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Diels-Alder Reactions of 2,4-Cyclohexadienones. I. Structural and Steric Orientation in the Dimerisation of 2,4-Cyclohexadienones*

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Salicyl alcohol (*3a*) and its methyl homologues *3b*—*3e* on treatment with periodate give the Diels-Alder dimers *5a*—*e* of the initially formed spiro(oxirane-2,4-cyclohexadienones) *4a*—*e*. Similarly, dimers *2a*—*e* are formed from 2,4-cyclohexadienones *1a*—*e* ("*o*-quinols").

Cleavage of the oxirane rings in *5a*—*e* by hydrogen bromide gave the bis(bromohydrins) *6a*—*e*, which on treatment with Raney nickel were converted to the corresponding *o*-quinol dimers *2c* and *2e* or to the further hydrogenated compounds *8*, *10*, and *11*, the three latter products also being obtained on Raney nickel reduction of *o*-quinol dimers *2a*, *2b* and *2d*, respectively.

Since the complete structure of dimer *5a* has been determined by X-ray crystallographic analysis of its bis(bromohydrin) *6a*, the final structure of *o*-quinol dimer *2a* now is established as well. Furthermore, the results of the Raney nickel reductions show that the Diels-Alder dimerisations of the spiro(oxirane-2,4-cyclohexadienones) *4b*—*e* and those of *o*-quinols *1b*—*e* are analogous with regard to regiospecificity and stereochemical specificity.

Recent X-ray analysis [16] elucidated the structures of *2b* and *2d* and showed these to be analogous to the structure of *2a* and, furthermore, photochemical work [14] proved that dimer *2e* is analogous to *2a* with regard to *endo* configuration and structural orientation. From the structural correlations revealed by the Raney nickel reductions it can be concluded that the orientation and the stereochemistry thus established for *o*-quinol dimers *2b*, *2d*, and *2e* are characteristic for the spirooxirane dimers *5b*, *5d*, and *5e* as well.

The steric arrangements of the *tert*-carbinol and oxirane groups in the two types of dimers can be ascribed to steric approach control in the dimerisation. Reasons for the regiospecificity in the dimerisation of 2,4-cyclohexadienones are briefly discussed.

In earlier communications [1-4] it has been shown that periodate oxidation of methyl homologues of *o*-cresol gives 6-hydroxy-6-methyl-2,4-cyclohexadienones ("*o*-quinols", *1b*—*1e*) which undergo rapid Diels-Alder reaction to give the *o*-quinol dimers *2b*—*2e*. The corresponding dimer (*2a*) of unsubstituted *o*-quinol (*1a*) has been obtained on acid hydrolysis of the acetate of *1a*.[5] Contrary to the free *o*-quinols, the acetates are comparatively stable at room temperature.

The aim of the present study was primarily to elucidate the structures of *o*-quinol dimers *2a*—*2e*.

Dimerisation of *o*-quinols *1a*—*e* formally offers several possibilities with regard to the structure of the products. Firstly, in the molecule acting as dienophile either the α,β or the γ,δ double bond of its conjugated carbonyl system may participate in the reaction. As observed earlier in similar cases,[6] the γ,δ double bond reacts specifically (see for instance, Refs. 2 and 3 and the review article, Ref. 7). Furthermore, there are the following alternative possibilities:

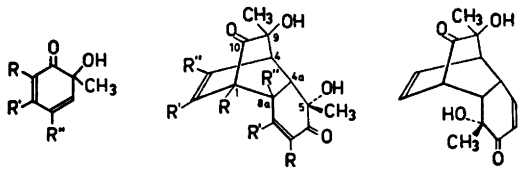
(*a*) The dimers may have *endo* or *exo* configuration.

(*b*) Due to the presence of an asymmetric C-atom in the monomers four isomeric dimers with different steric arrangements at C-atoms 5 and 9 are conceivable.

(*c*) There are two possible structural orientations of the diene and dienophile moieties, as illustrated by formulae *2a* and *2a'*.

Although the alternatives involved in items *a*—*c* make the formation of sixteen isomeric dimers (D,L pairs) possible, in each case only one dimeric product has been obtained. The

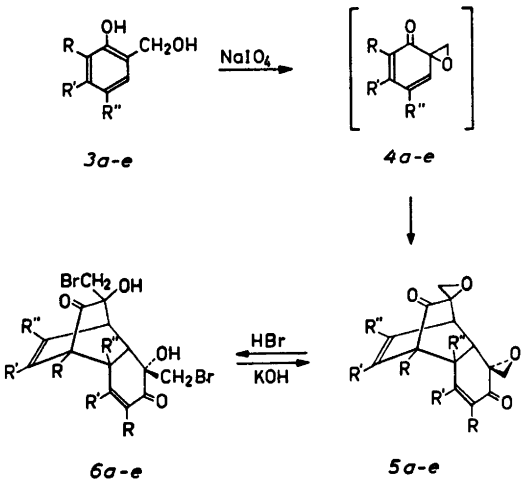
* Part XI in the series "Periodate Oxidation of Phenols". Preliminary communication, see Part X.[1]



1a-g *2a-g* *2a'*

1a, *2a* R = R′ = R″ = H
1b, *2b* R = CH_3; R′ = R″ = H
1c, *2c* R′ = CH_3; R = R″ = H
1d, *2d* R″ = CH_3; R = R′ = H
1e, *2e* R = R″ = CH_3; R′ = H
1f = *1b*, F instead of OH; *2f* = *2b*, F instead of OH
1g = *1b*, Cl instead of OH; *2g* = *2b*, Cl instead of OH

Chart 1.



