Organic Chemistry

Synthesis of 1,1-bis(trifluoromethyl)alkyl isocyanates, carbamates, and ureas

*A. V. Popov, A. N. Pushin, and E. L. Luzina**

Institute of Physiologically Active Substances, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax: +7 (095) 913 2113. E-mail: root@fluor.home.chg.ru

A convenient preparative method for the synthesis of 1,1-bis(trifluoromethyl)alkyl isocyanates was proposed. The reactions of the isocyanates with alcohols, phenols, and alkyl-, aryl-, and hetarylamines were studied.

Key words: perfluoroisobutylene, 2,2-bis(trifluoromethyl)alkanoyl fluorides, Curtius reaction, 1,1-bis(trifluoromethyl)alkyl isocyanates, carbamates, and ureas.

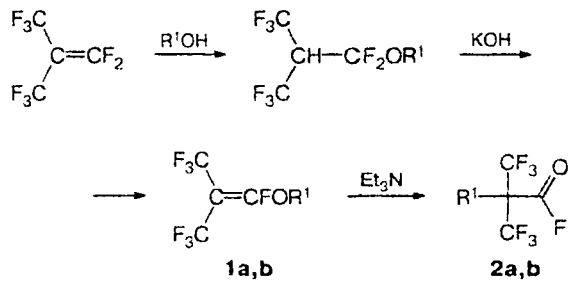
The interest in trifluoromethyl-containing compounds is due to their potential physiological activity and high lypophilicity.[1] Polyfluorine-containing isocyanates can be a basis for both the synthesis of new and modification of known biologically active substances. Rather convenient methods for the synthesis of 2-alkoxyhexafluoroprop-2-yl isocyanates[2] and their properties have been described. However, of 1,1-bis(trifluoromethyl)alkyl isocyanates, only the first representative of this series, (1,1,1,3,3,3-hexafluoro-2-methyl-prop-2-yl) isocyanate, has been described.[3]

Perfluoroisobutylene is an appropriate source of bistrifluoromethyl derivatives. It is transformed under successive treatment with alcohols, alkali, and Et_3N (Scheme 1) into 2,2-bis(trifluoromethyl)alkanoyl fluorides[4–7] **2a,b**, starting compounds for the synthesis of 1,1-bis(trifluoromethyl)alkyl isocyanates.

(1,1,1,3,3,3-Hexafluoro-2-methyl-prop-2-yl) isocyanate **3a** has previously been prepared[3] in a low yield by the reaction of **1a** with NaN_3.

In this work, we present a convenient preparative method for the synthesis of 1,1-bis(trifluoromethyl)alkyl isocyanates (Scheme 2) and describe some of their chemical properties.

Scheme 1



1a,b **2a,b**

R^1 = Me (**a**), Et (**b**)

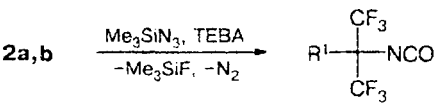
We found that the reaction of acyl fluorides **2** with Me_3SiN_3 in xylene in the presence of triethylbenzylammonium chloride (TEBAC) affords isocyanates **3** in high yields (Curtius reaction). As far as we know, this is the first example of the reaction of carboxylic acid

Published in *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 7, pp. 1205—1209, July, 2000.

1066-5285/00/4907-1202 $25.00

fluorides with trimethylsilyl azide. It was shown by control experiments that the replacement of the solvent and azide (for example, by NaN_3 in diglyme) resulted in a 2—3-fold decrease in the yield of the target products.

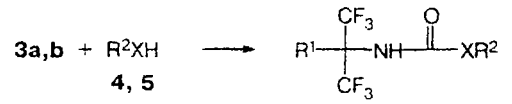
Scheme 2



3a,b

Compounds **3a,b** are mobile low-boiling liquids whose composition and structure were proved by the data of elemental analysis, ^1H and ^{19}F NMR spectrometry, IR spectra (Tables 1 and 2), and the reactions with some *O*- (**4**) and *N*-nucleophiles (**5**) (Scheme 3), which afforded carbamates **6** and ureas **7**.

