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Synthesis of fluorine containing N-heterocycles using oxides of terminal perfluoroolefins and urea

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ABSTRACT

The reaction of octafluoro-1,2-epoxybutane (**1**) with urea in Me_2SO, aqueous Me_2SO, aqueous dioxane, aqueous acetonitrile and of hexadecafluoro-1,2-epoxyoctane (**2**) with urea in aqueous Me_2SO gave perfluoroalkylhydantoins – 5-hydroxy-5-pentafluoroethylimidazolidine-2,4-dione (**4a**) (yield 40–42%) and 5-hydroxy-5-tridecafluorohexylimidazolidine-2,4-dione (**4b**) (yield 54%), respectively. Use of dioxane and acetonitrile in the reaction of oxiranes **1**, **2** with urea led to unexpected heterocyclic products – perfluoroalkyloxazoles **7a**, **b** (yield 11–82%). Perfluoroalkyl containing allantoin – 5-tridecafluorohexyl-5-ureidoimidazolidine-2,4-dione (**3b**) (yield 19%) and polyfluoroalkyl containing urea–(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-1-hydroxyheptyl)urea (**6b**) (yield 46%) have been first obtained by the reaction of oxirane **2** with urea in Me_2SO and aqueous Me_2SO, respectively.

The molecular and crystal structure of hydantoin **4a** has been studied by X-ray crystallography.

1. Introduction

The chemistry of N-heterocycles based on urea, such as glycolurils, imidazolidine-2-ones and oxazolines, is of great interest due to high physiological activity of these compounds [1,2]. So, one of representatives of glycolurils of octane series, 2,4,6,8-tetramethylglycoluril (mebicar), is used in medical practice as a daytime tranquilizer [1]. Among imidazolidine-2-ones phenytoin is known as antiepileptic drug. Antihypertensive substance, rilmenidine (albarel) has been prepared on the base of oxazoline derivatives [1]. Moreover, hydantoins and oxazolines can be used as insecticides and acaricides [3], herbicides [4], plant growth regulators [5], polymer stabilizers, plasticizers for rubber, *etc.* [5,6].

The principal methods known for preparation of glycolurils and 4,5-dihydroxyimidazolidine-2-ones, rather extensively studied compounds, are based on interaction of ureas with α-dicarbonyl compounds [7]. At the same time, literature data on synthesis and properties of their fluorine containing analogs are limited. So, the reaction between trifluoropyruvic acid hydrate and urea derivatives has been used to prepare 5-trifluoromethyl-5-hydroxyhydantoins [8,9]. 5-Acetoxyhydantoins have been obtained by the reaction of 2-amino-4-trifluoromethyloxazoles with excess bromine in acetic acid/sodium acetate [10]. Another way to 5-polyfluoroalkylhydantoins has been reported from of 2,4,5-imidazolidinetriones and alkylsilanes in the presence of tetrabutyl-ammonium fluoride [11]. In addition, we recently proposed a novel method for synthesis of fluorine containing glycolurils and oxazolines based on interaction of oxides of internal perfluoroolefins with urea [12].

It is known that oxides of terminal perfluoroolefins are convenient syntons, they easily react with mono- and bifunctional nucleophilic reagents resulting in fluorine containing polyfunctional and heterocyclic compounds [13–15]. It has been shown earlier that hexafluoropropylene oxide (HFPO) gives fluorine containing heterocyclic compounds, such as thiazolines [16], quinoxalines, benzoxazines and benzothiazines [17] when reacts with bifunctional nucleophilic reagents: thiourea, *o*-phenylenediamine, 2-aminophenol and 2-aminothiophenol, respectively; but there are no data in the literature on reactions of oxides of terminal perfluoroolefins with urea.

In this work we have studied the reaction of octafluoro-1,2-epoxybutane (**1**) and hexadecafluoro-1,2-epoxyoctane (**2**) [18,19] with urea for the purpose of the preparing N-heterocyclic compounds containing perfluoroalkyl substituent: perfluoroalkylallantoins, perfluoroalkylhydantoins and perfluoroalkyloxazoles.