3a-e *4a-e* *6a-e* *5a-e*

3a, *4a*, *5a*, *6a* R = R′ = R″ = H
3b, *4b*, *5b*, *6b* R = CH_3; R′ = R″ = H
3c, *4c*, *5c*, *6c* R′ = CH_3; R = R″ = H
3d, *4d*, *5d*, *6d* R″ = CH_3; R = R′ = H
3e, *4e*, *5e*, *6e* R = R″ = CH_3; R′ = H
7a-e = *6a-e*, OAc instead of OH

Chart 2.

dimerisation of the *o*-quinols (*1a-e*) thus proceeds with a very high degree of stereochemical selectivity (items *a* and *b*) and regioselectivity (item *c*). No further isomers could be detected by NMR analysis and thin layer chromatography of the crude reaction products. For simplicity, it will therefore be assumed in the following that the dimerisations are stereospecific and regiospecific.

By degrading the dimer of *o*-quinol *1a* to 1,7-dimethyl-2-naphthol, Metlesics and Wessely [5] proved the structural orientation in this dimer to be that given in formula *2a* rather than *2a'*. Experimental evidence for the *endo* configuration and the steric arrangements at C-5 and C-9, however, was still lacking.

Periodate oxidation of salicyl alcohol (*3a*) was found [8] to result in the formation of spiro(oxirane-2,4-cyclohexadienone) *4a* which rapidly dimerised to give the bis(spirooxirane) *5a*. Treatment of this dimer with hydrogen bromide afforded a bis(bromohydrin), for which structure *6a* was established by X-ray crystallography.[9] This also proved structure *5a* for the parent dimer.[8]

Reductive opening of the oxirane rings in *5a* or reductive debromination of *6a* could be expected to give the *o*-quinol dimer *2a*, provided that the latter had the same structural and steric arrangements as established for *5a* and *6a*. Attempts to perform these conversions by treating *5a* with $LiAlH_4$ or $NaBH_4$ or by treating *6a* or the corresponding bis(iodohydrin) with hydrogen in the presence of Pt and Pd catalysts as well as with various other reductants remained without success. Raney nickel in boiling ethanol, however, effected the conversion of the bromomethyl groups in *6a* into methyl groups with simultaneous hydrogenation of the C=C and C=O double bonds present to give the tetrahydroxy compound *8*. The same reduction product was obtained on similar treatment of *o*-quinol dimer *2a*. This constitutes unambiguous proof of structure *2a* and shows that the Diels-Alder dimerisation of *o*-quinol *1a* is completely analogous to that of spirooxirane *4a* with regard to both regiospecificity and stereospecificity.

Treatment of *8* with chromic acid in the presence of manganese(II) nitrate [10] resulted in rapid cleavage of the 1,2-diol groups to give the dicarboxylic acid *9*. The ease with which this cleavage takes place tends to indicate *cis* configuration for both 1,2-diol groups (*cf.* Ref. 11).

It was further of interest to examine whether the similarity in structural and steric characteristics thus established for the pair *5a* and *2a* is true also for other pairs of the two kinds

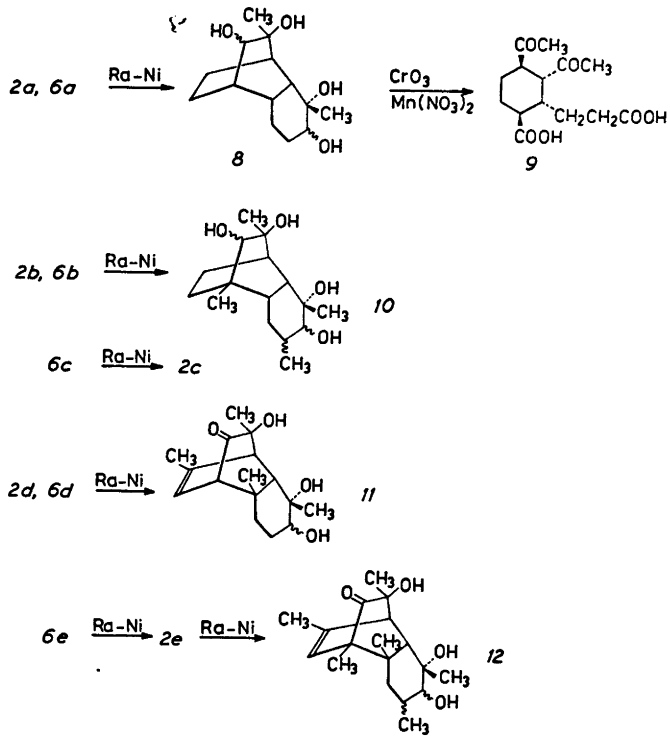


Chart 3.

of dimers. The bis(bromohydrins) (*6b – 6e*) obtained from the methyl-substituted dimers *5b – 5e* as well as the corresponding *o*-quinol dimers (*2b – 2e*) were therefore treated with Raney nickel (Chart 3).

