A solution of 10 g. (0.05 mole) of crude sodium β-methyl-β-phenylglycidate in 50 ml. of water, cooled to 0°, was made just acid to litmus with cold, 10% aqueous sulfuric acid. The resulting mixture was extracted with four 10-ml. portions of ether and the combined extracts were washed with water, dried over magnesium sulfate and concentrated. Distillation of the residue afforded 3.90 g. (59%) of α-phenylpropionaldehyde, b.p. 60° (1 mm.), $n^{29}D$ 1.5138 [lit.[38] 73–76° (4 mm.)]. The 2,4-dinitrophenylhydrazone of the product crystallized from a methanol–ethyl acetate mixture as yellow prisms, m.p. 137–138° (lit.[30] 136–137°). The vapor-phase chromatogram of the aldehyde indicated the presence of less than 2% acetophenone. The infrared spectrum[11] of the aldehyde has bands at 2710 and 2815 cm.$^{-1}$ (C–H of aldehyde) and at 1720 (C=O) as well as a very weak band at 1682 cm.$^{-1}$ (conj. C=O of acetophenone).

A sample of the aldehyde, b.p. 89–95° (11 mm.), $n^{29}D$ 1.5160, was prepared in 48% yield by the procedure of Newman and Closson.[16] The vapor-phase chromatogram of the crude product indicated the presence of 32% of acetophenone. The infrared spectrum[6] of the crude product had the same peaks present in the spectrum of the aldehyde sample previously described. However, the band at 1682 cm.$^{-1}$ (conj. C=O of acetophenone) was much more intense.

A solution (pH ~ 9) of 1 g. (0.005 mole) of crude sodium β-methyl-β-phenylglycidate in 10 ml. of water was heated to 80° for 1 hr., cooled and extracted with ether. The extract was dried, concentrated and treated with 2,4-dinitrophenylhydrazine in boiling ethanol. The cold, ethanolic solution deposited 0.16 g. (12%) of acetophenone 2,4-dinitrophenylhydrazone, m.p. 246–247°, identified by a mixed melting point determination with an authentic sample. Reaction of the aqueous layer with *p*-bromophenacyl bromide yielded the *p*-bromophenacyl ester of β-methyl-β-phenylglycidic acid, m.p. 128.5–130°, previously described, yield 0.80 g. (42%).

A 0.50-g. (0.0025 mole) sample of the less soluble sodium β-methyl-β-phenylglycidate, m.p. 256° dec., was converted to the crude, insoluble silver salt, m.p. 154–155° dec., by treatment with aqueous silver nitrate. The crude silver salt was stirred with excess ethyl iodide at room temperature for 30 min. The resulting mixture was diluted with ether and filtered. After the filtrate had been dried over magnesium sulfate and concentrated, the infrared spectrum[6] of the crude residue (350 mg.) was examined. The spectrum has all of the bands present in the spectrum of the original glycidic ester plus a new, strong band at 915 cm.$^{-1}$. The ultraviolet spectrum of the crude residue has a maximum at 239 mμ (ε 4200). Since attempts to separate the components of the crude re-esterified product by fractional distillation resulted in decomposition of the entire sample, a 300-mg. portion of the crude product was hydrolyzed with aqueous sulfuric acid as previously described. The only crystalline product which could be isolated was the lower-melting isomer of ethyl 2,3-dihydroxy-3-phenylbutyrate, m.p. 42.5–44°, yield 55 mg., which was identified by a mixed melting point determination with the diol sample previously described.

CAMBRIDGE 39, MASS.

(30) F. Ramirez and A. F. Kirby, THIS JOURNAL, **75**, 6026 (1953).

[CONTRIBUTION FROM THE ROHM & HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

A Re-examination of the Peroxyacid Cleavage of Ketones. I. Relative Migratory Aptitudes

BY M. FREDERICK HAWTHORNE,[1] WILLIAM D. EMMONS AND K. S. MCCALLUM

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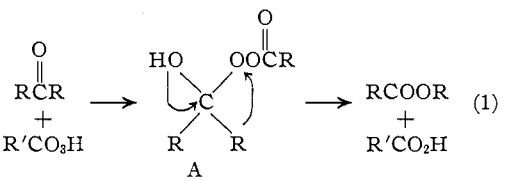
Relative migratory aptitudes of various groups in the cleavage of unsymmetrical ketones with trifluoroperoxyacetic acid have been measured. The results are compared with those of similar studies with other peroxyacids. Among alkyl groups, the usual sequence prim. < sec. < tert. is observed. The 1-apocamphyl group has nearly as high a migratory aptitude as does *t*-butyl. Among aryl groups, migratory aptitude is decreased by electron-attracting substituents on the aromatic nucleus. Migration aptitudes are significantly different in the reactions of ketones with trifluoroperoxyacetic acid and with peroxyacetic acid; the latter reagent is the more selective of the pair. Mechanistic implications are discussed.

The mechanism of the oxidation of ketones to esters by peroxyacids[2] has received considerable study during recent years. Criegee[3] proposed the mechanism shown in eq. 1. The intermediate, A, will be referred to as the "Criegee intermediate."



