The Oxidative Hydrolysis of Quinol Esters by Periodic Acid[1]

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Abstract: Reaction between periodic acid and *p*-quinol monoesters gives a *p*-quinone and iodate ion. The reaction rates of *p*-hydroxyphenyl acetate and benzoate are very similar, but a *t*-butyl group adjacent to the hydroxyl groups retards oxidative hydrolysis of the ester and oxidation of the quinol to similar extents. There is no evidence for formation of a periodate intermediate in high concentration, and it seems that the rate-limiting step is attack of periodate upon the hydroxyl group of the quinol ester. Both periodic acid and its monoanion are reactive species.

Periodic acid and its salts are very useful reagents for the oxidation of quinols to quinones.[2,3] Kaiser and Weidman found that the reaction of periodate with a *p*-quinol was first order with respect to each reactant, and the most reasonable mechanism involved formation of an intermediate aryl periodate which then decomposed to *p*-quinone and iodate ion.[4]

Quinol monoethers are also oxidized to quinones by periodate. (The term periodate, Per, will be applied to all species which have the same stoichiometry as HIO_4.) They are less reactive than quinols and it is the aryl oxygen bond which is broken during the reaction.[5]

Although there is kinetic, and other,[6] evidence that the oxidation of 1,2-diols occurs by formation of an intermediate, which can in favorable cases be present in high concentration, no intermediate was detected during the periodate oxidation of a *p*-quinol.[4] Therefore, either formation of the intermediate is the rate-limiting step of the reaction, or there is a preequilibrium formation of the intermediate, followed by a slow decomposition to products.

It seemed probable that periodate would react with monocarboxylic esters of *p*-quinol and oxidatively hydrolyze them to quinone and carboxylic acid, and in such a reaction either formation of an intermediate or its decomposition to products could be rate limiting.

Experimental Section

Materials. The *p*-quinols were commercial samples purified by recrystallization from hot water and had the following melting points: *p*-quinol, 172° (lit.[7] 171–172°); 2,5-di-*t*-butyl-*p*-quinol, 216–217° (lit.[8] 210–212°). Periodate solutions were analyzed in the usual way.[9] The kinetic solutions were made up with water which had been distilled and treated with ion-exchange resin and were saturated with nitrogen. Solutions were protected from light and air. Freshly made solutions were used for the kinetic runs.

p-Hydroxyphenyl acetate was prepared by acetylating *p*-quinol with acetic anhydride at 0° in aqueous sodium carbonate.[10] After complete reaction, diester was removed by filtration, and the solution extracted with ether. The ethereal solution was dried (Na_2SO_4) and evaporated. The solid was purified by extracting with hot pentane, which extracted the monoester, which was then recrystallized several times from hot water, mp 65–66° (lit.[10] 62–63°). Alternatively, the ethereal extract could be separated by Al_2O_3 chromatography and elution with ether. This ester was also prepared by controlled saponification of the diester, but the yield and purity of the sample were lower than those obtained by Olcott's method.[10] *p*-Hydroxyphenyl benzoate was prepared by benzoylating *p*-quinol with benzoyl chloride in aqueous sodium carbonate at room temperature for 1 hr with stirring.[11] The white precipitate was washed with dilute sodium carbonate and recrystallized from aqueous ethanol, mp 162–163° (lit.[11] 162–163°).

Two methods were used for the monoacetylation of *t*-butyl-*p*-quinol, with either sodium hydroxide or sodium carbonate as base. (i) *t*-Butyl-*p*-quinol (16.7 g, 0.1 mole) was dissolved in ice water (600 ml) containing NaOH (12 g), and acetic anhydride (24 ml) was added rapidly with stirring. The solution darkened and a gummy solid separated out, and was filtered off. The precipitate was extracted with *ca.* 100 ml of hot water, and a white solid, mp 110.5–111°, separated from the aqueous extract on cooling. The residue of the gummy precipitate was washed with cold pentane, the residue was reextracted with hot water, and a white solid, mp 110°, separated on cooling. The solids were combined and recrystallized twice from hot water to give 0.3 g of material, mp 111° (yield 1.5%). (ii) *t*-Butyl-*p*-quinol (16.7 g, 0.1 mole) was added to Na_2CO_3 (16 g) in ice water (500 ml), and acetic anhydride (12 ml) was added rapidly with stirring. A white solid slowly separated out and was filtered off and extracted into hot water. On cooling, the aqueous solution deposited white crystals, mp 109–111° (0.2 g), which were recrystallized twice from hot water to give 0.15 g of material, mp 111° (yield 0.7%). More solid could be obtained by concentrating the reaction solution, but it had a low melting point (89–92°) and appeared to be a mixture of the quinol and its monoacetate, and no attempt was made to isolate pure monoacetate from it.

