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1,3-Dipolar Cycloaddition of Difluoro-Substituted Azomethine Ylides. Synthesis and Transformations of 2-Fluoro-4,5-dihydropyrroles

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Abstract—2-Fluoro-4,5-dihydropyrrole-3,4-dicarboxylic acid derivatives were obtained by reaction of difluorocarbene with N-substituted ketone imines in the presence of fumaronitrile, maleonitrile, or dimethyl maleate. The reaction involves intermediate formation of azomethine ylides and their subsequent cycloaddition at the double bond. 11*H*-Dibenz[*b*,*e*]azepine and 3,4-dihydroisoquinolines react with difluorocarbene in the presence of fumaronitrile to give fluoro-substituted dibenzo[*c*,*f*]pyrrolo[1,2-*a*]azepine and pyrrolo[2,1-*a*]-isoquinoline derivatives. Treatment of 2-fluoro-4,5-dihydropyrrole-3,4-dicarbonitrile with amines and alkoxides affords the corresponding 2-amino- and 2-alkoxy derivatives, while its reactions with hydrazine hydrate and benzimidamide lead to formation of substituted pyrrolo[2,3-*c*]pyrazole and pyrrolo[2,3-*d*]-pyrimidine derivatives.

Pyrrole derivatives are widely used in synthetic and medical practice [1]. In the recent years, much attention was given to fluorinated pyrroles as potential biologically active substances. Several synthetic approaches to fluoropyrroles have been reported. Among these, direct fluorination of pyrrole derivatives [2, 3], transfunctionalization according to Schiemann [4], heterocyclization of fluorinated linear precursors [5], and 1,3-dipolar cycloaddition with participation of either fluorine-containing azomethine ylides [6–8] or fluorinated dipolarophiles [9, 10] must be noted.

2-Fluoro-4,5-dihydropyrroles attract interest not only as potential biologically active substances but also as useful building blocks having a labile fluorine atom in the α-position with respect to nitrogen. However, there are no convenient methods for the preparation of such compounds. Only two kinds of transformations are known to produce 2-fluoro-4,5-dihydropyrrole systems [11, 12]. Photolytic ring contraction in N-substituted perfluoroazepines to give perfluoro(3a,5a-dihydrocyclobuta[*b*]pyrroles) cannot be regarded as an acceptable synthetic route to 2-fluoro-4,5-dihydropyrroles, for its scope is limited to perfluorinated derivatives [11]. The reaction of *N*-methylpyrrolidone with carbonyl fluoride in the presence of cesium fluoride resulted in formation of only 4% of 2-fluoro-1-methyl-2,3-dihydropyrrole-3-carbonyl fluoride [12].

We recently found that reactions of difluorocarbene with Schiff bases in the presence of 2-butenedioic acid derivatives could lead to 2-fluoro-4,5-dihydropyrroles in good yields [13]. The present article reports the results of our detailed study on the reactions of various ketone imines with difluorocarbene in the presence of fumaric and maleic acid derivatives as a method of synthesis of substituted 2-fluoro-4,5-dihydropyrroles and building up of a 2-fluoro-4,5-dihydropyrrole fragment as a part of a polycyclic system. Difluorocarbene was generated *in situ* by reduction of dibromodifluoromethane with lead in the presence of tetrabutylammonium bromide.

The reactions of Schiff bases **Ia**–**Id** with difluorocarbene in the presence of fumaronitrile, maleonitrile, or dimethyl fumarate afforded dihydropyrroles **IIa**–**IId** and **III** which were isolated in good yields by column chromatography. The reaction mechanism includes attack by difluorocarbene on the lone electron pair on the nitrogen atom in Schiff base **Ia**–**Id** to give azomethine ylide **IVa**–**IVd**, cycloaddition of the latter at the double C=C bond of 2-butenedioic acid derivative,

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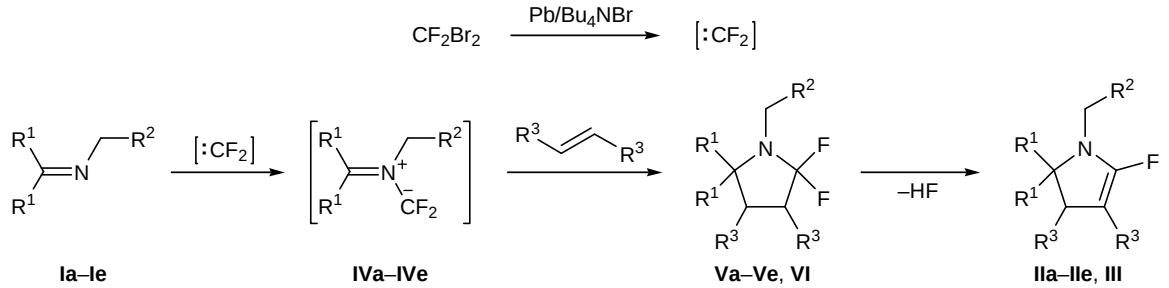
Scheme 1.



Ia–**Ie** **IVa**–**IVe** **Va**–**Ve**, **VI** **IIa**–**IIe**, **III**

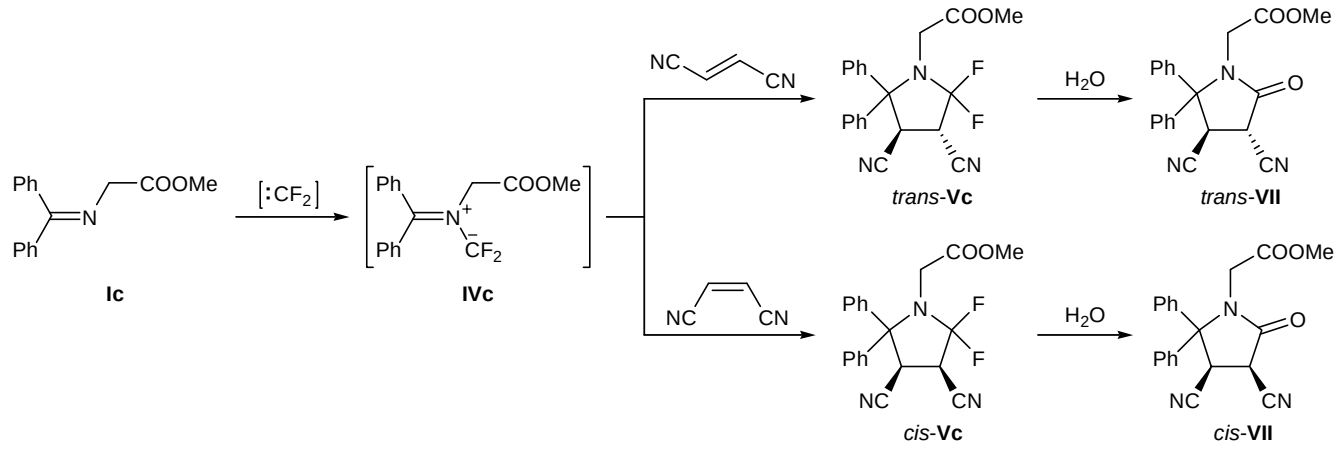
I, **IV**, R^1 = Ph, R^2 = H (**a**), $PhCH_2$ (**b**), MeOCO (**c**); R^1R^1 = 2,2'-biphenylene, R^2 = H (**d**); R^1R^1 = 2,2'-($C_6H_4OC_6H_4$), R^2 = H (**e**); **II**, **V**, R^1 = Ph, R^2 = H, R^3 = CN (**a**), R^2 = $PhCH_2$, R^3 = CN (**b**), R^2 = MeOCO, R^3 = CN (**c**); R^1R^1 = 2,2'-biphenylene, R^2 = H, R^3 = CN (**d**); R^1R^1 = 2,2'-($C_6H_4OC_6H_4$), R^2 = H, R^3 = CN (**e**); **III**, **VI**, R^1 = Ph, R^2 = H, R^3 = MeOCO.

and dehydrofluorination of difluoropyrrolidine **Va**–**Vd** or **VI** thus formed (Scheme 1). The isolated fluorodihydropyrroles are fairly stable: they can be stored for a long time below 5°C. However, they undergo slow hydrolysis to the corresponding lactams in chloroform solution.

