acid derivative was precipitated by acidification. The colorless crystalline material was dried and decarboxylated at 145°. The resulting propionic acid derivative was purified by distillation, b. p. 130–135° (0.5 mm.). The yield was 77%. The material crystallized on standing, m. p. 37–43°.

Anal. Calcd. for $C_9H_{16}O_3$: C, 62.76; H, 9.37. Found: C, 62.96; H, 9.28.

1-(4-Tetrahydropyranyl)-2-aminopropane (I).—α-Methyl-β-(4-tetrahydropyranyl)-propionyl chloride was obtained from the acid (XI) and excess thionyl chloride in a yield of 90%. The colorless liquid boiled at 85° (0.5 mm.). A solution of 12 g. (0.063 mole) of this acid chloride in 30 cc. of dry xylene was added slowly to a stirred mixture of 20 g. of (technical) sodium azide and 120 cc. of heated xylene. The calculated amount of nitrogen was evolved within two hours. Inorganic salts were filtered, and the clear xylene solution was refluxed with 135 cc. of 12 *N* hydrochloric acid for three hours. The acid layer was separated, made alkaline with sodium hydroxide and the precipitated oil was extracted into ether. A yield of 7.3 g. (81%) of a clear colorless liquid, b. p. 89° (20 mm.), was obtained. The base was converted to the colorless hydrochloride in ether solution, and the salt was recrystallized from methanol–ethyl acetate.

Anal. Calcd. for $C_8H_{17}NO\cdot HCl$: C, 53.45; H, 10.10; N, 7.80. Found: C, 53.63; H, 10.15; N, 7.98.

Summary

1. 1-(4-Tetrahydropyranyl)-2-aminopropane was synthesized in seven steps from 4-carboxytetrahydropyran, and 1-(4-phenyl-4-tetrahydropyranyl)-ethylamine from 4-acetyl-4-phenyltetrahydropyran.

2. A number of derivatives of 1-(4-phenyltetrahydropyranyl)-2-dialkylaminoethanol were prepared from 4-phenyl-4-carboxytetrahydropyran by way of 4-phenyl-4-bromoacetyltetrahydropyran through the corresponding bromohydrin or the corresponding amino ketones.

CHARLOTTESVILLE, VIRGINIA RECEIVED MAY 20, 1950

[CONTRIBUTION FROM HAVEMEYER LABORATORY, COLUMBIA UNIVERSITY]

The Peracetic Acid Cleavage of Unsymmetrical Ketones[1]

BY W. VON E. DOERING AND LOUISE SPEERS

Since Baeyer and Villiger[2] first discovered that Caro's acid would cleave menthone, tetrahydrocarvone and camphor to related lactones, numerous carbonyl compounds have been treated with Caro's acid or with the related reagents, peracetic and perbenzoic acid, to obtain the appropriate ester or lactone. Among alicyclic compounds may be mentioned cyclohexanone,[3] suberone,[4] C_{13}–C_{17} ring ketones,[5] 3-ketosteroid derivatives,[6,7,8,9] 17-ketosteroids,[10] sarsasapogenin,[11] 20-ketopregnanes[12,13,14] and, surprisingly, α,β-unsaturated ketones, which are cleaved to enol esters.[15] A few aliphatic–aromatic ketones, *p*-methoxyacetophenone,[16] and, very recently, acetophenone, propiophenone and β-acetonaphthone,[17] have been cleaved as have four aromatic ketones, benzophenone,[18] Michler's ketone,[19] *p*-nitrobenzophenone[19] and fluorenone.[20]

The behavior of the unsymmetrical ketones in the literature permits the generalization that $2°$[2,11,12,13,14] and $3°$[10,21] alkyl groups migrate to oxygen more readily than $1°$ groups. Theoretically related is the fact that the remarkable peracetic acid oxidations of benzaldehydes to phenylformates[16] proceed only when a hydroxyl or amino group is in the ortho or para position. From these few facts the hypothesis is suggested that groups which bear positive charge more readily (as judged from other reactions) will rearrange more rapidly in the peracid cleavage. As a further test of this hypothesis, the behavior of substituted benzophenones has been investigated.

