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Ring-chain isomerism of ethyl 7-polyfluoroalkyl-7-hydroxy-4,7-dihydro[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylates

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Ethyl-7-hydroxy-7-(trifluoromethyl)-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate **2a** (general procedure A). A mixture of ethyl-2-ethoxymethylidene-3-oxo-4,4,4-trifluorobutanoate **1a** (0.720 g, 0.003 mol) and 3-amino-1*H*-[1,2,4]triazole (0.444 g, 0.003 mol) in 1,4-dioxane (20 ml) was refluxed for 16-18 h. The reaction mixture was poured into water. The resulting precipitate was filtered off and recrystallized from ethanol to give 0.60 g (72 %) of product **2a**, mp 184-186 ºC. ^{1}H NMR ($(CD_3)_2SO$) δ: 1.23 (t, 3H, $OCH_2\underline{CH_3}$, J 7.0 Hz), 4.15 (m, 2H, $O\underline{CH_2}CH_3$, AB-system, Δ_{AB} 0.05 ppm, J_{AB} 10.8, J 7.0 Hz), 7.88, 7.91 (both s, 1H each, H-2, H-5), 8.48 (s, 1H, NH), 11.77 (br.s, 1H, OH). ^{19}F NMR ($(CD_3)_2SO$) δ: 83.94 (s, CF_3). IR (nujol, ν/cm^{-1}): 3200, 3114, (NH, OH), 1678 (CO_2Et), 1599, 1521 (C=C, C=N), 1267-1158 (C-F). Found (%): C, 38.86; H, 3.11; F, 20.47; N, 20.27. Calc. for $C_9H_9F_3N_4O_3$ (%): C, 38.86; H, 3.26; F, 20.49; N, 20.14.

Ethyl-7-hydroxy-7-(1,1,2,2-tetrafluoroethyl)-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate **2b.** Ethyl-2-ethoxymethylidene-3-oxo-4,4,5,5-tetrafluoro-pentanoate **1b** (0.817 g, 0.003 mol) gave by procedure A 0.633 g (68 %) of product **2b**, mp 155-157 ºC. ^{1}H NMR ($(CD_3)_2SO$) δ: 1.24 (t, 3H, $OCH_2\underline{CH_3}$, J 7.0 Hz), 4.16 (m, 2H, $O\underline{CH_2}CH_3$, AB-system, Δ_{AB} 0.03 ppm, J_{AB} 10.7, J 7.0 Hz), 6.70 (d.d.d.d, 1H, $H(CF_2)_2$, $^2J_{H,F}$ 53.2, $^2J_{H,F}$ 51.3, $^3J_{H,F}$ 10.5, $^3J_{H,F}$ 2.4 Hz), 7.86, 7.91 (both s, 1H each, H-2, H-5), 8.36 (s, 1H, NH), 11.68 (br.s, 1H, OH). ^{1}H NMR ($(CD_3)_2CO$) δ: **(*E*)-2b'** (26 %) 1.34 (t, 3H, $OCH_2\underline{CH_3}$, J 7.0 Hz), 4.36 (q, 2H, $O\underline{CH_2}CH_3$, J 7.0 Hz), 6.95 (t.t, $H(CF_2)_2$, $^2J_{H,F}$ 53.4, $^3J_{H,F}$ 5.8 Hz), 8.52 (br.s, 1H, H-5'), 8.98 (d, 1H, CH, J 13.5 Hz), 10.69 (br.d, 1H, NH, J 13.5 Hz), 13.27 (br.s, 1H,

