$K_4Fe(CN)_6$ solution: after the titration, americium returns to the initial three-valent state. The rate of oxidation increases with the increase in XeO_3 concentration and depends only slightly on the composition of the solution. In 1.5–3 *M* solutions of K_2CO_3 containing XeO_3 the photochemical oxidation of Am^{III} to Am^{VI} takes place.

Thus, xenon compounds are useful for oxidation of Am^{III} in carbonate solutions. A new reagent, XeF_2, useful for preparation of Am^{IV} by chemical methods in bicarbonate—carbonate solutions has been found; the oxidant is decomposed completely, and the small amount of F^- that is introduced into the solution, has no significant effect on the behavior of Am^{IV}. The presence of F^- ions in the solution can be avoided if XeO_3 is used, but the formation of Am^{IV} in that case proceeds only under UV irradiation. To obtain Am^{VI}, Na_4XeO_6 may be used, but a large excess of oxidant must be taken.

The present work was supported by the Russian Foundation for Basic Research (Project 93—03—4510).

Experimental

The quality of the reagents used, the procedures for the preparation of purified Am samples and carbonate solutions of americium, and the description of the spectrophotometrical investigations have been given elsewhere.[5,9] The procedure for the titration of Am^{IV} and Am^{VI} solutions has been described previously.[3] XeF_2 and Na_4XeO_6 were used without additional purification and were introduced into solutions in the crystalline state or in the form of a solution in ice-cold water. XeO_3 was obtained by hydrolysis of Na_4XeO_6 in a 0.1 *M* $HClO_4$ solution.

References

1. J. S. Coleman, T. K. Keenan, and L. H. Jones, *Inorg. Chem.*, 1963, **2**, 58.
2. V. A. Ermakov, A. G. Rykov, G. A. Timofeev, A. V. Dzhzadav, and G. N. Yakovlev, *Radiokhimiya*, 1973, **15**, 380 [*Sov. Radiochem.*, 1973, **15** (Engl. Transl.)].
3. D. E. Hobart, K. Samhoun, and J. R. Peterson, *Radiochim. Acta*, 1982, **31**, 139.
4. P. L. Khizhnyak, Ph. D. Thesis., Moscow, 1987 (in Russian).
5. A. B. Yusov and V. P. Shilov, *Mendeleev Commun.*, 1993, 83.
6. P. Berger, P. Blank, and J. Bourges, *Radiochim. Acta*, 1988, **43**, 217.
7. V. D. Klimov, V. N. Prusakov, and V. B. Sokolov, *Radiokhimiya*, 1971, **13**, 725 [*Sov. Radiochem.*, 1971, **13** (Engl. Transl.)].
8. E. H. Appelman and J. G. Malm, *J. Am. Chem. Soc.*, 1964, **86**, 2141.
9. V. P. Shilov and A. B. Yusov, *Radiokhimiya*, 1971, **13**, 725 [*Sov. Radiochem.*, 1971, **13** (Engl. Transl.)].

Received December 30, 1993;
in revised form February 8, 1994

Nucleophilic substitution of bromine in vicinal bromotrifluoroalkylamines

Yu. L. Ignatova,* N. M. Karimova, and I. N. Rozhkov†

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 117813 Moscow, Russian Federation.
Fax: + 7 (095) 135 5085

Secondary *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*-alkylamines cyclize under the action of bases to yield aziridines. Tertiary *N*-(2-bromo-3,3,3-trifluoropropyl)amines react with S-nucleophiles to give products of bromine substitution.

Key words: *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*-alkylamines, nucleophilic substitution; 2-trifluoromethylaziridines.

Compounds containing the CF_3 group are of significant interest as potentially biologically active substances. However, the methods for the synthesis of these compounds are rather limited, because the nucleophilic substitution in trifluoromethylated alkyl halides is hindered.[1–3] The rate of nucleophilic substitution of the halogen in α-fluorinated ethyl halides is several orders

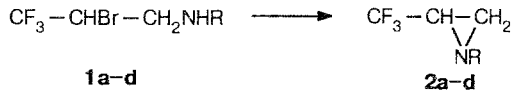
† Deceased in 1993.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 955—957, May, 1994.

of magnitude lower than in their nonfluorinated analogs.[3,4] The passivating influence of the CF_3 group is caused by steric and electronic effects.[1,5] If the nucleophile is a strong base, substitution reactions are accompanied by β-elimination of the F^- anion (*cf.* Ref. 6).

In the present work, the reactions of intra- and intermolecular substitution of bromine in *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*-alkylamines[7] (**1**) have been investigated. As expected, the bromine atom in compounds **1** is passivated by the neighbouring CF_3 group, and its replacement requires prolonged heating in aprotic polar solvents, which facilitate S_N2 reactions.

