Mechanism of C–C Cleavage of Cyclic 1,2-Diketones with Alkaline Hydrogen Peroxide. The Acyclic Mechanism and Its Application to the Basic Autoxidation of Pyrogallol

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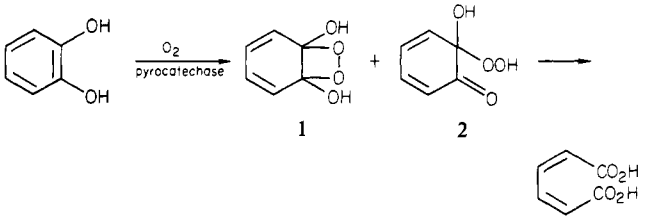
Abstract: The reaction of 3,5-di-*tert*-butyl-*o*-benzoquinone (**3**) with alkaline hydrogen peroxide was found to give a considerable amount of methyl ester **5** when H_2O_2 was added dropwise. In contrast, the corresponding diacids were not obtained from *o*-benzoquinone or 1,2-naphthoquinone on reaction with alkaline H_2O_2. An ^{18}O-tracer study of the reaction of **3** and 9,10-phenanthrenequinone indicated that the C–C cleavage reaction proceeds via the acyclic Baeyer–Villiger type mechanism and clearly eliminated possible dioxetane or epoxide mechanisms. A similar study of the base-catalyzed autoxidation of 4,6-di-*tert*-butylpyrogallol revealed that the C–C bond is cleaved in a similar way by hydrogen peroxide formed from O_2 and the polyphenol.

A number of enzymatic C–C cleavages are known to go by way of dioxygenases, e.g., the oxidation of catechol to muconic acid by pyrocatechase[1] and of quercetin by quercetinase.[2] Since these reactions involve incorporation of molecular oxygen, a dioxetane intermediate (e.g., **1**) is often written. However, this cyclic mechanism has been criticized because of the high endothermicity of dioxetane formation in comparison to an alternative acyclic mechanism involving **2**.[3] A model reaction for pyrocatechase

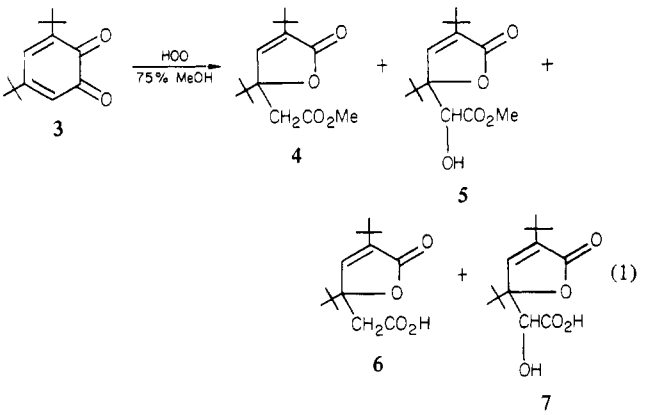


using cuprous chloride was reported to afford monomethyl muconate in methanol and was explained as involving methoxide attack on **2**.[4] However, the reaction has recently been shown to be an oxidative C–C fission by Cu(II) itself; oxygen is not required.[5]

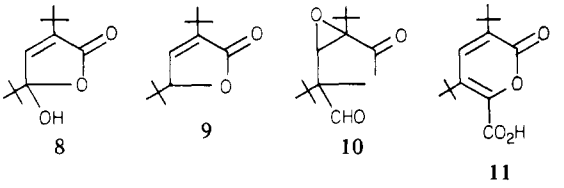
The same question of dioxetane intermediacy is also unsolved in the nonenzymatic oxidative C–C cleavage of catechols by superoxide[6] and their base-catalyzed autoxidation.[7] As a model for this type of reaction, we have reported previously that the reaction of benzils with alkaline hydrogen peroxide goes by way of an acyclic Baeyer–Villiger type mechanism rather than a dioxetane.[8] Here we wish to summarize product and ^{18}O studies on the alkaline H_2O_2 cleavage of some cyclic 1,2-diketones and on the base-catalyzed autoxidation of a pyrogallol, which lead to the same conclusion.

Results

3,5-Di-*tert*-butyl-*o*-benzoquinone (3). The *o*-quinone **3** was oxidized by alkaline H_2O_2 in 75% MeOH, and the major products, determined by GLC, were as follows:



Minor products (**8–10**) also were detected (0–5%). Most of thses



products (**6–10**) had been previously isolated from the reaction of KO_2 with **3** in aprotic solvents.[6a] The results in Table IA show that the product ratios change depending on the rate of addition of H_2O_2; a 32% yield of methyl ester **5** was obtained as a major product when H_2O_2 was slowly added dropwise (run **3**, Table I). As shown in run **8**, the reaction of ester **4** to give α-hydroxy ester **5** was not important, suggesting that ester **5** is a primary product from **3** and alkaline H_2O_2.

The reaction under neutral conditions (see Table IB) was very slow; the product was acid **6** in ether or the corresponding ester **4** in MeOH. In this case, we cannot say whether ester **4** is a primary product or not, since acid **6** was esterified by standing for 3 days in MeOH. The reaction in 75% formic acid (run 7) was complete within 1 h, affording only acid **6**, but this reaction probably actually involves the in situ formation of and reaction with performic acid. It is noteworthy that all the reactions under nonbasic conditions afforded acid **6** or its ester **4** but not α-hydroxy acid **7** or its ester **5**.