The bis(spirooxiranes) *5b – 5d* were prepared by periodate oxidation of the *o*-hydroxybenzyl alcohols *3b – 3d*, again only one isomer being obtained from each of the alcohols. Treatment of the dimers *5b – 5d* with hydrogen bromide provided the bis(bromohydrins) *6b – 6d*, which, when treated with methanolic potassium hydroxide, regenerated the bis(spirooxiranes) *5b – 5d*. Dimer *5e* and its bis(bromohydrin) *6e* have been described earlier.[8] The *o*-quinol dimers *2b*, *2d*, and *2e*, which are formed on periodate oxidation of 2,6-dimethyl-, 2,4-dimethyl-, and 2,4,6-trimethylphenol *via* the short-lived *o*-quinols *1b*, *1d*, and *1e*, respectively, have also been reported.[2,3] Dimer *2c* has now been prepared similarly from 2,5-dimethylphenol.

Whereas the periodate oxidation of 2,6- and 2,4-dimethylphenol as well as of 2,4,6-trimethylphenol is rapid, the phenols being consumed within a few minutes and the corresponding dimers being obtained in fair yields, 2,5-dimethylphenol reacts sluggishly, unconsumed phenol still being found after 1 h. In addition to the expected dimer *2c* (see Exptl.), the reaction mixture contained substantial amounts of 2,5-dimethyl-1,4-benzoquinone as well as a monocarboxylic acid formed from *2c* by ketol cleavage, as will be further described in a following paper.

Since periodate consumption by *o*-cresol is still slower than by 2,5-dimethylphenol, periodate oxidation of the former phenol cannot be used for the preparation of dimer *2a*, which, however, is available *via* the *o*-quinol acetate (*1a*, OAc instead of OH).[5]

Raney nickel reduction of bis(bromohydrins) *6b – 6e* revealed that these compounds and, consequently, the bis(spirooxiranes) *5b – 5e* as well have the same structural and steric arrangements as the corresponding *o*-quinol dimers *2b – 2e*. Thus, bis(bromohydrin) *6b* as well as *o*-quinol dimer *2b* gave the octahydro derivative *10* of dimer *2b*. Product *10* was obtained in fair yields, indicating high stereoselectivity of the Raney nickel reduction.

From the reaction mixture obtained on Raney

nickel reduction of *6c*, the corresponding *o*-quinol dimer *2c* could be isolated and, similarly, *6e* was reduced to *2e*. In the last-mentioned case, prolonged reduction converted both *6e* and *2e* into the partially hydrogenated *o*-quinol dimer *12*. Finally, a similarly hydrogenated *o*-quinol dimer (*11*) was obtained from both bis(bromohydrin) *6d* and *o*-quinol dimer *2d*.

It is noteworthy that hydrogenation of *o*-quinol dimer *2e* in acetic acid, using PtO_2 as catalyst (3 atm, 48 h), yielded a tetrahydro compound, m.p. 213 – 214°,[13] not identical with *12*, m.p. 240 – 242°, obtained with Raney nickel. The UV spectra (ethanol) of these compounds indicate that the homoconjugated carbonyl system is intact in both cases. The spectra exhibit the expected transannular charge transfer bands at 205 nm (log $\varepsilon = 3.61$) and 208 nm (log $\varepsilon = 3.65$), respectively, and enhanced $n \rightarrow \pi^*$ absorptions at 310 nm (log $\varepsilon = 2.25$) and 308 nm (log $\varepsilon = 2.35$), respectively. Apparently, the two compounds are stereoisomers arising by hydrogenation of the α,β-conjugated carbonyl system of *2e*. This indicates different stereochemical selectivity of the two hydrogenation systems used.

From the results of reduction summarized in Chart 3 it can be concluded that the dimerisation of *o*-quinols *1a – 1e* involves the same structural and steric orientation as the dimerisation of the correspondingly substituted spiro(oxirane-2,4-cyclohexadienones) *4a – 4e*. However, since only the structure of dimer *5a* was completely known,[8,9] the reduction experiments only established the complete structure of *o*-quinol dimer *2a* (structural orientation as in formula *2a* rather than *2a'*, *endo* configuration and steric arrangements at C-5 and C-9 as shown by formula *2a*).

Further experimental data are now available which indicate that the structures of *o*-quinol dimers *2b – 2e* as well as those of the bis(spirooxiranes) *5b – 5e* are analogous to those of *2a* and *5a*, respectively.

