dissolved in 250 cc. of phosphorus oxychloride and then the naphthalene-insoluble pitch resulting from the reaction was added (after it had been broken up into lumps), 250 g. of phosphorus pentachloride was added. The temperature was raised slowly to 110° and kept there for approximately 20 hours. Since it appeared that there was still unreacted material in the flask, another 41.5 g. of phosphorus pentachloride was added and heating was continued for 5 hours longer at 110°. Sulfur dioxide was bubbled through the reaction mixture to destroy any excess of phosphorus pentachloride. Then the phosphorus oxychloride and the phosphonic dichloride were distilled, the latter under reduced pressure. There was obtained 13 g. of 2-naphthylphosphonic dichloride.

Phosphonation of *o*-Xylene.—Two hundred sixty-five grams (2.5 moles) of *o*-xylene and 71.0 g. (0.25 mole) of P_4O_{10} were heated in a stainless steel shaker autoclave at 275° for 24 hours. When the phosphoric anhydride was mixed with the xylene a cherry red color developed which is very probably due to a thioxene content of the *o*-xylene used. After the autoclave had reached room temperature, its content consisted of an orange-brown liquid xylene phase, which was removed by decantation, and a dark brown pitch, which was chipped from the autoclave and weighed approximately 91.5 g. A sample of the pitch when dissolved in water gave a strong test with the ammonium molybdate reagent. In another similar experiment the xylene solution had been evaporated and had left approximately 30.5 g. of a brown sirup (essentially the anhydride of the phosphonic acid). In this experiment, however, both the comminuted pitch and the xylene solution were combined and treated with hot water to promote hydrolysis. The xylene was stripped off. The still residue consisted of an undissolved dark oil and a dark solution which was decanted and clarified. The filtrate (500 cc.) separated on cooling a first crop of 33.8 g. of *o*-xylylphosphonic acid and the mother liquor yielded on further concentration a second crop of 10.6 g. A sample when recrystallized from water and dehydrated by drying showed a melting point of 150–151.5°.

Anal. Calcd. for $C_8H_{11}O_3P$: C, 51.58; H, 5.96. Found: C, 51.4; H, 5.61.

BOUND BROOK, NEW JERSEY

[CONTRIBUTION FROM THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY]

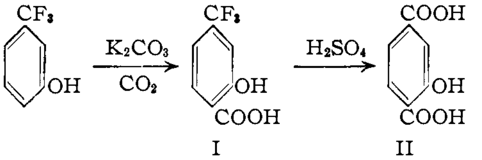
Trifluoromethyl Derivatives of Hydroxybenzoic Acids and Related Compounds[1]

BY MURRAY HAUPTSCHEIN, E. A. NODIFF AND A. J. SAGGIOMO

RECEIVED SEPTEMBER 28, 1953

4-Trifluoromethylsalicylic acid (I) has been synthesized in 88% yield by the reaction of *m*-trifluoromethylphenol with potassium carbonate and carbon dioxide, as well as by the Kolbe–Schmidt reaction on both sodium and potassium *m*-trifluoromethylphenolates. Hydrolysis of I with sulfuric acid affords an excellent synthesis of 2-hydroxyterephthalic acid. 3-Trifluoromethyl-5-hydroxybenzoic acid, 2-trifluoromethyl-4-hydroxybenzoic acid, and I, have been synthesized by reaction sequences involving intermediate formation of new trifluoromethyl derivatives of amino acids, nitro acids, and chloro-, nitro-, amino-, hydroxynitriles. Observations on the relative ease of acid hydrolysis of the trifluoromethyl group in certain isomeric compounds are reported. Acetyl-4-trifluoromethylsalicylic acid and methyl 4-trifluoromethylsalicylate, trifluoromethyl derivatives of well known pharmaceuticals, have been prepared.

