# Synthesis of new fluorine-containing pyrazolo[3,4-*b*]pyridinones as promising drug precursors

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Methods for the synthesis of 4-R-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones (R = $CF_2SAr$ and 4-CFHSAr) were developed. The derivatives with R = $CF_2SAr$ were obtained by both heterocyclization of 1-substituted 5-aminopyrazoles with ethyl 4,4-difluoro-3-oxo-4-phenylsulfanylbutanoate and replacement of the Br atom in 4-bromodifluoromethyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones by sodium arenethiolates. The fragment 4-CFHSAr was introduced by replacement of the Cl atom in 4-chlorofluoromethyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones by sodium arenethiolates. Oxidation of 4-$CF_2SPh$-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones gave the corresponding sulfoxides; their structures were confirmed by X-ray diffraction data.

**Key words:** pyrazolo[3,4-*b*]pyridines, fluorine-containing 6,7-dihydro-1*H*-pyrazolo[3,4-*b*]-pyridin-6-ones, 1-substituted 5-aminopyrazoles, heterocyclization, fluorine-containing ethyl acetoacetates, microwave irradiation, arylsulfanyl(difluoro)methyl group, arylsulfinyl(difluoro)-methyl group.

The pyrazolo[3,4-*b*]pyridine framework is a key structural fragment of many heterocyclic compounds showing a broad spectrum of biological activity.[1] In the last decade, some heterocycles of this class have been found to regulate the cardiovascular system[2] and possess antiviral,[3] antitumor,[4] antiinflammatory,[5] antimicrobial,[6] and antiparasitic properties.[7] Fluoroalkyl-containing pyrazolo-[3,4-*b*]pyridines are also believed to be candidates for medications and considered to be potential inhibitors of adenosine deaminase and inosine 5′-monophosphate dehydrogenase.[8] Primary attention has been given to the synthesis of $CF_3$-containing pyrazolo[3,4-*b*]pyridines **1**,[9] while derivatives containing the fragment $CF_2$ were represented by $CF_2H$-containing pyrazolo[3,4-*b*]pyridines.[8] At the same time, the structural fragment $CF_2$, which is sterically similar to the $CH_2$ group, contrasts sharply with the latter in polarity and reactivity.[10] In particular, this fragment is thought to be an isopolar and isosteric substitute for oxygen.[11] Some $CF_2$-containing compounds exhibit high physiological activity,[12] including antitumor[13] and antifungal effects[14] and inhibition of HIV-1 reverse transcriptase[15] and various protein kinases.[16] Thus, development of synthetic routes to compounds with functionalized fragments $CF_2$ is an important step in searching for novel biologically active molecules. Recently, we have published a method for the synthesis of 4-[(difluoro)(phenoxy)methyl]-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (**2**) from ethyl 4,4-difluoro-4-phenoxyacetoacetate and 5-amino-1-(3-chlorophenyl)-3-methylpyrazole.[17]

The goal of the present work was to develop methods for the synthesis of earlier unknown 6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones **3** containing arylsulfanyl(difluoro)methyl ($ArSCF_2$—) and arylsulfanyl(fluoro)methyl groups (ArSCHF—) at position 4.

Within the scope of the present work, we studied two synthetic routes to target compounds **3**. The first route involves heterocyclization of 1-substituted 5-aminopyrazoles with acyclic compounds already containing the fragment $ArSCF_2$ or ArSCHF (*e.g.*, earlier unknown esters of 4-arylthio-4,4-difluoroacetoacetic and 4-arylthio-4-fluoroacetoacetic acid **4**) (Scheme 1). The second route involves the formation of the fragments $ArSCF_2$ and ArSCHF in a heteromolecule *via* substitution of the arylsulfanyl group for the halogen atom in 4-$CF_2Br$- (or 4-$CF_2Cl$-) and 4-CHFCl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones (see Scheme 1).

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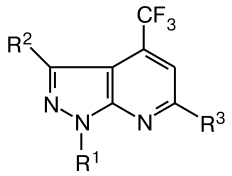
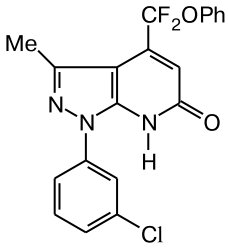


**1**



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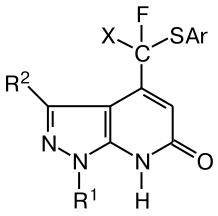
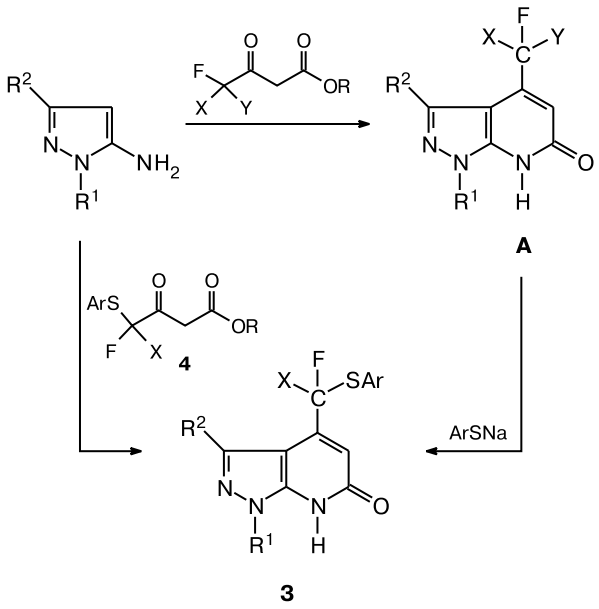


**3**

X = F, H

**Scheme 1**

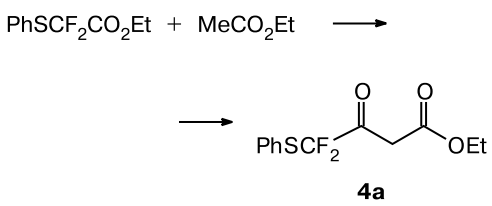


**A:** X = F, Y = Br (Cl); X = H, Y = Cl
**3, 4:** X = F, H

## Results and Discussion

For the first approach, we should previously synthesize 4-arylthio-4,4-difluoroacetoacetic and 4-arylthio-4-fluoroacetoacetic acid esters **4** (see Scheme 1). Ethyl 4,4-difluoro-4-phenylthioacetoacetate (**4a**) was obtained in two ways: (1) condensation of ethyl difluoro(phenylthio)acetate with ethyl acetate in the presence of NaH and (2) lithiation of ethyl acetate with lithium diisopropylamide (LDA) at −75 °C followed by acylation of the lithium derivative with ethyl difluoro(phenylthio)acetate at the same temperature (Scheme 2).

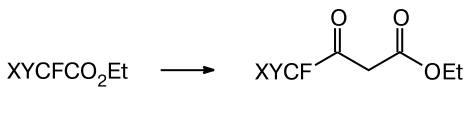
**Scheme 2**



**Conditions:** NaH, $Et_2O$ or LDA, −75 °C.

Ethyl 4-fluoro-4-phenylthioacetoacetate (**4b**) was obtained as shown in Scheme 3. Following this scheme, we also obtained known[18] ethyl 4-bromo-4,4-difluoroacetoacetate (**4c**) and ethyl 4-chloro-4,4-difluoroacetoacetate (**4d**) and undocumented ethyl 4-chloro-4-fluoroacetoacetate (**4e**).

**Scheme 3**

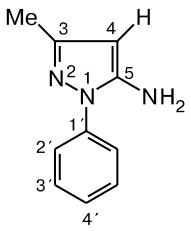


**4b—e**

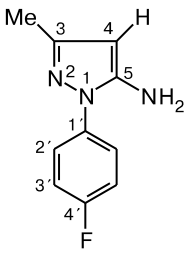
| 4 | X | Y | 4 | X | Y |
|---|---|---|---|---|---|
| **b** | H | PhS | **d** | F | Cl |
| **c** | F | Br | **e** | H | Cl |

**Conditions:** LDA, $MeCO_2Et$, $Et_2O$, −75 °C.

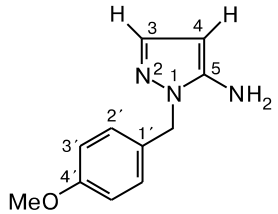
Then we studied heterocyclization reactions of acetoacetic derivatives **4a—e** with 1-substituted 5-aminopyrazoles **5a—c**.



**5a**



**5b**

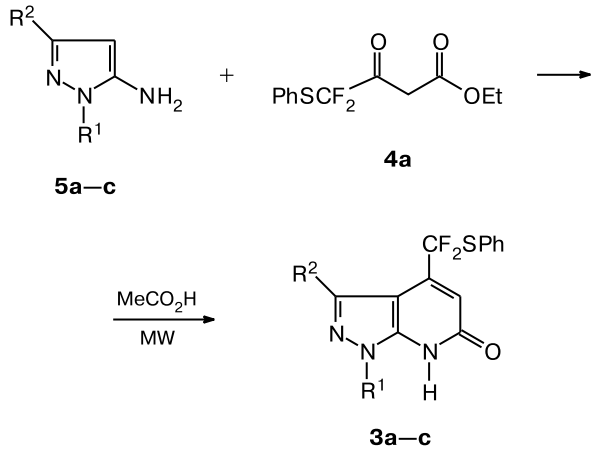


**5c**

A reaction of ethyl 4,4-difluoro-4-phenylthioacetoacetate **4a** with pyrazole **5a** in boiling acetic acid gave a complex mixture of products precluding isolation of the

target pyrazolo[3,4-*b*]pyridine (**3a**). A decrease in the reaction temperature to 70 °C, as well as heating in DMF at 80 °C, was ineffective. The target pyrazolo[3,4-*b*]pyridines **3a**—**c** were obtained when solutions of oxo ester **4a** and pyrazoles **5a**—**c** in acetic acid were exposed to microwave irradiation for 7 min (Scheme 4).

