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Received November 16, 1994

2-Alkoxyhexafluoropropyl-2-isocyanates

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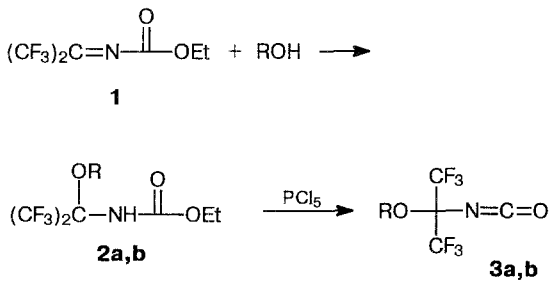
A convenient preparative method for the synthesis of 2-alkoxyhexafluoropropyl-2-isocyanates is proposed. The reactions of the isocyanates with amines and alcohols are studied.

Key words: 2-alkoxyhexafluoropropyl-2-isocyanates, synthesis; ureas, carbamates.

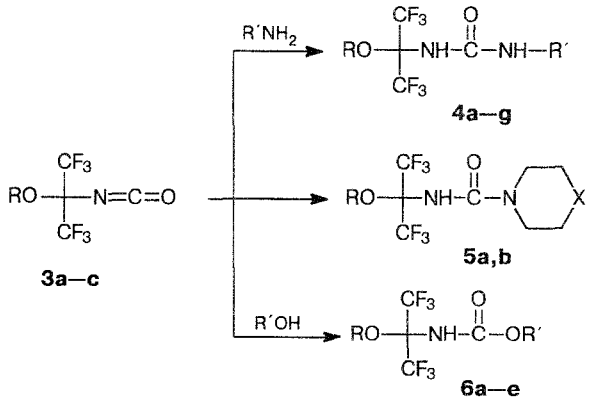
Alkylisocyanates are the main reagents for the modification of known physiologically active compounds and the synthesis of new ones. Isocyanates containing functional substituents at the α-position[1,2] occupy a special place in the series of alkylisocyanates. However, the data on the synthesis of α-alkoxypolyfluoroalkylisocyanates are scarce.[3] In the present report, a convenient preparative method for the synthesis of 2-alkoxyhexafluoropropyl-2-isocyanates is presented along with some of their chemical properties.

Previously we have found that the interaction of α-chlorohexafluoropropylisocyanate with EtOH in the presence of bases results in the formation of a mixture of the imine and ethoxyisocyanate. Therefore, the reaction of carbamates of the corresponding alcohols with PCl_5 is a more convenient and unambiguous method for the synthesis of the analogous isocyanates:



However, the reaction of the PhOH—α-chlorohexafluoropropylisocyanate adduct with one equivalent of a base (Py or Et_3N) turned out to be preferable for the preparation of phenoxyisocyanate **3c**.

Isocyanates **3a—c** are mobile low-boiling liquids, whose compositions and structures were confirmed by the data of elemental analysis, ^1H and ^{19}F NMR, IR spectra (Table 1, 2), and chemical transformations. Isocyanates **3** react with both primary and secondary amines to form the corresponding carbamide derivatives **4** and **5**, and react with alcohols to form carbamates **6**.



Compounds **4—6** are characterized by the CF_3 group signal in the 2 to 4 ppm range of the ^{19}F NMR spectra

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 2, pp. 390—392, February, 1995.

Table 1. Yield, properties, and elemental analysis data for the compounds obtained