3-*t*-Butyl-4-hydroxyphenyl acetate, mp 111°, has infrared peaks at 3460–3600 and 1720 cm^{-1} in a Nujol mull (*Anal.* Calcd: C, 69.4; H, 7.7. Found: C, 69.6; H, 7.9). The evidence for the position of the *t*-butyl group in this ester is (i) acetylation should go preferentially away from the *t*-butyl group, (ii) the rate of its hydrolysis is very similar to that of *p*-hydroxyphenyl acetate, whereas if the *t*-butyl group had been *ortho* to the acetoxy group, steric hindrance to hydrolysis (but not to oxidation) should have been observed, and (iii) in dilute solution the infrared spectrum in the OH stretching region is that expected for a phenol having a bulky group *ortho* to hydroxyl. The infrared spectra of phenols having bulky groups *ortho* to the hydroxyl group always have a small peak at a higher frequency than that of the large peak associated with the free OH group, because of restrictions to the free rotation of the OH group;[12] this small peak is otherwise absent. With 3-*t*-butyl-4-hydroxyphenyl acetate (0.003–0.004 *M*) in carbon tetrachloride (the conditions used by Goddu[12]) we observed peaks at 3478 cm^{-1}, due to

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[1] This work was supported by the National Science Foundation. This support is gratefully acknowledged.

[2] D. E. Pennington and D. M. Ritter, *J. Am. Chem. Soc.*, **68**, 1391 (1946); **69**, 187 (1947).

[3] E. Adler and S. Hemestam, *Acta Chem. Scand.*, **9**, 319 (1955).

[4] E. T. Kaiser and S. W. Weidman, *J. Am. Chem. Soc.*, **86**, 4354 (1964).

[5] E. Adler, I. Falkehag, and B. Smith, *Acta Chem. Scand.*, **16**, 529 (1962).

[6] C. A. Bunton in "Oxidation in Organic Chemistry, Part A," K. B. Wiberg, Ed., Academic Press Inc., New York, N. Y., 1965, Chapter 6.

[7] "Tables of Identification of Organic Compounds," C. D. Hodgman, Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p 53.

[8] P. F. Oesper, C. P. Smyth, and M. S. Kharasch, *J. Am. Chem. Soc.*, **64**, 937 (1942).

[9] E. L. Jackson, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p 341.

[10] H. S. Olcott, *J. Am. Chem. Soc.*, **59**, 392 (1937).

[11] O. N. Wittard and E. S. Johnson, *Ber.*, **26**, 1909 (1893).

[12] R. F. Goddu, *J. Am. Chem. Soc.*, **82**, 4533 (1960); K. U. Ingold and D. R. Taylor, *Can. J. Chem.*, **39**, 471 (1961); K. U. Ingold, *ibid.*, **40**, 111 (1962).

the hydrogen-bonded hydroxyl group, and at 3606 cm^{-1} and 3639 cm^{-1}, due to the free hydroxyl group. The intensity of the peak at 3639 cm^{-1} was approximately $^1/_{20}$ that of the peak at 3606, and their relative intensities did not depend upon concentration, whereas the relative intensity of the peak at 3478 cm^{-1} increased with concentration. With *p*-hydroxyphenyl acetate only the peaks at 3478 cm^{-1} and 3606 cm^{-1} were observed. These measurements were done on a Beckman IR7 spectrophotometer.

Kinetics. The reactions were followed spectrophotometrically, using either a Hitachi-Perkin-Elmer 139 or a Gilford 200 recording spectrophotometer with thermostated cell compartments. Reactions of *p*-hydroxyphenyl benzoate were slow, and were therefore followed by removing samples from stoppered flasks and measuring their absorbance. This procedure was also used for a few kinetic runs with *p*-hydroxyphenyl acetate, although most of the runs with this compound were followed directly in the spectrophotometer. Periodate solutions were made up from the acid, and the pH was adjusted by addition of concentrated H_2SO_4 or NaOH. Solutions were deoxygenated in a stream of nitrogen.

For reactions of *p*-hydroxyphenyl acetate the ester concentration was varied between 10^{-5} and 10^{-2} *M*, with periodate in at least tenfold excess over ester. For the lower concentrations of ester and periodate, reaction was followed by measuring the change of optical density at 2470 A, where the absorbance changes during reaction are largest. For the runs with higher concentrations of periodate and ester we followed the formation of *p*-benzoquinone at 4360 A. In all cases, the first-order rate constants, k_ψ, were calculated graphically using the integrated first-order rate equation. The absorbance at complete reaction was determined directly.

For reactions of *p*-hydroxyphenyl benzoate the concentration of ester was restricted by its low solubility, and was varied only between 4 and 7 × 10^{-5} *M*; periodate was in at least tenfold excess, except for the most dilute solutions. Reaction was followed by the decreasing absorbance at 2740 A, where the ester absorbs strongly. The absorbance corresponding to complete reaction was calculated from the known optical densities of the reactants and products at pH and concentrations used for the experiment, because with the low reagent concentrations reaction is inconveniently slow for direct determination of the absorbance corresponding to complete reaction.