**Scheme 4**



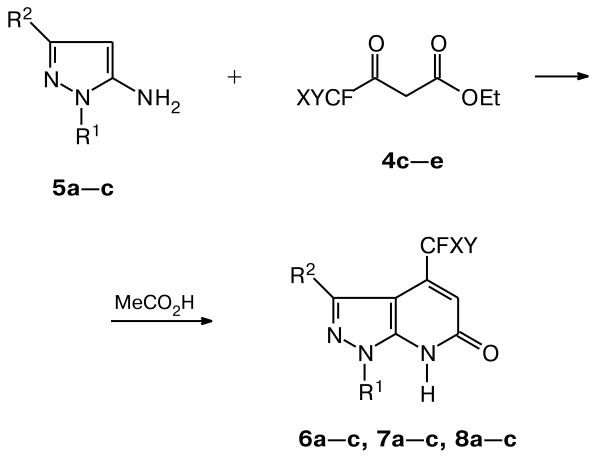

$R^1$ = Ph, $R^2$ = Me (**3a**); $R^1$ = 4-$FC_6H_4$, $R^2$ = Me (**3b**); $R^1$ = 4-$MeOC_6H_4CH_2$, $R^2$ = H (**3c**)
MW denotes microwave irradiation

With ethyl 4-fluoro-4-phenylthioacetoacetate **4b**, all our attempts to obtain the target 4-ArSCHF-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones **3** from oxo ester **4b** and pyrazoles **5a**—**c**, including heating in acetic acid under microwave irradiation, were unsuccessful.

Ethyl 4-bromo-4,4-difluoroacetoacetate (**4c**) reacts with aminopyrazoles **5a**—**c** in boiling acetic acid for 3 h to give pyrazolo[3,4-*b*]pyridines **6a**—**c** in high yields. Similar reactions of ethyl 4-chloro-4,4-difluoroacetoacetate (**4d**) and ethyl 4-chloro-4-fluoroacetoacetate (**4e**) produce pyrazolo[3,4-*b*]pyridines **7a**—**c** and **8a**—**c**, respectively, in high yields (Scheme 5).

Pyrazolopyridines **6a**—**8a** were used for the synthesis of the target products **3** according to the second approach. For instance, pyrazolo[3,4-*b*]pyridine **3a** was obtained by a reaction of 4-$CF_2$Br-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]-pyridin-6-one (**6a**) with an excess of PhSNa in DMF, in which the Br atom is replaced by the arylsulfanyl group. For this transformation to occur, we accurately selected appropriate reaction conditions. It turned out that the complete conversion of compound **6a**, as well as high yields of the target products, cannot be achieved unless oxygen is thoroughly removed from the solutions of the reagents in DMF. Under these conditions, the reaction was completed with mild heating (50 °C) in 2 h; pyrazolo[3,4-*b*]-pyridine **3a** and its 4-$ArSCF_2$ analogs **3d,e** were isolated in high yields (Scheme 6). Nevertheless, we failed to avoid

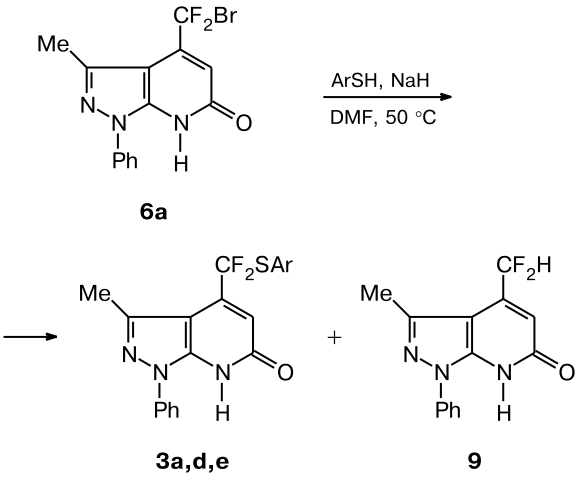
**Scheme 5**




| Compound | X | Y | $R^1$ | $R^2$ |
|---|---|---|---|---|
| **6a** | F | Br | Ph | Me |
| **6b** | F | Br | 4-$FC_6H_4$ | Me |
| **6c** | F | Br | 4-$MeOC_6H_4CH_2$ | H |
| **7a** | F | Cl | Ph | Me |
| **7b** | F | Cl | 4-$FC_6H_4$ | Me |
| **7c** | F | Cl | 4-$MeOC_6H_4CH_2$ | H |
| **8a** | H | Cl | Ph | Me |
| **8b** | H | Cl | 4-$FC_6H_4$ | Me |
| **8c** | H | Cl | 4-$MeOC_6H_4CH_2$ | H |

the reduction[19] of the 4-$CF_2$Br group to the 4-$CF_2$H group: in all cases, difluoromethylpyrazolopyridine **9** was formed as a by-product. Compound **9** was also obtained by condensation of aminopyrazole **5a** with ethyl 4,4-difluoroacetoacetate **4f** in boiling acetic acid.

**Scheme 6**



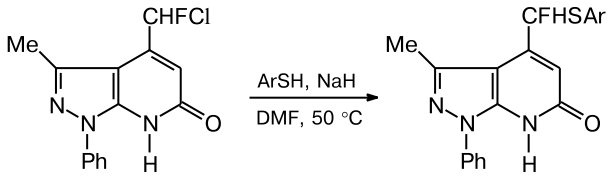

Ar = Ph (**3a**), 4-$ClC_6H_4$ (**3d**), 4-$MeC_6H_4$ (**3e**)

The Cl atom in 4-$CF_2$Cl-6,7-dihydro-1*H*-pyrazolo-[3,4-*b*]pyridin-6-one **7a** was not replaced by the arylthio

group under the action of excess PhSNa in DMF at 20—130 °C.

However, with 4-CHFCl-6,7-dihydro-1*H*-pyrazolo-[3,4-*b*]pyridin-6-one **8a**, this replacement easily occurred in the presence of a threefold excess of sodium benzenethiolate or sodium 4-chlorobenzenethiolate in DMF at 20 °C; compounds **3f** and **3g** were isolated in high yields (Scheme 7). Thus, the target compounds 4-ArSCHF-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones **3f**,**g** were obtained according to the second approach.

**Scheme 7**

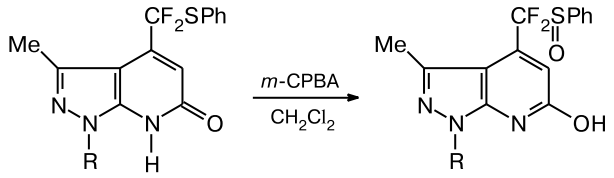



**8a** **3f,g**

Ar = Ph (**3f**), 4-$ClC_6H_4$ (**3g**)

Pyrazolo[3,4-*b*]pyridines containing the arylsulfinyl-(difluoro)methyl group ($ArSOCF_2$—) are unknown. We demonstrated that the difluoro(phenylsulfanyl)-methyl group ($PhSCF_2$—) in compounds **3a,b** can be oxidized with MCPBA into the difluoro(phenylsulfinyl)-methyl group ($PhSOCF_2$—). This transformation gave the corresponding sulfoxides **10a,b** in good yields (Scheme 8).

**Scheme 8**




**3a,b** **10a,b**

R = Ph (**3a**, **10a**), 4-$FC_6H_4$ (**3b**, **10b**)

The structures of the compounds obtained were confirmed by elemental analysis (Table 1), NMR spectroscopy (Table 2), IR spectroscopy, mass spectrometry (Table 3), and X-ray diffraction (for **10a,b** only). Clearly, the last data also provide evidence for the 1*H*-pyrazolo[3,4-*b*]-pyridine structure of, and the presence of the 4-fluoroalkyl substituent in, compounds **3a,b**, **6a,b**, and **7a,b** (precursors of sulfoxides **10a,b**) and compounds **3d,e** and **9**. The structures of 1*H*-pyrazolo[3,4-*b*]pyridines **8a**—**c**, their derivatives **3f,g**, and compounds **3c**, **6c**, **7c**, notably the presence of the 4-fluoroalkyl substituent, were confirmed by $^{13}C$ NMR spectroscopy and 2D NMR experiments (NOESY, HSQC, and HMBC).

It should be noted that the discussed[8,9c,9e,17,20] trends for the 1D $^{13}C$ NMR spectra of 4-methyl- and 4-fluoromethyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones and related 4-trifluoromethylquinolin-2-ones, which confirm the presence of the methyl (fluoromethyl) substituent at the γ-position of the pyridine ring of the 1*H*-pyrazolo[3,4-*b*]-pyridin-2-one (quinolin-2-one) system, are true for the compounds obtained here. For instance, the signals for the C(6) atom in their $^{13}C$ NMR spectra appear at δ 160—165, while the chemical shifts of the C(4) atom are δ 135—143 (see Table 2).

The IR absorption spectra of compounds **3a**—**g**, **6a**—**c**, **7a**—**c**, **8a**—**c**, and **9** (KBr pellets) differ from those of compounds **10a,b**. For instance, the IR spectra of the compounds of the former group contain very intense bands due to the C=O stretching vibrations (ν(CO) ≈ ≈ 1653—1667 $cm^{-1}$, see Table 3) and a wide band with several peaks at 3300—2400 $cm^{-1}$.[21] At the same time, the IR spectra of compounds **10a,b** show very weak bands in the range of the C=O vibrations. The spectrum of compound **10b** contains a wide band of medium intensity with a peak at 3208 $cm^{-1}$, which can be assigned to the OH stretching vibrations. A similar medium-intensity wide band with a peak at 3064 $cm^{-1}$ appears in the IR spectrum of compound **10a**. This spectral pattern for compounds **10a,b** agrees with the X-ray diffraction data (see above): according to them, both compounds in the crystal exist in the tautomeric hydroxy (or lactim) form, while compounds **3a**—**g**, **6a**—**c**, **7a**—**c**, **8a**—**c**, and **9** in the solid state mainly exist in the keto (or lactam) form.[9d] Apparently, the 4-difluoro(phenylsulfinyl)methyl group ($PhSOCF_2$-) in 6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones is a structural element enabling variation of the tautomeric nature of the heterocycle.[22]*

