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Periodate Oxidation of Phenols. XIX.* Nondimerizing *o*-Quinols, *o*-Quinol Ethers, and *o*-Quinone Ketals

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Several 6-hydroxy-6-methyl-2,4-cyclohexadienones (*o*-quinols) and their 6-ethoxy analogues carrying a CH_3 or OCH_3 substituent in the 5-position were obtained by oxidation of the appropriate phenols with sodium periodate in aqueous ethanol. The 6-methoxy analogues were prepared similarly, using periodic acid in methanol. These 2,4-cyclohexadienones showed no tendency to dimerize, in contrast to the corresponding dienones lacking the 5-substituent which undergo rapid Diels-Alder dimerization.

The *o*-quinol formed on oxidation of 2,3-dimethylphenol, although resistant to dimerization, could not be isolated since it gave Diels-Alder adducts with 2,3-dimethyl-*p*-quinone and 3,4-dimethyl-*o*-quinone being formed simultaneously. Part of the *o*-quinol suffered oxidative ring cleavage.

Treatment of 2,3-dimethoxyphenol with HIO_4/CH_3OH produced a nondimerizing *o*-quinone dimethyl ketal, 5,6,6-trimethoxy-2,4-cyclohexadienone.

A characteristic reaction of 2,4-cyclohexadienones [1] is their Diels-Alder dimerization. *o*-Quinols *1a*—*1e* and spiro-epoxydienones of type *2*, either unsubstituted or carrying small substituents such as CH_3 or OCH_3 in positions 2 to 4, dimerize so rapidly that they cannot be obtained as monomers.[2] The same is true for most of the *o*-quinone dimethyl ketals (*1*, $R = R^6 = OCH_3$) recently investigated.[3] Only the 3-methoxy derivative could be isolated as monomer, but it dimerized within two days at room temperature and thus behaved like *o*-quinol methyl ethers (*1*, $R = OCH_3$, $R^6 = CH_3$)[4] and 6,6-dialkyl-2,4-cyclohexadienones (*1*, $R = R^6 =$ alkyl).[1,5]

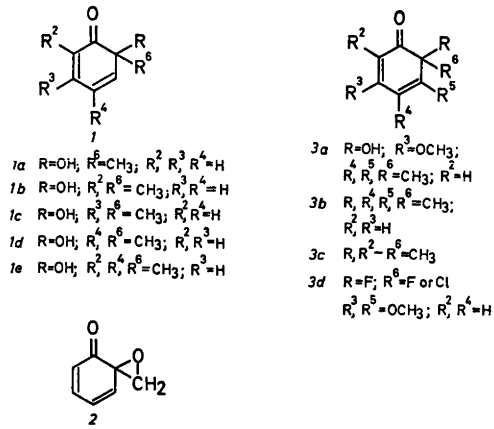

Chart 1.

The acetates derived from *o*-quinols *1a* and *1b*, although stable at room temperature, dimerize when heated at 120 °C,[6-8] whereas those of *1d* and *1e* proved to be stable even at 160 °C.[9] The dimerization of 2,4-cyclohexadienones is inhibited by bulky substituents such as aryl groups in the 2-, 4-, and 6-positions,[10] *t*-butyl [11] or iodine [8,11] in the 4-position, or a 2-cyclohexyl group.[11]

A few monomeric 2,4-cyclohexadienones lacking bulky substituents have been reported. Wessely *et al.*[12,13] obtained small amounts of *o*-quinols *4a* and *5a* (Chart 2) on thermolysis of the dimers of *1b* and *1e*, respectively. The retro Diels-Alder reaction of these dimers was followed by an acyloin rearrangement of the initially formed monomers, *1b* and *1e*.[7] *o*-Quinol *3a*,[14] the 6,6-dimethylcyclohexadienones

* Part XVIII, see Ref. 3.

3b [15] and *3c*,[16] and the 6,6-dihalo compounds *3d* [17] have also been described only as monomers.

In his review article (Ref. 1, p. 226), Waring assumed that substituents in positions 3 and 5 of a 2,4-cyclohexadienone hinder dimerization by steric interaction with the 6,6-groups of the other partner. This assumption seemed plausible as far as it concerned the 5-substituent, which is a common feature of compounds *3a-d*. It was incompatible, however, with the earlier reported spontaneous dimerization of *o*-quinol *1c*, which carries a 3-substituent [7,18] (*cf.* also Ref. 2a). The recently described dimerizations of a 3-methyl-substituted *o*-quinol ether [4] and of a similarly substituted spiro-epoxy-2,4-cyclohexadienone,[2a] as well as the dimerization of the above-mentioned 3-methoxy derivative of *o*-quinone dimethyl ketal,[3] also prove that a small 3-substituent is not critical in dimerization.

