Journal contents

The Development of Perfluoroalkyl Substituted Uracyl Derivatives Synthesis on the Base of Urea with Perfluoroalkenyl Groups

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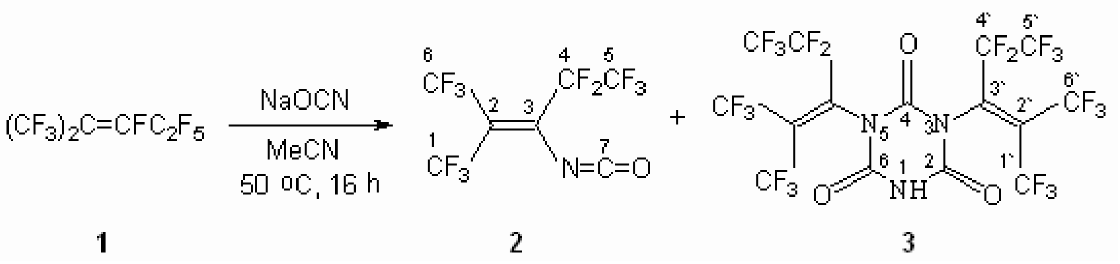
Perfluoro-2-methyl-2-pentene together with sodium cyanate produces the vinyl fluorine atom substitution product 1,1,1,4,4,5,5,5-octafluoro-3-isocyanato-2-(trifluoromethyl)pent-2-ene, which at heating undergoes intramolecular cyclization forming 1,3-bis-1,1,1,2,2,5,5,5-octafluoro-4-(trifluoromethyl)-pent-3-en-3-yl)-1,3,5-triazine-2,4,6-trion. Here we discuss the reactions of this isocyanate with sodium methylate and cyclohexylamine. Here it is shown, that at first urea derivatives are formed, which are transformed into uracyl derivatives under the action of potash. The products' structure is confirmed by spectral data.

Heterocyclic compounds with fluorine atoms are important for creating of medical products and pesticides [1]. Their key synthesis methods are based on condensation processes and intramolecular cyclization reactions which affect fluorine atoms in benzene ring and at multiply bond in perfluoroolefines at heteronuclephils' acting [2]. These transformations are typical exactly for poly-fluorinated unsaturated compounds. In view of high bio- activity of heterocyclic compounds with perfluoroalkyl groups we carried out a number of detailed researches on these reactions [3]. Pyrimidine derivatives play an important role for creating of medical products among heterocyclic compounds. Thus, in particular 5- fluorouracyl has found a wide application as a medicine for cancer treatment [4]. Its synthesis is based on direct elemental fluorine fluorination of uracyl. Earlier we [5] described an example of heterocyclic system construction using interaction of urea and perfluoro-2-methyl-2-penten, and in the work [6] α -(perfluoroalkyl)acrylic acid was used for this purpose. Here for heterocyclic construction we used the reaction of perfluorolefines with nucleophilic reagent, possessing two nucleophilic centres. The special feature of such reactions is the prime addition of nucleophile by carbon atom of multiply bond, and not than nucleophilic substitution of vinyl fluorine atom. The further stabilization of intermediate carbanion results in new multiply bond generation. In case of binucleophilic reagents the attack of second nucleophilic center by this multiply bond results in formation of heterocyclic one. At the same time we can use mononucleophilic reagents in case, if bond C=C is not affected as a result of interaction with perfluoroolefine, and instead new nucleophilic center is formed at expense of functional group. We had showed that rather extensively using example of pefluoro-2-methyl-2-pentene derivatives [2]. Another example is described in the work [7], where we showed, that we could construct the cycle of uracyl with perfluoroalkyl substituent by condensing of phosgene and tri-phosgene with oxazolyne and fluorinated nitriles interaction products.

In case of uracyl derivatives the intermediate formation of corresponding urea derivative should have been the main thing. The use of appropriate perfluoroalkenylisocyanate as starting substrate could have been one of approaches to that. This very thing became the goal of this work, in which we describe synthesis of such species and its synthetic opportunities to obtain some perfluoroalkyl uracyl derivatives.

