SOME TRISUBSTITUTED BENZOTRIFLUORIDES*

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A number of highly fluorinated aliphatic compounds have been known for some time, especially, some of the chlorofluoro derivatives of methane and ethane. Due to their unique properties they have found commercial application as refrigerants, as propellants in "bug bombs," as gaseous and liquid dielectrics, and in the synthesis of some very unusual polymers. These discoveries and applications warrant research in other types of compounds. Almost immediately the field of aromatic compounds suggests itself. Very few polyfluorides of such simple molecules as benzene and toluene have been described in the literature. The synthesis of two difluorobenzotrifluorides by Finger and Reed[1] in the Survey laboratories immediately brought requests for samples and for further information on these and other aromatic compounds. This paper represents a preliminary report on some of the intermediate compounds studied in trying to find an appropriate synthesis for a trifluorobenzotrifluoride.

The synthesis of higher fluorinated aromatic compounds presents two problems; (1) the usual fluorine substitution reactions tend to be inoperative as the degree of substitution increases, and (2) it is necessary to know the exact structure of the final compound in order to evaluate it properly. Ordinarily the second problem is solved if the structure of the compound just preceding the introduction of a fluorine atom is definitely known. These facts are, more or less, illustrated in this preliminary report.

As a first approach to a probable synthesis of a trifluorobenzotrifluoride, 2-acetylamino-5-fluorobenzotrifluoride (I) was used as the starting compound. This compound was available in the Survey laboratories as a result of some previous work[1].

The nitration of (I) followed by hydrolysis of the acetyl group gave 2-amino-3-nitro-5-fluorobenzotrifluoride (III). This was the compound desired although on a theoretical basis two other isomers could be formed, namely, the nitro group could have entered also into the 4 or 6 positions. These isomers were not isolated although they may have been present in small amounts. The structure of compound (III) was established by conversion to 2, 3-diphenyl-6-fluoro-8-trifluoromethylquinoxaline (V). After having established the structure of 2-amino-3-nitro-5-fluorobenzotrifluoride (III), it appeared that this nitroamine may be the basis for the synthesis of 2,3,5-trifluorobenzotrifluoride.

Attempts to apply the Schiemann reaction, in the usual way, to 2-amino-3-nitro-5-fluorobenzotrifluoride (III) so as to obtain 2,5-difluoro-3-nitrobenzotrifluoride failed. The nitroamine appears to be only slightly basic although it forms an amine hydrochloride in concentrated hydrochloric acid; the hydrochloride can also be formed in absolute ether by passing in dry hydrogen chloride. Indications are that diazotization did take place; however, when

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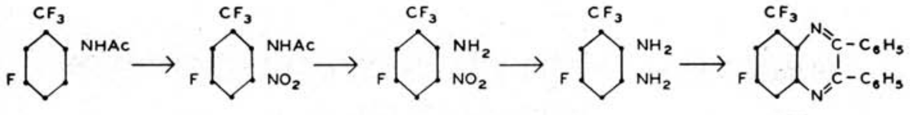

I II III IV V

sodium fluoborate was added a precipitate of sodium chloride and sodium fluoborate was formed.

Although these results did not achieve the original objective, the nitration data is significant in predicting the results which may be obtained in nitrating 2,5-difluorobenzotrifluoride. The orientation factors are, more or less, the same thus lending credence to the formation, of 2,5-difluoro-3-nitro-benzotrifluoride as the chief product. The nitration of 2,5-difluorobenzotrifluoride gave a nitro compound and its composition was established through the acetyl derivative of the amine resulting from reduction. Therefore, it is possible to assign a structure with some supporting evidence even though a more positive proof is necessary. The nitro compound is being studied further as to its structure and properties.

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EXPERIMENTAL

2-Amino-3-nitro-5-fluorobenzotrifluoride (III).—Twenty grams of 2-acetylamino-5-fluorobenzotrifluoride[1] (I) was dissolved in a mixture of 150 g. of concentrated sulfuric acid and 30 g. of glacial acetic acid at room temperature. After cooling to 10°, a solution of 12.6 g. of fuming nitric acid (sp. gr. 1.49-1.5) in 25 g. of concentrated sulfuric acid was added slowly with stirring, and the temperature maintained at 10-20° for ninety minutes. The reaction mixture was poured slowly into an ice-water mixture giving a white precipitate. After filtering and drying, the yield of crude product was 17 g. This crude product was found to be chiefly 2-acetylamino–3-nitro–5-fluorobenzotrifluoride (II) upon recrystallizing a sample from 50 percent aqueous ethanol. The crude material was heated on a water bath for one hour with 50 cc. of concentrated sulfuric acid, and poured into an ice-water mixture giving the crude nitroamine as a yellow precipitate. After filtering and drying, recrystallization from 60 percent aqueous ethanol gave 11.5 g. (57 percent) of 2-amino–3-nitro–5-fluorobenzotrifluoride (III) as yellow needles, m.p. 68-69°.

