[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AT THE OHIO STATE UNIVERSITY]

Fluoroform

BY ALBERT L. HENNE

The novelty of the synthesis of CHF_3 presented in this paper resides in the combined use of antimony fluoride and mercuric fluoride as fluorinating agents.

A minute amount of a substance which was probably impure fluoroform has been obtained by Meslans,[1] by the interaction of iodoform and dry silver fluoride, in chloroform: the reaction was quite violent, the yields very bad, and the vapor tension curve given for the finished product indicates that it was a mixture of CHF_3 and CHF_2I. Fluoroform has been prepared by Ruff[1a] from iodoform and a mixture of mercurous fluoride and calcium fluoride. The details reported by Ruff are in complete agreement with those appearing in the following paragraphs.[1b]

It has been shown in a previous paper from this Laboratory[2] that mercuric fluoride can be advantageously substituted for silver fluoride; and it was found that mercuric fluoride reacts violently with either iodoform or bromoform, even in a large quantity of chloroform. It also has been shown previously[3] that antimony fluoride readily replaces two halogen atoms by two fluorine atoms in halogenated derivatives of methane: after two fluorine atoms have been introduced into the molecule, the other remaining halogens are considerably less reactive than they were in the original substance. In view of the above it was therefore decided to attempt the synthesis of CHF_3 by the reactions

$$3CHBr_3 + 2SbF_3 = 3CHBrF_2 + 2SbBr_3$$
$$2CHBrF_2 + HgF_2 = 2CHF_3 + HgBr_2$$

A detailed description follows.

One kilogram of bromoform is placed in a steel container with a 20% excess of antimony fluoride and 50 cc. of bromine; the container is equipped with a piece of steel pipe, one meter long, to act as a dephlegmator. At the top, this pipe carries a pressure gage, a thermometer well and a needle valve, through which the reaction products are discharged. The container is immersed in a water-bath which is heated progressively. The reaction starts promptly. The pressure rises and is kept at about 4 atmospheres, by properly regulating the rate of discharge through the needle valve, and the rate of heating. The reaction product is washed through water, dried and condensed in a receiver cooled with solid carbon dioxide. When the reaction is properly conducted the discharge is a mixture of HBr, HF and CHF_2Br; since the latter boils at −14.5°, no condensation takes place in the washing water; but when the discharge is permitted to become excessive, incompletely fluorinated material comes over, and $CHFBr_2$, boiling at +64.5°, condenses in the water. When operating as described, a 60% yield of pure CHF_2Br is obtained in about one-half a day. By operating with a smaller quantity of bromine, and a slower rate of heating, the yield is increased to better than 80%.

Before subjecting CHF_2Br to fluorination with mercuric fluoride, it is imperative to purify it carefully by distillation, thus removing all $CHFBr_2$; otherwise, the reaction with mercuric fluoride proceeds too rapidly evolving much heat and accelerating automatically and it acquires explosive violence. With pure CHF_2Br, the regulation of the reaction rate is an easy task.

The fluorination of CHF_2Br to CHF_3 by means of mercuric fluoride is carried out in a piece of apparatus similar to the one described for the first part of the fluorination. The reaction container, with the mercuric fluoride, is cooled in solid carbon dioxide; the theoretical quantity of CHF_2Br, cooled to the same temperature, is poured into the container. The dephlegmator is rapidly screwed in place, and the whole outfit is allowed to warm to room temperature; this causes the pressure to rise to about 4 atmospheres. By means of a bath of water kept at about 50°, and applied intermittently, the pressure is raised progressively to 7 or 8 atmospheres; it will be noted that when this is reached, the rate of increase of the pressure accelerates suddenly. When this occurs, the water-bath is removed instantly, and a bath of liquid, thoroughly cooled by an excess of solid carbon dioxide, is placed be-

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(1) Meslans, *Ann. chim.*, [7] 1, 395 (1894).

(1a) Ruff, *Ber.*, **69**, 299 (1936).

(1b) The present work had been completed and submitted for publication before the author saw Ruff's article. The presentation of the paper consequently was slightly revised, but the experimental data have been left strictly intact.

(2) Henne and Midgley, THIS JOURNAL, **58**, 884 (1936).

