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Synthesis of 1-[4-(1,3-Diaryl-4,5-dihydro-1*H*-pyrazol-5-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-ols and Their Acrylates

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Abstract—(4-Hydroxypiperidin-1-yl)tetra- and -octafluorochalcones reacted with phenylhydrazine in acetic acid to give mixtures of polyfluoro-1,3,5-triaryl-4,5-dihydro-1*H*-pyrazoles and their *O*-acetyl derivatives. Analogous reactions in ethanol afforded in satisfactory yields 1-[4-(1,3-diaryl-4,5-dihydro-1*H*-pyrazol-5-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-ols which were treated with acryloyl chloride to obtain the corresponding acrylates that are promising as monomers for the preparation of fluorescent films.

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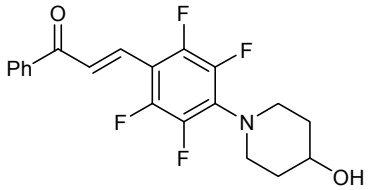
1,3,5-Triaryldihydropyrazoles and their derivatives are the most widely known heterocyclic organic fluorophores [1] which attract persistent attention due to their possible application as fluorescent probes [2], organic light-emitting diodes [3], organic one-dimensional nanomaterials [4], nonlinear optical materials [5], and biologically active compounds [6–9]. Some pyrazoline-based fluorescent monomers give rise to thin transparent polymer films with strong fluorescence [10].

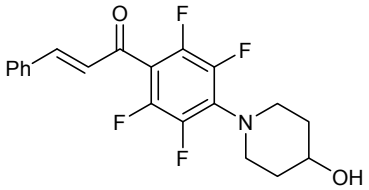
We have synthesized acryloyl-substituted 1,3,5-tris(polyfluoroaryl)-4,5-dihydro-1*H*-pyrazoles exhibiting a combination of fluorophore and monomer properties, which makes them promising starting materials for the preparation of fluorescent polymer films.

One of the main methods for the synthesis of 1,3,5-triaryl-4,5-dihydro-1*H*-pyrazoles is based on the reaction of chalcones with phenylhydrazine [11–13]. The presence of labile fluorine atoms in the molecules of polyfluorinated chalcones makes it possible to introduce various substituents, such as dialkylamino, phenoxy, and azido groups, via reactions with nucleophiles [14]. Substituents containing hydroxy or amino groups can be subjected to further functionalization [15, 16]. Our choice of piperidin-4-ol as nucleophile was based on the following considerations: the secondary amino group of piperidine is capable of replacing aromatic fluorine atoms under mild conditions [14]; free hydroxy group can be involved in further transformations, e.g., esterification; alicyclic skeleton acts as a linker connecting the heterocycle and functional group.

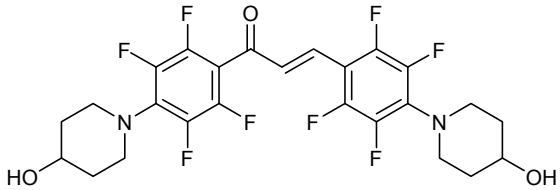
Reactions of chalcones with phenylhydrazine are usually carried out in acid medium, mostly in acetic acid. Pereyaslova et al. [17] were the first to report on reactions of polyfluorinated chalcones with phenylhydrazine [17]. Later on, we revealed some peculiar features of this reaction [13]. For example, 3-(penta-



1a

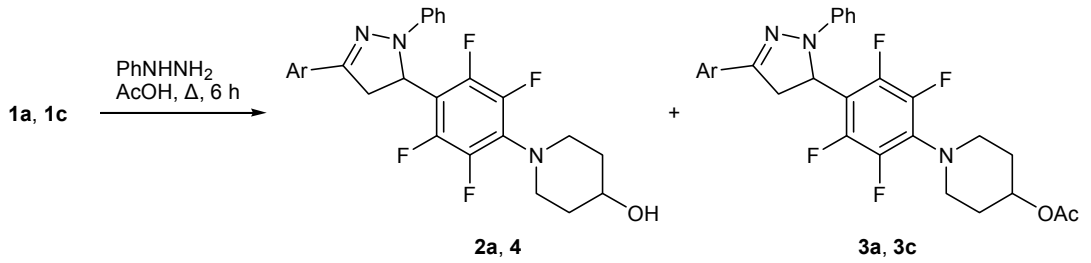


1b



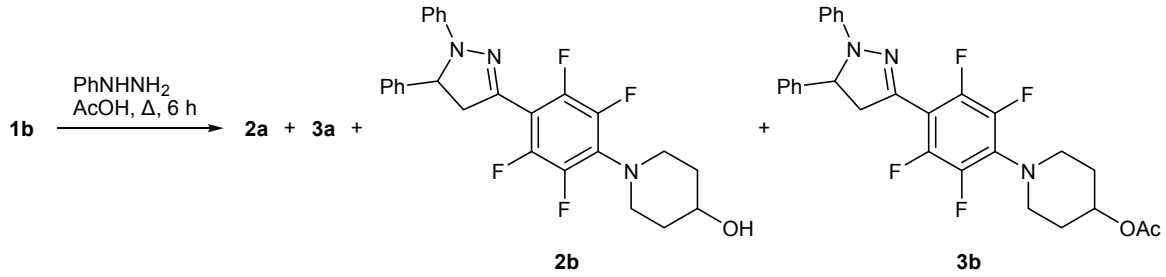
1c

Scheme 1.



2a, **3a**, Ar = Ph; **3c**, **4**, Ar = 4-(4-acetoxypiperidin-1-yl)-2,3,5,6-tetrafluorophenyl; **2a** : **3a** = 69 : 31, **3c** : **4** = 48 : 52.

