CHEMISTRY LETTERS, pp. 853-854, 1988. © 1988 The Chemical Society of Japan

Trapping of Trifluoromethyl Radical with Enolacetate and in situ Generated Enol

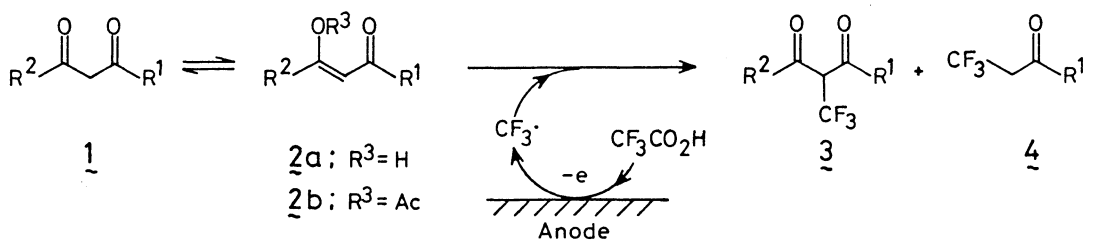
Kenji UNEYAMA* and Kunimasa UEDA
Department of Applied Chemistry, Faculty of Engineering, Okayama University, Okayama 700

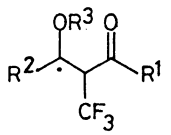
Electrochemically generated trifluoromethyl radical can be trapped with enolacetates and enol generated in situ from β-ketoesters and 1,3-diketones, affording trifluoromethylated active methylene compounds.

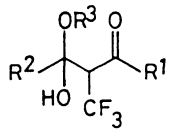
Because of the increasing attention to the trifluoromethyl compounds for the medicines and material science[1], trifluoromethyl copper, zinc, and tin complexes[2] have been extensively employed for trifluoromethylation of carbonyl compounds and aryl halides. Perfluoroalkanoyl peroxide[3] and N-trifluoromethyl-N-nitrosotrifluoromethanesulfonamide[4] can trifluoromethylate aromatic compounds. Here, we describe a novel trifluoromethylation on methylene carbon of octyl acetoacetate by electrochemically generated trifluoromethyl radical from trifluoroacetic acid (TFA). The electrogenerated trifluoromethyl radical can add to a carbon-carbon double bond.[5] Therefore, active-methylene compounds **1** and their enolates **2** can be in principle trifluoromethylated under electrolysis conditions where **1** are enolized. Questions to be solved are how to generate sufficiently **2** and how to suppress the oxidative dimerization of **1** since **1** is easily electrooxidized in the basic conditions.[6]

Thus, a typical constant-current electrolysis was conducted in a mixture of acetonitrile and water in the presence of a large excess amount of TFA using an undivided cell and platinum foil electrodes (H_2O : MeCN : TFA = 0.1 : 3.0 : 1.4 ml, 50 mA/cm^2). The use of sodium trifluoroacetate in the medium failed for the purpose.

The compound **4** (R^1 = OC_8H_{17}) was a sole product (47%) at -40 °C. On the




5


6

other hand, **3** (R^1= OC_8H_{17}, R^2=CH_3) was isolated in 31% yield and no **4** was obtained at 60 °C. In the electrolysis at 0 °C, both **3** (15%) and **4** (43%) were isolated. Interestingly, the electrolysis of the enolacetate **2b** (R^1= OC_8H_{17}, R^2=CH_3) afforded **3** (64%) exclusively and no **4** with 3 eq. of TFA under the similar conditions at 0 °C. Therefore, some enolacetates **2b** were subjected to the electrochemical trifluoromethylation. The result is shown in the table 1. Both enolacetates from β-ketoesters and 1,3-diketones gave resonable yields of **3**.

Table 1. Electrochemical Trifluoromethylation of Enolacetates

R^1	OC_8H_{17}	OC_2H_5	OC_2H_5	OC_2H_5	C_6H_{13}
R^2	CH_3	CH_3	C_2H_5	$(CH_3)_2CH$	CH_3
3 Yield/%	64	42	48	48	48

The electrochemically generated trifluoromethyl radical adds the enol **2a** to yield 5. The trifluoromethylated radical 5 would suffer further one-electron oxidation and the successive hydrolysis leading to an intermediate **6** which would undergo smooth carbon-carbon bond breaking at the low temperature and carbon-oxygen bond breaking at the higher temperature, affording **4** and **3**, respectively. No isolation of the dimer of **1**[6] supports the mechanism on the initial attack of trifluoromethyl radical to **2**. Meanwhile, electrolysis of the enol acetate **2b** provided exclusively **3** suggesting that a good leaving group (R^3=Ac) induces the ketone formation from **6**.

The authors are greatful to The Mazda and The Japan Securities Scholarship Foundations for the financial support and the SC-NMR Laboratory of Okayama University for the 500 MHz-NMR experiment.

References

1) R. Filler and Y. Kobayashi, "Biomedicinal Aspects of Fluorine Chemistry," Kodansha, Tokyo (1982); H. Hudlicky, "Chemistry of Organic Fluorine compounds," Ellisorwood, New York (1976).

2) Y. Kobayashi, K. Yamamoto, and I. Kumadaki, Tetrahedron Lett., 1979, 4071; N. V. Kondratenko, E. P. Vechirko, and L. M. Yagupolshii, Synthesis, 1980, 932 ; T. Kitazume and N. Ishikawa, Chem. Lett., 1981, 1337 and 1679; T. Kitazume and N. Ishikawa, ibid., 1982, 137; N. J. O'Relly, M. Maruta, and N. Ishikawa, ibid., 1984, 517.

3) H. Sawada, M. Yoshida, H. Hagii, K. Aoshima, and M. Kobayashi, Bull. Chem. Soc. Jpn., 59, 217 (1986); C. Zaho, G. M. El-Taliawi, and C. Walling, J. Org. Chem., 48, 4908 (1983).

4) T. Umemoto and A. Ando, Bull. Chem. Soc. Jpn., 59, 447 (1986).

5) C. J. Brookes, P. L. Coe, D. M. Owen, A. E. Pedler, and J. C. Taltow, J. Chem. Soc., Chem. Commun., 1974, 323; R. N. Renaud, P. J. Champagne, and M. Savard, Can. J. Chem., 57, 2617 (1979); N. Muller, J. Org. Chem., 48, 1370 (1983).

6) H. Shafer, Chem. Ing. Techn., 42, 164 (1970).

(Received March 7, 1988)