As part of a search for new chemotherapeutic agents, we wished to synthesize several trifluoromethylhydroxybenzoic acids as intermediates. Since *m*-trifluoromethylphenol was readily accessible, the most direct method for the preparation of trifluoromethylsalicylic acid and possibly 2-trifluoromethyl-4-hydroxybenzoic acid appeared to be the Kolbe–Schmidt reaction. The question remained, however, as to whether the strong electron-withdrawing influence of the trifluoromethyl group might deactivate this phenol sufficiently to seriously curtail its reactivity. It was therefore somewhat surprising to find that 4-trifluoromethylsalicylic acid (I) was formed in 88% yield when *m*-trifluoromethylphenol, anhydrous potassium carbonate and carbon dioxide were allowed to react under pressure by progressively heating the mixture from room temperature to 220°.



I II

I was also obtained from sodium and potassium *m*-trifluoromethylphenolates *via* the Kolbe–Schmidt reaction. The *p*-isomer, 2-trifluoromethyl-4-hydroxybenzoic acid (XII), was not detected in any of these experiments. In addition several attempts to convert the potassium salt of I into the *p*-isomer according to the procedure[2] for transforming salicylic acid into *p*-hydroxybenzoic acid, failed.

The very convenient method using potassium carbonate and the phenol (rather than its salt) has been described[3] for the carbonation of *p*-cresol in which case only one isomeric product was possible. In the present reaction it is obvious that three isomers could have been produced as two ortho and one para positions were unoccupied. The structure of the single isomer actually formed was determined by treatment with concentrated sulfuric acid, which gave 2-hydroxyterephthalic acid (II) in 85% yield (a most convenient synthesis of the latter acid!).

It was next considered interesting to determine which isomer would be formed on treating *m*-cresol, the hydrocarbon analog, with carbon dioxide and potassium carbonate under conditions identical to the above. 4-Methylsalicylic acid was formed in 88% yield, and similarly the *p*-isomer could not be detected.

4-Trifluoromethylsalicylic acid was next prepared by the following sequence of reactions

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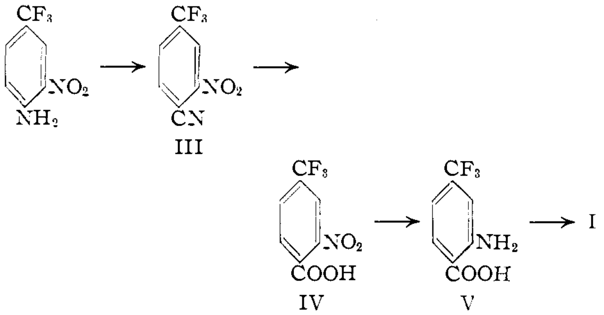
(1) Presented at the 124th Meeting of the American Chemical Society, Chicago, Illinois, Sept. 6–11, 1953.

(2) C. A. Buehler and W. E. Cate in "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 341.

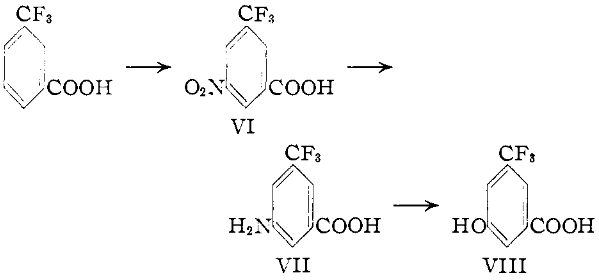
(3) D. Cameron, H. Jeskey and O. Baine, *J. Org. Chem.*, **15**, 233 (1950).



4-Trifluoromethyl-2-nitroaniline was converted into the nitrile III by diazotization in *ca.* 20% sulfuric acid followed by a Sandmeyer reaction using potassium nickelocyanide.[4,5] When the relatively insoluble nitroamine was dissolved in much more highly concentrated hot sulfuric acid, hydrolysis of the CF_3-group was noted. Apparently, in the presence of ortho and para amino groups, the trifluoromethyl group is rendered relatively more susceptible to hydrolytic attack. Hydrolysis of III with 55% sulfuric acid at 165° gave the nitro acid IV. However, when the hydrolysis was conducted at 190° with 70% sulfuric acid, the main product was 2-nitroterephthalic acid, which indicates the criticalness of the concentration of sulfuric acid employed. These findings should be compared with those of Caldwell and Sayin[5] where only the nitrile group of 3-trifluoromethyl-4-nitrobenzonitrile was hydrolyzed even though 75% sulfuric acid and a temperature of 190° was used.

