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Intramolecular 1,3-Dipolar Cycloaddition to Ester Carbonyl of Azomethinylides Prepared from Aldimines and Difluorocarbene

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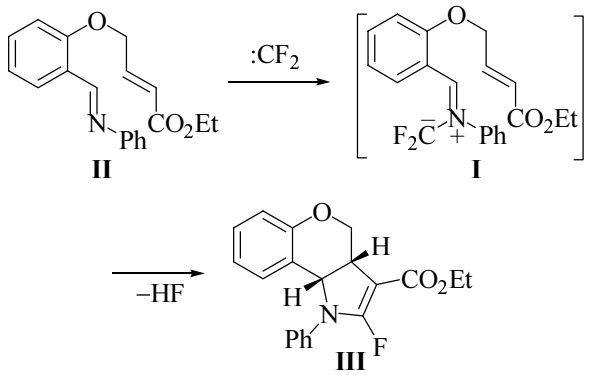
Abstract—Azomethinylides generated by reaction of difluorocarbene with N-alkyl- and N-arylimines of O-acylated salycilaldehyde undergo intramolecular 1,3-dipolar cycloaddition to the ester carbonyl group forming regioselectively 2,5-epoxy-1,4-benzoxazepine derivatives.

Reactions of 1,3-dipolar cycloaddition of azomethinylides are among the most promising synthetic approaches in the chemistry of the nitrogen-containing heterocycles [1]. An intramolecular version of this reaction became owing to recent investigations a convenient procedure for preparation of complex polycyclic and cage-like heterocyclic systems, including naturally occurring compounds [2]. The high synthetic potential of the intramolecular 1,3-dipolar addition of azomethinylides is due both to the large choice of methods for their generation and to the high regio- and stereoselectivity of the cycloaddition. Furthermore the intramolecular version of the reaction is relatively insensitive to variation of substituents attached to C=C and C≡C bond that serve as the most typical dipolarophile traps. The azomethinylides cycloaddition to the carbonyl bonds of aldehydes and ketones [3] and to imine C=N bonds [4–6] was performed only intermolecularly. The ester carbonyl group is famous for its passivity with respect to 1,3-dipoles and therefore it is often used for activation of C=C- and C≡C dipolarophiles [2, 3]. However we showed recently that under certain conditions the carbonyl bond of an ester functional group could serve for efficient capture of azomethinylides [7]. We report here the results of the study of intramolecular 1,3-dipolar cycloaddition to the ester carbonyl of azomethinylides generated by reaction of difluorocarbene with O-acylated salicylaldimines.

Among the main factors facilitating the intramolecular 1,3-dipolar cycloaddition should be named the nature of the chain (linker) connecting the dipole with the dipolarophile, and the activity of the multiple bond of the dipolarophile that grows in parallel with its electrophilic quality in case of nucleophilic azomethiylides. We formerly found that azomethinylides **I** generated from O-alkenylated salicylaldimines **II** and difluorocarbene readily added across a C=C bond connected to the ylide fragment of the molecule by a 4-atomic linker C_{sp^2}=C_{sp^2}–O–C_{sp^3}, affording chromenopyrrole derivatives **III**, Scheme 1.

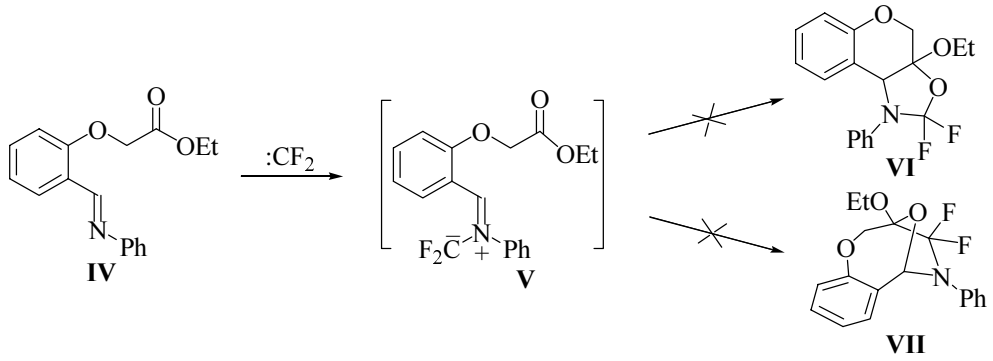
Scheme 1.



