

Short Communication

Electroreductive Intramolecular Cyclization of Olefinic Esters and its Application to the Synthesis of Muscone

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Dedicated to Professor Henning Lund on the occasion of his 70th birthday.

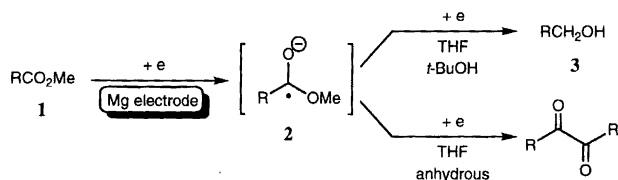
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It has been reported in our previous papers that the electroreduction of aliphatic ester (**1**) with Mg electrode gave the primary alcohol (**3**) or 1,2-diketone (**4**) depending on the reaction conditions (Scheme 1). Namely, the electroreduction of **1** in the presence of a proton donor such as *t*-BuOH gave **3**² and that of **1** under anhydrous conditions afforded **4**.^{3,4} In these reactions, an anion radical (**2**) formed by one-electron reduction of **1** seemed the key intermediate leading to the formation of **3** or **4**. Since the time that the formation of **2** from **1** was first proposed as the essential inter-

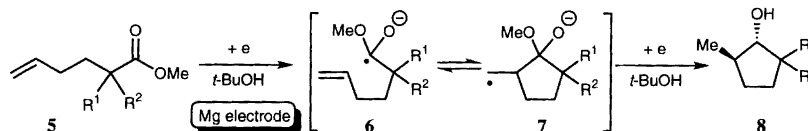
mediate in these reactions, the reactivity of **2** was almost unknown.⁴

In our continuing studies on the electroreduction of aliphatic esters, it has recently been found that the electroreduction of olefinic esters (**5**) with Mg electrode leads to the formation of cyclic products (**8**) through intramolecular cyclization of radical intermediates **6** or **7** (Scheme 2).⁵ The use of an Mg electrode was the crucial factor for the formation of **8**, since the electroreduction of **5** with other types of electrode such as C, Pt, Cu, Ni, Cu, and Pb did not give **8**, and **5** was recovered unchanged.

The electroreduction of **5** to **8** was carried out 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 LiClO₄ (10 mmol), molecular sieves 5 Å (1.5 g), and anhydrous THF (20 ml, dried over Na–benzophenol ester (**5**) (3 mmol) and *t*-BuOH (7.5 mmol) were added to the mixture after it had been



Scheme 1.



Scheme 2.

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Table 1. Electroreductive cyclization of olefinic esters.

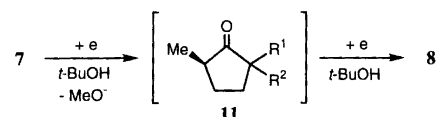
Run	Ester	Product	Yield (%) ^{a-c}	<i>trans/cis</i> ^d
1			64	83/17
2			76	79/21
3			77	— ^e
4			80	82/18
5			71	
6			75	

^aIsolated. ^b5 F mol⁻¹ of electricity based on **5** was passed. ^cAll products gave satisfactory spectroscopic values for the assigned structure. See Ref. 14. ^dRatio of isomers was determined by GLC. ^eThe product was a mixture of stereo isomers.

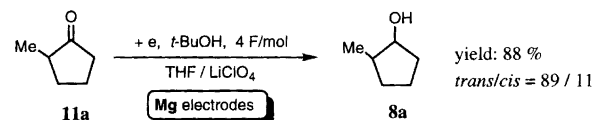
stirred overnight under an Ar atmosphere in order to remove the residual water. The constant current (0.05 A) electrolysis was performed at a cathode potential of ca. -2.7 V vs. SCE. The cathode and anode were alternated at the intervals of 15 s during the reaction. After 5 F mol⁻¹ of electricity (based on **5**) had passed through the cell, the products **8a–8d** were isolated by silica gel column chromatography (hexane–AcOEt = 20:1). Typical results are shown in Table 1. The electroreduction of **5a–5d** (runs 1–4) gave the corresponding cyclic products in reasonable yields, whereas methyl 2-heptenoate (**9**) (run 5) the methyl 1-heptenoate (**10**) (run 6) did not give cyclic products. The exclusive formation of a five-membered ring rather than a six-membered ring in the cathodic cyclization of **5** (**5a–5d**) may be explained by a usual intramolecular coupling reaction between a radical and a double bond.¹³ The products **8a–8d** gave satisfactory spectroscopic values for the assigned structures.¹⁴

