Reactions of 3-polyfluoroacylchromones with primary amines

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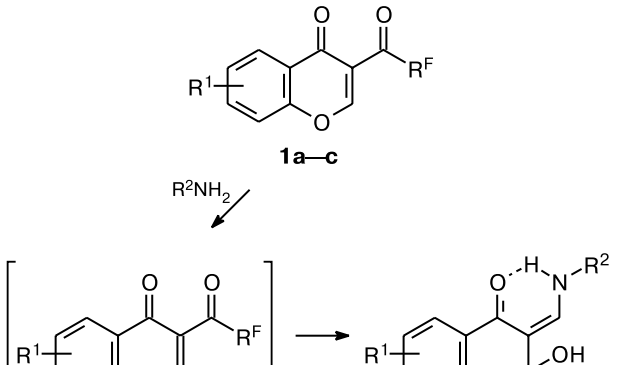
Recently,[1] we have described a simple and efficient method for the synthesis of 3-polyfluoroacylchromones from 2-polyfluoroalkyl-2-hydroxychroman-4-ones and diethoxymethyl acetate. In contrast to well studied 3-formyl-[2—5] and 3-acylchromones,[6—9] no data on the chemical properties of 3-polyfluoroacylchromones have been documented. This is quite surprising, especially because chromones containing an electron-withdrawing R^FCO group in position 3 should contain the highly electrophilic C(2) atom, which is usually attacked by nucleophilic reagents.

We found that reactions of 3-R^FCO-chromones **1a—c** with primary amines follow the 1,4-addition mechanism with subsequent opening of the pyran ring and cyclization into 3-alkyl(aryl)aminomethylene-2-hydroxy-2-polyfluoroalkylchroman-4-ones **2a—c** in 50—76% yields, whose structures were confirmed by elemental analysis and ^1H, ^{19}F, and ^{13}C NMR spectroscopy. Since these reactions easily occur with both aliphatic and aromatic amines, chromones **1** are highly reactive and promising substrates for the synthesis of various R^F-containing heterocycles. Note that reactions of 3-formylchromones with primary aromatic amines gave difficult-to-separate mixtures of 3-aryliminomethylchromone and 2-arylamino-3-arylaminomethylenechroman-4-one.[10]



	R^F	R^1	R^2
a	CF_3	H	*cyclo*-C_6H_{11}
b	CF_3	H	Ph
c	CF_2H	H	4-$MeOC_6H_4$

Synthesis of compounds 2a—c (general procedure). A solution of 3-polyfluoroacylchromone **1** (0.4 mmol) and a primary amine (0.6—0.8 mmol) in methanol (2—3 mL) was kept at ~20 °C for 2 to 3 days. The precipitate that formed was filtered off, washed with cold methanol or hexane—toluene, and dried.

3-Cyclohexylaminomethylene-2-hydroxy-2-trifluoromethylchroman-4-one (2a). The yield was 50%, a colorless powder, m.p. 133—134 °C (hexane—toluene, 1 : 1). Found (%): C, 58.91; H, 5.28; N, 3.94. $C_{17}H_{18}F_3NO_3 \cdot 0.25H_2O$. Calculated (%): C, 59.04; H, 5.39; N, 4.05. IR (KBr), ν/cm^{-1}: 3200, 2937, 2859, 1646, 1610, 1596, 1547. ^1H NMR (400 MHz, $CDCl_3$), δ: 1.30—1.97 (m, 10 H, $(CH_2)_5$); 3.12—3.22 (m, 1 H, CHN); 4.03 (br.s, 1 H, OH); 6.95 (dd, 1 H, H(8), J_o = 8.2 Hz, J_m = 1.0 Hz); 7.07 (ddd, 1 H, H(6), J_o = 7.8 Hz, J_o = 7.3 Hz, J_m = 1.0 Hz); 7.39 (ddd, 1 H, H(7), J_o = 8.2 Hz, J_o = 7.3 Hz, J_m = 1.7 Hz); 7.47 (d, 1 H, =CH, J = 13.4 Hz); 7.88 (dd, 1 H, H(5), J_o = 7.8 Hz, J_m = 1.7 Hz); 11.10 (br.s, 1 H, NH).

