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# Periodate Oxidation of Phenols. XIV.* Oxidation of *p*-Hydroxybenzyl Alcohol with Periodate and Bismuthate

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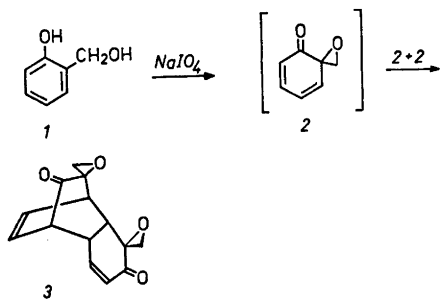
Treatment of *p*-hydroxybenzyl alcohol with sodium metaperiodate in acetic acid-water gives, in addition to amorphous material, *p*-benzoquinone (23 %) and *p*-hydroxybenzaldehyde (4 %). If sodium bismuthate is used as oxidant, the yield of *p*-benzoquinone is only 5 % and a new product, 1-oxaspiro[2.5]octa-4,7-dien-6-one (*5*), is formed in a yield of 20 %.

It was observed several years ago that *p*-hydroxybenzyl alcohols on treatment with aqueous sodium metaperiodate give formaldehyde and the corresponding *p*-benzoquinone.[1] *o*-Hydroxybenzyl alcohols were later found to react with the same oxidant to give the Diels-Alder *endo* dimers of the initially formed spiro(oxirane-2,4-cyclohexadienones).[2,3] For instance, periodate oxidation of salicyl alcohol (*1*) (Scheme 1) afforded a dimer (*3*) of the intermediary 2,4-cyclohexadienone *2* in a yield of 74 %, with only 1 % of salicyl aldehyde being formed simultaneously.[2] Similar oxidation of *o*-hydroxybenzyl alcohols carrying at least one bulky ring substituent gave the corresponding monomeric spiro compounds which, due to steric hindrance, did not dimerize.[4]

The primary aim of the present study was to find conditions under which oxidation of *p*-hydroxybenzyl alcohols leads to the formation of spiro(oxirane-2,5-cyclohexadienones) rather than to the oxidative cleavage to the corresponding *p*-benzoquinone and formaldehyde. It has been possible to perform the first-mentioned reaction with 4-hydroxybenzyl alcohol.




*Scheme 1.*

From the reaction mixture obtained on treatment of 4-hydroxybenzyl alcohol (*4*) for 30 min with a solution of sodium metaperiodate in acetic acid-water (4:1) only *p*-benzoquinone (yield, 23 %) and *p*-hydroxybenzaldehyde (yield, 4 %) could be isolated. A similar experiment with sodium bismuthate as oxidant gave, in addition to minor amounts of *p*-benzoquinone (5 %) and *p*-hydroxybenzaldehyde (2 %), 20 % of a product $C_7H_6O_2$ (m.p. 51 – 52 °C) which was the desired spiro compound *5*. Its structural assignment is based on the chemical behaviour and the spectral properties described below.

In the reaction mixtures obtained in the periodate and bismuthate oxidation experiments no unreacted 4-hydroxybenzyl alcohol could be detected. The major part of the starting material had been converted into a dark-coloured product which was strongly adsorbed on the silica gel column used in the separation of the reaction products. If the oxidation with periodate was carried out in water or in a 10 %, rather than the above-mentioned 80 %, aqueous acetic acid solution, a dark-brown amorphous material deposited. It is most probable that the

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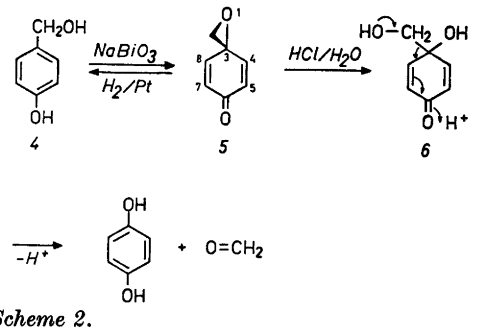
formation of this material is mainly due to *ortho* oxidation of *4*, the resulting *o*-quinone alcohol being unstable under the conditions used, as shown in separate studies.[5] It has been reported earlier that periodate oxidation of 2,4-dimethylphenol, possessing a free *ortho* position, gives 3,5-dimethyl-1,2-benzoquinone [6] among other products.