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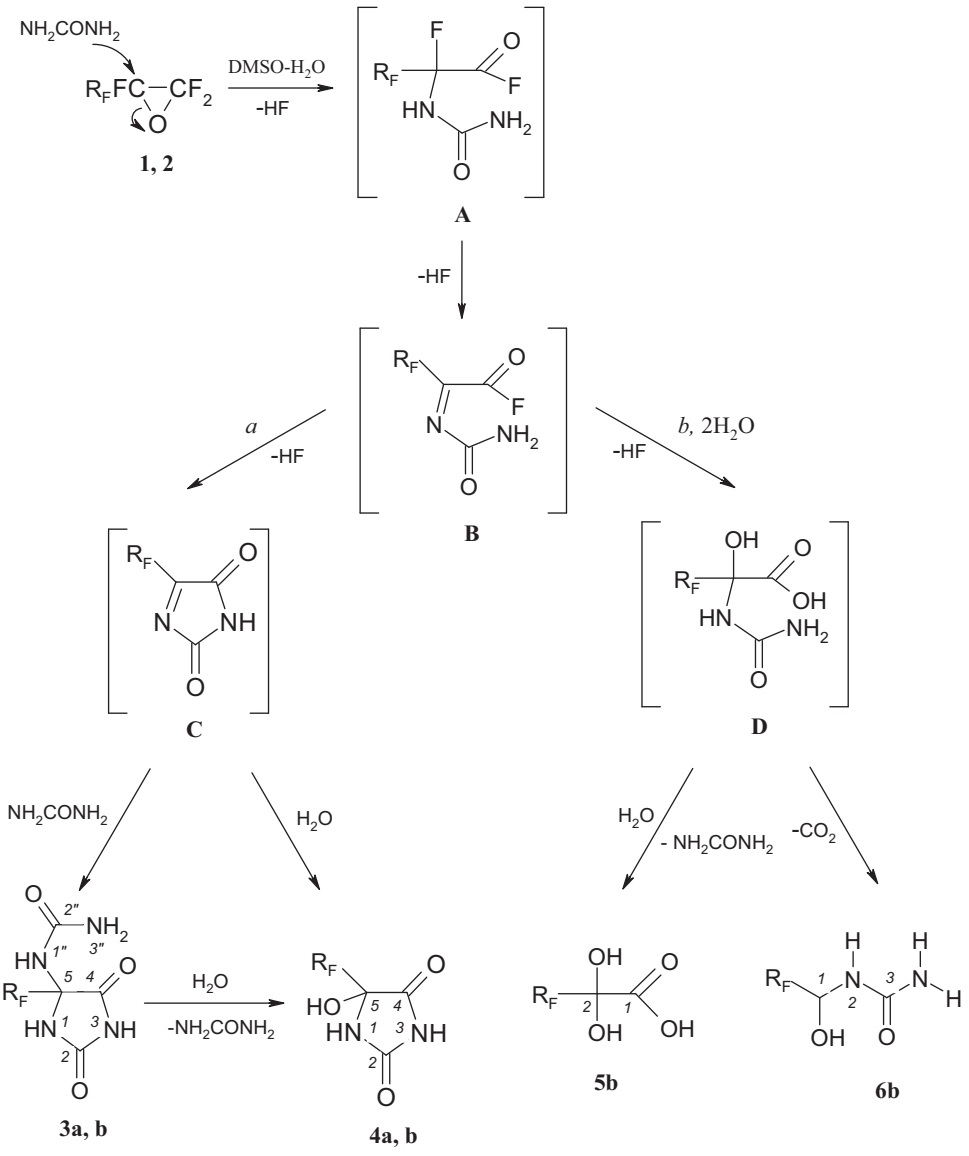
2. Results and discussion

We have found that the structure of the reaction products depends on a solvent type, temperature and volume of perfluoralkyl substituent in the starting oxirane.

So, oxirane **2** rather easily reacts with urea in Me_2SO (Me_2SO:H_2O ~ (99:1) at room temperature resulting in perfluoroalkyl containing allantoin – 5-tridecafluoro-5-ureidoimidazolidine-2,4-dione (**3b**) and hydantoine – 5-hydroxy-5-tridecafluorohexyl-5-ureidoimidazolidine-2,4-dione (**4b**) in a ratio ~1:1 (Scheme 1, Table 1, run 1). Probably, the reaction begins with the attack of one of amino groups of urea on the C-2 carbon atom of the oxirane **2**, followed by ring opening and formation of intermediate **A** and then – **B**, which gives the heterocycle **C** as a result of intramolecular cyclization. The latter is unstable under the reaction conditions and adds yet another molecule of urea at C=N bond, giving allantoin **3b**. Interestingly, in contrast to oxides of internal perfluoroolefins, which give glykolurils under the action of urea in Me_2SO [9], further intramolecular cyclization of allantoin **3b** to corresponding glykoluril is not observed in the reaction, apparently, due to relatively low electrophilicity of the carbonyl carbon atom C-4 of imidazolidine cycle **3b**. The other pathway for stabilization of the intermediate **C** is formation of hydantoin **4b** as a result of addition of water which is present in trace amounts in the solvent.

It should be noted that with increasing water content in the Me_2SO the fraction of hydantoin **4b** in the final product increases, and of allantoin **3b** – is reduced. Thus, in 94% aqueous Me_2SO at room temperature, compounds **3b, 4b** in a ratio of ~30:70 have been obtained as the reaction products (Scheme 1 and Table 1, run 2).



	R_F
1, 3a, 4a	$C^{2'}F_3C^{1'}F_2$
2, 3b-6b	$C^{6'}F_3C^{5'}F_2C^{4'}F_2C^{3'}F_2C^{2'}F_2C^{1'}F_2$

Scheme 1.

Table 1
Composition and molar ratios of the products of the reaction of oxiranes **1**, **2** with urea at the molar ratio oxirane:reagent ~ 1:3.

Run no.	Starting oxirane	Solvent	Temperature, °C	Reaction products (molar ratio (%), from ^{1}H, ^{19}F NMR)
1	**2**	Me_2SO–H_2O (99:1)	20	**3b**, **4b** (~50:50)
2	**2**	Me_2SO–H_2O (94:6)	20	**3b**, **4b** (~30:70)
3	**2**	Me_2SO–H_2O (94:6)	70–80	**4b**, **5b** (~74:26)
4	**2**	Me_2SO–H_2O (94:6)	100	**4b**, **6b** (~31:69)
5	**1**	Me_2SO–H_2O (99:1)	20	**4a**
6	**1**	Me_2SO–H_2O (94:6)	20	**4a**
7	**2**	Dioxane	100	**7b**
8	**2**	MeCN	70–80	**7b**
9	**1**	Dioxane	70–80	**7a**, **4a** (~30:70)
10	**1**	MeCN	70–80	**7a**, **4a** (~50:50)
11	**2**	Dioxane–H_2O (90:10)	100	**4b**, **7b** (~40:60)
12	**2**	MeCN–H_2O (93:7)	70–80	**4b**, **7b** (~33:67)
13	**1**	Dioxane–H_2O (95:5)	70–80	**4a**
14	**1**	MeCN–H_2O (93:7)	70–80	**4a**

As can be seen in Table 1, an increase in temperature of the reaction carried out in 94% aqueous Me_2SO up to 70–80 °C leads to formation of hydantoin **4b** and small amounts of 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-2,2-dihydroxyoctanoic acid (**5b**) (Scheme 1 and Table 1, run 3), and at 100 °C (2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-1-hydroxyheptyl)urea (**6b**) is formed along with heterocycle **4b** (Scheme 1 and Table 1, run 4). Apparently, the formation of compounds **5b, 6b** in this case proceeds by the path *b*: the stabilization of the intermediate fluoride **B** is realized through hydrolysis and acid **D** formation which gives the 2,2-dihydroxytridecafluorooctanoic acid **5b** as a result of elimination of urea molecule. Further acid cleavage of intermediate **D** with the elimination of CO_2 leads to the substituted urea **6b**.

