Synthesis and some properties of 6-di(tri)fluoromethyl- and 5-di(tri)fluoroacetyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones

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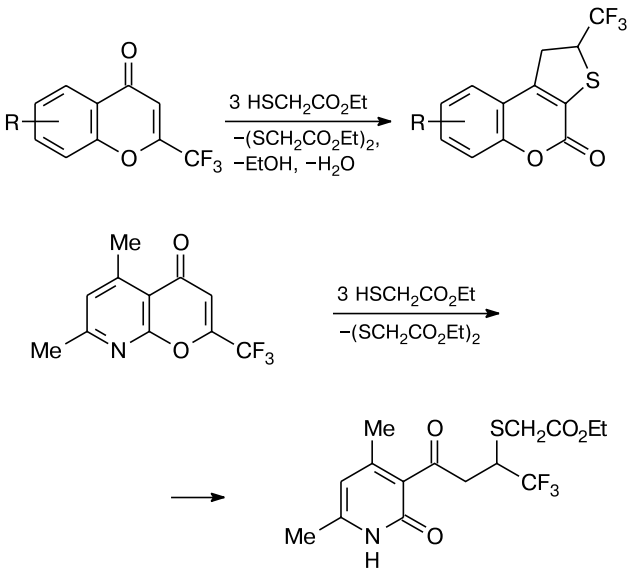
Condensation of 4-acetyl-5-hydroxy-3-methyl-1-phenylpyrazole with R^FCO_2Et (R^F = CF_2H, CF_3) in the presence of LiH affords 4-di(tri)fluoroacetoacetyl-5-hydroxy-3-methyl-1-phenylpyrazoles from which 6-di(tri)fluoromethyl- and 5-di(tri)fluoroacetyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones were synthesized. The reactions of pyranopyrazoles with hydrazine hydrate, ethyl mercaptoacetate, or aromatic amines proceed at the C(6) atom with pyrone ring opening and formation of aminoenones, pyrazoles, or thiophenes with the 5-hydroxy-3-methyl-1-phenyl-4-pyrazolyl fragment.

Key words: 6-di(tri)fluoromethyl- and 5-di(tri)fluoroacetyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones, diethoxymethyl acetate, substituted pyrazoles, thiophenes and thieno[3′,2′:4,5]pyrano[2,3-*c*]pyrazol-5(3*H*)-one.

It is known[1] that 2-polyfluoroalkylchromones can be used for syntheses of different R^F-containing heterocycles. For instance, the reaction of 2-CF_3-chromones with ethyl mercaptoacetate is a redox process that affords 1,2-dihydro-2-trifluoromethyl-4*H*-thieno[2,3-*c*]chromen-4-ones.[2,3] The replacement of the benzene ring in 2-CF_3-chromones by the pyridine cycle stops the reaction at the step of formation of ethyl [3-(4,6-dimethyl-2-oxo-1,2-dihydropyridin-3-yl)-3-oxo-1-trifluoromethylpropyl]sulfanyl acetate (Scheme 1).[4,5] Therefore, it was of interest to reveal the behavior in the reaction with ethyl mercaptoacetate of the heterocyclic system, whose pyrone ring containing the CF_3 group in the corresponding position is annelated to the pyrazole fragment.

Scheme 1



In the present work, we performed the condensation of 4-acetyl-5-hydroxy-3-methyl-1-phenylpyrazole with R^FCO_2Et (R^F = CF_2H, CF_3) and prepared for the first time 4-di(tri)fluoroacetoacetyl-5-hydroxy-3-methyl-1-phenylpyrazoles (**1a,b**). The latter were used, in turn, as the starting compounds for the synthesis of the target 6-di(tri)fluoromethyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones (**2a,b**) and 5-di(tri)fluoroacetyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones (**3a,b**). Owing to the presence of electron-withdrawing R^F- and R^FCO groups in compounds **2** and **3**, one could expect that they would be highly reactive and synthetically valuable R^F-containing compounds that allow the preparation of different heterocycles with a pharmacophoric pyrazolone substituent.[6]

Results and Discussion

Data on the synthesis and chemical properties of R^F-containing pyranopyrazoles **2** and **3** are lacking. At the same time, the methods for synthesis[7—10] and biological activity[11] of their nonfluorinated analogs, as well as the tautomeric structures of the starting 4-acyl-5-hydroxypyrazoles[12—15] and 4-acylacetyl-5-hydroxy-1-phenylpyrazoles,[7] were studied in rather detail. We found that the condensation of 4-acetyl-5-hydroxy-3-methyl-1-phenylpyrazole with ethyl di- and trifluoroacetates in