NMR spectra of dimers *2d* and *2e* clearly show the presence of the vicinal hydrogen atoms at positions 4 and 4a. In the NMR spectrum (DMSO-d_6) of *2d* H-4 gives rise to a triplet at δ 2.96, whereas the signal for H-4a is a doublet at δ 2.72 ($J_{4,4a} = J_{4,2} = 2.2$ Hz). Similarly, the NMR spectrum ($CDCl_3 + D_2O$) of *2e* shows H-4 as a triplet at δ 3.15 and H-4a as a doublet at δ 2.84 ($J_{4,4a} = J_{4,2} = 2.0$ Hz). This proves the structural orientation of dimers *2d* and *2e* to be of type *2a* rather than *2a'*. The same orientation then must be true for the bis(spirooxiranes) *5d* and *5e*, and has already been proven for the last-mentioned dimer by similar NMR analysis.[8] Furthermore, Becker [14] concluded from the photochemically induced intramolecular cycloaddition of *o*-quinol dimers *2b*, *2d*, and *2e* (*cf.* also Ref. 15) that these dimers had *endo* configuration and a structural orientation analogous to *2a*. Finally, recent X-ray crystallographic analysis completely established the structures of *o*-quinol dimers *2b* and *2d*,[16] revealing that the steric orientations at C-5 and C-9 in these two dimers are the same as found for dimers *2a* (Ref. 1 and present paper) and *5a*.[9] The correlations between the *o*-quinol dimers and the bis(spirooxiranes) reported above then imply that the complete structures of bis(spirooxiranes) *5b* and *5d* are as depicted in Chart 2.

Experimental proof is still lacking for the structures of *o*-quinol dimer *2c* and its bis(spirooxirane) counterpart *5c* as well as for the steric arrangements at carbon atoms 5 and 9 of the dimer pair *2e* and *5e*. It seems justified, however, to assume that the structural features of these dimers are analogous to those discussed above. Chemical evidence for the stereochemistry at C-5 and C-9 of the *o*-quinol dimers will be given in a forthcoming paper.

It is likely that the structural and steric specificity found in the dimerisation of *o*-quinols and spiro(oxirane-2,4-cyclohexadienones) is valid for the dimerisation of other 2,4-cyclohexadienones as well. On the basis of dipole moment measurements, the dimer of 2,6,6-trimethyl-2,4-cyclohexadienone [17] has been assigned the *endo* form as well as a structural orientation corresponding to that of the dimers discussed in the present paper. Furthermore, chemical and spectroscopic data indicated that the steric arrangement at C-5 of the dimers *2f* and *2g* of the fluorinated [18] and chlorinated [19] 2,4-cyclohexadienones *1f* and *1g* is analogous to that found in dimers *2a* and *5a* as well as in the pairs *2b*, *5b* and *2d*, *5d*.

To summarize, it can be concluded that the rapid Diels-Alder dimerisation of *o*-quinols *1a – e* as well as that of the spiro(oxirane-2,4-cyclohexadienones) *4a – e:*

(*a*) follows the *endo* rule,

(*b*) is stereospecific, the CH_3 groups at C-5 and C-9 of dimers *2a – e* as well as the CH_3

groups of the oxirane rings in dimers *5a–e* being oriented away from the reaction center, which indicates steric approach control,[20] and

(c) is regiospecific, the diene and the dienophile moieties being oriented to each other as illustrated by formula *2a* rather than *2a'*.

The factors responsible for the regiospecificity of Diels-Alder reactions involving unsymmetrical dienes and dienophiles so far are not well understood (for reviews, see Refs. 21–25). Neither steric interactions nor polar factors have been found to be of decisive importance. Although Diels-Alder reactions now are generally considered to be concerted $4\pi+2\pi$ cycloadditions, it has been pointed out that the preferred structural orientation is "consistent with reaction through the transition state in which build up of diradical character is best accomodated".[25] It is easily seen that diradicals which, in a formal sense, could be regarded as intermediates in the formation of 2,4-cyclohexadienone dimers of type *2a* are favoured, by greater resonance stabilisation, over those which would lead to the isomers of type *2a'*.

The view that Diels-Alder reactions may involve a diradical-like transition state has found support in a very recent theoretical study on the regioselectivity of concerted cycloadditions.[26]

EXPERIMENTAL

Ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer; IR and NMR spectra were obtained using Beckman 9A and Varian A-60 instruments, respectively. Chemical shifts are given in δ(ppm) units, TMS being used as internal standard. Melting points are uncorrected.

o-*Quinol dimers 2a, 2b, 2d,* and *2e* were prepared according to Refs. 5, 3, 2, and 3, respectively, and *bis(bromohydrins) 6a* and *6e* were obtained according to Ref. 8.

1,4a,5,8a-Tetrahydro-5,9-dihydroxy-2,5,8,9-tetramethyl-1,4-ethanonaphthalene-6,10(4H)-dione (2c).*,** A solution of sodium metaperiodate (54 g, 0.25 mol) in water (1.1 l) was added to a solution of 2,5-dimethylphenol (13.2 g, 0.10 mol) in water (3.3 l). After 1 h, unconsumed periodate was destroyed by addition of ethylene glycol (10 g), a small amount of amorphous material was filtered off and the solution was extracted with six 250 ml portions of methylene chloride. The dried extract on evaporation under vacuum left a deep red semi-solid residue. The solution of the latter in ethanol was treated with sulphur dioxide, and, after addition of sodium bisulfite, was concentrated under vacuum, water being added repeatedly. The aqueous mixture containing a crystalline deposit was made alkaline by addition of sodium bicarbonate and extracted with methylene chloride. Undissolved crystalline material was collected and identified as *2,5-dimethylhydroquinone*, m.p. 210°; yield, 13 %. The extract, after washing with aqueous bicarbonate and water, drying and evaporation, gave an oil, from which on treatment with ether (5 ml) almost colourless crystals of *2c* deposited (yield, 12 %). After recrystallisation from ethanol, m.p. 200–201°. (Found C 69.39; H 7.53. Calc. for $C_{16}H_{20}O_4$: C 69.54; H 7.30.) IR (KBr): ν_{max} (cm^{-1}) 1660 (conj. CO), 1725 (CO), 3450 (OH). UV (abs. ethanol), λ_{max} (nm) and log ε values: 210, 3.93 (charge transfer band, homoconjugated CO system); 233, 3.98 (conj. CO); 305, 2.45 (homoconj. and conj. CO). NMR (DMSO-d_6): δ 1.10 and 1.18 (singlets, 3 H each, 2 CH_3), 1.53 and 1.95 (doublets, 3 H each, 2 olefinic CH_3); 2.80–3.35 (4 H, 4 CH), 4.76 and 5.45 (singlets, 1 H each, 2 OH), 5.60–6.00 (2 H, 2 olefinic H).

