2-Polyfluoroalkylchromones
11.* Synthesis and structures of 5-hydroxy-3-(2-hydroxyaryl)-5-polyfluoroalkyl-Δ^2-pyrazolines and 3(5)-(2-hydroxyaryl)-5(3)-polyfluoroalkylpyrazoles

V. Ya. Sosnovskikh, M. A. Barabanov, and A. Yu. Sizov*

A. M. Gorky Urals State University,
51 prosp. Lenina, 620083 Ekaterinburg, Russian Federation.
Fax: +7 (343 2) 61 5978. E-mail: Vyacheslav.Sosnovskikh@usu.ru

The reaction of 2-hydroxy-2-polyfluoroalkylchroman-4-ones with hydrazine affords 5-hydroxy-3-(2-hydroxyaryl)-5-polyfluoroalkyl-Δ^2-pyrazolines, whereas 2-polyfluoroalkylchromones under similar conditions produce 3(5)-(2-hydroxyaryl)-5(3)-polyfluoroalkylpyrazoles. 5-(2-Hydroxyaryl)-1-methyl-3-polyfluoroalkylpyrazoles were synthesized in the reaction with methylhydrazine, and the reaction with phenylhydrazine afforded regioisomeric 3(5)-(2-hydroxyphenyl)-1-phenyl-5(3)-polyfluoroalkylpyrazoles.

Key words: fluorine-containing chromanones and chromones, hydrazine, methyl- and phenylhydrazines, pyrazolines, pyrazoles, isoxazoles, ^{1}H and ^{13}C NMR spectroscopy, conformations, regioisomers, tautomers.

Pyrazoles, including fluorine-containing, are rated in the well-studied class of organic compounds, which found wide use in technology, medicine, and agriculture. For example, pyrazoles with 2-hydroxyaryl substituents in positions 1, 3, or 5 possess high stability toward UV light,[2,3] and 5-aryl-3-trifluoromethylpyrazoles are selective inhibitors of cyclooxigenase and used for treatment of rheumatoid arthritis and osteoarthritis.[4,5] Many fluorine-containing pyrazoles manifest herbicidal, fungicidal, analgesic, and antiphlogistic properties (see Refs. 6 and 7 and literature cited therein). However, data on synthesis of pyrazoles containing simultaneously 2-hydroxyaryl and polyfluoroalkyl substituents are lacking.

To continue our works[8—11] on studying the reaction of 2-polyfluoroalkylchromones with N-nucleophiles, we studied the reactions of these compounds and their precursors, *viz.*, 2-hydroxy-2-polyfluoroalkylchroman-4-ones, with hydrazine and methyl- and phenylhydrazines and obtained a series of previously undescribed pyrazolines and pyrazoles with 2-hydroxyaryl and polyfluoroalkyl substituents in positions 3 and 5. The structures of the synthesized compounds, including the questions about regioisomerism, conformation, and tautomerism, were determined from the ^{1}H and ^{13}C NMR spectra, taking into account published data on related molecules.[1,2]

* For Part 10, see Ref. 1.

Results and Discussion

The reactions of nonsymmetrical aliphatic and aromatic β-diketones with hydrazines are well known to produce a mixture of regioisomeric pyrazoles, depending on the site of the initial nucleophilic attack.[12] The replacement of the alkyl or aryl group at one of the carbonyl carbon atoms by the R^F group substantially increases nonequivalency of the electrophilic centers to provide a high regioselectivity of the interaction of nonsymmetrical fluorine-containing β-diketones with various N-nucleophiles. For example, these compounds react with hydroxylamine almost only at the carbonyl group remote from the R^F group to yield 5-hydroxy-5-polyfluoroalkyl-Δ^2-isoxazolines.[13,14] Monosubstituted hydrazines react with RCOCHR´COR^F more ambiguously, although they exemplify regiospecific reactions under acid catalysis conditions.[5,15,16] As a whole, it was found[7] that, according to the HSAB principle, the terminal nitrogen atom of methylhydrazine attacks predominantly the COR^F group, and that of (het)arylhydrazines attacks the COR group. This provides the regioselective preparation of 3- and 5-R^F-pyrazoles, respectively.[15,17,18] Under mild conditions, the reaction with hydrazine[19,20] and some monosubstituted hydrazines[17—19] can be ceased at the stage of formation of intermediate 5-hydroxy-5-polyfluoroalkyl-Δ^2-pyrazolines, which is explained by the electron-acceptor influence of the R^F group that stabilizes the

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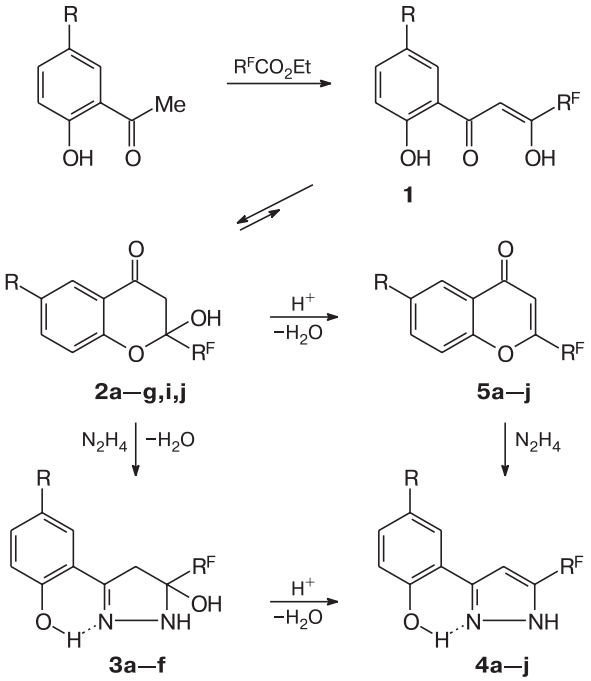
semiaminal fragment and hinders dehydration. Pyrazolines are usually aromatized to pyrazoles in an acidic medium, and the reaction conditions depend strongly on the nature of substituents in positions 1, 3, and 5 of the pyrazoline system.[19]

Condensation of 2-hydroxyacetophenones with R^FCO_2Et affords fluorine-containing β-diketones **1**, which exist as cyclic chromanone **2** due to the *ortho*-hydroxyl group.[21] Therefore, it was of interest to elucidate whether chromanones **2** in reactions with hydrazines behave similarly to the previously described linear β-diketones with the general formula $ArCOCH_2COR^F$. In this work we found that the reaction of 2-hydroxy-2-polyfluoroalkylchroman-4-ones **2a—f** with hydrazine hydrate under mild conditions (~20 °C, ethanol, 15 min) occurs with the chromanone system opening and formation of 5-hydroxy-3-(2-hydroxyaryl)-5-polyfluoroalkyl-Δ^2-pyrazolines (**3a—f**) (Scheme 1). The increase in the temperature and reaction duration is undesirable because results, in some cases, in the partial or complete dehydration of pyrazolines **3** to pyrazoles **4**. The same occurs when compounds **3** are kept for more than 2 months. The stability of 5-R^F-pyrazolines **3** decreases in the series $R^F = CF_3$, $H(CF_2)_2$, HCF_2 and, hence, pyrazolines with the HCF_2 group cannot be isolated in the analytically pure form because of their easy dehydration. Of trifluoromethylated pyrazolines **3a—c**, compound **3c** with the NO_2 group in position 5 of the aromatic ring is the most stable. This compound is not dehydrated even when recrystallized from a toluene—butanol mixture. Pyrazoline **3f** with the 2-hydroxy-5-chlorophenyl substituent is the most stable among compounds **3d—f** with the $H(CF_2)_2$ group. These data agree with the results in Ref. 19 in which the electron-withdrawing groups were shown to additionally stabilize 5-R^F-pyrazolines and prevent their aromatization. Note that only pyrazoles have been synthesized previously[22] from nonfluorinated β-diketones with 2-hydroxyaryl substituents (some of them can also exist in the cyclic form[23,24]).

Scheme 1



	R	R^F		R	R^F
a	H	CF_3	**f**	Cl	$(CF_2)_2H$
b	Me	CF_3	**g**	MeO	$(CF_2)_2H$
c	NO_2	CF_3	**h***	NO_2	$(CF_2)_2H$
d	H	$(CF_2)_2H$	**i**	H	CF_2H
e	Me	$(CF_2)_2H$	**j**	Me	CF_2H

* Chromone **5h** was prepared by the nitration of 2-(1,1,2,2-tetrafluoroethyl)chromone.

