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Dedicated to Full Member of the Russian Academy of Sciences V.I. Minkin on his 70th Anniversary

Intramolecular 1,3-Dipolar Cycloaddition of Geminal Difluoro Azomethine Ylides at Multiple Carbon–Carbon Bonds

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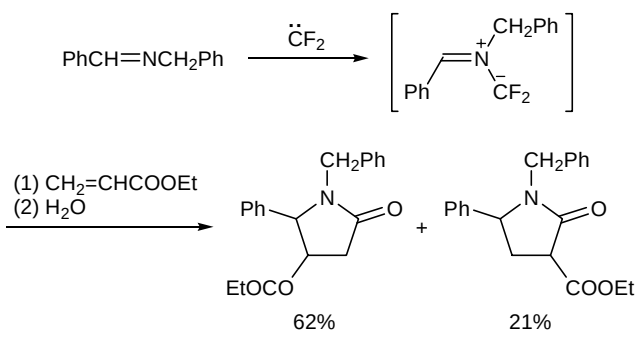
Abstract—*N*-Alkyl- and *N*-arylimines derived from *o*-allyl-, *o*-allyloxy-, and *o*-(2-propynyloxy)arenecarbaldehydes react with difluorocarbene to give indeno[1,2-*b*]pyrrole and chromeno[4,3-*b*]pyrrole derivatives. The reaction involves intermediate formation of difluoro-substituted azomethine ylides which undergo regio- and stereoselective intramolecular ring closure at the multiple bond.

1,3-Dipolar cycloaddition of azomethine ylides at multiple carbon–carbon bonds underlies important procedures for the synthesis of pyrrole derivatives. Reactions of functionally substituted ylides, in particular of geminal dihalo azomethine ylides, attract specific attention, for they lead to cycloadducts containing readily transformable functional groups, such as halogen atoms or oxo group. Intermolecular cycloadditions of geminal dichloro and difluoro azomethine ylides to alkenes and alkynes were studied, and methods for the synthesis of pyrrolidin-2-ones [1–4], 2-fluoro-4,5-dihydropyrroles [5], 2-fluoropyrroles [6], 3-chloropyridin-2-ones [1], and other heterocycles were developed on their base. Intramolecular cycloaddition of halogenated azomethine ylides could give rise to more complex structures in which the above listed functionally substituted heterocycles are fragments of fused or bridged polycyclic systems. We previously described the first example of such reaction [2].

In the present work we examined intramolecular cycloaddition of geminal difluoro azomethine ylides generated from difluorocarbene and *ortho*-substituted arenecarbaldehyde imines to double and triple carbon–carbon bonds. Specific attention was given to the effect of the length and nature of the bridging fragment between the dipole and dipolarophile moieties, as well as of the structure of the ylide and dipolarophile fragments, on the reactivity of azomethine ylides and regio- and stereoselectivity of the cycloaddition.

It is known that difluoro azomethine ylides generated *in situ* by reaction of difluorocarbene with *N*-alkyl- and *N*-arylbenzaldehyde imines readily add to such electron-deficient olefinic dipolarophiles as fumaric and maleic acid derivatives. In reactions with unsymmetrical dipolarophiles, e.g., methyl methacrylate and ethyl acrylate, cycloadducts with a distal arrangement of the CF_2 and CO_2R groups were mainly formed; hydrolysis of these products afforded substituted 5-oxopyrrolidine-3-carboxylic acid esters [3] (Scheme 1).

Scheme 1.



We have synthesized Schiff bases **Ia**–**Ic** whose reactions with difluorocarbene under analogous conditions should lead to ylide systems in which the 1,3-dipole and dipolarophile fragments (the latter being activated by the CO_2Et group) appear in a single molecule and are linked through a four-membered C_{sp^2}–C_{sp^2}–O–C_{sp^3} bridge. The reaction of *N*-phenyl-substituted Schiff base **Ia** with difluorocarbene gen-

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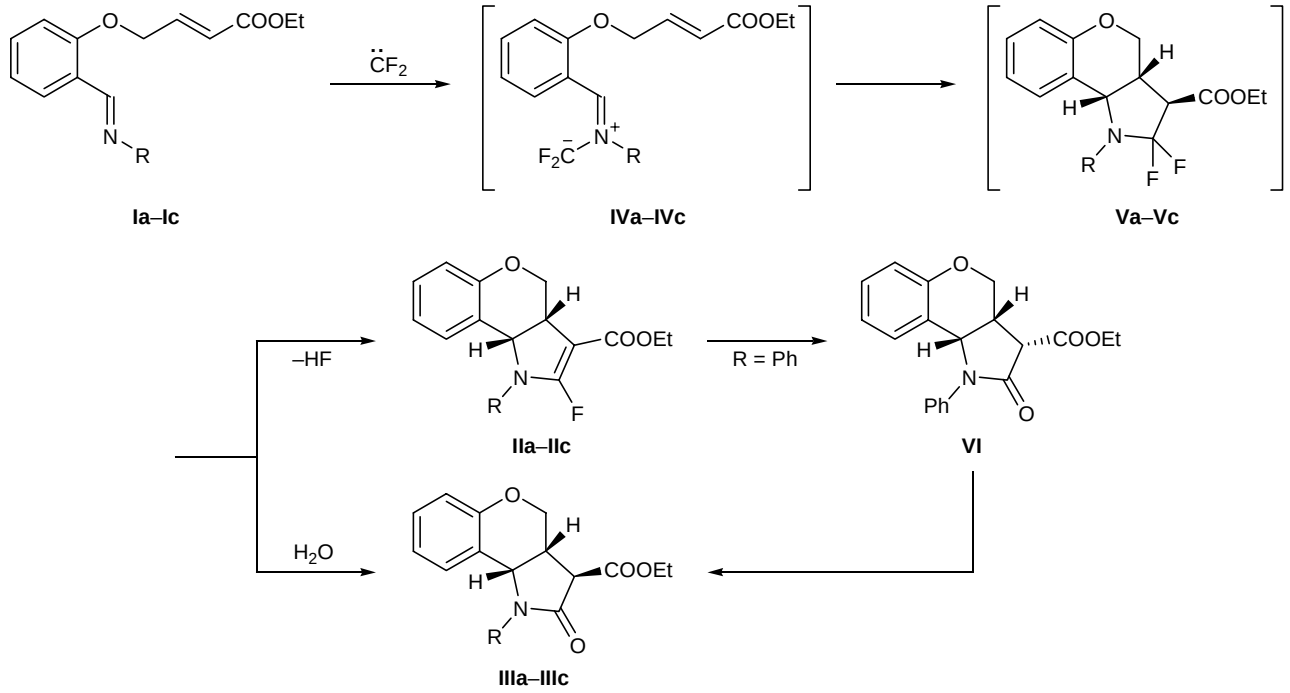
Scheme 2.