If the deep red semi-solid residue obtained above before the SO_2 treatment was extracted with hot benzene, the extract gave *2,5-dimethyl-1,4-benzoquinone*, m.p. 122°.

Diacetate of 2c. From *2c* by treatment with the $Ac_2O/HClO_4$ reagent according to Ref. 28. M.p. 190–191° after recrystallisation from ethanol. (Found: C 66.84; H 6.58; CH_3CO 23.10. Calc. for $C_{20}H_{24}O_6$: C 66.65; H 6.71; CH_3CO 23.89.)

o-*Hydroxybenzyl alcohols* 3b, 3c, *and* 3d. 2-Hydroxy-3-methylbenzyl alcohol (*3b*) and 2-hydroxy-5-methylbenzyl alcohol (*3d*) were prepared from the corresponding methylphenol, trioxane and boric oxide (B_2O_3) according to Ref. 12, whereas a slight modification of the method described there was used for 2-hydroxy-4-methylbenzyl alcohol (*3c*). The orthoborate obtained in 50 % yield from *m*-cresol (27 g), boric oxide (8.75 g) and trioxane (7.5 g) was collected and added to a stirred mixture of toluene (50 ml) and ice water (50 ml), and the mixture was made alkaline by addition of 18 g of a 30 % aqueous sodium hydroxide solution. The aqueous phase was washed with diisopropyl ether, then was made slightly acidic with aqueous H_2SO_4 and extracted with ether. The extract yielded a crystalline product (yield, 30 %), which was recrystallised from chloroform and from benzene. M.p. 107–108° (Lit.[27] m.p. 111°).

Dimeric spiro(oxirane-2,4-cyclohexadienones) 5b, 5c, *and* 5d. A solution of sodium metaperiodate (11.75 g, 0.055 mol) in water (250 ml)

* Nomenclature according to *Chem. Abstr. 76* (1972) 1445 CS.

** Preparation based on experiments carried out by Dr. Britt Berggren and tekn.lic. Ingrid Jansson.

was added to a solution of the *o*-hydroxybenzyl alcohol (*3b*, *3c*, and *3d*, respectively, 6.90 g, 0.050 mol) in water (700 ml). The mixture was kept in the refrigerator for 24 h. The almost colourless precipitate formed was recrystallised from chloroform.

1',4',4'a,8'a-Tetrahydro-1',7'-dimethyl-dispiro-[oxirane-2,5'(6'H)-[1,4]ethanonaphthalene-9',2''-oxirane]-6',10'-dione (5b).* From *3b* and periodate. Yield of crude product, 74 %. M.p. 206 – 207°. (Found: C 70.61; H 5.92. Calc. for $C_{16}H_{16}O_4$: C 70.57; H 5.92.) IR (KBr): ν_{max} (cm^{-1}) 1696 (conj. CO), 1731 (CO), 3076 (oxirane-CH_2). NMR (DMSO-d_6): δ 1.35 (s, 3 H, CH_3), 1.76 (t, 3 H, olefinic CH_3), 2.40 – 3.20 (7 H, 2 CH_2 and 3 CH), 5.80 and 6.48 (doublets, 1 H each, 2 olefinic H), 6.66 (m, 1 H, olefinic H).

1',4',4'a,8'a-Tetrahydro-2',8'-dimethyl-dispiro-[oxirane-2,5'(6'H)-[1,4]ethanonaphthalene-9',2''-oxirane]-6',10'-dione (5c). From *3c* and periodate. Yield of crude product, 71 %. M.p. 222.5 – 223.5°. (Found: C 70.42; H 5.99. Calc. for $C_{16}H_{16}O_4$: C 70.57; H 5.92.) IR (KBr): ν_{max} (cm^{-1}) 1698 (conj. CO), 1731 (CO), 3048 (oxirane-CH_2). NMR (DMSO-d_6): δ 1.71 and 2.09 (doublets, 3 H each, 2 olefinic CH_3), 2.71 and 2.93 (doublets, 1 H each, AB system with $J = 6.8$ Hz, oxirane-CH_2), 3.02 (broadened singlet, 2 H, oxirane-CH_2), 3.52 (broad, 2 H, 2 CH), 6.01 – 6.27 (2 H, olefinic H). Signals arising from 2 H are partially hidden by the signal due to incompletely deuterated DMSO.