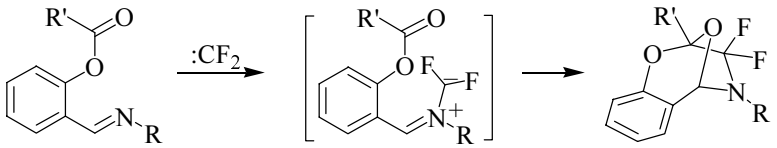
Moreover, in the molecules with this linker the intramolecular cycloaddition of a number of azomethinylides was performed even with so inert dipolarophile as the double bond of furan ring [8].

In order to test whether the intramolecular 1,3-dipolar cycloaddition of difluoromethylides would occur with a carbonyl of an ester group we generated from imine **IV** and difluorocarbene ylide **V** where the dipole and the potential dipolarophile were linked by the chain C_{sp^2}=C_{sp^2}–O–C_{sp^3} (Scheme 2).

Scheme 2.



Scheme 3.



The difluorocarbene was generated be reduction of CF_2Br_2 with active lead in the presence of tetrabutylammonium bromide under ultrasonic irradiation. However we failed to detect in the reaction mixture either cycloadduct **VI** or **VII**, and also their transformation products. The study of ylide system with a shorter, triatomic, linker C_{sp^2}=C_{sp^2}–O was carried o ut by an example of ylides **VIII** generated from imines **IX**. Successful intramolecular cycloadditions of azomethinylides connected to dipole with a triatomic linker are known for the bonds C=C [9–11], C≡C [12], and even for the multiple bond of the benzene ring (although under very severe conditions [13]).

Yields of compounds **Xa–Xo** and time of reaction of difluorocarbene with imines **IXa–IXo**

Imine	R	R'	Reaction time, h	Yield, %
IXa	Ph	Ph	72	74
IXb	Ph	4-$MeOC_6H_4$	19	92
IXc	Ph	4-NCC_6H_4	4	70
IXd	Ph	2,4-$Cl_2C_6H_3$	80	73
IXe	Ph	1-Naphthyl	95	75
IXf	Ph	CH_2=CMe	17	77
IXg	Ph	*trans*-MeCH=CH	110	68
IXh	Ph	*trans*, -PhCH=CH	20	56
IXi	Ph	*trans*-PhCH=CPh	80	70
IXj	4-BrC_6H_4	2-Furyl	37	75
IXk	4-BrC_6H_4	Ph	56	85
IXl	4-BrC_6H_4	4-$MeOC_6H_4$	11	[a]
IXm	4-BrC_6H_4	4-NCC_6H_4	44	[a]
IXn	2,4-$Cl_2C_6H_3$	Ph	85	70
IXo	$(4\text{-}ClC_6H_4)_2CH$	Ph	17	88

[a] Compounds **Xl, XIm** were isolated from mixtures obtained in runs of concurrent reactions.

Synthesis of arylimines **IXa–IXn** and N-alkylimine **IXo** was performed by condensation of the O-acylated salicylaldehyde with an appropriate amine. The synthesis of N-alkylimines by this procedure was not always successful due to fast hydrolysis of the ester group affording salicylaldimine. Therefore *O*-benzoylsalicylaldehyde *N*-trimethylsilylmethylimine **IXo** was prepared from *O*-benzoylsalicylaldehyde and trimethylsilylmethyl azide.

Keeping a mixture of O-benzoylsalicylaldehyde anil **IXa**, CF_2Br_2, active lead, and Bu_4NBr in dichloromethane at 45°C under ultrasonic irradiation of 160 W for 72 h resulted in formation of compound **Xa** that was isolated by column chromatography in 74% yield.

Compound **Xa** is a product of intramolecular 1,3-dipolar cycloaddition to the C=O bond of ester group of ylide **VIIIa** formed at difluorocarbene attack on the unshared electron pair of the nitrogen in imine **IXa**. Imines **IXb**–**IXo** reacted analogously to furnish adducts **Xb**–**Xo** (see

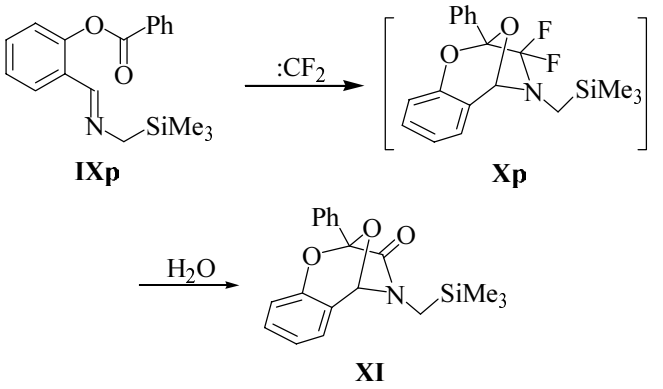
Scheme 3, and table). The reaction in all the cases occurred regioselectively affording exclusively bridged adducts **X**; no *ortho*-fused isomers of **VI** type was detected in the reaction mixtures. The regiochemistry of cycloaddition was consistent with that observed in intermolecular cycloaddition of difluoroazomethinylides to the carbonyl group of aldehydes and ketones [14]: the carbon atom of the difluoromethylene group of ylide always added to the carbon of the carbonyl group.

