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Quinones XVII [1]
The First Anthraquinone-(2,9): 1,3,4,5,8-Pentamethyl-2,9-dihydro-2,9-anthracenedione

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Of the possible nine anthraquinones (AQ's) only those with the carbonyl groups in the same ring are known. The reason is the high reactivity of the extended AQ's toward water, and – if there are *s-cis* diene partial structures in the molecule – the tendency to undergo [2+4] dimerization reactions. The reactivity of quinones has been treated quantitatively on the basis of PMO/MNDO calculations correlating the tendency to undergo [2+4] cycloadditions with the HOMO–LUMO gap [2] and the reactivity towards water with a reactivity index [3] The conclusion was, that only quinones with $S_{max}^{(H_2O)} < 2.5 \cdot 10^{-2}\,\beta$ are stable against water under normal conditions.

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

(E_{LUMO}: LUMO-energy of the quinone, IP_{H_2O} ionization potential of water, $c_{max}^{(LUMO)}$ the largest LUMO AO coefficients of the quinoid C-atoms, β the resonance integral, assumed to be constant for similar quinones).

All other quinones with $S_{max}^{(H_2O)} > 2.7 \cdot 10^{-2}\,\beta$ could only be obtained by introducing substituents which stabilize the quinone system by their +M effect (*e.g.* –Cl, –OH, $-NR_2$), enhancing the thermodynamic stability, or by means of sterical shielding (*e.g.* alkyl), enhancing the kinetic stability. Alkyl groups have the advantage of only minor influences on the *p*-electron system and thus on the spectral and electro-chemical properties of the quinone. Alkyl substituted 1,10- [4] and 2,6-AQ's [5] could be prepared and characterized, but neither 2,9-AQ itself nor derivatives have been described up to now [6].

2,9-AQ is not prone to dimerization reactions because it possesses no *s-cis* diene partial structures. However, the value (calculated with AM1 [7]) for $S_{max}^{(H_2O)}$ of $3.12 \cdot 10^{-2}\,\beta$ [8] suggests a very high reactivity towards water, with C-10 possessing the largest AO coefficient. As shown earlier in the case of 1,10-AQ [5], the *meso* position can be shielded effectively by two methyl groups in the neighbouring *peri* positions. Accordingly, we assumed, that a 2,9-AQ with methyl groups in 1,3,4, and 5 postion should be sufficiently stable against water or other nucleophiles.

Therefore, we tried to synthesize 1,3,4,5,8-pentamethyl-2,9-AQ (**8**). The additional methyl group in 8-position is necessary to facilitate the synthesis by means of symmetry.

Syntheses

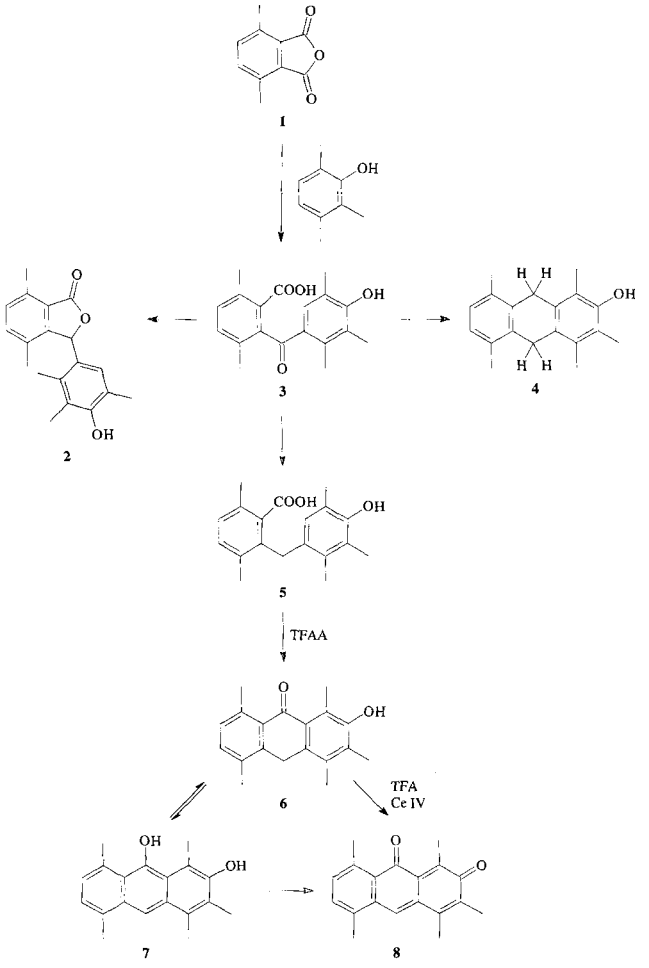
Quinones can be synthesized under especially mild conditions by dehydrogenation of the conjugate hy-droquinones. The first synthetic aim was therefore **7**, or its probably more stable tautomeric form, the anthrone **6**, respectively. This should be obtainable by Friedel–Crafts acylation of 2,3,6-trimethylphenol with 3,6-dimethylphthalic anhydride (**1**) to give **3** [9], followed by Clemmensen reduction (**5**) and ring closure under acid conditions.

