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Communications

Electroreductively Promoted Diastereoselective Coupling of Ketones with Allylic Alcohols. Synthesis of Optically Active 1,4-Diols[1]

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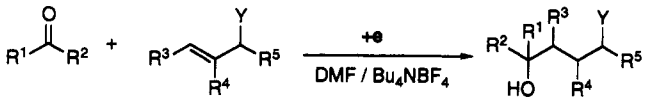
Summary: Cathodic coupling of ketones with allylic alcohols has been found to take place with high regio- and stereoselectivities at the position γ to the hydroxyl group to afford the corresponding 1,4-diols.

In our continuing studies on the cathodic coupling of ketones with olefinic systems,[3-6] we have reported[6] that the intermolecular coupling of ketones **1** with olefinic systems **2** (Y = H) is greatly influenced by the structure of **2** (Scheme 1). For example, the coupling of **1** with 1-olefins (R^3 = R^4 = H, R^5 = an alkyl group) gave the coupling products **4** in excellent yields (~80%), whereas the coupling with 2-substituted 1-olefins (R^3 = H, R^4 and R^5 = alkyl groups) resulted in the remarkable decrease in the yield of **4** (~20%) and that with inner olefins (R^3 and R^5 = alkyl groups, R^4 = H) did not take place at all.

In the present study we have found that allylic alcohols **3** (Y = OH) show quite unique reactivity in the cathodic coupling with **1**. Namely, the alkyl group (R^3 or R^4) located on the double bond of **3** does not obstruct the coupling (Scheme 1), and moreover, the coupling of optically active **3** with **1** gave **5** with excellent diastereoselectivity at the coupling position.

Some of the typical results of the electroreductive coupling of **1** with **3**, carried out in DMF using Bu_4NBF_4 as a supporting electrolyte,[7] are shown in Table 1 (runs 1–5). The unique reactivity of the allylic alcohols in this electroreductive coupling is explained on the basis of the unique role of the allylic hydroxyl group. As is clearly shown in Table 1, the position of a hydroxyl group at the allylic position of the olefin is essential to effectively promote this coupling reaction. For example, the coupling of acetone with *trans*-2-octen-4-ol (*trans*-**3e**, an allylic alcohol) took place with a reasonable yield (run 5), whereas that with *trans*-2-octen-5-ol (**6**, a homoallylic alcohol) showed a remarkable decrease in the yield (run 6) and that with *trans*-2-octen-6-ol (**8**, run 7) or *trans*-2-octene (**2a**, run 8) did not take place at all. In addition, the

Scheme 1



1

2; Y = H
3; Y = OH

4; Y = H
5; Y = OH

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(1) Electroorganic Chemistry. 143. For part 142, see: *Tetrahedron Lett.* **1993**, *22*, 3577.

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(3) Shono, T.; Mitani, M. *J. Am. Chem. Soc.* **1971**, *93*, 5284.

(4) Shono, T.; Mitani, M. *Nippon Kagaku Kaishi* **1973**, 975.

(5) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. *J. Am. Chem. Soc.* **1978**, *100*, 545.

(6) Shono, T.; Kashimura, S.; Mori, Y.; Hayashi, T.; Soejima, T.; Yamaguchi, Y. *J. Org. Chem.* **1989**, *54*, 6001.

(7) The cathodic reduction was carried out in a divided cell equipped with a bundle of carbon fiber (3000 carbon fiber filaments,[8] 15-cm length) as a cathode, a platinum anode (2 × 2 cm), and a glass filter diaphragm (no. 5). A solution of **1** (10 mmol) and **3** (2 mmol) in dry DMF (20 mL, dried over Al_2O_3) containing Bu_4NBF_4 (5 mmol) as a supporting electrolyte was put into the cathodic chamber of the cell. The anodic solution was 15 mL of dry DMF containing Bu_4NBF_4 (5 mmol). After 2.5 F/mol of electricity based on **1** was passed through the cell under the constant current of 0.2 A, the cathodic solution was poured into 100 mL of brine and extracted with ether (50 mL × 3). The combined organic layer was washed with 1 N HCl (50 mL), saturated aqueous $NaHCO_3$, and brine (50 mL) and then dried over $MgSO_4$. The residue obtained by evaporation of the solvent was column chromatographed (silica gel, EtOAc:hexane = 1:2) in order to give **5**.

(8) The carbon fiber used was carbonized polyacrylonitrile (Hi-Carbolon-3KS, diameter 7 μm, Asahi Kasei Carbon Fiber Co., Ltd.).