The other way of the acid **5b** formation can proceed *via* the interaction of oxirane **2** with H_2O [20]. The absence of the compound **3b** among the reaction products may be caused not only by the participation of water in stabilizing the intermediate **C**, but also the transformation of compound **3b** into the imidazolidine **4b** by hydrolysis (Scheme 1, path *a*).

The structure of compounds **3b**, **4b**, isolated in individual form, was confirmed by IR, ^{1}H, ^{19}F, ^{13}C NMR spectroscopy and elemental analysis.

In Me_2SO (Me_2SO:H_2O ~ 99:1, 94:6), a similar reaction of oxirane **1**, less spatially shielded in comparison with compound **2**, proceeds exothermically, with the formation of hydantoin **4a** and only trace amounts of allantoin **3a** (Scheme 1 and Table 1, runs 5 and 6). In the ^{1}H NMR spectra of the crude product obtained by reacting oxirane **1** with urea in Me_2SO, along with signals of imidazolidine **4a** there was a group of signals at 6.09 (br.s), 7.42 (s), 8.95 (s) and 11.17 (s) with a ratio of integral intensities of 2:1:1:1, which have been attributed to compound **3a**. Compound **4a** was isolated in pure form by crystallization and characterized by IR, ^{1}H, ^{19}F, ^{13}C NMR spectroscopy, elemental and X-ray analysis.

According to X-ray data, compound **4a** is crystallized in centrosymmetric space group. The imidazole ring is planar in limits 0.005 Å. CF_3-group is placed in anti-periplanar position towards OH-group and demonstrates strong libration of F-atoms. General geometry of the molecule **4a** is shown on Fig. 1. Molecular packing is characterized by system of intermolecular H-bonds (Table 2) and is formed by bimolecular layers (Fig. 2).

Another type of interacting oxirane **2** with urea takes place in dioxane and acetonitrile resulting in 2-amino-5-fluoro-5-trideca-fluorohexyloxazole-4-one (**7b**) (Scheme 2, path *a*, Table 1, lines 7, 8). Probably, in this case the reaction begins with the attack of the oxygen atom of urea on the epoxide carbon atom C2, leading to ring opening and formation of the adduct **H**, which forms heterocycle **7b** as a result of intramolecular cyclization. Such the reaction proceeding can be explained by the higher nucleophilicity of the

Table 2
Hydrogen bonds with H···A ⟨*r*(*A*) + 2.000 Å and angle D–H–A⟩ 110°.

D–H	*d*(D–H)	*d*(H···A)	∠DHA	*d*(D···A)	*A*
N2–H2	0.96(3)	2.04(3)	172(2)	2.986(3)	O1 [*x*, *y* − 1, *z*]
N1–H1	0.86(3)	2.11(3)	152(2)	2.893(3)	O3 [*x*, −*y* + 1/2, *z* + 1/2]
N1–H1	0.86(3)	2.56(3)	124(2)	3.124(3)	O2 [−*x*, −*y*, −*z* + 2]
O3–H3	0.79(3)	1.83(3)	173(2)	2.610(3)	O2 [*x*, −*y* − 1/2, *z* − 1/2]

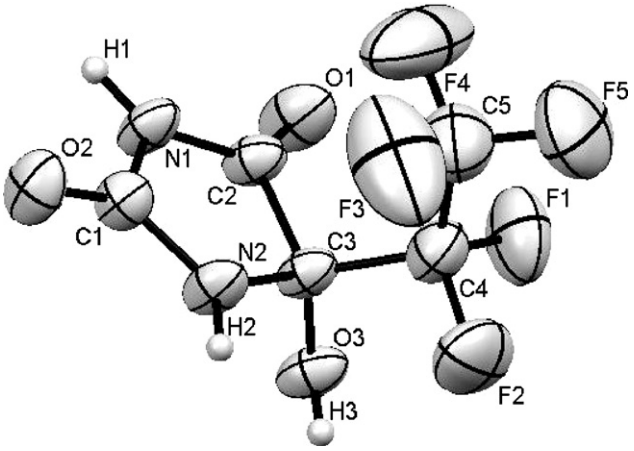


Fig. 1. Compound (**4a**) in thermal ellipsoids of 50% probability.