In the present work, 5-substituted *o*-quinols and *o*-quinol ethers, as well as a 5-substituted *o*-quinone dimethyl ketal, were prepared by the oxidation of phenols *4*–*8*, which carry a 3-methyl or a 3-methoxyl group, using either sodium periodate in water/ethanol (8:1) or periodic acid in methanol (Chart 2). No dimer of these 2,4-cyclohexadienones was detected in the reaction mixtures, nor could the isolated monomers be dimerized by heat treatment. These results firmly establish the dimerization-preventing effect of a small 5-substituent.

Oxidation with periodate in water/ethanol (Charts 2 and 3). Phenols *4*–*7* provided *o*-quinols (*5a* and *6a*) and *o*-quinol ethyl ethers (*4b*, *5b*, *7b*). Secondary reactions of these *ortho* oxidation products, as well as competing oxidation in the other *o*-position or in the *p*-position, gave rise to the additional products shown in Chart 3.

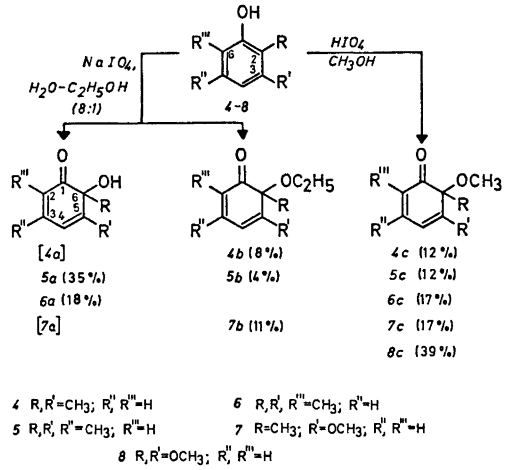

Chart 2.

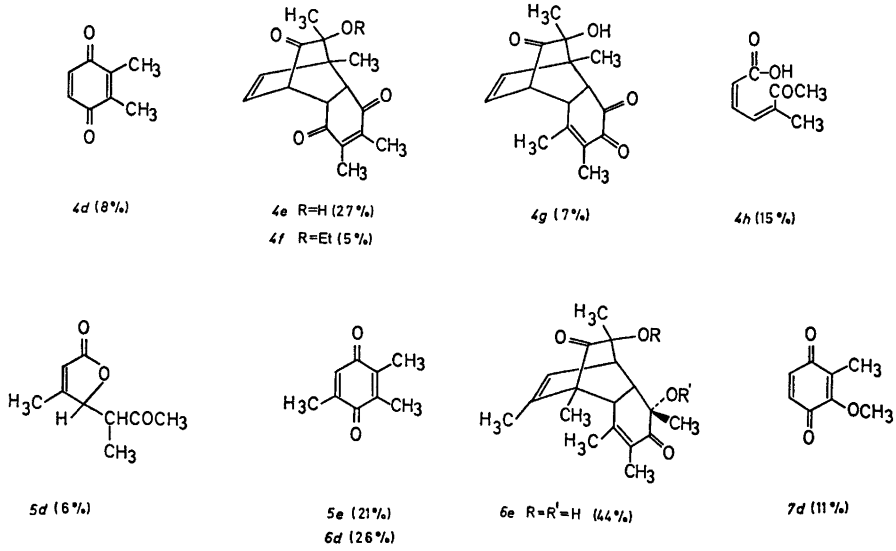

Chart 3. Products obtained, in addition to the 2,4-cyclohexadienones *a* and *b* (Chart 2), on oxidation of phenols *4*–*7* with $NaIO_4$ in H_2O/C_2H_5OH (8:1).

2,3-Dimethylphenol (*4*) was consumed very slowly, 33 % of the phenol being recovered after a reaction time of 21 h. (The yields of products derived from *4* are based on consumed phenol. The other phenols investigated were completely consumed within the reaction times used; see Experimental.) The expected *o*-quinol *4a* was not found in the reaction mixture. It had reacted as diene with simultaneously formed *p*-quinone *4d* and 3,4-dimethyl-*o*-benzoquinone to give the Diels-Alder adducts *4e* and *4g*, and had been also oxidized by periodate to the oxodienoic acid *4h*. A portion of the *o*-quinol ethyl ether also appeared as a *p*-quinone adduct (*4f*).

2,3,5-Trimethylphenol (*5*) gave, in addition to *5a* and *5b*, a minor amount of lactone *5d*, formed by comparatively slow periodate cleavage of *5a* followed by cyclization of the resulting oxodienoic acid. Furthermore, *para* oxidation produced the *p*-quinone *5e*.

In all the oxidations investigated (Chart 2), except for the oxidation of 2,3,6-trimethylphenol (*6*), the reaction mixtures acquired a red colour indicating the formation of the corresponding *o*-benzoquinones which, however, were removed during the work-up procedures (see Experimental). The presence of methyl groups in both *o*-positions of phenol *6* prevented *o*-quinone formation. Instead, oxidation at the 6-position of this phenol gave 2,3,6-trimethyl-*o*-quinol, which is isomeric with *6a*. Having no 5-substituent, it dimerized to give product *6e*. Competing *para* oxidation resulted in the formation of *6d*.

