0.1 mol), N,N′-dimethylethylenediamine (35.2 g, 0.4 mol), and $TiCl_4$ (19 g, 0.1 mol) were allowed to react for 6 days at 25° in ether. The reaction mixture was filtered and the precipitate was extracted with CH_2Cl_2 for 24 hr using a Soxhlet extractor. The resulting yellow solution was evaporated to dryness and the residue was treated with a solution of $NaPF_6$ (16.8 g, 0.1 mol) in hot methanol. On cooling, 1,4-dimethyl-1,2,3,4-tetrahydrocyclohepta[*b*]pyrazinium hexafluorophosphate crystallized out. The mother liquor was evaporated to dryness and the residue was extracted with hot CH_2Cl_2 to recover the remaining product. The two fractions were combined and recrystallized from CH_2Cl_2–Et_2O. Although it is apparently stable when crystalline, **6** decomposes quite rapidly in solution, possibly through oxidation; the chloride salt is quite sensitive in this respect.

Anal. Calcd for $C_{11}H_{15}N_2PF_6$: C, 41.26; H, 4.72; N, 8.75; F, 35.60. Found: C, 41.46; H, 4.58; N, 8.55; F, 35.69.

2-Phenyl-1,3-dimethylimidazolinium Hexafluorophosphate.—By method A, benzoic acid (6.1 g, 0.05 mol) and N,N′-dimethylethylenediamine (18 g, 0.2 mol) were allowed to react with $TiCl_4$ (5.6 ml, 0.051 mol) in THF for 48 hr. The filter cake from the reaction mixture was treated with CH_2Cl_2 to dissolve product, which was recovered by evaporation of the CH_2Cl_2. The chloride was exchanged for PF_6^- and the product was recrystallized from THF to yield 5.0 g (31%) of 2-phenyl-1,3-dimethylimidazolinium hexafluorophosphate, mp 118–120°.

Anal. Calcd for $C_{11}H_{15}N_2PF_6$: C, 41.26; H, 4.72; N, 8.75; F, 35.60. Found: C, 40.87; H, 4.75; N, 8.67; F, 35.61.

Registry No.—Titanium tetrachloride, 7550-45-0; **2**, 815-62-3; **4**, 23645-56-9; **5**, 23649-59-4; **6**, 23645-57-0.

Direct Fluorination of Amides[1]

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The fluorination of secondary amides was shown to be a general method for the synthesis of difluoramino compounds and N-alkyl-N-fluoroamides. Formation of difluoramino compounds by the displacement of acylium ions was evidenced by the isolation difluoramino acids from lactams and 2-difluoraminoethanol esters from N-acylethanolamines. Some chemical properties of difluoramino acids are described. Alkylfluoroammonium salts were prepared by the reaction of N-alkyl-N-fluoroamides with sulfuric acid. The fluorination of cyclohexanecarboxamide gave cyclohexyl isocyanate and cyclohexylcarboxylic acid, apparently by hydrolysis of the difluoroamide. Oxidation of the fluorination product of acetamide gave tetrafluorohydrazine.

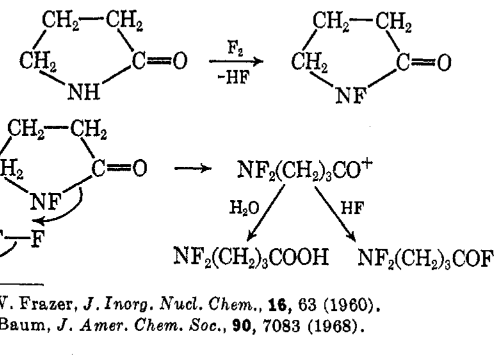
The direct fluorination of alkyl carbamates results in replacement of one or both hydrogens on nitrogen by fluorine,[2] whereas the fluorination of alkyl N-alkylcarbamates results in replacement of NH and subsequently acyl groups.[3] Fluorination studies of amides[4] have been limited to acetamide and N-methylacetamide. Aqueous fluorination of acetamide was reported to give only acetic acid, carbon dioxide, nitrous oxide, and a trace of tetrafluorohydrazine, and that of N-methylacetamide was reported to give acetic acid, carbon dioxide, and a 7% yield of difluoraminomethane. The present paper describes the fluorination of a variety of amides to give N-fluoroamides and difluoramino alkanes, as well as rearrangement products.

Products of the fluorination of secondary amides are shown in Table I. The fluorinations were generally conducted using solutions or suspensions of the substrates in water or acetonitrile, although in several cases no solvent was used. The reactions are similar to those of carbamates in that successive fluorination of NH and fluorinolysis of acyl groups takes place. The rates of the two reactions are of the same order of magnitude, and considerable amounts of difluoramino alkanes are formed, even at low fluorine to substrate ratios. The reactions, however, are characterized by high selectivity toward nitrogen and only two CH fluorination/products, 1,3-bis(difluoramino)-1-fluoropropane and 2-difluoraminoethyl fluoroacetate, were isolated in this work. As a practical synthesis method for difluoramino alkanes, the fluorination of secondary amides is comparable with that of carbamates, and therefore provides a more convenient choice of starting materials. The intermediates, N-fluoroamides, are isolated readily by conventional methods.

$$RNHC(=O)R' \xrightarrow{F_2} RNFC(=O)R' \xrightarrow{F_2} RNF_2$$

The products were characterized by elemental analysis and spectral data, or by comparison with authentic samples. Methyldifluoramine and ethyldifluoramine were prepared previously by reactions of N_2F_4 with alkyl iodides.[5] β-Difluoraminopropionic acid was prepared previously by the addition of difluoramine to acrylic acid,[6] and 1,3-bis(difluoramino)propane and 2-difluoraminoethanol, by the fluorination of the corresponding carbamates.[3]

The fluorinolysis of acyl groups can be rationalized as an electrophilic displacement of acylium ions by fluorine. In the case of lactams, the acyl fragment is retained in the product molecule. For example, 2-pyrrolidinone gave 3-difluoraminobutyric acid in aqueous solution, and 3-difluoraminobutyryl fluoride when no solvent was used in the fluorination.



