

Reaction of Chlorine Dioxide with Phenols: Formation of α,β -Epoxy Ketones from Mesityl and 2,6-Xylenol

BENGT O. LINDGREN and (in part) BIRGER ERICSSON

Swedish Forest Products Research Laboratory, Box 5604, S-114 86 Stockholm, Sweden

When 2,6-xylenol is oxidised with chlorine dioxide in an aqueous solution the following compounds are the main products: 2,6-dimethyl-1,4-benzoquinone, an α,β -epoxy ketone (Ia), and 4-chloro-2,6-dimethylphenol. If oxidised in carbon tetrachloride solution, the xylenol gives the Diels-Alder dimer (VIIc) of 6-chloro-2,6-dimethyl-cyclohexa-2,4-dien-1-one (VIc) in a low yield. Mesityl yields by oxidation in aqueous solution an α,β -epoxy ketone (Ib), a chlorination product (IX) of this epoxy ketone, and 2,4,6-trimethyl-*p*-quinol (XVI).

Some papers dealing with the action of chlorine dioxide on phenolic substances have been published. Purves *et al.*^{1,2} and Sarkanen *et al.*^{3,4} have studied the oxidation of guaiacol derivatives, and Paluch,⁵ that of chloro- and nitrophenols. The formation of *p*-quinones and the cleavage of the guaiacol ring to form substituted muconic acids have been observed.

This paper reports a study of the chlorine dioxide oxidation of two simple phenols: 2,6-xylenol and mesityl.

RESULTS

2,6-Xylenol. When 2,6-xylenol was treated with chlorine dioxide in an aqueous *t*-butanol solution, buffered to a pH of about 5, the main reaction product was 2,6-dimethyl-1,4-benzoquinone. It was formed in about 50 % yield but was isolated in pure form in only 21 % yield. An oily compound C₈H₁₀O₃ (b.p. about 80°C at 15 mm Hg), called *A* in the following, was obtained in a yield of about 9 %. (*A* was not obtained when the oxidation was carried out in an unbuffered solution.) Besides these products, small amounts of 2,2',6,6'-tetramethyl-4,4'-diphenoquinone (yield about 3 %) and 4-chloro-2,6-dimethylphenol (yield 0–8 %, see experimental section) were formed.

Substance *A* was found to be 5,6-epoxy-2-hydroxy-*cis*-2,6-dimethyl-cyclohex-3-en-1-one (Ia) in the following way. It contains a carbonyl group (IR) and an olefinic bond (NMR, IR). The carbonyl stretching band at 1718 cm⁻¹ shows that these two groups are not conjugated. The NMR signals

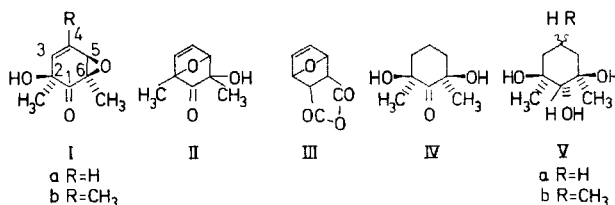
Table 1. NMR signals (δ -values) for the α,β -epoxy ketones (60 Mc). For numbering of the carbon atoms, see formula (I).

Assignment	A (Ia)		C (Ib)	D (IX)	
	CDCl ₃	C ₆ H ₆	CDCl ₃	CDCl ₃	C ₆ H ₆
2-CH ₃	} 1.33 or 1.55 3.60	} 1.30 3.03	} 1.27 or 1.52 3.43	} 1.27 or 1.57 3.90	} 1.15 or 1.22 3.23
6-CH ₃					
5-H					
4-Substituent	} 6.09 or 6.26 3.25	} 5.69 or 5.90 3.52	1.98 5.79 3.42	} 5.82 5.93 4.82 3.70	} 5.22 5.58 4.70 3.67
3-H					
OH					
Substituent in 4-position	-H		-CH ₃	=CH ₂	

Coupling constants: for *A*, $J_{3-H,4-H}$ is 9 cps; $J_{3-H,5-H}$, 2.5 or 3.5 cps; and $J_{4-H,5-H}$, 3.5 or 2.5 cps; for *C*, $J_{3-H,5-H}$ is 2.8 cps; and $J_{2-H,4-Me}$, 1.7 cps; for *D*, the sum of the values for $J_{5-H,4-CH_3}$ is less than 0.7 cps; and the values for $J_{3-H,4-CH_3}$ 1.5 and 1.7 cps.