The general view of structure **10b** with the atomic numbering adopted in crystallographic experiments is shown in Fig. 1, *b*. The molecule exists in a tweezers-like conformation folded along the bonds C(11)—C(8)—S(1)—C(1). The distance between the centroids of the phenyl substituent at the sulfinyl group and of the pyridine ring is 4.135 Å. The torsion angle O(1)—S(1)—C(8)—C(11) is 165.55°. The phenyl substituent at the N(1) atom is virtually coplanar with the pyrazolo[3,4-*b*]pyridine framework: the maximum deviation of the atoms from the mean-square plane does not exceed 0.130 Å. The bond lengths have nearly standard values. The C(1)—S(1) bond between the sulfur atom and the phenyl substituent is substantially shorter

* *N*-Oxide is a structural fragment that shifts the tautomeric equilibrium in 3-oxo-1*H*-pyrazolo[4,3-*c*]pyridines toward the lactim form.[22a] Attempts to change the tautomeric form in quinolin-2-ones by introduction of structural fragments have been described.[22b]

**Table 1.** Yields and selected physicochemical characteristics of compounds **3a—g**, **6a—c, 7a—c**, **8a—c**, **9**, and **10a,b**

| Compound | Yield (%) | M.p./°C (LP—EA)* | Found / Calculated (%) | | | Molecular formula |
|---|---|---|---|---|---|---|
| | | | C | H | N | |
| **3a** | 65 | 179—180 | 62.85<br>62.65 | 3.71<br>3.94 | 10.96<br>10.96 | $C_{20}H_{15}F_2N_3OS$ |
| **3b** | 67 | 196—198 | 59.64<br>59.84 | 3.34<br>3.52 | 10.29<br>10.47 | $C_{20}H_{14}F_3N_3OS$ |
| **3c** | 70 | 156—157 | 60.78<br>61.01 | 4.06<br>4.14 | 10.18<br>10.16 | $C_{21}H_{17}F_2N_3O_2S$ |
| **3d** | 77 | 199—200 | 57.12<br>57.49 | 3.09<br>3.38 | 9.88<br>10.06 | $C_{20}H_{14}ClF_2N_3OS$ |
| **3e** | 77 | 214—215 | 63.77<br>63.46 | 4.21<br>4.31 | 10.38<br>10.57 | $C_{21}H_{17}F_2N_3OS$ |
| **3f** | 89 | 173—174 | 65.67<br>65.74 | 4.37<br>4.41 | 11.32<br>11.50 | $C_{20}H_{16}FN_3OS$ |
| **3g** | 85 | 195—196 | 60.21<br>60.07 | 3.88<br>3.78 | 10.30<br>10.51 | $C_{20}H_{15}ClFN_3OS$ |
| **6a** | 77 | 156—157 | 47.60<br>47.48 | 2.82<br>2.85 | 11.87<br>11.86 | $C_{14}H_{10}BrF_2N_3O$ |
| **6b** | 73 | 170—171 | 45.32<br>45.19 | 2.33<br>2.44 | 11.09<br>11.29 | $C_{14}H_9BrF_3N_3O$ |
| **6c** | 85 | 205—206 | 47.07<br>46.90 | 3.08<br>3.15 | 10.92<br>10.94 | $C_{15}H_{12}BrF_2N_3O_2$ |
| **7a** | 70 | 157—158 | 54.43<br>54.30 | 3.23<br>3.25 | 13.55<br>13.57 | $C_{14}H_{10}ClF_2N_3O$ |
| **7b** | 74 | 184—185 | 51.15<br>51.31 | 2.88<br>2.77 | 12.78<br>12.82 | $C_{14}H_9ClF_3N_3O$ |
| **7c** | 87 | 197—198 | 52.89<br>53.03 | 3.66<br>3.56 | 12.24<br>12.37 | $C_{15}H_{12}ClF_2N_3O_2$ |
| **8a** | 72 | 182—183 | 57.86<br>57.64 | 3.68<br>3.80 | 14.35<br>14.40 | $C_{14}H_{11}ClFN_3O$ |
| **8b** | 74 | 223—224 | 54.42<br>54.30 | 3.24<br>3.25 | 13.56<br>13.57 | $C_{14}H_{10}ClF_2N_3O$ |
| **8c** | 79 | 187—188 | 56.00<br>56.00 | 4.03<br>4.07 | 12.97<br>13.06 | $C_{15}H_{13}ClFN_3O_2$ |
| **9** | 76 | 184—185 | 60.87<br>61.09 | 3.89<br>4.03 | 15.45<br>15.27 | $C_{14}H_{11}F_2N_3O$ |
| **10a** | 65 | 157—158 | 60.11<br>60.14 | 3.67<br>3.79 | 10.48<br>10.52 | $C_{20}H_{15}F_2N_3O_2S$ |
| **10b** | 60 | 188—189 | 57.45<br>57.55 | 3.27<br>3.38 | 10.02<br>10.07 | $C_{20}H_{14}F_3N_3O_2S$ |

* The solvent system is light petroleum—ethyl acetate.

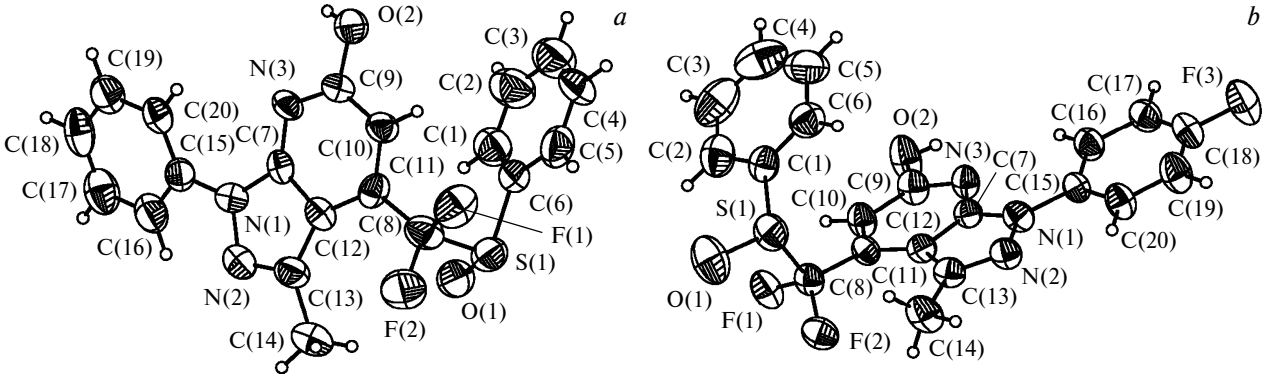



**Fig. 1.** General view of structures **10a** (*a*) and **10b** (*b*) with thermal displacement ellipsoids ($p = 50\%$).

**Table 2.** $^{1}H$, $^{13}C$, and $^{19}F$ NMR spectra of compounds **3a—c**, **3f**, **6a—c**, **7a—c**, **8a—c**, **9**, and **10a**

