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Dedicated to Full Member of the Russian Academy of Sciences O.N. Chupakhin on his 75th anniversary

Reactions of Internal Perfluoroolefin Oxides with Urea

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Abstract—Internal perfluoroolefin oxides reacted with urea to give, depending on the solvent nature, two types of new fluorine-substituted nitrogen-containing heterocycles. 1,5-Bis(perfluoroalkyl)tetraazabicyclo[3.3.0]octane-3,7-diones were formed in dimethyl sulfoxide, *N*,*N*-dimethylacetamide, and acetonitrile, while the reaction in dioxane resulted in the formation of unexpected products, 2-amino-5-fluoro-4,5-bis(perfluoroalkyl)-4,5-dihydrooxazol-4-ols, existing mainly as *trans* isomers. *trans* Orientation of perfluoroalkyl substituents in these compounds was determined by analysis of ^{19}F–^{19}F spin–spin coupling constants in the ^{19}F NMR spectra. The molecular structure of *trans*-2-amino-5-fluoro-4,5-bis(trifluoromethyl)-4,5-dihydrooxazol-4-ol was studied by X-ray analysis.

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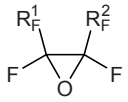
Interest in the chemistry of urea-based nitrogen-containing heterocycles, such as bicyclic glycolurils and their precursors (imidazolidin-2-ones), originates from their strong biological activity. Glycolurils of the octane series were shown to be promising neurotropic agents [1–3]. One of these, 2,4,6,8-tetramethylglycoluril (Mebicar), is used in medical practice as minor tranquilizer (anxiolytic) [1]. Among imidazolidin-2-ones, Phenytoin is known [1] as an antiepileptic drug. In addition, glycolurils and their derivatives may be used as spacer elements in molecular capsules [4], polymer stabilizers [5, 6], and fluorescent substances [7]. In the recent years, glycolurils have found wide application in supramolecular chemistry as building blocks for the preparation of nanoporous materials, synthetic receptors, and liquid crystals [8].

Known procedures for the synthesis of glycolurils are based on reactions of ureas with α-dicarbonyl compounds or 4,5-dihydroxyimidazolidin-2-ones [9]. However, there are no published data on the synthesis of fluorine-containing glycolurils. We previously showed that internal perfluoroolefin oxides readily react with difunctional nucleophiles and that they are convenient starting compounds for the preparation of perfluoroalkyl-containing N,O,S-heterocycles [10–13].

The present work was aimed at synthesizing new glycoluril derivatives and other nitrogen-containing heterocycles with perfluoroalkyl substitutents. For this purpose, we examined reactions of urea with 2,3-epoxyoctafluorobutane (**I**, *cis*/*trans* isomer ratio ~1 : 9), 3,4-epoxydodecafluorohexane (**II**, *cis*/*trans* isomer ratio ~1 : 9), and 2,3-epoxydodecafluorohexane (**III**, *cis*/*trans* isomer ratio ~1 : 9) [14]. In order to estimate solvent effect on the direction of nucleophilic attack, the reactions were carried out in aprotic solvents characterized by different polarities, namely dimethyl sulfoxide (DMSO), *N*,*N*-dimethylacetamide (DMA), acetonitrile, and dioxane.

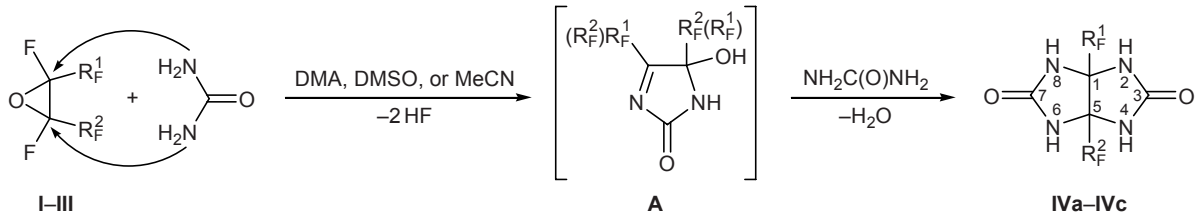


I–III

I, $R_F^1 = R_F^2 = CF_3$; **II**, $R_F^1 = R_F^2 = C_2F_5$; **III**; $R_F^1 = CF_3$, $R_F^2 = C_3F_7$.

Oxiranes **I**–**III** reacted with urea in polar DMSO, DMA, and acetonitrile to give the corresponding glycolurils, 1,5-bis(perfluoroalkyl)-2,4,6,8-tetraazabicyclo-[3.3.0]octane-3,7-diones **IVa**–**IVc**, in ~20–42% yield (Scheme 1). Presumably, the reaction begins with attack by the amino group of urea molecule on one carbon atom in the oxirane ring of **I**–**III**; the subsequent oxirane ring opening gives unstable intermediate **A** which takes up one more urea molecule to produce

Scheme 1.



