Competition between Complete and Partial Cleavage during Ozonation of Olefins

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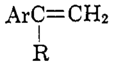
Abstract: Results are reported of a systematic study of the competition between complete cleavage (ozonolysis) and partial cleavage (epoxide, etc. formation) during ozonation of a series of compounds of type $RR'C{=}CH_2$, where R and R′ are aliphatic or aromatic groups which are systematically varied in regard to their bulk. As substitution is increased at the *ortho* positions of the aryl groups and at the β positions of the alkyl groups, the ratio of partial cleavage to complete cleavage products increases. The results are explained on the basis of a competition between purely electrophilic ozone attack (to give a π and/or σ complex, followed by loss of molecular oxygen) and 1,3-dipolar cycloaddition (to give an initial ozonide).

There are in the literature numerous examples of epoxide (and rearrangement products thereof) formation during ozonation of olefins.[1] We term these "partial cleavage" reactions. A classical example is 1-mesityl-1-phenylethylene (Ia), studied by Fuson, *et al.*[2] Ozonation in glacial acetic acid gave 2-mesityl-2-phenylvinyl alcohol (VII), mesitylphenylacetic acid (X), and 1-mesityl-2-phenyl-1,2-ethanedione (XI) in undisclosed yields. Similar results were obtained with 1-mesityl-1-*p*-tolylethylene and 1-isoduryl-1-phenylethylene.[2] Subsequently, Criegee[3] reported that if Ia were ozonized in the absence of acids (and presence of triethylamine), the epoxide (IX) was produced.

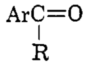
With many of the reported instances of partial cleavage product formation, the olefin was of the type illustrated by I and III, in which the bulky groups were on one side only of the double bond.[1] In other cases, a tri- or tetrasubstituted ethylene was involved.[4-7] Both π[1,8] and σ[3,9-12] complexes have been proposed as intermediates in the formation of the partial cleavage products.

The results in the literature suggest that a competition exists between ozonolysis and the formation of partial cleavage products during ozonation of certain olefins. However, no systematic study has been made of this competition. The present paper reports such a study with the compounds illustrated by I and III. The purpose of the study was: (1) to learn more about the course of the ozonation of the classical example Ia; (2) to study the effect, on the competition between ozonolysis and the partial cleavage reaction, of systematically increasing the bulk on one carbon atom of the double bond of olefins, using both aromatic (I) and aliphatic (III) substituents; and (3) to gain from these results a better understanding of the mechanism(s) of initial ozone attack upon carbon–carbon double bonds and of the partial cleavage reaction.



$$\underset{\displaystyle R}{\underset{|}{ArC}}{=}CH_2$$

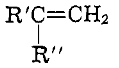
I



$$\underset{\displaystyle R}{\underset{|}{ArC}}{=}O$$

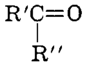
II

a; R = mesityl; Ar = phenyl
b, R = *o*-tolyl; Ar = phenyl
c, R = *o*-carboxyphenyl; Ar = phenyl
d, R = Ar = phenyl
e, R = *p*-*t*-butylphenyl; Ar = phenyl
f, R = H; Ar = mesityl



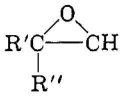
$$\underset{\displaystyle R''}{\underset{|}{R'C}}{=}CH_2$$

III

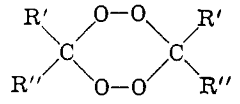


$$\underset{\displaystyle R''}{\underset{|}{R'C}}{=}O$$

IV

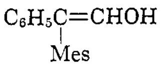


V



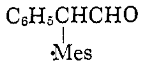
VI

a, R′ = R″ = neopentyl
b, R′ = R″ = *t*-butyl
c, R′ = *t*-butyl; R″ = isopropyl
d, R′ = *t*-butyl; R″ = methyl
e, R′ = *t*-butyl; R″ = H
f, R′ = neopentyl; R″ = CH_3
g, R′ = *t*-butyl
R″ = $C(CH_3)_2C(CH_3)_3$



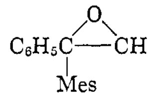
$$\underset{\displaystyle Mes}{\underset{|}{C_6H_5C}}{=}CHOH$$

VII

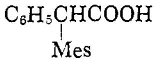


$$\underset{\displaystyle Mes}{\underset{|}{C_6H_5CH}}CHO$$

VIII

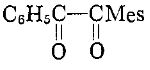


IX



$$\underset{\displaystyle Mes}{\underset{|}{C_6H_5CH}}COOH$$

X



$$C_6H_5\underset{\displaystyle O}{\underset{\|}{C}}{-}\underset{\displaystyle O}{\underset{\|}{C}}Mes$$

XI

Experimental Section

Equipment and Procedures. The ozonation setup and procedures, using either ozone–oxygen or ozone–nitrogen, and the method for determining molecular oxygen yields are described in earlier publications.[13,14] Active oxygen determinations were made

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[1] P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958).

[2] R. C. Fuson, M. D. Armstrong, W. E. Wallace, and J. W. Kneisley, *J. Am. Chem. Soc.*, **66**, 1274 (1944).

[3] R. Criegee, "Products of Ozonization of Some Olefins," Advances in Chemistry Series, No. 21, American Chemical Society, Washington, D. C., 1959, p 133.

[4] I. A. Kaye, M. Fieser, and L. F. Fieser, *J. Am. Chem. Soc.*, 77, 5936 (1955).

[5] R. O. Uhler, H. Shechter, and G. V. D. Tiers, *ibid.*, **84**, 3397 (1962).

[6] C. R. Enzell and B. R. Thomas, *Tetrahedron Letters*, 225 (1965).

[7] See A. Lane, Dissertation, University of Texas, 1967, for a more complete listing.

[8] E. A. Blair and A. Maggiolo, paper presented at the 134th National Meeting of the American Chemical Society, Chicago Ill., Sept 1958; Abstracts, p 6P.

[9] R. Criegee, *Record Chem. Progr.* (Kresge-Hooker Sci. Lib.), **18**, 111 (1957).

[10] P. S. Bailey, S. B. Mainthia, and C. J. Abshire, *J. Am. Chem. Soc.*, 82, 6136 (1960).