The composition and structure of compounds **Xa–o** were established basing on elemental analysis, ^{1}N and ^{13}C NMR and IR spectra, sometimes using also the data of ^{19}F NMR spectroscopy and mass spectra. In the ^{1}N NMR spectra of all compounds are present doublets from H^5 protons at 6.04–6.50 ppm ($^{4}J_{HF}$ 5.8–7.3 Hz). In the ^{13}C NMR spectra appears a singlet signal from C^5 at 85.8–88.6 ppm and doublets of doublets from atoms C^2 at 101.1–106.2 ppm ($^{2}J_{CF}$ 25.3–27.6, 33.1–37.0 Hz) and C^3 at 120.8–123.6 ppm ($^{1}J_{CF}$ 255–260, 259–268 Hz). In the ^{19}F NMR spectra of compounds **Xa, g** fluorine signals are observed at 57.5–59.8 and 84.5–88.7 ppm with respect to C_6F_6 with the coupling constant J_{FF} 176 Hz. In the mass spectra of compounds **Xa, Xd, Xe, Xg, Xi** molecular ion peaks were present. In addition the structure of compound **Xg** was solved by X-ray diffraction method [7].

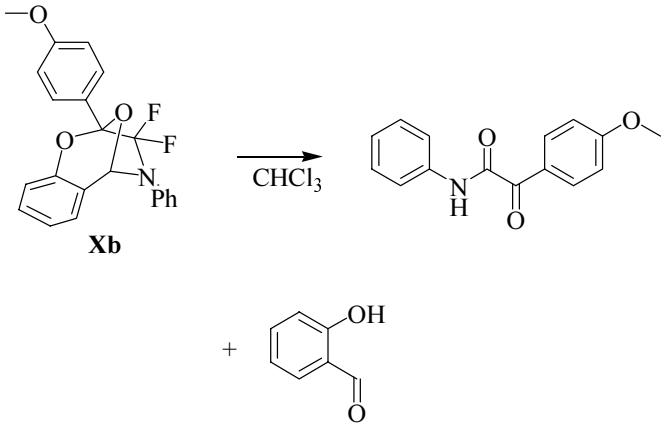
Difluoride **Xp** formed from N-alkyl-substituted imine **IXp** under conditions of difluorocarbene generation was unstable and at chromatography of the reaction mixture on silica gel suffered hydrolysis. Lactam **XI** was isolated in 67% yield (Scheme 4).

Compounds **Xa–Xo** and **XI**, mostly crystalline substances, are relatively stable and can be stored at 4°C for indefinitely long time. However at prolonged keeping on silica gel at room temperature compounds **Xa**–**o** are hydrolyzed to the corresponding lactams, and in weakly acidic solutions occurs decomposition of the bicyclic skeleton. For instance, after keeping a chloroform solution

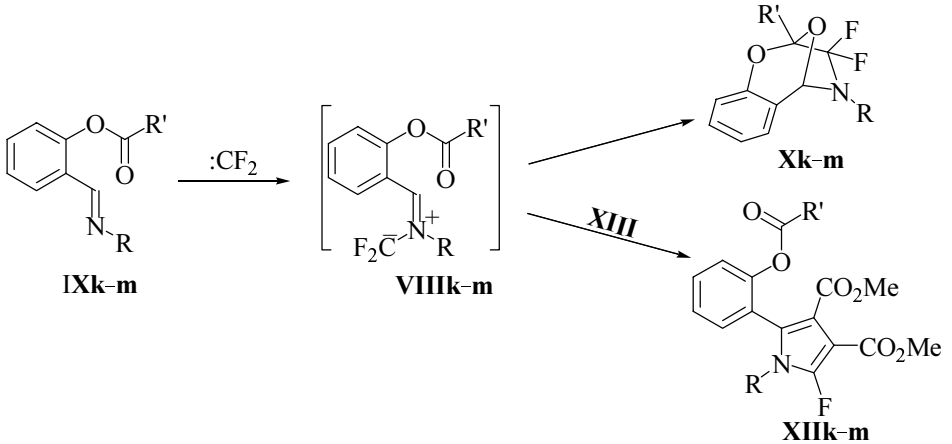
Scheme 4.



