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SHORT COMMUNICATIONS

Synthesis of Regioisomeric Polyfluoroalkylpyrazolo[1,5-*a*]pyrimidines

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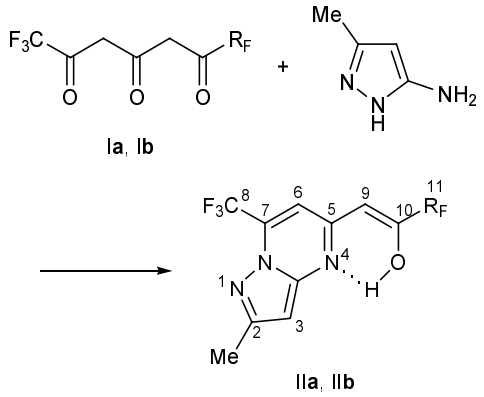
Polyfluoroalkyl-containing 1,3,5-triketones [1] are convenient and promising reagents for building up various heterocyclic systems [2]. In continuation of our studies on the reactivity of polyfluorinated 1,3,5-triketones toward difunctional nucleophiles, we examined reactions of triketones **Ia** and **Ib**, as well as of their dehydration products, 2,6-bis(fluoroalkyl)-4-pyranones **IVa** and **IVb** [3], with 5-amino-3-methylpyrazole (Scheme 1).

Scheme 1.

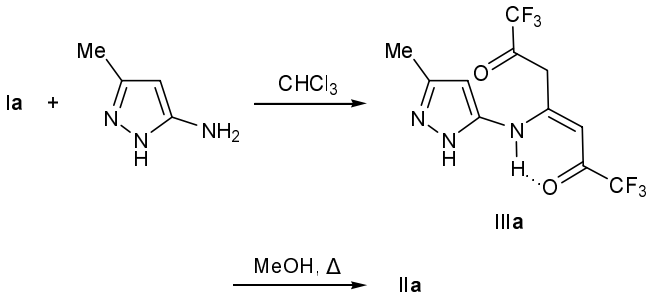


$R_F = CF_3$ (**a**), C_4F_9 (**b**).

We have found that 5-amino-3-methylpyrazole adds in a regioselective fashion at the dicarbonyl fragment neighboring to the trifluoromethyl group in the triketone to give 7-trifluoromethyl-5-polyfluoroacylmethylpyrazolo[1,5-*a*]pyrimidines **IIa** and **IIb** which exist in the enol form (Scheme 1). This follows from the presence in the ^{13}C NMR spectra of the products of multiplet signals at δ_C 164–167 ppm (quartet for **IIa** and triplet for **IIb**), as well as from similar chemical shifts of fluorine atoms in the trifluoromethyl groups at the pyrimidine ring in their ^{19}F NMR spectra.

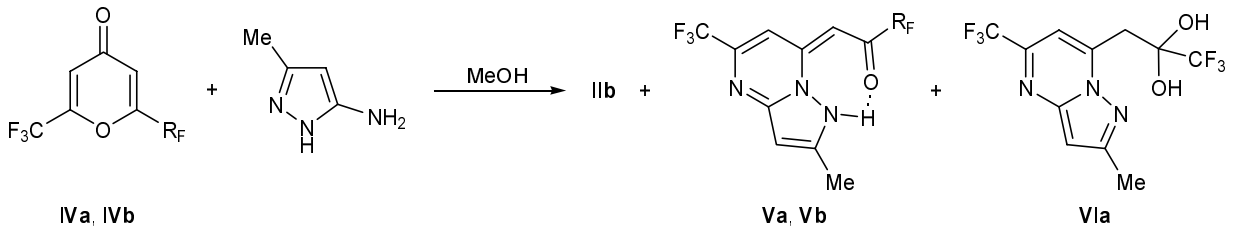
The reaction begins with nucleophilic attack by the amino group in 5-amino-3-methylpyrazole on the central carbonyl carbon atom to give intermediate amino enone **IIIa** (which can be isolated as a mixture with **IIa** when the reaction is carried out in chloroform). Enone **IIIa** undergoes ring closure to pyrazolopyrimidine **IIa** on heating in boiling methanol (Scheme 2).

