Mendeleev Commun., 2001, 11(2), 76–76

A route to ethyl α-pentafluorobenzoyl-β-oxobutanoate *via* its copper(II) chelate

Yanina V. Burgart, Sergei P. Kisil, Viktor I. Saloutin* and Oleg N. Chupakhin

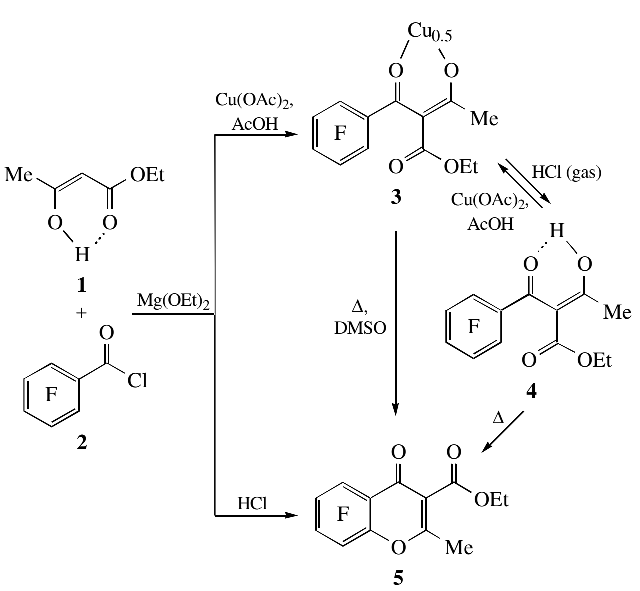
Institute of Organic Synthesis, Urals Branch of the Russian Academy of Sciences, 620219 Ekaterinburg, Russian Federation.
Fax: +7 3432 74 5954; e-mail: saloutin@ios.uran.ru

10.1070/MC2001v011n02ABEH001399

Ethyl 2-pentafluorobenzoyl-3-oxobutanoate has been prepared by the acylation of ethyl acetoacetate with pentafluorobenzoyl chloride *via* a copper(II) chelate.

The acylation of β-oxo esters by pentafluorobenzoyl chloride is known to form 2,3-substituted 5,6,7,8-tetrafluorochromones instead of the expected β,β′-dioxoesters.[1–4]

We prepared the copper chelate of ethyl 2-pentafluorobenzoyl-3-oxobutanoate **3** using a chelation stage in the reaction of ethyl acetoacetate **1** with pentafluorobenzoyl chloride **2**. The acylation was carried out in ethanol in the presence of magnesium ethoxide. The decomposition of chelate **3** by gaseous hydrogen chloride gives a free ligand, ethyl 2-pentafluorobenzoyl-3-oxobutanoate **4**. The treatment of the latter with an aqueous copper acetate solution gives chelate **3**.



Two groups of signals appeared in the ^{1}H and ^{19}F NMR spectra of β,β′-dioxoester **4** obtained in $CDCl_3$ solutions.† The resonance signal of a methine proton of the keto form is absent from the ^{1}H NMR spectrum. At the same time, two downfield signals at 17.44 and 14.65 ppm corresponding to two enol hydroxyl protons are observed. Thus, β,β′-dioxoester **4** exists in a $CDCl_3$ solution as a mixture of two enol tautomers in the ratio ~4:1.

The isolation of β,β′-dioxoester **4** was considered impossible[1–4] because of its instability and ready intramolecular cyclization into 3-ethoxycarbonyl-2-methyl-5,6,7,8-tetrafluorochromone **5**. In fact, β,β′-dioxoester **4** was readily converted into chromone **5** upon heating in the absence of solvents or in DMSO. Chromone **5** was also obtained when chelate **3** was heated in DMSO. The cyclization proceeds through the intramolecular substitution for an *ortho*-fluorine atom in the pentafluorophenyl substituent.

We found that, in contrast to the reports on the impossibility of the isolation of α-pentafluorobenzoyl-β-dicarbonyl compounds in the reactions of β-oxo esters and β-diketones with pentafluorobenzoyl chloride, these compounds can be obtained using interchelate stabilization. This method blocks the formation of chromone structures, which occur under usual reaction conditions. Thus, we developed a simple procedure for the synthesis of β,β′-tricarbonyl compounds containing *ortho*-fluorine atoms in a benzoyl substituent. These compounds may be of interest as novel building blocks for the synthesis of fluoroheterocycles.

This work was supported by the State Programme for Supporting Leading Scientific Schools of the Russian Federation (grant no. 00-15-97390).

References

1 N. N. Vorozhtsov, V. A. Barkhash, A. T. Prudchenko and T. I. Khomenko, *Dokl. Akad. Nauk SSSR*, 1965, **164**, 1046 [*Dokl. Chem.* (*Engl. Transl.*), 1965, 962].

