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New Reactivity of Methoxyhydridosilane in the Catalytic Activation System[1]

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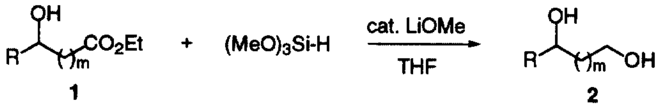
Abstract

Hydroxy esters are reduced by trimethoxysilane in the presence of a catalytic amount of lithium methoxide to yield diols, while for simple esters the alcohol exchange reaction takes place preferentially. Through the exchange reaction, lactones without a hydroxy group are reduced. Tosylimines are also reduced in the system.

Keywords: Silicon and compounds; Hypervalent elements; Reduction; Catalysis

Among highly coordinated silicon species, fluorosilicates have been used for the selective transformation of functional groups and the carbon-carbon bond formation in organic synthesis [1,2], while alkoxy-variants especially in the catalytic activation system are not well utilized [3-9]. We previously reported the stereoselective reduction of ketones by alkoxyhydridosilicates generated from trialkoxysilanes and a catalytic amount of alkoxides [10,11]. We describe here an interesting feature in the reactivity of alkoxyhydridosilicates generated in the catalytic activation system, the selective reduction of hydroxy esters, lactones and imines.

We found that methyl mandelate (**1a**) was converted to phenylethane-1,2-diol (**2a**) by trimethoxysilane in the presence of 6 mol% of lithium methoxide (eq 1, R = Ph, m = 0). Other hydroxy esters **1** were also reduced to the corresponding diols **2**.[2] These results are summarized in Table 1.



(1)

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[1] Studies on organosilicon chemistry. No. 146. For No. 145, see, Ito H, Ishizuka T, Tateiwa J, Sonoda M, Hosomi A. J. Am. Chem. Soc. in press.

[2] A typical procedure is as follows. To a solution of lithium methoxide in THF prepared at 0 °C for 30 min from methanol (0.06 mmol, 2.43 μL) in dry THF (1.2 mL) and butyllithium (1.64 M hexane solution, 0.06 mmol, 37 μL), trimethoxysilane (3.5 mmol, 428 mg, 446 μL) and **1a** (1 mmol) were added, and the mixture was refluxed for 9.5 h under nitrogen. After cooling the mixture, 1N HCl (5 mL) was introduced to the mixture, and subsequently solid $NaHCO_3$ was added. The resultant gel was washed with EtOAc (30 mL). Stirring the gel with MeOH (7 mL) gave a solid, which was again washed with EtOAc (30 mL). All combined organics were dried over Na_2SO_4 and passed through a Celite-pad, and the solvents were evaporated to give a crude mixture. The mixture was subjected to column chromatography on silica gel (R_f = 0.23, hexane/EtOAc = 1/1) to give **2a** (94%).

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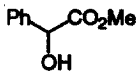
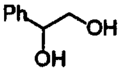
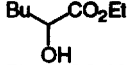
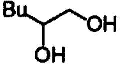
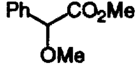
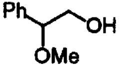
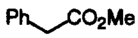
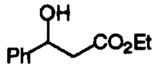
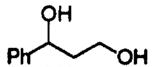
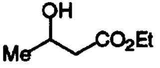
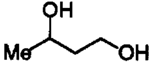
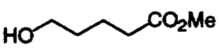
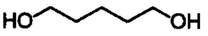
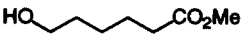
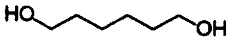
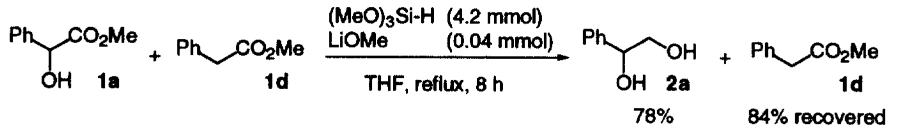
Table 1
Reduction of Esters 1 Using Trimethoxysilane in the Catalytic Activation System.[a]

Entry	Ester 1	Conditions	Product 2	Yield / %[b]
1	 **1a**	reflux, 9.5 h	 **2a**	94
2	 **1b**	reflux, 9.5 h	 **2b**	100
3	 **1c**	reflux, 9.5 h	 **2c**	76[c]
4	 **1d**	reflux, 16 h	 **2d**	13[d]
5	 **1e**	rt, 0.5 h	 **2e**	92
6	 **1f**	rt, 0.5 h	 **2f**	100
7	 **1g**	reflux, 27 h	 **2g**	80
8	 **1h**	reflux, 27 h	 **2h**	63

[a] For reactions of **1a-c** (entries 1-3), **1d** (entry 4), **1g-h** (entries 7-8), ester (1 mmol), $HSi(OMe)_3$ (3.5 mmol), LiOMe (0.06 mmol), and THF (1.2 mL) were used. For the reactions **1e,f** (entries 5 and 6), ester (1 mmol), $HSi(OMe)_3$ (3.0 mmol), LiOMe (0.05 mmol), and THF (1.2 mL) were used.
[b] Isolated yield.
[c] Ester **1c** (11%) was recovered.
[d] Ester **1d** (67%) was recovered.