IV, $R_F^1 = R_F^2 = CF_3$ (**a**), CF_3CF_2 (**b**); $R_F^1 = C^{3'}F_3C^{2'}F_2C^{1'}F_2$, $R_F^2 = C^{1''}F_3$ (**c**).

glycolurils **IVa**–**IVc**. We failed to isolate the primary addition products, hydroxyimidazol-2-ones **A**. In contrast, reactions of internal perfluorinated epoxy derivatives with other diamines such as ethane-1,2-diamine and benzene-1,2-diamine resulted in the formation of the corresponding 1 : 1 adducts, 2,3-bis(polyfluoroalkyl)-1,2,5,6-tetrahydropyrazin-2-ols and quinoxalines, as the only products [10, 12].

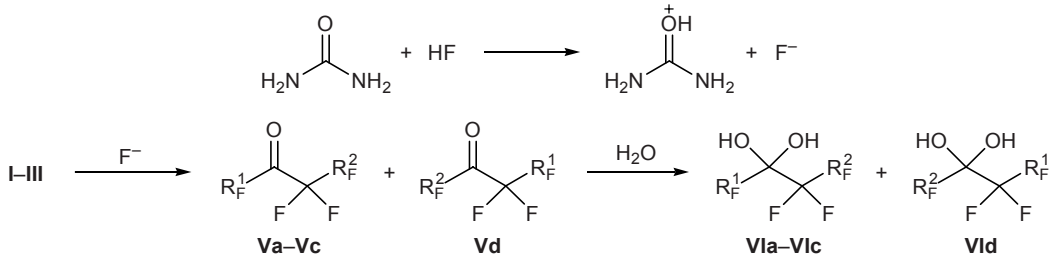
The structure of compounds **IVa**–**IVc** was confirmed by the IR, ^{1}H, ^{19}F, and ^{13}C NMR, and mass spectra (**IVa**, **IVc**) and elemental analyses. The ^{19}F NMR spectra of the reaction mixtures obtained in the reactions of compounds **I**–**III** with urea in DMSO, DMA, and acetonitrile revealed the presence of ~25–35% of hydrated ketones **VIa**–**VId** [12] which were likely to be formed as a result of hydration of isomeric ketones **Va**–**Vd** on treatment with water (Scheme 2). Ketones **Va**–**Vd** were obtained as the major products in the reactions with excess perfluorinated oxirane, whereas glycolurils **IVa**–**IVc** were formed in a small yield.

Oxiranes **I**–**III** reacted with urea in dioxane (sealed ampule, ~100°C) to give unexpected products, 2-amino-5-fluoro-4,5-bis(perfluoroalkyl)-4,5-dihydrooxazol-4-ols **VIIa**–**VIId** (Scheme 3). In this case, the initial reaction step is likely to be attack by the carbonyl oxygen atom of urea at one carbon atom in the oxirane ring of **I**–**III**; opening of the oxirane ring leads to intermediate **B** which loses HF molecule, and intramolecular ring closure in intermediate **C** thus formed yields heterocycles **VIIa**–**VIId**. This reaction direction may be rationalized assuming that dioxane as solvent favors high nucleophilicity of the carbonyl oxygen atom in urea molecule. Insofar as dioxane is a weakly polar solvent, it forms weak hydrogen bonds with hydrogen atoms in the amino groups of urea, and, unlike polar DMSO, DMA, and acetonitrile, ionization of N–H bonds in the nucleophile is not favored [15].

According to the ^{19}F NMR data, nucleophilic opening of the oxirane ring in unsymmetrically substituted 2,3-epoxydodecafluorohexane (**III**) by the action of urea takes both possible paths *a* and *b*, as shown in Scheme 3; as a result, regioisomeric oxazoles **VIIc** and **VIId** are formed (mainly as *trans* isomers). Approximately equal yields of these compounds (~53 and 47%, respectively; Table 1) indicate equal probabilities of nucleophilic attack at both oxirane carbon atoms, which may be interpreted in terms of electronic control (approximately equal stabilities of intermediate O-anions) [10]. On the whole, the observed relations are consistent with our previous data on reactions of 2,3-epoxyperfluoroalkanes with 2-aminophenol and ammonia [12, 16].

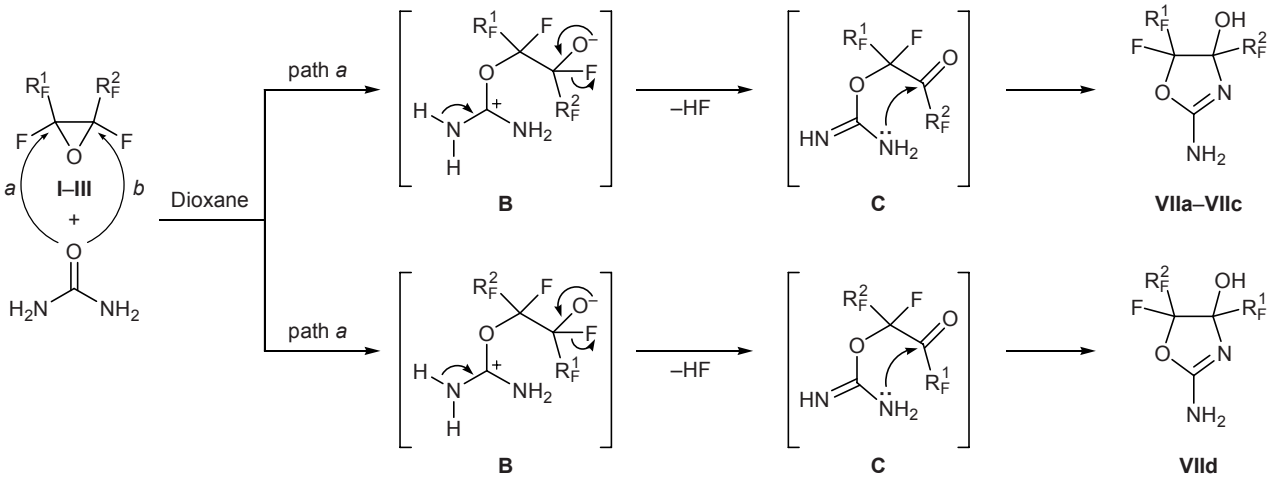
The structure of *trans*-isomeric dihydrooxazoles **VIIa**–**VIIc**, which were isolated by crystallization, was determined by ^{1}H, ^{19}F, and ^{13}C NMR and IR spectroscopy, mass spectrometry (**VIIc**), and elemental analysis. The structure of *trans*-**VIIa** was proved by X-ray analysis (Fig. 1). Single crystals of **VIIa** as solvate

