Studies on Quinones. Part 21.[1] Regioselective Synthesis of Tetracyclic Quinones related to Rabelomycin

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The Diels–Alder reaction of the hydroxyquinones **5**, **11** and **16** with (*E*)-1-trimethylsiloxybuta-1,3-diene **3** afforded the corresponding mixture of the regioisomers **6a,b**, **12a,b** and **17a,b** in the ratios 9:1, 8:1 and 11:1, respectively. From these mixtures, the quinones **8**, **14** and **19** were obtained by hydrolysis and subsequent oxidation.

The preparation of the diene **22** by chlorotrimethylsilylation of the anion of the ester **21** is described. Diels–Alder reaction of diene **22** with the quinones **23** and **24** yielded the corresponding 6-ethoxybenz[*a*]anthracenequinones **25** and **26**, together with the 6-hydroxybenz[*a*]anthracenequinones **19** and **20**. The quinones **19** and **20**, which were isolated in mixtures with the ester **21**, undergo selective aerial oxidation under basic conditions to give the corresponding benz[*a*]anthracene-1,7,12-triones **27** and **28**.

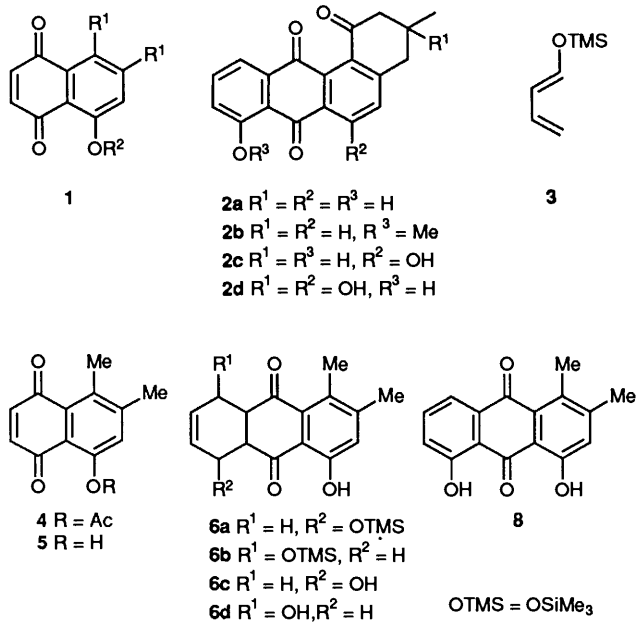
The angucyclinones, a growing family of naturally occurring quinones,[2] are of current interest due to their antibacterial,[3–5] enzyme inhibitory[6,7] and antitumour activities.[5,8,9] Synthetic efforts in this field, confined to the preparation of the ochromycinone **2a**,[10,11] X-14881C **2b**[10] and the non-naturally occurring 3-deoxyrabelomycin **2c**,[12] are based on two main strategies. In one of these, the benz[*a*]anthracene skeleton is assembled by regiospecific aromatic metallation;[10,12] in the other, the construction of the angular tetracyclic framework was achieved by Diels–Alder cycloaddition.[11]

As part of a programme aimed at constructing polycyclic angular quinones we have previously reported convenient routes[13–15] to 7,8-dimethyl- and 7,8-oligomethylene-1,4-naphthoquinones bearing an oxygenated substituent at C-5, of general formula **1**. The synthetic sequences required to obtain these quinones are based on acid-induced rearrangement of acylbenzo[*b*]furans[13–16] and on the dienone–phenol rearrangement of naphthalenetriones.[13–15] The structural analogy of the tetrahydrophenanthrene-1,4-quinone **1** (R^1R^1 = $[CH_2]_4$, R^2 = Ac)[15] (≡**15**) with the tricyclic portion of the rabelomycin antibiotic **2d**[3] led us to study the extension of the annular system in order to construct new tetrahydrobenz[*a*]anthracene-7,12-quinones related to rabelomycin **2d**.

This paper reports the synthesis of tri- and tetra-cyclic quinones, structurally related to rabelomycin **2d**, through regiocontrolled Diels–Alder reactions of quinones of type **1** with dienes bearing an oxygen substituent.

The hydroxyquinone **5** was used as a model substrate for the exploration of the construction of the 3,4-dialkyl-1,8-dihydroxyanthracene-9,10-quinone system by cycloaddition reaction with (*E*)-1-trimethylsiloxybuta-1,3-diene **3**. The quinone **5** was prepared in 86% yield by acid hydrolysis (aq. AcOH, HCl) of the corresponding acetate **4**. Reaction of compound **5** with an excess of the diene **3** in dichloromethane at room temperature gave a mixture of the isomeric adducts **6a,b** in 88% yield. The NMR signals of the chelated protons of the adducts **6a,b**, which appeared at δ 12.65 and 12.16 respectively, indicated that these adducts were generated in the ratio 9:1.