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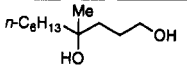
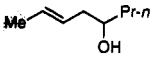
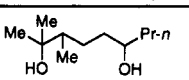
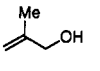
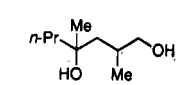
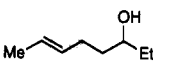
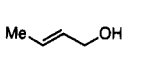
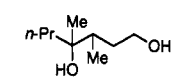
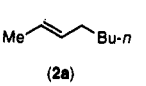
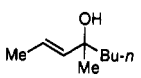
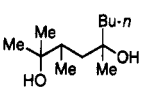
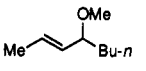
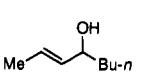
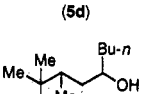
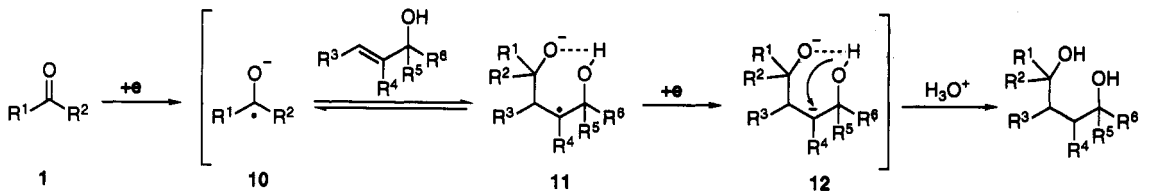
Table 1. Cathodic Coupling of Ketones with Olefins

run	ketone (1)	olefin	product (5)[a]	yield[b] (%)	run	ketone (1)	olefin	product (5)[a]	yield[b] (%)
1	*n*-C_6H_{13}COMe	 (3a)	 (5a)	89	6	MeCOMe	 (6)	 (7)	
2	*n*-PrCOMe	 (3b)	 (5b)		7	MeCOMe	 (8)		0
3	*n*-PrCOMe	 (3c)	 (5c)		8	MeCOMe	 (2a)		0
4	MeCOMe	 (3d)	 (5d)	85	9	MeCOMe	 (9)		0
5	MeCOMe	 (3e)	 (5e)	78					

[a] 2.5 F/mol of electricity based on 1 was passed. [b] Isolated.

Scheme 2



1 10 11 12

coupling reaction was completely inhibited when the hydroxyl group of *trans*-**3e** was transformed to a methoxyl group (run 9).

The pathway of the coupling is shown in Scheme 2 in which the first step of the reaction, that is, the coupling of a carbonyl anion radical with the double bond, is highly dependent on the ease of further reduction of the first radical intermediate (**11**). If **11** is not easily reduced to the corresponding anion intermediate **12** owing to the instability of **12**, the coupling does not take place. The fact that the coupling of 2-substituted 1-olefins or inner olefins takes place in low yield is explained by the instability of the anion intermediate corresponding to **12**. In the case of allylic alcohols, however, the carbanion **12** is protonated very rapidly with the intramolecular hydroxyl group so that **11** is reduced with a reasonable rate and, hence, the coupling takes place.

The hydroxyl group of **3** also plays an important role in promoting the coupling with high diastereoselectivity. For example, the cathodic coupling of acetone with *trans*-(*R*)-2-octen-4-ol [*trans*-(R)-**3e**] and *trans*-(*R*)-5-methyl-2-hexen-4-ol [*trans*-(*R*)-**3f**][9] gave (3*S*,5*R*)-2,3-dimethyl-2,5-nonanediol [(3*S*,5*R*)-**5e**][11-13] and (3*S*,5*R*)-2,3,6-trimethyl-2,5-heptanediol [(3*S*,5*R*)-**5f**],[13,14] respectively, with excellent diasteleoselectivity (Scheme 3). Also, the coupling of acetone with *cis*-(*R*)-2-octen-4-ol [*cis*-(*R*)-**3e**][9] gave (3*R*,5*R*)-2,3-dimethyl-2,5-nonanediol [(3*R*,5*R*)-**5e**][15] diastereoselectively (Scheme 4).

It seems reasonable that the stereo structure of the intermediate **11** is fixed by the interaction between the OH group and O anion. Therefore, in the case of the coupling of acetone with *trans*-(*R*)-**3**, for instance, two types of **11**, namely, **11A** and **11B**, are formed. The former corresponds to the *Si*-face attack of the radical on the double bond in **13** and the latter to the *Re*-face attack. As shown in Scheme 3, **11B** seems more unfavorable than **11A**. Therefore, (3*S*,5*R*)-**5** is preferentially formed through the intermediate **11A**. The selective formation of (3*R*,5*R*)-**5** in the coupling of acetone with *cis*-(*R*)-**3** is explained similarly since the intermediate **11C** is of lower energy than **11D** (Scheme 4).