An attempt to prepare IV from α,α,α-trifluoro-4-iodo-3-nitrotoluene (see Experimental) *via* the Grignard (CO_2) reaction, failed.

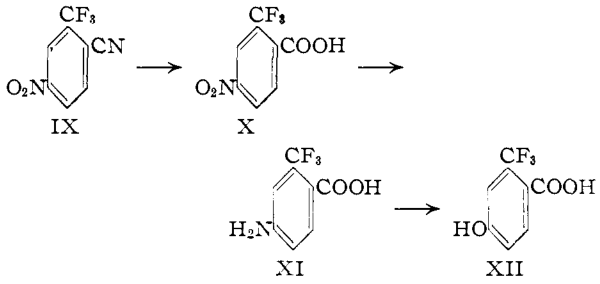
3-Trifluoromethyl-5-hydroxybenzoic acid (VIII) was synthesized as



m-Trifluoromethylbenzoic acid was nitrated in the expected meta position, and after reduction and diazotization the desired hydroxy acid VIII was produced.

2-Trifluoromethyl-4-hydroxybenzoic acid (XII) was synthesized by a sequence similar to that for the preparation of I.

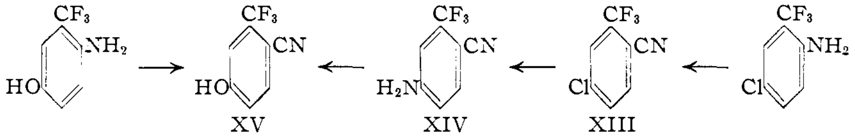
Amination of α,α,α-trifluoro-2-chloro-5-nitrotoluene with liquid ammonia followed by the Sandmeyer reaction gave the nitrile IX, which was hydrolyzed to X with sulfuric acid. It was again found that the concentration of sulfuric acid used is critical if concurrent attack of the CF_3^- group (ortho) is to



be prevented. Reduction of X gave 4-amino-2-trifluoromethylbenzoic acid (XI), a trifluoromethyl derivative of the physiologically interesting *p*-aminobenzoic acid.[5]

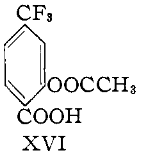
Whereas 4-trifluoromethylsalicylic acid (I) gave a deep violet-red ferric chloride reaction, both 2-trifluoromethyl-4-hydroxybenzoic acid (XII) and 3-trifluoromethyl-5-hydroxybenzoic acid (VIII) gave a hardly visible (negative) color change.

Prior attempts to prepare the pure trifluoromethyl derivative of *p*-hydroxybenzoic acid (XII) from 2-trifluoromethyl-4-hydroxybenzonitrile (XV) were unsuccessful. This hydroxynitrile was prepared by the two alternative routes

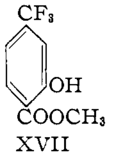


4-Amino-3-trifluoromethylphenol prepared by the method of Whalley[6] was diazotized and treated with potassium nickelocyanide to yield the hydroxynitrile XV. The alternative synthesis started from 4-chloro-2-trifluoromethylaniline which was converted into the chloronitrile XIII and then aminated with liquid ammonia to give the aminonitrile XIV. It is interesting to note here that although *p*-chloroaniline boils 8° higher than *p*-chlorobenzonitrile, in the case of these trifluoromethyl derivatives the boiling point relationship is reversed, the amine boiling 25° below the nitrile. This is attributed to intramolecular hydrogen bonding between the fluorine atoms and the hydrogens of the amino group as proposed by Jones[7] to explain the relatively low boiling point of the ortho isomer of trifluoromethylaniline itself.

Finally, 4-trifluoromethylsalicylic acid was converted into trifluoromethyl derivatives of "Aspirin" (XVI) and "Oil of Wintergreen" (XVII).