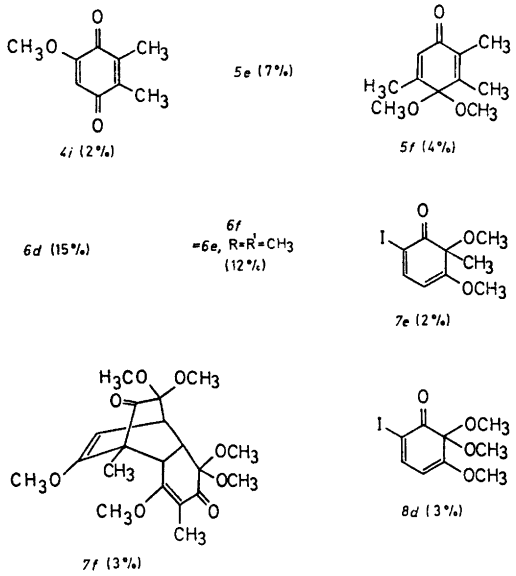

Chart 4. Products obtained, in addition to *4c – 8c* (Chart 2), on oxidation of phenols *4 – 8* with HIO_4 in CH_3OH.

Similar *para* oxidation of 3-methoxy-2-methylphenol (*7*) gave the *p*-quinone *7d* in addition to the *ortho* oxidation product *7b*. *o*-Quinol *7a* could not be detected, probably because it had suffered ketol cleavage.

Oxidation with periodic acid in methanol (Charts 2 and 4). Treatment of phenols *4 – 7* with HIO_4 in CH_3OH provided the *o*-quinol methyl ethers *4c – 7c*, and similar treatment of 2,3-dimethoxyphenol (*8*) gave the 5-methoxy-substituted 2,4-cyclohexadienone *8c*, an *o*-quinone dimethyl ketal (Chart 2).

Oxidative methoxylation at the free *o*-position of phenol *4*, followed by *para* oxidation, produced a small amount of *4i*. In the case of phenol *5*, two consecutive *para* methoxylations gave the *p*-quinone ketal *5f*, the *p*-quinone *5e* arising possibly by hydrolysis of *5f*. The formation of the dimeric *o*-quinone ketal *7f* can be understood as being due to a similar twofold *ortho*-oxidative methoxylation of phenol *7* with subsequent dimerization of the resulting 3,6,6-trimethoxy-2-methyl-2,4-cyclohexadienone.

The formation of the Diels-Alder dimer *6f* is similar to that of *6e* discussed above. As expected, both dimers have the same stereochemistry and regiochemistry, as shown by the methylation of *6e* to give *6f*. The orientations presented for *6e* and *6f* are analogous to those established earlier for other *o*-quinol dimers [2] and their dimethyl ethers.[4]

Initial iodination of the starting phenols, as observed previously in the system HIO_4/CH_3OH,[4] explains the formation of the 2-iodocyclohexadienones *7e* and *8d*.

In a following paper, mixed Diels-Alder reactions of nondimerizing 2,4-cyclohexadienones will be discussed.

EXPERIMENTAL

UV spectra were run in ethanol on a Beckman DK-2A, and IR spectra were recorded in KBr on a Beckman 9A instrument. ^1H NMR spectra were taken in $CDCl_3$ on a Varian A-60 spectrometer, unless otherwise stated. UV data

are noted as λ_{max} values in nm, with log ε values indicated in parentheses, IR data as ν_{max} values in cm^{-1}. Thin layer chromatography was performed on silica gel with benzene/ethyl acetate (4:1) as mobile phase.

Oxidation procedures. (A). For the oxidation in *aqueous* medium, a solution of the starting phenol (about 30 mmol) in a 7:1 mixture of water and ethanol (1600 ml) was mixed with an aqueous solution (200 ml) of $NaIO_4$ (about 90 mmol). After the reaction time (*t*) given below, the mixture was extracted with dichloromethane (6 × 100 ml), and the extract was dried over anhydrous $CaSO_4$ and evaporated. A solution of the resulting oil in ethyl acetate was passed through a column of aluminium oxide ("neutral", Woelm, 4 × 15 cm) which then was washed with the same solvent, dark-brown material remaining adsorbed in the upper part of the column. The combined filtrates, on evaporation, gave a yellow, oily or partly crystalline product which was chromatographed on a column (3 × 110 cm) of silica gel (Silicic Acid, Mallinckrodt, 100 mesh), benzene/ethyl acetate (4:1) being used as eluent.

Deviations from this general procedure are noted below.