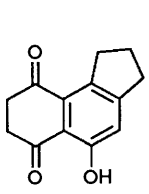
The mixture of the adducts **6a,b** was easily converted into the mixed allylic alcohols **7a,b** by treatment with hydrochloric acid in water–tetrahydrofuran (THF) (1:9) solution at room temperature. The resulting alcohols **7a,b** were oxidised with active manganese dioxide in dichloromethane and the major



product, characterised as the anthraquinone **8**, was purified by recrystallisation from ethanol–chloroform. The structure of compound **8** was established mainly on the basis of the carbonyl absorptions at 1660 and 1630 cm^{-1}, and by the carbonyl carbon signals which appeared at δ_C 192.47 and 184.34, in agreement with those of the carbonyl carbons of 1,8-dihydroxyanthracene-9,10-quinone.[17]

These results indicated that cycloaddition of the diene **3** with the quinone **5** proceeds with high regioselectivity to afford the adduct **6a** as the major isomer. The regiochemical control of this cycloaddition can be attributed to the intramolecular hydrogen bond in the quinone **5**, making C-4 the more electron-deficient carbon of the dienophilic system.[18,19]

Next we studied the cycloaddition of the angular quinone **11** with the diene **3**. For this purpose the preparation of the quinone **11** was attempted by oxidation of the dione **9**;[13] however, this substrate was inert under a variety of conditions. A successful preparation of the quinone **11** was eventually



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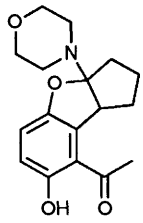

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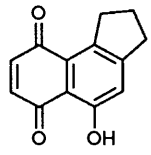
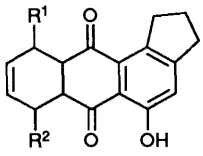
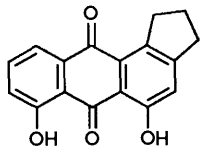


11



12a R^1 = H, R^2 = OTMS
12b R^1 = OTMS, R^2 = H
13a R^1 = H, R^2 = OH
13b R^1 = OH, R^2 = H



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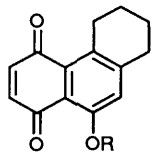
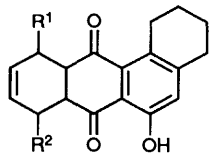
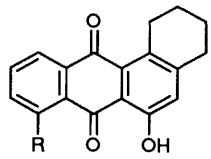


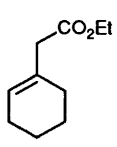
15 R = Ac
16 R = H



17a R^1 = H, R^2 = OTMS
17b R^1 = OTMS, R^2 = H
18 R^1 = H, R^2 = OH



19 R = OH
20 R = H



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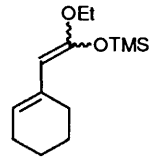

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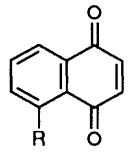
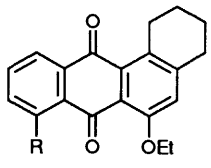
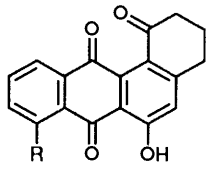


23 R = OH
24 R = H



25 R = OH
26 R = H



27 R = OH
28 R = H

achieved by acid-induced rearrangement of the *O,N*-acetal **10** in the presence of oxygen.

Compound **11** was subject to cycloaddition with the diene **3** to furnish a mixture of the cycloadducts **12a,b** in the ratio 8:1, respectively. This mixture was converted into the corresponding allyl alcohols **13a,b** in 95% yield, and these alcohols were oxidised with active manganese dioxide in dichloromethane solution. Purification of the reaction mixture by column chromatography on silica gel afforded the major tetracyclic quinone **14** in 47% yield.

The quinone **16** was prepared in 42% yield by acid hydrolysis of the corresponding acetate **15**, and was then subjected to the above annelation sequence employed in the synthesis of the quinones **8** and **14**. Cycloaddition of the phenanthrenequinone **16** with the diene **3** afforded a mixture of the adducts **17a,b** in the ratio 11:1, respectively. The major isomer **17a**, isolated in 91% yield by column chromatography followed by recrystallisation from light petroleum, was hydrolysed to the corresponding alcohol **18** and this was oxidised to the tetracyclic quinone **19** in 52% yield with pyridinium chlorochromate (PCC) in dichloromethane solution.