The Friedel–Crafts acylation of 2,3,6-trimethylphenol with 3,6-dimethylphthalic anhydride and aluminium chloride as catalyst in 1,2-dichlorobenzene gave **3** (51%) only at elevated temperatures (70 °C). This is obviously due to steric hindrance, because the acylation of 2,6-dimethylphenol was possible (76%) at room temperature. The success of the reduction of **3** with zinc amalgam depends on the concentration of the hydrochloric acid. Judging from the spectra with ~ 0.9M HCl, the lactone **2** (42%) was formed with ~ 6M HCl the dihydroanthracene **4** (18%), whereas ~ 2M HCl yielded eventually **5** (53%). The cyclisation of **5** was possible by heating in 80% sulfuric acid (39% **6**) or, at room temp., with trifluoroacetic anhydride [10] (48%).

The mild dehydrogenation of **6** to **8**, *e.g.* with high potential quinones, is only possible, if there exists at least a small equilibrium concentration of **7** and the equilibrium is established quickly. But as to be expected and judging from the NMR spectrum in dimethylsulfoxide or pyridine, **6** contains no traces of **7** and the signal of the methylene protons at C-10 remains unchanged for several days after addition of a drop of deuteriooxide. The absence of **7** may explain that the oxidation of **6** with dichlorodicyanobenzoquinone in

anhydrous chloroform gave a complex reaction mixture, containing no **8**. The anthrone/anthranol tautomerization is a vinylogous keto/enol reaction and should be catalyzed by traces of bases or acids. Indeed, a H/D exchange could be observed (vanishing of the NMR signal of the 10-H protons) in pyridine after addition of a drop of $NaOD/D_2O$. It was also complete in deuterio trifluoroacetic acid within 35 min and in chloroform/deuterio trifluoroacetic acid (2:1) after one day. In general, quinones are attacked very easily by bases but the highly labile *o*-benzoquinone is stable even in diluted aqueous sulfuric acid [11]. We decided therefore, to oxidize **6** in an acidic medium. Under exclusion of water the solution of **6** in chloroform containing small amounts of trifluoroacetic acid yielded at oxidation with excessive cer(IV) ammonium nitrate within 15 min at 45 °C, filtration and dry-freezing *in vacuo* at –196 °C nearly quantitatively **8** as yellow solid. Against our expectations, **8** showed to be extremely sensitive towards light, moisture and temperature. The structure was proven by the ^1H- and ^{13}C-NMR spectrum, the mass spectrum and the determination of the high resolution mass. The measurement of the UV/VIS and IR spectra were not possible. Alkyl-substituted 1,10-anthraquinones are red and show absorption bands in the range of 486–504 nm [4, 12]. However, the yellow colour of **8** is not unexpected. In contrast to the 1,10-anthraquinones with a *o*-quinonoid structure it contains the partial structure of a *p*-quinonemethide and *p*-quinones absorb generally at shorter wavelengths than *o*-quinones. Even the more extended *p*-quinonoid 3,7-di-*tert*-butyl-9,10-dimethyl-2,6-anthraquinone [5] shows a long wavelength absorption band only at 432 nm.

The high reactivity of **8** should not be caused – as in another sterically shielded extended quinone [3] – by steric overcrowding. As AM1 calculations revealed [7], **8** shows no severe distortions. The quinonoid part of the molecule is only slightly bent. Obviously, the methyl groups are not bulky enough for a more effective sterical shielding. But probably it is not possible to raise the stability of the 2,9-AQ using bulkier alkyl groups because this should also raise instability by higher intramolecular steric strains.



