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Communication

A Facile Synthesis of Partly-fluorinated Organic Compounds Using Perfluoropropoxyethylene and Amines

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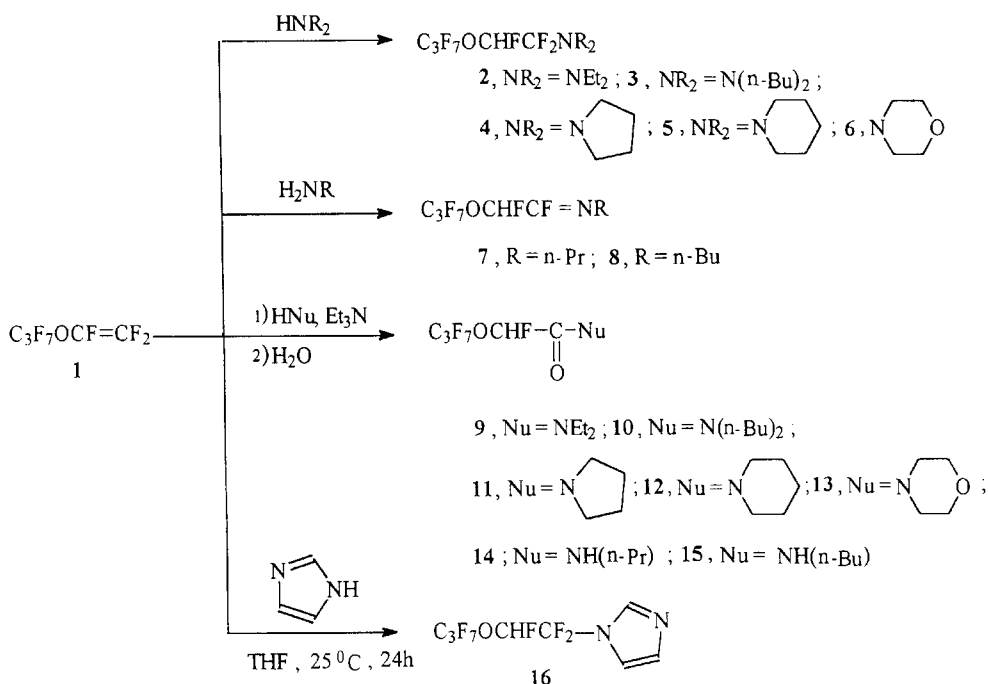
Because of their peculiar characteristics, perfluorinated amines have been used as a high temperature lubricant, a liquid dielectric or an artificial blood.¹ Recently, a perfluorinated amine was also applied in quantity for the production of polyurea resin.² This kind of compounds has a wide range of industrial application and the most promising applicable area with them would be related with medical field. It is, therefore, required to develop an effective methodology which enables us to synthesize tailor-made perfluoro-chemicals. However, conventional routes for the perfluorination of a non-fluorinated precursor using such methods as electrochemical fluorination and direct fluorination with F₂ are too rough to prepare a designed perfluoro-organic compound in pure form. These routes have a critical problem of poor yields in the synthesis of perfluorinated product. On the contrary, it has been known that fluorination with partly-fluorinated ethers or amines reduces decomposition during a perfluorination process and drastically increases the yield of perfluorinated product. The application of this methodology has been also limited since no easy way for the synthesis of partly-fluorinated compounds has been generalized. For instance, there have been only a few examples for the preparation of partly-fluorinated precursors starting with perfluoroolefins and N-nucleophilic reagents.³⁻⁷

In this paper, we would like to report a convenient method for the synthesis of partly-fluorinated amino, imino or amid ethers starting with perfluoropropoxyethylene (**1**)^{8,9} and various amines. The partly-fluorinated products are expected to be used in the effective synthesis of perfluorinated amine derivatives. Reactions of **1** with diethylamine (di-n-butylamine, pyrrolidine, piperidine, morpholine) in anhydrous THF yield the addition products **2-6** or N,N-dialkylamides **9-13** depending