The high regioselectivity of the cycloaddition of unsaturated ketene acetals with 5-hydroxy-1,4-naphthoquinone **23**[20–22] prompted us to explore the synthesis of the quinone **19** by cycloaddition reaction of the diene **22** with compound **23**. The required diene **22** was obtained from the ester **21** by deprotonation with lithium diisopropylamide (LDA) and subsequent quenching of the dienolate with chlorotrimethylsilane (TMSCl).

The cycloaddition of the diene **22** with quinone **23** was conducted at room temperature in benzene solution for ten days. The reaction mixture was passed through a column of silica gel in order to induce aromatisation of the adduct and was then chromatographed on preparative TLC plates. This procedure afforded the angular quinone **25** in 61% yield, and a 1:5.5 mixture of the quinone **19** and the ester **21**.

The structure of the angular quinone **25** was determined from its ^{1}H and ^{13}C NMR spectra. Furthermore, treatment of compound **25** with aluminium chloride in dichloromethane solution provided a hydroxy quinone which, on the basis of IR and ^{1}H NMR spectra, was identical with compound **19** obtained from the alcohol **18**.

Since attempted separation of compounds **19** and **21** using chromatographic techniques was unsuccessful, we attempted to isolate the hydroxy quinone **19** by acid–base extraction. The mixture of the products **19** and **21** in benzene solution was therefore rapidly extracted with cool aq. sodium hydroxide and the aqueous phase was acidified. After this treatment an unexpected compound was isolated. The new compound exhibited three carbonyl absorptions, at 1707, 1675 and 1630 cm^{-1}. The ^{1}H NMR spectrum displayed two types of coupled methylenic protons, at δ 2.18 and 2.86, signals of two chelated protons, at δ 11.72 and 12.31, and a singlet at δ 7.02 for an aromatic proton. The ^{13}C NMR spectrum of this compound showed the existence of three types of methylenic carbons, and the signals at δ_C 184.58, 192.59 and 198.27 confirmed the presence of three carbonyl groups. These spectral properties, along with the mass spectrum and decoupling experiments in which irradiation of the methylene protons signal at δ 2.86 sharpened the signal of the aromatic proton at δ 7.02, are in good agreement with the structure **27**. It is reasonable to assume that the quinone **27**, isolated in 79% yield from substrate **19**, was generated by aerial oxidation of the methylene group at C-1 under basic conditions.

We also studied the cycloaddition between the diene **22** and the 1,4-naphthoquinone **24** in benzene solution at room temperature. After ten days, the reaction mixture was subjected to the same chromatographic separation as mentioned in the reaction of the quinone **23** with the diene **22**. This procedure afforded the tetracyclic quinone **26** albeit in poor yield (9%), and a 1:6 mixture of the quinone **20** and the ester **21**. Further acid–base treatment of this mixture as previously described for the formation of compound **27** afforded the tetracyclic quinone **28** in 83% yield from substrate **20**.

There are several literature reports in which organic compounds with benzylic hydrogens (*e.g.*, diarylmethanes, diarylmethanols, fluorene, fluoren-9-ol and dihydroanthracenes) are oxidised with molecular oxygen in basic medium to afford carbonyl compounds.[23,24] The proposed mechanism of these oxidations involves a peroxyl free radical generated by reaction of a carbanion with molecular oxygen.[23] Triones **27** and **28** may probably be produced from the diones **19** and **20** through the corresponding carbanion intermediates at C-1, generated in

basic media. On the basis of this assumption, and considering that carbonyl C-7 in the substrates has lower electrophilic character than does carbonyl C-12, the selectivity of oxidation at C-1, could be explained by the greater resonance stabilisation of the carbanion on C-1 than on C-4.

Conclusions.—In summary, two routes have been developed for the preparation of benz[*a*]anthraquinones structurally related to rabelomycin, employing regiocontrolled Diels–Alder reactions as the key step. These synthetic routes and the selective aerial oxidation (under basic conditions) of the 1,2,3,4-tetrahydrobenz[*a*]anthracene-7,12-quinones, are potentially useful results to apply to synthesis of more complex benz[*a*]-anthraquinones.