Scheme 2.



$R_F^1 = R_F^2 = CF_3$ (**a**), CF_3CF_2 (**b**); $R_F^1 = C^{3'}F_3C^{2'}F_2C^{1'}F_2$, $R_F^2 = C^{1''}F_3$ (**c**, **d**).

Scheme 3.



VII, $R_F^1 = R_F^2 = CF_3$ (**a**), CF_3CF_2 (**b**); $R_F^1 = C^{1'}F_3$, $R_F^2 = C^{1''}F_AF_BC^{2''}F_AF_BC^{3''}F_3$ (**c**), $R_F^1 = C^{1''}F_3$, $R_F^2 = C^{3'}F_3C^{2'}F_AF_BC^{1'}F_AF_B$ (**d**).

with water and benzene were obtained by recrystallization from moist benzene. According to the X-ray diffraction data, the dihydrooxazole ring is flattened so that deviations of atoms from the mean-square plane do not exceed 0.06 Å. The trifluoromethyl groups appear in anticlinal conformation. The bond lengths and bond angles in molecule **VIIa** approach standard values. The amino and hydroxy groups are involved in hydrogen bond system (Table 2). The crystal packing of compound **VIIa** includes fairly unusual solvate shell consisting of one benzene molecule and one water molecule per two molecules of **VIIa**, $2(C_5H_3F_7N_2O_2)\cdot C_6H_6\cdot H_2O$. Water molecule is involved in intermolecular hydrogen bonds (Table 2), while benzene molecule occupies the space between the trifluoromethyl groups, giving rise to several weak shortened contacts like $O\cdots H–C_{arom}$ and $N–H\cdots C_{arom}$ (Fig. 2). Among other shortened contacts, intermolecular $O^1\cdots F^7$ contact should be noted [~2.9 Å; 1.5 – *x*, 0.5 – *y*, –*z*]; it links dihydrooxazole molecules to dimers. In addition, $F\cdots F$ contacts (~2.75–2.90 Å) are formed between the CF_3 substituents (hydrophobic interactions).

The ^{19}F NMR spectrum of **VIIa** (*trans* isomer) in DMSO-d_6 contained a doublet of quartets at δ_F 85.0 ppm, which was assigned to the 5-CF_3 group ($^3J_{FF}$ = 2.9, $^5J_{FF}$ = 1.7 Hz), and the other doublet of quartets (δ_F 84.1 ppm) was assigned to the 4-CF_3 group ($^4J_{FF}$ = 19.5, $^5J_{FF}$ = 1.7 Hz). The large long-range coupling constant between the 5-F atom and fluorine atoms in the trifluoromethyl group on C^4 ($^4J_{FF}$ = 19.5 Hz) is determined mainly by the through-space contribution which is possible when the interacting nuclei are spatially close to each other. Such arrangement is consistent with the X-ray diffraction data. The 5-F atom and the 4-CF_3 group in *trans*-**VIIa** are located at the same side of the five-membered ring, and the average distance between the interacting atoms in crystal is 3.15 Å (Fig. 1), the distances $F^7\cdots F^4$ (2.63 Å) and $F^7\cdots F^6$ (2.79 Å) being shorter than the sum of the corresponding van der Waals radii.

The ^{19}F NMR spectra of *trans*-isomeric dihydrooxazoles **VIIb**–**VIId** displayed more complex patterns due to nonequivalence of fluorine atoms in all difluoromethylene groups. The ^{19}F signals in the spectra of **VIIb**–**VIId** were assigned on the basis of two-dimensional homonuclear $^{19}F–^{19}F$ COSY spectra. The relative configuration of substituents in the five-membered ring may be determined by analysis of $^{19}F–^{19}F$ coupling constants through four bonds. In the spectrum

Table 1. Reactions of perfluorinated oxiranes **I**–**III** with urea

Initial oxirane no.	Solvent	Oxirane–urea molar ratio	Product[a]
I	DMSO	1:3	**IVa**
I	DMA	1:3	**IVa**
I	Acetonitrile	1:3	**IVa**
I	Dioxane	1:2	**VIIa**
II	DMSO	1:3	**IVb**
II	Dioxane	1:2	**VIIb**
III	DMSO	1:3	**IVc**
III	Dioxane	1:2	**VIIc** (~53 mol %), **VIId** (~47 mol %)

[a] According to the ^{19}F NMR data.