[11] P. R. Story, R. W. Murray, and R. D. Youssefyeh, *ibid.*, **88**, 3144 (1966).

[12] By the term σ complex we mean intermediates of either type XXI or XXII in which, in contrast to a π complex, one or both carbon atoms of the original double bond are now sp^3 hybridized.

[13] (a) P. S. Bailey, *J. Am. Chem Soc.*, 78, 3811 (1956); (b) P. S. Bailey, *J. Org. Chem.*, 22, 1548 (1957).

[14] (a) P. S. Bailey and A. M. Reader, *Chem. Ind.* (London), 1063 (1961); (b) P. S. Bailey, P. Kolsaker, B. Sinha, J. B. Ashton, F. Dobinson, and J. E. Batterbee, *J. Org. Chem.*, 29, 1400 (1964); (c) A. M. Reader, P. S. Bailey, and H. M. White, *ibid.*, 30, 784 (1965).

Table I. Ozonation of 1-Mesityl-1-phenylethylene (Ia)

Expt	Solvent	Carrier gas	Olefin, mmoles Start	Olefin, mmoles Reacting	Ozone, mmoles[a]	O_3/olefin	Partial cleavage[b] products, mmoles	Partial cleavage[b] products, %	O_2 evolvd, mmoles	%
1	CH_2Cl_2	N_2	5.0	5.0	5.0	1.0	3.9	78[c]	3.9	78
2	CH_2Cl_2	O_2	5.0	5.0	5.0	1.0	3.8	76[d]	...	...
3	CH_2Cl_2	N_2	4.7	2.4	2.5	1.0	1.9	79	2.1	87
4	CH_2Cl_2	N_2	14.7	8.2	10.0	1.2	7.2	88[e]	...	...
5	CH_2Cl_2	N_2	25.0	4.7	5.0	1.1	3.5	75	...	...
6	CH_2Cl_2	O_2	5.0	2.5	2.6	1.0	2.0	80	...	...
7	Pentane	N_2	10.0	10.0	10.0	1.0	...	...	8.2	82
8	Pentane	O_2	20.0	...	10.0[f]	...		81[g]		
9	CH_2Cl_2–CH_3OH	N_2	4.8	2.3	2.8	1.2	2.1	91	2.1	91
10	CH_3OH	N_2	10.0	9.3	10.0	1.1	8.4	90	...	...

[a] Unless otherwise stated, ozone absorption was quantitative. [b] Unless otherwise stated, yield was determined by vpc and represents the mixture of vinyl alcohol VII and aldehyde VIII. [c] Quantitative infrared determination, 42% vinyl alcohol VII, 36% aldehyde VIII. [d] Quantitative infrared determination, 42% VII, 34% VIII. [e] In this experiment 11% active oxygen (peroxide) and 13% of mesityl phenyl ketone IIa also were determined. [f] Only 9.2 mmoles of ozone reacted. [g] A 71% yield of epoxide IX was isolated and a 10% yield of aldehyde VII was estimated by infrared of the remainder.

on the methanol or methylene chloride–methanol reaction mixtures essentially by the method of Criegee, *et al.*,[15] in which excess sodium iodide in glacial acetic acid solution was added to the reaction mixture under a carbon dioxide cloud. Results generally were good with these methanolic reaction mixtures, since they contained alkoxy hydroperoxides as peroxidic ozonolysis products, but not always with purely methylene chloride, etc. reaction mixtures with which the peroxidic ozonolysis products presumably included dimeric and polymeric peroxides.[1,15] Analytical vpc determinations were made on an F & M Model 500 gas chromatograph and on a Wilkins Aerograph Model 1520, both equipped with a disk integrator. The columns were: (a) 2 ft × 0.25 in. (copper) with silicone gum rubber (methyl) SE-30 on 45–60 Chromosorb W, (b) 10 ft × 0.25 in. (copper) with 15% Silicone Dow Corning 710 on 45–60 Chromosorb W, (c) 10 ft × 0.25 in. (copper) with Carbowax 1500 on 60–80 Chromosorb P (for Aerograph 1520). Quantitative determinations were made by comparison of peak areas with those of standard solutions of similar concentrations of pure, known compounds. Preparative vpc separations were made on an Aerograph Model A-90-P3 Autoprep, using a 20 ft × $^3/_8$ in. aluminum column of either 30% silicone gum rubber (methyl) SE-30 or 20% Carbowax 20M on 45–60 Chromosorb W. Helium was the carrier gas. Tlc experiments were run using plates coated with 0.25-mm silica gel G layers prepared with a Desaga/Brinkman apparatus (Brinkman Instruments, Inc. Westbury, N. Y.). Quantitative infrared determinations were made on Beckman IR-5 and IR-7 spectrophotometers, using as standards solutions of similar concentrations of pure compounds. Nmr spectra were measured with a Varian Associates A-60 spectrometer using a TMS internal standard. Elemental analyses were obtained commercially. Melting points were corrected.

Materials. All solvents were pure and anhydrous unless otherwise stated. 1-Mesityl-1-phenylethylene (Ia) was prepared by the method of Fuson, *et al.*;[16] chromatographed over alumina with petroleum ether (bp 60–70°), n^{21}D 1,5830. 1-*o*-Tolyl-1-phenylethylene (Ib) was prepared from acetophenone and *o*-bromotoluene as described by Bergmann and Bondi;[17] chromatographed over alumina, purity established by vpc. 1-(*o*-Carboxyphenyl-1-phenylethylene (Ic) was prepared as described by Bergmann[18] (mp 136–137°). 1-(*p*-*t*-Butylphenyl)-1-phenylethylene (Ie) was prepared from 4-*t*-butylbenzophenone as described previously;[19] n^{25}D 1.5740, purity attested by vpc. 2-*t*-Butyl-3,3-dimethyl-1-butene (IIIb) was prepared from 2,2,4,4-tetramethyl-3-pentanone[20] by the method of Newman, *et al.*;[21] bp 149–150°, n^{26}D 1.4342. 3,3-Dimethyl-2-isopropyl-1-butene (IIIc) was prepared from 2,2,4-trimethyl-3-pentanone[22] by the same general procedure which Newman, *et al.*,[21] used to make IIIb; bp 120–121°, n^{25}D 1.4165 (*cf.* ref 22), purity attested by vpc. Other starting materials were of the highest grade available commercially. Their purity was checked by vpc and, if necessary, they were purified by standard procedures. Further details may be found elsewhere.[7]

