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Cathodic Intra- and Intermolecular Couplings of Ketones with Unsaturated Silanes¹

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Abstract : The electroreduction of 6-trimethylsilyl-6-hepten-2-one afforded *cis*-1-methyl-3-trimethylsilyl cyclohexanol, and γ -trimethylsilyl alcohols were yielded as the intermolecular coupling products when the cathodic reduction of ketones was carried out in the presence of unsaturated silanes.

In our continuing study on the cathodic intra- and intermolecular couplings of ketones with olefinic systems, $^{6-9}$ we have found that the cathodic reduction of nonconjugated olefinic ketones (1) afforded 5-membered tertiary alcohols (3) with high regio- and stereoselectivities (Scheme 1). The exclusive formation of a 5-membered ring rather than a 6-membered ring could be explained by the fact that 5-*exo*-cyclization was more favorable than the 6-*end*-cyclization in the radical cyclization.¹⁰⁻¹²



Scheme 1

It has also been found in the previous study that the electroreductive intermolecular couplings of ketones (4) with olefinic systems (5) was greatly influenced by the structure of 5 (Scheme 2).⁹ Namely, the reaction of 4 with 1-olefins (5a; $\mathbb{R}^3 = \mathbb{H}$, $\mathbb{R}^4 = an$ alkyl group) gave the coupling products (6) in excellent yields (~80 %), whereas the yield of coupling remarkably decreased (~20 %) in the reaction of 2-substituted 1-olefins (5b; \mathbb{R}^3 , $\mathbb{R}^4 = alkyl$ groups).



Scheme 2

In the present study we have found that both intra- and intermolecular couplings of a carbonyl group with a double bond was highly affected by the substituent located on the double bond. Namely, the use of unsaturated silane as the olefinic system led to an unprecedented and unique coupling reaction.

The electroreduction of 6-trimethylsilyl-6-hepten-2-one (7) carried out in DMF using Et₄NOTs as a supporting electrolyte was found to afford *cis*-1-methyl-3-trimethylsilyl-1-cyclohexanol (8) as a single product (Scheme 3).¹³ The formation of a 6-membered ring rather than a 5-membered ring is highly noteworthy since the 6-membered product has never been formed in any of the reactions shown in Scheme 1.



Scheme 3

Thus, the presence of a trimethylsilyl group on the double bond remarkably alters the regioselectivity of the cathodic cyclization. This difference may be explained by the steric and electronic effects of the trimethylsilyl group. As shown in Scheme 3, the cathodic reduction of 7 forms the corresponding radical species $9.^{14}$ The 5-exo-cyclization of 9 (path B) seems to be inhibited by steric hindrance of the trimethylsilyl group. Therefore, the only possible manner of cyclization of 9 is 6-endo-cyclization (path A) which is usually unfavorable in the reaction shown in Scheme 1. Although the cathodic 6-endo-cyclization of olefinic ketones has never been observed so far, the electronic effect of the trimethylsilyl group seems to enable this cyclization. Namely, the radical center of 9 attacks the terminal position of the double bond forming the intermediate 10 which is rather easily reduced to the anionic intermediate 11 due to stabilization by the trimethylsilyl group. Thus, the irreversible formation of a stabilized anion intermediate 11 promotes the 6-endo-cyclization.

As shown in Scheme 4, cathodic intermolecular coupling of 4 with 5c ($\mathbb{R}^4 = \operatorname{SiMe_3}$, $\mathbb{R}^3 = H$) was found to afford γ -trimethylsilyl alcohols 14 in satisfactory yields. The coupling of 4 with 2-substituted 1-olefins such as 5d ($\mathbb{R}^4 = \operatorname{SiMe_3}$, $\mathbb{R}^3 = \operatorname{Me}$) (Runs 6 and 7 in Table 1) and 5e ($\mathbb{R}^4 = \operatorname{SiMe_3}$, $\mathbb{R}^3 = n$ -Pr) (Run 8) also afforded the corresponding coupling products in satisfactory yields. This is a highly attractive result since the cathodic coupling of 4 with 2-substituted 1-olefins 5 (\mathbb{R}^3 , $\mathbb{R}^4 = \operatorname{alkyl}$ groups) usually gave very low yields.⁹



Since the formation of 14 seems to involve the intermediary formation of an anion species 13, the stabilization of 13 by the neighboring trimethylsilyl group^{15,16} is the crucial factor for the formation of 14.