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(2) Vanneste, W. H.; Zuberbuhler, A. "Molecular Mechanisms of Oxygen Activation"; Hayaishi, O., Ed.; Academic Press: New York, 1974; p 371.
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(4) (a) Tsuji, J.; Takayanagi, H. *J. Am. Chem. Soc.* **1974**, *96*, 7349. (b) Tsuji, J.; Takayanagi, H.; Sakai, I. *Tetrahedron Lett.* **1975**, 1245; (c) *Chem. Lett.* **1980**, 65.
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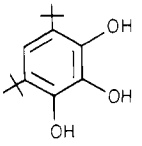
Table I. Alkaline H_2O_2 Oxidation of 3,5-Di-*tert*-butyl-*o*-benzoquinone (**3**) and Related Compounds

run no.	substrate	reagents, mmol: substrate	H_2O_2	NaOH	conditions[a]	addition[b]	products, %: 4	5	6	7	others
					(A) Alkaline Oxidation of **3**						
1	**3**	2.5	5	10		at once	0	2	0	28	yes
2	**3**	2.5	5	10		NaOH[f]	0	13	0	18	yes
3	**3**	2.5	5	10		H_2O_2[f]	<1	32	0	12	yes
4	**3**	5	5	5		H_2O_2[f]	7	17	3	16	yes
					(B) Neutral or Acidic Oxidation of **3**						
5	**3**	2.5	10	0	99% MeOH, 5 days	at once	10[d]	0	0	0	yes
6	**3**	2.5	10	0	Et_2O, 5 days	at once	0	0	10	0	yes
7[e]	**3**	2.5	5	0	75% HCO_2H, 1 h	at once	0	0	31	0	yes
					(C) Alkaline Oxidation of Other Substrates						
8	**4**	2.5	5	10	20 min	at once	12	0	28	27	no
9	**12**	2.5	5	10	O_2, 20 min	at once	0	<1	0	79	**11** (20%)
10	**12**	2.5	0	10	O_2, 20 min	at once	0	8	0	70	**11** (20%)
11	**12**	2.5	0	10	N_2, 20 min	at once	0	0	0	<5	**11** (3%)

[a] Reaction for 10 min (5 min addition and then 5 min stirring) in 75% MeOH solution of total 40 mL at ca. 23 °C, if not noted otherwise. [b] Final dropwise addition of 1 M H_2O_2 or 2 M NaOH for 5 min; "at once" means immediate fast addition and mixing. [c] Products were determined by GLC using *p*-chlorobenzil as an internal standard directly and after methylation with diazomethane. Other products from **3** were **8**, **9**, **10**, and **11**, each of which are in 0–5% yield. [d] Long standing (3 days) of **6** in MeOH afforded the corresponding ester **4**; thus, it is not certain whether the ester is a primary product or not. [e] Performic acid oxidation of **3**. [f] Dropwise addition.

The base-catalyzed autoxidation of 4,6-di-*tert*-butylpyrogallol (**12**) was also examined and shown to give mainly α-hydroxy acid **7** and 3,5-di-*tert*-butyl-2-pyrone-6-carboxylic acid (**11**). (It is

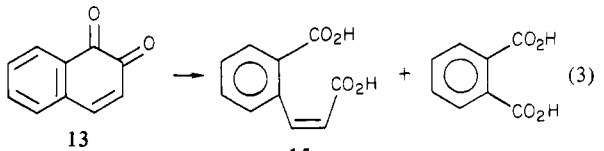


12

$\longrightarrow$ 5 + 7 + **11** (2)

not certain why the major product from **12** is **7** and **11** while α-hydroxy acid **5** or **7** is formed as a main product from *o*-quinone **3**.) The yield of ester **5** was again increased in the absence of added H_2O_2 (run 10).

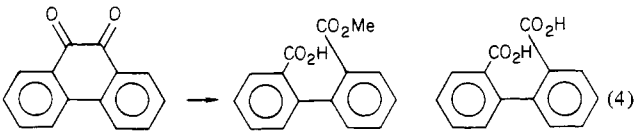
Other Cyclic 1,2-Diketones. The alkaline H_2O_2 oxidation of some other cyclic 1,2-diketones was found to be facile (Table II). However, no significant amount of the muconic acid analog or its methyl ester was obtained from 1,2-naphthoquinone (**13**) (run 12) or *o*-benzoquinone (**14**) (run 15). The corresponding muconic acid derivatives were found to be stable under the conditions. In the former case, a small amount of phthalic acid was formed. Reaction with H_2O_2 under neutral conditions (run 13) afforded a higher yield of *cis*-*o*-carboxycinnamic acid **15** and phthalic acid.



13 **15** (3)

However, peracid oxidation of **13** gave a good yield of diacid **15** without formation of phthalic acid (run 14). Peracid oxidation is, of course, an important synthetic route to *cis,cis*-muconic acid from catechol or phenol.[9] Although the reaction of *o*-benzoquinone **14** with H_2O_2 failed to give the muconic acid under the conditions of runs **15** and **16**, the reaction at −40 °C has been reported to afford 5–15% muconic acid together with many dimeric products.[10]

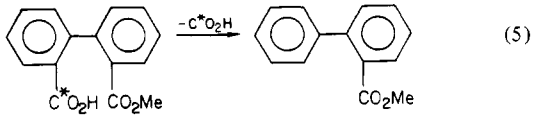
In contrast to these *o*-quinones, the oxidation of 9,10-phenanthrenequinone (**16**) resulted in a clean C–C cleavage. The oxidation with alkaline H_2O_2 afforded 41% of monoester **17** (run 17), while performic acid oxidation (run 18) gave a higher yield of **18**. In these respects, quinone **16** resembles the benzils[8] rather than the *o*-quinones **13** or **14**.