R = Ph (**a**), Me (**b**), *t*-Bu (**c**).

erated by reduction of dibromodifluoromethane with activated lead in the presence of tetrabutylammonium bromide afforded fluorodihydropyrrole **IIa** and lactam **IIIa**. The products were isolated by column chromatography on silica gel. The mechanism of their formation is shown in Scheme 2. It includes attack by difluorocarbene on the unshared electron pair on the nitrogen atom in the Schiff base to give intermediate ylide **IVa**, followed by intramolecular cycloaddition at the double bond. Difluoropyrrolidine **Va** thus formed undergoes dehydrofluorination to fluorodihydropyrrole **IIa**, and hydrolysis of **Va** gives lactam **IIIa**.

Table 1 contains data on the product compositions and their yields. It may be seen that the hydrolytic stability of fluorodihydropyrroles **II** strongly depends on the nature of the substituent on the nitrogen atom. The greatest yields were obtained from the *N*-*tert*-butyl derivative. While attempting to crystallize compound **IIa** at −15°C we found that it undergoes slow hydrolysis to lactam **VI**. The latter quantitatively rearranges into thermodynamically more stable isomer **IIIa** within several hours in $CDCl_3$. An analogous isomerization of structurally related systems is well known; it often occurs spontaneously in a few hours [1, 7]. Scheme 3 illustrates a plausible mechanism of acid hydrolysis of fluorodihydropyrrole **IIa** to lactam **VI**. Presumably, the crucial factor responsible for formation in the hydrolysis of thermodynamically less stable isomer **VI** is proton addition to the C^3 atom from the spatially more accessible side.

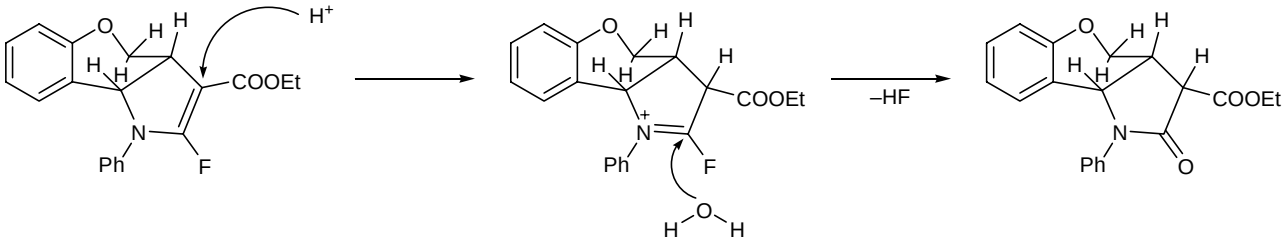
Table 1. Reaction of difluorocarbene with imines **Ia**–**Ic**[a]

Schiff base	R	Reaction time, h	Yield, %	
			II	**III**
Ia	Ph	2	17	50
Ib	Me	2 (34)	0 (0)	55 (32)
Ic	*t*-Bu	1	57	13

[a] In parentheses are given the data for the reactions carried out with nonactivated lead.

The syntheses of chromeno[4,3-*b*]pyrrole derivatives via intramolecular cycloaddition at the C=C bond in halogen-free azomethine ylides generated by noncarbene methods have been well documented [8–11]. A distinctive feature of the cycloaddition of difluoro-substituted ylides **IVa**–**IVc** is the perfect *cis*-stereoselectivity of the process: the reaction gives only systems with *cis*-fused pyran and pyrrolidine rings. This may be explained in terms of specificity of the carbene generation of azomethine ylide, which gives rise to the corresponding *Z*-dipole whose configuration is determined in turn by *E* configuration of the initial Schiff base. By contrast, such methods for generation of ylides as dehydration of the coupling product of

Scheme 3.



an aldehyde and secondary amine [8, 9] or prototropic isomerization of benzylidene derivatives of α-amino acids [10, 11] are equilibrium processes which often lead to formation of mixtures of isomeric ylides and hence mixtures of diastereoisomeric cycloaddition products.

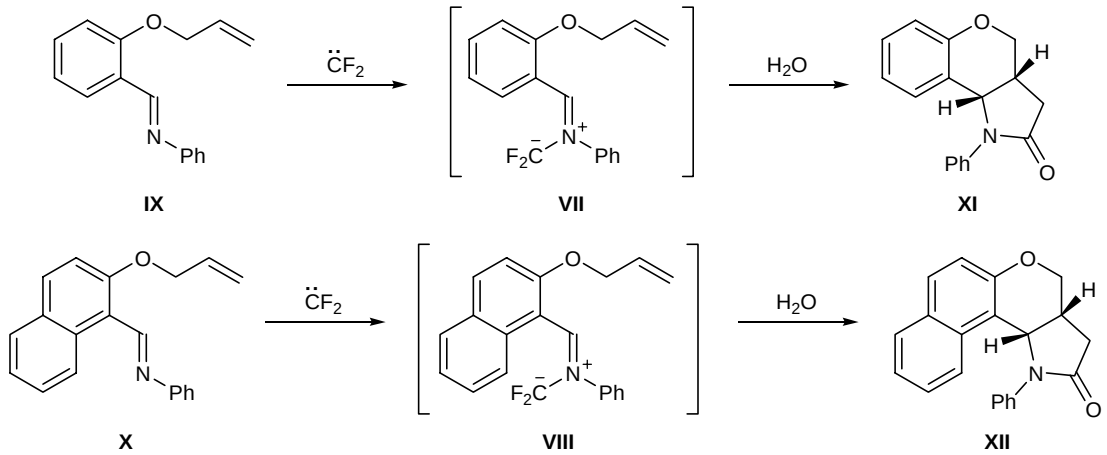
Using Schiff base **Ib** as an example we showed that the yield of lactam **IIIb** decreases while the reaction time considerably increases when difluorocarbene is generated with the use of common lead turnings instead of activated lead.

