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Reactions of 1,5-π-Cyclization of *gem*-Difluoro-Substituted Azomethine Ylides Involving an Aromatic Ring

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Abstract—Reactions of *N*-(5-R-furan-2-ylmethylidene)anilines with difluorocarbene proceeds through intermediate azomethine ylides suffering 1,5-π-cyclization to yield 6,6-difluorocyclopropa[*b*]furo[2,3-*c*]pyrrole and/or 4,4,6,6-tetrafluorocyclopropa[*b*]furo[2,3-c]pyrrole. The heating of these compounds without solvent resulted in high yields of 2,5-disubstituted 7-fluoro-4,5-dihydrofuro[3,2-*c*]pyridin-4(5*H*)-ones.

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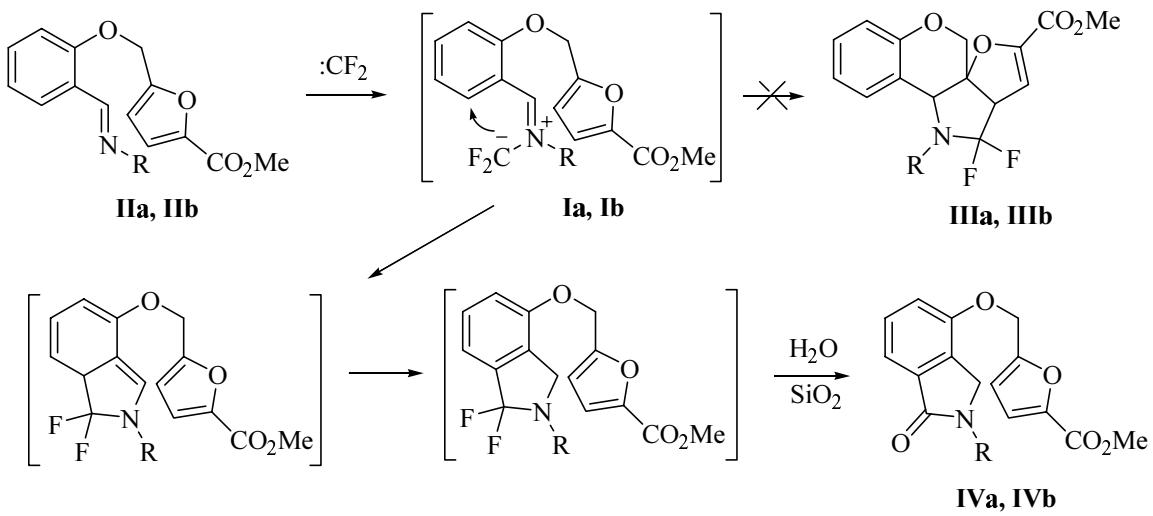
Reactions of difluorocarbene with imines is a convenient procedure for generation of *gem*-difluoro-substituted azomethine ylides, unstable intermediates used in the synthesis of 2-fluoropyrroles [1], 2-fluoro-2-pyrrolines [2], derivatives of pyrrolidine [3–5], oxazolidine [6], imidazolidine [7], 2,5-epoxy-1,4-benzoxazepine [8, 9], and 2,2-difluoro-1-azabicyclo[3.1.0]hex-3-ene [10, 11]. These synthetic methods are based on intermolecular and intramolecular cycloadditions of the difluoro-substituted ylide intermediate to the multiple bonds C=C, C≡C, C=O, and C=N. Incidentally it is known that the azomethine ylides alongside the cycloaddition reactions are capable to undergo 1,3-, 1,5-, and 1,7-π-cyclization affording 3-, 5-, and 7-membered nitrogen-containing heterocycles. For instance, the 1,3-cyclization is characteristic of many *gem*-dibromo-, *gem*-dichloro-, *gem*-bromochloro-, *gem*-bromofluoro-, and *gem*-fluorochloro-substituted azomethine ylide [12] generated from Schiff bases and the corresponding dihalocarbenes, and also ylides formed in Schiff bases reactions with metallocarbenoids from diazo compounds [13]. Several instances are known of 1,5-cyclizations of azomethine ylides involving C=C bond [14–17], C=O bond [18–21], and the pyridine ring [22]. Recently 1,7-cyclization of azomethine ylides was observed involving a benzene ring and resulting in formation of 2-benzazepine derivatives [23, 24]. No π-cyclization reactions are known for difluoro-substituted ylides. We report here on the first example of 1,5-electrocyclization of *gem*-difluoro-substituted azomethine ylides originating from the reaction of Schiff bases with difluorocarbene generated by reduction of dibromodifluoromethane with active lead in the presence of tetrabutylammonium bromide.

In the study of intramolecular 1,3-dipolar cycloaddition of difluoro-substituted ylides to endocyclic C=C-dipolarophiles imine **IIa** was introduced into the reaction with the difluorocarbene as ylide **Ia** precursor. However instead of the expected cycloaddition product **IIIa** isoindolone **IVa** was isolated in a 20% yield (Scheme 1). The formation of this compound is likely due to the low dipolarophile activity of the multiple bond in the furan ring favoring the competing process involving the 1,5-π-cyclization of intermediate ylide **Ia**, a formal proton shift and a hydrolysis during the chromatographic workup of the reaction mixture.