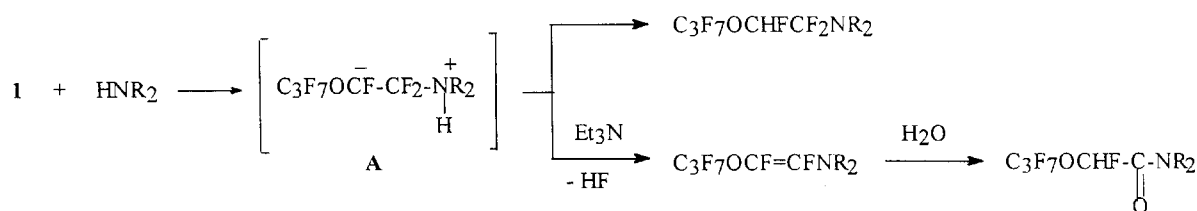
on the reaction conditions and the methods of separation of products. As shown in Scheme 1, treatments of equimolar amounts of the compound **1** with secondary amines produce the addition products **2-6** in 85-91% yields. On the other hand, reactions of **1** with dialkylamines in the presence of Et₃N followed by aqueous work-up provide the amides **9-13** in 71-95% yields. The pure products can be separated by a distillation of the reaction mixtures. The formation of amides was observed earlier in the reaction of hexafluoropropene with secondary amines in an aqueous-ether medium.¹⁰

Reaction of primary amine (n-propylamine or n-butylamine) with **1** in the presence of Et₃N followed by an aqueous work-up also provides the amide **14** or **15** respectively. The first step of that reaction might consist of the nucleophilic addition of a primary amine to the double bond of **1**. The product contains CF₂ group in next to NH fragment and elimination of HF by Et₃N undergoes to form a N=C bond. The fluorine atom at N=C bond is known to be reactive and a reaction with water transforms the imino group into a corresponding amide. On the contrary, a fractional distillation right after the reaction of **1** with n-propylamine or n-butylamine without any aqueous work-up gives the imine **7** or **8** even in the absence of triethylamine. Spectral data are entirely consistent with the proposed structures of **7** and **8**; the ¹⁹F NMR spectra showed the characteristic A-B system of F³ representing the presence of stereogenic center C⁴ and mass spectrometry gave M-1 ions. The ¹H NMR spectra of **7** and **8** also showed the typical resonance of H⁴ at δ_H 6.23 or 6.25 as a doublet (*J*_{HF} = 54.0 Hz) respectively.

It is interesting to note, however, that a treatment of imidazole with **1** produces only the addition product **16** irrespective of the presence of Et₃N. And the reason for the exclusive for-



Scheme 1



Scheme 2

mation of **16** out of **1** and imidazole is not clear yet.

The following Scheme 2 might be a plausible reaction mechanism between **1** and a secondary amine:

Without triethylamine, a nucleophilic attack of a secondary amine to the double bond on **1** ends up with an addition product. In the presence of triethylamine, however, elimination of HF from the addition product could be accompanied by the base to give an enamine. The resulting enamine might be easily converted into an amide by hydrolysis.

In short, reactions of perfluoropropoxyethylene (**1**) with secondary amines (diethylamine, dibutylamine, pyrrolidine, piperidine, morpholine) effectively provide the N,N-dialkyl amides **9-13** or the addition products **2-6** respectively depending on whether triethylamine exists as a base or not. Treatments of **1** with primary amines (n-propylamine, n-butylamine) in the presence of triethylamine followed by aqueous work-up also successfully produce the amides **14-15**. The partly-fluorinated products **2-16** are expected to be used as excellent precursors for a perfluorination reaction.

