[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

2,2,2-Trifluoroethylamine and 2,2,2-Trifluorodiazoethane

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2,2,2-Trifluoroethylamine has been prepared by the following reactions

$$CF_3CO_2Na + C_2H_5OH + H_2SO_4 \longrightarrow CF_3CO_2C_2H_5 + {}^1/_2Na_2SO_4 \quad [I]$$

$$CF_3CO_2C_2H_5 + NH_3 \longrightarrow CF_3CONH_2 + C_2H_5OH \quad [II]$$

$$CF_3CONH_2 + P_2O_5 \longrightarrow CF_3CN + H_3PO_4 \quad [III]$$

$$CF_3CN + H_2 \xrightarrow{[Pt]} CF_3CH_2NH_2 \quad [IV]$$

Reactions [I], [II] and [III] were carried out essentially as described by Swarts.[1a] However, a decided improvement in the yield of trifluoroacetamide was realized by treating ethyl trifluoroacetate with dry ammonia rather than with ammonium hydroxide. The catalytic hydrogenation [IV] was effected at a temperature of 50 to 60°, and hydrogen pressures above 1000 lb./sq. in., using a liberal quantity of Adams platinum catalyst. No secondary amine was formed under these conditions. The small quantity of ammonia obtained may have resulted from hydrogenolysis of the amine or by hydrolysis of some of the nitrile by traces of moisture.

The trifluoroethylamine appears to be uncommonly stable. This is hardly unexpected in view of the high stability reported by earlier workers[1] of compounds containing the trifluoromethyl group. 2-Fluoroethylamine[2] and 2,2-difluoroethylamine[3] have also been described as stable compounds. An interesting property of 2,2,2-trifluoroethylamine is its boiling point of 37°, which is 21° *higher* than the boiling point of ethylamine. It is significant that 2,2,2-trifluoroisopropylamine[4] also boils higher than isopropylamine. As a general rule, the other reported compounds containing the trifluoromethyl group have boiling points lower than those of the non-fluorinated types. A particularly striking illustration is trifluoroacetonitrile, which boils 145° lower than acetonitrile. Incidentally, we found our trifluoroacetonitrile to boil at −63.9°, and not at −61° as reported earlier.[1a]

The trifluoromethyl group has a pronounced effect on the chemical properties of trifluoroethylamine. This amine is a very weak base, and its hydrochloride reacts acid to methyl red. A most interesting reaction of trifluoroethylamine is with nitrous acid in aqueous solution, as a consequence of which 2,2,2-trifluorodiazoethane is formed.

$$CF_3CH_2NH_2 + HONO \longrightarrow CF_3CHN_2 + 2H_2O$$

Only aliphatic amines such as those with α-carbonyl groups have hitherto been reported to react with nitrous acid to form diazo compounds. Like many other aliphatic diazo compounds, trifluorodiazoethane is intensely yellow in color. It is stable in solution at ordinary temperatures, and an ether solution was kept for six weeks without undergoing any noticeable decomposition. The diazo compound was quite rapidly decomposed by acids, and it reacted normally with iodine, though rather slowly in dilute solution or in the cold.

$$CF_3CHN_2 + I_2 \longrightarrow CF_3CHI_2 + N_2$$

The diazo compound should prove useful in synthesis, and among other things has been employed in the preparation of trifluoroethyl iodide.[4]

It should be mentioned that unsuccessful attempts have been made to prepare trifluoromethylamine by the Hofmann degradation and by the treatment of trifluoroacetic acid with hydrazoic acid.[5]

Experimental

Ethyl Trifluoroacetate.—Anhydrous sodium trifluoroacetate[1a] (170 g., 1.25 mole) was treated with a cold mixture of 140 g. of absolute ethanol and 160 g. of concd. sulfuric acid. After standing at room temperature for three hours, the reaction mixture was heated on a water-bath, and the ester was distilled off during one and one-half hours up to a boiling point of 68°. The crude ester, collected in a receiver cooled in ice-water, was washed once with 100 cc. of cold 5% sodium carbonate solution then dried over 25 g. of calcium chloride at 0°. The product was finally purified by mixing with 15 g. of phosphorus pentoxide and distilling. The yield was 160 g. (90%) of pure ester boiling at 60–62°.