(Table 1) can be attributed to the structures (II), (Ia), and its *trans*-dimethyl epimer.

The structure (II) for *A* is not probable because electron impact on *A* did not induce a *retro*-Diels-Alder reaction as did electron impact on the Diels-Alder product (III) which yielded the cations of furan and maleic anhydride. The main fragmentations of *A* involve instead eliminations of CH₃, O, CHO, and CH₃CO. No peak for the molecular ion was observed. The oxygen atom is most probably eliminated from the epoxy group. Such a fragmentation has recently been reported for aliphatic α,β -epoxy ketones.⁶



Compound *A* was hydrogenated to a mixture of a dihydroxy ketone C₈H₁₄O₃ (m.p. 66–69°C) and a trihydroxy compound C₆H₁₆O₃ (m.p. 135.5–137.5°C). NMR, IR and mass spectra together with the finding that the 2,6-hydroxyl groups are *cis*-related (see below) indicate that the dihydroxy ketone has the formula (IV) and the trihydroxy compound the formula (Va) (see experimental section). The dihydroxy ketone (IV) was reduced by catalytic

hydrogenation or sodium borohydride treatment to the trihydroxy compound (Va).

The trihydroxy compound forms no borate complex as it does not migrate by electrophoresis in borate buffer.⁷ It has therefore no *cis*-1,2-diol group as such groups coordinate with borate.⁸ That establishes that the trihydroxy compound is the *xylo* isomer (Va) from which it follows that the methyl groups of the dihydroxy ketone and *A* are *cis*-related.

The dihydroxy ketone migrates by electrophoresis in a borate buffer. As neither a *cis*-1,3-diol nor a *trans*-1,3-diol in the cyclohexane series coordinate with borate,⁹ the complex is formed with the acetal form of the dihydroxy ketone.

Oxidation of 2,6-xylenol in carbon tetrachloride solution by chlorine dioxide gave in a yield of about 1% a compound — called *B* — with the formula $C_{16}H_{18}Cl_2O_2$ and the m.p. 192.5–196°C. Its NMR signals are mutually related to those of the Diels-Alder dimer (VIIa) of 2,6-dimethyl-*o*-quinol (VIa) and the diacetate of the same dimer (Table 2). This indicates that

Table 2. NMR signals (δ -values) for the compounds with the general formula (VII) (60 Mc). For numbering of the carbon atoms, see formula (VII).

Assignment	Compound <i>B</i> (Ia)		Compound <i>B'</i> (Ib)		The diacetate of (VIIa)		Signal charact. ^a	
	CDCl ₃	C ₆ H ₆	CDCl ₃	C ₆ H ₆	CDCl ₃	CDCl ₃ C ₆ H ₆		
Methyl-	4	1.38	1.02	1.38	1.02	1.27	1.42	1.13 s
	2,8	1.66	1.41	1.64	1.35	1.34	1.49	1.51 s
		1.80	1.51	1.79	1.69	1.35	1.72	1.64 s
6	1.88	1.55	1.88	1.77	1.87	1.84	1.67 t, <i>J</i> 1.5	
Methine-	4A	3.02	2.29	3.0	2.6	2.9	2.99	2.40 u, <i>W</i> 20
	1,8A	3.6	3.5	3.15	2.7	3.3	3.49	3.60
		3.7	3.6	3.89	3.88	3.4	3.77	3.92
Olefinic-	10	5.63	5.06	5.65	5.05	5.57	5.64	5.18 dd, <i>J</i> 8,2–3
	5	6.4	5.60	6.3	5.5 to 5.8	6.3	6.3	5.58 u, <i>W</i> 7
	9	6.4	5.95	6.3		6.3	6.3	6.02 t, <i>J</i> 7–8

^a s, singlet; d, doublet; t, triplet; u, unsolved; *J*, coupling constant and *W*, half-band width (both in cps).

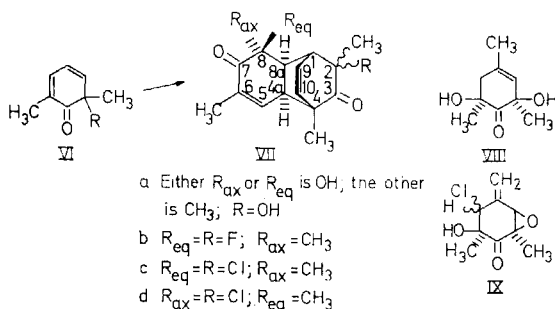
B is the dimer (VIIc) of 6-chloro-2,6-dimethyl-cyclohexa-2,4-dien-1-one (VIc). (The sterical relationship at carbon atom 8 is shown below.)