In Table I, which contains the pertinent results as well as most of the experimental details, the penultimate column shows that *p*-anisyl (expts. 8–10) and *p*-tolyl (expt. 11) migrate more rapidly than phenyl whereas *p*-chlorophenyl (expts. 14–17), *p*-bromophenyl (expt. 19), *p*-nitrophenyl[19] (expts. 20–22) and *p*-anilinium (expt. 27) migrate less rapidly than phenyl. In the absence of sulfuric acid (expts. 14 and 18) *p*-chloro- and *p*-bromobenzophenone react inexplicably to a slight

(1) This work is taken from a dissertation submitted January 21, 1949, in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University.

(2) Baeyer and Villiger, *Ber.*, **32**, 3625 (1899).

(3) Stoll and Schemer, *Helv. Chim. Acta*, **13**, 142 (1930).

(4) Baeyer and Villiger, *Ber.*, **33**, 858 (1900).

(5) Ruzicka and Stoll, *Helv. Chim. Acta*, **11**, 1159 (1928).

(6) Windaus, *Ber.*, **37**, 2027 (1904).

(7) Gardner and Godden, *Biochem. J.*, **7**, 588 (1913).

(8) Burckhardt and Reichstein, *Helv. Chim. Acta*, **25**, 821, 1434 (1942).

(9) Prelog, Ruzicka, Meister and Wieland, *ibid.*, **28**, 618 (1945); Ruzicka, Prelog and Meister, *ibid.*, **28**, 1651 (1945).

(10) (a) Jacobsen, *J. Biol. Chem.*, **171**, 61 (1947); (b) Levy and Jacobsen, *ibid.*, **171**, 71 (1947); (c) Jacobsen, Picha and Levy, *ibid.*, **171**, 81 (1947).

(11) Marker, Rohrmann, Crooks, Wittle, Jones and Turner, THIS JOURNAL, **62**, 525 (1940).

(12) Marker, *et al.*, *ibid.*, **62**, 650, 2543, 3003 (1940).

(13) Marker, *ibid.*, **62**, 2621 (1940).

(14) Sarett, *ibid.*, **69**, 2899 (1947).

(15) Böeseken and Kremer, *Rec. trav. chim.*, **50**, 827 (1931); Böeseken and Soesman, *ibid.*, **52**, 874 (1933); Böeseken and Jacobs, *ibid.*, **55**, 786 (1936).

(16) Wacek and Bézard, *Ber.*, **74**, 845 (1941).

(17) Friess, THIS JOURNAL, **71**, 14 (1949).

(18) Dilthey, Inckel and Stephan, *J. prakt. Chem.*, **154**, 219 (1939).

(19) Dilthey, Quint and Dierichs, *ibid.*, **151**, 25 (1938).

(20) Wittig and Pieper, *Ber.*, **73**, 295 (1940).

(21) The opposite behavior of camphor[2] in giving campholide may be attributed to the fact that the 3° substituent is part of a bridgehead.

