silyl)oxy]-1,3-butadiene was used (entry 4) but high in all other cases (entries 3, 5-7).

As an illustration of the applicability of 1 in synthesis, Diels-Alder adduct 14 (entry 7) was transformed into alcohol 17 (Scheme II), a crucial intermediate in a projected synthesis of gelsemine.[13] The acetyl function was easily removed from 14 through treatment with dimethylamine. Lactam 15 ($[\alpha]^{20}_D$ +55° (c 0.90, $CHCl_3$)) was then methylated with sodium hydride and methyl iodide, followed by an isopropoxy/ethoxy exchange to give lactam 16 ($[\alpha]^{20}_D$ +11° (c 1.15, $CHCl_3$)). This exchange was necessary, because the eventual BF_3·Et_2O-induced *N*-acyliminium cyclization to the tricyclic product 18[13] did not proceed well with isopropoxy as leaving group. Finally, the ester group in 16 was reduced with lithium borohydride in the presence of $LiBEt_3H$ to give alcohol 17 in 80% yield.[14] All spectroscopic data of 17 except rotation ($[\alpha]^{20}_D$ +5° (c 2.85, MeOH)) were in complete agreement with those of the racemic alcohol prepared before.[13] The product appeared to be enantiomerically pure within detection limits, according to analysis of its ^1H NMR spectrum with $Eu(hfc)_3$.[9]

In conclusion, we have shown that enantiomerically pure (*R*)-1-acetyl-5-isopropoxy-3-pyrrolin-2-one (1) can be readily prepared from (*S*)-malic acid and reacts with excellent stereo- and regioselectivity in Diels-Alder reactions without loss of enantiomeric purity. Further applications of this methodology as well as stereoselective conjugate additions to 1 will be reported in due course.

Acknowledgment. We are grateful to J. Fraanje and K. Goubitz of the Department of Crystallography of this University for the X-ray crystal structure determination. We thank C. Kruk and his staff for their help in obtaining and interpreting the NMR spectra, R. H. Balk and W. J. M. Steeman for the preparation of starting materials on large scale, and M. Avis and R. M. Schonk for pioneering experiments with 2. This investigation was supported by the Netherlands' Foundation for Chemical Research (SON) with financial aid from the Netherlands' Organization for the Advancement of Pure Research (NWO).

Registry No. 1, 138259-70-8; 5, 85319-59-1; *trans*-6, 138259-71-9; *cis*-6, 138259-72-0; 7, 138259-73-1; 8, 138259-74-2; 8 deacylated derivative, 138259-75-3; 9, 138259-76-4; 10, 138259-77-5; 11a, 138259-78-6; 11b, 138259-79-7; 12, 138259-80-0; 13, 138259-81-1; 14, 138259-82-2; 15, 138259-83-3; 16, 138259-84-4; 17, 138332-58-8; cyclopentadiene, 542-92-7; 2,3-dimethyl-1,3-butadiene, 513-81-5; 1-[(trimethylsilyl)oxy]-1,3-butadiene, 6651-43-0; 2-[(trimethylsilyl)oxy]-1,3-butadiene, 38053-91-7; 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene, 59414-23-2; 3,5-hexadien-1-ol, 5747-07-9; ethyl 3,5-hexadienoate, 81838-64-4.

Supplementary Material Available: Experimental procedures, physical properties, and spectral data (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(13) (a) Vijn, R. J.; Hiemstra, H.; Kok, J. J.; Knotter, M.; Speckamp, W. N. *Tetrahedron* **1987**, *43*, 5019. (b) Hiemstra, H.; Vijn, R. J.; Speckamp, W. N. *J. Org. Chem.* **1988**, *53*, 3882. (c) Fang, Y. Forthcoming Thesis, University of Amsterdam.
(14) Brown, H. C.; Narasimhan, S. *J. Org. Chem.* **1982**, *47*, 1604.
(15) (a) Martin, S. F.; Tu, C.; Chou, T. *J. Am. Chem. Soc.* **1980**, *102*, 5274. (b) Stevens, R. V.; Cherpeck, R. E.; Harrison, B. L.; Lai, J.; Lapalme, R. *J. Am. Chem. Soc.* **1976**, *98*, 6317.