Catalytic hydrogenation of *5* regenerated 4-hydroxybenzyl alcohol, as could be expected from the similar behaviour of spiro(oxirane-2,5-cyclohexadienones) carrying substituents in the six-membered ring.[7] Dilute aqueous hydrochloric acid caused rapid degradation of *5* to give formaldehyde and hydroquinone. It is assumed that, in this reaction, hydrolysis first gives the *p*-quinol *6* which in a rapid (proton-catalyzed) retro aldol condensation loses its hydroxymethyl group as formaldehyde, concomitant aromatization constituting a driving force (Scheme 2).

Similar loss of a 4-carbinol substituent takes place in 2,5-cyclohexadienone intermediates arising in certain modes of radical coupling involved in the biosynthesis of lignin,[8,9] in the oxidative degradation of *p*-hydroxybenzyl alcohols with dipotassium nitrosodisulfonate,[10] in the formation of oligomers of the polyphenylene oxide type from 3,5-disubstituted 4-hydroxybenzyl alcohols,[11,12] and in the colour reaction of 4-hydroxybenzyl alcohols with *N*-chloroquinone imide.[13]

The 60 MHz NMR spectrum of compound *5* in $CDCl_3$ exhibited two signals at $\delta$ 3.36 and 6.49, the ratio of their integrals being 1:2. The former signal can be ascribed to the protons of the oxirane ring. Since the plane of this ring is perpendicular to that of the dienone ring, the two oxirane protons are equivalent and the same is true for the vinyl protons H-4, H-8 and H-5, H-7, respectively. By a fortuitous shift coincidence the two last-mentioned pairs of protons give rise to a single signal.



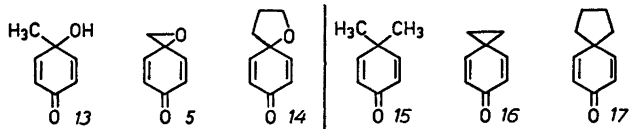

*Scheme 2.*

The presence of a group of three peaks at 1665, 1635, and 1622 $cm^{-1}$ in the IR spectrum of *5*, arising from the cross-conjugated carbonyl system is in accord with IR spectroscopic characteristics of other 2,5-cyclohexadienones. It may be noted, however, that in the spectrum of *5* these three bands are of high intensity, whereas in the spectra of previously investigated 2,5-cyclohexadienones the band of lowest frequency generally was rather weak.[14,15] A peak of medium strength at 3060 $cm^{-1}$ can be attributed to the $CH_2$ group of the oxirane ring.[16]

In the UV spectrum of *5* (in ethanol), the maximum of the $\pi \rightarrow \pi^*$ absorption was found at $\lambda$ 250 nm ($\log \varepsilon = 4.24$) and that of the $n \rightarrow \pi^*$ band at $\lambda$ 336 nm ($\log \varepsilon = 1.47$). As can be seen from Table 1, the former maximum is located at a considerably higher wavelength than the corresponding maxima of *p*-toluquinol (*13*) [17] and of the spiro(oxolane-2,5-cyclohexadienone) *14*,[18] the positions of the two latter maxima being in accord with that calculated for a $\beta$-substituted enone system (227 nm). The deviation from the Woodward rules found for *5* seems to be due to a conjugative effect of the oxirane ring.

For comparison, Table 1 also includes the $\lambda_{max}$ value of the spiro(cyclopropane-2,5-cyclohexadienone) *16*,[20] as well as those of the dimethyl dienone *15* and the spiro compound *17*.[19] The absorption maximum of *16* is found at a wavelength still higher than that of its oxa analogue *5*. It may further be noted that compound *17* absorbs at a higher wavelength than its oxa analogue *14* and the monocyclic compounds *13* and *15*.