Scheme 2.



2a : **3a** : **2b** : **3b** = 14 : 9 : 48 : 29

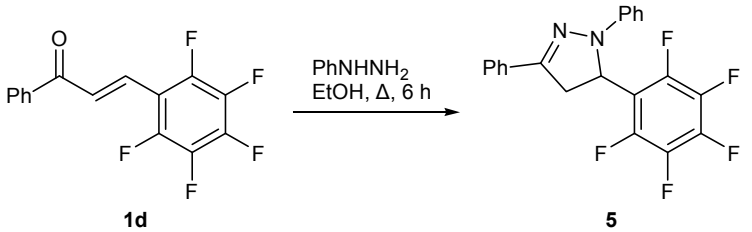
fluorophenyl)-1-phenylprop-2-en-1-one and its *para*-substituted derivatives reacted with phenylhydrazine to give a mixture of isomeric dihydropyrazoles differing by the substituents in positions *3* and *5*.

We used as starting compunds (4-hydroxypiperidin-1-yl)tetra- and -octafluorochalcones **1a**–**1c** which were prepared as described in [15] from the corresponding fluorinated chalcones, 1-(pentafluorophenyl)-3-phenylprop-2-en-1-one (**1d**), 3-(pentafluorophenyl)-1-phenylprop-2-en-1-one (**1e**), and 1,3-bis(pentafluorophenyl)-prop-2-en-1-one (**1f**). We have optimized the procedure for the synthesis of chalcone **1b** from **1e**: the use of DMF instead of ethanol made it possible to avoid formation of *ortho*-substituted isomer and improve the yield of **1b** to 94% against 60% in [15].

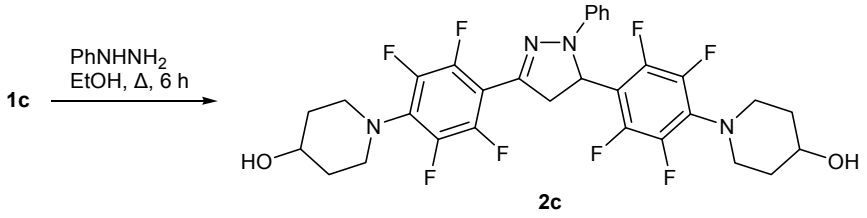
The presence of a hydroxy group in molecules **1a**–**1c** led us to expect that their reaction with phenylhydrazine in acetic acid could be accompanied by O-acetylation. In fact, by heating chalcones **1a** and **1c** with phenylhydrazine in acetic acid we obtained mixtures of (4-hydroxypiperidin-1-yl)-substituted triaryldihydropyrazoles and *O*-acetyl derivatives (Scheme 1; the product ratios were determined on the basis of the ^{19}F NMR spectra). Chalcone **1a** was converted to hydroxy and *O*-acetyl derivatives **2a** and **3a**, and chalcone **1c**, to di- and monoacetyl derivatives **3c** and **4**. In the latter case, preferential acetylation of hydroxy group in the substituent on C^3 of the pyrazole ring was observed.

Chalcone **1b** reacted with phenylhydrazine under analogous conditions to give a mixture of two pairs of isomeric dihydropyrazoles **2a**/**3a** and **2b**/**3b** differing by the substituents on C^3 and C^5 (cf. [13]; Scheme 2). We failed to isolate pure compounds **2b** and **3b**. Preparative thin-layer chromatography afforded two fractions which were mixtures of regioisomers **2a** and **2b** and their acetyl derivatives **3a** and **3b**. The structure of **3b** (in a mixture with **3a**) was determined by NMR

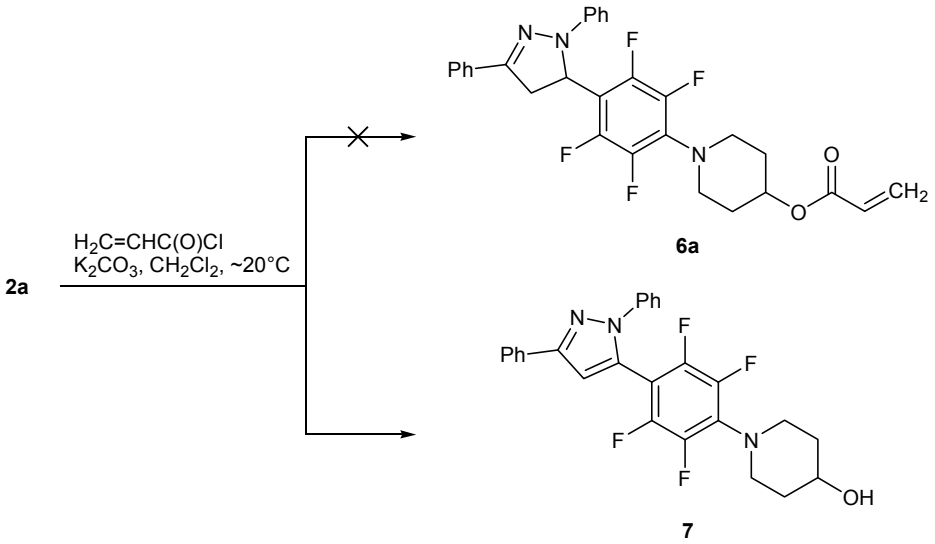
Scheme 3.



Scheme 4.



Scheme 5.



spectroscopy and was confirmed by gas chromatography/mass spectrometry.