The ^1H NMR spectra of compounds **3a—f** (in $CDCl_3$) are characterized by the AB system of methylene protons with J_{AB} = 17.8—18.2 Hz with a center at δ 3.35—3.51 and a downfield singlet of the phenolic OH group at 10.44—11.77 ppm, indicating its participation in intramolecular hydrogen bond (IMHB) formation with the iminic nitrogen atom of the pyrazoline cycle (Table 1). Since the molecule contains the asymmetric carbon atom, the signal from the proton of the $H(CF_2)_2$ group in pyrazolines **3d—f** is split into a triplet of doublets of doublets with $^3J_{H,F}$ = 6.8—7.1 and 4.6—4.7 Hz, whereas in related 5-hydroxy-5-(1,1,2,2-tetrafluoroethyl)-Δ^2-isoxazolines described previously[1] it usually appears as a triplet of triplets with $^3J_{H,F}$ = 5.6—5.7 Hz, despite the neighborhood with the chiral center. A comparison of the ^1H NMR spectra of pyrazolines **3a,b,d,e** and similarly substituted isoxazolines[1] shows that the replacement of the N(1) atom by the oxygen atom deshields signals from all protons by 0.04—0.34 ppm, including the methyl group of the benzene ring. At the same time, the singlet of the phenolic hydroxyl exhibits the upfield shift by ~1.4 ppm, probably pointing to the weakening of IMHB in isoxazolines compared to pyrazolines.

Unlike chromanones **2a—f**, whose reaction can be ceased at the stage of pyrazolines **3a—f**, chromones **5a—j** react with N_2H_4 in ethanol at ~20 °C during 1 day or on boiling for 5 min and afford pyrazoles **4a—j** in high yields. These compounds were also prepared from the corresponding pyrazolines on boiling in acetic acid in the presence of concentrated HCl for 5 min (see Scheme 1). Chromones and flavones react with hydrazine to form pyrazoles or azines, depending on the conditions.[25,26]

2-Hydroxy-5,7-dimethyl-2-(1,1,2,2-tetrafluoroethyl)chroman-4-one (**2k**) and related 5,7-dimethyl- and 5,7-dimethyl-6,8-dinitro-2-(1,1,2,2-tetrafluoroethyl)chromones (**5k,l**) described in the report[10] react

Table 1. ^{1}H and IR spectra of pyrazolines **3a—f,k** and **6a,b,d,m**

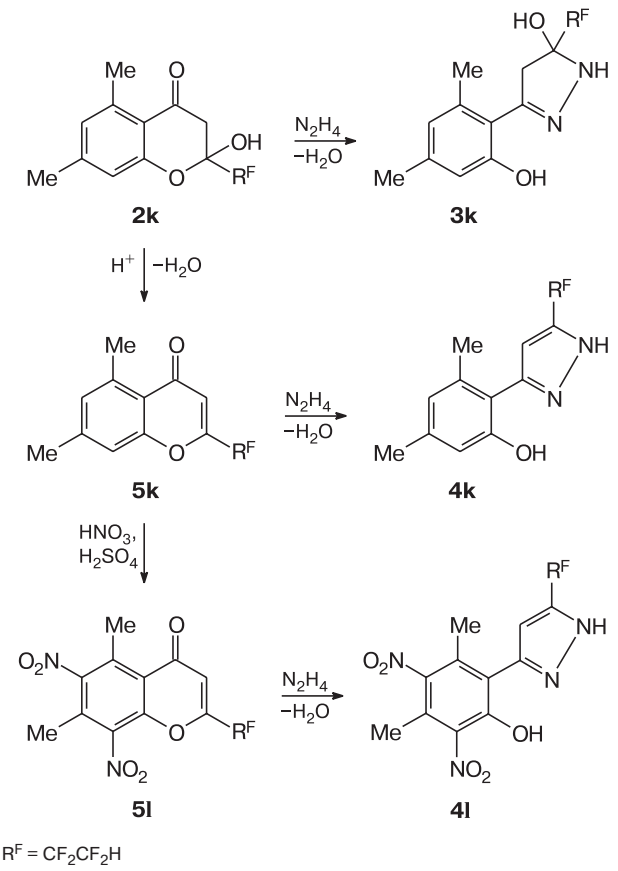
Compound	^{1}H NMR ($CDCl_3$, δ, J/Hz)								IR, ν/cm^{-1}
	C(4)H$_2$	H(3′)	H(4′)	H(5′)	H(6′)	OH	NH (s)	R^F	
3a	3.46[a] (J = 17.8, Δδ = 0.25)	7.01 (dd, J_o = 8.3, J_m = 1.0)	7.29 (ddd, J_o = 8.3, 7.4, J_m = 1.6)	6.90 (ddd,[b] J_o = 7.8, 7.4, J_m = 1.0)	7.11 (dd, J_o = 7.8, J_m = 1.6)	3.31 (s)[c] 10.49 (s)[d]	6.15	—	3330, 3240, 1625, 1605, 1575
3b	3.40[a] (J = 17.8, Δδ = 0.26)	6.88 (d, J_o = 8.3)	7.07 (dd, J_o = 8.3, J_m = 1.7)	2.25 (s, Me)	6.79 (br.s)[e]	4.05 (br.s)[c] 10.44 (s)[d]	6.11	—	3420, 3310, 1625, 1605
3c[f]	3.47[a] (J = 18.2, Δδ = 0.12)	7.07 (d, J_o = 9.1)	8.10 (dd, J_o = 9.1 J_m = 2.8)	—	8.25 (d, J_m = 2.8)	8.25 (s)[c] 11.69 (br.s)[d]	7.35	—	3330, 1625, 1595, 1565
3d	3.43[a] (J = 18.2, Δδ = 0.38)	6.98 (dd, J_o = 8.3, J_m = 1.0)	7.27 (ddd, J_o = 8.3, 7.4, J_m = 1.6)	6.87 (ddd,[b] J_o = 7.8, 7.4, J_m = 1.0)	7.06 (dd, J_o = 7.8, J_m = 1.6)	3.68 (br.s)[c] 10.67 (s)[d]	6.25	6.20 (tdd, ^2J = 53.0, ^3J = 6.9, ^3J = 4.7)	3360, 1630, 1605, 1570
3e	3.35[a] (J = 18.1, Δδ = 0.39)	6.83 (d, J_o = 8.3)	7.05 (dd, J_o = 8.3, J_m = 1.7)	2.23 (s, Me)	6.70 (d, J_m = 1.7)	4.44 (s)[c] 10.56 (s)[d]	6.18	6.21 (tdd, ^2J = 53.0, ^3J = 7.1, ^3J = 4.6)	3360, 1625, 1605, 1570
3f	3.43[a] (J = 18.2, Δδ = 0.40)	6.93 (d, J_o = 8.8)	7.23 (dd, J_o = 8.8, J_m = 2.5)	—	7.06 (d, J_m = 2.5)	3.43 (s)[c] 10.49 (s)[d]	6.34	6.20 (tdd, ^2J = 53.0, ^3J = 6.8, ^3J = 4.6)	3435, 3120, 1620, 1605, 1565
3k	3.51[a] (J = 18.1, Δδ = 0.40)	6.63 (s)[g]	2.26 (s)[g]	6.47 (s)[g]	2.28 (s)[g]	4.55 (s)[c] 11.77 (s)[d]	6.07	6.21 (tdd, ^2J = 53.0, ^3J = 6.7, ^3J = 5.0)	3360, 1635, 1585
6a[h]	3.85[a] (J = 19.1, Δδ = 0.27)	6.96 (d,[i] J_o = 8.2)	7.30 (ddd, J_o = 8.2, 7.3, J_m = 1.6)	6.94 (t,[i] J_o = 7.5)	7.57 (dd, J_o = 7.8, J_m = 1.6)	8.23 (s)[c] 10.29 (s)[d]	N—Ph: 7.07 (t,[i] *p*-H, J_o = 7.2); 7.30—7.41 (m, 4 H)		3390, 1615, 1590, 1570
6b[h]	3.83[a] (J = 19.1, Δδ = 0.27)	6.86 (d, J_o = 8.3)	7.11 (dd, J_o = 8.3, J_m = 1.6)	2.26 (s, Me)	[j]	8.24 (s)[c] 10.08 (s)[d]	N—Ph: 7.06 (tt, *p*-H, J_o = 7.2, J_m = 1.2); 7.31—7.41 (m, 5 H)		3320, 1620, 1590
6d	3.67[a] (J = 18.1, Δδ = 0.26)	7.01 (dd, J_o = 8.3, J_m = 1.1)	7.30 (ddd, J_o = 8.3, 7.3, J_m = 1.6)	6.92 (ddd, J_o = 7.8, 7.3, J_m = 1.1)	7.18 (dd, J_o = 7.8, J_m = 1.6)	3.26 (s)[c] 10.45 (s)[d]	N—Ph: 7.30 (m, *p*-H); 7.38—7.40 (m, 4 H); CF_2CF_2H: 6.15 (tdd, 1 H, $^2J_{H,F}$ = 52.9, $^3J_{H,F}$ = 6.7, 4.6)		3390, 1620, 1600, 1580
6m[h]	3.85[a] (J = 19.3, Δδ = 0.27)	6.98 (d, J_o = 8.8)	7.31 (dd, J_o = 8.8, J_m = 2.7)	—	7.65 (d, J_m = 2.7)	8.26 (s)[c] 10.44 (s)[d]	N—Ph: 7.06 (tt, *p*-H, J_o = 7.2, J_m = 1.1); 7.30—7.42 (m, 4 H)		3410, 1600, 1560