Trifluoroacetamide.—The ethyl trifluoroacetate (160 g., 1.13 mole) was mixed with 100 cc. of anhydrous ether.

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(1) (a) Swarts, *Bull. classe sci. Acad. roy. Belg.*, **8**, 343 (1922) [*C. A.*, **17**, 769 (1923)]; (b) Swarts, *ibid.*, **13**, 175 (1927) [*C. A.* **22**, 58 (1928)]. See, also, *Bull. soc. chim. Belg.*, **35**, 412 (1926); **43**, 471 (1934); **38**, 99 (1929); (c) For a recent review and general references, see Henne in Gilman, "Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 944; (d) Tinker, U. S. Patent 2,257,868 [*C. A.*, **36**, 495 (1942)]. (e) Simons and Ramler, THIS JOURNAL, **65**, 389 (1943).

(2) Träube and Peiser, *Ber.*, **53**, 1500 (1920).

(3) Swietoslawski and Bobinska, *J. chim. phys.*, **24**, 545 (1927) [*C. A.* **22**, 1267 (1928)].

(4) Unpublished studies.

(5) v. Braun, *Ann.*, **490**, 125 (1931).

This mixture was cooled in an ice-bath and saturated with dry gaseous ammonia. The resulting clear, colorless solution was subjected to distillation by heating on a water-bath at 60–70°. When no more distillate collected at this temperature, the vacuum of an aspirator was applied and heating at 60–70° was continued until the residue in the flask began to crystallize. At this point the heating bath was removed, but the vacuum was continued until crystallization was complete. The 116.5 g. of pure trifluoroacetamide obtained in this manner melted at 75°. The distillate was redistilled to yield an additional 10 g. of trifluoroacetamide which was carried over during the first distillation. The total yield was 126.5 g. or 99%.

Trifluoroacetamide was also prepared by adding ethyl trifluoroacetate to well cooled anhydrous methanol saturated with ammonia. The yield in this case was about 90%. The preparation of the amide by the reaction of aqueous ammonia with the ester as reported by Swarts[1a] gives only poor yields, apparently because of the ease with which trifluoroacetamide is hydrolyzed to ammonium trifluoroacetate.

Trifluoroacetonitrile.—An intimate mixture of 85 g. (0.75 mole) of powdered trifluoroacetamide and 200 g. of phosphorus pentoxide was made in a 2-liter round-bottomed flask. The flask was provided with a condenser from the top of which led a rubber tube to a trap cooled in an ice–salt mixture. This trap, in turn, was connected to two other traps in series cooled in "dry-ice"–acetone baths. A calcium chloride tube protected the end trap from atmospheric moisture. The flask with the reaction mixture was heated gradually in an oil-bath up to 145–150°, and held at this temperature for three hours. Trifluoroacetonitrile, which was evolved rapidly at first, collected as a colorless liquid in the first "dry-ice"–acetone trap. The yield was 52 g. (74%). The compound boiled at −63.9° (743 mm.). Observations on the boiling points of several different preparations gave concordant results. These observations were made by completely immersing the bulb of a low temperature thermometer in 50 g. of the boiling liquid.

Trifluoroethylamine Hydrochloride.—A 500-cc. Parr hydrogenation bomb was fitted with a large cork stopper which carried an inlet tube reaching to the bottom of the bomb, and an outlet protected with a calcium chloride tube. The inlet tube was connected by means of rubber tubing to a trap containing 50 g. (0.55 mole) of trifluoroacetonitrile cooled by a "dry-ice"–acetone mixture. In the bomb was placed 100 cc. of anhydrous ether and 2 g. of platinum oxide catalyst. The bomb was then immersed in a bath of acetone and "dry-ice" and allowed to cool for five or ten minutes. Fresh "dry-ice" was added to the bath from time to time so that the temperature was maintained at −75°. The trap containing the trifluoroacetonitrile was removed from its cooling bath and the nitrile was allowed to distil into the bomb. The cork stopper carrying the inlet tube was removed and the bomb was quickly assembled and sealed while cold. The cold bomb was charged with hydrogen to a pressure of 1000 lb./sq. in. It was then heated slowly. At 45° the pressure was 1500 lb., and agitation was begun. The uptake of hydrogen set in almost immediately. At 55 to 60° the absorption of hydrogen was very rapid and the reduction appeared to be complete within one to two hours.