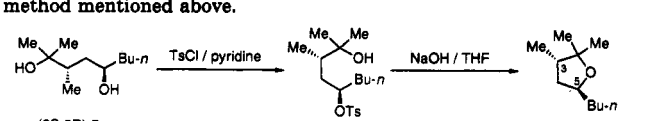
(9) *trans*-(*R*)-**3e** and *trans*-(*R*)-**3f** were prepared by the kinetic resolution of the corresponding racemic alcohols using a known method.[10]

(10) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

(11) (3*S*,5*R*)-**5e**: IR (neat) 3300, 2930, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.64 (m, 1H), 1.09–1.80 (m, 8H), 1.22 (s, 3H), 1.14 (s, 3H), 0.93 (d, 3H, J = 7.0 Hz), 0.91 (t, 3H, J = 6.0 Hz).

(12) The diastereomeric excess of (3*S*,5*R*)-**5e**, (3*S*,5*R*)-**5f**, or (3*R*,5*R*)-**5e** was determined in the presence of Eu(hfc)$_3$ by ^1H NMR analysis after the secondary hydroxyl group of (3*S*,5*R*)-**5e**, (3*S*,5*R*)-**5f**, or (3*R*,5*R*)-**5e** was transformed to the corresponding acetate.

(13) The absolute configuration of (3*S*,5*R*)-**5e** was determined as follows: The reaction of (3*S*,5*R*)-**5e** with TsCl/pyridine gave the tosylate [(3*S*,5*R*)-**15**], and the treatment of **15** with NaOH gave (3*S*,5*S*)-**16** through an intramolecular S_N2 reaction. **16**: IR (neat) 2920, 1360, 1150, 1010 cm^{-1}; NMR ($CDCl_3$) δ 3.93 (m, 1H), 1.89 (m, 1H), 1.76 (m, 2H), 1.58–1.14 (m, 6H), 1.22 (s, 3H), 1.01 (s, 3H), 0.92 (d, 3H, J = 7 Hz), 0.89 (t, 3H, J = 7 Hz). The stereochemical relation between a methyl group at the 3-position and a butyl group at the 5-position of **16** was determined to be *trans* since the irradiation of a proton at the 5-position (δ 3.93) showed a NOE at the methyl group at the 3-position (δ 0.92). The absolute configuration of (3*S*,5*R*)-**5f** was also determined by using the similar method mentioned above.