(B) The oxidations in *methanolic* solution were carried out by mixing a solution of the phenol (about 30 mmol) in absolute methanol (50 ml) with that of an equimolar amount of anhydrous periodic acid (HIO_4)[19] in the same solvent (400 ml). (This actually implies an excess of oxidant, since the iodic acid formed also oxidizes the phenol.[4]) After 5 – 10 min, the reaction mixture had acquired a red colour. After 2 h, water (400 ml) was added, the mixture was extracted with dichloromethane, and the products were separated as above.

The reaction products are given below in the order of their elution from the silica gel column.

Oxidation of 2,3-dimethylphenol (4). (A) With $NaIO_4$ in H_2O-EtOH; t = 21 h. The dichloromethane extract obtained from the reaction mixture was extracted with saturated aqueous sodium bicarbonate. The bicarbonate phase was acidified and extracted with dichloromethane. The dried extract on evaporation gave crystals of *5-methyl-6-oxo-2,4-heptadienoic acid* (4h), m.p. 114 – 117 °C (15 %, based on consumed *4*, see below), after recrystallization from isopropyl ether m.p. 118 – 119 °C. (Found: C 62.30; H 6.55. Calc. for $C_8H_{10}O_3$: C 62.32; H 6.54). Parent mass, found: 154.0631; calc. for $C_8H_{10}O_3$: 154.0630. UV 282 (4.42). IR 3000 – 2400 and 1698 (COOH), 1667 (conj. CO), 1623 and 1587 (C=C). NMR δ 1.97 (d, 3 H, CH_3-5), 2.42 (s, 3 H, CH_3-7), 6.00 (d, 1 H, H-2), 7.13 (t, 1 H, H-3), 8.30 (d, 1 H, H-4). The doublets of H-2 and H-4 are further split by allylic coupling. $J_{2,3} = J_{3,4} = 11$ Hz, $J_{H-4,CH_3-5} = 1$ Hz.

The dichloromethane solution remaining after the extraction with bicarbonate, when dried and evaporated, gave a residue which afforded the following products on silica gel chromatography:

(a) A brownish yellow crystalline product, which on TLC with benzene as eluent gave two spots, the R_F values of which were identical with those found for starting phenol *4* and *p*-quinone *4d*. The NMR spectrum of the crude product showed the signals expected for these two compounds, and the integrals of their CH_3 signals indicated that the product was composed of about 85 % of *4* and 15 % of *4d*. The amount of phenol present corresponded to 33 % of the amount used. The yields of products given below are based on consumed phenol.

For identification of the *p*-quinone, a solution of the crude fraction in ethyl acetate was passed through a column (4 × 5 cm) of Al_2O_3 (neutral, Woelm) which retained the phenol *4*; the filtrate gave *2,3-dimethyl*-p-*benzoquinone* (4d), m.p. 54 – 55 °C (8 %), identical by m.p. and mixed m.p. with an authentic sample.[20]

(b) 10-Ethoxy-1,4,4a,8a-tetrahydro-1,6,7,10-tetramethyl-1,4-ethanonaphthalene-5,8,9-trione (4f). The ethyl acetate solution of the crude material was purified with Al_2O_3 (see above) and then gave faintly yellow needles, m.p. 160 – 161 °C (ethyl acetate); yield, 5 %. (Found: C 71.45; H 7.29. Calc. for $C_{18}H_{22}O_4$: C 71.50; H 7.33). UV 203 (3.88), 252 (3.94), sh 315 (2.23), 365 (2.02); *cf.* Ref. 9. IR 1728 s, 1663 s, 1628 w. NMR δ 1.10 (t, 3 H, OCH_2CH_3), 1.25, 1.40 (s, 3 H each, CH_3-1, CH_3-10), 1.95 (s, 6 H, CH_3-6, CH_3-7), 3.3 – 3.8 (m, 5 H, OCH_2CH_3, H-4, H-4a, H-8a), 6.0 (m, 2 H, H-2, H-3).

(c) 6-Ethoxy-5,6-dimethyl-2,4-cyclohexadienone (4b), yellow oil, purified by distillation at 50 °C/1 mmHg; yield, 8 %. Parent mass, found: 166.0986; calc. for $C_{10}H_{14}O_2$: 166.0993. UV 316 (3.66), sh 385 (2.66); the former λ_{max} value ($\pi \rightarrow \pi^*$) is in accord with the value (320 nm) calculated according to the extended Woodward rules.[21] IR 1678 vs, 1640 s, 1570 m; for the IR spectra of 2,4-cyclohexadienones, see Refs. 1, 22 – 24.

