Pergamon

Tetrahedron Letters 41 (2000) 5873–5876

TETRAHEDRON LETTERS

Electrochemical oxidation of 2,2,2-trifluoroethanol to trifluoroacetaldehyde 2,2,2-trifluoroethyl hemiacetal

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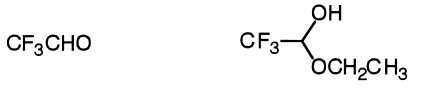
Received 5 April 2000; revised 15 May 2000; accepted 26 May 2000

Abstract

Electrochemical oxidation of 2,2,2-trifluoroethanol (**1**) gave trifluoroacetaldehyde 2,2,2-trifluoroethyl hemiacetal (**2b**), which was more reactive than commercially available trifluoroacetaldehyde ethyl hemiacetal (**2a**). The high reactivity of **2b** was utilized, for example, for the facile synthesis of 1-furyl-2,2,2-trifluoroethanol (**4**) from furan.

Keywords: electrochemistry; oxidation; alcohols; fluorine and compounds.

Trifluoroacetaldehyde (**1**) is an important source material to prepare compounds having a trifluoromethyl group,[1] while commercially available trifluoroacetaldehyde ethyl hemiacetal (**2a**) has often been used as an equivalent of **1** because of the troublesome handling of **1** due to its low boiling point.[2] The preparation methods[3] of **1** so far reported, however, have been rather limited: (i) Sn/Ru-catalyzed hydrogenation of trifluoroacetic acid;[4] (ii) reduction of trifluoroacetic acid;[2] (iii) reduction of trifluoroacetic acid esters;[5] (iv) reduction of trifluoroacetonitrile;[6] (v) oxidation of trifluoropropane;[7] and (vi) fluorination of chloral with hydrogen fluoride.[8] Although all of these methods consist of a number of simple steps, most of them are not always appropriate for large-scale production, except method (i); furthermore, some starting compounds are not easily available. Also, method (i) must be carried out under severe reaction conditions (400–450°C).[4]



1 **2a**

We report herein a new facile method for the preparation of trifluoroacetaldehyde 2,2,2-trifluoroethyl hemiacetal (**2b**) starting from 2,2,2-trifluoroethanol (**3**) (Eq. (1)) and also present data that shows that **2b** is superior to **2a** as an equivalent of **1**.

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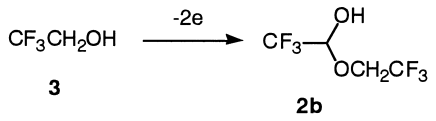
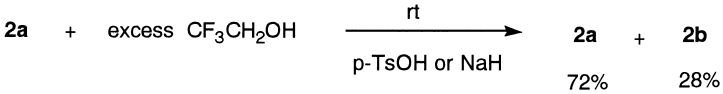
PII: S0040-4039(00)00880-7



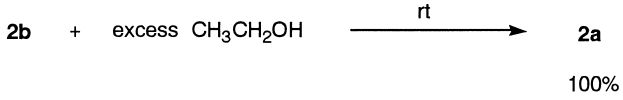
(1)

Our method uses an electrochemical oxidation of **3** for the preparation of **2b**. Thus, into a cell equipped with platinum plate electrodes (1×2 cm) without a diaphragm was charged a solution of **3** (10 g, 0.1 mol) containing Et_4NBF_4 (1.08 g, 5.0 mmol) as a supporting electrolyte. The solution was electrolyzed with a constant current (0.2 A) at –10°C. The terminal voltage was 25–30 V through the electrolysis. After 1.5 *F*/mol of electricity was passed, the solution was poured onto pentane:ether (1:1 (v/v), 100 mL) and then the organic portion was washed with water three times. The yield of **2b** was more than 70%.[9]

2,2,2-Trifluoroethyl hemiacetal **2b** seemed to be producible from ethyl hemiacetal **2a**. However, the transformation of **2a** to **2b** proved difficult. Namely, an addition of **2a** to a solution of an excess amount (10 equiv.) of 2,2,2-trifluoroethanol (**3**) containing a catalytic amount of *p*-TsOH or sodium hydride resulted in the 72% recovery of **2a** with 28% formation of **2b** (Eq. (2)). On the other hand, the transformation of **2b** to **2a** was easily achieved (Eq. (3)).

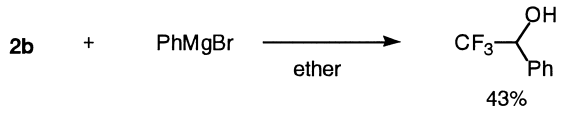


(2)

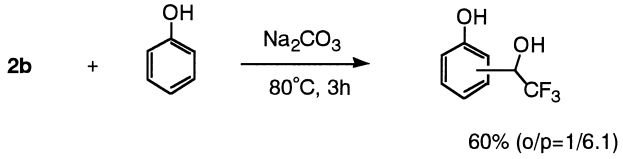


(3)

With **2b** in hand using the electrochemical method, we developed its utilization in organic synthesis. It was used as an equivalent of **1** as described in Eqs. (4) and (5),[10] in which **2b** showed a reactivity similar to **2a**.

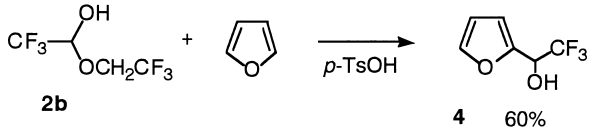


(4)



(5)

The synthetic advantage of **2b** over **2a** was shown by an acid-catalyzed α-hydroxy-trifluoroethylation of furan leading to 1-furyl-2,2,2-trifluoroethanol (**4**)[11] (Eq. (6)).