The structure of the products was determined by spectral methods, and the relative configurations of chiral centers in lactams **IIIa**–**IIIc** and **VI** were established on the basis of their ^{1}H NMR spectra and NOE experiments. According to the results of MNDO semiempirical calculations, the distances between the 3-H, 3a-H, and 9b-H protons in molecules **IIIa** and **VI** differ considerably. Irradiation of the 3a-H proton in **VI** increases the intensities of the 9b-H and 3-H signals by 11 and 12%, respectively. Irradiation of the same proton in **IIIa** increases the intensity of the 9b-H signal by 14%, whereas the 3-H signal grows by only 2%. Therefore, compound **IIIa** was assigned *trans,cis*-configuration, and **VI**, *cis,cis*. In addition, the *cis*-junction of the pyran and pyrrolidine rings in all the isolated products follows from a characteristic spin–spin coupling constant between 3a-H and 9b-H (J = 6.6–8.8 Hz). It is known that the coupling constant between protons in the bridgehead positions in analogous *cis*-5,6-fused systems ranges from 6 to 9 Hz and that the corresponding *trans* isomers are characterized by a value of 11–12 Hz [12].

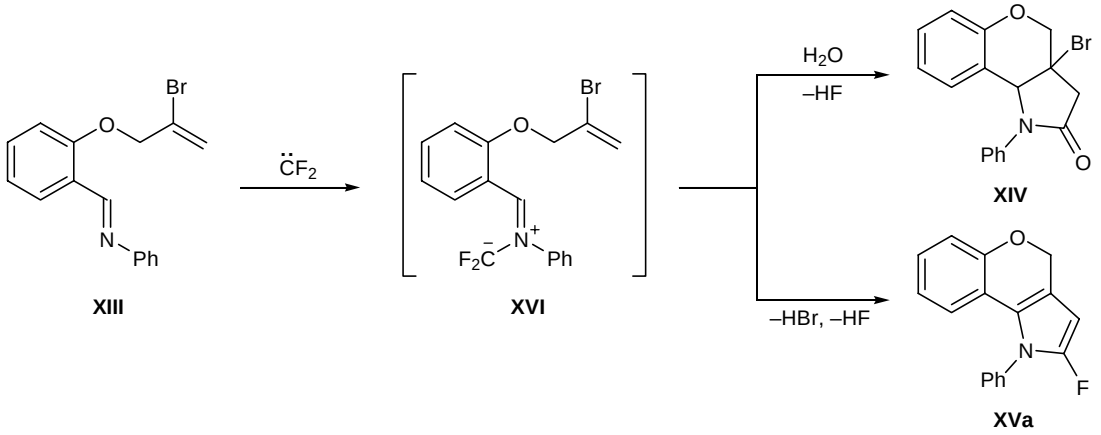
Study of the transformations of ylides **VII** and **VIII** in which the terminal double bond in the dipolarophile fragment is not activated showed that neither the reaction direction and its stereoselectivity nor the product yield change to an appreciable extent in the absence of an activating CO_2Et substituent. Schiff bases **IX** and **X** derived from aniline and 2-allyloxybenzaldehyde and 2-allyloxy-1-naphthaldehyde reacted with difluorocarbene to give, respectively, 56% of chromenopyrrole **XI** and 76% of benzochromenopyrrole **XII** (Scheme 4). The absence in the reaction mixtures of products having a cyclopropane ring indicates that there is no competition between the formation of azomethine ylide and difluorocyclopropanation of the double bond. The formation of geminal difluorocyclopropane derivatives in high yields is usually observed in reactions of difluorocarbene with nucleophilic alkenes [13].

Chromeno[4,3-*b*]pyrroles were also obtained by the reaction of difluorocarbene with Schiff base **XIII**

Scheme 4.



Scheme 5.

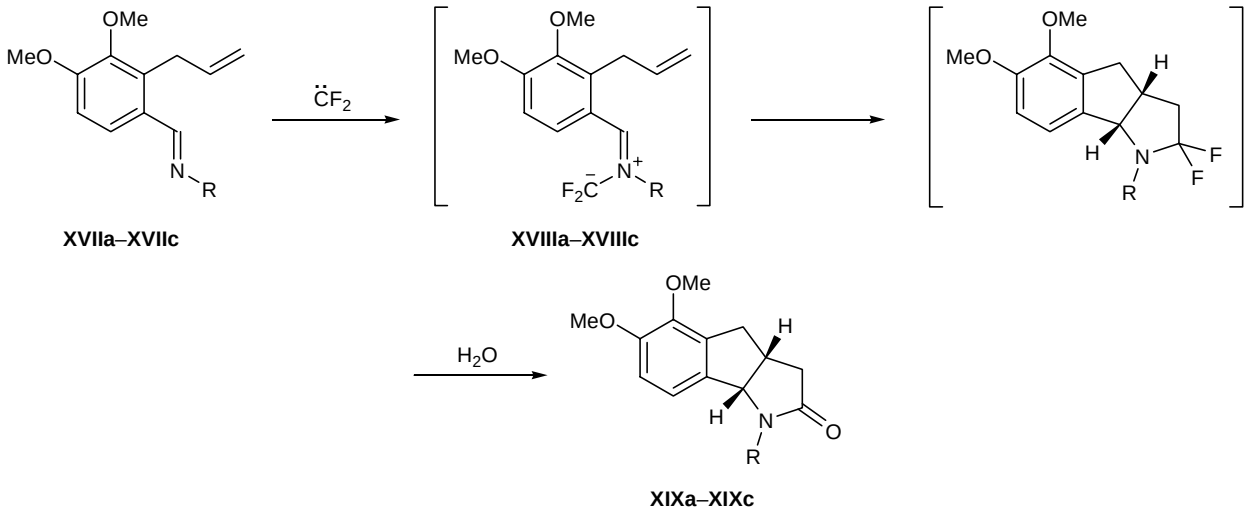


having a 2-bromo-2-propenyloxy group; in this case, apart from the expected product **XIV** (yield 23%), we isolated 18% of fluoropyrrole **XV** resulting from dehydrofluorination and dehydrobromination of primary cycloadduct **XVI** (Scheme 5).