(1)

Friess[4] and co-workers studied the kinetics of the reaction of various ketones with peroxybenzoic acid and concluded that the reaction was general acid catalyzed and that formation of A was the rate-determining step.

Turner[5] and Mislow and Brenner[6] proved that optically active alkyl groups migrated with complete retention of configuration. The product-determining step of the Baeyer–Villiger reaction thus appears to be related to the well known Lossen,[7] Curtius[8] and Schmidt[9] reactions as the Criegee mechanism would predict.

Doering and Speers[10] carried out a thorough product study of the reaction of unsymmetrical ketones with peroxyacetic acid. From this work and also from the work of Friess[11] it was concluded that the order of increasing migratory aptitudes of alkyl groups is generally prim. < sec. < tert. Similarly, it was shown[10] that aryl groups with electron-releasing substituents displayed enhanced migratory ability.

More recently, Doering and Dorfman[12] have shown, by O^{18}-labeling of the ketone carbonyl, that the oxygen of the carbonyl group of the ester formed in the reaction comes from the ketone. This extremely important result at once ruled out

(1) Presented at the Sixth Reaction Mechanisms Conference, Swarthmore, Pa., September, 1956.

(2) This general reaction will be referred to as the Baeyer–Villiger reaction throughout this and the succeeding papers of this series [A. v. Baeyer and V. Villiger, *Ber.*, **32**, 3625 (1899)].

(3) R. Criegee, *Ann.*, **560**, 127 (1948).

(4) S. L. Friess and A. H. Soloway, THIS JOURNAL, **73**, 3968 (1951).

(5) R. B. Turner, *ibid.*, **72**, 878 (1952).

(6) K. Mislow and J. Brenner, *ibid.*, **75**, 2318 (1953).

(7) E. S. Wallis and R. D. Dripps, *ibid.*, **55**, 1701 (1933).

(8) L. W. Jones and E. S. Wallis, *ibid.*, **48**, 169 (1926).

(9) J. V. Brown and E. Friehmelt, *Ber.*, **66**, 684 (1933).

(10) W. v. E. Doering and L. Speers, THIS JOURNAL, **72**, 5515 (1950).

(11) S. L. Friess and N. Farnham, *ibid.*, **72**, 5518 (1950).

(12) W. v. E. Doering and E. Dorfman, *ibid.*, **75**, 5595 (1953).

possible reaction paths which would involve equivalent oxygen atoms.

Yukawa and Yokoyama have carried out migration aptitude studies[13] with a series of phenyl cycloalkyl and phenyl alkyl ketones with peroxybenzoic acid. These same authors concluded from a comparison of oximation and Baeyer–Villiger rates[14,15] for a series of ketones that the rate-determining step of the latter was acid-catalyzed electrophilic attack of the peroxyacid upon the ketone carbonyl group.

The discovery of trifluoroperoxyacetic acid, its synthetic application to the Baeyer–Villiger reaction[16] and the demonstration[17] that it could be used as an analytical reagent for the estimation of the carbonyl function at once suggested its use in further studies of the Baeyer–Villiger reaction. The reagent offers some advantages over other peroxyacids in that it reacts rapidly at low temperatures with very clean stoichiometry. This paper reports the results of a study of relative migratory aptitudes.

Results

Two series of unsymmetrical ketones were examined. The first was a group of phenyl alkyl ketones and the second series were nuclearly substituted acetophenones. In an additional series of experiments, the action of peroxyacetic acid on phenyl cyclohexyl ketone was compared with that of trifluoroperoxyacetic acid.

Phenyl Alkyl Ketone Cleavage.—In this series of experiments the migratory ability of various prim. sec. and tert. alkyl groups were determined relative to that of the phenyl group. The reactions were carried out under conditions which prevented or at least minimized nuclear oxidation of the phenyl esters, and at the same time prevented transesterification of the reaction products with trifluoroacetic acid. This was accomplished by carrying out the reaction in the presence of an acid scavenger, disodium acid phosphate.[16] Table I presents the collected yield data and the migratory ratios obtained. In every case the material balance was such as to account for at least 90% of the reactant ketone as ester or recovered starting material.

Cleavage of Substituted Acetophenones.—Two negatively substituted acetophenones were employed in this study—*p*-chloroacetophenone and *p*-nitroacetophenone. Although both of these ketones reacted sluggishly with trifluoroperoxyacetic acid at room temperature in methylene chloride solvent, sufficient conversion to esters was obtained after 20–50 hours reaction to obtain analytical measurements. In all cases material recoveries were of the order of 100 to 106%. Table II summarizes the results of these experiments.

The Peroxyacetic Acid Oxidation of Phenylcyclohexyl Ketone.—In order to determine the effect of peroxyacid reactivity upon the selectivity of group migration during the oxidation of a representative ketone, the oxidation of phenyl cyclohexyl ketone was carried out using anhydrous peroxyacetic acid in the presence of trifluoroacetic acid catalyst and in ethylene chloride at 29.8°. Phenyl cyclohexyl ketone was employed since it had been shown in other experiments that the phenyl and cyclohexyl groups have similar migratory abilities.

