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Dedicated to Full Member of the Russian Academy of Sciences O.N. Chupakhin on his 80th anniversary

Fluoroalkyl-Substituted Lithium 1,3-Diketonates in Reactions with Hetarylhydrazines

N. S. Boltacheva[a], L. N. Dianova[b], P. A. Slepukhin[a], V. I. Filyakova[a], V. A. Bakulev[b], and V. N. Charushin[a]

[a] *Postovskii Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences, ul. S. Kovalevskoi/Akademicheskaya 22/20, Yekaterinburg, 620990 Russia*
e-mail: vif@ios.uran.ru

[b] *Institute of Chemical Technology, Ural Federal University, ul. Mira 28, Yekaterinburg, Russia*

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Abstract—Fluoroalkyl-substituted lithium 1,3-diketonates reacted with 4-hydrazinyl-6-methylpyrimidin-2-amine, 2,6-dimethylpyrimidin-4-ylhydrazine, 7-fluoroquinoxalin-6-ylhydrazine, and benzothiazol-2-ylhydrazine to give the corresponding hetaryl-substituted pyrazoles. The molecular and crystal structures of 4-methyl-6-(3-methyl-5-trifluoromethyl-1*H*-pyrazol-1-yl)pyrimidin-2-amine and 4-(5-difluoromethyl-4,5,6,7-tetrahydro-2*H*-indazol-2-yl)-6-methylpyrimidin-2-amine were determined by X-ray analysis.

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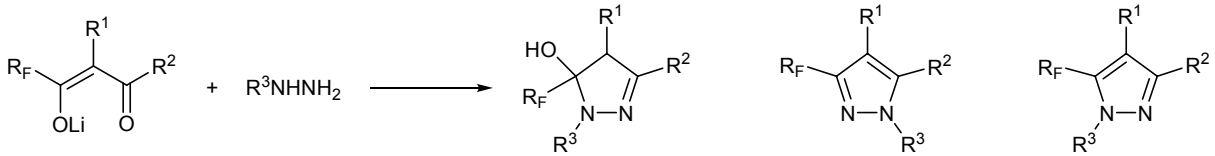
In recent years, systems composed of two or more heterocycles of different natures have attracted keen interest. A huge number of possible ring combinations make it possible to vary over a wide range properties and biological activity of the resulting compounds. 1,3-Dicarbonyl compounds and their derivatives, including fluorine-containing ones, are very important building blocks in the synthesis of numerous heterocycles. For example, the reaction of trifluoroacetylacetone with hetarylhydrazines (2-hydrazinylthiazoles, 2-hydrazinylbenzothiazoles [1–4], 2-hydrazinylbenzoxazole [5], 2-hydrazinylquinolines [6]) gave a series of bi- and tricyclic compounds containing a pyrazole ring. However, these reactions are not selective due to formation of fairly stable intermediate 4,4,4-trifluorobutane-1,3-dione hydrazones and mixtures of regioisomeric pyrazoles. The reaction selectivity can often be improved by using the corresponding lithium enolates instead of fluoroalkyl-substituted unsymmetrical 1,3-diketones [7–17]; such lithium enolates are more accessible, stable on storage, and convenient for use in chemical processes. We previously demonstrated advantages of lithium 1,3-diketonates **I** as three-carbon building blocks in the synthesis of fluoroalkyl-substituted heterocycles [7–11, 14, 16, 17], including *N*-unsubstituted and *N*-phenyl-substituted pyrazoles [7, 16, 17].

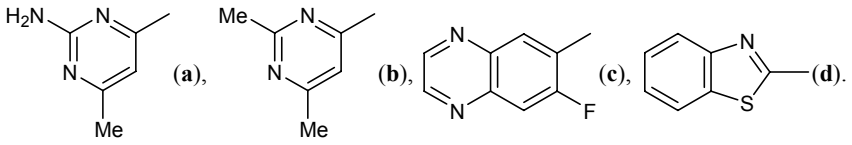
In the present work we examined reactions of fluoroalkyl-substituted lithium 1,3-diketonates **Ia**–**Ig** with 4-hydrazinyl-6-methylpyrimidin-2-amine (**IIa**), 2,6-dimethylpyrimidin-4-ylhydrazine (**IIb**), 7-fluoroquinoxalin-6-ylhydrazine (**IIc**), and benzothiazol-2-ylhydrazine (**IId**) (Table 1). These, at first glance simple and predictable, reactions could give rise to regioisomeric dihydropyrazole and/or pyrazole derivatives. However, structural specificities of hetarylhydrazines **IIa**–**IId** may favor alternative reaction paths. For instance, compound **IIa** possesses an amino group in the pyrimidine ring, while hydrazine **IIc** contains a labile fluorine atom in the quinoxaline fragment. In addition, opening of carbocycles in initial diketonates **Ie**, **If**, and **Ig** is possible. The latter transformation was observed previously in reactions of lithium diketonates containing cycloalkane fragments [$R^1R^2 = (CH_2)_n$] with benzene-1,2-diamine and 2-aminobenzenethiol [17, 18].

In this work we found that the examined reactions led to the formation of only pyrazole ring and that the heterocycle in the initial hetarylhydrazine remains unchanged (Scheme 1). The composition of products formed in the reactions of lithium diketonates **Ia**–**Ig**

Scheme 1.



For R_F, R^1, R^2, and R^3 in **I**, **III**–**V**, see table.

II, R^3 =  (**a**), (**b**), (**c**), (**d**).

with substituted hydrazines **IIa**–**IId** is determined by the natures of both fluoroalkyl substituent in initial diketonate **I** and substituents in hydrazines **II** (Table 1). The reaction of diketonate **Ia** with hydrazine **IIa** containing an amino group in the pyrimidine ring in ethanol–acetic acid gave a mixture of hydroxydihydropyrazole **IIIa** and its dehydration product, pyrazole **Va**. Compounds **IIIa** and **Va** were isolated as pure substances and characterized. Diketonates **Ib** and **Ic** reacted with hydrazine **IIa** to produce hydroxydihydropyrazoles **IIIb** and **IIIc**, respectively, and no subsequent dehydration was observed.

Reactions of diketonates **Ia**–**Ig** with hetarylhydrazines under more harsh conditions (in boiling glacial acetic acid) afforded either mixtures of 3-R_F (**IVa**–**IVc**, **IVf**) and 5-R_F isomers (**Va**, **Vb**, **Ve**, **Vi**) or 5-R_F isomers alone (**Vc**, **Vd**, **Vf**–**Vh**, **Vj**). An exception was the reaction of diketonate **Ib** with benzothiazolyl-

Table 1. Reaction of lithium 1,3-diketonates **Ia**–**Ig** with hetarylhydrazines **IIa**–**IId**

