Novel synthesis of 1,4,8-triazabicyclo[5.3.0]dec-4-ene derivatives

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We have hitherto reported[1] a simple synthesis of previously unknown representatives of the 1,4,8-triazabicyclo[5.3.0]dec-4-ene system from aromatic β-amino-β-polyfluoroalkylvinyl ketones and diethylenetriamine. Our attempt to expand this reaction to aminoenones with 2-hydroxyaryl substituents failed, thus stimulating further investigations in this sphere. We have found out that the reaction of 2-(polyfluoroalkyl)chromones (**1a—e**) with diethylenetriamine proceeds under mild conditions (at room temperature in ethanolic solution or without a solvent) and permits synthesis of 2-hydroxyaryl derivatives of 1,4,8-triazabicyclo[5.3.0]dec-4-ene (**2a—e**) in high yields (54—80 %), which we were unable to obtain from the corresponding aminoenones (see Scheme 1).

The first stage apparently involves nucleophilic attack of the primary amino group at the C(2) atom of the pyrone ring, which is attended with scission of chromones **1a—e** to give *N*-substituted aminoenones. The latter undergo cyclization to triazabicycles **2a—e** with the participation of both nucleophilic centers and release of a water molecule.

Thus, the reaction of 2-(polyfluoroalkyl)chromones with diethylenetriamine comprises a novel approach to the synthesis of the 1,4,8-triazabicyclo[5.3.0]dec-4-ene system and makes its 2-hydroxyaryl derivatives available.

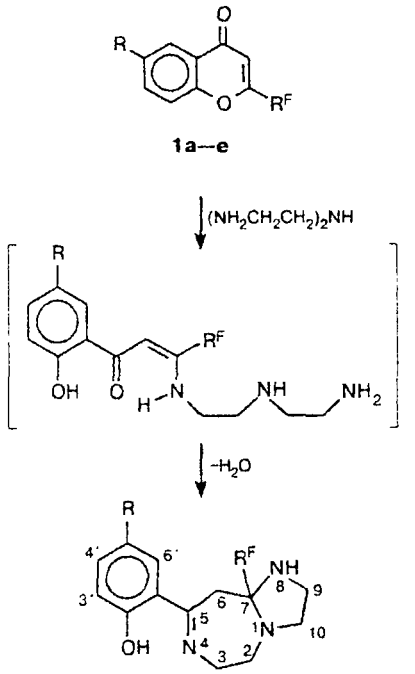
IR spectra were recorded on an IKS-29 instrument in Vaseline. ^{1}H NMR spectra were registered on a Bruker WM-250 spectrometer in $CDCl_3$ at a working frequency of 250 MHz with Me_4Si as the internal standard.

5-(2-Hydroxyphenyl)-7-trifluoromethyl-1,4,8-triazabicyclo-[5.3.0]dec-4-ene (2a). Chromone **1a** (214 mg, 1.0 mmol) and diethylenetriamine (215 μL, 205 mg, 2.0 mmol) were dissolved in 3 mL of ethanol. The reaction mixture was kept for 24 h at room temperature, and the precipitate of bicycle **2a** was washed with water and recrystallized from ethanol, yield 240 mg (50%), m.p. 152—153 °C. Found (%): C, 55.90; H, 5.62; N, 14.11. $C_{14}H_{16}F_3N_3O$. Calculated (%): C, 56.18; H, 5.39; N, 14.04. IR, ν/cm^{-1}: 3380 (NH); 1610, 1560, 1500 (C=N, benzene ring). ^{1}H NMR, δ: 2.12 (br.s, 1 H, NH); 2.94—3.14 (m, 4 H, C(9)H$_2$, C(10)H$_2$); 3.15—3.27 (m, 1 H, C(2)HH); 3.37 (s, 2 H, C(6)H$_2$); 3.44—3.57 (m, 1 H, C(2)HH); 3.96 (ddd, 1 H, C(3)HH, ^2J = 15.3 Hz, ^3J = 6.7 and 5.2 Hz); 4.16 (dt, 1 H, C(3)HH, ^2J = 15.3 Hz, ^3J = 6.0 Hz); 6.80 (td, 1 H, H(5′), J_o = 8.2 Hz, J_m = 1.2 Hz); 6.95 (dd, 1 H, H(3′)); 7.31 (td, 1 H, H(4′)); 7.51 (dd, 1 H, H(6′)); 15.90 (br.s, 1 H, OH).

5-(2-Hydroxy-5-methylphenyl)-7-trifluoromethyl-1,4,8-triazabicyclo[5.3.0]dec-4-ene (2b). Yield 67%, m.p. 114—115 °C (petroleum ether). Found (%): C, 57.41; H, 5.99; N, 13.36. $C_{15}H_{18}F_3N_3O$. Calculated (%): C, 57.50; H, 5.79; N, 13.41. IR, ν/cm^{-1}: 3380 (NH); 1620, 1600, 1575, 1500 (C=N, benzene ring). ^{1}H NMR, δ: 2.14 (br.s, 1 H, NH); 2.29 (s, 3 H, Me); 2.95—3.12 (m, 4 H, C(9)H$_2$, C(10)H$_2$); 3.16—3.27 (m, 1 H, C(2)HH); 3.37 (s, 2 H, C(6)H$_2$); 3.43—3.57 (m, 1 H, C(2)HH); 3.97 (ddd, 1 H, C(3)HH, ^2J = 15.3 Hz, ^3J = 7.0 and 5.2 Hz); 4.16 (dt, 1 H, C(3)HH, ^2J = 15.3 Hz, ^3J = 6.1 Hz); 6.87 (d, 1 H, H(3′), J_o = 8.5 Hz); 7.13 (dd, 1 H, H(4′), J_m = 1.7 Hz); 7.28 (td, 1 H, H(6′)); 15.60 (br.s, 1 H, OH).