Ozonation of 1-Mesityl-1-phenylethylene (Ia). A. General. Solutions of 5–20 mmoles of Ia in 100 ml of solvent were ozonized with 1 mole equiv or less of ozone in an oxygen or nitrogen stream at −78°. Ozone absorption was quantitative and the ozone:olefin reacting ratio was 1.0–1.2 as shown in Table I. In one instance 2 mole equiv of ozone was employed, absorption was quantitative through 1.25 mole equiv, and 1.5 mole equiv of ozone reacted. Vpc determinations of starting material and products were made on the 2-ft silicone gum rubber column (see Equipment and Procedures, above) at a column temperature of 180° and a flow rate of 30 cc/min. Determinations of unconsumed starting material and of partial cleavage products generally were made on freshly ozonized solutions, since it was shown that the results were the same as those obtained after iodide reduction. The retention times of the enol VII, aldehyde VIII, and epoxide IX were identical, probably due to equilibration on the column. Therefore, the enol VII was used as the standard and yields from these experiments are reported as total partial cleavage products in Table I. These yields agree well with the molecular oxygen yields (see Equipment and Procedures, above) determined from the ozone–nitrogen experiments. An active oxygen determination on an aliquot of one of the reaction mixtures showed a yield of 11% peroxidic material. A vpc analysis of the reduced reaction mixture showed a 13% yield of mesityl phenyl ketone[23] (IIa).

B. 2-Mesityl-2-phenylvinyl Alcohol (VII) and Mesitylphenylacetaldehyde (VIII). A solution of 1.12 g (5.0 mmoles) of 1-mesityl-1-phenylethylene (Ia) in 100 ml of methylene chloride was treated with 5.3 mmoles of ozone in oxygen at −78°. The reaction mixture was evaporated and the oily residue (1.16 g) was crystallized from 100 ml of commercial heptane, giving 0.4 g of crude vinyl alcohol (VII); mp 105–110°, recrystallized from petroleum ether, mp 113–115°, strong hydroxyl band in the infrared at 2.84 μ.[24] Concentration of the filtrate gave 0.29 g of crystals melting at 60–67° and shown to be largely mesitylphenylacetaldehyde (VIII) by the strong carbonyl peak at 5.78 μ and a very weak hydroxyl peak at 2.84 μ in the infrared and by the separation of only 0.07 g of the vinyl alcohol (VII) upon fractional recrystallization; recrystallized from commercial heptane until no hydroxyl peak in infrared, mp 70–71°.[25] Further concentration of the heptane filtrate gave additional crude vinyl alcohol and a small amount of material melting at 132–135° and assumed to be 1-mesityl-1-phenyl-1,2-ethanedione[2] (XI, strong bands at 5.80 and 6.13 μ in infrared).

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(15) R. Criegee, G. Blust, and G. Lohaus, *Ann.*, **583**, 2 (1953).

(16) R. C. Fuson, M. D. Armstrong, W. E. Wallace, and J. W. Kneisley, *J. Am. Chem. Soc.*, **66**, 681 (1944).

(17) E. Bergmann and A. Bondi, *Ber.*, **66**, 286 (1933).

(18) E. Bergmann, *J. Org. Chem.*, 4, 1 (1939).

(19) F. Bergmann and J. Szmuszkowicz, *J. Am. Chem. Soc.*, 70, 2748 (1948).

(20) Prepared by method of N. C. Cook and W. C. Percival, *ibid.*, 71, 4141 (1949).

(21) M. S. Newman, A. Arkell, and T. Fukunaga, *ibid.*, 82, 2498 (1960).

(22) F. C. Whitmore and K. C. Laughlin, *ibid.*, **55**, 3732 (1933).

(23) Pure sample prepared for standard by method of P. J. Montagne, *Rec. Trav. Chim.*, 27, 327 (1908); bp 175–180° (6 mm), purity demonstrated by vpc.

(24) *Cf.* R. C. Fuson, N. Rabjohn, and D. J. Byers, *J. Am. Chem. Soc.*, **66**, 1272 (1944).

(25) *Cf.* R. C. Fuson and T.-L. Tan, *ibid.*, 70, 602 (1948).

Table II. Ozonation of Other Olefins[a]

Olefin	Olefin, mmoles	Ozone, mole equiv	Active O, % yield[b]	Cleavage prodt,[c] % yield	O_2 evolvd, % yield	Partial cleavage prodt, % yield	Total act. $O + O_2$, %
Ib	5	1	71[d]	69	39[d]	*e*	110[f]
Ic	5–24	1	51[d]	50[d]	40[d]	35[g]	91[h]
Id	5–20	1	87[d]	82	14[d]	...	101
Ie	20	1	80	50	19	...	99
If	20	1	84	83	17	...	101
IIIa	5–20	0.5–1	60[d]	65	31[d]	22[i]	91[j]
IIIb	4–37	0.5–1	87	85	10[d]	15[i]	97
IIIc	10–40	0.5	91	72	11	...	102
IIId	15–60	0.5–1	77[d]	*k*	12[d]	...	89[l]
IIIe	30–60	0.5–1	91	*k*	9[d]	...	100
IIIf	40	0.5	89	*k*	11	...	100

[a] Solvent was CH_2Cl_2–CH_3OH (9:1 or 4:1) unless otherwise noted. [b] Per cent yield represents gram atoms of active oxygen per 100 moles of olefin reacting. [c] The cleavage product was the corresponding ketone or aldehyde, determined by vpc. [d] These values are averages of several runs. [e] Blank spaces indicate product not determined. [f] For some unknown reason, the molecular oxygen yields appear to be high with this compound. [g] Product determined was XIII; there may have been others. [h] The average active oxygen yield appears to be low. The range was 48–54%. [i] The partial cleavage product was the corresponding epoxide V. [j] The actual cleavage product yield of 65% appears to be more accurate than the active oxygen and/or molecular oxygen yields. Also other partial cleavage products appeared to be present. [k] Identified as the aldehyde or ketone, but not determined. [l] Active oxygen probably low due to rearrangements of peroxidic ozonolysis product; see ref 32.

