

## The Epoxidation and Cleavage of $\alpha,\beta$ -Unsaturated Ketones with Alkaline Hydrogen Peroxide

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Received September 10, 1969

The kinetics of the reaction between 4-phenyl-3-buten-2-one and aqueous alkaline hydrogen peroxide were studied. Four reactions occur in this system: epoxidation by hydroperoxide ion to form 4-phenyl-3,4-epoxy-2-butanone, oxidative cleavage of the epoxide by hydroperoxide to give benzaldehyde, retrograde aldol reaction, and cleavage of the epoxide by hydroxide. The rates of these reactions in water at 25° are 0.22, 0.05, 0.00016, and 0.0032 l. mol<sup>-1</sup> sec<sup>-1</sup>, respectively. The influence of substituents in the phenyl ring on reaction rates and the relative reactivities of hydroperoxide and hydroxide ions are discussed in terms of the reaction mechanisms. The oxidative cleavage of  $\alpha,\beta$ -epoxy ketones is mechanistically similar to several recently reported fragmentation reactions. The cleavage reaction was shown to have general synthetic utility in preparing diacids, keto acids, and ketones from  $\alpha,\beta$ -unsaturated ketones,  $\alpha,\beta$ -unsaturated aldehydes, and  $\beta$  diketones.

Treatment with alkaline hydrogen peroxide is the standard method for converting  $\alpha,\beta$ -unsaturated ketones into  $\alpha,\beta$ -epoxy ketones.<sup>1</sup> Our knowledge of the mechanism of this reaction is largely due to the work of Bunton and Minkoff.<sup>2</sup> The observed second-order kinetics and the rate-decreasing effect of methyl substituents at the double bond suggested that the rate-determining step is Michael addition of the hydroperoxide ion to the carbon-carbon double bond. Stereochemical studies also support this mechanism.<sup>3</sup> No general considerations of the reactions of the epoxide products under epoxidation conditions have been reported. In fact, standard references present  $\alpha,\beta$ -epoxy ketones as being stable under basic epoxidation conditions.<sup>4</sup>

We report here additional information on the epoxidation mechanism, along with the rates and probable mechanisms of several competing reactions which occur under epoxidation conditions.  $\alpha,\beta$ -Epoxy ketones undergo oxidative cleavage under these conditions. This reaction has synthetic utility and is mechanistically related to several other recently reported fragmentation reactions.

### Results

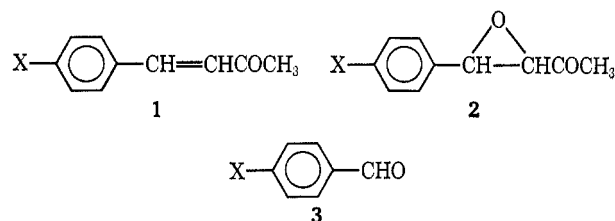
**Kinetics.**—Bunton and Minkoff<sup>2</sup> found that the epoxidation of 3-penten-2-one and 4-methyl-3-penten-2-one with aqueous alkaline hydrogen peroxide obeyed the rate equation

$$\text{initial rate} = k[\text{ketone}][\text{HOO}^-]$$

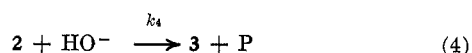
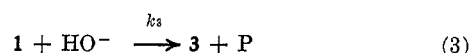
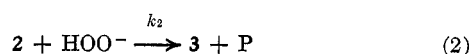
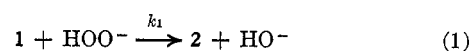
Although the kinetics apparently deviated from second order after long reaction times, these workers did not consider possible side reactions or reactions following the epoxidation.

Our initial results with 4-phenyl-3-buten-2-one (benzalacetone, 1a) indicated that the reaction was not simply conversion of the  $\alpha,\beta$ -unsaturated ketone into the epoxide. Ultraviolet spectra recorded during a typical run are shown in Figure 1. The intense ketone absorption at 290 nm decreases regularly with time, while the combined ketone and epoxide maximum

near 225 nm decreases much more slowly, as expected for formation of epoxide with disappearance of ketone. However, the lack of a simple isosbestic point near 250 nm and the subsequent appearance of a strong peak in this region accompanied by the disappearance of the epoxide 225-nm maximum show that the epoxide is being converted into a new product. This product was identified as benzaldehyde by ultraviolet and infrared spectroscopy, boiling point, and preparation of the *p*-nitrophenylhydrazone derivative. Analysis of the spectra shown in Figure 1 and other spectra recorded during this run shows that the concentrations of the three species vary as shown by the points in Figure 2. Kinetic and stoichiometry studies, discussed later in detail, indicated that reactions 1–4



a, X = H; b, X = Cl; c, X = OCH<sub>3</sub>



take place in this system, where 1 =  $\alpha,\beta$ -unsaturated ketone, 2 = epoxide, 3 = benzaldehyde, and P represents cleavage products containing three carbon atoms. Reaction 1 is the expected epoxidation reaction. Most of the benzaldehyde is produced by the epoxide fragmentation (reaction 2). Some benzaldehyde is also produced by reaction 3, the retrograde aldol reaction, and by cleavage of the epoxide by base (reaction 4). Reactions 3 and 4 are orders of magnitude slower than 1 and 2.

