonate and stored over 3 Å molecular sieves. Tetrahydrofuran was distilled from sodium–benzophenone.

The compounds **9**, **10**, **13**, **15**, **16** and **17** failed to give satisfactory microanalytical data.

2-Bromo-5-methyl-1,4-benzoquinone 6[15]

To a vigorously stirred suspension of 2-bromo-2-methylbenzene-1,4-diol (119 mg, 0.59 mmol) in dichloromethane (20 cm^3) was added potassium dichromate on silica (1.5 g of a 17.3% by wt dispersion, 1.76 mmol Cr^{6+}) in one portion and the suspension was stirred at room temperature for 7 min. Filtration of the mixture through a pad of silica, followed by evaporation of the filtrate, afforded **6** (109.9 mg, 93%) as a bright yellow solid, mp 107–108 °C (ethanol) (Found: C, 41.8; H, 2.4; Br, 39.3. $C_7H_5BrO_2$ requires: C, 41.8; H, 2.5; Br, 39.5%); ν_{max}(KBr)/cm^{-1} 1666, 1627, 1590 and 929; λ_{max}/nm 270 (sh); δ_H 2.04 (3H, d, *J* 1.6, 5-CH_3), 6.77 (1H, q, *J* 1.6, 6-H) and 7.24 (1H, s, 3-H); δ_C 15.50 (CH_3), 132.45 (CH), 137.32 (C), 137.99 (CH), 146.34 (C), 179.29 (C) and 184.96 (C); EIMS *m*/*z* 200 (70%) and 202 (100).

2-Bromo-6-methyl-1,4-benzoquinone 7[15]

To a stirred solution of 4,6-dibromo-2-methylphenol (1.06 g, 4 mmol) in glacial ethanoic acid (27 cm^3) and water (12 cm^3) at room temperature was added chromium trioxide (1.2 g, 12 mmol) in water (6 cm^3) over 10 min. The solution was stirred for a further 40 min and then partitioned between water (70 cm^3) and dichloromethane (3 × 50 cm^3). The combined organic extracts were washed with water (2 × 100 cm^3), dried (Na_2SO_4) and evaporated. The residue was passed through a pad of silica with dichloromethane as eluent to afford **7** (654 mg, 81%) as a bright yellow solid, mp 95–97 °C (ethanol) (Found: C, 41.7; H, 2.5; Br, 39.3. $C_7H_5BrO_2$ requires: C, 41.8; H, 2.5; Br, 39.5%); ν_{max}(KBr)/cm^{-1} 1666, 1627, 1590, 1315 and 929; λ_{max}/nm 270 (sh); δ_H 2.14 (3H, d, *J* 1.6, 6-CH_3), 6.65 (1H, q, *J* 1.6, 5-H) and 7.24 (1H, s, 3-H); δ_C 16.67 (CH_3), 133.38 (CH), 137.29 (C), 137.29 (CH), 138.06 (C), 179.86 (C) and 184.68 (C); EIMS *m*/*z* 200 (80%) and 202 (100).

3-Benzylaminocyclohex-2-en-1-one 8

A solution of cyclohexane-1,3-dione (9.00 g, 80.3 mmol), benzylamine (9.45 g, 88 mmol) and toluene-*p*-sulfonic acid monohydrate (150 mg, 0.8 mmol) in chloroform (150 cm^3) was boiled in a Dean–Stark apparatus for 8 h. The solution was then concentrated under reduced pressure to give the yellow enamino ketone (14.07 g, 89%), mp 125–127 °C (from ethyl acetate) (Found: C, 77.6; H, 7.5; N, 6.9. $C_{13}H_{15}NO$ requires: C, 77.6; H, 7.5; N, 7.0%); ν_{max}(KBr)/cm^{-1} 3315, 2934, 1599, 1575, 1519, 1434, 1369, 1236, 1187 and 1145; λ_{max}/nm 274 (sh); δ_H 1.91 (2H, quin, *J* 6.2, CH_2), 2.21 (2H, t, *J* 6.2, CH_2), 2.38 (2H, t, *J* 6.2, CH_2), 4.17 (2H, d, *J* 5.4, CH_2Ph, s with D_2O), 5.07 (1H, s, CH), 6.22 (1H, br s, NH) and 7.28 (5H, m, Ph); δ_C 22.00 (CH_2), 29.42 (CH_2), 36.45 (CH_2), 46.98 (CH_2), 96.69 (CH), 127.61 (CH), 127.70 (CH), 128.75 (CH), 137.03 (C), 164.97 (C) and 197.34 (C); *m*/*z* (CI) 202 (M^+ + 1, 100%) and 112 (30).