Compound	R	R′	Yield (%)	B.p. or m.p./°C (n_D)	Empirical formula	Found / Calculated (%)		
						C	H	N
2a	Me		85	161—163 (1.3634)	$C_7H_9F_6NO_3$	31.43 / 31.24	3.23 / 3.37	5.04 / 5.20
2b	Et		80	86(20) (1.3680)	$C_8H_{11}F_6NO_3$	34.12 / 33.93	3.80 / 3.92	5.07 / 4.95
3a	Me		58	72—78 (1.3259)	$C_5H_3F_6NO_2$	25.73 / 25.92	1.40 / 1.36	6.15 / 6.28
3b	Et		52	90—92 (1.3392)	$C_6H_5F_6NO_2$	30.22 / 30.39	2.32 / 2.13	5.75 / 5.91
3c	Ph		70	53—54 (10) (1.4055)	$C_{10}H_5F_6NO_2$	41.03 / 42.12	1.87 / 1.77	5.05 / 4.91
4a	Me	Ph	64	176—171	$C_{11}H_{10}F_6N_2O_2$	42.03 / 41.78	3.22 / 3.19	8.94 / 8.86
4b	Me	4-Me-C_6H_4	62	131—134	$C_{12}H_{12}F_6N_2O_2$	43.70 / 43.65	3.78 / 3.66	8.57 / 8.48
4c	Me	Et	69	61—62	$C_7H_{10}F_6N_2O_2$	31.20 / 31.35	3.72 / 3.76	10.55 / 10.45
4d	Et	Ph	86	162—163	$C_{12}H_{12}F_6N_2O_2$	43.44 / 43.65	3.54 / 3.66	8.34 / 8.48
4e	Et	Et	85	116—118	$C_8H_{12}F_6N_2O_2$	33.96 / 34.05	4.37 / 4.29	10.04 / 9.93
4f	Ph	Ph	83	134—136	$C_{16}H_{12}F_6N_2O_2$	51.02 / 50.80	3.01 / 3.20	7.58 / 7.41
4g	Ph	4-Me-C_6H_4	90	124—126	$C_{17}H_{14}F_6N_2O_2$	52.24 / 52.05	3.69 / 3.60	7.25 / 7.14
5a[a]	Me		59	63—65	$C_{10}H_{14}F_6N_2O_2$	38.72 / 38.97	4.73 / 4.58	8.98 / 9.09
5b[b]	Me		60	Oil	$C_{10}H_{15}F_6N_3O_2$	37.34 / 37.16	4.42 / 4.67	13.22 / 13.00
6a	Me	CH_2CH_2Cl	50	108—109 (10) (1.3965)	$C_7H_8ClF_6NO_3$	27.80 / 27.69	2.78 / 2.66	4.53 / 4.61
6b	Me	$PhCH_2$	50	110 (0.05) (1.4479)	$C_{12}H_{11}F_6NO_3$	43.68 / 43.52	3.31 / 3.35	4.02 / 4.23
6c	Ph	Pr	75	55—57	$C_{13}H_{13}F_6NO_3$	45.03 / 45.23	4.02 / 3.80	3.98 / 4.06
6d	Ph	CH_2CH_2Cl	68	67—69	$C_{12}H_{10}ClF_6NO_3$	39.52 / 39.42	2.88 / 2.76	3.74 / 3.83

Note. For **5** X = CH_2 (**5a**)[a], N—Me (**5b**)[b].

and the signals of the NH protons in the 6 to 11 ppm range of the ^1H NMR spectra.

Experimental

^1H and ^{19}F NMR spectra were recorded on a Bruker CXP 200 spectrometer in acetone-d_6, DMSO-d_6, or $CDCl_3$. IR spectra were obtained on a Specord IR-75 spectrometer (compounds were analyzed as films or in KBr). Melting points were determined in a capillary.

***N*-(2-Methoxyhexafluoroprop-2-yl)-*O*-ethylcarbamate (2a).** A solution of 23.7 g (0.1 mol) of imine **1** in 45 mL of ether was added dropwise at 20 °C with stirring to a solution of 3.42 g (0.107 mol) of MeOH in 20 mL of ether. The mixture was stirred for 2 h and kept over night. The reaction mixture was evaporated, and the residue was distilled to yield 22.7 g of **2a.**

***N*-(2-Ethoxyhexafluoroprop-2-yl)-*O*-ethylcarbamate (2b)** was synthesized by a similar procedure from 0.11 mol of EtOH and 0.1 mol of imine **1** in a yield of 22.6 g.

2-Methoxyhexafluoropropyl-2-isocyanate (3a). A mixture of 26.9 g (0.1 mol) of **2a** and 22.9 g (0.11 mol) of PCl_5 was refluxed at a temperature below 120 °C. The reaction was followed by IR spectroscopy. Four hours after the complete dissolution of PCl_5, **3a** obtained was distilled off with an efficient dephlegmator in a yield of 11.1 g.

