Quinones. Part 14.[1] Attempted synthesis of 9,10-dimethyl-2,6-anthraquinone. Desmotropic formation of secondary *ortho*-anthraquinoles instead of 1,2-anthrahydroquinones

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In connection with PMO calculations on the reactivity of quinones, we attempted to synthesize 9,10-dimethyl-2,6-anthraquinone 3a by oxidising 2,6-dihydroxy-9,10-dimethylanthracene 2. Even under exclusion of water, only addition products of water to 3a, *viz.* the secondary *ortho*-anthraquinols 1,6-dihydroxy-9,10-dimethylanthracen-2(1*H*)-one 4 and 2,6-dihydroxy-9,10-dimethylanthracen-1(2*H*)-one 6, could be isolated. The fully aromatic tautomer of compounds 4 and 6, 1,2,6-trihydroxy-9,10-dimethylanthracene 5 could not be detected. Acyloins 4 and 6 represent the first examples of secondary *ortho*-anthraquinoles.

Introduction

Anthraquinones (AQs) represent an important class of compounds. They are used as dyestuffs[2] and occur in biologically active compounds such as the anthracyclines.[3] Nevertheless, unsubstituted extended anthraquinones, *i.e.* with the carbonyl groups in different rings, are not known.[4] The reason is the high reactivity towards nucleophiles such as water and the high tendency to undergo Diels–Alder-type dimerisations if s-*cis* diene substructures are present.[5] The reactivity of the ipso cycloaddition can be correlated with the value of the HOMO–LUMO gap of the quinone molecule.[6] The reactivity towards water has been correlated with a reactivity index $S_{max}^{(H_2O)}$ on the basis of perturbational molecular orbital (PMO) calculations,[5] with eqn. (1), where E_{LUMO} = LUMO-energy of the quinone,

$$S_{max}^{(H_2O)} = -\frac{2(c_{max}^{(LUMO)})^2}{E_{LUMO} - IP_{H_2O}}\beta^{-1} \qquad (1)$$

IP_{H_2O} = ionisation potential of water, $c_{max}^{(LUMO)}$ = the largest LUMO AO coefficients of the quinoid C-atoms. The conclusion was that quinones with $S_{max}^{(H_2O)} > -2.5 \times 10^{-2}\ \beta$ are stable against water under normal conditions. All other quinones with $S_{max}^{(H_2O)} < -2.7 \times 10^{-2}\ \beta$ can only be prepared under anhydrous conditions and/or by introducing substituents which stabilise the quinone system by their electron-donating capability (*e.g.* OH, NR_2) or by means of sterical shielding (*e.g.* alkyl). The latter ones have the advantage of only minor influences on the π-electron system and thus on the spectral and electrochemical properties of the quinone. Alkyl derivatives of 1,10-,[7a] 2,9-[7b] and the 2,6-AQs [7c] could be prepared. In the case of the 2,6-AQ, this was the 3,7-di-*tert*-butyl-9,10-dimethyl derivative **3b**. However, even in spite of its sterical shielding, compound **3b** could only be obtained under anhydrous conditions. As the PMO calculations showed, the AO coefficients have their largest values at C-1 and -5, which are not sterically shielded by the *tert*-butyl groups.† In order to investigate the spectral and electrochemical properties of 2,6-AQ itself, we first tried to synthesize 9,10-dimethyl-2,6-AQ **3a**. We hoped that C-1 and -5 were sufficiently shielded by the methyl groups in *peri* positions, as was obviously the case in analogue **3b**.

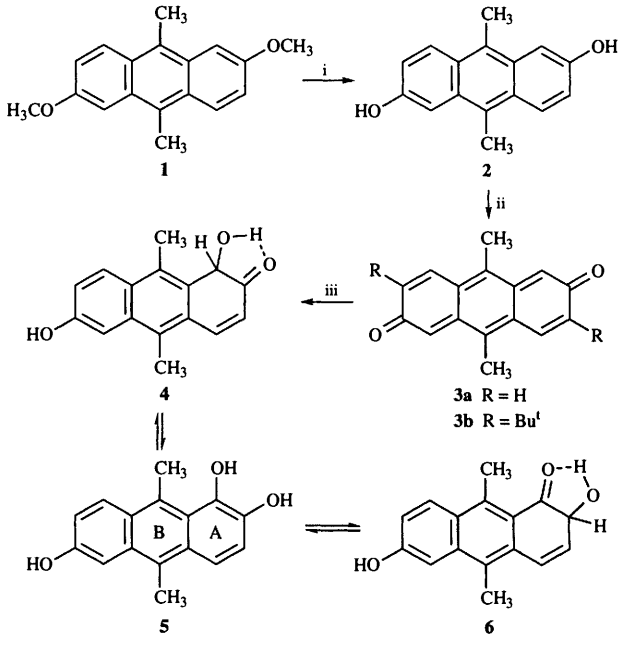
† A decomposition of 2,6-AQ by means of a (2 + 4) cyloaddition is not possible, because this molecule contains no s-*cis* double bonds.