Experimental

M.p.s were measured on a Kofler hot-stage apparatus and are uncorrected. Unless otherwise stated, IR spectra were recorded on a Perkin-Elmer 1310 spectrophotometer for KBr discs. ^{1}H NMR spectra were obtained on a Varian XL-100 or a XL-300 spectrometer; ^{13}C NMR were recorded on a Bruker WM 200 SY(200 MHz) or a Varian XL-300 spectrometer. Samples were dissolved in $CDCl_3$ and chemical shifts are expressed downfield from $SiMe_4$. *J*-values are given in Hz. Mass spectra were recorded on a VB-12-250 spectrometer. Silica gel Merck 60 (70–230 mesh) and DC-Alufolien $60F_{254}$ were normally used for preparative column chromatography and analytical TLC, respectively.

8-*Hydroxy*-5,6-*dimethyl*-1,4-*naphthoquinone* **5**.—A stirred solution of the acetate **4**[15] (170 mg, 0.84 mmol) in acetic acid (9 cm^3) was heated to 85–90 °C, hydrochloric acid (7 mol dm^{-3}; 1.3 cm^3) was immediately added in one portion, and the mixture was heated for 15 min. The deep red solution was poured into ice–water (200 cm^3) and extracted with chloroform (2 × 50 cm^3). The extract was washed successively with water, aq. sodium hydrogen carbonate and water, and dried ($MgSO_4$) to give *compound* **5** in 84% yield. The title compound was purified by column chromatography (benzene); m.p. 158–160 °C (from benzene–hexane) (Found: C, 71.2; H, 4.9. $C_{12}H_{10}O_3$ requires C, 71.3; H, 4.95%); ν_{max}/cm^{-1} 3450, 1660, 1650 and 1610; δ_H(100 MHz) 2.40 (3 H, s, 6-Me), 2.56 (3 H, s, 5-Me), 6.88 (2 H, s, 2- and 3-H), 7.12 (1 H, s, 7-H) and 12.60 (1 H, s, OH); δ_C 16.4, 21.7, 113.9, 125.1, 128.5, 133.9, 136.8, 141.1, 149.4, 160.4, 186.9 and 190.2.

Reaction of Quinone **5** *with* (E)-1-*Trimethylsiloxybuta*-1,3-*diene* **3**.—To a solution of the quinone **5** (100 mg, 0.50 mmol) in dichloromethane (7 cm^3) was added the diene **3** (0.3 cm^3) and the mixture was kept at room temperature for one day. The solvent was removed and the residue was heated at 70–80 °C for two hours under reduced pressure. The residue was dissolved in benzene and then filtered through silica gel to afford a 1:9 mixture of the adducts **6a,b** as a yellow liquid (150 mg, 88%); ν_{max}(film)/cm^{-1} 1710, 1640, 1250, 1060 and 850; δ_H(100 MHz) −0.21 (9 H, s, $OSiMe_3$), 2.07 (1 H, dd, *J* 18, 6, C*H*H), 2.35 [3 H, s, CO·C·C(Me)=C(*Me*)], 2.43 [3 H, s, CO·C·C(*Me*)=C(Me)], 2.86–3.50 (3 H, m, CH*H* and 2 × CO·CH), 4.43 (1 H, m, CHOSi), 5.68–6.16 (2 H, m, CH=CH), 7.00 (1 H, s, ArH), 12.16 (0.1 H, s, OH) and 12.65 (0.9 H, s, OH).

1,8-*Dihydroxy*-5,6-*dimethyl*-1,4,4a,9a-*tetrahydro*-9,10-*anthraquinone and* 1,5-*Dihydroxy*-7,8-*dimethyl*-1,4,4a,9a-*tetrahydro*-9,10-*anthraquinones* **7a,b**.—A solution of the adducts **6a,b** (115 mg, 0.33 mmol) and hydrochloric acid (1.3 mol dm^{-3}; 0.5 cm^3) in water–THF (20 cm^3; 1:9) was stirred at room temperature. After one hour the mixture was diluted with water (20 cm^3) and extracted with chloroform. The dried ($MgSO_4$) extract was evaporated and the solid residue was triturated with hot light petroleum (2 × 5 cm^3; 40–60 °C) to afford the alcohols **7a,b** (84 mg, 94%) in the ratio 9:1 (^{1}H NMR). An analytical sample of the *major isomer* **7a** was obtained by crystallisation from benzene, m.p. 156–158 °C (Found: C, 70.9; H, 5.85. $C_{16}H_{16}O_4$ requires C, 70.6; H, 5.9%); ν_{max}/cm^{-1} 3470, 1700, 1640 and 1230; δ_H(100 MHz), 2.20 (1 H, dd, *J* 18, 6, 4-H), 2.33 (3 H, s, 6-Me), 2.37 (3 H, s, 5-Me), 2.88 (1 H, dd, *J* 18, 3, 4-H′), 3.40 (2 H, m, 4a- and 9a-H), 4.46 (1 H, m, 1-H), 5.93 (2 H, m, 2- and 3-H) and 12.50 (1 H, s, OH).

