[CONTRIBUTION FROM THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY]

Trifluoromethylaminosalicylic Acids and Related Reactions[1]

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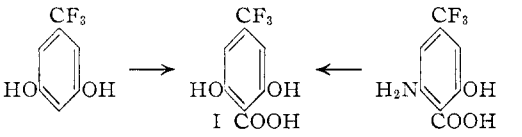
A novel conversion of a CF_3– group to a COOH– group is reported for a high temperature carboxylation of *m*-trifluoromethylphenol under anhydrous conditions. Hydroxyterephthalic acid was produced in 28% conversion. The reactions of 5-trifluoromethylresorcinol and 5-amino-3-trifluoromethylphenol with carbon dioxide and potassium carbonate are described. 4-Trifluoromethyl-2,6-dihydroxybenzoic acid and 6-amino-4-trifluoromethylsalicylic acid, respectively, were the sole isomers formed. Certain "alkylated 4-aminosalicylic acids" reported in the literature as the products of the carboxylation of 5-amino-3-alkylphenols are probably alkylated 6-aminosalicylic acids. In particular, the carboxylation of 5-amino-3-methylphenol has been demonstrated to yield 6-amino-4-methylsalicylic acid. 4-Trifluoromethylsalicylic acid was coupled with diazotized *m*-nitroaniline to form the dye, 4-trifluoromethyl-5-(3-nitro-1-phenylazo)-salicylic acid, which upon reductive cleavage yielded 5-amino-4-trifluoromethylsalicylic acid.

In previous communications[2,3] we reported th synthesis of various trifluoromethylhydroxybenzoic acids and derivatives. The fact that *m*-trifluoromethylphenol could be carboxylated in high yield to give a single isomer, *i.e.*, 4-trifluoromethylsalicylic acid, pointed to the likely utility of this reaction in the synthesis of various substituted trifluoromethylsalicylic acids. As part of a study of the pharmacological activity of new trifluoromethylsalicylic acid derivatives, we wished to synthesize certain trifluoromethylamino- and hydroxysalicylic acids.

Before discussing this phase of our work, certain interesting findings connected with the carboxylation of *m*-trifluoromethylphenol are mentioned briefly. Due to a faulty thermocouple this reaction was inadvertently carried out at a considerably higher temperature (300°) than that recommended.[2] Under these drastic conditions the conversion to 4-trifluoromethylsalicylic acid was reduced to only 6% as compared to the 88% conversion obtained under optimum conditions. Large quantities of potassium fluoride, indicative of the extensive destruction of the CF_3– group, were formed. Trace amounts of salicylic acid were isolated. For each mole of phenol used 4.2 moles of carbon were produced, which represents 60% of the available carbon in the *m*-trifluoromethylphenol. The principal organic product was hydroxyterephthalic acid (28%). This represents a most unusual conversion of a CF_3– to a COOH– group, particularly since the reaction was carried out under anhydrous conditions. The mechanism of this peculiar transformation and degradation is not known. The salicylic acid found, however, probably was produced by decarboxylation of the hydroxyterephthalic acid.

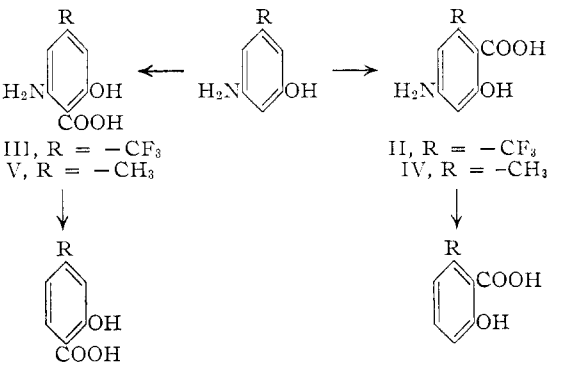
We next wished to study the carboxylation of 5-trifluoromethylresorcinol and 5-amino-3-trifluoromethylphenol. The former compound was prepared by a slight modification of the method of Whalley.[4] The latter is synthesized usually from the corresponding nitrophenol.[5] We have found that a superior method for preparing 5-amino-3-trifluoromethylphenol is the reaction of 3-trifluoromethyl-5-methoxyaniline with hydriodic acid. The amino group actually facilitates the reaction since it renders all the reactants miscible through salt formation with aqueous hydriodic acid.