The presence of an alkyl group at a double bond is known to reduce the activity of the latter as dipolarophile [10]; on the other hand, alkyl groups enhance the reactivity toward difluorocarbene [13]. Presumably, this is the reason why we failed to effect intramolecular cycloaddition of azomethine ylide generated from difluorocarbene and *N*-phenyl-*o*-(3-methyl-2-butenyl)-salicylaldehyde imine: after a long induction period, uncontrolled exothermic reaction has started; as a result, no identifiable compounds were isolated.

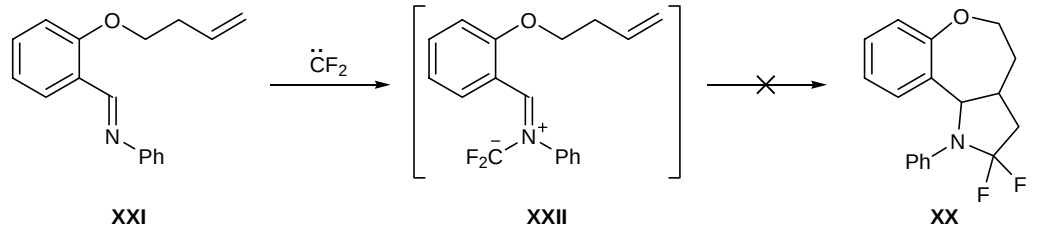
In order to estimate the effect of the length of the bridging group linking the dipole and dipolarophile fragments on the intramolecular 1,3-dipolar cycloaddition process, we synthesized a series of Schiff bases **XVIIa**–**XVIIc** from 2-allyl-3,4-dimethoxybenzaldehyde; compounds **XVIIa**–**XVIIc** are precursors of difluoro azomethine ylides **XVIIIa**–**XVIIIc** in which the bridging group is shorter than in **VII** by one atom. We have found that systems with a three-atom C_{sp^2}–C_{sp^2}–C_{sp^3} bridging group also readily undergo intramolecular cycloaddition with participation of the nonactivated C=C bond to afford indeno[1,2-*b*]pyrrole derivatives **XIXa**–**XIXc** in good yields (Scheme 6, Table 2). However, our attempts to build up benzoxepino[5,4-*b*]pyrrole system **XX** from *N*-phenyl-*o*-(3-butenyloxy)benzylideneamine (**XXI**) were unsuccessful: in the reaction mixture we detected no cycloaddition products which could be formed from intermediate ylide **XXII** with a five-membered C_{sp^2}–C_{sp^2}–

Scheme 6.



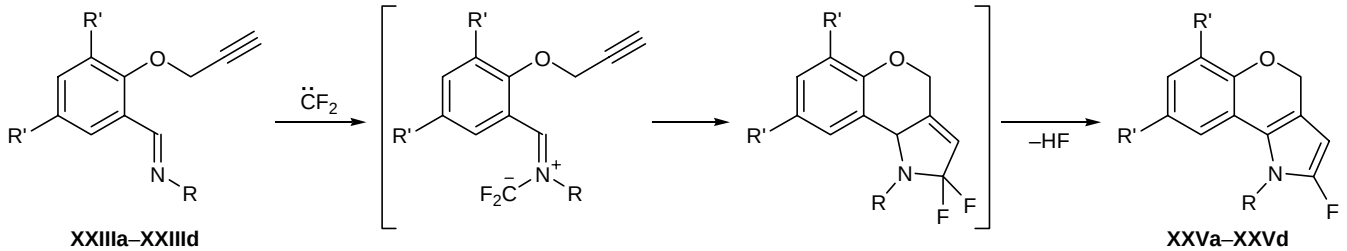
R = 4-BrC_6H_4 (**a**), $PhCH_2CH_2$ (**b**), *t*-Bu (**c**).

Scheme 7.

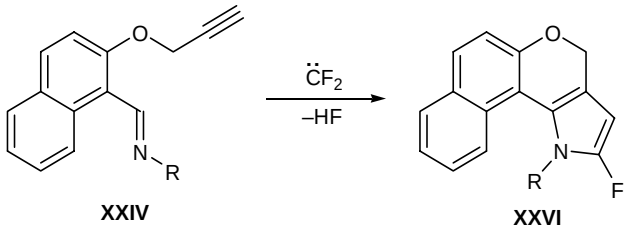


XXI **XXII** **XX**

Scheme 8.



XXIIIa–XXIIId **XXVa–XXVd**



XXIV **XXVI**

XXIII, R' = H, R = Ph (**a**), Me (**b**), *t*-Bu (**c**); R = 4-BrC_6H_4, R' = Br (**d**); **XXIV**, R = 4-BrC_6H_4.

O–C_{sp^3}–C_{sp^3} bridging group between the dipole and dipolarophile fragments (Scheme 7).

Intermolecular cycloaddition of difluoromethylides to acetylenes is known to afford fluoropyrroles [6]. Via the intramolecular version of this reaction, fused fluoropyrroles become accessible. Scheme 8 illustrates the reaction of difluorocarbene with Schiff bases **XXIIIa**–**XXIIId** and **XXIV** containing a terminal triple bond; the product yields are given in Table 3. Fluorochromenopyrroles **XXVa**–**XXVd** and **XXVI** are formed as a result of dehydrofluorination of unstable primary adducts having a difluorodihydropyrrole fragment. The structure of compounds **XXVa**–**XXVd** and **XXVI** was determined on the basis of their ^{1}H and ^{13}C NMR spectra and elemental compositions. The most characteristic signals in the ^{13}C NMR spectra were those from C^2 at δ_C ~150 ppm ($^1J_{CF} \approx$ 263–269 Hz) and C^3 at δ_C ~82 ppm ($^2J_{CF}$ = 12–16 Hz).