Scheme 5.



Scheme 6.

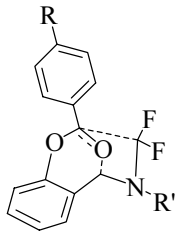


XII, R = 4-BrC_6H_4, R' = C_6H_5 (**k**); R = 4-BrC_6H_4, R' = $MeOC_6H_4$ (**l**); R = 4-BrC_6H_4, R' = CC_6H_4 (**m**).

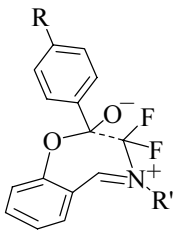
of compound **Xb** for 3.5 months were isolated *p*-methoxyphenylglyoxylic acid anilide and salicylaldehyde in 62% yield (Scheme 5).

The reactions of difluorocarbene with aromatic aldehydes N-alkyl- and N-arylimines in the presence of electron-deficient alkynes are known to afford fluoropyrroles [15]. The rate of intramolecular 1,3-dipolar cycloaddition to the C=O bond of ylide **VIIIl** proved to be comparable with the rate of intermolecular addition to one of the most active dipolarophiles, dimethyl acetylenedicarboxylate **XIII**.In reaction of imine **IXl** with difluorocarbene in the presence of double molar excess of compound **XIII** formed both difluoride **Xl** and fluoropyrrole **XIIl** the latter was isolated in 17% yield. According to ^{1}H NMR data compounds **Xl** and **XIII**formed in the ratio 1 : 1.08.

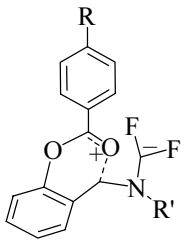
Similar experiments with imines **IXk**, m showed that the ratio of difluoride **Xk, Xm** to fluoropyrrole **XIIk, XIIm** was relatively weakly affected by the character of substituents in the benzoyl moiety of the initial imine (1 : 1.08 for imine **IXk** and 1 : 0.99 for imine **IXm**). Inasmuch as the substituents in the aromatic ring of the benzoyl group should not considerably affect the intermolecular cycloaddition for they are significantly removed from the reaction sites, the experimental data obtained indicate that the intramolecular cycloaddition to C=O group also is not notably sensitive to the electronic effect of substituents in the aromatic ring. This fact may be rationalized by analysis of the probable transition states A, B, and C in the cycloaddition reaction of ylides **VIII**.



A



B



C

The transition state A corresponds to a concerted cycloaddition with simultaneous formation of C–C and C–O bonds. The like cycloaddition mechanism is presumed for intermolecular reactions of difluoromethylides with C=C bonds [16]. The paths involving transition states B and C imply that the ylide addition to C=O bond is not concerted and occurs via zwitter-ion intermediates. These intermediates arising through transition state B are in particular the cause of rearranged products formation in reaction of sterically loaded C,C-diaryl-substituted difluoromethylides with aldehydes [14]. Structure C also cannot be ignored for here a positive charge might be delocalized to the aryl ring of the benzoyl group. In transition states B and C the charges on the atoms of the carbonyl group should suffer strong changes compared to the initial molecule, and hence if these transition states were operative a considerable influence of substituents R on the rate of intramolecular cycloaddition should be expected and therefore on the ratio of products **Xk–m** and **XIIk–m**. On the contrary, if the reaction goes via the concerted transition state A the substituents effect should not be very conspicuous. The experimentally observed weak effect of R substituents of quite different electronic character on the rate of the intramolecular cycloaddition leads to conclusion that the reaction occurs by the concerted mechanism.

Although the intramolecular cycloaddition of fluorinated azomethinylides **VIII** to the ester carbonyl occurred quite readily giving the corresponding cycloadducts in high yields our attempt to carry out the reaction in an intermolecular fashion under similar conditions (benzalaniline and difluorocarbene as the source of azomethinylide, and methyl benzoate as external dipolarophile) was unsuccessful. At the same time the imtermolecular cycloaddition of fluorinated azomethinylides to aldehydes occurs without difficulty [14]. Apparently the unfavorable electronic factor that decreases the activity of the ester carbonyl compared to that of aldehyde (relatively higher LUMO energy in the former) in the intramolecular version of the reaction is overcome with the favorable entropic facctor.