In the ^{1}H NMR spectrum of compound **IVa** apart from the signals of the methylene protons of the CH_2O group at 5.20 ppm a singlet signal is present corresponding to the methylene protons of the dihydroisoindole system at 4.78 ppm. In the ^{13}C NMR spectra the characteristic signals of two methylene carbon atoms appear at 48.2 and 62.2 ppm, those of carbonyl carbons, at 158.6 and 167.0 ppm. The mass spectrum contained two peaks of *m/z* 399 and 397 with the intensity ratio 1:3 corresponding to the molecular ion. The reaction with *p*-bromo-

Scheme 1.



R = 4-ClC_6H_4 (**a**), 4-BrC_6H_4 (**b**).

Scheme 2.

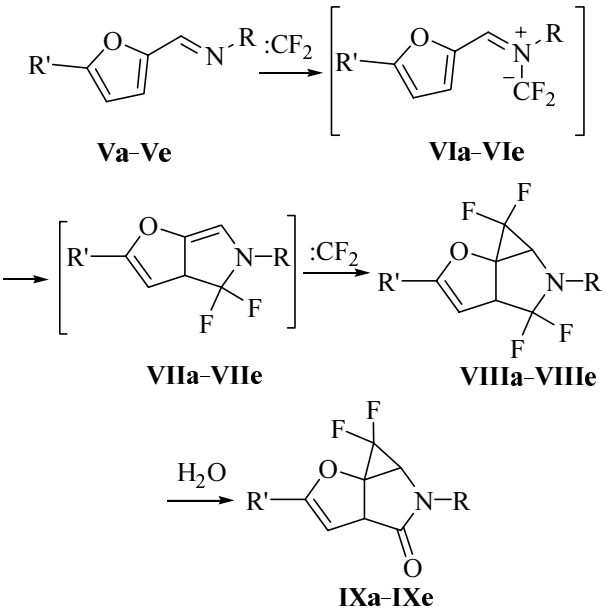


Table 1. Yields of products and time of reaction between imines **Va–Vf** and difluorocarbene

Imine no.	R	R'	Reaction time, h	Yields, %	
				VIII	**IX**
Va	Ph	H	5		53
Vb	4-BrC_6H_4	Me	5	36	36
Vc	Ph	4-$EtO_2CC_6H_4$	14		6
Vd	4-BrC_6H_4	2-FC_6H_4	12	51[a]	
Ve	4-$MeOC_6H_4$	Br	6		50
Vf	4-$MeOC_6H_4$	4-NCC_6H_4	4		34[b]

Imine conversion: [a] 70%, [b] 45%.

substituted analog **Ib** proceeded in the same fashion, and we isolated isoindolone **IVb** in a 4% yield.

The 1,5-cyclization of ylides generated from substituted *N*-benzylideneanilines and difluorocarbene proved to be sensitive to the structural parameters. For instance, we failed to obtain products of 1,5-cyclization analogous to compound **IV** from ylides generated from 2-methoxy- and 3,4,5-trimethoxybenzylideneanilines. We suggested that the replacement of the benzene ring by a furan one should significantly facilitate the 1,5-cyclization of the corresponding difluoroylide and thus increase the yields of the reaction products. Actually, the anils of substituted furfurals **Va–Vf** under conditions of difluorocarbene generation afford ylides **VIa–VIf** that sufficiently readily undergo the 1,5-cyclization involving the furan ring to furnish pyrroline ring (Scheme 2). We did not succeed in any case to isolate the primarily cyclization products, furopyrroles **VIIa–VIIf**, for the highly nucleophilic double bond of the pyrroline ring suffered fast cyclopropanation giving cyclopropa[*b*]furo[2,3-*c*]pyrroles **VIIIa–VIIIf** that were hydrolyzed in the course of chromatography on silica gel to furnish compounds **IXa, IXb, IXe**, and **IXf** (Table 1). In two cases, namely, in reactions of ylides generated from imines **Vc** and **Vd**, we succeeded to obtain the precursoes of lactams **IXc** and **IXd**, tetrafluorides **VIIIc** and **VIIId**.

The structure of compounds **VIII** and **IX** was proved by the data of NMR and IR spectroscopy and was confirmed by elemental analysis. In the ^1H NMR spectra of compounds **VIII** a triplet signal from H^{5a} proton was observed in the region 3.88–3.95 ppm (J_{HF} 7.3–7.5 Hz),

and the multiplet in the region 4.55–4.60 ppm (J ~13, 7, 4, 3 Hz), corresponded to proton H^{3a}. In the ^{13}C NMR spectra of compounds **VIII** difluoromethyl atoms C^6 and C^4 gave rise to doublets of doublets of doublets in the region 109.7–109.8 (J_{CF} 320, 301–302, 9.4–10.0 Hz) and 128.6–128.8 ppm (J_{CF} 259–260, 247–250, 5.5–7 Hz) respectively. In the ^1H NMR spectra of compounds **IX** two doublets of doublets are present in the 3.91–4.06 (J_{HF} 7.9–8.2, 1.4–1.8 Hz) and 4.20–4.40 ppm (J 2.4–4.5, 1.3–2.6 Hz) corresponding to protons H^{5a} and H^{3a} respectively. In the ^{13}C NMR spectra of compounds **IX** C^6 atom of the difluoromethyl group appeared as a doublet of doublets in the region 107.5–108.3 ppm (J_{CF} 319–320, 301 Hz). Atom C^4 of the carbonyl group appeared in the ^{13}C NMR spectra as a signal in the region 169.5–171.4 ppm; the frequency of the stretching vibrations of the C=O bond in the IR spectra was observed at 1725–1730 cm^{-1}.