In order to prove that mixtures of peroxyacetic acid and trifluoroacetic acid do not equilibrate as in (2) under the conditions employed, control experiments were carried out (see Experimental part) in which mixtures of peroxyacetic acid with trifluoroacetic acid and mixtures of trifluoroperoxyacetic acid with acetic acid were prepared and each mixture was analyzed simultaneously for both peroxyacids as a function of time. It was found that trifluoroperoxyacetic acid was not produced at a measurable rate under the reaction conditions employed for oxidation of phenyl cyclohexyl ketone.

$$CH_3CO_3H + CF_3CO_2H \rightleftharpoons CH_3CO_2H + CF_3CO_3H \quad (2)$$

In contrast to these results it was found that trifluoroperoxyacetic acid does react slowly with acetic acid in the presence of trifluoroacetic acid to produce peroxyacetic acid. It thus appears as though the rates of these exchange reactions are intimately related to the ability of the peroxyacid to donate hydroxyl cation and/or the nucleophilicity of the carboxylic acid.

TABLE I

OXIDATION OF PHENYL ALKYL KETONES WITH TRIFLUOROPEROXYACETIC ACID

R in C_6H_5COR	Ester products, % $RCOO-C_6H_5$	Ester products, % C_6H_5-COOR	Total yield, %	Alkyl/phenyl ratio
Methyl	90	Negl.	90	Very small
Ethyl	87	6	93	7×10^{-2}
n-Propyl	85	6	91	7×10^{-2}
i-Propyl	33	63	96	1.9
Cyclohexyl[a]	25	75	100	3.0
Cyclopentyl	44	48	92	1.1
Benzyl	39	51	90	1.3
Neopentyl	84	9	97[b]	1.1×10^{-1}
t-Butyl	2	77	90[c]	39
1-Apocamphyl[d]	2.5	97.5	[e]	39

[a] Data obtained by experimental methods outlined in both methods A and B of Experimental. [b] Total yield includes 4% recovered ketone. [c] Total yield includes 11% recovered ketone. [d] Data obtained by method B of Experimental. Yield assumed to be 100% in analytical experiments; preparative experiments produced a 90% yield of 1-apocamphanol.

TABLE II

OXIDATION OF *p*-X-ACETOPHENONES WITH TRIFLUOROPEROXYACETIC ACID

p-X	Recovery, % of ketone reactant: *p*-X-benzoic acid	*p*-X-phenol	*p*-X-acetophenone	Methyl migration, %
–Cl	1.2	41.5	64[a]	2.9
	1.2	40.9	64[a]	
$-NO_2$	9.0	61.0	33	13
	8.8	60.1	31	

[a] Pure by infrared but contained small amounts of solvent.

(13) Y. Yukawa and T. Yokoyama, *Mem. Inst. Sci. Ind. Research Osaka Univ.*, **13**, 171 (1956).

(14) Y. Yukawa and T. Yokoyama, *ibid.*, **9**, 180 (1952).

(15) Y. Yukawa and T. Yokoyama, *J. Chem. Soc. Japan*, **73**, 371 (1952).

(16) W. D. Emmons and G. B. Lucas, THIS JOURNAL, **77**, 2287 (1955).

(17) M. F. Hawthorne, *Anal. Chem.*, **28**, 340 (1956).

Table III records the results obtained in the experiments described above while Table IV presents similar data obtained by the use of the trifluoroperoxyacetic acid with phenyl cyclohexyl ketone.

TABLE III

PRODUCT DISTRIBUTION FROM PEROXYACETIC ACID CLEAVAGE OF PHENYL CYCLOHEXYL KETONE CATALYZED BY TRIFLUOROACETIC ACID IN ETHYLENE CHLORIDE SOLVENT AT 29.8°

Initial concentrations, moles/l.			Phenyl migration,
$C_6H_5COC_6H_{11}$	CH_3CO_3H	CF_3CO_2H	%
0.21	0.51	1.76	11.9
.20	.50	1.76	10.8
.21	.50	1.80	9.1
.20	.48	1.80	10.2

TABLE IV

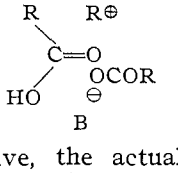
PRODUCT DISTRIBUTION FROM THE TRIFLUOROPEROXYACETIC ACID CLEAVAGE OF PHENYL CYCLOHEXYL KETONE CATALYZED BY TRIFLUOROACETIC ACID IN ETHYLENE CHLORIDE SOLVENT, 29.8°

Initial concentrations, moles/l.[a]			Phenyl migration,
CF_3CO_3H	CF_3CO_2H	$C_6H_5COC_6H_{11}$	%
0.409	0.495	1.00	21.4
.395	.476	1.20	21.9
.200	.242	1.00	22.0
.200	.242	1.00	21.5

[a] Calculated on the basis of the final volume of reaction mixture (10 ml.). In these latter cases the reaction mixtures were examined by infrared spectra after removal of solvent and trifluoroacetic acid *in vacuo* but prior to hydrolysis. In every case a strong band characteristic of trifluoroacetate esters was found at 5.60 μ. These esters must arise through transesterification of trifluoroacetic acid with the normal Baeyer-Villiger reaction products.[18]

