Pergamon

Tetrahedron Letters, Vol. 35, No. 8, pp. 1271-1274, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0050-8

A NEW REACTION SYSTEM FOR EFFICIENT ELECTROCHEMICAL OXIDATION OF N-METHOXYCARBONYL-2,2,2-TRIFLUOROETHYLAMINES

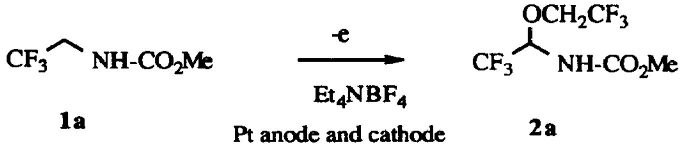
Yoshihiro MATSUMURA,* Takashi TOMITA, Masaki SUDOH, and Naoki KISE

Division of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Yoshida, Sakyo, Kyoto 606-01, Japan

Abstract: Electrochemical oxidation of N-methoxycarbonyl-2,2,2-trifluoroethylamine in a system of 2,2,2-trifluoroethanol/Et_4NBF_4 or 2,2,2-trifluoroethanol/acetonitrile/Et_4NBF_4 gave N-methoxycarbonyl-1-(2,2,2-trifluoroethoxy)-2,2,2-trifluoroethylamine in good yield and with good current efficiency.

We have already reported electrochemical α-methoxylation of N-alkyl- or N,N-dialkylamines protected with an electron-withdrawing group such as methoxycarbonyl group[1] and subsequently showed many examples indicating the usefulness of the α-methoxylated products as α-aminoalkylating reagents toward a variety of nucleophiles.[2] In continuation of these studies, electrochemical oxidation of 2,2,2-trifluoroethylamine derivatives is interesting since the expected products, 1-methoxy-2,2,2-trifluoroethylamine derivatives, might be usable as 2,2,2-trifluoroethylating reagent, which would be worthwhile in view of biological importance of trifluoromethylated compounds.[3] However, there has been no precedent for electrochemical α-methoxylation of perfluoroalkylamine derivatives except N-(2,2,2-trifluoroethyl)anilines.[4] This may be due to the high oxidation potentials of N-protected trifluoroethylamines.

In general, oxidation of organic substrates possessing high oxidation potentials does not efficiently proceed since oxidation of solvents and/or anion parts of supporting electrolytes competes or overwhelmingly takes place. We wish to report herein a new reaction system in which even substrates such as N-methoxycarbonyl-2,2,2-trifluoroethylamine **1a** can be efficiently oxidized (eq 1).



1a **2a** (1)

solvent	F/mol	Yield (%)
CF_3CH_2OH	2.5	87%
CF_3CH_2OH/CH_3CN (1 : 9)	2.3	88%

Our device is the use of 2,2,2-trifluoroethanol (TFE) instead of methanol as a solvent or a co-solvent. Methanol is electrochemically oxidizable[5] as shown in a current-potential curve of a system of methanol/CH_3CN(1:9) in which growing up of current was observed at around 1.1 V vs SCE (Fig.1, b) and in a cyclic voltammetry of a system containing methanol which indicated an oxidation wave at around 1.1 V (Fig.2, b). On the other hand, a reaction system consisting of TFE and CH_3CN showed a current-potential curve (Fig.1, a) and a cyclic voltammetry (Fig.2, a) which were identical with the back-grounds.

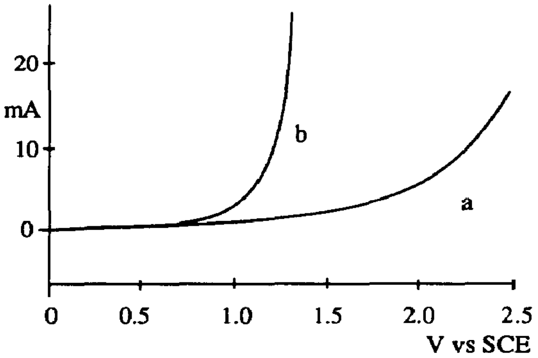


Fig. 1 Current-Potential Curve
a; $CF_3CH_2OH/CH_3CN(1/9)$
b; $MeOH/CH_3CN(1/9)$
supporting electrolyte;0.1M Et_4NBF_4

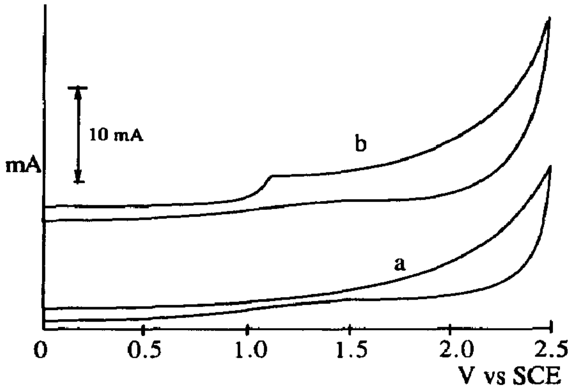
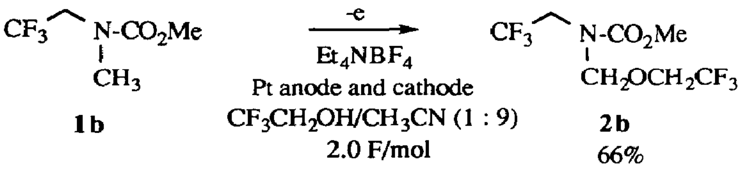