Compound no.	R_F	R^1	R^2	R^3NHNH_2	Method[a]	Product (yield, %)		
						III	**IV**	**V**
Ia	HCF_2	H	Ph	**IIa**	*a*	**IIIa** (47)	–	**Va** (21)
					b	–	**IVa**, **Va**, 3 : 1 (47)	
					c	–	–	**Va** (67)
Ib	CF_3	H	Ph	**IIa**	*a*	**IIIb** (60)	–	–
					b	–	**IVb**, **Vb**, 6 : 1 (42)	
Ic	HCF_2	H	Me	**IIa**	*a*	**IIIc** (58)[b]	–	–
					b	–	–	**Vc** (76)
Id	CF_3	H	Me	**IIa**	*b*	–	–	**Vd** (69)
Ie	HCF_2	$(CH_2)_3$		**IIa**	*b*	–	**IVc**, **Ve**, 1 : 5 (66)	
If	HCF_2	$(CH_2)_4$		**IIa**	*b*	–	–	**Vf** (81)
Ig	CF_3	$(CH_2)_4$		**IIa**	*b*	–	–	**Vg** (71)
Ia	HCF_2	H	Ph	**IIb**	*b*	–	**IVd** (56)	–
Ib	CF_3	H	Ph	**IIb**	*b*	–	–	**Vh** (49)
Ia	HCF_2	H	Ph	**IIc**	*b*	–	**IVe** (74)	–
Ib	CF_3	H	Ph	**IIc**	*b*	–	**IVf**, **Vi**, 1 : 1 (60)	
Ia	HCF_2	H	Ph	**IId**	*b*	–	**IVg**, **Vk**, 3 : 1	
Ib	CF_3	H	Ph	**IId**	*b*	**IIId** (69)	–	–
Ig	CF_3	$(CH_2)_4$		**IId**	*b*	–		**Vj** (49)

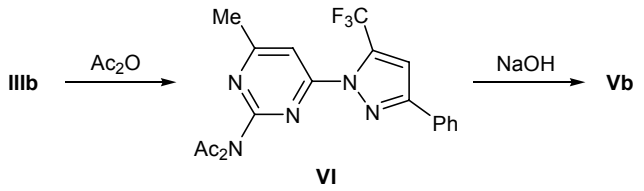
[a] *i*: EtOH, AcOH, reflux; *ii*: AcOH, reflux; *iii*: (1) CF_3COOH, reflux; (2) 2 N NaOH.
[b] Isolated as acetate.

hydrazine **IId**, which produced hydroxydihydropyrazole **IIId**. In the reaction of diketonate **Ia** with hydrazine **IIa** in boiling trifluoroacetic acid (which is known as one of the most efficient dehydrating agents) we obtained the corresponding trifluoroacetate, and treatment of the latter with 2 N NaOH gave pyrazole **Va**.

The structure of compounds **III**–**V** was confirmed by elemental analyses and IR and ^{1}H NMR spectra. Some compounds were additionally characterized by ^{19}F and ^{13}C NMR spectra, GC/MS data, and X-ray analysis. The ^{1}H NMR spectra of dihydropyrazoles **III** (R^1 = H) contained a singlet at δ 5–8 ppm due to OH proton and an *AB* pattern in the region δ 3–4 ppm (^2J = 18–24 Hz) due to diastereotopic methylene protons on C^3. Singlets at δ_F 81.40 and 80.37 ppm in the ^{19}F NMR spectra of **IIIb** and **IIId** are typical of CF_3 groups attached to sp^3-carbon atom (cf. [19]). The fluorine atoms in the HCF_2 group of **IIIa** and **IIIc** are diastereotopic, and they appeared as an *AB* spin system in the ^{19}F NMR spectra. Compounds **III** displayed in the ^{1}H and ^{19}F NMR spectra spin–spin coupling between the fluorine nuclei and methylene protons on C^3 with a coupling constant $^4J_{HF}$ of ~2.4–2.5 Hz. The above spectral parameters correspond to 5-hydroxy-5-R_F derivatives rather than to isomeric 3-hydroxy-5-R_F-dihydropyrazoles.

Dehydration of hydroxydihydropyrazoles **IIIa** and **IIIb** could produce exclusively 5-R_F isomers **Va** and **Vb**. In fact, compounds **Va** and **Vb** were obtained by heating hydroxy derivatives **IIIa** and **IIIb** in boiling acetic anhydride and subsequent treatment of *N*,*N*-diacyl derivatives with 2 N aqueous NaOH on heating. Intermediate *N*,*N*-diacetyl derivative **VI** was isolated and characterized by spectral data (Scheme 2).

Scheme 2.



VI

The structure of the condensation products of fluoroalkyl-substituted lithium 1,3-diketonates **Ia**–**Ig** with hetarylhydrazines **IIa**–**IId** was determined on the basis of the spectral data for compounds **Va**–**Vc** and **Vf**, taking into account the data of [4, 19, 20]* where some diagnostic features for the assignment of substituted pyrazoles to 3-R_F or 5-R_F isomers were formulated. In the ^{19}F NMR spectra of 3-R_F pyrazoles the CF_3 singlet is observed at δ_F 99–100 ppm (relative to C_6F_6)

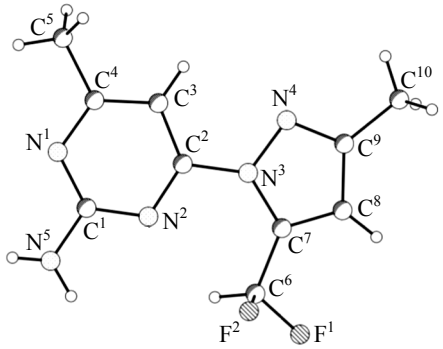


Fig. 1. Structure of the molecule of 4-(5-difluoromethyl-3-methyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (**Vc**) according to the X-ray diffraction data.

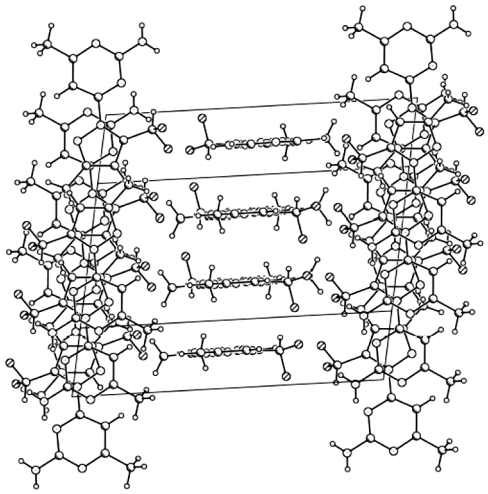


Fig. 2. A fragment of crystal packing of 4-(5-difluoromethyl-3-methyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (**Vc**).

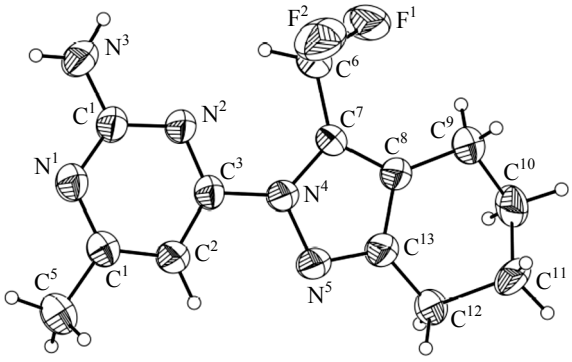


Fig. 3. Structure of the molecule of 4-[5-(difluoromethyl)-4,5,6,7-tetrahydro-2*H*-indazol-2-yl]-6-methylpyrimidin-2-amine (**Vf**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

* The chemical shifts of the fluorine nuclei in CF_3 groups given in [19, 20] were recalculated relative to hexafluorobenzene: $\delta(C_6F_6) = \delta(CFCl_3) + 162.9$.

