

Received: June 11, 1979

SYNTHESIS OF TRIFLUOROMETHYL AMINES, $CF_3N(X)H$, FROM $CF_3N(X)C(O)F$.

AKIRA SEKIYA and DARRYL D. DESMARTEAU [1]

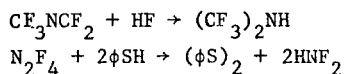
Department of Chemistry, Kansas State University, Manhattan, Kansas
66506, USA.

Summary

A new general synthesis of trifluoromethyl amines of the type, $CF_3N(X)H$, is reported. The amines are prepared in excellent yield by the hydrolysis $CF_3N(X)C(O)F$ in the presence of NaF. The N-acyl fluorides are now available in considerable variety from the reaction of nucleophiles with the oxaziridine $CF_3\overline{NCF_2O}$. Six new amines have been prepared and characterized [$X=CF_3O$, $(CF_3)_2CFO$, CH_3O , C_2H_5O , $(CH_3)_2CHO$ and $(CH_3)_3CO$] and improved syntheses of CF_3NHf and $CF_3NHOC(O)CH_3$ are reported. The new compounds are thermally stable at 22° and are characterized by IR, NMR and physical properties.

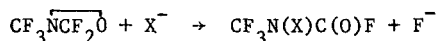
INTRODUCTION

The fluorinated amines $(CF_3)_2NH$ ^[2,3] and F_2NH ^[4,5] are well known and provide good examples of the inductive effect of fluorine and trifluoromethyl which render these compounds somewhat acidic. The compounds are commonly prepared by rather disparate methods.

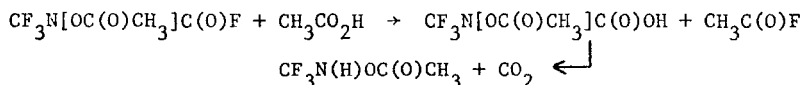


Bis(trifluoromethyl)amine is unstable in H_2O and HNF_2 can be prepared in aqueous systems. The mixed trifluoromethylfluoroamine, CF_3NHf , is known but its synthesis is difficult and very little is known about the compound.^[6] Other related compounds where one of the fluorines in HNF_2 or one of the CF_3 groups in $(CF_3)_2NH$ is substituted by a simple alkyl, alkoxy or other groups are very rare.

Recently in the study of the reaction chemistry of the perfluoro-oxaziridine, $\text{CF}_3\overline{\text{NCF}_2\text{O}}$, with nucleophiles, a variety of compounds of the type $\text{CF}_3\text{N(X)C(O)F}$ were obtained [7-9].



When the nucleophile was CH_3CO_2^- from $\text{CH}_3\text{CO}_2\text{H}$, a significant amount of $\text{CF}_3\text{N(H)OC(O)CH}_3$ was observed along with the expected acyl fluoride. This product was believed to form by the following reactions.



This suggested that the simple hydrolysis of $\text{CF}_3\text{N(X)C(O)F}$ might lead to $\text{CF}_3\text{N(X)H}$. This paper reports the synthesis of eight $\text{CF}_3\text{N(X)H}$ derivatives by this method.

EXPERIMENTAL

General

All volatile compounds were handled in glass and stainless steel vacuum systems as previously described [10]. Characterization of new compounds was carried out in the usual way.

All reagents other than $\text{CF}_3\overline{\text{NCF}_2\text{O}}$ were obtained from commercial sources. Solids were dried under vacuum and liquids were distilled before using. $\text{CF}_3\overline{\text{NCF}_2\text{O}}$ was prepared by the literature method^[9,10] and $\text{CF}_3\text{N(X)C(O)F}$ were prepared from the oxaziridine as previously described.^{7,8,9}

Reactions of $\text{CF}_3\text{N(X)C(O)F}$ with H_2O

Reactions were carried out in ~6 ml Kel-F reactors fitted with a stainless steel valve. In a typical reaction, dried NaF (0.2g) was placed in the reactor and pumped under vacuum. Dry air was then admitted and a weighed amount of H_2O was added onto the NaF. The vessel was then cooled to -193° , evacuated and the $\text{CF}_3\text{N(X)C(O)F}$ was added by vacuum transfer. The mixture was then allowed to warm from -111° to 22° in a CFCl_3 bath over 16 hrs. The products were then separated by pumping through traps at -111° and -193° . The -193° trap contained the CO_2 . The contents of the -111° trap were then separated by glc on 10' x 3/8" column packed with 40% halocarbon 11-21 oil on Chromosorb P. In the case of $\text{CF}_3\text{NFC(O)F}$, the products were separated directly by glc.

The reactions are summarized in Table 1. Characterization of the compounds follows.