To avoid acetylation, reactions of polyfluorinated chalcones with phenylhydrazine were carried out in ethanol which was used as solvent in some reactions of chalcones with hydrazine hydrate [18, 19]. By reaction of 1-(pentafluorophenyl)-3-phenylprop-2-en-1-one (**1d**) with phenylhydrazine in boiling ethanol we obtained dihydropyrazole **5** (Scheme 3).

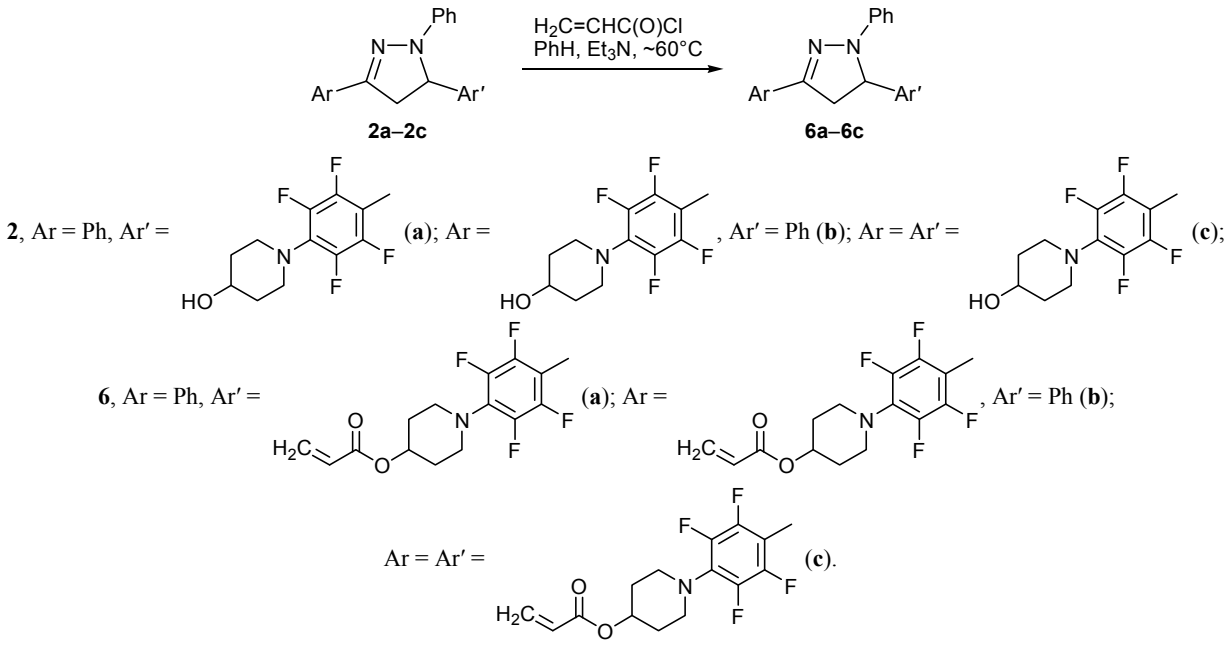
Polyfluorochalcones **1a**–**1c** reacted with phenylhydrazine in ethanol in a similar way. Chalcone **1a** was thus converted to dihydropyrazole **2a** in 50% yield. The reaction of **1b** with phenylhydrazine in ethanol was most efficient. Instead of a mixture of four compounds (**2a**, **2b**, **3a**, **3b**) formed in acetic acid, the reaction in ethanol gave 78% of **2b** as the only product. Under analogous conditions, octafluorochalcone **1c** was converted with high yield to dihydropyrazole **2c** which was not formed in acetic acid (Scheme 4).

Compounds **2a**–**2c** were then used to synthesize the corresponding acrylates. However, the reaction of **2a** with acryloyl chloride in methylene chloride in the presence of potassium carbonate produced pyrazole **7** rather than expected acrylate **6a** (Scheme 5), whereas no acylation of **7** occurred under these conditions. In keeping with published data, we presumed that the instability of dihydropyrazoles is determined by the presence of methylene chloride [17, 20]. When methylene chloride was replaced by benzene, and potassium carbonate, by triethylamine, target acrylates **6a**–**6c** were obtained with moderate yields (Scheme 6).

Triarylpyrazolines are strong fluorophores emitting in the blue and green regions of the spectrum. Fluorescence properties of compound **2b** depend on the solvent polarity. The electronic absorption and fluorescence spectra of triaryldihydropyrazoles **2a**–**2c**, **3a**, **3c**, and **4** and pyrazole **7** were recorded in toluene and ethanol (see table). The spectra of acrylates **6a**–**6c** were recorded only in toluene because of their poor solubility in ethanol.

The long-wave fluorescence maximum of 1,3,5-triaryldihydropyrazoles **2a**, **3a**, and **6a** with the fluorinated aromatic substituent on C^5 is located at λ ~450 nm in ethanol and λ 425–427 nm in toluene. The fluorescence maxima of isomers **2b** and **6b** are observed at longer wavelengths (Δλ = 22–27 nm) due to the presence of fluorinated aromatic substituent in the 3-position conjugated with the *N*-phenyl ring [1, 21]. Dihydropyrazoles **2c**, **3c**, **4**, and **6c** with polyfluorinat-

Scheme 6.



ed aromatic substituents on both C^3 and C^5 are characterized by intermediate position of the long-wave maximum in the absorption and fluorescence spectra. A small blue shift ($\Delta\lambda$ = 6–7 nm) of the absorption maxima is observed in going from toluene to ethanol, whereas the fluorescence maxima shift red by 16–23 nm, which is consistent with published data on the solvent effect on the fluorescence properties of fluorophores [21]. The Stokes shift in ethanol is larger by 22–30 nm than in toluene and is 100 nm. Pyrazole **7** showed fluorescence in the same region as dihydropyrazoles, but the intensity of the long-wave maximum was considerably lower.