XVI



XVII

Experimental

The Reaction of *m*-Trifluoromethylphenol with Carbon Dioxide and Potassium Carbonate.—*m*-Trifluoromethylphenol (48.6 g., 0.3 mole) and anhydrous potassium carbonate (124.4 g.) were intimately dispersed in a copper bomb of 250-ml. capacity, and carbon dioxide gas from a commercial cylinder was introduced at 300 p.s.i. at room temperature.

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[4] F. R. Storrie, *J. Chem. Soc.*, 1746 (1937).

[5] W. T. Caldwell and A. N. Sayin, THIS JOURNAL, **73**, 5125 1951).

[6] W. B. Whalley, *J. Chem. Soc.*, 3016 (1949).

[7] R. G. Jones, THIS JOURNAL, **69**, 2346 (1947).

The temperature was allowed to rise very slowly over a period of ten days to 220°. It was noted that some carbon dioxide was absorbed even at room temperature and that at 140° the reaction was essentially completed. As the carbon dioxide was taken up additional gas was introduced. The reaction time can be shortened greatly by raising the temperature much more rapidly. However, there are indications that a fairly slow rise in temperature is beneficial, and immediate increasing of the temperature to above 140° is not recommended. At the completion of the reaction the bomb was cooled, vented and opened. The product was a hard cake which was dissolved in hot water. The solution was extracted with ether, decolorized with charcoal and acidified with concentrated hydrochloric acid. An 88% yield of 4-trifluoromethylsalicylic acid (I) was isolated (only a trace of unreacted phenol was detected). On recrystallization from alcohol and water, I melted at 178–178.5° (white needles).

Anal.[8] Calcd. for $C_8H_5O_3F_3$: C, 46.61; H, 2.45; mol. wt., 206. Found: C, 46.55; H, 2.46; mol. wt. (neut. eq.), 208.

4-Trifluoromethylsalicylic acid (0.80 g.) was heated in a Pyrex tube on a bunsen flame with 6 ml. of concentrated sulfuric acid.[9] The solution turned deep brown and hydrogen fluoride fumes were liberated. After pouring on ice-water and recrystallizing the resultant precipitate with alcohol and water, there was isolated 0.60 g. (85%) of 2-hydroxyterephthalic acid (II), m.p. 327°[10]; dimethyl ester, m.p. 93–94°[10] (recrystallized from alcohol).

The more soluble *p*-isomer XII was demonstrated not to be present in more than trace amounts. This was also shown to be true even when the reaction temperature was taken up to 275°.

The Kolbe–Schmidt Reaction on Sodium and Potassium *m*-Trifluoromethylphenolates.—These reactions were carried out in the customary manner at temperatures up to 230° and the only product isolated in either case was 4-trifluoromethylsalicylic acid, m.p. 177°, 178°; mixed melting points with an authentic sample gave no depression.

Reaction of *m*-Cresol with Carbon Dioxide and Potassium Carbonate.—One-tenth of a mole of *m*-cresol was treated with carbon dioxide and potassium carbonate as described above for *m*-trifluoromethylphenol. This reaction appeared to be relatively more rapid at lower temperatures. 4-Methylsalicylic acid, m.p. 175–179°, was isolated in 88% yield. Recrystallization from benzene gave a m.p. of 176.5–177.5° (lit. m.p. 177°)[11]; ethyl ester, b.p. 253–254° (lit. b.p. 254°).[12]

Preparation of Acetyl 4-Trifluoromethylsalicylic Acid (XVI).—One and one-half grams of I was acetylated in the usual manner with 5 ml. of acetic anhydride and two drops of concentrated sulfuric acid. Acetyl 4-trifluoromethylsalicylic acid (XVI) was obtained in almost quantitative yield. Upon recrystallization from a petroleum ether–ether mixture, XVI which was a mat of fine white needles melted at 110–112° when placed in a bath previously heated to 108°. It was difficult to get consistent values for the melting point if the sample had been heated more slowly from room temperature.

Anal. Calcd. for $C_{10}H_7O_4F_3$: C, 48.40; H, 2.84. Found: C, 48.64; H, 3.00.