Discussion

Alkyl Group Migration in Concerted Rearrangement.—The foregoing experimental data clearly show that the migratory ability of alkyl groups in the Baeyer–Villiger reaction decreases in the order tertiary > secondary > primary > methyl. This effect has been observed previously and discussed[10] in terms of the ability of the migrating group to sustain positive charge in the transition state as in canonical structure C. Those alkyl groups which may stabilize positive charge by hyperconjugation or by inductive electron release appear to have superior migratory abilities. Although this explanation is attractive, the actually rather small rate differences observed in competitive migration processes such as in the extreme case of *t*-butyl and phenyl *vs.* ethyl and phenyl (for which the observed alkyl/phenyl ratios are *ca.* 39 and 7 × 10^{-2}, respectively) suggest that the carbonium ion character of R depicted in B is not tremendously important.[19]

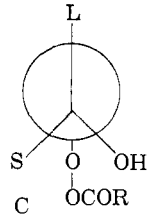


B

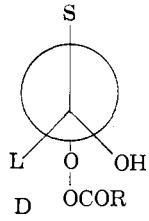
(18) In the following paper this is verified experimentally; M. F. Hawthorne and W. D. Emmons, THIS JOURNAL, **80**, 6398 (1958).

(19) The ratio 38/7 × 10^{-2} or 555 is small compared to the rate ratios observed in the solvolysis of ethyl and *t*-butyl halides which may be as high as 10^6 or 10^8. See A. Streitwieser, *Chem. Revs.*, **56**, 571 (1956), for examples.

A possible alternative explanation for the observed rate differences involves steric acceleration of migration of the more bulky alkyl group and the assumption that the alkyl group which migrates enters the transition state *trans* to the leaving carboxylic acid group.



C



D

The sterically favored transition state should be that which "staggers" the leaving group (–OOCOR) between the smaller alkyl group and the small hydroxyl group. Migration of the larger alkyl group would occur by way of the sterically preferred transition state C.

Further examination of Table I brings out three further interesting points. In favor of the electronic argument is the fact that the benzyl group migrates to oxygen at a relative rate which is comparable to those of secondary alkyl groups. The argument that the migrating benzyl group has some cationic character is further strengthened by the fact that the bulky neopentyl group has about the same migratory aptitude as ethyl and *n*-propyl.

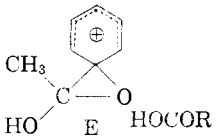
The cleavage of phenyl 1-apocamphyl ketone presents an apparent anomaly since carbonium ion character is relatively difficult to develop at a bridgehead carbon atom during the solvolysis of bridgehead-substituted halides. This has generally been attributed to difficulty in bringing the tertiary carbon atom into the trigonal planar configuration. The transition state which is produced in the decomposition of the Criegee intermediate is probably unique in that solvation of the cation-like migrating group probably is not required. If tertiary carbonium ions were not required to assume a planar configuration to attain stability, and if the lack of reactivity associated with bridgehead halides were actually due to steric hindrance of back-side solvation of the developing ion, the high migratory ability of the 1-apocamphyl group could be rationalized.

The true solution to the electronic *vs.* steric enigma is still an open question and in all probability both effects are important. The electronic interpretation appears to the authors to be the most promising.

Aryl Group Migration.—The observations of previous workers[10,11,13] with regard to the factors which determine the ease of aryl group migration are conclusive. It is always observed that electron-donating substituents enhance the migratory ability of aryl groups. The results reported above for the trifluoroperoxyacetic acid cleavage of substituted acetophenones confirm this conclusion. In going from phenyl to *p*-chlorophenyl to *p*-nitrophenyl the methyl/aryl migration ratio increases in the order: too small to measure, 3 × 10^{-2} and 1.5 × 10^{-1}.

The stabilization afforded the migration transition state by electron-donating groups can be effective only in the π-electron stabilization from

such structures as E rather than those corresponding to B and the transition state may resemble a heterocyclic "phenonium ion."



Peroxyacetic Acid Cleavage of Phenyl Cyclohexyl Ketone.—Greater selectivity between migrating groups is observed in cleavage with peroxyacetic acid than in the similar reaction with trifluoroperoxyacetic acid. This *proves* that migration must occur while the carboxylic acid residue is leaving the Criegee intermediate. It also suggests that more driving force is supplied by the migrating group when acetic acid leaves than when trifluoroacetic acid is expelled. The result is that which would be expected if the Criegee complex is a high energy intermediate which passes over an energy barrier in the ionization–rearrangement reaction. If this is the case, the more reactive adduct with trifluoroacetic acid as the leaving group would undergo the least change in arriving at the transition state.

Experimental

Materials.—All ketones, with the exception of 1-apocamphyl phenyl ketone, and esters either were obtained commercially or prepared by standard literature methods. In either case they were carefully distilled or recrystallized before use. Distillations were routinely carried out with a Heli-pak packed column of approximately fifty theoretical plates efficiency. Methylene chloride was purified by distillation through a large helix-packed column and ethylene chloride was purified by extraction with cold sulfuric acid until a colorless acid layer was obtained, washing with water, drying over anhydrous sodium carbonate, and by distillation of the resulting material from phosphorus pentoxide.

