Rates and Scope of the Oxidative Carbon–Carbon Cleavage of Epoxides by Alkaline Hydrogen Peroxide[1]

Yoshiro Ogata,* Yasuhiko Sawaki, and Hideo Shimizu

Department of Applied Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya 464, Japan

Received September 12, 1977

The scope and mechanism for the oxidative C–C cleavage of simple epoxides c-$R_1R_2COCR_3R_4$ with alkaline hydrogen peroxide has been studied. The cleavage occurs with most terminal epoxides ($R_3 = R_4 = H$), but was unsuccessful when R_1 = alkyl and $R_2 = H$, in this case affording the corresponding glycol. The cleavage proceeds via the β-hydroperoxy alcohol, which can be isolated in some cases. Base-catalyzed decomposition of β-hydroperoxy alcohols was studied kinetically. The substituent effect for the concerted fragmentation is explained by (i) an acceleration by the phenyl group via resonance with developing carbonyl, (ii) a possible steric acceleration, and (iii) the effect of acidities of the HOO and HO groups.

Ring-opening reactions of epoxides with nucleophiles have been extensively studied,[2] but reports on peroxides as nucleophiles are relatively limited. The acid-[3] and base-catalyzed[4] additions of hydroperoxides to epoxides have been shown to give β-hydroxy peroxides. Alkaline H_2O_2 cleavage of epoxides from α,β-unsaturated ketones was reported to proceed via a retro-Darzens condensation,[5] but α-methylstyrene oxide is the only simple epoxide reported to give C–C cleavage.[6] Here we wish to report our study on the scope and kinetics of the oxidative cleavage of some other simple epoxides.

Results and Discussion

Reaction of Epoxides with Alkaline Hydrogen Peroxide. The reaction of epoxides **1a–h** (Table I) with excess H_2O_2 was conducted in 70% MeOH containing 0.36 M KOH at 25 °C. The oxidative C–C cleavage occurred with epoxides **1a–d** to afford ketones. When $R_2 = H$, produced aldehyde R_1CHO was oxidized to acid R_1CO_2H (see Table I). No reaction took place for the case of **1e** and **1f**, which indicates no occurrence of S_N2 attack of HOO^- because of the steric retardation by methyl group.

$$R_1R_2C(O)CR_3R_4 \xrightarrow[70\%\ MeOH]{H_2O_2\text{–}KOH} R_1R_2C{=}O \qquad (1)$$

1

The reaction of **1g** and **1h** affords β-hydroperoxy alcohols, **2g** ($R_1 = n$-Pr; R_2 = Me; $R_3 = R_4 = H$) and **2h** ($R_1 = n$-C_7H_{15}; $R_2 = R_3 = R_4 = H$), respectively, together with other products. Interestingly, in spite of the occurrence of C–C cleavage with **2g**, peroxide **2h** is only converted slowly to 1,2-glycol. Likewise, cyclohexene oxide gave only cyclohexane 1,2-glycol after prolonged reaction.

$$R_1R_2C(O)CR_3R_4 \xrightarrow[S_N2]{H_2O_2\text{–}KOH} R_1R_2C(HO)CR_3R_4(OOH) \qquad (2)$$

1 2

The rates of disappearance of 1 were followed by NMR and/or GLC analysis. The relative rates are in the order **1h** > **1b** > **1a** > **1d** ≫ **1e, 1f**, which reflects the steric retardation by α substituents (R_3 and R_4) and also by β substituents (R_1 and R_2) in the S_N2 attack of HOO^- on the right side carbon of epoxide.

These results suggest that this kind of cleavage of epoxides is not always general but seems to be effective for terminal epoxides ($R_3 = R_4 = H$) except when R_1 = alkyl and $R_2 = H$ (e.g., **1h**).