Table 2. Parameters of hydrogen bonds D–H···A formed by molecules **VIIa** in crystal

D–H	*d*(D–H)	*d*(H···A)	∠DHA	*d*(D···A)	A
N^2–$H^{2\,a}$	0.83(2)	2.107	172(1)	2.93(2)	O^{1C} [–*x* + 1/2, –*y* + 1/2, –*z*]
O^2–H^{2C}	0.85(2)	1.84(2)	175(1)	2.70(2)	H^1 [–*x* + 1, –*y*, –*z*]
O^{1C}–H^1	0.87(2)	2.09(2)	150(1)	2.87(2)	O^2 [*x* – 1/2, *y* + 1/2, *z*]

of **VIId**, the coupling constant between 5-F and 4-CF_3 is $^4J_{FF}$ = 19.5 Hz, i.e., it is equal to that observed in the spectrum of **VIIa**. Compounds **VIIb** and **VIIc** displayed even larger $^4J_{FF}$ values for C^5 and 4-CF_2: $^4J(5\text{-F},F_A) \approx 40$, $^4J(5\text{-F},F_B) \approx 25$ Hz. Obviously, these values are typical of *cis* orientation of the interacting atoms; i.e., dihydrooxazoles **VIIb**–**VIId** have *trans* configuration.

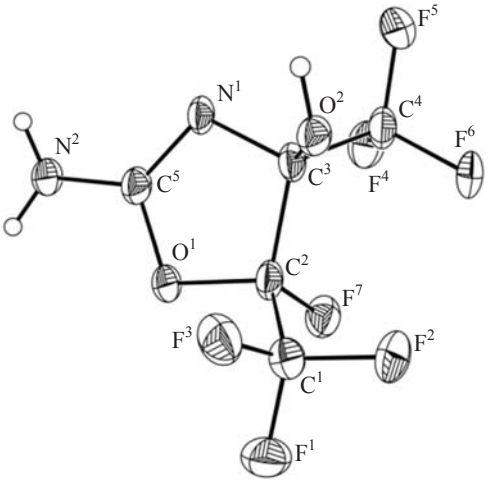


Fig. 1. Structure of the molecule of 2-amino-5-fluoro-4*t*,5*r*-bis(trifluoromethyl)-4,5-dihydrooxazol-4-ol (**VIIa**) according to the X-ray diffraction data.

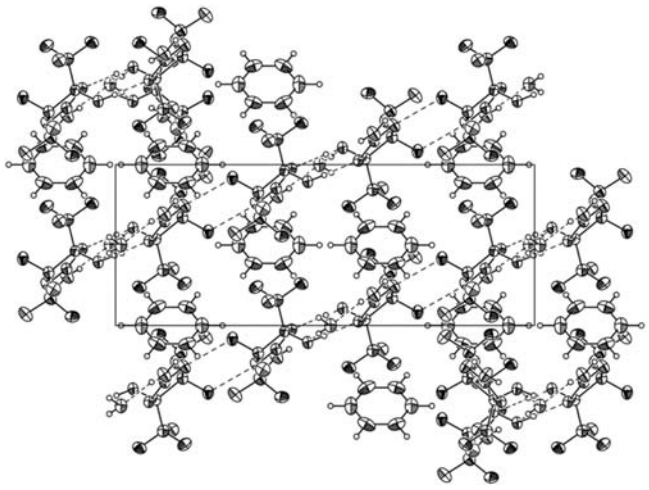


Fig. 2. A fragment of crystal packing of 4*t*,5*r*-2-amino-5-fluoro-4,5-bis(trifluoromethyl)-4,5-dihydrooxazol-4-ol (**VIIa**); a view along the *c* crystallographic axis is shown.

In the ^{1}H NMR spectra of **VIIa**–**VIId** in DMSO-d_6, the OH proton signal appears as a doublet with a coupling constant of ~2.0 Hz. It is reasonable to presume that the observed splitting results from coupling with 5-F through four bonds. Using the ^{19}F–{^{1}H} and ^{1}H–{^{19}F} double resonance techniques we found that, in fact, the OH signal in the spectra of **VIIa** and **VIId** (where the substituent on C^4 is trifluoromethyl group) is split into doublet due to interaction with F^5. However, suppression of the 5-F signal in the spectra of **VIIb** and **VIIc** led to only insignificant narrowing of the OH doublet, whereas the latter was converted into a singlet only upon suppression of resonance of one fluorine atom (downfield signal) in the difluoromethylene group on C^4.

Thus, we have proposed a new synthetic approach to previously unknown fluoroalkyl-substituted nitrogen-containing heterocycles, glycolurils **IVa**–**IVc** and dihydrooxazoles **VIIa**–**VIId**, which is based on reactions of urea with internal perfluoroolefin oxides. The reactions in polar aprotic solvents, such as DMSO, DMA, and acetonitrile, give 20–42% of bis(perfluoroalkyl)glycolurils **IVa**–**IVc**, whereas in weakly polar dioxane bis(perfluoroalkyl)dihydrooxazoles **VIIa**–**VIId** are formed with high selectivity (yield 60–66%) as a result of primary nucleophilic attack by the carbonyl oxygen atom in urea molecule on the oxirane carbon atom.