As expected for a Diels-Alder dimer, *B* gave on electron impact a distinct peak for half the molecular weight. The most predominant fragment from *B* was the cation of the xylenol or an isomer of it.

2,6-Xylenol is oxidised by periodate to (VIIa)¹⁰ and by perchloryl fluoride to (VIIb).¹¹ In the latter oxidation product, the steric relationship between the fluoro group of the cyclohexenone part and the ethyleno group was established¹¹ from the high value (1700 cm⁻¹) for the stretching frequency of the

conjugated carbonyl group which indicates that the fluoro group is pseudo-equatorial. As the corresponding frequency for *B* is also high (1698 cm^{-1}) the configuration (VIIc) is proved for compound *B*.¹²

The dimer (VIIa) of 2,6-dimethyl-*o*-quinol was converted by thionyl chloride into a compound — called *B'* — (m.p. 149–151°C), the stoichiometric formula of which is the same as that of *B*. Every NMR signal from *B'* corresponds with a signal from *B* with a similar δ -value and the same shape (Table 2). For all pairs of signals but one the difference in δ -value is below 0.3 ppm. The exception is a pair in which the signal from *B* is attributed to either the 1-H or the 8A-H, where the difference is 0.5–0.8 ppm. The mass spectrum of *B'* is identical to that of *B*. These findings indicate that *B'* is an epimer of *B*.



As the IR frequency of the conjugated carbonyl group of *B'* is 1680 cm^{-1} , the chloro group of the cyclohexenone part should be pseudo-axial.¹² *B'* has thus the configuration (VIIId). Such a dissimilarity between *B* and *B'* explains the relatively large difference in the NMR signals mentioned above if this pair of signals is attributed to the 1-protons. From simple stereochemical considerations it follows that *B'* is probably more stable than *B*.

The spatial arrangements of the second chloro groups of *B* and *B'* have not been determined.

The isolation of compound *B* by oxidation in a non-aqueous solution may suggest that the Diels-Alder dimer (VIIa) is formed by oxidation in aqueous solutions. The formation of this dimer in such solutions, however, was not observed. Further, the dimer (VIIa) did not react with chlorine dioxide under these conditions, and cannot therefore be a short-lived intermediate of the reaction.

Mesitol. In aqueous solution at pH 5, mesitol was transformed by chlorine dioxide into 2,4,6-trimethyl-*p*-quinol (XVI in Scheme 1) (isolated in a yield of 28 %), a compound *C*, $\text{C}_9\text{H}_{12}\text{O}_3$ (yield 26 %; oil b.p. about 100°C, 15 mm Hg), and a compound *D*, $\text{C}_9\text{H}_{11}\text{ClO}_3$ (yield 7 %; m.p. 90–95°C). GLC of the reaction mixture indicated that *C* was formed in a larger amount than the *p*-quinol (XVI) suggesting that *C* was partly destroyed during the working-up of the reaction mixture.

GLC showed that *C* is formed when mesitol is oxidised in unbuffered aqueous solution. *C* was, however, destroyed within some minutes, probably because the solution became too acidic.

The NMR (Table 1), mass and IR spectra of *C* suggested its being related to compound *A*, derived from 2,6-xylenol. Hydrogenation of *C* yielded a complicated mixture from which a trihydroxy compound $C_9H_{18}O_3$ (m.p. 141–142°C) was isolated. Its mass and NMR spectra and its immobility to borate electrophoresis showed that its structure is (Vb) (see experimental section). Compound *C* should thus possess structure (Ib). Further isolated hydrogenation products of *C* were mesitol and an oily compound, whose spectra indicate its having the structure (VIII).

Compound *D* contains two methyl groups and one methylene group as shown by IR and NMR (Table 1). An IR-band at 1708 cm^{-1} and a weak $n \rightarrow \pi^*$ absorption in the UV spectrum shown that the carbonyl group is unconjugated.

The mass spectrum of *D* is very complex; some of the fragments are interpreted as eliminations from the molecular ion of Cl, CH_3CO , and $(CO_3CO + Cl)$. No elimination of an oxygen atom, which occurs by electron impact on *A* and *C*, is detectable.