For reactions of 3-*t*-butyl-4-hydroxyphenyl acetate we could not directly determine the absorbance corresponding to complete reaction because the *t*-butyl-*p*-benzoquinone decomposes on prolonged treatment in periodate. Therefore the absorbance at complete reaction was determined by either of two methods. For reactions with the higher reagent concentrations, a sample of the ester was hydrolyzed at pH 1 in an atmosphere of nitrogen at 70° and then periodate was added in appropriate concentration to this solution, the pH adjusted to 1.0, and the absorbance of the quinone measured at 4340 A. The reaction was followed by the absorbance at 4340 A. For reactions at the lower reagent concentrations, the formation of quinone was followed at 2740 A, and the absorbance at complete reaction was calculated from the known absorbances of reactants and products. The effects of atmospheric oxidation were decreased by passing a stream of nitrogen gas through the cell compartment of the spectrophotometer, and all solutions were saturated with nitrogen, and stoppered cells were used. Reactions of the *t*-butyl compound were followed for approximately 40% of total reaction. Examples of kinetic runs are given in Figure 1.

The rate of oxidation of 2,5-di-*t*-butyl-*p*-quinol by periodate was measured at pH 1, using a quinol concentration ~10^{-5} *M* and following the formation of the quinone, which absorbs strongly at 2520 A. The solutions were deoxygenated in a stream of nitrogen immediately before reaction, which was done in stoppered cells; a stream of nitrogen gas was passed through the cell compartment of the spectrophotometer. The absorbance at complete reaction was determined experimentally, and agreed reasonably well with the calculated value. However, there appears to be a substantial decomposition of 2,5-di-*t*-butyl-*p*-quinone in the presence of oxygen and periodate or iodate, and the rate constants for oxidation of this quinol are therefore less reliable than those for the other compounds.

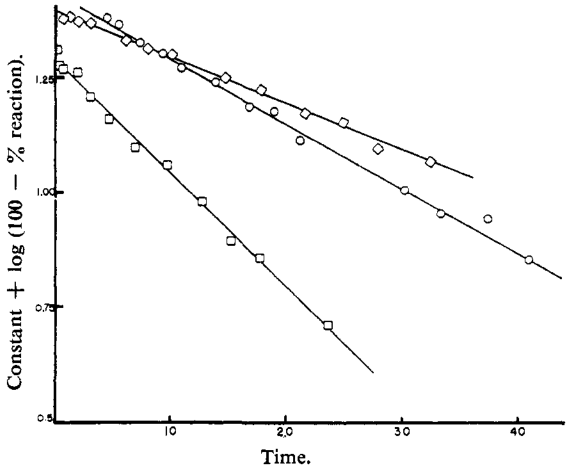
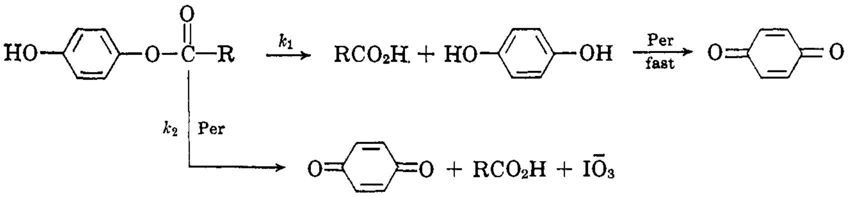


Figure 1. Reaction of *p*-hydroxyphenyl acetate at pH 1.0, time in minutes × 10, [Per] = 2.33 × 10^{-2} *M*, ○; reaction of *p*-hydroxyphenyl acetate at pH 2.0, time in hours, [Per] = 6.30 × 10^{-3} *M*, ◇; reaction of *p*-hydroxyphenyl benzoate at pH 0.5, [Per] = 6.33 × 10^{-4} *M*, time in hours × 10, □.

The hydrolysis of *p*-hydroxyphenyl benzoate was followed by withdrawing samples, adding standard periodate which reacts very rapidly with the quinol,[4] and then determining the quinone spectrophotometrically.

Results

Periodate reacts much more readily with *p*-quinols than with their esters (ref 4 and Table I), and under our conditions two reactions are occurring simultaneously. One is a slow hydrolysis of the ester followed by a very rapid oxidation of the quinol by peridoate (1) and the other is a direct oxidation by periodate (2).