Thus azomethine ylides generated by addition of difluorocarbene to *N*-substituted *o*-allyl-, *o*-allyloxy-, and *o*-(2-propynyloxy)arencarbaldehyde imines undergo regio- and stereoselective intramolecular cycloaddition at the double bond to give chromeno[4,3-*b*]pyrrole and indeno[1,2-*b*]pyrrole derivatives.

EXPERIMENTAL

The melting points were determined on a Boetius device and were not corrected. The IR spectra were recorded on a Carl Zeiss UR-20 instrument using 400-μm cells. The NMR spectra were measured on a Bruker DPX 300 spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C. The mass spectra (electron impact, 70 eV) were run on an MKh-1303 mass spectrometer. The elemental compositions were determined on an HP-185B CHN analyzer. The progress of reactions was monitored by TLC on Silufol-254 plates. The reaction mixtures were separated by column chromatography using LS silica gel (5–40 μm, Chemapol). Methylene chloride was distilled over P_2O_5.

Table 2. Reactions of difluorocarbene with Schiff bases **XVIIa**–**XVIIc**

Schiff base	R	Reaction time, h	Product	Yield, %
XVIIa	4-BrC_6H_4	8	**XIXa**	73
XVIIb	$PhCH_2CH_2$	2	**XIXb**	82
XVIIc	*t*-Bu	13	**XIXc**	69

Table 3. Reactions of difluorocarbene with Schiff bases **XXIIIa**–**XXIIId** and **XXIV**

Schiff base	R	R'	Reaction time, h	Product	Yield, %
XXIIIa	Ph	H	7	**XXVa**	69
XXIIIb	Me	H	1	**XXVb**	49
XXIIIc	*t*-Bu	H	1	**XXVc**	31
XXIIId	4-BrC_6H_4	Br	4.5	**XXVd**	81
XXIV	4-BrC_6H_4	H	5	**XXVI**	63

Schiff bases **I**, **IX**, **X**, **XIII**, **XVII**, **XXI**, and **XXIII** were synthesized by condensation of the corresponding aldehydes with amines in ethanol. The initial aldehydes were prepared by alkylation of salicylaldehyde, 3,5-dibromosalicylaldehyde, and 2-hydroxynaphthaldehyde with appropriate halogen derivatives in anhydrous dimethylformamide in the presence of anhydrous potassium carbonate. 2-Allyl-3,4-dimethoxybenzaldehyde was synthesized by the procedure reported in [14]. Lead was activated as described in [6].

Reactions of Schiff bases with difluorocarbene (*general procedure***).** A 50-ml flask was charged with 2 g (9.7 mmol) of activated lead, and 3.54 g (12 mmol) of tetrabutylammonium bromide, 12 ml of methylene chloride, 0.003 mol of Schiff base, and 1.2 ml (13 mmol) of dibromodifluoromethane were added in succession under argon. The flask was tightly capped, and the mixture was stirred using a magnetic stirrer at 45°C or kept in an ultrasonic bath at the same temperature until the black lead powder disappeared completely. After cooling, 10 g of silica gel (100–160 μm) was added, the solvent was removed under reduced pressure, the residue was applied to a column charged with silica gel (5–40 μm), and the column was eluted with a hexane–ethyl acetate mixture.

From 0.6 g (1.94 mmol) of Schiff base **Ia** [reaction time 2 h; chromatographic separation was performed using hexane–diethyl ether (3:1 as eluent], we isolated 0.113 g (17%) of ethyl (3a*RS*,9b*SR*)-2-fluoro-1-phenyl-1,3a,4,9b-tetrahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (**IIa**) and 0.329 g (50%) of ethyl (3*RS*,3a*RS*,9b*SR*)-2-oxo-1-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (**IIIa**). The physical constants and spectral parameters of compounds **IIa** and **IIIa** were reported in [2].

Ethyl (3*RS*,3a*RS*,9b*SR*)-1-methyl-2-oxo-1,2,3,-3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (IIIb) was obtained from 0.82 g (3.31 mmol) of Schiff base **IIb** (reaction time 2 h); the product was isolated by column chromatography using hexane–ethyl acetate (first 5:1 and then 3:1) as eluent. Yield 0.509 g (55%). mp 97–98°C (from diethyl ether). IR spectrum (CCl_4), ν, cm^{-1}: 1740, 1710 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.34 t (3H, C**H**$_3$CH$_2$O, J = 7.1 Hz), 2.94 s (3H, CH_3N), 3.21–3.27 m (1H, 3a-H), 3.43 d (1H, 3-H, J = 5.3 Hz), 3.93 d.d (1H, 4-H, J = 11.5, 7.1 Hz), 4.11 d.d (1H, 4-H, J = 11.5, 3.5 Hz), 4.28 q (2H, CH_2O, J = 7.1 Hz), 4.77 d (1H, 9b-H, J = 7.1 Hz), 6.94–7.30 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.8 (CH_2**C**H_3); 28.4 (NCH_3); 35.5 (C^{3a}); 49.7 and 55.2 (C^3, C^{9b}); 61.6 (CH_2); 65.3 (C^4); 117.7, 118.6, 121.0, 129.5, 130.4, 155.3 (C_{arom}); 168.0, 168.7 (C=O). Found, %: C 65.06; H 6.21; N 4.98. $C_{15}H_{17}NO_4$. Calculated, %: C 65.44; H 6.22; N 5.09.

In the reaction with 0.6 g (2.43 mmol) of Schiff base **IIb** and freshly prepared lead filings (instead of activated lead; reaction time 34 h) we isolated 0.21 g (32%) of lactam **IIIb**.

Ethyl (3a*RS*,9b*SR*)-1-*tert*-butyl-2-fluoro-1,3a,-4,9b-tetrahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (IIc) and ethyl (3*RS*,3a*RS*,9b*SR*)-1-*tert*-butyl-2-oxo-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (IIIc) were obtained from 0.2 g (0.69 mmol) of Schiff base **Ic** (reaction time 1 h); the products were isolated by column chromatography using hexane–ethyl acetate (3.5:1) as eluent.