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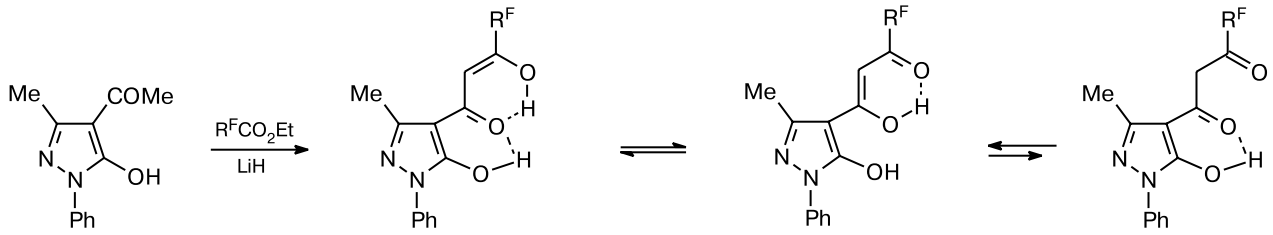
Scheme 2

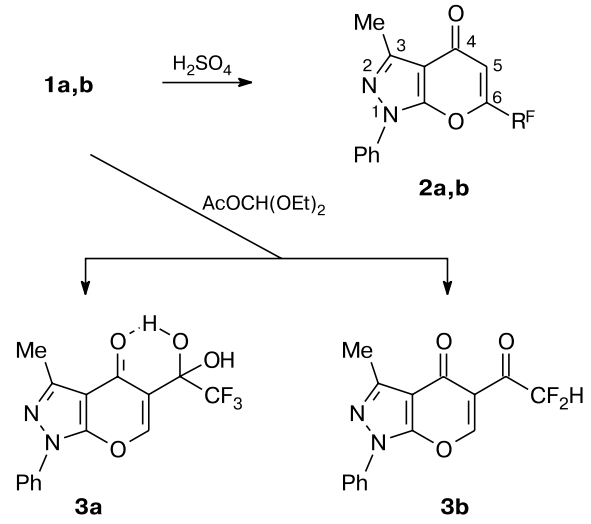


R^F = CF_3 (**a**), CF_2H (**b**)

the presence of LiH in THF affords diketones **1a** and **1b** in 93 and 87% yields, respectively. Diketones **1a** and **1b** exist in a $CDCl_3$ solution almost exclusively in the ketoenol form (Scheme 2). The ^{1}H NMR spectra of these compounds exhibit a singlet of the vinyl proton at δ 6.16—6.24 and two strongly broadened singlets of the enol (δ 14.4—14.5) and pyrazole (δ 11.7) hydroxyls, which agrees well with published data[7] for nonfluorinated analogs of diketones **1a,b**. The intensity of the singlet of the CH_2 group at δ 4.14—4.16 suggests that the content of the diketo form is only 3—4%, which is lower than that in the case of 4-acylacetyl-5-hydroxy-1-phenylpyrazoles (6—20%).[7]

The treatment of compounds **1a,b** with concentrated H_2SO_4 at ~20 °C is accompanied by pyrone ring closure, and 6-di(tri)fluoromethyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones **2a,b** are formed in 67—74% yields (Scheme 3). Their ^{1}H NMR spectra contain signals of aromatic protons and, in addition, a singlet of the methyl group (δ 2.64) and a singlet of the vinyl proton at δ 6.71 and 6.54 for compounds **2a** and **2b**, respectively.

Scheme 3



R^F = CF_3 (**a**), CF_2H (**b**)

The reaction of diketones **1a,b** with excess diethoxymethyl acetate at 140—150 °C for 15 min gives 5-di(tri)fluoroacetyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-ones **3a,b**. Trifluoromethylated pyranopyrazole **3a** is formed only as covalent hydrate, which is characteristic of 3-trifluoroacetylchromones,[16] whereas pyranopyrazole **3b**, according to the ^{1}H and ^{19}F NMR spectra, contains only 7—9% of the hydrate form (see Scheme 3).