Carboxylation of 5-trifluoromethylresorcinol by the previously reported technique[2,6] produced as the sole isomer 4-trifluoromethyl-2,6-dihydroxybenzoic acid (I) identical to the product formed by diazotization and hydrolysis of 6-amino-4-trifluoromethylsalicylic acid (*vide infra*). The hydrocarbon analog, orcinol, gives *p*-orsellinic acid (*i.e.*, 4-



methyl-2,6-dihydroxybenzoic acid),[7] which indicates that carboxylation takes place in an analogous manner.

The two possible isomers that can result from the carboxylation of 5-amino-3-trifluoromethylphenol are



By deamination, the position of the entering carboxyl group may be ascertained readily. Over a dozen trial experiments were made in order to determine the optimum conditions for carboxylation. Although *m*-aminophenol was carboxylated by us in 50% conversion at a maximum temperature of 135°, this trifluoromethyl derivative gave no product, other than some tar, under identical conditions. When the maximum temperature was raised to 152°, the conversion was only 6%. Good

(1) Presented at the 126th Meeting of the American Chemical Society, New York, N. Y., Sept. 12–17, 1954.

(2) M. Hauptschein, E. A. Nodiff and A. J. Saggiomo, THIS JOURNAL, **76**, 1051 (1954).

(3) M. Hauptschein, C. S. Stokes and A. J. Saggiomo, *ibid.*, **76**, 4476 (1954).

(4) W. B. Whalley, *J. Chem. Soc.*, 3235 (1951).

(5) W. B. Whalley, *ibid.*, 3016 (1949).

(6) D. Cameron, H. Jeskey and O. Baine, *J. Org. Chem.*, **15**, 233 (1950).

(7) F. v. Hemmelmayr, *Monatsh.*, **38**, 77 (1917).

conversions (>50%) were obtained only when the maximum temperature was higher than 190° and when the reaction was maintained at this temperature range for at least 20 hours. Although some tar was produced in all cases, very little was found under the above recommended conditions, especially when the additional precaution of removing all the air in the bomb was taken. Deamination, through reduction of the diazonium salt with hypophosphorous acid yielded 4-trifluoromethylsalicylic acid as the sole isomer; thus the carboxylation product was established as 6-amino-4-trifluoromethylsalicylic acid (III).

The fact that 5-amino-3-trifluoromethylphenol is carboxylated in the 6-position rather than in the 2-position as has been reported[8,9] for its hydrocarbon analog, 5-amino-3-methylphenol, seemed surprising to us, especially since we have found[2] that *m*-cresol and *m*-trifluoromethylphenol are carboxylated in identical positions. A perusal of the literature[8,9] revealed that actually no real structure proof was made. Apparently, the structural assignments were based on the fact that *m*-aminophenol and 3-amino-4-alkylphenols are known to be carboxylated in the position *para* to the amino group.[10] We therefore decided to repeat the work on the hydrocarbon analog. Carboxylation of 5-amino-3-methylphenol was carried out under conditions similar to those described by both groups of investigators.[8,9] Deamination of the carboxylated product made possible an unequivocal proof of structure. In this manner 6-amino-4-methylsalicylic acid (V), and not the reported[8,9] 4-amino-2-methylsalicylic acid (IV) was demonstrated to be formed, the carboxylation occurring in the same position as in the case of the CF_3–analog. It is therefore likely that the so-called "alkylated *p*-aminosalicylic acids" prepared by the carboxylation of 5-amino-3-alkylphenols and tested for tuberculostatic activity by the aforementioned authors[8,9] were instead probably alkylated 6-aminosalicylic acids.

