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

$$CH_3CO\boxed{NH_2{\cdot}BF_3 + H}OR \longrightarrow CH_3COOR + NH_3{\cdot}BF_2 \quad (1)$$

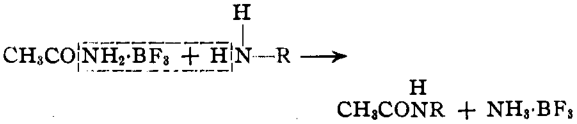
This reaction seems to indicate that if another compound with a labile hydrogen were substituted for ROH it should be possible to eliminate monoamminoboron fluoride.

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



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

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

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

---

[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).

TABLE I

SUBSTITUTED AMIDES PREPARED

Name of Amine used	Name of Amide formed	Amine used, g.	Yield of amide, %	B. p., °C.	M. p., °C.
Butylamine	N-Butylacetamide	36.5	37	229	
Isoamylamine	N-Isoamylacetamide	43.5	64	234	
Aniline	N-Phenylacetamide	46.5	99		114
1-Naphthylamine	N-1-Naphthylacetamide	71.5	45		159
2-Naphthylamine	N-2-Naphthylacetamide	71.5	17		132
Methylaniline	N-Methyl-N-phenylacetamide	53.5	54	255	98
Ethylaniline	N-Ethyl-N-phenylacetamide	60.5	45	115 (10 mm.)	
Dibutylamine	N,N-Dibutylacetamide	64.5	27	241	
Aniline	Benzanilide	60.5	95		161
Aniline	N-Phenylpropionamide	46.5	97	221	103

Acetamide and Acetic Acid.—One mole of acetamide was weighed in a 500-cc. Erlenmeyer flask fitted with an inlet tube that extended to within 2 cm. of the bottom and an outlet tube. The flask was immersed in cold water and 0.5 mole of boron fluoride was added. Five-tenths of a mole of acetic acid was poured into the flask and the contents refluxed for thirty minutes. A white solid separated, which proved to be monoamminoboron fluoride. The apparatus was arranged for distillation directly from the reaction flask. After careful fractionation the following results were obtained:

Fraction	B. p., °C.	Yield, g.
I	80–85	19.8
II	115–118	55.5
III	Residue	45.7

Fraction (I) was acetonitrile and corresponds to 97% of the theoretical yield. Fraction (II) was acetic acid and (III) was monoamminoboron fluoride.

The experiment was repeated except that 0.25 mole of acetic acid was used in place of 0.50 mole. The yield was 89% instead of 97% of the theoretical.

Propionamide and Acids.—The procedure in this reaction was the same as that described above except propionamide was used in place of acetamide. A second experiment was performed with propionamide and propionic acid. Propionitrile was formed in each case and in 80 to 95% yield.

Acetamide and Acids.—A series of experiments was run using exactly the same procedure as above except that propionic, butyric, hydrochloric or benzoic acids were used in place of acetic acid. The results were similar; in each experiment acetonitrile was obtained in yields from 75 to 89% except in the case of benzoic acid where only a 20% yield was isolated.

One experiment was performed using 0.5 mole of boron fluoride with one mole of acetamide in the absence of acids. Acetonitrile was again formed but in a yield of only 3 to about 15%.

Amides and Amines.—Since all of the substituted amides were prepared in a similar manner, a general method only will be described. One-half mole of acetamide (29.5 g.) was weighed into a 500-cc. Erlenmeyer flask, fitted with a stopper carrying an inlet tube, which extended to within 2 cm. of the bottom, and an outlet tube. One-half mole of boron fluoride (34 g.) was passed into the acetamide. The absorption of the boron fluoride was very rapid and exothermic. When 0.5 mole of the gas was added an orange colored solid appeared. To this compound was added 0.5 mole of the amine and the contents refluxed gently for thirty minutes. After cooling the reaction mixture was neutralized with a dilute solution of sodium carbonate, washed with water and then fractionally distilled; solid products were extracted with ether. After removing the ether, the products were distilled under reduced pressure or repeatedly crystallized from an alcohol–water solution.

The results of several runs are given in Table I.

By refluxing 0.25 of a mole of the amides formed in a 15% solution of sodium hydroxide, the original amines were recovered and identified.

Summary

A method for the preparation of nitriles from amides and acids in the presence of boron fluoride has been described. The reaction proceeds by the elimination of monoamminoboron fluoride.

A general method has been outlined for the preparation of mono and dialkyl or aryl alkyl substituted amide from an amide and an amine in the presence of boron fluoride. The reaction proceeds by the elimination of monoamminoboron fluoride.

The compound acetamide–boron fluoride is a good acetylating agent whenever the elements of ammonia can be eliminated.

NOTRE DAME, INDIANA RECEIVED MARCH 29, 1937