Compound **IIc**. Yield 0.028 g (13%), viscous liquid. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.28 t (3H, CH_2C**H**$_3$, J = 7.1 Hz), 1.46 s (9H, *t*-Bu, J_{HF} = 1.8 Hz), 3.76 d.d.d.d (1H, 3a-H, J = 8.4, 3.5, 3.5, J_{HF} = 6.6 Hz), 4.11 d.d.d (1H, 4-H, J = 11.5, 3.5, J_{HF} = 3.1 Hz), 4.15–4.27 m (2H, CH_2), 4.68 d.d (1H, 4-H, J = 11.5, 3.5 Hz), 4.71 d.d (1H, 9b-H, J = 8.8, J_{HF} = 4.9 Hz), 6.83–7.37 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.0 (CH_2**C**H_3); 29.4 (C**Me**$_3$); 40.7 (C^{3a}); 53.9 (C^{9b}); 57.4 (**C**Me$_3$); 59.1 (**C**H_2); 65.2 (C^4); 85.6 (C^3, J_{CF} = 10.0 Hz); 116.9, 121.0, 124.0, 128.2, 129.2, 156.5 (C_{arom}); 163.7 (C=O, $^3J_{CF}$ = 5.5 Hz); 165.9 (C^2, J_{CF} = 290 Hz).

Compound **IIIc**. Yield 0.126 g (57%). mp 153–154°C (from diethyl ether). IR spectrum (CCl_4), ν, cm^{-1}: 1730, 1700 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.32 t (3H, CH_2C**H**$_3$, J = 7.2 Hz), 1.60 s (9H, *t*-Bu), 3.12–3.19 m (1H, 3a-H), 3.63 d (1H, 3-H, J = 12.3 Hz), 4.17 d (2H, 4-H, J = 2.1 Hz), 4.23–4.31 m (2H, CH_2), 4.99 d (1H, 9b-H, J = 7.2 Hz), 6.84–7.44 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.8 (CH_3); 28.6 (CH_3); 39.4 (C^{3a}); 49.8, 53.0, 55.2 (C^3, C^{9b}, **C**Me$_3$); 61.3 (CH_2); 64.0 (C^4); 117.4, 121.2,

122.2, 128.9, 129.4, 153.9 (C_{arom}); 169.0, 169.7 (C=O). Found, %: C 68.16; H 7.16; N 4.42. $C_{18}H_{23}NO_4$. Calculated, %: C 68.12; H 7.30; N 4.41.

Ethyl (3*SR*,3a*RS*,9b*SR*)-2-oxo-1-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-3-carboxylate (VI) was obtained by keeping 0.2 g (0.59 mmol) of compound **IIa** in a mixture of hexane with diethyl ether at –15°C. Yield 0.154 g (77%). mp 92–94°C. IR spectrum ($CHCl_3$), ν, cm^{-1}: 1730, 1700 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.22 t (3H, CH_2CH_3, *J* = 7.1 Hz), 3.32 d.d.d.d (1H, 3a-H, *J* = 8.8, 7.5, 6.6, 4.0 Hz), 3.90 d (1H, 3-H, *J* = 8.8 Hz), 4.16–4.27 m (2H, OCH_2), 4.34 d.d (1H, 4-H, *J* = 11.9, 4.0 Hz), 4.43 d.d (1H, 4-H, *J* = 11.9, 7.5 Hz), 5.17 d (1H, 9b-H, *J* = 6.6 Hz), 6.42–7.33 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.5 (CH_3); 34.5 (C^{3a}); 50.3 (C^3); 56.2 (C^{9b}); 61.4, 63.5 (CH_2, C^4); 117.0, 118.3, 120.3, 127.6, 129.0, 129.3, 130.4 136.5, 154.7 (C_{arom}); 167.8, 168.6 (C=O). Found, %: C 70.65; H 5.65; N 4.27. $C_{20}H_{19}NO_4$. Calculated, %: C 71.20; H 5.68; N 4.15.

(3a*RS*,9b*SR*)-1-Phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrol-2-one (XI) was obtained from 0.84 g (3.54 mmol) of Schiff base **IX** (reaction time 1.5 h); the product was isolated by column chromatography using hexane–ethyl acetate (3:1) as eluent. Yield 0.521 g (56%). mp 126–127°C (from diethyl ether). IR spectrum (CCl_4): ν(C=O) 1710 cm^{-1}. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.63 d.d (1H, 3-H, *J* = 17.0, 6.2 Hz), 2.85 d.d (1H, 3-H, *J* = 17.0, 8.4 Hz), 2.98–3.09 m (1H, 3a-H), 4.11 d.d (1H, 4-H, *J* = 11.5, 6.8 Hz), 4.20 d.d (1H, 4-H, *J* = 11.5, 3.5 Hz), 5.23 d (1H, 9b-H, *J* = 7.1 Hz), 6.48–7.44 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 31.2 (C^{3a}); 33.0 (C^3); 57.2 (C^{9b}); 65.5 (C^4); 117.1, 119.4, 120.4, 126.9, 127.0, 128.9, 129.1, 130.4, 137.0, 154.7 (C_{arom}); 172.8 (C=O). Found, %: C 76.92; H 5.68; N 5.08. $C_{17}H_{15}NO_2$. Calculated, %: C 76.96; H 5.70; N 5.28.

(3a*RS*,11b*SR*)-1-Phenyl-1,2,3,3a,4,11b-hexahydrobenzo[6,7]chromeno[4,3-*b*]pyrrol-2-one (XII) was obtained from 0.73 g (2.54 mmol) of Schiff base **X** (reaction time 3 h); the product was isolated by column chromatography using hexane–ethyl acetate (3:1) as eluent. Yield 0.572 g (71%). mp 171–174, 187–191°C (dimorphic, from hexane–ethyl acetate). IR spectrum ($CHCl_3$): ν(C=O) 1695 cm^{-1}. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.43 d (1H, 3-H, *J* = 16.5 Hz), 2.92–3.01 m (1H, 3a-H), 3.09 d.d (1H, 3-H, *J* = 7.5, 16.5 Hz), 4.22 t (1H, 4-H, *J* = 11.0 Hz), 4.35 d.d (1H, 4-H, *J* = 4.9, 11.0 Hz), 5.61 d (1H, 11c-H, *J* = 4.9 Hz), 6.83–7.76 m (11H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 30.2, 33.7 (C^3, C^{3a}); 54.9 (C^{11c}); 64.8 (C^4); 110.0, 118.2, 121.7, 122.8, 125.5, 127.3, 127.7, 128.1, 128.4, 128.5, 130.6, 133.0, 136.6, 153.2 (C_{arom}); 173.1 (C=O). Found, %: C 80.18; H 5.51; N 4.42. $C_{21}H_{17}NO_2$. Calculated, %: C 79.98; H 5.43; N 4.44.