Chlorination of *C* yielded *D*. Of the possible chlorination products from *C* only the allylic chlorination product with the formula (IX) fits the NMR spectrum of *D*. From that it is concluded that *D* has structure (IX).

The steric arrangement of the chloro group in *D* is unknown: the large m.p.-interval may suggest *D* being a mixture of the two epimers but the sharpness of its NMR signals ($W_{1/2}$ for the methyl signals is 0.5 cps) indicates that our preparation is a pure compound.

The chlorination product of mesitol, 3-chloro-2,4,6-trimethyl-phenol, was not formed or formed in only a very low yield. When it was treated with chlorine dioxide, *D* was not obtained.

When the oxidation of mesitol is carried out in carbon tetrachloride solution the same reaction products as in the aqueous solution are formed, as shown by GLC. The yields of compounds *B* and *C* were, however, considerably lower than in aqueous solution at pH 5. No compound was obtained corresponding to *A* from 2,6-xylenol.

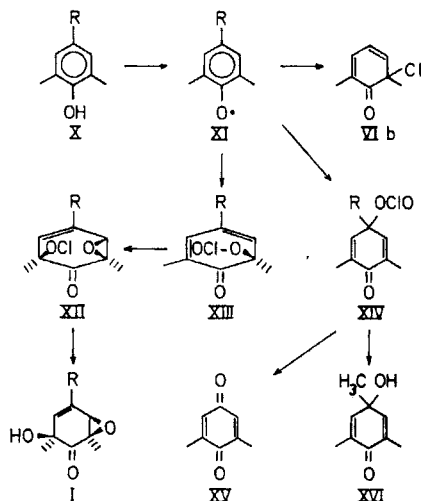
DISCUSSION OF OXIDATION MECHANISM

From the reaction products obtained as well as the general views of the radical oxidations of phenols,¹³ some ideas of the oxidation paths may be suggested (Scheme 1).

The phenol (X) and chlorine dioxide probably initially react to form the phenoxy radical (XI) and chlorous acid (Scheme 1). The radical may then add a molecule of chlorine dioxide in either the *para*- or one of the *ortho*-positions giving the chlorite esters of a *p*-quinol (XIV) or a *o*-quinol (XIII).

The chlorite esters are certainly very labile compounds and they probably react immediately after their formation. The *p*-quinol ester (XIV) from 2,6-xylenol may yield the *p*-quinone by a loss of hypochlorous acid. The *p*-quinol ester of mesitol may be transformed into 2,4,6-trimethyl-*p*-quinol by hydrolysis or a radical process.

Unexpectedly, the chlorine dioxide oxidation did not yield the *o*-quinol dimers. The *o*-quinol chlorite esters (XIII) eventually formed may then react



Scheme 1. The postulated pathways for oxidation of 2,6-xyleneol (X, R=H) and mesitol (X, R=CH₃) by chlorine dioxide.

differently from the *p*-quinol esters of mesitol. It is possible that they may rearrange to the hypochlorite esters of the α,β -epoxy ketones (XII), which then are transformed into the epoxy ketones (I) by hydrolysis or some radical reaction. The *cis*-relationship between the hydroxyl and epoxy groups is in agreement with the above-mentioned rearrangement.

The hypochlorous acid formed by these reactions evidently chlorinates 2,6-xyleneol and α,β -epoxy ketone (Ib). The *o*-quinol derivative (VIb) may be formed also over the phenoxyl radical (XI) (see Scheme 1).

EXPERIMENTAL

Reaction of 2,6-xyleneol with chlorine dioxide in aqueous solution

Analytical experiments. 2,6-Xyleneol was oxidised with varying amounts of chlorine dioxide in an aqueous acetate buffer solution (pH 4.6)/*t*-butanol solution (4/1 v/v). The reaction products were isolated by extraction with methylene chloride. GLC (QF-1; 86°C) of the extract showed the presence of 2,6-xyleneol (R_T 3.1 min), substance A (9.5 min), 2,6-dimethyl-1,4-benzoquinone (10.3 min), 4-chloro-2,6-dimethyl-phenol (11.3 min), and an unidentified compound (15.1 min, relatively small peak). At the molar ratio chlorine dioxide/phenol=1.3–1.7 almost all xyleneol had reacted and the maximum amounts of the quinone and the compound A were obtained. The amount of the chloro compound formed was largest at the ratio about 1.0 (estimated to be about 8 % from the peak area) and decreased if the ratio was raised.