Fig. 2 Cyclic Voltammetry
a; CH_3CN or $CF_3CH_2OH(2mM)/CH_3CN$
b; MeOH (2mM)/CH_3CN
supporting electrolyte;0.1M Et_4NBF_4;100mV/sec

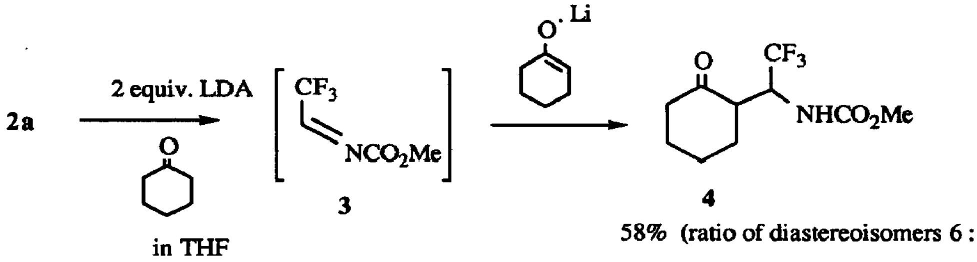
In fact, electrolysis of **1a** (2mmol) in a system of TFE(5mL)/Et_4NBF_4(1mmol) or TFE(1mL)/CH_3CN(9mL)/Et_4NBF_4(1mmol) using platinum electrodes (1cm x 1cm) and an undivided cell with a constant current (100mA) gave α-trifluoroethoxylated product **2a**[6] in good yields at 2.3-2.5*F*/mol of electricity (eq 1), though that of **1a** in a system of methanol /Et_4NOTs or Et_4NBF_4 resulted in the complete recovery of **1a**.

In order to elucidate a mechanism of this electrochemical oxidation, we tried oxidation of N-methoxycarbonyl-N-methyl-2,2,2-trifluoroethylamine **1b** and found that the substitution preferentially took place at the methyl group (eq 2).[6] This site selectivity was consistent with our previous results obtained in electrochemical α-methoxylation of unsymmetrical dialkyl-substituted carbamates[1] and anilines[7] in which the less substituted α-site was exclusively methoxylated, and also with the selectivity in electrochemical α-cyanation of 2,2,2-trifluoroethylated amines.[8] Thus, we propose a mechanism involving electron-transfer from **1a,b** to anode at the initiation step,[9] which is similar to a mechanism in electrochemical oxidation of carbamates[1] and amines.[7,8]



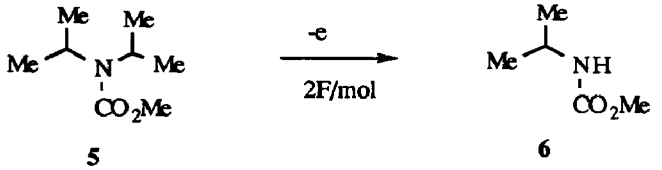
(2)

Synthetic utility of **2a** was realized as follows. Although the acid-promoted generation of α-trifluoromethylated iminium cation from **2a** was not achieved in contrast with the results of 1-methoxy-2,2,2-trifluoroethylaniline derivatives,[4] we succeeded in 1-amino-2,2,2-trifluoroethylation at the α-position of cyclohexanone by using 2 equivalents of LDA in which imine **3** might be involved as the intermediate to afford **4** (eq 3).[6]



(3)

Advantage of our new reaction system was also indicated by electrochemical oxidation of α-branched alkylamine derivatives which generally gave dealkylated amine derivatives.[1] For example, the oxidation of N-methoxycarbonyl-N,N-diisopropylamine **5** giving a dealkylated product **6** was a 16% current efficiency in a system of methanol/Et_4NOTs, but the current efficiency was largely improved under our new reaction system to 66% (eq 4). Fig.3 shows the reaction profile of these reactions.



(4)

$CF_3CH_2OH/CH_3CN(1/9)/Et_4NBF_4$	66%
$MeOH/Et_4NOTs$	16%

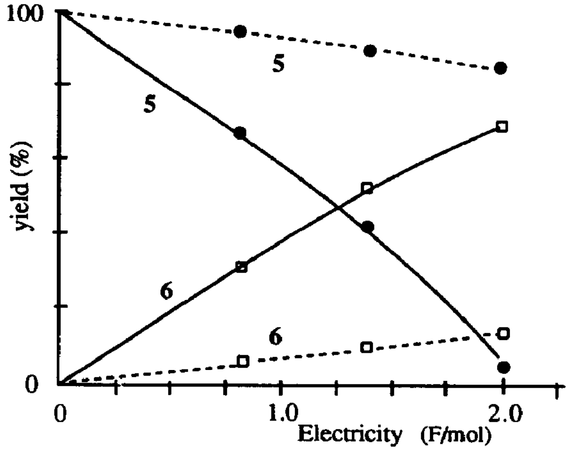


Fig. 3 Reaction Profile of Oxidation of **5**.
—— ; in CF_3CH_2OH/CH_3CN (1/9) ● ; 5
----- ; in MeOH □ ; 6

Although further mechanistic study of electrochemical oxidation of **1a,b** should be carried out, our system might possess a versatile synthetic utility since it might be applicable to a variety of substrates which have been hardly oxidized by electrochemical method so far. Such studies are now under investigation and the results will be reported in the near future.