No coloration with aqueous ferric chloride was given. However, on standing overnight, a violet-red color slowly developed due to hydrolysis of the ester. The ester was hydrolyzed intentionally with 25% sodium hydroxide at 70° for six hours, and after acidification the original acid, m.p. 177–178°, was isolated.

Preparation of Methyl 4-Trifluoromethylsalicylate (XVII).—Twenty and six-tenths grams of I was esterified with 35 ml. of methanol in the presence of 3.5 ml. of concentrated sulfuric acid at the reflux temperature for 6 hours. Upon working up in the usual manner, there was isolated in 80% yield (75% conversion), methyl 4-trifluoromethylsalicylate (XVII), b.p. 223° (760 mm.), 87° (14 mm.), f.p. *ca.* 21°.

Anal. Calcd. for $C_9H_7O_3F_3$: C, 49.10; H, 3.21. Found: C, 49.23; H, 3.29.

4-Trifluoromethyl-2-nitrobenzonitrile (III).—Into a 2-l., 3-necked flask equipped with a Hershberg stirrer were placed 665 ml. of water and 133 ml. of concentrated sulfuric acid, to which was added, with stirring, 61.8 g. (0.3 mole) of 4-trifluoromethyl-2-nitroaniline (Caribou Chemical Co.). This mixture was heated until a clear solution resulted and subsequently cooled to 0°, at which time 21.5 g. of sodium nitrite in 40 ml. of water was added over a period of 30 minutes. The temperature was allowed to rise to 5–10° where it was maintained for several hours. Twenty-two grams of insoluble material (essentially all of which was undiazotized amine) was filtered off and the clear diazonium solution was added slowly with stirring into a cold solution of potassium nickelocyanide prepared from 105 g. of potassium cyanide in 450 ml. of water and 90 g. of nickel sulfate in 150 ml. of water to which 450 g. of anhydrous sodium carbonate in 900 ml. of water had been added. During the pouring additional sodium carbonate solution was added to keep the solution neutral to slightly alkaline. The mixture was then heated to 30–35° and maintained there for half an hour. The mixture was allowed to stand overnight and was then heated to 70° with vigorous stirring for half an hour. After cooling to room temperature the crude blackish solid was filtered off and steam distilled. The pale yellow crystals of 4-trifluoromethyl-2-nitrobenzonitrile, m.p. 41–42.5°, weighed 19.9 g. (48% yield, 32% conversion). Upon recrystallization from aqueous alcohol the melting point rose to 44.5–45.5°.

Anal. Calcd. for $C_8H_3O_2N_2F_3$: C, 44.46; H, 1.40; N, 12.96. Found: C, 44.46; H, 1.32; N, 12.99.

4-Trifluoromethyl-2-nitrobenzoic Acid (IV).—One and sixty-four hundredths grams of III in 30 ml. of 55% sulfuric acid was heated at 165° for half an hour. The mixture was allowed to cool and then poured on ice. The precipitate formed was dissolved in 10% sodium hydroxide and was reprecipitated on acidification with concentrated hydrochloric acid. The yield of IV was 1.32 g. (74%). Upon recrystallization from hot distilled water and decolorization with charcoal it melted at 140–140.5°.

Anal. Calcd. for $C_8H_4O_4NF_3$: C, 40.86; H, 1.71; N, 5.96. Found: C, 41.27; H, 1.69; N, 5.83.

When the hydrolysis was carried out with 70% sulfuric acid at 190° the principal product was 2-nitroterephthalic acid, m.p. found 261–263°.

2-Amino-4-trifluoromethylbenzoic Acid (V).—Seventy-three hundredths gram (0.0031 mole) of IV was introduced in small portions to a stirred mixture of 1 g. of iron powder and a solution of 0.5 g. of ammonium chloride in 15 ml. of water at 50°. The mixture was refluxed with stirring for one hour during which time a considerable amount of foaming developed. After treating with 10% sodium hydroxide and filtering, the solution was neutralized with concentrated hydrochloric acid. On cooling in ice the solution only became turbid and it was necessary to extract the acid solution several times with ether. After evaporation 0.51 g. (80%) of V was obtained. It melted at 175–177°[13] (after a single crystallization from cold alcohol).