(1) This work was supported by the Office of Naval Research and the Advanced Research Projects Agency.

(2) V. Grakauskas and K. Baum, *J. Amer. Chem. Soc.*, **91**, 1679 (1969).

(3) V. Grakauskas and K. Baum, *J. Org. Chem.*, **34**, 2840 (1969).

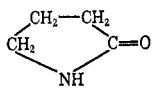
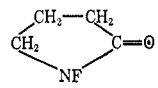
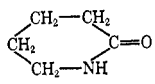
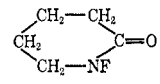
(4) R. E. Banks, R. N. Haszeldine, and J. P. Lalu, *J. Chem. Soc., C*, 1514 (1966).

(5) J. W. Frazer, *J. Inorg. Nucl. Chem.*, **16**, 63 (1960).

(6) K. Baum, *J. Amer. Chem. Soc.*, **90**, 7083 (1968).

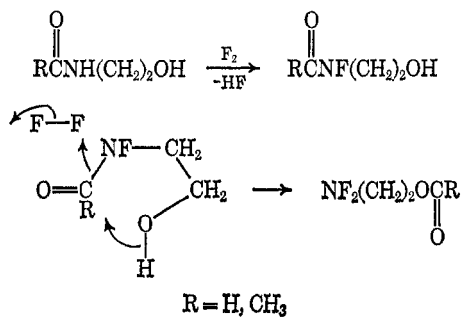
TABLE I

FLUORINATION OF SECONDARY AMIDES

Starting material	Products	Registry no.	Bp (mm), °C	Yield, %[a]
CH_3NHCHO	CH_3NFCHO	23649-62-9	76–77[b]	31
	CH_3NF_2		*c*	
C_2H_5NHCHO	C_2H_5NFCHO	23674-46-6	21–22 (25)	5.5
	$C_2H_5NF_2$		*c*	
$CH_3(CH_2)_3NHCOCH_3$	$CH_3(CH_2)_3NFCOCH_3$	23649-63-0	45–46 (25)[b]	1.5
$CH_3CONHCH_2CH_2CO_2H$	$NF_2CH_2CH_2CO_2H$	20955-66-2	60 (1)	36
		23649-65-2	37–38 (0.15)	16.5
	$NF_2(CH_2)_3COOH$	23649-66-3	52–54 (0.15)	11
	$NF_2(CH_2)_3COF$[d]	23649-67-4	<20 (0.2)[b]	
		23649-68-5	60–62 (0.2–0.3)	20
$HCONH(CH_2)_3NHCHO$	$NF_2(CH_2)_4COOH$		*e*	46
	$NF_2(CH_2)_3NF_2$	21298-22-6	26–30 (25)[b]	5.6
	$NF_2CHF(CH_2)_2NF_2$	23649-70-9		2.5
	$NF_2(CH_2)_3NFCHO$	23649-71-0	31–32 (0.2–0.3)[b]	2.5
$HCONHCH_2CH_2OH$	$NF_2CH_2CH_2OCHO$	23649-72-1	38–45 (25)	25
	$NF_2CH_2CH_2OH$	21298-33-9		3.7
$CH_3CONHCH_2CH_2OH$	$NF_2CH_2CH_2OCOCH_3$	23649-74-3	40–50 (25)[b]	13
	$NF_2CH_2CH_2OH$			3.6
	$NF_2CH_2CH_2OCOCH_2F$	23649-77-6	29–30 (0.1)[b]	0.8

[a] Yields were not optimized. [b] Impure distillate; analytical sample was isolated by gas chromatography. [c] Spectroscopic identification. [d] Nonhydrolytic fluorination conditions. [e] Purified through salt formation.

Further evidence for electrophilic acylium ion displacement is found in the fluorinations of N-acylethanolamines. The fluorinations of both the formyl and acetyl derivatives in aqueous solution gave 2-difluoraminoethanol and its corresponding esters. In the case of the acetyl compound, the fluoroacetate was also isolated. The alcohol function thus competes with the solvent to trap acylium ions.



R = H, CH_3

Simple N-fluoro-N-alkylamides were found to be hydrolytically stable in the presence of dilute aqueous acid. They underwent hydrolysis in concentrated sulfuric acid under the same conditions as the corresponding carbamates.[7] Thus methyl-N-fluoroformamide gave the previously identified[7] methylfluoroammonium ion. Ethyl-N-fluoroformamide gave ethylfluoroammonium ion. The fluorine nmr spectrum of the sulfuric acid solution, a triplet of triplets at −15.51 ppm from external trifluoroacetic acid (J_{NH_2-F} = 42.5 cps, J_{CH_2-F} = 28.7 cps), was consistent with previously reported fluoroammonium ion spectra.[7]

$$RNFCHO \xrightarrow[\Delta]{H_2SO_4} RNH_2F^+HSO_4^-$$

(7) V. Grakauskas, A. H. Remanick, and K. Baum, *J. Amer. Chem. Soc.*, **90**, 3839 (1968).

