



Synthesis of Symmetrical and Unsymmetrical 1,2-Diketones through Cathodic Intramolecular Coupling of Diesters.¹

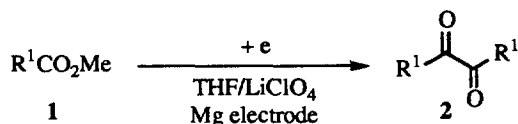
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Abstract: Electroreduction of diesters [R¹COO(CH₂)₂OCOR²] with Mg electrode has been found to give the corresponding unsymmetrical 1,2-diketones (R¹COCOR²) with excellent yields.

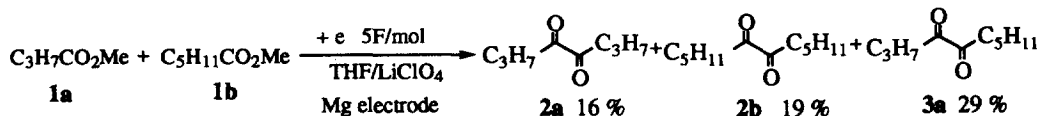
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It has been shown in our recent study that under aprotic conditions⁵, the electroreduction of aliphatic ester (1) with Mg electrode gives the corresponding symmetrical 1,2-diketone (2) in excellent yield (Scheme 1).⁷



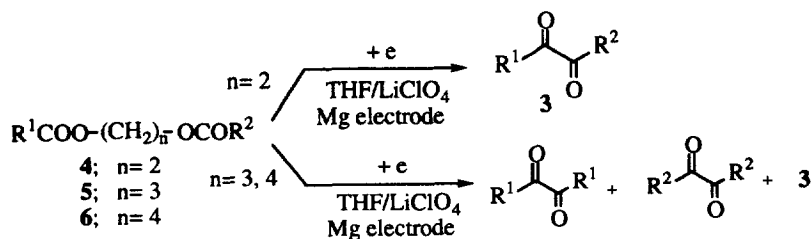
Scheme 1

The electrochemical method shown in the scheme 1 was useful for one step synthesis of 2, whereas the method was not applicable to the selective synthesis of unsymmetrical 1,2-diketone (3) since the electroreduction of a mixture of methyl butyrate (1a) and methyl hexanoate (1b) (1a : 1b=1:1), for example, gave a mixture of two types of symmetrical 1,2-diketones (2a, 2b) and an unsymmetrical 1,2-diketone (3a) (Scheme 2).



Scheme 2




On the contrary, it has been found in the present study that the electroreduction of diester 4 (n=2) with Mg electrode leads to the selective formation of 3 under aprotic conditions (Scheme 3), whereas the reduction of diester 5 (n=3) or 6 (n=4) gave a mixture of 2 (R¹COCOR¹ and R²COCOR²) and 3 under the same reduction conditions.



Scheme 3

The electroreduction of **4**⁸ was carried out as follows: Into an undivided electrolysis cell equipped with Mg (99.9% pure, Rare Metallic Co., LTD) cathode and anode (rod, diameter = 1 cm; length = 4 cm) were put anhydrous LiClO₄ (10 mmol), molecular sieve 5A (1.5 g), and anhydrous THF (20 mL, dried over Na-ketyl). After the mixture was stirred for overnight under an Ar atmosphere in order to remove the residual water, ester (**4**) (3 mmol) was added to the mixture. 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 interval of 15 sec. during the reaction. After 5 F/mol of electricity (based on **4**) was passed through the cell, product **3** was isolated by silica gel column (hexane : AcOEt = 20 : 1). As the typical results are shown in Table 1, the electroreduction of diester **4a** (run 1) gave the corresponding unsymmetrical 1,2-diketone **3a** in an excellent yield and the formation of symmetrical 1,2-diketones (**2a** and **2b**) was not observed at all. This method was successfully applicable for the synthesis of aliphatic (runs 2 and 3) and aromatic (run 4) unsymmetrical 1,2-diketones. It is also noteworthy that the electroreduction of aromatic diester **4e** gave the corresponding symmetrical 1,2-diketone **2e** in a high yield (run 5) since it has been shown in our previous study that the electroreductive intermolecular coupling of methyl benzoate according to the method shown in the scheme 1 gave **2e** only in 33 % yield.⁷ This result indicated that the intramolecular coupling of diester resulted in the remarkable increase in the yield of the symmetrical 1,2-diketone **2e** and this tendency was also observed in the cathodic coupling of aliphatic diester **4f** (run 6). The products (**3a-3d**, **2e**, and **2f**) gave satisfactory spectroscopic values for the assigned structures.¹⁰