5-(2-Hydroxyphenyl)-7-(1,1,2,2-tetrafluoroethyl)-1,4,8-triazabicyclo[5.3.0]dec-4-ene (2c). Yield 54%, m.p. 149—150 °C. Found (%): C, 54.52; H, 5.28; N, 12.61. $C_{15}H_{17}F_4N_3O$. Calculated (%): C, 54.38; H, 5.17; N, 12.68. IR, ν/cm^{-1}: 3370 (NH); 1620, 1575, 1510 (C=N, benzene ring). ^{1}H NMR, δ: 2.11 (br.s, 1 H, NH); 2.90—3.24 (m, 5 H, C(9)H$_2$, C(10)H$_2$, C(2)HH); 3.38 (AB-system, Δδ = 0.13, 2 H, C(6)H$_2$, J_{AB} = 15.3 Hz); 3.42—3.56 (m, 1 H, C(2)HH); 3.93 (ddd, 1 H, C(3)HH, ^2J = 14.9 Hz, ^3J = 6.9 and 4.9 Hz); 4.14 (dt, 1 H, C(3)HH, ^2J = 14.9 Hz, ^3J = 6.1 Hz); 6.11 (tdd, 1 H, CF_2CF_2H, $^2J_{H,F}$ = 53.4 Hz, $^3J_{H,F}$ = 7.9 and 4.6 Hz); 6.80 (td, 1 H, H(5′), J_o = 8.2 Hz, J_m = 1.2); 6.95 (dd, 1 H, H(3′)); 7.31 (td, 1 H, H(4′)); 7.53 (dd, 1 H, H(6′)); 15.95 (br.s, 1 H, OH).

Scheme 1



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5-(2-Hydroxy-5-methylphenyl)-7-(1,1,2,2-tetrafluoroethyl)-1,4,8-triazabicyclo[5.3.0]dec-4-ene (2d). Yield 65%, m.p. 184—185 °C. Found (%): C, 55.55; H, 5.56; N, 12.32. $C_{16}H_{19}F_4N_3O$. Calculated (%): C, 55.65; H, 5.55; N, 12.17. IR, ν/cm^{-1}: 3400 (NH); 1620, 1585, 1500 (C=N, benzene ring). ^1H NMR, δ: 2.12 (br.s, 1 H, NH); 2.30 (s, 3 H, Me); 2.86—3.22 (m, 5 H, C(9)H_2, C(10)H_2, C(2)H<u>H</u>); 3.37 (AB-system, Δδ = 0.12, 2 H, C(6)H_2, J_{AB} = 15.3 Hz); 3.42—3.55 (m, 1 H, C(2)H<u>H</u>); 3.93 (ddd, 1 H, C(3)<u>H</u>H, ^2J = 14.9 Hz, ^3J = 6.9 and 4.9 Hz); 4.13 (dt, 1 H, C(3)H<u>H</u>, ^2J = 14.9 Hz, ^3J = 6.0 Hz); 6.12 (tdd, 1 H, CF_2CF_2H, $^2J_{H,F}$ = 53.5 Hz, $^3J_{H,F}$ = 8.6 and 4.6 Hz); 6.86 (d, 1 H, H(3′), J_o = 8.5 Hz); 7.13 (dd, 1 H, H(4′), J_m = 1.7 Hz); 7.30 (d, 1 H, H(6′)); 15.64 (br.s, 1 H, OH).

7-Difluoromethyl-5-(2-hydroxyphenyl)-1,4,8-triazabicyclo[5.3.0]dec-4-ene (2e). Yield 54%, m.p. 124—125 °C. Found (%): C, 59.90; H, 6.24; N, 14.78. $C_{14}H_{17}F_4N_3O$. Calculated (%): C, 59.78; H, 6.09; N, 14.94. IR, ν/cm^{-1}: 3350 (NH); 1620, 1575, 1510 (C=N, benzene ring). ^1H NMR, δ: 2.08 (br.s, 1 H, NH); 2.92—3.21 (m, 5 H, C(9)H_2, C(10)H_2, C(2)H<u>H</u>); 3.28 (AB-system, Δδ = 0.16, 2 H, C(6)H_2, J_{AB} = 15.3 Hz); 3.36—3.47 (m, 1 H, C(2)H<u>H</u>); 3.93 (ddd, 1 H, C(3)<u>H</u>H, ^2J = 15.5 Hz, ^3J = 6.6 and 4.0 Hz); 4.14 (ddd, 1 H, C(3)H<u>H</u>, ^2J = 15.5 Hz, ^3J = 7.6 and 4.2 Hz); 5.50 (t, 1 H, CHF_2, $J_{H,F}$ = 56.1); 6.78 (td, 1 H, H(5′), J_o = 8.2 Hz, J_m = 1.2 Hz); 6.93 (dd, 1 H, H(3′)); 7.29 (td, 1 H, H(4′)); 7.54 (dd, 1 H, H(6′)); 16.09 (br.s, 1 H, OH).

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References

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