(d) 1,4,4a,8a-Tetrahydro-10-hydroxy-1,6,7,10-tetramethyl-1,4-ethanonaphthalene-5,8,9-trione (4e); yield, 27 %; faintly yellow prisms, m.p. 146 – 148 °C (isopropyl ether). (Found: C 69.98; H 6.65. Calc. for $C_{16}H_{18}O_4$: C 70.05; H 6.61). UV 203 (3.88), 252 (4.01), sh 315 (2.49), 360 (2.10); *cf.* Ref. 9. IR 3470, 1740, s, 1660 s, 1620 m. NMR, recorded on a Bruker WH 270 instrument: δ 1.23, 1.31 (s, 3 H each, CH_3-1, CH_3-10), 1.90, 1,96 (s, 3 H each, CH_3-6, CH_3-7), 2.55 (s, 1 H, OH-10, exchangeable with D_2O), 3.30 (dd, 1 H, H-4a), 3.60 (d, 1 H, H-8a), 3.68 (four doublets, 1 H, H-4), 6.00 (dd, 1 H, H-2), 6.12 (dd, 1 H, H-3). $J_{3,4} = 6$ Hz, $J_{4,4a} = 3$ Hz, $J_{2,4} = 1.5$ Hz, $J_{2,3} = 8$ Hz, $J_{4a,8a} = 9$ Hz.

(e) 1,4,4a,8a-Tetrahydro-9-hydroxy-4,7,8,9-tetramethyl-1,4-ethanonaphthalene-5,6,10-trione (4g); yield, 7 %; yellow needles of m.p. 150 – 151 °C (isopropyl ether). (Found: C 69.63; H 6.60. Calc. for $C_{16}H_{18}O_4$: C 70.05; H 6.61). UV 273 (3.79), sh 308 (3.29), 418 (1.87). IR ($CHCl_3$)

1730, 1715, 1675 (three CO groups), 1625 (C=C); in KBr: 3440 (OH), 1725 (broad), 1680, 1628. These UV and IR characteristics are similar to those of the adduct between 6-hydroxy-4,6-dimethyl-2,4-cyclohexadienone and 3,5-dimethyl-1,2-benzoquinone.[25] NMR, recorded on a Bruker WH 270 instrument: δ 1.23, 1.30 (s, 3 H each, CH_3-4, CH_3-9), 1.83, 2.07 (s, 3 H each, CH_3-7, CH_3-8), 2.32 (broad s, 1 H, OH, exchangeable with D_2O), 3.34 (d with broadened signals, 1 H, H-8a), 3.40 (d, 1 H, H-4a), 3.46–3.53 (m, 1 H, H-1), 6.00 (dd, 1 H, H-2), 6.05 (dd, 1 H, H-3). $J_{1,2}=6$ Hz, $J_{1,3}=1.5$ Hz, $J_{2,3}=7.5$ Hz, $J_{4a,8a}=8$ Hz.

*(B) With HIO_4 in CH_3OH. (a) 5-Methoxy-2,3-dimethyl-*p*-benzoquinone (4i)*, 2 % of yellow needles, m.p. 104–108 °C which was raised to 112–113 °C (lit.[26] m.p. 110–111 °C) by recrystallization from methanol. NMR δ 2.03 (s, 6 H, CH_3-2, CH_3-3), 3.80 (s, 3 H, OCH_3-6), 5.85 (s, 1 H, H-5).

(b) 6-Methoxy-5,6-dimethyl-2,4-cyclohexadienone (4c), 12 % of a yellow oil, which crystallized on cooling, m.p. 29–31 °C after distillation at 40 °C/15 mmHg. (Found: C 70.64; H 8.14; OCH_3 20.52. Calc. for $C_9H_{12}O_2$: C 71.02; H 7.95; OCH_3 20.39). The UV and IR spectra of *4c* were almost identical with those of *4b* (see above).

Oxidation of 6-hydroxy-5,6-dimethyl-2,4-cyclohexadienone (4a). The *o*-quinol[12] (600 mg) was treated for 6 h with aqueous-ethanolic $NaIO_4$ under the conditions given above for the oxidation of phenols. The reaction was terminated by the addition of ethylene glycol, and the mixture extracted with chloroform. Evaporation of the extract left 560 mg (84 %) of *4h*.

Oxidation of 2,3,5-trimethylphenol (5). (A) With $NaIO_4$ in H_2O-EtOH, $t=18$ h (cf. Ref. 7). The following products were obtained:

*(a) 2,3,5-Trimethyl-*p*-benzoquinone (5e)*; yield, 21 %. M.p. 33–34 °C (lit.[27] 34 °C).

(b) 6-Ethoxy-3,5,6-trimethyl-2,4-cyclohexadienone (5b), yellow oil; yield, 4 %. Parent mass, found: 180.1154; calc. for $C_{11}H_{16}O_2$: 180.1150.

(c) 6-Hydroxy-3,5,6-trimethyl-2,4-cyclohexadienone (5a), yellow crystals, m.p. 35–38 °C (lit.[12] 42 °C), in 35 % yield. The UV data were in agreement with those given in Ref. 28 for a compound wrongly designated as "mesityl-*o*-quinol", *i.e.*, *o*-quinol *1e* which, however, is not stable as monomer (see also Ref. 7). IR 3430 m, 1670 vs, 1642 s, 1570 m.