Scheme 3



X = O (**4**, **6**)
X = NR³ (**5**, **7**)

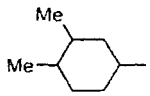
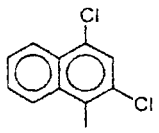
6a—k, 7a—p

The structures of compounds **6** and **7** were confirmed by the NMR spectra with the characteristic signal from the CF_3 groups in the ^{19}F spectra in the region of −1—6 ppm and the signals from the NH protons in the ^1H NMR spectra in the region of 5—11 ppm.

Experimental

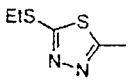
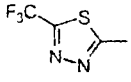
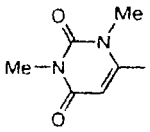
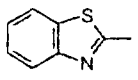
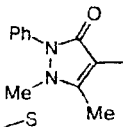
^1H and ^{19}F NMR spectra (CF_3COOH as the external standard) were obtained on Bruker CXP 200 and Bruker DPX

Table 1. Yields, properties, and elemental analysis data of the compounds

Compound	R^1	R^2	R^3	Yield (%)	M.p./°C, b.p./°C (*p*/Torr)	Found (%) / Calculated C	H	F	N	Molecular formula
3a	Me	—	—	89	62—64 (760) Ref.[7]: 61—62 (760)	28.83 / 29.00	1.52 / 1.46	55.46 / 55.05	6.84 / 6.76	$C_5H_3F_6NO$
3b	Et	—	—	92	82—84 (760)	32.48 / 32.59	2.35 / 2.28	51.42 / 51.55	6.23 / 6.34	$C_6H_5F_6NO$
6a	Me		—	83	Oil	45.03 / 44.86	5.57 / 5.33	34.33 / 35.48	4.19 / 4.36	$C_{12}H_{17}F_6NO_2$
6b	Me		—	89	53—56[a]	46.24 / 46.57	5.38 / 5.71	33.78 / 34.00	3.99 / 4.18	$C_{13}H_{19}F_6NO_2$
6c	Me	4-NO_2—C_6H_4—CH_2	—	91	97—98[b]	38.89 / 40.01	2.95 / 2.80	31.12 / 31.64	7.42 / 7.78	$C_{12}H_{10}F_6N_2O_4$
6d	Me		—	89	124—125[b]	43.06 / 42.88	2.31 / 2.16	26.55 / 27.13	3.39 / 3.33	$C_{15}H_6Cl_2F_6NO_2$
6e	Me	2,6-Me_2—C_6H_3	—	91	96—97[c]	46.81 / 47.43	3.71 / 3.98	35.02 / 34.62	4.04 / 4.25	$C_{13}H_{13}F_6NO_2$
6f	Et	$CH{\equiv}CCH_2$	—	88	60—61 (4)	38.79 / 39.00	3.18 / 3.27	41.70 / 41.13	4.93 / 5.05	$C_9H_9F_6NO_2$
6g	Et	$NCCH_2CH_2$	—	84	109—110 (2)	36.88 / 37.00	3.33 / 3.45	39.18 / 39.01	9.36 / 9.59	$C_9H_{10}F_6N_2O_2$
6h	Et	2-NO_2—$C_6H_4CH_2$	—	72	60—61[d] /120 (2)	41.49 / 41.72	3.15 / 3.23	30.28 / 30.46	7.63 / 7.49	$C_{13}H_{12}F_6N_2O_4$

(To be continued)

Table 1. (*Continued*)