[a] Center of the AB system.
[b] The signal looks like a triplet of doublets with J_o = 7.6 Hz.
[c] Semiaminal OH.
[d] Phenolic OH.
[e] The signal is broadened due to the *ortho*-benzyl interaction.
[f] The spectrum was recorded in DMSO-d$_6$/CCl_4.
[g] The signals can be re-assigned.
[h] The spectrum was recorded in DMSO-d$_6$.
[i] *meta*-Constants do not appear.
[j] The signal is disguised by protons of the Ph group.

with hydrazine hydrate similarly and yield compounds **3k** and **4k,l**, respectively, whose aryl substituent contains the 6′-Me group. Unfavorable interactions between this group and the H(4) atom of the pyrazole system hinder the formation of the planar conformer and weaken the IMHB, which, in turn, reflects in the spectral character-

istics of these molecules compared to their sterically nonhindered analogs **4a—j** (Scheme 2).

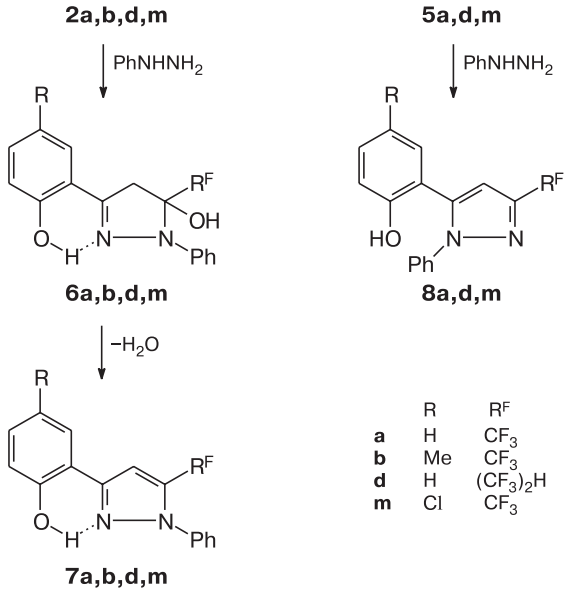
Scheme 2



$R^F = CF_2CF_2H$

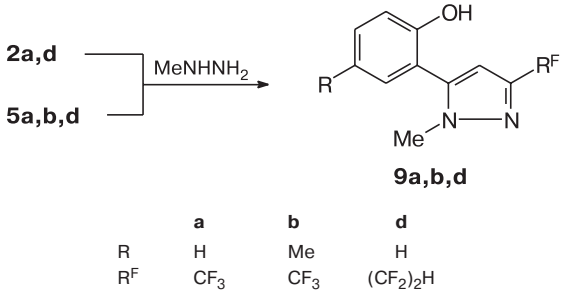
In the previous report[1] we described the highly regioselective reaction of hydroxylamine with chromanones **2** and chromones **5**, which affords 5-R^F-isoxazoles from chromanones **2** and 3-R^F-isoxazoles from chromones **5**. These data show that the NH_2 group of hydroxylamine reacts selectively with the C(4) atom in chromanones **2** and C(2) in chromones **5** and encourage that the reactions of methyl- and phenylhydrazines with compounds **2** and **5** are also highly regioselective. In fact, we succeeded in the preparation of regioisomeric 5- (**7**) and 3-R^F-pyrazoles (**8**) from phenylhydrazine and chromanones **2a,b,d,m** and chromones **5a,d,m**. The reactions with compounds **2a,b,d,m** proceeded through the formation of the corresponding pyrazolines **6**, which were further dehydrated to 1-Ph-5-R^F-pyrazoles **7a,b,d,m** by boiling in AcOH with a catalytic amount of HCl (Scheme 3). 3-R^F-1-Phenylpyrazoles **8a,d,m** were synthesized by boiling of ethanolic solutions of chromones **5a,d,m** with $PhNHNH_2$. However, the yields of these compounds were at most 20%.

Scheme 3



Unlike phenylhydrazine, methylhydrazine reacts with both **2a,d** and **5a,d** to form the same 3-R^F-1-methylpyrazoles **9a,d** (Scheme 4). The previously[15] studied reaction of methylhydrazine with $PhCOCH_2COR^F$ ($R^F = C_3F_7$, C_5F_{11}, C_7F_{15}) in the presence of HCl afforded 3-R^F-pyrazoles also with high regioselectivity. Therefore, we may conclude that the primary amino group of methylhydrazine preferentially attacks the carbon atom bound to the R^F group regardless of the molecule (diketone or chromone) containing this atom. The reaction of $MeNHNH_2$ with chromone **5b** yielded 3-CF_3-1-methylpyrazole **9b** in 27% yield. According to its ^1H NMR spectrum, compound **9b** contained ~5% regioisomeric 5-CF_3-pyrazole (a quartet of the N—Me group at 4.04 ppm with $^5J_{H,F} = 0.7$ Hz and a singlet of the phenolic OH group at 10.0 ppm).

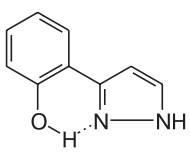
Scheme 4



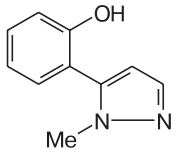
Chromone **5d** with the $H(CF_2)_2$ group is much less reactive than its trifluoromethylated analog **5a**, which is likely related to the steric factor.[7,27] For example,

pyrazoles **8d** and **9d** were prepared from chromone **5d** and methyl(phenyl)hydrazines only in low yields (10—15%) after several hours of boiling with two—three drops of HCl in ethanol, while compound **5a** reacts with $MeNHNH_2$ without acid catalysis for 1 h. Therefore, to obtain pyrazole **9d**, it is better to use chromanone **2d** as the initial compound because its reaction with methylhydrazine occurs in 51% yield on boiling for 10 min.

Since 3-(2-hydroxyphenyl)pyrazole (**10**) and its N- and O-methyl derivatives are photostable compounds and of interest as photostabilizers of polymeric materials, their structure was studied in detail by UV and NMR spectroscopies and X-ray diffraction analysis.[2] It has been shown that pyrazole **10** is a planar molecule, which exists as 1*H*-3-Ar-tautomer in the crystalline state and in solution due to the stabilization *via* IMHB between the phenolic hydroxyl group and pyridinic (iminic) nitrogen atom of the heterocycle. Unlike compound **10**, in crystalline 1-methyl-5-(2-hydroxyphenyl)pyrazole (**11**) the torsion angle between two rings is equal to 61.7°, and the nonplanar character of this molecule in solution was proved by the UV spectra.