If the oxidation was carried out in an unbuffered aqueous *t*-butanol solution the formation of 2,6-dimethyl-1,4-benzoquinone and 4-chloro-2,6-dimethyl-phenol but not that of compound A was observed by GLC.

Preparative experiments. An aqueous chlorine dioxide (28 mmoles) solution (500 ml) was added dropwise to a solution of 2,6-xyleneol (3 g, 24.6 mmoles) in a mixture of *t*-butanol (150 ml) and aqueous acetate buffer solution (300 ml, pH 4.6). The mixture was then stirred for half an hour. The temperature was kept below +15°C. Precipitated crystals of 3,3',4,4'-tetramethyl-4,4'-diphenylquinone (0.1 g) were removed.

The solution was extracted with methylene chloride, which was then washed with ice water, dried and evaporated. The evaporation residue (2.2 g) was chromatographed on a silica gel column (4 × 35 cm) using isopropyl ether as eluent. The temperature was kept at +6°C. The following fractions were collected:

a) 320–380 ml. The oily residue of evaporation (23 mg) contained 4-chloro-2,6-dimethylphenol according to GLC and TLC.

b) 440–700 ml. The residue of evaporation (1.80 g, yellow-brown crystals) was dissolved in boiling light petroleum (50 ml). By slow evaporation a small fraction of dark crystals was precipitated. They were removed and the residue from evaporation of the mother liquor was recrystallised from light petroleum, which yielded 2,6-dimethyl-1,4-benzoquinone (0.71 g, yield 21 %); m.p. 69.5–71°C, lit.¹⁴73°C.

c) 1000–1400 ml. The oily residue of evaporation (0.34 g) consisted mainly of compound *A* (see below). The yield of *A* calculated from the weight of this fraction was 9 %.

Compound A (= 5,6-epoxy-2-hydroxy-cis-2,6-dimethyl-cyclohex-3-en-1-one) (*Ia*). The product obtained as described above was distilled (bath temperature: 80°C at 15 mm Hg). The NMR signals of the oily distillate are presented in Table 1. ν_{\max} at 3450, 1718, 1100, and 820 cm^{-1} (oil between KBr plates). [Found: C 62.6; H 6.5; O 31.3. Calc. for $\text{C}_8\text{H}_{10}\text{O}_3$ (154.2): C 62.3; H 6.5; O 31.1]. The mass spectrum was determined directly on the eluate from a GLC apparatus. It showed distinct peaks at m/e 138 (8 % of the base peak), 125 (6), 111 (53), 109 (17), 95 (9), 83 (19), 55 (19), and 43 (100) m.u.

Hydrogenation of compound A. Compound *A* (517 mg) dissolved in ethanol was hydrogenated at room temperature and normal pressure using Adams' PtO_2 catalyst. The hydrogen consumption was about 2.2 moles per mole of *A*. The product obtained (417 mg) was purified by preparative TLC (silica gel, isopropyl ether). Two fractions were obtained.

The main fraction (154 mg) gave after sublimation cis-2,6-dimethylcyclohexan-2,6-diol-1-one (*IV*), m.p. 66–69°C, 77 mg, yield 15 %. [Found: C 61.2; H 9.1; O 30.0. Calc. for $\text{C}_8\text{H}_{14}\text{O}_3$ (158.2): C 60.7; H 8.9; O 30.3]. Its NMR signals in CDCl_3 were: δ 1.44 s (2 CH_3), 1.65–2.18 m (3 CH_2), and 3.92 s (2OH) ppm; and in C_6H_6 : δ 1.17 s (2 CH_3), 1.20–1.84 m (3 CH_2), 3.83 broad s (OH), and 5.91 broad s (OH). ν_{\max} at 3350 and 1718 cm^{-1} (KBr-plate); no peak was observed for olefinic hydrogen at 3000–3100 cm^{-1} .

The mass spectrum showed distinct peaks at m/e 158 (0.04 % of the base peak), 130 (13), 112 (33), 97 (33), 71 (54), 69 (16), 58 (31), 57 (22), 55 (13) and 43 (100) m.u. Metastable ions were observed for 130→112 and 112→97 m.u. The fragmentation starts with elimination of H_2O giving the fragment with m/e 130. This species then loses H_2O giving a fragment with m/e 112. The smaller fragments noted above (except that with m/e 71) can be formed from the fragments with m/e 130 and 112 according to well known principles.