1',4',4'a,8'a-Tetrahydro-3',8'a-dimethyl-dispiro[oxirane-2,5'(6'H)-[1,4] ethanonaphthalene-9',2''-oxirane]-6',10'-dione (5d). From *3d* and periodate. Yield of crude product, 87 %. M.p. 217.5 – 218.5°. (Found: C 70.44; H 5.98. Calc. for $C_{16}H_{16}O_4$: C 70.57; H 5.92.) IR (KBr): ν_{max} (cm^{-1}) 1698 (conj. CO), 1727 (CO), 3056 (oxirane-CH_2). NMR (DMSO-d_6): δ 1.34 (s, 3 H, CH_3), 1.80 (d, 3 H, olefinic CH_3), 2.23 (d, 1 H, CH), 2.74 and 3.00 (doublets, 1 H each, AB system with $J = 6.5$ Hz, oxirane-CH_2), 2.99 and 3.18 (doublets, 1 H each, AB system with $J = 6.2$ Hz, oxirane-CH_2), 5.78 (m, 1 H, H-2'), 6.09 and 6.60 (doublets, 1 H each, H-7' and H-8', $J = 10$ Hz). Signals from 2 H are hidden by the signal for incompletely deuterated DMSO.

Bis(bromohydrins) 6b, 6c *and* 6d. Aqueous hydrobromic acid (7.40 g of 66 % HBr solution, 0.060 mol HBr) was added dropwise to a solution of bis(spirooxirane) (*5b*, *5c*, and *5d*, respectively, 6.80 g, 0.025 mol) in dioxane (750 ml). After 8 h at room temperature the solution was brought to dryness under vacuum.

5,9-Bis(bromomethyl)-1,4a,5,8a-tetrahydro-5,9-dihydroxy-1,7-dimethyl-1,4-ethanonaphthalene-6,10(4H)-dione (6b). From *5b* and HBr. The solid residue obtained gave colourless crystals (64 %) from ethanol, m.p. 185.5 – 186.5°. (Found: C 44.47; H 4.11; Br 36.43. Calc. for $C_{16}H_{16}O_4Br_2$: C 44.27; H 4.18; Br 36.81.) IR (KBr): ν_{max} (cm^{-1}) 1688 (conj. CO), 1713 (CO), 3439 and 3483 (OH). NMR (DMSO-d_6): δ 1.26 (s, 3 H, CH_3), 1.78 (broadened singlet, 3 H, olefinic CH_3), 2.70 – 3.80 (7 H, 2 CH_2 and 3 CH), 5.37 and 6.20 (singlets, 1 H each, 2 OH), 5.62 (dd, 1 H, olefinic H), 6.14 (d, 1 H, olefinic H), 6.40 (m, 1 H, olefinic H).

5,9-Bis(bromomethyl)-1,4a,5,8a-tetrahydro-5,9-dihydroxy-2,8-dimethyl-1,4-ethanonaphthalene-6,10(4H)-dione (6c). From *5c* and HBr. The acetone solution of the light yellow oily residue was concentrated to a volume of 15 ml. The crystalline product deposited (63 %), after recrystallisation from benzene and from acetone, had m.p. 174 – 175° and contained 1 mol of acetone per mol. (Found: C 46.01; H 4.79; Br 32.71. Calc. for $C_{16}H_{16}O_4Br_2.C_3H_6O$: C 46.36; H 4.97; Br 32.47.) IR (KBr): ν_{max} (cm^{-1}) 1698 (conj. CO), 1719 (CO), 3440 (OH). NMR (DMSO-d_6): δ 1.58 (d, 3 H, olefinic CH_3), 1.98 (broadened singlet, 3 H, olefinic CH_3), 2.09 (s, 6 H, acetone), 2.87 – 3.70 (8 H, 2 CH_2 and 4 CH), 5.18 and 6.17 (singlets, 1 H each, 2 OH), 5.80 (broadened doublet, 1 H, olefinic H), 5.98 (broadened singlet, 1 H, olefinic H).

5,9-Bis(bromomethyl)-1,4a,5,8a-tetrahydro-5,9-dihydroxy-3,8a-dimethyl-1,4-ethanonaphthalene-6,10(4H)-dione (6d). From *5d* and HBr. The solid residue was recrystallised from ethanol to give *6d* (88 %), m.p. 211 – 212°. (Found: C 44.56; H 4.25; Br 36.54. Calc. for $C_{16}H_{16}O_4Br_2$: C 44.27; H 4.18; Br 36.81.) IR (KBr): ν_{max} (cm^{-1}) 1673 (conj. CO), 1730 (CO), 3394 and 3482 (OH). NMR (DMSO-d_6): δ 1.37 (s, 3 H, CH_3), 1.73 (d, 3 H, olefinic CH_3), 2.84 and 2.92 (doublets, 1 H each, 2 CH), 3.33 (t, 1 H, CH), 3.34 and 3.57 (doublets, 1 H each, AB system with $J = 11$ Hz, CH_2), 3.65 (s, 2 H, CH_2), 5.36 and 6.24 (singlets, 1 H each, 2 OH), 5.55 (d, further split by allylic coupling, 1 H, H-2), 6.05 and 6.40 (doublets, 1 H each, H-7 and H-8, $J = 10$ Hz).