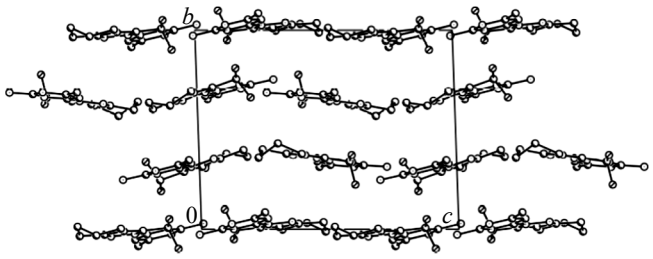


Fig. 4. A fragment of crystal packing of 4-[5-(difluoromethyl)-4,5,6,7-tetrahydro-2*H*-indazol-2-yl]-6-methylpyrimidin-2-amine (**Vf**). A view along the *a* axis; hydrogen atoms are not shown.

while the corresponding signal of the 5-CF_3 group is located at δ_F 102–103 ppm. It was difficult to assign substituted pyrazoles with R_F = HCF_2 to 3-R_F or 5-R_F isomers by the chemical shifts of the fluorine nuclei in the HCF_2 group, since the difference in the δ_F values of the 3-R_F or 5-R_F isomers was too small. The ^{19}F NMR spectrum of 5-R_F isomer **Vi** characteristically displayed spin–spin coupling of the 6′-F nucleus in the quinoxaline fragment with the CF_3 group; no such coupling is observed in 3-R_F isomer **IVf**. The ^1H and ^{19}F NMR spectra of the product obtained from diketonate **Ia** and hydrazine **IIc** were consistent with the structure of 3-R_F isomer **IVe**: there was no coupling between 6′-F and HCF_2, whereas the =CH singlet appeared in the ^1H NMR spectrum at δ 6.83 ppm.

GC/MS analysis of the product mixture obtained in the reaction of lithium diketonate **Ia** and hydrazine derivative **IId** revealed two components with retention times of 11.86 and 12.58 min. According to the ^1H and ^{19}F NMR data, isomer **IVg** predominated. Therefore, the peak with τ_r 11.86 min having a larger area was assigned to major isomer **IVg**, and the minor peak with τ_r 12.58 min, to isomer **Vk**. The mass spectra of **IVg** and **Vk** differed only by relative intensities of the main fragment ion peaks with the same *m*/*z* values: 327 $[M]^+$ (68.5 and 80.2%), 326 $[M - H]^+$ (83.6 and 15.1%), 250 $[M - Ph]^+$ (79.6 and 14.4%), 224 $[M - PhCN]^+$ (13.6 and 99.8%), 223 $[M - H - PhCN]^+$ (53.1 and 27.6%). The peaks with *m*/*z* 276 $[M - HCF_2]^+$ and 275 $[M - H - HCF_2]^+$ were present only in the mass spectrum of 3-R_F isomer **IVg**, while those with *m*/*z* 205, 197, 193 $[M - Ht]^+$, and 174 $[M - Ht - F]^+$ were observed only in the spectrum of 5-R_F isomer **Vk**. The fragment ion peaks with *m*/*z* 134 $[Ht]^+$, 116 $[M - Ht - Ph]^+$, 103 $[PhCN]^+$, 77 $[Ph]^+$, and 51 $[HCF_2]^+$ had comparable intensities in the spectra of both regioisomers.

Table 2. Selected bond lengths and bond angles in the molecule of 4-(5-difluoromethyl-3-methyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (**Vc**)

Bond	*d*, Å	Angle	ω, deg
C^1–N^5	1.345(2)	$N^1C^1N^2$	126.41(18)
C^1–N^1	1.341(2)	$N^5C^1N^2$	116.55(19)
C^1–N^2	1.346(2)	$N^1C^1N^5$	117.02(19)
C^4–C^5	1.495(2)	$F^2C^6F^1$	104.90(15)
N^3–C^2	1.408(2)	$F^2C^6C^7$	110.06(15)
N^4–N^3	1.370(2)	$F^1C^6C^7$	107.44(15)
F^1–C^6	1.364(2)	$C^8C^7C^6$	128.19(18)
F^2–C^6	1.363(2)	$N^3C^7C^6$	125.27(17)

The structure of compounds **Vc** and **Vf** was unambiguously determined by X-ray analysis (Figs. 1–4). Molecule **Vc** in crystal (Fig. 1) is planar; deviations of atoms from the mean-square plane do not exceed 0.05 Å, except for the difluoromethyl carbon atom which deviates from that plane by 0.082 Å. The bond lengths and bond angles in molecule **Vc** approach the corresponding standard values (Table 2). Molecules **Vc** in crystal are linked to dimers via intermolecular hydrogen bond system (Table 3), and the dimers are packed to form parallel and crosswise layers (Fig. 2). Within a layer, molecules **Vc** are linked through a system of π–π contacts with an interplanar distance of ~3.25 Å.

The crystal structure of compound **Vf** is formed by three crystallographically independent molecules **A**–**C**. The bond lengths and bond and torsion angles in molecules **A**–**C** differ insignificantly and are close to the corresponding standard values (Table 4). Figure 3 shows the structure of molecule **A**. Molecules **A**–**C** are planar; deviation of atoms from the mean-square plane does not exceed 0.05 (**A**) and 0.1 Å (**B**, **C**). The fluorine atoms in the difluoromethyl group and the cyclohexenyl fragment of molecule **A** are disordered by two positions with populations of 0.8/0.2 and 0.5/0.5, respectively. Molecules **Vf** in crystal are linked to dimers through a system of intermolecular hydrogen bonds (Table 4). The dimer formed by molecules **B** is centrosymmetric due to intermolecular hydrogen bond between the amino group and nitrogen atom of the pyrimidine ring: N^{3B}–$H^{3BA}\cdots N^{1B}$ [$-x + 2$, $-y + 3$, $-z$], while molecules **A** and **B** form noncentrosymmetric dimers where the mean-square planes of the heterocyclic systems are arranged at a dihedral angle of 21.5° and the distance $N^3\cdots N^{1A}$ 3.04 Å [$x + 1$, y, z] appears to be shorter than the distance $N^{3A}\cdots N^1$ 3.1 Å [$x - 1$, y, z]. As a result, layered structure with the positions of molecules modulated along the *b* axis is

Table 3. Parameters of hydrogen bonds in the crystal structures of compounds **Vc** and **Vf**

D–H[a]	D–H, Å	H···A	∠DHA, deg	D···A, Å	A
Compound **Vc**					
N^5–H^{5A}	0.88(2)	2.59(2)	174.7(2)	3.468(2)	F^1 [–x + 3/2, *y* + 1/2, –*z* – 1/2]
N^5–H^{5B}	0.83(2)	2.23(2)	174.4(2)	3.061(2)	N^1 [–*x* + 2, –*y* + 3, –*z*]
Compound **Vf**					
N^{3B}–H^{3BA}	0.860	2.197	178.77	3.057	N^{1B} [–*x* + 1, –*y*, –*z*]
N^{3A}–H^{3AA}	0.860	2.294	157.41	3.105	N^1 [*x* – 1, *y*, *z*]
N^3–H^{3B}	0.860	2.187	174.44	3.044	N^{1A} [*x* + 1, *y*, *z*]

[a] Atoms in molecule **A** are numbered without indices, in molecule **B**, with superscript "*A*", and in molecule **C**, with superscript "*B*".

obtained (Fig. 4). We believe that such modulation is related to perturbations introduced by the cyclohexenyl and difluoromethyl fragments into the common interlayer π–π contact system.

Thus, on the basis of fluoroalkyl-substituted lithium 1,3-diketonates and hetarylhydrazines we have synthesized new heterocyclic ensembles composed of pyrazole (or dihydropyrazole) and pyrimidine, quinoxaline, or benzothiazole rings.