The carboxylation of 4-amino-3-trifluoromethylphenol, prepared by the reductive cleavage of 2-(2-trifluoromethyl-4-hydroxy-1-phenylazo)-benzoic acid, was studied next. All attempts at carboxylation, however, failed. When the reaction was carried out at temperatures below 152°, no reaction occurred, whereas at temperatures above 152° loss of fluoride ion and tar formation resulted. These findings are attributed to the fact that the amino group is *ortho* to the CF_3–group.

Had the above carboxylation been successful, 5-amino-4-trifluoromethylsalicylic acid (VII) would have been the predicted isomer. The successful synthesis of VII was accomplished, however, by coupling 4-trifluoromethylsalicylic acid with diazotized *m*-nitroaniline to yield 4-trifluoromethyl-5-(3-nitro-1-phenylazo)-salicylic acid (VI) which was reduced with sodium dithionate in alkaline solution to yield 5-amino-4-trifluoromethylsalicylic acid (VII).

It was found that trifluoromethylsalicylic acid couples more slowly than salicylic acid, as might be predicted. Good yields of azo dyes are obtained, nevertheless, when the diazonium component is a negatively substituted amine and when the proper experimental conditions are used.

Experimental

The Reaction of *m*-Trifluoromethylphenol with Carbon Dioxide and Potassium Carbonate.—This reaction was carried out as previously described[2] except that due to a faulty thermocouple the upper temperature limit, which was maintained for several days, was estimated to be about 300°. *m*-Trifluoromethylphenol (97.2 g., 0.6 mole), anhydrous, granular potassium carbonate (250 g.) and 600 p.s.i. of carbon dioxide (at room temperature) were employed. On working up the reaction, there were isolated 30 g. (2.5 moles) of carbon, 7 g. (0.034 mole) of 4-trifluoromethylsalicylic acid[2] and 30.6 g. (0.17 mole) of hydroxyterephthalic acid,[11] m.p. 317–320°; dimethyl ester, m.p. 92–93°. The presence of considerable potassium fluoride was demonstrated and in addition trace amounts (*ca.* 0.1 g.) of salicylic acid, m.p. 157.5–158° (mixed melting point gave no depression with an authentic sample), were isolated.

Anal.[12] Calcd. for $C_7H_6O_3$: C, 60.87; H, 4.38. Found: C, 61.13, 61.07; H, 4.43, 4.65.

α,α,α-Trifluoro-3-methoxy-5-nitrotoluene.—Seventy and eight-tenths grams (0.3 mole) of α,α,α-trifluoro-3,5-dinitrotoluene[13] was dissolved in 720 ml. of absolute methanol and the solution added to a stirred solution of 20 g. (0.37 mole) of technical sodium methoxide in 150 cc. of absolute methanol. The red alcoholic solution then was allowed to reflux for 45 minutes after which time most of the alcohol was removed by distillation. The remaining solution was evaporated overnight and the resulting crude residue of product and inorganic salts was treated with hot petroleum ether and filtered. There was obtained from the filtrate 60 g. of product, m.p. 32–34°. A recrystallization from 65% methanol yielded 56 g. (84%) of α,α,α-trifluoro-3-methoxy-5-nitrotoluene, m.p. 34–35.5° (lit. m.p. 37.5°).[14]

3-Trifluoromethyl-5-methoxyaniline.—α,α,α-Trifluoro-3-methoxy-5-nitrotoluene (86.0 g., 0.389 mole) was introduced in portions to a mechanically stirred mixture of 126.6 g. of iron powder and 63.3 g. of ammonium chloride in 1580 ml. of water at 60°. The mixture was refluxed for 4 hours, 2 ml. of 10% hydrochloric acid solution being added after the first hour. Upon cooling to room temperature the mixture was filtered and the filtrate made alkaline. The precipitate that formed was collected and combined with the ether residue obtained from washing the material initially filtered from the reaction mixture with ether. After a recrystallization from petroleum ether there was obtained 63 g. (85%) of 3-trifluoromethyl-5-methoxyaniline as light tan needles, m.p. 48–49.5°, acetyl derivative from petroleum ether, m.p. 118–120° (lit. m.p. 151° and 120°, respectively).[14] The former literature value would appear to be a typographical error.