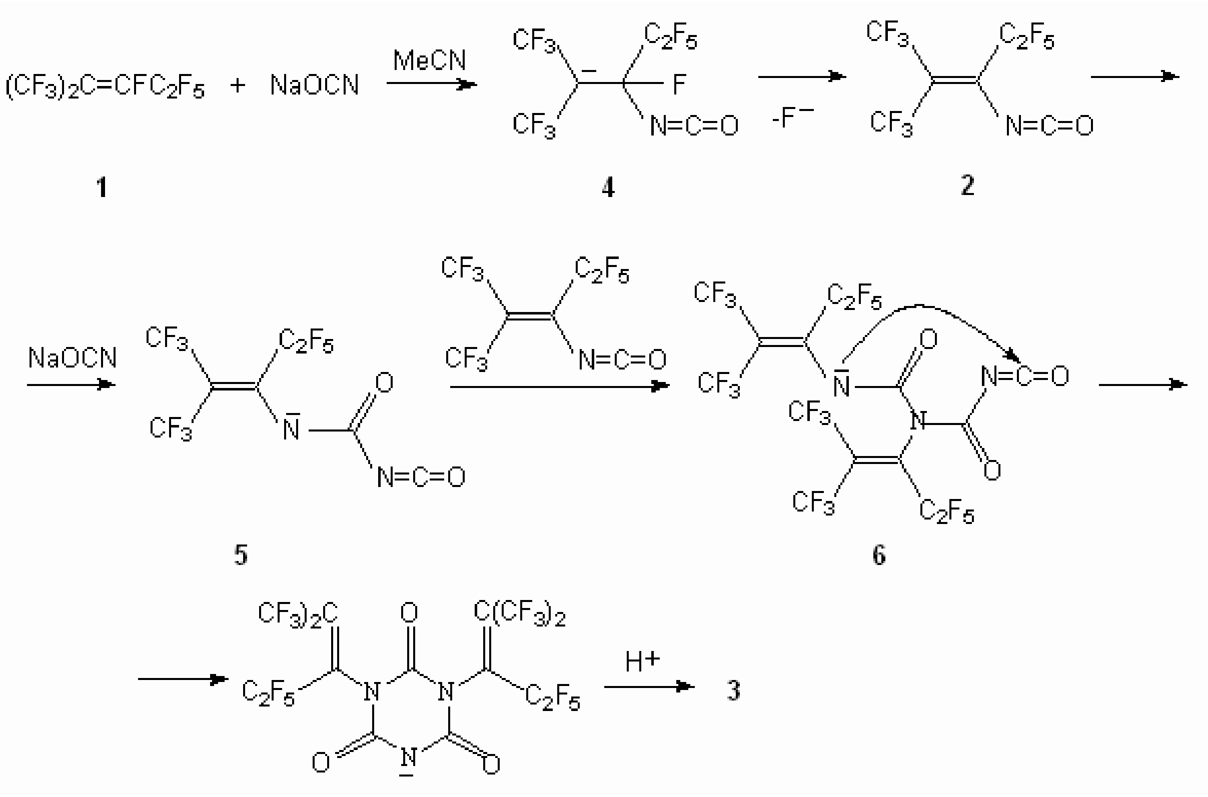
We showed that at interaction of perfluoro-2-methyl-2-pentene **1** and sodium cyanate in acetonitrile the mixture of fluorine atom vinyl replacement product (**2**) and heterocyclic compound (**3**) is formed. The increasing of reaction period up to 16 hours results in disappearing of compound **2** and compound **3** yield increase (Scheme 1).

Scheme 1



Reaction of perfluorolefine **1** and sodium cyanate should be going as follows (Scheme 2).

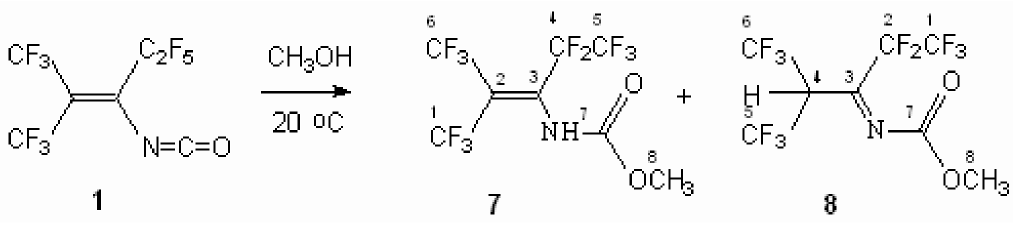
Scheme 2



It starts with the attack of nucleophile nitrogen atom according to internal multiply bond of compound **1** generating intermediate carbanion **4**, which stabilization is carried out by elimination of ion-fluoride out of CF fragment resulting in formation of compound **2**. Further interaction of sodium cyanate excess and compound **2** produces intermediate N - anion (**5**). Its reaction with compound (**2**) goes through generation N-anion (**6**) by intramolecular nucleophilic cyclization and results in formation of compound (**3**).

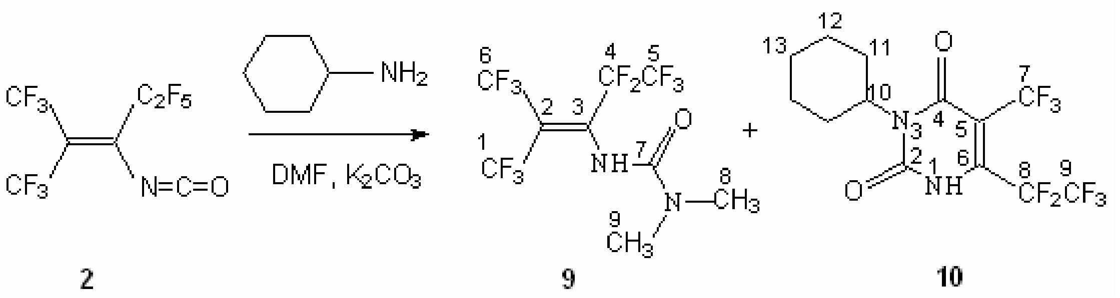
Compound (**2**) as we should have been expected shows high activity towards action of nucleophilic reagents. Thus, its dissolving in methyl alcohol or at sodium methylate acting in methyl alcohol results in formation of two (**7**) and (8) isomeric products mixture. Moreover the proportion of these products is determined by process conditions. Thus, in methyl alcohol the proportion of **7**:**8** is 69 : 31, while in the presence of sodium methylate it changes at little to 54:46.

