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Cathodic Coupling of Ketones with Trimethylsilyl Substituted Allyl Alcohols[1]

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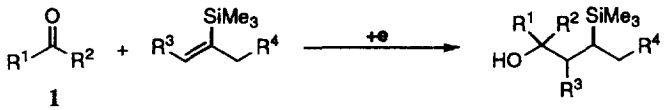
Abstract : Cathodic coupling of ketones with 3-(trimethylsilyl)allyl alcohols has been found to give trimethylsilyl substituted 1,3-diols with high diastereoselectivity, whereas that with 2-(trimethylsilyl)allyl alcohols afforded homoallylic alcohols through the Peterson elimination of intermediately formed trimethylsilyl substituted 1,4-diols. Copyright © 1996 Elsevier Science Ltd

It has been shown in our previous studies that cathodic coupling of ketones (**1**) with olefins is remarkably affected by the structure of olefin (terminal, exomethylene, or inner type olefin) and some types of heteroatom substituent. In the reaction of **1** with unsaturated silanes (Scheme 1, R^1, R^2= alkyl groups, R^3= H, R^4= H or alkyl group)[5], for instance, the coupling reaction was remarkably promoted by stabilization of the anionic intermediate by the trimethylsilyl group and hence, it took place at the neighboring position of trimethylsilyl group even though the type of olefin was exomethylene type. On the other hand, in the reaction of **1** with allyl alcohols (Scheme 2, R^1, R^2= alkyl groups, R^3, R^4, R^5 = H or alkyl group),[6] the hydroxyl group located at the allylic position played important roles in the coupling and the reaction took place at the position γ to hydroxyl group with high regio- and stereoselectivities even in the case that the olefin was inner type.



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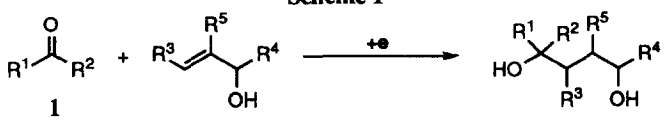
Scheme 1



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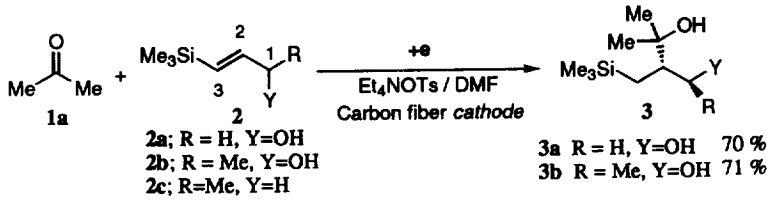
Scheme 2

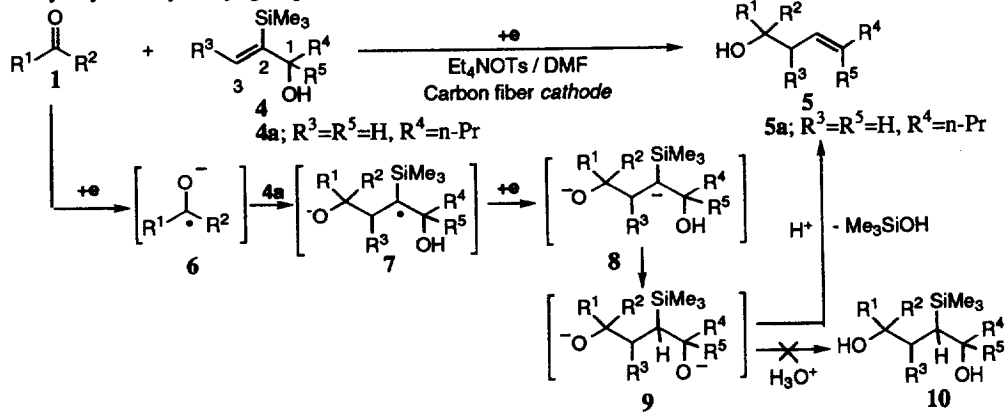
In the present study, the coupling of **1** with olefins having both trimethylsilyl and hydroxyl groups in the same molecule has been examined and it has been found that the regioselectivity of the reaction was controlled by the trimethylsilyl group, and the hydroxyl group played an important role in the stereoselectivity. The coupling reaction is useful for the regioselective synthesis of homoallylic alcohols.