3a-Bromo-1-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrol-2-one (XIV) and 2-fluoro-1-phenyl-1,4-dihydrochromeno[4,3-*b*]pyrrole (XV) were obtained from 1.55 g (4.9 mmol) of Schiff base **XIII** (reaction time 14 h); the products were isolated by column chromatography using hexane–ethyl acetate (3:1) as eluent.

Compound **XIV**. Yield 0.388 g (23%). mp 160–163°C (from hexane–diethyl ether). IR spectrum ($CHCl_3$): ν(C=O) 1710 cm^{-1}. ^1H NMR spectrum (C_6D_6), δ, ppm: 3.14 d (1H, 3-H, *J* = 17.6 Hz), 3.49 d (1H, 3-H, *J* = 17.6 Hz), 4.35 d (1H, 4-H, *J* = 11.5 Hz), 4.50 d (1H, 4-H, *J* = 11.5 Hz), 5.60 s (1H, 9b-H), 6.55–7.28 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 43.0 (C^3); 55.6 (C^{3a}); 67.6 (C^4); 70.1 (C^{9b}); 117.4, 119.8, 121.7, 125.9, 127.0, 128.8, 129.2, 129.6, 136.9, 152.4 (C_{arom}); 169.8 (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 345 (26) $[M]^+$, 343 (26) $[M]^+$, 264 (21), 262 (8), 236 (5), 223 (3), 197 (11), 171 (11), 145 (100), 131 (11), 115 (39), 104 (12), 91 (22), 77 (50).

Compound **XV**. Yield 0.234 g (18%).

(3a*RS*,8b*SR*)-1-(4-Bromophenyl)-5,6-dimethoxy-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrol-2-one (XIXa) was obtained from 1.47 g (4.08 mmol) of Schiff base **XVII** (reaction time 8 h); the product was isolated by column chromatography using hexane–ethyl acetate (3:1). Yield 1.16 g (73%). mp 157–160°C (from CH_2Cl_2–Et_2O). IR spectrum ($CHCl_3$): ν(C=O) 1695 cm^{-1}. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.51 d.d (1H, 3-H, *J* = 4.9, 17.6 Hz), 2.89–2.98 m and 3.29–3.41 m (5H, 3-H, 3a-H, 4-H), 3.82 s (3H, CH_3), 3.86 s (3H, CH_3), 5.55 d (1H, 8b-H, *J* = 7.0 Hz), 6.59 d.d and 6.64 d.d (2H, 7-H, 8-H), 7.37–7.55 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 34.8, 38.5 (C^3, C^4); 35.2 (C^{3a}); 55.7 (CH_3); 59.9 (CH_3); 67.9 (C^{8b}); 111.3, 118.7, 120.2, 125.3, 131.7, 133.3, 135.8, 136.7, 145.1, 152.5 (C_{arom}); 172.9 (C=O). Found, %: C 58.82; H 4.74; N 3.47. $C_{19}H_{18}BrNO_3$. Calculated, %: C 58.78; H 4.67; N 3.61.

(3a*RS*,8b*SR*)-5,6-Dimethoxy-1-phenethyl-1,2,3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrol-2-one (XIXb) was obtained from 1.11 g (3.59 mmol) of

Schiff base **XVIIb** (reaction time 2 h); the product was isolated by column chromatography using hexane–ethyl acetate (3:1). Yield 0.95 g (82%). mp 97–98°C (from hexane–diethyl ether). IR spectrum ($CHCl_3$): ν(C=O) 1680 cm^{-1}. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.38 d.d (1H, 3-H, J = 2.3, 17.1 Hz), 2.68–2.78 m and 2.94–3.38 m (8H, 3-H, 3a-H, 4-H, CH_2CH_2), 3.79–3.89 m (1H, CH_2CH_2), 3.84 s (3H, CH_3), 3.87 s (3H, CH_3), 4.70 d (1H, 8b-H, J = 6.6 Hz), 6.82 d (1H, 7-H, J = 8.2 Hz), 7.04 d (1H, 8-H, J = 8.2 Hz), 7.23–7.34 m (5H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 33.2, 35.7, 37.2, 41.6 (C^3, C^4, CH_2CH_2); 36.1 (C^{3a}); 55.7 (CH_3); 59.8 (CH_3); 66.5 (C^{8b}); 111.0, 120.0, 126.1, 128.2, 128.4, 133.3, 136.8, 138.6, 145.2, 152.5 (C_{arom}); 173.0 (C=O). Found, %: C 74.71; H 6.89; N 4.14. $C_{21}H_{23}NO_3$. Calculated, %: C 74.75; H 6.87; N 4.15.

(3a*RS*,8b*SR*)-1-*tert*-Butyl-5,6-dimethoxy-1,2,-3,3a,4,8b-hexahydroindeno[1,2-*b*]pyrrol-2-one (XIXc) was obtained from 1.10 g (4.2 mmol) of Schiff base **XVIIc** (reaction time 13 h); the product was isolated by column chromatography using hexane–ethyl acetate (3:1). Yield 0.84 g (69%). mp 126–127°C (from diethyl ether). IR spectrum ($CHCl_3$): ν(C=O) 1675 cm^{-1}. ^1H NMR spectrum (C_6D_6), δ, ppm: 1.68 s (9H, *t*-Bu), 2.02 d.d (1H, 3-H, J = 10.1, 16.4 Hz), 2.40 d.d (1H, 3-H, J = 9.0, 16.4 Hz), 2.52–2.64 m (1H, 3a-H), 2.69 d (2H, 4-H, J = 3.5 Hz), 3.52 s (3H, CH_3), 3.80 s (3H, CH_3), 4.78 d (1H, 8b-H, J = 6.9 Hz), 6.62 d (1H, 7-H, J = 8.3 Hz), 7.13 d (1H, 8-H, J = 8.3 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 28.5 (C**C**H_3); 31.4, 38.9 (C^3, C^4); 38.0 (C^{3a}); 53.7 (CH_3); 55.7 (CH_3); 60.0 (**C**CH_3); 66.7 (C^{8b}); 111.5, 120.5, 134.9, 135.3, 145.4, 151.8 (C_{arom}); 174.3 (C=O). Found, %: C 70.31; H 8.09; N 4.87. $C_{17}H_{23}NO_3$. Calculated, %: C 70.56; H 8.01; N 4.84.