The total crude yields were vinyl alcohol VII, 45%, mesitylphenylacetaldehyde (VIII), 18%, and the ethanedione XI, 3%.

In similar experiments, one with oxygen and one with nitrogen carrier, the reaction mixture was evaporated, and the yields of vinyl alcohol VII and aldehyde VIII in the residue were estimated by comparison of the infrared peaks at 2.84 μ (VII) and 5.78 μ (VIII) with those of standard solutions of pure VII and VIII. The results showed 42% VII and 34–36% VIII in the two cases.

C. 1-Mesityl-1-phenylethylene Epoxide (IX). A solution of 4.5 g (20 mmoles) of 1-mesityl-1-phenylethylene (Ia) in 50 ml of pure pentane was ozonized with 10 mmoles of ozone in a 3% ozone–oxygen stream (9.2 mmoles of ozone reacted) at −78°. After concentration of the reaction mixture to 10–20 ml and an overnight cooling period, 1.55 g of crystals melting at 90–95° was obtained (71% yield based on ozone reacting); recrystallized from acetone, mp 97–98°.[26] The infrared spectrum showed neither a hydroxyl nor a carbonyl band and was identical with the infrared spectrum of the product obtained from Ia and perbenzoic acid by the epoxidation procedure of Bartlett and Stiles.[27]

Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.74; H, 7.78.

An infrared spectrum of the residue from evaporation of the filtrate (from the epoxide) showed the presence of mesitylphenylacetaldehyde (VIII, about 10%), mesityl phenyl ketone (IIa), but no vinyl alcohol VII, judging from presence or absence of bands at 5.78, 6.01, and 2.84 μ, respectively.

The epoxide IX was dissolved in methylene chloride, and infrared spectra of the solution were taken at intervals. The characteristic epoxide bands (*e.g.*, 12.00 and 13.10 μ) gradually disappeared as characteristic bands of the vinyl alcohol VII (*e.g.*, 2.84 μ) and mesitylphenylacetaldehyde (VIII, *e.g.*, 5.78 μ) appeared. No isomerization in pentane solution occurred, however, unless a trace of acid was added. Ozonation in pentane with 1 mole equiv of ozone gave only the enol–aldehyde mixture.

Ozonation of 1-(*o*-Carboxyphenyl)-1-phenylethylene (Ic). A solution of 5.4 g (24 mmoles) of 1-(*o*-carboxyphenyl)-1-phenylethylene (Ic) in 200 ml of a 9:1 methylene chloride–methanol mixture was ozonized at −78° with an equivalent amount of ozone in an ozone–oxygen stream. The ozone was quantitatively absorbed. In a separate similar experiment an infrared spectrum of the residue, after evaporation of the reaction mixture, showed no unreacted olefin (absence of typical bands at 6.44, 7.12, and 7.30 μ). The reaction mixture was acidified with acetic acid and reduced with sodium iodide, and the released iodine titrated with standard thiosulfate. Two experiments of this type gave an average of 51% active oxygen-containing products. The organic layer was separated from the aqueous layer and extracted with 5% sodium bicarbonate solution. From the basic extract (acidification, extraction with ether, evaporation, drying at 70° for several hours) 2.9 g (54% yield) of *o*-benzoylbenzoic acid (mp 127–128°) was obtained. From several experiments this yield averaged 50%. Evaporation of the methylene chloride layer (neutral fraction) gave 2.0 g (35% yield) of material melting at 120–122°; recrystallized from benzene, mp 121–122°. It was identified as 3-phenyl-3-(α-hydroxymethyl)phthalide (XIII) by elemental analysis and by comparison of infrared spectra (OH, 2.96 μ; C=O, 5.76 μ), and a mixture melting point, with an auhentic sample.[28]

Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.98; H, 5.04; mol wt, 240. Found: C, 74.54; H, 5.02; mol wt (vapor pressure method (vp) in acetone), 232.

From several experiments using ozone–nitrogen, an average molecular oxygen yield of 40% was obtained. These results are summarized in Table II.

Ozonation of 2-Neopentyl-4,4-dimethyl-1-pentene (IIIa). Solutions of 10–20 mmoles of IIIa in 100 ml of pentane or 4:1 methylene chloride–methanol were ozonized at −78° with 0.5–1.0 mole equiv of ozone in an oxygen or nitrogen stream. The ozone was absorbed quantitatively. After iodide reduction of the acidified (glacial acetic acid) reaction mixtures and removal of the released iodine with thiosulfate, the organic layer was washed, dried, concentrated, and analyzed for unconsumed starting material and products on the Carbowax 1500 column (See Equipment and Procedures, above) at a column temperature of 92° and a helium flow rate of 64 cc/min. In all cases the ozone to olefin reacting ratio was essentially unity. Active oxygen determinations on the reaction mixtures averaged 60% (yield of peroxidic ozonolysis products) and molecular oxygen yields, using ozone–nitrogen (see Equipment and Procedures, above), averaged 31% (yield of partial cleavage products). In one experiment (20 mmoles of IIIa, 10 mmoles of ozone in a nitrogen stream, methylene chloride–methanol), the yields of the two principal products were shown to be 2,2,6,6-tetramethyl-4-heptanone (IVa), 65%, and the epoxide Va, of IIIa, 22%. A pure sample of the ketone IVa was obtained by preparative vpc and used as a standard, bp 183°, n^{26}D 1.4190,[29] carbonyl band in infrared at 5.84 μ, nmr singlets at τ 9.03 and 7.98 ppm in a ratio of 9:2. A pure sample of the epoxide Va was prepared by the method of Hickenbottom and Wood,[30] bp 95–100° (30 mm), n^{26}D 1.4301, no hydroxyl or carbonyl band in infrared; nmr showed two singlets at τ 9.02 (18 H) and 7.54 (2 H) ppm and two doublets centered at τ 8.26 (2 H) and 8.65 (2 H) ppm (*cf.* ref 31 for explanation of nonequivalence of these methylene groups). The epoxide

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[26] Criegee[3] reports mp 101–102° but gives no other characterization.