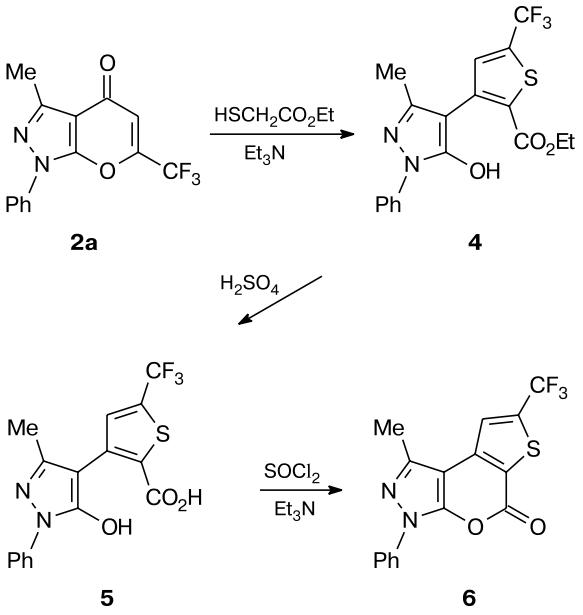
We found that the reaction of 6-CF_3-pyranopyrazole **2a** with excess ethyl mercaptoacetate in the presence of triethylamine proceeds at the C(6) atom followed by pyrone ring opening and intramolecular condensation of the aldol type. Unlike the earlier studied 2-CF_3-chromones[2,3] and their 8-aza analogs,[4,5] this transformation is not accompanied by the reduction of an intermediate under the action of ethyl mercaptoacetate and leads to the synthesis of ester **4**, which is hydrolyzed on heating with dilute H_2SO_4 to acid **5**. On reflux in toluene with thionyl chloride and triethylamine, acid **5** undergoes ring closure to form a new heterocyclic system: 1-methyl-3-phenyl-7-trifluoromethylthieno[3′,2′:4,5]pyrano[2,3-*c*]pyrazol-5(3*H*)-one (**6**) (Scheme 4).

Pyranopyrazole **2a** is nitrated at the *para*-position of the benzene ring to form 3-methyl-1-(4-nitrophenyl)-6-trifluoromethylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (**7**), and the reaction with hydrazine hydrate affords the expected bipyrazole **8** in 85% yield (Scheme 5). Compound **8** was prepared from diketone **1a** (76% yield).

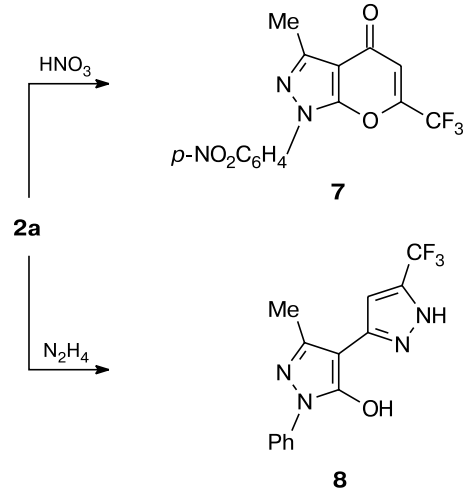
As a whole, pyranopyrazoles **2** are less reactive than earlier[17] studied 8-azachromones. For instance, we failed to perform the reactions of compound **2a** with pyrrolidine, ethylenediamine, hydroxylamine, methylhydrazine, and benzamidine. In all cases, either a complex mixture of products were formed, or the starting pyranopyrazole **2a** recovered.

Unlike compounds **2** in which the nucleophilic attack to the C(6) atom is sterically hindered, compounds **3** react readily at this center even with aromatic amines.