In order to examine the effect of trimethylsilyl and hydroxyl groups on the coupling, cathodic reduction of a solution of acetone (**1a**) and 3-(trimethylsilyl)allyl alcohol (**2a**; R = H, Y = OH) in DMF was carried in the presence of Et_4NOTs.[7] As shown in Scheme 3, the coupling of **1a** with **2a** took place at the position-2 of **2a** (position β to both trimethylsilyl and hydroxyl groups) with indicating that the regioselectivity was controlled not by the hydroxy group but by the trimethylsilyl group. Under similar conditions, the reaction of **1a** with 1-methyl-3-(trimethylsilyl)allyl alcohol (**2b**; R = Me, Y = OH) also took place at position-2 and afforded the product **3b** (R= Me, Y = OH) with high regio- and stereoselectivities[8] even though the type of olefin was the inner type, whereas the coupling of **1a** with 1-trimethylsilyl-1-butene (**2c**; R = Me, Y = H) did not take place at all as it was predicted. These results clearly show that the hydroxyl group also promotes the coupling of **1a** with **2b** and determines the stereoselectivity of the product **3b**.[9]



Scheme 3

The coupling of ketones **1** with 1-propyl-2-(trimethylsilyl)allyl alcohol (**4a**; $R^3 = R^5 = H$, $R^4 = n$-Pr) has been found to lead to an unprecedented type reaction that is useful for the regioselective synthesis of homoallylic alcohols. As shown in Scheme 4, coupling of **1** with **4a** did give not a trimethylsilyl substituted 1,4-diol (**10**; $R^3 = R^5 = H$, $R^4 = n$-Pr) but a homoallylic alcohol (**5a**; $R^3 = R^5 = H$, $R^4 = n$-Pr). The formation of **5a** may be explained by the mechanism shown in Scheme 4. Namely, the Peterson elimination of the trimethylsilyl and hydroxyl groups from the final intermediate dianion **9** affords the product **5a**.[11,12]



Scheme 4

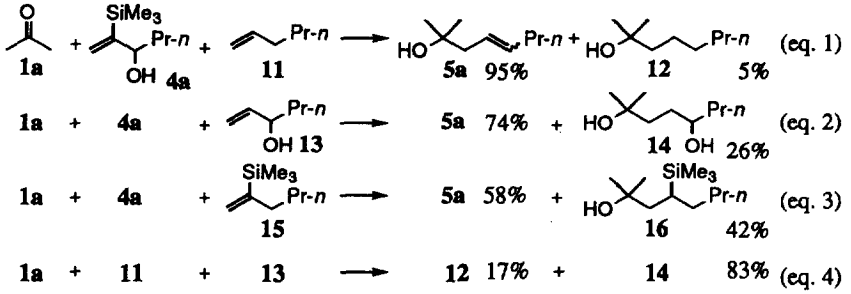
As typical results are summarized in Table 1, the cathodic coupling of **1** with 2-(trimethylsilyl)allyl alcohols (**4a-4e**) afforded the corresponding homoallylic alcohols in good yield (Run 1-7).[13] The presence of an alkyl group (R^3) on the double bond, namely the inner type olefin, was found to decrease the yield. The coupling of **1a** with **4f**, for instsnce, gave **5h** with 35 % yield (Run 8). Since the base induced Peterson elimination has been known to require a *syn* conformation,[14] the *trans-cis* ratio of the products shown in Table 1 may reflect the stereoselectivity of the protonation step of **8**. This reaction seems to be useful since the coupling of **1** and **4** provides a new route for the regioselective transformation of **1** to homoallylic alcohols **5**.

Table 1. Cathodic Coupling of Ketones with Vinylsilanes 2.