Base-Catalyzed Reaction of β-Hydroperoxy Alcohols. In order to study the base-catalyzed decomposition of **2**, some other β-hydroperoxy alcohols were synthesized by the trifluoroacetic acid-catalyzed addition of H_2O_2 to epoxides. Here, the course of addition was normal and gave the adduct **3** as the

$$R_1R_2C(O)CH_2 + H_2O_2 \xrightarrow[Et_2O,\ reflux]{CF_3CO_2H} R_1R_2C(OOH)CH_2OH \qquad (3)$$

1 3

only product. These structures were identified by NMR and by comparison with authentic glycols after reduction with KI.

The rates and products from the base-catalyzed decomposition of **2** and **3** are listed in Table II. In most cases the fission of C–C and O–O bonds occurred to give high yields of ketones; **3b** gave benzaldehyde instead of benzoic acid in contrast to the cleavage of epoxide **1b** with excess H_2O_2 (see Table I). But the peroxy alcohols **2h** and **3h** were only converted to the same glycol without any C–C fission. This slow conversion to glycol is the homolytic decomposition of the hydroperoxide. The homolysis is assumed, since H_2O_2 itself decomposes also gradually evolving O_2 under the same condition, which is significantly reduced by addition of EDTA.

The rate for **3a** increases with increasing [KOH] and approaches a constant value (Figure 1). For comparison, the decomposition of the corresponding β-*tert*-butylperoxy alcohol PhMeC(OO-*t*-Bu)CH_2OH (**4a**) was also studied; a linear increase of the rate with increasing [KOH] was observed in this case. Similar results were also reported for Me_2C(OO-*t*-Bu)CH_2OH (**4b**).[7] The reaction of **3a** with lower concentrations of base (i.e., [KOH] ≲ 0.1 M) is about two times faster than that of **4a** but becomes slower when [KOH] is above ca. 0.36 M (Figure 1). The linear relationship between the rate and [KOH] is explained by Scheme I.[7] The nonlinear relationship for the case of **3a** suggests that the dissociation of β-hydroperoxy group inhibits the fragmentation (Scheme II).

Hydroperoxides are much stronger acids than alcohols[8] and the K_7 value of **3a** can be estimated to be 4.0 M^{-1} in 70% MeOH according to the reported method.[9,10] The curvature

Scheme I

$$R_1R_2C(OO\text{-}t\text{-}Bu)CH_2OH + MeO^- \overset{K_4}{\rightleftharpoons} R_1R_2C(OO\text{-}t\text{-}Bu)CH_2O^- + MeOH \qquad (4)$$

4

$$R_1R_2C(OO\text{-}t\text{-}Bu)CH_2O^- \xrightarrow{k_5} R_1R_2C{=}O + CH_2O + t\text{-}BuO^- \qquad (5)$$

0022-3263/78/1943-1760$01.00/0

Table I. Rates and Products for the Reaction of Epoxides with Alkaline Hydrogen Peroxide in 70% MeOH at 25.0 °C[a]

	Registry no.	$R_1R_2C(O)CR_3R_4$ R_1, R_2, R_3, R_4	10^5k_{obsd},[b] M^{-1} s^{-1}	Products (%)[c]
1a	2085-88-3	Ph, Me, H, H	3.69	PhCOMe (71)
1b	96-09-3	Ph, H, H, H	5.33	$PhCO_2H$ (85)
1c[d]	17619-97-5	Ph, H, H, Ph	*e*	$PhCO_2H$
1d	882-59-7	Ph, Ph, H, H	1.22	PhCOPh (88)
1e	4741-91-7	Ph, Ph, H, Me	Too slow	none
1f	60227-39-6	Ph, Ph, Me, Me	Too slow	none
1g	3657-41-8	*n*-Pr, Me, H, H	ca. 3	**2g**[f] (38), *n*-PrCOMe (~45)
1h	28114-20-7	*n*-C_7H_{15}, H, H, H	10	**2h**[f] (60–80), glycol (10–30)

[a] Reaction with 0.1 M **1**, 1–3 M H_2O_2, and 0.36 M KOH in 70 vol % MeOH at 25.0 °C. [b] Second-order rate constants were calculated according to $v = k_{obsd}[1][HOO^-]$. $[HOO^-]$ was estimated from the corresponding K_7 value of 15 M^{-1} for H_2O_2. [c] Products were determined after 48 h's reaction by GLC, NMR, and/or UV analyses. Other minor products are the corresponding 1,2-glycols and/or α-methoxy alcohols (i.e., the addition products of MeO^-). [d] Reaction in 95% MeOH. [e] Not determined. [f] See Table II for structures. Prolonged reaction afforded the corresponding ketone and the glycol, respectively.