| Compound | NMR (DMSO-$d_6$, δ, *J*/Hz) | | |
|---|---|---|---|
| | $^{1}H$ | $^{13}C$ | $^{19}F$ |
| **3a** | 2.71 (s, 3 H, Me); 6.61 (s, 1 H, H(5)); 7.32 (t, 1 H, Ar, *J* = 6.7); 7.46—7.57 (m, 5 H, Ar); 7.62 (d, 2 H, Ar, *J* = 7.0); 8.12 (d, 2 H, Ar, *J* = 7.4); 12.03 (br.s, 1 H, NH) | 16.29 ($CH_3$); 103.77 (C(5)); 105.66 (C(3a)); 121.60 (C(2′)(NPh)); 125.61 (C1′(SPh)), 126.05 (t, $CF_2S$, $J_{C,F}$ = 277.5); 126.42 (C(4′)(NPh)); 129.47, 130.13 (C(3′)(NPh), C(3′)(SPh)); 131.37 (C(4′)(SPh)); 136.71 (C(2′)(SPh)); 139.12 (C(1′)(NPh)); 139.91 (t, C(4), $J_{C,F}$ = 26.5); 141.52 (C(3)), 150.93 (C(7a)); 163.65 (C(6)) | 7.70 (s, $CF_2SPh$) |
| **3b** | 2.72 (s, 3 H, Me); 6.62 (s, 1 H, H(5)); 7.40 (t, 2 H, Ar, *J* = 8.8); 7.52 (t, 2 H, Ar, *J* = 7.5); 7.58 (d, 1 H, Ar, *J* = 7.5); 7.65 (d, 2 H, Ar, *J* = 7.0); 8.15 (m, 2 H, Ar); 12.07 (br.s, 1 H, NH) | 16.01 ($CH_3$); 103.61 (C(5)); 105.47 (C(3a)); 115.86 (d, C(3′)(NAr), $J_{C,F}$ = 23.2); 123.19 (d, C(2′)(NAr), $J_{C,F}$ = 7.8); 125.50 (C(1′)(SPh)); 125.75 (t, $CF_2S$, $J_{C,F}$ = 278.0); 129.75 (C(3′)(SPh)); 131.03 (C(4′)(SPh)); 135.31 (C(1′)(NAr)); 136.46 (C(2′)(SPh)); 139.90 (t, C(4), $J_{C,F}$ = 26.5); 141.48 (C(3)); 150.54 (C(7a)); 160.18 (d, C(4′)(NAr), $J_{C,F}$ = 241.2); 163.46 (C(6)) | −38.04 (m, 1 F, ArF); 7.44 (s, $CF_2SPh$, 2 F) |
| **3c*** | 3.83 (s, 3 H, OMe); 5.56 (s, 2 H, $CH_2$); 6.50 (s, 1 H, H(5)); 6.91 (d, 2 H, Ar, *J* = 8.7); 7.41—7.54 (m, 5 H, Ar); 7.66 (d, 2 H, Ar, *J* = 8.7); 7.93 (s, 1 H, HC(3)); 13.69 (br.s, 1 H, NH) | 51.23 ($CH_2$); 55.27 ($OCH_3$); 102.98 (C(3a)); 109.90 (C(5)); 114.11 (C(3′)($NCH_2Ar$)); 125.59 (t, $CF_2S$, $J_{C,F}$ = 279.7); 125.85 (C(1′)(SPh)); 127.68 (C(1′)($NCH_2Ar$)); 129.29 (C(3′)(SPh)); 129.62 (C(2′)($NCH_2Ar$)); 130.59 (C(4′)(SPh)); 134.15 (C(3)); 136.70 (C(2′)(SPh)); 141.62 (C(7a)), 142.63 (t, C(4), $J_{C,F}$ = 27.7); 159.52 (C(4′)($NCH_2Ar$)); 164.88 (C(6)) | 3.05 (s, $CF_2SPh$) |
| **3f** | 2.68 (s, 3 H, Me); 6.58 (s, 1 H, H(5)); 7.32 (t, 1 H, Ar, *J* = 7.3); 7.44—7.60 (m, 7 H, Ar); 7.68 (d, 1 H, CHF, $J_{H,F}$ = 53.4); 8.17 (d, 2 H, Ar, *J* = 7.8); 11.70 (br.s, 1 H, NH) | 15.60 ($CH_3$); 97.80 (d, CHFS, $J_{C,F}$ = 224.5); 103.23 (d, C(5), $J_{C,F}$ = 7.7); 106.40 (C(3a)); 121.69 (C(2′)(NPh)); 125.81 (C(4′)(NPh)); 128.87 (C(3′)(NPh)); 128.98 (C(4′)(SPh)); 129.41 (C(3′)(SPh)); 131.74 (C(1′)(SPh)); 132.63 (C(2′)(SPh)); 139.24 (C(1′)(NPh)); 141.66 (C(3)); 142.52 (d, C(4), $J_{C,F}$ = 24.3); 149.96 (C(7a)); 163.93 (C(6)) | −75.79 (d, $J_{H,F}$ = 53.4) |
| **6a** | 2.61 (s, 3 H, Me); 6.80 (s, 1 H, H(5)); 7.34 (t, 1 H, Ar, *J* = 7.15); 7.53 (t, 2 H, Ar, *J* = 7.5); 8.09 (d, 2 H, Ar, *J* = 7.8); 12.21 (br.s, 1 H, NH) | 16.00 (t, $CH_3$, $J_{C,F}$ = 4.5); 101.88 (t, C(5), $J_{C,F}$ = 6.6); 104.14 (C(3a)); 115.39 (t, $CF_2Br$, $J_{C,F}$ = 302.0); 121.83 (C(2′)); 126.62 (C(4′)); 129.48 (C(3′)); 138.94 (C(1′)); 140.82 (C(3)); 141.35 (t, C(4), $J_{C,F}$ = 26.5); 151.07 (C(7a)); 163.80 (C(6)) | 30.06 (s, $CF_2Br$) |
| **6b** | 2.67 (s, 3 H, Me); 6.87 (s, 1 H, H(5)); 7.44 (t, 2 H, Ar, *J* = 8.5); 8.16 (m, 2 H, Ar); 12.21 (br.s, 1 H, NH) | 15.80 ($CH_3$); 101.90 (t, C(5), $J_{C,F}$ = 6.3); 103.90 (C(3a)); 115.25 (t, $CF_2Br$, $J_{C,F}$ = 302.6); 116.14 (d, C(3′), $J_{C,F}$ = 23.0); 123.65 (d, C(2′), $J_{C,F}$ = 8.3); 135.19 (C(1′)); 140.93 (C(3)); 141.33 (t, C(4), $J_{C,F}$ = 26.2); 150.81 (C(7a)); 160.42 (d, C(4′), $J_{C,F}$ = 243.7); 163.80 (C(6)) | −37.73 (m, 1 F, ArF); 31.35 (s, 2 F, $CF_2Br$) |
| **6c**** | 3.83 (s, 3 H, OMe); 5.58 (s, 2 H, $CH_2$); 6.64 (s, 1 H, H(5)); 6.92 (d, 2 H, Ar, *J* = 8.4); 7.47 (d, 2 H, Ar, *J* = 8.4); 7.96 (s, 1 H, HC(3)); 13.59 (br.s, 1 H, NH) | 50.24 ($CH_2$); 55.24 ($OCH_3$); 102.65 (C(3a)); 104.22 (C(5)); 114.04 (C(3′)); 115.68 (t, $CF_2Br$, $J_{C,F}$ = 303.5); 128.81 (C(1′)); 129.14 (C(2′)); 131.66 (C(3)); 141.05 (t, C(4), $J_{C,F}$ = 26.2); 147.48 (C(7a)); 159.17 (C(4′)); 163.48 (C(6)) | 28.11 (s, $CF_2Br$) |
| **7a** | 2.54 (s, 3 H, Me), 6.85 (s, 1 H, H(5)); 7.34 (t, 1 H, Ar, *J* = 7.3); 7.53 (t, 2 H, Ar, *J* = 7.5); 8.05 (d, 2 H, Ar, *J* = 7.8); 12.31 (br.s, 1 H, NH) | 15.33 ($CH_3$); 102.69 (t, C(5), $J_{C,F}$ = 6.5); 104.37 (C(3a)); 121.71 (C(2′)); 124.17 (t, $CF_2Cl$, $J_{C,F}$ = 289.4); 126.64 (C(4′)); 129.47 (C(3′)); 138.77 (C(1′)); 139.30 (t, C(4), $J_{C,F}$ = 28.7); 140.93 (C(3)); 150.93 (C(7a)); 163.76 (C(6)) | 23.45 (s, $CF_2Cl$) |

(*to be continued*)

**Table 2** (*continued*)

| Compound | NMR (DMSO-$d_6$, δ, *J*/Hz) | | |
|---|---|---|---|
| | $^1$H | $^{13}$C | $^{19}$F |
| **7b** | 2.63 (s, 3 H, Me); 6.94 (s, 1 H, H(5)); 7.44 (t, 2 H, Ar, *J* = 8.5); 8.15 (m, 2 H, Ar); 12.31 (br.s, 1 H, NH) | 15.25 ($CH_3$); 102.71 (t, C(5), $J_{C,F}$ = 2.0); 104.22 (C(3a)); 116.10 (d, C(3´), $J_{C,F}$ = 22.7); 123.54 (d, C(2´), $J_{C,F}$ = 8.1); 124.13 (t, $CF_2Cl$, $J_{C,F}$ = 289.7); 135.17 (C(1´)); 139.27 (t, C(4), $J_{C,F}$ = 28.7); 140.92 (C(3)); 150.77 (C(7a)); 160.39 (d, C(4´), $J_{C,F}$ = 243.1); 163.80 (C(6)) | −37.84 (m, 1 F, ArF); 28.41 (s, 2 F, $CF_2Cl$) |
| **7c**** | 3.83 (s, 3 H, OMe); 5.59 (s, 2 H, $CH_2$); 6.69 (s, 1 H, H(5)); 6.92 (d, 2 H, Ar, *J* = 6.4); 7.48 (d, 2 H, Ar, *J* = 6.4); 7.94 (s, 1 H, H—C(3)); 13.59 (br.s, 1 H, NH) | 50.31 ($CH_2$); 55.24 ($OCH_3$); 102.96 (C(3a)); 105.29 (t, C(5), $J_{C,F}$ = 5.2); 114.06 (C(3´)); 124.40 (t, $CF_2Cl$, $J_{C,F}$ = 290.2); 128.77 (C(1´)); 129.09 (C(2´)); 131.72 (C(3)); 139.52 (t, C(4), $J_{C,F}$ = 29.0); 147.43 (C(7a)); 159.25 (C(4´)); 163.54 (C(6)) | 23.96 (s, $CF_2Cl$) |
| **8a** | 2.63 (s, 3 H, Me); 6.80 (s, 1 H, H(5)); 7.31 (t, 1 H, Ar, *J* = 6.8); 7.52 (t, 2 H, Ar, *J* = 7.2); 7.98 (d, 1 H, CHFCl, *J* = 48.1); 8.13 (d, 2 H, Ar, *J* = 7.4); 11.95 (br.s, 1 H, NH) | 15.53 (d, $CH_3$, $J_{C,F}$ = 2.2); 98.13 (d, CHFCl, $J_{C,F}$ = 241.0); 103.03 (d, C(5), $J_{C,F}$ = 4.4); 106.14 (C(3a)); 121.41 (C(2´)); 126.29 (C(4´)); 129.49 (C(3´)); 139.28 (C(1´)); 141.69 (C(3)); 143.03 (d, C(4), $J_{C,F}$ = 22.1); 150.84 (C(7a)), 164.13 (C(6)) | −56.88 (d, $J_{H,F}$ = 48.1) |
| **8b** | 2.67 (s, 3 H, Me); 6.84 (s, 1 H, H(5)); 7.43 (t, 2 H, Ar, *J* = 8.2); 8.04 (d, 1 H, CHFCl, *J* = 48.2); 8.19 (m, 2 H, Ar); 12.02 (br.s, 1 H, NH) | 15.35 (d, $CH_3$, $J_{C,F}$ = 2.3); 97.93 (d, CHFCl, $J_{C,F}$ = 242.0); 103.01 (d, C(5), $J_{C,F}$ = 9.5); 105.85 (d, C(3a), $J_{C,F}$ = 3.2); 116.14 (d, C(3´), $J_{C,F}$ = 22.7); 123.32 (d, C(2´), $J_{C,F}$ = 8.3); 135.44 (d, C(1´), $J_{C,F}$ = 2.3); 141.76 (C(3)); 143.03 (d, C(4), $J_{C,F}$ = 22.7); 150.50 (C(7a)); 160.26 (d, C(4´), $J_{C,F}$ = 243.1); 164.10 (C(6)) | −56.93 (d, 1 F, CHFCl, $J_{H,F}$ = 48.1); −38.28 (m, 1 F, ArF) |
| **8c**** | 3.79 (s, 3 H, OMe); 5.54 (s, 2 H, $CH_2$); 6.50 (s, 1 H, H(5)); 6.87 (d, 2 H, Ar, *J* = 9.0); 7.11 (d, 1 H, CHFCl, *J* = 49.3); 7.44 (d, 2 H, Ar, *J* = 9.0); 7.91 (s, 1 H, HC(3)); 13.59 (br.s, 1 H, NH) | 49.36 ($CH_2$); 54.24 ($OCH_3$); 96.93 (d, CHFCl, $J_{C,F}$ = 242.8); 102.29 (C(3a)); 105.90 (d, C(5), $J_{C,F}$ = 7.8); 112.96 (C(3´)); 127.65 (C(1´)); 128.15 (C(2´)); 131.41 (C(3)); 141.44 (d, C(4), $J_{C,F}$ = 23.0); 144.70 (C(7a)); 158.13 (C(4´)); 162.72 (C(6)) | −59.15 (d, $J_{H,F}$ = 48.1) |
| **9** | 2.64 (s, 3 H, Me); 6.65 (s, 1 H, H(5)); 6.84 (t, 1 H, $CF_2H$, *J* = 54.6); 7.34 (t, 1 H, Ar, *J* = 7.15); 7.44 (t, 2 H, Ar, *J* = 7.5); 7.68 (d, 2 H, Ar, *J* = 7.5); 12.30 (br.s, 1 H, NH) | 14.70 ($CH_3$); 104.88 (t, C(5), $J_{C,F}$ = 8.8); 106.39 (C(3a)); 112.75 (t, $CF_2H$, $J_{C,F}$ = 239.9); 121.79 (C(2´)); 125.86 (C(4´)); 128.71 (C(3´)); 138.56 (t, C(4), $J_{C,F}$ = 21.3); 138.86 (C(1´)); 141.66 (C(3)); 149.89 (C(7a)); 163.62 (C(6)) | −35.93 (d, $J_{H,F}$ = 54.6) |
| **10a*** | 2.52 (dd, 3 H, Me, *J* = 2.3, *J* = 3.7); 6.32 (s, 1 H, H(5)); 7.30 (m, 1 H, Ar); 7.42 (m, 2 H, Ar); 7.59 (m, 2 H, Ar); 7.68 (m, 3 H, Ar); 7.80 (m, 2 H, Ar); 9.59 (br.s, 1 H, OH) | 15.23 (d, AB system, $J_{AB}$ = 4.5); 15.33 (d, AB-systema, $J_{AB}$ = 4.5); 105.57, 108.17 (t, $J_{C,F}$ = 8.0); 122.23, 122.40 (d, AB system, $J_{C,F}$ = 291); 126.31, 126.35 (d, AB system, $J_{C,F}$ = 291); 126.98, 129.11, 129.23, 133.32, 135.12 (t, $J_{C,F}$ = 23.5); 136.44, 137.60, 142.82, 146.57, 161.71 | −27.72 (d, AB system, $J_{AB}$ = 223.1); −20.00 (d, AB system, $J_{AB}$ = 223.1) |