The bomb was cooled to −70°, blown off and opened, and the contents together with anhydrous ether washings were transferred to a distilling flask. The mixture was distilled and two fractions were collected. The first and largest boiled from 30 to 40° and the second from 40 to 130°. Each fraction, cooled to −15°, was treated with an excess of cold ethereal hydrogen chloride, and then the ether was removed by distillation leaving the amine hydrochloride as a white powder. The salt from the first fraction was entirely soluble in hot alcohol and was almost pure trifluoroethylamine hydrochloride. The salt from the second fraction was treated with 20 times its weight of hot absolute ethanol, and the small quantity of insoluble product was collected on a filter. This alcohol-insoluble salt weighed 2.0 g. It was shown by analysis to be ammonium chloride.

Anal. Calcd. for NH_4Cl: Cl, 66.5. Found: Cl, 66.3, 66.4.

The total yield of trifluoroethylamine hydrochloride was 57 g. (80%).

Anal. Calcd. for $CF_3CH_2NH_3Cl$: Cl, 26.2. Found: Cl, 26.6.

Trifluoroethylamine hydrochloride is a white crystalline solid, insoluble in ether, fairly soluble in absolute alcohol, and easily soluble in water, but not hygroscopic. The compound sublimes readily above 125°. A melting point could not be observed even in a sealed capillary tube.

The high-pressure hydrogenation of trifluoroacetonitrile under the conditions just described did not always proceed smoothly. Although yields as high as 80% of trifluoroethylamine were obtained in a number of runs, the yields sometimes dropped as low as 50% when the reduction took place more slowly or a lower temperature was maintained during the reduction. In all cases the only products isolated were trifluoroethylamine and a little ammonia. Small quantities of ammonium trifluoroacetate also appeared to be present. Exhaustive searches were made for secondary amine.

Trifluoroethylamine.—In a Claisen flask provided with a condenser and a receiver cooled in an ice–salt-bath was placed 50 g. (0.37 mole) of trifluoroethylamine hydrochloride. From a dropping funnel was added 200 cc. of saturated aqueous potassium hydroxide solution. The mixture was heated on a water-bath until no more distillate came over. The distillate was treated with 5 g. of barium oxide and distilled through a small packed column with an efficiency of about 10 plates. The amine distilled completely between 37 and 37.3° (737 mm.) and the yield was 33.5 g. (90%). Two determinations of the density gave the values d^{25}_4 1.2452 and 1.2457. A small quantity of the pure amine was added to dry ether containing hydrogen chloride. The salt was collected, dried, and analyzed. *Calcd.* for $CF_3CH_2NH_3Cl$: Cl, 26.2. Found: Cl, 26.29, 26.30.

Trifluoroethylamine appeared to be entirely stable. A sample underwent no change upon standing at room temperature for several months. The compound is highly volatile and has an unpleasant odor remindful of anima glue. The fact that methyl red reacts acid with a water solution of the amine hydrochloride indicates that the amine is a very weak base.

Ether Solution of Trifluorodiazoethane.—A solution of 13.5 g. (0.10 mole) of trifluoroethylamine hydrochloride in 30 cc. of water was chilled in an ice–salt-bath and then treated with a solution of 7.5 g. of 95% sodium nitrite (0.103 mole) in 20 cc. of water. The resulting solution was placed in a separatory funnel and layered with 20 cc. of ether. About 1 cc. of 10% sulfuric acid was added dropwise with good agitation. The mixture was shaken for about five seconds, and after the layers separated the aqueous solution was quickly drained off and returned to the flask cooled in an ice–salt-bath. The ether solution was placed in another well-stoppered flask cooled in an ice–salt bath. This treatment of the cold aqueous solution with acid and extraction with ether was repeated as rapidly as possible about ten times or until the ether extracts were no longer colored yellow. The combined ether extracts (about 200 cc.) were washed quickly with ice-cold 5% sodium carbonate solution; then placed in a tightly stoppered flask with 10 g. of anhydrous calcium chloride; and kept in an ice-bath for two hours. The dried ether solution was decanted into a dry distilling flask and distilled on a water-bath. The bright yellow ether distillate was collected in a dry receiver cooled to −15°. There was apparently no decomposition of the diazo compound during this distillation.