Table II. Rates and Products from the Base-Catalyzed Decomposition of α-Hydroperoxy Alcohols[a]

	$R_1R_2C(OOH)CH_2OH$ R_1	R_2	10^3k_{obsd},[b] s^{-1}	Products (%)[a]
3a	Ph	Me	4.20	PhCOMe (94)[c]
3b	Ph	H	0.32	PhCHO (89)
3d	Ph	Ph	2.19	PhCOPh (98)[c]
3g	*n*-Pr	Me	0.083	*n*-PrCOMe (81)[c]
3h	*n*-C_7H_{15}	H	0.022	*n*-$C_7H_{15}CH(OH)CH_2OH$ (100)
2g	*n*-PrMeC(C(OH)CH_2OOH		0.0019	*n*-PrCOMe (~65)[c]
2h	*n*-$C_7H_{15}CH(OH)CH_2OOH$		<0.001[d]	*n*-$C_7H_{15}CH(OH)CH_2OH$ (100)

[a] Reaction with 0.1 M **2** or **3** and 0.36 M KOH in 70 vol % MeOH at 25.0 °C. Products were determined by GLC and/or NMR analyses. [b] First-order rate constants were determined iodometrically from the rate equation $v = k_{obsd}$[**2** or **3**]. [c] Glycols or other products were not detected by GLC or NMR. [d] Reproducibility of the reaction rate was poor.

Scheme II

$$R_1R_2C(OOH)CH_2OH + MeO^- \underset{}{\overset{K_3}{\rightleftharpoons}} R_1R_2C(OOH)CH_2O^- + MeOH \quad (6)$$

3 **5**

$$3 + MeO^- \overset{K_7}{\rightleftharpoons} R_1R_2C(OO^-)CH_2OH + MeOH \quad (7)$$

6

$$5 \xrightarrow{k_8} R_1R_2C{=}O + CH_2O + HO^- \quad (8)$$

in Figure 1 can be reproduced by assuming $K_7 = 4.0$ M^{-1} for **3a**. Similar curves were obtained for the other peroxy alcohols, **3b** and **3g**, and the estimated K_7 values are 4.5 and 2.7 M^{-1}, respectively. These facts suggest that peroxy anion **6** is stable and the fragmentation proceeds via alkoxide ion **5**.

Since the same magnitude of the pK_a value may be assumed for primary alcohols,[7] $K_4 \simeq K_6 \simeq 1$, which means that only 1/300 of **3** is dissociated into **5** (molar ratio of MeOH:**3** is 300:1). Thus, a rough estimate of k_5 and k_8 values is possible: k_5 for **4a** is 3.5 s^{-1} and k_8 for **3a** is 8.3 s^{-1} in 70% MeOH at 25 °C.[12] That is, k_8 for **3a** is 2.4 times larger than k_5 for **4a**; the order is reasonable, since the HO group is a better leaving group than *t*-BuO.

Substituent Effects. The rate data for the base-catalyzed fragmentation of β-hydroperoxy alcohols in Table II can be summarized as follows:

(i) The peroxy alcohol **3a** (R_1 = Ph) is decomposed 50 times faster than **3g** (R_1 = *n*-Pr). The k_{obsd} value of 6.33×10^{-3} s^{-1} for **4a** (R_1 = Ph) with 0.08 M KOH in 40% MeOH at 30 °C is 18 times larger than the corresponding value of 0.372×10^{-3} s^{-1} for **4b** (R_1 = Me).[7] This indicates that resonance stabilization of the developing carbonyl by the phenyl group is important in the transition state for fragmentation (**7**).