Acknowledgements: One of the authors (Y.M.) wishes to thank the Japanese Ministry of Education, Science and Culture for a Grant-in-Aid for Scientific Research on Priority Areas (No. 236). We also thank Daikin Industries, Ltd. for a generous gift of 2,2,2-trifluoroethanol.

References and Notes

1. (a) Shono, T; Hamaguchi, H.; Matsumura, Y. *J.Am.Chem.Soc.*, **1975**, *97*, 4264. b) Shono, T.; Matsumura, Y.; Tsubata, K. *Org.Synth.*, **1984**, *63*, 206.
2. Shono, T.; Matsumura, Y.; Tsubata, K. *J.Am.Chem.Soc.*, **1981**, *103*, 1172.
3. Fuchigami, T.; Yamamoto, K.; Nakagawa, Y. *J.Org.Chem.*, **1991**, *56*, 137, and references cited therein.
4. Fuchigami, T.; Nakagawa, Y.; Nonaka, T. *J.Org.Chem.*, **1987**, *52*, 5491.
5. Hammerich, O.; Svensmark, B. in "Organic Electrochemistry" ed. by Lund, H; Baizer, M.M. Mercel Dekker, New York, 1991, 3rd ed., pp 615-657.
6. **2a**; mp 62°C; IR (KBr) 3400, 1735, 1715, 1630, 1330, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200MHz) δ 3.80 (s, 3H), 4.07 (q, 2H, J=8.4Hz), 5.52 (br s, 2H); ^{13}C NMR ($CDCl_3$, 50MHz) δ 53.13, 66.11 (q, J_{CCF}=35.8 Hz), 80.05 (q, J_{CCF}=36.0Hz), 121.54 (q, J_{CF}=280.0Hz), 123.18 (q, J_{CF}=276.0Hz), 156.75.
   2b; liquid; IR (neat) 2950, 1720, 1450, 1400, 1275, 1100, 960, 825, 775 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200MHz) δ 3.82 (s, 3H), 3.70-4.20 (m, 4H), 5.00 (s, 2H); ^{13}C NMR ($CDCl_3$, 50MHz) δ 46.35 (q, J_{CCF}=34.4Hz), 53.78, 66.21 (q, J_{CCF}=32.4Hz), 78.74, 124.13 (q, J_{CF}=277.4Hz), 124.61 (q, J_{CF}=277.8Hz), 157.11.
   4; major isomer: R_f 0.5 (hexane/AcOEt=2/1); mp 107°C; IR (KBr) 3300,1705, 1300, 1250, 1180, 1130, 1110, 1100, 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200MHz) δ 1.60-2.03 (m, 4H), 2.07-2.22 (m, 2H), 2.36-2.48 (m, 2H), 2.86-2.98 (m, 1H), 3.72 (s, 3H), 4.18-4.40 (m, 1H), 6.33 (d, 1H, J=12Hz); ^{13}C NMR ($CDCl_3$, 50MHz) δ 24.92, 27.99, 33.03, 42.92, 48.39, 52.61, 54.77 (q, J_{CCF}=31.7 Hz), 124.70 (q, J_{CF}=282Hz), 157.18, 210.98.
   minor isomer; R_f 0.4 (hexane/AcOEt=2/1); mp 131°C; IR (KBr) 3320, 1700, 1285, 1240, 1175, 1130, 1050 cm^{-1};^{1}H NMR ($CDCl_3$, 200MHz) δ 1.50-2.28 (m, 6H), 2.30-2.42 (m, 1H), 2.48-2.60 (m, 2H), 2.70-2.83 (m, 1H), 3.76 (s, 3H), 4.98-5.18 (m, 1H), 5.63 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50MHz) δ 24.25, 26.70, 28.16, 41.55, 48.93, 50.41 (q, J_{CCF}=30.3 Hz), 122.55 (q, J_{CF}=282 Hz), 156.57, 208.16.
7. Shono, T.; Matsumura, Y.; Inoue, K.; Ohmizu, H.; Kashimura, S. *J.Am.Chem.Soc.*, **1982**, *104*, 5753.
8. Konno, A.; Fuchigami, T.; Fujita, Y.; Nonaka, T. *J.Org.Chem.*, **1990**, *55*, 1952.
9. Since oxidation waves of **1a,b** were not observed below 2.5 V, direct electron transfer mechanism is not conclusive yet.

*(**Received in Japan** **28 September** 1993; **accepted** **17 December** 1993)*