Although primary difluoramino compounds have been reported to undergo facile dehydrofluorination in the presence of bases,[8] it was found that analytically pure 6-difluoraminohexanoic acid could be isolated in 46% overall yield by extraction of the ε-caprolactam fluorination mixture with cold bicarbonate solution. On the other hand, aqueous sodium hydroxide at 0 to 3° reacted with the acid to give a 59% yield of 5-cyanovaleric acid in 15 min. Reactions of 6-difluoraminohexanoic acid and 4-difluoraminobutyric acid with alcohols in the presence of a trace of acid gave high yields of the corresponding esters.

3-Difluoraminobutyric acid reacted with thionyl chloride to give the acid chloride or the anhydride depending on the reactant ratio. The acid chloride reacted with sodium azide in benzene to give an 85% yield of the isocyanate. The isocyanate reacted with ethanol to give ethyl N-(3-difluoraminopropyl)carbamate, a compound previously obtained in impure form from the fluorination of ethyl trimethylenedicarbamate.[3]

$$NF_2(CH_2)_3COOH \xrightarrow{SOCl_2} NF_2(CH_2)_3COCl \xrightarrow[C_6H_6,\,\Delta]{NaN_3}$$

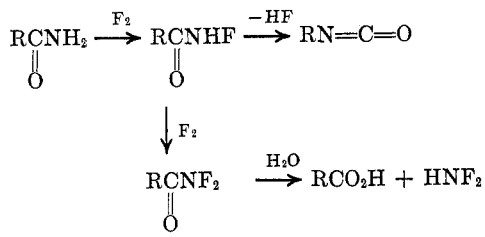
$$NF_2(CH_2)_3NCO \xrightarrow{EtOH} NF_2(CH_2)_3NHCO_2Et$$

A more limited study was made of fluorinations of primary amides. The expected initial products, N-fluoroamides, could be expected to undergo further fluorination to give N,N-difluoroamides. Another possible reaction path of N-fluoroamides leads to isocyanates by the Hofmann rearrangement. Isocyanates

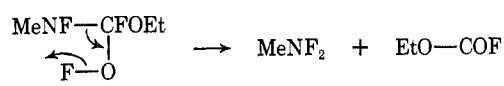
(8) R. C. Petry and J. P. Freeman, *J. Org. Chem.*, **32**, 4034 (1967); F. A. Johnson, C. Haney, and T. E. Stevens, *ibid.*, **32**, 466 (1967); G. N. Sausen and A. L. Logothetis, *ibid.*, **33**, 2330 (1968); A. L. Logothetis and G. N. Sausen, *ibid.*, **31**, 3689 (1966); S. K. Brauman and M. E. Hill, *J. Amer. Chem. Soc.*, **89**, 2127 (1967); A. S. Filatov and M. A. Englin, *Zh. Obshch. Khim.*, **38**, 1408 (1968).

have been isolated from reactions of primary amides with iodine pentafluoride,[9] and similar nucleophilic rearrangements were observed in reactions of fluoroammonium salts with carbonyl compounds. N,N-Difluoroamides were prepared previously from tetrafluorohydrazine and acyl radical sources[10] and were reported to react readily with hydroxylic compounds; reactions with HF, the fluorination by-product, would therefore be expected.

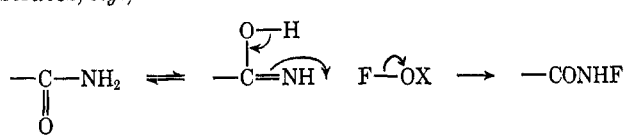
Fluorination of cyclohexanecarboxamide in acetonitrile with 2 mol of fluorine gave an 18% yield of cyclohexyl isocyanate and a 48% yield of cyclohexanecarboxylic acid (after aqueous bicarbonate extraction). The starting material was not hydrolyzed by HF under the fluorination conditions in a control experiment, indicating that the difluoroamide is a precursor to the acid. Additional evidence for a difluoroamide intermediate was obtained by fluorinating acetamide in acetonitrile and oxidizing the solution with chromic acid; a 50% yield of tetrafluorohydrazine was isolated. Tetrafluorohydrazine has been prepared from difluorocarbamates by this method.[11]



Banks, Haszeldine, and Laln[4] have proposed a mechanism for the formation of alkyldifluoramines from carbamates and amides in which fluorine adds to the carbonyl group of the N-fluoro intermediate, followed by intramolecular fluorination by the OF, *e.g.*,



For the first step of the fluorinations in aqueous solutions, they proposed the reaction of oxygen difluoride or hypofluorous acid with the enolic forms of the substrates, *e.g.*,



There now appears to be no reason to invoke oxygen difluoride or hypofluorous acid as intermediates, since similar results (aside from product hydrolysis) are obtained with water or acetonitrile as fluorination solvents. Enolization of the substrates is unnecessary since simple amines can be fluorinated in buffered aqueous solutions,[12] and weakly basic amines, in liquid HF.[13] There is no evidence of fluorine addition to carbonyl groups in the uncatalyzed fluorination of simple esters.[14] The displacement of acylium ions is well known with other electrophilic reagents. The simplest mechanism consistent with the available experimental data is the electrophilic displacement of hydrogen and acylium ions by molecular fluorine.

(9) T. E. Stevens, *J. Org. Chem.*, **31**, 2025 (1966).
(10) R. C. Petry and J. P. Freeman, *J. Amer. Chem. Soc.*, **83**, 3912 (1961).
(11) V. Grakauskas, U. S. Patent 3,350,172 (Oct 31, 1967).
(12) C. M. Sharts, *J. Org. Chem.*, **33**, 1008 (1968).
(13) C. L. Coon, M. E. Hill, and D. L. Ross, *ibid.*, **33**, 1387 (1968).
(14) V. Grakauskas, *ibid.*, **34**, 963 (1969).