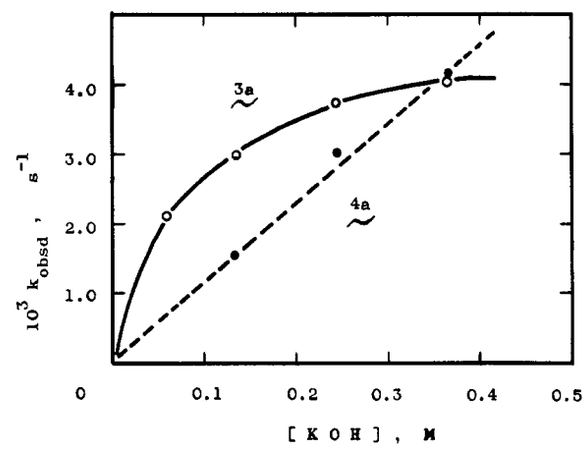
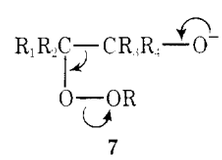


Figure 1. Effect of [KOH] on the decomposition of peroxy alcohols, **3a** and **4a**, in 70% MeOH at 25.0 °C.



7

Similar acceleration by the phenyl group has been reported for related peroxide reactions, e.g., the base-catalyzed reaction of α-hydroperoxy ketones[13] and α-ketols with H_2O_2.[14]

(ii) The rate for **3a** is much faster than **3b**; the fragmentation of **2g** and **3g** occurs, but that of **2h** and **3h** does not. These facts probably reflect a steric acceleration in the C–C fission as a second driving force for the fragmentation. Molecular models for **2** and **3** show their crowded structures. It is natural that the transition state **7** for the fragmentation is sterically assisted by releasing the steric strain.

Table III. NMR Data for β-Peroxy Alcohols (2, 3, and 4) and 1,2-Glycols[a]

β-Peroxy	Registry no.	Alcohols (R_1, R_2)	Corresponding 1,2-glycols
3a (Ph, Me)	33334-31-5	1.55 (s, CH_3), 3.87 and 3.90 (asym CH_2), 7.28 (s, ArH)	1.52 (s, CH_3), 3.63 and 3.68 (asym CH_2), 7.24 (s, ArH)
3b (Ph, H)	61040-96-8	3.70, 3.79, and 3.82 (asym CH_2), 5.03 (q, J = 5 and 7 Hz, CH), 7.24 (s, ArH)	3.53, 3.57, and 3.66 (asym CH_2), 4.74 (q, J = 5 and 7 Hz, CH), 7.25 (s, ArH)
3d (Ph, Ph)	33334-32-6	4.46 (s, $-CH_2O-$), 7.27 (s, ArH)	4.10 (s, $-CH_2O-$), 7.26 (s, ArH)
2g (*n*-Pr, Me)	65311-38-8	0.94 (m, CH_3), 1.10 (s, CH_3), 1.45 (m, $(CH_2)_2$), 3.83 (s, CH_2OO)	0.88 (m, CH_3), 1.08 (s, CH_3), 1.44 (m, $(CH_2)_2$), 3.30 (s, $-CH_2O-$)
3g (*n*-Pr, Me)	65311-39-9	0.89 (m, CH_3), 1.10 (s, CH_3), 1.45 (m, $(CH_2)_2$), 3.45 (s, $-CH_2O-$)	
2h (C_7H_{15},H)	65311-40-2	0.89 (m, CH_3), 1.33 (m, $(CH_2)_6$), 3.85 (m, $-CH_2O-$), 3.85 (m, CH)	0.88 (m, CH_2), 1.34 (m, $(CH_2)_6$), 3.40 (m, $-CH_2O-$), 3.55 (m, CH)
3h (C_7H_{15}, H)	65311-41-3	0.89 (m, CH_3), 1.32 (m, $(CH_2)_6$), 3.70 (m, CH_2), 3.83 (m, CH)	
4a (Ph, Me)	65311-42-4	1.27 (s, $C(CH_3)_3$), 1.50 (s, CH_3), 3.86 and 3.89 (asym CH_2), 7.26 (s, ArH)	

[a] Chemical shifts (δ vs. Me_4Si) in $CDCl_3$ for **3a, 3b, 3d,** and the corresponding glycols or in CCl_4 for **2g, 3g, 2h, 3h, 4a,** and the corresponding glycols. Ratios of peak areas are in accord with each structure. Peaks of OOH and OH protons were broad and their chemical shift changed by each determination.