For a complete kinetic treatment of this system, the rapid degradation of product P must also be considered. Stoichiometry studies suggest that the de-

(1) E. Weitz and A. Scheffer, *Chem. Ber.*, **54**, 2327 (1921).

(2) C. A. Bunton and G. J. Minkoff, *J. Chem. Soc.*, **1949**, 665.

(3) H. O. House and R. S. Ro, *J. Amer. Chem. Soc.*, **80**, 2428 (1958); H. E. Zimmerman and G. A. Zimmerman, Abstracts, 149th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1965, p 8P.

(4) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley & Sons, Inc., New York, N. Y., 1967, p 466.

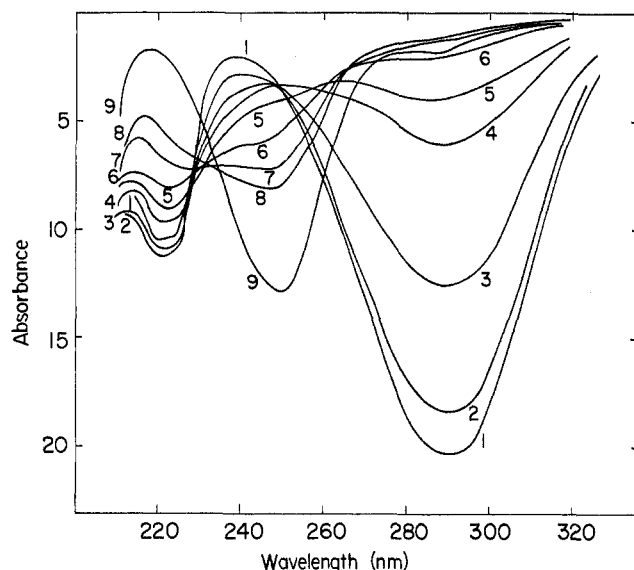


Figure 1.—Spectra recorded during reaction of benzalacetone (initially 0.001075 *M*) with hydrogen peroxide (0.00497 *M*) and sodium hydroxide (0.00644 *M*) in water at 25°. Spectra were recorded at the following times (in seconds): 1, 0; 2, 320; 3, 1020; 4, 2480; 5, 3700; 6, 7130; 7, 12,600; 8, 21,100. Spectrum 9 is a spectrum of 0.001075 *M* benzaldehyde.

struction of P consumes *ca.* 1 equiv each of base and peroxide, as in reaction 5.



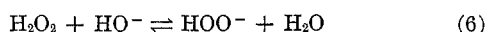
The total titrable base ( $\text{HO}^- + \text{HOO}^-$ ) stoichiometry results shown in Table I indicate that *ca.* 2 mol of base are used up for every 1 mol of epoxide converted into aldehyde. This agrees with the stoichiometry required by reactions 2 (or 4) and 5. Product Q has not been identified, but by stoichiometry is likely an equimolar mixture of  $\text{HCOO}^-$  and  $\text{CH}_3\text{COO}^-$ .

TABLE I  
BASE STOICHIOMETRY IN REACTION 2<sup>a</sup>

Time, sec	$\Delta[2a]^b$	$\Delta[3a]^b$	$\Delta[\text{NaOH}]^b$	$\Delta[\text{NaOH}]/\Delta[2a]$	$\Delta[\text{NaOH}]/\Delta[3a]$
330	3.51	2.81	7	2.0	1.8
500	5.05	4.49	9	1.8	2.0
990	5.90	6.36	14	2.4	2.2
1090	6.05	6.74	14	2.3	2.1
1480	7.39	6.65	17	2.3	2.6
1570	6.95	7.55	17	2.4	2.2
2000	7.40	7.38	19	2.6	2.6
2180	7.78	7.96	19	2.4	2.4
2600	8.25	7.49	20	2.4	2.7
3120	7.94	7.63	21	2.5	2.6
				2.3	2.3
				(avg)	(avg)

<sup>a</sup> In water at 25.0°. Initial concentrations: 2a,  $9.30 \times 10^{-4}$  *M*;  $\text{H}_2\text{O}_2$ ,  $4.07 \times 10^{-2}$  *M*; NaOH,  $1.68 \times 10^{-2}$  *M*. <sup>b</sup>  $\Delta[X]$  is the change in concentration of compound X at the time given. All values are  $10^{-4}$  *M*.