Analysis of our results and the data published in [1–8, 12, 16, 17] showed that fluoroalkyl-substituted lithium 1,3-diketonates react with hydrazine derivatives to produce compounds containing a pyrazole ring, namely 5-hydroxy-5-R_F-dihydropyrazoles and regioisomeric 3-R_F and/or 5-R_F pyrazoles. 3-Hydroxy-3-R_F-dihydropyrazoles were not isolated, presumably due to their facile dehydration to the corresponding 3-R_F pyrazoles. The possibility for the isolation of 5-hydroxy-5-R_F-dihydropyrazoles is consistent with the known stabilization of adducts with a fluoroalkyl substituent and a hydroxy group attached to the same carbon atom. The reaction of fluoroalkyl-substituted lithium 1,3-diketonates with hydrazine derivatives in organic acids ensures preparation of 3-R_F and/or 5-R_F pyrazoles without intermediate isolation of 5-hydroxy-5-R_F-dihydropyrazoles. Unlike the corresponding 1,3-diketones, no hydrazones were formed from their lithium enolates. As in reactions of fluoroalkyl-substituted 1,3-diketones with hydrazines, it is impossible to predict *a priori* the reaction selectivity on the basis of the initial reactant structure. Nevertheless, the use of fluoroalkyl-substituted lithium 1,3-diketonates instead of the corresponding 1,3-diketones seems to be more advantageous due to appreciable reactant and time economy as a result of elimination of several steps related to the isolation and purification of intermediate products.

Table 4. Selected bond lengths and bond angles in crystallographically independent molecules **A**–**C** of compound **Vf**

Parameter	Molecule **A**	Molecule **B**	Molecule **C**
Bond length, Å			
N^1–C^4	1.346(2)	1.342(2)	1.342(2)
N^2–C^4	1.339(2)	1.348(2)	1.346(2)
N^3–C^4	1.341(2)	1.339(2)	1.336(2)
N^4–N^5	1.3666(19)	1.369(2)	1.3715(19)
N^4–C^3	1.414(2)	1.407(2)	1.410(2)
N^4–C^7	1.384(2)	1.382(2)	1.379(2)
C^1–C^5	1.502(2)	1.498(2)	1.499(2)
Bond angle, deg			
$N^1C^4N^2$	126.05(18)	126.22(18)	125.79(18)
$N^3C^4N^1$	116.48(18)	116.78(17)	117.07(17)
$N^3C^4N^2$	117.47(18)	117.00(18)	117.14(18)

Table 5. Principal crystallographic parameters of compounds **Vc** and **Vf** and parameters of X-ray diffraction experiments

Parameter	**Vc**	**Vf**
Formula	$C_{10}H_{11}F_2N_5$	$C_{13}H_{15}F_2N_5$
Molecular weight	239.24	279.30
Temperature, K	295(2)	295(2)
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/n$	P-1
Unit cell parameters:		
a, A	13.374(4)	11.8378(7)
b, A	5.3977(8)	12.0160(6)
c, A	15.2818(17)	15.3079(7)
α, deg	90	82.942(4)
β, deg	102.826(16)	73.893(4)
γ, deg	90	70.802(5)
V, Å^3	1075.6(4)	1974.43(18)
Z	4	6
d, g/cm^3	1.477	1.409
μ, mm^{-1}	0.120	0.109
Θ range, deg	$2.73 \le \Theta \le 31.78$	$2.61 \le \Theta \le 28.28$
Completeness, % (Θ, deg)	99.1 (27.00)	97.4 (26.00)
Total number of reflections	13401	16501
Number of independent reflections	3303	9266
R_{int}	0.0667	0.0232
Number of reflections with $I > 2\sigma(I)$	1088	3828
Number of variables	162	586
Goodness of fit (F^2)	1.000	1.003
R_1 [$I > 2\sigma(I)$]	0.0460	0.0466
wR_2 [$I > 2\sigma(I)$]	0.0778	0.0949
R_1 (all reflections)	0.1673	0.1191
wR_2 (all reflections)	0.0845	0.1005
$\Delta e_{max/min.}$, e/Å^3	0.288/–0.290	0.358/–0.258

EXPERIMENTAL

Lithium diketonates **Ia**–**Ig** were prepared according to the procedure described in [7]; their characteristics were reported in [21]. 4-Hydrazinyl-6-methylpyrimidin-2-amine (**IIa**), 2,6-dimethylpyrimidin-4-ylhydrazine (**IIb**), 7-fluoroquinoxalin-6-ylhydrazine (**IIc**), and benzothiazol-2-ylhydrazine (**IId**) were synthesized as described in [22–25]. The progress of reactions was monitored by TLC (Silufol UV-254, $CHCl_3$); spots were developed by treatment with aqueous solutions of $Cu(OAc)_2$ and $KMnO_4$. The NMR spectra were recorded on a Bruker DRX-400 spectrometer [400 (^{1}H), 376 (^{19}F), and 100 MHz (^{13}C)] using tetramethylsilane (^{1}H, ^{13}C) and C_6F_6 (^{19}F) as internal standards. The IR spectra were measured on a Perkin Elmer Spectrum One spectrometer with Fourier transform from samples dispersed in mineral oil. The elemental compositions were determined on a Perkin Elmer 2400 analyzer. The mass spectra were obtained on a Varian Saturn 2100T GC/MS (GC 3900) system [VF-5ms column, 30 m× 0.25 mm; carrier gas helium, flow rate 1 mL/min; oven temperature programming from 40 (3 min) to 200°C at a rate of 20 deg/min].

The X-ray diffraction data for compounds **Vc** and **Vf** were acquired according to a standard procedure on an Xcalibur 3 automatic four-circle diffractometer equipped with a CCD detector (λMoK_α radiation, graphite monochromator, ω-scanning, scan step 1.0°) from a 0.51×0.12×0.08-mm colorless needle-shaped single crystal of **Vc** and a 0.45×0.35×0.29-mm colorless prismatic crystal of **Vf**. No correction for absorption was applied because of its insignificance. The structure was solved by the direct method using SHELXS97 [26] and was refined against F^2 by the full-matrix least squares procedure in anisotropic approximation (isotropic for hydrogen atoms) using SHELXL97 [26]. Hydrogen atoms were visualized by the electron density maps, and their positions were refined according to the riding model with dependent thermal parameters. The sets of crystallographic data for compounds **Vc** and **Vf** were deposited to the Cambridge Crystallographic Data Centre (entry nos. CCDC 1002976, 1002977) and are available at *www.ccdc.cam.ac.uk/data_request/cif*. The principal crystal structure parameters and parameters of X-ray diffraction experiments are collected in Table 5, and selected bond lengths and bond angles are given in Tables 2 and 4.

Reaction of lithium 1,3-diketonates Ia–Ig with hetarylhydrazines IIa–IId (*general procedures***).** *a*. *In EtOH–AcOH*. Equimolar amounts of diketonate **I** and hydrazine **II** were dissolved in a minimum amount of ethanol, 2 equiv of glacial acetic acid was added, and the mixture was heated under reflux until the initial compounds disappeared (TLC). The mixture was then poured into 20 mL of water, the precipitate was filtered off, and the filtrate was extracted with two portions of chloroform. The solvent was removed from the extract, and the residue was combined with the precipitate and

subjected to column chromatography using chloroform as eluent, the separation process being monitored by TLC. The collected fractions were evaporated, and compounds **V**, **IV**, and **III** (hereinafter, in order of elution) were recrystallized from chloroform–hexane (1:3).

b. *In AcOH*. Equimolar amounts of diketonate **I** and hetarylhydrazine **II** were dissolved in a minimum amount of glacial acetic acid, and the mixture was heated under reflux until the initial compounds disappeared (TLC). The mixture was cooled to room temperature and poured into water, the products were extracted into chloroform, the extract was filtered through a layer of silica gel, the solvent was removed, and the residue was recrystallized from chloroform–hexane (1:10).