Scheme 3



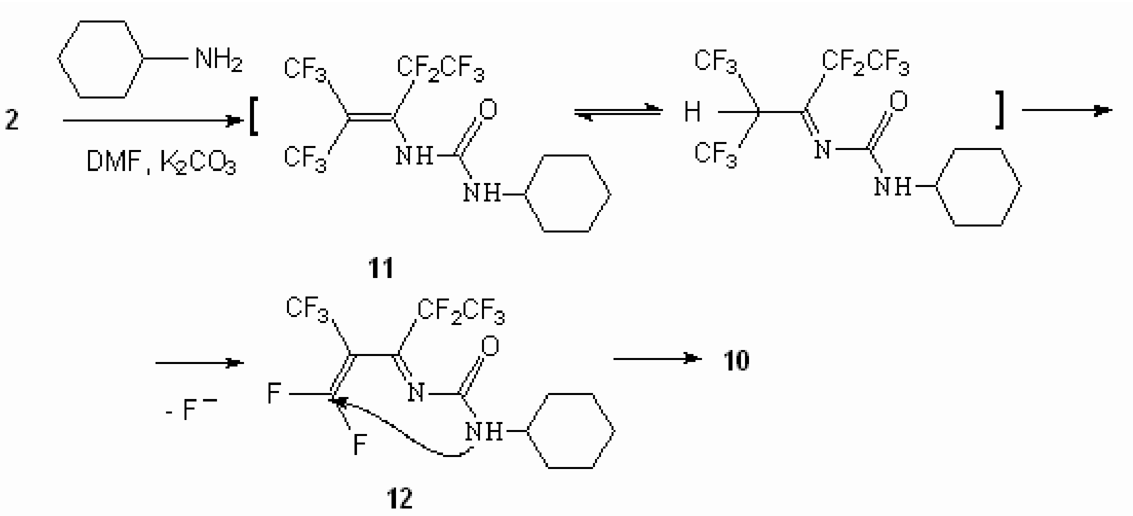
This data allowed to expect the formation of urea derivatives at N- nucleophilic reagents action on perfluorolefine **2**. Indeed, in case of interaction of compound (**2**) with cyclohexylamine in dimethylformamide in the presence of potash we get the mixture of (**9**) and (**10**) compounds (Scheme 4).

Scheme 4



We didn't succeed in finding the expected 1- cyclohexyl-3-(1,1,1,4,4,5,5,5,-octafluoro- 2-trifluoromethylpent-2-ene-3-yl) urea (**11**) probably because it had transformed into compound (**10**) due to intramolecular nucleophilic cyclization. Compound (**9**) must be formed due to attack of dimethylamine, produced out of dimethylformamide under the action of potash.

Scheme 5

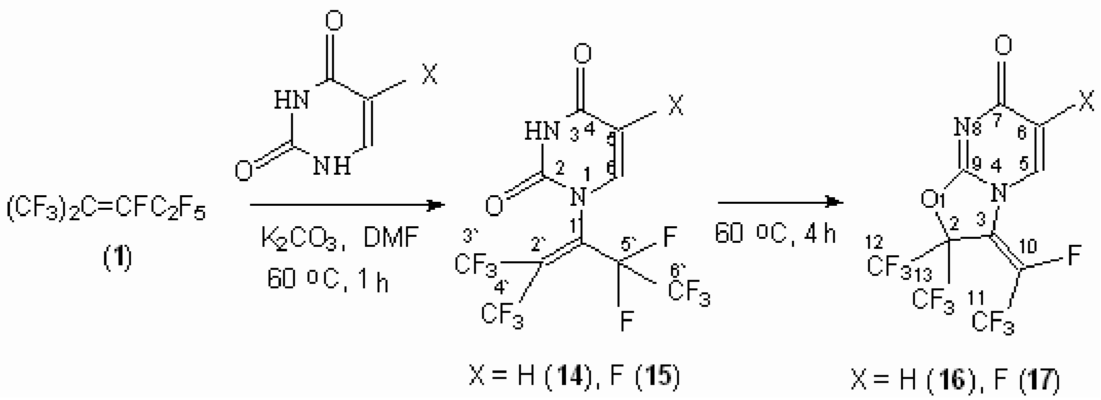


It can be interesting to mention, that dissolving of compound (**10**) in DMSO results in formation of salt (**13**), which is probably formed by interaction of enol form of compound (**10**) and DMSO.

Compound **10** possesses nucleophilic center and can act as nucleophile towards perfluorolefine **1**. Can such nucleophile compete with another N-nucleophile at interaction with pefluorolefine **2** reaction product? To this end we have studied the behaviour of uracyl in the perfluorolefine **1** medium in the presence of base.

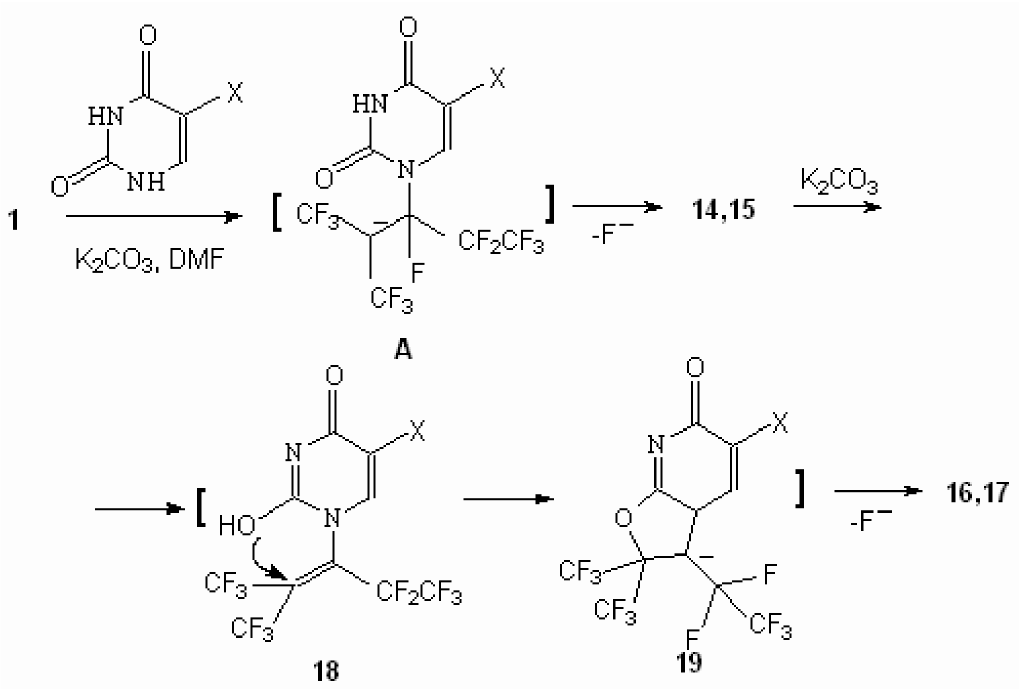
It is stated, that at interaction of perfluorolefine **1** and uracyl and 5-fluorouracyl in dimethylformamide in the presence of K_2CO_3 the (**14**) and (**15**) vinyl fluorine atom replacement products are formed correspondingly. The increasing of reaction temperature up to 60^{o}C and reaction period to 4-5 hours results in disappearing of **14** and **15** compounds and formation of (**16**) and (**17**) intramolecular nucleophilic cyclization products correspondingly (Scheme 6).