Scheme 4

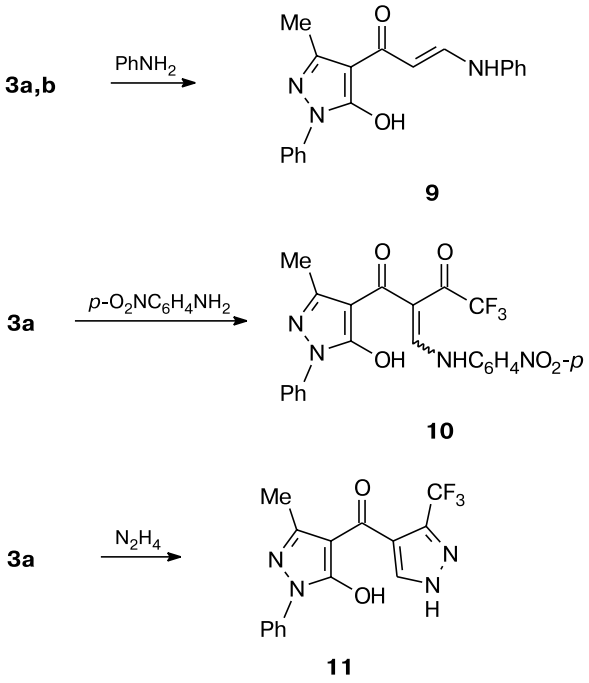


Scheme 5



However, it turned out that when reacting with aniline, they lose the di(tri)fluoroacetyl group and gave aminoenone **9** as a mixture of *E*- and *Z*-isomers in a ratio of 9 : 1 (J_{trans} = 12.5 Hz, J_{cis} = 7.9 Hz), while the reaction of **3a** with less basic *p*-nitroaniline ceased at the step of pyrone ring opening, due to which trifluoroacetylated aminoenone **10** was formed in 72% yield (the configuration of the double bond was not determined). Based on the elemental analysis data and a broadened singlet at δ 3.6 in the ^{1}H NMR spectrum, one can conclude that this compound exists as hydrate. The treatment of pyranopyrazole **3a** in propan-2-ol with hydrazine hydrate at ~20 °C produces dipyrazolyl ketone **11** in 52% yield (Scheme 6).

Scheme 6



Thus, the reaction of 6-R^F- and 5-R^FCO-containing pyranopyrazoles **2** and **3** with N- and S-nucleophiles starts from the attack at the C(6) atom and affords, depending on the nature of the reactant, aminoenones, pyrazoles, and thiophenes with the 5-hydroxy-3-methyl-1-phenyl-4-pyrazolyl fragment.

Experimental

IR spectra were recorded on a Perkin—Elmer Spectrum BX-II instrument in KBr pellets. ^{1}H and ^{19}F NMR spectra were obtained on a Bruker DRX-400 spectrometer with working frequencies of 400.1 and 376.5 MHz, respectively, and Me_4Si and C_6F_6 as internal standards. 4-Acetyl-5-hydroxy-3-methyl-1-phenylpyrazole was synthesized by the procedure described elsewhere.[18]

1-(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-4,4,4-trifluorobutane-1,3-dione (1a). Finely powdered LiH (0.28 g, 35.0 mmol) was added to a solution of ethyl trifluoroacetate (2.0 g, 14.1 mmol) and 4-acetyl-5-hydroxy-3-methyl-1-phenylpyrazole (2.0 g, 9.3 mmol) in anhydrous THF (10 mL). The resulting reaction mixture was refluxed for 3 h. Then the solvent was distilled off to dryness in a water bath under reduced pressure, and a mixture of AcOH (5 mL) and concentrated HCl (4 mL) was added to the residue. The mixture was refluxed for 5 min and poured onto crushed ice (40 g). The precipitate that formed was filtered off, washed with water, dried, and recrystallized from toluene. Diketone **1a** was obtained as yellowish crystals in a yield of 2.7 g (93%), m.p. 116—117 °C. Found (%): C, 53.66; H, 3.39; N, 8.74. $C_{14}H_{11}F_3N_2O_3$. Calculated (%): C, 53.85; H, 3.55; N, 8.97. IR, ν/cm^{-1}: 1655, 1590, 1568, 1501. ^{1}H NMR ($CDCl_3$), δ: 2.50 (s, 3 H, Me); 6.24 (s, 1 H, =CH);

7.34 (tt, 1 H, H(4′), J_o = 7.5 Hz, J_m = 1.3 Hz); 7.45—7.50 (m, 2 H, H(3′), H(5′)); 7.77—7.81 (m, 2 H, H(2′), H(6′)); 11.7 (br.s, 1 H, OH of pyrazole); 14.5 (br.s, 1 H, OH of enol).