Heating of the secondary bromoalkylamines **1a—d** in DMF in the presence of Et_3N or Na_2CO_3 affords aziridines.



1a–d **2a–d**

R = Me (**a**), Et (**b**), *cyclo*-C_6H_{11} (**c**), $PhCH_2$ (**d**)

In the case of nonfluorinated vicinal halodialkylamines, this cyclization proceeds exceptionally readily, and it is the main method for the synthesis of aziridines. Thus, for the first time we have managed to apply the Gabriel reaction to the synthesis of 1-alkyl-2-trifluoromethylaziridines[8] (**2a—d**).

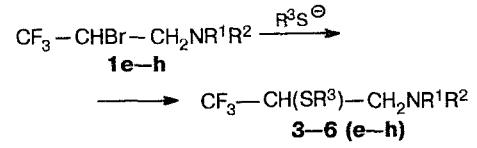
All attempts to replace bromine in primary and secondary bromotrifluoroalkylamines with sulfur-containing nucleophiles were unsuccessful: compounds **1a—d** and unsubstituted amine did not change after prolonged heating with thiourea and potassium thiocyanate in MeCN or DMF. Tertiary bromoalkylamines **1e—h** reacted with sulfur-containing nucleophiles to give a series of products of bromine substitution (**3—6**).

The data[9] about the basicity of bromoalkylamines **1** fail to explain the difference in the reactivity, since no correlation between the reactivity and basicity of the amino group has been observed. Probably, in the case of primary and secondary bromotrifluoroalkylamines, the attack of the nucleophilic species is passivated by the amino group proton, which suppresses the nucleophilic substitution.

Table 1. Conditions for the synthesis of compounds **2—6** and their characteristics

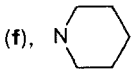
Compound	NR (NR^1R^2)	SR^3	Reaction conditions			Yield (%)	M.p./°C or b.p./°C	Found / Calculated (%)					Molecular formula
			T/°C	Reaction time/h	Solvent		(*p*/Torr)	C	H	F	N	S	
2a	NMe	—	120	3	DMF	70	67 (760)	37.8 38.4	4.72 4.80	—	10.8 11.2	—	$C_4H_6F_3N$
2b	NEt	—	120	3	DMF	70	77 (760)	43.3 43.2	5.74 5.75	40.7 41.0	—	—	$C_5H_8F_3N$
2c	*cyclo*-NC_6H_{11}	—	120	4	DMF	65	65 (15)	56.1 55.9	7.25 7.25	29.1 29.5	—	—	$C_9H_{14}F_3N$
3e	NMe_2	SCN	70	25	MeCN	90	88 (10)	36.2 36.3	4.67 4.54	—	13.8 14.1	—	$C_6H_9F_3N_2S$
3f		SCN	110	4	DMF	52	102 (7)	42.7 42.8	5.09 4.91	25.8 25.4	—	—	$C_8H_{11}F_3N_2S$
3g		SCN	120	1.5	DMF	54	125 (10)	45.3 45.4	5.45 5.46	—	—	13.3 13.4	$C_9H_{13}F_3N_2S$
3h		SCN	115	6	DMF	40	132 (10)	40.4 40.0	4.68 4.58	—	—	13.3 13.3	$C_8H_{11}F_3N_2OS$
4e*	NMe_2	$SC(=NH)NH_2$	70	10	MeCN	81	127	23.3 23.8	4.35 4.39	—	14.2 14.2	—	$C_6H_{13}BrF_3N_3S$
4g*		$SC(=NH)NH_2$	70	6.5	MeCN	83	180	32.1 32.2	4.99 5.06	—	12.6 12.5	—	$C_9H_{17}BrF_3N_3S$
4h*		$SC(=NH)NH_2$	70	6	MeCN	80	183	28.4 28.4	4.62 4.43	—	12.4 12.4	—	$C_8H_{15}BrF_3N_3OS$
5e	NMe_2	SPh	70	36	MeCN	41	114 (10)	53.2 53.0	5.54 5.62	—	—	13.2 12.9	$C_{11}H_{14}F_3NS$
6g		SAc	150	3	DMF	65	92 (7)	47.1 47.0	6.27 6.46	—	—	—	$C_{10}H_{16}F_3NOS$

* Hydrobromide.