(iii) The effect of the acidity of the peroxy alcohols is also important. That is, the fragmentation occurs for most of the primary alcohols, i.e., **3a,b,d,g,** while the secondary alcohol **2g** is cleaved more slowly. This sharp difference is explicable by reaction via **5,** since the acidities of secondary alcohols are less than one-tenth of primary alcohols.[15]

Considering the above arguments, the nature of the oxidative cleavage of epoxides may be summarized as follows. The successful C–C cleavage of epoxides may be due to any of three factors, i.e., the stabilization of developing carbonyl by the phenyl group, steric acceleration, or the acidity of the intermediary alcohols. On the other hand, the unsuccessful cleavage of **1h** and cyclohexene oxide may be due to the intermediary formation of less reactive peroxy alcohols.

Of course, a very important driving force for fragmentation is the strong electron-releasing effect of α-oxy anion. A similar effect of the α-oxy anion is well known for other peroxides fragmentations, e.g., the base-catalyzed reactions of β-peroxy alcohols,[7] carboxylic acids,[16] α-hydroperoxy ketones,[13] esters,[17] and α-ketols with H_2O_2.[14]

Experimental Section

Melting points were measured by a Yanagimoto micro melting point apparatus and are corrected. Boiling points are uncorrected. IR spectra were recorded with a Perkin-Elmer 337 grating spectrophotometer, UV spectra with a Hitachi 124 spectrophotometer, and ^1H NMR spectra with a Hitachi R-24B spectrometer. GLC analyses were performed with a Yanagimoto G 180 gas chromatograph with a flame ionization detector using diphenyl as an internal standard and two different columns: PEG 20M, 20% on Chamelite CK; Silicon OV17, 5% on Shimalite W.

Substituted Epoxides. α-Methylstyrene oxide (**1a**), styrene oxide (**1b**), 2-methyl-1-pentene oxide (**1g**), and 1-nonene oxide (**1h**) were prepared by treating the corresponding olefins with acetonitrile and alkaline H_2O_2.[18] Stilbene oxide (**1c**), 1,1-diphenylpropylene oxide (**1e**), and 1,1-diphenyl-2-methylpropylene oxide (**1f**) were prepared by treating the corresponding olefins with peracetic acid.[19] 1,1-Diphenylethylene oxide (**1d**) was prepared by Zaugg's method.[20] The compounds were purified by distillation and/or recrystallization; **1a,** bp 107–112 °C (47 mm) (lit.[21] bp 75–76 °C (12 mm)); **1b,** bp 95–98 °C (30 mm) (lit.[18] bp 86–87 °C (27 mm)); **1c,** mp 68–69 °C (lit.[19] mp 68–69 °C); **1d,** mp 52 °C (lit.[20] mp 56–57 °C); **1e,** bp 150–155 °C (7 mm) (lit.[22] bp 178–180 °C (21 mm)); **1f,** bp 140–142 °C (6 mm) (lit.[23] bp 162–163 °C (15 mm)), mp 61 °C (lit.[23] mp 61–62 °C); **1g,** bp 108–110 °C; **1h,** bp 92–94 °C (30–31 mm).