[27] P. D. Bartlett and M. Stiles, *J. Am. Chem. Soc.*, 77, 2806 (1955).

[28] G. Berti, *J. Org. Chem.*, 24, 934 (1959).

[29] *Cf.* F. C. Whitmore and J. D. Surmatis, *J. Am. Chem. Soc.*, **63**, 2200 (1941).

[30] W. J. Hickenbottom and D. G. M. Wood, *J. Chem. Soc.*, 1600 (1951).

[31] G. M. Whitesides, D. Holtz, and J. D. Roberts, *J. Am. Chem. Soc.*, **86**, 2628 (1964).

gave two peaks on the vpc which varied in size with the column temperature, indicating that it was equilibrating with some decomposition product. Only one peak was obtained on the 2-ft silicone gum rubber column at 135–195°

During ozonations in pentane, a small amount of a white precipitate was produced (about 3% yield, mp 145–146°). The material slowly released iodine from 34% hydriodic acid in glacial acetic acid, but not from sodium iodide. The nmr spectrum of the material in chloroform showed two singlets, at τ 7.89 and 8.92 ppm in the ratio of 4:1, the infrared spectrum showed no hydroxyl, carbonyl, or olefinic bands. The material appears to be a dimeric peroxide VIa.

Anal. Calcd for $C_{22}H_{44}O_4$: C, 70.92; H, 11.90; active O, 8.59; mol wt, 372.59. Found: C, 70.85; H, 11.23; active O, 8.6; mol wt (ebullioscopic in $CHCl_3$), 347.

Vpc of a pentane reaction mixture on the Carbowax 20M column at 200° and a flow rate of 100 cc/min showed five significant products: the dimeric peroxide VIa, dineopentyl ketone IVa, a small amount of *t*-butylacetic acid, and two minor unidentified materials. The epoxide must decompose completely at this temperature. The *t*-butylacetic acid was collected by preparative vpc (bp 183–184°, n^{26}D 1.4100) and identified by comparison of infrared and nmr spectra with those of a pure commercial sample.

Ozonations of Other Olefins (I and III). The ozonations and active oxygen and molecular oxygen determinations were carried out as described for Ia, Ic, or IIIa. After iodide reduction, the aromatically substituted olefin (Ib, Id, Ie, and If) reaction mixtures were analyzed by vpc on the 2-ft silicone rubber column; the aliphatic olefin (IIIb and IIIc) reaction mixtures were analyzed on the Carbowax 1500 column (see Equipment and Procedures, above). In most cases only the complete cleavage (ozonolysis) products were determined, since results with Ia, Ic, and IIIa showed that the molecular oxygen yield was equal to the yield of partial cleavage product. In the cases of IIId, e, and f, the cleavage (ozonolysis) products were identified through the respective DNP; no depression in mixture melting points with authentic samples (melting points of DNP: IVd, 209–210°; IVe, 125–126°, IVf, 100–101°) and only one spot by tlc (eluting with either methylene chloride or benzene–petroleum ether) which corresponded with the known sample. The active oxygen determinations were used for the yields of these products since this was shown to be valid in the other cases. The results are summarized in Table II.

During ozonation of IIIb and IIId in nonparticipating solvents (methylene chloride etc.) white precipitates formed, as described for IIIa. The material from IIIb exploded during attempted purification. The material from IIId melted at 123–124° and is thought to be a dimeric peroxide (VId).[32] The infrared spectrum showed no hydroxyl or carbonyl peaks. The nmr spectrum (CCl_4) showed two bands, at τ 8.99 and 8.33 ppm in the ratio 2.7:1.

Anal. Calcd for $C_{12}H_{24}O_4$: C, 62.04; H, 10.41; mol wt, 232. Found: C, 61.73; H, 9.50; mol wt (vp in benzene), 228.

Results

The principal results obtained are summarized in Tables I and II. In general, ozone absorption was quantitative, and the ratio of ozone to olefin reacting was unity throughout the reaction. The most thorough studies were made with 1-mesityl-1-phenylethylene (Ia), 1-(*o*-carboxyphenyl)-1-phenylethylene (Ic), 2-neopentyl-4,4-dimethyl-1-pentene (IIIa), and 2-*t*-butyl-3,3-dimethyl-1-butene (IIIb), in which both the ozonolysis (complete cleavage) and the partial cleavage (epoxides, etc.) products were quantitatively determined. In addition, with compounds Ib, Id, Ie, If, and IIIc, the ozonolysis product was quantitatively determined. As can be seen from Tables I and II, the yields of the ozonolysis products agreed closely with the values of the active oxygen determinations (yield of peroxidic ozonolysis product) made on the reaction mixtures, except in the cases of Ie and IIIc where the vpc determinations appear to be low, for reasons unknown. In the cases of Ia, Ic, IIIa, and IIIb, it was shown that 1 mole of molecular oxygen per mole of partial cleavage product was evolved, as shown by reasonably good agreement between the two values in Tables I and II. Because of these findings, the active oxygen determination values are used for the yields of ozonolysis products in the cases of Ie, IIIc, IIId, IIIe, and IIIf, and the molecular oxygen yields are utilized for the yields of partial cleavage products for compounds Ib, Id, Ie, If, IIIc, IIId, IIIe, and IIIf. That such substitutions are justified is shown by the fact that in most cases the sum of the active oxygen and molecular oxygen yields is very close to 100. From these determinations, estimates were made of the percentages of the partial cleavage reaction occurring with the compounds studied; these are listed in Table III.

Table III. Percentages of Partial Cleavage Reaction

Aromatic series I		Aliphatic series III	
Compd	% partial cleavage[a]	Compd	% partial cleavage[a]
Ia	75–90	IIIa	35[c]
Ib	30[b]	IIIb	15[d]
Ic	40	IIIc	10
Id	15	IIId	10
Ie	20	IIIe	10
If	15	IIIf	10
		IIIg	50[e]

[a] Approximate figures, rounded off to closest 5%, based on molecular oxygen yield unless otherwise stated. [b] Based on active oxygen and ozonolysis product yield, rather than molecular oxygen yield. [c] Based on cleavage product yield. [d] Based on epoxide yield. [e] Approximate yield reported by Bartlett and Stiles.[27] Preliminary results from this laboratory indicate it may be as high as 70–80%.