Compound **III** formed by addition of ylide **IVa** to dimethyl maleate is less stable. We succeeded in isolating this product by chromatography using an eluent containing anhydrous triethylamine. Dihydropyrrole **III** can be stored for several months at –18°C. It was obtained in a good yield (64%) when activated lead was used instead of lead filings [7], presumably due to shortened reaction time. The primary adducts, compounds **V** and **VI** are extremely unstable, and we failed to isolate or detect them by chromatography. An exception was compound **Vc**. It was obtained as an analytically pure substance in 38% yield (together with 18% of dihydropyrrole **IIc**) from Schiff base **Ic** and fumaronitrile. When the reaction mixture was treated with anhydrous triethylamine before chromatographic treatment, the yield of **IIc** increased to 63%.

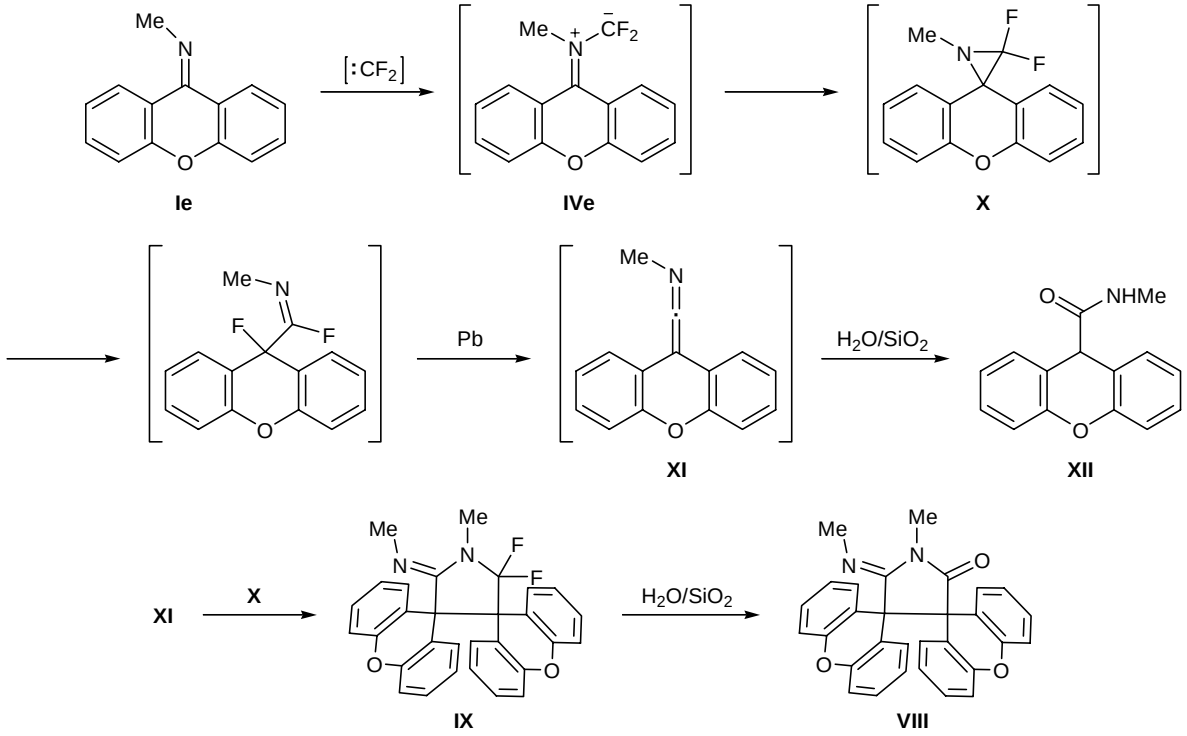
The reaction of Schiff base **Ic** with difluorocarbene in the presence of fumaronitrile is the only example of intermolecular cycloaddition in iminiodifluoromethanide, in which the primary adduct, intermediate 2,2-difluorodihydropyrrole, was isolated. This reaction provides a convenient model for studying stereoselectivity in the cycloaddition of geminal difluoro-substituted azomethine ylides. According to the ^1H and ^{13}C NMR data, the reactions of ketone imine **Ic** with difluorocarbene in the presence of fumaronitrile and maleonitrile give different isomeric dihydropyrroles: *trans*-**Vc** and *cis*-**Vc**, respectively (Scheme 2). The ^1H NMR spectrum of *trans*-**Vc** contains a doublet at δ 4.63 ppm (J_{HH} = 12.4 Hz) from the 3-H proton, while the corresponding signal of *cis*-**Vc** is located at δ 4.64 ppm (J_{HH} = 8.2 Hz). The 4-H signal of *trans*-**Vc** appears as a double doublet of doublets at δ 3.74 ppm (J_{HH} = 12.4, J_{HF} = 8.8, 5.3 Hz), while isomer *cis*-**Vc** is characterized by a doublet of doublets at δ 4.16 ppm (4-H, J_{HH} = 8.2, J_{HF} = 15.4 Hz). Compounds *trans*-**Vc** and *cis*-**Vc** in $CDCl_3$ undergo gradual hydrolysis with traces of water to give lactams *trans*-**VII** and *cis*-**VII**.

Scheme 2.



Ic **IVc** *trans*-**Vc** *trans*-**VII** *cis*-**Vc** *cis*-**VII**

Scheme 3.

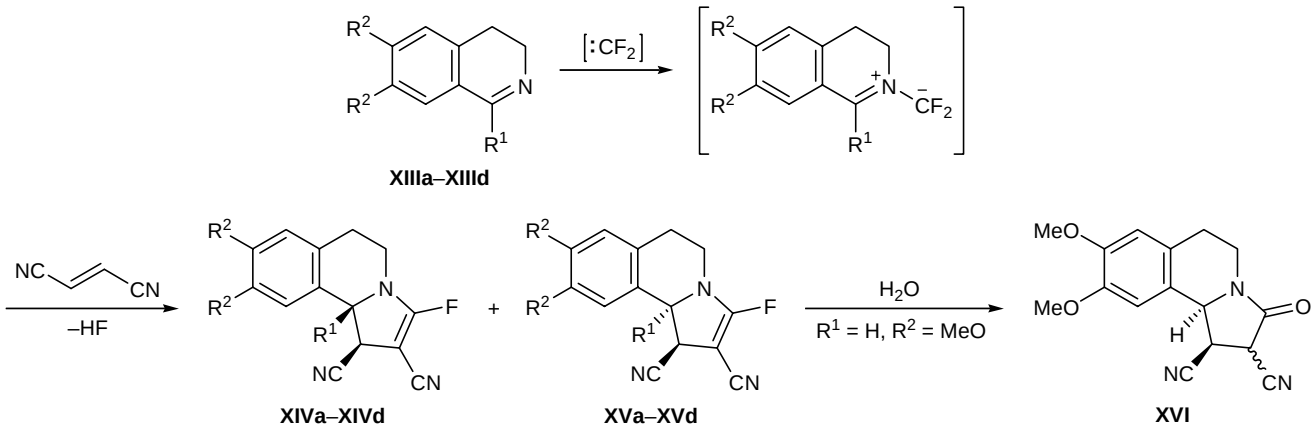


Thus the addition of ylide **IVc** to fumaronitrile and maleonitrile occurs with retention of the configuration of the double bond, which is typical of concerted processes.

9-Methyliminoxanthene (**Ie**) also revealed a specific behavior under conditions of difluorocarbene generation, and the corresponding dihydropyrrole derivative **Ve** was isolated in only 7% yield. The other product was compound **VIII** (26%) (Scheme 3). In the absence of fumaronitrile, the yield of **VIII** was 72%. By varying conditions for chromatographic treatment of the reaction mixture, we succeeded in isolating precursor of **VIII**, difluoride **IX** (using benzene–chloroform–ethyl acetate as eluent). Spirocyclic pyrrolidinone **VIII** is likely to be formed by hydrolysis of **IX** over silica gel. In fact, compound **VIII** was obtained in 42% yield when difluoride **IX** was applied to silica gel and kept for 12 h. The ^{13}C NMR spectrum of **IX** contained triplet signals from C^5 at δ_C 125.3 ppm (J_{HF} = 255 Hz) and C^4 at δ_C 60.2 ppm (J_{HF} = 18.5 Hz).