Experimental Section

General.—Fluorinations were conducted in a glass standard taper three-necked flask fitted with a mechanical stirrer, a glass tube extending below the liquid level used as a gas inlet, and a standard taper thermometer well with an opening for gas exit. Standard fluorine-handling hardware[15] was used, and the fluorine was diluted fourfold to sixfold with nitrogen. Exit gases were vented through an aqueous potassium iodide trap. Safety shielding is required for the fluorinations and for handling NF compounds.

Methyl-N-fluoroformamide.—Methylformamide (100 g, 1.7 mol) was fluorinated without a solvent with 0.67 mol of fluorine at −30 to −40° over a 2.5-hr period. A mixture of methyldifluoramine[5] and hydrogen fluoride (12 g, ir identification) was removed at 10–15° (25 mm), and the remaining product was vacuum transferred at 25° (0.2 mm) into a −80° receiver. Distillation of the condensate gave 18.0 g (31% yield) of 93% pure (gc analysis) methyl-N-fluoroformamide, bp 76–77°. An analytical sample was isolated by gas chromatography (10 ft × 0.25 in. column of 25% butyl phthalate on Chromosorb P, 75°, 50-cc/min He flow), which showed four more volatile compounds.

Anal. Calcd for C_2H_4NFO: C, 31.17; H, 5.23; N, 18.18; F, 24.66. Found: C, 31.31; H, 5.39; N, 18.0; F, 24.1.

The proton nmr spectrum ($CDCl_3$ solution) showed a doublet (J = 26.2 cps) at δ 3.34 for the methyl and a doublet (J = 13 cps) at 8.58 for –CHO. The fluorine spectrum showed a broad signal at ϕ^* +67.1. The infrared spectrum showed the following peaks (μ): 3.45 (w), 5.86 (s), 6.74 (w), 7.0 (w), 7.60 (m), 8.70 (m), 9.0 (m), 9.69 (m), 9.9 (sh), and 12.2 (s).

When the fluorination was conducted in aqueous solution only methyldifluoramine was obtained.

Ethyl-N-fluoroformamide.—A solution of 73 g (1.0 mol) of ethylformamide in 350 ml of water was treated with 1 mol of fluorine at 0–5°. Ethyldifluoroamine (4.5 ml), identified by its infrared spectrum,[5] was collected in a −80° trap in series with the fluorination flask. The aqueous layer was extracted with three 100-ml portions of ether, dried, and distilled to give 5.0 g (5.5% yield) of ethyl-N-fluoroformamide, bp 20–21° (25 mm), $n^{25}D$ 1.3930.

Anal. Calcd for C_3H_6NFO: C, 39.55; H, 6.64; N, 15.38; F, 20.86. Found: C, 39.60; H, 6.81; N, 15.4; F, 21.1.

The proton nmr spectrum ($CDCl_3$ solution) consisted of a triplet (J = 7.5 cps) at δ 1.31 for the methyl, a doublet (J_{HF} = 31.2 cps) of quartets (J_{HH} = 7.5 cps) at 3.84 for the methylene, and a doublet (J_{HF} = 13.3 cps) at 8.53 for –CHO. The fluorine spectrum showed a broad unresolved signal at ϕ^* +81.7. The infrared spectrum showed a carbonyl band at 5.8 and an NF band at 10.5 μ.

The fluorination of 100 g (1.37 mol) of ethylformamide (no solvent) with 0.32 mol of diluted fluorine at −40 to −45° over a 2.5-hr period gave 4 ml of ethyldifluoramine and 12.0 g (41% yield based on fluorine) of ethyl-N-fluoroformamide.

Butyl-N-fluoroacetamide.—A solution of 86.5 g (0.75 mol) of butylacetamide in 450 ml of water was fluorinated with 0.75 mol of fluorine at 0–5°. The product was extracted with three 50-ml portions of methylene chloride, dried over sodium sulfate, and distilled to give 2.0 g (1.5% yield) of 75% pure butyl-N-fluoroacetamide, bp 45–46° (25 mm). An analytical sample was prepared by gas chromatography (6 ft × 0.25 in. column of 10% Ucon 50 HB100 on Fluoropak 80, 115°, 75-cc/min He flow, rention time 28 min).

Anal. Calcd for $C_6H_{12}NFO$: C, 54.12; H, 9.08; N, 10.52; F, 14.27. Found: C, 54.00; H, 9.11; N, 10.8; F, 14.6.

The proton nmr spectrum (CCl_4 solution) showed an irregular triplet at δ 0.95 for $-CH_2CH_3$, a doublet of triplets at 3.73 (J_{HF} = 33.8 cps) for $-NFCH_2CH_2-$, a multiplet at 1.5 for the other methylenes, and a doublet (J_{HF} = 7.6 cps) at 2.12 for CH_3CONF-. The fluorine spectrum consisted of a triplet (J = 33.8 cps) of quartets (J = 7.3 cps) at ϕ^* + 66.37. The infrared spectrum showed a carbonyl at 5.90 and relatively weak bands in the NF region at 10.01, 10.5, 11.0, and 11.4 μ.

β-Difluoraminopropionic Acid.—Fluorination of 26.2 g (0.20 mol) of N-acetyl-β-alanine in water (0.4 mol of fluorine, 5 hr),

(15) Allied Chemical Corp. Data Sheet PD-TA-85413A.

extraction with ether, drying over Drierite, and distillation gave 9.0 g (36% yield) of β-difluoraminopropionic acid, identical with that prepared previously.[6]

Fluorination of 2-Pyrrolidinone.—A solution of 85 g (1.0 mol) of 2-pyrrolidinone in 1 l. of water was treated with 1.0 mol of fluorine (0–5°, 1.5 hr). The product was extracted with five 75-ml portions of methylene chloride, dried, and distilled to give 17 g (16.5% yield) of N-fluoro-2-pyrrolidinone, bp 37–38° (0.15 mm), $n^{25}D$ 1.4390, and 15 g (11% yield) of 4-difluoraminobutyric acid, bp 52–54° (0.15 mm).