The hydrogen peroxide acid-base equilibrium (reaction 6) must also be included in the kinetic scheme. The equilibrium constant for reaction 6 can be ob-



tained from literature data:  $K_6 = K_p/K_w = 222$ , where  $K_p$  is the ionization constant of hydrogen per-

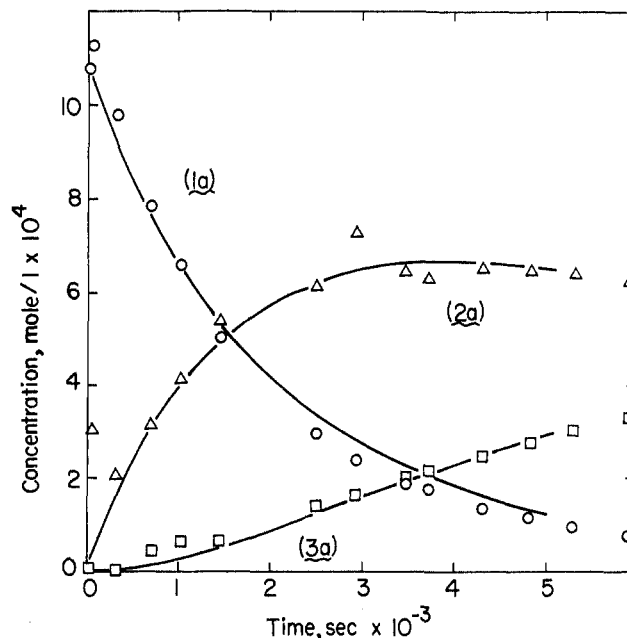
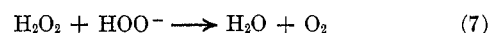


Figure 2.—Zero-order kinetic plot of the run shown in Figure 1. The symbols are experimental points. The solid lines are calculated as described in text: 1a,  $\circ$ ; 2a,  $\triangle$ ; 3a,  $\square$ .

oxide ( $2.24 \times 10^{-12}$ )<sup>5</sup> and  $K_w$  is the self-ionization constant of water. Finally, the base-catalyzed decomposition of hydrogen peroxide (reaction 7) cannot be ignored in our system. The value of  $k_7$  in control



runs averaged *ca.*  $5 \times 10^{-3}$  l. mol<sup>-1</sup> sec<sup>-1</sup>. Fast, irregular peroxide decomposition rates were occasionally encountered, probably owing to adventitious catalytic impurities. Kinetic runs in which such rapid decomposition was evident were discarded.

The complete set of differential equations describing reactions 1–5 and including the acid–base equilibrium of reaction 6 cannot be solved explicitly and subjected to the usual kinetic analysis. However, the rates of reactions 3 and 4 can be determined accurately, independent of the other processes. The rate constants obtained for the reaction of hydroxide ion with  $\alpha,\beta$ -unsaturated ketones 1a–1c and with the epoxide 2a are given in Table II. Adherence to second-order kinetics was excellent in every case, and ultraviolet spectra showed that the corresponding aldehyde, 3a–3c, was always the reaction product.

Rough estimates of the rate constants for reactions 1 and 2 can be obtained from pseudo-first-order (in 1 or 2) plots or second-order (in 1 or 3 and hydroperoxide) plots of kinetic data from runs with peroxide, base, and compound 1 or 2 initially present. The averages of several runs suggested that  $k_1$  was *ca.* 0.3 in the a series, 0.4 in the b series, and 0.1 in the c series, and that  $k_2$  was *ca.* 0.03 in the a series (all rate constants in l. mol<sup>-1</sup> sec<sup>-1</sup>). These values were refined and the validity of the entire reaction scheme was checked through the use of a computer simulation technique. An analog model of the proposed scheme was set up on an IBM 360/44 computer using a modified IBM

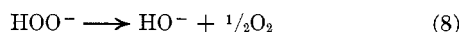
(5) M. G. Evans and N. Uri, *Trans. Faraday Soc.*, **45**, 224 (1949).

TABLE II  
RATES OF REACTIONS 3 AND 4.  
CLEAVAGE OF UNSATURATED KETONES (1) AND  
EPOXIDES (2) BY HYDROXIDE ION<sup>a</sup>

Substrate	Initial concn, —mol/l. $\times 10^2$ —		Rate constant, —l. mol <sup>-1</sup> sec <sup>-1</sup> $\times 10^4$ —	
	Substrate	NaOH	$k_3$	$k_4$
1a	0.524	17.2	1.40	...
1a	0.685	25.2	1.76	...
1a (avg)			1.6	
2a	0.730	17.2	...	33
2a	0.620	25.2	...	29.8
2a	0.688	11.2	...	32.2
2a (avg)				32
1b	0.668	25.2	5.27	...
1b	0.445	25.2	7.09	...
1b (avg)			6.2	
1c	0.775	25.2	1.94	...
1c	0.388	31.5	1.78	...
1c (avg)			1.9	

<sup>a</sup> In water at 25.0°.