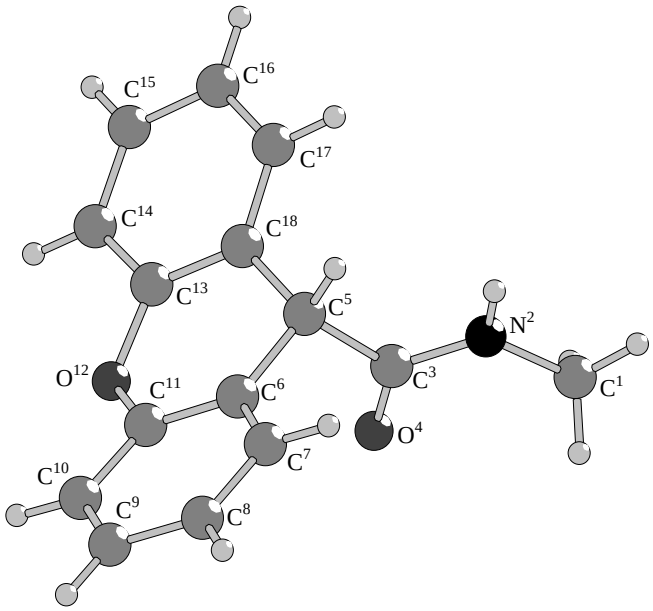
A probable scheme of formation of geminal difluoro derivative **IX** (Scheme 3) includes successive genera-

Scheme 4.



R^1 = Ph, R^2 = MeO (**a**), H (**b**); R^1 = 3,4-$(CH_2O_2)C_6H_3$, R^2 = H (**c**); R^1 = H, R^2 = MeO (**d**).

tion of ylide **IVe** and its transformation into ketene imine **XI** through aziridine **X**. Some analogies of the transformation **X** → **XI** are known from the literature. For example, reductive opening of the three-membered ring in 2,2-dichloroaziridines by the action of zinc dust was reported [14] to produce ketene imines. Taking into account our previous data on the stability of fluorine- and chlorine-containing 1,2-diaryl-3,3-dihaloaziridines [15], we anticipated that aziridine **X** should be extremely unstable due to the presence of strong π-donor substituents in the benzene rings and of a fluorine atom at C^3 in the aziridine ring. Both these factors favor opening of the aziridine ring at the C–N bond opposite to the CF_2 group. Apart from compounds **VIII** and **IX**, we isolated a small amount of amide **XII** whose structure was proved by the X-ray diffraction data (see figure). It is known that ketene imines readily undergo hydrolysis to the corresponding amides [16]; therefore, the presence of compound **XII** among the products is a strong evidence in support of inter-mediate formation of ketene imine **XI**.



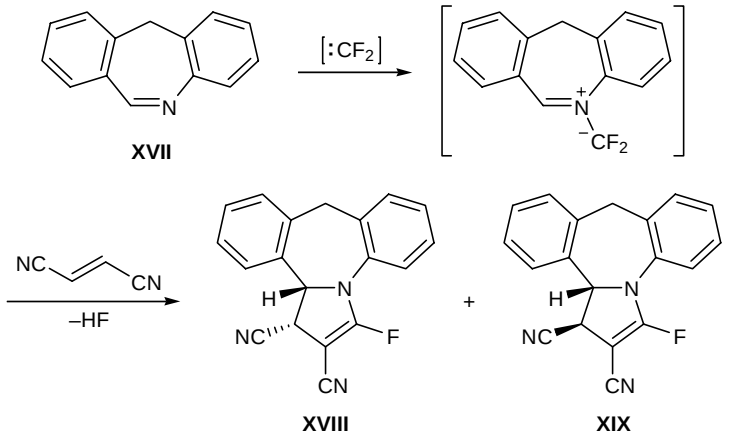
Structure of the molecule of *N*-methyl-9*H*-xanthene-9-carboxamide (**XII**) according to the X-ray diffraction data.

It should be emphasized that the behavior of ylide **IVe** is not typical of geminal difluoro-substituted azomethine ylides [17] which as a rule readily react with electron-deficient unsaturated compounds according to the cycloaddition pattern rather than undergo intramolecular ring closure to aziridines. Presumably, the reason for the anomalous reactivity of ylide **IVe** is considerable rotation of the xanthene ring system with respect to the plane of the C–N(Me)–CF_2 ylide fragment (53°, PM3), which facilitates conrotatory closure of aziridine ring, on the one hand, and increases steric hindrances to cycloaddition to a dipolarophile, on the other. For comparison, the corresponding dihedral angle in C,C-diphenyl-substituted ylide **IVa** is 17° (see also [18]).

1-Phenyl-3,4-dihydroisoquinolines **XIIIa**–**XIIIc** reacted with difluorocarbene in the presence of fumaronitrile in a way similar to acyclic Schiff bases **Ia**–**Id**, but the products were mixtures of stereoisomeric pyrroloisoquinolines **XIVa**–**XIVc**/**XVa**–**XVc** (overall yield 59–69%, Scheme 4). The relative configuration of the chiral centers in molecules **XIVa** and **XVa** was determined by NOE experiments. Irradiation of the 1-H proton in **XIVa** gave a response on the 10-H signal which increased in intensity by 14%. Irradiation of the same proton in **XVa** did not change the 10-H signal intensity, but an 11% response was observed on the *ortho* proton in the benzene ring. These data indicate that the cyano group on C^1 in **XVa** is oriented *trans* with respect to the benzene ring on C^{10b}; correspondingly, the 1-CN and 10b-Ph substituents in **XIVa** are arranged *cis*. Compounds **XIVa**–**XIVd** are characterized by smaller hydrogen–fluorine coupling constants for the 10b-H proton (J_{HF} = 2.5–3.1 Hz) than those for stereoisomers **XVa**–**XVd** (J_{HF} = 4.4–4.6 Hz).

Fluorodihydropyrroles derived from aldehyde imines are less hydrolytically stable than the corresponding ketone derivatives, and they cannot be synthesized by the above method [19, 20]. On the other hand, cyclic analogs of such Schiff bases can be converted into fused fluoropyrrole systems provided that no traces of acids are present at the stage of chromatographic treatment of the reaction mixture. From 6,7-dimethoxy-3,4-dihydroisoquinoline (**XIIId**) and fumaronitrile we obtained a mixture of stereoisomeric pyrroloisoquinolines **XIVd** and **XVd** in an overall yield of 39% (Scheme 4), which were isolated by chromatography using an eluent containing triethylamine. According to the ^{1}H NMR data, the isomer ratio **XIVd**:**XVd** was 3:1. Compound **XIVd** was isolated in the pure state as a stable crystalline substance and was characterized by the ^{1}H and ^{13}C NMR and IR spectra; its elemental composition was consistent with the assumed structure. We failed to isolate compound **XVd** as individual substance (it was characterized only by the ^{1}H NMR spectrum), for it readily underwent hydrolysis to lactam **XVI** upon attempted purification by crystallization or chromatography. Lactam **XVI** showed in the ^{13}C NMR spectrum a signal at δ_C 160.3 ppm from the carbonyl carbon atom, and its mass spectrum

Scheme 5.