TABLE I

Expt.	Ketone A-CO-B A	B	Used, mole	Acid reagents, cc. 40% peracetic	HAc	Concd. H_2SO_4	Time, hr.	Yield of products in %[a] AOH-BCOOH	BOH-ACOOH	Yield of rec. ketone in %
1	C_6H_5	C_6H_5	0.032	20	50	...	96		38, 28 (27)[b]	49
2	C_6H_5	C_6H_5	.032	20	50	...	192		42, 44	37
3	C_6H_5	C_6H_5	.02	8	8	...	192		45, 45	46
4	C_6H_5	C_6H_5	.02	8	..	50	0.5		5, 13	69
5	C_6H_5	C_6H_5	.02	8	50	30	0.5		46	24
6	C_6H_5	C_6H_5	.02	8	40	7	0.5		82	..
7	C_6H_5	C_6H_5	.02	8	50	1	38		7, 10	82
8	p-$CH_3OC_6H_4$	C_6H_5	.01	5	5	...	192	86	...	..
9	p-$CH_3OC_6H_4$	C_6H_5	.02	8	25	0.25	0.5	14, 17	...	73
10	p-$CH_3OC_6H_4$	C_6H_5	.02	8	25	.25	72	96	...	..
11	p-$CH_3C_6H_4$	C_6H_5[c]	.02	8	8	...	192	27[d], 47	...	39
12	Mesityl	C_6H_5[e]	.023	8	8	...	192	0, 7	...	92
13	Mesityl	C_6H_5	.02	8	30	8	1	0, 10	...	52
14	p-ClC_6H_4	C_6H_5[f]	.02	8	8	...	192	2[g]	.., 20	74
15	p-ClC_6H_4	C_6H_5	.03	12	..	60	0.5	...	.., 8	90
16	p-ClC_6H_4	C_6H_5	.015	6	40	7	0.5	...	15, 26	72
17	p-ClC_6H_4	C_6H_5	.02	8	40	7	72	...	32 / 45, 60 [h]	0
18	p-BrC_6H_4	C_6H_5[i]	.02	8	30	...	192	0, 3	...	94
19	p-BrC_6H_4	C_6H_5	.015	6	30	20	0.5	...	60[j]	..
20	p-$NO_2C_6H_4$	C_6H_5[k]	.01	10	50	...	336	...	.., 29	..
21	p-$NO_2C_6H_4$	C_6H_5	.02	8	50	30	0.5	...	95[l]	..
22	p-$NO_2C_6H_4$	C_6H_5	.02	8	..	30	0.5	...	67 / 0, 6 [h]	.. ..
23	p-$NO_2C_6H_4$	p-$NO_2C_6H_4$[m]	.005	10	90	...	480		1, 7	84
24	p-$NO_2C_6H_4$	p-$NO_2C_6H_4$	.01	4	..	75	0.5		54, 82	..
25	p-$NO_2C_6H_4$	p-$NO_2C_6H_4$	.02	8	50	30	0.5		33, 62	23
26	p-$NO_2C_6H_4$	o-$NO_2C_6H_4$[m]	.01	4	..	50	0.5[n]	0, 0	0, 0	92
27	p-$NH_2C_6H_4$	C_6H_5[o]	.009	4	25	17	0.5	...	39, 0 (38)[b,p]	30
28	CH_3	C_6H_5	.06	12	10	...	120	..,4	14	41
29	CH_3	C_6H_5	.10	25	20	8	1	..,7	3 / 27, .. [q]	34
30	Cyclohexyl	C_6H_5	.046	20	50	5	18	6, 33	5, 5[r]	..
31	Fluorenone		.02	8	45	5	21		55[s]	25

[a] A single figure signifies isolation as the ester. Two figures indicate that the products were isolated after hydrolysis. In contrast to a dash, 0% implies that an attempt to isolate product was made. [b] Isolated from another aliquot without hydrolysis. [c] Prepared according to Bourcet, *Bull. soc. chim.*, [3] **15**, 945 (1896). [d] *p*-Cresol was identified as *p*-methylphenoxyacetic acid, m. p. 135–137° (Gabriel, *Ber.*, **14**, 919 (1881), reports m. p. 135–136°). [e] Prepared according to Louise, *Ann. chim. phys.*, [6] **6**, 174 (1885). [f] Prepared according to Gomberg and Cone, *Ber.*, **39**, 3274 (1906). [g] *p*-Chlorophenol was isolated and identified as *p*-chlorophenoxyacetic acid, m. p. 153–155° (Minton and Stephen, *J. Chem. Soc.*, **121**, 1598 (1922) report m. p. 155–156°). [h] The precipitated ester was isolated directly; the remainder by hydrolysis of the concentrated filtrate. The total yield is the sum of the ester and acid. [i] Prepared according to Cone and Long, THIS JOURNAL, **28**, 518 (1906). [j] Phenyl *p*-bromobenzoate was identified by m. p. 113–115° (Jackson and Rolfe, *Am. Chem. J.*, **9**, 82 (1887), report 117°), and by saponification to *p*-bromobenzoic acid, m. p. 248–250° (amide, m. p. 185–188°), and phenol. [k] Prepared according to Schroeter, *Ber.*, **42**, 3356 (1909). [l] Phenyl *p*-nitrobenzoate, m. p. 128–130°, was saponified to *p*-nitrobenzoic acid and phenol. [m] Prepared according to Städel, *Ann.*, **194**, 307 (1878); **283**, 151, 164 (1894). [n] No product was isolated after 168 hours either. [o] Prepared according to the second method of Clarke and Esselen, THIS JOURNAL, **33**, 1135 (1911). [p] Identified by mixed m. p. with an authentic sample prepared from phenyl *p*-nitrobenzoate. [q] In neutralizing the sulfuric acid in the residue remaining after distillation of the acetic acid, only this small amount of phenyl acetate remained unhydrolyzed. [r] The somewhat complicated isolation is summarized by these figures and reported in more detail in the experimental section. [s] The lactone of 2'-hydroxydiphenyl-2-carboxylic acid m. p. 91.5–92.5° (Graebe and Schestakow, *Ann.*, **284**, 306 (1895), report m. p. 92.5°), was identified *via* the mono bromo derivative, m. p. 195–196° (Richter, *J. prakt. Chem.*, **28**, 273 (1883), reports m. p. 193°).