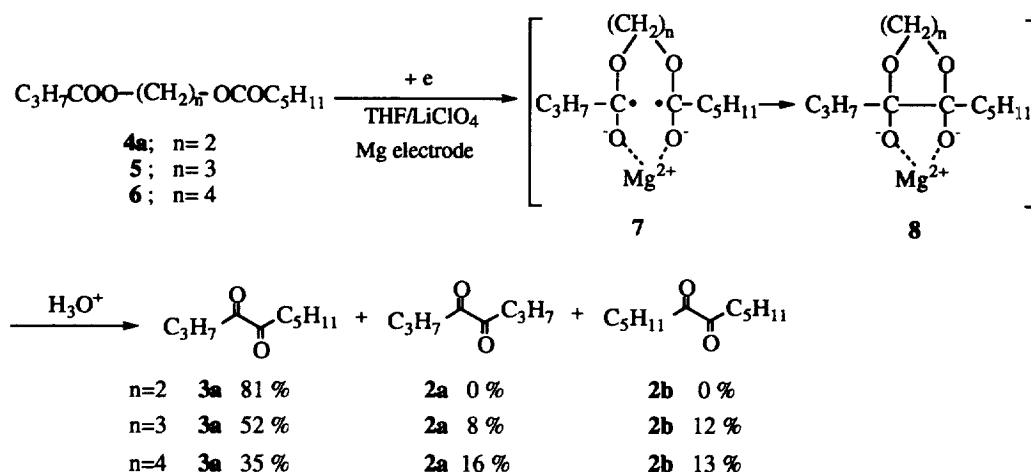
Table 1. Synthesis of 1,2-Diketone.

Run	Diester	n=	R ¹	R ²	Product Yield (%) ^{a,b,c}		
					3	2	
1	(4a)	2	C ₃ H ₇ -	C ₅ H ₁₁ -	(3a) 81	(2a) 0	(2b) 0
2	(4b)	2	C ₃ H ₇ -	C ₇ H ₁₅ -	(3b) 87	0	
3	(4c)	2	<i>iso</i> -C ₃ H ₇ -	C ₇ H ₁₅ -	(3c) 78	0	
4	(4d)	2	C ₃ H ₇ -		(3d) 82	0	
5	(4e)	2				(2e) 71 (33) ^d	
6	(4f)	2	C ₆ H ₁₃ -	C ₆ H ₁₃ -		(2f) 88 (63) ^d	

a) Isolated. b) 5 F/mol of electricity based on **4** was passed. c) All products gave satisfactory spectroscopic values for the assigned structures. See ref. 10. d) The number in the parenthesis shows the yield of the product obtained by the intermolecular coupling of esters. See ref. 7.

The formation of **3** by the electroreduction of **4** with Mg electrode is highly interesting since so far, the simple and reliable method for the synthesis of unsymmetrical 1,2-diketones **3** has never been reported.¹¹

To have an insight into the reaction mechanism, the electroreduction of **4a**, **5**, and **6** (Scheme 4) was investigated. After 5 F/mol of electricity was passed through the solution of **4a**, the reaction mixture was filtered prior to the treatment with water. The analysis of the contents of THF filtrate and filter cake showed that the THF filtrate did not contain **3a** but the hydrolysis of the filter cake with an aqueous solution of NH_4Cl gave the corresponding diketone (**3a**) in 81 % yield. These results indicated that the coupling of the anion radical intermediate **7** ($n=2$) formed an intermediate **8** ($n=2$) which was a magnesium salt. Since the salt **8** ($n=2$) was insoluble in THF and precipitated from THF solution, the hydrolysis of the filter cake gave **3a** in high yield. These results showed that the presence of Mg ion was important for the formation of **3**.^{13,14} The electroreduction of diester **5** ($n=3$) gave **3a** along with the symmetrical 1,2-diketones (**2a** and **2b**), and that of **6** ($n=4$) under same reaction conditions also gave a mixture of diketones **3a**, **2a** and **2b**. The ratio of the products obtained by the electroreduction of **6** was almost the same as that of intermolecular reaction shown in the scheme 2. These results suggested that the selective formation of **3a** highly depended on the stereochemical relation between two radical centers of **7**. Namely, the electroreduction of **4a** formed the radical intermediate **7** ($n=2$) in which two radical centers were situated in the pattern forming a 6-membered ring and this was important for the selective formation of **3a**. On the other hand, in the electroreduction of **5** and **6**, the radical centers formed were located in 1,7- and 1,8- positions respectively which obstructed the formation of the cyclic intermediate and hence, led to the formation of a mixture of diketones **3a**, **2a** and **2b**.