16 **17** **18** (4)

^{18}O-Tracer Study. The ^{18}O-tracer study was done with labeled $H_2{}^*O_2$ (M + 2 = 16.4%; M + 4 = 8.4% excess) or $^*O_2$(M + 2 = 8.22% and M + 4 = 4.17% excess); the results are summarized in Table III. As described previously,[8] percent excess ^{18}O was determined in comparison to the M + 1 peak because the parent peak (M) is off scale.

The results from phenanthrenequinone (**16**) and alkaline $H_2{}^*O_2$ indicate that only one labeled atom from $H_2{}^*O_2$ is incorporated in the product diphenic acid (**18**). It is noteworthy that one atom of oxygen in monoester **17** comes from $H_2{}^*O_2$ and that the oxygen atom is located entirely in the acid group, as shown by the fact that mass spectral cleavage of CO_2H results in loss of all the excess isotope, whereas cleavage of CO_2CH_3 retains it.



m/e 256 ^{18}O = 12.5% *m/e* 211 ^{18}O = 0% (5)

Since the corresponding parent peaks were too small, the ^{18}O contents for compounds **4**, **5**, and **7** were determined from the M − 15 (CH_3) or M − 56 (isobutylene) peaks. Only a single ^{18}O was incorporated in these products.

The ^{18}O-tracer study indicates clearly that the oxygen atom is derived from H_2O_2 but not from O_2 in the base-catalyzed autoxidation of pyrogallol **12** in the presence of H_2O_2. Autoxidation in the presence of $H_2{}^{18}O_2$ resulted in a considerable amount of ^{18}O incorporation in product **11**, while oxidation with $^{18}O_2$ in the presence of H_2O_2 gave much lower incorporation of $^{18}O_2$. Although the yield of **11** was quite low from the autoxidation with $^*O_2$ in the absence of added H_2O_2, in this case acid **11** contained a considerable amount of ^{18}O. These results show that H_2O_2 has an important role in the C–C cleavage during aut-

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Table II. Alkaline H_2O_2 Oxidation of Other Cyclic 1,2-Diketones

run no.	reagents, mmol: diketone	H_2O_2	NaOH	conditions[a]	products, %[b]: monomethyl ester	dicarboxylic acid	others
				(A) 1,2-Naphthoquinone (13)			
12	2.5	10	5	75% MeOH, 10 min	<1	<1	phthalic acid (5%)
13	2.5	10	0	98% MeOH, 5 days	<1	7	phthalic acid (10%)
14	2.5	5	0	75% HCO_2H, 1 h	0	54[c]	
				(B) 1,2-Benzoquinone (14)			
15	1	5	0	*d*, 0 °C, 1 h	<1	<1	yes[e]
16	1	5	9	*d*, 0 °C, 1 h	<1	<1	yes[e]
				(C) Phenanthrenequinone (16)			
17	2.5	5	5	*f*, 10 min	41[g]	56[g]	
18	2.5	5	0	*h*, 1 h	0	90[c]	

[a] Reaction at ca. 23 °C with total 40 mL solution for runs 12–16. The reaction with alkaline H_2O_2 was started by dropwise addition of 1 M H_2O_2 for 5 min, and then the mixture was stirred for 5 min. [b] Products were determined by GLC after methylation with diazomethane. The diacids for A and B were *cis*-(*o*-carboxyl)cinnamic and *cis,cis*-muconic acids, respectively. [c] Isolated yields. [d] MeOH/ether (7:10). [e] Not determined. [f] MeOH-THF-H_2O, 30 mL each. [g] Determined by NMR. [h] HCO_2H-THF-H_2O, 30 mL each.

Table III. ^{18}O-Tracer Study Using $H_2{}^*O_2$ or $^*O_2$[a]

reaction	products (%)[b]	obsd ^{18}O, %[c] excess	calcd ^{18}O, %[d] excess: dioxetane	acyclic[d]
(16 + $H_2{}^*O_2$)[e]	acid **18** (34%)	(M + 2) 25.8 ± 0.5	16.4	30.8
		(M + 4) 2.04 ± 0.25	8.4	2.35
	monoester **17** (25%)	(M + 2) 12.5 ± 0.8	no	15.3
		(M + 4) 0.01 ± 0.17	no	0.0
(3 + $H_2{}^*O_2$)[f]	ester **4** (1%)	(M + 2) 13.4 ± 1.2[g]	no	15.3
		(M + 4) 0.2 ± 0.12[g]	no	0.0
	α-HO ester **5** (36%)	(M + 2) 29.2 ± 3.4[g]	no	30.8
		(M + 4) 2.0 ± 1.0[g]	no	2.35
	α-HO acid **7** (10%)	(M + 2) 32.0 ± 2.0[h]	32.8	46.1
		(M + 4) 5.8 ± 0.5[h]	11.1	7.07
(12 + O_2 + $H_2{}^*O_2$)[i]	acid **11** (47%)	(M + 2) 13.5 ± 1.0	16.4[j]	30.8[j]
		(M + 4) 0.40 ± 0.38	8.4	2.35[j]
(12 + $^*O_2$ + H_2O_2)[k]	acid **11** (31%)	(M + 2) 1.04 ± 0.12	0[j]	0[j]
		(M + 4) 0.09 ± 0.06	0[j]	0[j]
(12 + $^*O_2$)[l]	acid **11** (3%)	(M + 2) 6.37 ± 0.38		
		(M + 4) 0.13 ± 0.17		