* In $CDCl_3$.
** In $CDCl_3$ ($^1$H and $^{19}$F) and $CDCl_3$—10% DMSO-$d_6$ ($^{13}$C).

than the S(1)—C(8) bond between sulfur and the fluoroalkyl group (Tables 4, 5). The molecular packing is made up of oppositely directed chains of molecules, the chains being held together by intermolecular hydrogen bonds between the sulfinyl and hydroxy groups. The parameters of these bonds are given in Table 6.

**Table 3.** IR and mass spectra of compounds **3a—c**, **3f**, **6a—c**, **7a—c**, **8a—c**, **9**, and **10a**

| Compound | IR (KBr), ν/cm$^{-1}$ | MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)) |
|---|---|---|
| **3a** | 1661 vs (C=O) | 384 $[M + H]^+$ (13), 383 $[M]^+$ (53), 275 (19), 274 (100), 226 (7), 206 (9) |
| **3b** | 1667 vs (C=O) | 402 $[M + H]^+$ (13), 401 $[M]^+$ (66), 293 (15), 292 (100), 244 (6), 224 (9) |
| **3c** | 1661 vs (C=O) | 413 $[M]^+$ (11), 305 (13), 304 (57), 303 (7), 149 (8), 122 (10), 121 (100) |
| **3f** | 1653 vs (C=O) | 366 $[M + H]^+$ (14), 365 $[M]^+$ (51), 257 (18), 256 (100), 218 (14), 208 (10), 149 (16), 109 (11) |
| **6a** | 1653 vs (C=O) | 356 $[M + H]^+$ (5), 355 $[M]^+$ (24), 354 $[M + H]^+$ (5), 353 $[M]^+$ (28), 275 (19), 274 (100), 247 (4), 226 (7), 206 (8) |
| **6b** | 1662 vs (C=O) | 374 $[M + H]^+$ (6), 373 $[M]^+$ (31), 372 $[M + H]^+$ (6), 371 $[M]^+$ (33), 293 (18), 292 (100), 265 (3), 244 (7), 224 (10) |
| **6c** | 1658 vs (C=O) | 385 $[M]^+$ (8), 383 $[M]^+$ (8), 305 (13), 304 (62), 303 (7), 122 (9), 121 (100) |
| **7a** | 1655 vs (C=O) | 311 $[M]^+$ (37), 310 $[M - H]^+$ (22), 309 $[M]^+$ (100), 308 $[M - H]^+$ (22), 294 (11), 274 (28), 268 (17), 267 (13), 246 (9), 226 (8) |
| **7b** | 1660 vs (C=O) | 329 $[M]^+$ (37), 328 $[M - H]^+$ (22), 327 $[M]^+$ (100), 326 $[M - H]^+$ (22), 293 (15), 292 (38), 286 (14), 265 (10), 244 (9), 224 (8) |
| **7c** | 1661 vs (C=O) | 341 $[M]^+$ (6), 340 $[M - H]^+$ (9), 339 $[M]^+$ (20), 338 $[M - H]^+$ (18), 305 (9), 304 (45), 303 (12), 122 (10), 121 (100) |
| **8a** | 1654 vs (C=O) | 293 $[M]^+$ (35), 292 $[M - H]^+$ (24), 291 $[M]^+$ (100), 290 $[M - H]^+$ (22), 257 (8), 256 (33), 236 (9), 208 (11) |
| **8b** | 1661 vs (C=O) | 311 $[M]^+$ (32), 310 $[M - H]^+$ (21), 309 $[M]^+$ (100), 308 $[M - H]^+$ (15), 275 (11), 274 (41), 254 (8), 246 (8), 226 (12) |
| **8c** | 1653 vs (C=O) | 323 $[M]^+$ (7), 322 $[M - H]^+$ (8), 321 $[M]^+$ (16), 320 $[M - H]^+$ (14), 287 (12), 286 (64), 285 (16), 122 (10), 121 (100) |
| **9** | 1662 vs (C=O) | 276 $[M + H]^+$ (17), 275 $[M]^+$ (100), 274 $[M - H]^+$ (41), 260 (12), 234 (15), 226 (7), 206 (6) |
| **10a** | 3064 m, br (OH) | 399 $[M]^+$ (7), 275 (20), 274 (77), 272 (19), 271 (100), 270 (27), 256 (15), 230 (21), 223 (10), 222 (13), 195 (13), 194 (14) |

The general view of structure **10a** with the atomic numbering is shown in Fig. 1, *a*. The molecule exists in a tweezers-like conformation folded along the C(11)—C(8)—S(1)—C(6) bond. However, the phenyl substituent at the sulfoxide group is substantially shifted relative to the pyridine ring: the distance between the centroids of these rings is 4.476 Å and the torsion angle O(1)—S(1)—C(8)—C(11) is 51.90°. The phenyl substituent at the N(1) atom makes an angle of −22.86° with the plane of the fused heterocycle. The bond lengths in sulfoxide **10a** are close to those in structure **10b**. The C(15) and C(16) atoms ($1 - x$, $1 - y$, $-z$) are linked by a shortened intermolecular π—π-contact. The molecules form helical chains along the axis *b*, which are held together by intermolecular hydrogen bonds, thereby producing the molecular packing (see Table 6).

To sum up, we developed novel approaches to the synthesis of earlier unknown 6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones containing the 4-Ar$SCF_2$ and 4-ArSCHF groups. The approaches involve (1) direct annulation of 1-substituted 5-aminopyrazoles with ethyl 4,4-difluoro-4-phenylthioacetoacetate **4a** and (2) replacement of the Br atom of 4-$CF_2$Br group (or the Cl atom of the 4-CFHCl group) by sodium arenethiolates. Using these procedures, one can obtain 6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones with various (including aryl and hetaryl) substituents R in the sulfur-containing fragments $CF_2SR$ and CHFSR.

Oxidation of 4-Ar$SCF_2$-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-ones yielded the corresponding sulfoxides; their structures were confirmed by X-ray diffraction.

## Experimental

$^1$H and $^{13}$C{$^1$H} NMR spectra were recorded on a Bruker Avance$^{TM}$600 spectrometer (600.22 and 150.925 MHz, respectively). The $^1$H and $^{13}$C chemical shifts were referenced to the residual signal of chloroform (δ 7.27) or $CDCl_3$ (δ 77.0), respectively, and converted to $SiMe_4$. The accuracy of δ determination is no less than 0.001 and 0.03 ppm, respectively. $^{19}$F and $^{19}$F{$^1$H} NMR spectra were recorded on a Bruker Avance$^{TM}$300 spectrometer (288.38 MHz). The $^{19}$F chemical shifts were referenced to trifluoroacetic acid as the external standard. The accuracy of δ determination is no less than 0.01 ppm.