Facile Electroreduction of Methyl Esters and *N*,*N*-Dimethylamides of Aliphatic Carboxylic Acids to Primary Alcohols[1]

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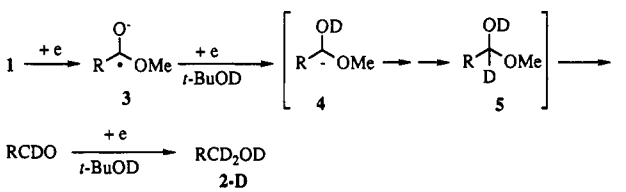
Summary: In the presence of *t*-BuOH, methyl esters and *N*,*N*-dimethylamides of aliphatic carboxylic acids are electroreduced at a Mg cathode to the corresponding primary alcohols. In the presence of *t*-BuOD instead of *t*-BuOH, the electroreduction of the esters gives the corresponding 1,1-dideuterated alcohol. In all cases, the yields are excellent.

The transformation of esters of aromatic carboxylic acids to benzyl-type alcohols can be achieved by electrochemical reduction.[2,3] However, the electroreduction of esters of aliphatic carboxylic acids to primary alcohols has never been achieved because such esters display highly negative reduction potentials (~-3.0 V vs SCE).[4-6]

Scheme I



We have found that when Mg is used as the electrode material, the electroreduction of esters of aliphatic carboxylic acids 1 is possible. Thus, the electroreduction of 1 at a Mg cathode in the presence of a proton donor like *t*-BuOH gives primary alcohols 2 (RCH_2OH) in excellent

(1) Electroorganic chemistry. 134. For part 133, see: Shono, T.; Nozoe, T.; Yamaguchi, Y.; Ishifune, M.; Sakaguchi, M.; Masuda, H.; Kashimura, S. *Tetrahedron Lett.* **1991**, *32*, 1051.
(2) Coleman, G. H.; Johnson, H. L. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 61.
(3) Popp, F. D.; Schultz, H. P. *Chem. Rev.* **1962**, *62*, 19 and references cited therein.
(4) Weinberg, N. L.; Ed. *Technique of Electroorganic Synthesis*; John Wiley: New York, 1974-1982; Vols. 1-3.
(5) Baizer, M. M.; Lund, H., Eds. *Organic Electrochemistry*, 2nd ed.; Marcel Dekker: New York, 1983.
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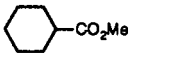
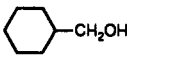
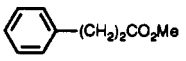
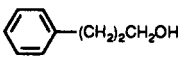
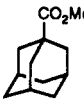
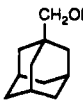
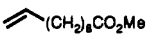
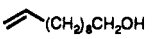
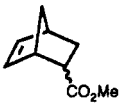
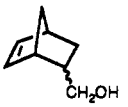
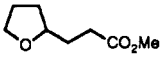
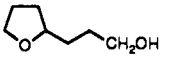
0022-3263/92/1957-1061$03.00/0

Table I. Electroreduction of Methyl Esters 1 of Aliphatic Carboxylic Acids[a]

run	ester 1	product 2[b]	yield[c] (%)
1	$Me(CH_2)_5CO_2Me$ (1a)	$Me(CH_2)_5CH_2OH$ (2a)	88
2	1a	2a	74[d]
3	 (1b)	 (2b)	81
4	 (1c)	 (2c)	86
5	 (1d)	 (2d)	87
6	 (1e)	 (2e)	90
7	 (1f)	 (2f)	80
8	 (1g)	 (2g)	87
9	$MeO_2C(CH_2)_8CO_2Me$ (1h)	$HOCH_2(CH_2)_8CH_2OH$ (2h)	70[e]