Experimental Section

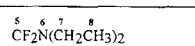
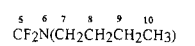

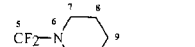
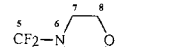
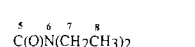
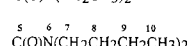
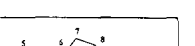
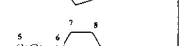
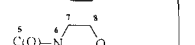
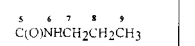
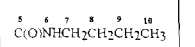
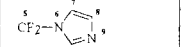
¹⁹F NMR spectra were recorded at 282.2 MHz with a Varian UNITY plus-300 spectrometer and obtained in the

presence of C₆F₆ as an internal standard; ¹³C and ¹H NMR spectra were measured with a Bruker AM-300 spectrometer (75.4 and 300.1 MHz respectively) in ppm using tetramethylsilane as an external standard in neat liquids (*J*_{CH} not recorded). IR spectra were obtained on a Mattson 5000 FTIR (NICAM) spectrometer (5% in CCl₄). Mass spectra were run on a JEOL LMS-DX 303 spectrometer and GC/MS data

Table 1. Yields, Boiling-points and HRMS Data of the Partly-fluorinated Products

Com-pound	Yield, %	b.p. °C/Torr	Found amu	Formula	Calculated amu
2	88	46-47/15	339.0664	C ₉ H ₁₁ F ₈ NO ₂	339.0669
3	86	45-46/2	395.1441	C ₁₃ H ₁₉ F ₁₀ NO	395.1307
4	88	36-37/0.8	337.0522	C ₉ H ₉ F ₁₀ NO	337.0524
5	90	66-67/15	351.0683	C ₁₀ H ₁₁ F ₁₀ NO	351.0681
6	91	76-78/15	353.0470	C ₉ H ₉ F ₁₀ NO ₂	353.0473
9	71	76-77/15	317.0663	C ₉ H ₁₁ F ₈ NO ₂	317.0662
11	95	78-73/0.3	315.0512	C ₉ H ₉ F ₈ NO ₂	315.0505
12	81	74-75/0.3	329.0664	C ₁₀ H ₁₁ F ₈ NO ₂	329.0662
13	75	85-86/0.3	331.0469	C ₉ H ₉ F ₈ NO ₃	331.0454
14	80	76-78/2	303.0502	C ₈ H ₉ F ₈ NO ₂	303.0505
15	74	87-88/2	317.0737	C ₉ H ₁₁ F ₈ NO ₂	317.0662

Table 2. ^{19}F and ^1H NMR Data of the Partly-fluorinated Products

R	$\text{CF}_3\text{CF}_2\text{CF}_2\text{OCH-R}$						*A-B system					
	F ¹	F ²	δ_{F} F ^{3*} (J_{FF})		F ⁴ (J_{FH})	F ^{5*} (J_{FF})		δ_{H} H ⁴	H ⁷	H ⁸	H ⁹	H ¹⁰
	82.4	33.8	78.9	76.4	23.2	75.5	72.8	6.04	3.00	1.10		
	82.5	33.5	78.7	75.9	23.4	75.9	73.0	5.94	2.88	1.50	1.34	0.91
	82.3	34.0	79.1	76.6	22.8	68.2	66.7	6.00	3.05	1.81		
	82.5	33.7	78.8	76.1	22.7	66.2	65.0	5.99	2.88	1.54	1.54	
	81.9	34.0	78.9	76.8	22.8	64.0	63.6	6.16	3.64	3.64		
	82.2	34.2	79.6	77.0	33.1			6.01	3.20	1.21		
	80.7	33.7	80.7	78.3	33.5			6.54	3.35	1.54	1.30	0.91
	82.5	34.3	79.7	77.3	30.2			6.47	3.32	1.82		
	82.2	33.9	79.3	76.6	33.1			6.56	3.00	1.53	1.53	
	82.3	34.1	80.3	75.9	32.7			6.64	3.61			
	81.2	33.8	78.7	77.2	29.3			6.30	3.27	1.58	0.91	
	81.9	33.8	78.9	77.3	29.3			6.39	3.34	1.60	1.35	0.91
	81.2	32.9	78.0	75.7	19.5	66.9	68.5	7.29	7.87	7.25	7.08	

were checked using a 4.8 cm×0.32 cm column packed with 10% OV-202 on 100-200 mesh Gas Chrom RZ. Reactions were routinely monitored with ^{19}F NMR spectroscopy. All chemicals were of analytical grade and used without further purification. Tetrahydrofuran was distilled from sodium benzophenone ketyl. The yields, boiling points and HRMS data of the new products are shown in Table 1. The ^1H , ^{13}C and ^{19}F NMR spectral data of them are also shown in Table 2 and 3.