Figure 1 shows fluorescence spectra of **2a**–**2c** in ethanol and toluene, and the fluorescence spectra of acrylates **6a**–**6c** are given in Fig. 2. It is seen that compound **2b** fluoresces green in ethanol (λ_{max} 473 nm) and blue in toluene (λ_{max} 454 nm). The lowest fluorescence intensity is observed for dihydropyrazoles with the fluorinated aromatic ring on C^5,

Long-wave absorption and fluorescence maxima of compounds **2a**–**2c**, **3a**, **3c**, **4**, **6a**–**6c**, and **7**

Compound no.	Ethanol		Toluene	
	λ_{max}, nm (logε)	λ_{max}, nm (I_{fl})[a]	λ_{max}, nm (logε)	λ_{max}, nm ($I_{fl.}$)[a]
2a	352 (4.32)	451 (650)	358 (4.32)	427 (621)
2b	367 (4.42)	473 (648)	373 (4.42)	454 (654)
2c	361 (4.43)	460 (605)	368 (4.43)	444 (461)
3a	352 (4.21)	452 (594)	358 (4.29)	425 (528)
3c	362 (4.44)	462 (553)	368 (4.45)	442 (533)
4	363 (4.47)	463 (675)	369 (4.36)	442 (657)
6a	–	–	358 (4.30)	427 (521)
6b	–	–	373 (4.41)	459 (663)
6c	–	–	368 (4.38)	443 (684)
7	276 (4.53)	450 (404)	283 (4.38)	459 (140)

[a] $\lambda_{excit} \approx 350$ nm.

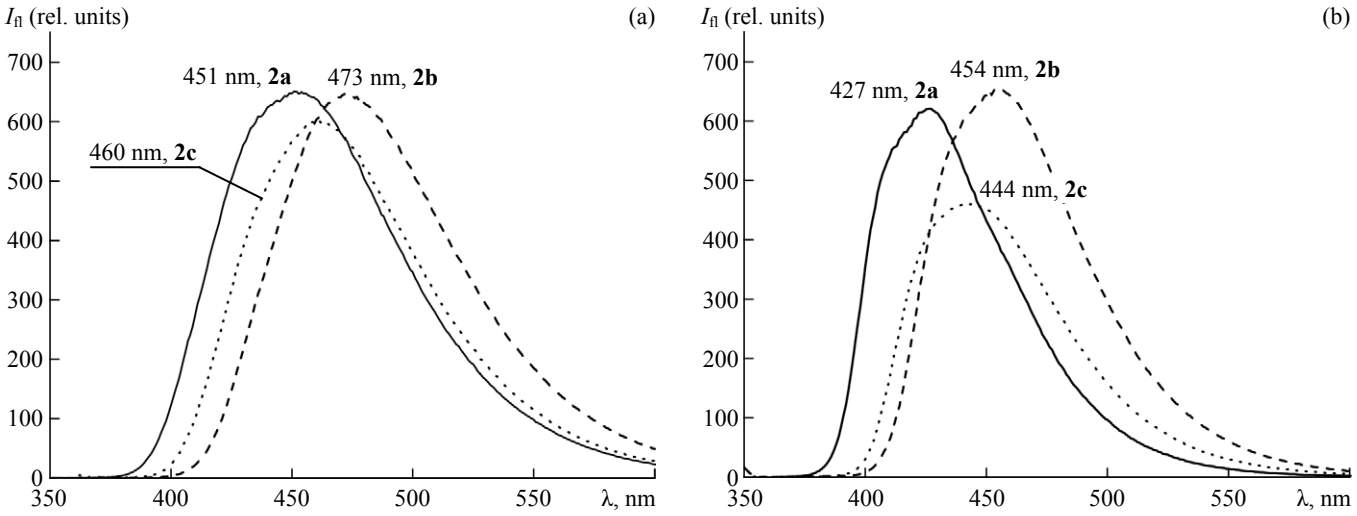


Fig. 1. Fluorescence spectra of compounds **2a**–**2c** in (a) ethanol and (b) toluene.

which is consistent with the data of [13]. Acrylates **6a**–**6c** are characterized by strong fluorescence with an intensity comparable with the emission intensity of the corresponding hydroxy and acetyl derivatives. Therefore, it may be presumed that polymerization of **6a**–**6c** would lead to formation of polymer films with bright blue fluorescence.

Thus, the use of ethanol instead of acetic acid as solvent in the reactions of (4-hydroxypiperidin-1-yl)-substituted polyfluorochalcones **1a**–**1c** with phenylhydrazine makes it possible to avoid side formation of *O*-acetyl derivatives, as well as the formation of regioisomer mixture in the reaction with chalcone **1b**, and to improve the yield of dihydropyrazoles **2a**–**2c** with a free hydroxy group which can be subjected to further functionalization.

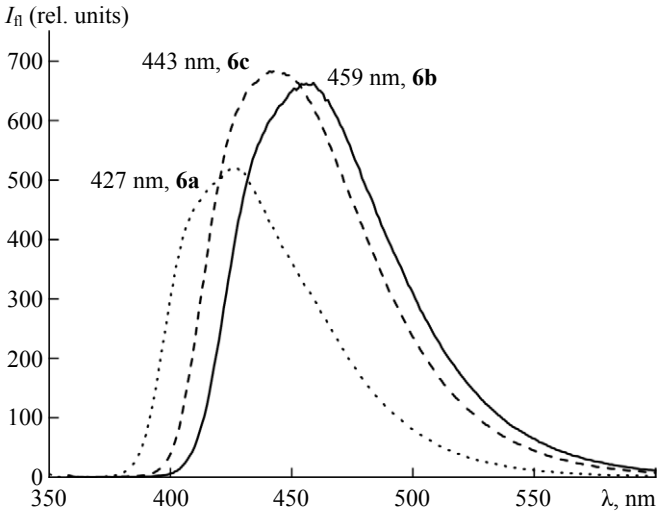


Fig. 2. Fluorescence spectra of compounds **6a**–**6c** in toluene.