Anal. Calcd. for $C_8H_6O_2NF_3$: C, 46.84; H, 2.95; N, 6.83. Found: C, 46.93; H, 3.14; N, 6.92.

4-Trifluoromethylsalicylic Acid (I).—2-Amino-4-trifluoromethylbenzoic acid (0.205 g.) in a solution of 0.5 ml. of concentrated sulfuric acid and 10 ml. of water was diazotized at 4° with 0.07 g. of sodium nitrite in 2 ml. of water. After 15 minutes the mixture was gradually heated to the reflux temperature where it was kept for 20 minutes. From the cooled solution there was collected 0.16 g. (78%) of solid which was redissolved in potassium carbonate solution and reprecipitated with concentrated hydrochloric acid (m.p. 175–177.5°). A second recrystallization raised the melting point of I to 177.5–178.5°. A mixed melting point of this product with that obtained from the reaction of *m*-trifluoromethylphenol with carbon dioxide showed no depression.

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(8) Microanalyses by Clark Microanalytical Laboratory.

(9) G. M. LeFave, THIS JOURNAL, **71**, 4148 (1949), converted *m*-trifluoromethylphenol into *m*-hydroxybenzoic acid with 100% sulfuric acid.

(10) R. Kuhn, F. Zilliken and H. Trischmann, *Chem. Ber.*, **83**, 304 (1950), gives for the melting point of the acid and diester, 325 and 94°, respectively.

(11) Zmerzlikar, *Monatsh.*, **31**, 899 (1910).

(12) Pinner, *Ber.*, **23**, 2938 (1890).

(13) A. Mooradian and C. M. Suter, THIS JOURNAL, **71**, 3507 (1949), prepared this compound in the course of proving the structure of 4-hydroxy-3-methyl-7-trifluoromethylquinoline by degradation with alkaline permanganate solution. They report a melting point of 172–174°.

α,α,α-Trifluoro-4-iodo-3-nitrotoluene.—4-Trifluoromethyl-2-nitroaniline was diazotized exactly as described in the preparation of 4-trifluoromethyl-2-nitrobenzonitrile. Potassium iodide reacted in the usual manner, affording a 92% yield of α,α,α-trifluoro-4-iodo-3-nitrotoluene, m.p. 32.5–33.5° (pale yellow crystals from alcohol).

Anal. Calcd. for $C_7H_3O_2NIF_3$: C, 26.52; H, 0.95. Found: C, 26.47, 26.81; H, 0.93, 0.89.

3-Trifluoromethyl-5-nitrobenzoic Acid (VI).—*m*-Trifluoromethylbenzoic acid[14] was prepared in high yield by the reaction of the Grignard reagents of *m*-bromo- and *m*-iodobenzotrifluoride with carbon dioxide. Eighty-one grams (0.426 mole) of this acid, m.p. 103–104°, was added with stirring to 500 g. of fuming sulfuric acid. Nitric acid (90%, sp. gr. 1.5, 125 g.), was introduced gradually to the mixture with efficient stirring, the temperature being maintained below 70°. The reaction mixture was heated on a water-bath for an additional 4–5 hours and then poured upon crushed ice, filtered, washed thoroughly with water, and dried at 70°. There was isolated 90 g. (90%) of the white 3-trifluoromethyl-5-nitrobenzoic acid, m.p. 127–129°; recrystallized from water, m.p. 128–129°.

Anal. Calcd. for $C_8H_4O_4NF_3$: C, 40.86; H, 1.71; N, 5.96. Found: C, 41.01; H, 1.78; N, 6.04, 5.94.

3-Amino-5-trifluoromethylbenzoic Acid (VII).—Thirty-five grams (0.149 mole) of VI was added in portions to a stirred mixture of 48 g. of iron powder and a solution of 24.5 g. of ammonium chloride in 400 ml. of water at 50°. The mixture was refluxed with stirring for three hours, during which time so much foaming was encountered that it was necessary to replace the 2 l. reaction flask with a 3 l. one. The mixture was then treated with 10% sodium carbonate, filtered and neutralized with concentrated hydrochloric acid. After standing overnight 21.6 g. of precipitate was collected. This crude product was redissolved in 10% sodium hydroxide and reprecipitated with acid. There was isolated 16.7 g. (55%) of white 3-amino-5-trifluoromethylbenzoic acid (VII), m.p. 141–142.5°.