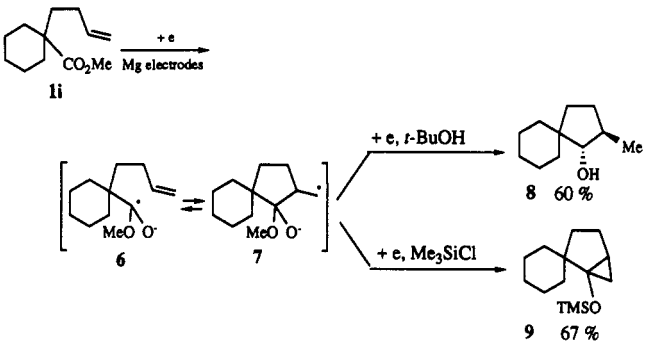
[a] The reduction was performed in an undivided cell in the presence of *t*-BuOH (6 equiv relative to 1). [b] All products gave satisfactory spectra. [c] Isolated yield after 7 F/mol of electricity had been passed. [d] the electroreduction was performed with Al electrodes. [e] 14 F/mol of electricity was passed.

yields. It was also found that the alternation of cathode and anode at the interval of 15 s was important for the reduction of 1 to 2.

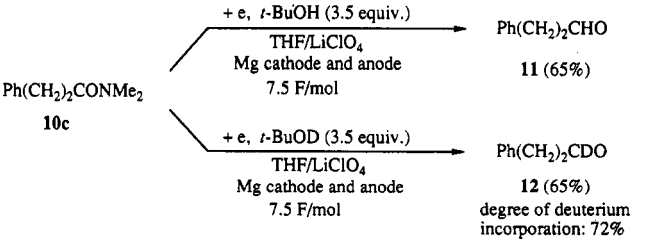
We report here what is undoubtedly the first finding that esters of aliphatic carboxylic acids can be electroreduced.[7,9] The use of Mg as the electrode material is essential. Esters 1 are not electroreduced at electrodes constructed of, for example, Zn, Pb, Ni, Cu, Pt, or C.[12] The presence of a proton donor is also essential. *t*-BuOH gave the best results. The use of other alcohols (MeOH, EtOH, and *i*-PrOH) and an amine (*i*-Pr_2NH) led to a significant decrease in the yield of 2.[14]

Some typical results of the electroreduction of esters 1 in THF in the presence of 6 equiv of *t*-BuOH are summarized in Table I. They clearly show that the method described here can be applied to the reduction of a variety of esters of aliphatic mono- and dicarboxylic acids.[15] In addition, it was found that other functional groups, e.g., aryl (run 4), alkenyl (runs 6,7), and alkoxy groups (run 8)

Scheme II



Scheme III



(7) The exact role played by Mg remains to be established. Attempts to *chemically* reduce esters 1 by the use of active Mg, e.g., Rieke's Mg,[8] were unsuccessful.

(8) Xiong, H.; Rieke, R. D. *J. Org. Chem.* **1989**, *54*, 3249.

(9) The so-called electrochemical reduction of aliphatic esters and amides in $MeNH_2$[10] or $liqNH_3$[11] has also been reported. However, the mechanism of reduction appears to be almost identical to that of a Birch-type reduction. Thus, reduction is not the result of a direct transfer of electrons from the cathode to the substrate. Rather, electrolysis serves only to generate solvated electrons, which then effect the reduction.

(10) Benkeser, R. A.; Watanabe, H.; Mels, S. J.; Sabol, M. A. *J. Org. Chem.* **1970**, *35*, 1210.

(11) Chaussard, J. C.; Combellas, A.; Thiebault. *Tetrahedron Lett.* **1987**, *28*, 1173.

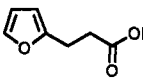
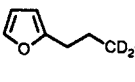
(12) We have reported[13] that the use of a Mg cathode and anode is effective in forming disilanes and polysilanes by the electroreduction of chlorosilanes.

(13) Shono, T.; Kashimura, S.; Ishifune, M.; Nishida, R. *J. Chem. Soc., Chem. Commun.* **1990**, 1160.