Reaction of diketonate Ia with 4-hydrazinyl-6-methylpyrimidin-2-amine (IIa). *a*. From 1.64 g (8.1 mmol) of compound **Ia** and 1 g (8.1 mol) of hydrazine **IIa** in 10 mL of ethanol containing 0.98 g (16.0 mmol) of glacial acetic acid we obtained 0.5 g (21%) of compound **Va** and 1.2 g (47%) of **IIIa**.

4-(5-Difluoromethyl-3-phenyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (Va). White crystals, mp 184–185°C. IR spectrum, ν, cm^{-1}: 3470 m, 3297 m, 3162 (NH), 1637 s, 1569 (C=N, C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.33 s (3H, CH_3), 4.89 br.s (2H, NH_2), 6.67 s (1H, CH), 6.69 s (1H, CH), 6.78 t (1H, HCF_2, $^2J_{HF}$ = 54.8 Hz), 7.26–7.40 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 24.11 s, 103.10 s, 106.93 s, 110.95 t (HCF_2, $^1J_{CF}$ = 234.6 Hz), 128.17 s, 128.86 s, 128.95 s, 130.51 s, 130.53 s, 145.99 s, 148.59 t ($^2J_{CF}$ = 30.2 Hz), 159.21 s, 162.14 s, 170.44 s. ^{19}F NMR spectrum ($CDCl_3$): δ_F 49.11 ppm, d.d (HCF_2, $^2J_{FH}$ = 54.8, $^4J_{FH}$ = 0.9 Hz). Found, %: C 59.73; H 4.47; F 12.60; N 23.23. $C_{15}H_{13}F_2N_5$. Calculated, %: C 59.79; H 4.35; F 12.61; N 23.25.

1-(2-Amino-6-methylpyrimidin-4-yl)-5-difluoromethyl-3-phenyl-4,5-dihydro-1*H*-pyrazol-5-ol (IIIa). White powder, mp 165–166°C. IR spectrum, ν, cm^{-1}: 3418 s, 3285 s (NH), 3133 br (OH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.32 s (3H, CH_3), 3.17 d.t (1H, 4-H, J_{AB} = 24.1, $J_{HF} \approx$ 2.6 Hz) and 3.52 d.t (1H, 4-H, J_{AB} = 24.1, $J_{HF} \approx$ 2.4 Hz) (*AB* system), 4.59 br.s (2H, NH_2), 5.88 br.s (1H, OH), 6.47 t (1H, HCF_2, $^2J_{HF}$ = 54.2 Hz), 6.57 s (1H, CH), 7.26–7.38 m (5H, Ph). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: 43.5 d.d (1F, F_A, J_{FF} = 321.4, $^2J_{FH}$ = 54.2 Hz), 44.42 d.d (1F, F_B, J_{FF} = 321.4, $^2J_{FH}$ = 54.3 Hz). Found, %: C 56.66; H 4.62; F 11.91; N 22.12. $C_{15}H_{15}F_2N_5O$. Calculated, %: C 56.42; H 4.74; F 11.89; N 21.93.

b. From 1 g (4.9 mmol) of diketonate **Ia** and 0.6 g (4.9 mmol) of hydrazine **IIa** we obtained 0.7 g (48%) of a mixture of isomers **Va** and **IVa** at a ratio of 2:1. IR spectrum, ν, cm^{-1}: 3450, 3230, 3150 (NH), 1638 s, 1567 m (C=N, C=C). The ^1H and ^{19}F NMR spectra each contained two sets of signals belonging to isomers **IVa** and **Va**. The spectral parameters of **Va** coincided with those given above. Found, %: C 59.71; H 4.38; F 12.71; N 23.18. $C_{15}H_{13}F_2N_5$. Calculated, %: C 59.79; H 4.35; F 12.61; N 23.25.

4-(3-Difluoromethyl-5-phenyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (IVa). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.45 s (CH_3), 5.17 br.s (2H, NH_2); the other signals were overlapped by those of the phenyl protons. ^{19}F NMR spectrum ($CDCl_3$): δ_F 48.04 ppm, d (HCF_2, $^2J_{HF}$ = 53.9 Hz).

c. *In CF_3COOH*. Trifluoroacetic acid, 3 mL, was added to a solution of 1.71 g (8.4 mmol) of compound **Ia** and 1.04 g (8.4 mmol) of hydrazine **IIa**, and the mixture was heated under reflux until the initial compounds disappeared (TLC). The solvent was distilled off, and the solid residue was washed with a 2 N solution of sodium hydroxide until neutral reaction and dissolved in chloroform. The solution was filtered through a layer of silica gel, the solvent was removed, and the residue was recrystallized from chloroform–hexane (1:10) to isolate 1.7 g (67%) of **Va**, mp 184–185°C.

1-(2-Amino-6-methylpyrimidin-4-yl)-3-phenyl-5-trifluoromethyl-4,5-dihydro-1*H*-pyrazol-5-ol (IIIb). *a*. From 1.8 g (8 mmol) of diketonate **Ib** and 1 g (8 mmol) of hydrazine **IIa** in 10 mL of ethanol containing 0.98 g (16 mmol) of glacial acetic acid we obtained 1.8 g (67%) of compound **IIIb**. White powder, mp 245–247°C. IR spectrum, ν, cm^{-1}: 3394, 3333, 3065 br (NH, OH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.39 s (3H, CH_3), 3.86 d and 4.12 d (1H each, 4-H, *AB* system, J_{AB} = 19.5 Hz), 6.90 s (1H, CH), 7.50–7.58 m (3H, Ph), 7.87 br.s (1H, NH), 7.89–7.92 m (2H, Ph), 8.30 br.s (1H, NH), 13.58 br.s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 18.73 s, 44.02 s, 93.05 q ($^2J_{CF}$ = 33.7 Hz), 96.17 s, 125.80 q (CF_3, $^1J_{CF}$ = 287.6 Hz), 127.03 s, 128.87 s, 129.55 s, 131.32 s, 154.85 s, 155.56 s, 155.91 s, 160.81 s. ^{19}F NMR spectrum (DMSO-d_6): δ_F 81.4 ppm, s (CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 337 (21.3) $[M]^+$, 336 (7.7), 320 (20.7), 319 (100), 318 (19.2), 268 (47.9), 251 (8.3), 226 (16.8), 212 (22), 108

(12.2), 77 (15.2), 69 (23.5). Found, %: C 53.66; H 4.22; F 16.92; N 20.81. $C_{15}H_{14}F_3N_5O$. Calculated, %: C 53.41; H 4.18; F 16.89; N 20.76. *M* 337.

b. From 1.16 g (5.2 mmol) of diketonate **Ib** and 0.65 g (5.2 mmol) of hydrazine **IIa** we obtained 0.7 g (42%) of a mixture of 4-methyl-6-(5-trifluoromethyl-3-phenyl-1*H*-pyrazol-1-yl)pyrimidin-2-amine (**Vb**) and 4-(3-difluoromethyl-5-phenyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (**IVb**) at a ratio of 6:1. The ^{1}H NMR spectrum contained two sets of signals belonging to isomers **IVb** and **Vb**. Found, %: C 56.46; H 3.84; F 17.88; N 21.89. $C_{15}H_{12}F_3N_5$. Calculated, %: C 56.42; H 3.79; F 17.85; N 21.93.