Table 1

Hydrolysis of $\text{CF}_3\text{N}(\text{X})\text{C}(\text{O})\text{F}^{\text{a}}$

X^{b}	$\text{H}_2\text{O}^{\text{b}}$	Products ^c		Recovered $\text{CF}_3\text{N}(\text{X})\text{C}(\text{O})\text{F}$
		$\text{CF}_3\text{N}(\text{X})\text{H}$	CO_2	
F, 1.0	1.4	43	100	0
OCF_3 , 1.4	1.5	65	93	0
$\text{OCF}(\text{CF}_3)_2$, 0.40	0.83	63	88	~0
OCH_3 , 0.73	1.4	74	100	0
OCH_2CH_3 , 0.82	1.1	41	72	28
$\text{OCH}(\text{CH}_3)_2$, 0.82	1.2	48	51	37
$\text{OC}(\text{CH}_3)_3$, 1.0	1.2	8	12	51
$\text{OC}(\text{CH}_3)_3$, 0.51 ^d	1.25	54	57	42
$\text{OC}(\text{O})\text{CH}_3$, 0.21	0.23	63	95	0
SCH_2CH_3 , 0.25	0.83	0	0	~90

a. -111 to 22° , 16 hr with 5 mmol NaF

b. amounts in mmol

c. % based on $\text{CF}_3\text{N}(\text{X})\text{C}(\text{O})\text{F}$

d. 22° for 20 hr.

CF_3NHF : m.p. -103 to -101° ; mol. wt. 101.0, calcd. 103.02; IR 3310(m), 1422(s), 1317(s), 1216(vs), 1030(s), 948R, 941Q(s), 933P, 858(m), 675(w), 610(w), 455(vw), cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{NH}^{\text{B}}\text{F}^{\text{C}}$, ϕ^*_{A} 74.2, d-d; δ_{B} 7.88, br-d; ϕ^*_{C} 127.6, d-q; $J_{\text{AB}}=9.5$, $J_{\text{BC}}=51.0$, $J_{\text{AC}}=26.7$ Hz.

$\text{CF}_3\text{N}(\text{H})\text{OCF}_3$: m.p. -100 to -99° ; mol. wt. 169.1, calcd. 169.03; IR 3356(w), 1462(m), 1324(s), 1288(s), 1230(vs), 1181(vs), 1967(w), 924(m), 857(m), 663(m), 623(w), 464(m), cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{N}(\text{H}^{\text{B}})\text{OCF}_3^{\text{C}}$, ϕ^*_{A} 71.5, d-q; δ_{B} 6.64, br.; ϕ^*_{C} 67.7, q; $J_{\text{AB}}=8.3$, $J_{\text{BC}}\sim 0$, $J_{\text{AC}}=2.8$ Hz.

$\text{CF}_3\text{N}(\text{H})\text{OCF}(\text{CF}_3)_2$: m.p. $< -125^\circ$; mol. wt. 270.1, calcd. 269.04; IR 3340(w), 1457(m), 1440(sh), 1330(m), 1314(vs), 1250(vs), 1228(s), 1208(w), 1164(m), 1120(s), 1027(s), 960(m), 920(m), 849(m), 736(m), 720(w), 660(m), 620(w), 588(w), 550(w), 463(m), cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{N}(\text{H}^{\text{B}})\text{OCF}^{\text{C}}(\text{CF}_3^{\text{D}})_2$, ϕ^*_{A} 71.4, d-d; δ_{B} 6.70, br-q; ϕ^*_{C} 140.5, m; ϕ^*_{D} 78.1, m; $J_{\text{AB}}=8.2$, $J_{\text{AC}}=5.9$, $J_{\text{AD}}=0.8$, $J_{\text{BD}}=0.4$, $J_{\text{CD}}=2.3$ Hz.

$\text{CF}_3\text{N}(\text{H})\text{OCH}_3$: m.p. -88 to -85° ; mol. wt. 116.5, calcd. 115.06; IR 3340(w), 2978(m), 2920(w), 2835(vw), 1446(m), 1307(s), 1212(vs), 1182(s), 1086(m), 947(w), 910(m), 826(w), 668(m), 622(w), 580(w), 480(vw), 462(m) cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{N}(\text{H}^{\text{B}})\text{OCH}_3^{\text{C}}$, $\phi_{\text{A}}^* 71.3$, d; $\delta_{\text{B}} 6.32$, br; $\delta_{\text{C}} 3.91$, s; $J_{\text{AB}}=0.6\text{Hz}$.