Experimental

NMR-spectra were measured with an AM 400 (magnetic field strength 9.4 T, ^1H: 400, 13 MHz, ^{13}C: 100,61 MHz), Bruker Analytische Meßtechnik. Mass spectra were measured with a Finnigan Mat 8430 (70 eV), the UV/VIS spectra with a Beckman UV 5230 and the IR spectra with a Perkin Elmer 1420 and Nicolet Ft-IR 320. Elemental analyses were carried out by Institut für Pharmazeutische Chemie, Technische Universität Braunschweig. Thin-layer chromatography (TLC) was performed on POLYGRAM SIL G/UV_{254}-foil, Macherey–Nagel, Düren, column chromatography (CC) with silica gel 60 (70–230 mesh, Merck, Darmstadt) and flash-chromatography (FCC) with silica gel (particle size 0.003–0.06 mm, Baker Chem.). Melting points are not corrected. The NMR signals were correlated by increment calculations [13]. For the AM1 calculations MOPAC 5.00 [14] with the parametrization of Dewar and Thiele [15] was used.

2-(4-Hydroxy-2,3,5-trimethylbenzoyl)-3,6-dimethylbenzoic acid (**3**)

A mixture of 20.4 g (0.15 mol) 3,6-dimethylphthalic anhydride, 22.0 g (0.13 mol) tri-methylphenol, 90 g (0.68 mol) anhydrous aluminium chloride and 1 l 1,2-dichlorobenzene was heated 24 h to 70 °C and then poured on 1 kg ice/hydrochloric acid (1:1). The organic phase was combined with the ether extract of the aqueous phase and extracted with 2N sodium hydroxide. The alkaline phase yielded after acidification, filtration, drying and recrystal-lization from chloroform 19.6g (0.063 mol, 51%) colourless crystals of **3**, *m. p.* 175–215 °C. – IR: ν/cm^{-1} = 2700–3350, 3420 (OH), 1655, 1715 (CO). – ^1H NMR (CD_3OD): δ/ppm = 2.08, 2.11, 2.18, 2.34, 2.48 (5 s, 15H, CH_3), 6.92 (s, 1H, H-6'), 7.27, 7.28 (2 s, 2H, H-4, 5). – MS, *m/z* (%): 312 (44), 297 (44), 267 (100).

$C_{19}H_{20}O_4$	calcd.:	C 73.06	H 6.45
(312,4)	found:	C 73.24	H 6.38.

Clemmensen Reduction of 2-(4-Hydroxy-2,3,5-trimethylbenzyl)-3,6-dimethylbenzoic acid (**3**)

a) *2-(4-Hydroxy-2,3,5-trimethylbenzyl)-3,6-dimethylbenzoic acid* (**5**)

A mixture of 1,0 g (3,2 mmol) **3**, 6 g zinc amalgam, 10 ml acetic acid, 30 ml water and 5 ml concd. hydrochloric acid was refluxed for 90 min and the solution decanted into water.

The precipitate gave after filtration, drying and recrystallization from dichloromethane 0,50 g (1,7 mmol, 53%) **5** as colourless crystals. *m. p.* 175–185 °C. – IR: ν/cm^{-1}= 2700–3300, 3520 (OH), 1700 (CO). – ^{1}H NMR(CD_3OD): δ/ppm = 1.99, 2.03, 2.18, 2.23, 2.33 (5 s, 15H, CH_3), 3.88 (s, 2H, CH_2) 6.14 (s, 1H, H-6'), 7.05 (d, J = 7.8 Hz, 1H, H-4), 7.12 (d, J = 7.8 Hz, 1H, H-5). – ^{13}C NMR(CD_3OD): δ/ppm = 12.8, 15.4, 16.7, 19.4, 19.6 (CH_3), 34.7 (CH_2), 127.9, 129.1 (C-4, C-6'), 130.1 (C-arom.), 132.9 (C-5), 132.5, 133.6, 136.3, 136.4, 137.8 (C-arom.), 151.8 (C-4'), 174.4 (COOH). – MS, *m/z* (%): 298 (78), 280 (78), 265 (100).