10



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In addition, criteria that allow conclusions about the conformation of pyrazoles with the 2-hydroxy(methoxy)phenyl substituent from the ^1H and ^{13}C NMR spectra are available.[2] The ^1H NMR spectra of planar pyrazoles in a $CDCl_3$ solution are characterized by the chemical shifts of the aromatic H(6′) proton at ~7.6 ppm and of the pyrazolic H(4) proton at ~6.7 ppm. Meanwhile, for nonplanar pyrazoles $\delta_{H(6')} \approx 7.2$ and $\delta_{H(4)} \approx 6.3$, *i.e.*, on going from the planar to nonplanar molecules, the H(6′) and H(4) atoms are shielded by ~0.4 ppm. In the ^{13}C NMR spectra the difference between the chemical shifts of the C(6′) and C(5′) atoms is $\Delta\delta_C = \delta_{C(6')} - \delta_{C(5')} \approx 7.0$ for planar and $\Delta\delta_C \approx 10.4$ for nonplanar pyrazoles.

The data of the ^1H NMR spectra of fluorine-containing pyrazoles **4**, **7—9** are presented in Table 2 along with the spectra of nonfluorinated analogs **10** and **11** given for comparison.[2] The absence of the *J* constant between the *meta*-situated H(3′) and H(5′) aromatic protons in compounds **4a,d,i** and its appearance in the spectra of N-substituted pyrazoles **7**, **8**, and **9a,d** and upon addition of DMSO-d_6 to a solution of compound **4a** in $CDCl_3$ are, most likely, a consequence of the tautomeric equilibrium in solutions of N-nonsubstituted pyrazoles **4**. The signals were assigned from their multiplicity. A comparison of the ^1H NMR spectra of pyrazoles **10** and **4a,d,i**, as well as **11** and **9a,d**, shows that the introduction of the polyfluoroalkyl group into the pyrazole ring has no noticeable effect on the chemical shifts of

Table 2. ^1H NMR and IR spectra of pyrazoles **4a—l**, **7a,b,d,m**, **8a,d,m**, **9a,b,d**, **10**, and **11**

Compound	^1H NMR ($CDCl_3$, δ, *J*/Hz)								IR, ν/cm^{-1}
	H(4)	H(3′)	H(4′)	H(5′)	H(6′)	OH	NH	R^F	
4a[a,b]	6.94 (s)	6.98 (d, J_o = 8.1)	7.26 (t)[c]	7.02 (t, J_o = 7.6)	7.61 (d, J_o = 7.7, J_m = 1.4)	7.9 (br.s)	11.3 (br.s)	–62.7 (s)[d]	3410, 3150, 1625, 1605, 1570
4a[e]	6.89 (s)	7.02 (dd, J_o = 8.1, J_m = 1.0)	7.19 (ddd, J_o = 8.1, 7.3, J_m = 1.6)	6.92 (ddd, J_o = 7.8, 7.3, J_m = 1.0)	7.59 (dd, J_o = 7.8, J_m = 1.6)	11.3 (br.s)		—	—
4b[a]	6.93 (s)	6.85 (d, J_o = 8.3)	7.07 (dd, J_o = 8.3, J_m = 1.6)	2.34 (s, Me)	7.41 (br.s)[f]	[g]	11.1 (br.s)	—	3420, 3150, 1620, 1570
4c[a]	7.17 (s)	7.12 (d, J_o = 9.1)	8.18 (dd, J_o = 9.1, J_m = 2.7)	—	8.52 (d, J_m = 2.7)	[g]	10.7 (br.s)	—	3390, 1630, 1605, 1535
4d[b]	6.96 (s)	6.99 (d, J_o = 8.2)	7.26 (ddd, J_o = 8.2, 7.4, J_m = 1.6)	6.99 (t, $J_o \approx 7.5$)	7.61 (dd, J_o = 8.0, J_m = 1.6)	9.2 (br.s)	10.9 (br.s)	6.09 (tt, ^2J = 53.7, ^3J = 2.85)	3405, 1620, 1605, 1570
4d[h]	6.91 (s)	6.95 (dd, J_o = 8.1, J_m = 1.0)	7.22 (ddd, J_o = 8.1, 7.4, J_m = 1.6)	6.98 (ddd, J_o = 7.8, 7.4, J_m = 1.0)	7.61 (dd, J_o = 7.8, J_m = 1.6)	—	—	6.07 (tt, ^2J = 53.6, ^3J = 3.20)	—
4d[i]	7.04 (s)	7.01 (d, J_o = 8.2)	7.36 (ddd, J_o = 8.2, 7.4, J_m = 1.5)	7.07 (ddd, J_o = 7.8, 7.4, J_m = 0.9)	7.67 (dd, J_o = 7.8, J_m = 1.5)	—	—	6.07 (tt, ^2J = 53.6, ^3J = 2.00)	—

(*to be continued*)

Table 2 (*continued*)

Compound	^{1}H NMR ($CDCl_3$, δ, *J*/Hz)								IR, ν/cm^{-1}
	H(4)	H(3′)	H(4′)	H(5′)	H(6′)	OH	NH	R^F	
4d[j]	7.03 (s)	7.00 (dd, J_o = 8.2, J_m = 1.1)	7.23 (ddd, J_o = 8.2, 7.3, J_m = 1.6)	6.91 (ddd, J_o = 7.8, 7.3, J_m = 1.1)	7.67 (dd, J_o = 7.8, J_m = 1.6)	10.4 (br.s)	13.4 (br.s)	6.82 (tt, ^2J = 52.2, ^3J = 5.05)	—
4e	6.95 (s)	6.87 (d, J_o = 8.3)	7.06 (dd, J_o = 8.3, J_m = 1.6)	2.33 (s, Me)	7.42 (br.s)[f]	8.1 (br.s)	11.2 (br.s)	6.10 (tt, ^2J = 53.7, ^3J = 2.95)	3410, 1620, 1570
4f	6.98 (s)	6.96 (d, J_o = 8.7)	7.21 (dd, J_o = 8.7, J_m = 2.5)	—	7.56 (d, J_m = 2.5)	9.8 (br.s)	10.8 (br.s)	6.08 (tt, ^2J = 53.7, ^3J = 2.10)	3450, 3360, 1630, 1600
4g	6.92 (s)	6.91 (d, J_o = 8.8)	6.83 (dd, J_o = 8.8, J_m = 2.9)	3.82 (s, MeO)	7.12 (d, J_m = 2.9)	8.0 (br.s)	11.5 (br.s)	6.10 (tt, ^2J = 53.6, ^3J = 2.90)	3390, 3120, 1620, 1560
4h[a]	7.16 (s)	7.12 (d, J_o = 9.1)	8.18 (dd, J_o = 9.1, J_m = 2.7)	—	8.54 (d, J_m = 2.7)	10.4 (br.s)	11.0 (br.s)	6.09 (tt, ^2J = 53.8, ^3J = 1.55)	3200, 1635, 1605, 1575, 1530
4h[j]	7.21 (s)	7.17 (d, J_o = 9.1)	8.16 (dd, J_o = 9.1, J_m = 2.8)	—	8.66 (d, J_m = 2.8)	12.1 (br.s)	13.9 (br.s)	6.85 (tt, ^2J = 52.2, ^3J = 4.90)	—
4i[b]	6.88 (s)	7.01 (d, J_o = 8.1)	7.26 (ddd, J_o = 8.1, 7.4, J_m = 1.4)	6.98 (t, $J_o \approx$ 7.5)	7.59 (dd, J_o = 7.7, J_m = 1.4)	9.6 (br.s)		6.85 (t, ^2J = 55.0)	3420, 1625, 1610, 1570
4j	6.87 (s)	6.88 (d, J_o = 8.3)	7.05 (dd, J_o = 8.3, J_m = 1.6)	2.33 (s, Me)	7.39 (br.s)[f]	8.8 (br.s)	10.9 (br.s)	6.83 (t, ^2J = 55.1)	3445, 1620, 1560
4k	6.75 (s)	6.72 (s)[k]	2.30 (s, Me)[k]	6.64 (s)[k]	2.35 (Me)[k]	[g]		6.14 (tt, ^2J = 53.6, ^3J = 3.55)	3440, 1615, 1600, 1565
4k[j]	6.54 (s)	6.61 (s)[k]	2.08 (s, Me)[k]	6.59 (s)[k]	2.22 (Me)[k]	9.6 (br.s)	13.3 (br.s)	6.81 (tt, ^2J = 52.2, ^3J = 5.10)	—
4l	6.82 (s)	—	2.38 (s, Me)[k]	—	2.44 (Me)[k]	10.8 (br.s)		6.14 (tt, ^2J = 53.6, ^3J = 2.75)	3290, 3210, 1630, 1540
7a[j]	7.59 (s)	7.01 (dd, J_o = 8.2, J_m = 1.0)	7.25 (ddd, J_o = 8.2, 7.3, J_m = 1.7)	6.91 (ddd, J_o = 7.8, 7.3, J_m = 1.0)	7.88 (dd, J_o = 7.8, J_m = 1.7)	10.12 (s)	7.61 (s, NPh)	—	3150, 1620, 1600
7b	7.18 (s)	6.94 (d, J_o = 8.3)	7.08 (dd, J_o = 8.3, J_m = 2.1)	2.34 (s, Me)	7.39 (d,[f] J_m = 1.6)	9.97 (s)	7.52 (s, NPh)	—	3160, 1635, 1600, 1560
7d	7.15 (s)	7.04 (dd, J_o = 8.3, J_m = 1.0)	7.27 (ddd, J_o = 8.3, 7.4, J_m = 1.6)	6.96 (ddd, J_o = 7.8, 7.4, J_m = 1.0)	7.61 (dd, J_o = 7.8, J_m = 1.6)	10.20 (s)	7.51 (s, NPh)	5.84 (tt, ^2J = 53.4, ^3J = 3.15)	3150, 1630, 1590
7d[j]	7.51 (s)	6.99 (d, J_o = 8.2)	7.23 (ddd, J_o = 8.2, 7.3, J_m = 1.6)	6.89 (ddd, J_o = 7.8, 7.3, J_m = 0.9)	7.87 (dd, J_o = 7.8, J_m = 1.6)	10.06 (s)	7.58 (s, NPh)	6.93 (tt, ^2J = 51.9, ^3J = 4.40)	—
7m	7.17 (s)	6.98 (d, J_o = 8.8)	7.22 (dd, J_o = 8.8, J_m = 2.5)	—	7.56 (d, J_m = 2.5)	10.16 (s)	7.53 (s, NPh)	—	1620, 1605, 1590
8a	6.79 (s)	6.85 (dd, J_o = 8.2 J_m = 1.0)	7.27 (ddd, J_o = 8.2, 7.5, J_m = 1.7)	6.88 (ddd,[l] J_o = 7.7, 7.5, J_m = 1.0)	7.04 (dd, J_o = 7.7, J_m = 1.7)	5.14 (s)	7.31 (s, NPh)	—	3240, 1620, 1595
8d	6.81 (s)	6.86 (dd, J_o = 8.2 J_m = 0.9)	7.27 (ddd, J_o = 8.2, 7.4, J_m = 1.7)	6.88 (ddd,[l] J_o = 7.8, 7.4, J_m = 0.9)	7.03 (dd, J_o = 7.8, J_m = 1.7)	5.01 (s)	7.30 (s, NPh)	6.23 (tt, ^2J = 53.4, ^3J = 4.40)	3360, 1620, 1600