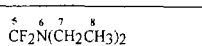
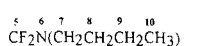
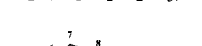
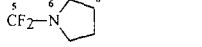
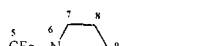
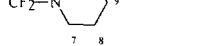
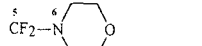

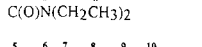
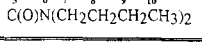
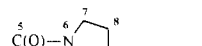
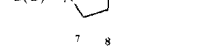
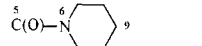

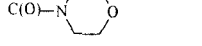
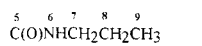
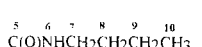
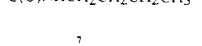
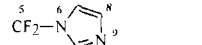
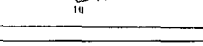

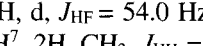
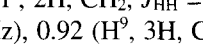
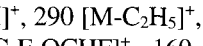

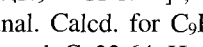
Typical procedures for the preparation of partly-fluorinated compounds

Method A. To a solution of **1** (26.6 g, 0.10 mol) in THF (50 mL) at 0 °C was slowly added imidazole (6.8 g, 0.10 mol) in THF (20 mL) for 0.5 h. The reaction mixture was stirred at 25°C overnight and the resulting solution was diluted with water (200 mL). The organic phase was separated and dried over anhydrous MgSO_4 . The crude product was distilled to give **16** (24.0 g, 72% yield) as a pale yellow liquid: b.p. 37-38 °C (0.1 Torr); Anal. Calcd. for $\text{C}_8\text{H}_4\text{F}_{10}\text{N}_2\text{O}$: C, 28.74; H, 1.20; F, 56.88, Found: C, 28.64; H, 1.17; F, 56.68; HRMS Calcd. 334.0164, Found 334.0163. The compounds **2-6** were prepared respectively by the Method A.

Method B. To a solution of **1** (13.3 g, 0.05 mol) in THF (20 mL) at 0 °C was added a solution of n-propylamine (5.9

g, 0.10 mol) in THF (10 mL). The reaction mixture was stirred for 1 h at 0 °C, 3 h at room temperature, and then 2 h at 45 °C. The solvent was distilled off under reduced pressure and the resulting organic phase was distilled to give **7** (12.0 g, 79% yield) as a colorless liquid: b.p. 37-38 °C (3 Torr); ^{19}F NMR (CDCl_3) δ_{F} 110.2 (F⁵, 1F, m), 81.9 (F¹, 3F, CF₃, s), 78.6 and 76.5 (F³, 2F, AB-system J_{FF} = 148.7 Hz), 33.7 (F², 2F, CF₂, s), 30.5 (F⁴, 1F, CHF, d, J_{FH} = 54.0 Hz); ^1H NMR (CDCl_3) δ_{H} 6.23 (H⁴, 1H, d, J_{HF} = 54.0 Hz), 3.40 (H⁶, 2H, t, J_{HH} = 7.8 Hz), 1.59 (H⁷, 2H, CH₂, sept, J_{HH} = 7.8 Hz), 0.91 (H⁸, 3H, CH₃, t, J_{HH} = 7.8 Hz); ^{13}C NMR (CDCl_3) δ_{C} 142.2 (C⁵, $^1J_{\text{CF}}$ = 355.8 Hz; $^2J_{\text{CF}}$ = 29.6 Hz), 117.6 (C¹, $^1J_{\text{CF}}$ = 286.2 Hz; $^2J_{\text{CF}}$ = 33.1 Hz), 116.2 (C³, $^1J_{\text{CF}}$ = 286.2 Hz; $^2J_{\text{CF}}$ = 32.9 Hz), 107.4 (C², $^1J_{\text{CF}}$ = 266.6 Hz; $^2J_{\text{CF}}$ = 38.8 Hz), 98.4 (C⁴, $^1J_{\text{CF}}$ = 236.8 Hz; $^2J_{\text{CF}}$ = 54.7 Hz; $^3J_{\text{CF}}$ = 5.4 Hz), 47.5 (C⁶), 22.9 (C⁷), 10.7 (C⁸); GC/MS 304 [M-H]⁺, 290 [M-CH₃]⁺, 276 [M-C₂H₅]⁺, 169 [C₃F₇]⁺, 120 [C₃H₇N=CFCHF]⁺, 88 [C₃H₇N=CF]⁺, 69 [CF₃]⁺, 43 [C₃H₇]⁺. The compound **8** was also prepared with n-butylamine in 75% yield by the Method B: b.p. 42-43 °C (3 Torr); ^{19}F NMR (CDCl_3) δ_{F} 110.8 (F⁵, 1F, m), 82.0 (F¹, 3F, CF₃, s), 78.6 and 77.4 (F³, 2F, AB-system J_{FF} = 148.9 Hz), 33.9 (F², 2F, CF₂, s), 29.2 (F⁴, 1F, CHF, d, J_{FH} = 54.0 Hz); ^1H NMR (CDCl_3) δ_{H} 6.25 (H⁴,