$\text{CF}_3\text{N}(\text{H})\text{OCH}_2\text{CH}_3$: m.p. -60.0 to -58.5° ; mol. wt. 128.0, calcd. 129.08; IR 3340(w), 2999(w), 2950(w), 2908(vw), 1439(s), 1397(w), 1305(s), 1210(vs), 1186(s), 1128(m), 1096(vw), 1068(m), 1028(s), 913(m), 834(w), 667(m), 620(m), 462(m) cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{N}(\text{H}^{\text{B}})\text{OCH}_2^{\text{C}}\text{CH}_3^{\text{D}}$, $\phi_{\text{A}}^* 70.9$, d; $\delta_{\text{B}} 6.16$, q; $\delta_{\text{C}} 4.14$, q; $\delta_{\text{D}} 1.46$, t; $J_{\text{AB}}=9.6$, $J_{\text{CD}}=7.0$ Hz.

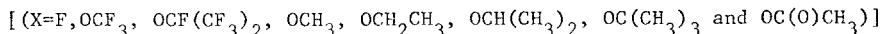
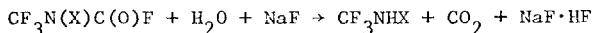
$\text{CF}_3\text{N}(\text{H})\text{OCH}(\text{CH}_3)_2$: m.p. -124 to -122° ; mol. wt. 144.3, calcd. 143.11; IR 3330(w), 2990(m), 2950(w), 1441(s), 1383(m), 1303(vs), 1270(w), 1209(vs), 1182(s), 1146(m), 1124(vw), 1047(m), 912(s), 810(w), 667(m), 620(w), 463(w) cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{N}(\text{H}^{\text{B}})\text{CH}^{\text{C}}(\text{CH}_3^{\text{D}})_2$, $\phi_{\text{A}}^* 70.5$, d; $\delta_{\text{B}} 5.74$, br; $\delta_{\text{C}} 4.02$, sep; $\delta_{\text{D}} 1.27$, d; $J_{\text{AB}}=9.6$, $J_{\text{CD}}=7.0\text{Hz}$.

$\text{CF}_3\text{N}(\text{H})\text{OC}(\text{CH}_3)_3$: m.p. -19.5 to -18.5° ; mol. wt. 156.4, calcd. 157.14; IR 3315(w), 2993(m), 2950(vw), 2890(vw), 1446(s), 1395(w), 1374(m), 1312(vs), 1256(w), 1203(vs), 1173(vs), 1035(s), 915(s), 871(w), 840(m), 755(vw), 667(m), 618(w), 462(m) cm^{-1} ; NMR $\text{CF}_3^{\text{A}}\text{N}(\text{H}^{\text{B}})\text{OC}(\text{CH}_3^{\text{C}})_3$, $\phi_{\text{A}}^* 69.7$, d; $\delta_{\text{B}} 5.67$, br; $\delta_{\text{C}} 1.51$, s; $J_{\text{AB}}=9.5\text{Hz}$.

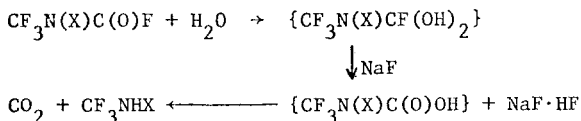
$\text{CF}_3\text{N}(\text{H})\text{OC}(\text{O})\text{CH}_3$: see ref. 8.

RESULTS AND DISCUSSION

The hydrolyses of $\text{CF}_3\text{N}(\text{X})\text{C}(\text{O})\text{F}$ are summarized in Table 1. The reactions proceed according to the equation.



Nothing certain can be stated about the mechanism of this reaction but it probably proceeds via an unstable acid, $\text{CF}_3\text{N}(\text{X})\text{C}(\text{O})\text{OH}$, formed via the attack of H_2O on the acyl group.



No evidence could be found for the acid intermediate, although some of the reactions are slow. This implies that the rate determining step is the initial reaction of H_2O with the acyl fluoride. The attack of H_2O on the acyl fluoride could occur in several different ways and the intermediate shown is speculative. The NaF may accelerate the loss of HF but the hydrolysis of $CF_3NFC(O)F$ will proceed without it. The other reactions were not examined in the absence of NaF and we viewed the NaF simply as a base to absorb HF.

From Table 1, it is obvious that electron donating groups on the nitrogen, decrease the reactivity of the acyl fluoride as would be expected for the above proposal. Comparison of $X=(CF_3)_2CFO$ with $(CH_3)_2CHO$ suggests that steric hindrance by the group attached to nitrogen is not important. The correlation between the percent CO_2 and recovered starting material is good but not between the latter and the amine. Either some of the amine is lost by our procedures, or other reactions occur in the system. Because only the volatile products were analyzed, the missing amine is probably in the NaF/HF/ H_2O residue. The isolated yields of the amines would probably increase if the reactions were run on a larger scale.