EXPERIMENTAL

Chalcones **1a** and **1c** were synthesized according to the procedure described in [15]. The spectral and analytical data were obtained at the Joint Chemical Service Center, Siberian Branch, Russian Academy of Sciences. The ^{1}H and ^{19}F NMR spectra were recorded on a Bruker AV-300 spectrometer at 300.13 and 282.37 MHz, respectively, using $CDCl_3$ as solvent and reference for ^{1}H ($CHCl_3$, δ 7.24 ppm); the ^{19}F chemical shifts were measured relative to hexafluorobenzene. Gas chromatographic–mass spectrometric analysis was performed on an Agilent Technologies instrument consisting of an Agilent 6890N gas chromatograph and an Agilent 5973N mass-selective detector [electron impact, 70 eV; HP-5MS capillary column, 30 m × 0.25 mm, film thickness 0.25 μm; carrier gas helium, flow rate 1 mL/min; oven temperature programming from 50°C (2 min) to 280°C at a rate of 10 deg/min; 30 min at 280°C; injector temperature 280°C, ion source temperature 230°C; scan rate 1.2 scan/s; a.m.u. range 30–800]. The melting points were determined on a Kofler hot stage (Carl Zeiss Jena).

1-[4-(4-Hydroxypiperidin-1-yl)-2,3,5,6-tetrafluorophenyl]-3-phenylprop-2-en-1-one (1b). Piperidin-4-ol, 1.36 g (13.4 mmol), was added to a solution of 2.0 g (6.7 mmol) of chalcone **1e** in 20 mL of DMF, and the mixture was stirred for 5 h at room temperature. The mixture was then poured onto ice and left overnight at room temperature, and the precipitate was filtered off, washed with water and hexane, and dried in air. Yield 2.40 g (94%). Compound **1b** was identical to that described in [15] in the melting point and ^{1}H and ^{19}F NMR spectra.

1,3-Diphenyl-5-(pentafluorophenyl)-4,5-dihydro-1*H*-pyrazole (5). Chalcone **1d**, 0.1 g (0.34 mmol), was added to a solution of 0.17 mL (1.7 mmol) of phenylhydrazine in 4 mL of ethanol, and the mixture was refluxed for 6 h with stirring and left overnight at room temperature. The precipitate was filtered off, washed with water, and dried in air. Yield 0.05 g (38%). Compound **5** was identical to that described in [13] in the melting point and ^{1}H and ^{19}F NMR spectra.

Reaction of chalcone 1a with phenylhydrazine. *a*. Chalcone **1a**, 3.26 g (8.6 mmol), was added to a solution of 4.26 mL (43.0 mmol) of phenylhydrazine in 10 mL of glacial acetic acid, and the mixture was refluxed for 6 h with stirring and left overnight at room temperature. The precipitate was filtered off, washed with water, and dried in air. The product (5.55 g) was analyzed by ^{1}H and ^{19}F NMR and subjected to column chromatography on aluminum oxide to isolate two fractions. The first fraction (hexane–methylene chloride, 4:1) contained compound **3a**, and the second (methylene chloride), compound **2a**.

1-[4-(1,3-Diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-ol (2a). Yield 1.59 g (39%), colorless crystals, mp 142–145°C (from 75% aq. EtOH). ^{1}H NMR spectrum, δ, ppm: 1.57–1.71 m (3H, CH_2, OH), 1.89–2.00 m (2H, CH_2), 3.00–3.16 m (2H, CH_2), 3.22–3.42 m (3H, CH_2, 4-H), 3.71–3.90 m (2H, C**H**OH, 4-H), 5.66 d.d (1H, 5-H, J = 13.2, 6.5 Hz), 6.76–6.83 m (1H, H_{arom}), 7.03–7.12 m (2H, H_{arom}), 7.15–7.23 m (2H, H_{arom}), 7.29–7.42 m (3H, H_{arom}), 7.66–7.78 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 11.14 m (2F), 16.80 br.s (2F). Found: *m/z* 469.1772 $[M]^+$. $C_{26}H_{23}F_4N_3O$. Calculated: *M* 469.1774.

1-[4-(1,3-Diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-yl acetate (3a). Yield 0.82 g (19%), colorless crystals, mp 185–188°C (from EtOAc–hexane, 2:3). ^{1}H NMR spectrum, δ, ppm: 1.68–1.81 m (2H, CH_2), 1.90–1.99 m (2H, CH_2), 2.05 s (3H, $COCH_3$), 3.08–3.19 m (2H, CH_2), 3.23–3.39 m (3H, CH_2, 4-H), 3.81 d.d (1H, 4-H, J = 17.3, 13.2 Hz), 4.89 m [1H, CHOC(O)], 5.66 d.d (1H, 5-H, J = 13.2, 6.5 Hz), 6.76–6.83 m (1H, H_{arom}), 7.04–7.11 m (2H, H_{arom}), 7.16–7.23 m (2H, H_{arom}), 7.31–7.42 m (3H, H_{arom}), 7.68–7.76 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 11.17 m (2F), 16.94 br.s (2F). Found, %: C 65.75; H 4.93; F 14.86; N 8.21. $C_{28}H_{25}F_4N_3O_2$. Calculated, %: C 65.34; H 5.13; F 14.86; N 8.18.