NH); **(*Z*)-2b'** (15 %) 1.35 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.0 Hz), 4.29 (q, 2H, $O\underline{CH_2}CH_3$, *J* 7.0 Hz), 6.66 (t.t, $H(CF_2)_2$, $^2J_{H,F}$ 52.7, $^3J_{H,F}$ 5.9 Hz), 8.48 (br.s, 1H, H-5'), 8.79 (d, 1H, CH, *J* 13.5 Hz), 11.08 (br.d, 1H, NH, *J* 13.5 Hz), 13.20 (br.s, 1H, NH); **2b** (59 %)1.24 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.29 (q, 2H, $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 6.73 (d.d.d.d, 1H, $H(CF_2)_2$, $^2J_{H,F}$ 52.1, $^2J_{H,F}$ 53.0, $^3J_{H,F}$ 10.4, $^3J_{H,F}$ 2.3 Hz), 7.34 (br.s, 1H, NH), 7.85, 8.09 (both s, 1H each, H-2, H-5), 10.69 (s, 1H, OH). ^{19}F NMR ($(CD_3)_2SO$) δ: 26.04 (t.d.d, 1F, HCF_2, $^2J_{F,F}$ 293.7, $^2J_{F,H}$ 53.2, $J_{F,F}$ 19.6 Hz), 31.02 (d.d.d.d, 1F, HCF_2, $^2J_{F,F}$ 293.7, $^2J_{F,H}$ 51.3, $^3J_{F,F}$ 10.6, $J_{F,F}$ 1.4 Hz), 32.97 (d.d.d, 1F, CF_2, $^2J_{F,F}$ 261.2, $^3J_{F,F}$ 19.6, $^3J_{F,H}$ 10.5 Hz), 41.66 (d.d.d, 1F, CF_2, $^2J_{F,F}$ 261.2, $^3J_{F,F}$ 10.6, $^3J_{F,H}$ 2.4 Hz). IR (nujol, ν/cm^{-1}): 3220, 3108, (NH, OH), 1682 (CO_2Et), 1614, 1529 (C=C, C=N), 1206-1078 (C-F). Found (%): C, 38.96; H, 3.20; F, 24.52; N, 18.03. Calc. for $C_{10}H_{10}F_4N_4O_3$ (%): C, 38.72; H, 3.25; F, 24.50; N, 18.06

Ethyl-7-(1,1,2,2,3,3,3-heptafluoropropyl)-7-hydroxy-4,7-dihydro[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate **2c.** Ethyl-2-ethoxymethylidene-3-oxo-4,4,5,5,6,6,6-heptafluoro-hexanoate **1c** (1.021 g, 0.003 mol) gave by procedure A 0.681 g (60 %) of product **2c**, mp 136-138 ºC. ^{1}H NMR ($(CD_3)_2SO$) δ: **(*E*)-2c'** (9 %) 1.25 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.26 (q, 2H, $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 8.58 (s, 1H, H-5'), 8.77 (d, 1H, CH, *J* 13.9 Hz), 11.81 (d, 1H, NH, *J* 13.9 Hz), 14.22 (br.s, 1H, NH); **(*Z*)-2c'** (11 %) 1.25 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.27 (q, 2H, $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 8.56 (s, 1H, H-5'), 8.60 (d, 1H, CH, *J* 13.9 Hz), 11.29 (d, 1H, NH, *J* 13.9 Hz), 14.13 (br.s, 1H, NH); **2c** (80 %) 1.25 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.2 Hz), 4.18 (m, 2H, $OC\underline{H_2}CH_3$, AB-system, Δ_{AB} 0.04 ppm, J_{AB} 10.8, *J* 7.2 Hz), 7.89, 7.92 (both s, 1H each, H-2, H-5), 8.56 (s, 1H, NH), 11.81 (br.s, 1H, OH). ^{19}F NMR ($(CD_3)_2SO$) δ: **(*E*)-2c'** (9 %): 39.64 (m, 2F, β-CF_2), 49.61 (m, 2F, α-CF_2, *J* 9.3 Hz), 82.92 (t, 3F, γ-CF_3, *J* 9.3 Hz); **(*Z*)-2c'** (11 %): 38.43 (m, 2F, β-CF_2), 49.96 (m, 2F, α-CF_2, *J* 9.3 Hz), 82.94 (t, 3F, γ-CF_3, *J* 9.3 Hz); **2c** (80 %) 37.44 (m, 2F, β-CF_2, AB-system, Δ_{AB} 1.4 ppm, J_{AB} 290.0, *J* 4.0 Hz), 46.26 (m, 2F, α-CF_2, *J* 11.6, *J* 4.0 Hz), 82.34 (t, 3F, γ-CF_3, *J* 11.6 Hz). ^{13}C NMR ($(CD_3)_2SO$) δ: 105.81-121.88 (m, C_3F_7 (**(*E*)-2c', (*Z*)-2c', 2c**)); **(*E*)-2c'** (9 %) 13.85 (CH_3), 60.69 (OCH_2), 100.63 (C-2), 144.73 (C-5'), 154.90 (C-4), 156.69 (C-3'), 164.11 (C-1), 180.74 (br.t, C-3, $J_{C\text{-}F}$ 25.0 Hz); **(*Z*)-2c'** (11 %) 13.74 (CH_3), 60.86 (OCH_2), 101.77 (C-2), 144.52 (C-5'), 151.52 (C-4'), 157.15 (C-3'), 165.09 (C-1), 179.43 (br.t, C-3, $J_{C\text{-}F}$ 25.4 Hz); **2c** (80 %) 14.03 (CH_3), 59.89 (OCH_2), 86.53 (t,