The infrared spectrum of N-fluoro-2-pyrrolidinone showed a carbonyl band at 5.73 and bands in the NF region at 10.0 (s), 10.85 (w), and 11.18 μ (w). The proton nmr spectrum (CCl_4 solution) consisted of a doublet (J_{HF} = 9.6 cps) of irregular triplets at δ 3.67 for $-CH_2NF-$ and a multiplet at 2.25 for the other methylenes. The fluorine spectrum consisted of a broad signal at ϕ^* +71.2.

Anal. Calcd for C_4H_6NFO: C, 46.60; H, 5.87; N, 13.57; F, 18.43. Found: C, 46.22; H, 5.70; N, 13.4; F, 18.9.

The proton nmr spectrum (CCl_4 solution) of 4-difluoraminobutyric acid consisted of a singlet at δ 12.37 for –COOH, a triplet of triplets (J_{HF} = 30 cps) for NF_2CH_2- at 3.63, a triplet at 2.58 for $-CH_2COOH$, and a quintet at 2.07 for the internal methylene. The fluorine spectrum consisted of a triplet (J = 30 cps) at ϕ^* −55.0.

Anal. Calcd for $C_4H_7NF_2O_2$: C, 34.54; H, 5.07; N, 10.07; F, 27.32. Found: 34.47; H, 5.13; N, 9.88; F, 27.0.

In another experiment, 140 g (1.65 mol) of 2-pyrrolidinone was fluorinated with no solvent (0.5 mol of fluorine, 2.5 hr, 0–5°). Some localized ignition at the inlet and charring took place. Volatile products were vacuum transferred at ambient temperature into a −80° receiver. Distillation of the condensate gave 12.5 g (24% yield) of N-fluoro-2-pyrrolidinone, bp 38–39° (0.2 mm). The forecut of this distillation, bp <20° (0.2 mm), 1.5 g, was found by gas chromatography (14 ft × 0.25 in. column of 10% 10% diethylene glycol adipate on Fluoropak 80, 80°, 50-cc/min He flow) to consist of 95% 3-difluoraminobutyryl fluoride. An analytical sample was isolated by gas chromatography.

Anal. Calcd for $C_4H_6NF_3O$: C, 34.05; H, 4.29; N, 9.93; F, 40.39. Found: C, 34.20; H, 4.23; N, 10.05; F, 39.2.

The proton nmr spectrum (CCl_4 solution) consisted of a triplet of triplets at δ 3.58 (J_{HF} = 28.9 cps) for NF_2CH_2-, a quintet at 2.08 for $CH_2CH_2CH_2$, and a triplet at 2.68 for $-CH_2C(=O)-$. The fluorine spectrum consisted of a triplet at ϕ^* −54.16 for NF_2 and a singlet at −43.87 for –CF. The infrared spectrum

showed a carbonyl band at 5.48 and bands in the NF region at 9.85 (m), 10.3 (m), 11.0 (m), 11.37 (m), 11.6 (m), and 12.3 μ (s).

N-Fluoro-ε-caprolactam.—A solution of 113 g (1.0 mol) of ε-caprolactam in 1 l. of water was treated with 1.0 mol of fluorine (0–5°, 3 hr). The product was extracted with four 75-ml portions of methylene chloride, and the methylene chloride solution was extracted with cold aqueous sodium bicarbonate solution. The methylene chloride solution was dried and distilled to give 26 g (20% yield) of N-fluoro-ε-caprolactam, bp 60–62° (0.2–0.3 mm), $n^{25}D$ 1.4640.

Anal. Calcd for $C_6H_{10}NFO$: C, 54.94; H, 7.69; N, 10.68; F, 14.49. Found: C, 54.61; H, 7.52; N, 10.2; F, 15.0.

The proton nmr spectrum (CCl_4 solution) consisted of a doublet of triplets (J_{HF} = 28.5 cps) at δ 3.89 for CH_2NFCO-, a multiplet at 2.4 for $-CH_2CO-$, and a multiplet at 1.77 for the other methylenes. The fluorine spectrum consisted of a triplet (J = 29.6 cps) at ϕ^* +44.0. The infrared spectrum showed a carbonyl band at 5.88 and bands in the NF region at 9.8 (w), 10.18 (s), 10.42 (m), 10.70 (s), 11.82 (s), 12.4 (m), and 12.6 μ (s).

The distillation residue contained ε-caprolactam, and acidification of the bicarbonate solution gave 6-difluoraminohexanoic acid.

6-Difluoraminohexanoic Acid.—A solution of 56.5 g (0.50 mol) of ε-caprolactam in 650 ml of water was treated with 1.0 mol of fluorine at 0–5°. The product was extracted with ether and the ether solution was extracted with sodium bicarbonate solution at 0–5°. The sodium bicarbonate solution was acidified with sulfuric acid, and the product was extracted with methylene chloride, dried, and stripped of solvent to give 40 g (46% yield) of 6-difluoraminohexanoic acid. Unreacted ε-caprolactam was recovered from the ether layer.

Anal. Calcd for $C_6H_{11}NF_2O_2$: C, 43.12; H, 6.63; N, 8.4; F, 22.7. Found: C, 43.47; H, 6.24; N, 8.3; F, 21.9.