(*to be continued*)

Table 2 (*continued*)

Compound	^{1}H NMR ($CDCl_3$, δ, *J*/Hz)								IR, ν/cm^{-1}
	H(4)	H(3′)	H(4′)	H(5′)	H(6′)	OH	NH	R^F	
8d[j]	6.86 (s)	6.83 (d, J_o = 8.2)	7.23 (ddd, J_o = 8.2, 7.3, J_m = 1.7)	6.82 (ddd,[l] J_o = 7.6, 7.3, J_m = 0.9)	7.16 (dd, J_o = 7.6, J_m = 1.7)	9.74 (s)	7.28—7.40 (m, NPh)	6.89 (tt, ^2J = 52.1, ^3J = 5.00)	—
8m[j]	7.06 (s)	6.81 (d, J_o = 8.6)	7.29 (dd, J_o = 8.6, J_m = 2.7)	—	7.31 (d, J_m = 2.7)	10.10 (s)	7.32—7.42 (m, NPh)	—	3200,1605
9a	6.58 (s)	6.99 (dd, J_o = 8.2, J_m = 0.9)	7.37 (ddd, J_o = 8.2, 7.4, J_m = 1.7)	7.03 (ddd,[l] J_o = 7.6, 7.4, J_m = 0.9)	7.22 (dd, J_o = 7.6, J_m = 1.7)	5.70 (s)	3.82 (s, NMe)	—63.1 (s)[d]	3150, 1620, 1595, 1550
9b	6.56 (s)	6.88 (d, J_o = 8.3)	7.17 (dd, J_o = 8.3, J_m = 1.7)	2.32 (s, Me)	7.01 (d, J_m = 1.7)	5.32 (s)	3.82 (s, NMe)	—	3240, 1620, 1600
9d	6.60 (s)	6.99 (dd, J_o = 8.2, J_m = 0.9)	7.37 (ddd, J_o = 8.2, 7.4, J_m = 1.7)	7.03 (ddd,[l] J_o = 7.6, 7.4, J_m = 0.9)	7.22 (dd, J_o = 7.6, J_m = 1.7)	5.56 (s)	3.82 (s, NMe)	6.14 (tt, ^2J = 53.5, ^3J = 4.05)	3210, 1620, 1595, 1550
9d[h]	6.57 (s)	6.97 (dd, J_o = 8.2, J_m = 0.9)	7.35 (ddd, J_o = 8.2, 7.4, J_m = 1.7)	7.00 (ddd,[l] J_o = 7.6, 7.4, J_m = 0.9)	7.22 (dd, J_o = 7.6, J_m = 1.7)	—	3.82 (s, NMe)	6.14 (tt, ^2J = 53.5, ^3J = 4.10)	—
9d[i]	6.62 (s)	6.99 (dd, J_o = 8.2, J_m = 0.9)	7.40 (ddd, J_o = 8.2, 7.5, J_m = 1.7)	7.06 (ddd,[l] J_o = 7.7, 7.5, J_m = 0.9)	7.24 (dd, J_o = 7.7, J_m = 1.7)	—	3.86 (s, NMe)	6.07 (tt, ^2J = 53.6, ^3J = 3.05)	—
9d[j]	6.60 (s)	7.01 (dd, J_o = 8.2, J_m = 0.9)	7.33 (ddd, J_o = 8.2, 7.4, J_m = 1.7)	6.92 (ddd,[l] J_o = 7.6, 7.4, J_m = 0.9)	7.24 (dd, J_o = 7.6, J_m = 1.7)	10.09 (s)	3.74 (s, NMe)	6.80 (tt, ^2J = 52.2, ^3J = 5.00)	—
10[m]	6.74 (d, J = 2.6)	7.04 (dd, J_o = 8.2 J_m = 1.2)	7.24 (ddd, J_o = 8.2, 7.2, J_m = 1.7)	6.93 (ddd, J_o = 7.7, 7.2, J_m = 1.2)	7.61 (dd, J_o = 7.7, J_m = 1.7)	10.4 (br.s)		—	—
11[m]	6.35 (d, J =1.9)	7.02 (d, J_o = 8.1)	7.34 (ddd, J_o = 8.1, 7.4, J_m = 1.7)	—	7.20 (dd, J_o = 7.6, J_m = 1.7)	5.89 (s)	3.79 (s, NMe)	—	—

[a] Poorly soluble in $CDCl_3$.
[b] *meta*-Constants between the H(3) and H(5) protons do not appear.
[c] *ortho*-Constants cannot be measured because of the superposition of the signal from the solvent.
[d] ^{19}F NMR spectrum relative to $CFCl_3$.
[e] In $CDCl_3$+DMSO-d_6.
[f] The signal is broadened due to the *ortho*-benzyl interaction.
[g] The signal is not detected.
[h] In $CDCl_3$+CD_3CO_2D.
[i] In $CDCl_3$+CF_3CO_2H.
[j] In DMSO-d_6.
[k] The signals can be re-assigned.
[l] The signal looks like a triplet of doublets with J_o = 7.5 Hz.
[m] Published data.[2]

the aromatic protons, which change slightly when solvents are replaced and acids are added (**4d**, **9d**).