Scheme 6



Perfluorolefine **1** and uracyles reaction must be going according to the following scheme (Scheme 7).

Scheme 7



It starts with an attack of nucleophile (uracyl) according to internal multiply bond with generation of intermediate carbanion **A**, which stabilization is carried out by elimination of fluoride-ion out of CF fragment. Later enon-enol isomerization occurs due to base (K_2CO_3 in dimethylformamide) action forming compound **18**, the action of K_2CO_3 on which results in generation of O-nucleophilic center, conducting intramolecular nucleophilic cyclization forming carbanion **19**, which is stabilized by elimination of fluoride-ion out of CF_2 fragment, which produces end reaction product **16** and **17** respectively. The elimination of fluoride-ion out of CF_2 fragment of pentafluoroethyl group has been postulated before by the authors of the work [8].

However, the introduction of electron acceptor perfluoroalkyl groups must sharply low the basicity of N-nuleophilic center and it will result in absence of corresponding reaction. Nevertheless we should not exclude such an opportunity.

The structure of **2, 3, 7 – 11, 14-17** molecules is justified by NMR spectroscopy data, which is interpreted taking into account the relevant data re compounds of similar type.

Experimental

^1H, ^{13}C, ^{19}F NMR spectra were obtained at Bruker WP 200 SY spectrometer (200, 50 and 188 MHz respectively, internal standards - TMDS and C_6F_6 , spin-spin coupling constants $J_{C\text{-}H}$ were not metered; IR-spectra of 5% solutions of new compounds in CCl_4 were recorded at using Specord M-80 spectrometer; electronic spectra was recorded using Specord UV VIS spectrophotometer in ethyl alcohol. Molecular mass was determined using mass-spectrometer method at Finnigan MAT 8200 chromatography-mass spectrometer at the power of ionizing electrons equal to 70 eV.

General Methods of Compound 1 and Sodium Cyanate Interaction.

6.5 g (100 mmoles) of NaOCN were added to 50 g (100 mmoles) of compound **1** suspension in 50 ml of DMF, then this mixture was being stirred for one half hour at room temperature, further at 45 °C for 3 h (or 16h) after that mixture was filtrated and the filtrate was distilled in vacuum of water-jet pump. We obtained 11 g (33%) of compound **1**, boiling point 42-43 °C and compound **2**. Compound 3 was obtained from vat residue by re-crystallization from CH_2Cl_2.

1,1,1,4,4,5,5,5-Octa-3-iso-cyanato-2-(trifluoromethyl)pent-2-en 2.

Distillation of reaction mixture produced 10 grams (49 %) of compound **2**, boiling point 119-120 °C. IR-spectra, (KBr), ν /cm^{-1} : 2280 (antisym. N=C=O), 1640 (C=C), 1322 (sym. N=C=O), 1239 (C-O), 1203, 1184 (C-F). Mass-spectra, *m/z* (I_{rel} (%)) : 323 $[M]^+$ (30.36), 304 $[M\text{-}F]^+$ (42.93), 254 $[M\text{-}CF_3]^+$ (13.53), 204 $[M\text{-}C_2F_5]^+$ (42.23), 178 $[(CF_3)_2C{=}C\text{-}O]^+$ (20.26), 138 $[CF_3CF_3]^+$ (10.30), 119 $[C_2F_5]^+$ (13.25), 100 $[CF_2{=}CF_2]^+$ (6.20), 92 $[CF_2NCO]^+$ (73.70), 69 $[CF_3]^+$ (100). Found, *m/z* = 322.98019. $C_7F_{11}NO$. Calculated, *m/z* = 322.98041. NMR ^{19}F spectra ($CDCl_3$, δ , ppm, J/Hz) : 107.6 qt (3F, FC(6), $J_{F(6),F(1)}$ = 10.5; $J_{F(6),F(4)}$ = 21.0); 104.1 (3F, FC(1), $J_{F(1),F(6)}$ = 10.5; $J_{F(1),F(5)}$ = 10.5); 82.8 q (3F, FC(5), $J_{F(5),F(1)}$ = 10.5); 52.1 q (2F, FC(4), $J_{F(4),F(6)}$ = 21.0). NMR ^{13}C spectra ($CDCl_3$, δ , ppm., J/Hz) : 134.9 (C(3), $^2J_{C,F}$ = 30.7); 126.4 (C(7); 121.8 (C(2), $^2J_{C,F}$ = 33.0); 120.3 (C(1),$^1J_{C,F}$ = 277.2); 119.6 (C(6), $^1J_{C,F}$ = 273.9); 117.9 (C(5), $^1J_{C,F}$ = 287.5; $^2J_{C,F}$ = 29.9); 110.3 (C(4), $^1J_{C,F}$ = 262.9; $^2J_{C,F}$ = 40.7).

1,3-Bis-(1,1,1,2,2,5,5,5-octafluoro-4-(trifluoromethyl)pent-3-en-3-yl))-1,3,5triazine-2,4,6-trion 3.