As can be seen in Table 1, irrespective of the position of a hydroxy group to the ester moiety, the reduction of hydroxy esters **1** giving diols **2** proceeds, while the conversion of α-methoxy ester **1c** was moderate (entry 3). In the case of an ester without a hydroxy function (**1d**), the reduction took place only to a slight extent (entry 4). In this reaction system, β-hydroxy esters **1e,f** were easily reduced, and even at room temperature 1,3-diols **2e,f** were obtained in high yields (entries 5 and 6). A remote hydroxy group seems not to be so beneficial to the present reduction (entry 8). These results suggest that this catalytic system appropriately lowers the reactivity of the original tetramethoxyhydridosilicate [12], and the specific coordination of an oxy-functionality to the reagent is the key to the successful reduction of esters [13].[3] Although it might be possible that a product diol acts as a bidentate ligand to generate a more reactive species [14], the following experiment shows this is not the case. When a mixture of hydroxy ester **1a** and ester **1d** was subjected to the reduction system, only hydroxy ester **1a** was reduced (eq 2), showing that the intramolecular coordination of a hydroxy group is essential to the reduction.



(2)

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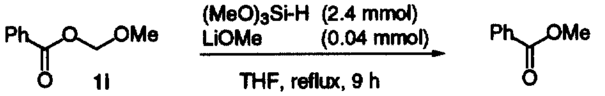
[3] The selective reduction of esters with intramolecular assistance of the Lewis basic functionality using other hydride reagents, see ref. 13.

Aiming at the reduction of carboxylic esters bearing an additional oxy-group only in an alcohol part, we examined the reduction of ester **1h**, in expectation of the intramolecular assistance of a hydroxy group in an alcohol part of the ester. Unfortunately, this attempt resulted in an alcohol exchange reaction to afford methyl benzoate (eq 3). By virtue of the exchange reaction, lactones **3** can be successfully reduced to diols **2** (eq 4, Table 2).[4,5] In the reduction of lactones, ring-opening intermediates produced through the alcohol exchange reaction may react further with hydridosilicate as in eq 1, although, at the moment, the reason why the yields in entry 7 in Table 1 and entry 4 in Table 2 were so different is not clear.



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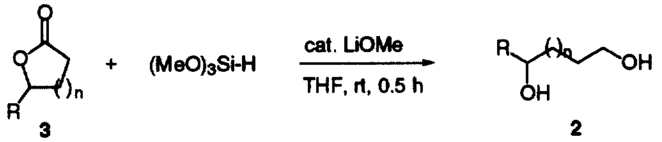
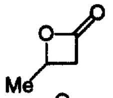
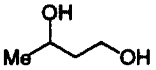
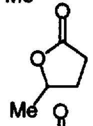
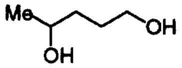
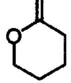
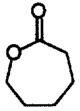


3 **2** (4)

Table 2
Reduction of Lactones **3** Using Trimethoxysilane in the Catalytic Activation System.[a]

Entry	Lactone 3		Conditions	Product 2		Yield / %[b]
1		**3a**	rt, 0.5 h		**2f**	48[c]
2		**3b**	rt, 0.5 h		**2j**	56[d]
3		**3c**	rt, 0.5 h		**2k**	100
4		**3d**	rt, 0.5 h		**2h**	95

[a] All reactions were carried out using lactone **3** (1 mmol) and $HSi(OMe)_3$ (4.5 mmol) in THF (1.2 mL) in the presence of LiOMe (0.08 mmol).
[b] Isolated yield.
[c] Lactone **3a** (24%) was recovered.
[d] Lactone **3b** (3%) was recovered.

Next, we tried the reaction of tosylimines **4** (eq 5, Table 3).[6] Both aldimine and ketimine were reduced to tosylamides **5** in high yields, and a nitro group tolerates the reaction. This system is applicable even to the reduction of aliphatic imines, which are in equilibrium between two tautomers, imine- and enamine-form (entries 6-8).

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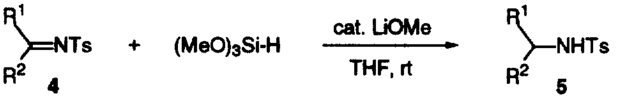
[4] In the reduction of hydroxy esters (Table 1) and lactones (Table 2), we sometimes encountered low yields of products. Such a problem was overcome with trimethoxysilane freshly distilled under nitrogen without a drying agent.

[5] For the workup procedure, the reaction mixture was directly subjected to chromatography on silica gel.

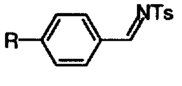
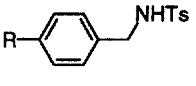
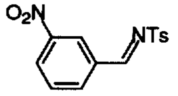
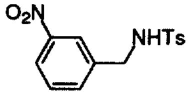
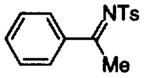
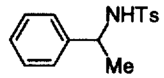
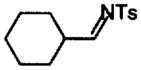
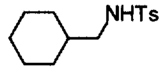
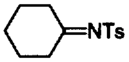
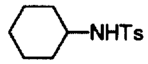
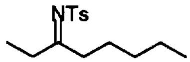
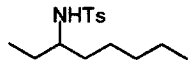
[6] *N*-benzylideneaniline, benzaldoxime and its *O*-silyl ethers were not reduced in the present reaction system.



(5)

Table 3

Reduction of Imines 4 Using Trimethoxysilane in the Catalytic Activation System.[a]

Entry	Imine 4		Conditions	Product 5		Yield / %[b]
1		4a R = H	rt, 42 h		5a	100
2		4b R = Me	rt, 59 h		5b	97
3		4c R = MeO	rt, 50 h		5c	80
4		4d	rt, 56 h		5d	92
5		4e	rt, 59 h		5e	63
6		4f	rt, 67 h		5f	84
7		4g	rt, 48 h		5g	62
8		4h	rt, 50 h		5h	80

[a] All reactions were carried out using imine 4 (1 mmol), and $HSi(OMe)_3$ (1.2 mmol) in THF (1.2 mL) in the presence of LiOMe (0.04 mmol).

[b] Isolated yield.

Acknowledgments

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