Anal. Calcd. for $C_8H_6O_2NF_3$: C, 46.84; H, 2.95; N, 6.83. Found: C, 46.72; H, 3.23; N, 6.89, 6.72.

3-Trifluoromethyl-5-hydroxybenzoic Acid (VIII).—One gram of VII was diazotized in sulfuric acid and then hydrolyzed essentially as described previously affording 0.6 g. (60%) of white 3-trifluoromethyl-5-hydroxybenzoic acid (VIII), m.p. 191.5–192.5° (decolorized and recrystallized from hot water).

Anal. Calcd. for $C_8H_5O_3F_3$: C, 46.61; H, 2.45. Found: C, 46.87; H, 2.79.

2-Trifluoromethyl-4-nitroaniline.—α,α,α-Trifluoro-2-chloro-5-nitrotoluene was aminated with an excess of liquid ammonia at 140°. 2-Trifluoromethyl-4-nitroaniline was isolated in 76% yield, m.p. 90–92°.[15]

2-Trifluoromethyl-4-nitrobenzonitrile (IX).—2-Trifluoromethyl-4-nitroaniline was converted into IX *via* the Sandmeyer reaction using potassium nickelocyanide in 32.5% yield. It melted at 48–49.5° (recrystallized from 20% aqueous alcohol).

Anal. Calcd. for $C_8H_3O_2N_2F_3$: C, 44.46; H, 1.40; N, 12.96. Found: C, 44.73; H, 1.32; N, 12.90.

2-Trifluoromethyl-4-nitrobenzoic Acid (X).—Two and seven-tenths grams of IX in 25 ml. of 63% sulfuric acid was heated slowly to 182° and kept at that temperature for half an hour. The cooled solution was thrown on ice and there was collected 2.6 g. (92%) of X, m.p. 137–140°. A single recrystallization from water gave white platelets, m.p. 138.5–140°.

Anal. Calcd. for $C_8H_4O_4F_3N$: C, 40.86; H, 1.71; N, 5.96. Found: C, 40.77; H, 1.61; N, 6.15.

When 75% sulfuric acid was used, 4-nitrophthalic acid was formed due to hydrolysis of the trifluoromethyl group, while 55–60% sulfuric acid yielded some of the amide due to incomplete hydrolysis of the nitrile.

4-Amino-2-trifluoromethylbenzoic Acid (XI).—Reduction of X with iron and ammonium chloride gave white crystals of XI, m.p. 185.5–187°, in 75% yield.

Anal. Calcd. for $C_8H_6O_2NF_3$: C, 46.84; H, 2.95; N, 6.83. Found: C, 46.85; H, 2.94; N, 6.93.

2-Trifluoromethyl-4-hydroxybenzoic Acid (XII).—Eighty-two hundredths gram of XI was dissolved in a solution of 4 ml. of concentrated sulfuric acid and 20 ml. of water, and was diazotized with 0.28 g. of sodium nitrite in 4 ml. of water. The diazonium solution was then added in portions to a refluxing solution of 4 ml. of concentrated sulfuric acid in 32 ml. of water and heated for one hour. After cooling and extracting with ether there was isolated 0.7 g. of crude material which melted below 100° and probably contained much water of hydration. After a recrystallization from benzene the product melted at 150–153.5° (0.5 g., 61%). Two additional recrystallizations from benzene afforded pure white 2-trifluoromethyl-4-hydroxybenzoic acid (XII), m.p. 152.5–154°.

Anal. Calcd. for $C_8H_5O_3F_3$: C, 46.61; H, 2.45. Found: C, 46.78; H, 2.75.