The ozonation of Ia was studied in several different solvents, as shown in Table I. As seen, the yield of partial cleavage products lies in the range of 75–91%. There is no noticeable difference in results using oxygen or nitrogen as the carrier (nor was there with the other olefins), but there does appear to be a small solvent effect. The yield of partial cleavage products was usually 75–82% with methylene chloride or pentane solvent and 90–91% with methanol or a mixture of methanol and methylene chloride. However, in one experiment with methylene chloride solvent an 88% yield was obtained and in another experiment a molecular oxygen yield of 87% was observed. In most cases the yield of partial cleavage product was that of the mixture of the enol VII, the aldehyde VIII, and (possibly) the epoxide IX, since these could not be differentiated on the vpc column. In two instances, however, quantitative infrared estimations on methylene chloride reaction mixtures showed 42% enol VII and 34–36% aldehyde VIII. In another experiment there was obtained by actual isolation 45% enol VII, 18% aldehyde VIII, and 3% diketone XI. This indicates that some isomerization of the aldehyde to enol occurs during the isolation procedure, which is to be expected.[25] The substituted benzil XI is thought to arise from further ozonation of the enol.[2]

Attempts to obtain epoxide IX by ozonations of Ia in methylene chloride solvent failed, whether or not triethylamine was present (*cf.* ref 3). However, when the olefin was ozonized in pure pentane with 0.5 mole

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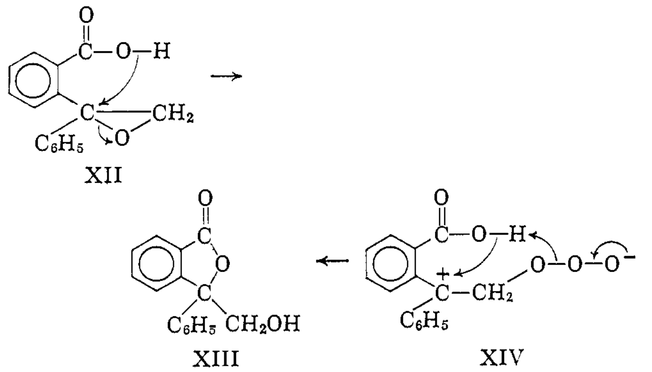
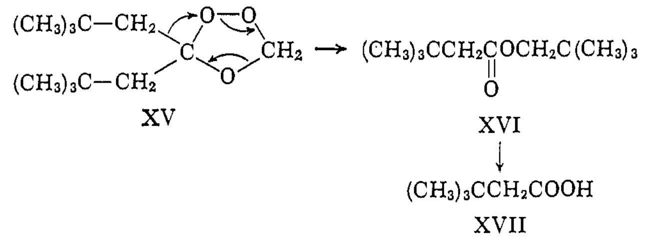
(32) *Cf.* R. Criegee, A. Kerchow and H. Zinke, *Chem. Ber.*, **88**, 1878 (1955).

equiv of ozone, the epoxide was obtained in 71% yield. An infrared spectrum of the remainder of the reaction mixture showed the aldehyde VIII, but no enol VII, also to be present in about 10% yield. Upon ozonation in pure pentane with 1 mole equiv of ozone, only the enol and aldehyde were obtained. The epoxide was shown to isomerize rapidly to a mixture of the enol and aldehyde in methylene chloride or in pentane with a trace of acid present. Apparently ozonation in pentane with more than 0.5 mole equiv of ozone produces enough organic acids to catalyze the isomerization.

Ozonation of 1-(*o*-carboxyphenyl)-1-phenylethylene (Ic), followed by a reductive work-up, gave isolated yields of 50% *o*-benzoylbenzoic acid (IIc) and 35% phthalide XIII. The latter could arise either by the acid-catalyzed rearrangement of epoxide XII or by a concerted reaction during ozone attack on Ic, as illustrated in XIV. Active oxygen and molecular oxygen determinations averaged 51 and 40%, respectively.





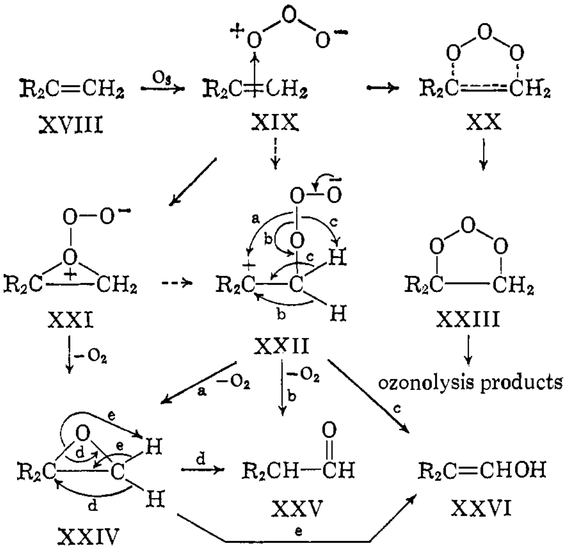
Ozonation of 2-neopentyl-4,4-dimethyl-1-pentene (IIIa) gave as major products the corresponding ketone IVa and epoxide Va. A small amount of *t*-butylacetic acid (XVII) was also obtained, presumably *via* a route such as XV → XVI → XVII. In some runs a peroxidic ozonolysis product, characterized as VIa, was isolated in low yield. A dimeric peroxide VId was also obtained during ozonation of IIId. A similar material precipitated during ozonation of IIIb, but proved to be too unstable to purify, probably due to polymeric peroxide impurities.