Continuous System Modeling Program (CSMP).<sup>6</sup> Reactions 1–7 were included in the model system, with the exception that reaction 7 was replaced for simplicity by a pseudo-reaction, 8. The accurately known rate and equilibrium constants discussed previously were used in the CSMP without modification. Reaction 5



was assigned an arbitrary rapid rate,  $k_5 = 1.0 \text{ l. mol}^{-1} \text{ sec}^{-1}$ . It was found that  $k_3 = 1.0 \times 10^{-5} \text{ sec}^{-1}$  worked well in most cases to account for peroxide disappearance; this would typically be equivalent to *ca.*  $5 \times 10^{-8} \text{ l. mol}^{-1} \text{ sec}^{-1}$  for  $k_7$ . Starting with the estimated values given above,  $k_1$  and  $k_2$  were varied systematically until the CSMP-calculated concentration–time data agreed with the observed concentrations of compounds 1–3 (compounds 1 and 3 only in the **b** and **c** series). The rate constants which give the best fit to data from several different kinetic runs are given in Table III. A typical fit of calculated

TABLE III  
RATES OF REACTIONS 1 AND 2.  
REACTION OF HYDROPEROXIDE ION WITH  
UNSATURATED KETONES (1) AND EPOXIDES (2)<sup>a</sup>

Series <sup>b</sup>	Rate constant, l. mol <sup>-1</sup> sec <sup>-1</sup>	
	$k_1$	$k_2$
a	0.22	0.05
b	0.28	0.06
c	0.08	0.03

<sup>a</sup> In water at 25.0°. <sup>b</sup> Series a, unsubstituted benzalacetone; b, *p*-chloro; c, *p*-methoxy.

to experimental data is shown by the solid lines in Figure 2. Peroxide and total base concentrations calculated using the constants in Tables II and III are in satisfactory agreement with the observed values.<sup>7</sup>

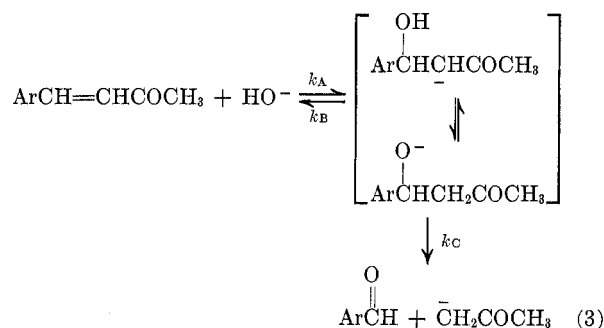
(6) International Business Machines Corp., "1130 Continuous System Modeling Program (1130-CX-13X) Program Reference Manual," IBM No. H20-0282-0, White Plains, N. Y., 1966.

(7) For examples of the use of similar computer techniques for determining rate constants in complex reactions, see D. F. DeTar, *J. Amer. Chem. Soc.*, **89**, 4058 (1967); J. E. Leffler and R. D. Temple, *ibid.*, 5235 (1967).

**Mechanism and Substituent Effects.**—Our results are consistent with a mechanism for reaction 1 which involves nucleophilic addition of perhydroxide ion to the activated double bond of the  $\alpha,\beta$ -unsaturated ketone as the rate-determining step. This is essentially the mechanism outlined by earlier investigators,<sup>2,3</sup> and is very similar to the Michael addition of various other nucleophiles to activated double bonds, including the retrograde aldol reaction (3). A close inspection of the rate constants given in Tables II and III, however, reveals some apparent anomalies which call for a detailed discussion of the rates and mechanisms of reactions 1–4.

The logarithms of the three rate constants (series a–c) for reaction 1 correlate roughly with the Hammett  $\sigma$  values<sup>8</sup> of the *para* substituents, with a slope ( $\rho$  value) of *ca.* +1.2. This value suggests that considerable negative charge is developed in the neighborhood of the double bond on passing from reagents to transition-state species, and is thus consistent with the suggested mechanism. Rate constants for reaction 2 are also correlated roughly, with a  $\rho$  value of *ca.* +0.6. With reaction 3, however, the straight-line correlation breaks down completely: the order of reactivity is  $\text{H} < p\text{-OCH}_3 < p\text{-Cl}$  instead of  $p\text{-OCH}_3 < \text{H} < p\text{-Cl}$  as required by the Hammett relationship. Since we have suggested that reactions 1 and 3 are similar, yet substituent effects are different, an apparent anomaly exists.

The problem is readily resolved by considering the details of the mechanism. The retrograde aldol reaction (3) is represented in more detail by the following scheme.



By applying the steady-state approximation (*i.e.*,  $k_A \ll k_B + k_C$ ) to the enolate intermediate, it can easily be shown that the observed second-order rate constant,  $k_3$ , is a composite given by

$$k_3 = \frac{k_A k_C}{k_B + k_C}$$

From this relationship it can then be shown that the observed  $\rho$  value is also a composite given by

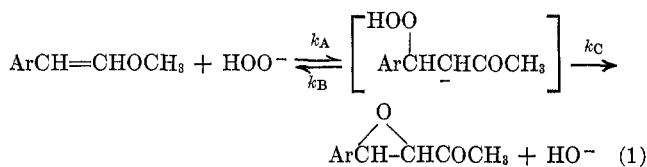
$$\rho_3 = \rho_A + \rho_C - \delta_R \log(k_B + k_C)$$

where  $\delta_R$  is the substituent stabilization operator.<sup>8</sup> A complex  $\rho$  of this type is not in general a constant; instead, in the case in which  $k_B \geq k_C$ , a U-shaped Hammett plot should result. Since we have only three data points, a detailed consideration of substituent effects on the rate of reaction 3 would be inappropriate, but

(8) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York, N. Y., 1963.

the points can clearly be placed on a U-shaped  $\rho$ - $\sigma$  plot.<sup>9</sup>

The epoxidation reaction (1) is similarly represented by the following mechanism.