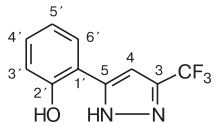
It is seen from Table 2 that for N-nonsubstituted pyrazoles **4a,d,i** $\delta_{H(6')}$ = 7.59—7.61 and $\delta_{H(4)}$ = 6.88—6.96, whereas for N-methylpyrazoles **9a,d** $\delta_{H(6')}$ = 7.22 and $\delta_{H(4)}$ = 6.58—6.60. Thus, taking into account the deshielding effect of the R^F group on the pyrazolic H(4) proton (0.14 ppm for CF_2H and 0.20—0.25 ppm for the CF_3 and CF_2CF_2H groups), the chemical shifts of the H(6′) and H(4) atoms in the fluorine-containing pyrazoles correlate well with the shifts indicated above for the planar and nonplanar pyrazoles. This allows us to ascribe the "planar" conformation to compounds **4a—j** and "nonplanar" conformation to compounds **9a,b,d** in the sense that the torsion angle between the 2-hydroxyaryl substituent and pyrazole ring in molecules **9** should be much greater than that in compound **4**. This is related to unfavorable interactions ap-

peared between the N—Me group of pyrazole and *o*-H atom or OH group of the aryl substituent. When $CDCl_3$ is replaced by DMSO-d_6, the chemical shift of the H(6′) atom remains unchanged ($\delta_{H(6')}$ = 7.59 for **4a** and $\delta_{H(6')}$ = 7.24 for **9d**) and, hence, the replacement of the solvent has no effect on the conformational composition. The appearance of the 6′-Me group in the 2-hydroxyaryl substituent of pyrazole **4k** results in deviation from the planar conformation, which is manifested as shielding of the H(4) proton (6.75 ppm) compared to compounds **4a,b,d—g** (6.92—6.98 ppm) and **4c,h** (7.16—7.17 ppm). Applying $\delta_{H(6')}$ as a criterion of planarity for regioisomeric *N*-phenylpyrazoles **7** and **8**, we can conclude that in compound **7** the pyrazole ring and 2-hydroxyphenyl group are planar and in compound **8** they are nonplanar. The singlets or narrow multiplets from the N—Ph group at 7.51—7.61 ppm for compound **7** and 7.28—7.42 ppm for **8** indicate that the phenyl group at the nitrogen atom is shifted from the plane of the pyrazole cycle in both regioisomers and is not involved in conjugation.[15]

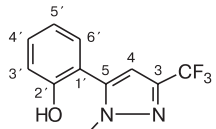
The data of the ^{13}C NMR spectra of pyrazoles **4a** and **9a** recorded in a DMSO-d_6 solution without proton decoupling are presented in Table 3. The signals were assigned from the comparison with published data for related molecules[2] taking into account the $^nJ_{C,H}$ constants (n = 1—4). It is seen from Table 3 that for **4a** $\Delta\delta_C = \delta_{C(6')} - \delta_{C(5')}$ = 6.44 in $CDCl_3$ and 8.31 in DMSO-d_6, whereas for **9a** $\Delta\delta_C$ = 12.08 in DMSO-d_6, which agrees well with the $\Delta\delta_C$ criterion for nonfluorinated planar and nonplanar pyrazoles.[2] If we accept that the spectral regularities found for pyrazoles with the 2-hydroxyphenyl substituent are valid for the isoxazole series, then both 3-(2-hydroxyphenyl)-5-R^F- and 5-(2-hydroxyphenyl)-3-R^F-isoxazoles should be considered as planar molecules with $\delta_{H(4)}$ = 7.00—7.13, $\delta_{H(6')}$ = 7.51, and $\Delta\delta_C$ = 7.8 for 5-R^F-isoxazoles and $\delta_{H(4)}$ = 6.96—7.01, $\delta_{H(6')}$ = 7.83—7.88, and $\Delta\delta_C$ = 6.4 for 3-R^F-isoxazoles ($CDCl_3$).[1]

Although the signals from mobile protons of the NH and OH groups in solutions of $CDCl_3$ and DMSO-d_6 appear as strongly broadened singlets due to the fast intermolecular exchange, their chemical shifts are very indicative and can be fruitful for establishment of the tautomeric and regioisomeric compositions of the pyrazoles under study (see Table 2). It is known from published data[28,29] that the proton of the NH group is strongly deshielded (12—14 ppm), and for pyrazoles with the 2-hydroxyaryl substituents it usually appears in a weaker field than the proton of the phenolic hydroxyl group.[2,3] A similar situation was observed in our case. In pyrazoles **4a—j** the proton of the NH group appears at 10.7—11.5 ppm in $CDCl_3$ and at 13.3—13.9 ppm in DMSO-d_6, and the proton of the OH group is observed

Table 3. ^{13}C NMR spectra of pyrazoles **4a** and **9a** (δ, J/Hz)



4a



9a

Compound	C(3)	C(4)	C(5)	CF_3	C(1′)	C(2′)	C(3′)	C(4′)	C(5′)	C(6′)
4a[a]	[b]	101.38 (d, ^1J = 179.3)	[b]	120.83 (q, ^1J_F = 267.8)	115.02 (t, $^3J \approx 7.0$)	153.50 (m)	116.95 (dd, ^1J = 158.1, ^3J = 7.8)	130.22 (dd, ^1J = 159.8, ^3J = 9.2)	121.11 (dd, ^1J = 162.4, ^3J = 7.9)	127.55 (dd, ^1J = 158.5, ^3J = 8.8)
4a[c]	141.14 (br.q, ^2J_F = 40.5)	102.46 (dq, ^1J = 181.3, ^3J_F = 1.6)	141.32 (br.s)	122.01 (q, ^1J_F = 268.0)	115.00 (t, ^3J = 6.5)	154.32 (tt, ^3J = 8.9, ^2J = ^4J = 1.6)	116.39 (dm, $J \approx 159.5$)	129.95 (dm, ^1J = 158.1)	119.43 (ddd, ^1J = 162.1, ^3J = 7.9, ^2J = 0.9)	127.74 (ddd, ^1J = 158.3, ^3J = 8.5, ^2J = 1.9)
9a[c,d]	139.32 (qd, ^2J_F = 37.2, ^2J = 4.5)	104.88 (dq, ^1J = 181.1, ^3J_F = 2.1)	142.49 (m)	121.65 (q, ^1J_F = 268.0)	115.81 (t, ^3J = 6.9)	155.10 (ddt, ^3J = 9.6, 8.2, ^2J = ^4J = 1.7)	115.99 (ddt, ^1J = 159.3, ^3J = 8.0, ^2J = ^4J = 1.3)	131.05 (ddd, ^1J = 159.4, ^3J = 8.8, ^2J = 1.6)	119.24 (dd, ^1J = 162.1, ^3J = 7.8)	131.32 (ddd, ^1J = 159.6, ^3J = 8.6, ^2J = 2.1)

[a] In $CDCl_3$.
[b] Measurements failed.
[c] In DMSO-d_6.
[d] N—Me, δ: 37.77 (q, ^1J = 141.2 Hz).

at 7.9—10.4 ppm in $CDCl_3$ and at 10.4—12.1 ppm in DMSO-d_6. For the previously[1] studied 5-R^F-isoxazoles, the phenolic proton is observed at 8.8—9.1 ppm in $CDCl_3$ and at 10.5—10.8 ppm in DMSO-d_6. Note that for pyrazoles **4a—j** the chemical shift of the OH group depends substantially on the nature of the substituent in the *para*-position toward this group (7.9—9.2 ppm for R = H, Me, MeO and 9.8—10.4 ppm for R = Cl, NO_2 in $CDCl_3$; 10.4 ppm for R = H and 12.1 ppm for R = NO_2 in DMSO-d_6). These data and the planar conformation of N-nonsubstituted pyrazoles indicate that in $CDCl_3$ the phenolic hydroxyl is involved in the formation of IMHB with the iminic nitrogen atom. This IMHB is strengthened when electron-withdrawing substituents appear in position 5′ of the benzene ring (**4f,h**) to enhance its acidic character. Therefore, pyrazoles **4a—j** as pyrazole **10** containing no R^F group[2] exist in $CDCl_3$ predominantly in the form of the 3-(2-hydroxyaryl)-5-R^F-tautomer stabilized by the IMHB (O—H···N=). It is important that in the absence of IMHB the equilibrium shifts toward the more thermodynamically stable 3-R^F-tautomer, as it occurs in the case of pyrazoles prepared from 2-polyfluoroacylcycloalkanones[7] and 3(5)-methyl-5(3)-trifluoromethylpyrazole, whose 3-CF_3-tautomer is by ~2.4 kcal mol^{-1} more stable that the 5-CF_3-tautomer.[30]