For preparation of compounds **VIII** and **IX** the optimum ratio of imine and the components for carbene generation (CF_2Br_2–Pb*—Bu_4NBr) equals 1:4:3:3. The decrease in the carbene excess in the reaction mixture reduces the conversion of the initial imine, and the greater excess of carbene leads to difluorocyclopropanation of the double bond in the furan ring of compounds **VIII**. For instance, at the reagents ratio (**Vg**) : CF_2Br_2 : Pb* : Bu_4NBr = 1 : 8 : 6 : 6 a mixture was obtained consisting of compounds **VIIIg** and **X** in a ratio 1:0.8 (Scheme 3) which we failed to separate by chromatography, but succeeded in assignment of individual peaks in the ^1H and ^{13}C NMR spectra. In the ^1H NMR spectrum of compound **VIIIg** the singlet belonging to the olefin atom H^3 was observed at 5.68 ppm, whereas the corresponding H^{3b} atom in compound **X** was attached to the cyclopropane ring and appeared in the spectrum as a doublet at 3.05 ppm (J_{HF} 14.5 Hz). In the ^{13}C NMR spectrum of compound **X** an additional carbon signal was observed as a doublet of doublets at 109.7 ppm (J_{CF} 305, 297 Hz) that belonged to atom C^4 of the cyclopropane difluoromethyl group. The keeping of the mixture of compounds **VIIIg** and **X** on silica gel at room temperature for 24 h furnished a mixture of compounds **IXg** and **XI** in the same ratio. In the ^1H NMR spectrum of the latter mixture the doublet at 3.13 ppm (J_{HF} 13.8 Hz) corresponded to H^{3b} proton of compound **XI**, and the doublet of doublets at 5.85 ppm (J 2.6, 1.7 Hz) belonged to proton H^3 of compound **IXg**. The ^{13}C NMR spectrum of the mixture contained two characteristic doublets of doublets of difluoromethylene groups of atoms C^1 and C^4 in compound **XI** at 107.4 (J 319, 301 Hz) and 109.8 ppm (J 307, 298 Hz), and a single doublet of doublets from atom C^6 in compound **IXg** at 108.3 ppm (J 319, 301 Hz). The singlets at 170.0 and 170.8 ppm belong to the carbon atoms of the lactam carbonyls in these compounds.

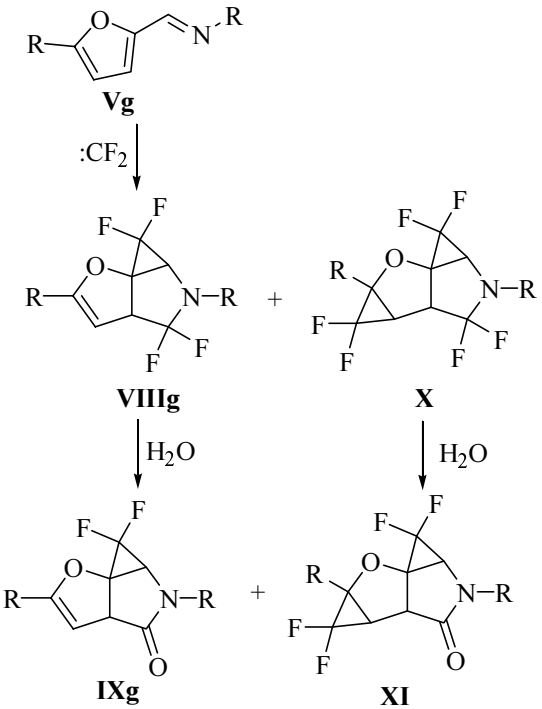
Table 2. Yields of thermolysis products from compounds **VIII** and **IX**

Compd. no.	R	R'	Yield of compound **XII**, %
VIIIc	Ph	4-$EtO_2CC_6H_4$	86
IXa	Ph	H	83
IXb	4-BrC_6H_4	Me	80
IXf	4-$MeOC_6H_4$	4-NCC_6H_4	93

The heating of compounds **IXa, IXb**, and **IXf** without solvent for 10 min at 160°C is accompanied with HF liberation and formation of 7-fluoro-4,5-dihydrofuro-[3,2-*c*]pyridin-4-ones **XIIa, XIIb**, and **XIIf** which were isolated in 80–93% yields. Analogous result was obtained in the thermolysis of the tetrafluoride **VIIIc** (Scheme 4, Table 2).