[a] Reaction at 23 °C with $H_2{}^*O_2$ (M + 2 = 16.4%, M + 4 = 8.4% excess) or with $^*O_2$ (M + 2 = 8.22%, M + 4 = 4.17% excess). See Experimental Section for details. [b] Isolated yield. [c] (M + 4)% is the percent of the molecules that have two ^{18}O atoms. [d] ^{18}O % excess calculated for each mechanism. The values for the epoxide mechanism (eq 7) are the same as those for the acyclic mechanism. See text for details. "No" means that none of these products are expected from the corresponding mechanism. [e] Reaction with **16** (1.25 mmol), NaOH (2.5 mmol), and $H_2{}^*O_2$ (1.25 mmol, added dropwise in MeOH-THF-H_2O (15 mL each) for 10 min). [f] Reaction with **3** (1.25 mmol), NaOH (2.5 mmol), and $H_2{}^*O_2$ (1.25 mmol, added dropwise in 85% MeOH for 10 min). [g] Determined from *m/e* 212 and 228 peaks, respectively (parent – isobutylene), since the parent peaks (268 and 284) were too small to obtain accurate values. [h] Determined from *m/e* 269, i.e., parent peak – 15 (methyl). [i] Reaction with **3** (1.25 mmol), NaOH (2.5 mmol), $H_2{}^*O_2$ (1 mmol), and O_2 bubbled in 75% MeOH (35 mL) for 20 min. [j] Calculated by assuming that the added $H_2{}^*O_2$ is the only oxidant for the C–C cleavage. [k] Mixture of **12** (0.5 mmol), NaOH (2 mmol, H_2O_2 (1 mmol), and $^*O_2$ in 75% MeOH (35 mL) was stirred under $^*O_2$ atmosphere for 20 min. [l] Reaction similar to *k* except without added H_2O_2.

oxidation of pyrogallol. Again, the second oxygen from *O–*O is lost in the product acid.

Discussion

C–C Cleavage Mechanism. The three mechanisms conceivable or proposed for the reaction of cyclic 1,2-diketone and alkaline $H_2{}^*O_2$ may be written as in Scheme I. In mechanisms B and C, the initial ^{18}O content (8.4%) should be different from that in $H_2{}^*O_2$ since the two ^{18}O atoms in the diacid are derived from different molecules of $H_2{}^*O_2$. It is assumed that the peroxyacid formed from anhydride and $H_2{}^*O_2$ reacts rapidly with another starting diketone yielding the diacid (as shown in eq 7b and 8b) and another molecule of anhydride. The reaction of HO^- with anhydride is less important than the reaction of MeO^- or HOO^- since both the nucleophilicity and the concentration of HOO^- and MeO^- are much greater than that of HO^-.[12]

The calculated percent ^{18}O values in Table III were obtained according to these reactions; the $H_2{}^*O_2$ used contained 16.4% singly and 8.4% doubly labeled ^{18}O (percent ^{18}O values are always calculated on the basis of ^{16}O = 100%). The ^{18}O content for products of the dioxetane mechanism (eq 6) are the same as that of the starting $H_2{}^*O_2$. The calculated ^{18}O content for monoester by mechanisms B and C (eq 7a and 8a) is half of the total ^{18}O content in the M + 2 peak and zero in the M + 4, because only one atom of oxygen is incorporated.

$$\frac{M+2}{M} = \frac{16.4\%/2 + 8.4\%}{100\% + 16.4\%/2} = 15.3\%$$

$$M + 4 = 0.0\%$$

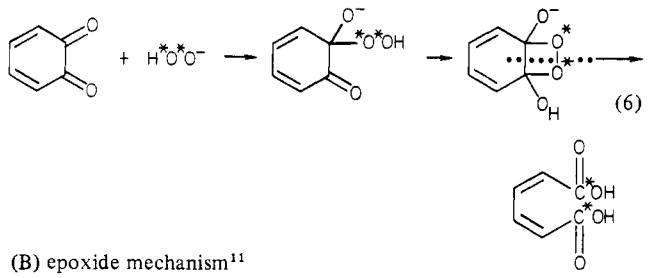
Although the calculated ^{18}O content is the same for the half ester from eq 7a or 8a, the position of the *O is different in the two mechanisms, i.e., the carboxyl or the ester carbonyl oxygen (eq 7a and 8a).

A second incorporation of *O from another $H_2{}^*O_2$ molecule is involved in diacid formation via the anhydride (eq 7b and 8b). The ^{18}O content by this scheme is calculated as follows: since

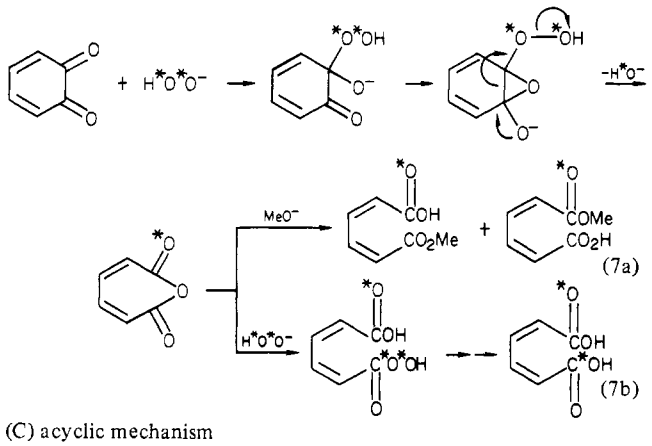
(12) (a) It is known that MeO^- and HOO^- are much stronger nucleophiles than HO^- (Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1968**, *90*, 2622). (b) Marto, J. In "The Chemistry of the Hydroxyl Group"; Patai, S., Ed.; Interscience: London, **1971**; Part 2, p 1087.