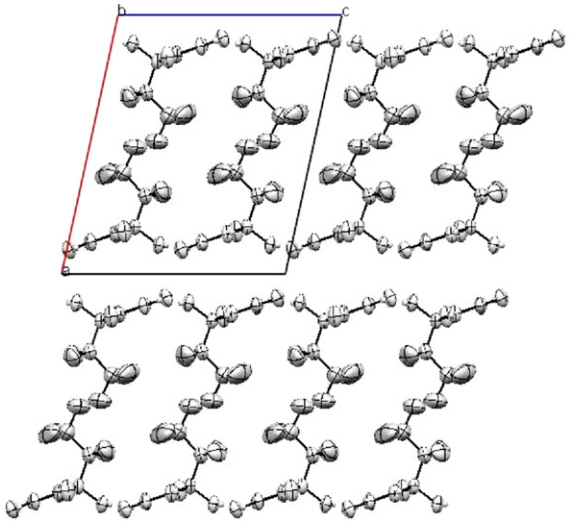
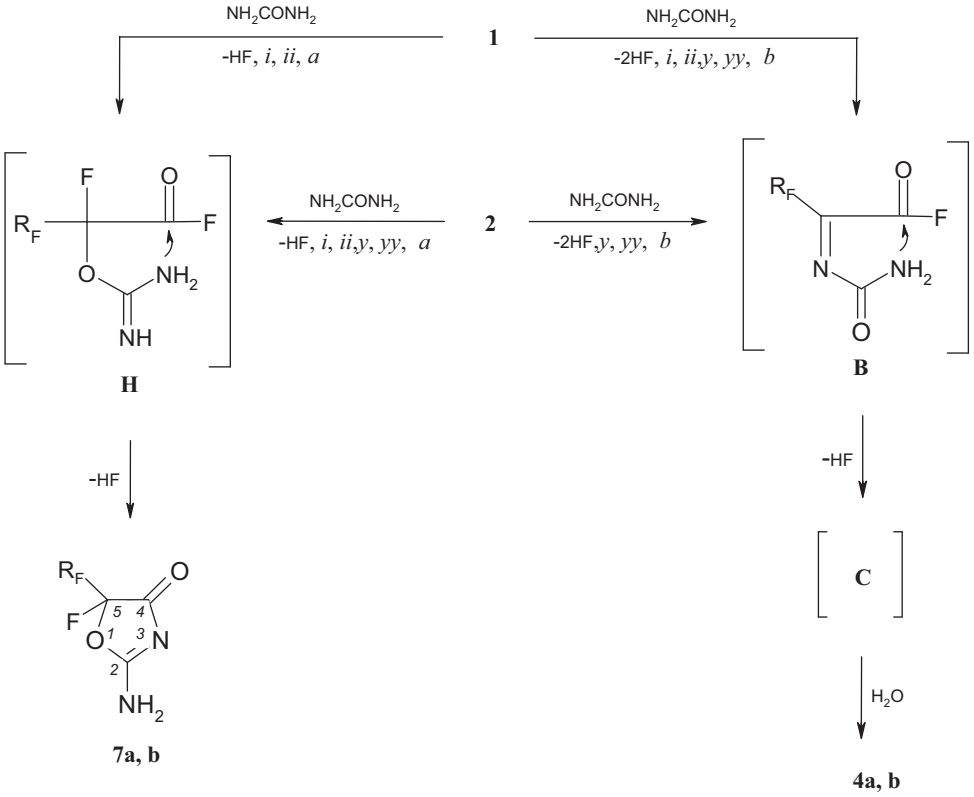


Fig. 2. Molecular packing of compound (**4a**).



	R_F
4a, 7a	$C^{2'}F_3C^{1'}F_AF_B$
4b, 7b	$C^{6'}F_3C^{5'}F_2C^{4'}F_2C^{3'}F_2C^{2'}F_2C^{1'}F_AF_B$

Scheme 2. (*i*) Dioxane, 70–100 °C; (*ii*) MeCN, 70–80 °C; (*y*) dioxane–H_2O, 70–100 °C; (*yy*) MeCN–H_2O, 70–80 °C.

urea carbonyl oxygen atom in these solvents – low-polar dioxane, which forms hydrogen bonds with H atoms of amino groups of the nucleophile does not promote N–H bond ionization, in contrast to the polar Me_2SO; in acetonitrile there is a specific solvation of urea with a hydrophilic CN group of the solvent, which also makes it difficult to attack the amino groups on C-2 atom of the oxirane **2** [21].

In contrast to oxirane **2**, the reaction of compound **1** with urea in dioxane and acetonitrile occurs both by path *a* and path *b* with the formation of oxazole **7a** and imidazolidine **4a** (Scheme 2 and Table 1, runs 9 and 10). Oxazole **7a** was not isolated in individual form and was characterized by ^1H, ^{19}F and ^{13}C NMR spectroscopy.

The reaction between oxirane **2** and urea in aqueous dioxane and aqueous acetonitrile gives mixtures of oxazole **7b** and imidazolidine **4b** (Scheme 2 and Table 1, runs 11 and 12), and compound **7b** can be easily isolated in the pure form by crystallization. In both solvents, proceeding the reaction by path *b* with the formation of heterocycle **4b** is likely due to participation of water in solvation of urea along with dioxane and acetonitrile, which leads to ionization of N–H bond and its activation [21].

A similar reaction of oxirane **1** with urea gives exclusively compound **4a**. This is probably due to greater stability of intermediates **B** and **C** in aqueous dioxane and aqueous acetonitrile as compared with intermediate **H** (Scheme 2 and Table 1, runs 13 and 14).

3. Conclusion

Thus, we have reported an approach to the synthesis of fluorine containing N-heterocyclic compounds – allantoin **3b**, hydantoins **4a**, **b** and oxazoles **7a**, **b** based on interaction of oxides of terminal perfluoroolefins **1**, **2** with urea. The reaction of octafluoro-1,2-epoxybutane (**1**) with urea in Me_2SO, aqueous Me_2SO, aqueous dioxane and aqueous acetonitrile and of hexadecafluoro-1,2-epoxioctane (**2**) with urea in aqueous Me_2SO gives perfluoroalkylhydantoins **4a**, **b** in yields 40–54%. In contrast to it, oxiranes **1**, **2** afford heterocyclic compounds of the other type – perfluoroalkyloxazoles **7a**, **b**, when interacting with urea in dioxane or acetonitrile. Perfluoroalkyl containing allantoin – 5-hexadecafluorohexyl-5-ureidoimidazolidine-2,4-dione (**5b**) and polyfluoroalkyl containing urea – (2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoro-1-hydroxyheptyl)urea (**6b**), which are of interest as biologically active compounds [22,23], have been first obtained by the reaction of oxirane **2** with urea in Me_2SO and aqueous Me_2SO, respectively.

