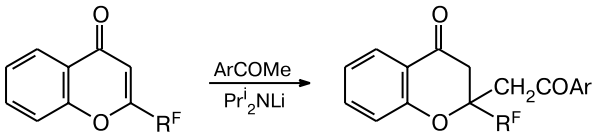
Synthesis of 2-aroylmethyl-2-polyfluoroalkylchroman-4-ones

V. Ya. Sosnovskikh, B. I. Usachev, and A. Yu. Sizov*

A. M. Gorky Ural State University,
51 prosp. Lenina, 620083 Ekaterinburg, Russian Federation.
Fax: +7 (343 2) 61 5978. E-mail: Vyacheslav.Sosnovskikh@usu.ru

Data on the reactions of 2-polyfluoroalkylchromones with C-nucleophiles are rather limited. It is known that 2-CF_3-chromones react with CF_3SiMe_3 to form 2,2-bis(trifluoromethyl)chroman-4-ones,[1—3] whereas 2-CF_3-chromene-4-imines react with malonic acid affording 2-methyl-2-trifluoromethylchroman-4-ones.[4] Aromatic methyl ketimines act as 1,3-C,N-dinucleophiles in the reaction with 2-R^F-chromones yielding 2,6-diaryl-4-polyfluoroalkylpyridines.[5,6]

We found that the reaction of 2-R^F-chromones **1** with acetophenones in the presence of lithium diisopropylamide at −30 °C in a mixture of diethyl ether and THF as solvent produces 2-aroylmethyl-2-polyfluoroalkylchroman-4-ones **2a—d** in 21—71% yields. Compounds **2a—d** are products of the Michael addition of lithium acetophenone enolates to the activated double bond of the pyrone ring. This reaction is a new transformation involving the chromone system, which occurs, most likely, due to the presence of an electron-withdrawing R^F group at the C(2) atom. The resulting products are promising R^F-containing substrates, whose open form represents a poorly studied class of unsaturated 1,5-diketones.



1 **2a—d**

	a	b	c	d
R^F	CF_3	CF_3	CF_3	$(CF_2)_2H$
Ar	Ph	4-ClC_6H_4	4-$MeOC_6H_4$	Ph

Synthesis of 2-aroylmethyl-2-polyfluoroalkylchroman-4-ones (2a—d) (general procedure). Diisopropylamine (0.81 g, 8.0 mmol) was added to a solution of BuLi (8.0 mmol) in Et_2O (8 mL). The mixture was stirred at ~20 °C for 30 min and then cooled to −30 °C, and a solution of aryl methyl ketone (8.0 mmol) in Et_2O (3 mL) was added. The resulting mixture was stirred for 1 h at ~20 °C and then cooled to −30 °C, and a solution of chromone **1** (7.0 mmol) in THF (5 mL) was added. The reaction mixture was stirred at ~20 °C for 5 h and poured into dilute HCl (1 : 3) (50 mL). The resulting solution was extracted with ether (2×25 mL), the ether was evaporated, an oily product was triturated with hexane to solidification, and the residue was filtered off, dried, and recrystallized.

2-Phenacyl-2-trifluoromethylchroman-4-one (2a). The yield was 32%, m.p. 81—83 °C (hexane—CCl_4, 2 : 1), colorless powder. Found (%): C, 64.63; H, 3.92. $C_{18}H_{13}F_3O_3$. Calculated (%): C, 64.67; H, 3.92. IR, ν/cm^{-1}: 1695, 1680 (C=O), 1605, 1600, 1580 (arom.). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.07 (d, 1 H, CHH(3), J = 17.5 Hz); 3.24 (d, 1 H, CHH, J = 15.8 Hz); 3.77 (dq, 1 H, CHH(3), J = 17.5 Hz, $J_{H,F}$ = 0.7 Hz); 3.87 (d, 1 H, CHH, J = 15.8 Hz); 6.88 (dd, 1 H, H(8), J_o = 8.4 Hz, J_m = 1.0 Hz); 7.04 (ddd, 1 H, H(6), J_o = 7.8, 7.3 Hz, J_m = 1.0 Hz); 7.45 (ddd, 1 H, H(7), J_o = 8.4, 7.3 Hz, J_m = 1.7 Hz); 7.48—7.51 (m, 2 H, H(3′), H(5′)); 7.61 (tt, 1 H, H(4′), J_o = 7.4 Hz, J_m = 1.3 Hz); 7.86 (dd, 1 H, H(5), J_o = 7.8 Hz, J_m = 1.7 Hz); 7.94—7.96 (m, 2 H, H(2′), H(6′)).