The amines are all colorless liquids or solids at 22° . No decomposition of the compounds was evident at 22° during handling in glass or stainless steel vacuum systems. The characterization of the compounds by IR, NMR and mol. wt. is straightforward. The broad resonance for hydrogen on nitrogen is due to nitrogen quadrupolar effects and possibly traces of H_2O . The half-widths of the CF_3 on nitrogen are typically 2-4 Hz. In the case of CF_3NFH , the half-width of the fluorine on nitrogen is about 30 Hz. The other proton and fluorine resonances in the amines were sharp. The chemical shifts of CF_3-N vary in a regular way, decreasing as the electron withdrawing effect of the substituents decreases. The NH chemical shift follows the same trend, except that $CF_3N(H)OC(O)CH_3$ is larger than CF_3NHF . This is probably due to inter- and intramolecular hydrogen bonding between N-H and C=O. The latter is also evident from the IR spectrum which shows two N-H stretches and multiple bands in the C=O region [8].

The IR spectra for these compounds contain characteristic $\nu(N-H)$, $\nu(N-O)$, $\nu(N-C)$, $\nu(CF_3)$, $\nu(C-O)$ and $\delta(NH)$ frequencies. Other assignments other than

C-H stretching are less obvious. The tentative assignments for these frequencies in the three smaller members of this series are shown in Table 2, along with the assignments for HNF_2 [11] and related values for

Table 2
Infrared Frequencies of CF_3NHX and HNF_2 (cm^{-1})

Description	X				
	F	OCF_3	OCH_3	CF_3^a	HNF_2^b
$\nu(\text{NH})$	3310	3356	3340	3455	3193
$\delta(\text{NH})$	1422	1462	1446	1493	1424, 1307
$\nu(\text{CF}_3)$	1317	1324	1307	1340	----
	1216	1288	1212	1255	
	1216	1230	1182	1195	
		1181		1138	
$\nu(\text{NX})$	1030	1067	1086	947	972
$\nu(\text{CN})$	941	857	826	880	888 ^c
$\nu(\text{CO})$	---	924	910	---	---

a. Our values and assignments

b. ref. 11

c. $\nu(\text{NF})$

$(\text{CF}_3)_2\text{NH}$. In CF_3NHF , the 1216 cm^{-1} band is probably degenerate and amounts for the observation of only two of the three expected C-F stretches. The assignment of the 941 band in CF_3NHF to $\nu(\text{CN})$ is consistent with its pronounced PQR band shape. The $\nu(\text{NO})$, $\nu(\text{CN})$ value for $\text{X}=\text{OCF}_3$ and OCH_3 are very reasonable when compared to a variety of $(\text{CF}_3)_2\text{NOX}$ derivatives [12,13].

In summary the hydrolysis of $\text{CF}_3\text{NXC(O)F}$, which can be obtained in considerable variety from $\text{CF}_3\text{NCF}_2\text{O}$, provides an excellent route to variety of secondary trifluoromethyl amines. The easy synthesis of CF_3NHF by this method is especially noteworthy. This novel molecule completes the series $(\text{CF}_3)_2\text{NH} - \text{CF}_3\text{NHF} - \text{F}_2\text{NH}$ and merits further study for comparison to the parent compounds. In particular, the elimination of HF from the compound should be of interest.

ACKNOWLEDGMENT

The financial support of this work by the Army Research Office-Durham (Grant No. DAAG29-77-G-0071) is gratefully acknowledged.

REFERENCES

- 1 Alfred P. Sloan Fellow 1975-77.
- 2 D. A. Barr and R. N. Haszeldine, *J. Chem. Soc.*, 2532 (1955).
- 3 J. A. Young, S. N. Tsoukalas and R. D. Dresdner, *J. Am. Chem. Soc.*, 80, 3604 (1958).
- 4 A. Kennedy and C. B. Colubrn, *J. Am. Chem. Soc.*, 81, 2906 (1959).
- 5 J. K. Ruff, *Chem. Rev.*, 67, 665 (1967).
- 6 V. A. Gensburg and K. N. Smirnov, *Zh, Obshih, Khim.*, 39, 1331 (1969); *C. A.*, 71, #101206t (1969).
- 7 A. Sekiya and D. D. DesMarteau, *J. Org. Chem.*, 44, 1131 (1979).
- 8 A. Sekiya and D. D. DesMarteau, *J. Fluorine Chem.*, 13, 000 (1979).
- 9 A. Sekiya and D. D. DesMarteau, *Inorg. Chem.*, 18, 1919 (1979).
- 10 E. R. Falardeau and D. D. DesMarteau, *J. Am. Chem. Soc.*, 98, 3529 (1976)
- 11 J. J. Comeford, D. E. Mann, L. J. Schoenard, D. R. Lide, Jr., *J. Chem. Phys.*, 38, 461 (1963).
- 12 P. M. Spaziante in 'MTP International Review of Science, Inorganic Chemistry Series One', Vol. 3 V. Gutmann, Ed., Butterworths, London, 1972, Chapter 5.
- 13 K. O. Christie, C. J. Scharf, R. D. Wilson and D. Pillipovich, *J. Fluorine Chem.*, 4, 423 (1974).