Results and discussion

We planned to synthesize compound **3a** by lead dioxide oxidation of diol **2**, obtainable in good yields by ether cleavage of substrate **1** with boron tribromide (Scheme 1). However, after oxidation, instead of dione **3a** a mixture of acyloins **4** and **6** in the ratio 1 : 1 was obtained. The complex ^{1}H NMR spectrum could be analysed by subtracting the spectrum of product **4**. The remaining signals could be assigned to isomer **6**. This assignment and the assignment of the ^{13}C NMR signals has been confirmed by ^{1}H–^{13}C COLOC (correlation *via* long range coupling).

Pure compound **4** was formed in *one* case by oxidation of diol **2** followed by addition of water. It has been characterised by ^{1}H NMR, ^{13}C NMR, IR and mass spectroscopy and by elemental analysis. Water was added to ensure complete reaction of the tentatively formed intermediate **3a**. In *all other* attempts to obtain compound **4** under the same conditions with or without addition of water only a mixture of isomers **4** and **6** could be obtained.

Surprisingly, the mixture of acyloins **4** and **6** slowly formed



Scheme 1 *Reagents:* i, BBr_3; ii, PbO_2, −PbO, −water; iii, water

Table 1 LUMO energies (E_{LUMO}) and the largest AO coefficients in the LUMO (c_{LUMO}^{max}) of the quinones 2,6-AQ, **3a** and **3b** as calculated by MNDO. The $S_{max}^{(H_2O)}$-values were calculated by eqn. (1)

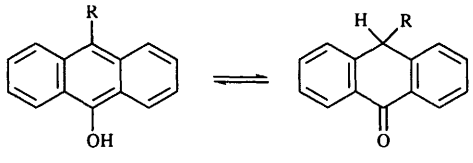
Quinone	2,6-AQ	**3b**	**3a**
E_{LUMO} (eV)	−2.161 [15]	−1.930 01	−2.084 64
$c_{max}^{(LUMO)}$	0.388 [15]	0.352 41	0.359 74
$-S_{max}^{(H_2O)}$ (10^{-2} β)	2.895 4	2.336 6	2.470 8

diol **2**, as has been verified by NMR spectroscopy. Obviously, the quinols were reduced by the solvent $(CD_3)_2SO$ ([$^2H_6$]-DMSO). The reaction was complete after 3 days at room temperature.

Compound **4** should have been formed by a 1,8 addition of a molecule of water to dione **3a**. The formation of acyloin **6** is only possible by tautomeric rearrangements *via* triol **5** as shown in Scheme 1. In spite of the fact that triol **5** should possess a higher aromatisation energy, it could not be detected by NMR spectroscopy in the reaction mixture.

Obviously, dione **3a** adds a molecule of water under conditions [lead dioxide–desiccated Na_2SO_4–anhydrous tetrahydrofuran (THF)] under which its analogue **3b** remains stable. Since the *tert*-butyl groups of compound **3b** cannot shield positions 1 and 5 by means of steric effects, obviously they exert a $+I$ effect by lowering the LUMO energy, *i.e.* this is the electrophilic behaviour of compound **3b**. This is reflected by a lowering of the calculated $S_{max}^{(H_2O)}$-value of -2.34×10^{-2} β for **3b** compared with -2.47×10^{-2} β for **3a** (Table 1). The fact that even compound **3b** is only stable in the absence of water shows that the stability borderline of $S_{max}^{(H_2O)} = -2.6 \times 10^{-2}$ β should be shifted at least to a value of $S_{max}^{(H_2O)} = -2.3 \times 10^{-2}$ β for AQs.

Quinols are the tautomeric forms of hydroquinones. Normally, the aromatic hydroquinoid structure prevails. Quinols have been observed only in the case of 9,10-dihydroxyanthracene **7** (with 3% equilibrium concentration of the quinole **8**).[8] The explanation is that the stabilisation energy of two benzene rings (2×151 kJ mol^{-1}) nearly equals the stabilisation energy of anthracene (352 kJ mol^{-1}).[9] An additional thermodynamic effect comes from the high bonding energy of the carbonyl group in structure **8**. The same is true in the case of the anthrone/anthranole tautomerism **9** ⟶ **10**. In this case the equilibrium is even known to lie on the side of the keto form.