EXPERIMENTAL

The IR spectra were recorded in the range from 400 to 4000 cm^{-1} on a Perkin–Elmer Spectrum One spectrometer with Fourier transform from samples dispersed in mineral oil. The ^{1}H, ^{13}C–{^{1}H}, and ^{19}F NMR spectra were obtained on a Bruker DRX-400 spectrometer at 400, 100, and 376 MHz, respectively, using tetramethylsilane (^{1}H, ^{13}C) or C_6F_6 (^{19}F) as internal reference and DMSO-d_6 as solvent (unless otherwise stated). The mass spectra (electron impact, 70 eV) were recorded on a GV 7070 E instrument. The ele-

mental compositions were determined with the aid of a Perkin–Elmer PE 2400 analyzer.

Initial perfluorooxiranes **I–III** were synthesized according to the procedure described in [14]. The solvents used in this work were purified and dehydrated by standard methods [17]. The product ratios were calculated from the intensities of the corresponding signals in the ^{19}F NMR spectra of the reaction mixtures.

X-Ray analysis of compound VIIa. Single crystals of *trans*-**VIIa** were obtained by crystallization from moist benzene; a fragment of a 0.43×0.36×0.28-mm crystal (colorless prism) was taken for the analysis. The X-ray diffraction data were acquired at 100(2) K according to standard procedure on an Xcalibur 3 four-circle automatic diffractometer equipped with a CCD detector (MoK_α irradiation, graphite monochromator, ω-scanning with a step of 1°). Total of 11821 reflection intensities were measured, 3422 of which were independent (R_{int} = 0.056), and 1963 reflections had intensities $I > 2\sigma(I)$. Completeness of edge scans (Θ < 26.00°) 98.1%. Monoclinic crystal system, space group $C2/c$; unit cell parameters: a = 7.4461(9), b = 19.0773(18), c = 16.551(2) Å; β = 100.957(12)°; V = 2308.2(5) Å^3. The structure was solved by the direct method and was refined using the full-matrix least-squares procedure in anisotropic approximation (isotropic for hydrogen atoms). Hydrogen atoms involved in hydrogen bonds were localized by the direct method, and their positions were refined independently. The other hydrogen atoms were involved in the refinement procedure using the riding model with dependent thermal parameters. No correction for absorption was introduced, taking into account its small value (μ = 0.200 mm^{-1}). The final divergence factors were R_1 = 0.0908, wR_2 = 0.1107 for all reflections and R_1 = 0.0478, wR_2 = 0.1029 for reflections with $I > 2\sigma(I)$; goodness of fit 1.000. The maximal and minimal residual electron densities were 0.423 and –0.261 e/Å^3, respectively. All calculations were performed using SHELX97 software package [18]. The complete set of crystallographic data was deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 732101) and are available upon request (*www.ccdc.cam.ac.uk/data_request/cif*).

Reaction of 2,3-epoxyoctafluorobutane (I) with urea. *a*. A glass ampule was charged with 8.0 g (37 mmol) of compound **I**, 7.1 g (118.3 mmol) of urea, and 20 ml of DMSO, and the ampule was sealed and heated for 6 h on a boiling water bath with occasional shaking. The ampule was cooled to –70°C and opened, the mixture was poured into 200 ml of ice water, and the precipitate was filtered off, washed with acetone, and dried at ~60–70°C. We thus isolated 2.2 g (21%) of compound **IVa**. An analytical sample of **IVa** was obtained by recrystallization from anhydrous acetone.

1,5-Bis(trifluoromethyl)-2,4,6,8-tetraazabicyclo-[3.3.0]octane-3,7-dione (IVa). White powder, decomposition point 328–330°C. IR spectrum, ν, cm^{-1}: 1690, 1704, 1742 (C=O), 2500–3500 (NH). ^1H NMR spectrum: δ 8.83 ppm, s (NH). ^{13}C NMR spectrum, δ_C, ppm: 77.11 q (C^1, C^5, $^2J_{CF}$ = 35.3 Hz), 121.89 q (CF_3, $^1J_{CF}$ = 285.3 Hz), 158.27 s (C^3, C^7). ^{19}F NMR spectrum: δ_F 86.67 ppm, s (CF_3). Mass spectrum, m/z (I_{rel}, %): 279 (2.2) $[M + 1]^+$, 278 (10.3) $[M]^+$, 235 (29.1) $[M – NHCO]^+$, 209 (100) $[M – CF_3]^+$, 196 (30.2) $[M – C_2F_3H]^+$, 166 (36.2) $[M – CF_3 – CONH]^+$, 140 (9.6) $[M – 2CF_3]^+$, 139 (46.4) $[M – H – 2CF_3]^+$, 138 (11.0) $[M – 2CF_3H]^+$, 123 (46.5) $[CF_3C(NH)C(NH)]^+$, 113 (25.8), 112 (25.7) $[M – 2CF_3 – CO]^+$, 97 (14.5) $[M – 2CF_3 – CONH]^+$, 96 (55.3) $[M – 2CF_3 – CON]^+$, 92 (6.6), 77 (12.9), 76 (6.9), 70 (7.3) $[CF_3H]^+$, 69 (79.8) $[CF_3]^+$. Found, %: C 26.0; H 1.3; F 41.0; N 20.1. $C_6H_4F_6N_4O_2$. Calculated, %: C 25.9; H 1.4; F 41.0; N 20.1.