4 g (17%) of compound 3 are obtained by recrystallization of vat residue out of CH_2Cl_2, melting temperature 131-132 °C . IR-

spectra, (KBr), ν /cm^{-1} : 3700, 3500 (NH); (KBr), ν /cm^{-1} : 1760, 1700 (C=O), 1650, 1645 (C=C), 1450 (C-N), 1361, 1310 (C-N), 1270, 1227 (C-O), 1200 (C-F). Mass-spectra, *m/z* (**I$_{rel}$** (%)) : 689 [M]$^+$ (2.58), 688 [M-H]$^+$ (14.58); 670 [M-F]$^+$ (2.27), 669 [M-HF]$^+$ (13.50); 620 [M-CF$_3$]$^+$ (5.25), 619 [M-CF$_3$,H]$^+$ (30.83), 297 [(CF$_3$)$_2$C=C(O)C$_2$F$_5$]$^+$ (30.18), 119 [C$_2$F$_5$]$^+$ (9.58), 70 [OCNCO]$^+$ (100), 69 [CF$_3$]$^+$ (62.00), 31 [CONH]$^+$ (20.35); 28 [CO]$^+$ (13.18). Found, *m/z* = 688.96157. $C_{15}H_1F_{22}N_3O_3$. Calculated, *m/z* = 688.96664. Found, % : C, 24.65; 24.12; H, 0.00; 0.15; F, 61.20; 61.50; N, 5.78. $C_{15}H_1F_{22}N_3O_3$. Calculated, % : C, 26.12; H, 0.15; F, 60.67; N, 6.10. NMR ^{1}H spectra (CDCl$_3$, δ , ppm, J/Hz) : 7.69 (d, H5, J = 6.00). NMR^{19}F spectra (CDCl$_3$, δ, ppm., J/Hz) : 106.1 qt (3F, FC(6'), $J_{F(6'),F(5')}$ = 20; $J_{F(6'),F(1')}$ = 10); 102.3 q (3F, FC(1'), $J_{F(1'),F(4')}$ = 10); 84.5 q (3F, FC(5'), $J_{F(5'),F(6')}$ = 10); 54.7 and 54.3 q (2F, FC(4'), $J_{F(4'),F(6')}$ = 20).

Methyl-1,1,1,4,4,5,5,5-octafluoro-2-(trifluoromethyl)pent-2-en-3-ylcarbamate 7. Boiling point 51-53 ^{o}C / 15 Torr. UV-spectra (EtOH, λ_{max} , nm ,(ε) : 201 (2600), 252 (2630). NMR spectra ^{1}H (CDCl$_3$, δ , ppm, J/Hz) : 7.90 (d, H (NH), J = 7.00); 3.89 (s, H(8). ^{19}F NMR spectra (CDCl$_3$, δ , ppm, J/Hz) : 107.6 qt (3F, FC(6), $J_{F(6),F(5)}$ = 20; $J_{F(6),F(1)}$ = 10); 102.3 q (3F, FC(1), $J_{F(1),F(4)}$ = 10); 81.8 q (3F, FC(5), $J_{F(5),F(6)}$ = 10); 48.4 q (2F, FC(4), $J_{F(4),F(6)}$ = 20). ^{13}C NMR spectra (CDCl$_3$, δ , ppm, J/Hz) : 152.9 (C(7); 135.7 (C(3) $^2J_{C,F}$ = 28.5); 120.9 (C(2), $^2J_{C,F}$ = 35.0); 120.2 (C(1),$^1J_{C,F}$ = 274.9); 120.7 (C(6), $^1J_{C,F}$ = 273.4); 117.6 (C(5), $^1J_{C,F}$ = 287.1; $^2J_{C,F}$ = 34.9); 109.3 (C(4), $^1J_{C,F}$ = 265.3; $^2J_{C,F}$ = 40.9); 53.6 (C(8)). Found, *m/z* = 355.00613. $C_8H_4F_{11}N_1O_2$. Calculated, *m/z* = 355.00662.

Methyl-1,1,1,2,2,5,5,5-octafluoro-4-(trifluoromethyl)pentan-3-ilydenecarbamate 8.

1H NMR spectra (CDCl$_3$, δ , ppm, J/Hz) : 4.61 (m, H (4)); 3.77 (s, H(8). ^{19}F NMR spectra (CDCl$_3$, δ , ppm, J/Hz) : 100.6 m (6F, FC(1,6)); 82.7 s (3F, FC(5)); 44.4 m (2F, FC(4)). ^{13}C NMR spectra (CDCl$_3$, δ , ppm., J/Hz) : 157.1 (C(7); 146.9 (C(3) $^2J_{C,F}$ = 28.6); 121.0 (C(1,6), $^1J_{C,F}$ = 282.7); 118.1 (C(5), $^1J_{C,F}$ = 282.6; $^2J_{C,F}$ = 35.2); 113.3 (C(2) $^2J_{C,F}$ = 30.4); 110.6 (C(4), $^1J_{C,F}$ = 259.6; $^2J_{C,F}$ = 39.9); 50.7 (C(8)). Found *m/z* = 355.00613. $C_8H_4F_{11}N_1O_2$. Calculated, *m/z* = 355.00662.

(Z)-1,1-dimethyl-3-(1,1,1,2,2,5,5,5-octafluoro-4-(trifluoromethyl)pentan-3-iliden)-urea 9. Boiling point 42-43 ^{o}C/ 15 Torr. NMR spectra ^{1}C (CDCl$_3$, δ , ppm, J/Hz) : 7.98 (m, H (NH)); 2.92 and 2.75 (s, H(8,9). ^{19}F NMR spectra (CDCl$_3$, δ , ppm, J/Hz) : 110. m (6F, FC(1,6)); 84.7 s (3F, FC(5)); 51.5 m (2F, FC(4)). NMR spectra ^{13}C (CDCl$_3$, δ , ppm, J/Hz) : 161.0 (C(7); 121.7 (C(1), $^1J_{C,F}$ = 275.0); 120.7 (C(6) $^1J_{C,F}$ = 275.9); 117.5 (C(5), $^1J_{C,F}$ = 287.1; $^2J_{C,F}$ = 36.2); 117.6 (C(3) $^2J_{C,F}$ = 30.4); 109.7 (C(4), $^1J_{C,F}$ = 262.4; $^2J_{C,F}$ = 35.9); 101.2 (C(2) $^2J_{C,F}$ = 33.2); 50.7 (C(8,9)). Found, *m/z* = 352.04249. $C_9H_7F_{11}N_2$. Calculated, *m/z* = 352.04334.