5-Amino-3-trifluoromethylphenol.—3-Trifluoromethyl-5-methoxyaniline was dissolved in 120 ml. of hydriodic acid (d. 1.7, 55–58% HI) and refluxed for 15 hours, the water condenser then being replaced by a long Vigreux column. There was collected initially 11 g. of methyl iodide, b.p. 42°. An additional 10 g. was obtained after an additional 180 ml. of hydriodic acid was added. After removal of most of the excess acid by distillation, the mixture was cooled, made alkaline with concentrated sodium hydroxide solution and filtered. On acidification of the filtrate there was collected *ca.* 34 g. of light brown material which, after several recrystallizations from a 3:5 benzene–petroleum ether mixture, yielded 28 g. (78%) of 5-amino-3-trifluoromethylphenol as pale buff-colored needles, m.p. 80–81° (lit. m.p. 81°).[5] It was found to be quite important to distil off the low-boiling

(8) F. Wessely, H. Eibl and G. Friedrich, *Monatsh.*, **83**, 24 (1952).

(9) M. N. Shchukina, Y. F. Markova and A. M. Pozharskaya, *Zhur. Obshchei Khim.*, **22**, 2019 (1952).

(10) References 8 and 9 are entitled "Alkylated *p*-Aminosalicylic Acids" and "Homologs of *p*-Aminosalicylic Acid," respectively. The carboxylation of the symmetrically alkylated *m*-aminophenols is said to give alkylated *p*-aminosalicylic acids. Only ref. 9 states that no rigid proof of structure was made.

(11) R. Kuhn, F. Zilliken and H. Trischmann, *Chem. Ber.*, **83**, 304 (1950).

(12) Microanalyses by Clark Microanalytical Laboratory.

(13) G. C. Finger and F. H. Reed, THIS JOURNAL, **66**, 1972 (1944).

(14) A. Robertson, W. B. Whalley and J. Yates, *J. Chem. Soc.*, 2013 (1951).

methyl iodide as the reaction proceeds. This affords a higher reaction temperature which is very beneficial, since prior reactions carried out for even 20 hours under customary conditions, *i.e.*, total reflux, gave much lower conversions.

5-Trifluoromethylresorcinol.—The following sequence was used[4,14]; 3-trifluoromethyl-5-methoxyaniline → 3-trifluoromethyl-5-methoxyphenol → 5-trifluoromethylresorcinol.

The Reaction of 3-Amino-5-trifluoromethylphenol with Carbon Dioxide and Potassium Carbonate.—3-Amino-5-trifluoromethylphenol (4.6 g., 0.026 mole) and 20.0 g. of granular anhydrous potassium carbonate were intimately mixed and added to a stainless steel pressure reactor. After repeated evacuations and filling with nitrogen, 500 p.s.i. of carbon dioxide was introduced at room temperature. The temperature was allowed to rise progressively over a period of 40–60 hours to 222°, the reaction starting at *ca.* 160°. The bomb was then vented, opened, and the grayish-white solid cake dissolved in a minimum of hot water. The solution was cooled and filtered to remove 0.6 g. of a black crystalline solid and then slightly acidified to a *p*H of 6, whereupon it was decolorized with Norite. Extraction with ether yielded 3.15 g. (55%) of 6-amino-4-trifluoromethylsalicylic acid (III), m.p. 162° dec. Recrystallization from hot water raised the melting point of the pale yellow solid to 166° dec.

Anal. Calcd. for $C_8H_6O_3NF_3$: C, 43.45; H, 2.74; N, 6.34. Found: C, 43.94; H, 2.66; N, 6.23.

For some unknown reason, it was found that the melting point rose to 171° after standing for several days. III exhibits a violet aqueous ferric chloride reaction.