Thus, the cathodic coupling of 4 with unsaturated silanes 5c-5e was promoted by the electronic effect of trimethylsilyl group. In fact, the coupling reaction of acetone (4i) with 2-trimethylsilyl-1,5-hexadiene (5f) (Scheme 5) took place predominantly at the silylated double bond of 5f and formed 15 in 86% yield.



Scheme 5

The cathodic reduction was carried out in a divided electrolysis cell (100 mL) equipped with a carbon fiber cathode, a platinum anode $(2 \times 2 \text{ cm})$, and a glass filter diaphragm (No.5). A solution of a ketone 4 (5 mmol)

and an unsaturated silane (5c-5f) (10 mmol) in dry DMF (20 mL) containing Et4NOTs (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 Et4NOTs (5 mmol). After 3F/mol of electricity based on 4 (constant current condition of 0.2 A) was passed through the cell with cooling by ice cold water, the cathodic solution was poured into 100 mL of brine and extracted with ether (50 mL \times 3). The residue obtained by evaporation of solvent was distilled under reduced pressure (bulb to bulb distillation) in order to give 14. All products gave satisfactory spectroscopic values for the assigned structure.¹⁷

Run	Ketone 4		Unsaturated Silane 5 Product 14		
	\mathbf{R}^{1}	R ²		R ³	Yield / %ª
1	Į	Q [×]	4a	Н 5 с	14a 74
2	-(CH ₂) ₅ -	4b	5c	1 4b 74
3	n-C ₅ H	11 <i>n</i> -C ₅ H ₁₁	4c	5c	14c 78
4	Me	<i>n</i> -C ₆ H ₁₃	4d	5c	14d 72
5	Me	CH ₂ CH ₂ CO ₂ Me	4 e	5c	
					14e 31
6	Me	n-Pr	4f	Me 5d	1 4f 75
7	Me	iso-Pr	4g	5d	14g 68
8	Me	Et	4h	<i>n</i> -Pr 5d	14h 69

Table 1. Cathodic Coupling of Ketones with Unsaturated Silanes

a) Isolated yields based on 4.

The results summarized in Scheme 4 and Table 1 are also interesting not only in mechanistic but also in synthetic points of view. Namely, the fact that 14 was formed by the cathodic coupling of 4 and 5 ($\mathbb{R}^4 = \text{SiMe}_3$) indicates that this cathodic coupling is an equivalent of the reaction of 4 with the anion 16 which is usually unstable and not easily preparable by the conventional nonelectrochemical method.¹⁸

$$\begin{bmatrix} -\overset{\mathsf{R}^3}{\swarrow}_{\mathsf{SiMe}_3} \end{bmatrix}$$

Since product 14 is easily transformed to the corresponding olefin, it is a key intermediate for the substitution of the carbonyl group of ketone by an alkenyl group (Scheme 6). The treatment of 14a (\mathbb{R}^1 , $\mathbb{R}^2 = 2$ -adamantyl) with BF₃-AcOH, for example, afforded 17 in quantitative yield.¹⁹



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- 17) 14a: IR (neat) 3400, 2960, 1255, 865, 840 cm⁻¹; ¹H NMR (CDCl₃) δ 0.00 (s, 9H), 0.40-0.50 (m, 2H), 1.43-1.88 (m, 16H)); 223 (79), 151 (100); Anal. Calcd for C₁₅H₂₈SiO : C, 71.36; H, 11.20. Found : C, 71.20; H, 11.47.