2 N. N. Vorozhtsov, V. A. Barkhash, A. T. Prudchenko and G. S. Shchegoleva, *Zh. Obshch. Khim.*, 1965, **35**, 1501 [*J. Gen. Chem. USSR* (*Engl. Transl.*), 1965, **35**, 1503].

3 A. T. Prudchenko, V. A. Barkhash and N. N. Vorozhtsov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1965, 1798 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1965, **14**, 1762).

4 R. Filler, Y. S. Rao, A. Biezais, F. N. Miller and V. D. Beacaire, *J. Org. Chem.*, 1970, **35**, 930.

Received: 15th November 2000; Com. 00/1725

---

† New compounds **3** and **4** were characterised by IR (Vazeline oil), ^{19}F (75.3 MHz, C_6F_6) and ^{1}H NMR (400 and 100 MHz) spectroscopy.

Bis(ethyl 2-pentafluorobenzoyl-3-hydroxy-2-butenoato)copper(II) **3**. (*a*) Ethyl acetoacetate (11.7 g, 0.09 mol) was added to a solution of $Mg(OEt)_2$ prepared from Mg chips (1.84 g, 0.07 mol). The reaction mixture was stirred for 1 h at 50 °C. A solution of pentafluorobenzoyl chloride **2** (18.4 g, 0.08 mol) in benzene (45 ml) was added. The reaction mixture was stirred for 1 h at 20 °C and for 15 min at 50 °C. After cooling, a solution of copper acetate (6.5 g) and acetic acid (3 g) in 40 ml of water was added. The organic layer was separated. The aqueous layer was extracted with diethyl ether (3×30 ml). The organic layer was dried over $MgSO_4$. The solvent was removed in a vacuum at 20 °C. The residue was reprecipitated from MeOH with water to give compound **3** (8.3 g, 29%); mp 162–164 °C. IR (ν/cm^{-1}): 1680 (C=O), 1630, 1580 [C=O, C=C (chelate)], 1495, 1450 (C=C), 980 (C–F). Found (%): C, 43.89; H, 2.22; F, 26.70. Calc. for $C_{26}H_{16}F_{10}O_8Cu$ (%): C, 43.99; H, 2.27; F, 26.76.

(*b*) To a solution of ester **4** (0.26 g, 0.8 mmol) in methanol (5 ml), a solution of copper acetate (0.3 g, 1.6 mmol) in water (10 ml) was added. The resulting precipitate was filtered off and dried at 100 °C to give chelate **3** (0.26 g, 91%).

Ethyl 2-pentafluorobenzoyl-3-oxobutanoate **4**. Dry gaseous hydrogen chloride was passed through a solution of chelate **3** (0.3 g, 0.845 mmol) in anhydrous diethyl ether (50 ml). The resulting precipitate was filtered off. Diethyl ether was removed in a vacuum at 20 °C to give compound **4** (0.27 g, 99%) as an oil. ^{1}H NMR ($CDCl_3$, a mixture of two tautomers in the ratio 4:1) δ: 1.12, 1.39 (t, 3H, OCH_2*Me*, *J* 7.1 Hz), 2.57, 2.47 (s, 3H, Me), 4.10, 4.40 (q, 2H, OC*H*$_2$Me, *J* 7.1 Hz), 17.44, 14.65 (br. s, 1H, OH). ^{19}F NMR ($CDCl_3$, a mixture of two tautomers in the ratio 4:1) δ: 20.21, 18.42 (2F, m), 9.95 (1F, m), 1.11, –2.93 (2F, m). IR (ν/cm^{-1}): 2930 (OH), 1710 (C=O), 1650, 1570 [C=O, C=C (enol)]; 1520, 1500 (C=C), 985 (C–F). Found (%): C, 47.93; H, 2.73; F, 29.15. Calc. for $C_{13}H_9F_5O_4$ (%): C, 48.16; H, 2.80; F, 29.30.

*3-Ethoxycarbonyl-2-methyl-5,6,7,8-tetrafluoro-4*H*-1,4-dihydrobenzopyran-4-one* **5**. (*a*) Compound **4** (6.48 g, 0.02 mol) was heated at 100–110 °C for 1 h. The resulting solid was recrystallised from CCl_4–hexane (1:2) to give product **5** (5.6 g, 92%); mp 91–92 °C. The physico-chemical properties were identical to published data.[1] (*b*) A solution of chelate **3** (0.5 g, 1.41 mmol) in DMSO (12 ml) was heated at 80 °C for 3 h and allowed to stand at 20 °C for 24 h. A mixture of concentrated HCl (12 ml) and water (12 ml) was added. The mixture was extracted with diethyl ether (3×15 ml). The extracts were washed with water and dried with $MgSO_4$. The solvent was removed in a vacuum. The residue was recrystallised from CCl_4–hexane (1:2) to give product **5** (0.2 g, 47%).