1-Apocamphyl Phenyl Ketone.—One-tenth mole (18.7 g.) of apocamphane-1-carboxylic acid chloride, prepared by the method of Bartlett and Knox,[20] was dissolved in 150 ml. of dry ether and one-tenth mole of phenylmagnesium bromide in 100 ml. of ether was added with stirring at such a rate as to maintain reflux. The reaction mixture was neutralized immediately by addition of dilute hydrochloric acid. The ether layer was washed well with water, dried over magnesium sulfate and the solvent was evaporated. The residual oil was cooled and scratched to induce crystallization. The crude product (16 g. or 70%) was recrystallized from pentane at −70° to yield 10.5 g. of ketone, m.p. 52–53°.

Anal. Calcd. for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.0; H, 8.95.

Trifluoroperoxyacetic acid in methylene or ethylene chloride solution was prepared by the method of Emmons and Lucas[16] for use in the preparative experiments which determined migratory aptitudes. In experiments which employed more refined analytical techniques these solutions were prepared as follows: About 20 ml. of pure trifluoroacetic anhydride was distilled through a small Heli-pak column into a micro-buret of 5-ml. capacity. About 0.8 g. of standardized 90% hydrogen peroxide (actually 88.0% pure) was weighed accurately into a 25-ml. volumetric flask and 15 ml. of ethylene chloride was added. To this mixture was added from the micro-buret exactly 4.90 ml. of trifluoroacetic anhydride for each gram of 88% peroxide taken. The flask was stoppered and shaken to effect reaction. The solution was then made up to volume at 29.8° and a 1-ml. aliquot was hydrolyzed with ice-water and titrated iodometrically. Calculated and observed titers agreed to within 3%.

Peroxyacetic acid in ethylene chloride was prepared by addition of 5.00 ml. of a solution prepared from 33.25 g. of acetic anhydride and 1.0 g. of trifluoroacetic acid diluted to 25 ml. with ethylene chloride to 1.00 g. of 88.0% hydrogen peroxide. The flask was shaken, cooled with an ice-bath, and allowed to stand for one hour. The solution was then diluted to 25 ml. with ethylene chloride to produce an approximately 1 *M* solution. Solutions prepared in this manner were titrated for hydrogen peroxide with standard ceric sulfate and for peroxyacetic acid by the iodimetric titration of peroxyacetic acid.[18] Analyses by this method indicated 99% conversion to peroxyacetic acid with 1% residual hydrogen peroxide. No diacetyl peroxide was present.

Procedure for Trifluoroperoxyacetic Acid Oxidation of Phenyl Alkyl Ketones (Method A).—With the exceptions of pivalophenone and phenyl 1-apocamphyl ketone all the ketones of Table I were oxidized in the following manner: A solution of trifluoroperoxyacetic acid was prepared by the dropwise addition of 19 ml. (0.09 mole) of trifluoroacetic anhydride to a stirred suspension of 2.1 ml. (0.075 mole) of 90% hydrogen peroxide in 25 ml. of methylene chloride stirred in an ice-bath. The solution so obtained then was added dropwise over a 30-minute period to a vigorously stirred suspension of 28.0 g. (0.20 mole) of disodium hydrogen phosphate in 150 ml. of methylene chloride containing 0.05 mole of phenyl alkyl ketone. After addition the mixture was heated under reflux for one hour and then was poured into 300 ml. of water. The organic layer was separated and dried over magnesium sulfate. The volatile solvent was evaporated at reduced pressure and the residua oil was diluted to 250 ml. with carbon tetrachloride. T infrared analyses of these solutions are described below.

Trifluoroperoxyacetic Acid Oxidation of Pivalophenone.—This experiment was carried out as described above. The product was contaminated with a hydroxy trifluoroacetate ester believed to have come from small amounts of isobutylene oxide formed in this reaction. Accordingly, the crude product was fractionated in a semi-micro spinning band column and a fraction (8.0 g., 90%) boiling at 106–108° (15 mm.) was obtained. An infrared spectrum of this material showed that it contained unreacted ketone as well as *t*-butyl benzoate and phenyl pivalate but no other detectable impurities. The mixture was analyzed for total ester content by saponification. A sample of the mixture was refluxed six hours with 0.50 *N* potassium hydroxide in ethylene glycol under a nitrogen atmosphere. Control experiments with authentic esters gave 99% recoveries under these conditions. The total ester was determined by back titration and unreacted ketone (12%) was determined by difference. Phenyl trimethylacetate (2.2%) was determined by the bromometric titration of the phenol liberated in the saponification.

Trifluoroperoxyacetic Acid Oxidation of Phenyl 1-Apocamphyl Ketone (Method B).—To 0.842 g. of 88.0% hydrogen peroxide suspended in 15 ml. of ethylene chloride was added 4.11 ml. of trifluoroacetic anhydride and the solution was then diluted to 25 ml. This solution was shown by titration to be 0.87 *M* in trifluoroperoxyacetic acid and 1.3 *M* in trifluoroacetic acid.