b. The reaction of 1.5 g (6.9 mmol) of compound **I** with 1.3 g (21.7 mmol) of urea in 20 ml of DMA was carried out in a similar way (reaction time 5 h). Yield of **IVa** 0.6 g (31%).

c. The reaction of 1.5 g (6.9 mmol) of compound **I** with 1.7 g (28.5 mmol) of urea in 40 ml of acetonitrile was carried out in a similar way. Yield of **IVa** 0.8 g (42%).

d. A glass ampule was charged with 3.0 g (13.9 mmol) of compound **I**, 1.7 g (28.3 mmol) of urea, and 50 ml of dioxane, and the ampule was sealed and heated for 20 h on a boiling water bath with occasional shaking. The ampule was cooled and opened, and the mixture was poured into 300 ml of ice water. The aqueous dioxane solution was extracted with diethyl ether, the extract was dried over $MgSO_4$ and evaporated, and the solid residue, 4.0 g, was dried at ~40–50°C and recrystallized from benzene–hexane. Yield of compound **VIIa** 2.2 g (62%).

***trans*-2-Amino-5-fluoro-4,5-bis(trifluoromethyl)-4,5-dihydrooxazol-4-ol (VIIa).** White powder, mp 111–111.5°C. IR spectrum, ν, cm^{-1}: 1595 (δNH), 1680 sh, 1700, (C=N), 3030 br (OH), 3185, 3260, 3330, 3380, 3400 sh, 3520 (OH, NH). ^1H NMR spectrum, δ, ppm: 7.80 br.s (2H, NH_2), 8.03 d (1H, OH,

J_{HF} = 2.2 Hz). ^{13}C NMR spectrum, δ_C, ppm (acetone-d_6): 99.16 q.d (C^4, $^2J_{CF}$ = 32.2, 24.5 Hz), 112.68 d.q (C^5, $^1J_{CF}$ = 251.5, $^2J_{CF}$ = 35.9 Hz), 120.40 q.d (5-CF_3, $^1J_{CF}$ = 283.3, $^2J_{CF}$ = 39.4 Hz), 123.28 q (4-CF_3, $^1J_{CF}$ = 285.2 Hz), 162.78 s (C^2). ^{19}F NMR spectrum, δ_F, ppm: 30.62 q.q.d (1F, 5-F, $^4J_{FF}$ = 19.5, $^3J_{FF}$ = 2.9, $^4J_{FH}$ = 2.2 Hz), 84.07 d.q (3F, 4-CF_3, $^4J_{FF}$ = 19.5, $^5J_{FF}$ = 1.7 Hz), 84.98 d.q (3F, 6-CF_3, $^3J_{FF}$ = 2.9, $^5J_{FF}$ = 1.7 Hz). Found, %: C 23.5; H 1.0; F 52.1; N 11.2. $C_5H_3F_7N_2O_2$. Calculated, %: C 23.4; H 1.2; F 52.0; N 10.9.

Reaction of 3,4-epoxydodecafluorohexane (II) with urea. *a*. As described above for the reaction of compound **I** with urea (method *a*), the reaction of 7.2 g (22.8 mmol) of compound **II** with 4.1 g (68.3 mmol) of urea in 20 ml of DMSO gave 2.5 g (29%) of compound **IVb**.

1,5-Bis(pentafluoroethyl)-2,4,6,8-tetraazabicyclo-[3.3.0]octane-3,7-dione (IVb). White powder, mp 324–326°C (decomp.). IR spectrum, ν, cm^{-1}: 1700, 1745 (C=O); 3240 br, 3110 sh, 3440 br (NH). ^1H NMR spectrum: δ 8.49 ppm, s (NH). ^{13}C NMR spectrum (acetone-d_6), δ_C, ppm: 79.33 t.t (C^1, C^5, $^2J_{CF}$ = 27.8, $^3J_{CF}$ = 13.1 Hz), 111.72 t.q (CF_2, $^1J_{CF}$ = 267.8, $^2J_{CF}$ = 35.9 Hz), 118.33 q.t (CF_3, $^1J_{CF}$ = 289.2, $^2J_{CF}$ = 36.6 Hz), 158.63 s (C^3, C^7). ^{19}F NMR spectrum, δ_F, ppm: 84.66 s (CF_3), 43.59 s (CF_2). Found, %: C 25.4; H 1.2; F 50.0; N 14.8. $C_8H_4F_{10}N_4O_2$. Calculated, %: C 25.4; H 1.1; F 50.3; N 14.8.

b. Likewise, by reaction of 3.1 g (9.8 mmol) of **II** with 1.2 g (20 mmol) of urea in 50 ml of dioxane we obtained 2.1 g (60%) of dihydrooxazole **VIIb**.