4. Experimental

^1H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400, 100 and 376 MHz, respectively. Chemical shifts are reported in ppm (δ) from internal $(CH_3)_4Si$ for hydrogen and carbon and external CCl_3F for fluorine (Me_2SO-d_6). Infrared spectra were obtained on a Perkin Elmer Spectrum One FT-IR instrument in the interval 400–4000 cm^{-1} in the solid state as powders on a stick using a diffuse reflectance attachment (DRA) or as suspensions in fluorocarbon oil on KBr films. The ν_{max} is reported in cm^{-1}. Elemental analyses were carried out on a Perkin Elmer PE 2400 elemental analyzer. Melting points were measured in open capillaries and are reported uncorrected. Oxiranes **1**, **2** were prepared according to reported procedures [18,19]. Solvents were purified and dried according to standard procedures [24].

X-ray structural analysis of compound **4a** was accomplished for colorless crystal with crystal size 0.48 mm × 0.41 mm × 0.21 mm by using "Xcalibur 3" diffractometer (Mo Kα, 295(2) K, $\omega/2\theta$-scanning with step 1°, θ range for data collection 3.36–26.37°). Reflections collected 3688, independent reflections 1647 (R_{int} = 0.0277), reflections with $I > 2\sigma(I)$ 939. Crystal is monoclinic, space group $P2_1/c$, a = 12.4237(13) Å, b = 6.4159(6) Å, c = 10.4913(11) Å, β = 102.332(9)°, V = 816.96(14) Å^3. Limiting indices $-15 < h < 14$, $-6 < k < 8$, $-12 < l < 13$. Completeness to θ = 26.37° 98.6%. For Z = 4 empirical formula $C_5H_3F_5N_2O_3$, D_{calc} = 1.903 g/cm^3, μ = 0.222 mm^{-1}, F(0 0 0) 464. Structure was solved and refined with using SHELX-97 program package [25] by full-matrix least-squares on F^2. All non-hydrogen atoms were solved and refined anisotropically, H-atoms were solved by direct methods and refined in isotropic approximation. Final results of refinement: S = 1.004, R_1 = 0.0511, wR_2 = 0.1373 [$I > 2\sigma(I)$], R_1 = 0.0850, wR_2 = 0.1508 (all data), largest diff. peak and hole 0.325 and −0.368ē Å^{-3}.

Crystallographic data for the structure **4a** reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary no. CCDC 868931. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223/336 033; deposit@ccdc.cam.ac.uk.

4.1. The reaction of oxirane (1) with urea

4.1.1. Procedure 1 (Table 1, run 5)

A mixture of oxirane **1** (2.4 g, 11.11 mmol) and urea (2.0 g, 33.33 mmol) in 99% Me_2SO (4 mL) was allowed to stand at room temperature for 0.5 h in a sealed tube, with intermittent shaking (a moderate heating was observed). After cooling (−70 °C), the tube was opened and the content was poured into ice water (200 mL). The resultant solution was extracted with Et_2O, the extract was dried under $MgSO_4$, and the ether was removed by evaporation. The solid residue was washed with $CHCl_3$ and recrystallized from ethylacetate–benzene mixture to give 1.1 g (42.3%) of colorless crystals of hydantoine **4a**.

*4.1.1.1. 5-Hydroxy-5-pentafluoroethylimidazolidine-2,4-dione (**4a**), mp 197–198 °C.* IR (film): ν 3309, 3089, 2920 (NH, OH), 1798, 1749, 1723 (C=O). ^{1}H NMR: δ 8.42 (s, 1H, NH), 9.29 (s, 1H, NH), 11.35 (s, 1H, OH). ^{13}C NMR: δ 83.65 (t, $^2J_{CF}$ 26.3 Hz, C^5), 111.26 (tq, $^1J_{CF}$ 261.5, $^2J_{CF}$ 36.2 Hz, C$^{1'}$), 118.26 (qt, $^1J_{CF}$ 287.5, $^2J_{CF}$ 35.3 Hz, C$^{2'}$), 155.62 (s, C^2), 169.00 (s, C^4). ^{19}F NMR: δ −125.68 (d, 1F, $^2J_{FF}$ 277.4 Hz, C$^{1'}$F$_B$), −124.49 (d, 1F, $^2J_{FF}$ 277.4 Hz, C$^{1'}$F$_A$), −79.17 (s, 3F, C$^{2'}$F$_3$). Anal. calcd. for $C_5H_3F_5N_2O_3$: C, 25.64; H, 1.28; F, 40.59; N, 11.96. Found: C, 25.77; H, 1.21; F, 40.60; N, 11.68.

4.1.2. Procedure 2 (Table 1, run 6)

Similarly, oxirane **1** (3.1 g, 14.3 mmol) was treated with urea (2.6 g, 43.33 mmol) in 10 mL of 94% aqueous Me_2SO for 1 h. The reaction mixture was worked up as described above in Section 4.1.1. A solid residue obtained (1.6 g) was washed with $CHCl_3$ and recrystallized from ethylacetate–benzene mixture to give 1.3 g, 38.7% yield of compound **4a**.

4.1.3. Procedure 3 (Table 1, run 9)

Similarly, oxirane **1** (2.6 g, 12.04 mmol) was treated with urea (2.2 g, 36.67 mmol) in 20 mL of anhydrous dioxane for 1 h at 70–80 °C. The reaction mixture was worked up as described above in Section 4.1.1. A solid residue obtained (2.0 g) was washed with $CHCl_3$ and recrystallized from $CHCl_3$–MeCN mixture to give 1.3 g of oxazole **7a** and imidazolidine **4a** (~25:75, from ^{19}F, ^{1}H NMR) as colorless crystals.