7 R = OH
9 R = H

8 R = OH
10 R = H

The difference between the stabilisation energy of anthracene and naphthalene (102 kJ mol^{-1})[9] should favour structure **5**, but obviously the dominating effect which leads to the formation of acyloin **4** and/or **6** is the destabilisation of triol **5** by a strong steric tension between the *meso* methyl group and the hydroxy group in a *peri* position. As MM2 calculations[10] show, in triol **5** a strong deformation of the ring system is caused by this effect. In acyloin **4** sterical tensions are less, because the dihedral angle between the hydroxy and methyl group should be in the range of 50°. As our MM2 calculations showed, the possibility of planar steric tension between the *meso* methyl and the keto group in acyloin **6** is avoided by a nonplanar arrangement of the keto group with respect to the plane of the ring system.

Though 1,2-dihydroxy-5,8-dimethylnaphthalene represents the partial structure of compound **5** (rings A and B), no hydroquinone/quinole tautomerism can be observed. As our calculation showed, steric stress is avoided in this case by a bending of the methyl group, which seems not to be possible in the case of compound **5** owing to the buttressing effect of the 8-H atom. A steric effect is further confirmed by the fact that no quinole could be detected in the ^1H and ^{13}C spectra of 1,2-dihydroxyanthracene. The same is true for 1,2,5,6-tetrahydroxyanthracene, which excludes a possible electronic effect of the 6-hydroxy group in compound **5**.

Experimental

General methods

NMR spectra were measured with an AM 400 (Magnetfeldstärke 9.4 T; ^1H, 400.13 MHz; ^{13}C, 100.61 MHz) and an AC 200 (Magnetfeldstärke 4.7 T; ^1H, 200.13 MHz; ^{13}C, 50.32 MHz) from Bruker Analytische Meβtechnik. [$^2H_6$]DMSO served as internal standard when NMR spectra were measured in this solvent. *J* Values are given in Hz. Mass spectra were measured with a Finnigan Mat 8430 (70 eV) and UV–VIS spectra with a Beckman UV 5230. Elemental analyses were carried out by Mikroanalytisches Laboratorium Beller, Göttingen. Mps (not corrected) were determined on a Kofler-Heiztischmikroskop. IR spectra were measured in KBr discs on a Nicolet FT-IR 320. MNDO calculations were carried out at Rechenzentrum, Technical University of Braunschweig with the IBM 3090/600J, software MOPAC 5.0, obtainable at QCPE, Number 560. Input structures were calculated with PC-MODEL 4.0 with an MMX force field.[10]

2,6-Dihydroxy-9,10-dimethylanthracene 2

To a solution of 6 ml (63 mmol) of boron tribomide in 55 ml of methylene dichloride under nitrogen was added dropwise a suspension of 5.85 g (22 mmol) of compound **1** in 120 ml of methylene dichloride. This reaction mixture was stirred for 12 h and hydrolysed with 150 ml of water. The product was filtered off, washed successively with cold ethanol and diethyl ether, and dried *in vacuo* for 8 h at 80 °C. Purification *via* the acetate (see below) yielded *diol* **2** (4.85 g, 92%) as green microcrystals, mp 260–280 °C (decomp.) (Found: C, 80.6; H, 6.0. $C_{16}H_{14}O_2$ requires C, 80.65; H, 5.92%); δ_H(400 MHz; [$^2H_6$]DMSO) 8.23 (2 H, d, *J* 9.4, 4- and 8-H), 7.49 (2 H, d, *J* 2.4, 1- and 5-H), 7.23 (2 H, dd, *J* 9.4 and 2.4, 3- and 7-H) and 2.39 (6 H, s, Me); δ_C(100 MHz; [$^2H_6$]DMSO) 153.28 (2 C, s, C-2 and -6), 129.25, 125.90 and 124.70 (6 C, each s, C-9, -10, -4a, -8a, -9a and -10a), 126.64, 119.53 and 104.65 (6 C, each d, C-1, - 3, -4, -5, -7 and -8) and 13.97 (2 C, q, Me); ν_{max}(KBr)/cm^{-1} 3330s (OH) and 1194vs (CO); λ_{max}(MeOH)/nm (log ε) 209 (4.352), 233 (4.401), 268 (4.380), 297 (3.915), 314 (3.689), 336 (3.660), 354 (3.580), 380 (3.452), 406 (3.401) and 425 (3.287); *m/z* (%) 239 (24) [$M^+ + 1$], 238 (100) [M^+], 236 (26) [$M^+ - 2$], 223 (28), 209 (8) and 194 (8).