4,5-*Dihydroxy*-1,2-*dimethyl*-9,10-*anthraquinone* **8**.—A solution of the alcohols **7a,b** (103 mg, 0.38) in dichloromethane (5 cm^3) containing active manganese dioxide[25] (0.5 g) was vigorously stirred for two hours. After this time further manganese dioxide (0.5 g) was added and the mixture was stirred overnight. The mixture was filtered and the solids were washed thoroughly with dichloromethane. The filtrate was evaporated and the residue was chromatographed on silica gel with benzene as eluent to afford *compound* **8** (90 mg, 89%), m.p. 202–205 °C (from EtOH–$CHCl_3$) (Found: C, 71.6; H, 4.7. $C_{16}H_{12}H_4$ requires C, 71.6; H, 4.5%); ν_{max}/cm^{-1} 1660, 1630 and 1605; δ_H(300 MHz) 2.39 (3 H, s, 2-Me), 2.59 (3 H, s, 1-Me), 7.07 (1 H, s, 3-H), 7.21 (1 H, dd, *J* 8, 1.5, 6-H), 7.50–7.75 (2 H, m, 7- and 8-H) 11.98 (1 H, s, OH) and 12.49 (1 H, s, OH); δ_C 17.2, 22.0, 114.6, 115.5, 119.5, 123.2, 125.2, 130.5, 134.5, 135.1, 136.8, 150.2, 161.2, 161.6, 184.3 and 192.5.

5-*Hydroxy*-2,3-*dihydro*-1H-*cyclopenta*[a]*naphthalene*-6,9-*quinone* **11**.—A solution of the heterocycle **10**[13] (298 mg, 0.99 mmol) in sulphuric acid (30 cm^3; 10%) was heated at 70–80 °C and stirred under oxygen for ten hours. The mixture was diluted with water and extracted with chloroform. The extract was washed with water and dried ($MgSO_4$). The solvent was removed and the residue was dissolved in chloroform and filtered through silica gel with chloroform as eluent to give the *quinone* **11** (83 mg, 39%), m.p. 148–149 °C (Found: C, 72.5; H, 4.7. $C_{13}H_{10}O_3$ requires C, 72.9; H, 4.7%); ν_{max}/cm^{-1} 1650 and 1630; δ_H(100 MHz) 2.13 (2 H, q, *J* 7, 2-H), 2.93 (2 H, t, *J* 7, 3-H_2), 3.25 (2 H, t, *J* 7, 1-H_2), 6.87 (1 H, d, B of AB, *J* 10, 7-H), 6.96 (1 H, d, A of AB, *J* 10, 8-H), 7.16 (1 H, s, 4-H) and 12.47 (1 H, s, OH).

Reaction of Quinone **11** *with the Diene* **3**.—A solution of the quinone **11** (102 mg, 0.47 mmol) in dichloromethane (3 cm^3) containing the diene **3** (136 mg, 0.96 mmol) was kept at room temperature for eight days. The solvent was removed under reduced pressure to yield an 8:1 mixture of the adducts **12a,b** as a pale yellow oil, in quantitative yield; ν_{max}/cm^{-1} 3200, 1680 and 1640; δ_H(100 MHz) −0.37 (9 H, s, $OSiMe_3$), 1.80–2.30 [2 H, m, 2- and 7(10)-H], 2.85 (2 H, t, *J* 7, 3-H_2), 2.96–3.60 (5 H, m, 1-H_2, 7(10)-H, 6a-H and 10a-H), 4.32 (1 H, m, 6-H), 5.50–6.20 (2 H, m, 8- and 9-H), 7.00 (1 H, s, 4-H), 12.08 (0.11 H, s, OH) and 12.53 (0.89 H, s, OH).

Hydrolysis of the Adducts **12a,b**.—A solution of the adducts **12a,b** (170 mg, 0.49 mmol) and hydrochloric acid (1.3 mol dm^{-3}; 0.4 cm^3) in water–THF (20 cm^3; 1:9) was stirred for two hours at room temperature. The mixture was diluted with water and extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated to afford an 8:1 mixture of the *alcohols* **13a,b** (129 mg, 95%); m.p. 130–133 °C (Found: C, 71.6; H, 5.7. $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.6%); ν_{max}/cm^{-1} 3500, 1680 and 1620; δ_H(100 MHz) 1.90–2.60 [4 H, m, 2- and 7(10)-H_2], 2.94 (2 H, t, *J* 8, 3-H_2), 3.10–3.50 (4 H, m, 1-H_1, 6a-H, and 10a-H), 4.5 (1 H, br s, OH), 5.95 (2 H, m, 8- and 9-H), 7.13 (1 H, s, 4-H) and 12.42 (1 H, s, OH).