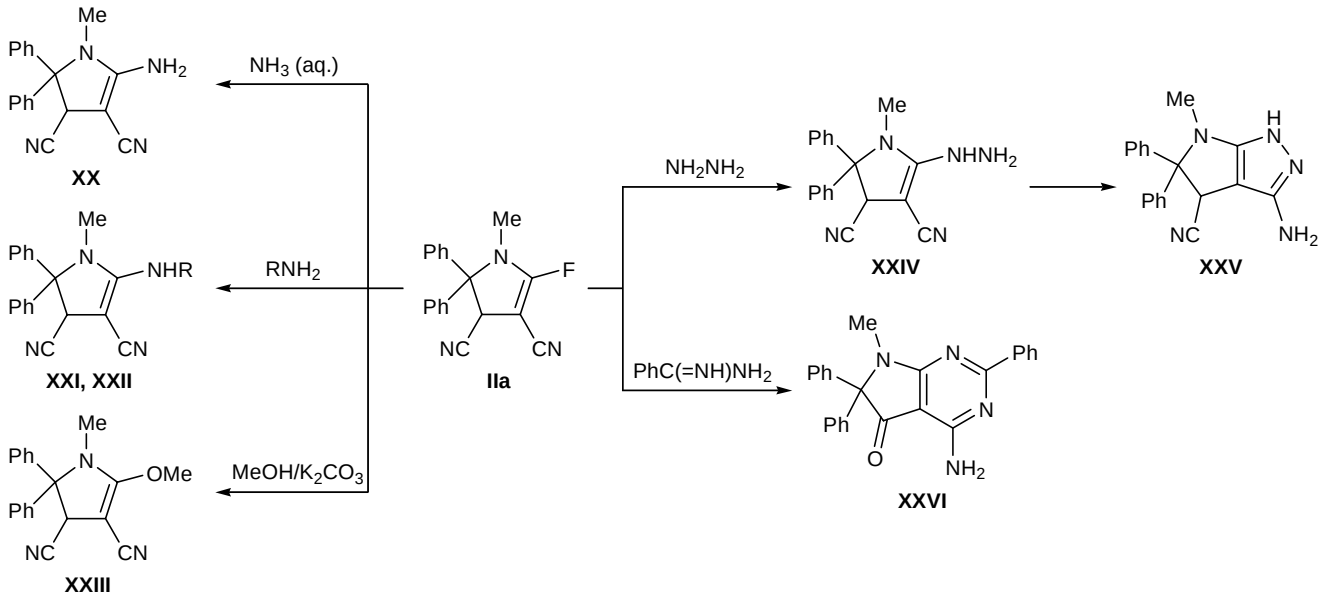


contained the molecular ion peak $[M]^+$ with *m*/*z* 297 (50%). On the basis of spin–spin coupling constats in the ^{1}H NMR spectra, isomer **XIVd** was assigned *trans* configuration with respect to the substituents on C^1 and C^{10b} (J_{HH} = 4.2 Hz), and compound **XVd**, *cis* configuration (J_{HH} = 10.1 Hz) [21]. 3-Oxo-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile **XVI** was isolated in 9% yield.

Under analogous conditions, the reaction of 11*H*-dibenz[*b*,*e*]azepine (**XVII**) with difluorocarbene in the presence of fumaronitrile gave stereoisomeric fluorodihydropyrroledinitriles **XVIII** and **XIX** (Scheme 5). Compounds **XVIII** and **XIX** are more stable to hydrolysis than **XIVd** and **XVd**, and they can be isolated as analytically pure substances. The overall yield in this reaction (36%) was considerably lower than in analogous reactions with ketone imines **Ia**–**Id**.

Compounds **IIa**–**IIe**, **III**, **XIVa**–**XIVd**, **XVa**–**XVd**, **XVIII**, and **XIX** contain several functional groups which make them promising from the viewpoint of further transformations, in particular those leading to polyheterocyclic systems. By treatment of fluorodihydropyrrole **IIa** with aqueous ammonia, methylamine, and 2-phenylethylamine we obtained the corresponding 2-amino-, 2-methylamino-, and 2-(2-phenylethylamino)-4,5-dihydropyrroles **XX**–**XXII** (Scheme 6). The reaction of **IIa** with methanol in the presence of potassium carbonate afforded 2-methoxy derivative **XXIII** which was isolated in 72% yield. Compound **IIa** reacted with hydrazine hydrate to give 74% of

Scheme 6.



XXI, R = Me; **XXII**, R = $PhCH_2CH_2$.

2-hydrazino-1-methyl-5,5-diphenyl-4,5-dihydropyrrole-3,4-dicarbonitrile (**XXIV**) which underwent intramolecular ring closure to pyrrolo[2,3-*c*]pyrazole **XXV** on heating at 100°C in toluene (yield 84%). The reaction of **IIa** with benzimidamide involved both cyano groups of the former, leading to formation of pyrrolo-[2,3-*d*]pyrimidine **XXVI** (Scheme 6).

Thus difluorocarbene generated *in situ* by reduction of dibromodifluoromethane with lead is a convenient synthon for the preparation of 2-fluoro-4,5-dihydropyrroles via three-component reaction with 2-butenedioic acid derivatives and Schiff bases. The reaction follows a domino pattern involving intermediate formation of azomethine ylides and is characterized by good yields of the final products. Analogous derivatives are also available from cyclic aldehyde imine analogs, but the products are as a rule less stable, and their yields are lower.

The 1,3-dipolar cycloaddition of difluoro azomethine ylides to fumaronitrile and maleonitrile is stereoselective, indicating a concerted mechanism of the process. 2-Fluoro-4,5-dihydropyrroles thus obtained are convenient intermediate products for the preparation of various 4,5-dihydropyrrole, pyrrolo[2,3-*c*]-pyrazole, and pyrrolo[2,3-*d*]pyrimidine derivatives.

EXPERIMENTAL

The melting points were determined on a Boetius melting point apparatus and are uncorrected. The IR spectra were recorded on a Carl Zeiss UR-20 spectrometer using 400-μm cells. The NMR spectra were obtained on a Bruker DPX 300 instrument 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 using a Hewlett–Packard HP-185B CHN analyzer. The progress of reactions was monitored by TLC on Silufol UV-254 plates. Silica gel LS (5–40 μm, Chemapol) was used for column chromatography.

Compounds **Ia**, **Ib**, **Id**, **Ie** [22], **Ic** [23], **XIIIa**–**XIIId** [24], and **XVII** [25] were synthesized according to published procedures.

Reactions of compounds Ia–Ie, XIIIa–XIIId, and XVII with difluorocarbene in the presence of fumaronitrile (*general procedure***).** A 50-ml flask was filled with argon and charged in succession with 15 ml of methylene chloride, 1.7 g (8.2 mmol) of freshly prepared lead filings, 2.7 g (8.4 mmol) of tetrabutylammonium bromide, 2.64 mmol of Schiff base **Ia**–**Ie**, **XIIIa**–**XIIId**, or **XVII**, 0.41 g (5.2 mmol) of fumaronitrile, and 1.72 g (8.3 mmol) of dibromodifluoromethane. The flask was hermetically plugged with a cap and was placed in an ultrasonic bath (160 W). The mixture was irradiated at 45°C until lead filings disappeared completely. When the reaction was complete, 5.4 g of silica gel (a double amount with respect to tetrabutylammonium bromide, by weight) was added to the mixture, the solvent was evaporated to dryness under reduced pressure, and the residue was applied to a column charged with silica gel. The column was eluted with solvent systems indicated below, and the isolated products were additionally purified by recrystallization.

The physical constants and spectral parameters of compounds **IIa**–**IIc**, **III**, **XIVa**, **XIVd**, **XVa**, **XVI**, **XVIII**, and **XIX** were reported previously [13].

5-Fluoro-1-methyl-2,2-diphenyl-2,3-dihydropyrrole-3,4-dicarbonitrile (IIa) was obtained from 0.51 g (2.6 mmol) of *N*-(diphenylmethylidene)-*N*-methylamine (**Ia**) and 0.41 g (5.2 mmol) of fumaronitrile according to the general procedure (reaction time 7 h) with the use hexane–ethyl acetate as eluent. Yield 0.66 g (84%).

5-Fluoro-2,2-diphenyl-1-(2-phenylethyl)-2,3-dihydropyrrole-3,4-dicarbonitrile (IIb) was obtained from 0.7 g (2.45 mmol) of *N*-(diphenylmethylidene)-*N*-(2-phenylethyl)amine (**Ib**) and 0.38 g (4.9 mmol) of fumaronitrile according to the general procedure (reaction time 14 h) with the use of hexane–ethyl acetate as eluent. Yield 0.62 g (64%).