The structures of these epoxides were ascertained by their IR and NMR spectra. NMR data for epoxides are as follows (δ vs. Me_4Si in CCl_4): Ratios of peak areas are in accord with each structure. Data for **1a:** 1.63 (s, CH_3), 2.58 and 2.77 (two d, J = 6 Hz, CH_2), 7.27 (s, ArH). Data for **1b:** 2.62 and 2.94 (two q, J = 6 and 3.5 Hz and J = 6 and 4.5 Hz, CH_2), 3.65 (q, J = 4.5 and 3.5 Hz, CH), and 7.12 (s, ArH). Data for **1c:** 3.66 (s, CH), 7.19 (s, ArH). Data for **1d:** 3.08 (s, CH_2), 7.20 (s, ArH). Data for **1e:** 1.12 (d, J = 6 Hz, CH_3), 3.26 (q, J = 6 Hz, CH), 7.10 and 7.20 (s, ArH). Data for **1f:** 1.13 (s, CH_3), 7.18 (m, ArH). Data for **1g:** 0.95 (m, CH_3), 1.22 (s, CH_3), 1.45 (m, CH_2CH_2), 2.38 (s, $-CH_2O-$). Data for **1h:** 0.89 (m, CH_3), 1.32 (m, $(CH_2)_6$), 2.28 and 2.51 (two q, J = 5.5 and 3 Hz and J = 5.5 and 5 Hz, CH_2), 2.67 (m, CH).

β-Hydroperoxy Alcohols. α-Methylstyrene oxide (2 g, 0.015 mol) and CF_3CO_2H (0.05 mL) were added with stirring to a Na_2SO_4-dehydrated ether solution of 90% H_2O_2 (10 mL of 90% H_2O_2 in 100 mL of Et_2O). After refluxing for 4 h, the reaction mixture was washed twice with a small amount of aqueous NaCl[24] and then with aqueous $NaHCO_3$ and dried over Na_2SO_4. The removal of the solvent under slightly reduced pressure gave crude 2-hydroperoxy-2-phenyl-1-propanol (**3a**) (0.53 g, 21% yield), which was purified by recrystallization from ether–*n*-hexane to give 0.18 g (7% yield) of pure **3a,** mp 60–61 °C (lit.[3b] mp 65–67 °C), 94% pure by iodometry.

The other β-hydroperoxy alcohols, **3b, 3d, 3g,** and **3h,** were prepared similarly from the corresponding epoxides. Peroxy alcohols, **3b** and **3d,** were purified by recrystallization, mp being 71–73 °C (97.3% pure) and 124–125 °C (96.4% pure) (lit.[3b] mp 123–124 °C). The peroxy alcohols, **3g** and **3h,** could not be crystallized but were pure enough for our use, i.e., over 80% pure by NMR. These β-hydroperoxy alcohols were identified by their IR and NMR spectra and by the KI reduction to the corresponding 1,2-glycol.[25] The IR spectra of **3a–h** are practically the same as those of the corresponding 1,2-glycols, but the NMR spectra differ from each other characteristically (see Table III).

***β-tert*-Butylperoxy Alcohol.** α-Methylstyrene oxide (2 g, 0.015 mol) and then CF_3CO_2H (0.05 mL) were added with stirring to a ethereal 10% solution of *t*-BuOOH (100 mL). After refluxing for 4 h, the mixture was washed twice with aqueous NaCl and then with aqueous $NaHCO_3$. Drying over Na_2SO_4 and evaporation of the solvent gave 2-*tert*-butylperoxy-2-phenyl-1-propanol (**4a**) of over 90% purity.

The Reaction of Epoxides with Alkaline Hydrogen Peroxide. The reaction of **1** (ca. 0.1 M) with 1–3 M H_2O_2 was carried out in 70% aqueous methanol containing 0.36 M KOH at 25.0 °C for 48 h. The reaction mixture was poured into water and extracted with CH_2Cl_2 and/or ether. 1,2-Glycols and the peroxy alcohol **2** are soluble only in ether. Products were identified by means of IR, NMR, and GLC analyses. The yields of products were determined mostly by GLC.

The formation of product (a carbonyl compound) was followed spectrophotometrically in the UV for **1a, 1b,** and **1d.** For the case of **1g** and **1h,** the consumption of epoxide was followed by GLC and/or NMR.

Base-Catalyzed Reaction of β-Hydroperoxy Alcohols. The base-catalyzed reaction of peroxy alcohols **2** or **3** (0.1 M) with KOH (mostly 0.36 M) was carried out in 70% aqueous MeOH at 25.0 °C. The consumption of β-hydroperoxy alcohol was followed by iodometry.[13] Products were determined as described above.