Run	Ketone 1			Vinylsilane 4				Product 5[a]		
	R^1	R^2			R^3	R^4	R^5		Yields (%)	*trans / cis*[b]
1	Me	Me	**1a**	**4a**	H	*n*-Pr	H	**5a**	70	4.7
2	-$(CH_2)_2$-		**1b**	**4a**				**5b**	67	4.0
3	**1a**			**4b**	H	*iso*-Pr	H	**5c**	87	4.0
4	Me	Et	**1c**	**4b**				**5d**	74	5.5
5	**1a**			**4c**	H		H	**5e**	88	4.6
6	**1a**			**4d**	H	Et	Et	**5f**	96	
7	**1a**			**4e**	H	-$(CH_2)_5$-		**5g**	79	
8	**1a**			**4f**	Me	*n*-Pr	H	**5h**	35	6.9

a) Isolated yield. d) Determined by IR and ^{1}H NMR.

In order to estimate the extent of promotion effect of trimethylsilyl and hydroxyl groups in the cathodic coupling, the electroreduction of a solution of **1a** (5 mmol) and **4a** (2 mmol) was carried out in the presence of 1-hexene (**11**) (2 mmol) (Scheme 5, eq. 1), 1-hexene-3-ol (**13**) (2 mmol) (eq. 2), or 2-trimethylsilyl-1-hexene (**15**) (2 mmol) (eq. 3). The results shown in Scheme 5 (eq. 1 or eq. 2) indicate that the reactivity of double bond is highly enhanced and also mainly determined by the trimethylsilyl group since the reaction exclusively took place with **4a** and yielded **5a** rather than **12** (eq. 1) or **14** (eq. 2). The effect of the hydroxyl group at allylic position seems much less than the trimethylsilyl group since the reaction of the mixture of **1a**, **4a**, and 2-trimethylsilyl-1-hexene (**15**) gave the products **5a** (58%) and **16** (42%) in comparable yields (Scheme 5, eq. 3). Although the promotion effect of the hydroxyl group is not obviously seen in the reactions shown in eqs. 1, 2, and 3, its remarkable effect was clearly shown in the competitive reaction of **1a** with **11** and **13** (Scheme 5, eq. 4), in which **14** was formed as the main product (83%).

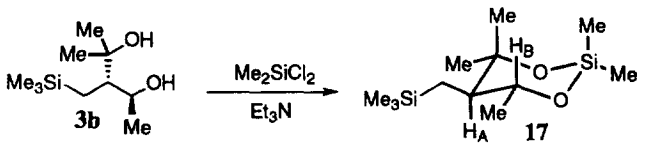


Scheme 5

References and Notes

1) Electroorganic Chemistry 151, For part 150, *Chem. Lett.* **1996**, 309-310.
2) Department of Metallurgy.
3) Department of Applied Chemistry.
4) Research Institute for Science and Technology.
5) Kashimura, S.; Murai, Y.; Ishifune, M.; Masuda, H.; Murase, H.; Shono, T. *Tetrahedron Lett.* **1995**, *36*, 5041-5044.
6) Shono, T.; Morishima, Y.; Moriyoshi, N.; Ishifune, M.: Kashimura, S. *J. Org. Chem.* **1994**, *59*, 273-275.
7) The cathodic reduction was carried out in a divided electrolysis cell (100 mL) equipped with a carbon fibier cathode, a platinum anode (2 x 2 cm), and a glass filter diaphragm (No.5). A solution of **1** (10 mmol) and **2** (2 mmol) in dry DMF (20 mL) containing Et_4NOTs (10 mmol) as a supporting electrolyte was put into a cathodic chamber of the cell. The anodic solution was 15 mL of dry DMF containing Et_4NOTs (5 mmol). After 2 F/mol of electricity based on **1** (constant current conditions of 0.2 A) was passed through the cell with cooling by ice cold water, the cathodic solution was poured into 100 mL of saturated aqueous NH_4Cl and extracted with ether (50 mL x 3). The residue obtained by evaporation of solvent was distilled under reduced pressure (bulb to bulb distillation) in order to get **3**.
8) We have recently reported that the interaction between a hydroxyl group located at the allylic position and a ketyl radical formed by the electroreduction of **1a** resulted in the diastereoselective coupling of **1a** with allyl alcohols.[6]
9) The stereochemistry of **3b** was determined as follows: The reaction of **3b** with Me_2SiCl_2 / Et_3N gave the cyclic siloxane **17** [^{1}H NMR ($CDCl_3$) δ 0.03 (s, 9H), 0.13 (s, 3H), 0.15 (s, 3H), 0.18 (dd, J = 16.3, 3.8 Hz, 1H), 0.36 (dd, J = 16.3, 3.8 Hz, 1H), 1.17 (s, 3H), 1.19 (d, J = 6.0 Hz, 3H), 1.27 (s, 3H), 1.55-1.70 (m, H_A), 3.89 (qd, J = 6.2, 9.7 Hz, H_B) The stereochemical relation between H_A and H_B was

determined to be *trans* since the coupling constant of ^1H NMR between H_A and H_B was measured to be 9.7 Hz.[10]