Compound **IVb**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.37 s (CH_3), 4.83 br.s (2H, NH_2), 6.69 s (1H, CH), 6.84 m (1H, CH), 7.41–7.49 m (3H, Ph), 7.87–7.89 m (2H, Ph). ^{19}F NMR spectrum ($CDCl_3$): δ_F 99.07 ppm, s (CF_3).

The spectral parameters of compound **Vb** are given below.

4-(5-Difluoromethyl-5-hydroxy-3-methyl-4,5-dihydro-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-aminium acetate (IIIc). *a*. Compound **IIIc** was synthesized from 0.4 g (2.8 mmol) of diketonate **Ic**, 0.35 g (2.8 mmol) of hydrazine **IIa**, and 0.35 g (5.8 mmol) of acetic acid in 10 mL of ethanol. Yield 0.52 g (58%), white powder, mp 128–130°C. IR spectrum, ν, cm^{-1}: 3296 s (NH), 2995 br (OH). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 1.96 s (3H, CH_3), 2.12 s (3H, CH_3), 2.17 s (3H, CH_3), 2.90 d.d (1H, $^2J_{HH}$ = 18.9, $^4J_{HF}$ = 3.2 Hz) and 3.38 d (1H, $^2J_{HH}$ = 18.9 Hz) (4-H), 5.79 br.s (1H, OH), 6.43 s (1H, CH), 6.53 d.d (1H, HCF_2, $^2J_{HF}$ = 58.06, $^2J_{HF}$ = 56.40 Hz). ^{19}F NMR spectrum (acetone-d_6), δ_F, ppm: 31.15 d.d (1F, $^2J_{FF}$ = 283.56, $^2J_{FH}$ = 58.06 Hz) and 37.55 d.d.d (1F, $^2J_{FF}$ = 283.56, $^2J_{FH}$ = 56.40, $^4J_{FH}$ = 0.81 Hz) (HCF_2). Found, %: C 45.32; H 5.43; F 11.80; N 22.04. $C_{10}H_{13}F_2N_5O\cdot CH_3CO_2H$. Calculated, %: C 45.42; H 5.40; F 11.98; N 22.07.

4-(5-Difluoromethyl-3-methyl-1*H*-pyrazol-1-yl)-6-methylpyrimidin-2-amine (Vc). *b*. From 0.4 g (2.8 mmol) of diketonate **Ic** and 0.35 g (2.8 mmol) of hydrazine **IIa** we obtained 0.5 g (76%) of compound **Vc** with mp 205–206°C. IR spectrum, ν, cm^{-1}: 3496, 3305, 3162 (NH), 1650 s, 1564 m (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.29 s (3H, Me), 2.40 s (3H, Me), 5.01 br.s (2H, NH_2), 6.59 s (1H, CH), 7.12 s (1H, CH), 7.67 t (1H, HCF_2, $^2J_{HF}$ = 54.8 Hz). ^{19}F NMR spectrum ($CDCl_3$): δ_F 48.09 ppm, d (HCF_2, $^2J_{FH}$ = 54.8 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.72 s, 24.20 s, 99.54 s, 108.88 t (HCF_2, $^1J_{CF}$ = 236.47 Hz), 110.12 s, 139.07 t ($^2J_{CF}$ = 31.13 Hz), 151.29 s, 158.97 s, 161.80 s, 170.44 s. Found, %: C 50.36; H 4.65; F 15.71; N 29.26. $C_{10}H_{11}F_2N_5$. Calculated, %: C 50.21; H 4.64; F 15.88; N 29.28.

4-Methyl-6-(3-methyl-5-trifluoromethyl-1*H*-pyrazol-1-yl)pyrimidin-2-amine (Vd). *b*. From 0.64 g (4.0 mmol) of diketonate **Id** and 0.5 g (4.0 mmol) of hydrazine **IIa** (after treatment with 2 N aqueous NaOH and recrystallization from chloroform–hexane, 1:10) we obtained 0.7 g (69%) of compound **Vd** with mp 171–172°C. IR spectrum, ν, cm^{-1}: 3508, 3302, 3107 (N–H), 1644 s, 1564 (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.35 s (3H, CH_3), 2.41 s (3H, CH_3), 5.13 br.s (2H, NH_2), 6.67 s (1H, CH), 7.04 s (1H, CH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.57 s, 24.24 s, 100.30 s, 112.64 q ($^4J_{CF}$ = 3.36 Hz), 119.84 q (CF_3, $^1J_{CF}$ = 268.40 Hz), 133.31 q ($^2J_{CF}$ = 41.1 Hz), 150.44 s, 158.29 s, 162.13 s, 170.43 s. ^{19}F NMR spectrum ($CDCl_3$): δ_F 103.99 ppm, s (CF_3). Found, %: C 46.61; H 3.87; F 22.21; N 27.37. $C_{10}H_{10}F_3N_5$. Calculated, %: C 46.69; H 3.92; F 22.16; N 27.23.

4-[3-(Difluoromethyl)-5,6-dihydrocyclopenta[*c*]-pyrazol-1(4*H*)-yl]-6-methylpyrimidin-2-amine (IVc) and 4-[5-(difluoromethyl)-3,6-dihydrocyclopenta-[*c*]pyrazol-1(4*H*)-yl]-6-methylpyrimidin-2-amine (Ve). *b*. From 1.35 g (8.0 mmol) of diketonate **Ie** and 1 g (8.0 mmol) of hydrazine **IIa** we obtained a mixture of compounds **IVc** and **Ve** at a ratio of 5:1. Yield 1.4 g (66%), white powder. IR spectrum, ν, cm^{-1}: 3507 m, 3302 m, 3167 m (NH), 1634 s, 1566 m (C=N, C=C). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: **IVc**: 2.39 s (3H, CH_3), 2.54–2.65 m (2H, CH_2), 2.71–2.75 m (2H, CH_2), 3.15–3.19 m (2H, CH_2), 5.05 br.s (2H, NH_2), 6.65 t (1H, HCF_2, $^2J_{HF}$ = 54.9 Hz), 7.08 s (1H, CH); **Ve**: 2.37 s (3H, CH_3), 2.44–2.50 m (2H, CH_2), 2.75–2.78 m (2H, CH_2), 2.79–2.82 m (2H, CH_2), 5.05 br.s (NH_2), 7.06 s (1H, CH), 7.67 t (1H, HCF_2, $^2J_{HF}$ = 55.0 Hz). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: **IVc**: 48.88 d (HCF_2, $^2J_{HF}$ = 54.9 Hz); **Ve**: 48.68 d.d.d. (HCF_2, $^2J_{FH}$ = 55.0, $^5J_{FH}$ = 2.6, 2.5 Hz). Found, %: C 54.35; H 4.99; F 14.33; N 26.35. $C_{12}H_{13}F_2N_5$. Calculated, %: C 54.34; H 4.94; F 14.32; N 26.40.