Single crystals of compounds **10a** and **10b** were grown by crystallization from light petroleum—diethyl ether. X-ray diffraction experiments were carried out on an Xcalibur-3 diffractometer fitted with a CCD detector (graphite monochromator, ω scan mode, scan step 1°). The structures were solved by the direct methods and refined by the full-matrix least-squares method on $F^2$ with the SHELX program package.[23] The coordinates and thermal parameters of the non-hydrogen atoms were refined isotropically and then anisotropically by the full-matrix least-

**Table 4.** Selected crystallographic parameters and the data collection and refinement statistics for structures **10a** and **10b**

| Parameter | **10a** | **10b** |
|---|---|---|
| Molecular formula | $C_{20}H_{15}F_2N_3O_2S$ | $C_{20}H_{14}F_3N_3O_2S$ |
| Molecular mass | 399.41 | 417.40 |
| $T$/K | 295(2) | 295(2) |
| λ/Å | 0.71073 | 0.71073 |
| Crystal system | Monoclinic | Triclinic |
| Space group | $P2_1/n$ | $P\bar{1}$ |
| $a$/Å | 10.594(3) | 9.122(2) |
| $b$/Å | 15.264(2) | 9.429(2) |
| $c$/Å | 11.651(3) | 11.047(2) |
| α/deg | 90 | 89.828(19) |
| β/deg | 103.73(2) | 78.62(2) |
| γ/deg | 90 | 79.05(2) |
| $Z$ | 4 | 2 |
| $d_{calc}$/g cm$^{-3}$ | 1.449 | 1.517 |
| μ/mm$^{-1}$ | 0.218 | 0.230 |
| $F$(000) | 824 | 428 |
| Crystal dimensions/mm | 0.46×0.37×0.18 | 0.43×0.36×0.28 |
| θ scan range/deg | 2.67—26.37 | 2.84—26.39 |
| Completeness at $\theta_{max}$ (%) | 99.8 | 99.4 |
| Ranges of $h$, $k$, $l$ indices | $-12 < h < 13$ | $-11 < h < 11$ |
| | $-18 < k < 19$ | $-10 < k < 11$ |
| | $-8 < l < 14$ | $-13 < l < 13$ |
| Number of measured reflections | 7860 | 5335 |
| Number of independent reflections | 3728 ($R_{int}$ = 0.0483) | 3716 ($R_{int}$ = 0.0243) |
| Number of reflections with $I > 2\sigma(I)$ | 1343 | 1442 |
| Number of parameters refined | 257 | 266 |
| Absorption correction | — | — |
| GOOF (on $F^2$) | 1.004 | 1.003 |
| $R$ Factors (for reflections with $I > 2\sigma(I)$) | | |
| $R_1$ | 0.0398 | 0.0463 |
| $wR_2$ | 0.0521 | 0.0780 |
| $R$ Factors (for all reflections) | | |
| $R_1$ | 0.1215 | 0.1111 |
| $wR_2$ | 0.0546 | 0.0818 |
| $\Delta\rho_{max}/\Delta\rho_{min}$/e Å$^{-3}$ | 0.212/−0.229 | 0.584/−0.437 |

squares method. The hydrogen atoms were located from the electron density maxima and refined using a riding model. Selected crystallographic parameters, data collection and refinement statistics, bond lengths, and hydrogen bond parameters for structures **10a** and **10b** are given in Tables 4—6.

IR absorption spectra were recorded on a Magna IR-750 Nicolet FTIR spectrometer (KBr pellets) in the 4000—400 cm$^{-1}$ range. Nujol was also used for compounds **3b** and **10a**,**b**. Mass spectra were recorded on a Finnigan Polaris Q instrument (ion trap, ionizing energy 70 eV, direct inlet probe). Syntheses involving microwave radiation were carried out in a Milestone MicroSynth system (radiation power 600 W, closed test tube, heating mode: 25—120 °C for 5 min and 120 °C for 7 min. For column chromatography, Kieselgel 60 silica gel (0.06—0.20 mm, Merck) was used. Compounds were detected by visualization on TLC plates covered with Kieselgel 60 $F_{254}$ (Merck). *n*-Butyllithium (a 1.6 *M* solution in hexane) was purchased from Acros. Sodium hydride (a 60% dispersion in mineral oil) was purchased from Aldrich. Ethyl acetate (extra dry, with molecular sieves, water <50 ppm) was purchased from Acros. Elemental analysis was carried out at the Microanalysis Laboratory of the A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences. Light petroleum (LP), ethyl acetate (EA), and diethyl ether (DE) were used as solvents.

**Table 5.** Selected bond lengths ($d$) in compounds **10a,b**

| **10a** | | **10b** | |
|---|---|---|---|
| Bond | $d$/Å | Bond | $d$/Å |
| S(1)—O(1) | 1.4878(16) | S(1)—O(1) | 1.454(2) |
| S(1)—C(6) | 1.788(2) | S(1)—C(1) | 1.772(3) |
| S(1)—C(8) | 1.890(3) | S(1)—C(8) | 1.901(3) |
| C(8)—F(2) | 1.363(2) | F(2)—C(8) | 1.349(3) |
| F(1)—C(8) | 1.373(3) | F(1)—C(8) | 1.338(3) |
| N(1)—N(2) | 1.375(2) | F(3)—C(18) | 1.361(3) |
| O(2)—C(9) | 1.339(3) | O(2)—C(9) | 1.345(3) |

**Table 6.** Parameters of the intermolecular hydrogen bonds in compounds **10a,b**

| Compound | D—H | *d*(D—H) | *d*(H..A) | *d*(D..A) | Angle D—H—A | A |
|---|---|---|---|---|---|---|
| **10a** | O(2)—H(2) | 0.70(3) | 2.02(3) | 2.669(3) | 153(1) | O(1) [$-x + 1/2, y + 1/2, -z + 1/2$] |
| | O(2)—H(2) | 0.70(3) | 3.02(3) | 3.663(3) | 153(1) | S(1) [$-x + 1/2, y + 1/2, -z + 1/2$] |
| **10b** | O(2)—H(2) | 0.73(3) | 1.97(3) | 2.660(3) | 156(1) | O(1) [$x, y - 1, z$] |

Compounds **3a**—**f**, **6a**—**c**, **7a**—**c**, **8a**—**c**, and **9** are colorless crystalline solids; compounds **10a,b** are light yellow crystals.

**Ethyl fluoro(phenylsulfanyl)acetate** was prepared from ethyl chloro(fluoro)acetate and benzenethiol as described earlier.[24] The reaction time was 3 h. The yield was 89%, light yellow low-viscosity liquid, b.p. 104—105 °C (1 Torr). The spectroscopic characteristics of ethyl fluoro(phenylsulfanyl)acetate are identical with the literature data.[24]

**Ethyl difluoro(phenylsulfanyl)acetate** was prepared from chloro(difluoro)acetic acid according to a known procedure.[25] The spectroscopic and physicochemical characteristics of ethyl difluoro(phenylsulfanyl)acetate are identical with the literature data.[26]

**4-[Difluoro(phenylsulfanyl)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3a).** ***A.*** A solution of oxo ester **4a** (1.3 g, 4.7 mmol) and 5-amino-3-methyl-1-phenylpyrazole **5a** (0.8 g, 4.7 mmol) in acetic acid (5 mL) was irradiated in a microwave oven (the heating conditions are described in the preamble to the Experimental). The reaction mixture was cooled, diluted with water (50 mL), and kept in a refrigerator for 16 h. The crystals that formed were filtered off, washed repeatedly with water on the filter, dried in air, and recrystallized from LP—EA (1 : 1). The yield of compound **3a** was 0.8 g. An additional crop (0.4 g) was obtained by column chromatography of the mother liquor with LP—EA (3 : 1) as an eluent.

***B.*** A flask with an inert gas outlet was charged with a 60% dispersion of NaH (0.24 g, 6 mmol). Then DMF (10 mL) and benzenethiol (0.5 g, 4.5 mmol) were added. The reaction mixture was stirred until gas evolution ceased. The resulting transparent solution was degassed several times by passing an inert gas *in vacuo*. Then pyrazolopyridine **6a** (0.5 g, 1.5 mmol) was added under an inert gas. The reaction mixture was stirred at 50 °C for 2 h until the starting compound **6a** was completely consumed ($^{19}$F NMR data), cooled to 20 °C, and poured into a saturated solution of $NH_4Cl$ (100 mL). The products were extracted with EA (3×40 mL). The organic extracts were combined, washed with brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with LP—EA (3 : 1) as an eluent. The first eluted fraction contained compound **3a** (0.41 g, 76%). Its spectroscopic and physicochemical characteristics are identical with those of pyrazolopyridine **3a** obtained according to method *A*. Further elution gave **4-difluoromethyl-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (9)** (0.07 g). Its spectroscopic and physicochemical characteristics are identical with those of pyrazolopyridine **9** obtained by condensation of oxo ester **4f** with 5-amino-3-methyl-1-phenylpyrazole (**5a**) (see above).

**4-[Difluoro(phenylsulfanyl)methyl]-1-(4-fluorophenyl)-3-methyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3b)** was obtained from oxo ester **4a** and 5-amino-1-(4-fluorophenyl)-3-methylpyrazole **5b** as described for compound **3a** (method ***A***).

**4-[Difluoro(phenylsulfanyl)methyl]-1-(4-methoxybenzyl)-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3c)** was obtained from oxo ester **4a** and 5-amino-1-(4-methoxybenzyl)pyrazole **5c** as described for compound **3a** (method ***A***).

**4-[4-Chlorophenylsulfanyl(difluoro)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3d)** was obtained from pyrazolopyridine **6a** and 4-chlorobenzenethiol as described for compound **3a** (method ***B***). IR (KBr), ν/cm$^{-1}$: 1660 vs (C=O). $^1$H NMR ($CDCl_3$), δ: 2.78 (s, 3 H, Me); 6.61 (s, 1 H, HC(5)); 7.34 (t, 1 H, Ar, $J$ = 7.5 Hz); 7.41—7.50 (m, 4 H, Ar); 7.60 (d, 2 H, Ar, $J$ = 8.0 Hz); 7.77 (d, 2 H, Ar, $J$ = 8.0 Hz). $^{19}$F NMR ($CDCl_3$), δ: 5.1 (s). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 420 $[M + H]^+$ (2), 419 $[M]^+$ (11), 418 $[M + H]^+$ (7), 417 $[M]^+$ (27), 275 (22), 274 (100).

**4-[Difluoro(4-methylphenylsulfanyl)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3e)** was obtained from pyrazolopyridine **6a** and 4-methylbenzenethiol as described for compound **3a** (method ***B***). IR (KBr), ν/cm$^{-1}$: 1662 vs (C=O). $^1$H NMR ($CDCl_3$), δ: 2.46 (s, 3 H, Me); 2.82 (s, 3 H, Me); 6.60 (s, 1 H, H(5)); 7.26—7.34 (m, 3 H, Ar); 7.45 (t, 1 H, Ar, $J$ = 7.8 Hz); 7.57 (d, 2 H, Ar, $J$ = 7.9 Hz); 7.75 (d, 2 H, Ar, $J$ = 7.9 Hz). $^{19}$F NMR ($CDCl_3$), δ: 4.7 (s). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 398 $[M + H]^+$ (11), 397 $[M]^+$ (46), 275 (27), 274 (100), 226 (6), 206 (6).