In a 50-ml. three-necked flask having a stirrer, dropping funnel and drying tube were placed 1.05 g. (4.6×10^{-3} mole) of phenyl 1-apocamphyl ketone and 5 ml. of ethylene chloride. This solution was placed in a thermostat at 29.8° and 2.0 ml. of the above peroxyacid solution (1.7×10^{-3} mole peroxyacid and 2.6×10^{-3} mole of trifluoroacetic acid) was added slowly over the course of one hour. The dropping funnel was washed with 1 ml. of solvent and this added to the reaction mixture. The reaction mixture was allowed to stand at 29.8° for five hours and the volatile solvent removed by evaporation at reduced pressure. The residual oil was refluxed for 12 hours with 50 ml. of 2 *N* potassium hydroxide in a nitrogen atmosphere. The hydrolysate was cooled and extracted with ether to remove all organic material other than phenol. The resulting aqueous potassium phenolate solution was freed of residual ether by a rapid stream of air, diluted to 100 ml. with water and the phenol determined as follows: A 25-ml. aliquot of phenol solution was mixed with 1 g. of sodium bromide and a slight excess of hydrochloric acid at 0°. Ten ml. of 0.100 *N* potassium bromate was added and the solution was allowed to stand for 3–4 minutes. The excess bromine was determined by titration of the iodine produced on the addition of sodium iodide by 0.1 *N* sodium thiosulfate solution. In this manner 2.63×10^{-1} meq. of bromine was consumed per 100 ml. of phenol solution. Assuming 100% conversion of

(20) P. D. Bartlett and L. H. Knox, THIS JOURNAL, **61**, 3184 (1939).

peroxyacid to ester mixture (1.7 mmoles) the ratio of apocamphyl to phenyl migration was calculated as 97.5 to 2.5. A similar series of experiments were conducted with phenyl cyclohexyl ketone and the results are presented in Table IV.

Preparation of 1-Apocamphanol.—To 4.1 ml. (0.15 mole) of 90% hydrogen peroxide suspended in 100 ml. of methylene chloride with stirring was added 26 ml. (0.18 mole) of trifluoroacetic anhydride in an ice-bath. Phenyl 1-apocamphyl ketone (2.28 g., 0.01 mole) was dissolved in 5 ml. of methylene chloride and 20 ml. of the above peroxyacid solution added with cooling and stirring. After the addition the solution was allowed to stand at room temperature overnight and the solvent was then removed by evaporation at reduced pressure. The residue (2.00 g.) was heated under reflux with 3.0 g. of sodium hydroxide and 20 ml. of diethylene glycol. As hydrolysis proceeded 1-apocamphanol collected on the cold condenser. After about two hours hydrolysis was complete. The product was removed from the condenser by ether; the ether solution was dried over magnesium sulfate, and the solvent was removed at reduced pressure. The crystalline residual solid (1.25 g., 90%) was recrystallized from petroleum ether to yield 1.0 g. of material melting at 160° (sealed tube).

Infrared Analysis of Ester Mixtures.—The reaction products were diluted to 250 ml. with carbon tetrachloride giving solutions which were 0.20 *M* based on starting ketone. Infrared spectra of these solutions were obtained with a Perkin–Elmer model 21 spectrophotometer using a sodium chloride prism. Concentrations of the esters were estimated by comparing the absorption at the carbonyl stretching frequency with that of standard solutions of the pure esters. When the molar ratio of the major product to the minor product did not exceed 5:1 the concentrations of both esters could be obtained directly. Where this ratio was greater, only the major component was determined and a reference solution of this component of the same concentration was prepared. The reaction product solution then was run against this reference and the absorption spectrum of the minor component was recorded. Results were finally checked by running the spectrum of the products with a solution containing the computed concentrations in the reference beam. This technique checked the calculated results and demonstrated the absence of trifluoroacetate esters and ketone in the reaction products. The analytical frequencies given in Table V were employed.

TABLE V

ANALYTICAL FREQUENCIES OF ESTER PAIRS

Ester	Analytical frequency, cm.$^{-1}$
Cyclopentyl benzoate	1708
Phenyl cyclopentylcarboxylate	1746
Cyclohexyl benzoate	1708
Phenyl cyclohexylcarboxylate	1733
Phenyl phenylacetate	1745
Benzyl benzoate	1708
Phenyl isobutyrate	1747
Isopropyl benzoate	1708
Ethyl benzoate	1705
Phenyl propionate	1756
Phenyl *n*-butyrate	1746
n-Propyl benzoate	1706
Phenyl *t*-butylacetate	1742
Neopentyl benzoate	1709

Transoxidation of Peroxyacetic and Trifluoroacetic Acids.—A solution which was 0.253 *M* in peroxyacetic acid and 0.210 *M* in trifluoroacetic acid was prepared in ethylene chloride at 29.8°. Immediately after mixing, and at various time intervals thereafter, 2 ml. aliquots were withdrawn and analyzed for trifluoroperoxyacetic acid (ceric ion titration) and peroxyacetic acid (thiosulfate titration). The reaction was followed over a 20-hour period during which the ceric titers remained constant at 0.20 ml. of 0.0835 *N* solution as did the thiosulfate titers at 10.50 ml. of 0.1014 *N* thiosulfate.

Transoxidation of Trifluoroperoxyacetic Acid and Acetic Acids.—A reaction mixture which was 0.517 *M* in trifluoroperoxyacetic acid and 3.34 *M* in acetic acid was prepared in ethylene chloride at 29.8°. Two-ml. aliquots were titrated for trifluoroperoxyacetic acid as before. The data appear in Table VI.