4-[5-(Difluoromethyl)-4,5,6,7-tetrahydro-2*H*-indazol-2-yl]-6-methylpyrimidin-2-amine (Vf). *b*. From 1.17 g (6.0 mmol) of diketonate **If** and 0.8 g (6.0 mmol) of hydrazine **IIa** we obtained 1.36 g (81%) of compound **Vf**. White powder, mp 220–221°C. IR spectrum, ν, cm^{-1}: 3510, 3308, 3165 (N–H), 1630 s,

1560 m (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.76–1.86 m (4H, CH_2), 2.71–2.81 m (4H, CH_2), 2.37 s (3H, Me), 5.63 br.s (NH_2), 7.08 s (1H, CH), 7.82 t (HCF_2, $^2J_{HF}$ = 54.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 21.19 s, 22.66 s, 22.70 s, 23.62 s, 24.20 s, 99.62 s, 110.38 t (HCF_2, $^1J_{CF}$ = 235.38 Hz), 121.77 t ($^4J_{CF}$ = 1.14 Hz), 132.89 t ($^2J_{CF}$ = 31.0 Hz), 152.61 t ($^3J_{CF}$ = 2.1 Hz), 159.39 s, 161.91 s, 170.31 s. ^{19}F NMR spectrum ($CDCl_3$): δ_F 48.04 ppm, d.d.d (HCF_2, $^2J_{FH}$ = 54.5, $^5J_{FH}$ = 2.9, 2.8 Hz). Found, %: C 55.87; H 5.49; F 13.58; N 25.16. $C_{13}H_{15}F_2N_5$. Calculated, %: C 55.91; H 5.41; F 13.60; N 25.07.

4-Methyl-6-[5-(trifluoromethyl)-4,5,6,7-tetrahydro-2*H*-indazol-2-yl]pyrimidin-2-amine (Vg). *b*. From 1.05 g (0.0052 mol) of diketonate **Ig** and 0.65 g (0.0052 mol) of hydrazine **IIa** we obtained 1.1 g (71%) of compound **Vg**. White powder, mp 202–203°C. IR spectrum, ν, cm^{-1}: 3496, 3288, 3138 (NH), 1637 s, 1572 m (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.75–1.86 (4H, CH_2), 2.39 s (3H, Me), 2.73–2.77 m (4H, CH_2), 5.13 br.s (2H, NH_2), 6.97 m (1H, CH). ^{19}F NMR spectrum ($CDCl_3$): δ_F 106.23 ppm, m (CF_3). Found, %: C 52.57; H 4.84; F 19.19; N 23.51. $C_{13}H_{14}F_3N_5$. Calculated, %: C 52.52; H 4.75; F 19.17; N 23.56.

6-[3-(Difluoromethyl)-5-phenyl-1*H*-pyrazol-1-yl]-2,4-dimethylpyrimidine (IVd). *b*. From 0.5 g (2.4 mmol) of diketonate **Ia** and 0.34 g (2.4 mmol) of hydrazine **IIb** we obtained 0.4 g (56%) of compound **IVd**. White powder, mp 89–90°C. IR spectrum, ν, cm^{-1}: 1605 s, 1549 m (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.38 s (6H, Me), 6.73 s (1H, CH), 6.85 t (HCF_2, $^2J_{HF}$ = 54.6 Hz), 6.96 s (1H, CH), 7.26–7.34 m (5H, Ph). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 23.73 s, 106.16 s, 111.16 t (HCF_2, $^1J_{CF}$ = 233.9 Hz), 118.98 s, 127.93 s, 128.42 s, 128.75 s, 130.97 s, 146.50 s, 148.48 t ($^2J_{CF}$ = 30.5 Hz), 156.50 s, 169.03 s. ^{19}F NMR spectrum ($CDCl_3$): δ_F 49.47 ppm, d.d (HCF_2, $^2J_{FH}$ = 54.6, $^4J_{FH}$ = 1.0 Hz). Found, %: C 63.95; H 4.71; F 12.61; N 18.70. $C_{16}H_{14}F_2N_4$. Calculated, %: C 63.99; H 4.69; F 12.65; N 18.65.

2,4-Dimethyl-3-phenyl-6-[5-(trifluoromethyl)-1*H*-pyrazol-1-yl]pyrimidine (Vh). *b*. From 1 g (4.5 mmol) of diketonate **Ib** and 0.62 g (4.5 mmol) of hydrazine **IIb** we obtained 0.7 g (49%) of compound **Vh** with mp 82.5–83.5°C. IR spectrum, ν, cm^{-1}: 1610 s, 1520 m (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.59 s (6H, Me), 7.05 s (1H, CH), 7.21 s (1H, CH), 7.39–7.46 m (3H, Ph), 7.92–7.95 m (2H, Ph). ^{19}F NMR spectrum ($CDCl_3$): δ_F 104.03 ppm, s (CF_3). Found, %: C 60.28; H 4.07; F 17.61; N 17.83. $C_{16}H_{13}F_3N_4$. Calculated, %: C 60.38; H 4.12; F 17.91; N 17.60.

7-[3-(Difluoromethyl)-5-phenyl-1*H*-pyrazol-1-yl]-6-fluoroquinoxaline (IVe). *b*. From 0.6 g (2.9 mmol) of diketonate **Ia** and 0.5 g (2.9 mmol) of hydrazine **IIc** we obtained 0.9 g (92%) of compound **IVe**. White powder, mp 134–135°C. IR spectrum, ν, cm^{-1}: 1510 s, 1490 m (C=N, C=C). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.81 t (HCF_2, $^2J_{HF}$ = 54.7 Hz), 6.83 s (1H, CH), 7.23–7.35 m (5H, Ph), 7.79 d (1H, $^3J_{HF}$ = 10 Hz), 8.29 d (1H, $^4J_{HF}$ = 7.6 Hz), 8.88 d (1H, $^3J_{HH}$ = 1.7 Hz), 8.90 d (1H, $^3J_{HH}$ = 1.7 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: 49.42 d (HCF_2, $^2J_{HF}$ = 54.7 Hz), 46.25 d.d (1F, 6-F, $^3J_{FH}$ = 10.00, $^4J_{FH}$ = 7.6 Hz). Found, %: C 63.55; H 3.24; F 16.76; N 16.44. $C_{18}H_{11}F_3N_4$. Calculated, %: C 63.53; H 3.26; F 16.75; N 16.46.

6-Fluoro-7-[3-phenyl-5-(trifluoromethyl)-1*H*-pyrazol-1-yl]quinoxaline (Vi) and 6-fluoro-7-[5-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]-quinoxaline (IVf). *b*. From 0.93 g (4.2 mmol) of diketonate **Ib** and 0.74 g (4.2 mmol) of hydrazine **IIc** we obtained a mixture of compounds **Vi** and **IVf** at a ratio of 1:1. Yield 0.9 g (60%), white powder. The ^{1}H and ^{19}F NMR spectra each contained two sets of signals. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: **IVf**: 6.86 s (1H, CH), 7.24–7.37 m (5H, Ph), 7.78 d (1H, $^3J_{HF}$ = 9.9 Hz), 8.34 d (1H, $^4J_{HF}$ = 7.8 Hz), 8.89 d (1H, J_{HH} = 2.3 Hz), 8.90 d (1H, J_{HH} = 2.3 Hz); **Vi**: 7.21 s (1H, CH), 7.38–7.47 m (3H) and 7.86–7.88 m (2H) (Ph), 7.97 d (1H, $^3J_{HF}$ = 9.8 Hz), 8.36 d (1H, $^4J_{HF}$ = 7.9 Hz), 8.94 d (1H, $^3J_{HH}$ = 1.68 Hz), 8.95 d (1H, $^3J_{HH}$ = 1.68 Hz). ^{19}F NMR spectrum ($CDCl_3$), δ_F, ppm: **IVf**: 99.32 s (3F, CF_3), 46.13 d.d (1F, 6-F, $^3J_{FH}$ = 9.9, $^4J_{FH}$ = 7.8 Hz); **Vi**: 102.75 d (3F, CF_3, J_{FF} = 4.88 Hz), 44.82 m (1F, 6-F). Found, %: C 60.35; H 2.83; F 21.29; N 15.62. $C_{18}H_{10}F_4N_4$. Calculated, %: C 60.34; H 2.81; F 21.21; N 15.64.