**4-[Fluoro(phenylsulfanyl)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3f).** Benzenethiol (0.66 g, 6 mmol) was added to a suspension of NaH (60% dispersion, 0.24 g, 6 mmol) in DMF (10 mL). The reaction mixture was stirred until gas evolution ceased. This resulted in a transparent solution to which pyrazolopyridine **8a** (0.6 g, 2 mmol) was added. The reaction mixture was stirred at 20 °C for ~3 h until the starting compound **8a** was completely consumed ($^{19}$F NMR data) and poured into a cooled saturated solution of $NH_4Cl$ (100 mL). The product was extracted with EA (3×40 mL). The organic extracts were combined, washed with brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with LP—EA (2 : 1) as an eluent. The yield of compound **3f** was 0.67 g (89%).

**4-[4-Chlorophenylsulfanyl(fluoro)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (3g)** was obtained from pyrazolopyridine **8a** and 4-chlorobenzenethiol as described for compound **3f**. IR (KBr), ν/cm$^{-1}$: 1657 vs (C=O). $^1$H NMR ($CDCl_3$), δ: 2.70 (s, 3 H, Me); 6.52 (s, 1 H, H(5)); 7.00 (d, 1 H, CHF, $J_{H,F}$ = 54.0 Hz); 7.34—7.60 (m, 7 H, Ar); 7.74 (d, 2 H, Ar, $J$ = 8.0 Hz). $^{19}$F NMR ($CDCl_3$), δ: −75.60 (d, $J_{H,F}$ = = 54.0 Hz). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 402 $[M + H]^+$ (2), 401 $[M]^+$ (13), 400 $[M + H]^+$ (8), 399 $[M]^+$ (32), 257 (19), 256 (100).

**Ethyl 4,4-difluoro-3-oxo-4-phenylsulfanylbutanoate (4a).** ***A.*** Sodium hydride as a 60% dispersion in mineral oil (1.80 g, 0.045 mol) was added to an ice-cooled (5 °C) solution of ethyl

difluoro(phenylthio)acetate (9.6 g, 0.042 mol) in ethyl acetate (10.2 g, 0.123 mol). The resulting suspension was warmed to 20 °C and vigorously stirred for ~15 min. This resulted in a violent reaction with a sharp temperature rise and foaming. The reaction mixture was stirred to complete homogenization. When the temperature decreased to 30 °C, diethyl ether (150 mL) was added. The reaction mixture was refluxed for 12 h and concentrated. The residue was dissolved in diethyl ether and treated with precooled 20% $H_2SO_4$. The organic layer was separated and the product from the aqueous layer was extracted with diethyl ether (3×70 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was distilled *in vacuo* to give ethyl 4,4-difluoro-3-oxo-4-phenylsulfanylbutanoate (9.1 g, 80%) as a yellowish viscous liquid, b.p. 148—150 °C (1 Torr). The keto/enol ratio for compound **4a** in $CDCl_3$ was 59 : 41. (According to $^1$H and $^{19}$F NMR data, compound **4a** also contains the *gem*-diol form $PhSCF_2C(OH)_2CH_2CO_2Et$ (~7%).[18a])

Keto form. $^1$H NMR ($CDCl_3$), δ: 1.31 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 3.71 (s, 2 H, $COCH_2$); 4.24 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 7.39—7.68 (m, 5 H, Ph). $^{19}$F NMR ($CDCl_3$), δ: −8.55 (s, $CF_2SPh$).

Enol form. $^1$H NMR ($CDCl_3$), δ: 1.32 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 4.26 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 5.40 (s, 1 H, CH=); 7.39—7.68 (m, 5 H, Ph); 12.03 (s, 1 H, OH). $^{19}$F NMR ($CDCl_3$), δ: −5.02 (s, $CF_2SPh$).

Both forms. $^{13}$C NMR ($CDCl_3$), δ: 13.98, 14.03, 43.21, 61.31, 62.04, 91.27 (t, $J_{C,F}$ = 4.3 Hz); 121.94 (t, $J_{C,F}$ = 291.1 Hz); 122.89 (t, $J_{C,F}$ = 279.3 Hz); 123.92, 125.38, 129.17, 129.51, 130.47, 130.85, 136.76, 136.81, 164.92 (t, $J_{C,F}$ = 30.0 Hz); 165.49, 171.76, 188.26 (t, $J_{C,F}$ = 31.3 Hz). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 275 $[M + H]^+$ (6), 274 $[M]^+$ (35), 228 (10), 227 (19), 209 (17), 189 (13), 181 (47), 165 (29), 164 (34), 161 (16), 160 (39), 159 (100). Found (%): C, 52.06; H, 4.13. $C_{12}H_{12}F_2O_3S$. Calculated (%): C, 52.55; H, 4.41.

***B.*** A 1.6 *M* solution of *n*-butyllithium (56.3 mL) in hexane was added to a solution of diisopropylamine (9.11 g, 90 mmol) in anhydrous diethyl ether (60 mL), while maintaining the temperature in a range from −5 to 0 °C. The reaction mixture was stirred at 0 °C for 1 h. Ethyl acetate (7.93 g, 90 mmol) in diethyl ether (20 mL) was added at −75 °C and the reaction mixture was stirred at this temperature for 20 min. Then ethyl difluoro(phenylthio)acetate (10.45 g, 45 mmol) in diethyl ether (20 mL) was added and the reaction mixture was stirred at −75 °C for 3 h. A saturated solution of $NH_4Cl$ (20 mL) was added and the reaction mixture was warmed to 0 °C. The organic layer was separated and the product from the aqueous layer was extracted with diethyl ether (3×40 mL). The organic extracts were combined and washed with precooled 1 *M* HCl to a distinct acid reaction. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The residue was distilled *in vacuo* to give ethyl 4,4-difluoro-3-oxo-4-phenylsulfanylbutanoate **4a** (10.1 g, 82%) as a yellowish liquid. The spectroscopic and physicochemical characteristics of oxo ester **4a** obtained according to methods ***A*** and ***B*** are identical.

**Ethyl 4-fluoro-3-oxo-4-phenylsulfanylbutanoate (4b)** was obtained from ethyl fluoro(phenylsulfanyl)acetate according to method ***B***. The yield was 87%. Crude compound **4b** was used in heterocyclization reactions. Its analytically pure sample (as a yellow viscous liquid) was isolated using column chromatography on silica gel with LP—EA (10 : 1) as an eluent. The keto/enol ratio for compound **4b** in $CDCl_3$ was 4 : 1.

Keto form. $^1$H NMR ($CDCl_3$), δ: 1.31 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 3.50 (AB system, 2 H, $COCH_2$); 4.22 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 6.27 (d, 1 H, CHFSPh, $J$ = 51.7 Hz); 7.37—7.62 (m, 5 H, Ph). $^{13}$C NMR ($CDCl_3$), δ: 14.05, 45.41, 61.74, 99.09 (d, $J_{C,F}$ = 235.6 Hz); 129.17, 129.49, 129.67, 134.12 (d, $J_{C,F}$ = 1.5 Hz); 166.08, 194.17 (d, $J_{C,F}$ = 27.6 Hz). $^{19}$F NMR ($CDCl_3$), δ: −82.96 (d, $J_{H,F}$ = 51.7 Hz).

Enol form. $^1$H NMR ($CDCl_3$), δ: 1.33 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 4.22 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 5.30 (dd, 1 H, CH=, $J$ = 1.3 Hz, $J$ = 0.7 Hz); 6.16 (dd, 1 H, CHFSPh, $J$ = 51.7 Hz, $J$ = 0.7 Hz); 7.37—7.62 (m, 5 H, Ph); 12.23 (d, 1 H, OH, $J$ = 1.8 Hz). $^{13}$C NMR ($CDCl_3$), δ: 14.14, 60.76, 90.42 (d, $J_{C,F}$ = = 5.5 Hz); 97.06 (d, $J_{C,F}$ = 225.0 Hz); 128.89, 129.17, 129.28, 133.84 (d, $J_{C,F}$ = 1.7 Hz); 168.78 (d, $J_{C,F}$ = 28.7 Hz); 172.03. $^{19}$F NMR ($CDCl_3$), δ: −80.66 (d, $J_{H,F}$ = 51.7 Hz). Found (%): C, 55.87; H, 5.03. $C_{12}H_{13}FO_3S$. Calculated (%): C, 56.24; H, 5.11.

**Ethyl 4-bromo-4,4-difluoro-3-oxobutanoate (4c)**, **ethyl 4-chloro-4,4-difluoro-3-oxobutanoate (4d)**, **ethyl 4-chloro-4-fluoro-3-oxobutanoate (4e)**, and **ethyl 4,4-difluoro-3-oxobutanoate (4f)** were obtained according to method ***B*** from ethyl bromo(difluoro)acetate, ethyl chloro(difluoro)acetate, ethyl chloro(fluoro)acetate, and ethyl difluoroacetate, respectively.

**Ethyl 4-bromo-4,4-difluoro-3-oxobutanoate (4c).** Yield 87%, colorless low-viscosity liquid, b.p. 80—84 °C (12 Torr; *cf.* Ref. 27: b.p. 78—82 °C (10 Torr)). The keto/enol/*gem*-diol[18a] ratio for compound **4c** in $CDCl_3$ was 35 : 50 : 15.

Keto form. $^1$H NMR ($CDCl_3$), δ: 1.40 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 3.86 (s, 2 H, $COCH_2$); 4.27 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz). $^{19}$F NMR ($CDCl_3$), δ: 12.62 (s).

Enol form. $^1$H NMR ($CDCl_3$), δ: 1.38 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 4.36 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 5.61 (s, 1 H, CH=); 12.09 (s, 1 H, OH). $^{19}$F NMR ($CDCl_3$), δ: 18.52 (s).

*gem*-Diol form. $^1$H NMR ($CDCl_3$), δ: 1.39 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 2.92 (s, 2 H, $C(OH)_2C\underline{H}_2$); 4.27 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 4.93 (br.s, 2 H, 2 OH). $^{19}$F NMR ($CDCl_3$), δ: 13.67 (s).

**Ethyl 4-chloro-4,4-difluoro-3-oxobutanoate (4d).** Yield 85%, colorless low-viscosity liquid, b.p. 59—63 °C (12 Torr; *cf.* Ref. 18b: b.p. 96 °C (70 Torr)). The keto/enol/*gem*-diol[18a] ratio for compound **4d** in $CDCl_3$ was 33 : 53 : 14.