3-(4-Methoxybenzylamino)cyclohex-2-en-1-one 11

A solution of cyclohexane-1,3-dione (1.12 g, 10.0 mmol), 4-methoxybenzylamine (1.51 g, 11.0 mmol) and toluene-*p*-sulfonic acid monohydrate (50 mg, 0.27 mmol) in chloroform (50 cm^3) was heated to reflux in a Dean–Stark apparatus for 8 h.

The solution was then concentrated under reduced pressure to give the yellow enamino ketone (1.20 g, 52%), mp 150–151 °C (from EtOH–H_2O) (Found: C, 72.1; H, 7.3; N, 6.0. $C_{14}H_{17}NO_2$ requires: C, 72.7; H, 7.4; N, 6.1%); ν_{max}(KBr)/cm^{-1} 3242, 2960, 1600, 1537, 1245 and 1176; λ_{max}/nm 277 (sh); δ_H (DMSO-d_6) 1.79 (2H, quin, *J* 7.5, CH_2), 2.06 (2H, t, *J* 7.5, CH_2), 2.35 (2H, t, *J* 7.5, CH_2), 3.73 (3H, s, OMe), 4.12 (2H, d, *J* 6.8, CH_2Ph, s with D_2O), 4.81 (1H, s, CH), 6.89 (2H, d, *J* 10.6, Ar), 7.21 (2H, d, *J* 10.6, Ar) and 7.43 (1H, s, NH); δ_C (DMSO-d_6) 21.66 (CH_2), 28.37 (CH_2), 36.41 (CH_2), 45.06 (CH_2), 54.94 (CH_3), 95.45 (CH), 113.71 (CH), 128.53 (CH), 129.74 (C), 158.31 (C), 164.18 (C) and 194.36 (C); CIMS *m*/*z* (CI) 232 (M^+ + 1, 100%).

9-Benzyl-4,5,6,7,8,9-hexahydro-3-methyl-1*H*-carbazole-1,4,5-trione 9

A mixture of 2-bromo-5-methylbenzoquinone **6** (199 mg, 1.00 mmol), enamino ketone **8** (201 mg, 1.00 mmol), sodium hydrogen carbonate (378 mg, 4.50 mmol), cupric chloride (19 mg, 0.2 mmol) and 3 Å molecular sieves (2 g) in dry acetonitrile (50 cm^3) was stirred at 40 °C for 48 h in dry air. The suspension was then filtered on Celite and evaporated *in vacuo* to give a brown residue. The crude residue, taken up in dichloromethane, was purified on a dry column of silica eluted with a mixture of dichloromethane and methanol. The bright yellow *product* **9** (96 mg, 30%) had mp 182–184 °C (from acetone–water) (Found: C, 73.8; H, 5.5; N, 4.3. $C_{20}H_{17}NO_3$ requires: C, 75.2; H, 5.4; N, 4.4%); ν_{max}(KBr)/cm^{-1} 2953, 1683, 1651, 1619, 1497, 1477 and 1265; λ_{max}/nm 270 (sh), 325 and 405; δ_H 2.10 (3H, d, *J* 1.6, CH_3), 2.15 (2H, quin, *J* 7.0, CH_2), 2.57 (2H, t, *J* 7.0 , CH_2), 2.75 (2H, t, *J* 7.0, CH_2), 5.67 (2H, s, CH_2Ph), 6.37 (1H, q, *J* 1.6, CH) and 7.05–7.30 (5H, m, Ph); δ_C 16.30 (CH_3), 21.92 (CH_2), 22.53 (CH_2), 38.80 (CH_2), 48.96 (CH_2), 118.42 (C), 122.95 (C), 126.0 (CH), 127.50 (CH), 128.65 (CH), 130.60 (C), 131.61 (CH), 135.70 (C), 146.92 (C), 148.96 (C), 179.11 (C), 180.60 (C) and 191.33 (C); FABMS *m*/*z* 322 (M^+ + 3, 100%), 321 (84), 320 (47) and 230 (28).