As mentioned above, compound *5* is obtained on oxidation of *4* with bismuthate but seems not to be formed when periodate is used as oxidant. This is remarkable, since the two oxidants are generally considered equivalent as glycol-cleaving agents [21] and have been shown to act similarly in the oxidation of guaiacol to *o*-benzoquinone and methanol.[22] An attempt to rationalize the different action of bismuthate and periodate in the present case has been made in Scheme 3. The oxidation of *4* is believed to be initiated by nucleophilic attack by the phenolic



| | 13 | 5 | 14 | 15 | 16 | 17 |
|---|---|---|---|---|---|---|
| $\lambda_{max}$, nm | 227 | 250 | 228 | 227 | 274 | 242 |
| log ε | 4.25 | 4.24 | 4.08 | 4.1 | 4.34 | 4.20 |

*Table 1.* Ultraviolet maxima ($\pi \rightarrow \pi^*$ bands) of some 2,5-cyclohexadienones. Solvents: Ethanol for *13*,[17] *5*, *14* [18] and *17* [19]; methanol for *16* [20]. The $\lambda_{max}$ value of *15* has been calculated by application of Woodward's rules; the log ε value is that of the 2-methyl derivative.[20]

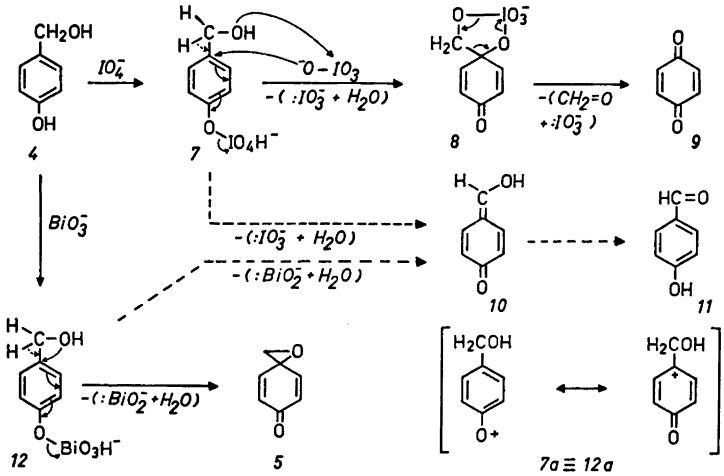
oxygen on the iodine and bismuth atoms of the oxidants, resulting in the formation of aryl esters *7* and *12*, respectively. In the bismuthate system, the formation of *5* is then assumed to proceed by a concerted reaction involving two-electron transfer to the bismuth atom with simultaneous nucleophilic attack by the alcoholic oxygen atom on the aromatic ring. In the periodate system, the oxygen of a second molecule of periodate rather than the alcoholic hydroxyl group may attack the ring, subsequent (or preceding) coordination of the latter group to the iodine atom giving intermediate *8*. This cyclic glycol periodic ester would decompose in the normal way [23] to give formaldehyde and *p*-benzoquinone (*9*).

The different behaviour of esters *7* and *12* can possibly be attributed to the fact that the concentration of bismuthate ions in 80 % acetic acid solution of *4* is low, most of the sodium bismuthate during the reaction being present as a solid, whereas the sodium periodate is completely dissolved.

The formation of small amounts of *p*-hydroxybenzaldehyde (*11*) in both systems may be understood as being due to the loss of a proton from the carbinol carbon atom in *7* and *12* giving the enol *10* which tautomerizes to *11* (see dashed line arrows in Scheme 3).

Instead of the one-step concerted reactions indicated in formulae *7* and *12*, one may as well assume two-step reactions, involving, in a first step, two-electron transfer to the periodate and bismuthate residue with formation of a resonance-stabilized phenoxonium ion (*7a*≡ *12a*), the latter reacting further to give the postulated intermediates *8* and *10*, as well as product *5*.