3-Cyclohexyl-6-(trifluoroethyl)-5-(trifluomethyl)pyrimidine-2,4(1H,3H)-dione 10.

Melting point 222-223^{o}C. IR-spectra, (KBr), ν /cm^{-1} : 2928, 2851 (C-H); (KBr), 1627, 1575 (C=O), 1536 (C=C), 1448, 1437 (C-N), 1312, 1271 (C-O), 1088, 1069, 1047 (C-F). NMR spectra ^{1}H (CDCl$_3$, δ , ppm, J/Hz) : 7.95 (d, H (NH), J = 7.00); 1.25, 1.67 (s, H, cyclohexyl). NMR spectra ^{19}F (CDCl$_3$, δ , ppm, J/Hz) : 106.0 qt (3F, FC(7), $J_{F(7),F(9)}$ = 10; $J_{F(7),F(8)}$ = 23); 83.1 q (3F, FC(9), $J_{F(9),F(7)}$ = 10); 52.3 q (2F, FC(8), $J_{F(8),F(7)}$ = 23). Found, *m/z* = 380.07851. $C_{13}H_{12}F_8N_2O_2$. Calculated, *m/z* = 380.07709.

The Complex of Dimethylsulfoxide and 3-cyclohexyl-2-hydroxy-6-(perfluoroethyl)-5-(trifluoroethyl)-5-(trifluoromethyl)-pyrimidine-4(3H)-on 13. Melting point 240-241^{o}C. IR-spectra, (KBr), ν /cm^{-1} : 3449 (OH), 3328 (NH), 2929, 2852 (C-H); 1627, (C=O), 1575 (C=N), 1537 (C=C), 1448, 1437 (C-N), 1342, 1312 (C-O), 1088, 11187 (C-F). NMR spectra ^{19}F (CDCl$_3$, δ , ppm., J/Hz) : 108.6 qt (3F, FC(7), $J_{F(7),F(9)}$ = 10; $J_{F(7),F(8)}$ = 23); 83.6 q (3F, FC(9), $J_{F(9),F(7)}$ = 10); 50.7 q (2F, FC(8), $J_{F(8),F(7)}$ = 23).

General Methods of Compound 1 and Uracyles Interaction.

5.6 g (50 mmoles) of uracyl (5-fluorouracyl) and 6.9 g (50mmoles) of K_2CO_3 were added to solution of 15 g (50 mmoles) of compound 1 in 50 ml of DMF, it was stirred for 1 hour at room temperature, then 1 hour (or 4-5 h) at 60 ^{o}C, poured into water, CH_2Cl_2 was extracted, it was washed out with 5% HCl and water, dried using $MgSO_4$ and then the reaction mixture was processed.

1(3,3,3-Trifluoro-1-pentafluoroethyl-2-trifluoromethyl-propenyl)-1H-pyrimidine-2,4-dione 14. After **treatment** the reaction mixture of compound 1and uracyl for 1 hour at 60^{o}C we obtained 16.9 g of mixture, distilling which we isolated 13.7 g o(70%) of compound **14**, boiling point 139-140^{o}C (0.3 Torr), m.p. 157-158 ^{o}C. IR-spectra (KBr), ν /cm^{-1} : 3110, 3056 (N-H), 1736 (C=O), 1676, 1656 (C=C), 1455, 1419 (C=C), 1382, 1317 (C-N), 1292, 1260 (C-O), 1054, 1189, 1146 (C-F). Mass spectra, *m/z*, (**I$_{rel}$** (%)) : 392 [M]$^+$ (19.40), 373 [M-F]$^+$ (6.59), 323 [M-CF$_3$]$^+$ (98.09), 230 [M-(CF$_3$)$_2$CC]$^+$ (100), 204 [M-(CF$_3$)$_2$CC,CN]$^+$ (28.06), 182 [C$_2$F$_5$C(NCC)CH]$^+$ (12.65), 158 [C$_2$F$_5$C(N)C=CH]$^+$ (28.57), 119 [C$_2$F$_5$]$^+$ (3.51), 70 [CONCO]$^+$ (13.48), 69 [CF$_3$]$^+$ (43.44). Found : *m/z* = 392.00234. $C_{10}H_3F_{11}N_2O_2$. Calculated : *m/z* = 392.00187. Found,% : C,30.64; 30.68; H, 0.83; 0.77; F, 53.11; 53.05; N, 6.67. Calculated, % : C, 30.61; H, 0.76; F, 53.3; N, 7.14. NMR ^{1}H spectra(CD$_3$CN, δ , ppm, J/Hz) : 5.51 (H3), 7.95 (d, H6, J = 7.00). NMR ^{19}F spectra (CD$_3$CN, δ , ppm, J/Hz) : 106.3 (3 F, FC(1') $J_{F(1'),F(5')}$ = 9, $J_{F(1'),F(4')}$ = 18, $J_{F(1'),F(6')}$ = 9); 102.5 (3 F, FC(6'), $J_{F(6'),F(1')}$ = 9); 52.3 and 52.2 (2 F, FC(4'), AB-system $J_{F(4'),F(4'')}$ = 175). NMR ^{13}C spectra(CD_3CN, δ , ppm, J/Hz) : 162.2 (C(4)), 148.6 (C(2)), 140.7 (C(5)), 140.5 (C(3), $^{1}J_{CF}$ = 24.5), 134.4 (C(2)), 2JCF = 31.6), 119.2 (C(6), $^{1}J_{CF}$ = 278.5), 118.5 (C(1), $^{1}J_{CF}$ = 277), 117.5 (C(5)), $^{1}J_{CF}$ = 287.8; $^{2}J_{CF}$ = 35.5), 110.0 (C(4)), $^{1}J_{CF}$ = 262.2; $^{2}J_{CF}$ = 40).