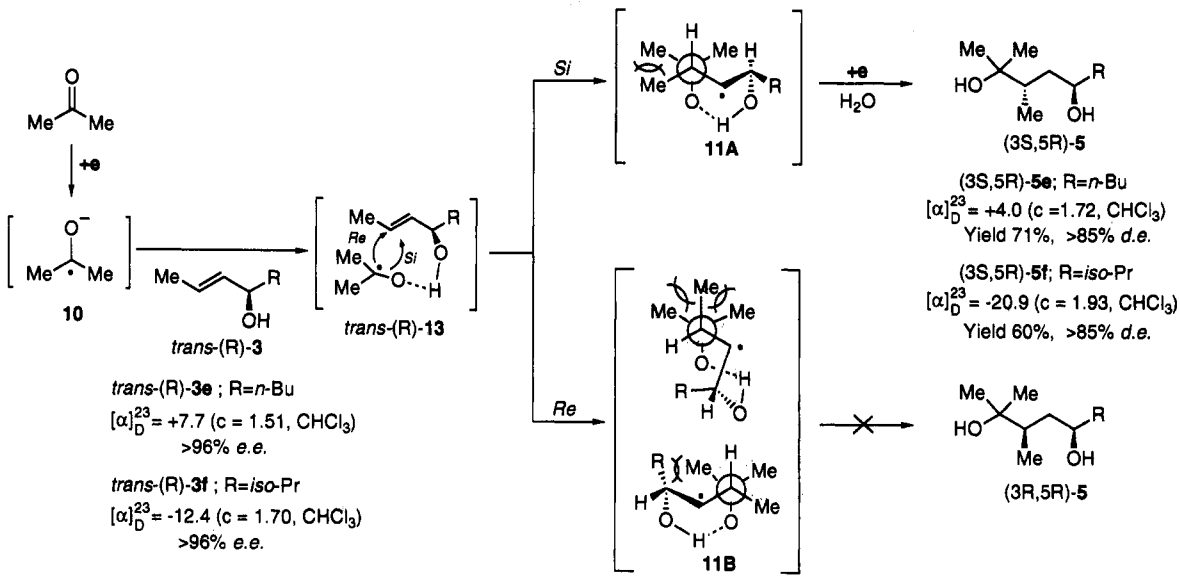


(3S,5R)-5e (3S,5R)-15 (3S,5S)-16

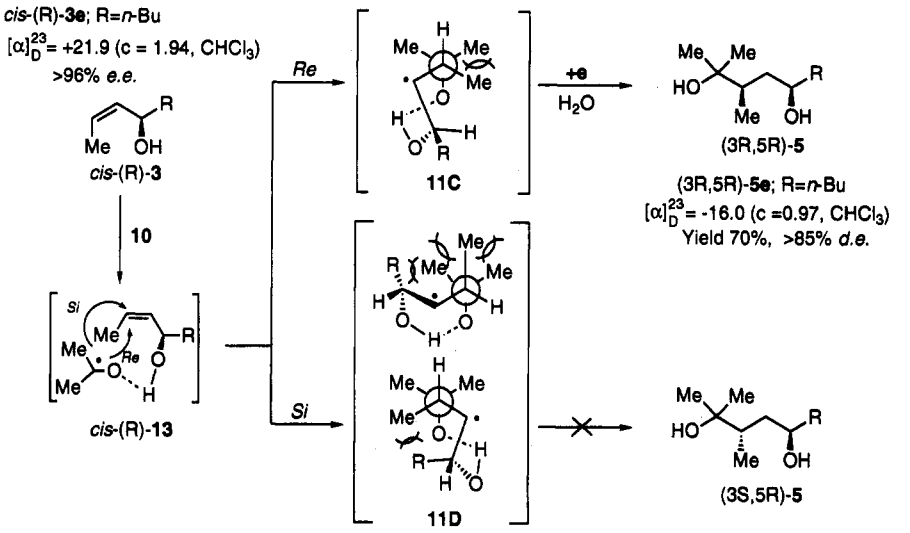
(14) (3*S*,5*R*)-**5f**: IR (neat) 3600, 2920, 1360 cm^{-1}; NMR ($CDCl_3$) δ 3.40 (m, 1H), 1.79–1.55 (m, 4H), 1.23 (s, 3H), 1.14 (s, 3H), 0.93 (d, 6H, J = 7 Hz).

(15) (3*R*,5*R*)-**5e**: IR (neat) 3350, 2930, 1360 cm^{-1}; NMR ($CDCl_3$) δ 3.77 (m, 1H), 1.80–1.09 (m, 9H), 1.24 (s, 3H), 1.17 (s, 3H), 0.96 (d, 3H, J = 7 Hz), 0.91 (t, 3H, J = 6 Hz).

Scheme 3

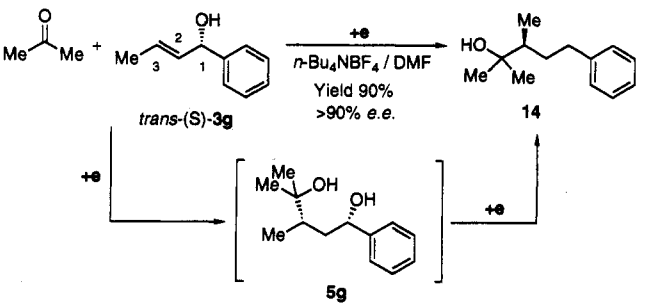


Scheme 4



It is noteworthy that the cathodic coupling of acetone with *trans*-(*S*)-1-phenyl-2-buten-1-ol [*trans*-(*S*)-**3g**] gave (*S*)-2,3-dimethyl-5-phenyl-2-pentanol (**14**)[16] in 90% yield and with higher than 90% ee (Scheme 5). The formation of **14** is reasonably explained as follows: The coupling of acetone with *trans*-(*S*)-**3g** takes place diastereoselectively affording the coupling product **5g**, while the hydroxyl group on the benzyl position of **5g** is reduced to form **14**.[19] The overall reaction shown in Scheme 5 is useful in organic synthesis since the 1,3-transcription of chirality is easily attained under mild and simple reaction conditions.

Scheme 5



(16) The authentic sample of **14** was prepared using a known method.[17,18]

(17) Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.

(18) Sonnet, P. E.; Heath, R. T. *J. Org. Chem.* **1980**, *45*, 3137.

(19) It has been reported that the cathodic reduction of benzyl alcohols results in the cleavage of the carbon–oxygen bond at the benzylic position and affords the corresponding hydrocarbons.[20]

(20) *Organic Electrochemistry*, 2nd ed.; Baizer, M. M., Lund, H., Eds.; marcel Dekker: New York, 1983; pp 757–774.

Supplementary Material Available: General experimental procedure and characterization data for all new compounds (5 pages). This material is contained in 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.