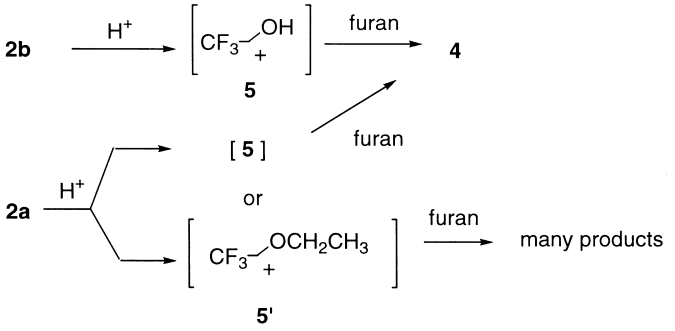


(6)

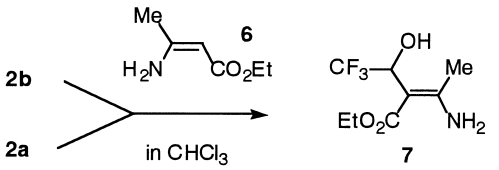
This type of reaction was first presumed to be achievable by using **2a**, but the reaction of **2a** with furan in the presence of *p*-TsOH resulted in the formation of many unidentified products

together with a trace amount of **4**. Fortunately, on the other hand, the reaction of **2b** with furan in the presence of *p*-TsOH afforded **4** in 60% yield. A similar satisfactory result was also obtained by using an electrolyzed solution of **3** without isolation of **2b**.

The unsuccessful result in the case of **2a** can be explained as follows. It has been known that an ethoxyl group is less reactive than a trifluoroethoxyl group as a leaving group.[12] Thus, an acid treatment of **2a** may give two kinds of cationic intermediates **5** and **5′** which lead to the formation of complex products (Scheme 1). In contrast with **2a**, an acid-catalyzed reaction of **2b** might afford mainly **4** because of the feasibility of the trifluoroethoxyl group leaving from **2b**.



Another example indicating a difference in the reactivity between **2a** and **2b** was the reaction with ethyl 3-aminocrotonate (**6**) to give hydroxy-trifluoromethylated product **7**[13] (Eq. (7)). The reaction of **2b** with **6** proceeded faster than that of **2a** with **6** as shown in Fig. 1.



(7)

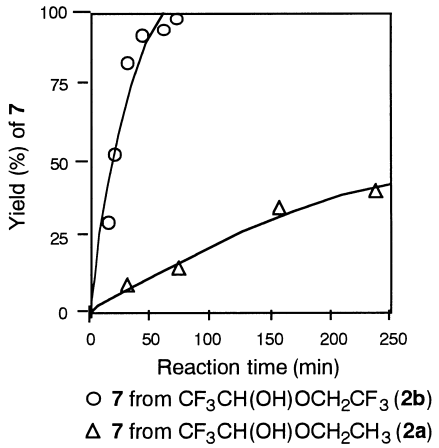


Figure 1. Reaction of **2a**,**b** with **6**

The high reactivity of **2b** in comparison with **2a** in this type of reaction can also be explained in terms of the ability of the trifluoroethoxyl group as a leaving group.

In summary, we have found a new preparation method of **2b** using an electrochemical oxidation of **3**. The method is very convenient not only for large-scale production but also for laboratory-scale experimentation since the starting compound **3** is easily available and the electrochemical method allows us to achieve the aimed oxidation without any oxidizing reagent. Also, we have demonstrated the novel reactivity of **2b** which could be utilized as an equivalent of **1** in a different way from the corresponding ethyl derivative **2a**. Further utilization of **2b** for the synthesis of trifluoromethyl-containing compounds is now under investigation.

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9. The product **2b** contaminated with a small amount of **3** (~5%) was obtained. The obtained **2b** could be utilized without purification for further synthetic use. The NMR and IR spectra of the obtained **2b** are as follows: IR ν_{max}: 3400, 1287, 1125, 1173, 1121, 841 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.01 (q, 2H, $J=5.5$ Hz), 4.99 (q, 1H, $J=3.4$ Hz). The identification of **2b** was achieved by its conversion to the benzoylated compound: IR ν_{max}: 3069, 2967, 1752, 1603, 1455, 1402, 1362, 1302, 1219, 1136, 1082, 1069, 1030, 1001, 963, 918, 716, 687, 664, 613 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.18–4.41 (m, 2H), 6.26 (q, 1H, $J=3.6$ Hz), 7.46–7.58 (m, 2H), 7.62–7.74 (m, 1H), 8.06–8.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 67.1 (q, $J=35.7$ Hz), 91.4 (q, $J=37.6$ Hz), 120.6 (q, $J=279.2$ Hz), 122.9 (q, $J=276.6$ Hz), 127.6, 128.9, 130.5, 134.7, 165.2. Anal. calcd for $C_{11}H_8F_6O_3$: C, 43.72; H, 2.67. Found C, 43.50; H, 2.73.
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13. Compound **7**: IR ν_{max}: 3420, 2986, 1721, 1613, 1518, 1269, 1240, 1161, 1127 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, 3H, $J=7.1$ Hz), 2.06 (s, 3H), 3.0 (br s, 1H), 4.15–4.32 (m, 2H), 4.60–4.75 (br s, 1H), 5.0 (br s, 1H), 8.7 (br s, 1H).