extent in the opposite direction. Phenyl mesityl ketone (expts. 12 and 13) gives some benzoic acid, but the failure to isolate mesitol makes questionable the conclusion that the mesityl group migrates more readily than phenyl. Finally it is interesting but uninformative that the alkyl groups in acetophenone (expts. 28 and 29)[22] and phenyl cyclohexyl ketone (expt. 30) migrate about as well as phenyl. However, the greater ease of migration of the 2° cyclohexyl group as compared with

(22) This result contrasts that of Friess[17] wherein the oxidative cleavage with perbenzoic acid gives only phenyl acetate.

the 1° methyl is consistent and agrees with the finding of Friess[17] that methyl cyclohexyl ketone with perbenzoic acid gives cyclohexyl acetate.

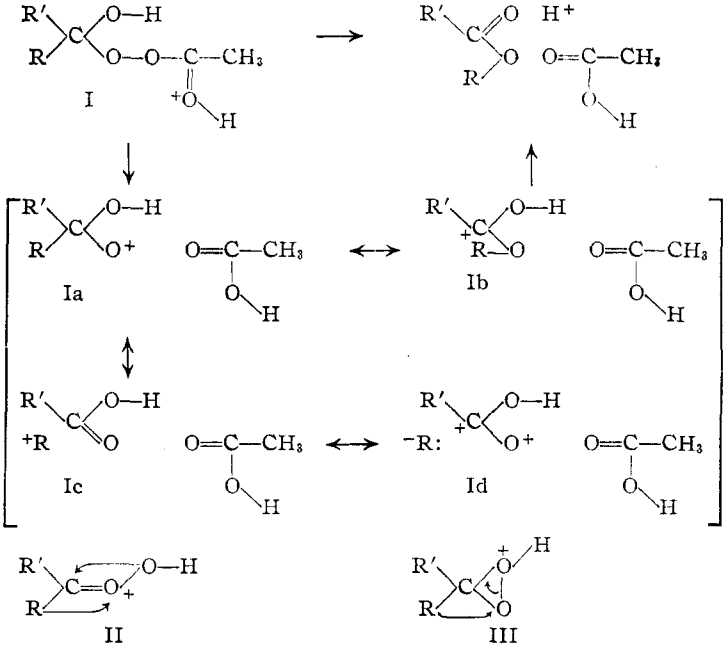
The order of the rates, very approximate at best,[23] parallels the migration aptitudes. Under comparable conditions, *p*-methoxybenzophenone (expt. 8) reacts more rapidly than benzophenone (expt. 3) and *p*-methylbenzophenone (expt. 11) which in turn react faster than *p*-chlorobenzophenone (expt. 14) and *p*-bromobenzophenone (expt. 18). *p,p'*-Dinitrobenzophenone (expt. 23) reacts very much slower.

The marked catalytic action of sulfuric acid is well illustrated by comparing the yield and reaction time in the pairs of experiments 3 and 6, 14 and 17, 18 and 19, 20 and 21, and 23 and 24. The observation of acid catalysis is not new, Wacek and Bézard[16] having reported the use of *p*-toluenesulfonic acid in peracetic acid oxidations and Dilthey, Quint and Dierichs[19] having found that *p,p'*-dinitrobenzophenone, stable in 88% sulfuric acid–hydrogen peroxide, is cleaved by 95% sulfuric acid–hydrogen peroxide to *p*-nitrophenol and *p*-nitrobenzoic acid. Establishment of acid catalysis[24] gives support to the hypothesis of an electron-deficient intermediate in these oxidations.