Table 3. ^{13}C NMR Data of the Partly-fluorinated Products

R	C ¹ ($^1J, ^2J_{\text{CF}}$)	C ² ($^1J, ^2J_{\text{CF}}$)	C ³ ($^1J, ^2J_{\text{CF}}$)	C ⁴ ($^1J, ^2J_{\text{CF}}$)	C ⁵ ($^1J, ^2J_{\text{CF}}$)	C ⁷	C ⁸	C ⁹	C ¹⁰
	117.8	106.5	115.7	98.9	117.0	38.8	12.2		
	(291, 33)	(267, 39)	(280, 32)	(245, 49)	(251, 29)				
	117.7	106.5	115.9	100.5	117.3	46.9	31.8	20.8	13.9
	(292, 33)	(267, 39)	(278, 30)	(245, 47)	(254, 29)				
	118.0	106.4	115.8	98.8	116.8	47.4	22.9		
	(290, 33)	(267, 40)	(280, 32)	(245, 49)	(254, 29)				
	116.9	106.5	115.5	98.8	117.5	44.0	24.6	23.5	
	(352, 33)	(282, 39)	(280, 32)	(244, 44)	(251, 27)				
	117.7	106.6	115.4	98.8	117.2	66.6	44.7		
	(290, 33)	(267, 40)	(280, 32)	(243, 45)	(254, 29)				
	116.4	105.9	115.1	98.4	159.2	39.7	11.9		
	(286, 33)	(276, 39)	(280, 29)	(244, 25)					
	116.7	106.2	115.3	99.2	159.5	44.8	28.2	18.8	11.9
	(287, 33)	(267, 38)	(279, 41)	(268, 25)					
	117.3	106.8	115.9	99.2	159.6	46.4	24.2		
	(286, 33)	(267, 39)	(280, 31)	(243, 26)					
	120.2	109.7	118.8	102.4	162.2	48.4	28.7	26.6	
	(286, 34)	(267, 39)	(281, 30)	(243, 25)					
	116.2	105.3	114.6	98.2	158.2	64.5	43.9		
	(288, 32)	(267, 32)	(290, 33)	(244, 15)					
	117.2	106.7	115.9	98.4	161.8	41.0	21.8	10.0	
	(286, 33)	(267, 39)	(279, 31)	(243, 25)					
	117.2	106.2	115.8	98.3	161.7	39.1	30.7	19.5	12.5
	(286, 33)	(267, 39)	(304, 33)	(243, 25)					
	116.9	106.6	115.6	100.2	117.3	135.8	131.4		117
	(287, 32)	(268, 39)	(279, 31)	(241, 43)	(254, 28)				