2,6-Diacetoxy-9,10-dimethylanthracene

A mixture of 11.7 g (49 mmol) of diol **2**, 65 ml of acetic anhydride and 0.6 ml of pyridine was refluxed for 0.5 h. After 1 h at 0 °C the product was filtered off. Recrystallisation from 500 ml of acetic anhydride yielded 2,6-*diacetoxy*-9,10-*dimethylanthracene* (10.40 g, 66%) as leaflets, mp 257 °C (from acetic anhydride) (Found: C, 74.55; H, 5.7. $C_{20}H_{18}O_4$ requires C, 74.52; H, 5.63%); δ_H(400 MHz; $CDCl_3$; Me_4Si) 8.30 (2 H, d, *J* 9.5, 4- and 8-H), 7.96 (2 H, d, *J* 2.3, 1- and 5-H), 7.29 (2 H, dd, *J* 9.5 and 2.3, 3- and 7-H), 3.01 (6 H, s, OAc) and 2.40 (6 H, s, Me); δ_C(100 MHz; $CDCl_3$; Me_4Si) 169.85 (2 C, s, *C*OMe), 147.61 (2 C, s, C-2 and -6), 130.02, 128.57 and 128.54 (6 C, each s, C-9, -10, -4a, -8a, -9a and -10a), 127.07, 121.10 and 115.51 (6 C, each d, C-1, -3, -4, -5, -7 and -8) and 21.26 and 14.45 [4 C, each q, Me, OC(O)*Me*]; λ_{max}(MeOH)/nm (log ε) 223 (4.278), 257 (4.691), 263 (4.914), 327 (3.345), 341 (3.486), 357 (3.546), 380 (3.546), 399 (3.599) and 410 (3.358); *m/z* (%) 322 (20) [M^+],

281 (2), 280 (23), 239 (18), 238 (100), 237 (14), 223 (14), 209 (17), 194 (10), 178 (3) and 165 (11).

To a boiling suspension of 5.80 g (18 mmol) of 2,6-diacetoxy-9,10-dimethylanthracene in 250 ml of acetic acid were added 100 ml (12.5 mol) of conc. hydrochloric acid dropwise. The product was filtered off, washed successively with cold ethanol and diethyl ether, and dried *in vacuo* for 8 h at 80 °C to give compound **2** (3.95 g, 92%).

1,6-Dihydroxy-9,10-dimethylanthracen-2(1*H*)-one 4 and 2,6-dihydroxy-9,10-dimethylanthracen-1(2*H*)-one 6

0.5 g (2.1 mmol) of dried 2,6-dihydroxy-9,10-dimethylanthracene **2** was added in small portions under nitrogen to a stirred suspension of 1.00 g (4.2 mmol) lead dioxide in 150 ml of absolute THF. After 2 h the residue was filtered off. The filtrate was concentrated under reduced pressure. After being cooled to 0 °C the precipitate (orange microcrystals) was filtered off and dried *in vacuo* for 8 h at 80 °C. NMR spectroscopy showed the signals of products **4** and **6** in the ratio 1:1. The yield was quantitative. The reaction product could not be separated by TLC, sublimation or crystallisation. Subtraction of the ^{1}H NMR spectrum of compound **4**, allowed the remaining signals to be assigned to compound **6**. This assignment and the assignment of the ^{13}C NMR signals has been confirmed by ^{1}H–^{13}C COLOC spectroscopy; δ_H(400 MHz; [$^2H_6$]DMSO) 10.00 (1 H, s, OH), 7.78 (1 H, d, *J* 9.1, 8-H), 7.59 (1 H, d, *J* 10.3, 4-H), 7.40 (1 H, d, *J* 2.4, 5-H), 7.18 (1 H, dd, *J* 9.1 and 2.4, 7-H), 5.77 (1 H, d, *J* 10.3, 3-H), 4.39 (1 H, s, 2-H), 2.47 (3 H, s, Me) and 1.98 (3 H, s, Me); δ_C(100 MHz; [$^2H_6$]DMSO) 198.90 (1 C, s, C-1), 155.61 (1 C, s, C-6), 141.95 (1 C, d, C-4), 133.15, 131.29, 130.87, 127.49, 126.90 and 126.81 (6 C, each s, C-4a, -8a, -9a, -10a, -9 and -10), 126.51 (1 C, d, C-8), 124.65 (1 C, d, C-3), 119.15 (1 C, d, C-7), 107.61 (1 C, d, C-5), 56.77 (1 C, d, C-2) and 13.60 and 13.42 (2 C, each q, Me).