Ylides **VIIIf–I** alongside the ester carbonyl contain one more dipolarophile fragment , C=C bond activated by a carbonyl group and connected to 1,3-dipole through a 4-atomic linker C_{sp^2}=C_{sp^2}–O–C_{sp^2}. The lack of competition between C=O dipolarophile and activated C=C dipolarophile is unexpected: the cycloaddition in all cases occurs only at the ester carbonyl. However the

activated and even nonactivated C=C bond connected to 1,3-dipole with a 4-atomic linker C_{sp^2}=C_{sp^2}–O–C_{sp^3} is known to readily undergo intramolecular cycloaddition [17]. This difference in reactivity is apparently caused by a higher rigidity of the first linker (containing one additional sp^2-center) that hampers efficient overlapping of orbitals from the dipole and the C=C bond.

Hence the intramolecular 1,3-dipolar cycloaddition of difluoroazomethinylides **VIII** to the ester carbonyl group occurs by concerted mechanism with complete regioselectivity yielding 2,5-epoxy-1,4-benzoxazepine derivatives. The rate of the reaction is comparable with the rate of intermolecular cycloaddition to the most active acetylene dipolarophiles.

EXPERIMENTAL

Melting points of compounds synthesized were measured on Boëtius heating block; the values obtained are presented without correction. IR spectra were recorded on a spectrophotometer Carl Zeiss UR-20, a cell 400 μm of thickness. NMR spectra were registered on a spectrometer Bruker DPX- 300, operating frequencies 300 (^{1}H) and 75 (^{13}C) MHz. Mass spectra were measured on MKh-1303 and HP-59970C instruments (ionizing energy 70 eV). The elemental analysis was "carried out on a CHN-analyzer HP-185B. The reaction progress was monitored by TLC on Silufol-254 plates. The reaction mixtures separation by column chromatography was performed on silica gel LS 5/40 (Chemapol). Dichloromethane, the solvent for imines reactions with difluorocarbene, was dried by distillation from P_2O_5.

O-Acylsalicylaldehydes were obtained by acylation of salicylaldehyde with appropriate acyl chlorides in anhydrous DMF in the presence of anhydrous K_2CO_3. Imines **IXa–o** were prepared by aldehydes condensation with amines in ethanol. Imine **IXp** was synthesized from O-benzoylsalicylaldehyde and trimethylsilylmethyl azide by procedure from [18]. Active lead was prepared by the method described in [15].

General procedure for reactions between imines and difluorocarbene. Into a flask of 50 ml capacity containing 1.2 g (5.8 mmol) of active lead was charged in succession under argon atmosphere 7 ml of anhydrous dichloromethane, 2.0 g (6.0 mmol) of tetrabutylammonium bromide, and 2.7 mmol of imine. The mixture was cooled to 10–15°C with cold water, and into the flask was charged 1.95 g (9.3 mmol) of dibromodifluoromethane. Then the flask was tightly stoppered and placed into an ultrasonic bath (160 W), and the reaction mixture was subjected to ultrasonic irradiation at 45°C till complete dissolution of lead. Then 4.0 g of silica gel (LS 40/100, Chemapol) was added to the reaction mixture, the solvent was evaporated to dryness in a vacuum, and the powder obtained was charged to the top of a chromatographic column packed with silica gel (LS 5/40, Chemapol). The products were eluted by a mixture hexane–ethyl acetate. Crystalline products were additionally recryatallized.

Physical and spectral characteristics of compounds **Xa, f** and **XI** were published in [7].

2-(4-Methoxyphenyl)-4-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xb). mp 139–141°C (hexane–EtOAc). ^{1}N NMR spectrum ($CDCl_3$), δ, ppm: 3.89 s (3H, MeO), 6.36 d (1H, H^5, $^4J_{HF}$ 6.6 Hz), 6.95–7.84 m (13H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 55.0 (MeO), 86.0 (C^5), 104.3 d.d (C^2, J_{CF} 26.5, 33.7 Hz), 113.3, 115.0, 116.1, 120.5 (C arom), 121.2 d.d (C^3, J_{CF} 257, 261 Hz), 121.5, 122.1 d (J_{CF} 5.0 Hz), 124.0, 127.4 d (J_{CF} 1.7 Hz), 129.1, 130.4, 136.4 d.d (J_{CF} 2.2, 4.0 Hz), 150.5, 160.7 (C arom). Found, %: C 69.02; H 4.41; N 3.47. $C_{22}H_{17}F_2NO_3$. Calculated, %: C 69.29; H 4.49; N 3.67.