3-Anilinomethylene-2-hydroxy-2-trifluoromethylchroman-4-one (2b). The yield was 76%, yellow crystals, m.p. 143—144 °C (hexane—toluene, 1 : 1). Found (%): C, 60.70; H, 3.45; N, 4.19. $C_{17}H_{12}F_3NO_3$. Calculated (%): C, 60.90; H, 3.61; N, 4.18. IR (KBr), ν/cm^{-1}: 3228, 1639, 1599, 1588, 1548. ^1H NMR (400 MHz, DMSO-d_6), δ: 7.07 (dd, 1 H, H(8), J_o = 8.3 Hz, J_m = 1.0 Hz); 7.15 (ddd, 1 H, H(6), J_o = 7.7 Hz, J_o = 7.3 Hz, J_m = 1.0 Hz); 7.18—7.23 (m, 1 H, H(4′)); 7.40—7.46 (m, 4 H, H(2′), H(3′), H(5′), H(6′)); 7.55 (ddd, 1 H, H(7), J_o = 8.3 Hz, J_o = 7.3 Hz, J_m = 1.7 Hz); 7.83 (dd, 1 H, H(5), J_o = 7.7 Hz, J_m = 1.7 Hz); 8.00 (d, 1 H, =CH, J = 12.9 Hz); 9.12 (s, 1 H, OH); 12.53 (d, 1 H, NH, J = 12.9 Hz). When CD_3CO_2D was added, the last two signals disappeared and the doublet at δ 8.00 changed into a singlet. ^{19}F NMR (376 MHz, DMSO-d_6, C_6F_6), δ: 77.75 (s, CF_3). ^{13}C NMR (100 MHz, DMSO-d_6), δ: 97.98 (q, C(2), $^2J_{C,F}$ = 32.6 Hz); 98.98, 116.53, 117.45, 119.98, 122.21, 122.87 (q, CF_3, $^1J_{C,F}$ = 290.3 Hz), 124.98, 125.67, 129.87, 135.03, 139.18, 147.21, 155.80, 179.81.

3-(*p*-Anisidinomethylene)-2-difluoromethyl-2-hydroxychroman-4-one (2c). The yield was 75%, orange crystals, m.p. 178—179 °C. Found (%): C, 62.32; H, 4.29; N, 4.02. $C_{18}H_{15}F_2NO_4$. Calculated (%): C, 62.25; H, 4.35; N, 4.03. IR (KBr), ν/cm^{-1}: 3287, 1637, 1604, 1587, 1544, 1516. ^1H NMR (400 MHz, DMSO-d_6), δ: 3.77 (s, 3 H, MeO); 6.07 (t, 1 H, CF_2H, $^2J_{H,F}$ = 55.4 Hz); 6.99 (dd, 1 H, H(8), J_o = 8.3 Hz, J_m = 1.0 Hz); 7.00 (d, 2 H, H(2′), H(6′), J_o = 9.0 Hz); 7.08 (ddd, 1 H, H(6), J_o = 7.8 Hz, J_o = 7.3 Hz, J_m = 1.0 Hz); 7.34 (d, 2 H, H(3′), H(5′), J_o = 9.0 Hz); 7.48 (ddd, 1 H, H(7), J_o = 8.3 Hz, J_o = 7.3 Hz, J_m = 1.7 Hz); 7.79 (dd, 1 H, H(5), J_o = 7.8 Hz, J_m = 1.7 Hz); 7.82 (d, 1 H, =CH, J = 12.8 Hz); 8.33 (s, 1 H, OH); 12.57 (d, 1 H, NH, J = 12.8 Hz).

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