2,2-Bis(trifluoromethyl)-3-tetraethylidene-2,3-dihydrooxazole[3,2-a]pyrimidin-7-one 16. At the same feedings as at standard synthesis in 4 hours at 60 ^{o}C we have obtained 17.4 g of mixture, which was distilled at column, filled with silicagel in the CH_2Cl_2-acetone (5:1) system. 11.9 g (64 %) of compound 16 are obtained, b.p. 160-162 ^{o}C (0.5 Torr), m.p. 87-88 ^{o}C. Mass-spectra, *m/z* (**I_{rel}** (%)) : 372 $[M]^+$ (2.23), 371 $[M\text{-}H]^+$ (13.99), 321 $[M\text{-}CF_2H]^+$ (100), 278 $[M\text{-}C_4HFN_2O]^+$ (18.33), 112 $[C_4NFN_2O]^+$ (3.16), 93 $[C_4NFN_2O,F]^+$ (4.74), 69 $[CF_3]^+$ (41.64). Found : *m/z* = 371.99610. $C_{10}H_2F_{10}N_2O_2$. Calculated : *m/z* = 371.99565. IR-spectra, (KBr), ν /cm^{-1} : 1729 (C=O), 1699 (C=C), 1388 (C=N), 1358 (C=C), 1269, 1222 (C-O), 1165, 963 (C-F). NMR ^{1}H spectra ($CDCl_3$, δ , ppm, J/Hz) : 8.13 (d, H6. J = 8.00), 5.75 (d, H5, J = 8.00). NMR ^{19}F spectra($CDCl_3$, δ , ppm, J/Hz) : 95.3 (3F, FC(11), $J_{F(11),F(6)}$ = 5.9); 91.6 (3F, FC(12), $J_{F(12),F(11}$ = 8.6; $J_{F(12),F(10)}$ = 24.6); 90.6 (3F, FC(13), $J_{F(13),F(11)}$ = 8.6; $J_{F(13),F(10)}$ = 24.6); 49.7 (1F, FC(10), $J_{F(10),F(12,13)}$ = 24.7; $J_{F(10),F(6)}$ = 5.9). NMR ^{13}C spectra($CDCl_3$, δ , ppm, J/Hz) : 161.5 (C(7)); 150.2 (C(10), $^{1}J_{C,F}$ = 276.2; $^{2}J_{C,F}$ = 30.1); 148.7 (C(9)); 142.7 (C(6)); 120.7 (C(12,13), $^{1}J_{C,F}$ = 188.2; $^{2}J_{C,F}$ = 26.9); 118.2 (C(3), $^{2}J_{C,F}$ = 31.7); 116.2 (C(11), $^{1}J_{C,F}$ = 266.6; $^{2}J_{C,F}$ = 40.2); 101.6 (C(5)); 52.7 (C(2)).

5-Fluoro-1(3,3,3-trifluoro-1-pentafluoroethyl-2-trifluoromethyl-propenyl)-1H-pyrimidine-2,4-dion 15. At the same feedings in one hour at 60 ^{o}C we have obtained 19.0 g of mixtures, containing compounds **15** and **17** in proportion close to 3:2 according to NMR ^{19}F and GLC. Distillation of mixture produced 12.5 g (61 %) of compound **15**, b.p. 140-143^{o}C (0.5 Torr), m.p. 138-139 ^{o}C. In addition, the compound was distilled at the column, filled with silicagel, in the system CH_2Cl_2- acetone (5:1). IR-spectra, (KBr), ν /cm^{-1} : 3202, 3084 (N-H), 1719 (C=O), 1674, 1448 (C=C), 1378 (C-N), 1317, 1240 (C-O), 11.94, 1048 (C-F). Mass-spectra, *m/z* (**I_{rel}** (%)) : 410 $[M]^+$ (22.56), 391 $[M\text{-}F]^+$ (10.53), 341 $[M\text{-}CF_3]^+$ (100), 271 $[M\text{-}2CF_3,H]^+$ (6.92), 248 $[M\text{-}CF_3\text{-}CF_3CC]^+$ (79.140, 194 $[C_2F_5CCCHF_2]^+$ (23.24), 143 $[CF_3CCCF_2]^+$ (16.75), 119 $[C_2F_5]^+$ (7.39), 93 $[CF_3CC]^+$ (14.04), 69 $[CF_3]^+$ (91.01), 43 $[CONH]^+$ (5.10), 28 $[CO]^+$ (19.71).Found, *m/z* = 409.99245. $C_{10}H_2F_{12}N_2O_2$. Calculated, *m/z* = 409.99247. ^{19}F NMR Spectra ($CDCl_3$, δ , ppm, J/Hz) : 106.4 (3F, FC(1'), $J_{F(1'),F(5')}$ = 10.5; $J_{F(1'),F(4')}$ = 24.7; $J_{F(1'),F(6')}$ = 10.5); 102.6 (3F, FC(6'), $J_{F(6'),F(1')}$ = 10.5); 83.0 (3F, FC(5'), $J_{F(5'),F(1')}$ = 9); 52.3 (2F, FC(4'), $J_{F(4'),F(1')}$ = 24.7; $J_{F(4'),F(5')}$ = 5.5); -0.3 (1F, FC(5)). ^{13}C NMR spectra ($CDCl_3$, δ , ppm, J/Hz) : 156.8 (C(4), $^{2}J_{C,F}$ = 36.7), 147.6 (C(2)), 140.6 (C(5),$^{1}J_{C,F}$ = 241.5), 126.4 (C(6), $^{2}J_{C,F}$ = 36.9), 140.5 (C(3'), $^{2}J_{C,F}$ = 24.5); 134.4 (C(2'), $^{2}J_{C,F}$ = 31.6); 119.2 (C(6'), $^{1}J_{C,F}$ = 278.5); 118.5 (C(1'), $^{1}J_{C,F}$ = 277); 117.5 (C(5'), $^{1}J_{C,F}$ = 287.8; $^{2}J_{C,F}$ = 35.5); 110.0 (C(4'), $^{1}J_{C,F}$ = 262.2; $^{2}J_{C,F}$ = 40).