Regioisomeric N-substituted pyrazoles can easily be distinguished by the chemical shift of the phenolic proton in a solution of $CDCl_3$. For nonplanar 3-R^F-pyrazoles **8** and **9**, this shift is observed in a strong field as a narrow singlet at 5.0—5.7 ppm (disappears when CD_3CO_2D is added), whereas for planar 5-R^F-pyrazoles **7** it is observed at 10.0—10.2 ppm due to IMHB formation. In a solution of DMSO-d_6 the hydroxyl group of the phenolic fragment is involved in the formation of the intermolecular hydrogen bond with molecules of a basic solvent, due to which for 3-R^F-pyrazoles **8** and **9** its signal is displaced by almost 5 ppm to a low field and is observed at δ_{OH} = 9.7—10.1, whereas for 5-R^F-pyrazoles **7** it remains virtually unchanged (~10.1 ppm). Therefore, regioisomers **7** and **8** cannot be distinguished by δ_{OH} in this solvent. Note a good correlation in chemical shifts of the phenolic protons in N-substituted 5- and 3-R^F-pyrazoles and 5- and 3-R^F-isoxazoles. For the latter it appeared at 5.9 ppm in $CDCl_3$ and at 10.9 ppm in DMSO-d_6.[1]

The ^{1}H NMR spectra of regioisomeric pyrazoles **7** and **8** exhibit additional characteristic features along with the chemical shift of the phenolic proton in a solution of $CDCl_3$. For example, signals from the protons of the N—Ph group in 3-R^F-pyrazoles **8** are observed at 7.3—7.4 ppm, and for 5-R^F-pyrazoles **7** they lie at 7.5—7.6 ppm. In addition, a comparison of the spectra of the regioisomeric pair **7d** and **8d** shows that only in the case of **7d** the replacement of $CDCl_3$ by DMSO-d_6 results in the substantial deshielding of the H(4) and H(6′) protons. The changes in the $^3J_{H,F}$ constant and chemical shift of the terminal proton in the $H(CF_2)_2$ group are observed on going from **7d** to **8d** and for solvent replacement.*

As shown above, in $CDCl_3$, due to the IMHB between the phenolic proton and iminic nitrogen atom (O—H···N=), pyrazoles **4a—j** exist predominantly (if not exclusively) as 5-R^F-tautomers. However, in a solution of DMSO-d_6, when this bond is changed by the intermolecular hydrogen bond with the solvent molecules (O—H···O=S), the prototropic equilibrium can be shifted toward the thermodynamically more stable 3-R^F-tautomer. To verify this assumption, let us return to the ^{13}C NMR spectra of pyrazoles **4a** and **9a**. The chemical shifts of the C(3) and C(5) atoms are considered to be the most reliable spectral criterion for distinguishing regioisomeric pyrazoles. It is known that for 5-R^F-pyrazoles $\delta_{C(3)} \approx 149$ and $\delta_{C(5)} \approx 133$, and for 3-$R^F$-pyrazoles $\delta_{C(3)} \approx \delta_{C(5)} \approx 140—145$ ppm.[7,16,17] The $\delta_{C(3)} \approx 150$ and $\delta_{C(5)} \approx 130$ values were reported for 3-arylpyrazoles containing no R^F group, while for 5-arylpyrazoles $\delta_{C(3)} \approx 138$ and $\delta_{C(5)} \approx 140$.[2] A comparison of $\delta_{C(3)}$ and $\delta_{C(5)}$ in the ^{13}C NMR spectra of compounds **4a** and **9a** (see Table 3) shows that in DMSO-d_6 both pyrazole **9a**, which is incapable of tautomerism, and pyrazole **4a**, which exists in $CDCl_3$ as 5-R^F-tautomer, have the structure of 3-R^F-pyrazoles, *i.e.*, going from $CDCl_3$ to DMSO-d_6, the tautomeric equilibrium shifts, in fact, toward the 1*H*-3-R^F form. Unfortunately, we failed to measure the chemical shifts of the C(3) and C(5) atoms in $CDCl_3$ because of a low solubility of pyrazole **4a** in this solvent. Note that a similar shift of the tautomeric equilibrium with the replacement of a solvent has previously[31] been observed in the series of 5(7)-aryl-7(5)-polyfluoroalkyl-2,3-dihydro-1*H*-1,4-diazepines, which exist in a solution of $CDCl_3$ as 7-R^F-tautomers if they contain the hydroxyl group in the *ortho*-position of the aryl substituent and as 5-R^F-tautomers if this group is absent or in a solution of DMSO-d_6.

Our conclusions about the structure of pyrazoles **7—9** and decisive role of the IMHB on the position of tautomeric equilibrium in pyrazoles **4** were confirmed by the spin-spin coupling constant $^3J_{H,F}$ of the $H(CF_2)_2$ group,* whose value is dependent on the nearest environment of the carbon atom bound to this group.[31]

Thus, the reaction of 2-hydroxy-2-polyfluoroalkylchroman-4-ones and 2-polyfluoroalkylchromones with hydrazine is a simple and convenient method for synthesis of 3(5)-(2-hydroxyaryl)-5(3)-polyfluoroalkylpyrazoles **4a—j**, which have a planar conformation and exist in a $CDCl_3$ solution predominantly in the form of 1*H*-5-R^F-pyrazoles and in a DMSO-d_6 solution as

* Unpublished results.

1*H*-3-R^F-pyrazoles. The reaction with methyl- and phenylhydrazines affords 5-(2-hydroxyaryl)-1-methyl-3-polyfluoroalkylpyrazoles **9** and regioisomeric 3(5)-(2-hydroxyphenyl)-5(3)-polyfluoroalkyl-1-phenylpyrazoles **7** and **8**.

Experimental

IR spectra were recorded on an IKS-29 instrument in Nujol. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 spectrometer in $CDCl_3$ with working frequencies of 400.13 and 100.62 MHz, respectively. ^{19}F NMR spectra were obtained on a Tesla BS-587A instrument with a working frequency of 75.3 MHz. Me_4Si was used as internal standard for ^{1}H and ^{13}C NMR spectra, and $CFCl_3$ served as internal standard for ^{19}F NMR. Initial chromanones **2** and chromones **5** were described in Refs. 1 and 10. The data of the ^{1}H NMR and IR spectra of pyrazolines **3** and **6** are presented in Table 1, and those for pyrazoles **4**, **7—9** are presented in Table 2. The data of the ^{13}C NMR spectra of pyrazoles **4a** and **9a** are presented in Table 3. The physicochemical characteristics of the synthesized compounds are presented in Table 4.

5-Hydroxy-3-(2-hydroxyaryl)-5-polyfluoroalkyl-Δ^2-pyrazolines (3). Chromanone **2** (1.3 mmol) was dissolved in a minimum volume of ethanol (2—3 mL) at ~20 °C, and 25% hydrazine hydrate (0.5 mL) was added. The solution was left at ~20 °C for 15 min and then diluted with water (10—15 mL). The crystalline product that precipitated (sometimes it was oil, which is gradually solidified) was filtered off, washed with water, dried, and recrystallized from a hexane—toluene mixture (toluene with a butanol additive was used for compound **3c**).