(1)

(2)

With an excess of periodate and at a fixed pH the rate equation should be

$$k_\psi = k_1 + k_2[\text{Per}]$$

Figures 2 and 3 show plots of k_ψ against [Per] over a range of pH, and the values of k_1 and k_2 are given in Table II for 4-hydroxyphenyl acetate and benzoate and 3-*t*-butyl-4-hydroxyphenyl acetate. The values of k_1, obtained by extrapolation of these plots of k_ψ against periodate concentration, agree reasonably with those determined directly. As expected, the hydrolysis of the acetate is much faster than that of the corresponding benzoate, and the *t*-butyl group *meta* to the acetoxy group has very little effect upon the hydrolysis rate. The reaction of 4-hydroxyphenyl acetate was not examined at low pH because the rate of hydrolysis becomes similar to that of the direct oxidation. The solubility of 4-hydroxyphenyl benzoate is small, and this fact prevented our examining its reaction at pH 3, where k_ψ would be very small unless we used a high

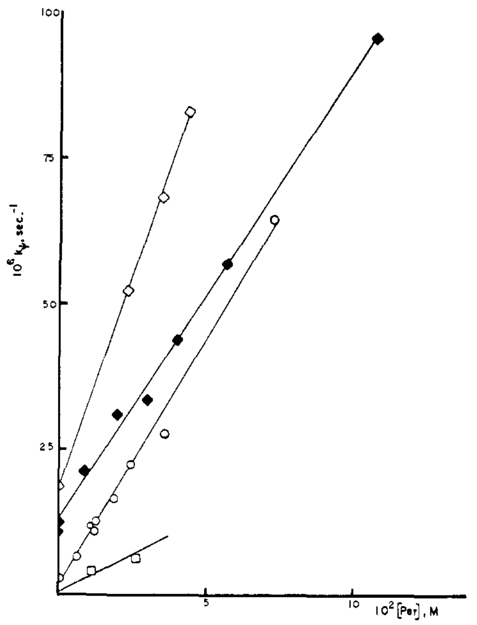


Figure 2. First-order rate constants for reactions between periodate and *p*-hydroxyphenyl and 3-*t*-butyl-4-hydroxyphenyl acetate; *p*-hydroxyphenyl acetate: ◇, pH 1.00; ○, pH 2.00; □, pH 3.00; 3-*t*-butyl-4-hydroxyphenyl acetate: ◆, pH 1.00.

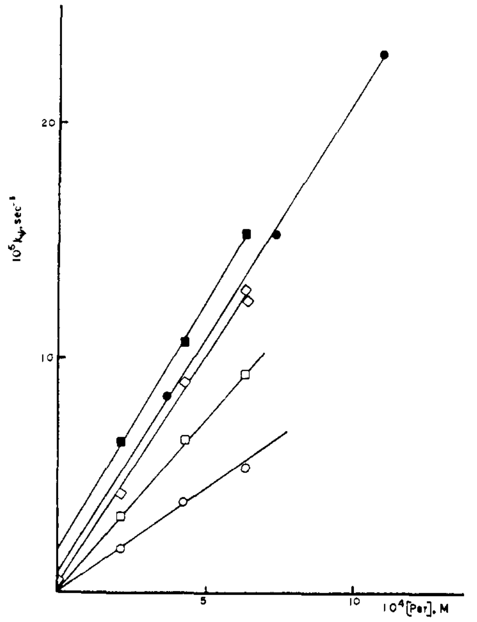


Figure 3. First-order rate constants for reaction between periodate and *p*-hydroxyphenyl benzoate: ■, pH 0.50; ●, pH 0.70; ◇, pH 1.00; □, pH 1.50; ○, pH 2.00.

concentration of periodate, in which case the absorption of the periodate would swamp that of the ester.

In their original kinetic work on the oxidation of *p*-quinols, Kaiser and Weidman did not examine the effect of alkyl substituents in the ring upon reaction rate.[4] We measured the rate of oxidation of 3-*t*-butyl-4-hydroxyphenyl acetate at pH 1.0 (Table II), and also measured the rate of oxidation of 2,4-di-*t*-butyl-*p*-quinol (Table III) so that we could compare the effects of a *t*-butyl group upon these two reactions. We did not examine the effects of pH changes upon the rates of these reactions.

Table I. First-Order Rate Constants for Reactions of Quinol Esters[a]

pH	10^4[Per], *M*	$10^6 k_\psi$, sec^{-1}
	p-Hydroxyphenyl Acetate	
3.00	118	4.25[b]
3.00	265	6.40[b]
2.00	1.83	2.90[b]
2.00	63.0	6.58[b]
2.00	109	12.0[b]
2.00	121	11.0[b]
2.00	127	12.8[b]
2.00	190	16.7[b]
2.00	242	22.4[b]
2.00	360	27.8[c]
2.00	722	64.7[c]
1.00	1.83	18.8[b]
1.00	233	54.3[b]
1.00	350	68.3[b]
1.00	418	83.0[b]
	3-*t*-Butyl-4-hydroxyphenyl Acetate	
1.00	3.15	10.8[d]
1.00	6.30	12.7[d]
1.00	84.0	21.3[d]
1.00	200	31.1[e]
1.00	300	33.5[e]
1.00	400	44.0[e]
1.00	570	57.0[e]
1.00	1077	95.9[e]
	p-Hydroxyphenyl Benzoate	
2.00	2.11	0.194[d]
2.00	4.22	0.386[d]
2.00	6.33	0.522[d]
1.50	2.11	0.323[d]
1.50	4.22	0.647[d]
1.50	6.33	0.934[d]
1.00	0	0.045[d]
1.00	2.11	0.423[d]
1.00	4.22	0.896[d]
1.00	6.33	1.29[d]
1.00	6.38	1.24[d]
0.70	3.67	0.832[d]
0.70	7.33	1.53[d]
0.70	11.0	2.30[d]
0.50	2.11	0.642[d]
0.50	4.22	1.07[d]
0.50	6.33	1.53[d]

[a] In water at 25.0°. [b] Followed at λ 2470 A. [c] Followed at λ 4360 A. [b] Followed at λ 2740 A. [e] Followed at λ 4340 A.