(14) When the electroreduction of 1 at a Mg cathode was performed in the absence of a ready source of protons, α-diketones (RCOCOR) were produced.

(15) A typical procedure is as follows: Into an undivided electrolysis cell equipped with a Mg (99.9% pure, Rare Metallic Co., LTD) cathode and anode (rod, diameter = 1 cm; length = 4 cm) were placed anhydrous $LiClO_4$ (10 mmol), molecular sieves (5A, 1.5 g), and dry THF (20 mL). The mixture was stirred overnight under Ar in order to remove residual water. Then, ester 1 (3 mmol) and freshly distilled *t*-BuOH (18 mmol) were added. The subsequent constant-current (0.05A) electrolysis was performed at a cathode potential of ca. −2.7 V vs SCE. The cathode and anode were alternated at the interval of 15 s during the reaction. After 7 F/mol of electricity (based on 1) had been passed through the cell, the product 2, was isolated by distillation.

Table II. Electroreduction of Esters 1 in the Presence of *t*-BuOD[a]

run	ester 1	alcohol 2-D	yield[b] (%)	deg of deuterium incorp[c] (%)
1	$Me(CH_2)_5CO_2Me$ (1a)	$Me(CH_2)_5CD_2OH$ (2a-D)	88	93
2	$Me(CH_2)_5CH(OH)CH{=}CH(CH_2)_8CO_2Me$ (1j)	$Me(CH_2)_5CH(OH)CH{=}CH(CH_2)_8CD_2OH$ (2j-D)	93	90
3	 (1k)	 (2k-D)	86	89

[a] The reduction was performed in an undivided cell in the presence of *t*-BuOD (6 equiv relative to 1). [b] Isolated yield after 7 F/mol of electricity had been passed. [c] Determined by 200-MHz ^{1}H-NMR analysis.

present in the ester remain unaffected. The use of Al electrodes was also effective in electroreducing methyl heptanoate (**1a**) (run 2). However, the yield of alcohol was lower than that obtained by the use of Mg electrodes.

When *t*-BuOD was present instead of *t*-BuOH, the electroreduction of esters **1** gave 1,1-dideuterated alcohols (**2-D**) (Scheme I). This result is important for both synthetic and mechanistic reasons. A method by which alcohols **2-D** can be synthesized under mild conditions from esters **1** and in which *t*-BuOD serves as the deuterium source is highly economical because such alcohols are usually prepared by reducing **1** with expensive lithium aluminum deuteride.[16] The results summarized in Table II indicate that, in each case, the yield and degree of deuterium incorporation are acceptable.

That the deuterated alcohol **2-D** is formed clearly suggests a reaction pathway (Scheme I) in which the electroreduction of **1** initially yields a radical anion **3**. That species is then further reduced to an anion **4**. The intermediacy of the radical **3** and of the hemiacetal **5** is also suggested by the results shown in Schemes II and III.

The results of electroreduction of the unsaturated ester **1i** at a Mg cathode are unprecedented (Scheme II). The cathodic reduction of **1i** in the presence of *t*-BuOH afforded the cyclic alcohol **8**[17] and, in the presence of Me_3SiCl, gave the bicyclic compound **9**.[18] That a 5-membered ring, rather than a 6-membered ring, was formed exclusively suggests that the radical **6** is the key intermediate in the cyclization.[19] The intramolecular addition of a radical species to a carbon–carbon double bond is known to preferentially yield a 5-membered ring.[20]

The electroreduction of amides of aliphatic carboxylic acids is known to be difficult. However, *N,N*-dimethylamides **10** ($RCONMe_2$) can be electroreduced to alcohols **2** (RCH_2OH) at a Mg cathode in the presence of *t*-BuOH (10 equiv relative to **10**). Thus, the electroreduction of **10a** (R = n-C_6H_{13}), **10b** (R = c-C_6H_{11}), and **10c** (R = $PhCH_2CH_2$) gave the corresponding alcohols **2** in yields of 82%, 75%, and 72%, respectively.

