Reductive Cleavage of VI.—The sodium salt of VI (35 g., 0.0927 mole) was poured into 425 ml. of hot water with stirring, and then a solution of 20 g. (0.5 mole) of sodium hydroxide in 75 ml. of water was added. At 60–70° commercial sodium dithionite (45 g., 0.26 mole) was added in portions until the deep red solution became pale yellow. It then was cooled and filtered. The filtrate was made slightly acid and was extracted several times with ether. There was isolated 12 g. (58%) of crude VII, which then was dissolved in anhydrous ether. Anhydrous hydrogen chloride was bubbled through the ethereal solution. The hydrochloride formed was filtered off and neutralized with dilute sodium bicarbonate solution to yield 5-amino-4-trifluoromethylsalicylic acid (VII); a recrystallization from water with decolorization gave pale yellow crystals melting at 185–186°; sublimation *in vacuo* at 150° gave white crystals, m.p. 191.5–192°.

Anal. Calcd. for $C_8H_6O_3NF_3$: C, 43.45; H, 2.74; N, 6.34. Found: C, 43.71; H, 2.99; N, 6.52.

Various attempts to decarboxylate VII thermally failed. In evacuated sealed tubes both VII and its hydrochloride when heated liberated hydrogen fluoride with excessive etching of the Pyrex tubes before any signs of decarboxylation occurred.

Acknowledgment.—This investigation was supported by a Research Corporation grant, for which we express our gratitude.

PHILADELPHIA, PENNSYLVANIA

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

Peroxytrifluoroacetic Acid. V. The Oxidation of Ketones to Esters[1]

BY WILLIAM D. EMMONS AND GEORGE B. LUCAS

RECEIVED OCTOBER 22, 1954

Peroxytrifluoroacetic acid has been found to oxidize ketones to esters in excellent yields. A noteworthy application of this reaction is the oxidation of methyl cyclopropyl ketone to cyclopropyl acetate in 53% yield.

Peroxytrifluoroacetic acid[2] has been found to be a remarkably efficient reagent for oxidation of ketones to the corresponding esters. This reaction,

$$R_2C{=}O \xrightarrow{CF_3CO_3H} ROCOR$$

first described by Baeyer and Villiger,[3] has been carried out previously with peracetic, perbenzoic and Caro's acid.[4] It generally has been applied, however, to alicyclic ketones, aralkyl ketones and to aromatic ketones. Furthermore, the yields in most cases are not extremely good, and this makes separation of the ester product from the original ketone somewhat tedious since these materials normally boil very close to one another.

Peroxytrifluoroacetic acid, in contrast to other peracids, smoothly and rapidly converts most ketones to esters in excellent yields. In addition, the products obtained from this reaction are in general uncontaminated by any of the ketonic starting material. The experimental results are summarized in Table I together with the physical constants of the esters obtained. In initial work it was observed that transesterification of the ester by trifluoroacetic acid produced small amounts (usually 5 to 10%) of the alkyl trifluoroacetate. This was eliminated, however, by conducting the oxidation in the presence of dibasic sodium phosphate, since this base removes most of the trifluoroacetic acid as soon as it is formed. The reaction was normally carried out by addition of peroxytrifluoroacetic acid to a boiling solution of the ketone in methylene chloride in which sodium phosphate was slurried. The physical constants of the esters so obtained were in every case essentially identical to those reported for these compounds in the literature. To further confirm the identity and purity of these products, their infrared spectra were compared with those of authentic samples prepared by independent methods and in each case the spectra were identical. It is our opinion that the oxidation reaction itself is quantitative and that the lower yields appearing in Table I simply represent mechanical losses in the experimental procedure.

The oxidation of methyl cyclopropyl ketone to cyclopropyl acetate was the only case where some unreacted ketone was found in the reaction product. Consequently, it was necessary to use Girard's reagent P to separate the ketone from cyclopropyl acetate. The cyclopropyl acetate so obtained was characterized by its physical properties and by comparison of its infrared spectrum with that of an authentic sample prepared by Roberts' procedure.[5] It is interesting to note that Friess[6] reported that methyl cyclopropyl ketone was unreactive toward perbenzoic acid. The synthesis of cyclopropyl acetate from methyl cyclopropyl ketone with peroxytrifluoroacetic acid is certainly the method of choice for preparation of this compound. The procedure utilized by Roberts[5] involved the intermediate cyclopropanol and the preparation of this material is tedious. Furthermore, the acetylation of cyclopropanol was an unsatisfactory reaction and could only be carried out in low yield.