In a separate experiment, in which the purification of the crude product mixture on Al_2O_3 was omitted, the silica gel chromatography afforded the lactone *5d* (see below) as an additional product in a yield of 6 %.

(B) With HIO_4 in CH_3OH. (a) p*-Benzoquinone* 5e (see above); yield, 7 %.

(b) 4,4-Dimethoxy-2,3,5-trimethyl-2,5-cyclohexadienone (5f), crystals of m.p. 70–75 °C in 4 % yield. After sublimation at 35 °C/0.1 mmHg and recrystallization from isopropyl ether, m.p. 74–75 °C. (Found: C 67.45; H 8.29; OCH_3 31.84. Calc. for $C_{11}H_{16}O_3$: C 67.32; H 8.22; OCH_3 31.63). UV 230 (4.17), 278 (3.28), sh 340 (1.88). IR 1679, sh 1640, 1632. NMR δ 1.93 (s, 9 H, 3 CH_3), 3.02 (s, 6 H, 2 OCH_3), 6.31 (q, 1 H, H-6). $J_{CH_3\text{-}5,H\text{-}6}=1.5$ Hz.

(c) 6-Methoxy-3,5,6-trimethyl-2,4-cyclohexadienone (5c), yellow oil in 12 % yield, distillable at 60 °C/15 mmHg. Parent mass, found 166.0991; calc. for $C_{10}H_{14}O_2$: 166.0993. UV spectrum very similar to that of *4c*. IR 1668 vs, 1650 s, 1580 m. In the NMR spectrum, the signal of the OCH_3 group appears at δ 3.00.

Oxidation of 6-hydroxy-3,5,6-trimethyl-2,4-cyclohexadienone (5a). The *o*-quinol (890 mg) was treated with $NaIO_4$ in H_2O-EtOH (conditions see "Oxidation procedures") for 63 h. Extraction with chloroform gave an oil, which on silica gel chromatography provided 270 mg of unchanged *o*-quinol *5a* (30 %) and 29 % of *4-methyl-5-(1-methyl-2-oxopropyl)-2(5H)-furanone* (5d) as a colourless oil which distilled at 40 °C/0.1 mmHg. Parent mass, found: 168.0798; calc. for $C_9H_{12}O_3$: 168.0786. UV 210 (4.14). IR 1765 (α,β-unsat. γ-lactone), 1715 (2-oxo group), 1645 (C=C). NMR δ 1.24 (d, 3 H, $CHCH_3$, $J=7$ Hz), 2.08 (d, 3 H, CH_3-4, $J=1.5$ Hz), 2.23 (s, 3 H, $COCH_3$), 3.09 (q, split into doublets with $J=3.5$ Hz, 1 H, $CHCH_3$), 5.24 (d, 1 H, H-5, $J=3.5$ Hz; further split by coupling with H-3), 5.98 (m, 1 H, H-3).

Oxidation of 2,3,6-trimethylphenol (6). (A) With $NaIO_4$ in H_2O-EtOH; $t=3$ h. Since no *o*-quinone is formed in this case, the aluminium oxide step could be omitted. The dichloromethane extract was dried and evaporated, leaving a partly crystalline product which on treatment with cold hexane gave a yellow solution and as a residue:

(a) 1,4a,5,8a-Tetrahydro-5,9-dihydroxy-1,2,5,-7,8,9-hexamethyl-1,4-ethanonaphthalene-6,10-(4H)-dione (6e) in a yield of 44 %; colourless crystals of m.p. 191–192 °C (ethyl acetate). (Found: C 70.97; H 7.95. Calc. for $C_{18}H_{24}O_4$: C 71.03; H 7.95). UV 203 (3.80), 253 (3.86), sh 310 (2.36). IR 3390, 1725, 1658, 1628. NMR δ 1.20 (s, 3 H) and 1.26 (s, 6 H), due to the CH_3 groups at C-1, C-5 and C-9; 1.46 (d, 3 H, CH_3-2), 1.85 (s, 3 H, CH_3-8), 2.02 (d, 3 H, CH_3-7), 2.8–3.2 (m, 2 H, H-4a, H-8a), 3.36 (dd, 1 H, H-4), 3.06 and 4.20 (s, 1 H each, OH-5, OH-9, exchangeable with D_2O), 6.00 (dq, 1 H, H-3). $J_{CH_3\text{-}2,H\text{-}3}=1.5$ Hz, $J_{3,4}=7$ Hz, $J_{4,4a}=2$ Hz, $J_{CH_3\text{-}7,H\text{-}8a}$ about 1 Hz.

The above-mentioned hexane solution was evaporated and the resulting oil chromatographed on silica gel to give two further products:

*(b) 2,3,5-Trimethyl-*p*-benzoquinone (6d)*; yield, 26 %.