***trans*-2-Amino-5-fluoro-4,5-bis(pentafluoroethyl)-4,5-dihydrooxazol-4-ol (VIIb).** White powder, mp 129°C. IR spectrum, ν, cm^{-1}: 1589, 1605 (δNH); 1706, 1733 (C=N); 3118 br, 3360, 3510, 3521 (OH, NH). ^1H NMR spectrum, δ, ppm: 7.89 br.s (2H, NH_2), 7.99 d (1H, OH, J_{HF} = 1.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 100.53 q (C^4, $^2J_{CF}$ = 24.4 Hz), 109.46 t.d.q (5-CF_2, $^1J_{CF}$ = 264.9, $^2J_{CF}$ = 43.3, 37.3 Hz), 112.31 t.q (4-CF_2, $^1J_{CF}$ = 264.6, $^2J_{CF}$ = 34.5 Hz), 112.62 d.d.d (C^5, $^1J_{CF}$ = 252.6, $^2J_{CF}$ = 36.4, 25.8 Hz), 117.90 q.t (CF_3, $^1J_{CF}$ = 288.8, $^2J_{CF}$ = 34.8 Hz), 118.60 q.t (CF_3, $^1J_{CF}$ = 288.6, $^2J_{CF}$ = 35.7 Hz), 160.79 s (C^2). ^{19}F NMR spectrum, δ_F, ppm: 33.92 m (1F, 5-F), 36.13 d.d.d (1F, 5-CF_B, $^2J_{FF}$ = 291.4, J_{FF} = 24.5, 7.4 Hz), 41.86 d.d (1F, 6-CF_A, $^2J_{FF}$ = 291.4, $^3J_{FF}$ = 10.3 Hz), 37.56 d.t (1F, 4-CF_B, $^2J_{FF}$ = 275.6, J_{FF} = 24.5 Hz), 44.04 d.d.d (1F, 4-CF_A, $^2J_{FF}$ = 275.6, $^4J_{FF}$ = 39.8, $^4J_{FH}$ = 1.9 Hz), 82.78 d.d (3F, 5-$CF_2C\mathbf{F}_3$, J_{FF} = 13.2, 1.3 Hz), 84.69 d.d (3F, 4-$CF_2C\mathbf{F}_3$, J_{FF} = 2.6, 1.6 Hz). Found, %: C 23.8; H 0.6; F 59.0; N 8.1. $C_7H_3F_{11}N_2O_2$. Calculated, %: C 23.6; H 0.8; F 58.7; N 7.9.

Reaction of 2,3-epoxydodecafluorohexane (III) with urea. *a*. The reaction was performed as described above (method *a*) with 7.5 g (18.7 mmol) of compound **III** and 4.3 g (57 mmol) of urea in 17 ml of DMSO. Yield of **IVc** 2.1 g (23%).

1-Heptafluoropropyl-5-trifluoromethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (IVc). mp 326–328°C (decomp.). IR spectrum, ν, cm^{-1}: 1705, 1735 sh (C=O); 3095 br, 3220 br (NH). ^1H NMR spectrum, δ, ppm: 8.64 s (2H, NH), 8.93 s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 78.22 t (C^5, $^2J_{CF}$ = 29.0 Hz), 79.03 q (C^1, $^2J_{CF}$ = 34.7 Hz), 108.76–116.12 m ($C^{1'}$, $C^{2'}$), 114.65 q ($C^{3'}$, $^1J_{CF}$ = 294.5 Hz), 121.97 q ($C^{1''}$, $^1J_{CF}$ = 284.3 Hz), 158.32 s (C^3, C^7). ^{19}F NMR spectrum, δ_F, ppm: 41.03 m (2F, 2′-F), 46.01 m (2F, 1′-F), 81.88 t (3F, 3′-F, J_{FF} = 10.9 Hz), 88.23 t.t (3F, 1″-F, J_{FF} = 21.5, 4.9 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 379 (2.2) $[M + 1]^+$, 378 (6.7) $[M]^+$, 336 (7.2) $[M - NCO]^+$, 335 (82.3) $[M - NHCO]^+$, 296 (34.7) $[M - C_2F_3H]^+$, 281 (5.9) $[M - C_2F_3H - NH]^+$, 276 (8.6) $[M - C_2F_3]^+$, 273 (17.2), 266 (7.3) $[M - CF_3 - CONH]^+$, 239 (35.9) $[M - 2CF_3 - H]^+$, 223 (9.1) $[C_3F_7C(NH)C(NH)]^+$, 216 (23.7), 213 (21.4), 210 (6.1), 209 (85.0) $[M - C_3F_7]^+$, 201 (8.5), 196 (18.5) $[M - 2CF_3H - CON]^+$, 181 (5.6) $[M - C_3F_7 - CN]^+$, 173 (6.1), 169 (20.4) $[C_3F_7]^+$, 166 (47.8), 146 (5.7), 140 (9.5) $[M - CF_3 - C_3F_7]^+$, 139 (61.3) $[M - CF_3H - C_3F_7]^+$, 138 (9.2) $[M - C_3F_7H - CF_3H]^+$, 131 (8.6), 123 (55.3) $[CF_3CNCO]^+$, 121 (6.4), 120 (5.7), 119 (15.3) $[C_2F_5]^+$, 113 (44.2), 112 (21.7), 108 (6.1) $[CF_3C(NH)C]^+$, 78 (5.7), 77 (8.7), 76 (5.1), 70 (8.9) $[CF_3H]^+$, 69 (100) $[CF_3]^+$. Found, %: C 25.6; H 0.9; F 50.0; N 14.7. $C_8H_4F_{10}N_4O_2$. Calculated, %: C 25.4; H 1.1; F 50.3; N 14.8.