4-(4-Phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepin-2-yl)benzonitrile (Xc). mp 149–150°C (EtOH). IR spectrum ($CNCl_3$), ν, cm^{-1}: 2240. ^{1}N NMR spectrum ($CDCl_3$), δ, ppm: 6.41 d (1H, H^5, $^4J_{HF}$ 6.5 Hz), 6.99–8.00 m (13H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 86.5 (C^5), 103.6 d.d (C^2, J_{CF} 26.5, 34.3 Hz), 113.9, 115.4, 116.1, 117.9, 121.07 (C arom), 121.1 d.d (C^3, J_{CF} 258, 262 Hz), 121.9 d (J_{CF} 5.0 Hz), 122.0, 124.2, 126.9 d (J_{CF} 1.7 Hz), 129.2, 130.6, 131.8, 136.0 d.d (J_{CF} 2.2, 4.4 Hz), 136.5 d (J_{CF} 1.7 Hz), 150.0 (C arom). Found, %: C 70.27; H 3.86; N 7.43. $C_{22}H_{14}F_2N_2O_2$. Calculated, %: C 70.21; H 3.75; N 7.44.

2-(2,4-Dichlorophenyl)-4-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xd). ^{1}N NMR spectrum ($CDCl_3$), δ, ppm: 6.39 d (1H, H^5, $^4J_{HF}$ 6.3 Hz), 6.96–7.96 m (12H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 85.9 d (C^5, J_{CF} 2.2 Hz), 104.4 d.d (C^2, J_{CF} 27.4, 36.2 Hz), 115.7 t (J_{CF} 2.5 Hz), 116.2, 120.9 (C arom), 121.00 d.d (C^3, J_{CF} 258, 268 Hz), 121.6 d (J_{CF} 4.4 Hz), 122.0, 124.3, 126.5, 128.8, 129.1, 129.5, 130.6, 131.1, 133.7, 136.2 d.d (J_{CF} 1.4, 4.1 Hz), 136.5, 150.1 (C arom). Mass spectrum (70 eV), *m/z* (I_{rel}, %): 423 (2) $[M]^+$, 421 (11) $[M]^+$, 419 (17) $[M]^+$, 246 (28), 196 (10), 173 (95), 163 (67), 161 (100), 77 (46), 51 (28).

2-(1-Naphthyl)-4-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xd). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.50 d (1H, H^5, $^4J_{HF}$ 5.9 Hz), 6.99–8.82 м (16H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 85.7 (C^5), 106.2 d.d (C^2, J_{CF} 27.6, 35.6 Hz), 115.4 t (J_{CF} 2.3 Hz), 116.2, 120.8, 121.7, 121.8 d.d (C^3, J_{CF} 258, 264 Hz), 122.0 d (J_{CF} 3.4 Hz), 124.3 d (J_{CF} 3.4 Hz), 125.3, 125.6, 125.9, 126.0, 126.2, 126.3, 128.2, 128.4, 129.1, 130.2, 130.5, 131.1, 133.9, 136.4 d.d (J_{CF} 2.3, 4.5 Hz), 150.4 (C arom). Mass spectrum (70 eV), *m/z* (I_{rel}, %): 401 (5) $[M]^+$, 335 (5), 246 (12), 196 (3), 181 (3), 177 (3), 155 (100), 152 (3), 127 (23), 77 (11).

(*E*)-2-(Prop-1-enyl)-4-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xg). mp 108–110°C (hexane–Et_2O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.96 d (3H, Me, *J* 6.6 Hz), 5.89 d.q (1H, H^1 propenyl, *J* 1.6, 15.7 Hz), 6.21 d (1H, H^5, $^4J_{HF}$ 6.2 Hz), 6.61 d.q (1H, H^2 propenyl, *J* 6.6, 15.0 Hz), 6.93–7.37 m (9H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 17.7 (Me), 86.0 (C^5), 102.8 d.d (C^2, J_{CF} 27.1, 33.1 Hz), 115.0, 116.0, 120.4 t (J_{CF} 2.2 Hz) (C arom), 121.1 d.d (C^3, J_{CF} 257, 261 Hz), 121.5, 122.4 d (J_{CF} 3.9 Hz), 124.0, 129.0, 130.3, 134.4 d (J_{CF} 1.7 Hz), 136.4 d.d (J_{CF} 2.2, 4.4 Hz), 135.4 (C arom). Found, %: C 68.53; N 4.83; N 4.07. $C_{18}H_{15}F_2NO_2$. Calculated, %: C 68.57; N 4.79; N 4.44.