Considerable work has been done on the mechanism of the Baeyer–Villiger reaction[4,7] and there is little doubt that the mechanism of peroxytrifluoroacetic oxidation is grossly similar to that of perbenzoic and peracetic acid. The reaction very probably proceeds through decomposition of the peroxytrifluoroacetic acid–ketone adduct (I), which by loss of trifluoroacetate anion and the

---

[1] This research was carried out under Army Ordnance Contract W-01-021-ORD-334.

[2] For the preceding paper in this series, see W. D. Emmons and A. S. Pagano, THIS JOURNAL, **77**, 89 (1955).

[3] A. Baeyer and V. Villiger, *Ber.*, **32**, 3625 (1899).

[4] For leading references, see W. von E. Doering and L. Speers, THIS JOURNAL, **72**, 5515 (1950).

[5] J. D. Roberts and V. C. Chambers, *ibid.*, **73**, 3176 (1951).

[6] S. L. Friess, *ibid.*, **71**, 14 (1949).

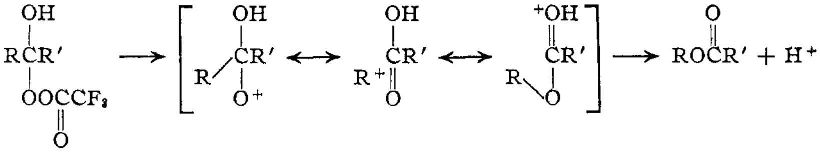
[7] W. von E. Doering and E. Dorfman, *ibid.*, **75**, 5595 (1953); S. L. Friess and N. Farnham, *ibid.*, **72**, 5518 (1950); R. B. Turner, *ibid.*, **72**, 878 (1950); S. L. Friess, *ibid.*, **71**, 2571 (1949); K. Mislow and J. B. Brenner, *ibid.*, **75**, 2318 (1953).

TABLE I

OXIDATION OF KETONES TO ESTERS WITH PEROXYTRIFLUOROACETIC ACID

Ketone	Ester	Yield, %	B.p., °C.	$n^{20}\text{D}$
Methyl ethyl ketone	Ethyl acetate	72	76–77	1.3729
Diethyl ketone	Ethyl propionate	78	99–100	1.3838
Methyl *n*-propyl ketone	*n*-Propyl acetate	78	99–100	1.3842
Methyl isopropyl ketone	Isopropyl acetate	81	86–87.5	1.3770
Methyl *n*-butyl ketone	*n*-Butyl acetate	81	122–123	1.3948
Methyl isobutyl ketone	Isobutyl acetate	84	114–115.5	1.3905
Methyl *n*-amyl ketone	*n*-Amyl acetate	87	143–145	1.4013
Methyl cyclopropyl ketone	Cyclopropyl acetate	53	109–111	1.4060
Di-*n*-propyl ketone	*n*-Propyl butyrate	80	142–143	1.4000
Diisobutyl ketone	Isobutyl isovalerate	81	164–166	1.4057
Benzophenone	Phenyl benzoate	88	68–69 (m.p.)	

concerted migration of an alkyl group yields the ester III. The excellence of peroxytrifluoroacetic acid in this reaction is undoubtedly due to the facile heterolysis of the oxygen–oxygen bond induced by the highly electronegative trifluoroacetyl substituent. It also has been established that structural features in the migrating group which are able to best accommodate a positive charge facilitate the rearrangement. This is presumably due to the large contribution of resonance structures such as IIb to the transition state.[4,7] On this basis, then, the migrating group will normally be that which is most stabilized by hyperconjugative electron release and this is completely true for every ketone examined here. Thus in the oxidation of methyl alkyl ketones, the alkyl group is the only one which migrates. Indeed the specificity of the reaction makes it a very elegant method for degradation of methyl ketones to alkyl acetates and, if desired, to the corresponding alcohols by hydrolysis. It should also be mentioned that peroxytrifluoroacetic acid recently has been applied successfully to the oxidation of cyclopentanone and cyclohexanone to the corresponding lactones in excellent yields.[8] Further work on migratory aptitudes and the stereochemistry of this reaction with peroxytrifluoroacetic acid is in progress.