Table II. Rate Constants for Hydrolysis and Oxidative Hydrolysis[a]

Substrate	pH	$10^7 k_1$, sec^{-1}	$10^4 k_2$, l. mole^{-1} sec^{-1} Obsd	$10^4 k_2$, l. mole^{-1} sec^{-1} Calcd[c]
p-Hydroxylphenyl acetate	3.00	...	2.8	2.8
p-Hydroxylphenyl acetate	2.00	18	8.6	8.3
p-Hydroxylphenyl acetate	1.00	190	15.2	15.2
3-*t*-Butyl-4-hydroxyphenyl acetate	1.00	126	7.6	...
p-Hydroxyphenyl benzoate	2.00	...	9.1	9.7
p-Hydroxyphenyl benzoate	1.50	0.15	14.5	14.5
p-Hydroxyphenyl benzoate	1.00	0.43[b]	19.5	18.9
p-Hydroxyphenyl benzoate	0.70	0.8	20.8	20.7
p-Hydroxyphenyl benzoate	0.50	1.8	21.3	21.6

[a] In water at 25.0°. [b] $k_1 = 0.45 \times 10^{-7}$ sec^{-1} by direct measurement. [c] Calculated taking $k^0 = 19.6 \times 10^{-4}$ and $k^- = 2.2 \times 10^{-4}$ l. mole^{-1} sec^{-1} for the acetate, and $k^0 = 24 \times 10^{-4}$ and $k^- = 3.9 \times 10^{-4}$ l. mole^{-1} sec^{-1} for the benzoate.

Table III. Oxidation of 2,5-Di-*t*-butyl-*p*-quinol[a]

10^4[Per], *M*	$10^3 k_\psi$, sec^{-1}
1.25	3.3
1.25	2.9
1.50	4.6
1.50	6.5

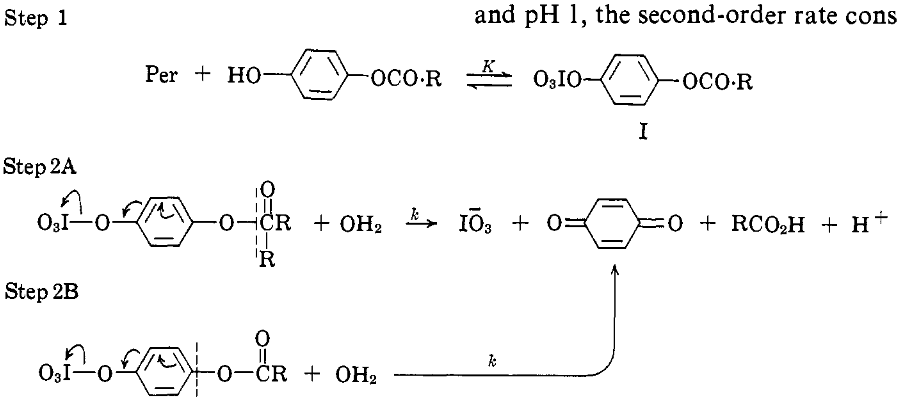
[a] In water, pH 1.0 at 25.0°; [quinol] 6–8 × 10^{-6} *M*.

Discussion

That part of the reaction which involves hydrolysis of the ester and subsequent rapid oxidation of the quinol is of no particular interest so far as the mechanism of oxidative hydrolysis is concerned. So far as the direct oxidation is concerned, the main questions are those of the timing of the various reaction steps and the nature of the reactive species.

Rate-Limiting Step of Oxidation. The rate-limiting step of the direct oxidative hydrolysis is almost certainly not the hydrolysis of a preformed intermediate periodate ester, for the following reasons.

(i) If the intermediate I was in equilibrium with the reactants, step 1, and was hydrolyzed slowly to products in steps 2A or 2B.



The (hypothetical) equilibrium constant, *K*, should be insensitive to small structural changes in the carboxyl residue, but if the slow decomposition of the intermediate involved nucleophilic attack upon the acyl residue (step 2A) the acetate should be more reactive than the benzoate, as it is in direct hydrolysis (Table II). Generally, the rate of nucleophilic attack upon an acyl group is reduced by approximately 10–10^2-fold by substitution of a phenyl for a methyl group (ref 13 and Table II), because reaction destroys the conjugation between the carbonyl and aryl groups. On the other hand, nucleophilic attack upon the aryl residue (step 2B) should be more rapid for the benzoate, because benzoate should be a better leaving group than acetate. Therefore if the decomposition of the intermediate were slow, quinol acetate and benzoate should have different reactivities toward periodate, although in the absence of further information one cannot predict which should be the more reactive.