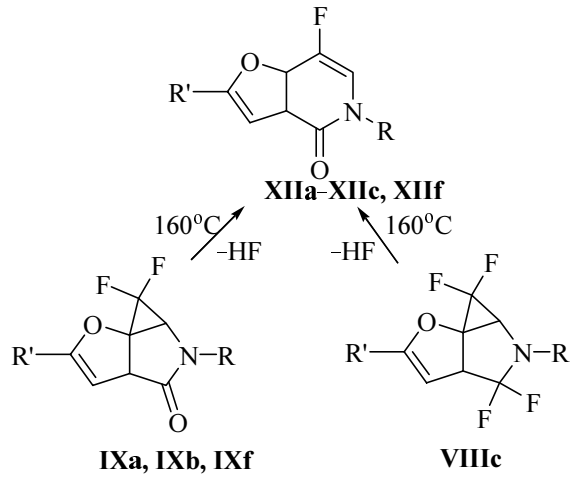
We have consequently established that the *gem*-difluoro-substituted azomethine ylides apart from the intramolecular cycloaddition and ylide-ylide isomerization are capable to undergo one more type of intramolecular

Scheme 3.



R = 4-BrC_6H_4.

Scheme 4.



transformation, 1,5-electrocyclization with the participation of the aromatic ring. Difluoroylides generated from *N*-(furylmethylidene)anilines undergo cyclization essentially more readily than the ylides obtained from *N*-benzylideneanilines obviously due to the difference in the resonance energy of the furan and benzene systems. Nevertheless, even with the furan derivatives the 1,5-cyclization of difluoroylides occurs with a rate relatively low for an intramolecular process for it cannot compete, for example, with the reaction of intermolecular 1,3-dipolar cycloaddition to dimethyl acetylenedicarboxylate: The reaction of *N*-(furylmethyidene)aniline with difluorocarben in the presence of dimethyl acetylenedicarboxylate affords the corresponding 2-fluoropyrrole in a 69% yield, and not the products of 1,5-cyclization of **VIII** or **IX** type [1]. The cleanly occurring thermal isomerization of furopyrroles **VIII** or **IX** suggests a simple procedure for the synthesis of 2,5-disubstituted 7-fluoro-4,5-dihydrofuro[3,2-*c*]pyridin-4(5*H*)-ones from cheap and available compounds.

EXPERIMENTAL

Melting points of the substances have been measured on the Boëtius heating block and are reported without correction. IR spectra were recorded on a spectrophotometer Carl Zeiss UR-20 using a cell with the absorbing layer thickness 400 μm. NMR spectra were registered on a spectrometer Bruker DPX-300 at operating frequancies 300 (^{1}H) and 75 (^{13}C) MHz. Mass spectra were obtained on MKh-1303 instrument (ionizing energy 70 eV). Elemental analysis was carried out on a CHN-analyzer HP-185B. The reaction progress was monitored by TLC on Silufol-254 plates. In separation of the reaction mixtures by column chromatography was used silica gel LS 5/40 (Chemapol). Dichloromethane was dried by distillation from P_2O_5.

Imines **I, IX, X, XIII, XVII, XXI**, and **XXIII** were prepared by condensation of aldehydes with amines in ethanol. The active lead was obtained by the method described in [1].

General procedure for imines reactions with the difluorocarbene. Into a flask of 50 ml capacity containing 1.2 g (5.8 mmol) of active lead was added in succession under an argon atmosphere 7 ml of dichloromethane, 2.0 g (6 mmol) of tetrabutylammonium bromide, 2.7 mmol of imine, and 1.95 g (9.3 mmol) of dibromodifluoromethane. The flask was tightly stoppered and was immersed into an ultrasonic bath (160 W) at 45°C for a time interval sufficient for the lead to react completely. On cooling 4 g of silica gel was added to the mixture, the solvent was evaporated in a vacuum, and the powder obtained was charged into a chromatographic column packed with silica gel, and the products were eluted with a mixture hexane–EtOAc.

The physical and spectral characteristics of compounds **VIIId**, **IXa**, and **XIIa** were reported in [25].

From 0.96 g (2.60 mmol) of imine **IIa** (reaction time 23 h) using as eluent hexane–EtOAc, 3:1, at chromatographic purification of the mixture we obtained 0.207 g (20%) of **methyl 5-{[1-oxo-2-(4-chlorophenyl)-2,3-dihydro-1*H*-isoindol-4-yl]oxymethyl}-2-furancarboxylate** (**IVa**), mp 200–201°C (EtOH–CH_2Cl_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.93 s (3H, CH_3), 4.78 s (2H, NCH_2), 5.20 s (2H, OCH_2), 6.60 d (1H, H_{furyl}, *J* 2.3 Hz), 7.13–7.87 m (8H, H_{furyl}, H_{arom}). Mass spectrum, *m/z* (I_{rel}, %): 399 (23) $[M]^+$, 397 (69) $[M]^+$, 260 (15), 258 (46), 230 (19), 167 (15), 139 (950), 137 (100), 111 (81), 79 (100), 59 (27), 51 (42), 41 (15), 38 (12).