Reaction of Schiff base Ic with difluorocarbene in the presence of fumaronitrile and maleonitrile. The reaction was carried out according to the general procedure with 1 g (3.95 mmol) of compounds **Ic** and 0.48 g (6.14 mmol) of fumaronitrile; chromatographic separation of the product mixture using hexane–ethyl acetate as eluent gave 0.274 g (18%) of methyl 2-(3,4-dicyano-5-fluoro-2,2-diphenyl-2,3-dihydro-1*H*-pyrrol-1-yl)acetate (**IIc**) and 0.596 g (38%) of methyl (3*RS*,4*SR*)-2-(3,4-dicyano-5,5-difluoro-2,2-diphenylpyrrolidin-1-yl)acetate (**Vc**, *trans* isomer).

Compound **Vc**. mp 144–150°C (decomp., from hexane–ethyl acetate). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1760 (C=O), 2270 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.32 s (3H, CH_3), 3.57 d.d (1H, CH_2, J = 18.1, 3.1 Hz), 4.16 d.d.d (1H, 4-H, J = 12.8, 8.8, 5.3 Hz), 3.88 d.d (1H, CH_2, J = 18.1, 3.1 Hz), 4.63 d (1H, 3-H, J = 12.4 Hz), 7.28–7.33 m (10H, H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 39.0 d.d (C^4, J = 29.3,

26.0 Hz); 40.0 (C^3); 42.0 d (CH_2, J = 1.7 Hz); 51.6 (CH_3); 74.3 (C^2); 111.4 (CN); 113.3 (CN); 121.5 d.d (C^5, J = 252, 247 Hz); 128.3, 128.4, 128.5, 128.6, 129.2, 129.4, 135.5 d (J = 6.1 Hz), 136.0 d (J = 2.2 Hz) (C_{arom}); 168.2 (C=O). Found, %: C 66.18; H 4.60; N 11.03. $C_{21}H_{17}F_2N_3O_2$. Calculated, %: C 66.14; H 4.49; N 11.02.

A solution of 45 mg of *trans* isomer **Vc** in 0.5 ml of $CDCl_3$ was kept for 24 h; the solution turned dark, and hydrogen fluoride evolved. By column chromatography on silica gel we isolated 17 mg (40%) of methyl (3*RS*,4*SR*)-2-(3,4-dicyano-2-oxo-5,5-diphenylpyrrolidin-1-yl)acetate (**VI**, *trans* isomer). mp 187–189°C (from CH_2Cl_2–Et_2O). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1760, 1730 (C=O); 2265 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.36 s (3H, CH_3), 3.56 d (1H, CH_2, J = 17.2 Hz), 3.87 d (1H, 4-H, J = 11.9 Hz), 4.50 d (1H, CH_2, J = 17.2 Hz), 4.69 d (1H, 3-H, J = 11.9 Hz), 7.20–7.39 m (10H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 35.9 (C^4); 39.7 (C^3); 42.8 (CH_2); 51.9 (CH_3); 72.4 (C^5); 113.1 (CN); 113.8 (CN); 127.8, 128.5, 128.6, 129.7, 128.8, 129.7, 129.9, 134.3, 134.7 (C_{arom}); 162.9 (C=O, lactam); 166.3 (C=O, ester). Found, %: C 70.10; H 4.83; N 11.74. $C_{21}H_{17}N_3O_3$. Calculated, %: C 70.18; H 4.77; N 11.69.

Following an analogous procedure, the reaction was performed with 0.51 g (2.01 mmol) of Schiff base **Ic** and 0.24 g (3.07 mmol) of fumaronitrile. When the reaction was complete, 0.5 ml of anhydrous triethylamine was added, and the mixture was stirred for 0.5 h and was then treated as described above. Yield of **IIc** 0.45 g (63%).

Following an analogous procedure, the reaction was performed with 1 g (3.95 mmol) of Schiff base **Ic** and 0.48 g (6.14 mmol) of maleonitrile. When the reaction was complete, the mixture was subjected to column chromatography using hexane–ethyl acetate as eluent. The fraction with an R_f range corresponding to compounds **IIc** and **Vc** was examined by ^1H NMR spectroscopy. It contained methyl (3*RS*,4*RS*)-2-(3,4-dicyano-5,5-difluoro-2,2-diphenylpyrrolidin-1-yl)acetate (**Vc**, *cis* isomer) and methyl (3*RS*,4*RS*)-2-(3,4-dicyano-2-oxo-5,5-diphenylpyrrolidin-1-yl)acetate (**VII**, *cis* isomer) at a ratio of ~2:1. Difluoride *cis*-**Vc** in $CDCl_3$ completely decomposed in a few hours with evolution of hydrogen fluoride.

Compound *cis*-**Vc**. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.39 s (3H, CH_3), 3.66 d.d (1H, CH_2, J = 17.4, 3.1 Hz), 3.89 d.d (1H, CH_2, J = 17.4, 3.1 Hz), 4.16 d.d (1H, 4-H, J = 15.4, 8.2 Hz), 4.64 d (1H, 3-H, J = 8.2 Hz), 7.20–7.46 m (10H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 39.9 d.d (C^4, J = 35.4, 26.0 Hz), 122.3 t (C^5, J = 250 Hz).

Compound *cis*-**VII**. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.35 d (1H, CH_2, J = 18.4 Hz), 3.43 d (1H, CH_2, J = 18.4 Hz), 4.07 d (1H, 4-H, J = 6.2 Hz), 4.47 d (1H, 3-H, J = 7.1 Hz), 7.20–7.46 m (10H, H_{arom}).

5-Fluoro-1-methyl-2,3-dihydro-9'*H*-spiro[pyrrole-2,9'-fluorene]-3,4-dicarbonitrile (IId) was obtained from 0.5 g (2.59 mmol) of *N*-methylfluorenylideneamine (**Id**) and 0.403 g (5.16 mmol) of fumaronitrile according to the general procedure (reaction time 32 h) with the use of hexane–diethyl ether as eluent. Yield 0.49 g (63%), mp 124–127°C (from EtOAc). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2215 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.36 s (3H, CH_3), 4.46 d (1H, 3-H, J = 2.8 Hz), 7.28–7.78 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 27.0 (CH_3); 40.0 d (C^3, J = 3.9 Hz); 52.1 d (C^4, J = 15.5 Hz); 74.1 (C^2); 113.2 d (CH, J = 3.8 Hz); 115.0 d (CH, J = 2.2 Hz); 120.5, 122.7, 125.2, 128.3, 128.7, 130.8, 131.0, 138.3, 139.7, 140.1, 142.1 (C_{arom}); 165.9 d (C^5, $^1J_{CF}$ = 287 Hz). Found, %: C 75.71; H 4.03; N 13.90. $C_{19}H_{12}FN_3$. Calculated, %: C 75.74; H 4.01; N 13.95.

Reaction of 9-methylimino-9*H*-xanthene (Ie) with difluorocarbene in the presence of fumaronitrile. The reaction was performed according to the general procedure with 0.5 g (2.38 mmol) of compound **Ie** and 0.372 g (4.76 mmol) of fumaronitrile (reaction time 10 h). The product mixture was separated by column chromatography using hexane–methylene chloride as eluent to isolate 0.053 g (7%) of 5-fluoro-1-methyl-2,3-dihydro-9'*H*-spiro[pyrrole-2,9'-xanthene]-3,4-dicarbonitrile (**IIe**) and 0.14 g (26%) of 1'-methyl-5'-methylimino-9*H*,9"*H*-dispiro[xanthene-9,3'-pyrrolidine-4',9"-xanthene]-2'-one (**VIII**).

Compound **IIe**. mp 124–127°C (from EtOAc). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2215 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.69 s (3H, CH_3), 4.34 d (1H, 3-H, J = 3.4 Hz), 7.26–7.50 m (8H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 27.6 (NCH_3), 48.6 d (C^3, J = 3.3 Hz); 49.2 d (C^4, J = 12.7 Hz); 63.3 (C^2); 113.1 d (4-CN, J = 3.8 Hz); 114.5 (3-CN, J = 2.2 Hz); 115.2, 117.5, 117.6, 124.1, 124.5, 125.0, 126.6, 130.9, 131.4, 149.9, 150.4 (C_{arom}); 164.9 d (C^5, J_{CF} = 286 Hz). Found, %: C 71.74; H 3.86; N 13.20. $C_{19}H_{12}FN_3O$. Calculated, %: C 71.92; H 3.81; N 13.24.