The proton nmr spectrum (CCl_4 solution) consisted of a triplet of triplets (J_{HF} = 30 cps, J_{HH} = 8 cps) at δ 3.52 for NF_2CH_2-, multiplets at 1.75 and 2.4 for the other methylenes, and a singlet at 12.20 for –COOH. The fluorine spectrum consisted of a triplet (J = 30 cps) of doublets (J = 7 cps) at ϕ^* −55.7. The infrared spectrum showed broad OH–CH absorption at 3–4, carbonyl at 5.88, and bands in the NF region at 9.8, 10.75, 11.0, and 11.7 μ.

Fluorination of N,N′-Diformyl-1,3-diaminopropane.—Fluorination of 26 g (0.20 mol) of N,N′-diformyl-1,3-diaminopropane in 350 ml of water (0.8 mol of fluorine, 0–5°), extraction with methylene chloride, and distillation gave 2.5 g of colorless liquid, bp 26–30° (25 mm). Gas chromatography (6 ft × 0.25 in column of 10% dioctyl phthalate on Fluoropak 80, 70°) showed that the sample contained, in the order of elution, 33% (2.5% yield) 1,3-bis(difluoramino)-1-fluoropropane and 55% (5.6% yield) 1,3-bis(difluoramino)propane. The latter was identified by its spectra.[3]

The proton nmr spectrum of 1,3-bis(difluoramino)-1-fluoropropane (CCl_4 solution) consisted of a triplet of triplets (J_{HF} = 27.6 cps) at δ 3.73 for $NF_2CH_2CH_2-$, a broad multiplet at 5.45 for the methine, and a multiplet at 2.27 for the other methylene. The fluorine spectrum consisted of a poorly resolved triplet ($J \sim 25$ cps) at ϕ^* −53.37 for NF_2CH_2-, a broadened AB quartet [ϕ^*_A −29.2, ϕ^*_B −19.3 (J_{AB} = 610 cps)] for $CHFNF_2$, and a doublet (51 cps) of triplets (19 cps) at +173.41 for $-CH_2CHF-$. Lack of observable coupling between adjacent CF and NF_2 groups has been observed previously.[3]

Anal. Calcd for $C_3H_5N_2F_5$: C, 21.95; H, 3.05; N, 17.05; F, 57.9. Found: C, 21.67; H, 3.31; N, 16.2; F, 56.2.

In another experiment, the fluorination of 130 g (1.0 mol) of N,N′-diformyl-1,3-diaminopropane (no solvent, 1.5 mol of fluorine) was carried out at 10–20° over a 6.5-hr period. The mixture was washed with water, dried, and distilled to give 8 g of impure 1,3-bis(difluoramino)propane and 4.0 g of N,N,N′-trifluoro-N′-formyl-1,3-diaminopropane, bp 31–32° (0.2–0.3 mm), of approximately 95% purity. An analytical sample was obtained by gas chromatography.

Anal. Calcd for $C_4H_7N_2F_3O$: C, 30.77; H, 4.52; N, 17.94; F, 36.51. Found: C, 30.41; H, 4.60; N, 18.0; F, 36.6.

The proton nmr spectrum (CCl_4 solution) showed a quintet (J = 8 cps) at δ 2.14 for $CH_2CH_2CH_2$, a triplet of triplets (J_{HF} = 28.7, J_{HH} = 8 cps) at 3.61 for $NF_2CH_2CH_2$, a doublet (J_{HF} = 32.6 cps) of triplets at 3.92 for CH_2CH_2NF-, and a doublet (J = 11.3 cps) at 8.59 for CHO. The fluorine spectrum consisted of a triplet (J = 32 cps) of doublets (J = 11 cps) at ϕ^* +79.1 for CH_2NFCHO, and a triplet (J = 28 cps) at ϕ^* −54.6 for NF_2.

Fluorination of N-Formylethanolamine.—The product of fluorination of 44.5 g (0.5 mol) of N-formylethanolamine (350 ml of water, 1 mol of fluorine, 0–5°, 2 hr) was extracted with five 25-ml portions of methylene chloride, drie dover sodium sulfate, treated with solid sodium bicarbonate, and distilled to give 17.5 g of liquid, bp 38–45° (25 mm). Gas chromatography indicated a mixture consisting of 11% 2-difluoraminoethanol and 89% 2-difluoraminoethyl formate.

The infrared spectrum of the latter showed carbonyl at 5.85 and bands in the NF region at 9.77 (m), 10.34 (s), 11.22 (w), 11.9 (s), and 12.5 μ (s).

Anal. Calcd for $C_3H_5NF_2O_2$: C, 28.8; H, 4.03; N, 11.2; F, 30.4. Found: C, 28.7; H, 4.15; N, 11.2; F, 30.4.

A solution of 10.0 g of the above mixture in 15 ml of methanol containing 1 drop of sufuric acid was heated at 55–60° for 2 hr and then distilled to give 6.1 g of 90% 2-difluoraminoethanol.

Fluorination of N-Acetylethanolamine.—The product of fluorination of 103 g (1.0 mol) of N-acetylethanolamine (650 ml of water, 2 mol of fluorine, 0–5°) was extracted with five 40-ml portions of methylene chloride, dried over sodium sulfate, treated with solid sodium bicarbonate, and distilled to give 23 g of colorless liquid, bp 40–50° (2t mm), and 5.0 g, bp 29–30° (0.1 mm). Gas chromatography showed that the 23-g fraction contained 15% 2-difluoraminoethanol (3.6% yield) and 80% 2-difluoraminoethyl acetate (13% yield), and that the 5-g portion contained 69% unidentified nonfluorinated compound and 26% 2-difluoraminoethyl fluoroacetate (0.8% yield). Analytical samples were prepared by gas chromatography.