From 1.08 g (2.61 mmol) of imine **IIa** (reaction time 17 h) using as eluent hexane–EtOAc, 3:1, at chromatographic purification of the mixture we obtained 0.044 g (4%) of **methyl 5-{[2-(4-bromophenyl)-1-oxo-2,3-dihydro-1*H*-isoindol-4-yl]oxymethyl}-2-furancarboxylate** (**IVb**), mp 205–207°C (MeOH–CH_2Cl_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.93 s (3H, CH_3), 4.77 s (2H, NCH_2), 5.20 s (2H, OCH_2), 6.60 d (1H, H_{furyl}, *J* 3.5 Hz), 7.13–7.82 m (8H, H_{furyl}, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 48.2 (C^3), 51.8 (Me), 62.2 (CH_2O), 111.7, 114.2, 116.8, 118.3, 120.3, 128.4, 129.9, 131.7, 134.6, 138.3, 144.6, 152.5, 153.2 (C_{furyl}, C_{arom}), 158.6 (C=O), 167.0 (C=O).

From 0.38 g (2.22 mmol) of imine **Va** (reaction time 5 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.295 g (53%) of **5-phenyl-6,6-difluoro-5*a*,6-dihydro-3*aH*-cyclopropa[*b*]furo[2,3-*c*]-pyrrol-4(5*H*)-one (IXa)**.

From 1.32 g (5.0 mmol) of imine **Vb** (reaction time 5 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.61 g (36%) of **5-(4-bromophenyl)-2-methyl-6,6-difluoro-5*a*,6-dihydro-3*aH*-cyclopropa[*b*]furo[2,3-*c*]pyrrol-4(5*H*)-one (IXb)**, mp 121–123°C (hexane–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1725 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.97 s (3H, Me), 3.91 d.d (1H, H^{5a}, *J* 8.0, 1.4 Hz), 4.18 d.d (1H, H^{3a}, *J* 4.4, 2.2 Hz), 5.13 s (1H, H^3), 7.40–7.54 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.3 (Me), 49.1 d.d (C^{5a}, *J* 17.6, 15.6 Hz), 52.4 d (C^{3a}, *J* 2.3 Hz), 68.2 d.d (C^{6a}, *J* 19.4, 10.4 Hz), 94.9 d (C^3, *J* 1.1 Hz), 108.3 d.d (C^6, *J* 319, 301 Hz), 118.5, 122.0, 131.8, 136.6 (C_{arom}), 157.7 (C^2), 171.4 d.d (C^4, *J* 4.2, 2.6 Hz). Found, %: C 49.07; H 3.10; N 3.98. $C_{14}H_{10}BrF_2NO_2$. Calculated, %: C 49.15: H 2.95; N 4.09.

From 0.70 g (2.2 mmol) of imine **Vc** (reaction time 14 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.336 g (36%) of **ethyl 4-(5-phenyl-4,4,6,6-tetrafluoro-4,5,5*a*,6-tetrahydro-3*aH*-cyclopropa-[*b*]furo[2,3-*c*]pyrrol-2-yl)benzoate (VIIIc)** and 0.052 g (6%) of **ethyl 4-(4-oxo-5-phenyl-6,6-difluoro-4,5,5*a*,6-tetrahydro-3*aH*-cyclopropa[*b*]furo[2,3-*c*]-pyrrol-2-yl)benzoate (IXc)**. Compound **VIIIc**, mp 158–161°C (decomp.) (hexane–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1725 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 t (3H, CH_3, *J* 7.1 Hz), 3.95 t (1H, H^{5a}, *J* 7.4 Hz), 4.43 q (2H, CH_2, *J* 7.1 Hz), 4.58 d.d.d.d (1H, H^{3a}, *J* 13.2, 6.8, 4.2, 2.6 Hz), 5.79 br.s (1H, H^3), 7.07–8.11 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.9 (CH_3), 50.8 t (C^{5a}, *J* 15.6 Hz), 58.0 d.d (C^{3a}, *J* 32.3, 2.2 Hz), 60.9 (CH_2), 71.7 m (C^{6a}), 94.9 (C^3), 109.8 d.d.d (C^6, J_{CF} 320, 302, 10 Hz), 116.9 t (*J* 2.2 Hz), 122.6, 125.1 (C_{arom}), 128.6 d.d.d (C^4, *J* 259, 248, 7 Hz), 128.9, 129.4, 131.3, 132.1, 138.5 d (C_{arom}, *J* 4.4 Hz), 158.0 (C^2), 165.5 (C=O). Found, %: C 63.21; H 4.16; N 3.15. $C_{22}H_{17}F_4NO_3$. Calculated, %: C 63.01; H 4.09; N 3.34. Compound **IXc**, mp 143–145, 149–151°C dimorphous (hexane–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1730 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.43 t (3H, CH_3, *J* 7.1 Hz), 4.06 d.d (1H, H^{5a}, *J* 8.2, 1.7 Hz), 4.41 q (2H, CH_2, *J* 7.1 Hz), 4.41 m (1H, H^{3a}), 5.97 d.d (1H, H^3, *J* 2.9, 1.5 Hz), 7.23–8.10 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.0 (Me), 49.5 d.d (C^{5a}, *J* 17.7, 15.5 Hz), 52.7 d (C^{3a}, *J* 2.2 Hz), 60.9 (CH_2), 68.3 d.d (C^{6a}, *J* 19.6, 11.1 Hz), 96.3 (C^3), 108.3 d.d (C^6, *J* 319, 301 Hz), 120.8, 124.9, 125.8, 128.9, 129.5, 131.1, 132.1, 137.2 (C_{arom}), 157.0 (C^2), 165.5 (CO_2Et), 170.6 t (C^4, *J* 3.5 Hz). Found, %: C 66.60; H 4.37; N 3.42. $C_{22}H_{17}F_2NO_4$. Calculated, %: C 66.50; H 4.31; N 3.52.