Table 2. NMR spectra of the compounds obtained

Compound	^1H, δ	^{19}F, δ	Solvent
2a	1.26 (t, 3 H, CH_3C); 3.54 (s, 3 H, CH_3O); 4.20 (q, CH_2); 5.92 (br.s, 1 H, NH)	1.38 (s)	$CDCl_3$
2b	1.28 (t, 6 H, CH_3C); 3.81 (q, 2 H, CH_2O); 4.22 (q, 2 H, CH_2O); 5.78 (s, 1 H, NH)	1.20 (s)	$CDCl_3$
3c[a]	3.62 (s)	-1.99 (s)	$CDCl_3$
3b[b]	1.30 (t, 3 H); 3.97 (q, 2 H)	-1.81 (s)	$CDCl_3$
3c[c]	7.28 (d, 2 H); 7.45 (m, 3 H)	-2.50 (s)	$CDCl_3$
4a	3.62 (s, 3 H, CH_3O); 7.02 (t, 1 H); 7.30 (m, 2 H); 7.48 (m, 2 H); 8.37 (s, 1 H, NH)	3.62 (s)	$CDCl_3$
4b	2.25 (s, 3 H, CH_3C); 2.56 (s, 3 H, CH_3O); 6.32 (s, 1 H, NH); 7.08 (d+d, 4 H, C_6H_4); 7.68 (s, 1 H, NH)	3.05 (s)	$CDCl_3$
4c	1.03 (t, 3 H, CH_3C); 3.08 (m, 2 H, CH_2); 3.33 (s, 3 H, CH_3O); 6.26 (s, 1 H, NH); 7.62 (s, 1 H, NH)	4.76 (s)	DMSO-d_6
4d	1.20 (t, 3 H, CH_3C); 3.86 (q, 2 H, CH_2)	3.50 (s)	Acetone-d_6
4e	1.13 (t, 3 H, CH_3); 1.28 (t, 3 H); 3.18 q (2 H, CH_2N); 3.83 (m, 2 H, CH_2O); 6.30 (s, 1 H, NH); 6.70 (s, 1 H, NH)	2.30 (s)	$CDCl_3$
4f	6.95 (m, 1 H, *p*-CH); 7.15 (m, 5 H, Ar); 7.30 (m, 4 H, Ar); 8.24	5.59 (s)	Acetone-d_6
4g	2.25 (s, 3 H, CH_3); 7.10 (m, 4 H); 7.30—7.50 (m, 5 H); 8.20 (s, 1 H, NH)	5.62 (s)	Acetone-d_6
5a	1.60 (m, 6 H, $-CH_2-$); 3.37 (m, 4 H, CH_2N); 3.56 (s, 3 H, CH_3O); 5.16 (s, 1 H, NH)	2.62 (s)	$CDCl_3$
5b	2.20 (s, 3 H, CH_3N); 2.40 (m, 4 H, $\underline{CH_2}NCH_3$); 3.52 (m, 4 H, CH_2N); 3.60 (s, 3 H, CH_3O); 5.75 (s, 1 H, NH)	4.40 (s)	$CDCl_3$
6a	3.60 (s, 3 H); 3.76 (m, 2 H, CH_2Cl); 4.40 (m, 2 H, CH_2O); 6.04 (br.s, 1 H, NH)	2.11 (s)	DMSO-d_6
6b	3.52 (s, 3 H, CH_3O); 5.14 (s, 2 H, CH_2O); 5.66 (br.s, 1 H, NH); 7.30 (m, 5 H, Ph)	2.35 (s)	$CDCl_3$
6c	0.90 (t, 3 H); 1.52 (sext, 2 H); 3.95 (t, 2 H); 7.20 (m, 3 H, Ph); 7.40 (m, 2 H, Ph); 8.05 (s, 1 H, NH)	5.20 (s)	Acetone-d_6
6d	3.75 (m, 2 H, CH_2Cl); 4.30 (m, 2 H, CH_2O); 7.26 (m, 3 H, Ph); 7.45 (m, 2 H, Ph); 8.30 (s, 1 H, NH)	4.80 (s)	Acetone-d_6
6e	1.15 (t, 3 H); 3.50 (m, 4 H, CH_2OCH_2); 4.12 (m, CH_2O); 7.20—7.50 (m, 5 H, Ph); 8.18 (s, 1 H, NH)	5.32 (s)	Acetone-d_6

Note. IR spectrum (N=C=O), ν/cm^{-1}: [a] 2257, [b] 2250, [c] 2270.

2-Ethoxyhexafluoropropyl-2-isocyanate (3b) was synthesized by a similar procedure from 0.05 mol of **2b** in a yield of 7.36 g.

2-Phenoxyhexafluoropropyl-2-isocyanate (3c). A solution of 1.4 g (0.015 mol) of phenol in 10 mL of ether was added dropwise at 20 °C to a solution of 3.5 g (0.015 mol) of α-chlorohexafluoroisopropylisocyanate in 20 mL of ether. After 30 min, a solution of 1.19 g (0.015 mol) of Py in 10 mL of ether was added to the reaction mixture. The precipitate that formed was filtered off, and the filtrate was evaporated and distilled to yield 3.1 g of **3c**.

Interaction of 3 with primary amines. A solution of 0.005 mol of the amine in 5 mL of ether was added to a solution of 0.005 mol of isocyanate **3** in 10 mL of ether. The reaction mixture sat over night. The precipitate that formed was filtered off and washed with hexane.

Synthesis of compounds 5a,b and 6a—e. The corresponding amine or alcohol (0.005 mol) was added to a solution of 0.005 mol of isocyanate **3** in 10 mL of ether. The mixture sat over night. The ether was evaporated, and the residue was recrystallized from hexane.

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Received November 23, 1994