$CF_3-CHBr-CH_2NR^1R^2$ **1e–h** $\xrightarrow{R^3S^\ominus}$ $CF_3-CH(SR^3)-CH_2NR^1R^2$ **3–6 (e–h)**

3: $SR^3 = SCN$
4: $SR^3 = SC(=NH)NH_2$
5: $SR^3 = SPh$
6: $SR^3 = SAc$

$R^1 = R^2 =$ Me (**e**), $NR^1R^2 =$  (**f**),  (**g**),

 (**h**)

Experimental

^1H NMR spectra were recorded on a Bruker WP-200SY (200 MHz) spectrometer with TMS as the external standard. The reaction conditions, yields, and characteristics of compounds **2—6** are given in Table 1, and the ^1H NMR spectral parameters are given in Table 2.

2-Trifluoromethyl-1-methylaziridine (2a). A mixture of 4.12 g (20 mmol) of *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*-methylamine (**1a**) and 2.33 g (22 mmol) of dry powdered Na_2CO_3 in 10 mL of abs. DMF was stirred with heating, and the reaction product, aziridine **2a**, was simultaneously distilled off.

1-Ethyl-2-trifluoromethylaziridine (2b) was prepared analogously from 0.1 mol of *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*-ethylamine (**1b**) and 0.11 mol of Na_2CO_3.

1-Cyclohexyl-2-trifluoromethylaziridine (2c) was prepared from 3.6 g (13 mmol) of *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*-cyclohexylamine (**1c**) and 1.5 g (15 mmol) of Et_3N in 5 mL of abs. DMF. The reaction mixture was poured into 15 mL of water and extracted with ether (3×10 mL). The extract was dried with $MgSO_4$, ether was removed, and aziridine **2c** was distilled in a vacuum.

***N*-(2-Thiocyanato-3,3,3-trifluoropropyl)-*N*,*N*-dimethylamine (3e).** A mixture of 4.4 g (20 mmol) of *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*,*N*-dimethylamine (**1e**) and 2.42 g (25 mmol) of KSCN was heated in 10 mL of abs. MeCN. The reaction mixture was diluted with water and extracted with ether (2×10 mL). The extract was dried with $MgSO_4$, ether was removed, and the residue was distilled in a vacuum.

***N*-(2-Thiocyanato-3,3,3-trifluoropropyl)pyrrolidine (3f), *N*-(2-thiocyanato-3,3,3-trifluoropropyl)piperidine (3g), and *N*-(2-thiocyanato-3,3,3-trifluoropropyl)morpholine (3h)** were prepared analogously from 50 mmol of the corresponding bromotrifluoropropylamine **1** and 60 mmol of KSCN in abs. DMF.

***N*-[2-(2-Isothioureido)-3,3,3-trifluoropropyl]-*N*,*N*-dimethylamine hydrobromide (4e).** A mixture of 4.73 g (21 mmol) of *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*,*N*-dimethylamine (**1e**) and 1.52 g (20 mmol) of thiourea was heated in 10 mL of abs. MeCN. After cooling, the precipitated salt **4e** was filtered and washed with ether, and dried in the air and recrystallized from MeCN.

***N*-[2-(2-Isothioureido)-3,3,3-trifluoropropyl]piperidine hydrobromide (4g) and *N*-[2-(2-isothioureido)-3,3,3-trifluoropropyl]morpholine hydrobromide (4h)** were prepared analogously from 21 mmol of the corresponding bromotrifluoroalkylamine **1** and 20 mmol of thiourea.

***N*-(2-Phenylthio-3,3,3-trifluoropropyl)-*N*,*N*-dimethylamine (5e).** 2.9 g (22 mmol) of sodium thiophenolate was added to a solution of 4.4 g (20 mmol) of *N*-(2-bromo-3,3,3-trifluoropropyl)-*N*,*N*-dimethylamine (**1e**) in 30 mL of abs. MeCN. The reaction mixture was heated in a sealed tube. The tube was