The electroreduction of **10** can be arrested at the aldehyde stage if a smaller amount of *t*-BuOH is present. As Scheme III shows, the electroreduction of *N,N*-dimethyl 3-phenylpropionamide (**10c**) in the presence of 3.5 equiv of *t*-BuOH gave the aldehyde **11** in reasonable yield. The deuterated aldehyde **12** was similarly obtained when, instead of *t*-BuOH, *t*-BuOD was present. That compounds like **12** can be formed under such mild conditions is remarkable because the preparation of deuterated aldehydes by nonelectrochemical methods is often long and arduous.[21,22]

Registry No. **1a**, 106-73-0; **1b**, 4630-82-4; **1c**, 103-25-3; **1d**, 711-01-3; **1e**, 111-81-9; **1f**, 6203-08-3; **1g**, 69248-88-0; **1h**, 106-79-6; **1i**, 127827-61-6; **1j**, 138353-72-7; **1k**, 37493-31-5; **2a**, 111-70-6; **2a**-D, 80094-80-0; **2b**, 100-49-2; **2c**, 122-97-4; **2d**, 770-71-8; **2e**, 112-43-6; **2f**, 95-12-5; **2g**, 767-08-8; **2h**, 112-47-0; **2j**, 138353-73-8; **2k**-D, 138353-74-9; **8**, 127827-67-2; **9**, 138353-75-0; **10c**, 5830-31-9; **11**, 104-53-0; **12**, 29372-37-0; THF, 109-99-9; $LiClO_4$, 7791-03-9; Me_3SiCl, 75-77-4; *t*-BuOH, 75-65-0; Mg, 7439-95-4; *t*-BuOD, 3972-25-6.

(16) Fetizon, M.; Henry, Y.; Moreau, N.; Moreau, G.; Golfier, M.; Prange, T. *Tetrahedron* **1973**, *29*, 1011.

(17) The cis:trans ratio (13:87) was established by ^{1}H NMR analysis. **8**: IR (neat) 3350, 2910, 1450, 1060 cm^{-1}; NMR ($CDCl_3$) δ 1.04 (d, 3 H, J = 6.2 Hz), 1.00–1.95 (m, 15 H), 3.02 (d, 1 H, J = 8.5 Hz); HRMS calcd for $C_{11}H_{20}O$ 168.1515, found 168.1506.

(18) The conversion of **1i** to **9** was achieved by electrolyzing **1i** in the presence of Me_3SiCl instead of *t*-BuOH. **9**: IR (neat) 1450, 1350, 1250, 840 cm^{-1}; NMR ($CDCl_3$) δ 0.08 (s, 9 H), 0.52–0.77 (m, 3 H), 1.05–1.92 (m, 14 H); HRMS calcd for $C_{14}H_{26}OSi$ 238.1754, found 238.1733.

(19) The mechanism of the formation of **8** and **9** from **7** will be discussed in a forthcoming paper.

(20) For example, see: Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386.

(21) Degani, I.; Fochi, R.; Regondi, V. *Tetrahedron Lett.* **1981**, *22*, 1821.

(22) Kalvin, D. M.; Woodard, R. W. *Tetrahedron* **1984**, *18*, 3387 and references cited therein.

Enzyme-Catalyzed Formation of Chiral Monosubstituted Mixed Diesters and Half Esters of Malonic Acid in Organic Solvents

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Summary: Enzymes in organic solvents were used to develop a strategy for the formation of heretofore unknown chiral monosubstituted malonate diesters and half esters. This enzymatic approach is not feasible in aqueous solutions because the activated malonic hydrogen invariably undergoes fast exchange accompanied by racemization.

Optically active monosubstituted half esters of malonic acid (1) would be useful as chiral synthons and substrates for mechanistic and kinetic studies on racemization, but their synthesis has not yet been reported. The failure to prepare these compounds in optically active form was due to the inapplicability of the conventional approach, i.e.,

0022-3263/92/1957-1063$03.00/0