From 0.53 g (1.54 mmol) of imine **Vd** (reaction time 12 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.350 g (51% with respect to applied imine, 73% with respect to reacted imine) of **5-(4-bromophenyl)-4,4,6,6-tetrafluoro-2-(2-fluorophenyl)-4,5,5*a*,6-tetra-hydro-3*aH*-cyclopropa[*b*]furo[2,3-*c*]pyrrole (VIIId)** and 0.085 g (30%) of 5-(2-fluorophenyl)furfural.

From 0.71 g (2.53 mmol) of imine **Ve** (reaction time 6 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.455 g (50%) of **2-bromo-5-(4-methoxyphenyl)-6,6-difluoro-5*a*,6-dihydro-3*aH*-cyclopropa[*b*]furo-[2,3-*c*]pyrrol-4(5*H*)-one (IXe)**, mp 111–112°C (hexane–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1730 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.82 s (3H, Me), 4.05 d.d (1H, H^{5a}, *J* 8.1, 1.9 Hz), 4.20 t (1H, H^{3a}, *J* 2.3 Hz), 5.56 d.d (1H, H^3, *J* 2.3, 1.7 Hz), 6.95 d (2H, H_{arom}, *J* 9.0 Hz), 7.37 d (2H, H_{arom}, *J* 9 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 49.8 d.d (C^{5a}, *J* 17.6, 15.6 Hz), 51.9 d (C^{3a}, *J* 2.3 Hz), 55.2 (Me), 69.4 d.d (C^{6a}, *J* 20.1, 10.4 Hz), 100.9 (C^3), 107.5 d.d (C^6, *J* 319, 301 Hz), 114.1, 122.9, 129.7, 132.6 (C_{arom}), 157.7 (C^2), 169.5 d.d (C^4, *J* 4.0, 2.9 Hz). Found, %: C 46.75; H 2.92; N 3.70. $C_{14}H_{10}BrF_2NO_3$. Calculated, %: C 46.95; H 2.81; N 3.91.

From 0.73 g (2.41 mmol) of imine **Vf** (reaction time 4 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.307 g (34% with respect to applied imine, 76% with respect to reacted imine) of **4-{5-(4-methoxyphenyl)-4-oxo-6,6-difluoro-4,5,5*a*,6-tetra-hydro-3*aH*-cyclopropa[*b*]-furo[2,3-*c*]pyrrol-2-yl}benzonitrile (IXf)** and 0.175 g (55%) of 4-(5-formyl-2-furyl)benzonitrile. Compound **IXf**, mp 145–147°C (CH_2Cl_2–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2235 (C≡N), 1725 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.82 s (3H, Me), 4.03 d.d (1H, H^{5a}, *J* 7.9, 1.4 Hz), 4.40 d.d (1H, H^{3a}, *J* 2.8, 1.6 Hz), 6.00 d.d (1H, H^3, *J* 2.8, 1.4 Hz), 6.94 d (2H, 4-$MeOC_6H_4$, *J* 9.0 Hz), 7.39 d (2H, 4-$MeOC_6H_4$, *J* 9.0 Hz), 7.70 s (4H, 4-NCC_6H_4). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 49.8 d.d (C^{5a}, *J* 17.1, 15.5 Hz), 52.4 d (C^{3a}, *J* 2.2 Hz), 55.1 (Me), 68.4 d.d (C^{6a}, *J* 19.4, 11.1 Hz), 97.7 (C^3), 108.2 d.d (C^6, *J* 320, 301 Hz), 112.8, 114.1 (C_{arom}), 117.9

(C≡N), 112.9, 125.5, 129.8, 132.0, 132.3 (C_{arom}), 156.0, 157.6 (C^2, C_{arom}), 170.3 t (C^4, *J* 3.3 Hz). Found, %: C 66.31; H 3.74; N 7.32. $C_{21}H_{14}F_2N_2O_3$. Calculated, %: C 66.31; H 3.71; N 7.37.