As in the benzpinacol rearrangement[25] the effect of substituents on migration aptitude in the peracid cleavage generally parallels the effect on the rate of aromatic substitution. In terms of the transition state theory, the effect of a substituent is accommodated in terms of an activated state, itself probably electron deficient, in which the migrating group is more electron-deficient than it was in the ground-state. In this manner *o,p*-directing substituents like methoxyl and methyl contribute lower-energy resonance structures to the transition state which decrease the activation energy and accelerate the reaction, whereas substituents like nitro and ammonium have the opposite effect.

We have considered three reaction mechanisms that accommodate the apparently consistent hypothesis that the migrating group is more electron deficient in the transition state than it is in the starting state. The first of these is the concerted[17] version of Criegee's[26] mechanism (I); the second involves attack of positive hydroxyl at the carbonyl oxygen to give either a linear peroxide (II) of the type proposed by Wittig and Pieper[21] or, third, a three-membered peroxide (III) as proposed by Baeyer and Villiger.[2] Experimental grounds for choosing among these three are now being sought.

Although the transition states in all three mechanisms are at present equally satisfactory, that from I is considered in more detail by writing four of the many resonance structures required for a reasonable representation. The oxygen–oxygen bond has increased in length and the group R is roughly equidistant from the carbon atom it is leaving (Ia) and the oxygen to which it is migrating (Ib), these two atoms having a partial positive charge. In order to explain consistently the migration aptitudes, structure Ic in which R is bearing some of the positive charge must be of importance, whereas the structure Id in which R has a negative charge must be of high energy and no appreciable significance. (The pinacol rearrangement and others have been described as involving migration of a group with its pair of electrons. Although this description accurately represents the structural relationship of starting material and rearranged product in the peracid reaction, it should not be applied to the transition state where the situation is quite the reverse: the group migrates with a smaller share in its bonding electrons (Ic) than it had in the ground state (I).)



Structural effects in R which lower the energy of R^+ can therefore be expected to increase the rate of rearrangement.

Experimental[27]

General Procedure.—A solution of the ketone, either

(23) Attempts to follow the reaction rates quantitatively were made futile by the fact that the spontaneous rate of decomposition of peracetic acid was increased by the presence of reaction product, *e. g.*, phenyl benzoate, even though the product seemed to be stable.

(24) From expts. 4–7, 15–16, 21–22 and 24–25, the suggestion can be derived that the acid catalysis is more complicated than a simple first-order dependence in that the catalytic action of sulfuric acid goes through a maximum varying with the ketone being oxidized. This suggestion is presently being scrutinized explicitly.

(25) *Cf.* Stempel, *J. Chem. Education*, **23**, 434 (1946).

(26) Criegee, *Ann.*, **560**, 127 (1948).

(27) Melting points are corrected. Microanalyses were done by Miss Lois E. May, the Clark Microanalytical Laboratory and the Elek Microanalytical Laboratory.

in acetic acid, sulfuric acid or a mixture of the two was added to cooled 40% peracetic acid.[28] The oxidation was allowed to proceed at room temperature. The product was determined, either directly by recrystallization of the ester, by saponification of the residue that remained after evaporating the acetic acid solvent or by saponification of the ether extract of the neutralized aqueous solution of the reaction mixture. Since the isolation procedures are commonplace and take customary advantage of the difference in acidity of phenols and acids, only in exceptional cases are more details given. References to the preparation of starting materials are given in Table I. Common hydrolysis products and starting materials were identified by melting point and mixed melting point. Esters were identified by hydrolysis or by mixed melting point with authentic samples. Phenol was characterized as the 2,4,6-tribromide, m. p. 92–94°.

p-**Methoxyphenylbenzoate.**—Isolated from experiment 8, Table I, by recrystallizing from hexane the precipitate formed when the reaction mixture was diluted with water, *p*-methoxyphenylbenzoate, m. p. 87.5–88.0°, was characterized by saponification to benzoic acid, m. p. 121–122°, and *p*-methoxyphenol, m. p. 53.5–54.0° (reported[29] m. p. 53°).

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.66; H, 5.30. Found: C, 73.56; H, 5.50.

Phenyl *p*-Chlorobenzoate.—Recrystallization of the crystalline material present at the conclusion of experiment 17, Table I, from hexane gave phenyl *p*-chlorobenzoate, m. p. 104–104.5°, identified by saponification to *p*-chlorobenzoic acid, m. p. 237–240°, and phenol.