(*E*)-2-Styryl-4-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xh). mp 92–94°C (hexane–Et_2O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.27 d (1H, H^5, $^4J_{HF}$ 6.8 Hz), 6.50 d.d (1H, H^1 styryl, J_{HH} 16.2, $^4J_{HF}$ 2.5 Hz), 6.96–7.60 m (13H, H^2 styryl, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 86.2 (C^5), 103.4 d.d (C^2, J_{CF} 26.5, 33.2 Hz), 115.2 t (J_{CF} 2.5 Hz), 116.1, 117.7, 120.6 (C arom), 121.2 d.d (C^3, J_{CF} 258, 262 Hz), 121.6, 122.3 d (J_{CF} 5.0 Hz), 124.0, 127.1, 128.4, 128.8, 129.1, 130.4, 134.8, 136.5 d (J_{CF} 1.7 Hz), 150.3 (C arom). Found, %: C 73.16; N 4.57; N 3.30. $C_{23}H_{17}F_2NO_2$. Calculated, %: C 73.20; N 4.54; N 3.71.

(*Z*)-2-(1,2-Diphenylvinyl)-4-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xi). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.29 d (1H, H^5, $^4J_{HF}$ 6.9 Hz), 6.93–7.51 m (20H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 85.8 (C^5), 104.6 d.d (C^2, J_{CF} 25.3, 34.5 Hz), 115.1 t (J_{CF} 2.5 Hz), 116.1, 120.5, 121.5 (C arom), 121.6 d.d (C^3, J_{CF} 258, 263 Hz), 122.0 d (J_{CF} 5.0 Hz), 123.9, 127.6, 127.7, 128.1, 129.0, 129.6, 130.3, 130.4,132.4, 132.5, 134.5, 134.8, 136.3 d.d (J_{CF} 2.5, 4.4 Hz), 150.6 (C arom). Mass spectrum (70 eV), *m/z* ($I_{rel.}$, %): 453 (6) $[M]^+$, 387 (23), 246 (16), 207 (62), 196 (5), 179 (100), 178 (27), 152 (8), 77 (19), 39 (11).

4-(4-Bromophenyl)-3,3-difluoro-2-(2-furyl)-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xj). mp 159–160°C (hexane–EtOAc). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.26 d (1H, H^5, $^4J_{HF}$ 6.2 Hz), 6.56 t (1H, H furyl, *J* 1.8 Hz), 6.93–7.64 m (10H, H furyl, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 86.3 (C^5), 101.1 d.d (C^2, J_{CF} 27.4, 34.0 Hz), 110.3, 111.3 d (J_{CF} 1.7 Hz), 114.7, 116.3, 117.1 t (C arom, J_{CF} 2.8 Hz), 120.8 d.d (C^3, J_{CF} 260, 263 Hz), 121.0, 121.6 d (J_{CF} 4.4 Hz), 124.1, 130.8, 132.1, 135.2 d.d (J_{CF} 2.2, 3.9 Hz), 144.0, 144.3, 149.8 (C arom). Found, %: C 54.43; H 3.02; N 3.17. $C_{19}H_{12}BrF_2NO_3$. Calculated, %: C 54.31; H 2.88; N 3.33.

4-(4-Bromophenyl)-2-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xk). mp 134–135°C (hexane–EtOAc). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.32 d (1H, H^5, $^4J_{HF}$ 6.3 Hz), 6.95–7.87 m (13H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 86.2 (C^5), 104.2 d.d (C^2, J_{CF} 25.3, 34.5 Hz), 114.4, 116.3, 116.8, 120.7 (C arom), 121.1 d.d (C^3, J_{CF} 259, 262 Hz), 121.7 d (J_{CF} 4.6 Hz), 123.9, 125.8, 128.0, 130.0, 130.6, 131.6, 132.0, 135.4 m, 150.4 (C arom). Found, %: C 58.44; H 3.34; N 3.08. $C_{21}H_{14}BrF_2NO_2$. Calculated, %: C 58.62; H 3.28; N 3.26.

4-(4-Bromophenyl)-2-(4-methoxyphenyl)-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xl). mp 150–151°C (hexane–EtOAc). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.89 s (3H, MeO), 6.29 d (1H, H^5, $^4J_{HF}$ 5.8 Hz), 6.94–7.81 m (12H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 55.0 (MeO), 86.0 (C^5), 104.3 d.d (C^2, J_{CF} 26.5, 33.7 Hz), 113.4, 114.2, 116.2, 116.7 t (J_{CF} 2.8 Hz), 120.6 (C arom), 121.1 d.d (C^3, J_{CF} 258, 263 Hz), 121.7 d (J_{CF} 5.0 Hz), 123.8, 123.9, 127.4, 130.6, 132.0, 135.4 d.d (J_{CF} 2.2, 4.4 Hz), 150.4, 160.7 (C arom).