2-[5-(Difluoromethyl)-3-phenyl-1*H*-pyrazol-1-yl]-1,3-benzothiazole (Vk) and 2-[3-(difluoromethyl)-5-phenyl-1*H*-pyrazol-1-yl]-1,3-benzothiazole (IVg). *b*. From 0.6 g (2.9 mmol) of diketonate **Ia** and 0.49 g (2.9 mmol) of hydrazine **IId** we obtained a mixture of compounds **Vk** and **IVg** at a ratio of 1:3. Yield 0.4 g (43%). The ^{1}H and ^{19}F NMR spectra each contained two sets of signals. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: **IVg**: 6.80 t (1H, HCF_2, $^2J_{HF}$ = 54.6 Hz), 6.73 s (1H, CH), 7.38–7.54 m and 7.74–7.80 m (9H, H_{arom}); **Vk**: 7.17 s (1H, CH), 7.38–7.54 m and 7.74–7.80 m (10H, HCF_2, H_{arom}). ^{19}F NMR spec-

trum ($CDCl_3$), δ_F, ppm: **IVg**: 48.74 d (HCF_2, $^2J_{HF}$ = 54.6 Hz); **Vk**: 47.07 d (HCF_2, $^2J_{HF}$ = 53.8 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): **IVg**): 327 (68.5) $[M]^+$, 326 (83.6), 276 (23.4), 250 (79.6), 77 (72.6), 51 (100); **Vk**: 327 (80.2) $[M]^+$, 326 (15.1), 250 (14.4), 224 (99.8), 193 (12.7), 134 (21.5), 77 (86.2), 51 (100). Found, %: C 62.55; H 3.32; F 11.56; N 12.90; S 9.82. $C_{17}H_{11}F_2N_3S$. Calculated, %: C 62.37; H 3.39; F 11.60; N 12.84; S 9.79.

1-(1,3-Benzothiazol-2-yl)-3-phenyl-5-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol (IIId). *b*. From 0.98 g (4.8 mmol) of diketonate **Ib** and 0.79 g (4.8 mmol) of hydrazine **IId** we obtained 1.2 g (69%) of compound **IIId**. White powder, mp 116–117°C. IR spectrum, ν, cm^{-1}: 3442, 3059 br (OH), 1596 s, 1541 m (C=N, C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.69 d and 3.81 d (1H each, 4-H, J_{AB} = 18.4 Hz), 7.22–7.45 m (5H, H_{arom}), 7.67–7.45 m (4H, H_{arom}), 8.00 br.s (1H, OH). ^{19}F NMR spectrum ($CDCl_3$): δ_F 80.37 ppm, s (CF_3). Found, %: C 56.25; H 3.36; F 15.65; N 11.62; S 8.56. $C_{17}H_{12}F_3N_3OS$. Calculated, %: C 56.19; H 3.33; F 15.69; N 11.56; S 8.82.

2-[3-(Trifluoromethyl)-4,5,6,7-tetrahydro-2*H*-indazol-2-yl]-1,3-benzothiazole (Vj). *b*. From 0.88 g (4.4 mmol) of diketonate **Ig** and 0.73 g (4.4 mmol) of hydrazine **IId** we obtained 0.7 g (49%) of compound **Vj**. White powder, mp 132.5–133.5°C. IR spectrum, ν, cm^{-1}: 1596 s, 1520 m (C=N, C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.78–1.89 m (4H, CH_2), 2.77–2.81 m (4H, CH_2); 7.36–7.46 m (1H), 7.38–7.47 m (1H), 7.81–7.83 m (1H), and 7.93–7.95 m (1H) (H_{arom}). ^{19}F NMR spectrum ($CDCl_3$): δ_F: 104.53 ppm, s (CF_3). Found, %: C 55.65; H 3.69; F 17.59; N 13.02, S 9.54. $C_{15}H_{12}F_3N_3S$. Calculated, %: C 55.72; H 3.74; F 17.63; N 12.99; S 9.92.

***N*-Acetyl-*N*-[4-methyl-6-(3-phenyl-5-trifluoromethyl-1*H*-pyrazol-1-yl)pyrimidin-2-yl]acetamide (VI).** A solution of 0.8 g (2.37 mmol) of dihydropyrazole **IIIb** in 40 mL of acetic anhydride was heated for 5 h under reflux. Excess acetic anhydride was distilled off, the residue was treated with 10 mL of water, and the precipitate was filtered off and recrystallized from ethanol. Yield 0.95 g (98%), mp 163°C. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.26 s (6H, MeCO), 2.68 s (3H, Me), 7.49–7.57 m (3H, Ph), 7.96 s (1H, CH), 8.07–8.09 m (2H, Ph), 8.11 s (1H, CH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 23.81 s, 25.51 s, 25.76 s, 109.39 s, 112.03 q ($^3J_{CF}$ = 3.3 Hz), 119.39 q (CF_3, $^1J_{CF}$ = 268.7 Hz), 126.13 s, 128.95 s, 128.98 s, 129.79 s, 130.02 s, 133.10 q ($^2J_{CF}$ = 41.1 Hz), 153.03 s, 157.24 s, 158.14 s, 171.60 s, 173.00 s. ^{19}F NMR spectrum (DMSO-d_6): δ_F 105.62 ppm, s (CF_3). Found, %: C 56.50; H 3.88; F 14.16; N 17.46. $C_{19}H_{16}F_3N_5O_2$. Calculated, %: C 56.58; H 3.99; F 14.13; N 17.36.

4-Methyl-6-[3-phenyl-5-(trifluoromethyl)-1*H*-pyrazol-1-yl]pyrimidin-2-amine (Vb). A solution of 0.36 g (1.1 mmol) of compound **IIIb** in 10 mL of acetic anhydride was heated for 5 h under reflux. Acetic anhydride was distilled off, the residue was poured into water, and the precipitate was filtered off. The product was heated in 2 N aqueous NaOH for 20 min under reflux, and the precipitate was filtered off and recrystallized from chloroform–hexane (1:10). Yield 0.33 g (97%), white powder, mp 187–188°C. IR spectrum, ν, cm^{-1}: 3562, 3238 (NH), 1638 s, 1567 m (C=N, C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.45 s (3H, Me), 5.05 br.s (2H, NH_2), 7.19 s (1H, CH), 7.21 s (1H, CH), 7.41–7.49 m (3H) and 7.87–7.90 m (2H) (Ph). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 23.81 s, 98.72 s, 110.12 q ($^3J_{CF}$ = 3.3 Hz), 119.62 q (CF_3, $^1J_{CF}$ = 268.4 Hz), 125.88 s, 126.11 s, 128.89 s, 129.27 s, 130.59 s, 132.63 q ($^2J_{CF}$ = 40.7 Hz), 151.64 s, 157.69 s, 162.61 s, 170.36 s. ^{19}F NMR spectrum ($CDCl_3$): δ_F 104.11 ppm, s (CF_3). Found, %: C 56.43; H 3.82; F 17.89; N 21.90. $C_{15}H_{12}F_3N_5$. Calculated, %: C 56.42; H 3.79; F 17.85; N 21.93.

Likewise, from 0.5 g (0.0015 mol) of **IIIa** we obtained 0.4 g (85%) of compound **Va**. White powder, mp 184–185°C. The IR and ^1H and ^{19}F NMR spectra of the product were consistent with those of a sample prepared by reaction of lithium diketonate **Ia** with hydrazine **IIa**.

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