The paper-electrophoretic migration rate in a borate buffer was 0.20–0.25 of that of glucose (30 V/cm; 1.5 h; pH 10; hydroxymethyl-furfural used to mark the starting point; glucose moved about 10 cm).

The minor fraction, which moved more slowly on silica gel than the major fraction, gave 1,3-dimethyl-cyclohexan-xylo-1,2,3-triol (*Va*) m.p. 135.5–137.5°C after recrystallisation from ethyl ether/acetone. [Found: C 59.7; H 10.0. Calc. for $\text{C}_8\text{H}_{16}\text{O}_3$ (160.2): C 60.0; H 10.1].

Its NMR signals in $(\text{CD}_3)_2\text{SO}$ were δ 1.08 s (2 CH_3); 1.25–1.50 m (3 CH_2); 2.97 d, $J_c = 6.5$ cps (CH); 4.92 d, $J_c = 6.5$ cps (OH); 5.22 s (2OH). No peaks were observed for carbonyl and olefinic hydrogen (IR, KBr-plates).

The mass spectrum showed distinct peaks at m/e 142 (3 % of the base peak), 127 (1), 124 (6), 111 (25), 109 (2), 185 (7), 84 (100), 83 (6), 81 (7), 74 (4), 72 (8), 71 (45), 69 (3), 59 (10), 58 (10), 57 (9), 56 (7), 55 (10), 43 (62), 41 (12) and 39 (6). A metastable ion was observed for 142→124. No peak was thus observed for the molecular ion. The main fragmentations involve an elimination of one and two molecules of H_2O (m/e 142 and 124). The $\Delta^{1,6}$ -double bond introduced into the fragment or one of the fragments with m/e 142 may start a retro-Diels-Alder reaction leading to the ion with m/e 84, which gives the base peak.

The compound did not migrate by electrophoresis in a borate buffer [the same experimental conditions as for (*IV*)].

When the dimethyl-cyclohexan-diol-one (IV) was hydrogenated as described above for *A* or reduced by sodium borohydride the dimethyl-cyclohexan-triol (Va) was obtained as shown by gas chromatography.

If the hydrogenation of *A* was performed for a longer time, 2.6 moles of hydrogen was absorbed during the hydrogenation. The dimethyl-cyclohexan-triol (Va) was then the main reaction product obtained (yield 28 %).

Reaction of 2,6-xyleneol with chlorine dioxide in a carbon tetrachloride solution

Compound B (=1,4-ethyleno-2,8-dichloro-2,4,6,8-tetramethyl-octahydronaphthal-5-en-3,7-dione) (VIIc). Dry chlorine dioxide (about 30 mmole) was passed into a solution of 2,6-xyleneol (5.0 g, 41 mmoles) in carbon tetrachloride (100 ml) during 15 h. GLC (QF-1, 165°C) of the solution obtained showed the presence of 2,6-xyleneol (7.4 mmoles), 2,6-dimethyl-1,4-benzoquinone (6.6 mmoles), and 4-chloro-2,6-dimethylphenol (8.3 mmoles).

The carbon tetrachloride solution was shaken 10–15 times with N aqueous sodium hydroxide solution until GLC showed a low content of the phenol. From the alkaline solution 4-chloro-2,6-dimethylphenol was isolated. The evaporation residue of the carbon tetrachloride solution was digested with boiling light petroleum, from which 2,6-dimethyl-1,4-benzoquinone was then isolated.

The petroleum insoluble material (0.18 g) was repeatedly recrystallised (methanol and ethanol) to the m.p. 192.5–196°C. TLC (chloroform) have only one spot. ν_{\max} at 1727 and 1698 cm^{-1} (KBr). [Found: C 61.8; H 6.0; Cl 23.2; O 10.7. Calc. for $\text{C}_{16}\text{H}_{18}\text{Cl}_2\text{O}_2$ (313.2): C 61.4; H 5.8; Cl 22.6; O 10.2]. The NMR signals are presented in Table 2. The mass spectrum showed distinct peaks for m/e 158 (5 % of the base peak), 156 (14) [both peaks are ascribed to the cation of (VIc)], 122 (100), 121 (45), 107 (69) and 91 (19).