2,3-*Dihydro*-5,7-*dihydroxy*-2H-*cyclopent*[a]*anthracene*-6,11-

quinone **14**.—A solution of the alcohols **12a,b** (99 mg, 0.35 mmol) in dichloromethane (5 cm^3) and active manganese dioxide (0.6 g) was vigorously stirred at room temperature for two hours. After this time an additional portion of the oxidant (0.6 g) was added and the mixture was vigorously magnetically stirred overnight. The insoluble solids were removed by filtration and thoroughly washed with dichloromethane. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with benzene furnished the angular *quinone* **14** (47 mg, 47%), m.p. 166–167 °C (Found: C, 72.8; H, 4.8. $C_{17}H_{12}O_4$ requires C, 72.9; H, 4.3%); ν_{max}/cm^{-1} 1650 and 1620; δ_H(100 MHz) 1.90–2.30 (2 H, m, 2-H), 2.91 (2 H, t, *J* 8, 3-H_2), 3.30 (2 H, *J* 8, 1-H_2), 7.05 (1 H, s, 4-H), 7.22 (1 H, d, *J* 6, 3, 8-H), 7.50–7.80 (2 H, m, 9- and 10-H), 12.09 (1 H, s, OH) and 12.37 (1 H, s, OH); δ_C 24.8, 32.9, 33.8, 113.9, 115.9, 119.4, 119.9, 123.8, 127.7, 134.0, 136.7, 140.9, 158.1, 162.1, 162.8, 183.2 and 192.4.

5-*Hydroxy*-7,8,9,10-*tetrahydrophenanthrene*-1,4-*quinone* **16**.—A solution of the acetate **15**[15] (120 mg, 0.44 mmol) in 1,4-dioxane (30 cm^3) and hydrochloric acid (5 mol dm^{-3}; 3 cm^3) was heated to reflux for one hour. The mixture was diluted with water and extracted with chloroform. The extract was washed with water (2 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography with benzene as eluent to yield *compound* **16** (50 mg, 50%), m.p. 139–141 °C (Found: C, 73.4; H, 5.1. $C_{14}H_{12}O_3$ requires C, 73.7; H, 5.3%); ν_{max}/cm^{-1} 3450, 1660, 1645 and 1610; δ_H(300 MHz) 1.78 (4 H, m, 8- and 9-H_2), 2.85 (2 H, t, *J* 5.5, 7-H_2), 3.14 (2 H, t, *J* 5.5, 10-H_2), 6.63 (1 H, d, *J* 10, 3-H), 6.86 (1 H, d, *J* 10, 2-H), 7.02 (1 H, s, 6-H) and 12.41 (1 H, s, OH); δ_C 21.7, 23.0, 28.4, 31.6, 114.3, 124.3, 128.3, 135.1, 136.6, 141.0, 149.8, 159.9, 186.7 and 190.7; *m/z* 228 (M^+, 100), 213, 199, 185 and 115.

Reaction of Quinone **16** *with the Diene* **3**.—A solution of quinone **16** (42 mg, 0.18 mmol) and the diene **3** (0.3 cm^3) in dichloromethane (10 cm^3) was kept at room temperature for 24 h. The solvent was removed under reduced pressure and the residue was heated *in vacuo* at 70–80 °C for two hours. The crude residue was purified by column chromatography on silica gel with benzene as eluent to give the *adduct* **17a** (62 mg, 91%), m.p. 112.5–114 °C (from hexane) (Found: C, 67.95; H, 6.9. $C_{21}H_{26}O_4Si$ requires C, 68.1; H, 7.0%); ν_{max}/cm^{-1} 1700, 1635, 1055 and 845; δ_H(300 MHz) 1.50–2.20 (5 H, m, 2- and 3-H_2 and 11-H), 2.70–3.40 (8 H, m, 1- and 4-H_2, 11-H, 7a-H, and 11a-H), 4.39 (1 H, t, *J* 4, 8-H), 5.70–5.90 (2 H, m, 9- and 10-H), 6.89 (1 H, s, 5-H) and 12.49 (s, 1 H, OH).