The proton nmr spectrum of 2-difluoraminoethanol ($CDCl_3$ solution) consisted of a singlet at δ 2.25 for the hydroxyl and multiplets for the methylenes. The fluorine spectrum consisted of a triplet (J = 26 cps) at ϕ^* −54.88. The infrared spectrum

showed prominent bands at 3.0, 9.28, 9.56, 10.43, 11.1, 11.9, and 12.61 μ.

Anal. Calcd for $C_2H_5NF_2O$: C, 24.75; H, 5.16; N, 14.44; F, 39.15. Found: C, 24.59; H, 5.30; N, 14.3; F, 38.5.

The proton nmr spectrum (CCl_4 solution) of 2-difluoraminoethyl acetate consisted of a singlet at δ 2.04 for $-\overset{\overset{O}{\|}}{C}CH_3$, a triplet of triplets (J_{HF} = 28, J_{HH} = 7 cps) at 3.70 for NF_2CH_2-CH_2, and a multiplet at 4.2 for the other methylene. The fluorine spectrum showed a triplet (J = 25 cps) at ϕ^* −54.57. The infrared spectrum showed carbonyl at 5.78 μ.

Anal. Calcd for $C_4H_7NF_2O_2$: C, 34.54; H, 5.07; N, 10.07; F, 27.3. Found: C, 34.40; H, 5.16; N, 9.87; F, 27.8.

The proton nmr spectrum of 2-difluoraminoethyl fluoroacetate (CCl_4 solution) consisted of a triplet of triplets (J_{HF} = 25, J_{HH} = 6 cps) at δ 3.78 for $NF_2CH_2CH_2$, a triplet (J = 7 cps) at 4.58 for $-\overset{\overset{O}{\|}}{C}CH_2-$, and a doublet ($J$ = 46.4 cps) at 4.83 for CH_2F-. The fluorine spectrum showed a triplet (J = 27 cps) at ϕ^* −54.2 for NF_2 and a triplet (J = 46.7 cps) at ϕ^* +231.7 for CF.

Anal. Calcd for $C_4H_6NF_3O_2$: C, 30.57; H, 3.85; N, 8.92; F, 36.3. Found: C, 30.96; H, 3.65; N, 9.07; F, 35.5.

Ethylfluoroammonium Bisulfate.—A solution of 0.4 g of ethyl-N-fluoroformamide in 2 g of concentrated sulfuric acid was heated at 65–70° for 45 min; gas evolution began at 45°. The fluorine nmr spectrum, which consisted of a triplet (J_{NH-F} = 42.5 cps) of triplets (J_{CH-F} = 28.7 cps) at −15.51 ppm from external trifluoroacetic acid, was consistent with those of previously reported fluoroammonium salts.[7]

Methylfluoroammonium Bisulfate.—The above procedure using methyl-N-fluoroformamide gave a methylfluoroammonium bisulfate solution in sulfuric acid identified by nmr spectra.[7]

5-Cyanovaleric Acid.—A solution of 5 g of sodium hydroxide in 20 ml of water was added dropwise over a 15-min period to a solution of 5.0 g (0.030 mol) of 6-difluoraminohexanoic acid in 25 ml of water at 0–3°. The solution was than allowed to stand at ambient temperature for 15 min and was acidified with sulfuric acid. The product was extracted with three 20-ml portions of methylene chloride, dried, and distilled to give 2.0 g (59% yield) of 5-cyanovaleric acid with the reported physical properties.[16]

Ethyl 6-Difluoraminohexanoate.—A solution of 3.8 g (0.023 mol) of 6-difluoraminohexanoic acid in ethanol containing 0.1 ml of sulfuric acid was refluxed for 8 hr. Ice (100 g) was added and the product was extracted with methylene chloride and distilled to give 3.5 g (78% yield) of ethyl 6-difluoraminohexanoate, bp 49–50° (0.2 mm), $n^{25}D$ 1.4060.

Anal. Calcd for $C_8H_{15}NF_2O_2$: C, 49.2; H, 7.74; N, 7.17; F, 19.5. Found: C, 48.9; H, 7.2; N, 7.10; F, 19.8.

The proton nmr spectrum (CCl_4 solution) consisted of a triplet at δ 1.23 and a quartet at 4.05 for CH_3CH_2O-, a triplet of triplets (J_{HF} = 29, J_{HH} = 7 cps) at 3.43 for NF_2CH_2-, and multiplets at 1.57 and 2.25 for the other methylenes. The fluorine spectrum consisted of a triplet (J = 30 cps) at ϕ^* −55.8. The infrared spectrum showed carbonyl at 5.8 μ and weak bands in the NF region at 10.3, 10.8, 11.1, and 11.65 μ.

Similarly, **methyl 6-difluoraminohexanoate** and **ethyl γ-difluoraminobutyrate** were prepared, bp 45–46° (0.2 mm), $n^{25}D$ 1.4050, and bp 26–27° (0.2 mm), $n^{25}D$ 1.3932, respectively.

Anal. Calcd for $C_7H_{13}NF_2O_2$: C, 46.41; H, 7.20; N, 7.7; F, 21.0. Found: C, 46.1; H, 7.10; N, 7.4; F, 21.5.

Anal. Calcd for $C_6H_{11}NF_2O_2$: C, 43.10; H, 6.63; N, 8.38; F, 22.73. Found: C, 42.82; H, 6.41; N, 8.69; F, 23.0.

γ-Difluoraminobutyryl Chloride and γ-Difluoraminobutyric Anhydride.—Thionyl chloride (40 g, 0.33 mol) was added dropwise, with stirring, to a solution of 42 g (0.30 mol) of γ-difluoroaminobutyric acid in 220 ml of dry benzene. With a reflux condenser in place, the solution was heated at 60–65° for 45 min. Distillation gave 43 g (91% yield) of γ-difluoraminobutyryl chloride, bp 29° (0.2 mm), $n^{25}D$ 1.4145.