Compound	R^1	R^2	R^3	Yield (%)	M.p./°C, b.p./°C (*p*/Torr)	Found / Calculated (%) C	H	F	N	Molecular formula
6i	Et	4-Bu^{t}CH$_2$CMe$_2$C$_6$H$_4$	—	77	57—58[c]	56.43 56.20	6.45 6.37	26.47 26.67	3.20 3.28	$C_{20}H_{27}F_6NO_2$
6j	Et	4-Ph—C$_6$H$_4$—	—	84	93—94[c]	55.34 55.25	3.92 3.86	28.98 29.13	3.46 3.58	$C_{18}H_{15}F_6NO_2$
6k	Et	4-Me—2-Pr^i—C$_6$H$_3$	—	92	61—62[b]	51.87 51.75	5.22 5.16	30.43 30.70	3.66 3.77	$C_{16}H_{19}F_6NO_2$
7a	Me	$(CH_2)_5N$	—	95	92—93[b]	41.34 41.10	4.90 4.83	38.87 39.01	9.74 9.59	$C_{10}H_{14}F_6N_2O$
7b	Me	PhCH$_2$CH$_2$	H	100	137—138[b]	47.71 47.57	4.40 4.30	34.18 34.73	8.68 8.53	$C_{13}H_{14}F_6N_2O$
7c	Me	Bu^t	H	86	183—184[b]	38.73 38.58	5.20 5.01	39.98 40.68	10.23 10.00	$C_9H_{14}F_6N_2O$
7d	Me	4-MeO—C$_6$H$_4$	H	97	172—173[b]	43.81 43.65	3.74 3.66	34.10 34.52	8.63 8.48	$C_{12}H_{12}F_6N_2O_2$
7e	Me	TsNH	H	93	144—145[b]	36.67 36.65	3.34 3.33	27.86 28.98	10.49 10.68	$C_{12}H_{13}F_6N_3O_3S$
7f	Me		H	99	131—132[b]	29.13 29.35	2.83 2.74	30.53 30.95	15.08 15.21	$C_9H_{10}F_6N_4OS_2$
7g	Me		H	93	121—122[b]	25.38 25.54	1.25 1.34	45.53 45.45	14.96 14.89	$C_8H_5F_9N_4OS$
7h	Me	2-PhO—C$_6$H$_4$	H	99	220—221[c]	52.20 52.05	3.72 3.60	28.88 29.06	6.97 7.14	$C_{17}H_{14}F_6N_2O_2$
7i	Me		H	77	167—168[c]	36.28 36.47	3.40 3.34	31.34 31.47	15.35 15.47	$C_{11}H_{12}F_6N_4O_3$
7j	Et	Bu^i	Bu^i	99	60—61[b]	47.87 48.00	6.79 6.91	32.38 32.54	8.11 8.00	$C_{14}H_{24}F_6N_2O$
7k	Et	PhCH$_2$CH$_2$	H	97	107—108[c]	49.29 49.13	4.83 4.71	33.19 33.30	8.26 8.18	$C_{14}H_{16}F_6N_2O$
7l	Et	4-NC—C$_6$H$_4$	H	85	169—170[c]	45.87 46.03	3.15 3.27	33.83 33.60	12.48 12.39	$C_{13}H_{11}F_6N_3O$
7m	Et		H	93	157—158[b]	33.49 33.65	2.77 2.82	35.56 35.48	12.96 13.08	$C_9H_9F_6N_3OS$
7n	Et		H	75	167—168[c] (decomp.)	41.86 42.05	2.80 2.99	30.83 30.70	11.18 11.32	$C_{13}H_{11}F_6N_3OS$
7o	Et		H	96	189—190[b]	47.96 48.12	4.30 4.28	27.00 26.86	13.06 13.20	$C_{17}H_{18}F_6N_4O_2$
7p	Et		H	95	150—153[b]	33.27 33.44	3.35 3.43	35.40 35.26	12.86 13.00	$C_9H_{11}F_6N_3OS$

[a] From $CHCl_3$.
[b] From C_6H_6.
[c] From heptane.
[d] Crystallized after distillation.