One of the referees suggested the possibility that the intermediate I might be extensively hydrated by attack of water upon the acyl residue and that this hydrate could then decompose slowly to products. Although this mechanism cannot be vigorously excluded, it has the disadvantage of explaining the similarity of the reaction rates of acetate and benzoate in terms of the adventitious cancellation of several factors. In addition such a mechanism seems improbable from all that is known about the mechanisms of hydrolysis of aryl esters.[13]

(ii) The variations of k_ψ with pH are very similar for the oxidations of *p*-quinols[4] and the oxidative hydrolyses of their esters (Tables I and II). This result would be unexpected unless the rate-limiting steps of both reactions were chemically similar, and therefore both rate-limiting steps must involve formation of quinol periodates whose decomposition must be fast.

(iii) The effect of a *t*-butyl group adjacent to the hydroxyl group upon the value of k_2 is consistent with the proposed mechanism (although it does not exclude a preequilibrium formation of a periodate intermediate). For the direct reaction between periodate and the ester, the *t*-butyl group cuts the value of k_2 approximately twofold (Table II).

This steric effect is very similar to that found for the direct oxidation of 2,4-di-*t*-butylquinol. (It was necessary in this case to use two *t*-butyl groups, because reaction can occur at either of two hydroxyl groups.) For the reaction between *p*-quinol and periodate,[4] at 25° and pH 1, the second-order rate constant is 62 l. mole^{-1} sec^{-1}, whereas for the 2,5-di-*t*-butyl derivative it is 30 l. mole^{-1} sec^{-1} (Table III). This effect is probably steric, and it is not particularly large because the *t*-butyl group will block electrophilic attack upon the hydroxyl group from one side only.

Effect of pH upon Reaction. The value of k_2 increases uniformly with decreasing pH. For the oxidations of quinol and quinol monomethyl ether by periodate, Kaiser and Weidman found that both periodate ion and undissociated periodic acid reacted with the quinol.[4]

The second-order rate constant for the direct reaction between periodate and ester is given by

$$k_2[\text{Per}] = k^0[\text{Per}^0] + k^-[\text{Per}^-] \qquad (3)$$

where the superscripts ^{0} and $^-$ denote reactions of undissociated periodic acid and periodate monoanion respectively, and we do not differentiate between hydrated and dehydrated species. The concentration of periodate dianion will be negligible at the acidities used.[14]

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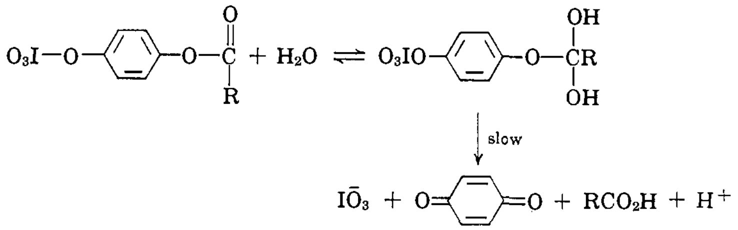
(13) (a) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 758; (b) M. L. Bender, *Chem. Rev.*, 60, 53 (1960).

(14) C. E. Crouthamel, H. V. Meek, D. S. Martin, and C. V. Banks, *J. Am. Chem. Soc.*, 71, 3031 (1949); C. E. Crouthamel, A. M. Hayes, and D. S. Martin, *ibid.*, 73, 82 (1951); G. J. Buist and J. D. Lewis, *Chem. Commun.*, 66 (1965).



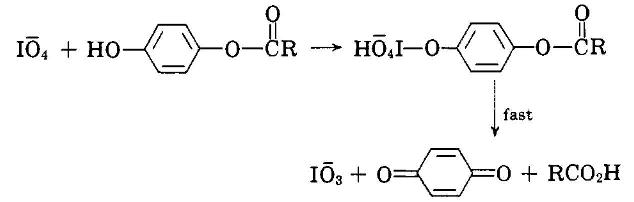
The proportions of periodate present as undissociated acid and monoanion can be calculated at any given pH, using the apparent classical first dissociation constant, $\bar{K}_1$, of periodic acid. In our calculation we use the value of $\bar{K}_1$ appropriate to the ionic strength, I, of the solution, interpolated from the following values of $10^2\bar{K}_1$ of 3.0 at $I = 0.052$, 4.23 at $I = 0.29$, and 5.5 at $I = 0.99$.[15] Using the values of k_2 at various pH and the proportions of periodate present as acid and monoanion we calculate the following values for k^0 and k^- at 25°: *p*-hydroxyphenyl acetate, $k^0 = 19.6 \times 10^{-4}$, $k^- = 2.2 \times 10^{-4}$ l. sec^{-1} mole^{-1}, and for *p*-hydroxyphenyl benzoate, $k^0 = 24 \times 10^{-4}$ and $k^- = 3.9 \times 10^{-4}$ l. sec^{-1} mole^{-1}. These second-order rate constants were calculated from values of k_2 at pH 1.0 and 3.0 for the acetate and pH 0.5, 0.7, and 1.5 for the benzoate. The value of k^0 is good, because the amount of reaction involving undissociated periodic acid is large at low pH. The value of k^- is much less reliable, because the amount of reaction involving periodate monoanion is never large, especially with the benzoate, where we were unable to follow the reaction at pH 3.0.