9-Benzyl-4,5,6,7,8,9-hexahydro-2-methyl-1*H*-carbazole-1,4,5-trione 10

Same procedure as for **9**; the *trione* **10**, yield 35%, mp 132–134 °C (Found: C, 73.7; H, 5.5; N, 4.4. $C_{20}H_{17}NO_3$ requires: C, 75.2; H, 5.4; N, 4.4%); ν_{max}(KBr)/cm^{-1} 2952, 1678, 1651, 1621, 1498 and 1479; λ_{max}/nm 270 (sh), 325 and 405; δ_H 2.03 (3H, d, *J* 1.6, 2-CH_3), 2.14 (2H, m, 7-H), 2.58 (2H, t, *J* 6.5, 6-H or 8-H), 2.77 (2H, t, *J* 6.2, 6-H or 8-H), 5.70 (2H, s, CH_2Ph), 6.49 (1H, q, *J* 1.6, 3-H) and 7.02–7.37 (5H, m Ph); δ_C 15.25 (CH_3), 22.09 (CH_2), 22.52 (CH_2), 39.05 (CH_2), 48.86 (CH_2), 118.54 (C), 123.62 (C), 126.20 (CH), 128.00 (CH), 129.08 (CH), 130.79 (C), 134.68 (CH), 135.46 (C), 144.01 (C), 150.50 (C), 179.40 (C), 181.23 (C) and 191.46 (C); FABMS *m*/*z* 322 (M^++3, 60%), 321 (71), 320 (100), 319 (10) and 230 (24).

9-Benzyl-4,5,6,7,8,9-hexahydro-3-methyl-1*H*-carbazole-1,4,5-trione 5-(4-methylphenyl)sulfonylhydrazone 14

To a solution of the carbazoletrione **9** (50 mg, 0.156 mmol) in glacial acetic acid (10 cm^3) was added a solution of *p*-tolylsulfonylhydrazine (58 mg, 0.313 mmol) in glacial acetic acid (10 cm^3), and the mixture was stirred at room temperature for 2 h. The mixture was then taken up in water (50 cm^3) and extracted with dichloromethane. The extracts were washed successively with water, saturated sodium bicarbonate solution, brine, and dried over magnesium sulfate. Evaporation of the solvent *in vacuo* gave the deep purple *hydrazone* **14** (2.81 g, 84%), mp > 250 °C (decomp.) (Found: C, 65.8; H, 5.1; N, 8.5; S, 6.6. $C_{27}H_{25}N_3SO_4$ requires: C, 66.5; H, 5.2; N, 8.6; S, 6.6%); ν_{max}(KBr) 2924, 1634, 1495, 1454, 1428, 1282, 1141, 1110 and 1082 cm^{-1}; λ_{max} 270 (sh), 330 (sh) and 545 nm; δ_H 1.98 (2H, quin, *J* 1.6, CH_2), 2.19 (3H, d, *J* 1.6, CH_3), 2.35 (3H, s, $ArCH_3$), 2.69 (2H, t, *J* 6.5, CH_2), 2.92 (2H, t, *J* 6.5, CH_2), 5.67 (2H, s, CH_2Ph), 6.47 (1H, q, *J* 1.6, CH), 7.02–7.31 (8H, m, Ar) and 7.91 (2H, m, Ar); *m*/*z* (FABMS) 490 (M^+ + 2, 28%), 489 (M^+ + 1, 9) and 488 (M^+, 11).