An alternative and perhaps better method of preparing an ether solution of trifluorodiazoethane was as follows: In a heavy walled 250-cc. flask was placed a solution of 13.5 g. (0.10 mole) of trifluoroethylamine hydrochloride in 50 cc. of water. To this was added 75 cc. of ether followed by 7.5 g. of powdered sodium nitrite. The flask was tightly stoppered and shaken for about five minutes and then cooled in an ice–salt-bath. The yellow ether layer was separated and stored in a tightly-stoppered, well-cooled flask. The aqueous solution was layered with another 75 cc. of ether and allowed to stand in the tightly stoppered flask with occasional shaking. After standing for one hour at room temperature, the mixture was again cooled and the ether layer separated. The aqueous solution was treated in the same way once more. The combined ether extract (225 cc.) was washed with sodium carbonate solution, dried and distilled as described above.

Analyses of the ether solutions of trifluorodiazoethane were carried out by titrating with a standard iodine solution in dry ether. The gas evolved during the titration was quantitatively collected and identified as nitrogen. The quantity of nitrogen evolved was almost exactly equivalent to the quantity of iodine decolorized. For example, 15.0 cc. of the diazo solution decolorized 7.0 cc. of 0.300 molar iodine solution (0.00210 mole of I_2) and evolved 0.00207 mole of nitrogen; 50.0 cc. of diazo solution decolorized 23.0 cc. of 0.300 molar iodine solution (0.0069 mole) and evolved 0.0069 mole of nitrogen. The yields of trifluorodiazoethane were from 50 to 70%.

Trifluorodiazoethane.—A di-*n*-butyl ether solution of trifluorodiazoethane was prepared exactly as the ethyl ether solution described above (preferably by the second method). This solution was dried over calcium chloride and then placed in a distilling flask carrying a one-foot Vigreux column. Three traps in series served as receivers. The first trap was cooled in ice-salt, and the second and third were cooled in "dry-ice"–acetone baths. The outlet from the end trap was connected to an aspirator by means of rubber tubing which could be closed with a screw-clamp. The butyl ether solution in the distilling flask was heated on a water-bath up to 80°. A vacuum of about 200 mm. was applied by means of the aspirator, then the system was closed off. As the distillation proceeded the yellow color of the butyl ether solution gradually faded. The tube leading to the aspirator was momentarily opened from time to time in order to maintain a low enough pressure to keep the distillation in progress. When the butyl ether had become practically colorless the distillation was stopped. All of the trifluorodiazoethane collected in the first "dry-ice"–acetone trap as an intensely yellow liquid. The boiling point of the pure compound, observed by immersing the bulb of a thermometer in the boiling liquid, was 13 to 13.5° (752 mm.). A yield of 7.4 g. (67%) was obtained starting from 0.10 mole of the amine hydrochloride. In another similar preparation the yield was 65%.

1,1,1-Trifluoroethyldiiodide.—The ether solutions from the titration of trifluorodiazoethane with iodine were concentrated to a small volume by distilling through a packed column. The residual liquid distilled at 134.5–135.5°, with the liberation of a little iodine indicating some decomposition. The compound was redistilled at reduced pressure and obtained as a colorless liquid boiling at 54° (39 mm.) and 48.5° (27.5 mm.). The melting point was −15 to −13.5°, and $d^{22}{}_4$ 2.595.

Anal. Calcd. for CF_3CHI_2: I, 75.58. Found: I, 75.65, 75.10.

The yield from 0.023 mole of the diazo compound was 6.7 g. (87%).

Summary

2,2,2-Trifluoroethylamine has been prepared by a series of reactions starting with sodium trifluoroacetate. The amine is very stable and weakly basic.

From the amine and nitrous acid there has been prepared 2,2,2-trifluorodiazoethane, CF_3CHN_2. Hitherto, this reaction has been confined to aliphatic amines containing groups like the α-carbonyl.

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