The bis(bromohydrins) *6b* – *6d* on treatment with a 2.4-fold excess of 0.1 M methanolic KOH during 10 min regenerated the corresponding bis(spirooxiranes) *5b* – *5d* (yields, 70 – 90 %), identified by m.p., mixed m.p. and IR spectra.

Diacetates 7b, *7c* and *7d* were obtained by dissolving the bis(bromohydrins) (*6b*, *6c*, and *6d*, respectively, in the EtOAc-Ac_2O-$HClO_4$ reagent [28] and working up the reaction mixture after 15 min. Recrystallisation from ethanol gave colourless products.

Diacetate 7b. From *6b* (68 %), m.p. 165 – 166°. (Found: C 46.34; H 4.36; Br 31.41. Calc. for $C_{20}H_{22}O_6Br_2$: C 46.35; H 4.28; Br 30.84.) IR (KBr): ν_{max} (cm^{-1}) 1653 (C=C), 1709 (conj. CO), 1741 – 1750 (CO and ester-CO).

Diacetate 7 c. From *6c* (70 %), m.p. 156 – 157°. (Found: C 46.53; H 4.33; Br 30.05. Calc. for $C_{20}H_{22}O_6Br_2$: C 46.35; H 4.28; Br 30.84.) IR (KBr): ν_{max} (cm^{-1}) 1623 (C=C), 1700 (conj. CO), 1740 and 1756 (CO and ester-CO).

Diacetate 7 d. From *6d* (65 %), m.p. 147.5 –

* Nomenclature according to *Chem. Abstr. 76* (1972) 1319 CS.

148.5°. (Found: C 46.44; H 4.35; Br 30.89. Calc. for $C_{20}H_{22}O_6Br_2$: C 46.35; H 4.28; Br 30.84.) IR (KBr): ν_{max} (cm^{-1}) 1630 (C=C), 1718 (conj. CO), 1738 and 1759 (CO and ester-CO).

Reductions with Raney nickel

Perhydro-2,3,5,6-tetrahydroxy-3,5-dimethyl-1,4-ethanonaphthalene (8). *(a) From bis(bromohydrin)* 6a. The stirred solution of *6a* containing 0.5 mol of dioxane per mol (1.015 g) in 95 % ethanol (125 ml) was refluxed for 5 h with Ra-Ni "W-6"[29] (10 g) and then filtered through celite and evaporated to dryness under vacuum. The solid residue was treated with boiling acetone (30 ml), which dissolved the major part of the product. The hot solution was filtered and, on cooling, gave colourless crystals (yield, 6 %), m.p. 251 – 252°, which rose to 253 – 254° on recrystallisation from methanol-acetone. (Found: *M*, by mass spectrometry, 256.1689. Calc. for $C_{14}H_{24}O_4$: *M*, 256.1674.) IR (KBr) ν_{max} (cm^{-1}) 3400 and 3450 (broad, OH), The NMR spectrum (CD_3OD) shows two singlets at δ 1.26 and 1.33 (3 H each, 2 CH_3) and signals between δ 1.40 and 3.67 (14 H, 6 CH and 4 CH_2). There were no signals due to olefinic protons.

(b) From o-*quinol dimer* 2a. The procedure was similar to that described under (a). From the cooled acetone solution a crude crystalline product of m.p. 210 – 215° (15 %) was obtained. Two recrystallisations from methanol-acetone gave pure *8*, m.p. 252 – 253°, identical with the product obtained according to (a) by mixed m.p., IR, NMR, and mass spectra.

2,3-Diacetyl-6-carboxycyclohexanepropanoic acid (9). To the solution of compound *8* (484 mg) in a mixture of acetic acid (7 ml), water (0.75 ml) and 1.5 ml of an aqueous solution of manganese(II) nitrate (500 g $Mn(NO_3)_2$/l), after cooling to 10°, a solution of chromic acid (0.8 g of CrO_3 in 2.3 ml of water) was added in portions during a period of 3 min. The solution was again cooled to 10° and conc. H_2SO_4 (0.45 ml) was added during 1 min. The reaction mixture was kept at 30° for 8 min and after addition of water (30 ml in portions) neutralised with aqueous bicarbonate and finally extracted with ethyl acetate. The extract gave a yellow oil which on treatment with a small amount of ether provided crystals, m.p. 179 – 180° (yield, 54 %) after recrystallisation from acetone. (Found: *M*, by mass spectrometry, 284.1274. Calc. for $C_{14}H_{20}O_6$: *M*, 284.1260.) IR (KBr): ν_{max} (cm^{-1}) 1702 and 1742 (CO and COOH), 2400 – 3600 (COOH). The NMR spectrum (DMSO-d_6) shows 2 singlets at δ 2.10 and 2.12, due to 2 CH_3CO.

Perhydro-2,3,5,6-tetrahydroxy-1,3,5,7-tetramethyl-1,4-ethanonaphthalene (10). *(a) From bis(bromohydrin)* 6b. The stirred solution of *6b* (1.085 g) in 95 % ethanol (110 ml) was refluxed for 7 h with Ra-Ni (19 g). Removal of the solvent from the filtered solution gave a semi-solid product, which was extracted with boiling acetone (30 ml). After cooling to 0° the mixture was filtered and the filtrate concentrated to a volume of 10 ml. Addition of hexane until beginning precipitation, followed by cooling in the refrigerator, provided *10* (25 %), m.p. 199 – 200° after recrystallisation from acetone. (Found: C 67.33; H 9.91. Calc. for $C_{16}H_{28}O_4$: C 67.57; H 9.92.) IR (KBr): ν_{max} (cm^{-1}) 3275, 3370, 3412, 3494 and 3519 (OH). The NMR spectrum (DMSO-d_6) indicates the presence of 4 OH (δ 3.51, 3.92, 4.14 and 4.22) and shows no absorption due to olefinic H.