Scheme 2.



Pyrazolo[1,5-*a*]pyrimidines **Va** and **Vb**, which are isomeric to **IIa** and **IIb**, were obtained by reaction of 5-amino-3-methylpyrazole with 4-pyranones **IVa** and **IVb** (Scheme 3). The product composition depends on the length of the polyfluoroalkyl substituents. Both compounds, **IVa** and **IVb** give rise to expected 5-trifluoromethyl-7-polyfluoroacylmethylidenepyrazolo-[1,5-*a*]pyrimidines **Va** and **Vb**, respectively, but the reaction with nonafluorobutyl-substituted pyranone **IVb** is accompanied by formation of compound **IIb**, presumably via initial attack by the amino group of pyrazole on the C^4=O carbonyl group. The 1-H proton in the pyrazole ring of **Va** and **Vb** is involved in strong

Scheme 3.



$R_F = CF_3$ (**a**), C_4F_9 (**b**).

intramolecular hydrogen bond with the carbonyl oxygen atom of the fluoroacyl group; the corresponding signal appears in the ^{1}H NMR spectra in a very weak field (δ ~16 ppm). Insofar as trifluoromethylcarbonyl group is known to readily take up water molecule, the ^{1}H and ^{19}F NMR spectra of pyrazolopyrimidine **Va** contained signals belonging to its hydrated form **VIa**. Signals from the hydroxy protons of diol **VIa** disappear from the ^{1}H NMR spectrum upon addition of CD_3COOD.

Reaction of polyfluorinated 1,3,5-triketones Ia and Ib with 5-amino-3-methylpyrazole (*general procedure*). A mixture of 1.9 mmol of triketone **Ia** or **Ib** and 0.18 g (1.9 mmol) of 5-amino-3-methylpyrazole in 3 ml of methanol was kept for 24 h. The solvent was evaporated, and the residue was recrystallized from benzene or hexane.

1,1,1-Trifluoro-3-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)propan-2-one (IIa). Yield 51%, yellow crystals, mp 137–138°C (from hexane). IR spectrum, ν, cm^{-1}: 3173 (OH); 3091 (=CH); 1666, 1612, 1578, 1502 (C=N, C=C). ^{1}H NMR spectrum, δ, ppm: 2.52 s (3H, CH_3), 5.99 s (1H, 9-H), 6.31 s (1H, 3-H), 6.76 s (1H, 6-H), 14.1 br.s (1H, OH). ^{19}F NMR spectrum, δ_F, ppm: 86.71 s (3F, CF_3CO), 93.39 s (3F, 7-CF_3). ^{13}C NMR spectrum, δ_C, ppm (*J*, Hz): 14.65, 93.48 q (C^9, *J* = 3.1), 93.67, 104.90 q (C^6, *J* = 4.5), 118.16 q (C^{11}, *J* = 280.1), 118.80 q (C^8, *J* = 274.8), 134.64 q (C^7, *J* = 37.7), 143.40, 153.31, 156.94, 164.79 q (C^{10}, *J* = 35.5). Found, %: C 42.31; H 2.29; F 36.68; N 13.37. $C_{11}H_7F_6N_3O$. Calculated, %: C 42.46; H 2.27; F 36.63; N 13.50.

3,3,4,4,5,5,6,6,6-Nonafluoro-1-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)hexan-2-one (IIb). Yield 56%, yellow crystals, mp 148°C (from benzene). IR spectrum, ν, cm^{-1}: 3088 (=CH); 1666, 1625, 1609, 1573, 1515 (C=N, C=C). ^{1}H NMR spectrum, δ, ppm: 2.51 s (3H, CH_3), 6.02 s (1H, 9-H), 6.28 s (1H, 3-H), 6.75 s (1H, 6-H), 14.3 br.s (1H, OH). ^{19}F NMR spectrum: δ_F 93.47 ppm, s (3F, 7-CF_3) (hereinafter, signals from fluorine atoms in the nonafluorobutyl group are omitted). ^{13}C NMR spectrum, δ_C, ppm (J_{CF}, Hz): 14.68, 94.83 t (C^9, *J* = 4.4), 93.40, 105.01 q (C^6, *J* = 4.4), 117.46 q.t (**C**F_3CF_2, *J* = 288.3, 33.4), 118.88 q (C^8, *J* = 274.9), 134.86 q (C^7, *J* = 37.7), 142.85, 152.96, 156.99, 167.23 t (C^{10}, *J* = 25.9). Found, %: C 36.45; H 1.49; F 49.46; N 9.03. $C_{14}H_7F_{12}N_3O$. Calculated, %: C 36.45; H 1.53; F 49.43; N 9.11.