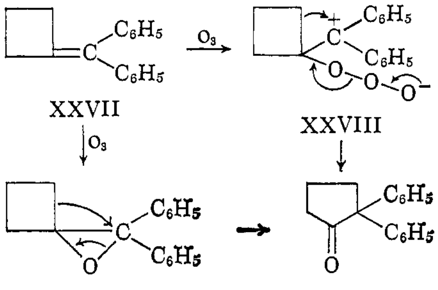
Discussion

The data shown in Table III clearly demonstrate a competition between ozonolysis and ozone attack leading to partial cleavage products which is strongly dependent upon the bulk of groups Ar, R, R′, and R″ in compounds I and III. With compounds I, as would be expected from a steric effect, substitution at the *ortho* positions has a strong effect on the competition. A comparison of compounds Ia, Ib, and Id, in which the number of *ortho* substituents decreases from 2 to 1 to 0, shows a corresponding decrease in the amount of partial cleavage reaction from 75–90 to 30 to 15. There is little effect from the *p*-*t*-butyl group in Ie and the loss of a phenyl group in If (in comparison to Id) is compensated by the presence of two *ortho* substituents in the Ar group. The apparent difference in results with Ib and Ic is probably due to the greater bulk of the carboxyl group than of the methyl group, rather than to an electrical effect.

In the aliphatic series III, as also should be expected,[33] substitution at the β positions of alkyl groups R′ and R″ had a much greater effect than substitution at the α positions, as shown by comparison of IIIa and IIIb. There is surprisingly little difference in the results with compounds IIIb–e. With compound IIIg, in which both α and β substitution is heavy, at least 50% yields of partial cleavage products are reported.[27]

As stated earlier, the formation of either a π or a σ complex, followed by loss of molecular oxygen, has been proposed as the route to partial cleavage products. The route to ozonolysis products is, at present, best explained by a 1,3-dipolar cycloaddition[34] of ozone to the olefinic double bond to give a five-membered 1,2,3-trioxolane ring,[35] called an initial ozonide.[36] Thus, a reasonable explanation for the competition between ozonolysis and the partial cleavage reaction is that, as the bulk of groups Ar, R, R′, and R″ in I





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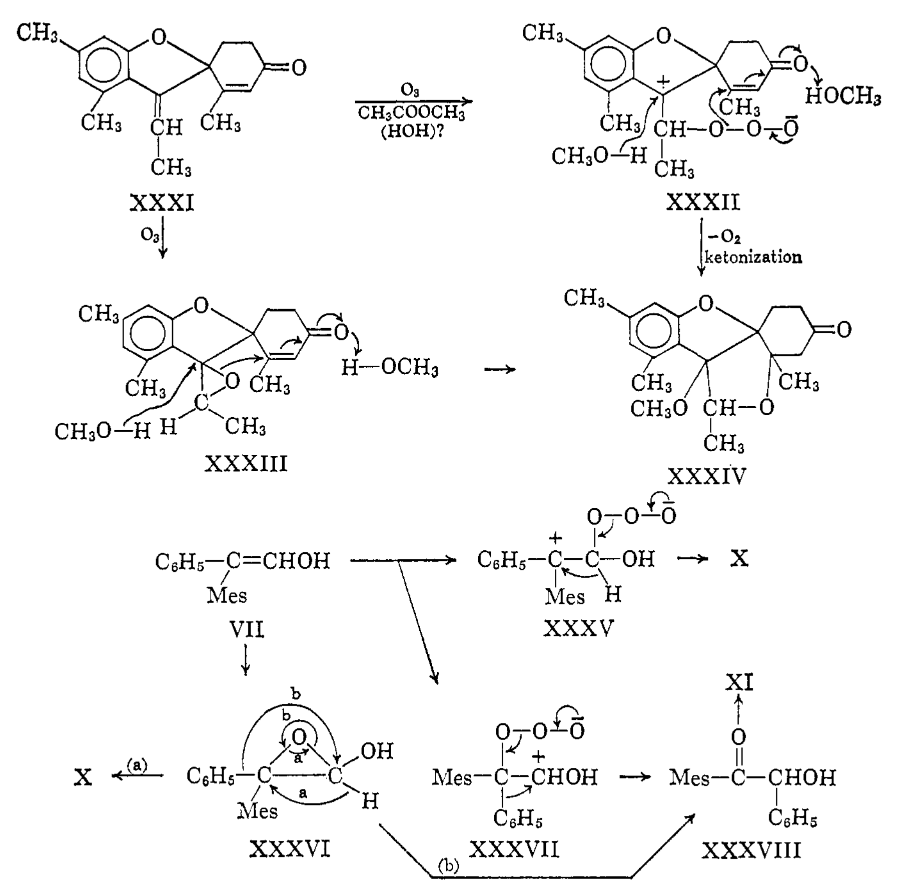
[33] M. S. Newman in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, pp 203–217.

[34] R. Huisgen, *Angew. Chem. Intern. Ed. Engl.*, **2**, 565, 633 (1963).

[35] P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *J. Am. Chem. Soc.*, **88**, 4098 (1966).

[36] Translation of Criegee's[3,9] "primarozonid." The term "molozonide" used by several authors today is a poor choice, since it refers to Staudinger's four-membered ring,[1] and no longer has any obvious meaning.



and III increases, the 1,3-dipolar cycloaddition of ozone becomes more and more hindered, and the alternative formation of a π or a σ complex, followed by loss of molecular oxygen to give partial cleavage products, occurs instead.[37]

An attractive description of the partial cleavage reaction is the formation of an unbalanced, open σ complex XXII,[12] involving the more stable carbonium ion, followed by loss of oxygen and the formation of an epoxide XXIV, an aldehyde XXV (or ketone), or an enol XXVI, *via* routes a, b, or c. Such a mechanism nicely explains the formation of XIII from Ic (*via* XIV) and reactions such as illustrated by XXVII → XXVIII → XXX[38] and XXXI → XXXII → XXXIV,[39] as well as the reported ozonation of VII to X (possibly *via* XXXV) and XI (possibly *via* XXXVII and XXXVIII).[24] This also seemed to be the best explanation for the production of VII and VIII from Ia, until it was found that epoxide IX apparently is produced first, and easily rearranges to VII and VIII (*via* routes d and e illustrated in XXIV). Similar rearrangements of epoxides can also explain the other reactions mentioned, as illustrated with XII, XXIX, XXXIII, and XXXVI.