$C_{19}H_{22}O_3$	calcd.:	C 76.48	H 7.43
(298,4)	found:	C 76.25	H 7.49.

b) *3-(4-Hydroxy-2,3,5-trimethylphenyl)-4,7-dimethyl-1,3-dihydro-1-isobenzofuranone* (**2**)

The same procedure as described under a) using 10 ml acetic acid and only 10 ml water and 2 ml concd. hydrochloric acid and a refluxing time of 2 h gave 0,40 g (1,34 mmol, 42%) **2**. Colourless crystals, *m. p.* 220 °C (methanol). – IR: ν/cm^{-1} = 3400 (OH), 1725 (CO). – ^{1}H NMR(CF_3COOH): δ/ppm = 2.01, 2.19, 2.32, 2.45, 2.72 (5 s, 15H, CH_3), 3.88 (s, 2H, CH_2) 6.81 (s, 1H, H-6'), 7.35, 7.44 (2d, J = 8,0 Hz, 2H, H-4,5). – MS, *m/z* (%): 296 (100).

c) *1,3,4,5,8-Pentamethyl-9,10-dihydro-2-anthracenol* (**4**)

To a solution of 1,0 g (3,2 mmol) **3** in 10 ml ethanol 4,6 g zinc amalgam and 15 ml concd. hydrochloric acid were added. The mixture was refluxed for 3 h, 2 ml concd. hydrochloric acid beeing added hourly. Processing as described above (a) yielded 160 mg (0,58 mmol, 18%) **4**. Colourless needles, *m. p.* 213 °C (methanol/water). – IR: ν/cm^{-1}= 3450 (OH), 1580–1590 (CC_{arom}). – ^{1}H NMR($CDCl_3$): δ/ppm = 2.24–2.36 (15H, CH_3), 3.83 (s, 4H, CH_2) 6.97 (s, 2H, H_{arom}). – MS, *m/z* (%): 266 (45), 251 (100).

Methyl 2-(4-hydroxy-2,3,5-trimethylbenzoyl)-3,6-dimethylbenzoate [9]

A solution of 4,0 g (0,013 mol) **3** and a drop of trifluoroacetic acid in 10 ml methanol was heated for 10 min. After cooling to room temp., filtration and drying we got 4,0 g (0,013 mol) of methyl 2-(4-hydroxy-2,3,5-trimethylbenzoyl)-3,6-dimethylbenzoate, *m. p.* 175–178 °C. – ^{1}H NMR($CDCl_3$): δ/ppm = 2.08, 2.19, 2.23, 2.40, 2.68 (5 s, 15H, CH_3), 3.12 (s, 3H, OCH_3, 6.58 (s, 1H, H-6'), 7.30 (d, J = 7.7 Hz, 1H, H-4), 7.39 (d, J = 7.7 Hz, 1H, H-5). – ^{13}C NMR($CDCl_3$): δ/ppm = 12.1, 15.9, 17.1, 17.3, 17.5 (CH_3), 50.6 (OCH_3),), 111.1, 118.4, 124.2, 126.0 (C-arom.), 126.8, 132.7, 135.8 (C-4,5, C-6'), 127.1, 136.2, 137.1, 144.3 (C-arom.), 152.6 (C-4'), 168.8 (COOR). – MS, *m/z* (%): 362 (30), 295 (18), 279 (38), 267 (100).

$C_{20}H_{22}O_4$	calcd.:	C 73.60	H 6.79
(326,4)	found:	C 73.58	H 6.81.

2-Hydroxy-1,3,4,5,8-pentamethyl-9,10-dihydro-9-anthracenone (**6**)

To an anhydrous solution of 250 mg (0,85 mmol) **5** in 20 ml chloroform were added at 0 °C 1,2 ml trifluoroacetic acid anhydride. After 2 h at room temp. the solvent was removed *in vacuo*. The residue yielded after recrystallization from methanol 115 mg (0,41 mmol, 48%) colourless needles of **6**, *m. p.* 210 °C (dec.). – IR: ν/cm^{-1} = 3500 (OH), 1640 (CO). – ^{1}H NMR($(CH_3)_2SO$): δ/ppm = 2.22, 2.23, 2.32, 2.46, 2.56 (5s, 15H, CH_3), 3.79 (s, 2H, CH_2), 7.08, 7.24 (2 d, J = 7.6 Hz, 2H, H-6,7), 8.25 (s, 1H, OH). – ^{13}C NMR($(CH_3)_2SO$): δ/ppm = 12.7, 13.3, 14.1, 17.8, 20.9 (CH_3), 28.0 (CH_2), 120.9, 128.0 (C-arom.), 151.1 (HOC), 189.4 (OC). – MS, *m/z* (%): 280 (82), 265 (100).

$C_{19}H_{20}O_2$	calcd.:	C 81.40	H 7.19
(298,4)	found:	C 81.57	H 7.01.