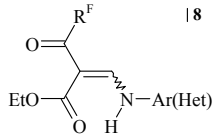
C-7, J_{C-F} 27.2 Hz), 96.86 (C-6), 139.09 (C-5), 147.19 (C-3a), 150.56 (C-2), 163.98 (C-9). IR (nujol, ν/cm^{-1}): 3200, 3115 (NH, OH), 1693 (CO_2Et), 1602, 1599 (C=C, C=N), 1220-1119 (C-F). Found (%): C, 34.94; H, 2.11; F, 35.25; N, 14.81. Calc. for $C_{11}H_9F_7N_4O_3$ (%): C, 34.93; H, 2.40; F, 35.16; N, 14.81.

Ethyl-7-(trifluoromethyl)-5H-[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate **3a** (general procedure B). The solution of pyrimidine **2a** (0.278 g, 0.001 mol) in glacial acetic acid was refluxed for 60 h. The reaction mixture was poured into water and was reduced to pH 7. The resulting precipitate was filtered off and recrystallized from hexane to give 0.247 g (95 %) of product **3a**, mp 77-78 ºC. ^{1}H NMR ($(CD_3)_2SO$) δ: 1.37 (t, 3H, $OCH_2\underline{CH_3}$, J 7.2 Hz), 4.41 (q, 2H, $O\underline{CH_2}CH_3$, J 7.2 Hz), 9.05 (s, 1H, H-5), 10.16 (s, 1H, H-2). ^{19}F NMR ($(CD_3)_2SO$) δ: 98.46 (s, CF_3). IR (nujol, ν/cm^{-1}): 3069, 3018 (C-H), 1719 (CO_2Et), 1627, 1511 (C=C, C=N), 1191-1129 (C-F). Found (%): C, 41.69; H, 2.80; F, 21.78; N, 21.69. Calc. for $C_9H_7F_3N_4O_2$ (%): C, 41.55; H, 2.71; F, 21.91; N, 21.53.

Ethyl-7-(1,1,2,2,-tetrafluoroethyl)-5H-[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate **3b.** Pyrimidine **2b** (0.310 g, 0.001 mol) gave by procedure B 0.228 g (78 %) of product **3b**, mp 93-95 ºC. ^{1}H NMR ($(CD_3)_2SO$) δ: 1.36 (t, 3H, $OCH_2\underline{CH_3}$, J 7.1 Hz), 4.41 (q, 2H, $O\underline{CH_2}CH_3$, J 7.1 Hz), 7.19 (t.t, 1H, $H(CF_2)_2$, J 51.8, J 6.0 Hz), 9.02 (s, 1H, H-5), 10.12 (s, 1H, H-2). ^{19}F NMR ($(CD_3)_2SO$) δ: 24.69 (d.m, 2F, HCF_2, J 51.8 Hz), 48.38 (m, 2F, CF_2, J 6.0 Hz). IR (nujol, ν/cm^{-1}): 3118, 3079, 3029 (C-H), 1707 (CO_2Et), 1620, 1506 (C=C, C=N), 1164-1071 (C-F). Found (%): C, 41.25; H, 2.81; F, 25.89; N, 18.95. Calc. for $C_{10}H_8F_4N_4O_2$ (%): C, 41.11; H, 2.76; F, 26.01; N, 19.17.