9-Benzyl-4,7,8,9-tetrahydro-3-methyl-1*H*-carbazole-1,4-dione 15

A solution of the hydrazone **14** (262 mg, 0.537 mmol) in dichloromethane (30 cm^3) was shaken with a solution of sodium dithionite (200 mg, 1.15 mmol) in water (30 cm^3) in a separatory funnel until yellow. The organic solution was then washed with water, dried over magnesium sulfate under nitrogen atmosphere, and evaporated *in vacuo*. The residue was taken up in dry THF (20 cm^3) and kept under nitrogen atmosphere. A solution of *n*-butyllithium in hexane (1 M, 3.0 cm^3, 3.0 mmol) was then added slowly under nitrogen, at room temperature and under rapid stirring. After 30 min of stirring at room temperature, the reaction was quenched by a slow addition of water in THF. The mixture was taken up in water, acidified with 0.1 M aqueous HCl and extracted with dichloromethane, extracts were washed with water, dried over magnesium sulfate and evaporated *in vacuo*. After purification on a dry column of silica (eluant: dichloromethane and methanol) the purple *quinone* **15** (65 mg, 41%) was obtained, mp 96–97 °C (Found: C, 77.5; H, 5.0; N, 4.4. $C_{20}H_{17}NO_2$ requires: C, 79.2; H, 5.7; N, 4.6%); ν_{max}(KBr)/cm^{-1} 1637, 1462, 1377 and 1078; λ_{max}/nm 270 (sh), 380 and 505; δ_H 2.04 (3H, d, *J* 1.6, CH_3), 2.44 (2H, m, CH_2), 2.67 (2H, d, *J* 9.0, CH_2), 5.59 (2H, s, CH_2Ph), 6.33 (1H, q, *J* 1.6, CH) and 6.90–7.35 (7H, m, Ar + vinyl); δ_C 15.40 (CH_3), 19.66 (CH_2), 23.20 (CH_2), 48.40 (CH_2), 119.20 (C), 121.11 (CH), 125.80 (CH), 126.5 (CH), 127.3 (CH), 128.5 (C), 129.0 (CH), 134.40 (C), 136.23 (C), 138.29 (C), 145.02 (C), 177.38 (C) and 184.86 (C); CIMS *m*/*z* 304 (M^++1, 100%) and 305 (35).

9-Benzyl-4,9-dihydro-3-methyl-1*H*-carbazole-1,4-dione 16

A solution of carbazoledione **15** (25 mg, 0.085 mmol) and dichlorodicyanobenzoquinone (39 mg, 0.172 mmol) in dry 1,4-dioxane (5 cm^3) was heated to reflux for 1 h. The solution was then taken up in water, extracted with dichloromethane, extracts were washed with water, dried over magnesium sulfate, and evaporated *in vacuo*. The residue taken up in dichloromethane was filtered through a pad of silica, and evaporation gave the orange *N-benzylmurrayaquinone-A* **16** (22 mg, 89%) mp 181–183 °C (Found: C, 77.5; H, 5.0; N, 4.4. $C_{20}H_{15}NO_2$ requires: C, 79.7; H, 5.0; N, 4.7%); ν_{max}(KBr)/cm^{-1} 1637, 1462, 1377 and 1078; λ_{max}/nm 270 (sh) and 395; δ_H 2.15 (3H, d, *J* 1.6, CH_3), 5.85 (2H, s, CH_2Ph), 6.44 (1H, q, *J* 1.6, CH), 7.1–7.5 (8H, m, Ar) and 8.32 (1H, m, Ar); δ_C 15.82 (CH_3), 48.15 (CH_2), 111.59 (CH), 119.53 (C), 123.27 (CH), 123.96 (C), 124.60 (CH), 126.72 (C), 126.87 (CH), 126.96 (CH), 127.87 (CH), 128.87 (CH), 132.91 (CH), 135.95 (C), 147.52 (C), 174.60 (C) and 181.41 (C); EIHRMS *m*/*z* 301.110227 (M^+, 100%), calc. for $C_{20}H_{15}NO_2$: 301.110278.

4,9-Dihydro-3-methyl-1*H*-carbazole-1,4-dione (murrayaquinone-A) 1

A solution of *N*-benzylmurrayaquinone-A **16** (10 mg, 0.033 mmol) in trifluoroacetic acid (1 cm^3) and one drop of trifluoromethanesulfonic acid was heated to reflux for 15 min. The solution was then taken up in water and extracted with dichloromethane, the extracts were washed with water and dried over magnesium sulfate. Purification by preparative thin layer chromatography gave murrayaquinone-A as an orange solid **1** (4 mg, 60%), ν_{max}(KBr)/cm^{-1} 3216, 2925, 1685, 1636 (sh) and 1405; λ_{max}/nm 270 (sh) and 392; δ_H 2.18 (3H, d, *J* 1.5, CH_3), 6.52 (1H, q, *J* 1.5, CH), 7.35–7.47 (4H, m, Ar) and 9.05 (1H, br s, NH); CIHRMS *m*/*z* 211.06331 (M^+, 100%), calc. for $C_{13}H_9NO_2$: 211.063328.