Keto form. $^1$H NMR ($CDCl_3$), δ: 1.40 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 3.84 (s, 2 H, $COCH_2$); 4.27 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz). $^{19}$F NMR ($CDCl_3$), δ: 9.54 (s).

Enol form. $^1$H NMR ($CDCl_3$), δ: 1.38 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 4.36 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 5.64 (s, 1 H, CH=); 12.09 (s, 1 H, OH). $^{19}$F NMR ($CDCl_3$), δ: 14.63 (s).

*gem*-Diol form. $^1$H NMR ($CDCl_3$), δ: 1.39 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 2.92 (s, 2 H, $C(OH)_2C\underline{H}_2$); 4.27 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 4.90 (br.s, 2 H, 2 OH). $^{19}$F NMR ($CDCl_3$), δ: 6.89 (s).

**Ethyl 4-chloro-4-fluoro-3-oxobutanoate (4e).** Yield 89%, colorless low-viscosity liquid, b.p. 96—98 °C (20 Torr). The keto/enol ratio for compound **4e** in $CDCl_3$ was 65 : 35.

Keto form. $^1$H NMR ($CDCl_3$), δ: 1.31 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 3.76 (AB system, 2 H, $COCH_2$); 4.24 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 6.37 (d, 1 H, CHFCl, $J$ = 51.0 Hz). $^{13}$C NMR ($CDCl_3$), δ: 13.96, 42.73, 61.96, 95.52 (d, $J_{C,F}$ = = 256.0 Hz); 165.65, 191.60 (d, $J_{C,F}$ = 26.4 Hz). $^{19}$F NMR ($CDCl_3$), δ: −70.29 (d, $J_{H,F}$ = 51.0 Hz).

Enol form. $^1$H NMR ($CDCl_3$), δ: 1.32 (t, 3 H, $C\underline{H}_3CH_2O$, $J$ = 7.5 Hz); 4.26 (q, 2 H, $OC\underline{H}_2CH_3$, $J$ = 7.5 Hz); 5.49 (s, 1 H, CH=); 6.41 (d, 1 H, CHFCl, $J$ = 49.0 Hz); 11.97 (br.s, 1 H,

OH). $^{13}$C NMR ($CDCl_3$), δ: 14.03, 61.15, 90.18 (d, $J_{C,F}$ = = 7.0 Hz); 94.80 (d, $J_{C,F}$ = 244.3 Hz); 167.32 (d, $J_{C,F}$ = 25.3 Hz); 171.83. $^{19}$F NMR ($CDCl_3$), δ: –68.83 (d, $J_{H,F}$ = 49.0 Hz). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 185 $[M + H]^+$ (5), 183 $[M]^+$ (12), 139 (16), 137 (55), 119 (20), 115 (68), 91 (29), 89 (20), 87 (100). Found (%): C, 39.88; H, 4.83. $C_6H_8ClFO_3$. Calculated (%): C, 39.47; H, 4.42.

**Ethyl 4,4-difluoro-3-oxobutanoate (4f).** Yield 77%, colorless low-viscosity liquid, b.p. 50—53 °C (12 Torr; *cf.* Ref. 18b: b.p. 100 °C (100 Torr)). The keto/enol/*gem*-diol[18a] ratio for compound **4f** in $CDCl_3$ was 27 : 56 : 17.

Keto form. $^1$H NMR ($CDCl_3$), δ: 1.35 (t, 3 H, $CH_3CH_2O$, $J$ = 7.5 Hz); 3.75 (s, 2 H, $COCH_2$); 4.28 (q, 2 H, $OCH_2CH_3$, $J$ = 7.5 Hz); 5.95 (t, 1 H, $CHF_2$, $J$ = 54.0 Hz). $^{19}$F NMR ($CDCl_3$), δ: –50.11 (d, $J_{H,F}$ = 54.0 Hz).

Enol form. $^1$H NMR ($CDCl_3$), δ: 1.37 (t, 3 H, $CH_3CH_2O$, $J$ = 7.5 Hz); 4.31 (q, 2 H, $OCH_2CH_3$, $J$ = 7.5 Hz); 5.54 (s, 1 H, CH=); 6.08 (t, 1 H, $CHF_2$, $J$ = 54.0 Hz); 11.84 (s, 1 H, OH). $^{19}$F NMR ($CDCl_3$), δ: –48.78 (d, $J_{H,F}$ = 54.0 Hz).

*gem*-Diol form. $^1$H NMR ($CDCl_3$), δ: 1.33 (t, 3 H, $CH_3CH_2O$, $J$ = 7.5 Hz); 2.78 (s, 2 H, $C(OH)_2CH_2$); 4.25 (q, 2 H, $OCH_2CH_3$, $J$ = 7.5 Hz); 4.60 (br.s, 2 H, 2 OH); 5.63 (t, 1 H, $CHF_2$, $J$ = 55.5 Hz). $^{19}$F NMR ($CDCl_3$), δ: –56.96 (d, $J_{H,F}$ = 55.5 Hz).

**5-Amino-1-(4-methoxybenzyl)pyrazole (5c)** was obtained as described earlier[28] for 5-amino-1-benzylpyrazole. At the final step of the synthesis, *n*-BuONa in *n*-butanol[4d] was used instead of solid-state NaOH in *n*-propanol. 5-Amino-1-(4-methoxybenzyl)pyrazole was isolated by column chromatography on silica gel with LP—EA (3 : 1) as an eluent, m.p. 70—71 °C. $^1$H NMR ($CDCl_3$), δ: 3.44 (br.s, 2 H, $NH_2$); 3.84 (s, 3 H, OMe); 5.21 (s, 2 H, $CH_2$); 5.61 (d, 1 H, H(4), $J$ = 1.8 Hz); 6.92 (d, 2 H, Ar, $J$ = 8.6 Hz); 7.18 (d, 2 H, Ar, $J$ = 8.6 Hz); 7.36 (d, 1 H, H(3), $J$ = 1.8 Hz). $^{13}$C NMR ($CDCl_3$), δ: 51.22, 55.30, 91.77, 114.30, 128.27, 128.63, 138.53, 144.37, 159.19. MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 203 $[M]^+$ (21), 122 (9), 121 (100), 91 (12), 77 (14).

**4-[(Bromo)(difluoro)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (6a).** A solution of ethyl 4-bromo-4,4-difluoro-3-oxobutanoate **4c** (2.45 g, 0.01 mol) and 5-amino-3-methyl-1-phenylpyrazole **5a** (1.7 g, 0.01 mol) in glacial acetic acid (30 mL) was refluxed for 3 h, cooled, poured into water with ice (100 mL), and kept in a refrigerator for 16 h. The precipitate that formed was filtered off, dried in air, and recrystallized from LP—EA (1 : 1). The yield of compound **6a** was 1.9 g. An additional crop (0.8 g) was obtained by column chromatography of the mother liquor with LP—EA (3 : 1) as an eluent.

In a similar way, **4-[(bromo)(difluoro)methyl]-1-(4-fluorophenyl)-3-methyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (6b)** and **4-[(bromo)(difluoro)methyl]-1-(4-methoxybenzyl)-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (6c)** were obtained by reactions of ethyl 4-bromo-4,4-difluoro-3-oxobutanoate **4c** with 5-amino-1-(4-fluorophenyl)-3-methylpyrazole **5b** and 5-amino-1-(4-methoxybenzyl)pyrazole **5c**, respectively. In a similar way, **4-[(chloro)(difluoro)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (7a)**, **4-[(chloro)(difluoro)methyl]-1-(4-fluorophenyl)-3-methyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (7b)**, and **4-[(chloro)(difluoro)methyl]-1-(4-methoxybenzyl)-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (7c)** were obtained by reactions of ethyl 4-chloro-4,4-difluoro-3-oxobutanoate **4d** with pyrazoles **5a**—**c**, respectively. In a similar way, **4-[(chloro)(fluoro)methyl]-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (8a)**, **4-[(chloro)(fluoro)methyl]-1-(4-fluorophenyl)-3-methyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (8b)**, and **4-[(chloro)(fluoro)methyl]-1-(4-methoxybenzyl)-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (8c)** were obtained by reactions of ethyl 4-chloro-4-fluoro-3-oxobutanoate **4e** with pyrazoles **5a**—**c**, respectively. In a similar way, **4-difluoromethyl-3-methyl-1-phenyl-6,7-dihydro-1*H*-pyrazolo[3,4-*b*]pyridin-6-one (9)** was obtained from ethyl 4,4-difluoro-3-oxobutanoate **4f** and pyrazole **5a**.

**4-[(Difluoro)(phenylsulfinyl)methyl]-1-(4-fluorophenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-6-ol (10b).** *m*-Chloroperoxybenzoic acid (17.3 mg, 0.1 mmol) in anhydrous $CH_2Cl_2$ (10 mL) was added at 20 °C for 1 h to a solution of pyrazolopyridine **3b** (40 mg, 0.1 mmol) in anhydrous $CH_2Cl_2$ (5 mL). The resulting solution was stirred for 1 h and treated with 5% $Na_2S_2O_3$. The organic layer was separated, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with LP—DE (5 : 2) as an eluent. The yield of compound **10b** was 25 mg. IR (KBr), ν/cm$^{-1}$: 3208 m, br (OH). $^1$H NMR ($CDCl_3$—$CD_3OD$), δ: 2.52 (t, 3 H, Me, $J$ = 3.0 Hz); 6.14 (s, 1 H, H(5)); 7.09 (m, 2 H, Ar); 7.42 (d, 4 H, Ar, $J$ = 4.4 Hz); 7.52 (m, 1 H, Ar); 7.90 (m, 2 H, Ar). $^{19}$F{$^1$H} NMR ($CDCl_3$—$CD_3OD$), δ: –38.06 (s, 1 F, Ar—F); –27.19 (d, AB system, 1 F, $J_{AB}$ = 223.1 Hz); –19.85 (d, AB system, 1 F, $J_{AB}$ = 223.1 Hz). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 417 $[M]^+$ (9), 293 (22), 292 (100), 290 (13), 289 (60), 288 (9), 274 (6), 248 (6), 241 (11), 213 (9).

**4-[(Difluoro)(phenylsulfinyl)methyl]-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-6-ol (10a)** was obtained from pyrazolopyridine **3a** as described for compound **10b**.

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