Anal. Calculated for $C_7H_4F_4N_2O_2$: C, 37.51; H, 1.8; N, 12.50. Found: C, 37.63; H, 1.85; N, 12.56.

The acetyl compound (II) upon recrystallization from 50 percent aqueous ethanol gave white needles, m.p. 179.5-180°.

Anal. Calculated for $C_9H_6F_4N_2O_3$: C, 40.61; H, 2.27; N, 10.53. Found: C, 40.70; H, 2.26; N, 10.45.

2,3-Diphenyl–6-fluoro–8-trifluoromethylquinoxaline (V).—To a refluxing solution of 2 g. of 2-amino-3-nitro-5-fluorobenzotrifluoride (III) in 100 cc. of 50 percent aqueous acetic acid, 6 g. of powdered zinc was added in small portions. After the mixture was light yellow in color, the unreacted zinc was removed by filtration. The 2,3-diamino-5-fluorobenzotrifluoride (IV) was not isolated.

To the filtrate was added slowly, a warm solution containing 30 cc. of 40 percent aqueous sodium bisulfite, 3 g. of benzil, and 40 cc. of ethanol. The yellow flocculent precipitate which formed was removed by filtration, washed, and dried. Recrystallization from methanol gave 2,3-diphenyl–6-fluoro–8-trifluoromethylquinoxaline (V) as white needles, m.p. 133-133.5°. The formation of the quinoxaline proved the adjacency of the nitro and amino groups in III.

Anal. Calculated for $C_{21}H_{12}F_4N_2$: C, 68.48; H, 3.28; N, 7.61. Found: C, 68.46 H, 3.28; N, 7.74.

Diazotization of 2-Amino-3-nitro-5-fluorobenzotrifluoride (III).—Attempts were made to diazotize 2-amino-3-nitro-5-fluorobenzotrifluoride (III) under a variety of conditions. The amine hydrochloride may be formed in concentrated hydrochloric acid or by dissolving the nitroamine in absolute ether and passing in anhydrous hydrogen chloride. In a concentrated hydrochloric acid solution, the amine hydrochloride appears to diazotize slowly with sodium nitrite to give a clear solution. Upon the addition of a strong sodium fluoborate solution, a white precipitate of inorganic salt (probably sodium chloride or sodium fluoborate) was formed. Diazotization with nitrosyl sulfuric acid in the presence of phosphoric acid[2] or glacial acetic acid[3] or 60 percent fluoboric acid failed to give a diazonium fluoborate.

2,5-Difluoro-3(?)-nitrobenzotrifluoride.—To a mixture of 40 cc. of fuming sulfuric acid (40 percent SO_3) and 19.3 g. of fuming nitric acid (sp. gr. 1.49-1.5), 18.3 g. of 2,5-difluorobenzotrifluoride was added at such a rate with stirring that the temperature was maintained at 50° for ninety minutes. The entire reaction mixture was poured into an ice-water mixture, and the crude nitro compound was isolated as a heavy yellow oil. The crude yield was 14.8 g. or 62 percent. A preliminary fractional distillation showed that 2,5-difluoro-3(?)-nitrobenzotrifluoride boils about 191-192° or 91.5-92.5°/19 mm. The sample was not pure indicating the possible presence of isomers and also a trace of a dinitro derivative.

A small sample of the crude nitro compound was reduced with iron filings in an ammonium chloride (0.78 N) solution[4] to the amine. The amine was isolated as an oil, and converted to the acetyl derivative by the usual method. Recrystallization from high-boiling petroleum ether gave 2,5-difluoro-3(?)-acetylaminobenzotrifluoride as white needles, m.p. 104.5-105.5°.

Anal. Calculated for $C_9H_6F_5NO$: C, 45.20; H, 2.53; N, 5.86. Found: C, 45.33; H, 2.43; N, 5.82.

SUMMARY

2-Amino-3-nitro-5-fluorobenzotrifluoride was synthesized from 2-acetylamino-5-fluorobenzotrifluoride.

Attempts to convert 2-amino-3-nitro-5-fluorobenzotrifluoride to 2,5-difluoro-3-nitrobenzotrifluoride by the Schiemann reaction failed.

The nitration of 2,5-difluorobenzotrifluoride gives a nitro compound which is probably 2,5-difluoro-3-nitrobenzotrifluoride.

BIBLIOGRAPHY

1. Finger and Reed, J. Am. Chem. Soc. *66*, 1972 (1944)
2. Welsh, ibid., *63*. 3278 (1941).
3. Hodgson and Walker, J. Chem. Soc. *1933*, 1620.
4. Lukasevich and Vorshilova, Compt. rend, acad. sci. U.R.S.S. *2*, 344 (1935).