14b: IR (neat) 3370, 2920, 1245, 860, 835 cm⁻¹; ¹H NMR (CDCl₃) δ -0.02 (s, 9H), 0.40-0.52 (m, 2H), 1.10-1.65 (m, 12H); Anal. Calcd for C₁₁H₂₄SiO: C, 65.93; H, 12.07. Found : C, 65.87; H, 12.34.

14c: IR (neat) 3460, 2940, 1255, 870, 845 cm⁻¹; ¹H NMR (CDCl₃) δ 0.00 (s, 9H), 0.30-0.48 (m, 2H), 0.80-0.97 (t, J = 6.0 Hz, 6H), 1.15-1.48 (m, 18H); Anal. Calcd for C₁₆H₃₆SiO: C, 70.51; H, 13.31. Found : C, 70.57; H, 13.58.

14d : IR (neat) 3400, 2970, 1255, 865, 840 cm⁻¹; ¹H NMR (CDCl₃) δ -0.05 (s, 9H), 0.34-0.48 (m, 2H), 0.85 (t, J = 6.7 Hz, 3H), 1.09 (s, 3H), 1.16-1.30 (m, 10H), 1.30-1.46 (m, 2H) ; Anal. Calcd for C₁₃H₃₀SiO : C, 67.75 ; H, 13.12. Found : C, 67.64 ; H, 13.39.

14e: IR (neat) 2960, 1770, 1250, 1165, 860, 835 cm⁻¹; ¹H NMR (CDCl₃) δ 0.03 (s, 9H), 0.45-0.60 (m, 2H), 1.42 (s, 3H), 1.58-1.72 (m, 2H), 1.90-2.22 (m, 2H), 2.57-2.70 (m, 2H); Anal. Calcd for C₁₀H₂₀SiO₂ : C, 59.95 ; H, 10.06. Found : C, 59.83, H, 10.02.

14f: IR (neat) 3400, 2970, 1255, 860, 840 cm⁻¹; ¹H NMR (CDCl₃) δ -0.06 (s, 9H), 0.66-0.84 (m, 1H), 0.91 (t, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 7.7 Hz, 3H), 1.14 (s, 3H), 1.20-1.62 (m, 6H); Anal. Calcd for C₁₁H₂₆SiO : C, 65.27; H, 12.95. Found : C, 65.05; H, 13.19.

14g: IR (neat) 3470, 2960, 1250, 860, 840 cm⁻¹; ¹H NMR (CDCl₃) δ -0.05 (s, 9H),.0.70-0.86 (m, 1H), 0.84, 0.88, 0.89, 0.93 (four doublets, J = 6.9 Hz, 6H), 1.05 (d, J = 7.7 Hz, 3H), 1.08 (OH), 1.12-1.28 (m, 1H), 1.52-1.82 (m, 2H) ;Anal. Calcd for C₁₁H₂₆SiO: C, 65.27 ; H, 12.95. Found : C, 65.04 ; H, 13.19. **14h** : IR (neat) 3400, 1460, 1380, 1250, 855, 835 cm⁻¹; ¹H NMR (CDCl₃) δ -0.027, -0.031 (s, 9H),.0.71 (m, 1H), 0.86 (m, 3H), 0.88, 0.89 (t, J = 6.9 Hz, 3H), 1.11, 1.12 (s, 3H), 1.20-1.60 (m, 8H) ;Anal. Calcd for C₁₂H₂₈SiO: C, 66.59 ; H, 13.04. Found: C, 66.49 ; H, 13.32.

18) It has been reported that the reaction of 2-bromoethyltrimethylsilane (18) with tert-BuLi or Mg metal gave the corresponding anion equivalent 16 (R³=H), though 18 was unstable and prepared by the hydrobromination of vinyltrimethylsilane.¹⁹

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