*4.1.3.1. 2-Amino-5-fluoro-5-pentafluoroethyloxazole-4-one (**7a**).* ^{1}H NMR: δ 10.05 (s, 1H), 10.25 (s, 1H) (NH_2). ^{13}C NMR: δ 102.12 (ddd, $^1J_{CF}$ 250.8; $^2J_{CF}$ 35.9, 30.2 Hz, C^5), 108.64 (tdq, $^1J_{CF}$ 265.0, $^2J_{CF}$ 38.9 Hz, C$^{1'}$), 117.32 (qt, $^1J_{CF}$ 287.8, $^2J_{CF}$ 34.2 Hz, C$^{2'}$), 173.15 (s, C^2), 173.48 (d, $^2J_{CF}$ 18.4 Hz, C^4). ^{19}F NMR: δ −132.43 (dq, 1F, $^3J_{FF}$ 10.1, $^4J_{FF}$ 7.7 Hz, C^{5}F), −128.27 (dd, 1F, $^2J_{FF}$ 290.1, $^3J_{FF}$ 10.1 Hz, C$^{1'}$F$_B$), −127.10 (d, 1F, $^2J_{FF}$ 290.1 Hz, C$^{1'}$F$_A$), −80.58 (d, 3F, $^4J_{FF}$ 7.7 Hz, C$^{2'}$F$_3$).

4.1.4. Procedure 4 (Table 1, run 10)

Similarly, oxirane **1** (1.7 g, 7.87 mmol) was treated with urea (1.4 g, 23.33 mmol) in 8 mL of anhydrous MeCN for 0.5 h at 70–80 °C. The reaction mixture was worked up as described above in Section 4.1.1. A solid residue obtained (1.3 g) was washed with $CHCl_3$ and recrystallized from $CHCl_3$–MeCN mixture to give 1.0 g of oxazole **7a** and imidazolidine **4a** (~48:52, from ^{19}F, ^{1}H NMR) as colorless crystals.

4.1.5. Procedure 5 (Table 1, run 13)

Similarly to procedure Section 4.1.3, oxirane **1** (3.3 g, 15.28 mmol) was treated with urea (2.7 g, 45 mmol) in 30 mL of 95% aqueous dioxane. A solid residue obtained (1.7 g) was washed with $CHCl_3$ and recrystallized from MeCN–benzene mixture to give 1.5 g, 42% yield of imidazolidine **4a**.

4.1.6. Procedure 6 (Table 1, run 14)

Similarly to procedure Section 4.1.4, oxirane **1** (1.8 g, 8.33 mmol) was treated with urea (1.5 g, 25 mmol) in 10 mL of 93% aqueous MeCN. A solid residue obtained (1.1 g) was washed with $CHCl_3$ and recrystallized from $CHCl_3$–ethylacetate mixture to give 0.8 g, 41% yield of imidazolidine **4a**.

4.2. The reaction of oxirane (2) with urea

4.2.1. Procedure 1 (Table 1, run 1)

A mixture of oxirane **2** (1.4 g, 3.36 mmol) and urea (0.6 g, 10 mmol) in 7 mL Me_2SO (Me_2SO:H_2O ~ 99:1) was stirred at room temperature over 1 h until disappearance of lower layer of the oxirane. After that ice water (200 mL) was poured into the reaction mixture. The resultant precipitate (1.4 g) was separated by filtration, dried at room temperature and washed with $CHCl_3$, then hot MeCN and Et_2O to afford 0.3 g, yield 18.8% of compound **3b** as a white powder. The extracts were evaporated to give a solid residue which was recrystallized from $CHCl_3$–ethylacetate mixture to give 0.5 g, 34.2% yield of colorless crystals of imidazolidine **4b**.

*4.2.1.1. 5-Tridecafluorohexyl-5-ureidoimidazolidine-2,4-dione (**3b**), mp 250–252 °C (decomp.).* IR (powder): ν 3490, 3370, 3080, 2760 (NH_2), 1800, 1724, 1673 (C=O), 1597, 1542 (NH). ^{1}H NMR: δ 6.11 (br.s, 2H, NH_2), 7.39 (s, 1H, NH), 8.95 (s, 1H, NH), 11.18 (s, 1H, NH). ^{13}C NMR: δ 73.08 (t, $^2J_{CF}$ 23.4 Hz, C^5), 107.96 (tq, $^1J_{CF}$ 273.6, $^2J_{CF}$ 35.8 Hz, C$^{5'}$), 109.84 (tt, $^1J_{CF}$ 271.9, $^2J_{CF}$ 32.3 Hz, CF_2), 110.50 (tt, $^1J_{CF}$ 272.2, $^2J_{CF}$ 33.6 Hz, CF_2), 113.91 (tt, $^1J_{CF}$ 268.2, $^2J_{CF}$ 31.4 Hz, CF_2), 116.64 (qt, $^1J_{CF}$ 288.7, $^2J_{CF}$ 33.1 Hz, C$^{6'}$), 156.21 (s, C^2), 156.64 (s, C$^{2''}$), 168.05 (s, C^4). ^{19}F NMR: δ −126.06 (m, 2F, C$^{5'}$F$_2$), −122.78 (m, 2F, C$^{4'}$F$_2$), −121.91 (m, 2F, C$^{3'}$F$_2$), −118.94 (m, 2F, C$^{2'}$F$_2$), −119.20 (dt, 1F, $^2J_{FF}$ 286, J_{FF} 14.7 Hz, C$^{1'}$F$_B$), −117.93 (dt, 1F, $^2J_{FF}$ 286, J_{FF} 14.7 Hz, C$^{1'}$F$_A$), −80.60 (t, 3F, $^4J_{FF}$ 9.7 Hz, C$^{6'}$F$_3$). Anal. calcd. for $C_{10}H_5F_{13}N_4O_3$: C, 25.22; H, 1.06; F, 51.87; N, 11.76. Found: C, 25.21; H, 1.16; F, 52.15; N, 11.47.