b. Chalcone **1a**, 0.1 g (0.26 mmol), was added to a solution of 0.13 mL (1.3 mmol) of phenylhydrazine in 2 mL of ethanol, and the mixture was refluxed for 6 h with stirring and left overnight at room temperature. The precipitate was filtered off, washed with water, and dried in air. The filtrate was extracted with ethyl acetate, the extract was washed with water and dried over $CaCl_2$, and the solvent was removed under reduced pressure. The products were analyzed by ^{1}H and ^{19}F NMR, combined (overall weight 0.16 g), and subjected to preparative thin-layer chromatography on Al_2O_3 plates using hexane–ethyl acetate (4:1) as eluent to isolate 0.06 g (50%) of compound **2a** which was identical to a sample obtained as described above in *a* in the melting point and ^{1}H and ^{19}F NMR spectra.

Reaction of chalcone 1b with phenylhydrazine. *a*. Chalcone **1b**, 1.0 g (2.6 mmol), was added to a solution of 1.31 mL (13.2 mmol) of phenylhydrazine in 5 mL of glacial acetic acid, and the mixture was refluxed for 6 h with stirring and left overnight at room temperature. A viscous material separated and was extracted with ethyl acetate, the extract was washed with water and dried over $CaCl_2$, and the solvent was removed under reduced pressure. The residue (1.53 g) was analyzed by ^{1}H and ^{19}F NMR and was subjected to preparative thin-layer chromatography on Al_2O_3 plates using hexane–ethyl acetate (25:3) as eluent. The first fraction was a mixture of compounds **3a** and **3b** at a ratio of 23:77, and the second was a mixture of **2a** and **2b** (23:77).

1-[4-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-yl acetate (3b). Yield 29% (according to the NMR data). ^{1}H NMR spectrum, δ, ppm: 1.73–1.85 m (2H, CH_2), 1.94–2.01 m (2H, CH_2), 2.07 s (3H, $COCH_3$), 3.15–3.25 m (2H, CH_2), 3.36–3.48 m (3H, CH_2, 4-H), 3.88 d.d (1H, 4-H, J = 17.6, 12.6 Hz), 4.94 m [1H, C**H**OC(O)], 5.24 d.d (1H, 5-H, J = 12.6, 7.3 Hz), 6.76–6.84 m (1H, H_{arom}), 7.00–7.06 m (2H, H_{arom}), 7.11–7.17 m (2H, H_{arom}), 7.24–7.32 m (5H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 9.96 m (2F), 20.36 m (2F).

b. Chalcone **1b**, 1.0 g (2.6 mmol), was added to a solution of 1.3 mL (13.2 mmol) of phenylhydrazine in 10 mL of ethanol, and the mixture was refluxed for 6 h with stirring and left overnight in a refrigerator. The precipitate of **2b** was filtered off, washed with water, and dried in air (0.93 g). An additional amount of compound **2b** (0.04 g) was isolated from the filtrate by extraction with ethyl acetate, followed by column chromatography on Al_2O_3 (ethyl acetate–hexane, 1:3). Yield 0.97 g (78%).

1-[4-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-ol (2b). Yield 0.97 g (78%), light yellow crystals, mp 142–145°C (from 75% aq. EtOH). ^{1}H NMR spectrum, δ, ppm: 1.51 br.s (1H, OH), 1.61–1.75 m (2H, CH_2), 1.92–2.05 m (2H, CH_2), 3.08–3.27 m (3H, CH_2, 4-H), 3.36–3.51 m (2H, CH_2), 3.79–3.96 m (2H, C**H**OH, 4-H), 5.24 d.d (1H, 5-H, J = 12.7, 7.2 Hz), 6.74–6.83 m (1H, H_{arom}), 6.99–7.06 m (2H, H_{arom}), 7.11–7.20 m (2H, H_{arom}), 7.24–7.38 m (5H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 9.95 m (2F), 20.25 m (2F). Found, %: C 66.52; H 4.94; F 16.19; N 8.95. $C_{26}H_{23}F_4N_3O$. Calculated, %: C 66.44; H 4.94; F 16.24; N 8.94.

Reaction of chalcone 1c with phenylhydrazine. *a*. Chalcone **1c**, 1.0 g (1.8 mmol), was added to a solution of 0.90 mL (9.1 mmol) of phenylhydrazine in 5 mL of glacial acetic acid, and the mixture was refluxed for 6 h with stirring and left overnight at room temperature. The precipitate was filtered off, washed with water, and dried in air. The product (0.75 g) was analyzed by ^{1}H and ^{19}F NMR and subjected to preparative thin-layer chromatography on Al_2O_3 (hexane–ethyl acetate, 3:1). The first fraction contained compound **3c**, and the second, compound **4**.

(1-Phenyl-4,5-dihydro-1*H*-pyrazole-3,5-diyl)bis[(2,3,5,6-tetrafluoro-1,4-phenylene)piperidine-1,4-diyl] diacetate (3c). Yield 0.18 g (14%), light yellow crystals, mp 155–157°C (from EtOAc–hexane, 2:3). ^{1}H NMR spectrum, δ, ppm: 1.68–1.86 m (4H, CH_2), 1.90–2.03 m (4H, CH_2), 2.05 s (3H, CH_3), 2.07 s (3H, $COCH_3$), 3.08–3.27 m (4H, CH_2), 3.29–3.48 m (5H, CH_2, 4-H), 3.86 d.d (1H, 4-H, J = 17.7, 13.3 Hz), 4.84–5.00 m [2H, CHOC(O)], 5.67 d.d (1H, 5-H, J = 13.3, 6.2 Hz), 6.76–6.89 m (1H, H_{arom}), 7.02–7.11 m (2H, H_{arom}), 7.15–7.23 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 10.03 m (2F), 11.24 m (2F), 16.97 br.s (2F), 20.39 m (2F). Found, %: C 58.01; H 4.45; F 20.97; N 7.73. $C_{35}H_{32}F_8N_4O_4$. Calculated, %: C 57.90; H 4.53; F 21.34; N 7.90.