*p*-Benzoquinone (*9*) is also formed in the bismuthate oxidation system, although in considerably smaller amounts than in the periodate system, the yields obtained after a reaction time of 30 min being 5 and 23 %, respectively (*cf.* p. 883). Prolonged bismuthate oxidation slowly increased the yield of *9*, whereas the yield of *5* decreased, the total of *9* and *5* remain-



*Scheme 3.*

ing approximately constant. This indicates that, in the bismuthate system, the *p*-benzoquinone is formed *via* the spiro compound *5*. In fact, treatment of *5* with bismuthate in 80 % aqueous acetic acid for 30 min gave *p*-benzoquinone in a yield of 22 %, in addition to unreacted *5* (65 %).

The possibility of *5* being an intermediate in the formation of *p*-benzoquinone in the periodate system seems to be ruled out by the fact that only 28 % of compound *5* was converted to the quinone when treated with periodate in 80 % aqueous acetic acid for 30 min.

These conversions of *5* to *p*-benzoquinone must be due to hydrolytic opening of the oxirane ring followed by loss of formaldehyde, the resulting hydroquinone (*cf.* the similar hydrolysis by aqueous HCl, Scheme 2) being dehydrogenated by the oxidant present. The hydrolysis of *5* in 80 % aqueous acetic acid, in the absence of oxidant, was followed by UV spectrometry revealing a decrease in absorbance at 250 nm ($\lambda_{max}$ of *5*) and an increase at 290 nm ($\lambda_{max}$ of hydroquinone). Expectedly, hydrolysis in this solvent was much slower than that found in aqueous hydrochloric acid (*cf.* p. 884). After 24 h treatment of *5* with 80 % acetic acid, however, hydroquinone could be isolated in a yield of 82 %.

Compound *5* proved to be stable in an aqueous solution of $NaIO_4$, but was rapidly converted to formaldehyde and *p*-benzoquinone in aqueous $H_5IO_6$, acid hydrolysis of the oxirane ring again being the initial step.

Treatment with aqueous sodium hydrogen carbonate did not appreciably affect compound *5*; however, addition of aqueous NaOH caused immediate conversion into dark brown products. At room temperature, solid *5* slowly deteriorates, whereas it can be stored essentially unchanged for several months at −20 °C.

Some compounds with the basic structure *5* carrying substituents in the dienone ring have been reported earlier. They were prepared by the action of alkali upon 2,5-cyclohexadienones with a halohydrine grouping in the 4-position [24] or by the action of diazomethane on substituted *p*-quinones.[7] A tricyclic analogue of *5* carrying the spirooxirane ring in the 10-position of anthrone has also been described.[25]

## EXPERIMENTAL

UV 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 $\delta$ (ppm) units, TMS being used as internal standard.

*Oxidation of 4-hydroxybenzyl alcohol (4) with sodium metaperiodate.* A solution of $NaIO_4$ (0.06 mol) in a mixture of 100 ml of water and 80 ml of acetic acid was added to a solution of *4* (0.03 mol) in 320 ml of acetic acid. After 30 min at room temperature ethylene glycol (5 ml) was added in order to remove excess periodate and the dark red-brown solution was extracted with three 150 ml portions of dichloromethane. The combined extracts were washed twice with aqueous hydrogen carbonate and with water and, after being dried over anhydrous $Na_2SO_4$, were brought to dryness under vacuum, leaving a brown oil. The latter was chromatographed on a silica gel column (4 × 60 cm) using benzene-ethyl acetate (4:1) as eluent. The first eluted yellow fraction gave p-*benzoquinone* ($R_F = 0.39$) in a yield of 23 %. A following fraction provided 4-*hydroxybenzaldehyde* ($R_F = 0.21$); yield, 4 %. The products were identified by m.p. and mixed m.p. with authentic samples.

*Oxidation of 4-hydroxybenzyl alcohol (4) with sodium bismuthate.* A solution of *4* (0.03 mol) in 300 ml of an acetic acid-water (4:1) mixture was stirred for 30 min at room temperature with $NaBiO_3$ (0.06 mol). Unconsumed bismuthate was filtered off and the dark brown-red filtrate worked up as described above. Elution of the silica gel column gave:

(*a*) p-*Benzoquinone* ($R_F = 0.39$) in a yield of 5 %.