Anal. Calcd. for $C_{13}H_9O_2Cl$: C, 67.11; H, 3.90. Found: C, 67.19; H, 4.01.

(28) Peracetic acid, 40%, was obtained from the Buffalo Electro-Chemical Company, Buffalo, N. Y.

(29) Hlasiwetz and Habermann, *Ann.*, **177**, 334 (1875).

Oxidation of Cyclohexyl Phenyl Ketone.—The mixture resulting from the oxidation of 8.65 g. of cyclohexyl phenyl ketone[30] (expt. 30, Table I) was concentrated *in vacuo* leaving 8.41 g. of dark oil. Distillation through a small Vigreux column gave fraction A, 1.32 g., b. p. 67–136° (14 mm.) and fraction B, 4.53 g., b. p. 136–157° (14 mm.). Saponification of A gave a bicarbonate-soluble oil (0.57 g.) which was molecularly distilled to give 0.28 g. (5%) of a colorless liquid identified as cyclohexane carboxylic acid by conversion to the amide, m. p. 137–139°. On the cold finger of the apparatus, 0.28 g. (5%) of benzoic acid was obtained. The bicarbonate-insoluble portion afforded 0.22 g. (5%) of phenol. Fraction B was redistilled giving two fractions, b. p. 135–157° (19 mm.) (1.66 g.) and b. p. 157–159° (19 mm.) (2.25 g.). Saponification of the first gave 0.26 g. (6%) of cyclohexanol, micro b. p. 162°, identified as the urethan, m. p. 81–82° (reported[31] m. p. 82.5°), and 0.60 g. (11%) of benzoic acid. After being redistilled, the second fraction, which was saponifiable to cyclohexanol and benzoic acid (17%), was analyzed; $n^{23}D$ 1.5195.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.45; H, 7.90. Found: C, 76.29; H, 8.09.

Summary

The cleavage of several unsymmetrical benzophenones with peracetic acid has been investigated. It is concluded that the migration aptitude and existence of acid catalysis support mechanisms in which the rearranging group is electron-deficient in the transition state.

(30) Prepared according to Meyer and Scharvin, *Ber.*, **30**, 1940 (1897).

(31) Bouveault, *Bull. soc. chim.*, [3] **29**, 1051 (1903).

NEW YORK 27, N. Y. RECEIVED DECEMBER 7, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

Reactions of Peracids. IV. The Reaction of Cyclohexylphenyl Ketone with Perbenzoic Acid

BY S. L. FRIESS AND N. FARNHAM

In a previous communication[1] in this series, it was noted that in the reaction

$$R{-}COCH_3 + C_6H_5CO_3H \xrightarrow[25^\circ]{CHCl_3} R{-}OCOCH_3 + C_6H_5CO_2H$$

I, R = phenyl
II, R = cyclohexyl

compound I consumed peracid far more slowly than II. For a rough comparison, a reaction period of ten days at room temperature was observed to result in complete uptake of 1.0 mole of perbenzoic acid by II, while under identical conditions the reaction of I has progressed to the extent of only 65%. Accordingly, it was of some utility in the present study to first investigate the relative rates of reaction in a more quantitative manner, employing runs at constant temperature, in order to evaluate the effect of the degree of saturation of ring R on the rate of uptake of peracid.

(1) Friess, THIS JOURNAL, **71**, 14 (1949).

A logical extension of this work was concerned with a ketone possessing both the phenyl and cyclohexyl groups in the same molecule, making possible a study in which the relative migration aptitudes of the two groups might be obtained. The cyclohexyl phenyl ketone (III) required for this objective was prepared and its rate of reaction with perbenzoic acid measured under the same conditions employed to study I and II. In addition, several larger scale runs on III were made to determine the relative proportions of the isomeric esters obtained as products, resulting from the competitive migration of the phenyl and cyclohexyl groups during some stage of the reaction.

Discussion

In the comparative rate work on compounds I, II and III, it was found that the presence of a phenyl nucleus conjugated with the carbonyl group markedly decreases the rate of reaction with peracid. In Fig. 1, for example, is shown a set of representative runs on the three ketones, with