Compound **VIII**. mp 229–231°C (from hexane–EtOAc). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1720 (C=O), 1680 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm:

2.71 s (3H, CH_3), 3.65 s (3H, CH_3), 6.64–6.83 m (12H, H_{arom}), 7.02–7.07 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 26.5 (CH_3); 37.8 (CH_3); 59.0 (C^4); 63.4 (C^3); 115.8, 116.1, 119.6, 120.2, 122.2, 122.3, 127.5, 128.0, 128.1, 128.3, 151.1, 152.3 (C_{arom}); 156.9 (C=N); 174.2 (C=O). Found, %: C 78.73; H 4.80; N 6.04. $C_{30}H_{22}N_2O_3$. Calculated, %: C 78.59; H 4.84; N 6.11.

Following the general procedure, from 1 g (4.76 mmol) of Schiff base **Ie** we obtained [after chromatographic separation using first benzene–chloroform (4:1) and then benzene–chloroform–ethyl acetate (3:1:0.01) as eluents] 0.041 g (3.6%) of *N*-methyl-*N*-(5',5'-difluoro-1'-methyl-9*H*,9"*H*-dispiro[xanthene-9,3'-pyrrolidine-4',9"-xanthene]-2'-ylidene)amine (**IX**), 0.37 g (34%) of compound **VIII**, and 1.5 mg of *N*-methyl-9*H*-xanthene-9-carboxamide (**XII**).

Compound **IX**. mp 193–195°C (from hexane–EtOAc). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2200 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.61 s (3H, CH_3), 3.41 s (3H, CH_3), 6.76–6.84 m (10H, H_{arom}), 7.10–7.21 m (6H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 25.3 (CH_3); 37.4 (CH_3); 60.2 t (C^4, J = 18.5 Hz); 61.0 (C^3); 116.0, 116.8, 119.4, 121.4, 122.1 (C_{arom}); 125.3 t (C^5, J = 255 Hz); 128.2, 128.3, 128.5, 129.5 t (C_{arom}, J = 7.2 Hz); 151.7, 151.8 (C_{arom}); 155.9 (C^2). Mass spectrum, m/z (I_{rel}, %): 480 (100) $[M - HF]^+$, 387 (1.3), 230 (3), 206 (68), 199 (39), 181 (42). Found, %: C 74.83; H 4.78; N 5.79. $C_{30}H_{22}F_2N_2O_2$. Calculated, %: C 74.99; H 4.61; N 5.83.

Compound **XII**. X-Ray diffraction data: $C_{15}H_{13}NO_2$. M 239.26. Unit cell parameters: a = 15.4459(3), b = 9.4460(19), c = 16.339(3) Å; α = β = γ = 90°; V = 2386.0(8) $Å^3$; Z = 8; d = 1.332 mg/mm^3. Orthorhombic crystals, space group *Pbca*; MoK_α irradiation, λ = 0.71073 Å, 133 K; R_{All} = 0.046, wR_2 = 0.0884. Total of 6900 reflections were measured, 2040 of which were independent (R_{int} = 0.0658).

Following an analogous procedure, but in the absence of fumaronitrile, from 0.5 g (2.48 mmol) of Schiff base **Ie** (reaction time 20 h) we obtained 0.39 g (72%) of compound **VIII** (which was isolated by column chromatography using hexane–methylene chloride as eluent).

A mixture of 15 mg (0.031 mmol) of compound **IX** and 0.5 g of silica gel in 1 ml of methylene chloride was kept for 0.5 h under reduced pressure (20 mm) and then for 9 h under atmospheric pressure. The resulting material was transferred to a Schott filter and was washed with 30 ml of methylene chloride. The solvent was evaporated, and the residue was recrystallized from hexane–ethyl acetate to obtain 6 mg (42%) of compound **VIII**.

Reaction of Schiff base Ia with difluorocarbene in the presence of dimethyl maleate. Following the general procedure, but using activated lead instead of lead filings, from 0.64 g (3.3 mmol) of *N*-(diphenylmethylidene)-*N*-methylamine (**Ia**) and 0.41 g (5.2 mmol) of dimethyl maleate (reaction time 3 h) we obtained 0.77 g (64%) of dimethyl 5-fluoro-1-methyl-2,2-diphenyl-2,3-dihydropyrrole-3,4-dicarboxylate (**III**) which was isolated by column chromatography using hexane–ethyl acetate as eluent.

(1*RS*,10b*SR*)-3-Fluoro-8,9-dimethoxy-10b-phenyl-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (XIVa) and (1*RS*,10b*RS*)-3-fluoro-8,9-dimethoxy-10b-phenyl-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (XVa) were obtained from 0.8 g (3.0 mmol) of 6,7-dimethoxy-1-phenyl-3,4-dihydroisoquinoline (**XIIIa**) and 0.94 g (12.0 mmol) of fumaronitrile according to the general procedure (reaction time 25 h); by column chromatography using hexane–ethyl acetate as eluent we isolated 0.35 g (31%) of compound **XIVa** and 0.31 g (28%) of compound **XVa**; the latter contained 35% of **XIVa** as an impurity

Following the general procedure, from 0.8 g (3.86 mmol) of 1-phenyl-3,4-dihydroisoquinoline (**XIIIb**) and 0.6 g (7.72 mmol) of fumaronitrile (reaction time 30 h) we obtained 0.26 g (21%) of (1*RS*,10b*SR*)-3-fluoro-10b-phenyl-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (**XIVb**) and 0.58 g (48%) of (1*RS*,10b*RS*)-3-fluoro-10b-phenyl-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (**XVb**) which were isolated by column chromatography using hexane–ethyl acetate as eluent.

Compound **XIVb**. mp 143–145°C (from EtOAc–CH_2Cl_2). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2217 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.59–2.68 m (1H, CH_2), 2.96–3.07 m (1H, CH_2), 3.31–3.40 m (1H, CH_2), 3.70–3.78 m (1H, CH_2), 4.78 d (1H, 1-H, J = 2.7 Hz), 7.22–7.41 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 26.6 (C^6); 38.2 (C^5); 43.8 d (C^1, $^3J_{CF}$ = 4.5 Hz); 52.6 d (C^2, J = 13.8 Hz), 70.5 (C^{10b}); 112.9 d (CH, J = 3.8 Hz); 115.5 d (CH, J = 3.5 Hz); 125.8, 126.8, 127.2, 128.5, 128.6, 129.2, 129.6, 133.3, 135.8, 137.1 (C_{arom}); 165.4 d (C^3, $^1J_{CF}$ = 286 Hz). Found, %: C 76.21; H 4.40; N 13.25. $C_{20}H_{14}FN_3$. Calculated, %: C 76.18; H 4.47; N 13.32.

Compound **XVb**. mp 190–192°C (from EtOAc–CH_2Cl_2). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2217 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.84–2.89 (1H, CH_2), 3.11–3.22 (1H, CH_2), 3.25–3.35 (1H, CH_2), 3.81–3.86 m (1H, CH_2), 4.73 d (1H, 1-H, J = 4.4 Hz), 7.15–7.45 m (9H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 28.3 (C^6); 37.8 (C^5); 44.3 d (C^1; J = 2.8 Hz); 53.4 d (C^2, J = 14.4 Hz); 68.7 (C^{10b}); 113.1 d (CH, J = 4.4 Hz); 115.8 d (CH, J = 1.7 Hz); 125.7, 126.7, 128.5, 128.6, 128.7, 129.0, 129.1, 132.9, 133.6, 141.7 (C_{arom}); 163.2 d (C^3, J = 286 Hz). Found, %: C 76.31; H 4.48; N 13.23. $C_{20}H_{14}FN_3$. Calculated, %: C 76.18; H 4.47; N 13.32.

Following the general procedure, from 0.505 g (2 mmol) of 1-(1,3-benzodioxol-5-yl)-3,4-dihydroisoquinoline (**XIIIc**) and 0.31 g (4 mmol) of fumaronitrile (reaction time 64 h) we obtained 0.29 g (40%) of (1*RS*,10b*SR*)-10b-(1,3-benzodioxol-5-yl)-3-fluoro-1,5,6,10b-tetrahydropyrrolo-[2,1-*a*]isoquinoline-1,2-dicarbonitrile (**XVc**) and 0.21 g (29%) of a mixture of **XVc** and (1*RS*,10b*RS*)-10b-(1,3-benzodioxol-5-yl)-3-fluoro-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (**XIVc**) at a ratio of 1.3:1. The products were isolated by column chromatography using hexane–ethyl acetate as eluent, followed by recrystallization from diethyl ether–methylene chloride.