^1H , d, $J_{\text{HF}} = 54.0$ Hz), 3.69 (H^6 , 2H, t, $J_{\text{HH}} = 7.8$ Hz), 1.54 (H^7 , 2H, CH_2 , $J_{\text{HH}} = 7.8$ Hz), 1.36 (H^8 , 2H, CH_2 , $J_{\text{HH}} = 7.8$ Hz), 0.92 (H^9 , 3H, CH_3 , t, $J_{\text{HH}} = 7.8$ Hz); GC/MS 318 [$\text{M}-\text{H}$] $^+$, 290 [$\text{M}-\text{C}_2\text{H}_5$] $^+$, 276 [$\text{M}-\text{C}_3\text{H}_7$] $^+$, 257 [$\text{M}-\text{C}_3\text{H}_7-\text{F}$] $^+$, 217 [$\text{C}_3\text{F}_7\text{OCHF}$] $^+$, 169 [C_3F_7] $^+$, 134 [$\text{C}_4\text{H}_9\text{N}=\text{CFCHF}$] $^+$, 102 [$\text{C}_4\text{H}_9\text{N}=\text{CFCHF}$] $^+$, 119 [C_2F_5] $^+$, 69 [CF_3] $^+$, 43 [C_3H_7] $^+$; Anal. Calcd. for $\text{C}_9\text{H}_{10}\text{F}_9\text{NO}$: C, 33.86; H, 3.13; F, 53.61. Found: C, 33.64; H, 3.17; F, 53.68.

Method C. To a solution of **1** (21.3 g, 0.08 mol) in THF (60 mL) at 0°C was added a solution of dibutylamine (10.3 g, 0.08 mol) and Et_3N (8.3 g, 0.08 mol) in THF (10 mL) for 0.5 h. The reaction mixture was stirred at room temperature overnight and then diluted with water (200 mL). The organic phase was separated and dried over anhydrous MgSO_4 . The crude product was distilled to give **10** (21.9 g, 73% yield) as a pale yellow liquid: b.p. $93-94^\circ\text{C}$ (0.2 torr); IR (5% in CCl_4) 2980, 2910, 1690 ($\text{C}=\text{O}$), 1200-1100 ($\text{C}-\text{F}$) cm^{-1} ; Anal. Calcd. for $\text{C}_{13}\text{H}_{19}\text{F}_8\text{NO}_2$: C, 43.70; H, 5.30; F, 42.60. Found: C, 43.96; H, 5.48; F, 43.17. The compounds **9**, **11-15** were also prepared respectively by the Method C.

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References

- (a) Liebman, J. F.; Greenberg, A.; Dolbier, W. R. Jr. *Fluorine-Containing Molecules: Structure, Reactivity, Synthesis, and Applications*; VCH Publishers, Inc.: New York, 1988. (b) Olah, G. A.; Chambers, R. D.; Prakash, G. K. S. *Synthetic Fluorine Chemistry*; Wiley Interscience: New York, 1992.
- Esipov, Yu. L.; Kitaev, L. G.; Moldavskii, D. D.; Shkultezkay, L. V.; Furin, G. G. *Patent Russia* 2005732, 1994.
- Snegirev, V. F.; Zacharova, E. V.; Makarov, K. N.; Knun-yants, I. L. *Izv. Akad. Nauk SSSR Ser. Khim.* **1983**, 2561.
- Ono, T.; Yamanouchi, K.; Scherer, K. V. *J. Fluorine Chem.* **1995**, *73*, 267.
- Kadyrov, A. A.; Gervits, L. L.; Komarova, L. F.; Makarov, K. N. *J. Fluorine Chem.* **1989**, *45*, 152.
- Moldavsky, D. D.; Kaurova, G. I.; Bispin, T. A.; Furin, G. G. *J. Fluorine Chem.* **1993**, *63*, 193.
- Moldavsky, D. D.; Furin, G. G. *Zh. Prikl. Khim.* **1995**, *65*, 1721.
- Yuminov, V. S. *Zh. Org. Khim.* **1995**, *31*, 1142.
- Fritz, C. G.; Selman, S. *U.S. Patent* 3291843, 1966.
- Kuroboshi, M.; Ishihara, T. *Bull. Chem. Soc. Jpn* **1990**, *64*, 1191.