1-(2,3,5,6-Tetrafluoro-4-{5-[4-(4-hydroxypiperidin-1-yl)-2,3,5,6-tetrafluorophenyl]-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl}phenyl)piperidin-4-yl acetate (4). Yield 0.48 g (39%), light yellow crystals, mp 200–203°C (from EtOAc–hexane, 2:3). ^{1}H NMR spectrum, δ, ppm: 1.52 br.s (1H, OH), 1.56–1.71 m (2H, CH_2), 1.74–1.86 m (2H, CH_2), 1.90–2.04 m (4H, CH_2), 2.07 s (3H, $COCH_3$), 3.02–3.15 m (2H, CH_2), 3.16–3.27 m (2H, CH_2), 3.29–3.48 m (5H, CH_2, 4-H), 3.76–3.95 m [2H, C**H**OH, 4-H], 4.94 m [1H, CHOC(O)], 5.67 d.d (1H, 5-H, J = 13.3, 6.3 Hz), 6.77–6.87 m (1H, H_{arom}), 7.02–7.10 m (2H, H_{arom}), 7.16–7.24 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 10.03 m (2F), 11.21 m (2F), 16.84 br.s (2F), 20.39 m (2F). Found, %: C 58.06; H 4.43; F 22.27; N 8.21. $C_{33}H_{30}F_8N_4O_3$. Calculated, %: C 58.13; H 4.49; F 22.38; N 8.17.

b. Chalcone **1c**, 1.0 g (1.8 mmol), was added to a solution of 0.9 mL (9.1 mmol) of phenylhydrazine in 10 mL of ethanol. The mixture was refluxed for 6 h with stirring, cooled to room temperature, and poured into water. The precipitate was filtered off, washed with water, and dried in air.

1,1′-[(1-Phenyl-4,5-dihydro-1*H*-pyrazole-3,5-diyl)bis(2,3,5,6-tetrafluoro-1,4-phenylene)]dipiperidin-4-ol (2c). Yield 1.07 g (92%), light yellow powder, mp 170–173°C (from 75% aq. EtOH). ^{1}H NMR spectrum, δ, ppm: 1.56–1.76 m (6H, OH, CH_2), 1.90–2.05 m (4H, CH_2), 3.01–3.24 m (5H, CH_2, 4-H), 3.30–3.51 m (4H, CH_2), 3.78–3.92 m (3H, C**H**OH, 4-H), 5.67 d.d (1H, 5-H, J = 13.3, 6.2 Hz), 6.79–6.86 m (1H, H_{arom}), 7.03–7.09 m (2H, H_{arom}), 7.17–7.24 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 10.01 m (2F), 11.20 m (2F), 16.84 br.s (2F), 20.28 m (2F). Found, %: C 58.13; H 4.41; F 23.73; N 8.75. $C_{31}H_{28}F_8N_4O_2$. Calculated, %: C 57.74; H 4.38; F 23.74; N 8.75.

1-[4-(1,3-Diphenyl-4,5-dihydro-1*H*-pyrazol-5-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-yl acrylate (6a). A solution of 0.16 mL (1.92 mmol) of acryloyl chloride in 5 mL of benzene was added dropwise at room temperature to a solution of 0.3 g (0.64 mmol) of compound **2a** and 0.18 mL (1.28 mmol) of triethylamine in 10 mL of benzene. The mixture was stirred for 5 h at 55°C and left overnight in a refrigerator. The mixture was then diluted with 20 mL of benzene, washed with ~5% aqueous HCl, and the acidic aqueous phase was extracted with ethyl acetate. The organic fractions were combined, washed with water, and dried over $CaCl_2$, and the solvent was removed under reduced pressure with slight heating. The residue (0.25 g) was subjected to column chromatography on Al_2O_3 using ethyl acetate–hexane (1:4) as eluent, the eluate was evaporated, and the residue was washed with hexane. Yield 0.11 g (33%), colorless powder, mp 154–156°C (from benzene–hexane, 1:1). ^{1}H NMR spectrum, δ, ppm: 1.74–1.89 m (2H, CH_2), 1.95–2.05 m (2H, CH_2), 3.11–3.22 m (2H, CH_2), 3.24–3.42 m (3H, CH_2, 4-H), 3.81 d.d (1H, 4-H, J = 17.7, 13.1 Hz), 5.00 m [1H, CHOC(O)], 5.67 d.d (1H, 5-H, J = 13.1, 6.6 Hz), 5.82 d.d (1H, C**H**$_2$=CH, J = 10.4, 1.5 Hz), 6.12 d.d (1H, C**H**$_2$=CH, J = 17.4, 10.4 Hz), 6.41 d.d (1H, CH_2=C**H**, J = 17.4, 1.5 Hz), 6.80 m (1H,

H_{arom}), 7.04–7.12 m (2H, H_{arom}), 7.17–7.24 m (2H, H_{arom}), 7.29–7.43 m (5H, H_{arom}), 7.68–7.76 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 11.20 m (2F), 16.96 br.s (2F). Found: *m*/*z* 523.1877 $[M]^+$. $C_{29}H_{25}F_4N_3O_2$. Calculated: *M* 523.1869.