Compound **XIVc**. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.62–2.71 m (1H, CH_2), 2.95–3.06 m (1H, CH_2), 3.34–3.44 m (1H, CH_2), 3.66–3.77 m (1H, CH_2), 4.77 d (1H, 1-H, J = 3.1 Hz), 6.01 (OCH_2O), 6.72–6.83 m (3H, H_{arom}), 7.15–7.27 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 26.5 (C^6); 38.1 (C^5); 43.8 d (C^1, J = 5.7 Hz); 52.3 d (C^2, J = 13.8 Hz); 70.2 (C^{10b}); 101.4 (OCH_2O); 107.6, 107.8 (C_{arom}); 113.0 d (CH, J = 4.6 Hz); 115.6 d (CH, J = 3.5 Hz); 118.1, 121.5, 125.7, 126.8, 129.5, 131.1, 133.2, 136.0, 147.9, 148.0 (C_{arom}); 165.2 d (C^3, J = 286 Hz).

Compound **XVc**. mp 192–194°C (from Et_2O–CH_2Cl_2). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2217 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.81–2.89 m (1H, CH_2), 3.09–3.20 m (1H, CH_2), 3.24–3.33 m (1H, CH_2), 3.79–3.86 m (1H, CH_2), 4.66 d (1H, 1-H, J = 4.63 Hz), 6.01 (OCH_2O), 6.72–6.77 m (3H, H_{arom}), 7.15–7.40 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 28.3 (C^6); 37.6 (C^5); 44.5 d (C^1, J = 2.8 Hz); 53.2 d (C^2, J = 14.4 Hz); 68.7 (C^{10b}); 101.4 (OCH_2O); 106.4, 107.8 (C_{arom}); 113.1 d (CH, J = 5.0 Hz); 115.7 (CH); 119.8, 126.8, 128.6, 128.7, 129.2, 133.1, 133.6, 135.8, 148.0, 148.1 (C_{arom}); 163.1 d (C^3, J = 285 Hz). Found, %: C 70.26; H 4.00; N 11.67. $C_{21}H_{14}FN_3O_2$. Calculated, %: C 70.19; H 3.93; N 11.69.

(1*RS*,10b*SR*)-3-Fluoro-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (XIVd) and (1*RS*,10b*RS*)-3-fluoro-8,9-dimethoxy-1,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (XVd) were obtained from 0.53 g (2.8 mmol) of 6,7-dimethoxy-3,4-dihydroisoquinoline (**XIIId**) and 0.44 g (5.6 mmol) of fumaronitrile according to the general procedure (reaction time 47 h). By column chromatography using hexane–ethyl acetate as eluent we isolated 0.22 g (26%) of compound **XIVd**. Compound **XVd** was detected by ^1H NMR spectroscopy as a mixture with **XIVd**. Repeated chromatographic treatment resulted in hydrolysis of **XVd** to (1*RS*,10b*SR*)-8,9-dimethoxy-3-oxo-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-1,2-dicarbonitrile (**XVI**) (0.075 g, 9%).

5-Amino-1-methyl-2,2-diphenyl-2,3-dihydro-1*H*-pyrrole-3,4-dicarbonitrile (XX). A mixture of 0.3 g (0.99 mmol) of dihydropyrrole **IIa** and 5 ml of 25% aqueous ammonia was stirred for 7 days at room temperature. The mixture was poured into 25 ml of water, and the precipitate was filtered off, washed with water, dried in air, and recrystallized from ethanol. Yield 0.224 g (53%), colorless crystals with mp 189°C (decomp.). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3500, 3410 (N–H); 2250, 2190 (C≡N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.46 s (3H, CH_3), 4.97 s (1H, 3-H), 7.02 s (2H, NH_2), 7.21–7.45 m (10H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 30.9 (CH_3); 45.9 (C^4); 46.9 (C^3); 77.3 (C^2); 119.8 (CN); 121.2 (CN); 128.3, 128.9, 129.1, 129.2, 129.3, 140.2, 140.6 (C_{arom}); 163.6 (C^5). Found, %: C 75.64; H 5.54; N 17.91. $C_{19}H_{16}N_4$. Calculated, %: C 75.98; H 5.37; N 18.68.

1-Methyl-5-methylamino-2,2-diphenyl-2,3-dihydro-1*H*-pyrrole-3,4-dicarbonitrile (XXI). A mixture of 0.2 g (0.66 mmol) of compound **IIa**, 0.045 g (0.67 mmol) of methylamine hydrochloride, 0.2 g (1.45 mmol) of calcined potassium carbonate, and 3 ml of anhydrous 1,2-dimethoxyethane was stirred for 1 h at room temperature. The mixture was poured into 25 ml of water, and the precipitate was filtered off, dried in air, and recrystallized from methanol. Yield 0.157 g (75%), colorless crystals with mp 212–215°C (decomp.). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3460 (N–H); 2250, 2185 (C≡N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.44 s (3H, 1-CH_3), 3.14 d (3H, 5-NHC**H**$_3$, J = 5.1 Hz), 4.57 s (1H, 3-H), 5.09 q (1H, NH, J = 5.1 Hz), 7.29–7.40 m (10H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.8 (CH_3); 30.3 (CH_3); 46.6 (C^4); 46.9 (C^3); 76.5 (C^2); 117.7 (CN); 121.0 (CN); 127.0, 128.0, 128.2, 128.3, 128.4, 128.5, 138.4, 139.7 (C_{arom});

160.8 (C^5). Found, %: C 76.44; H 5.79; N 17.84. $C_{20}H_{18}N_4$. Calculated, %: C 76.41; H 5.77; N 17.82.

1-Methyl-2,2-diphenyl-5-(2-phenylethylamino)-2,3-dihydro-1*H*-pyrrole-3,4-dicarbonitrile (XXII). A mixture of 0.2 g (0.66 mmol) of compound **IIa**, 0.16 g (1.32 mmol) of 2-phenylethylamine, and 5 ml of anhydrous DMF was stirred for 1 h at room temperature. The mixture was poured into 30 ml of water and extracted with 5 ml of ethyl acetate, and the extract was washed with water (3×20 ml) and a saturated solution of NaCl and dried over Na_2SO_4. Removal of the solvent gave 0.258 g (96%) of compound **XXII** as a glassy material. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3440 (N–H); 2250, 2185 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.34 s (3H, CH_3), 2.98 t (2H, C**H**$_2$Ph, J = 6.9 Hz), 3.75–3.85 m (2H, CH_2N), 4.58 s (1H, 3-H), 7.17–7.43 m (15H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.6 (CH_3); 35.5 (Ph**C**H_2); 44.1 (NCH_2); 46.7 (C^3); 47.4 (C^4); 76.5 (C^2); 117.4 (CN); 120.3 (CN); 126.5, 127.0, 127.9, 128.3, 128.3, 128.4, 128.5, 128.6, 137.3, 138.2, 139.6 (C_{arom}); 159.5 (C^4).

5-Methoxy-1-methyl-2,2-diphenyl-2,3-dihydro-1*H*-pyrrole-3,4-dicarbonitrile (XXIII). A mixture of 0.3 g (0.99 mmol) of compound **IIa**, 0.3 g (2.18 mmol) of potassium carbonate, and 3 ml of methanol was stirred for 1 h at room temperature. The mixture was poured into 25 ml of water, and the precipitate was filtered off and recrystallized from methanol. Yield 0.227 g (72%), colorless crystals with mp 195–197°C (from MeOH). IR spectrum ($CHCl_3$), ν, cm^{-1}: 2250, 2200 (C≡N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.49 s (3H, NCH_3), 4.31 s (3H, OCH_3), 4.67 s (1H, 3-H), 7.31–7.48 m (10H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.9 (NCH_3); 46.1 (C^3); 49.7 (C^4); 60.2 (OCH_3); 75.0 (C^2); 116.5 (CN); 117.5 (CN); 126.9, 127.9, 128.3, 128.5, 128.7, 137.6, 139.22 (C_{arom}); 166.7 (C^5). Found, %: C 76.21; H 5.40; N 13.24. $C_{20}H_{17}N_3O$. Calculated, %: C 76.17; H 5.43; N 13.32.