1-(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-4,4-difluorobutane-1,3-dione (1b) was synthesized similarly to compound **1a** in 87% yield as colorless needle-like crystals, m.p. 89—90 °C (toluene). Found (%): C, 57.37; H, 4.23; N, 9.64. $C_{14}H_{12}F_2N_2O_3$. Calculated (%): C, 57.15; H, 4.11; N, 9.52. IR, ν/cm^{-1}: 1643, 1563, 1495. ^{1}H NMR ($CDCl_3$), δ: 2.50 (s, 3 H, Me); 6.10 (t, 1 H, CF_2H, $^2J_{H,F}$ = 54.2 Hz); 6.16 (s, 1 H, =CH); 7.33 (tt, 1 H, H(4′), J_o = 7.5 Hz, J_m = 1.3 Hz); 7.45—7.49 (m, 2 H, H(3′), H(5′)); 7.78—7.82 (m, 2 H, H(2′), H(6′)); 11.7 (br.s, 1 H, OH of pyrazole); 14.4 (br.s, 1 H, OH of enol).

3-Methyl-6-trifluoromethyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (2a). Diketone **1a** (4.7 g, 0.015 mol) was added by small portions with stirring to concentrated H_2SO_4 (19 mL), and the resulting solution was kept for 24 h at ~20 °C. Then the reaction mixture was poured onto ice, and the precipitate that formed was filtered off, dried, and recrystallized from a hexane—toluene (1 : 1) mixture. Compound **2a** was obtained as colorless needle-like crystals in a yield of 2.95 g (67%), m.p. 129—130 °C. Found (%): C, 57.03; H, 3.07; N, 9.47. $C_{14}H_9F_3N_2O_2$. Calculated (%): C, 57.15; H, 3.08; N, 9.52. IR, ν/cm^{-1}: 3039, 1672, 1598, 1557, 1530. ^{1}H NMR ($CDCl_3$), δ: 2.64 (s, 3 H, Me); 6.71 (s, 1 H, =CH); 7.42 (tt, 1 H, H(4′), J_o = 7.5 Hz, J_m = 1.3 Hz); 7.52—7.57 (m, 2 H, H(3′), H(5′)); 7.75—7.78 (m, 2 H, H(2′), H(6′)). ^{19}F NMR ($CDCl_3$), δ: 91.49 (s, CF_3).

6-Difluoromethyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (2b) was synthesized similarly to compound **2a** as colorless needles in 74% yield, m.p. 135—136 °C. Found (%): C, 60.88; H, 3.71; N, 10.25. $C_{14}H_{10}F_2N_2O_2$. Calculated (%): C, 60.87; H, 3.65; N, 10.14. IR, ν/cm^{-1}: 3038, 1669, 1597, 1553, 1527. ^{1}H NMR ($CDCl_3$), δ: 2.64 (s, 3 H, Me); 6.48 (t, 1 H, CF_2H, $^2J_{H,F}$ = 53.5 Hz); 6.54 (s, 1 H, =CH); 7.40 (tt, 1 H, H(4′), J_o = 7.5 Hz, J_m = 1.3 Hz); 7.51—7.56 (m, 2 H, H(3′), H(5′)); 7.75—7.79 (m, 2 H, H(2′), H(6′)). ^{19}F NMR ($CDCl_3$), δ: 39.84 (dd, CF_2H, $^2J_{H,F}$ = 53.5 Hz, $^4J_{H,F}$ = 0.6 Hz).

3-Methyl-1-phenyl-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)pyrano[2,3-*c*]pyrazol-4(1*H*)-one (3a). A solution of diketone **1a** (0.31 g, 1 mmol) in diethoxymethyl acetate (1.0 g, 6.0 mmol) was stored for 15 min at 140—150 °C. After cooling, the resulting mixture was diluted with hexane (3 mL), and the crystals that precipitated upon keeping were filtered off, washed with hexane, and dried. Hydrate **3a** was obtained as colorless crystals in a yield of 205 mg (60%), m.p. 150—151 °C. Found (%): C, 52.61; H, 3.21; N, 7.90. $C_{15}H_{11}F_3N_2O_4$. Calculated (%): C, 52.95; H, 3.26; N, 8.23. IR, ν/cm^{-1}: 3220, 1654, 1597, 1538, 1490. ^{1}H NMR (DMSO-d_6), δ: 2.54 (s, 3 H, Me); 7.46 (t, 1 H, H(4′), J_o = 7.4 Hz); 7.57—7.62 (m, 2 H, H(3′), H(5′)); 7.80—7.84 (m, 2 H, H(2′), H(6′)); 8.25 (br.s, 2 H, 2 OH); 8.48 (s, 1 H, =CH).