Compound B' (=1,4-ethyleno-2,8-dichloro-2,4,6,8-tetramethyl-octahydronaphthal-5-en-3,7-dione) (VIIId). Compound (VIIa) (2.5 g) was mixed with pyridine (45 ml). Thionyl chloride (5 ml) was added (ice cooling) and the mixture was stirred for 2 days at room temperature. Ice was added and the product obtained was fractionated by preparative TLC (chloroform): the zones containing the fractions were visible under UV light. The fastest moving fraction (140 mg) was recrystallised (methanol) to the m.p. 149–151°C. [Found: C 61.4; H 5.8. Calc. for $\text{C}_{16}\text{H}_{18}\text{Cl}_2\text{O}_2$ (313.2): C 61.4; H 5.6]. ν_{\max} at 1730 and 1680 cm^{-1} (KBr). The NMR signals are presented in Table 2. The mass spectrum was identical with that of the dimer (VIIc), also in the relative peak heights. On TLC (isopropyl ether or chloroform) (VIIc) moved slightly faster than (VIIId).

Treatment of the dimer (VIIa) with chlorine dioxide. A solution of compound (VIIa) (0.5 g) in *t*-butanol (25 ml), acetate buffer solution (pH 4.8, 150 ml), and an aqueous chlorine dioxide solution (0.09 M, 40 ml) was left at room temperature for 17 h. From the solution, compound (VIIa) (456 mg) was recovered, m.p. 195–198°C, lit.¹⁰ 194–196°C.

Reactions of mesitol with chlorine dioxide

Aqueous solution, pH 4.5. An aqueous chlorine dioxide solution (100 ml: about 8 mmole of chlorine dioxide) was added to a solution of mesitol (1 g, 7.4 mmole) in *t*-butanol (50 ml) and an aqueous acetate buffer solution (100 ml: pH 4.5). After 30 min, GLC of the reaction product showed the presence of 2,4,6-trimethyl-*p*-quinol (XVI) (relative peak area was 10), compound *C* (Ib) (area, 20), and compound *D* (IX) (area, 2). Only a very weak peak was observed for a compound moving with the same rate as 3-chloro-2,4,6-trimethyl-phenol.

The solution was then extracted three times with methylene chloride. The methylene chloride solution was washed with a sodium bicarbonate solution and with water. It was then dried with sodium sulphate and evaporated to dryness. The residue was chromatographed on a silica column (diameter 4 cm, height 30 cm). The column was first eluted with isopropyl ether/light petroleum 1/1 v/v. The following fractions were collected:

640–1040 ml. The crystalline material (111 mg: m.p. 87–91°C, yield 7 %) consisted mainly of substance *D* (see below).

1140–1300 ml. The oily material (327 mg, yield 26 %) was homogeneous in TLC and GLC, and consisted mainly of substance *C* (see below).

When 3000 ml had been eluted, the eluent was changed to isopropyl ether/light petroleum ether 3/1 v/v.

3200–4000 ml. The oil obtained (314 mg, yield 28 %) was indistinguishable from 2,4,6-trimethyl-*p*-quinol (XVI) by GLC, TLC, and IR.

Aqueous solution, unbuffered. An aqueous chlorine dioxide solution (110 ml, 0.18 M) was added to mesitol (5 g) in *t*-butanol/water (125 ml). GLC showed peaks for mesitol, 2,4,6-trimethyl-*p*-quinol and compound *C*. The peak height for *C* decreased by half in 22 minutes.

Carbon tetrachloride solution. Dry chlorine dioxide was passed into a solution of mesitol in carbon tetrachloride. Preparative TLC followed by GLC on the fractions obtained showed the presence of 2,4,6-trimethyl-*p*-quinol, *C* and *D*.

Compound C (=5,6-epoxy-2,4,6-trimethyl-cyclohex-3-en-2-ol-1-one) (*Ib*). The raw material from the chlorine dioxide oxidation of mesitol in aqueous solution (pH 4.5) was distilled (bath temperature, 100°C; 15 mm Hg). The NMR signals of the oily distillate are shown in Table 1. ν_{\max} at 3520, 3015 and 1722 cm^{-1} (oil). [Found: C 64.0; H 7.5; Cl 1.2. Calc. for $\text{C}_9\text{H}_{12}\text{O}_3$ (168.2): C 64.3; H 7.2]. The mass spectrum (determined as for *A*) showed distinct peaks at m/e 152 (3 % of the base peak), 139 (11), 125 (42), 123 (14), 109 (8), 97 (10), 83 (12) and 43 (100).

Attempts to reduce compound *C* with lithium aluminium hydride and to acetylate it with acetic anhydride using perchloric acid or pyridine as catalyst gave complex mixtures.