1,3,4,5,8-Pentamethyl-2,9-dihydro-2,9-anthracenedione (**8**)

A mixture of 100 mg (0,36 mmol) **6**, 500 mg (0,9 mmol) cer(IV) ammonium nitrate, 10 ml chloroform, 0,2 ml trifluoroacetic acid and 0,1 ml trifluoroacetic acid anhydride was stirred at 45 °C for 15 min and then cooled to –196 °C. After filtration and removing the solvents by sublimation *in vacuo* at –196 °C we yielded a solid yellow residue of **8** (90 mg, 90%). All operations were performed under nitrogen and with severe exclusion of water. The small amount of trifluoroacetic acid anhydride has been added to ensure the removal of last traces of water. – *m. p.* 175–180 °C (dec.). – ^{1}H NMR ($CDCl_3$): δ/ppm = 2.00, 2.07, 2.30, 2.51, 2.56 (5 s, 15H, CH_3), 6.83 (s, 1H, H-10), 7.23, 7.30 (2 d, J = 7.9 Hz, 2H, H-6,7). – ^{13}C NMR($CDCl_3$): δ/ppm = 12.6, 16.5, 19.0, 22.1, 24.5 (CH_3), 81.7 (HC-10), 93.4, 129.4, 130.3, 134.3, 135.3, 135.4, 140.4, 141.2, 144.2 (C-arom.), 134.9, 135.5 (HC-6,7), 183,5 (OC-2), 190,9 (OC-9). – MS, *m/z* (%): 278 (100), 253 (16), 235 (18), 191 (10), 165 (12), 43 (36).

$C_{19}H_{18}O_2$:	calcd.:	C 278, 1306
	found:	278, 1306 (MS).

References

[1] Part XVI: P. Boldt, S. Zippel, G. Haucke, J. Chem. Res. (1997), in press

[2] H. L. K. Schmand, H. Kratzin, P. Boldt, Liebigs Ann. Chem. **1976**, 1560

[3] K.–H. Menting, W. Eichel, K. Riemenschneider, H. L. K. Schmand, P. Boldt, J. Org.Chem. **48** (1983) 2814

[4] F. Setiabudi, P. Boldt, Liebigs Ann. Chem. **1985**, 1272.

[5] P. Boldt, P. Hilmert–Schimmel, R. Müller, D. Heuer, Chem. Ber. **120** (1987) 497

[6] P. Boldt, Extended Quinones in: The Chemistry of Quinonoid Compounds, S. Patai, Z. Rappoport eds., Wiley 1988, 1419

[7] T. Knoblauch, Synthese des 1,3,4,5,8-Pentamethylanthrachinon-(2,9) und chinoider Merocyanine für die nichtlineare Optik, Cuvillier, Göttingen,1994, S. 7

[8] The $S_{max}^{(H_2O)}$ values of all AQ's calculated with AM1 in this work differ only slightly from that calculated earlier [3] with MNDO. *E.g.* 2,9-AQ: $S_{max}^{(H_2O)}$ (AM1) = 3.17·10^{-2} β. An exception is 2,3-AQ: $S_{max}^{(H_2O)}$(MNDO) = 3.07 and $S_{max}^{(H_2O)}$ (AM1) = 5.87·10^{-2} β. For details [7]

[9] In the first instance, the elemental analysis of **3** showed no correct values. Therefore the ester of **3** was prepared, which showed besides the expected spectra a correct elemental analysis (see exp. part)

[10] T. M. Nicoletti, C. L. Raston, M. V. Sargent, J. Chem. Soc., Perkin Trans. 1 **1990**, 133

[11] R. Brockhaus, Liebigs Ann. Chem. **1974**, 1167
[12] A. Topp, P. Boldt, H. Schmand, Liebigs Ann. Chem. (1974), 1167; M. V. Gorelik, S. P. Titova, V. A. Trdatyan, Zh. Org. Khim. **15** (1979) 1033: J. Org. Chem. USSR (Engl. Transl.) **15** (1979) 139
[13] M. Hesse, H. Meier, B. Zeeh, Spektroskopische Methoden der organischen Chemie. G. Thieme, Stuttgart 1987, 3. Auflage, S. 153
[14] F. J. Seiler Res. Lab., U. S. Air Force Acad., Colorado Springs, Co 80840
[15] M. J. S. Dewar, W. Thiele, J. Am. Chem. Soc. **99** (1977) 4899

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