Table 2. NMR spectra of the compounds

Compound	^{1}H NMR (δ)	^{19}F NMR (δ)	Solvent
3a[a]	1.85 (s)	−0.52 (s)	$CDCl_3$
3b[b]	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 6.6 Hz); 2.10 (q, 2 H, CH_2, $^3J_{HH}$ = 6.6 Hz)	2.92 (s)	$CDCl_3$
6a	0.80–1.00 (m, 4 H, $C\underline{H}_3CH$ + CH_2); 1.10–1.90 (m, 8 H, CH_2 + $C\underline{H}CH_3$); 1.97 (s, 3 H, CH_3C); 4.60 (m, 0.7 H, CHO[c]); 4.95 (m, 0.3 H, CHO[d]); 5.10 (s, 1 H, NH)	−0.34 (s)	$CDCl_3$
6b[e]	0.80–0.95 (m, 6 H, $C\underline{H}_3CH$); 1.00–2.00 (m, 8 H, CH_2 + $C\underline{H}CH_3$); 1.95 (s, 3 H, CH_3C); 4.60 (m, 0.6 H, CHO); 4.80 (m, 0.4 H, CHO); 5.05 (s, 1 H, NH)	−0.35 (s)	$CDCl_3$
6c	1.80 (s, 3 H, CH_3); 5.00 (s, 2 H, CH_2); 5.15 (s, 1 H, NH); 7.30 (m, 2 H, Ar); 8.00 (m, 2 H, Ar)	−0.22 (s)	$CDCl_3$
6d	2.05 (s, 3 H, CH_3); 5.92 (s, 1 H, NH); 7.60 (m, 3 H, Ar); 7.85 (m, 1 H, Ar); 8.20 (m, 1 H, Ar)	−0.50 (s)	$CDCl_3$
6e	2.00 (s, 3 H, CH_3CCF_3); 2.20 (s, 6 H, CH_3); 5.60 (s, 1 H, NH); 7.05 (s, 3 H, Ar)	−0.30 (s)	$CDCl_3$
6f	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 6.7 Hz); 2.50 (m, 3 H, $C\underline{H}_2CH_3$ + CH≡); 4.80 (d, 2 H, CH_2O, $^4J_{HH}$ = 2.5 Hz); 5.40 (s, 1 H, NH)	4.05 (s)	$CDCl_3$
6g	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 6.2 Hz); 2.50 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{HH}$ = 6.7 Hz); 2.80 (t, 2 H, CH_2CN, $^3J_{HH}$ = 6.2 Hz); 4.30 (t, 2 H, CH_2O, $^3J_{HH}$ = 6.7 Hz); 5.70 (s, 1 H, NH)	4.43 (s)	$CDCl_3$
6h	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 6.7 Hz); 2.50 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{HH}$ = 6.7 Hz); 5.25 (s, 1 H, NH); 5.55 (s, 2 H, CH_2O); 7.45–7.75 (m, 3 H, Ar); 8.15 (m, 1 H, Ar)	5.79 (s)	$CDCl_3$
6i	0.75 (s, 9 H, $(C\underline{H}_3)_3C$); 1.15 (t, 3 H, $C\underline{H}_3CH_3$, $^3J_{HH}$ = 6.7 Hz); 1.38 (s, 6 H, $(C\underline{H}_3)_2C$); 1.75 (s, 2 H, $CC\underline{H}_2C$); 2.55 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{HH}$ = 6.7 Hz); 5.40 (s, 1 H, NH); 7.05 (m, 2 H, Ar); 7.35 (m, 2 H, Ar)	0.05 (s)	$CDCl_3$
6j	1.20 (t, 3 H, CH_3, $^3J_{HH}$ = 6.7 Hz); 2.55 (q, 2 H, CH_2, $^3J_{HH}$ = 6.7 Hz); 5.45 (s, 1 H, NH); 7.30–7.65 (m, 9 H, Ar)	3.80 (s)	$CDCl_3$
6k	1.15 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{HH}$ = 6.5 Hz); 1.20 (d, 6 H, $(C\underline{H}_3)_2CH$, $^3J_{HH}$ = 6.2 Hz); 2.30 (s, 3 H, CH_3); 2.55 (q, 2 H, CH_2, $^3J_{HH}$ = 6.5 Hz); 3.02 (sept, 1 H, $C\underline{H}CH_3$, $^3J_{HH}$ = 6.2 Hz); 5.45 (s, 1 H, NH); 6.85 (s, 1 H, Ar); 7.05 (d, 1 H, Ar); 7.20 (d, 1 H, Ar)	3.67 (s)	$CDCl_3$
7a	1.60–1.80 (m, 6 H, CH_2); 2.05 (s, 3 H, CH_3); 3.50 (m, 6 H, CH_2N); 6.20 (s, 1 H, NH)	2.10 (s)	Acetone-d_6
7b	1.90 (s, 3 H, CH_3); 2.70 (t, 2 H, CH_2Ph, $^3J_{HH}$ = 6.3 Hz); 3.30 (q, 2 H, CH_2N, $^3J_{HH}$ = 6.3 Hz); 5.90 (t, 1 H, $N\underline{H}CH_2$, $^3J_{HH}$ = 6.3 Hz); 6.05 (s, 1 H, NH); 7.05–7.30 (m, 5 H, Ar)	0.11 (s)	$CDCl_3$
