

Tetrahedron Letters 40 (1999) 2203-2204

TETRAHEDRON LETTERS

Electrochemical Synthesis of Ethyl Pentafluoroacetoacetate.

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Received 2 October 1998; accepted 19 January 1999

Abstract: Electrochemical reduction of ethyl trifluoroacetate in the presence of chlorotrimethylsilane (TMSCI) is followed by a Claisen condensation to produce the ethyl (trimethylsilyl)ketal of ethyl pentafluoroacetoacetate (1). Ethyl pentafluoroacetoacetate is available in high yield by the hydrolysis of (1) under mild conditions. © 1999 Elsevier Science Ltd. All rights reserved. Keywords; Fluorine and compounds, Electrochemistry, Keto acids and derivatives.

Ethyl pentafluoroacetoacetate has been prepared in 20% yield by the condensation of difluoro- and trifluoroacetates [1]. Although little is known about it's chemistry, it has interest as a precursor of biologically active compounds. The reduction of ethyl trifluoroacetate with sodium sand leads to γ , γ , γ -trifluoroacetoacetate *via* the intermediate formation of ethyl pentafluoroacetoacetate [2]. Electrochemical reduction of trifluoroacetic acid esters is believed to take place as a two electron process at a high cathodic potential -2.65 V. Preparative scale electrolysis in the presence of a proton donor shows no carbonyl group reduction, instead substitution of two fluorine atoms by hydrogen with a yield 70 - 90 % [3]. So, it was reasonable to expect, that the electrochemical reduction of ethyl trifluoroacetate in aprotic media could provide a route to ethyl pentafluoroacetoacetate (5).

We carried out preparative electrochemical reduction of ethyl trifluoroacetate in acetonitrile (undivided cell, stainless steel cathode, sacrificial Al anode) and obtained ethyl pentafluoroacetoacetate in low yield (<10%). The low yield is probably due to the difference in the reduction potentials: the potential of the starting compound is 0.5 V more cathodic than that of the product, the initially formed acetoacetate undergoing further reduction [4].

Electrolysis under the same conditions, but with an excess of chlorotrimethylsilane (TMSCl) provided ethyl pentafluoroacetoacetate ethyl(trimethylsilyl)ketal (1) in 51% yield. Obviously, difluorocarboxylate anion (2), generated after two-electron transfer [5,6], adds to the molecule of starting ester (see scheme 1). Silylation of the intermediate anion (3) is more rapid than elimination of ethoxide, and the resulting ketal (1) was not electroactive under the reaction conditions.

Silulation of the anion (2) also occurs to small extent, but contrary to the silulation of (2) generated by reduction of ethyl iododifluoroacetate with Zn [7], C-silulation was observed to give (4) [8].

Scheme 1.

$$CF_{3}CO_{2}Et \xrightarrow{+2e} - CF_{2}CO_{2}Et \xrightarrow{CF_{3}CO_{2}Et} CF_{3}C-CF_{2}CO_{2}Et \xrightarrow{TMSCl} CF_{3}C-CF_{2}CO_{2}Et \xrightarrow{(1)} OEt (3) \xrightarrow{TMScl} CF_{3}C-CF_{2}CO_{2}Et \xrightarrow{(1)} OEt (1)$$

$$TMSCl \xrightarrow{F_{3}CO_{2}Et} CF_{3}C-CF_{2}CO_{2}Et \xrightarrow{(1)} OEt (1)$$

$$TMS CF_{2}CO_{2}Et \xrightarrow{CF_{3}CO_{2}Et} CF_{3}C-CF_{2}CO_{2}Et \xrightarrow{(1)} OEt (1)$$

A typical experiment is as follows: into the electrochemical cell, equipped with a stainless steel cathode (50 cm²), sacrificial Al anode, magnetic stirrer and inert gas inlet, 60 ml dry acetonitrile, 0.1 g Et₄NBF₄ and 8.6 g (79 mM, 10 ml) TMSCI were charged and pre-electrolysis was carried out for 30 min at current density of 4 mA cm⁻². Then 10.7 g (75 mM, 9 ml) of ethyl trifluoroacetate was added and electrolysis continued at a current density of 12 mA cm⁻² until 2F had been consumed. The electrolyte was poured on ice and extracted with 50 ml hexane. The hexane extract was washed with 10 ml of water, dried over anhydrous MgSO₄, and distilled to obtain 6.9 g of (1) [9].

Ethyl pentafluoroacetoacetate is readily available by mild hydrolysis of the ketal (1): it may be achieved, for instance, by heating under reflux in ethanol or by stirring with $NaHF_2$ in acetonitrile, but in this case it is difficult to separate the product (5). If hydrolysis is carried out in concentrated sulphuric acid at ambient temperature, pure product may be condensed into a cold trap at reduced pressure [10].

(1)
$$\xrightarrow{H_2SO_4}$$
 $CF_3CCF_2CO_2Et$ 82 %

REFERENCES AND NOTES

1. McBee, E. T.; Pierce, O. R.; Kilbourne, H. W.; Wilson, E. R. J. Am. Chem. Soc. 1953; 75: 3152 - 153

2. McBee, E. T.; Pierce, O. R.; Kilbourne, H. W.; Baron, J. A. J. Am. Chem. Soc. 1953; 75: 4090 - 4091

3. Mayranovsky, V. G.; Ponomarev, A. M. Zh. Obsch. Khim. 1977; 47: 2343 -46.

4. The reduction potentials were determined on the "Polarografic analyzer PA-2" (Praha) in 0.1 M acetonitrile solution of Et₄NBF₄ at the glassy carbon electrode vs SCE. Potentials of the reduction peaks for CF₃CO₂Et, CF₃CO₂Me and CF₃COCF₂CO₂Et were correspondingly: -2.58, -2.37, -1.96 V.

5. On the basis of voltammetric data two electron transfer was verified by the analysis of the Randles-Ševcik equation. The average diffusion coefficient obtained from it was 1¹⁰⁴.

6. The possibility of the initial TMSCl reduction was not taken into account because of it's high reduction potential: Martynov, B.I.; Stepanov, A.A. J. Fluor. Chem. 1997; 85: 127 - 8

7. Kitagawa, O; Taguchi, T.; Kobayashi, Y. Tetrahedron Lett. 1988; 29: 1803 - 1806

8. TMSCF₂CO₂Et structure was confirmed by NMR¹⁹F (δ_F vs external CF₃COOH is 46.4, s) and ethyl diffuoroacetate formation by acidic hydrolysis.

9. Ketal (1) is a liquid with b.p. 94 - 7°C at 15 mm Hg; δ_F (external CF₃COOH): -1.3 (3F, t, J = 11.0 Hz); 35.73 and 37.77 (2F, J_{AB} = 262.5 Hz). Found: C, 39.10; H, 5.58; F, 27.83; Si, 8.34. Calc. for C₁₁H₁₉F₅O₄Si: C, 39.05; H, 5.66; F, 28.08; Si, 8.30%.

10. Boiling point of the obtained ester (5) is 105 - 7°C (lower than reported in [1]). δ_F (external CF₃COOH): 4.8 (3F, t, J = 9 Hz); 42.3 (2F, q, J = 9 Hz). Found: C, 32.59; H, 2.24; F, 43.16. Calc. for C₆H₅F₅O₂: C, 32.74; H, 2.29; F, 43.16 %.