Proof of Structure III by Deamination.—The product III (0.20 g., 0.000905 mole) was dissolved in 2.5 ml. of concentrated hydrochloric acid, cooled to 0°, and diazotized with 0.063 g. (0.000913 mole) of sodium nitrite in 2 ml. of water. The solution was stirred for an additional 15 minutes, and 0.7 ml. of 50% hypophosphorous acid was then added drop by drop with stirring. The solution on standing overnight at 10–15° gave 0.13 g. of a yellow product which was dissolved in dilute sodium bicarbonate solution and decolorized with Norite. On acidification there was obtained 0.12 g. (64%) of a product, m.p. 173–175°. Washed with hot water, the melting point rose to 177–178.5°. A mixed melting point with 4-trifluoromethylsalicylic acid, m.p. 177.5–178.5°, gave no depression. Thus the carboxylation product was proven to be 6-amino-4-trifluoromethylsalicylic acid (III).

The Reaction of 5-Trifluoromethylresorcinol with Carbon Dioxide and Potassium Carbonate.—5-Trifluoromethylresorcinol (0.5 g.) and 2.66 g. of anhydrous granular potassium carbonate were mixed thoroughly and placed in a stainless steel pressure vessel to which was introduced carbon dioxide at 330 p.s.i. at room temperature. The reactor was heated over a period of two weeks from room temperature to 120° and then cooled, vented and opened. The solid light brown cake was dissolved in a minimum of hot water, slightly acidified and then decolorized with Norite. The filtrate, upon cooling and further acidification, yielded white 4-trifluoromethyl-2,6-dihydroxybenzoic acid (I), m.p. 183–185° dec., which gave no depression when a mixed melting point was taken with the product obtained by diazotization and hydrolysis of III.

Anal. Calcd. for $C_8H_5O_4F_3$: C, 43.26; H, 2.27. Found: C, 43.25; H, 2.56.

Diazotization and Hydrolysis of III.—Compound III (2.55 g., 0.0115 mole) was dissolved in 9 ml. of concentrated hydrochloric acid and diazotized at 0° with 0.82 g. (0.0117 mole) of sodium nitrite in 6 ml. of water. After 15 minutes the diazonium solution was added drop by drop with stirring to 30 ml. of concentrated hydrochloric acid in 60 ml. water at 80° and then refluxed for an hour. Extraction with ether and recrystallization of the residue from water with decolorization gave I (1.1 g., 43%), m.p. 183–184.5° dec. An additional 15% of I was estimated to be dissolved in the filtrate. I exhibits a reddish-violet and bluish-violet ferric chloride reaction in water and ethanol, respectively.

The Reaction of 5-Amino-3-methylphenol with Carbon Dioxide and Potassium Carbonate.[8,9]—5-Amino-3-methylphenol was carboxylated under conditions similar to those described. The temperature of this reaction was allowed to rise from room temperature to 154° over a period of 21 hours. The yield of 6-amino-4-methylsalicylic acid (V), the structure of which is proved below, was 60%. After several recrystallizations from 80% acetone it melted at 132–133° dec.[15]

Anal. Calcd. for $C_8H_9O_3N$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.28; H, 5.26; N, 8.23.

V gives a reddish-violet ferric chloride reaction.

Proof of Structure V by Deamination.—The compound V (0.15 g., 0.00090 mole) was dissolved in 2.5 ml. of concentrated hydrochloric acid, cooled to 0° and diazotized with 0.063 g. of sodium nitrite in 2 ml. of water. After several minutes, 0.7 ml. of cold 50% hypophosphorous acid was added drop by drop with stirring, and the solution allowed to stand overnight at 10–15°. There was isolated 0.09 g. (66%) of 4-methylsalicylic acid, m.p. 174–176°; after recrystallization, m.p. 176.5° (lit. m.p. 177°).[16] A mixed melting point with an authentic sample gave no depression. 2-Methylsalicylic acid, m.p. 168°,[17] was not isolated. The carboxylation product therefore was established as 6-amino-4-methylsalicylic acid (V).