(c) 6-Hydroxy-2,5,6-trimethyl-2,4-cyclohexadienone (6a), yellow oil (18 %), distillable at 40 °C/1 mmHg. Parent mass, found: 152.086; calc. for $C_9H_{12}O_2$: 152.084. UV 317 (3.46), sh 362 (2.98). IR 3436 m, 1664 vs, 1642 s, 1588 m.

(B) With HIO_4 in CH_3OH. Three products

were obtained:

(a) 2,3,5-Trimethyl-p-*benzoquinone* (6d); yield, 15 %.

(b) 6-Methoxy-2,5,6-trimethyl-2,4-cyclohexadienone (6c), yellow crystals of m.p. 47–51 °C (17 % yield), after recrystallization from hexane m.p. 51–52 °C. (Found: C 72.04; H 8.53; OCH_3 18.82. Calc. for $C_{10}H_{14}O_2$: C 72.25; H 8.49; OCH_3 18.67). UV 321 (3.68), sh 390 (2.82). IR 1667 vs, 1652 s, 1598 m.

(c) 1,4a,5,8a-Tetrahydro-5,9-dimethoxy-1,2,5,-7,8,9-hexamethyl-1,4-ethanonaphthalene-6,10-(4H)-dione (6f), colourless crystals of m.p. 149–152 °C (yield, 12 %), prisms of m.p. 153–154 °C from ethyl acetate. (Found: C 71.94; H 8.67; OCH_3 18.98. Calc. for $C_{20}H_{28}O_4$: C 72.25; H 8.49; OCH_3 18.67). UV 206 (3.79), 252 (3.91), 311 (2.50). IR 1718, 1680, 1634. The NMR spectrum of *6f* is very similar to that of *6e*; the signals of the OCH_3 groups in the former compound appear at 3.34 and 3.52 ppm.

The dimethyl ether 6f was also obtained by methylation of *dimer 6e* with CH_3I/Ag_2O [29] as described in Part XVII.[4] Silica gel chromatography of the crude reaction product gave, in addition to *6f* (46 %), 24 % of *the monomethyl ether* (*6e*, R = CH_3, R′ = H), m.p. 105–106 °C (isopropyl ether). (Found: C 71.80; H 8.18; OCH_3 10.10. Calc. for $C_{19}H_{26}O_4$: C 71.68; H 8.23; OCH_3 9.75). UV 208 (3.82), 252 (3.91), 305 (2.86). IR 3458, 1716, 1660, 1625. The position of the peak due to the unconjugated CO (1716) of the monomethyl ether is very close to the corresponding peak of the dimethyl ether *6f* (1718), but differs from that of the nonmethylated dimer *6e* (1725), whereas the peak due to the α,β-conjugated CO (1660) is very close to that of *6e* (1658), but differs by 20 cm^{-1} from that of *6f* (1680). This indicates that the methoxyl group is located at C-9, *i.e.*, adjacent to the unconjugated CO. In the NMR spectrum, which is very similar to the spectra of *6e* and *6f*, a signal for a single OCH_3 group is found at 3.34 ppm.

Oxidation of 3-methoxy-2-methylphenol (7). *(A) With $NaIO_4$ in H_2O-EtOH*, $t = 21$ h. The following two products were isolated:

(a) 3-Methoxy-2-methyl-p-*benzoquinone* (7d), yellow oil [30] (11 %). The IR data of the compound were in agreement with those reported in the literature.[31]

(b) 6-Ethoxy-5-methoxy-6-methyl-2,4-cyclohexadienone (7b); yield, 11 %. Yellow crystals of m.p. 100–101 °C (hexane.) (Found: C 65.91; H 7.80. Calc. for $C_{10}H_{14}O_3$: C 65.91; H 7.74). UV 347 (3.70), sh 362 (3.60). IR 1669 vs, 1632 s, 1550 vs. NMR δ 1.17 (t, 3 H, OCH_2CH_3), 1.42 (s, 3 H, CH_3-6), 3.32 (q, 2 H, OCH_2CH_3), 3.80 (s, 3 H, OCH_3), 5.42 (d, 1 H, H-4), 5.83 (d, 1 H, H-2), 7.10 (dd, 1 H, H-3). $J_{2,3} = 10$ Hz, $J_{3,4} = 7$ Hz.

(B) With HIO_4 in CH_3OH. The following three products were obtained:

(a) 2-Iodo-5,6-dimethoxy-6-methyl-2,4-cyclohexadienone (7e); yield, 2 %. Yellow prisms of m.p. 183–184 °C (ethyl acetate-hexane). (Found: C 36.51; H 3.68; OCH_3 20.80; I 43.11. Calc. for $C_9H_{11}O_3I$: C 36.76; H 3.77; OCH_3 21.10; I 43.15). UV 388 (3.75). IR 1668 vs, 1625 s, 1527 vs. NMR δ 1.48 (s, 3 H, CH_3-6), 3.02 (s, 3 H, OCH_3-6), 3.83 (s, 3 H, OCH_3-5), 5.38 (d, 1 H, H-4), 7.82 (d, 1 H, H-3). $J_{3,4} = 7.5$ Hz.