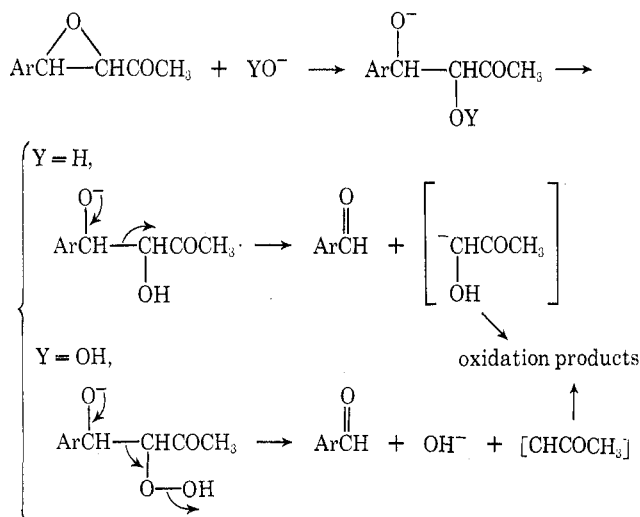


The observed  $k_1$  and  $\rho$  values are again composites, as in reaction 3. The results become explicable if we postulate that  $k_B \ll k_C$ , instead of  $k_B \geq k_C$  as suggested for reaction 3. It is reasonable that  $k_C/k_B$  for reaction 1 should be larger than for reaction 3. Other workers<sup>10</sup> have suggested that the elimination of hydroxide from  $\beta$ -hydroxy ketone carbanions (analogous to the  $k_B$  step in reaction 3) is rapid relative to retro aldol cleavage (the  $k_C$  step in reaction 3). The intramolecular displacement of  $\text{HO}^-$  ( $k_C$ ) in reaction 1 should be easier than the carbon-carbon bond cleavage in reaction 3, and  $k_C$  in reaction 1 does not depend on the position of an intermediate prototropic equilibrium as it does in reaction 3. If  $k_B \ll k_C$ , the expression for  $\rho_1$  can be simplified as follows.

$$\begin{aligned} \rho_1 &= \rho_A + \rho_C - \delta_R \log (k_B + k_C) \\ &\cong \rho_A + \rho_C - \delta_R \log k_C = \rho_A \end{aligned}$$

The Hammett plot for reaction 1 should then be approximately rectilinear, as observed.

Another apparent anomaly appears when we compare the relative reactivities of hydroxide and perhydroxide, respectively, with substrates **1a** and **2a**. The relative reactivity with **1a** is  $k_1/k_3 = 1400$ , while with **2a** it is  $k_2/k_4 = 16$ . The relative reactivities of  $\text{HOO}^-$  and  $\text{HO}^-$  can vary widely with substrate,<sup>11</sup> but a



(9) A referee has suggested as an alternative explanation that the *p*-methoxy compound is oxidized more rapidly owing to a competing Dakin or Baeyer-Villiger reaction. This possibility is ruled out by product analysis. No *p*-methoxyphenol, *p*-methoxyphenylacetic acid, or *p*-methoxycinnamic acid was found, though as little as a few per cent of any one could easily have been detected (nmr).

(10) M. F. Zinn, T. M. Harris, D. G. Hill, and C. R. Hauser, *J. Amer. Chem. Soc.*, **85**, 71 (1963); B. W. Rockett, T. M. Harris, and C. R. Hauser, *ibid.*, **85**, 3491 (1963); J. Warkentin and L. K. M. Lam, *Can. J. Chem.*, **42**, 1676 (1964).

TABLE IV  
PRODUCTS FROM THE REACTION OF  $\alpha,\beta$ -UNSATURATED  
CARBONYL COMPOUNDS WITH ALKALINE HYDROGEN PEROXIDE

Compd	Product <sup>a</sup>	Yield, % <sup>b</sup>
2-Cyclohexen-1-one	Glutaric acid	72
1-Acetyl-1-cyclohexene	Adipic acid	67
Isophorone	3,3-Dimethyl-5-keto- hexanoic acid	84
Pulegone	3-Methyladipic acid	60
Verbenone	Pinonic acid <sup>c</sup>	85
Citral	2-Methyl-2-hepten-6-one	77 <sup>d</sup>
5,5-Dimethyl-1,3- cyclohexanedione	3,3-Dimethylglutaric acid	80

<sup>a</sup> Reaction conditions and product identification are given in the Experimental Section. <sup>b</sup> No attempt to optimize yield was made in most cases. <sup>c</sup> Mixture of *cis* and *trans* isomers, *ca.* 1:1. <sup>d</sup> By gas chromatography.

factor of 100 seems excessive for reactions postulated to be similar. We suggest that  $k_2/k_4 = 16$  for the epoxide cleavage is of the order of magnitude of a "normal" reactivity ratio,<sup>12</sup> and that the mechanisms of reactions 2 and 4 are in fact very similar.