Hydrogenation of compound C. Compound *C* (207 mg) dissolved in ethanol was hydrogenated at room temperature and normal pressure using Adams' PtO_2 catalyst. The hydrogenated product was chromatographed [silica gel column 0.7×32 cm; chloroform-methanol (5/1 v/v)]. The first fractions obtained were a complex mixture of incompletely hydrogenated substances.

The last fraction (18 mg) consisted of 1,3,5-trimethyl-cyclohexan-xylo-1,2,3-triol (*Vb*) (m.p. 141–142°C). Its NMR signals in $(\text{CD}_3)_2\text{SO}$ were: δ 0.85 d, $J=3.5$ cps (5- CH_3); 1.00 s (1- and 3- CH_3); 1.1–1.7 m (4- and 6- CH_2 and 5-CH); 3.29 s and d (H_2O and 2-CH); 4.08 s (1- and 3-OH); 4.29 d, $J=4$ cps (2-OH). The mass spectrum showed distinct peaks at m/e 156 (0.6 % of the base peak), 141 (5), 138 (3), 125 (3), 123 (6), 99 (100), 95 (10), 85 (69), 83 (12), 74 (8), 72 (8), 71 (29), 69 (12), 67 (8), 58 (10), 55 (8), 43 (65), 41 (14). The fragmentation pattern is similar to that of 1,3-dimethyl-cyclohexan-xylo-1,2,3-diol (*Va*). It did not migrate on electrophoresis in a borate buffer; the experiment was carried out as described for (*IV*).

In another experiment compound *C* (397 mg) was hydrogenated as described above. The reduction was interrupted after the consumption of about 100 ml of hydrogen. The reaction product (350 mg) was fractionated on a silica column (1×30 cm) using chloroform/methanol (50/1 v/v) as solvent. Two fractions were collected. The first fraction (165 mg) consisted of mesitol (m.p., mixed m.p., and IR). The second fraction (82 mg) was an oil which was homogeneous in GLC (SE-30; 75°C) and borate electrophoresis [carried out as described above for (*IV*); R_{glucose} was 0.46]. It consisted of cis-2,6-dihydroxy-2,4,6-trimethyl-cyclohex-3-en-1-one (*VIII*). Its NMR signals in CDCl_3 were: δ 1.44 s and 1.49 s (2- and 6- CH_3); 1.80 s, $W_{1/2}$ 3 cps (4- CH_3); 2.52 s, $W_{1/2}$ 3.5 cps (5- CH_2); about 3.5 s (broad) (2OH); 5.50 s, $W_{1/2}$ 4 cps (3-CH). The mass spectrum (determined as for *A*) showed distinct peaks for m/e 152 (33 % of the base peak) [$\text{M}^+ - 18$], 150 (100), 136 (25), 135 (45), 121 (30), 111 (25), 110 (60), 109 (60), 108 (60), 107 (45), 95 (70), and 91 (24). The fragment m/e 150 may be due to an impurity which could not be traced in the NMR spectrum. The IR spectrum showed characteristic bands at 3400 and 1725 cm^{-1} .

Chlorination of compound C. An aqueous chlorine solution (1 ml, 90 mM) was added to a solution of compound *C* (18 mg) in *t*-butanol (0.1 ml) and an aqueous acetate buffer solution (0.2 ml, pH 4.6). After 15 min the solution was extracted with methylene chloride. Evaporation yielded a crystalline material (m.p. 85–90°C) which was indistinguishable from compound *D* [IR and GLC (XE-60, 86°C)].

Compound D (=3-chloro-5,6-epoxy-cis-2,6-dimethyl-4-methylene-cyclohexan-2-ol-1-one) (*IX*). The raw material from the chlorine dioxide oxidation of mesitol in aqueous solution (pH 4.5) was recrystallised from hexane to a m.p. of 90–95°C. The NMR signals are shown in Table 1. ν_{\max} at 3510, 3010, 1708, and 908 cm^{-1} (KBr) and at 3082 cm^{-1} (weak,

observed in carbon tetrachloride solution). UV maximum at 298 nm (ϵ , 37). [Found: C 53.2; H 5.4. Calc. for $C_9H_{11}ClO_3$ (202.7); C 53.4; H 5.4].

Its mass spectrum had distinct peaks for m/e 204/202 (0.2/0.7 % of the base peak), 167 (16), 161/159 (10/27), 149 (10), 142 (10), 139 (18), 125 (46), 124 (100), 123 (18), 117 (10), 111 (12), 97 (11), 95 (22), 43 (100).

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