6,8-*Dihydroxy*-1,2,3,4-*tetrahydrobenz*[a]*anthracene*-7,12-*quinone* **19**.—A solution of the adduct **17a** (60 mg, 0.16 mmol), in water–THF (10 cm^3; 1:9) containing 1.3 mol dm^{-3} hydrochloric acid (seven drops) was kept at room temperature for 90 min. The mixture was diluted with water and extracted with chloroform, and the extract was dried ($MgSO_4$). The solvent was removed and the alcohol **18** was dissolved in dichloromethane (2 cm^3). This solution was added dropwise to a stirred mixture of PCC (200 mg) and dry sodium acetate (100 mg). The reaction mixture was stirred at room temperature for two hours and was then filtered through silica gel and eluted with dichloromethane. Evaporation of the eluate afforded the *tetracyclic quinone* **19** as red crystals (22 mg, 49%), m.p. 174–177 °C (Found: C, 73.3; H, 5.0. $C_{18}H_{14}O_3$ requires C, 73.5; H, 4.8%); ν_{max}/cm^{-1} 1660 and 1615; δ_H(100 MHz) 1.72–2.04 (4 H, m, 2- and 3-H), 2.74–3.06 (2 H, m, 4-H_2), 3.18–3.46 (2 H, m, 1-H_2), 7.20–7.48 (1 H, m, 9-H), 7.30 (1 H, s, 5-H), 7.58–7.92 (2 H, m, 10- and 11-H), 12.02 (1 H, s, OH) and 12.48 (1 H, s, OH); δ_C 21.7, 23.2, 29.0, 31.7, 115.0, 115.4, 119.5, 123.2, 124.5, 130.3, 135.1, 135.8, 136.8, 150.6, 160.7, 161.6, 184.0 and 192.7.

(E)-*and*(Z)-1-(2′-*Ethoxy*-2′-*trimethylsiloxyvinyl*)*cyclohexene* **22**.—To a stirred solution of LDA (380 mg, 3.6 mmol) in anhydrous THF (5 cm^3) at −78 °C under nitrogen was added a solution of the ester **21**[26] (500 mg, 2.98 mmol) in the same solvent (2 cm^3). After being stirred at −78 °C for two hours the mixture was treated with a solution of chlorotrimethylsilane (390 mg, 3.6 mmol) in THF (5 cm^3) added dropwise and the reaction mixture was stirred and allowed to warm to room temperature overnight. After removal of the solvent the residue was taken up in pentane and the insoluble solids were filtered off. Evaporation of the filtrate afforded a mixture of the title compounds **22** (0.62 g, 87%) as a slightly yellow oil, which was used directly in the next step; ν_{max}/cm^{-1} 1650, 1610, 1200 and 845; δ_H(100 MHz) 0.16 (9 H, s, $OSiMe_3$), 1.16 (2.1 H, t, *J* 7, CH_2*Me*), 1.22 (0.9 H, t, *J* 7, CH_2*Me*), 1.35–1.70 (4 H, m, 4- and 5-H_2), 1.84–2.30 (4 H, m, 3- and 6-H_2), 3.77 (1.4 H, q, *J* 7, CH_2Me), 3.84 (0.6 H, q, *J* 7, CH_2Me), 4.04 (0.3 H, s, 1′-H), 4.23 (0.7 H, s, 1′-H) and 5.47 (1 H, m, 2-H).

Reaction of 5-*Hydroxy*-1,4-*naphthoquinone* **23** *with the Diene* **22**.—A solution of quinone **23** (290 mg, 1.66 mmol) and the crude diene **22** (540 mg, 2.5 mmol) in anhydrous benzene (5 cm^3) was kept at room temperature for ten days. The mixture was passed through silica gel (benzene) and the filtrate was evaporated. The residue was chromatographed by preparative TLC (benzene) to give a 5.5:1 mixture (310 mg) of the quinone **19** and the ester **21** (^{1}H NMR), and the *tetracyclic quinone* **25** (330 mg, 61%), m.p. 185–186 °C (Found: C, 74.1; H, 5.6. $C_{20}H_{18}O_4$ requires C, 74.5; H, 5.6%); ν_{max}/cm^{-1} 1660 and 1635; δ_H(100 MHz) 1.55 (3 H, t, *J* 7, CH_2*Me*), 1.66–1.98 (4 H, m, 2- and 3-H_2), 2.68–2.96 (2 H, m, 4-H_2), 3.03–3.32 (2 H, m, 1-H_2), 4.19 (2 H, q, *J* 7, CH_2Me), 6.98 (1 H, s, 5-H), 7.08–7.33 (1 H, m, 9-H) and 7.25–7.48 (2 H, m, 10- and 11-H); δ_C 14.8, 21.8, 23.4, 29.1, 31.7, 65.3, 116.6, 118.2, 120.2, 120.6, 123.1, 133.7, 134.3, 134.6, 135.4, 148.0, 157.9, 161.5, 185.9 and 189.0; *m/z* 322 (M^+), 279 (100%), 247, 189, 165 and 115.