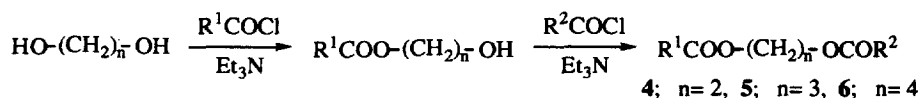


Scheme 4

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References and Notes

- 1) Electroorganic Chemistry 154. For part 153, see *Tetrahedron Lett.*, *in press* 1997.
- 2) Department of Metallurgy.
- 3) Research and Development Department, Osaka Gas Co. Ltd. 1 Chyudoji-Machi, Simogyo, Kyoto 600.
- 4) Research Institute for Science and Technology.
- 5) We have previously reported that the electroreduction of **1** under protic conditions gave the corresponding primary alcohols.⁶
- 6) Shono, T.; Masuda, H.; Murase, H.; Shimomura, M.; Kashimura, S. *J. Org. Chem.* **1992**, *57*, 1061.
- 7) Kashimura, S.; Murai, Y.; Ishifune, M.; Masuda, H.; Murase, H.; Shono, T. *Tetrahedron Lett.* **1995**, *36*, 4805.
- 8) The preparation of diesters (**4**, **5** and **6**) was carried out by the known method shown below.⁹



- 9) Horton, D. *Org. Synth. Collect. Vol. 5*, **1973**, 1.
- 10) **3a**: IR (neat) 2930, 1714, 1460, 1446cm⁻¹; NMR (CDCl₃) δ 0.86 (t, 3H, J = 6 Hz), 0.92 (t, 3H, J = 6 Hz), 1.27 (m, 2H), 1.57 (m, 6H), 2.71 (t, 2H, J = 6.0 Hz), 2.74 (t, 2H, J = 6.0 Hz); HRMS Calcd for C₁₀H₁₈O₂: 170.1307; Found: 170.1310.
3b: IR (neat) 2952, 1709, 1460, 1440cm⁻¹; NMR (CDCl₃) δ 0.87 (t, 3H, J = 6 Hz), 0.94 (t, 3H, J = 6 Hz), 1.26 (m, 6H), 1.54 (m, 6H), 2.71 (t, 2H, J = 6.0 Hz), 2.73 (t, 2H, J = 6.0 Hz); HRMS Calcd for C₁₂H₂₂O₂: 198.1620; Found: 198.1624.
3c: IR (neat) 2916, 1711, 1456cm⁻¹; NMR (CDCl₃) δ 0.89 (t, 3H, J = 6 Hz), 1.08 (d, 6H, J = 6 Hz), 1.30 (m, 6H), 1.60 (m, 4H), 2.73 (t, 2H, J = 6.0 Hz), 3.35 (m, 1H); HRMS Calcd for C₁₂H₂₂O₂: 198.1620; Found: 198.1615.
3d: IR (neat) 3020, 2963, 1712, 1673, 1457, 1450cm⁻¹; NMR (CDCl₃) δ 0.87 (t, 3H, J = 6 Hz), 1.26 (m, 2H), 2.83 (t, 2H, J = 6.0 Hz), 7.14-8.00 (m, 5H); HRMS Calcd for C₁₁H₁₂O₂: 176.0837; Found: 176.0842.
2e: IR (neat) 3020, 1660, 1600, 1450, 1320, 1210, 880 cm⁻¹; NMR (CDCl₃) δ 7.44-7.56 (m, 4H), 7.60-7.70 (m, 2H), 7.93-8.00 (m, 4H); HRMS Calcd for C₁₄H₁₀O₂: 210.0681; Found: 210.0679.
2f: IR (neat) 2920, 1710, 1460, 1400, 710 cm⁻¹; NMR (CDCl₃) δ 0.86 (t, 6H, J = 6 Hz), 1.27 (m, 12H), 1.55 (m, 4H), 2.71 (t, 4H, J = 6.0 Hz); HRMS Calcd for C₁₄H₂₆O₂: 226.1934; Found: 226.1936.
- 11) Recently it has been reported that the electroreduction of an aromatic ester gave the corresponding symmetrical 1,2-diketone.¹²
- 12) Heintz, M.; Devaud, M.; Hebri, H.; Dunach, E.; Troupel, M. *Tetrahedron*, **1993**, *49*, 2249.
- 13) The reduction of **4a** with sodium metal did not give **3a** but yielded a complex mixture of products.
- 14) Electroreduction of **4a** with Pt anode and cathode in the presence of Mg²⁺ [MgCl₂, MgBr₂, Mg(ClO₄)₂] did not give **3a**, and **4a** was recovered.