1,6-Dihydroxy-9,10-dimethylanthracen-2(1*H*)-one 4

0.5 g (2.1 mmol) of 2,6-dihydroxy-9,10-dimethylanthracene **2** was added in small portions to a stirred suspension of 1.50 g (6.3 mmol) of lead dioxide in 250 ml of absolute THF. To ensure complete reaction of the possibly formed intermediate **3a**, 0.04 ml (2.2 mmol) of water were added after 1 h. Stirring of the mixture was continued for an additional 0.5 h. The residue was filtered off and the filtrate was evaporated under reduced pressure. The residue was dried *in vacuo* for 8 h at 80 °C to give 0.50 g *compound* **4** (95%) as orange microcrystals, mp 205–206 °C (decomp.) (Found: C, 75.6; H, 5.4. $C_{16}H_{14}O_3$ requires C, 75.58; H, 5.55%); δ_H(400 MHz; [$^2H_6$]DMSO) 10.00 (1 H, s, OH), 8.14 (1 H, d, *J* 10.2, 4-H), 7.39 (1 H, d, *J* 2.3, 5-H), 7.30 (1 H, d, *J* 9.1, 8-H), 7.01 (1 H, dd, *J* 9.1 and 2.3, 7-H), 6.10 (1 H, d, *J* 10.2, 3-H), 4.00 (1 H, s, 1-H), 2.66 (3 H, s, Me) and 1.30 (3 H, s, Me). The second OH signal could not be observed; δ_C(100 MHz; [$^2H_6$]DMSO) 201.19 (1 C, s, C-2), 155.61 (1 C, s, C-6), 141.52 (1 C, d, C-4), 133.15, 132.22, 131.42, 126.76, 126.57 and 126.20 (6 C, each s, C-4a, -8a, -9a, -10a, -9 and -10), 126.34 (1 C, d, C-8), 124.22 (1 C, d, C-3), 119.04 (1 C, d, C-7), 107.58 (1 C, d, C-5), 57.85 (1 C, d, C-1) and 13.94 and 13.01 (2 C, each q, Me); ν_{max}(KBr)/cm^{-1} 3217s (OH) and 1642vs (C=O); *m*/*z* (%) (CI NH_3, pos.) 257 (73), 256 (100), 255 (30), 254 (40) [M^+], 224 (15), 199 (21), 191 (14), 136 (14), 124 (30), 111 (17), 106 (46), 97 (14), 90 (28), 89 (100), 88 (19), 78 (30) and 73 (18).

1,2-Dihydroxyanthracene

The synthesis was performed as described in ref. 11, but no spectroscopical data were previously given; δ_H(200 MHz; [$^2H_6$]DMSO) 9.36 (1 H, s, OH), 9.02 (1 H, s, OH), 8.65 (1 H, s, 9-H), 8.37 (1 H, s, 10-H), 8.06–7.93 (2 H, m, 5- and 8-H), 7.52 (1 H, d, *J* 9.0, 3-H), 7.46–7.33 (2 H, m, 6- and 7-H) and 7.29 (1 H, d, *J* 9.0, 4-H); δ_C(50 MHz; [$^2H_6$]DMSO) 138.6 (1 C, s, C-1), 136.2 (1 C, s, C-2), 130.9, 129.5 and 128.2 (3 C, each s, C-4a, -8a and -10a), 128.2 and 128.1 (2 C, each d, C-5 and -8), 126.1 (1 C, s, C-9a), 125.8, 125.3 and 124.4 (3 C, each d, C-6, -7 and -10) and 120.8, 119.7 and 118.8 (3 C, each d, C-3, -4 and -9).

1,2,5,6-Tetrahydroxyanthracene

The synthesis was performed as described in ref. 12, but no spectroscopical data were previously given; δ_H(200 MHz; [$^2H_6$]DMSO) 8.97 (4 H, s, OH), 8.44 (2 H, s, 9- and 10-H), 7.45 (2 H, d, *J* 8.7, 3- and 7-H) and 7.16 (2 H, d, 4- and 8-H); δ_C(50 MHz; [$^2H_6$]DMSO) 137.5 (2 C, s, C-1 and -5), 136.1 (2 C, s, C-2 and -6), 127.8 (2 C, s, C-4a and -8a), 124.1 (2 C, s, C-9a and -10a), 120.3, 119.5 and 118.5 (6 C, each d, C-3, -4, -7, -8, -9 and -10).

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