Scheme I

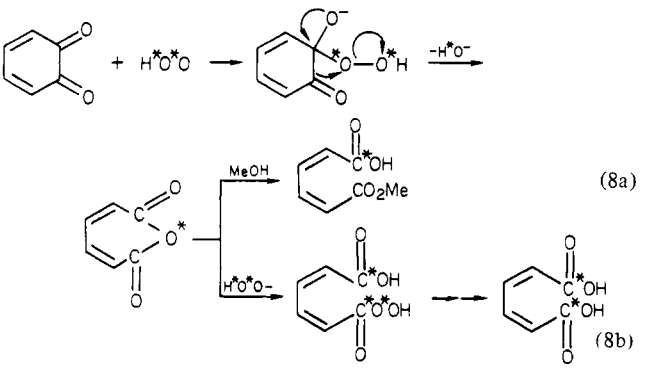
(A) dioxetane mechanism



(B) epoxide mechanism[11]



(C) acyclic mechanism



the fractions of M and M + 2 for one *O incorporation are 0.867 and 0.133, the amounts of excess ^{18}O (percent) for the diacid are

$$\frac{M+2}{M} = \frac{15.3\% \times 0.867 + 100\% \times 0.133}{100\% \times 0.867} = 0.308 = 30.8\%$$

$$\frac{M+4}{M} = \frac{15.3\% \times 0.133}{100\% \times 0.867} = 0.0235 = 2.35\%$$

When the third *O is incorporated after the above reaction, the labeling consequences are as follows:

$$\frac{M+2}{M} = \frac{30.8\% \times 0.867 + 100\% \times 0.133}{100\% \times 0.867} = 46.1\%$$

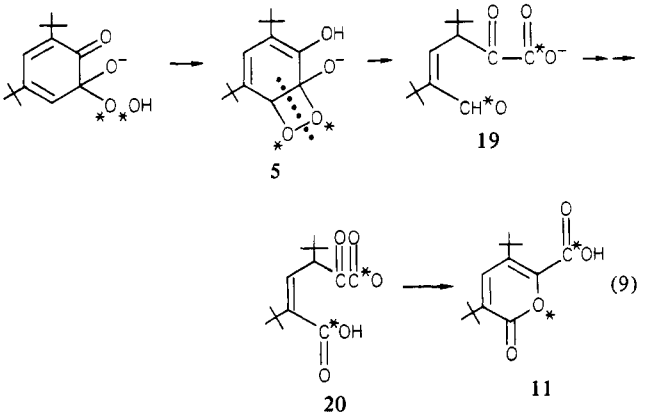
$$\frac{M+4}{M} = \frac{2.35\% \times 0.867 + 30.8\% \times 0.133}{100\% \times 0.867} = 7.07\%$$

All the calculated values in Table III were obtained as shown above.

In the previous studies on substituted benzils,[8] it has been shown that the major reaction is the acyclic Baeyer–Villiger type mechanism. Examination of the product and labeling consequences for the present cyclic 1,2-diketones **3** and **16** leads to the same conclusion.

Although the dioxetane mechanism is simple and attractive, it cannot explain the formation of half-esters (Table I) and the ^{18}O results for the diacids from **16** or **3**, which are far from the expected values (Table III). For example, the observed ^{18}O incorporation values (M + 2 = 25.8% and M + 4 = 2.04%) for diphenic acid are far from the calculated ones (16.4 and 8.4%, respectively) for the dioxetane mechanism (eq 6).

The following alternative cyclic mechanism is also conceivable:



A similar C–C fission scheme was proposed to explain the formation of **11** from KO_2 and **3**.[6a] However, the ^{18}O content from this reaction should be M + 2 = 16.4% and M + 4 = 8.4% according to eq 9, which is inconsistent with the observed values, M + 2 = 32.0% and M + 4 = 5.8%, making the scheme shown in eq 9 unlikely.

On the other hand, the formation of half esters and the ^{18}O contents in products coincide with either the epoxide (eq 7) or the acyclic mechanism (eq 8). The calculated ^{18}O contents according to these two mechanisms agree well with the observed values (Table III). However, the mass spectral results shown in eq 5 clearly eliminate the epoxide mechanism on the basis of the absence of ^{18}O in the decarboxylated ester, as in the previous case for acyclic compounds. Thus, it is concluded that the C–C cleavage proceeds via the acyclic Baeyer–Villiger type mechanism, the same as that of the acyclic diketones.