In Table II we show the agreement between the experimental and calculated values of k_2, using the above values of k^0 and k^-.

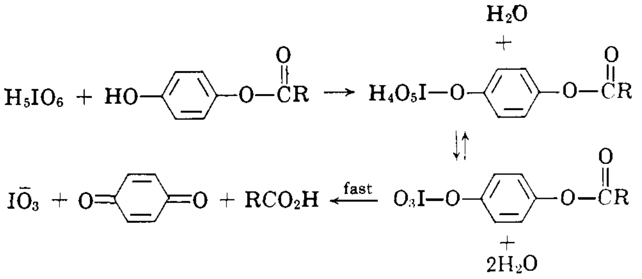
The variation of k_2 with pH can be explained in terms of formation of an aryl periodate by attack of the quinol ester upon undissociated periodic acid, H_5IO_6, and upon the monoanion, either in the form IO_4^- or $H_4IO_6^-$. Reaction with undissociated acid would have the same kinetic form as a reaction between quinol ester and monoanion catalyzed by a proton, and we cannot at present distinguish between these possibilities.

At low pH periodic acid exists wholly as H_5IO_6, and we cannot differentiate between direct reaction between this acid and the ester of quinol, and an equilibrium dehydration to give H_3IO_5 which then reacts. (The fully dehydrated acid HIO_4 should be very strong,[16] and its concentration should be vanishingly small at pH 0.5 or higher.) The most electrophilic monoanion should be IO_4^-, and because it is also the predominant monoanion[14] (*cf.* ref 17), we assume that there is also a direct reaction between it and the ester of quinol.

Although in reactions of simple 1,2-diols with periodate it is the monoanion of the cyclic intermediate which decomposes to products,[6] the formation of the cyclic intermediate can occur by reaction between the diol and either periodic acid or its monoanion.[6,15] The situation is similar for reactions between periodate and quinol or quinol esters. For both these reactions undissociated periodic acid is more reactive than its monoanion. Two factors influence the electrophilicity of these periodate species. The negative charge of the monoanion should decrease its electrophilicity, but at the same time reaction between the quinol or quinol ester and periodate monoanion involves addition to a predominantly dehydrated species

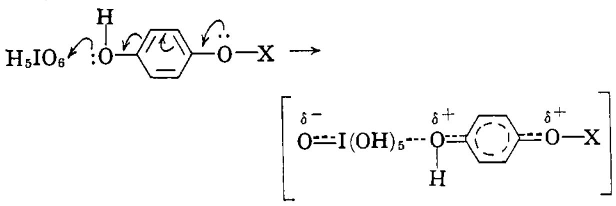


whereas reaction with the acid presumably involves formation of a new iodine–oxygen bond and displacement of at least one water molecule.



These two factors of charge and hydration approximately balance each other, because for oxidation of these quinol esters the acid is six to ten times as reactive as the monoanion, and the rate difference is, as expected, somewhat less for oxidation of the quinols,[4] because these less reactive quinol esters discriminate more between periodic acid and its monoanion than do the quinols.

The carboxyl group strongly hinders reaction with periodate. For reaction between *p*-quinol and undissociated periodic acid the second-order rate constant is 71.7 l. sec^{-1} mole^{-1} at 25°,[4] whereas for *p*-quinol acetate it is 19.6×10^{-4} l. sec^{-1} mole^{-1}, and this reactivity difference is caused by the strong electron attraction of the carboxy group, which is particularly important in these reactions where conjugative electron release from one oxygen atom to another assists nucleophilic attack upon the periodate. A transition state



X = H, R, RCO

can be formulated for reaction with the periodate monoanion.

Other reactions which are akin to these oxidations of the quinol esters are reactions of *p*-hydroxylphenyl phosphates with oxidizing agents such as the halogens,[18,19]

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and there is a reaction between aqueous periodate and p-hydroxyphenyl phosphate which gives p-quinone and inorganic phosphate, and which is very much faster than the direct hydrolysis of the phosphate.[20]

For reactions of p-hydroxyphenyl phosphate in the presence of oxidizing agents both phosphorus– and carbon–oxygen fission is observed.[18,19] In our reactions the very low solubility of the carboxylic esters in water makes it very difficult to use tracer methods to differentiate between the two possible bond fissions.