(b) 5,6-Dimethoxy-6-methyl-2,4-cyclohexadienone (7c); yield, 17 %. Light-yellow rods, m.p. 109–110 °C (hexane). (Found: C 64.24; H 7.02; OCH_3 36.91. Calc. for $C_9H_{12}O_3$: C 64.27; H 7.19; OCH_3 36.90). UV and IR spectra closely similar to those of *7b*.

Treatment of *7c* with zinc dust in 50 % aqueous acetic acid at room temperature for 30 min regenerated phenol *7*.

(c) 1,4a,5,8a-Tetrahydro-2,5,5,8,9,9-hexamethoxy-1,7-dimethyl-1,4-ethanonaphthalene-6,10-(4H)-dione (7f); yield, 3 %. Colourless needles of m.p. 159–160 °C (ethyl acetate-hexane). (Found: C 60.82; H 6.97; OCH_3 46.53. Calc. for $C_{20}H_{28}O_8$: C 60.59; H 7.12; OCH_3 46.97). UV 270 (4.03) (α,β-enone, calc.[21] 267), sh 315 (3.08). IR 1740 (CO), 1680 (conj. CO), 1640 and 1629 (CH_3O-substituted C=C bonds), all peaks strong. NMR δ 1.25 (s, 3 H, CH_3-1), 1.82 (s, 3 H, CH_3-7), singlets at 3.00, 3.26, 3.40, 3.41, 3.44, 3.75 (6 OCH_3) overlapping a multiplet (3 H, H-4, H-4a, H-8a), 4.84 (d, 1 H, H-3). $J_{3,4} = 7.5$ Hz.

Oxidation of 2,3-dimethoxyphenol (8) [32] *with HIO_4 in CH_3OH.** The crystalline product obtained after passage through the Al_2O_3 column was separated on silica gel into two compounds.

(a) 2-Iodo-5,6,6-trimethoxy-2,4-cyclohexadienone (8d); yield, 3 %. After purification by preparative TLC and recrystallization from hexane, yellow crystals of m.p. 85–87 °C. (Found: C 34.90; H 3.56; OCH_3 29.65; I 40.56. Calc. for $C_9H_{11}O_4I$: C 34.86; H 3.58; OCH_3 30.02; I 40.92). UV 394 (3.73). IR 1680 s, 1668 s, 1634 vs, 1531 vs. NMR δ 3.32 (s, 6 H, 2 OCH_3 at C-6), 3.80 (s, 3 H, OCH_3-5), 5.29 (d, 1 H, H-4), 7.70 (d, 1 H, H-3). $J_{3,4} = 7.5$ Hz.

(b) 5,6,6-Trimethoxy-2,4-cyclohexadienone (8c); yield, 39 %. Yellow needles, m.p. 77–78 °C (hexane). (Found: C 58.61; H 6.63; OCH_3 50.58. Calc. for $C_9H_{12}O_4$: C 58.68; H 6.57; OCH_3 50.54). UV 358 (3.66). IR 1670 vs, 1638 s, 1555 vs. NMR δ 3.37 (s, 6 H, 2 OCH_3 at C-6), 3.83 (s, 3 H, OCH_3-5), 5.45 (dd, 1 H, H-4), 5.84 (dd, 1 H, H-2), 7.07 (dd, 1 H, H-3). $J_{2,4} = 1$ Hz, $J_{2,3} = 10$ Hz, $J_{3,4} = 7$ Hz.

Treatment with zinc dust in 50 % aqueous acetic acid (room temperature, 15 min) reduced the *o*-quinone ketal *8c* to the phenol *8*.

Heat treatment of 2,4-cyclohexadienones. (a) Solutions of the *o*-quinol methyl ethers *4c–7c*, of the ethyl ether *7b*, and of the *o*-quinone ketal *8c* (10 mg each) in toluene (2 ml) were heated in sealed tubes at 110 °C for 17 h. In all cases,

* Experiment performed by H. Thomelius.

TLC gave only a single spot revealing the presence of unchanged monomer.

(b) *o*-Quinone ketal *8c* was heated first at 120 °C for 3 h and then at 150 °C for 1.5 h. After both heating periods, TLC gave an intense single spot (*8c*) located within a continuous band. When heating was continued at 120 °C for 11 d, the intensity of the spot due to *8c* gradually decreased, whereas that of the band increased. Attempts to isolate a defined reaction product by column chromatography (silica gel, benzene/ethyl acetate 1:1) were unsuccessful.

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