6-Fluoro-2,2-bis(trifluoromethyl)-3-tetrafluoroethylidene-2,3-dihydrooxazole[3,2-a]pyrimidin-7-one 17. At the same feedings in 5 hours at 60 ^{o}C we have obtained 18.0 g of mixture, containing compounds **15** and **17** in proportion about 1:5 according to the GLC and NMR ^{19}F . Distilling the mixture we have obtained 10.3 g (52.8 %) of compound **17**, b.p. 140-143 ^{o}C (0.5 Torr). In addition, we have distilled the compound **in CH_2Cl_2- acetone (5:1) system** at the column, filled with silicagel . IR-spectra (KBr), ν /cm^{-1} : 1722 (C=O), 1674 (C=C), 1643 (C=N), 1361, 1351 (C-N), 1283, 1227 (C-O), 1160, 1048 (C-F). Mass-spectra, *m/z* (**I_{rel}** (%)) : 390 $[M]^+$ (27.79), 371 $[M\text{-}F]^+$ (16.13), 321 $[M\text{-}CF_3]^+$ (100), 301 $[M\text{-}CF_3,HF]^+$ (11.12), 278 $[M\text{-}C_4HFN_2O]^+$ (14.90), 258 $[M\text{-}CF_3,CCF]^+$ (3.36), 236 $[M\text{-}CF_3,CCFCON]^+$ (20.28), 180 $[M\text{-}CF_3,CCF,HF, CCCONC]^+$ (39.92), 112 $[C_4NFN_2O]^+$ (1.17), 93 $[C_4NFN_2O,F]^+$ (2.24), 69 $[CF_3]^+$ (17.61), 42 $[CON]^+$ (22.81). Found, *m/z* = 389.98587. $C_{10}H_1F_{11}N_2O_2$. Calculated, *m/z* = 389.98622. NMR ^{1}H spectra($CDCl_3$, δ , ppm, J/Hz) : 7.69 (d, H5, J = 6.00). NMR ^{19}F spectra ($CDCl_3$, δ , ppm , J/Hz) : 94.7 (3F, FC(11), $J_{F(11),F(6)}$ = 5.8); 91.1 (3F, FC(12), $J_{F(12),F(11)}$ = 8.6; $J_{F(12),F(10)}$ = 24.7); 90.0 (3F, FC(13), $J_{F(13),F(11)}$ = 8.6; $J_{F(13),F(10)}$ = 24.7); 50.1 (1F, FC(10), $J_{F(10),F(12,13)}$ = 24.7; $J_{F(10),F(6)}$ = 5.8); -3.2 (1F, FC(6), $J_{F(6),F(10)}$ = 5.8). NMR ^{13}Cspectra ($CDCl_3$, δ , ppm, J/Hz) : 156.6 (C(7), $^{2}J_{C,F}$ = 26.3); 150.6 (C(10), $^{1}J_{C,F}$ 275.7; $^{2}J_{C,F}$ = 29.5); 147.2 (C(9)); 138.7 (C(6), $^{1}J_{C,F}$ = 238.8); 126.8 (C(5), $^{2}J_{C,F}$ = 35.0); 120.0 (C(12,13), $^{1}J_{C,F}$ = 285.4; $^{2}J_{C,F}$ = 20.3); 117.7 (C(3), $^{2}J_{C,F}$ = 23.9); 115.5 (C(11), $^{1}J_{C,F}$ = 276.0; $^{2}J_{C,F}$ = 38.5); 47.2 (C(2)).

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The List of References

1. Новое в технологии соединений фтора. / Под ред. Н. Исикавы. М. : Мир. 1984. 592с.
2. G.G. Furin // Fluorine Containing Heterocyclic Compounds. Synthesis and Application. Novosibirsk : Science. 2001. 304 c.
3. Chambers R.D., Sargent C.R. // *Adv. Heterocyclic Chem.* / Eds. A.R. Katritzky, A.J. Boulton. N.Y. : Academic Press. Inc.

1981. Vol. 28. P. 1-71.

4. Nucleosides and Nucleotides as Antitumor and Antiviral Agents. // Eds. C.K. Chu, D.C. Baker. New York : Plenum Press. 1993.

5. Chi K.-W., Furin G.G., Gatilov Yu.V., Bagryanskay I.Yu., Zhuzhgov E.L. // *J. Fluorine Chem.* 2000. Vol. 103. P. 105-115.

6. Kato K., Takemitsu M., Mizumoto H., Takoyaka K., Arai S. // *Ger. Offen DE* 19835866 (1999); Chem. Abstr. 1999. Vol. 130. 168166k.

7. Fustero S., Salavert E., Sanz-Cervera J.F., Piera J., Asensio A. // *J. Chem. Soc., Chem. Commun.*, 2003. P. 844-845.

8.R.D. Chambers, A.A. Lindley, P.D. Philpot et al. , *J. Chem. Soc., Perkin Trans, 1,* 1979, 214.

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