A solution of the quinone **19** and the ester **21** (310 mg) in benzene (15 cm^3) was extracted in a separatory funnel with ice-cold aq. sodium hydroxide (2.8 mol dm^{-3}; 2 × 15 cm^3) by vigorous shaking for one minute. The deep purple aq. phase was acidified with 3 mol dm^{-3} hydrochloric acid, extracted with chloroform, and dried ($MgSO_4$). Removal of the solvent afforded the *trione* **27** (60 mg, 79% based on **19**), m.p. 226.5–228 °C (Found: M^+, 308.067 33. $C_{18}H_{12}O_3$ requires M, 308.068 46); ν_{max}/cm^{-1} 1707, 1675 and 1630; δ_H(300 MHz) 2.18 (2 H, quin, *J* 6.7, 3-H_2), 2.86 (4 H, t, *J* 6.7, 2- and 4-H_2), 7.02 (1 H, s, 5-H), 7.24–7.30 (2 H, m, 9- and 10-H), 7.68 (1 H, dd, *J* 4.6 and 0.6, 11-H), 11.72 (1 H, s, OH) and 12.31 (1 H, s, OH); δ_C 22.3, 30.4, 39.1, 115.1, 116.6, 120.1, 120.9, 124.0, 130.4, 135.3, 137.5, 137.7, 154.4, 162.1, 163.3, 184.6, 192.6 and 198.3.

Dealkylation of the Quinone **25**.—To a solution of the quinone **25** (70 mg, 0.22 mmol) in dichloromethane (5 cm^3) at 0 °C was added anhydrous aluminium chloride (145 mg, 1.09 mmol) and the mixture was stirred at room temperature for ten minutes. The resulting deep purple solution was quenched with ice–water and extracted with dichloromethane, and the organic phase was dried ($MgSO_4$). The solvent was evaporated off at reduced pressure to give the quinone **19** (60 mg, 94%).

Reaction of the Diene **22** *with the Quinone* **24**.—Following the same procedure previously described for the reaction of the quinone **23** with the diene **22**, treatment of quinone **24** (180 mg, 1.14 mmol) with the crude diene **22** (400 mg, 1.85 mmol) afforded a 6:1 mixture (220 mg) of the quinone **20** and the ester **21**, and the *tetracyclic quinone* **26** (36 mg, 9%), m.p. 153–155 °C (Found: M^+, 306.125 99. $C_{20}H_{18}O_3$ requires M, 306.125 64); ν_{max}/cm^{-1} 1680 and 1650; δ_H(300 MHz) 1.57 (3 H, t, *J* 7,

CH_2Me), 1.75–1.90 (4 H, m, 2- and 3-H_2), 2.85–2.90 (2 H, m, 4-H_2), 3.20–3.30 (2 H, m, 1-H_2), 4.21 (2 H, q, *J* 7, CH_2Me), 7.05 (1 H, s, 5-H), 7.62–7.78 (2 H, m, 9- and 10-H) and 8.06–8.23 (2 H, m, 8- and 11-H).

A solution of compounds **20** and **21** (220 mg) in benzene (15 cm^3) was extracted in a separatory funnel with ice-cold aq. sodium hydroxide (2.8 mol dm^{-3}; 2 × 15 cm^3) by vigorous shaking for one minute. The purple aq. phase was acidified with 3 mol dm^{-3} hydrochloric acid and extracted with chloroform, and the extract was dried ($MgSO_4$). Evaporation of the solvent afforded the benz[*a*]anthracenequinone **28** (40 mg, 83% based on **20**) as red crystals, m.p. 187.5–189.5 °C; ν_{max}/cm^{-1} 1700, 1675 and 1640; δ_H(100 MHz) 2.00–2.40 (2 H, quin, *J* 6, 3-H_2), 2.86 (4 H, t, *J* 6, 2- and 4-H_2), 7.00 (1 H, s, 5-H), 7.86–7.92 (2 H, m, 9- and 10-H), 8.05–8.35 (2 H, m, 8- and 11-H) and 12.78 (1 H, s, OH); δ_C 22.3, 30.5, 39.2, 116.9, 120.6, 126.6, 126.7, 129.9, 130.9, 132.2, 133.7, 135.0, 135.3, 153.9, 163.5, 183.61, 188.3 and 198.3; *m/z* 292 (M^+), 264 (100%), 208, 180 and 152.

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