*4.2.1.2. 5-Hydroxy-5-tridecafluorohexylimidazolidine-2,4-dione (**4b**), mp 220–221 °C.* IR (powder): ν 3245, 3055 (NH_2), 1778, 1673 (C=N, C=O), 1590 (NH). ^{1}H NMR: δ 8.47 (s, 1H, NH), 9.29 (s, 1H, NH), 11.37 (s, 1H, OH). ^{13}C NMR: δ 84.45 (t, $^2J_{CF}$ 26.5 Hz, C$^{5'}$), ~105–116 (m, C$^{1'}$–C$^{5'}$), 116.74 (qt, $^1J_{CF}$ 289.3, $^2J_{CF}$ 32.4 Hz, C$^{6'}$), 155.68 (s,

C^2), 168.97 (s, C^4). ^{19}F NMR: δ −126.07 (m, 2F, $C^{5'}F$), −122.86 (m, 2F, $C^{4'}F_2$), −122.18 (m, 2F, $C^{3'}F_2$), −121.48 (dm, 1F, $^2J_{FF}$ 282 Hz, $C^{2'}F_B$), −120.57 (dm, 1F, $^2J_{FF}$ 283 Hz, $C^{2'}F_A$), −120.46 (dm, 1F, $^2J_{FF}$ 295 Hz, $C^{1'}F_B$), −119.49 (dm, 1F, $^2J_{FF}$ 295 Hz, $C^{1'}F_A$), −80.58 (t, 3F, $^4J_{FF}$ 9.8 Hz, $C^{6'}F_3$). Anal. calcd. for $C_9H_3F_{13}N_2O_3$: C, 24.88; H, 0.69; F, 56.91; N, 6.45. Found: C, 24.87; H, 0.55; F, 56.89; N, 6.37.

4.2.2. Procedure 2 (Table 1, run 2)

Similarly, oxirane **2** (0.9 g, 2.16 mmol) was treated with urea (0.4 g, 6.67 mmol) in 4.5 mL of 94% aqueous Me_2SO for 1.5 h. A powder obtained (0.9 g) which contained allantoin **3b** and hydantoin **4b** in a ratio ~30:70 (from ^{19}F, ^1H NMR) was worked up as above in Section 4.2.1 to give 0.15 g, 14.6% yield of compound **3b** and 0.45 g, 48% yield of compound **4b**.

4.2.3. Procedure 3 (Table 1, run 3)

A mixture of oxirane **2** (0.8 g, 1.92 mmol) and urea (0.35 g, 5.83 mmol) in 94% Me_2SO (5 mL) was heated at 70–80 °C for 15 min in a sealed tube, with intermittent shaking, until disappearance of lower layer of the oxirane. After cooling (−70 °C), the tube was opened and the content was poured into ice water (150 mL). The resultant precipitate was separated by filtration, dried at room temperature, then washed with $CHCl_3$ and recrystallized from $CHCl_3$–ethylacetate mixture to give 0.45 g, 54% yield of compound **4b**. The filtrate Me_2SO–H_2O was extracted with Et_2O, the extract was dried over $MgSO_4$, and the ether was removed by evaporation. The solid residue was recrystallized from $CHCl_3$ to give 0.15 g, 19% yield of colorless crystals of acid **5b**.

*4.2.3.1. 3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-2,2-dihydroxyoctanoic acid (**5b**), mp 99–100 °C.* IR (powder): ν 3478 br, 3147 br, 2593, 2464 (OH), 1767, 1731 (C=O). ^1H NMR: δ 7.71 (s, OH), 13.7 (br.s, COOH). ^{13}C NMR: δ 92.20 (t, $^2J_{CF}$ 25.8 Hz, C^2), 108.08 (tq, $^1J_{CF}$ 272.9, $^2J_{CF}$ 34.1 Hz, $C^{5'}$), 110.06 (tt, $^1J_{CF}$ 272.8, $^2J_{CF}$ 30.9 Hz, CF_2), 111.55 (tt, $^1J_{CF}$ 266.5, $^2J_{CF}$ 31.5 Hz, CF_2), 113.76 (tt, $^1J_{CF}$ 265.6, $^2J_{CF}$ 29.6 Hz, CF_2), 116.79 (qt, $^1J_{CF}$ 288.5, $^2J_{CF}$ 33.4 Hz, $C^{6'}$), 168.25 (s, C^1). ^{19}F NMR: δ −126.15 (m, 2F, $C^{5'}F_2$), −122.83 (m, 2F, $C^{4'}F_2$), −122.10 (m, 2F, $C^{3'}F_2$), −120.69 (m, 2F, $C^{2'}F_2$), −119.95 (m, 2F, $C^{1'}F_2$), −80.61 (t, 3F, $^4J_{FF}$ 9.8 Hz, $C^{6'}F_3$). Anal. calcd. for $C_8H_3F_{13}O_4$: C, 23.41; H, 0.73; F, 60.24. Found: C, 23.64; H, 0.60; F, 59.96.

4.2.4. Procedure 4 (Table 1, run 4)

Similarly to procedure Section 4.2.3, a mixture of oxirane **2** (2.9 g, 6.97 mmol), urea (1.3 g, 21.67 mmol) and 10 mL of 94% aqueous Me_2SO was heated in a sealed tube in a boiling water bath for 1 h. A powder obtained after processing the reaction mixture (2.4 g) was dried at room temperature, then washed with $CHCl_3$ and underwent fractional crystallization from $CHCl_3$–ethylacetate mixture to give 1.3 g, 45.8% yield of urea **6b** as a white powder and 0.5 g, 16.5% yield of imidazolidine **4b**. The extraction of the filtrate Me_2SO–H_2O with Et_2O gave additionally 0.2 g, 6.6% yield of compound **4b**.

