

Letters to the Editor

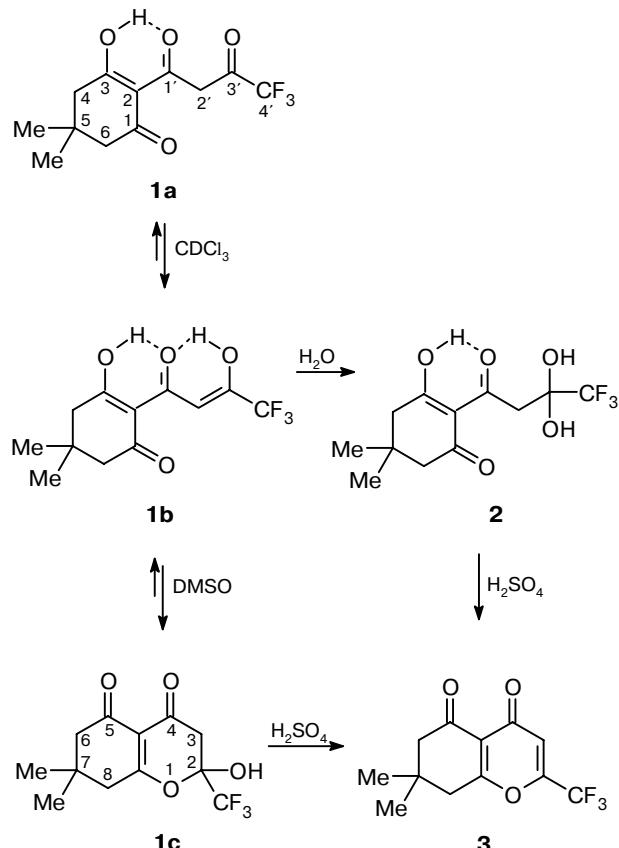
Trifluoroacetylation of 2-acetylacetone

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Considerable recent attention has been given to the problem of introduction of the trifluoromethyl group into hydrogenated and partially hydrogenated heterocyclic compounds. The increased interest in this problem arises from the fact that not only are trifluoromethylated heterocycles being of importance by themselves due to their potential biological activities,^{1,2} but they also serve as highly reactive synthons for preparing new fluorine-containing heterocyclic systems.³

Recently,⁴ we have reported the synthesis of 2-poly-fluoroalkyl-7-methylpyrano[4,3-*b*]pyran-4,5-diones from dehydroacetic acid and polyfluorocarboxylic esters. In the present study, we performed trifluoroacetylation of 2-acetylacetone. We found that condensation of 2-acetylacetone with ethyl trifluoroacetate in the presence of LiH upon refluxing in THF for 5 h afforded tetraketone **1** in 65% yield. In a solution in CDCl₃, compound **1** exists as an equilibrium mixture of the triketoenol (**1a**) and diketodienol (**1b**) tautomers with the latter predominating (**1a** : **1b** = 33 : 67). In a 1 : 1 mixture of DMSO-d₆ and CCl₄, compound **1** occurs as cyclic hemiketal **1c** (95%) and open forms **1a** and **1b** (5%). In the crystalline state, the product of condensation of 2-acetylacetone with CF₃CO₂Et exists in cyclic form **1c** as evidenced by its IR spectrum recorded in Nujol mulls (the band of the hydroxy group of hemiketal at 3290 cm⁻¹ and the band of the nonconjugated C=O group at 1715 cm⁻¹). It should be noted that this spectrum is almost identical with the IR spectrum of the



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product in DMSO, but it differs essentially from the spectrum of its solution in CDCl_3 .

Tetraketone **1** was isolated from acetic acid solution as large crystals. In these crystals, the compound under study occurred in hydrated form **2**, which readily lost water upon vacuum distillation. The ^1H NMR spectrum of a solution of compound **2** in CDCl_3 has signals of tautomers **1a** and **1b** along with the signals of hydrate **2** (**2** : **1a** : **1b** = 44 : 19 : 37). Treatment of compound **1** or its hydrate **2** with concentrated H_2SO_4 at $\sim 20^\circ\text{C}$ for 5 h afforded tetrahydrochromone derivative **3** in good yield. Nonfluorinated analogs of compounds **1** and **3** have been synthesized previously by the reactions of acetone with diketene^{5,6} and dimethylacetamide dimethylacetal, respectively.⁷ In these reactions, cyclic form **1c** was not detected.