Preparation of 2-Trifluoromethyl-4-hydroxybenzonitrile (XV). A. Via **4-Amino-3-trifluoromethylphenol.**—Two grams of 4-amino-3-trifluoromethylphenol, prepared by the method of Whalley[6] was dissolved in a solution of 8 ml. of concentrated sulfuric acid and 6 ml. of water and then diazotized at 0° with a solution of 0.8 g. of sodium nitrite in 5 ml. of water. The cold diazonium solution was treated with potassium nickelocyanide as described previously. The black precipitate (1.6 g.) was dissolved in hot water, decolorized with charcoal, and filtered. The filtrate was cooled in an ice-bath and 0.63 g. (30%) of fine white needles of 2-trifluoromethyl-4-hydroxybenzonitrile, m.p. 119–120°, was collected.

Anal. Calcd. for $C_8H_4ONF_3$: C, 51.35; H, 2.15; N, 7.49. Found: C, 51.51; H, 2.30; N, 7.46, 7.75.

B. **Via 4-Chloro-2-trifluoromethylaniline. Preparation of 4-Chloro-2-trifluoromethylbenzonitrile** (XIII).—To 78.2 g. (0.4 mole) of 4-chloro-2-trifluoromethylaniline,[16] b.p. 84° at 10 mm., in 133 ml. of cold concentrated sulfuric acid, a cold 20% solution of sodium nitrite (27.6 g.), was added gradually with vigorous shaking. The diazonium solution was then added to potassium nickelocyanide as described above. On steam distillation, 34.46 g. (42%) of XIII was collected, essentially all of which boiled at 109° at 10 mm., $n^{26}D$ 1.4902.

Anal. Calcd. for $C_8H_3NClF_3$: C, 46.74; H, 1.47; N, 6.81. Found: C, 47.26; H, 1.74; N, 6.45.

4-Cyano-3-trifluoromethylaniline (XIV).—4-Chloro-2-trifluoromethylbenzonitrile was aminated with an excess of liquid ammonia in a stainless steel pressure reactor at 130°. There was isolated in *ca.* 50% yield 4-cyano-3-trifluoromethylaniline (XIV), m.p. 142° (recrystallized from water).

Anal. Calcd. for $C_8H_5N_2F_3$: C, 51.62; H, 2.71. Found: C, 52.07; N, 3.15.

Conversion of XIV to 2-Trifluoromethyl-4-hydroxybenzonitrile (XV).—Ninety-three hundredths gram (0.005 mole) of XIV was diazotized in a solution of 10 ml. of concentrated sulfuric acid and 20 ml. of water with 0.35 g. of sodium nitrite in 5 ml. of water. The diazonium solution was added in portions to a refluxing solution of 5 ml. of concentrated sulfuric acid and 40 ml. of water. The solution was refluxed for 3/4 hour, cooled in ice, and 0.79 g. of crude material was recovered after separation of a red dye was made mechanically. On recrystallization from hot water (decolorized with charcoal), 0.6 g. (64%) of pure white XV, m.p. 119–120°, was recovered.

Attempted Conversion of XV to XII.—The nitrile XV was heated with 55% sulfuric acid. A low yield of product was isolated which dissolved in bicarbonate solution with evolution of carbon dioxide. After several recrystallizations from water and then benzene this product melted over the range 134–138° and probably contained impure XII, described previously, as well as hydroxyphthalic acid resulting from hydrolysis of the trifluoromethyl group. In addition there was isolated considerable bicarbonate-insoluble material resulting from only partial hydrolysis to the amide. When the concentration of sulfuric acid used was raised to 63%, the trifluoromethyl group was attacked more extensively.

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PHILADELPHIA, PENNSYLVANIA

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[14] F. Swarts, *J. chim. phys.*, **17**, 32 (1919).

[15] (a) H. W. Daudt and H. E. Woodward, U. S. Patent 2,194,926 (1940), gives m.p. about 88°; (b) M. R. Pettit and J. C. Tatlow, *J. Chem. Soc.*, 3459 (1951), gives m.p. 94°; (c) J. B. Dickey, *et al.*, *Ind. Eng. Chem.*, **45**, 1730 (1953), gives m.p. 90–92°.

[16] I. G. Farbenind, A.G., French Patent 800,343 (1936), reports b.p. 76–77° (4–5 mm.).