5-Difluoroacetyl-3-methyl-1-phenylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (3b) was synthesized similarly to compound **3a** in 64% yield, m.p. 185—186 °C. Found (%): C, 59.20; H, 3.28; N, 9.23. $C_{15}H_{10}F_2N_2O_3$. Calculated (%): C, 59.22; H, 3.31; N, 9.21. ^{1}H NMR ($CDCl_3$), δ, compound **3b**: 2.66 (s, 3 H, Me); 6.91 (t, 1 H, CF_2H, $^2J_{H,F}$ = 53.3 Hz); 7.43 (tt, 1 H, H(4′), J_o = 7.5 Hz, J_m = 1.3 Hz); 7.52—7.57 (m, 2 H, H(3′), H(5′)); 7.73—7.77 (m, 2 H, H(2′), H(6′)); 8.35 (s, 1 H, =CH); hydrate (7%): 2.63 (s, 3 H, Me); 5.57 (s, 2 H, 2 OH); 5.77 (t, 1 H, CF_2H, $^2J_{H,F}$ = 56.1 Hz); 8.09 (s, 1 H, =CH). ^{19}F NMR ($CDCl_3$), δ, compound **3b**: 31.03 (d, CF_2H, $^2J_{H,F}$ = 53.3 Hz); hydrate (9%): 28.98 (d, CF_2H, $^2J_{H,F}$ = 56.1 Hz).

Ethyl 3-(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-5-trifluoromethylthiophene-2-carboxylate (4). A mixture of pyranopyrazole **2a** (0.52 g, 1.77 mmol), ethyl mercaptoacetate (0.64 g, 5.3 mmol), and triethylamine (0.1 mL) was kept for 10 h at 80 °C, then methanol (3 mL) was added, and the mixture was cooled. The yellowish precipitate that formed was filtered off, washed with 70% methanol and water, dried, and recrystallized from a hexane—toluene (2 : 1) mixture. Compound **4** was obtained as colorless crystals in a yield of 0.22 g (31%), m.p. 194—195 °C. Found (%): C, 54.46; H, 3.81; N, 7.12. $C_{18}H_{15}F_3N_2O_3S$. Calculated (%): C, 54.54; H, 3.81; N, 7.07. IR, ν/cm^{-1}: 1727, 1614, 1594, 1557, 1500. ^{1}H NMR ($CDCl_3$), δ: 1.42 (t, 3 H, Me, J = 7.1 Hz); 2.33 (s, 3 H, Me); 4.43 (q, 2 H, CH_2, J = 7.1 Hz); 7.29 (br.t, 1 H, H(4′), J_o = 7.4 Hz); 7.42—7.47 (m, 3 H, =CH, H(3′), H(5′)); 7.77—7.81 (m, 2 H, H(2′), H(6′)); 9.3 (br.s, 1 H, OH). ^{1}H NMR (DMSO-d_6), δ: 1.22 (t, 3 H, Me, J = 7.1 Hz); 2.12 (s, 3 H, Me); 4.25 (q, 2 H, CH_2, J = 7.1 Hz); 7.25 (t, 1 H, H(4′), J_o = 7.4 Hz); 7.45—7.49 (m, 2 H, H(3′), H(5′)); 7.73—7.76 (m, 2 H, H(2′), H(6′)); 7.84 (q, 1 H, =CH, $^4J_{H,F}$ = 1.0 Hz); 10.8—12.2 (br.s, 1 H, OH).

3-(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-5-trifluoromethylthiophene-2-carboxylic acid (5). Ester **4** (0.21 g, 0.53 mmol) was added to a solution containing concentrated H_2SO_4 (2 mL) and water (1 mL), and the resulting mixture was kept for 1 h at 110 °C: until the formation of a homogeneous solution from which acid **5** began to crystallize soon. The mixture was diluted with cold water (5 mL) and left to stand for 24 h at 4 °C. The precipitate that formed was filtered off, washed with water (10 mL), and dried. Acid **5** was obtained as colorless crystals in a yield of 0.13 g (67%), m.p. 216—218 °C. Found (%): C, 52.27; H, 2.94; N, 7.57. $C_{16}H_{11}F_3N_2O_3S$. Calculated (%): C, 52.17; H, 3.01; N, 7.61. IR, ν/cm^{-1}: 3060, 1730, 1597, 1575, 1547, 1501. ^{1}H NMR (DMSO-d_6), δ: 2.12 (s, 3 H, Me); 7.25 (br.t, 1 H, H(4′), J_o = 7.4 Hz); 7.45—7.50 (m, 2 H, H(3′), H(5′)); 7.74—7.78 (m, 3 H, =CH, H(2′), H(6′)); 9.0—14.0 (br.s, 2 H, OH, CO_2H).