The high  $k_1/k_3$  ratio can be accounted for by the suggested complex nature of the measured rate constants. As postulated for reaction 1,  $k_B \ll k_C$ , and

$$k_1 = \frac{k_A k_C}{k_B + k_C} \cong \frac{k_A k_C}{k_C} = k_A$$

so the observed rate is a good approximation for the actual rate of nucleophilic attack by  $\text{HOO}^-$  on the unsaturated ketone. For reaction 3, however,  $k_B$  is approximately equal to or greater than  $k_C$ , and the observed rate constant  $k_3 = k_A k_C / (k_B + k_C)$ , which can be much smaller than  $k_A$  itself. We thus attribute the large  $k_1/k_3$  ratio to the contribution of the factor  $k_C / (k_B + k_C)$  to  $k_3$ .

**Scope and Synthetic Utility.**—The epoxidation and cleavage sequence of reactions 1 and 2 seems to be a general one and to have synthetic utility. A variety of  $\alpha,\beta$ -unsaturated aldehydes and ketones (Table IV) were converted in good yield into the products expected on the basis of this sequence. 1,3 diketones react similarly, presumably *via* epoxidation of the enol.

The alkaline hydrogen peroxide epoxidation-cleavage reaction has advantages over the use of base alone (reaction 3), which sometimes yields the same products. For example, the cleavage of citral to 2-methyl-2-hepten-6-one in 1 *M* aqueous methanolic sodium hydroxide at 25° is *ca.* 50 times faster when the solution is made 1 *M* in hydrogen peroxide. In addition, the reaction mixture assumes a deep yellow color when base alone is used, while no noticeable colored by-products are formed when peroxide is present.

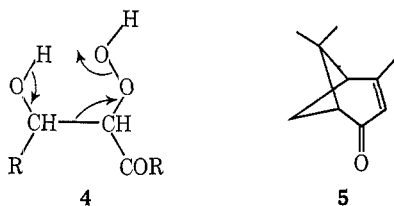
The alkaline peroxide treatment often yields products different from those obtained on cleavage with base alone. Cleavage by peroxide of the  $\alpha$ -dicarbonyl compounds obtained on initial oxidative epoxide cleavage is an obvious example. Treatment of  $\alpha,\beta$ -epoxy ketones with base often leads to products of benzylic

(11) (a) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 18 (1962). (b) R. G. Pearson and D. N. Edgington, *ibid.*, **84**, 4607 (1962).

(12) For example, in the displacement of bromide from benzyl bromide,  $k(\text{HOO}^-)/k(\text{HO}^-) = 34$  (ref 11); from  $\alpha$ -bromo-*p*-toluic acid,  $k(\text{HOO}^-)/k(\text{HO}^-) = 11$  (J. E. McIsaac, Jr., H. A. Mulhausen, and E. J. Behrman, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968).

acid type rearrangement<sup>13</sup> or Favorskii rearrangement,<sup>14</sup> not cleavage as in reaction 2.

The production of pinonic acid from verbenone in high yield probably rules out a cyclic mechanism such as **4** for the cleavage reaction (2). The rigid geometry



of the intermediate *trans*- $\beta$ -hydroxyhydroperoxide derived from verbenone (**5**) precludes a transition state of this type.

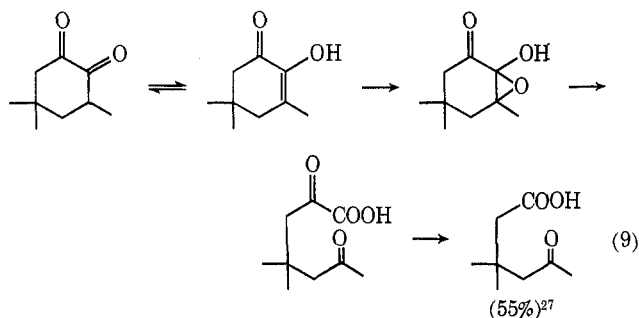
### Discussion

Two groups of workers<sup>15</sup> have observed specific examples of epoxidation-cleavage reaction sequences, one in a keto steroid and one in a cyano olefin. The generality of the reaction, however, has apparently not been appreciated. Two other reactions in which epoxides are cleaved by hydrogen peroxide are reported in the literature. Thus  $\alpha$ -methylstyrene oxide is slowly converted into acetophenone on treatment with alkaline hydrogen peroxide,<sup>16</sup> and 3,4-epoxy-4-methyl-2-pentanone reportedly reacts with hydrogen peroxide without solvent or added base to give acetone, acetic acid, and formic acid.<sup>17</sup> The cleavage with neutral peroxide is surprising.  $\alpha$ -Methylstyrene oxide is not cleaved in the absence of added base,<sup>16</sup> and we also find that little or no cleavage product results from epoxides and hydrogen peroxide alone. An acid-catalyzed analog of reaction 2 has been proposed recently.<sup>18</sup>