The base-catalyzed reaction of β-*tert*-butylperoxy alcohol **4a** was performed similarly. The rate was followed by determining acetophenone produced by means of UV spectrophotometry.

References and Notes

(1) Contribution No. 244.
(2) (a) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959); (b) A. Rosowski, "Heterocyclic Compounds with Three- and Four-Membered Rings", Part I, A. Weissberger, Ed., Interscience, New York, N.Y., 1964, Chapter 1.
(3) (a) W. H. Richardson and R. S. Smith, *J. Org. Chem.*, **33**, 3882 (1968); (b) W. Adam and A. Rios, *Chem. Commun.*, 822 (1971).
(4) (a) M. R. Barusch and J. Q. Payne, *J. Am. Chem. Soc.*, **75**, 1987 (1953); (b) H. Kropf, M. Ball, H. Schröder, and G. Witte, *Tetrahedron*, **30**, 2943 (1974).
(5) R. D. Temple, *J. Org. Chem.*, **35**, 1275 (1970).
(6) J. Hoffman, *J. Am. Chem. Soc.*, **79**, 503 (1957).
(7) W.H. Richardson and T. C. Heesen, *J. Org. Chem.*, **37**, 3416 (1972).
(8) R. Curci and J. O. Edwards, "Organic Peroxides", Vol. I, D. Swern, Ed., Interscience, New York, N.Y., 1970, p 205.
(9) W. H. Richardson and V. F. Hodge, *J. Org. Chem.*, **35**, 4012 (1970).
(10) From Taft's equation: $pK_a = -0.51\sigma^*$ for $ROOH$[9] and σ^* value of $PhMe(HOCH_2)C$[11] (the σ^* value for $HOCH_2CH_2$ was assumed to be $\frac{1}{3}$ of that for $HOCH_2$), K_7 for **3a** is calculated to be 2.0 times higher than that of *t*-BuOOH. Since the corresponding K_7 value of *t*-BuOOH is determined to be 2.0 M^{-1} in 70% MeOH from UV absorbance (280 nm), the K_7 value of **3a** is then 4.0 M^{-1}.
(11) J. E. Leffler and E. Grunwald, "Rates and Equillibria of Organic Reactions", Wiley, New York, N.Y., 1963, p 224.
(12) This was estimated from $k_{obsd} = 4.1 \times 10^{-3}\ s^{-1}$ for **3a** with 0.36 M KOH in 70% MeOH. That is, $k_8 = 4.1 \times 10^{-3}/(0.36 \times 0.41 \times (1/300)) = 8.3$, where 0.41 is a factor of undissociated **3a** (cf. $K_7 = 4\ M^{-1}$) and 1/300 is the molar ratio of **5:3.**
(13) Y. Sawaki and Y. Ogata, *J. Am. Chem. Soc.*, **97**, 6983 (1975).
(14) Y. Ogata, Y. Sawaki, and M. Shiroyama, *J. Org. Chem.*, **42**, 4061 (1977).
(15) J. Murto, "The Chemistry of the Hydroxyl Group", Part 2, S. Patai, Ed., Interscience, London, 1971, p 1087.
(16) W. H. Richardson and R. S. Smith, *J. Am. Chem. Soc.*, **91**, 3610 (1969).
(17) Y. Sawaki and Y. Ogata, *J. Org. Chem.*, **42**, 40 (1977).
(18) Y. Ogata and Y. Sawaki, *Tetrahedron*, **20**, 2063 (1964).
(19) D. J. Reif and H. O. House, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 860.
(20) H. E. Zaugg and R. J. Michaels, *J. Am. Chem. Soc.*, **80**, 2770 (1958).
(21) S. Ishida, *Bull. Chem. Soc. Jpn.*, **33**, 924 (1960).
(22) Beilsteins Handbuch der Organische Chemie, Vol. I, No. 17, 1952, p 75.
(23) Reference 22, p 76.
(24) Washing with a large amount of aqueous NaCl lowered the yield significantly.
(25) Authentic 1,2-glycols were prepared by hydrolysis of epoxides; their spectra were identical with the reduction products.

