

H, 10.12; P, 10.05. $C_{36}H_{66}N_2O_4P_2$. Calculated (%): C, 66.23; H, 10.19; P, 9.49. IR. ν/cm^{-1} : 1612 (C=O), 2149 (CN). ^{31}P NMR (C_6D_6), δ : 32.0. 1H NMR (C_6D_6), δ : 0.98 (t, 9 H, $CH_3(CH_2)_2P$, $J = 7.0$ Hz); 1.19 (m, 6 H, CH_2CH_2P); 1.52 (m, 8 H, $(CH_2)_4CH_2O$); 1.70 (m, 6 H, CH_2CH_2P); 3.12 (d, 2 H, CH_2P , $J_{H-P} = 6.9$ Hz); 4.01 (m, 2 H, CH_2O).

In the study of the anticholine esterase effect of compound 3, choline esterases from different biological sources were used as enzymes¹: acetylcholine esterase (KF 3.1.1.7) from erythrocytes of blood of man (ACEM) and bull (ACEB); butyrylcholine esterases (KF 3.1.1.8) from the blood serum of horse (BuCEH), fish (BuCEF), and pigeon (BuCEP); choline esterase (KF 3.1.1.8) from the blood serum of hen (CEH) and the cerebral tissue of New Zealand squid (CENS).

Catalytic activity of enzymes in the absence and presence of an inhibitor was determined by the photometric Ellman method⁶ at 25 °C and pH 7.5 using acetylcholine (2 mmol L^{-1}) as a substrate. Efficiency of the inhibition effect of a compound was estimated from its concentration (I_{50}) that results in a 50% decrease in the hydrolysis rate of the substrate. Conditions of determination of the catalytic activity and I_{50} were similar to those in Ref. 1.

References

1. Yu. G. Zhukovskii, L. P. Kuznetsova, E. E. Sochilina, E. N. Dmitrieva, Yu. G. Gololobov, and E. Yu. Bykovskaya, *Zh. Evolyuts. Biokhim. Fiziol.*, 1996, **32**, 212 [*J. Evolut. Biochem. Physiol.*, 1996, **32** (Engl. Transl.)].
2. T. O. Krylova, G. D. Kolomnikova, I. A. Garbuzova, and Yu. G. Gololobov, *Zh. Obshch. Khim.*, 1994, **64**, 409 [*Russ. J. Gen. Chem.*, 1994, **64** (Engl. Transl.)].
3. A. P. Brestkin, L. P. Kuznetsova, S. N. Moralev, E. V. Rozengart, and L. M. Epshtein, *Kholinesterazy nazemnykh zhivotnykh i gidrobiontov* [*Choline Esterases of Terrestrial Animals and Hydrobionts*], TINRO-tsentr [Center of the Pacific Institute for Fish Economy and Oceanography], Vladivostok, 1997, 137 (in Russian).
4. Yu. G. Gololobov and I. V. Chernoglazova, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 997 [*Russ. Chem. Bull.*, 1993, **42**, 961 (Engl. Transl.)].
5. A. P. Brestkin, T. N. Vinyar, and E. V. Rozengart, *Ukr. Biokhim. Zh.*, 1983, **55**, 77 [*Ukr. Biochem. J.*, 1983, **55** (Engl. Transl.)].
6. G. L. Ellman, K. D. Courtney, V. Andress, and R. M. Featherstone, *Biochem. Pharmacol.*, 1961, No. 2, 7, 251.

Received January 6, 1999;
in revised form May 12, 1999

Synthesis of 5-fluoro-2,4,6-tris(perfluoroalkyl)pyrimidines

O. E. Petrova,* M. A. Kurykin, and D. V. Gorlov

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 117813 Moscow, Russian Federation.
Fax: +7 (095) 135 5085. E-mail: mak@ineos.ac.ru

5-Fluoro-2,4,6-tris(perfluoroalkyl)pyrimidines were synthesized by reactions of polyfluorinated iminoenamines with perfluorocarboxylic acid anhydrides and perfluorobutanoyl chloride.