In this cathodic cyclization, the formation of a *trans*-isomer of **8** rather than a *cis*-isomer may be explained by the intermediate formation of a cyclic ketone (**11**) from **7** followed by the electroreduction of **11** to **8** (Scheme 3), since the electroreduction of 2-methyl-

cyclopentanone (**11a**) with an Mg electrode in the presence of *t*-BuOH, for example, gave *trans*-**8a** as the main product (Scheme 4) and the *trans/cis* ratio was very similar to that obtained in the electroreductive cyclization of **5a** to **8a** (Table 1, run 1).¹⁷

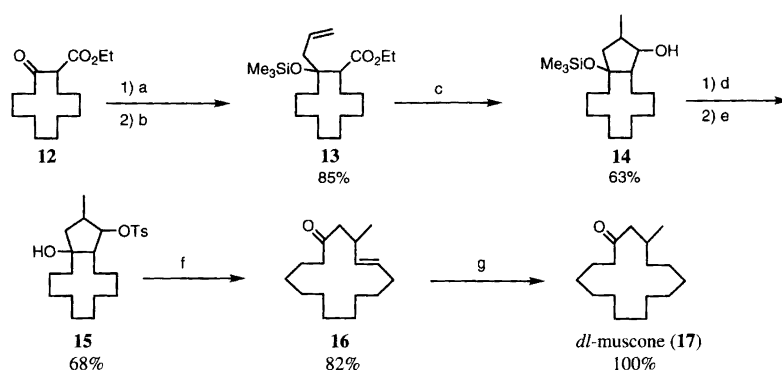


Scheme 3.



Scheme 4.

This cyclization reaction was found to be useful for the synthesis of (±)-muscone (**17**) (Scheme 5) and as shown in Scheme 5, the transformation of **12** into **17** was successfully accomplished by using the cathodic cyclization of **13** to **14** as the key reaction.¹⁹



Scheme 5. (a) Allyl bromide–Zn–DMF; (b) TMSCl–1m–DMF; (c) *t*-BuOH + e; Mg electrode; (d) TsCl–Py; (e) 2 M HCl aq–THF; (f) *t*-BuOK–*t*-BuOH; (g) H₂–Raney Ni.

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References and notes

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5. We have previously reported some unique reactions of anion radicals formed by the electroreduction of aliphatic ketones.^{6,7} Other groups have also reported the electroreductive cyclization of unsaturated ketones or activated olefins.⁸⁻¹²
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14. The main products (*trans*-**8a**, *trans*-**8b** and *trans*-**8d**) were separated by TLC (silica gel). these products gave satisfactory spectroscopic values for the assigned structures:^{15,16} *trans*-**8a**, IR (neat) 3350, 2970, 1090 cm⁻¹. NMR (CDCl₃). δ 0.97 (d, 3 H, $J=6.6$ Hz), 1.05–2.03 (m, 7 H) 3.64–3.79 (m, 1 H). HRMS: Calc. for C₆H₁₂O₂: 116.0837. Found: 116.0922. *trans*-**8b**, IR (neat) 3360, 2950, 1065 cm⁻¹. NMR (Cl₃): δ 0.86 (s, 3 H), 0.98 (s, 3 H), 1.05 (d, 3 H, $J=6.3$ Hz), 1.20–1.92 (m, 5 H), 3.10 (d, 1 H, $J=8.0$ Hz). HRMS: Calc. for C₈H₁₆O: 128.1202. Found: 128.1221. **8c** (mixture of stereo isomers), IR (neat) 3350, 2950, 1065 cm⁻¹. NMR (CDCl₃): δ 0.83–2.05 (m, 14 H), 3.04–3.20 or 3.62–3.74 (m, 1 H). HRMS: Calc. for C₈H₁₆O: 128.1202. Found: 128.1194. *trans*-**8d**, IR (neat) 3350, 2910, 1450, 1060 cm⁻¹. NMR (CDCl₃): δ 1.04 (d, 3 H, $J=6.2$ Hz), 1.00–1.95 (m, 16 H), 3.02 (d, 1 H, $J=8.5$ Hz). HRMS: Calc. for C₁₁H₂₀O: 168.1515. Found: 168.1506.
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19. Transformation of **12** into **13** as carried out by our previously reported method using Zn as the reagent²⁰ and the synthesis of **17** from **15** was accomplished by a known procedure.²¹ **14**, IR (neat) 3400, 2940, 1040 cm⁻¹. NMR (CDCl₃): δ (CDCl₃) 0.16 (s, 9 H), 1.14 (d, 3 H, $J=6.6$ Hz), 1.10–1.80 (m, 24 H), 3.56–3.61 (m, 1 H). HRMS: Calc. for C₁₉H₃₈O₂Si: 326.2642. Found: 326.2607.
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