Table 4. Main characteristics of pyrazolines **3**, **6** and pyrazoles **4**, **7—9**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) C	H	N	Molecular formula
3a	75	133—134	48.85 48.78	3.72 3.68	11.30 11.38	$C_{10}H_9F_3N_2O_2$
3b	68	151—152	50.87 50.77	4.37 4.26	10.84 10.77	$C_{11}H_{11}F_3N_2O_2$
3c	51	209—210	41.09 41.25	2.52 2.77	14.47 14.43	$C_{10}H_8F_3N_3O_4$
3d	65	137—138	47.51 47.49	3.77 3.62	10.17 10.07	$C_{11}H_{10}F_4N_2O_2$
3e	83	129—130	49.37 49.32	4.12 4.14	9.48 9.59	$C_{12}H_{12}F_4N_2O_2$
3f	64	119—120	42.26 42.26	2.78 2.90	8.94 8.96	$C_{11}H_9ClF_4N_2O_2$
3k	57	145—146	50.94 50.98	4.56 4.61	9.14 9.15	$C_{13}H_{14}F_4N_2O_2$
4a	89	197—198	52.72 52.64	2.91 3.09	12.09 12.28	$C_{10}H_7F_3N_2O$
4b	66	210—211	54.29 54.55	3.77 3.75	11.43 11.57	$C_{11}H_9F_3N_2O$
4c	48	236—237	43.95 43.97	2.13 2.21	15.21 15.38	$C_{10}H_6F_3N_3O_3$
4d	52	138—139	50.88 50.78	3.03 3.10	10.83 10.77	$C_{11}H_8F_4N_2O$
4e	71	164—165	52.58 52.56	3.61 3.68	10.28 10.22	$C_{12}H_{10}F_4N_2O$
4f	48	155—156	44.88 44.84	2.25 2.39	9.56 9.51	$C_{11}H_7ClF_4N_2O$
4g	54	122—123	49.67 49.66	3.56 3.47	9.69 9.65	$C_{12}H_{10}F_4N_2O_2$
4h	83	248—249	43.21 43.29	2.09 2.31	13.66 13.77	$C_{11}H_7F_4N_3O_3$
4i	77	168—169	57.40 57.15	3.82 3.84	13.44 13.33	$C_{10}H_8F_2N_2O$
4j	68	183—184	62.66 62.82	4.73 5.01	11.09 10.99	$C_{11}H_{10}F_2N_2O\cdot$ $\cdot 1/3PhMe$
4k	38	158—159	54.30 54.17	4.13 4.20	9.73 9.72	$C_{13}H_{12}F_4N_2O$
4l	77	204—205	41.35 41.28	2.53 2.66	14.78 14.81	$C_{13}H_{10}F_4N_4O_5$
6a	62	179—180	59.74 59.63	4.29 4.07	8.55 8.69	$C_{16}H_{13}F_3N_2O_2$
6b	39	139—140	60.86 60.71	4.66 4.50	8.37 8.33	$C_{17}H_{15}F_3N_2O_2$
6d	37	130—131	57.59 57.63	3.93 3.98	7.89 7.91	$C_{17}H_{14}F_4N_2O_2$
6m	46	132—133	53.88 53.87	3.17 3.39	7.78 7.85	$C_{16}H_{12}ClF_3N_2O_2$
7a	81	79—80	63.19 63.16	3.64 3.64	9.19 9.21	$C_{16}H_{11}F_3N_2O$
7b	63	90—91	64.24 64.15	4.03 4.12	8.64 8.80	$C_{17}H_{13}F_3N_2O$
7d	32	64—65	60.73 60.72	3.51 3.60	8.38 8.33	$C_{17}H_{12}F_4N_2O$
7m	91	130—132	56.92 56.74	3.10 2.98	8.38 8.27	$C_{16}H_{10}ClF_3N_2O$
8a	13	144—145	63.00 63.16	3.47 3.64	8.94 9.21	$C_{16}H_{11}F_3N_2O$
8d	15	127—128	55.67 55.36	3.29 3.31	7.68 7.45	$C_{17}H_{12}F_4N_2O\cdot$ $\cdot 1/3CHCl_3$
8m	20	143—144	56.60 56.74	2.83 2.98	8.21 8.27	$C_{16}H_{10}ClF_3N_2O$
9a	24[a] 23[b]	123—124	54.59 54.55	3.82 3.74	11.60 11.57	$C_{11}H_9F_3N_2O$
9b	27[b]	139—140	53.54 53.63	4.37 4.31	10.31 10.42	$C_{12}H_{10}F_3N_2O\cdot$ $\cdot 3/4H_2O$
9d	51[a] 10[b]	135—136	52.61 52.56	3.57 3.68	10.34 10.22	$C_{12}H_{10}F_4N_2O$

[a] From chromanone **2**.
[b] From chromone **5**.

3(5)-(2-Hydroxyaryl)-5(3)-polyfluoroalkylpyrazoles (4). ***A.*** 25% Hydrazine hydrate (0.5 mL) was added to a solution of chromone **5** (1.5 mmol) in 2 mL of ethanol. The mixture was boiled for 5 min, cooled, and diluted with water (10 mL). The crystalline precipitate was filtered off, washed with water, dried, and recrystallized from a hexane—toluene mixture.

B. A mixture of pyrazoline **3** (0.01 mmol), glacial acetic acid (10 mL), and concentrated HCl (0.1 mL) was boiled for 5 min, cooled, and diluted with water (50 mL). The precipitated crystals were filtered off, washed with water, dried, and recrystallized from a hexane—toluene mixture. Pyrazoles **4** prepared according to procedures ***A*** and ***B*** had identical IR spectra and gave no melting point depression.

5-Hydroxy-3-(2-hydroxyphenyl)-1-phenyl-5-trifluoromethyl-Δ^2-pyrazoline (6a). A solution obtained from ethanol (2 mL), chromanone **2a** (0.30 g, 1.29 mmol), and phenylhydrazine (0.30 g, 2.77 mmol) was left for 2 days at ~20 °C. The white crystals that precipitated were washed with 70% ethanol and dried.

5-Hydroxy-3-(2-hydroxyaryl)-1-phenyl-5-polyfluoroalkyl-Δ^2-pyrazolines (6). Chromanone **2** (1.15 mmol) was dissolved in 2—3 mL of ethanol at ~20 °C, and a 4 *M* ethanolic solution (0.3 mL) of phenylhydrazine was added. The solution was left at ~20 °C for 1 week, then the solvent was evaporated, and the residue was washed with 70% ethanol, dried, and recrystallized from a hexane—toluene mixture.

3-(2-Hydroxyaryl)-1-phenyl-5-polyfluoroalkylpyrazoles (7). Pyrazoline **6** (1.0 mmol) was dissolved in 2 mL of acetic acid, and one droplet of concentrated HCl was added. The resulting solution was boiled for 30 min, cooled, and diluted with water (10 mL). The precipitate was filtered off, dried, and recrystallized from hexane.

5-(2-Hydroxyaryl)-1-phenyl-3-polyfluoroalkylpyrazoles (8a,m). Chromone **5a** or **5m** (1.4 mmol) was dissolved in ethanol (2—3 mL), and a 4 *M* ethanolic solution (0.5 mL) of phenylhydrazine was added. The resulting solution was boiled for 30 min and diluted with 10 mL of water. The oily product, which was formed and gradually solidified, was filtered off, dried, and recrystallized from a hexane—toluene mixture.

5-(2-Hydroxyphenyl)-1-phenyl-3-(1,1,2,2-tetrafluoroethyl)pyrazole (8d). Two—three drops of concentrated HCl were added to a solution of chromone **5d** (0.22 g, 0.89 mmol) and phenylhydrazine (0.40 g, 3.70 mmol). The obtained mixture was boiled for 4 h, diluted with water (10 mL) containing 0.5 mL of concentrated HCl, and left for 2 days. The precipitated brown mixture was filtered off, dried, and recrystallized from a hexane—chloroform mixture.

5-(2-Hydroxyaryl)-1-methyl-3-polyfluoroalkylpyrazoles (9a,d). A 1.4 *M* aqueous-ethanolic solution (1.5 mL) of methylhydrazine prepared from methylhydrazine sulfate and KOH was added to a solution of chromanone **2a** or **2d** (1.3 mmol) in ethanol (3 mL). The mixture was boiled for 10 min, cooled, and diluted with water (15 mL) containing concentrated HCl (0.5 mL). The crystalline product that precipitated was filtered off, washed with water, and recrystallized from a hexane—toluene mixture. Pyrazoles **9a,b,d** were prepared from the corresponding chromones **5** using a similar procedure by boiling for 1 h for **5a,b** and by boiling for 5 h with a drop of concentrated HCl for **5d**.

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