9,9′-Bis(4-methoxybenzyl)-3,3′-dimethylbi[4,5,6,7,8,9-hexahydro-1*H*-carbazole]-1,1′4,4′,5,5′-hexone 13

A mixture of 2-bromo-5-methylbenzoquinone (3.01 g, 15.0 mmol), enamino ketone **11** (3.46 g, 15.0 mmol), sodium hydrogen carbonate (5.04 g, 60.0 mmol), cupric chloride (0.40 g, 3.0 mmol) and 3 Å molecular sieves (4 g) in dry acetonitrile (100 cm^3) was stirred at room temperature for 9 days in dry air. The suspension was then filtered on Celite and evaporated *in vacuo* to give a brown residue. The crude, taken up in dichloromethane, was purified on a dry column of silica eluted with a mixture of dichloromethane and methanol. The bright yellow *product* **13** (376 mg, 7%), mp 254 °C (decomp.) (from EtOH–H_2O) (Found: C, 70.8; H, 5.4; N, 3.8. $C_{42}H_{36}N_2O_8$ requires: C, 72.4; H, 5.2; N, 4.0%); ν_{max}(KBr)/cm^{-1} 2948, 1683, 1646, 1613, 1515, 1474, 1427 and 1252; λ_{max}/nm 270 (sh), 328 and 410; δ_H 1.93 (6H, s, CH_3), 2.15 (4H, quin, *J* 7.0, CH_2), 2.57 (4H, t, *J* 7.0, CH_2), 2.77 (4H, t, *J* 7.0, CH_2), 3.75 (6H, s, OMe), 5.57 (4H, s, CH_2Ar), 6.80 (4H, d, Ar) and 7.01 (4H, d, *J* 7.5, Ar); δ_C 14.22 (CH_3), 22.28 (CH_3), 22.61 (CH_2), 39.08 (CH_2), 48.55 (CH_2), 55.31 (CH_2), 114.44 (CH), 119.02 (C), 123.42 (C), 127.31 (C), 128.05 (CH), 130.45 (C), 136.91 (C), 145.04 (C), 150.59 (C), 159.38 (C), 177.27 (C), 180.36 (C) and 191.47 (C); FABMS *m*/*z* 697 (M^+, 20%), 699 (60).

9,9′-Bis(4-methoxybenzyl)-3,3′-dimethylbi[4,5,6,7,8,9-hexahydro-1*H*-carbazole]-1,1′,4,4′5,5′-hexone 5,5′-bis[(4-methylphenyl)sulfonylhydrazone] 17

To a solution of the bicarbazolehexone **13** (110 mg, 0.158 mmol) in glacial acetic acid (30 cm^3) was added a solution of *p*-tolylsulfonylhydrazine (65 mg, 0.350 mmol) in glacial acetic acid (10 cm^3), and the mixture was stirred at room temperature for 2 h. The mixture was then taken up in water (150 cm^3) and extracted with dichloromethane. The extracts were washed successively with water, saturated sodium bicarbonate solution, brine, and dried over magnesium sulfate. Purification by dry column chromatography (ethyl acetate and then dichloromethane) gave the deep purple *hydrazone* **17** (124 mg, 76%), mp 218 °C (decomp.) (from EtOH–$CHCl_3$) (Found: C, 64.3; H, 5.5; N, 7.6; S, 5.8. $C_{56}H_{52}N_6S_2O_{10}$ requires: C, 65.1; H, 5.1; N, 8.1; S, 6.2%); ν_{max}(KBr)/cm^{-1} 3452, 1639, 1510, 1297 and 1248; λ_{max}/nm 270 (sh), 330 (sh) and 570; δ_H (CD_2Cl_2) 2.01 (3H, s, CH_3), 2.06 (4H, m, CH_2), 2.09 (3H, s, CH_3), 2.37 (6H, s, $ArCH_3$), 2.71 (4H, m, CH_2), 2.92 (4H, m, CH_2), 3.74 (6H, s, OCH_3), 5.55 (4H, s, CH_2Ar), 6.81 (4H, d, *J* 9.0, Ar), 7.01 (4H, d, *J* 9.0, Ar), 7.24 (4H, d, *J* 8.0, Ar) and 7.86 (4H, d, *J* 8.0, Ar); FABMS *m*/*z* 1037 (M^+ + 5, 100%), 1036 (78), 1035 (59), 1034 (18) and 1033 (5).