7c	0.88 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{HH}$ = 6.7 Hz); 1.08 (d, 3 H, $C\underline{H}_3CH$, $^3J_{HH}$ = 6.3 Hz); 1.43 (m, 2 H, CH_2); 1.98 (s, 3 H, $C\underline{H}_3C$); 3.65 (m, 1 H, CH); 5.70 (br.s, 1 H, NH); 6.05 (s, 1 H, NH)	−0.07 (s)	Acetone-d_6
7d[f]	2.00 (s, 3 H, $C\underline{H}_3C$); 3.75 (s, 3 H, $C\underline{H}_3O$); 6.85 (m, 2 H, Ar); 7.35 (m, 2 H, Ar)	1.10 (s)	Acetone-d_6
7e	1.90 (s, 3 H, $C\underline{H}_3CCF_3$); 2.50 (s, 3 H, $C\underline{H}_3Ar$); 6.61 (s, 1 H, NH); 7.40 (m, 2 H, Ar); 7.80 (m, 2 H, Ar); 8.10 (s, 1 H, NH); 8.70 (br.s, 1 H, NH)	1.00 (s)[g]	Acetone-d_6
7f	1.40 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{HH}$ = 6.8 Hz); 1.98 (s, 3 H, $C\underline{H}_3CCF_3$); 3.23 (q, 2 H, CH_2, $^3J_{HH}$ = 6.8 Hz); 7.50 (s, 1 H, NH); 10.80 (br.s, 1 H, NH)	1.30 (s)	DMSO-d_6
7g	2.10 (s, 3 H, CH_3C); 7.50 (s, 1 H, NH); 10.80 (br.s, 1 H, NH)	−0.40 (s, 6 F); 17.40 (s, 3 F)	Acetone-d_6
7h	2.10 (s, 3 H, CH_3C); 6.80 (d, 1 H, Ar); 6.95–7.20 (m, 7 H, Ar + 2 NH); 7.30–7.50 (m, 2 H, Ar); 8.30 (m, 1 H, Ar)	1.33 (s)	Acetone-d_6
7i	2.00 (s, 3 H, CH_3C); 3.30 (s, 3 H, CH_3N); 3.50 (s, 3 H, CH_3N); 5.50 (br.s, 1 H, CH=); 11.10 (s, 2 H, NH)	0.93 (s)	$CDCl_3$
7j	0.85 (d, 12 H, $C\underline{H}_3CH$, $^3J_{HH}$ = 6.2 Hz); 1.05 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{HH}$ = 6.7 Hz); 1.95 (m, 2 H, $C\underline{H}CH_3$); 2.55 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{HH}$ = 6.7 Hz); 3.10 (d, 4 H, CH_2N, $^3J_{HH}$ = 6.2 Hz); 4.80 (s, 1 H, NH)	4.32 (s)[h]	$CDCl_3$
7k	1.05 (t, 3 H, CH_3, $^3J_{HH}$ = 6.7 Hz); 2.45 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{HH}$ = 6.7 Hz); 2.80 (t, 2 H, CH_2Ph, $^3J_{HH}$ = 6.3 Hz); 3.30 (q, 2 H, CH_2N, $^3J_{HH}$ = 6.3 Hz); 5.90 (t, 1 H, $N\underline{H}CH_2$, $^3J_{HH}$ = 6.3 Hz); 7.10–7.30 (m, 6 H, Ar + NH)	4.40 (s)	$CDCl_3$
7l	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 6.7 Hz); 2.60 (q, 2 H, CH_2, $^3J_{HH}$ = 6.7 Hz); 6.80 (s, 1 H, NH); 7.70 (s, 4 H, Ar); 8.80 (s, 1 H, NH)	4.12 (s)	Acetone-d_6
7m	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 7 Hz); 2.70 (q, 2 H, CH_2, $^3J_{HH}$ = 7 Hz); 7.10 (d, 1 H, CH, $^3J_{HH}$ = 4 Hz); 7.40 (d, 1 H, CH, $^3J_{HH}$ = 4 Hz); 7.90 (br.s, 1 H, NH); 8.90 (br.s, 1 H, NH)	4.45 (s)[h]	Acetone-d_6
7n[f]	1.15 (t, 3 H, CH_3, $^3J_{HH}$ = 7 Hz); 2.70 (q, 2 H, CH_2, $^3J_{HH}$ = 7 Hz); 7.35 (t, 1 H, Ar, $^3J_{HH}$ = 7 Hz); 7.50 (td, 1 H, Ar, $^3J_{HH}$ = 7 Hz, $^4J_{HH}$ = 2 Hz); 7.75 (dd, 1 H, Ar, $^3J_{HH}$ = 7 Hz, $^4J_{HH}$ = 2 Hz); 7.95 (d, 1 H, Ar, $^3J_{HH}$ = 2 Hz); 8.40 (br.s, 1 H, NH)	4.65 (s)	Acetone-d_6
7o	1.10 (t, 3 H, $C\underline{H}_3CH_2$, $^3J_{HH}$ = 7 Hz); 2.15 (s, 3 H, CH_3C); 2.60 (q, 2 H, CH_2, $^3J_{HH}$ = 7 Hz); 3.05 (s, 3 H, CH_3N); 7.25–7.40 (m, 4 H, Ar + NH); 7.50–7.65 (m, 2 H, Ar); 7.75 (s, 1 H, NH)	6.08 (s)	DMSO-d_6
7p[f]	1.10 (t, 3 H, CH_3, $^3J_{HH}$ = 7 Hz); 2.50 (q, 2 H, $C\underline{H}_2CH_3$, $^3J_{HH}$ = 7 Hz); 3.30 (t, 2 H, CH_2S, $^3J_{HH}$ = 6.2 Hz); 3.85 (t, 2 H, CH_2N, $^3J_{HH}$ = 6.2 Hz)	4.85 (s)	Acetone-d_6