(*b*) *1-Oxaspiro[2.5]octa-4,7-dien-6-one (5)*, $R_F$ = 0.33, colourless crystals of m.p. 51 – 52 °C after sublimation (40 °C, 1 mmHg); yield, 20 %. (Found: C 69.01; H 5.04. Calc. for $C_7H_6O_2$: C 68.84; H 4.95). UV, IR and NMR spectra, *cf.* p. 884.

(*c*) 4-*Hydroxybenzaldehyde* ($R_F = 0.21$); yield, 2 %.

*Catalytic hydrogenation of* 5. A solution of *5* (124 mg) in acetone (10 ml) was added to the suspension of prehydrogenated $PtO_2$ (30 mg) in acetone (5 ml). The mixture was stirred under hydrogen for 30 min after which time 1 mol of $H_2$ per mol of *5* had been consumed and further hydrogen uptake was slow. Removal of the solvent from the filtered solution and recrystallization of the crystalline residue from ether gave *4-hydroxybenzyl alcohol*, identical by m.p. and mixed m.p. with authentic material. Yield, 80 %.

*Hydrolysis of 5 with 2 M aqueous hydrochloric acid.* (a) A solution of *5* (110 mg) in 2 M aqueous HCl (25 ml) was kept at room temperature for 3 min and then extracted with three 100 ml portions of ether. The combined extracts were dried over anhydrous $Na_2SO_4$ and brought to dryness. The crystalline residue was recrystal-

lized from ether and was found to be identical to *hydroquinone* by m.p. (168–170 °C) and mixed m.p. Yield, 74 %. (b) Compound *5* (21.7 mg, 0.18 mmol) was dissolved in 2 M aqueous HCl. After 5 min, the solution was neutralized with aqueous NaOH. A 0.1 M NaOAc-HCl (2:1) buffer solution (300 ml) of pH 4.6 was added, followed by 30 ml of a saturated aqueous solution of dimedone (*cf.* Ref. 26). Filtration after 15 h gave *dimedone-formaldehyde compound*, m.p. 185–187 °C, identical by mixed m.p. with an authentic sample. Yield, 53.2 mg (100 %).

*Hydrolysis of 5 with 80 % aqueous acetic acid.* A solution of *5* (300 mg) in a 4:1 acetic acid-water mixture (50 ml) was kept at 25 °C for 24 h. The solution was then concentrated under vacuum to one third of its volume and extracted with 3 × 25 ml of chloroform. Removal of the solvent from the combined extracts gave an oily residue which crystallized on addition of a few milliliters of ether. The product after recrystallization from acetone had m.p. 170–171 °C and was identical by mixed m.p. with authentic *hydroquinone*. Yield, 82 %.

*Treatment of 5 with $NaIO_4$ and $NaBiO_3$ in 80 % aqueous acetic acid.* (a) Solutions of *5* (300 mg) in acetic acid (60 ml) and of $NaIO_4$ (920 mg) in 60 % aqueous acetic acid (60 ml) were mixed and after 30 min the mixture was extracted with chloroform (3 × 40 ml). The residue obtained on evaporation of the combined extracts was chromatographed (silica gel, benzene-ethyl acetate, 4:1) giving p-*benzoquinone* in a yield of 28 % and unreacted *5* (62 %). (b) $NaBiO_3$ (1.2 g) was added to a stirred solution of *5* (300 mg) in 80 % aqueous acetic acid (60 ml). After 30 min, the filtered solution was worked up as described under (*a*), affording p-*benzoquinone* (22 %) in addition to unreacted *5* (65 %).

*Treatment of 5 with $H_5IO_6$ in aqueous solution.* Aqueous solutions of *5* (300 mg, 15 ml) and $H_5IO_6$ (1.1 g, 80 ml) were mixed and the mixture was extracted after 17 h with 3 × 100 ml of chloroform. The combined extracts, after being dried and evaporated, gave a residue which was purified by sublimation (25 °C, 0.05 mmHg) to give p-*benzoquinone* in a yield of 85 %. In a separate experiment, formaldehyde present in the reaction mixture was converted into the dimedone compound; yield, 80 %.

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