Reaction of imine Vg with difluorocarbene. The reaction was carried out by the general procedure using a 6-fold excess of the difluorocarbene source. From 0.300 g (0.74 mmol) of imine **Vg**, 0.92 g (4.44 mmol) of active lead, 1.43 g (4.44 mmol) of tetrabutylammonium bromide, and 0.55 ml (6.0 mmol) of CBr_2F_2 (reaction time 4 h) using as eluent hexane–EtOAc, 5:1, at chromatographic purification of the mixture we obtained 0.124 g of a mixture of **2,5-bis(4-bromophenyl)-4,4,6,6-tetrafluoro-4,5,5*a*,6-tetrahydro-3*a*H-cyclopropa[*b*]furo-[2,3-*c*]pyrrole (VIIIg) and 2,4*a*-bis(4-bromophenyl)-1,1,3,3,4,4-hexafluoro-octahydrocyclopropa[*b*]cyclopropa[4,5]-furo[2,3-*c*]-pyrrole (X)** in a ratio 1:0.8 according to the data of ^{1}H NMR spectrum, and 0.113 g of 5-(4-bromophenyl)-furfural. Compound **VIIIg**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.93 t (1H, H^{5a}, *J* 7.5 Hz), 4.55 d.d.d.d (1H, H^{3a}, *J* 13.1, 6.4, 4.2, 2.7 Hz), 5.68 br.s (1H, H^3), 7.12–7.61 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 50.8 t (C^{5a}, *J* 15.2 Hz), 58.0 d.t (C^{3a}, *J* 32.9, 2.2 Hz), 70.8 m (C^{6a}), 93.3 d.d (C^3, *J* 1.4, 1.1 Hz), 109.7 d.d.d (C^6, *J* 320, 302, 9.4 Hz), 116.9 t (*J* 2.3 Hz), 122.6, 123.7, 124.9, 126.8 (C_{arom}), 128.8 d.d.d (C^4, *J* 260, 250, 6 Hz), 128.9, 131.8, 138.2 d (C_{arom}, *J* 4.4 Hz), 157.9 (C^2). Compound **X**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.05 d (1H, H^{3b}, *J* 14.5 Hz), 3.73 t (1H, H^{1a}, *J* 7.4 Hz), 4.06 d.d.d (1H, H^{3a}, *J* 11.8, 7.2, 1.2 Hz), 7.12–7.61 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 31.4 d.t (C^{3b}, *J* 12.0, 5.0 Hz), 47.8 t (C^{1a}, *J* 16.0 Hz), 54.2 t.t (C^{3a}, *J* 30.8, 2.9 Hz), 70.8 m (C^{4a}), 75.3 t (C^{4a}, *J* 12.2 Hz), 109.0 d.d.d (C^1, *J* 320, 302, 9.4 Hz), 109.7 d.d (C^4, *J* 305, 297 Hz), 117.1 t (*J* 2.3 Hz), 123.1, 123.9 (C_{arom}), 126.3 d.d.d (C^3, J_{CF} 261, 249, 6 Hz), 127.2, 128.9 t (*J* 1.5 Hz), 129.0, 131.5, 138.1 d (*J* 5.0 Hz) (C_{arom}).

Into a solution of 0.08 g of a mixture of compounds **VIIIg** and **X** in 2 ml of chloroform was added 0.5 g of silica gel, the solvent was evaporated in a vacuum, and the mixture obtained was maintained at room temperature for 24 h. The reaction products were extracted with chloroform and analyzed by ^{1}H NMR spectroscopy. According to the spectral data the sample obtained consisted of a mixture of **2-(4-bromophenyl)-5-phenyl-6,6-difluoro-5*a*,6-dihydro-3*a*H-cyclopropa[*b*]furo-[2,3-*c*]-pyrrol-4(5*H*)-one (IXg)** and **4*a*-(4-bromophenyl)-2-phenyl-1,1,4,4-tetrafluorohexahydro-cyclopropa-[*b*]cyclopropa[4,5]furo[2,3-*c*]pyrrol-3(1*H*)-one (XI)** in a ratio 1:0.8. Compound **IXg**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.04 d.d (1H, H^{5a}, *J* 8.1, 1.7 Hz), 4.38 d.d (1H, H^{3a}, *J* 2.6, 2.1 Hz), 5.85 d.d (1H, H^3, *J* 2.6, 1.7 Hz), 7.27–7.59 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 49.5 d.d (C^{5a}, *J* 17.6, 16.0 Hz), 52.7 d (C^{3a}, *J* 2.5 Hz), 68.2 m (C^{6a}), 94.7 d (C^3, *J* 1.1 Hz), 108.3 d.d (C^6, *J* 319, 301 Hz), 120.5, 123.2, 125.8, 126.6, 127.2, 128.9, 131.5, 137.3 (C_{arom}), 157.0 (C^2), 170.8 (C^4). Compound **XI**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.13 d (1H, H^{3b}, J_{HF} 13.8 Hz), 3.89 d.d (1H, H^{1a}, *J* 8.3, 1.8 Hz), 3.95 d.d (1H, H^{3a}, *J* 3.0, 1.8 Hz), 7.27–7.59 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 33.9 t (C^{3b}, *J* 11.9 Hz), 47.0 d.d (C^{1a}, *J* 17.6, 16.0 Hz), 49.1 t (C^{3a}, *J* 3.6 Hz), 68.1 m (C^{5a}), 74.5 t (C^{4a}, *J* 12 Hz), 107.4 d.d (C^1, *J* 319, 301 Hz), 109.8 d.d (C^4, *J* 307, 298 Hz), 120.8, 123.7, 126.2, 127.9 t (*J* 1.7 Hz), 128.5, 129.0, 131.7, 137.0 (C_{arom}), 170.0 (C^3).