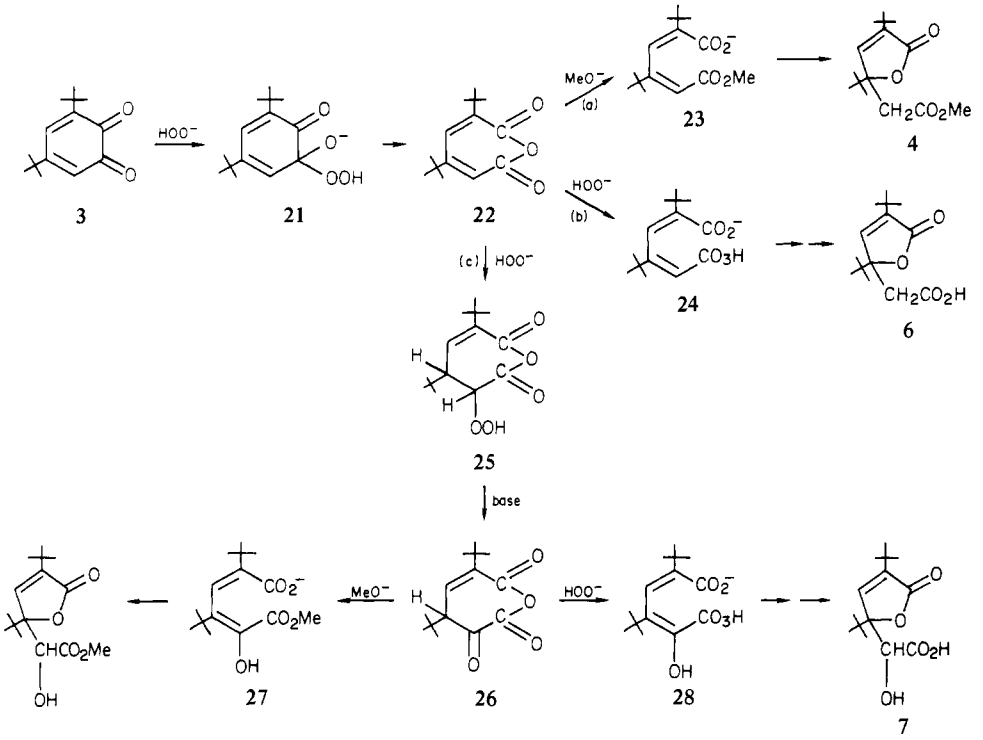
Overall Scheme for Reaction of *o*-Quinone 3. The mechanism for phenanthrenequinone is straightforward, as shown in eq 8. The route to the furanones **4**–**7** from *o*-quinone **3** is somewhat complicated because of many steps involving intramolecular cyclization. Compounds **4**–**7** are reported to be produced in the reaction of **3** with alkaline H_2O_2[7a] or KO_2[6a] and in the photosensitized[13] and base-catalyzed[7b] oxygenation of 3,5-di-*tert*-butylcatechol. It is always true that products formed under neutral conditions do not contain derivatives of α-hydroxy acid **5** or **7**, as in the present case (Table I). The product and ^{18}O labeling results both argue strongly against a cyclic dioxetane mechanism.

The reaction pathways a and b in Scheme II provide simple and attractive explanations for the formation of furanones **4** and **6**. Since the cyclization is complete under the basic conditions, acidic conditions are not required for the lactonization or the intramolecular Michael reaction (**23** → **4**, 24 → **6**). An explanation for the formation of α-hydroxy acid **7** or ester **5** is not so straightforward. The control experiment with **4** (run 8, Table I) indicates that **4** is stable under the reaction conditions and that α-hydroxy ester **5** is not formed from **4**. One possible mechanism is the peroxidation of anhydride **22** (pathway c, Scheme I); base-catalyzed decomposition of **25** would give **26**, leading to **5** or **7**. However, this pathway cannot explain the increased formation of α-hydroxy ester **5** when H_2O_2 is added slowly by dropwise addition. According to Scheme II, a lower concentration of HOO^- should decrease the yield of **5** or **7** and increase ester **4**, which was not the case (see Table I).

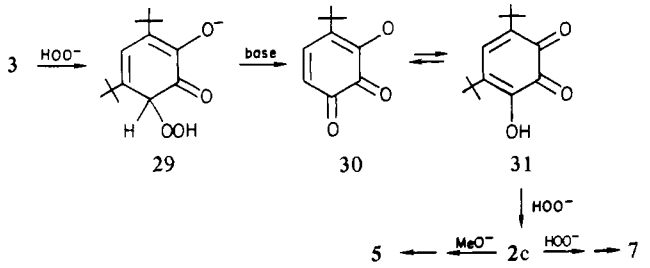
This consideration suggests that Scheme III is a more probable pathway for the formation of α-hydroxy acid **7** and ester **5**. Since α-hydroperoxy ketones are known to be decomposed by base to diketones when an α-hydrogen is available,[14] the base-catalyzed

(13) Matsuura, T.; Matsushima, H.; Kato, S.; Saito, I. *Tetrahedron* **1972**, *28*, 5119.