2-(*p*-Chlorobenzoylmethyl)-2-trifluoromethylchroman-4-one (2b). The yield was 21%, m.p. 141—143 °C (toluene—hexane, 2 : 1), colorless powder. Found (%): C, 58.62; H, 3.44. $C_{18}H_{12}ClF_3O_3$. Calculated (%): C, 58.63; H, 3.28. IR, ν/cm^{-1}: 1695, 1665 (C=O), 1605, 1580 (arom.). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.07 (d, 1 H, CHH(3), J = 17.5 Hz); 3.19 (d, 1 H, CHH, J = 15.5 Hz); 3.72 (dq, 1 H, CHH(3), J = 17.5 Hz, $J_{H,F}$ = 0.8 Hz); 3.83 (d, 1 H, CHH, J = 15.5 Hz); 6.88 (dd, 1 H, H(8), J_o = 8.4 Hz, J_m = 1.0 Hz); 7.05 (ddd, 1 H, H(6), J_o = 7.8 Hz, 7.3, J_m = 1.0 Hz); 7.44—7.48 (m, 3 H, H(7), H(3′), H(5′)); 7.86 (dd, 1 H, H(5), J_o = 7.8 Hz, J_m = 1.8 Hz); 7.89 (d, 2 H, H(2′), H(6′), J_o = 8.7 Hz).

2-(*p*-Anisoylmethyl)-2-trifluoromethylchroman-4-one (2c). The yield was 71%, m.p. 69—71 °C (toluene—hexane, 2 : 1), cream-colored powder. Found (%): C, 62.55; H, 4.06. $C_{19}H_{15}F_3O_4$. Calculated (%): C, 62.64; H, 4.15. IR, ν/cm^{-1}: 1695, 1655 (C=O), 1600, 1570 (arom.). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.05 (d, 1 H, CHH(3), J = 17.5 Hz); 3.16 (d, 1 H, CHH, J = 15.5 Hz); 3.77 (d, 1 H, CHH(3), J = 17.5 Hz); 3.82 (d, 1 H, CHH, J = 15.5 Hz); 6.89 (dd, 1 H, H(8), J_o = 8.4 Hz, J_m = 1.0 Hz); 6.94 (d, 2 H, H(3′), H(5′), J_o = 9.0 Hz); 7.03 (ddd, 1 H, H(6), J_o = 7.8, 7.3 Hz, J_m = 1.0 Hz); 7.45 (ddd, 1 H, H(7), J_o = 8.4 Hz, 7.3, J_m = 1.7 Hz); 7.85 (dd, 1 H, H(5), J_o = 7.8 Hz, J_m = 1.7 Hz); 7.94 (d, 2 H, H(2′), H(6′), J_o = 9.0 Hz).

2-Phenacyl-2-(1,1,2,2-tetrafluoroethyl)chroman-4-one (2d). The yield was 66%, m.p. 99—101 °C (toluene), light yellow powder. Found (%): C, 62.26; H, 3.72. $C_{19}H_{14}F_4O_3$. Calculated (%): C, 62.30; H, 3.85. IR, ν/cm^{-1}: 1700, 1675 (C=O), 1610, 1590, 1575 (arom.). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.18 (d, 1 H, CHH(3), J = 17.6 Hz); 3.31 (dd, 1 H, CHH, J = 16.2, 2.1 Hz); 3.70 (dd, 1 H, CHH(3), J = 17.6, 1.5 Hz); 3.90 (d, 1 H, CHH, J = 16.2 Hz); 6.16 (tdd, 1 H, CF_2CF_2H, $^2J_{H,F}$ = 52.5 Hz,

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$^3J_{H,F}$ = 7.4, 3.8 Hz); 6.87 (dd, 1 H, H(8), J_o = 8.3 Hz, J_m = 1.0 Hz); 7.06 (ddd, 1 H, H(6), J_o = 7.8, 7.1 Hz, J_m = 1.0 Hz); 7.44—7.49 (m, 3 H, H(7), H(3´), H(5´)); 7.59 (tt, 1 H, H(4´), J_o = 7.4 Hz, J_m = 1.3 Hz); 7.88 (dd, 1 H, H(5), J_o = 7.8 Hz, J_m = 1.7 Hz); 7.90—7.92 (m, 2 H, H(2´), H(6´)).

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References

1. V. Ya. Sosnovskikh, D. V. Sevenard, B. I. Usachev, and G.-V. Röschenthaler, *Tetrahedron Lett.*, 2003, **44**, 2097.
2. V. Ya. Sosnovskikh, B. I. Usachev, D. V. Sevenard, and G.-V. Röschenthaler, *J. Org. Chem.*, 2003, **68**, 7747.
3. D. V. Sevenard, V. Ya. Sosnovskikh, A. A. Kolomeitsev, M. H. Königsmann, and G.-V. Röschenthaler, *Tetrahedron Lett.,* 2003, **44**, 7623.
4. V. Ya. Sosnovskikh and B. I. Usachev, *Synthesis,* 2002, 2341.
5. V. Ya. Sosnovskikh, B. I. Usachev, A. Yu. Sizov, I. I. Vorontsov, and Yu. V. Shklyaev, *Org. Lett.*, 2003, **5**, 3123.
6. V. Ya. Sosnovskikh, B. I. Usachev, and A. Yu. Sizov, *Synthesis*, 2004, 942.

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