2-Fluoro-1-phenyl-1,4-dihydrochromeno[4,3-*b*]-pyrrole (XXVa) was obtained from 0.84 g (3.57 mmol) of Schiff base **XXIIIa** (reaction time 7 h); the product was isolated by column chromatography using hexane–ethyl acetate (5:1). Yield 0.652 g (69%). The physical constants and spectral parameters of compound **XXVa** were given in [2].

2-Fluoro-1-methyl-1,4-dihydrochromeno[4,3-*b*]-pyrrole (XXVb) was obtained from 0.89 g (5.14 mmol) of Schiff base **XXIIIb** (reaction time 1 h); the product was isolated by column chromatography using hexane–diethyl ether (~200:1). Yield 0.511 g (49%). mp 47–49°C (from hexane). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.73 s (3H, CH_3), 5.15 s (2H, 4-H), 5.43 d (1H, 3-H, J_{HF} = 4.0 Hz), 6.94–7.37 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 30.2 (CH_3, J_{CF} = 3.3 Hz); 65.0 (C^4, J_{CF} = 2.8 Hz); 81.5 (C^3, J_{CF} = 12.7 Hz); 112.1 (J_{CF} = 5.5 Hz); 115.7 (C^{3a}, C^{9b}); 116.9, 118.7, 118.8, 121.2, 125.8 (C_{arom}); 148.5 (C^2, J_{CF} = 263 Hz); 152.4 (C^{5a}, J_{CF} = 2.2 Hz). Found: C 70.86, H 4.99; N 6.99. $C_{12}H_{10}FNO$. Calculated, %: C 70.93; H 4.96; N 6.89.

1-*tert*-Butyl-2-fluoro-1,4-dihydrochromeno-[4,3-*b*]pyrrole (XXVc) was obtained from 1.18 g (5.48 mmol) of Schiff base **XXIIIc** (reaction time 1 h); the product was isolated by column chromatography using hexane–diethyl ether (~100:1). Yield 0.412 g (31%). mp 85–87°C (from hexane). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.78 d (9H, *t*-Bu, J = 2.7 Hz), 4.89 s (2H, 4-H), 5.47 d (1H, 3-H, J_{HF} = 3.3 Hz), 6.98–7.41 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 31.2 (C**C**H_3, J_{CF} = 6.1 Hz); 58.6 (**C**CH_3, J_{CF} = 2.2 Hz); 65.4 (C^4, J_{CF} = 2.8 Hz); 83.3 (C^3, J_{CF} = 16.6 Hz); 117.3 (C_{arom}); 117.8 (J_{CF} = 2.8 Hz), 120.2 (J_{CF} = 5.0 Hz) (C^{3a}, C^{9b}); 120.9, 121.8, 123.9, 124.8 (C_{arom}); 152.1 (C^2, J_{CF} = 269 Hz); 152.6 (C^{5a}). Found, %: C 73.48; H 6.65; N 5.71. $C_{15}H_{16}FNO$. Calculated, %: C 73.45; H 6.57; N 5.71.

6,8-Dibromo-1-(4-bromophenyl)-2-fluoro-1,4-dihydrochromeno[4,3-*b*]pyrrole (XXVd) was obtained from 0.6 g (1.27 mmol) of Schiff base **XXIIId** (reaction time 4.5 h); the product was isolated by column chromatography using hexane–diethyl ether (3:1). Yield 0.516 g (81%). mp 165–166°C (from hexane–diethyl ether). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 5.30 s (2H, CH_2), 5.59 d (1H, 3-H, J_{HF} = 4.4 Hz,), 6.35 d (1H, H_{arom}, J = 2.2 Hz,), 7.23–7.71 m (5H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 65.8 d (CH_2, J_{CF} = 2.2 Hz); 83.4 d (C^3, J_{CF} = 12.7 Hz); 111.5 (C_{arom}); 113.2 (C_{arom}); 114.0, 115.7 d (C^{3a}, C^{9b}, J_{CF} = 4.4 Hz); 120.1, 121.0, 122.9, 128.6, 132.0, 132.6, 133.2 (C_{arom}); 148.1 d (C^{5a}, J_{CF} = 2.2 Hz); 148.6 d (C^2, J_{CF} = 269 Hz). Found, %: C 40.47; H 1.90; N 2.53. $C_{17}H_9Br_3FNO$. Calculated, %: C 40.68; H 1.81; N 2.79.

1-(4-Bromophenyl)-2-fluoro-1,4-dihydrobenzo-[5,6]chromeno[4,3-*b*]pyrrole (XXVI) was obtained from 0.56 g (1.54 mmol) of Schiff base **XXIV** (reaction time 5 h); the product was isolated by column chromatography using hexane–diethyl ether (3:1). Yield 0.38 g (63%). mp 152–154°C (from hexane–diethyl ether). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 5.11 s (2H, CH_2), 5.76 d (1H, 3-H, J_{HF} = 4.4 Hz), 6.87–7.37 m (10H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 64.8 d (CH_2, J_{CF} = 2.2 Hz); 83.9 (C^3, J_{CF} =

13.3 Hz); 112.1, 115.9 (C^{3a}, C^{11c}, J_{CF} = 4.4 Hz); 118.2, 120.6, 123.3, 124.5, 125.1, 126.3, 126.96, 126.94, 127.47, 127.5, 129.6, 135.4 (C_{arom}); 149.0 d (C^{2}, J_{CF} = 268 Hz); 152.2 d (C^{5a}, J_{CF} = 2.2 Hz). Found, %: C 63.95; H 3.33; N 3.49. $C_{21}H_{13}BrFNO$. Calculated, %: C 63.98; H 3.32; N 3.55.

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