I IIa IIb IIc III

Experimental[9]

Oxidation of Methyl Isobutyl Ketone.—A solution of peroxytrifluoroacetic acid was prepared by dropwise addition of 50.8 ml. (0.36 mole) of trifluoroacetic anhydride to a suspension of 8.2 ml. (0.3 mole) of 90% hydrogen peroxide in 50 ml. of cold methylene chloride. This solution was then added over a 20-minute period to a stirred suspension of 130 g. of dry, finely ground disodium hydrogen phosphate in a mixture of 150 ml. of methylene chloride and 20.0 g. (0.2 mole) of methyl isobutyl ketone. During the addition the exothermic reaction caused the solution to boil vigorously. After addition was complete, the solution was heated under reflux for 30 minutes and the insoluble salts were then collected on a filter. The salts were washed with 100 ml. of methylene chloride. The combined filtrates were then washed with 50 ml. of 10% sodium carbonate solution and dried over magnesium sulfate. Most of the solvent was distilled at atmospheric pressure and the residual liquid, still containing some solvent, was fractionated in a Todd column packed with a Monel metal spiral and equipped with a variable reflux ratio head. There was obtained 19.5 g. (84%) of colorless isobutyl acetate, b.p. 114–115.5°, $n^{20}\text{D}$ 1.3905 (lit. $n^{18.8}\text{D}$ 1.3907[10]). The infrared spectrum of this product was also identical in all respects to that of an authentic sample of isobutyl acetate.

Oxidation of Methyl Cyclopropyl Ketone.—A solution of peroxytrifluoroacetic acid was prepared from 67.6 ml. (0.48 mole) of trifluoroacetic anhydride, 10.8 ml. (0.4 mole) of 90% hydrogen peroxide and 100 ml. of methylene chloride. This solution was added over a 25-minute period to a well-stirred mixture of 142 g. (1.0 mole) of disodium hydrogen phosphate and 16.8 g. (0.2 mole) of methyl cyclopropyl ketone in 200 ml. of methylene chloride. After addition was complete, the mixture was heated under reflux for one hour. The mixed salts were then collected on a filter and washed with 100 ml. of methylene chloride. The combined filtrates were washed with 150 ml. of 10% sodium carbonate solution and dried over magnesium sulfate. Most of the methylene chloride was removed by distillation and the residual liquid was dissolved in a mixture of 180 ml. of methanol and 20 ml. of acetic acid containing 37.4 g. of Girard's reagent P. The resulting solution was boiled for 12 hours and poured into 600 ml. of ice-water. It was partially neutralized with 25.2 g. of sodium bicarbonate in 100 ml. of water and was then extracted with six 50-ml. portions of methylene chloride. The extracts were washed with 50 ml. of 10% bicarbonate solution, dried, and most of the solvent was distilled at atmospheric pressure. The residual liquid on fractionation through the Todd column yielded 10.5 g. (53%) of colorless cyclopropyl acetate, b.p. 109–111°, $n^{25}\text{D}$ 1.4060 (lit. $n^{25}\text{D}$ 1.4059[5]). The infrared spectrum of this product was identical in all respects to that of an authentic specimen of cyclopropyl acetate.

Oxidation of Benzophenone to Phenyl Benzoate.—A solution of peroxytrifluoroacetic acid prepared from 8.2 ml. (0.3 mole) of 90% hydrogen peroxide and 50.8 ml. (0.36 mole) of trifluoroacetic anhydride in 50 ml. of methylene chloride was added over a 30-minute period to 36.4 g. (0.2 mole) of benzophenone and 130.0 g. (0.92 mole) of dibasic sodium phosphate in 150 ml. of methylene chloride. After addition was complete, the solution was heated under reflux for one hour. The inorganic salts were then collected on a filter and and the organic filtrate was washed with 100 ml. of 10% sodium carbonate solution. The methylene chloride extract was dried over magnesium sulfate and the volatile solvent was then evaporated. There was obtained 34.0 g. (86%) of fairly pure phenyl benzoate, m.p. 65–67°. After one recrystallization from ethanol the product melted at 68–69° and showed no depression in melting point when mixed with an authentic specimen of phenyl benzoate.

Acknowledgment.—We are indebted to Mr. A. S. Pagano for certain preliminary experiments in connection with this work.

HUNTSVILLE, ALABAMA

---

[8] W. F. Sager and A. Duckworth, THIS JOURNAL, **77**, 188 (1955).

[9] All boiling points are uncorrected.

[10] I. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1946, p. 412.