TABLE VI

TRANSOXIDATION OF TRIFLUOROPEROXYACETIC AND ACETIC ACIDS IN ETHYLENE CHLORIDE AT 29.8°

Time, min.	Ceric ion titer, ml. 0.0835 *N*	Thiosulfate titer
0.7	24.60	0.20
12.8	24.60	.30
65	24.2	.70
121	23.5	1.00
190	23.0	1.30
272	22.3	1.60
1238	18.3	4.50

Peroxyacetic Acid Cleavage of Phenyl Cyclohexyl Ketone.—To 1.07 g. of phenyl cyclohexyl ketone in a 50-ml. glass stoppered flask was added 20 ml. of a 0.50 *M* ethylene chloride solution of peroxyacetic acid which contained 1.76 *M* trifluoroacetic acid. The solution was placed in a 29.8° thermostat for three days. After this period the thiosulfate titer of a 1-ml. aliquot of solution indicated the disappearance of peracid equivalent to 130% of the original ketone. The remaining solution was concentrated under reduced pressure to an oil and a trace of material taken for an infrared spectrum. Trifluoroacetate ester was shown to be present by the observation of the carbonyl stretching band characteristic of trifluoroacetate esters. The remaining material was refluxed overnight under a nitrogen atmosphere with 50 ml. of 2 *N* potassium hydroxide. The resulting hydrolysate was cooled and extracted with ether. Removal of ether solvent gave cyclohexanol which was identified by its infrared spectrum. The aqueous hydrolysate was purged of ether in a brisk air stream and made up to 100 ml. with water. Bromometric analysis of aliquots of this phenol solution by the procedure described above gave reproducible titers which showed 10% phenyl migration; 100% conversion of ketone to esters is assumed.

Control experiments using known quantities of phenyl cyclohexanecarboxylate and cyclohexyl benzoate proved the analytical method to be accurate to within ±0.2%.

Trifluoroperoxyacetic Acid Cleavage of *p*-Nitroacetophenone.—A solution of trifluoroperoxyacetic acid was prepared by slow addition of 8.5 ml. (0.06 mole) of trifluoroacetic anhydride to a suspension of 1.7 g. of 90% hydrogen peroxide in 25 ml. of methylene chloride. This solution was added to 5.0 g. (0.03 mole) of pure *p*-nitroacetophenone dissolved in 50 ml. of methylene chloride. The reaction mixture was allowed to stand at room temperature for two days. The solvent then was removed by evaporation under reduced pressure. The residue was hydrolyzed by refluxing and stirring in the presence of 100 ml. of 6 *N* hydrochloric acid for 3 hours. The acidic hydrolysate was extracted five times with 50-ml. portions of methylene chloride. These combined extracts were extracted twice with 50-ml. portions of 10% sodium hydroxide. The basic extracts was acidified with 40 ml. of concentrated hydrochloric acid and extracted five times with 50-ml. portions of methylene chloride. These combined extracts were evaporated under reduced pressure and the residue (3.1 g.) diluted to 100 ml. with glacial acetic acid and analyzed for *p*-nitrophenol and *p*-nitrobenzoic acid as described below.

The neutral material remaining after sodium hydroxide extraction was extracted with 3:1 hydrochloric acid, washed with water, dried over magnesium sulfate and evaporated to dryness. In this manner 1.65 g. (0.01 mole) of ketone was recovered.

Analysis of the reaction product mixture indicated that 1.83×10^{-2} mole of *p*-nitrophenyl acetate and 2.68×10^{-3} mole of methyl *p*-nitrobenzoate were produced. The analytical procedure is described below.

Trifluoroperoxyacetic Acid Cleavage of *p*-Chloroacetophenone.—A trifluoroperoxyacetic acid solution prepared in 25 ml. of methylene chloride from 4.2 ml. (0.03 mole) of trifluoroacetic anhydride and 0.85 g. (0.025 mole) of 90% hydrogen peroxide was added to 7.8 g. (0.05 mole) of *p*-chloroacetophenone dissolved in 75 ml. of methylene chloride. The reaction mixture was allowed to stand at room temperature for 20 hours. The solvent was removed and the residue was refluxed for two hours with 4.0 g. of sodium hydroxide in 50 ml. of methanol and then poured into 100

ml. of water. This aqueous mixture was extracted five times with 50-ml. portions of methylene chloride to yield 5.0 g. (0.032 mole) of recovered *p*-chloroacetophenone. The aqueous solution was acidified with 15 ml. of concentrated hydrochloric acid and extracted overnight with ether in a continuous extraction apparatus. The ether extract was dried over magnesium sulfate and the solvent was removed under reduced pressure. The residue was diluted to 100 ml. with glacial acetic acid and analyzed as described below. The analysis showed that 2.08×10^{-2} mole of *p*-chlorophenylacetate and 5.9×10^{-4} mole of methyl *p*-chlorobenzoate were produced in the reaction.