Preparation of 4-Amino-3-trifluoromethylphenol by the Reductive Cleavage of 2-(2-Trifluoromethyl-4-hydroxy-1-phenylazo)-benzoic Acid.—Anthranilic acid (5.48 g., 0.040 mole) was dissolved in a stirred solution of 16 ml. of concentrated hydrochloric acid (0.192 mole) and 40 ml. of water with heating and then cooled to 0.5°. Diazotization was carried out with 2.8 g. (0.0405 mole) of sodium nitrite in 12 ml. of water. After stirring for 15 additional minutes the diazonium solution was added slowly with mechanical stirring to the coupling solution prepared by dissolving 6.48 g. (0.040 mole) of *m*-trifluoromethylphenol in 40 ml. of water containing 2.4 g. of sodium hydroxide (0.060 mole), and then adding 14 g. of sodium carbonate (0.132 mole) in 225 ml. of water. The solution was stirred at 5–10° for several hours and then allowed to stand overnight at room temperature. Upon acidification with concentrated hydrochloric acid there was obtained an 80% yield of the orange dye.

2-(2-Trifluoromethyl-4-hydroxy-1-phenylazo)-benzoic acid (0.020 mole) was dissolved in 50 ml. of water containing 2.4 g. (0.060 mole) of sodium hydroxide at 60–70°, and 8.5 g. (0.048 mole) of sodium dithionite was added in portions till decolorizing was complete. Upon cooling, there was obtained a crude precipitate which yielded 2 g. (57%) of 4-amino-3-trifluoromethylphenol, m.p. 156–158° (lit. m.p. 158°)[5] after recrystallization from benzene–petroleum ether.

The Reaction of 4-Amino-3-trifluoromethylphenol with Carbon Dioxide and Potassium Carbonate.—Four reactions were carried out essentially as described for previous carboxylations. When the reaction was carried out at a maximum temperature of 152° for 72 hours, only unreacted phenol was isolated. When kept at maximum temperatures of 185, 190 and 195° for 12 to 48 hours, the products were tar and potassium fluoride due to decomposition.

The Coupling of 4-Trifluoromethylsalicylic Acid with Diazotized *m*-Nitroaniline.—*m*-Nitroaniline (13.8 g., 0.1 mole) was dissolved in a solution of 25 ml. of concentrated hydrochloric acid (0.3 mole) and 25 ml. of water, cooled to 0–5°, and diluted with an additional 40 ml. of cold water. Diazotization was carried out with 6.95 g. (0.101 mole) of sodium nitrite in 15 ml. of water over a period of 20 minutes. The diazonium solution then was poured slowly in a fine stream into the cold coupling solution prepared as follows: 20.6 g. (0.1 mole) of 4-trifluoromethylsalicylic acid was dissolved in 150 ml. of water containing 8.2 g. (0.205 mole) of sodium hydroxide; 10.6 g. (0.1 mole) of sodium carbonate then was added; stirring was continued for several hours in the cold; after approximately two-thirds of the diazonium solution had been added, the sodium salt of the dye precipitated. There finally was isolated 35 g. (93%) of pure orange sodium 4-trifluoromethyl-5-(3-nitro-1-phenylazo)-salicylic acid, m.p. 280–281° dec. The acid dye VI was red and melted at 250–252°.

Anal. Calcd. for $C_{14}H_8O_5N_3F_3$: N, 11.83. Found: N, 11.54.

(15) References 8 and 9 report for the melting point of this carboxylation product, which was assumed to be 4-amino-2-methylsalicylic acid (IV), 159° dec. and 127.5–128° with loss of CO_2, respectively. Such large discrepancies in the m.p.'s have been noted in the literature for compounds with similar structures.

(16) F. Zmerzlikar, *Monatsh.*, **31**, 899 (1910).

(17) O. Jacobsen, *Ber.*, **16**, 1962 (1883).

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.

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PHILADELPHIA, PENNSYLVANIA

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

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

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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.*, **73**, 2318 (1953).