Application of the Hammett Equation to Equilibrium Acidities of Meta- and Para-Substituted Acetophenones

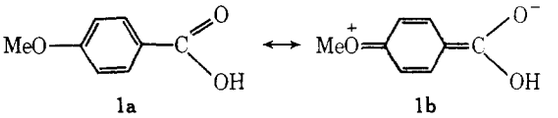
F. G. Bordwell* and Frederick J. Cornforth

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

Received May 31, 1977

Equilibrium acidities in dimethyl sulfoxide solution are reported for 23 meta- and para-substituted acetophenones. A plot of the pK values for 14 of these vs. Hammett σ constants gave a linear correlation with $\rho = 3.55 \pm 0.05$ and $r = 0.9990$. The fit of these points to the line appears to be within the experimental error of the measurements. The slightly greater deviations for the remaining nine points can be rationalized. The excellent correlation argues against direct ("through") conjugative effects for *p*-Me_2N, *p*-MeO, and like groups in benzoic acids and acetophenones. Also, for at least 14 substituents solvation effects must be proportional in water and in dimethyl sulfoxide solutions. The absence of direct conjugative effects and solvent effects for most substituents accounts for the general success of the Hammett equation. The close similarity in geometry between the benzoic acids and their carbon analogues, the acetophenones, accounts for the good correlation observed in this particular instance.

The Hammett equation has proved to be of great utility in physical–organic chemistry[1] and has found application in various other areas of chemistry as well.[1d] Both kinetic and equilibrium data have been correlated by the equation in many types of benzenoid and heterocyclic systems in all types of media, including the gas phase. Its influence may be judged by the fact that a review of the subject by Jaffe,[1b] published in 1953, 13 years after the appearance of the first edition of Hammett's classical text,[1a] has become one of the most cited papers in all of chemistry. The literature in this area has continued to grow at a rapid pace in the ensuing years.[1] Despite its remarkable success, there are a number of problems with the Hammett treatment. In particular, the Hammett σ constants are empirical in nature and do not appear to be "constants" at all in the true sense of the word, since they contain resonance components which vary with the nature of the reactive site. For example, the σ_p constants for substituents having one or more electron pairs on the atom attached to the benzene ring (Me_2N, H_2N, MeO, HO, F, Cl, Br, I, and the like) are believed to be composed of two component parts, an electron-withdrawing polar (inductive) component and an electron-releasing resonance (mesomeric) component. When Me_2N, H_2N, MeO, or HO is substituted into the para position of benzoic acid, the resonance component is dominant, and these substituents are acid weakening. This was accounted for as a direct resonance effect by Ingold in 1933,[2] as depicted by resonance contributor **1b,** and this interpretation has gained general acceptance.[1]



1a **1b**

In benzenoid systems where CO_2H has been replaced by some other reactive site, the size of the resonance component varies with the degree of interaction between the two para substituents. When a saturated center intervenes between the benzenoid ring and the reactive site, such as in the arylacetic acids, direct conjugative interactions of type **1b** and **3b** are not possible and the use of σ^n and σ^0 constants has been proposed.[1] When the reactive site is an ion or radical directly attached to the aryl ring, conjugative interactions reach extremes. For cationic sites the use of Brown's σ_p^+ constants (based on rates of formation of cumyl "cations", i.e., ion pairs, in 90% aqueous acetone) is common, whereas for anionic sites σ_p^- constants (based on equilibrium acidities of phenols or anilinium ions in water) are generally used. The degree of direct conjugation of this type is believed to vary with the systems under scrutiny.

The σ_p constants for substituents in which the atom attached to the benzene ring is part of a multiple bond (NO_2, CN, $COCH_3$, SO_2CH_3, etc.) also have polar and resonance components. In this instance both components exert electron-withdrawing effects. Direct resonance interaction between these substituents and the carboxyl group in benzoic acid is not possible, but the presence of the resonance component is indicated by the fact that the effects are larger from

0022-3263/78/1943-1763$01.00/0