1-Methyl-3-phenyl-7-trifluoromethylthieno[3′,2′:4,5]pyrano[2,3-*c*]pyrazol-5(3*H*)-one (6). A mixture of acid **5** (0.1 g, 0.27 mmol), triethylamine (0.07 g, 0.7 mmol), and thionyl chloride (0.16 g, 1.4 mmol) in anhydrous toluene (15 mL) was refluxed for 20 min. Then the darkened solution was cooled, filtered off from the precipitate, and concentrated by evaporation. The crystals that precipitated were filtered off and recrystallized from hexane containing several drops of toluene. Compound **6** was obtained as light yellow needle-like crystals in a yield of 0.04 g (42%), m.p. 208—209 °C. Found (%): C, 54.97; H, 2.61; N, 8.00. $C_{16}H_9F_3N_2O_2S$. Calculated (%): C, 54.86; H, 2.59; N, 8.00. IR, ν/cm^{-1}: 3094, 1745, 1575, 1518. ^{1}H NMR (DMSO-d_6), δ: 2.60 (s, 3 H, Me); 7.44 (tt, 1 H, H(4′), J_o = 7.4 Hz, J_m = 1.2 Hz); 7.58—7.63 (m, 2 H, H(3′), H(5′)); 7.81—7.84 (m, 2 H, H(2′), H(6′)); 8.38 (q, 1 H, =CH, $^4J_{H,F}$ = 1.1 Hz).

3-Methyl-1-(4-nitrophenyl)-6-trifluoromethylpyrano[2,3-*c*]pyrazol-4(1*H*)-one (7). Pyranopyrazole **2a** (0.2 g, 0.68 mmol) was introduced with stirring and cooling into a mixture of 68% HNO_3 (0.22 mL) and concentrated H_2SO_4 (0.22 mL). The reaction mixture was heated for 20 min at 60 °C, cooled, and poured onto crushed ice (30 g). The precipitate that

formed was filtered off, washed with water, dried, and recrystallized from ethanol. Compound **7** was obtained as colorless crystals in a yield of 140 mg (61%), m.p. 183—184 °C. Found (%): C, 49.59; H, 2.28; N, 12.55. $C_{14}H_8F_3N_3O_4$. Calculated (%): C, 49.57; H, 2.38; N, 12.39. IR, ν/cm^{-1}: 3046, 1674, 1613, 1597, 1563, 1525, 1503. ^{1}H NMR ($CDCl_3$), δ: 2.65 (s, 3 H, Me); 6.77 (s, 1 H, =CH); 8.05 (d, 2 H, H(2′), H(6′), J_o = 9.2 Hz); 8.43 (d, 2 H, H(3′), H(5′), J_o = 9.2 Hz).

5-Hydroxy-3-methyl-1-phenyl-4-[3(5)-trifluoromethylpyrazol-5(3)-yl]pyrazole (8). A solution of diketone **1a** or pyranopyrazole **2a** (0.6 mmol) and 25% hydrazine hydrate (0.4 g, 2 mmol) in ethanol (3 mL) was refluxed for 15 min, cooled, and diluted with water (7 mL) containing 0.3 mL of concentrated HCl. The precipitate that formed was filtered off, washed with water, dried, and recrystallized from toluene containing several drops of butanol. The yields were 76% from **1a** and 85% from **2a**, colorless needles, m.p. 236—237 °C. Found (%): C, 54.58; H, 3.42; N, 18.03. $C_{14}H_{11}F_3N_4O$. Calculated (%): C, 54.55; H, 3.60; N, 18.18. IR, ν/cm^{-1}: 3326, 3069, 1670, 1630, 1591, 1556, 1502. ^{1}H NMR (DMSO-d_6), δ: 2.34 (s, 3 H, Me); 6.75 (s, 1 H, =CH); 7.28 (br.t, 1 H, H(4′), J_o = 7.4 Hz); 7.47—7.52 (m, 2 H, H(3′), H(5′)); 7.72—7.76 (m, 2 H, H(2′), H(6′)); 12.0 (br.s, 1 H, OH); 13.37 (s, 1 H, NH).