General procedure for thermolysis of compounds VIIIc, IXa, IXb, and IXf. Furopyrroles **VIIIc, IXa, IXb,** and **IXf** were kept for 10 min in a test tube placed into an oil bath heated at 160°C. Therewith the initial compounds melted with HF liberation. On cooling the solid reaction product was recrystallized from a mixture $CHCl_3$–CH_2Cl_2 or CH_2Cl_2–Et_2O.

From 0.130 g (0.52 mmol) of compound **IXa** was obtained 0.099 g (83%) of **5-phenyl-7-fluoro-4,5-dihydro-furo[3,2-*c*]pyridin-4-one (XIIa)**.

From 0.090 g (0.21 mmol) of compound **VIIIc** was obtained 0.070 g (86%) of **ethyl 4-(4-oxo-5-phenyl-7-fluoro-4,5-dihydrofuro[3,2-*c*]pyridin-2-yl)benzoate (XIIc)**, mp 220–221°C (CH_2Cl_2–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1735 (C=O), 1700 (C=O), 1630 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 t (3H, CH_3, *J* 6.8 Hz), 4.42 q (2H, CH_2, *J* 6.8 Hz), 7.34 d (1H, H^6, *J* 6.0 Hz), 7.43–8.16 m (10H, H^3, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.0 (CH_3), 60.9 (CH_2), 104.6 d (C^3, *J* 2.3 Hz), 119.4 d (C^{3a}, *J* 3.1 Hz), 120.5 d (C^6, *J* 32.2 Hz), 124.0, 126.5, 128.3, 129.1, 129.9, 130.2, 132.4 (C_{arom}), 138.0 d (C^7, *J* 239 Hz), 140.0 (C_{arom}), 148.7 d (C^{7a}, *J* 15.0 Hz), 155.1 (C^2), 156.8 (C^4), 165.6 (CO_2Et). Found, %: C 70.26; H 4.40; N 3.63. $C_{22}H_{16}FNO_4$. Calculated, %: C 70.02; H 4.27; N 3.71.

From 0.120 g (0.35 mmol) of compound **IXb** was obtained 0.091 g (80%) of **5-(4-bromophenyl)-2-methyl-7-fluoro-4,5-dihydrofuro[3,2-*c*]pyridin-4-one (XIIb)**, mp 251–253°C (CH_2Cl_2–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1695 (C=O), 1630 (C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.50 s (3H, Me), 6.67 m (1H,

H^{3}), 7.17 d (1H, H^{6}, *J* 5.7 Hz), 7.30 d (2H, H_{arom}, *J* 8.7 Hz), 7.62 d (2H, H_{arom}, *J* 8.7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.4 (Me), 104.0 d (C^{3}, J_{CF} 2.2 Hz), 118.2 d (C^{6}, *J* 32.6 Hz), 118.9 d (C^{3a}, *J* 3.3 Hz), 122.0, 128.3, 132.2 (C_{arom}), 138.0 d (C^{7}, *J* 239 Hz), 139.2 (C_{arom}), 148.2 d (C^{7a}, *J* 15 Hz), 155.8 (C^{2}), 156.6 (C^{4}). Found, %: C 52.02; H 2.90; N 4.15. $C_{14}H_9BrFNO_2$. Calculated, %: C 52.20; H 2.82; N 4.35.

From 0.049 g (0.129 mmol) of compound **IXf** was obtained 0.049 g (93%) of **4-{5-(4-methoxyphenyl)-4-oxo-7-fluoro-4,5-dihydrofuro[3,2-*c*]pyridin-2-yl}-benzonitrile (XIIf)** as a monohydrate, mp 285–286°C ($CHCl_3$–CH_2Cl_2). ^{1}H NMR spectrum (DMCO-d_6), δ, ppm: 3.83 s (3H, MeO), 7.07 d (2H, 4-$MeOC_6H_4$, *J* 8.7 Hz), 7.39 d (2H, 4-$MeOC_6H_4$, *J* 8.7 Hz), 7.97 d (2H, 4-NCC_6H_4, *J* 8.7 Hz), 7.97 d (1H, H^{3}, *J* 2.8 Hz), 8.06 d (1H, H^{6}, *J* 6.5 Hz), 8.10 d (2H, 4-NCC_6H_4, *J* 8.7 Hz). ^{13}C NMR spectrum (DMCO-d_6), δ, ppm: 52.9 (Me), 104.1 d (C^{3}, *J* 2.2 Hz), 108.4, 111.7 (C_{arom}), 115.8 (C≡N), 115.9 d (C^{3a}, *J* 3.0 Hz), 120.5 d (C^{6}, *J* 32.0 Hz), 122.4, 125.7, 130.0, 130.3, 130.5 (C_{arom}), 133.9 d (C^{7}, *J* 235 Hz), 146.4 d (C^{7a}, *J* 15.5 Hz), 151.1 (C_{arom}), 153.8 (C^{2}), 156.4 (C^{4}). Found, %: C 66.82; H 3.69; N 7.36. $C_{21}H_{13}FN_2O_2 \cdot H_2O$. Calculated, %: C 66.66; H 4.00 N 7.40.

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