4-(2,4-Dichlorophenyl)-2-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4-benzoxazepine (Xn). mp 100–101°C (pentane). ^{1}N NMR spectrum ($CDCl_3$), δ, ppm: 6.04 d (1H, H^5, $^4J_{HF}$ 6.6 Hz), 6.82–7.93 m (12H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 88.6 (C^5), 104.1 d.d (C^2, J_{CF} 26.8, 33.0 Hz), 116.0, 120.6 (C arom), 121.7 d.d (C^3, J_{CF} 259, 259 Hz), 122.4 d (J_{CF} 3.3 Hz), 123.9, 125.9 d (J_{CF} 1.7 Hz), 127.6, 127.9, 129.8, 130.1, 130.4, 131.8 t (J_{CF} 2.5 Hz), 132.0, 134.5, 135.6 d.d (J_{CF} 1.1, 2.8 Hz), 150.4 (C arom). Found, %: C 60.00; H 3.19; N 3.14. $C_{21}H_{13}Cl_2F_2NO_2$. Calculated, %: C 60.02; H 3.12; N 3.33.

4-[Bis(4-chlorophenyl)methyl]-2-phenyl-3,3-difluoro-2,3,4,5-tetrahydro-2,5-epoxy-1,4- benzo-

xazepine (Xo). mp 192–194°C (hexane–EtOAc). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.92 d (1H, $CHAr_2N$, $^4J_{HF}$ 4.9 Hz), 5.73 d (1H, H arom, $^6J_{HF}$ 5.7 Hz), 6.41 d.d (1H, H^5, $^4J_{HF}$ 7.3, $^4J_{HH}$ 1.1 Hz), 6.87–7.80 m (16H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 61.7 d ($CHAr_2N$, J_{CF} 5.0 Hz), 88.0 d (C^5, $^3J_{CF}$ 4.4 Hz), 104.7 d.d (C^2, J_{CF} 26.0, 37.0 Hz), 120.2 d (J_{CF} 3.9 Hz), 120.3 (C arom), 123.6 d.d (C^3, J_{CF} 255, 268 Hz), 124.9, 125.6 d (J_{CF} 1.1 Hz), 127.9, 128.3, 128.5, 129.0, 129.7, 130.6, 132.4, 133.5, 133.7, 137.8, 138.4, 150.6 (C arom). Found, %: C 65.71; N 3.79; N 2.46. $C_{28}H_{18}Cl_2F_2NO_2$. Calculated, %: C 65.90; N 3.75; N 2.74.

Dimethyl 1-(4-bromophenyl)-2-[2-(4-methoxybenzoyloxy)phenyl]-5-fluoropyrrole-3,4-dicarboxylate (XIII). The reaction was carried out along the general procedure using as internal dipolarophile a double excess of dimethyl acetylenedicarboxylate ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.72 s (3H, CO_2Me), 3.85 s (3H, CO_2Me), 3.91 s (3H, MeOAr), 6.96–7.98 m (12H, H arom). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 51.3; 51.4 (Me), 55.1 (Me), 94.6 d (J_{CF} 5.0 Hz), 113.5, 120.7, 122.1, 122.5, 122.7, 123.5 d (J_{CF} 2.8 Hz), 125.0, 128.3 d (J_{CF} 1.1 Hz), 130.0, 131.7, 131.97, 132.05, 132.1 (C arom), 146.9 d (CF, J_{CF} 278 Hz), 149.5 (C arom), 161.6 d (J_{CF} 5.0 Hz), 163.6 d (MeO<u>C</u>=O, J_{CF} 2.8 Hz), 163.7 (Ar<u>C</u>=O).

Concurrent reactions. Concurrent reactions of intra- and intermolecular cycloaddition with dimethyl acetylenedicarboxylate were carried out taking a double molar excess of the latter with respect to imine and at equal concentrations of the corresponding reagents in all experiments. Imine conversion was 50–95%. Ratio of compounds **Xk–Xm** and **XIIk–XIIm** was determined by comparison of intensity in the ^{1}N NMR spectra of the reaction mixtures of proton signal from H^5 belonging to compounds **VIIIk–VIIIm** (δ, ppm: 6.32, 6.29, 6.32 respectively), and of signal from methoxycarbonyl group of compounds **XIIk–XIIm** (δ 3.72 ppm).

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