(*E*)-3-Anilino-1-(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)prop-2-en-1-one (9). A solution of pyranopyrazole **2b** (70 mg, 0.23 mmol) and aniline (43 mg, 0.46 mmol) in methanol (1 mL) was kept for 24 h at ~20 °C. The precipitated crystals were filtered off, washed with methanol, and dried. Compound **9** was obtained as yellow crystals in a yield of 40 mg (55%), m.p. 156—157 °C. The same compound was obtained from pyranopyrazole **2a** on reflux for 10 min with aniline in propan-2-ol (43%). Found (%): C, 70.11; H, 5.23; N, 12.99. $C_{19}H_{17}N_3O_2 \cdot 0.25H_2O$. Calculated (%): C, 70.46; H, 5.45; N, 12.97. IR, ν/cm^{-1}: 1671, 1643, 1600, 1591, 1531, 1499. ^{1}H NMR ($CDCl_3$), δ, *E*-isomer (90%): 2.44 (s, 3 H, Me); 5.87 (d, 1 H, =CH, J = 12.5 Hz); 7.07—7.22 (m, 5 H, NH, H arom.); 7.35—7.44 (m, 4 H, H arom.); 7.92—7.96 (m, 2 H, H arom.); 8.30 (t, 1 H, =CHN, J = 13.0 Hz); *Z*-isomer (10%): 2.49 (s, 3 H, Me); 5.53 (d, 1 H, =CH, J = 7.9 Hz); 7.07—7.44 (m, 8 H, H arom.); 7.85—7.88 (m, 2 H, H arom.); 11.24 (d, 1 H, NH, J = 13.0 Hz).

1-(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(4-nitroanilinomethylene)-4,4,4-trifluorobutane-1,3-dione (10). A solution of pyranopyrazole **2a** (100 mg, 0.29 mmol) and *p*-nitroaniline (60 mg, 0.44 mmol) in propan-2-ol (3 mL) was refluxed for 10 min. Then the solvent was evaporated, and the residue was recrystallized from methanol. Compound **10** was obtained as yellow crystals in a yield of 100 mg (72%), m.p. 157—158 °C. Found (%): C, 52.76; H, 3.60; N, 11.48. $C_{21}H_{15}F_3N_4O_5 \cdot H_2O$. Calculated (%): C, 52.73; H, 3.58; N, 11.71. IR, ν/cm^{-1}: 1644, 1599, 1555, 1534, 1504, 1490. ^{1}H NMR (DMSO-d_6), δ: 2.44 (s, 3 H, Me); 3.58 (br.s, 2 H, H_2O); 7.41 (t, 1 H, H(4′), J_o = 7.4 Hz); 7.55—7.60 (m, 2 H, H(3′), H(5′)); 7.61—7.73 (m, 4 H, C_6H_4); 7.95 (d, 1 H, =CH, J = 12.3 Hz); 8.22—8.26 (m, 2 H, H(2′), H(6′)); 10.25 (br.s, 1 H, OH); 12.14 (br.d, 1 H, NH, $J \approx$ 12.0 Hz).

(5-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)[3(5)-trifluoromethyl-1*H*-pyrazol-4-yl]methanone (11). Pyranopyrazole **2a** (100 mg, 0.29 mmol) was dissolved on heating in propan-2-ol (3 mL), and a 25% solution of hydrazine hydrate (80 mg, 0.4 mmol) was added. The resulting yellow solution was kept for 24 h at ~20 °C, after which the solvent was evaporated, and the residue was washed with methanol and dried. Compound **11** was obtained as light yellow crystals in a yield of 51 mg (52%), m.p. 255—257 °C. Found (%): C, 52.25; H, 3.18; N, 16.04. $C_{15}H_{11}F_3N_4O_2 \cdot 0.5H_2O$. Calculated (%): C, 52.18; H, 3.50; N, 16.23. IR, ν/cm^{-1}: 3140, 3049, 1627, 1597, 1568, 1503. ^{1}H NMR (DMSO-d_6), δ: 2.34 (s, 3 H, Me); 7.32 (tt, 1 H, H(4′), J_o = 7.4 Hz, J_m = 1.2 Hz); 7.47—7.52 (m, 2 H, H(3′), H(5′)); 7.66—7.70 (m, 2 H, H(2′), H(6′)); 8.60 (s, 1 H, =CH); 13.84 (br.s, 1 H, NH); no OH signal is observed. ^{19}F NMR (DMSO-d_6), δ: 102.70 (s, CF_3).

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