[a,b] IR (N=C=O), ν/cm^{-1}: [a] 2270, [b] 2276.
[c] (*E*)-Isomer.
[d] (*Z*)-Isomer.
[e] The exact isomeric composition was not determined.
[f] One or two signals from NH were not observed because of the exchange with the solvent.
[g] In acetone-d_6.
[h] In $CDCl_3$.

200 spectrometers. IR spectra were recorded on a Bruker IFS 113v spectrometer. Trimethylsilyl azide was synthesized according to the previously described method.[8] The ratio of (*Z*)- and (*E*)-isomers of the starting 2-methylcyclohexanol was 1 : 2. 3,4-Dimethylcyclohexanol was a mixture of isomers in a ratio of 1 : 3 : 5. The melting point was determined in a capillary.

(1,1,1,3,3,3-Hexafluoro-2-methylprop-2-yl) isocyanate (3a). A solution of Me_3SiN_3 (115 g, 1 mol) in xylene (100 mL) was slowly added dropwise to a boiling solution of acid fluoride **2a** (212 g, 1 mol) and TEBAC (1 g, 0.004 mol) in xylene (150 mL, a mixture of isomers) in a round-bottom two-necked flask with a dropping funnel and an efficient reflux condenser. After the addition of the azide, the reaction mixture was boiled for 2 h. The reaction was monitored by ^{19}F NMR. The fraction boiling below 140 °C was distilled off from the reaction mixture. The repeated distillation of this fraction gave 184.2 g of isocyanate **3a**.

(1,1,1-Trifluoro-2-(trifluoromethyl)-but-2-yl) isocyanate (3b) was synthesized by a similar procedure from acyl fluoride **2b** (226 g, 1 mol), Me_3SiN_3 (115 g, 1 mol), and TEBAC (1 g, 0.004 mol). After the addition of a solution of the azide, the reaction mixture was boiled for 4 h, and isocyanate **3b** (203.3 g) was obtained.

Preparation of *O*-(2-methylcyclohexyl)-*N*- (6a), *O*-(3,4-dimethylcyclohexyl)-*N*-(1,1,1,3,3,3-hexafluoro-2-methylprop-2-yl) (6b), *N*-(1,1,1,3,3,3-hexafluoro-2-methylprop-2-yl) *O*-(4-nitrobenzyl) carbamate (6c); *O*-(prop-2-inyl)-*N*- (6f), *O*-(2-cyanoethyl)-*N*- (6g), *O*-(2-nitrobenzyl)-*N*-(1,1,1-trifluoro-2-trifluoromethylbut-2-yl) carbamate (6h); 1-(5-ethylthio-1,3,4-thiadiazol-2-yl)-3- (7f), 1-(5-trifluoromethyl-1,3,4-thiadiazol-2-yl)-3-(1,1,1,3,3,3-hexafluoro-2-methylprop-2-yl)urea (7g); 1-(4-cyanophenyl)-3- (7l), 1-(benzothiazol-2-yl)-3-(1,1,1-trifluoro-2-trifluoromethylbut-2-yl)urea (7n) (general procedure). Isocyanate **3** (0.006 mol) and the catalyst Me_3N in a saturated ethereal solution (0.2 mL) were added with stirring to a solution of the hydroxy or amino derivative (0.005 mol) in Et_2O (20 mL). The reaction mixture was left to stand for 12 h. The solvent and volatiles were evaporated. Compounds **6f—h** were isolated by vacuum distillation, and **6c**, **7f,g,l,n** were recrystallized; **6a,b** were dissolved in $CHCl_3$ (10 mL) and passed through a thin silica gel L 40/100 layer, and the solvent was evaporated.