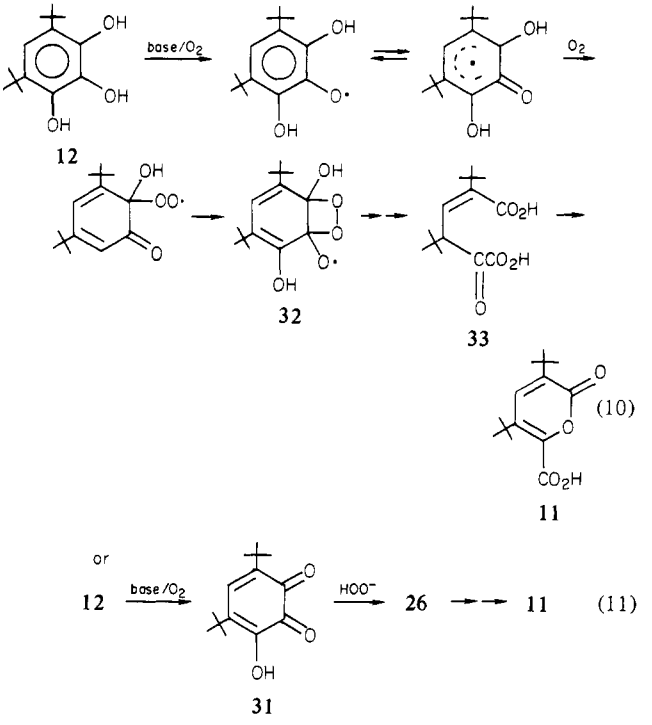
Scheme II



Scheme III



Scheme IV



conversion of adduct **29** into **30** is possible. Diketone **31** would be easily oxidized by HOO^- to anhydride **26**, followed by the attack of MeO^- or HOO^- affording ester **5** or acid **7**. The last steps from **26** are the same as in pathway c in Scheme II. The key step in Scheme III is the reaction of *o*-quinone **3** with HOO^-, which may explain why muconic acids were not obtained from HOO^- and *o*-benzoquinone (**14**) or 1,2-naphthoquinone (**13**) (Table II), although they are stable under the reaction conditions.

Autoxidation of Pyrogallol. In the base-catalyzed autoxidation of polyphenols, it is an interesting problem to determine whether the C–C cleavage proceeds via an intermediate formed by addition of O_2 to a phenoxy radical (e.g., **32** in eq 10) or via the reaction of H_2O_2, formed in the reaction (Scheme IV). Previous studies[7b,15] have given no clear answer to this question. The results of the study using $^*O_2$ or $H_2{}^*O_2$ (Table III) clearly indicate that the incorporated oxygen in product **11** is not from O_2 but from $H_2{}^*O_2$. Since H_2O_2 is easily formed from O_2 and phenolate,[16] it is reasonable that the C–C cleavage proceeds via an intermediate *o*-quinone and HOO^-. Thus, in the base-catalyzed autoxidation of polyphenols, the C–C cleavage also proceeds via the acyclic mechanism involving diketone (eq 11) rather than a cyclic one such as eq 10. As suggested by Nishinaga et al.,[7b] the interconversion **11** → **33** → **7** probably occurs, but ^{18}O exchange with solvent H_2O does not occur, since these acids are in the form of carboxylate anions under the alkaline conditions used.

Relation to Dioxygenase Cleavages. Although di-*tert*-butyl-*o*-quinone (**3**) gives a substantial amount of C–C cleavage products, the reaction of unsubstituted *o*-benzoquinone or 1,2-naphthoquinone with alkaline H_2O_2 did not afford the corresponding muconic acids (Table II). Moreover, the reaction of *o*-benzoquinone **14** with H_2O_2 at −40 °C gave only 5–15% of muconic acid, dimeric products being major.[10] On the contrary, enzymatic reactions[1] and a model reaction for catechases[4,5] give

(14) (a) Bailey, E. J.; Barton, D. H. R.; Elbs, J.; Templeton, J. F. *J. Chem. Soc.* **1962**, 1578. (b) Biellmann, J. F.; Rajic, M. *Bull. Soc. Chim. Fr.* **1962**, 441. (c) Hanna, R.; Ourisson, G. *Ibid.* **1967**, 3742.

(15) (a) Campbell, T. W.; Coppinger, G. M. *J. Am. Chem. Soc.* **1951**, *73*, 2708. (b) Campbell, T. W. *Ibid.* **1951**, *73*, 4190. (c) Schulze, V. H.; Flaig, W. *Liebigs Ann. Chem.* **1952**, *575*, 231.

(16) See, for example: Ogata, Y.; Kosugi, Y.; Nate, N. *Tetrahedron* **1971**, *27*, 2905.

a high yield of muconic acid or its ester. A ternary complex of enzyme or metal, catechol, and molecular oxygen is presumably involved in these reactions and is probably the origin of the high selectivity in enzymatic reactions. These facts suggest that no scheme for the enzymatic reaction will be complete without considering metal complexing. It is clear from these results that these nonenzymatic reactions do *not* provide an adequate model for the dioxygenase system, since the labeling results are *different*. In contrast to the present systems, the dioxygenase products incorporate *both* oxygen atoms from one molecule of molecular oxygen.

Experimental Section

Melting points are corrected. NMR spectra were recorded on a Varian Model T-60, and mass spectra on an AEI MS-9 (organics) and on a Consolidated Electrodynamics 21-620 mass spectrometer (O_2). Mass spectral data were analyzed as described previously.[8] GLC analysis was performed on a HP Model 5720A, using a 50-cm column packed with 10% UC W982 on Chromosorb W and a 75-cm column packed with Carbowax 20M on Anachrom. Bibenzyl or *p*-chlorobenzophenone was used as an internal standard. Carboxylic acids were determined by GLC after methylation with diazomethane.

Materials. *o*-Quinones **3**, **13**, and **16** were from commercial sources. *o*-Benzoquinone[17] and 4,6-di-*tert*-butylpyrogallol (**12**)[18] were synthesized according to literature procedures. Preparation of labeled $H_2{}^*O_2$ has been described previously;[8] the $H_2{}^*O_2$ contained M + 2 = 16.4% and M + 4 = 8.4% excess, and $^*O_2$ gas had M + 2 = 8.22% and M + 4 = 4.17% excess.