Ethyl-7-(1,1,2,2,3,3,3-heptafluoropropyl)-5H-[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylate **3c.** Pyrimidine **2c** (0.378 g, 0.001 mol) gave by procedure B 0.234 g (65 %) of product **3c**, mp 125-126 ºC. ^{1}H NMR ($CDCl_3$) δ: 1.43 (t, 3H, $OCH_2\underline{CH_3}$, J 7.2 Hz), 4.49 (q, 2H, $O\underline{CH_2}CH_3$, J 7.2 Hz), 8.78 (s, 1H, H-5), 9.39 (s, 1H, H-2). ^{19}F NMR ($CDCl_3$) δ: 39.12 (m, 2F, β-CF_2, J 1.9 Hz), 54.73 (m, 2F, α-CF_2, J 1.9, J 10.0 Hz), 81.86 (t, 3F, γ-CF_3, J 10.0 Hz). IR (nujol, ν/cm^{-1}): 3049, 3104 (C-H), 1727 (CO_2Et), 1622, 1502 (C=C, C=N), 1236-1124 (C-F). Found (%): C, 36.36; H, 2.00; F, 36.94; N, 15.28. Calc. for $C_{11}H_7F_7N_4O_2$ (%): C, 36.68; H, 1.96; F, 36.92; N, 15.55.

Table Characteristic shifts and coupling constants in ^{1}H NMR of compounds **2a-c** in comparison with literature data.

proton fragment	δ, ppm, (J, Hz)			
	2a	**2b**	**2c**	 **8**
=CH (*E*)-2'	8.91 (d, *J* 13.2)[b]	8.86 (d, *J* 13.5) [b] 8.98 (d, *J* 13.5) [c]	8.77 (d, *J* 13.9) [a] 8.84 (d, *J* 13.7) [b] 8.96 (d, *J* 13.6) [c]	8.44 (d, *J* 14.5) [a] 8.09-9.36 (d, *J* 13.2-14.5) [d]
=CH (*Z*)-2'	8.73 (d, *J* 13.8)[b]	8.70 (d, *J* 13.5) [b] 8.79 (d, *J* 13.5) [c]	8.60 (d, *J* 13.9) [a] 8.67 (d, *J* 13.2) [b] 8.75 (d, *J* 13.2) [c]	8.26 (d, *J* 14.5) [a] 7.97-9.23 (d, *J* 13.2-14.5) [d]
NH (*E*)-2'	11.78 (d, *J* 13.2)[b]	11.87 (d, *J* 13.5) [b] 11.08 (d, *J* 13.5) [c]	11.81 (d, *J* 13.9) [a] 11.67 (d, *J* 13.7) [b] 11.85 (d, *J* 13.6) [c]	12.10 (d, *J* 14.5) [a] 10.42-12.27(d, *J* 13.2-14.5) [d]
NH (*Z*)-2'	11.02 (d, *J* 13.8) [b]	10.87 (d, *J* 13.5) [b] 10.69 (d, *J* 13.5) [c]	11.29 (d, *J* 13.9) [a] 10.97 (d, *J* 13.2) [b] 11.14 (d, *J* 13.2) [c]	10.97 (d, *J* 14.5) [a] 9.47-11.41 (d, *J* 13.2-14.5) [d]

[a] in $(CD_3)_2SO$; [b] in CD_3CN; [c] in $(CD_3)_2CO$; [d] in $CDCl_3$