(*Z*)-1,1,1,7,7,7-Hexafluoro-4-(3-methyl-1*H*-pyrazol-5-ylamino)hept-3-ene-2,6-dione (IIIa). A mixture of 1.9 mmol of triketone **Ia** and 0.18 g (1.9 mmol) of 5-amino-3-methylpyrazole in 3 ml of chloroform was kept for 48 h, and the colorless precipitate (a mixture of compounds **IIIa** and **IIa** at a ratio of 9:1, according to the ^{1}H NMR data) was filtered off and washed with a small amount of chloroform. ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 3.29 s (2H, CH_2), 5.69 s and 5.76 s (1H each, CH), 12.2 br.s (1H, OH).

Reaction of 2,6-bis(polyfluoroalkyl)pyran-4-ones IVa and IVb with 5-amino-3-methylpyrazole (*general procedure*). A mixture of 2 mmol of 4-pyranone **IVa** or **IVb** and 0.19 g (2 mmol) of 5-amino-3-methylpyrazole in 3 ml of methanol was kept for 24 h, the solvent was evaporated, and the residue was recrystallized from benzene or hexane.

1,1,1-Trifluoro-3-(2-methyl-5-trifluoromethyl-1*H*-pyrazolo[1,5-*a*]pyrimidin-7-ylidene)propan-2-one (Va). Yield 48%, yellow crystals, mp 115–120°C (from hexane). According to the ^{1}H NMR data, the product was a mixture of **Va** and hydrate **VIa** at a ratio of 52:48 (freshly prepared solution) to 69:31 (after 7 days). ^{1}H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 5.85 s (1H, CH), 6.67 s and 6.86 s (1H each, 3-H, 6-H), 16.2 br.s (1H, OH). ^{19}F NMR spectrum, δ_F, ppm: 88.69 s (3F, CF_3CO), 92.89 s (3F, 5-CF_3).

1,1,1-Trifluoro-3-(2-methyl-5-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-7-yl)propane-2,2-diol (VIa). ^{1}H NMR spectrum, δ, ppm: 2.58 s (3H, CH_3), 3.73 s (2H, CH_2), 6.01 s (2H, OH), 6.74 s and 7.06 s

(1H each, 3-H, 6-H). ^{19}F NMR spectrum, δ_F, ppm: 75.03 s (3F, CF_3COH), 93.30 s (3F, 5-CF_3).

3,3,4,4,5,5,6,6,6-Nonafluoro-1-(2-methyl-5-trifluoromethyl-1*H*-pyrazolo[1,5-*a*]pyrimidin-7-ylidene)-hexan-2-one (Vb). Yield 60%, yellow crystals (a mixture of **Vb** and **VIb** at a ratio of 3:7). ^1H NMR spectrum, δ, ppm: 2.59 s (3H, CH_3), 5.84 s (1H, CH), 6.67 s and 6.87 s (1H each, 3-H, 6-H), 16.3 br.s (1H, OH). ^{19}F NMR spectrum: δ_F 92.90 ppm, s (3F, 5-CF_3).

The IR spectra were recorded on a Perkin–Elmer Spectrum I spectrometer from samples dispersed in mineral oil. The NMR spectra were measured on a Bruker DRX-400 instrument at 400 (^1H), 375 (^{19}F), and 100 MHz (^{13}C) from solutions in $CDCl_3$ using tetramethylsilane (^1H and ^{13}C) and hexafluorobenzene (^{19}F) as internal references.

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