In larger context, the mechanism of reaction 2 is typical of a class of heterolytic fragmentation mechanisms reviewed recently.<sup>19</sup> Similar peroxide fragmentations, presumably proceeding by the same mechanism, have been reported in the cases of  $\beta$ -hydroxy peroxides,<sup>20,21</sup>  $\alpha$ -peroxycarboxylic acids,<sup>21,22</sup> the ozonide of an  $\alpha,\beta$ -unsaturated carboxylic acid,<sup>23</sup> and  $\beta$ -amino peroxides.<sup>24</sup> The instability of  $\beta$ -halohydroperoxides

to base has recently been documented also.<sup>25,26</sup> Both elimination and carbon-carbon bond cleavage can occur with these compounds.<sup>26</sup> We suggest that the latter reaction may proceed *via* hydrolysis to the  $\beta$ -hydroxy compound followed by cleavage as in reaction 2.<sup>26b</sup>

Certain  $\alpha$  diketones<sup>27</sup> and  $\beta$ -dicarbonyl compounds<sup>28</sup> reportedly react with alkaline hydrogen peroxide to give cleavage products very much like those obtained from  $\alpha,\beta$ -unsaturated ketones in this work. We suggest that these reactions may proceed *via* epoxidation of the enol followed by oxidative cleavage of the epoxide by hydroperoxide ion (*e.g.*, reaction 9). A similar mechanism could also account for the recently reported oxidative cleavage of phenyl-2-propanone.<sup>29</sup>



### Experimental Section<sup>30</sup>

**Materials.**—Reagents were obtained from commercial sources, with the exceptions of 4-*p*-chlorophenyl-3-buten-2-one (**1b**), bp 105–108° (0.35 mm), mp 58.5–59.5° (lit.<sup>31</sup> mp 59–59.5°), which was prepared by Claisen-Schmidt condensation of *p*-chlorobenzaldehyde with acetone; 4-phenyl-3-epoxy-2-butanone (**2a**), bp 88–90° (0.08 mm), mp 44–45°, mmp 10–15° with 4-phenyl-3-buten-2-one (**1a**) (lit.<sup>1</sup> mp 52–53°), prepared by oxidation of **1a** with alkaline methanolic hydrogen peroxide at 0–5°; and verbenone, obtained from Dr. W. F. Erman of these laboratories. Commercial samples of **1a** and 4-*p*-methoxyphenyl-3-buten-2-one (**1c**) were recrystallized from hexane, mp 41–42° (lit.<sup>32</sup> mp 40–42°) and 74–75.5° (lit.<sup>32</sup> mp 72–74°), respectively. Compounds **1a** and **2a** were the *trans* isomers, as indicated by their nmr spectra: **1a**, vinyl protons at  $\tau$  2.51 and 3.33 (d,  $J = 16$  Hz); **2a**, oxirane protons at  $\tau$  6.05 and 6.58 (d,  $J = 2$  Hz). Hydrogen peroxide (30%, Matheson Coleman and Bell) and sodium hydroxide (Baker Analyzed Reagent) were used without further purification.

**Kinetic Methods.**—In a typical kinetic run, the required amounts of water, aqueous  $\alpha,\beta$ -unsaturated ketone or  $\alpha,\beta$ -epoxy

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ketone solution, and sodium hydroxide solution were pipeted into a volumetric flask immersed in a constant-temperature bath at  $25.0 \pm 0.05^\circ$ . The mixture was shaken and allowed to equilibrate for a few minutes, and then hydrogen peroxide solution was added to initiate the reaction. Samples were withdrawn periodically and analyzed as described in the next section.

Rate constants were first estimated graphically from second-order or pseudo-first-order kinetic plots, then refined by use of the CSMP digital analog simulation technique discussed in the text.

**Analytical Methods.**—Hydrogen peroxide solutions were analyzed titrimetrically with potassium permanganate in acidic solution. In kinetic runs in which peroxide concentration was followed, samples were withdrawn periodically and the titanium-(IV)-hydrogen peroxide complex was determined spectrophotometrically at 405 nm.<sup>38</sup> Base concentration was followed in some runs by titration with standard 0.05 *N* hydrochloric acid.