Anal. Calcd for $C_4H_6NF_2ClO$: C, 30.50; H, 3.84; N, 8.89; F, 24.12. Found: C, 30.48; H, 3.82; N, 9.12; F, 24.0.

The proton nmr spectrum (CCl_4 solution) showed a quintet for $CH_2CH_2CH_2$ at δ 2.53, a triplet of triplets (J_{HF} = 29, J_{HH} = 8 cps) at 3.57 for $NF_2CH_2CH_2$, and a triplet at 3.10 for $-CH_2$-COCl. The fluorine spectrum consisted of a triplet (J = 28 cps) at ϕ^* −54.6. The infrared spectrum showed carbonyl at 5.60 and bands in the NF region at 10.4 (s), 10.62 (m), 11.17 (m), 11.45 (s), and 11.92 μ (s).

A similar reaction using 15.3 g (0.11 mol) of γ-difluoraminobutyric acid and 12.0 g (0.10 mol) of thionyl chloride gave 9.0 g (57% yield) of γ-difluoraminobutyryl chloride and 4.0 g (30% yield) of γ-difluoraminobutyric anhydride, bp 105–106° (0.1–0.2 mm), $n^{25}D$ 1.4130.

Anal. Calcd for $C_8H_{12}N_2F_4O_3$: C, 36.93; H, 4.65; N, 10.77; F, 29.17. Found: C, 36.62; H, 4.56; N, 10.6; F, 30.5.

The infrared spectrum showed carbonyl bands at 5.50 and 5.71 μ.

γ-Difluoraminopropyl Isocyanate.—A stirred suspension of 13.7 g (0.21 mol) of recrystallized sodium azide in a solution of 31.5 g (0.20 mol) of γ-difluoraminobutyryl chloride in 360 ml of dry benzene was heated (using a reflux condenser) at 70–73° until nitrogen evolution ceased (50 min). The solution was filtered and distilled to give 23.0 g (85% yield) of γ-difluoraminopropyl isocyanate, bp 66–67° (45 mm), $n^{25}D$ 1.4028.

Anal. Calcd for $C_4H_6F_2N_2O$: C, 35.30; H, 4.44; N, 20.58; F, 27.92. Found: C, 35.11; H, 4.40; N, 20.2; F, 27.9.

The fluorine nmr spectrum (CCl_4 solution) consisted of a triplet (J = 28 cps) at ϕ^* −55.2. The infrared spectrum showed NCO at 4.42 and bands in the NF region at 10.17, 10.98, 11.27, and 11.7 μ.

Ethyl N-(3-Difluoraminopropyl)carbamate.—A solution of 1.36 g (0.010 mol) of γ-difluoraminopropyl isocyanate in 10 ml of ethanol was allowed to stand at ambient temperature for 18 hr. Distillation gave 1.64 g (90% yield) of ethyl N-(3-difluoraminopropyl)carbamate, bp 66–67° (0.1–0.2 mm), $n^{25}D$ 1.4190.

Anal. Calcd for $C_6H_{12}N_2F_2O_2$: C, 39.56; H, 6.64; N, 15.38; F, 20.86. Found: C, 39.89; H, 6.51; N, 15.1; F, 21.2.

Fluorination of Cyclohexanecarboxamide.—A suspension of 12.7 g (0.10 mol) of cyclohexanecarboxamide in 350 ml of acetonitrile was treated with 0.2 mol of fluorine at −15°. Half of the solution was stirred with solid sodium sulfate and distilled to give 1.1 g (18% yield) of cyclohexyl isocyanate, bp 28–30° (0.1 mm), identified by spectral comparison with an authentic sample. The remaining acetonitrile solution was concentrated to 10 ml under vacuum and the residue was added to 100 ml of aqueous 10% sodium bicarbonate. The aqueous phase was acidified and was extracted with 3–15-ml portions of methylene chloride. Removal of the solvent gave 3.1 g (48% yield) of cyclohexanecarboxylic acid, identical with an authentic sample.

Fluorination of 0.1 mol of the amide in 350 ml of water (0–5°, 0.2 mol of fluorine) gave, after extraction with hexane, 2.0 g (16% conversion, 43% yield) of cyclohexyl isocyanate and 8.0 g of the insoluble starting material.

Tetrafluorohydrazine.—A suspension of 23.6 g (0.40 mol) of acetamide in 25 ml of acetonitrile was fluorinated (0.8 mol of fluorine, 2 hr, −10 to −20°). A 10% aliquot of the resulting solution was added dropwise under a stream of helium to a stirred solution of 2.0 g of chromic anhydride in 40 ml of water at 5–7°. The reaction flask was connected, in series, to a 0° trap, a calcium sulfate drying tower, a −78° trap, and a −195° trap. After 20 min, the final trap contained 0.010 mol (50% yield by volumetric measurement) of tetrafluorohydrazine identified by its infrared spectrum.[17]

Registry No.—γ-Difluoraminobutyric anhydride, 236-49-82-3; γ-difluoraminopropyl isocyanate, 23649-83-4; ethyl N-(3-difluoraminopropyl)carbamate, 21298-39-5; N-fluoro-ϵ-caprolactam, 23649-75-4; 6-difluoraminohexanoic acid, 23649-76-5; ethyl 6-difluoraminohexanoate, 23649-78-7; methyl 6-difluoraminohexanoate, 23649-79-8; ethyl γ-difluoraminobutyrate, 23649-80-1; γ-difluoraminobutyryl chloride, 23649-81-2.

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