10) Narasaka, K.; Pai, F.-C. *Tetrahedron* **1984**, *40*, 2233-2238.
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12) Top, S.; Jaouen, G.; Sayer, B. G.; McGlinchey, M. J. *J. Am. Chem. Soc.* **1983**, *105*, 6426-6429.
13) **5a:** IR (neat) 3350, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, *J* = 7.4 Hz, 3H), 1.20 (*trans* isomer), 1.23 (*cis* isomer) (s, 6H), 1.30-1.50 (m, 2H), 1.54 (OH), 1.96-2.10 (m, 2H), 2.15-2.18 (*trans* isomer), 2.22-2.28 (*cis* isomer) (m, 2H), 5.45-5.56 (m, 2H); Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.79; H, 13.04.
5b: IR (neat) 3360, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (*trans* isomer), 0.91 (*cis* isomer) (t,*J* = 7.3 Hz, 3H), 1.20-1.70 (m, 12H), 1.96-2.10 (m, 2H), 2.10-2.16 (*tans* isomer) 2.19-2.25 (*cis* isomer) (m, 2H) 5.45-5.60 (m,2H); Anal.Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.07; H, 12.04.
5c: IR (neat) 3370, 980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (*trans* isomer), 0.95 (*cis* isomer) (d, *J* = 6.7 Hz, 6H), 1.20 (*trans* isomer), 1.23 (*cis* isomer) (s, 6H), 1.65 (OH), 2.10-2.40 (m, 3H), 5.35-5.60 (m, 2H); Anal. Calcd for $C_9H_{18}O$: C, 76.00; H, 12.76. Found: C, 75.60; H, 13.03.
5d: IR (neat) 3400, 980 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (*trans* isomer), 0.95 (*cis* isomer) (t, *J* = 7.6 Hz, 6H), 0.99 (d, *J* = 6.7 Hz, 6H), 1.13 (*trans* isomer), 1.16 (*cis* isomer) (s, 3H),1.40-1.55 (m, 2H), 1.65 (OH), 2.14 (*trans* isomer), 2.22 (*cis* isomer) (d, *J* = 5.9 Hz, 2H), 2.20-2.40 (m, 1H), 5.30-5.60 (m, 2H).
5e: IR (neat) 3350, 3025, 980, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (*trans* isomer), 1.24 (*cis* isomer) (s, 6H), 1.30-1.50 (m, 1H), 1.57 (OH), 1.70-1.95 (m, 2H), 2.00-2.10 (m, 3H), 2.15-2.30 (m, 3H), 5.45-5.55 (m, 2H), 5.66-5.70 (m, 2H).
5f: IR (neat) 3350, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (t, *J* = 7.6 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H), 1.22 (s, 6H), 1.70 (OH), 2.00-2.15 (m, 4H), 2.21 (d, *J* = 7.7 Hz, 2H), 5.19 (t, *J* = 7.7 Hz, 1H); Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.63; H, 13.15.
5g: IR (neat) 3360, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (s, 6H), 1.45-1.60 (m, 6H), 1.50 (OH), 2.10-2.22 (m, 6H), 5.15-5.25 (m, 1H); Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.31; H, 12.18.
5h: IR (neat) 3400, 2970, 2880, 1460, 1380, 1140, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, *J* = 7.3 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 1.13 (*trans* isomer), 1.15 (*cis* isomer) (s, 3H), 1.18 (*trans* isomer), 1.19 (*cis* isomer) (s, 3H), 1.30-1.50 (m, 2H), 1.60 (OH), 1.95-2.22 (m, 3H), 5.29-5.60 (m, 2H).
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