Table 2. ^1H NMR spectra of compounds **2—6**

Compound	Solvent	δ (*J*/Hz)
2a	C_6D_6	1.05 (d, 1 H, CH_2, J = 6.45); 1.6—1.7 (m, 1 H, CH); 1.8 (d, 1 H, CH_2, J = 3.2); 2.1 (s, 3 H, NCH_3)
2b	C_6D_6	0.75 (d, 1 H, CH_2, J = 6.2); 0.9 (t, 3 H, CH_3, J = 7.1); 1.4 (m, 1 H, CH); 1.7 (m, 1 H, CH_2, J = 2.9, 0.2); 1.9 (m, 2 H, $C\underline{H}_2CH_3$)
2c	C_6D_6	1.1—2.2 (m, 14 H, CH, CH_2, C_6H_{11})
3e	CD_3OD	2.15 (s, 6 H, $N(CH_3)_2$); 3.0 (d, 1 H, CH_2, J = 7.1); 3.15—3.25 (m, 2 H, CH_2, CH)
3f	$CDCl_3$	1.8 (br.s, 4 H, $N(CH_2C\underline{H}_2)_2$); 2.9 (m, 4 H, $N(C\underline{H}_2CH_2)_2$); 3.3 (dd, 1 H, CH_2, J = 12.7, 5.1); 3.5 (dd, 1 H, CH_2, J = 12.7, 0.2); 3.7 (m, 1 H, CH)
3g	$CDCl_3$	1.2 (br.s, 6 H, $CH_2NCH_2(C\underline{H}_2)_3$); 2.1 (m, 2 H, $N(CH_2)_2$); 2.5 (m, 2 H, $N(CH_2)_2$); 2.7—2.9 (m, 3 H, CH_2, CH)
3h	$CDCl_3$	2.65—2.75 (m, 2 H, $N(CH_2)_2$); 2.9—3.0 (m, 2 H, $N(CH_2)_2$); 3.3—3.5 (m, 2 H, CH_2); 3.7 (m, 5 H, CH, $O(CH_2)_2$)
4e	CD_3OD	2.5 (s, 6 H, $N(CH_3)_2$); 3.3 (d, 1 H, CH_2 J = 9.6); 3.8 (m, 2 H, CH_2, CH); 4.8—4.9 (m, 4 H, 2 NH_2)
4g	CD_3OD	1.2 (br.s, 6 H, $CH_2NCH_2(C\underline{H}_2)_3$); 2.1 (m, 2 H, $N(CH_2)_2$); 2.5 (m, 2 H, $N(CH_2)_2$); 3.6—3.8 (m, 3 H, CH_2, CH); 4.8—4.9 (m, 4 H, 2 NH_2)
4h	CD_3OD	2.8—3.05 (m, 4 H, $N(CH_2)_2$); 3.5 (d, 1 H, CH_2, J = 10.7); 3.7—3.8 (m, 6 H, CH_2, CH, $O(CH_2)_2$); 4.8—4.9 (m, 4 H, 2 NH_2)
5e	$CDCl_3$	2.6 (s, 6 H, $N(CH_3)_2$); 3.2—3.3 (m, 3 H, CH_2, CH); 7.3 (m, 5 H, SC_6H_5)
6g	$CDCl_3$	1.5 (br.s, 6 H, $CH_2NCH_2(C\underline{H}_2)_3$); 2.3 (s, 3 H, $SCOCH_3$); 2.6 (m, 2 H, $N(CH_2)_2$); 2.8 (m, 2 H, $N(CH_2)_2$); 3.0 (dd, 1 H, CH_2, J = 13.5, 9.6); 3.2 (dd, 1 H, CH_2, J = 13.5, 5.1)

opened, the solvent was evaporated, and the residue was dissolved in ether. The precipitate was filtered off, the etheral solution was dried with $MgSO_4$ and evaporated, and the residue was distilled in a vacuum.

***N*-(2-Acetylthio-3,3,3-trifluoropropyl)piperidine (6g).** 3.04 g (40 mmol) of thioacetic S-acid was added to a solution of 1.68 g (40 mmol) of $LiOH \cdot H_2O$ in 5 mL of water. Then the water was evaporated, and 9.1 g (35 mmol) of *N*-(2-bromo-3,3,3-trifluoropropyl)pyperidine (**1g**) in 20 mL of abs. DMF was added to the residue. The mixture was heated, diluted with 20 mL of water, and extracted with ether (2×10 mL). The extract was dried with $MgSO_4$ and evaporated. The residue was distilled in a vacuum.

References

1. F. G. Bordwell and W. T. Brannen, *J. Am. Chem. Soc.*, 1964, **86**, 4645.
2. T. Uemoto and J. Gotoh, *J. Fluor. Chem.*, 1986, **31**, 231.
3. E. T. McBee and R. D. Battershell, *J. Am. Chem. Soc.*, 1962, **84**, 3157.
4. J. Hine and R. G. Chirardelly, *J. Org. Chem.*, 1958, **23**, 1550.
5. G. P. Brendline and E. T. McBee, in *Uspekhi khimii ftora*, [*Progress in the Chemistry of Fluorine*], Khimiya, Leningrad, 1970, III—IV, 232 (Russ. Transl.).
6. T. Nakai, K. Tanaka, and N. Ishikawa, *J. Fluor. Chem.*, 1977, **9**, 89.
7. Yu. L. Ignatova, N. M. Karimova, and O. V. Kil'disheva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 480 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, **38**, 423].
8. Yu. L. Ignatova, N. M. Karimova, O. V. Kil'disheva, and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, 732 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1986, **35**, 675].
9. I. N. Rozhkov, N. M. Karimova, Yu. L. Ignatova, and A. G. Matveeva, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 279 [*Russ. Chem. Bull.*, 1994, **43**, 258].

Received February 9, 1994