*4.2.4.1. (2,2,3,3,4,4,5,5,6,6,7,7,7-Tridecafluoro-1-hydroxyheptyl)urea (**6b**), mp 152–153 °C.* IR (powder): 3490, 3370, 3080, 2760 (NH), 1800, 1724, 1673 (C=O), 1597, 1542 (NH). ^1H NMR: δ 5.65 (dddd, 1H, $^3J_{HF}$ 14.5, 8.5; $^3J_{HH}$ 9.8, 6.2 Hz, C^1H), 5.90 (br.s, 2H, NH_2), 6.97 (d, 1H, $^3J_{HH}$ 9.8 Hz, OH), 7.16 (d, 1H, $^3J_{HH}$ 6.2 Hz, NH). ^{13}C NMR: δ 71.13 (dd, $^2J_{CF}$ 26.5, 22.7 Hz, C^1), 116.68 (qt, $^1J_{CF}$ 289.2, $^2J_{CF}$ 33.7 Hz, $C^{6'}$), ~105–117 (m, $C^{1'}$–$C^{5'}$), 156.83 (s, C^3). ^{19}F NMR: δ −127.23 (dm, 1F, $^2J_{FF}$ 277.1 Hz, CF_B), −121.33 (dm, 1F, $^2J_{FF}$ 277.1 Hz, CF_A), −126.40 (dm, 1F, $^2J_{FF}$ 289.2 Hz, CF_B), −125.86 (dm, 1F, $^2J_{FF}$ 289.2 Hz, CF_A), −122.95 (2F, center of AB-system), −122.29 (2F, center of AB-system), −121.95 (m, 2F, CF_2), −80.61 (t, 3F, $^4J_{FF}$ 9.8 Hz, $C^{6'}F_3$). Anal. calcd. for $C_8H_5F_{13}N_2O_2$: C, 23.54; H, 1.23; F, 60.54; N, 6.86. Found: C, 23.57; H, 1.26; F, 60.44; N, 6.87.

4.2.5. Procedure 5 (Table 1, run 7)

Similarly to procedure Section 4.2.3, a mixture of oxirane **2** (1.4 g, 3.36 mmol) and urea (0.62 g, 10.01 mmol) in 10 mL of anhydrous dioxane was heated in a sealed tube in a boiling water bath for 20 min. The solid obtained after processing the reaction mixture with water (1.3 g) was dried at room temperature, then washed with $CHCl_3$ and recrystallized from benzene–Et_2O mixture to give 1.1 g, 75% yield of colorless crystals of oxazole **7b**.

*4.2.5.1. 2-Amino-5-fluoro-5-tridecafluorohexyloxazole-4-one (**7b**), mp 174–175 °C.* IR (powder): ν 3245, 3055, 1590 (NH_2), 1778, 1673 (C=N, C=O). ^1H NMR: δ 10.04 (s, 1H), 10.26 (s, 1H) (NH_2). ^{13}C NMR: δ 102.62 (ddd, $^1J_{CF}$ 252.2; $^2J_{CF}$ 37.8, 30.6 Hz, C^5F), ~105.37–113.83 (m, $C^{1'}$–$C^{5'}$), 116.58 (qt, $^1J_{CF}$ 288.6, $^2J_{CF}$ 33.0 Hz, $C^{6'}F_3$), 173.15 (s, C^2), 173.51 (d, $^2J_{CF}$ 18.3 Hz, C^4). ^{19}F NMR: δ −131.08 (dm, 1F, J_{FF} 7.5 Hz, C^5F), −126.09 (m, 2F, CF_2), −124.38 (dm, 1F, $^2J_{FF}$ 291.0 Hz, CF_B), −122.73 (dt, 1F, $^2J_{FF}$ 291.0, J_{FF} 14.2 Hz, CF_A), −122.81 (m, 2F, CF_2), −122.23 (m, 2F, CF_2), −121.40 (m, 2F, center of AB-system), −80.55 (t, 3F, $^4J_{FF}$ 9.6 Hz, $C^{6'}F_3$). Anal. calcd. for $C_9H_2F_{14}N_2O_2$: C, 24.77; H, 0.46; F, 61.01; N, 6.42. Found: C, 24.85; H, 0.40; F, 61.13; N, 6.55.

4.2.6. Procedure 6 (Table 1, run 8)

Similarly to procedure Section 4.2.3, a mixture of oxirane **2** (1.4 g, 3.36 mmol) and urea (0.62 g, 10.01 mmol) in 10 mL of anhydrous MeCN was heated in a sealed tube in a boiling water bath for 15 min. The solid obtained after processing the reaction mixture (1.3 g) was dried at room temperature and recrystallized from benzene–Et_2O mixture to give 1.2 g, 81.8% yield of oxazole **7b**.

4.2.7. Procedure 7 (Table 1, run 11)

Similarly to procedure Section 4.2.3, a mixture of oxirane **2** (1.7 g, 4.09 mmol) and urea (0.72 g, 12.0 mmol) in 15 mL of 90% aqueous dioxane was heated in a sealed tube in a boiling water bath for 0.5 h. The solid obtained after processing the reaction mixture (1.5 g) was dried at room temperature and recrystallized from dioxane to give 0.68 g, 38.2% yield of oxazole **7b**.

4.2.8. Procedure 8 (Table 1, run 12)

Similarly to procedure Section 4.2.3, a mixture of oxirane **2** (2.1 g, 5.05 mmol) and urea (0.9 g, 15.0 mmol) in 11 mL of 93% aqueous MeCN was heated in a sealed tube in a boiling water bath for 0.5 h. The solid obtained after processing the reaction mixture with water (1.9 g) was dried at room temperature and recrystallized from dioxane to give 0.98 g, 44.5% yield of oxazole **7b**.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2012.03.017.

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