b. The reaction of 3.2 g (10.1 mmol) of compound **III** with 2.1 g (35 mmol) of urea in 50 ml of dioxane was carried out in a similar way. When the reaction was complete, the ampule was cooled to –70°C and opened, the mixture was poured into 200 ml of ice water, and the precipitate was filtered off, washed with water, dried at ~40–50°C, and recrystallized from hexane–benzene to isolate 0.7 g (19%) of compound **VIIc** as white powder. The filtrate was extracted with diethyl ether, dried over $MgSO_4$, and evaporated. The solid residue was a mixture of regioisomeric dihydrooxazoles **VIIc** and **VIId**; it was dried at ~40–50°C and recrystallized from benzene–hexane. We thus isolated 1.7 g (47%) of a mixture of *trans* isomers of **VIIc** and **VIId** at a ratio of 2:1 (white powder).

***trans*-2-Amino-5-fluoro-4-heptafluoropropyl-5-trifluoromethyl-4,5-dihydrooxazol-4-ol (VIIc).** mp 112–113°C. IR spectrum, ν, cm^{-1}: 1596 (δNH); 1702, 1732 sh (C=N); 3100 br, 3380, 3500 (OH, NH). ^1H NMR spectrum, δ, ppm: 7.90 br.s (2H, NH_2), 8.07 d (1H, OH, J_{HF} = 2.0 Hz). ^{19}F NMR spectrum, δ_F, ppm: 31.11 d.d.m (1F, 5-F, $^4J_{FF}$ = 38.9, 24.6 Hz), 38.19 d.d.m (1F, 2″-F_B, $^2J_{FF}$ = 287.1, J_{FF} = 9.9 Hz), 41.74 d.m (1F, 1″-F_B, $^2J_{FF}$ = 282.4 Hz), 41.85 d.m (1F, 2″-F_A, $^2J_{FF}$ = 287.1 Hz), 46.35 d.d.q.d (1F, 1″-F_A, $^2J_{FF}$ = 282.4, $^4J_{FF}$ = 38.7, J_{FF} = 11.3, 9.6 Hz), 82.36 d.d (3F, 3″-F, $^4J_{FF}$ = 11.3, 8.1 Hz), 85.18 d (3F, 1′-F, J_{FF} = 7.3 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 339 (10.9) $[M - OH]^+$, 337 (10.9) $[M - F]^+$, 289 (6.0), 240 (38.2) $[M - CF_3CFO]^+$, 220 (6.7) $[M - CF_3CFO - HF]^+$, 197 (11.5), 188 (5.5) $[M + 1 - C_3F_7]^+$, 187 (100) $[M - C_3F_7]^+$, 169 (32.2) $[C_3F_7]^+$, 121 (38.0), 119 (8.2) $[C_2F_5]^+$, 111 (7.1), 109 (8.5), 100 (9.4) $[C_2F_4]^+$, 97 (17.1), 78 (8.6), 71 (21.9), 70 (15.2) $[CF_3H]^+$, 69 (100) $[CF_3]^+$. Found, %: C 23.9; H 0.6; F 58.7; N 7.9. $C_7H_3F_{11}N_2O_2$. Calculated, %: C 23.6; H 0.8; F 58.7; N 7.9.

***trans*-2-Amino-5-fluoro-5-heptafluoropropyl-4-trifluoromethyl-4,5-dihydrooxazol-4-ol (VIId).** IR spectrum, ν, cm^{-1}: 1596 (δNH); 1702, 1732 sh (C=N); 3100 br, 3380, 3500 (OH, NH). ^1H NMR spectrum, δ, ppm: 7.83 br.s (2H, NH_2), 8.02 d (1H, OH, J_{HF} = 2.2 Hz). ^{19}F NMR spectrum, δ_F, ppm: 32.99 m (1F, 5-F), 37.30 d.d.d (1F, 2′-F_B, $^2J_{FF}$ = 288.3, J_{FF} = 11.4, 10.1 Hz), 39.74 d.d.d.d (1F, 2′-F_A, $^2J_{FF}$ = 288.3, J_{FF} = 24.1, 11.0, 5.1 Hz), 40.50 d.m (1F, 1′-F_B, $^2J_{FF}$ = 298.6 Hz), 44.41 d.d.q (1F, 1′-F_A, $^2J_{FF}$ = 298.6, J_{FF} = 22.6, 11.4 Hz), 82.21 d.d.d (3F, 3′-F, J_{FF} = 11.4, 8.5, 3.0 Hz), 84.41 d.d (3F, 1″-F, J_{FF} = 20.2, 7.0 Hz).

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