(3) Henne and Midgley, *ibid.*, **58**, 882 (1936).

low the reaction vessel. At the same time the needle valve is opened slightly, to permit the CHF_3 to escape. By proper manipulation of the cold bath and the delivery valve, the pressure is kept at about 12 atm.; when it increases above this, the cold bath is raised, thus immersing the reaction vessel and quickly reducing the pressure; in a properly run reaction the cold bath is applied only two or three times for one or two minutes.

When starting from purified CHF_2Br, there is no acid in the reaction products; consequently, washing the product in water is superfluous. The product from the releasing needle valve passes through a large test-tube cooled in solid carbon dioxide, and thence to a gasometer filled with a salt solution. The test-tube collects practically all the CHF_2Br carried over by the fluoroform, together with an appreciable amount of CHF_3 remaining dissolved in the condensed CHF_2Br. After the reaction has been completed, this mixture gathered in the solid carbon dioxide is returned to the reaction container, after adequate cooling, and the procedure is repeated.

The fluoroform collected in the gasometer is condensed in liquid air (as it freezes at about $-163°$, it is apt to plug the inlet of the receiver, if run too slowly). Its purification is effected by distillation through a dephlegmator maintained at $-80°$ by means of solid carbon dioxide. It boils at $-82.2°$ and as CHF_2Br, boiling at $-14.5°$ is the only impurity the separation is as efficient as it is simple to carry out. The yield of distilled fluoroform is about 80%, and about 15% of CHF_2Br (containing some CHF_3) is recovered. The mercuric salt remaining in the reaction vessel is white, crystalline and without a trace of carbon or resinous material. Its analysis shows it to be a mixture of about 90% of $HgBr_2$ and 10% of HgF_2. This indicates that the mechanical losses are small. Moreover, it has been found, on pilot runs, that the use of an excess of CHF_2Br permits the complete utilization of the fluorine available in HgF_2, but as the mercury residue generally is to be subjected to a treatment with fluorine to obtain fresh HgF_2, this mode of operation is not advisable.

Fluoroform is characterized by its great stability, and almost complete chemical as well as physiological inertness. White hot silica decomposes it very slowly, though completely, thus making it possible to analyze it by means of the method previously recommended,[4] and determining its molecular weight at the same time (assuming that it behaves as a perfect gas). Decomposition by calcium oxide is also slow, and proceeds only at elevated temperature (red hot), where it is complete. Metals are indifferent to it. Caustic solutions, even at the boiling point, are without effect. Concentrated acids are not effective. Even in bright sunlight, there is no reaction with bromine; with chlorine, in bright sunlight, and in a quartz vessel, the hydrogen is replaced slowly to yield CF_3Cl. With fluorine a vigorous reaction occurs, but without carbonization, and yields carbon tetrafluoride and hydrogen fluoride.

The vapor tension has been measured between 3 and 1500 mm.; the logarithm of the pressure *versus* the reciprocal of the absolute temperature is a straight line: $\log p = -939.0 \times 1/T + 7.7935$. The Trouton constant is 22.6. The freezing point is $-163°$; the vapor pressure at the triple point about 2 mm.

It is to be noted that the boiling point depression caused by the replacing of bromine by fluorine in CHF_2Br is 67.7°; if, however, the boiling point of CHF_3 ($-82.2°$) is compared to that of $CClF_3$ ($-81.1°$), it is seen that replacing H by Cl causes only a 1° rise in the boiling point, a rather unique occurrence.

The atomic distance between the carbon atom and the fluorine atoms is 1.35 Å., as measured by electron diffraction.[5]

With regard to the physiological effect, it is sufficient to state that exposure of a guinea pig for one hour to a 50–50% mixture of CHF_3 and air by volume caused no effect whatsoever. The animal was not apparently aware of the presence of the gas. In a second experiment, a guinea pig was maintained in an "artificial atmosphere" of 80 volumes of fluoroform and 20 volumes of oxygen for one hour, and again did not exhibit any symptoms of discomfort, though it was patiently aware of unusual conditions, at the start of the experiment.

Summary

Fluoroform has been produced and described; it is a substance characterized by exceptional physiological and chemical inertness. The novel feature of its preparation is the introduction of

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(4) Henne and Hubbard, THIS JOURNAL, **58**, 406 (1936), and **56**, 1078 (1934).