Thus, in view of the present state of knowledge, we suggest that the initial attack of ozone on an olefinic double bond involves a π complex XIX which, if steric hindrance is not too great, proceeds into a 1,3-dipolar cycloaddition, *via* transition state XX, to give an initial ozonide XXIII and, from it, ozonolysis products. Blair and Maggiolo[8] have suggested, in line with the 1,3-dipolar cycloaddition mechanism,[34] that there should be more hindrance to the formation of XX, which still has sp^2 hybridization, than to the initial ozonide XXIII itself. When the formation of XX or XXIII is too strongly hindered, however, the π complex XIX proceeds, instead, to a σ complex and partial cleavage products.[40] The σ complex[12] probably is of type XXI in most cases and yields first, through loss of molecular oxygen, an epoxide XXIV, which may or may not rearrange to other partial cleavage products. The possiblity is not eliminated, however, that aldehydes XXV (or ketones) and enols XXVI may be formed directly, at least in some cases, from XXI *via* XXII, as previously indicated.

Story, *et al.*,[11] have suggested that in some cases, especially hindered *cis*-olefins, ozonolysis products may arise through the σ complex rather than an initial ozonide. This does not seem likely with compounds of types I or III in view of the data just presented, but could be a competing reaction with compounds having bulky substituents on both carbon atoms of the double bond. A complete understanding of the various competitions occurring during ozonation of olefins cannot come until systematic studies such as those reported here with I and III are carried out with compounds of types XXXIX, XL, and XLI, where groups R are bulky and constant, and groups R′ are progressively increased in bulk. Such studies are in progress.

$R_2C{=}CHR'$	$RCH{=}CHR'$	$R_2C{=}CRR'$
XXXIX	XL	XLI

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[37] A referee raised the question as to whether or not an ozonide (1,2,4-trioxolane) could decompose to an epoxide, etc. This not only seems highly unlikely, but many ozonides are now known (*e.g.*, ref 1 and 11) and no such reaction has ever been observed. The fact that 1 mole of molecular oxygen is evolved per mole of epoxide, etc., produced shows that no epoxidation of olefin by a peroxidic ozonolysis product is occurring.

[38] S. H. Graham and A. J. S. Williams, *J. Chem. Soc.*, 4066 (1959).

[39] F. M. Dean, T. Francis, and K. Manunapichu, *ibid.*, 4551 (1958).

[40] The π complex XIX is an attractive, but not absolutely necessary, precursor to XX and XXI.

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Base-Catalyzed β-Elimination Reactions in Aqueous Solution. I. Elimination from β-Acetoxy Ketones

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Abstract: 4-Methyl-4-acetoxy-2-pentanone reacts with tertiary amines and with hydroxyl ion in aqueous solution to form 4-methyl-3-penten-2-one. Reactivity of the bases is related to their pK_a by the Brønsted relationship, log $k_2 = 0.46\mathrm{p}K_a - 5.0$. Negative deviations of rate constants from this equation are presumed due to steric inhibition of proton abstraction, a conclusion supported by the greater reactivity of 4-acetoxy-2-butanone with hydroxyl ion.

Several biologically important reactions may be classified formally as β-elimination reactions and are represented by eq 1.[1] A particular example of

$$\underset{\mathbf{1}}{\mathrm{RCHX{-}CHY{-}CO{-}R_1}} \rightleftarrows \underset{\mathbf{2}}{\mathrm{RCH{=}CY{-}CO{-}R_1}} + \mathrm{HX} \qquad (1)$$

such reactions is the enzyme-mediated interconversion of D-(−)-β-hydroxybutyryl-ACP and crotonyl-ACP in fatty acid biosynthesis in *E. coli.*[2] Although the over-all sequence of reactions in fatty acid biosynthesis has been established, very little is known of the chemical mechanism employed by enoyl hydrase in mediating the interconversion of hydroxybutyrate and crotonate.[3]

Catalysis by hydronium ion[4-11] and by hydroxyl ion[12-14] of nonenzymic reversible dehydrations of β-hydroxycarbonyl compounds (eq 1: **1**, X = OH; Y = H)[15] is well established. Also, intramolecular carboxyl group catalysis of hydration of fumaric acid[16] as well as general acid catalysis of hydration of type **2** compounds are known.[11,17] The preceding establishes hydronium ion and hydroxyl ion catalysis as well as general acid catalysis of hydration–dehydration reactions of type **1** and type **2** compounds. However, general base catalysis of elimination from type **1** compounds by amine bases in aqueous solution has not been established although such catalysis is predictable on the basis of previous investigations.[18]

Since many enzymic reactions are believed to be catalyzed in a Brønsted general base sense by functional groups of the protein, it was of interest to determine if type **1** compounds (eq 1) undergo nonenzymic general base catalyzed β elimination. An experimentally convenient compound for such a study is 4-methyl-4-acetoxy-2-pentanone (**3**) which undergoes base-catalyzed β elimination, forming 4-methyl-3-penten-2-one (**4**).[22] The β-acetoxy ketone is not labile to retrograde aldol-type condensation as is the parent 4-methyl-4-hydroxy-2-pentanone (**5**) since **3** does not possess the requisite acidic alcohol group.[14,25] Further, acetyla-

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(15) No attempt is made to survey the voluminous literature of elimination reactions which are not closely related to type **1** compounds. For recent discussions of elimination reactions in general, see J. F. Bunnett, *Angew. Chem. Intern. Ed. Engl.*, 1, 225 (1962); D. V. Banthorpe in "Reaction Mechanisms in Organic Chemistry," Vol. 2, E. D. Hughes, Ed., Elsevier Publishing Co., New York, N. Y., 1963.

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(17) T. H. Fife, *ibid.*, **87**, 1084 (1965).

(18) General base catalysis in elimination reactions of compounds structurally dissimilar to type **1** compounds is well known. Thus Crowell and Francis[19] and Kim[20] have established general base catalysis by acetate ion and hydroxyl ion in the solvolysis of 3,4-methylenedioxy-β-nitrostyrene. Similarly, Weinstock, Pearson, and Bordwell[21] have established general base catalysis by trimethylamine, triethylamine, and piperidine in *cis* and *trans* eliminations in the cyclopentane and cyclohexane series.

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