1-[4-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-yl acrylate (6b) was synthesized in a similar way. The product (0.30 g) was purified by column chromatography on Al_2O_3 (EtOAc–hexane, 1:3) and was additionally precipitated from benzene with hexane. Yield 0.14 g (42%), light yellow powder, mp 130–133°C (from benzene–hexane, 1:1). ^1H NMR spectrum, δ, ppm: 1.78–1.91 m (2H, CH_2), 1.97–2.09 m (2H, CH_2), 3.14–3.30 m (3H, CH_2, 4-H), 3.37–3.52 m (2H, CH_2), 3.88 d.d (1H, 4-H, *J* = 12.5, 18.0 Hz), 5.03 m [1H, CHOC(O)], 5.24 d.d (1H, 5-H, *J* = 12.5, 7.3 Hz), 5.84 d.d (1H, C**H**$_2$=CH, *J* = 10.5, 1.4 Hz), 6.13 d.d (1H, C**H**$_2$=CH, *J* = 17.2, 10.5 Hz), 6.42 d.d (1H, CH_2=C**H**, *J* = 17.2, 1.4 Hz), 6.79 m (1H, H_{arom}), 6.99–7.08 m (2H, H_{arom}), 7.11–7.19 m (2H, H_{arom}), 7.25–7.37 m (5H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 10.01 m (2F), 20.40 m (2F). Found: *m*/*z* 523.1877 $[M]^+$. $C_{29}H_{25}F_4N_3O_2$. Calculated: *M* 523.1869.

(1-Phenyl-4,5-dihydro-1*H*-pyrazole-3,5-diyl)bis[(2,3,5,6-tetrafluoro-4,1-phenylene)piperidine-1,4-diyl] bisacrylate (6c). A solution of 0.15 mL (1.9 mmol) of acryloyl chloride in 5 mL of benzene was added dropwise at room temperature to a solution of 0.3 g (0.47 mmol) of dihydropyrazole **2c** and 0.26 mL (1.9 mmol) of triethylamine in 10 mL of benzene. The procedure was the same as that described above for compound **6a**. The product isolated by chromatography was dissolved in benzene, and the solvent was slowly evaporated at room temperature (from an open vessel). Yield 0.09 g (26%), yellow powder, mp 87–90°C (from benzene–hexane, 1:1). ^1H NMR spectrum, δ, ppm: 1.75–1.91 m (4H, CH_2), 1.95–2.09 m (4H, CH_2), 3.11–3.30 m (4H, CH_2), 3.30–3.51 m (5H, CH_2, 4-H), 3.87 d.d (1H, 4-H, *J* = 17.6, 13.6 Hz), 5.02 m (2H, 4-H), 5.67 d.d (1H, 5-H, *J* = 13.5, 6.0 Hz), 5.82 d.d (1H, C**H**$_2$=CH, *J* = 10.4, 1.5 Hz), 5.84 d.d (1H, C**H**$_2$=CH, *J* = 10.4, 1.5 Hz), 6.10 d.d (1H, C**H**$_2$=CH, *J* = 17.3, 10.4 Hz), 6.15 d.d (1H, C**H**$_2$=CH, *J* = 17.3, 10.4 Hz), 6.40 d.d (1H, CH_2=C**H**, *J* = 17.3, 1.5 Hz), 6.43 d.d (1H, CH_2=C**H**, *J* = 17.3, 1.5 Hz), 6.82 m (1H, H_{arom}), 7.02–7.10 m (2H, H_{arom}), 7.15–7.23 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 10.06 m (2F), 11.27 m (2F), 16.98 br.s (2F), 20.42 m (2F). Found: *m*/*z* 748.2290 $[M]^+$. $C_{37}H_{32}F_8N_4O_4$. Calculated: *M* 748.2304.

1-[4-(1,3-Diphenyl-1*H*-pyrazol-5-yl)-2,3,5,6-tetrafluorophenyl]piperidin-4-ol (7). Compound **2a**, 0.3 g (0.64 mmol), was dissolved in 6 mL of methylene chloride, 0.13 g (0.96 mmol) of potassium carbonate was added, the mixture was cooled to 2–4°C, and a solution of 0.08 mL (0.96 mmol) of acryloyl chloride in 4 mL of methylene chloride was added. The mixture was stirred for 2 h at 2–4°C and for 3 h at room temperature. When the reaction was complete, the mixture was diluted with 20 mL of methylene chloride, washed with distilled water, dried over $CaCl_2$, and left overnight in a refrigerator. The solvent was removed under reduced pressure with slight heating, and the residue (0.26 g) was purified by column chromatography on Al_2O_3 (ethyl acetate–hexane, 1:3). Yield 0.1 g (27%), colorless powder, mp 162–164°C (from EtOAc–hexane, 2:3). ^1H NMR spectrum, δ, ppm: 1.52 br.s (1H, OH), 1.61–1.75 m (2H, CH_2), 1.93–2.04 m (2H, CH_2), 3.08–3.22 m (2H, CH_2), 3.38–3.52 m (2H, CH_2), 6.85 s (1H, 4-H), 7.28–7.39 m (3H, H_{arom}), 7.39–7.46 m (2H, H_{arom}), 7.85–7.92 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: 10.99 m (2F), 20.92 m (2F). Found, %: C 66.80; H 4.53; F 16.26; N 8.99. Found: *m*/*z* 467.1615 $[M]^+$. $C_{26}H_{21}F_4N_3O$. Calculated, %: C 66.38; H 4.61; F 16.20; N 9.10. *M* 467.1619.

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