(5) Private communication from Dr. L. O. Brockway; see *J. Phys. Chem.*, **41**, 185 (1937).

two atoms of fluorine into the molecule by means of antimony fluoride, followed by the introduction of the third fluorine atom by means of mercuric fluoride, a mode of synthesis which can be extended to other compounds.

COLUMBUS, OHIO RECEIVED APRIL 3, 1937

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Organic Reactions with Boron Fluoride. XIV. The Reaction of Amides with Acids and Amines[1]

BY FRANK J. SOWA AND JULIUS A. NIEUWLAND

In a recent publication[2] a process was described whereby ammonia was removed as monoamminoboron fluoride from the boron fluoride addition compound of acetamide and a second compound of the type ROH; a second product, an ester, was also formed. The reaction which takes place may be illustrated by the following equation

$$CH_3CO\boxed{NH_2\cdot BF_3 + H}OR \longrightarrow CH_3COOR + NH_3\cdot BF_3 \quad (1)$$

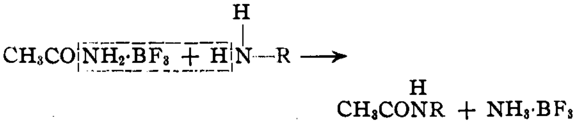
This reaction seems to indicate that if another compound with a labile hydrogen were substituted for ROH it should be possible to eliminate monoamminoboron fluoride.

The purpose of this investigation was to study the reaction of amides with acids and amines. When acetamide–boron fluoride was treated with acetic acid, acetic anhydride was expected as the product with the elimination of monoamminoboron fluoride. Instead of the expected product, however, acetonitrile was formed. The molar ratio of the latter to acetamide used was one to two. Monoamminoboron fluoride was also formed and in the same molar proportion as acetonitrile. In other words, on this basis practically the theoretical yield of acetonitrile was formed. Relatively low quantities of acetic acid can be used with only small losses in the yield of acetonitrile. Without any acetic acid, to serve as an initial catalyst or as a solution medium, the maximum yield of acetonitrile was 15%. The reaction may be represented as follows with acetic acid to aid the reaction

$$CH_3CONH_2\cdot BF_3 + CH_3CONH_2 \xrightarrow{CH_3COOH} CH_3CN + CH_3COOH + NH_3\cdot BF_3$$

When propionic, butyric, hydrochloric or benzoic acids were treated with acetamide in the presence of boron fluoride, acetonitrile resulted in each case. From propionamide and acetic acid this reaction gave propionitrile. In each case tried the nitrile that formed corresponded to the acid amide used.

When the vapors of acetamide were heated to 500° and passed directly into cold aniline Hurd, Dull and Martin[3] obtained a 28% yield of acetanilide. This reaction was accompanied by the evolution of ammonia. The reaction using boron fluoride should be applicable in this case for the removal of ammonia from acetamide and alkyl or aryl amines. Such was found to be the case. Aniline and acetamide–boron fluoride gave the theoretical yield of acetanilide by warming the mixture for only a few minutes. Other amines such as methylaniline gave N-methylphenylacetamide, butylamine gave N-butylacetamide, etc. The reaction may be represented as follows



$$CH_3CO\boxed{NH_2\cdot BF_3 + H}\overset{H}{\overset{|}{N}}-R \longrightarrow CH_3CO\overset{H}{N}R + NH_3\cdot BF_3$$

Both mono and dialkyl or aryl alkyl substituted amides have been prepared by this method. The compound acetamide–boron fluoride is a good acetylating agent whenever the elements of ammonia can be eliminated. This procedure is rapid and of general application for the preparation of substituted amides. Other methods usually involve long heating or sealed tube reactions or are not of a general application.

The boron fluoride could be recovered easily by adding concentrated sulfuric acid to the residue of monoamminoboron fluoride, from either of the above reactions, and warming it. The reaction takes place according to the equation

$$NH_3\cdot BF_3 + H_2SO_4 \longrightarrow BF_3\uparrow + NH_4HSO_4$$

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[1] For previous article, see McKenna and Sowa, THIS JOURNAL, 59, 470 (1937).

[2] Sowa and Nieuwland, *ibid.*, 55, 5052 (1933).

[3] Hurd, Dull and Martin, *ibid.*, 54, 1975 (1932).