(b) From o-*quinol dimer* 2b. Treatment of *2b* (1.90 g) with Ra-Ni (15 g) in ethanol (2.5 h reflux) and work-up as above. The semi-solid residue after treatment with 25 ml of a chloroform-hexane mixture (2:1) gave crystals of *10* (48 %), m.p. 200 – 201° after recrystallisation from ethyl acetate and from acetone. Identical with the product obtained according to (a) by mixed m.p., IR and NMR spectra.

o-*Quinol dimer* 2c *from bis(bromohydrin)* 6c. The stirred solution of *6c* (2.17 g) in 95 % ethanol (130 ml) was refluxed with Ra-Ni (6 g) for 1.5 h. The filtered solution on evaporation gave a light yellow oil which was chromatographed on a silica gel column using acetone-hexane (2:1) as solvent. Dimer *2c* (R_F = 0.65), m.p. 199 – 200° (from ethanol), was obtained in 15 % yield and shown to be identical with the product prepared by periodate oxidation of 2,5-dimethylphenol (p. 469) by mixed m.p., IR and NMR spectra.

1,4,4a,5,6,7,8,8a-Octahydro-5,6,9-trihydroxy-3,5,8a,9-tetramethyl-1,4-ethanonaphthalen-10-one (11). *(a) From bis(bromohydrin)* 6d. The stirred solution of *6d* (2.17 g) in 95 % ethanol (130 ml) was refluxed for 2 h with Ra-Ni (20 g), then filtered and evaporated giving a semi-crystalline residue which on treatment with a mixture of chloroform (10 ml) and acetone (10 ml) left crystals of *11* (22 %), m.p. 240 – 241° after recrystallisation from acetone. (Found: *M*, by mass spectrometry, 280.1676. Calc. for $C_{16}H_{24}O_4$: *M*, 280.1674.) IR (KBr): ν_{max} (cm^{-1}) 1718 (CO), 3272, 3480, and 3536 (OH). NMR (DMSO-d_6): δ 1.11 (s, 6 H, 2 CH_3), 1.18 (s, 3 H, CH_3), 1.30 – 2.10 (4 H, 2 CH_2), 1.87 (d, 3 H, olefinic CH_3), 2.27, 2.32, and 3.36 (doublets, 1 H each, 3 CH), 3.62 and 5.08 (singlets, 1 H each, 2 OH), 4.52 (d, 1 H, sec. OH), 5.44 (d, further split by allylic coupling, 1 H, olefinic H). The signal for 1 CH is hidden by the signal for incompletely deuterated DMSO.

(b) From o-*quinol dimer* 2d. The stirred solution of *2d* (1.90 g) in 95 % ethanol (125 ml) was refluxed for 3 h with Ra-Ni (15 g), then filtered and evaporated to dryness. The solid residue on recrystallisation from chloroform gave *11* (39 %), m.p. 239 – 240° after further recrystallisation from acetone. The product was identical by mixed m.p., IR and NMR spectra with *11* obtained according to (a).

o-Quinol dimer 2e *from bis(bromohydrin)* 6e. Compound *6e* (1.386 g) was treated for 4 h with Ra-Ni (9 g) in refluxing 95 % ethanol (140 ml). The filtered solution was brought to dryness, leaving crude crystalline *2e*, m.p. 170 – 175° (67 %). After recrystallisation from acetone and from benzene, the product had m.p. 181 – 182° and was identical by mixed m.p., IR and NMR spectra with *2e* prepared by periodate oxidation of mesitol.

1,4,4a,5,6,7,8,8a-Octahydro-5,6,9-trihydroxy-1,3,5,7,8a,9-hexamethyl-1,4-ethanonaphthalen-10-one (12). *o*-Quinol dimer *2e* (912 mg) was treated for 5 h with Ra-Ni (18 g) in refluxing 95 % ethanol. The filtered solution was concentrated under vacuum to a volume of 10 ml. After 2 h at 0° the crystalline product deposited was collected and recrystallised from 95 % ethanol, m.p. 240 – 242° (35 %). (Found: *M*, by mass spectrometry, 308.1996. Calc. for $C_{18}H_{28}O_4$: *M*, 308.1987) IR (KBr): ν_{max} (cm^{-1}) 1710 (CO), 3270, 3530 (OH). NMR (DMSO-d_6): δ 0.92 (s, 6 H, 2 CH_3), 1.05, 1.13, and 1.26 (singlets, 3 H each, 3 CH_3), 1.89 (d, 3 H, olefinic CH_3), 1.60 – 3.52 (partly overlapped by H_2O signal, 6 H, CH_2 and 4 CH), 3.60 (s, 1 H, OH), 4.58 (d, 1 H, *sec.* OH), 5.09 (broad singlet, 2 H, OH and olefinic H). UV data, see p. 468.

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