The organic compounds were determined spectrophotometrically. The ultraviolet spectra of aqueous solutions of the benzalacetones, epoxides, and aldehydes were determined, and extinction coefficients were calculated from the optical densities of at least five different samples of each compound. Adherence to Beer's Law was excellent in every case. The extinction coefficients are given in Table V. The spectra of all three classes of

TABLE V  
EXTINCTION COEFFICIENTS OF COMPOUNDS 1-3

Compd	Wavelength, nm						
	225	250	260	285	290	300	320
1a	8750	2700	...	...	19000	...	...
1b	...	...	5620	...	...	23140	...
1c	...	...	...	8410	...	...	20370
2a	10600	770	...	...	170	...	...
3a	2050	12400	...	...	1270	...	...
3b	...	...	15710	...	...	575	...
3c	...	...	...	15520	...	...	820

compounds (1a-3a) were followed in the a series ( $X = H$ ), and the concentrations of 1 and 3 were followed in the b and c series. Approximate correction for overlapping of the absorption bands was made using a computer program which solves the matrix equation

$$\begin{Bmatrix} A(\lambda_1) \\ A(\lambda_2) \\ A(\lambda_3) \end{Bmatrix} = \begin{Bmatrix} \epsilon(\lambda_1, 1) & \epsilon(\lambda_1, 2) & \epsilon(\lambda_1, 3) \\ \epsilon(\lambda_2, 1) & \epsilon(\lambda_2, 2) & \epsilon(\lambda_2, 3) \\ \epsilon(\lambda_3, 1) & \epsilon(\lambda_3, 2) & \epsilon(\lambda_3, 3) \end{Bmatrix} \begin{Bmatrix} c(1) \\ c(2) \\ c(3) \end{Bmatrix}$$

where  $A$  is the absorbance,  $\epsilon$  is the extinction coefficient,  $c$  is the concentration,  $\lambda$ 's designate three wavelengths, and boldface numerals stand for the three compounds. The wavelengths used with each series of compounds can be inferred from Table V.

**Preparative Oxidation Procedure.**—To a solution of 0.01 mol of the  $\alpha,\beta$ -unsaturated carbonyl compound in 50 ml of methanol,

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12 ml of 30% aqueous hydrogen peroxide and then 30 ml of 1 *N* aqueous sodium hydroxide solution were added with cooling. The mixture was then stirred overnight at 40-50° (1 hr at 40° for the reaction with citral). The resulting solution was evaporated to about half the original volume on a rotary evaporator and then washed with ether. The aqueous solution was made acidic with sulfuric acid, saturated with sodium sulfate, and extracted thoroughly with ether. The extract was treated with  $\text{FeSO}_4$  or  $\text{Na}_2\text{SO}_3$  to destroy peroxides, dried ( $\text{MgSO}_4$ ), and evaporated. The residue, which was essentially pure product, was recrystallized, distilled, or converted into a suitable derivative as outlined below.

**Identification of Products.**—The above treatment converted 2-cyclohexen-1-one into glutaric acid, mp and mmp 94-95°.

1-Acetyl-1-cyclohexene yielded adipic acid, mp and mmp 150-151°.

Isophorone was converted into 3,3-dimethyl-5-ketohexanoic acid, a slightly yellowish oil (lit.<sup>34</sup> mp 28°). This product showed a positive iodoform test and gave a crystalline semicarbazone, mp 167-169° (lit.<sup>34</sup> mp 170-172°).

Oxidation of pulegone gave 3-methyladipic acid. A sublimed sample had a melting point of 86-87.5° (lit. mp 85-89°,<sup>35</sup> 92-94°<sup>36</sup>) and an ir spectrum identical with that reported.<sup>36</sup>

Verbenone was oxidized to a mixture (ca. 1:1) of *cis*- and *trans*-pinonic acid (3-acetyl-2,2-dimethylcyclobutanecarboxylic acid). The nmr spectrum of the noncrystalline product mixture clearly indicated an essentially pure mixture of the two isomers. The most important features were two sets of three methyl singlets:  $\tau$  7.9, 8.5, and 9.0 (*cis* acid) and  $\tau$  7.8, 8.6, and 8.8 (*trans* acid). The spectrum of the authentic *cis* acid<sup>37</sup> has singlets at  $\tau$  7.9, 8.5, and 9.0. The mass spectrum of the methyl ester mixture obtained by treating the acids with diazomethane showed a parent peak at  $m/e$  184 (calcd mol wt 184). Important fragment ions were  $m/e$  169, 152, 141, 124, and 114.

Citral (ca. 40:60 mixture of geranial and neral) yielded 2-methyl-2-hepten-6-one, a colorless liquid with a characteristic odor. The ir and nmr spectra and the gas chromatographic retention time were identical with those of authentic material.

5,5-Dimethyl-1,3-cyclohexanedione was oxidized to 3,3-dimethylglutaric acid, mp and mmp 96-100°.

**Registry No.**—Hydrogen peroxide, 7722-84-1; 1a, 122-57-6; 1b, 3160-40-5; 1c, 943-88-4; 2a, 6249-79-2; 3a, 100-52-7; 3b, 104-88-1; 3c, 123-11-5.

**Acknowledgment.**—The author wishes to acknowledge the capable assistance of Mr. H. H. Lorange in the experimental part of this work.

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