Key words: polyfluorinated iminoenamines; condensation with perfluorocarboxylic acid anhydrides and perfluorobutanoyl chloride; perfluoropyrimidines.

Pyrimidines constitute an abundant class of natural bases and are widespread among drugs possessing a pronounced antiviral,¹ gastric antisecretory,² diuretic,³ anti-malarial,⁴ and anti-HIV-1-activity.^{5,6} It is also known that the presence of fluorine atoms in a molecule increases the physiological activity of compounds as compared with their nonfluorinated analogs.⁷ Therefore, interest in the synthesis of new fluorine-containing pyrimidines, which is the subject of this work, seems to be quite natural.

It is known that reactions of polyfluorinated imidoylamidines with perfluorocarboxylic acid anhy-

Table 1. Characteristics of compounds 1a–c

Com- pound	Yield (%)	B.p./°C (p/Torr)	Found Calculated (%)			Molecular formula
			C	F	N	
1a	71.3	111—112	<u>28.0</u> 27.8	<u>61.75</u> 62.90	<u>9.04</u> 9.27	C ₇ F ₁₀ N ₂
1b	73.0	44 (50)	<u>27.27</u> 27.27	<u>64.94</u> 64.77	<u>8.00</u> 7.95	C ₈ F ₁₂ N ₂
1c	88.0	50—51 (24)	<u>27.07</u> 26.87	<u>66.19</u> 66.17	<u>6.93</u> 6.97	C ₉ F ₁₄ N ₂

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 11, pp. 2195–2196, November, 1999.

1066-5285/99/4811-2169 \$22.00 © 1999 Kluwer Academic/Plenum Publishers

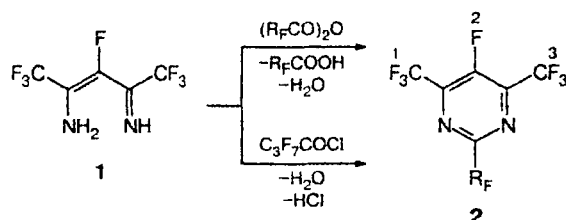
Table 2. Spectral characteristics of compounds **1a–c**

Compound, R _F	IR spectrum, v/cm ⁻¹	Mass spectrum, m/z (I _{rel} (%))	¹⁹ F NMR spectrum, δ, J/Hz
1a , CF ₃ ⁴	1470 br, 1595 s, 1800 m	302 [M] ⁺ (94), 283 [M - F] ⁺ (100), 233 [M - CF ₃] ⁺ (70), 119 [C ₂ F ₅] ⁺ (40), 69 [CF ₃] ⁺ (100)	-8.0 (d, 6 F, F(1), F(3), J = 15.0); -4.8 (s, 3 F, F(4)); 51.5 (hept, 1 F, F(2), J = 15.0)
1b , CF ₂ ⁴ CF ₃ ⁵	1470 br, 1595 s	352 [M] ⁺ (100), 333 [M - F] ⁺ (85), 283 [M - CF ₃] ⁺ (79), 233 [M - C ₂ F ₅] ⁺ (41), 119 [C ₂ F ₅] ⁺ (70), 69 [CF ₃] ⁺ (60)	-8.0 (d, 6 F, F(1), F(3), J = 15.0); 5.5 (s, 3 F, F(5)); 41.5 (s, 2 F, F(4)); 51.5 (hept, 1 F, F(2), J = 15.0)
1c , CF ₂ ⁴ CF ₂ ⁵ CF ₃ ⁶		402 [M] ⁺ (9), 383 [M - F] ⁺ (47), 283 [M - C ₂ F ₅] ⁺ (100), 169 [C ₃ F ₇] ⁺ (6), 69 [CF ₃] ⁺ (48)	-7.7 (d, 6 F, F(1), F(3), J = 15.0); 5.9 (t, 3 F, F(6), J = 11.5); 39.0 (br.d, 2 F, F(4), J = 11.5); 50.7 (s, 2 F, F(5)); 51.5 (hept, 1 F, F(2), J = 15.0)

drides⁸ and halides⁹ proceed by a common mechanism to give heterocyclic compounds, namely, triazines.