9,9′-Bis(4-methoxybenzyl)-3,3′dimethylbi[4,9-dihydro-1*H*-carbazole]-1,1′4,4′-tetrone 18

A solution of the hydrazone **17** (103 mg, 0.099 mmol) in dichloromethane (30 cm^3) was shaken with a solution of sodium dithionite (200 mg, 1.15 mmol) in water (30 cm^3) in a separatory funnel until yellow. The organic solution was then washed with water, dried over magnesium sulfate under nitrogen atmosphere, and evaporated *in vacuo*. The residue was taken up in dry THF (50 cm^3) and kept under nitrogen atmosphere. A solution of *n*-butyllithium in hexane (1.6 M, 1.5 cm^3, 2.4 mmol) was then added slowly under nitrogen, at room temperature and under rapid stirring. After 30 min of stirring at room temperature, the reaction was quenched by a slow addition of water in THF. The mixture was taken up in water, acidified with 0.1 M aqueous HCl and extracted with dichloromethane, extracts were washed with water, dried over magnesium sulfate and evaporated *in vacuo*. Purification on a dry column of silica (eluant: dichloromethane and methanol) gave the intermediate as a mauve solid. This intermediate was dissolved in dry 1,4-dioxane (4 cm^3) with dichlorodicyanobenzoquinone (45 mg, 0.199 mmol) and was heated to reflux for 1 h. The solution was then taken up in water, extracted with dichloromethane, extracts were washed with water, dried over magnesium sulfate, and evaporated *in vacuo*. The residue taken up in dichloromethane was filtered through a pad of silica, and evaporation gave the orange *bisquinone* **18** (21 mg, 32%), mp 224–225 °C; ν_{max}(KBr)/cm^{-1} 1646, 1613, 1519, 1466 and 1249; λ_{max}/nm 270 (sh) and 395; δ_H 2.03 (6H, s, CH_3), 3.72 (6H, s, OCH_3), 5.75 (4H, s, CH_2Ar), 6.77 (4H, d, *J* 8.6, Ar), 7.13 (4H, d, *J* 8.6, Ar), 7.36–7.49 (6H, m, Ar) and 8.34 (2H, m, Ar); δ_C 13.97 (CH_3), 47.87 (CH_2), 55.33 (CH_3), 111.74 (CH), 113.77 (C), 114.28 (CH), 117.53 (C), 123.44 (CH), 124.04 (C), 124.78 (CH), 127.21 (CH), 128.45 (CH), 130.42 (C), 133.24 (C), 137.82 (C), 139.27 (C), 145.37 (C), 179.28 (C) and 182.64 (C); FABMS 664 (M^+ + 4, 100%), 663 (74), 662 (67) and 661 (40); CIHRMS *m*/*z* 660.226017 (M^+, 60%), calc. for $C_{42}H_{32}N_2O_6$: 660.226037.

(±)-Bismurrayaquinone-A 5

A solution of the bis-*N*-benzylmurrayaquinone-A **18** (10 mg, 0.033 mmol) in trifluoroacetic acid (1 cm^3) and one drop of trifluoromethanesulfonic acid was heated to reflux for 15 min. The solution was then taken up in water and extracted with dichloromethane, the extracts were washed with water and dried over magnesium sulfate. Evaporation gave (±)-bismurrayaquinone-A as an orange solid (4 mg, 60%); ν_{max}(KBr)/cm^{-1} 2927, 1734, 1640, 1466, 1397, 1381 and 1325; λ_{max}/nm 270 (sh) and 390; δ_H 2.06 (6H, s, CH_3), 7.37–7.47 (6H, m, Ar), 8.26 (2H, d, *J* 7.4, Ar) and 9.26 (2H, br s, NH); CIHRMS *m*/*z* 420.110965 (M^+, 30%), calc. for $C_{26}H_{16}N_2O_4$: 420.111007.

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