Therefore, we performed for the first time trifluoroacetylation of 2-acetylacetone, which proceeded at the methyl group to give highly reactive compounds **1–3**. These compounds are of interest in the synthesis of new CF_3 -containing heterocycles.

5,5-Dimethyl-2-(3'-oxo-4',4'-trifluorobutyroyl)cyclohexane-1,3-dione (1). The yield was 65%, m.p. 71–72 °C, b.p. 121–126 °C (5 Torr). Found (%): C, 51.81; H, 4.89. $\text{C}_{12}\text{H}_{13}\text{F}_3\text{O}_4$. Calculated (%): C, 51.80; H, 4.71. IR (Nujol mulls), ν/cm^{-1} : 3290 (OH), 1715, 1645 (C=O), 1575 (C=C); DMSO: 3460 (OH), 1715, 1665 (C=O), 1585 (C=C); CDCl_3 : 1660 (C=O), 1570 sh, 1555 (C=O, C=C). ^1H NMR (400 MHz, CDCl_3), δ : **1a** (33%): 1.09 (s, 6 H, 2 Me); 2.34 (s, 2 H, C(4)H₂); 2.60 (s, 2 H, C(6)H₂); 4.20 (s, 2 H, C(2')H₂); 16.99 (s, 1 H, OH); **1b** (67%): 1.11 (s, 6 H, 2 Me); 2.39 (s, 2 H, C(4)H₂); 2.61 (s, 2 H, C(6)H₂); 7.55 (s, 1 H, =CH); 13.19 (br. s, 1 H, OH); 16.41 (s, 1 H, OH in the ring). ^1H NMR (400 MHz, DMSO- d_6 + CCl_4), δ : **1c** (95%): 1.06 (s, 6 H, 2 Me); 2.23 (AB system, $\Delta\delta$ = 0.09, 2 H, C(8)H₂, J_{AB} = 15.2 Hz); 2.56 (AB system, $\Delta\delta$ = 0.02, 2 H, C(6)H₂, J_{AB} = 18.5 Hz), 2.61 (d, 1 H, C(3)HH, J_{AX} = 16.0 Hz); 3.03 (d, 1 H, C(3)HH, J_{AX} = 16.0 Hz); 9.11 (s, 1 H, OH).

2-(3',3'-Dihydroxy-4',4'-trifluorobutyroyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (2), m.p. 104–105 °C.

Found (%): C, 49.03; H, 5.14. $\text{C}_{12}\text{H}_{15}\text{F}_3\text{O}_5$. Calculated (%): C, 48.65; H, 5.10. IR (Nujol nulls), ν/cm^{-1} : 3435, 3240 (OH), 1650 (C=O), 1570 (C=C). ^1H NMR (250 MHz, CDCl_3), δ : **1a** (19%): 1.09 (s, 6 H, 2 Me); 2.34 (s, 2 H, C(4)H₂); 2.61 (s, 2 H, C(6)H₂); 4.20 (s, 2 H, C(2')H₂); 16.96 (s, 1 H, OH); **1b** (37%): 1.10 (s, 6 H, 2 Me); 2.38 (s, 2 H, C(4)H₂); 2.61 (s, 2 H, C(6)H₂); 7.53 (s, 1 H, =CH); 13.28 (br. s, 1 H, OH); 16.38 (s, 1 H, OH in the ring); **2** (44%): 1.11 (s, 6 H, 2 Me); 2.45 (s, 2 H, C(4)H₂); 2.61 (s, 2 H, C(6)H₂); 3.47 (s, 2 H, C(2')H₂); 5.34 (s, 2 H, 2 OH), 17.40 (s, 1 H, OH in the ring).

7,7-Dimethyl-2-trifluoromethyl-7,8-dihydro-6H-chromene-4,5-dione (3). The yield was 73%, m.p. 102–103 °C. Found (%): C, 55.51; H, 4.28. $\text{C}_{12}\text{H}_{11}\text{F}_3\text{O}_3$. Calculated (%): C, 55.39; H, 4.26. IR (Nujol mulls), ν/cm^{-1} : 1710, 1680 w. (C=O), 1650, 1600 (C=C). ^1H NMR (400 MHz, CDCl_3), δ : 1.17 (s, 6 H, 2 Me); 2.46 (s, 2 H, C(8)H₂); 2.83 (s, 2 H, C(6)H₂); 6.76 (s, 1 H, =CH).

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