Preparation of 1,1-dimethyl-3- (7a), 1-phenethyl-3- (7b), 1-*sec*-butyl-3- (7c), 1-(4-methoxyphenyl)-3-(2-methyl-1,1,1,3,3,3-hexafluoroprop-2-yl)urea (7d); 4-(2-methyl-1,1,1,3,3,3-hexafluoroprop-2-yl)-1-tosyl semicarbazide (7e); 3-(1,1,1,3,3,3-hexafluoro-2-methylprop-2-yl)-1-(2-phenoxyphenyl)urea (7h); 1-*sec*-butyl-3- (7j), 1-phenethyl-3- (7k), 1-(thiazol-2-yl)-3- (7m), 1-(2,3-dimethyl-5-oxo-1-phenylpyrazol-3-in-4-yl)-3- (7o), 1-(thiazol-2-in-2-yl)-3-(2-trifluoromethyl-1,1,1-trifluorobut-2-yl)urea (7p) (general procedure). Isocyanate **3** (0.006 mol) was added along with stirring to a solution of amine (0.005 mol) in Et_2O (20 mL). The reaction mixture was left to stand for 12 h. The solvent and volatiles were evaporated. The residue was recrystallized.

Preparation of *O*-(2,4-dichloronaphthyl)-*N*- (6d), *O*-(2,6-dimethylphenyl)-*N*-(1,1,1,3,3,3-hexafluoro-2-methylprop-2-yl) carbamate (6e); *O*-[4-(2,4,4-trimethylpent-2-yl)phenyl]-*N*- (6i), *O*-biphenyl-4-yl-*N*- (6j), *O*-(2-isopropyl-4-methylphenyl)-*N*-(1,1,1-trifluoro-2-trifluoromethylbut-2-yl) carbamate (6k); 1-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-6-yl)-3-(2-methyl-1,1,1,3,3,3-hexafluoroprop-2-yl)urea (7i) (general procedure). The hydroxy or amino derivative (0.005 mol), isocyanate **3** (0.006 mol), Et_2O (20 mL), and a saturated ethereal solution of Me_3N (0.2 mL) were loaded in tubes. In the case of compounds **6d,e,i—k**, the sealed tubes were heated on a water bath, and for compound **7i**, the tube was heated on an oil bath (140 °C) for 3 h. The solvent and volatiles were evaporated, and the residues were recrystallized.

The characteristics of the compounds are presented in Tables 1 and 2.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 98-03-33007).

References

1. K. L. Kirk and L. A. Cohen, in *Biochemistry Involving Carbon-Fluorine Bond*, Ed. R. Filler, Am. Chem. Soc., Washington, 1976, 23.
2. O. V. Korenchenko, A. Yu. Aksinenko, V. B. Sokolov, and A. N. Pushin, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 390 [*Russ. Chem. Bull.*, 1995, **44**, 381 (Engl. Transl.)].
3. C. G. Krespan, *J. Org. Chem.*, 1969, **34**, 1278.
4. I. L. Knunyants, L. S. German, and B. L. Dyatkin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1956, 1353 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1956, **5**, 1387 (Engl. Transl.)].
5. R. J. Koshar, T. C. Simmons, and W. F. Hoffmann, *J. Am. Chem. Soc.*, 1957, **79**, 1741.
6. S. Misaki, *J. Fluorine Chem.*, 1985, **29**, 471.
7. I. L. Knunyants, E. G. Abduganiev, S. T. Kocharyan, M. V. Urushadze, V. A. Livshits, Yu. E. Aronov, and E. M. Rokhlin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1971, 110 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1971, **20**, 93 (Engl. Transl.)].
8. S. S. Washburne and W. R. Peterson, Jr., *J. Organomet. Chem.*, 1971, **33**, 153.

Received November 24, 1999;
in revised form March 1, 2000