It could be expected that 2-amino-4-iminoperfluoropent-2-ene (**1**), which we synthesized recently¹⁰ and which is structurally similar to the above-mentioned imidoylamidines, will enter into analogous reactions.

Actually, we established that compound **1** reacts with perfluorocarboxylic acid anhydrides and perfluorobutanoyl chloride to give 5-fluoro-2,4,6-tris(perfluoroalkyl)pyrimidines (**2**).



R_F = CF₃ (**a**), C₂F₅ (**b**), C₃F₇ (**c**)

It is likely that the formation of pyrimidines **2** includes two stages, namely, acylation of iminoenamine followed by dehydration of this intermediate acyl derivative, resulting in ring closure. It should be noted that ¹⁹F NMR spectra of the reaction mass contain signals of end products only, which indicates the absence of side reactions.

Experimental

¹⁹F NMR spectra were recorded on a Bruker AC-200F spectrometer operated at 188.3 MHz (¹⁹F). Chemical shifts are reported in δ relative to CF₃COOH (external standard) and spin-spin coupling constants are reported in Hz. IR spectra were recorded on an UR-20 spectrometer (thin layer) and mass spectra were obtained on a VG-7070E instrument at an ionizing voltage of 70 eV. The yields and characteristics of compounds obtained are listed in Tables 1 and 2.

5-Fluoro-2,4,6-tris(trifluoromethyl)pyrimidine (2a), **2-pentafluoroethyl- (2b)**, and **2-heptafluoropropyl-5-fluoro-4,6-bis(trifluoromethyl)pyrimidine (2c)**. Trifluoroacetic anhydride (6 g, 28 mmol) was added dropwise with stirring to 2-amino-4-iminoperfluoropent-2-ene (**1**, 3.0 g, 13 mmol) in dry ether (50 mL) on cooling to 1–3 °C. The reaction mass was neutralized with aqueous NaHCO₃, the organic layer was separated, dried over CaCl₂, and distilled to give **2a**. Pyrimidines **2b**, **2c** were obtained analogously by reactions of **1** with pentafluoropropionic anhydride and heptafluorobutanoyl chloride, respectively.

References

- L. M. Beauchamp, B. L. Serling, J. E. Kelsey, K. K. Biron, P. Collins, J. Selway, J.-C. Lin, and H. I. Schaeffer, *J. Med. Chem.*, 1988, **31**, 144.
- M. Sugiyama, T. Sakamoto, and H. Fukumi, *Heterocycles*, 1989, **29**, 985.
- A. Monge, V. Martinier-Merino, C. Sammartin, M. C. Ochoa, and E. Fernandez-Alvarez, *Arz. Forsch.*, 1990, **40**, 1349.
- T. Ishihara, Y. Okada, M. Kuroboshi, T. Shinozaki, and T. Ando, *Chem. Lett.*, 1988, **5**, 819.
- T. Miyasaka, H. Tanaka, M. Baba, H. Hayakawa, R. T. Walker, J. Balzarini, and E. De Clercq, *J. Med. Chem.*, 1989, **32**, 2507.
- H. Tanaka, H. Takashima, M. Ubasawa, K. Sekiya, I. Nitta, M. Baba, S. Shigeta, R. T. Walker, E. De Clercq, and T. Miyasaka, *J. Med. Chem.*, 1992, **35**, 337.
- J. T. Welch, *Tetrahedron*, 1987, **43**, 3123.
- G. M. Tolmachev, S. P. Krukovskii, A. V. Ignatenko, and V. A. Ponomarenko, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 580 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1979, **28** (Engl. Transl.)].
- R. G. Spain, *Behavior of Some Elastomers in Petroleum Based Fluids at Elevated Temperatures, Division of Rubber Chemistry. A. C. S. Meeting*, Cincinnati, Ohio, May 15, 1985.
- O. E. Petrova, M. A. Kurykin, and D. V. Gorlov, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 1710 [*Russ. Chem. Bull.*, 1999, **48**, 1688 (Engl. Transl.)].

Received March 25, 1999;
in revised form May 17, 1999