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The Base-Induced Rearrangements of α-Epoxy Ketones

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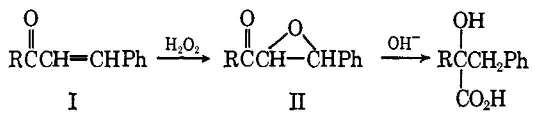
Abstract: Although 1,3-diaryl-2,3-epoxypropanones generally yield glycolic acids *via* a benzylic acid type rearrangement on treatment with aqueous or alcoholic alkali, the related 1-aryl-3-cycloalkyl-2,3-epoxypropanones ordinarily react by a different pathway. The 3-cyclohexyl, 3-cyclopentyl, and 3-cyclobutyl derivatives rearrange to a mixture of γ-lactones and β,γ-unsaturated acids. The 3-cyclopropyl derivative is, however, converted into the glycolic acid on base treatment.

In connection with work in these laboratories on the biological activity of certain glycolate esters, a variety of acids of the general structure III were required. The planned synthetic procedure involved the conversion by known methods of the appropriate α,β-unsaturated ketone I *via* the epoxy ketone II to the glycolic acid III.



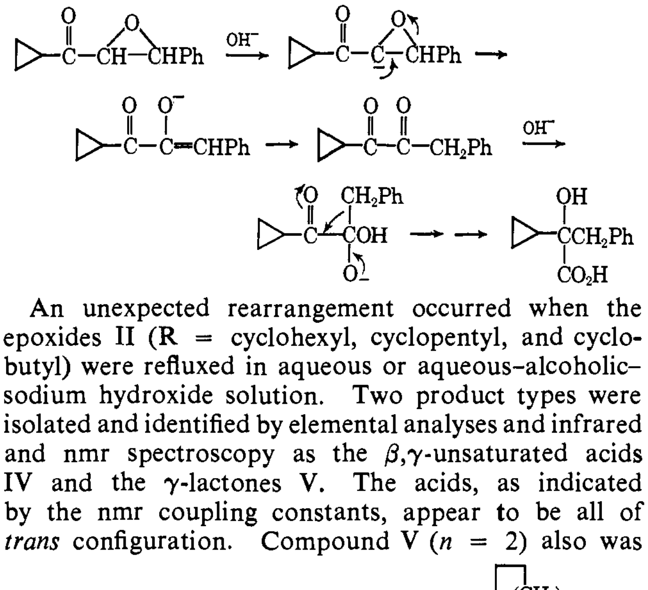
I II III

R = cycloalkyl

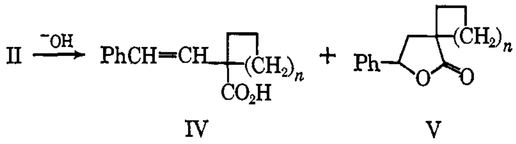
The readily synthesized α,β-unsaturated ketones I appear to be the *trans* isomers as judged by the nmr chemical shifts and coupling constants (Table I). These were successfully converted to the α-epoxy ketones II with hydrogen peroxide and sodium hydroxide in an aqueous–ethanolic–acetone solution. An examination of the nmr coupling constants between the two epoxide protons reveals that these compounds are also of the *trans* configuration (Table I). Further, Black and Lutz[1] have shown that both the *cis* and *trans* isomers of chalcone react with alkaline hydrogen peroxide to produce the same *trans*-epoxy ketone.

When the epoxy ketones II were treated with an aqueous or aqueous–alcoholic–sodium hydroxide solution only 1-cyclopropyl-3-phenyl-2,3-epoxypropan-1-one (II, R = cyclopropyl) gave the "normal" benzilic acid type rearrangement product, the substituted glycolic acid III (R = cyclopropyl). This rearrangement has been accomplished with a number of related epoxidized benzylideneacetophenones[2] and the mechanism studied in careful detail.[3] By analogy with this work, the mechanism of rearrangement of II (R = cyclopropyl) is pictured in Scheme I.

Scheme I

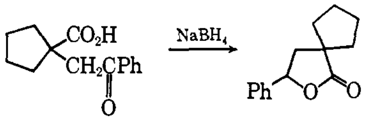


An unexpected rearrangement occurred when the epoxides II (R = cyclohexyl, cyclopentyl, and cyclobutyl) were refluxed in aqueous or aqueous-alcoholic–sodium hydroxide solution. Two product types were isolated and identified by elemental analyses and infrared and nmr spectroscopy as the β,γ-unsaturated acids IV and the γ-lactones V. The acids, as indicated by the nmr coupling constants, appear to be all of *trans* configuration. Compound V (n = 2) also was obtained from the known keto acid VI[4,5] by reduction with sodium borohydride. The mechanism we



IV V

$n = 1,2,3$



VI V (n = 2)

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