Analytical Procedure for the Determination of *p*-Nitrobenzoic Acid and *p*-Nitrophenol.—Solutions of *p*-nitrophenol and of *p*-nitrobenzoic acid (1×10^{-4} *M*) were prepared in glacial acetic acid solvent and the ultraviolet absorption spectra of these solutions were determined with a Beckman model DK-1 spectrophotometer using 1-cm. silica cells. *p*-Nitrophenol was found to have an extinction coefficient of 1.08×10^4 at λ_{max} 308 mμ while *p*-nitrobenz ic acid absorbed most strongly at 259 mμ with an extinction coefficient of 1.28×10^4. Since the absorption of *p*-nitrobenzoic acid was negligible at 308 mμ, mixtures of the two compounds could be analyzed directly for *p*-nitrophenol by determining the absorbence of the unknown solution at 308 mμ. *p*-Nitrobenzoic acid was determined by subtracting 17% of the absorbence of the unknown solution at 308 mμ from its absorbence at 259 mμ. Several known mixtures were analyzed in this manner with great accuracy (±2% error).

Analytical Procedure for the Determination of *p*-Chlorophenol and *p*-Chlorobenzoic Acid.—The spectra of both pure materials were determined as for *p*-nitrophenol and *p*-nitrobenzoic acid. *p*-Chlorophenol had λ_{max} 281 mμ and an extinction coefficient of 1.70×10^3 while *p*-chlorobenzoic acid had λ_{max} 248 mμ and an extinction coefficient of 1.27×10^4. The *p*-chlorobenzoic acid did not interfere with the *p*-chlorophenol absorbence at 281 mμ. Therefore, the concentration of *p*-chlorophenol was determined directly from the absorbance of the unknown solution at 281 mμ. The absorbance of *p*-chlorobenzoic acid was determined by subtracting 6% of the absorbance of the solution at 281 mμ from the absorbance at 248 mμ. The precision of the method was shown to be excellent since known mixtures could be analyzed to within ±2%.

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[CONTRIBUTION FROM THE ROHM & HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

A Re-examination of the Peroxyacid Cleavage of Ketones. II. Kinetics of the Baeyer–Villiger Reaction

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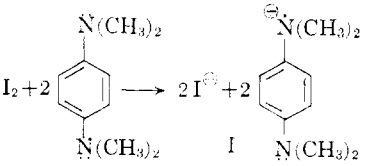
The kinetics of the reaction of a series of ketones with trifluoroperoxyacetic acid has been determined in ethylene chloride and 10:1 acetonitrile–ethylene chloride solvents. The results lead to the conclusion that the rate-determining step of the Baeyer–Villiger reaction is the acid-catalyzed decomposition of the peroxyacid–ketone adduct.

The quantitative reaction of trifluoroperoxyacetic acid with ketones[2] allowed a study of the kinetics of this reaction to be made and the results of this investigation are reported here. Our prime objective in this study was identification of the rate-controlling step and this problem was attacked in several ways. Among the experimental approaches were: (1) an examination of acid catalysis, (2) an attempted correlation of reaction rates with migratory abilities of the aryl or alkyl groups attached to the ketonic carbonyl group, (3) an attempted correlation of carbonyl group reactivity in other reactions with rates of Baeyer–Villiger reactions, (4) the effect of solvent type on ketone reactivity and (5) a study of rate as a function of peroxyacid structure.

Results

Kinetic Methods.—Phenyl alkyl ketones and substituted acetophenones, with which product distributions had been previously determined, were examined kinetically as were the simple cycloalkanones with from five to seven ring members and a series of methyl alkyl ketones. Two reaction solvents of greatly different character were employed: ethylene chloride and 10:1 (volume) acetonitrile–ethylene chloride. In every case the reaction temperature was 29.8°, a temperature which allowed rate measurements to be made throughout the wide spectrum of ketone reactivities encountered. The change in concentration of trifluoroperoxyacetic acid was followed as a measure of the extent of reaction. The analytical method employed was an adaptation of a previously described method[3] which involved the following reactions and the spectrophotometric determination of I.

$$CF_3CO_3H + H^+ + 2I^- \longrightarrow CF_3CO_2^- + I_2 + H_2O \qquad (I)$$



(II)

Kinetics Measurements in Acetonitrile–Ethylene Chloride Solution.—Owing to the fact that trifluoroperoxyacetic acid was stable in acetonitrile solution it was possible to carry out rate measurements in this highly polar and nucleophilic solvent. Rate measurements were carried out under pseudo first-order conditions using a large excess of ketone and varied amounts of trifluoroacetic acid catalyst. The observed rates were found to fit the rate expression (1).

$$-d[CF_3CO_3H]/dt = k_3[CF_3CO_2H][R_2CO][CF_3CO_3H] \quad (1)$$

Since trifluoroacetic acid is a product of the reaction, it was not surprising to find that after approximately 25% reaction the pseudo first-order plots of log $[CF_3CO_3H]$ *vs.* time developed curvature as would be required of an autocatalytic reaction.

(1) Presented at the Sixth Reaction Mechanisms Conference, Swarthmore, Pa., September, 1956.

(2) M. F. Hawthorne, W. D. Emmons and Keith S. McCallum, THIS JOURNAL, **80**, 6393 (1958).

(3) M. F. Hawthorne, *ibid.*, **79**, 2510 (1957).