Reaction of Phenanthrenequinone 16 with $H_2{}^*O_2$. To a stirred mixture of **16** (0.271 g, 1.25 mmol), 2 M NaOH (1.25 mL, 2.5 mmol), THF (15 mL), and MeOH (15 mL) was added dropwise 0.5 M $H_2{}^*O_2$ (2.5 mL, 1.25 mmol) for 5 min, and the mixture was stirred for 5 min. After dilution with aqueous NaCl, unreacted quinone and traces of neutral products were extracted with ether. The aqueous solution was then neutralized by adding 1 N HCl (2.5 mL, 2.5 mmol) and extracted with ether. After drying with Na_2SO_4, solvent was evaporated under reduced pressure; the addition of CH_2Cl_2 (20 mL) caused crystallization of diphenic acid (**18**), which was recrystallized from MeOH/H_2O (1:2), affording a 20% yield of a pure sample: mp 223–226 °C.

Monomethyl diphenate (**17**) was obtained from the CH_2Cl_2 solution, from which diphenic acid was removed by crystallization after 20 min of standing. Crystallization of the half ester was started by rubbling the wall of the vessel with a spatula to afford half ester **17** in 25% yield, and recrystallization from MeOH/H_2O (1:2) gave crystals: mp 107–108.5 °C (lit.[19] mp 110 °C); mass spectral analysis was done as described previously.[8]

Reaction of 3,5-Di-*tert*-butylbenzoquinone (3) with $H_2{}^*O_2$. To a mixture of *o*-quinone **3** (0.275 g, 1.25 mmol), 2 N NaOH (1.25 mL, 2.5 mmol), and MeOH (30 mL) was added dropwise (5 min) 0.5 M $H_2{}^*O_2$ (3 mL, 1.5 mmol), and the mixture was stirred for 5 min. After dilution with aqueous NaCl, extraction with ether gave a crude sample of 3,5-di-*tert*-butyl-5-((methoxycarbonyl)hydroxymethyl)-2-furanone (**5**), which was recrystallized from hexane in 36% yield: mp 104–105 °C (lit.[6a] mp 103–105 °C). In the first filtrate, a small amount of 3,5-di-*tert*-butyl-5-((methoxycarbonyl)methyl)-2-furanone (**4**) could be detected by GLC and mass spectrum.

The aqueous layer was acidified with 1 N HCl (2.5 mL, 2.5 mmol); ether extraction gave crude acid **7**, which was methylated with diazomethane and crystallized from hexane, affording the methyl ester of **7** in 10% yield: mp 103–105 °C. The results of mass spectral analysis of these products are shown in Table III.

Reaction of 4,6-Di-*tert*-butylpyrogallol (12) with $H_2{}^*O_2$. Oxygen was bubbled into a solution of pyrogallol **12** (0.12 g, 0.5 mmol), 2 N NaOH (1 mL, 2 mmol), and 0.5 M $H_2{}^*O_2$ (2 mL, 1 mmol) in 10 mL MeOH for 20 min. After dilution with aqueous NaCl, traces of neutral products were extracted with ether; the aqueous solution was neutralized with 1 N HCl and extracted with ether. Drying over Na_2SO_4, evaporation of the ether, and crystallization from benzene/hexane (1:1) gave 3,5-di-*tert*-butyl-2-pyrone-6-carboxylic acid (**11**) in 47% yield: mp 192–194 °C (lit.[15b] mp 203–205 °C); NMR ($CDCl_3$) δ 1.32 (s, 9 H), 1.35 (s, 9 H), 3.86 (s, 3 H), 7.28 (s, 1 H).

The reaction of pyrogallol **12** under $^*O_2$ in the presence or absence of H_2O_2 was carried out in a similar manner, except that $^*O_2$ gas was introduced in a closed 10-mL flask with a septum, the scale being half of the above reaction, and stirred vigorously for 20 min. The mass spectral results are listed in Table III.

Reaction of 1,2-Naphthoquinone (13) with H_2O_2 in Aqueous Formic Acid. *o*-Quinone **13** (0.396 g, 2.5 mmol) was dissolved in 88% formic acid (30 mL), and 3% H_2O_2 (5 mL, 5 mmol) was added. After standing for 1 h, precipitated acid was filtered and washed with water and methanol to give a pure sample of *o*-carboxyallocinnamic acid (**15**) in 54% yield: mp 204–207 °C dec (lit.[20] mp 198–203 °C).

Registry No. 3, 3383-21-9; **12**, 3934-77-8; **13**, 524-42-5; **16**, 84-11-7; H_2O_2, 7722-84-1; oxygenase, 9037-29-0; SDS, 151-21-3; CTAC, 112-02-7; Brij-35, 9002-92-0; acetone, 67-64-1; acetaldehyde, 75-07-0; 2-butanone, 78-93-3; biphenyl, 92-52-4; 4,4'-dimethylbiphenyl, 613-33-2.

(17) Dyer, E.; Baudish, O. *J. Biol. Chem.* **1932**, *95*, 483.
(18) Schulz, V. H.; Flaig, W. *Liebigs Ann. Chem.* **1952**, *575*, 231.
(19) Graebe, C.; Aubin, C. *Liebigs Ann. Chem.* **1888**, *247*, 267.
(20) Boeseken, J.; Sloof, G. *Recl. Trav. Chim. Pays-Bas* **1930**, *49*, 91.