5-Hydrazino-1-methyl-2,2-diphenyl-2,3-dihydro-1*H*-pyrrole-3,4-dicarbonitrile (XXIV). A solution of 0.8 g (2.64 mmol) of compound **IIa** in 4 ml of 1,4-dioxane was added dropwise under stirring to 10 ml of hydrazine hydrate. The mixture was stirred for 30 min and poured into 30 ml of water. The precipitate was filtered off, washed with water, and dried in air. The product was isolated as a solvate with dioxane, $C_{19}H_{17}N_5 \cdot 0.5C_4H_8O_2$, yield 0.705 g (74%), mp 116°C (decomp., from EtOH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 3.57 s (3H, dioxane), 4.62 m (2H, NH_2), 4.93 s (1H, 3-H), 7.22–7.44 m (10H, H_{arom}), 8.25 m (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 31.4 (CH_3); 46.9 (C^3); 48.3 (C^4); 67.2 (OCH_2); 77.2 (C^2); 119.8 (CN); 121.7 (CN); 128.4, 128.9, 129.0, 129.1, 129.2, 129.3, 140.4, 140.5 (C_{arom}); 163.8 (C^5). Found, %: C 70.18; H 5.62; N 20.47. $C_{19}H_{17}N_5 \cdot 0.5C_4H_8O_2$. Calculated, %: C 70.18; H 5.89; N 19.48.

3-Amino-6-methyl-5,5-diphenyl-2,4,5,6-tetrahydropyrrolo[2,3-*c*]pyrazole-4-carbonitrile (XXV). A solution of 50 mg (0.159 mmol) of compound **XXIV** in 0.5 ml of anhydrous toluene was heated for 3 h at 100°C. The solvent was removed under reduced pressure, and the residue was recrystallized from THF–Et_2O. Yield 42 mg (84%), mp 126–130°C (decomp., from EtOH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.23 s (3H, CH_3), 4.78 s (1H, 4-H), 5.34 s (2H, NH_2), 7.12–7.44 m (10H, H_{arom}), 10.19 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 31.7 (CH_3); 31.8 (C^4); 84.5, 85.5 (C^{3a}, C^5); 119.5 (CN); 128.4, 128.6, 128.8, 128.9, 129.0, 141.0, 141.8, 143.6 (C_{arom}). Found, %: C 72.38; H 5.49; N 22.20. $C_{19}H_{17}N_5$. Calculated, %: C 72.36; H 5.43; N 22.21.

4-Amino-7-methyl-2,6,6-triphenyl-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidin-5-one (XXVI). A mixture of 0.4 g (1.32 mmol) of compound **IIa**, 0.2 g (1.66 mmol) of benzimidamide, 0.25 g (2.45 mmol) of anhydrous triethylamine, and 4 ml of anhydrous DMF was stirred for 5 days at room temperature. The mixture was poured into 25 ml of water, and the precipitate was filtered off, washed with water, dried in air, and recrystallized from DMF. Yield 0.245 g (47%), colorless crystals with mp 320–322°C (from DMF). IR spectrum (KBr), ν, cm^{-1}: 3510 (OH), 3380 (N–H). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.20–7.53 m (14H, H_{arom}, NH), 8.15 s (1H, NH), 8.43 d (2H, H_{arom}, J = 7.3 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 27.9 (CH_3); 79.7 (C^6); 90.3 (C^{4a}); 129.0, 129.1, 129.1, 129.6, 132.4, 138.1, 138.2 (C_{arom}); 160.6 (C^2); 169.7 (C^4); 172.4 (C^{7a}); 195.5 (C^5). Mass spectrum, m/z (I_{rel}, %): 394 (3) $[M + 2]^+$, 393 (27) $[M + 1]^+$, 392 (100) $[M]^+$, 365 (3), 264 (27), 393 (99), 315 (32), 287 (44), 244 (10), 157 (7), 118 (11), 104 (14). Found, %: C 76.69; H 5.16; N 14.43. $C_{25}H_{20}N_4O$. Calculated, %: C 76.51; H 5.14; N 14.28.

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REFERENCES

1. *Pyrroles. Part I*, Jones, R.A., Ed., New York: Wiley, 1990.

2. Wang, J. and Scott, A.I., *Tetrahedron Lett.*, 1994, vol. 35, p. 3679.
3. Wang, J. and Scott, A.I., *Tetrahedron*, 1994, vol. 50, p. 6181.
4. Onda, H., Toi, H., Aoyama, Y., and Ogoshi, H., *Tetrahedron Lett.*, 1985, vol. 26, p. 4221.
5. Shi, G. and Cai, W., *J. Org. Chem.*, 1995, vol. 60, p. 6289.
6. Novikov, M.S.,. Khlebnikov, A.F, Sidorina, E.S., and Kostikov, R.R., *J. Fluorine Chem.*, 1998, vol. 90, p. 117.
7. Novikov, M.S., Khlebnikov, A.F., Sidorina, E.S., and Kostikov, R.R., *J. Chem. Soc., Perkin Trans. 1*, 2000, p. 231.
8. Novikov, M.S., Khlebnikov, A.F., Besedina, O.V., and Kostikov, R.R., *Tetrahedron Lett.*, 2001, vol. 42, p. 533.
9. Leroy, J. and Wakselman, M., *Tetrahedron Lett.*, 1994, vol. 35, p. 8605.
10. Leroy, J., Bergmark, C.W., and Pashayan, D., *J. Am. Chem. Soc.*, 1969, vol. 91, p. 2659.
11. Barlow, M.G., Culshaw, S., Haszeldine, R.N., and Morton, W.D., *J. Chem. Soc., Perkin Trans. 1*, 1982, p. 2105.
12. Fawcett, F.S., Tullock, C.W., and Coffman, D.D., *J. Am. Chem. Soc.*, 1962, vol. 84, p. 4275.
13. Novikov, M.S., Khlebnikov, A.F., and Shevchenko, M.V., *J. Fluorine Chem.*, 2003, vol. 123, p. 117.
14. Khlebnikov, A.F., Novikov, M.S., and Kostikov, R.R., *Synlett*, 1997, p. 929.
15. Kostikov, R.R., Khlebnikov, A.F., and Ogloblin, K.A., *Khim. Geterotsikl. Soedin.*, 1978, p. 48.
16. Khlebnikov, A.F., Novikov, M.S., and Kostikov, R.R., *Zh. Org. Khim.*, 1990, vol. 26, p. 1899.
17. Khlebnikov, A.F., Novikov, M.S., and Kostikov, R.R., *Ros. Khim. Zh.*, 1999, vol. 43, p. 70.
18. Khlebnikov, A.F., Novikov, M.S., Nikiforova, T.Yu., and Kostikov, R.R., *Russ. J. Org. Chem.*, 1999, vol. 35, p. 91.
19. Novikov, M.S., Khlebnikov, A.F., Sidorina, E.S., Masalev, A.E., Kopf, J., and Kostikov, R.R., *Russ. J. Org. Chem.*, 2002, vol. 38, p. 672.
20. Novikov, M.S., Khlebnikov, A.F., and Kostikov, R.R., *Russ. J. Org. Chem.*, 2002, vol. 38, p. 1647.
21. Huisgen, R. and Niklas, K., *Heterocycles*, 1984, vol. 22, p. 21.
22. Padwa, A., Bergmark, W., and Pashayan, D., *J. Am. Chem. Soc.*, 1969, vol. 91, p. 2659.
23. O'Donnell, M.J. and Polt, R.L., *J. Org. Chem.*, 1982, vol. 47, p. 2663.
24. Whaley, W.M. and Meadow, M., *J. Chem. Soc.*, 1953, p. 1067.
25. Werner, L.H., Ricca, S., Mohacsi, E., Rossi, A., and Arya, V.P., *J. Med. Chem.*, 1965, vol. 8, p. 74.