

# A Practical Method for Activation of Commercial Lithium Hydride: Reductive Silylation of Carbonyl Compounds with Lithium Hydride and Chlorotrimethylsilane

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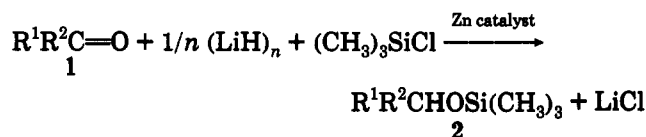
Commercially available lithium hydride, an essentially inert metal hydride, can be activated as a hydride source by an equimolar amount of chlorotrimethylsilane and a catalytic amount of a Zn salt or Zn powder. Aromatic and aliphatic ketones, as well as nonenolizable aldehydes, are reductively converted to the trimethylsilyl ethers of the corresponding alcohols in high yields by treatment with this reagent system in dichloromethane or toluene at 28 to 40 °C for 25–50 h. This procedure has many advantages including the safety and low cost of the reagents and operational simplicity and provides a practical method for carbonyl reduction. X-ray induced Auger electron spectroscopy analysis suggests that a Zn(II) species is the catalyst of the heterogeneous reaction.

## Introduction

Since metal hydride reduction of carbonyl compounds is one of the most fundamental synthetic reactions,<sup>1</sup> development of practical procedures is still desirable. At this moment, most hydride reagents are expensive. Their sensitivity to moisture, air, and heat often requires special precautions for their use. The exothermicity of the reaction often requires external cooling. Furthermore, isolation of the alcoholic product is not always easy.

Lithium hydride (LiH) is an extremely attractive material for several reasons. The solid hydride can be purchased at a low price from distributors. In addition, this ionic crystalline material is stable up to 900 °C. Because it has the highest lattice energy (920 kJ/mol) among the alkali metal hydrides,<sup>2</sup> commercial solid (LiH)<sub>n</sub> is known as an essentially inert hydride. For example, it is unaffected by oxygen below red heat, by chlorine, or by hydrogen chloride.<sup>3</sup> In addition, it fails to react with tertiary alcohols at room temperature.<sup>4</sup> These properties in turn provide a great operational advantage, allowing one to handle LiH in open air and to safely store the pure material without deterioration. This low sensitivity contrasts with the combustibility of NaH and KH. Because of their combustibility, NaH and KH must be stored in mineral oil, which is frequently troublesome for their synthetic use. In spite of these advantageous properties, commercial LiH remains untouched on the shelves of almost all organic laboratories. Although LiH is a useful precursor for the synthesis of mixed bimetallic hydride reagents,<sup>5</sup> LiH itself has scarcely been used in organic synthesis.<sup>6</sup> The limited use is simply due to the

lack of effective methods to activate the stable metal hydride as nucleophile or base.<sup>7,8</sup> We now wish to report a method for the direct activation of commercially available LiH and to show its ability as a hydride donor for reductive silylation of carbonyl compounds, 1 → 2. To our knowl-



- a: R<sup>1</sup> = C<sub>6</sub>H<sub>5</sub>, R<sup>2</sup> = CH<sub>3</sub>    e: R<sup>1</sup>, R<sup>2</sup> = (CH<sub>2</sub>)<sub>2</sub>CH(t-C<sub>4</sub>H<sub>9</sub>)(CH<sub>2</sub>)<sub>2</sub>  
b: R<sup>1</sup> = n-C<sub>6</sub>H<sub>13</sub>, R<sup>2</sup> = CH<sub>3</sub>    f: R<sup>1</sup> = C<sub>6</sub>H<sub>5</sub>, R<sup>2</sup> = H  
c: R<sup>1</sup> = (CH<sub>3</sub>)<sub>3</sub>C, R<sup>2</sup> = CH<sub>3</sub>    g: R<sup>1</sup> = (CH<sub>3</sub>)<sub>3</sub>C, R<sup>2</sup> = H  
d: R<sup>1</sup>-R<sup>2</sup> = (CH<sub>2</sub>)<sub>6</sub>    h: R<sup>1</sup> = (E)-C<sub>6</sub>H<sub>5</sub>CH=CH, R<sup>2</sup> = CH<sub>3</sub>

edge, this reaction is the first example of carbonyl reduction with commercial (LiH)<sub>n</sub> as a hydride source.<sup>9</sup> This reduction method is very practical and would be particularly useful for large-scale reactions.

## Results and Discussion

**Search for the Reaction Conditions.** We used powdered (LiH)<sub>n</sub> (30 mesh, 95% purity) purchased from Aldrich Chemical Co. and acetophenone (1a) as a model substrate to find suitable reaction conditions. No reaction

(6) Synthetic uses of commercial LiH as base: (a) Liu, H.-J.; Lamoureaux, G. V.; Llinas-Brunet, M. *Can. J. Chem.* 1986, 64, 520. (b) Bare, T. M.; House, H. O. *Organic Syntheses*; John Wiley & Sons: New York, 1973; Collect. Vol. 5, p 775. (c) Bartlett, P. A.; Johnson, W. S. *Tetrahedron Lett.* 1970, 4459. (d) Kříž, J.; Beneš, M. J.; Peška, J. *Tetrahedron Lett.* 1965, 2881. As reducing agent: (e) Caglioti, L.; Grasselli, P.; Maina, G. *Chim. Ind. (Milan)* 1963, 45, 559. (f) Taylor, M. D.; Grant, L. R. *J. Am. Chem. Soc.* 1955, 77, 1507.

(7) Active LiH is obtained by the hydrogenolysis of alkyl lithium at 4000 psi of hydrogen at rt. A mixture of this LiH and an equimolar amount of VCl<sub>3</sub> has a high reducing ability toward carbonyl compounds: (a) Ashby, E. C.; Noding, S. A. *J. Org. Chem.* 1980, 45, 1041. See also: (b) Pi, R.; Friedl, T.; Schleyer, P. v. R.; Klusener, P.; Brandsma, L. *J. Org. Chem.* 1987, 52, 4299. (c) Kowalski, C. J.; Lal, G. S. *J. Am. Chem. Soc.* 1986, 108, 5356.

(8) For activation of commercial NaH and KH see: (a) Soderquist, J. A.; Rivera, I. *Tetrahedron Lett.* 1988, 29, 3195. (b) Hubbard, J. L. *Tetrahedron Lett.* 1988, 29, 3197.

(9) Reduction of alkyl bromides with a mixture of LiH and triethylborane: Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* 1973, 95, 1669.

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(1) Recent review: Greeves, N. In *Comprehensive Organic Synthesis*; Fleming, I., Ed.; Pergamon Press: Oxford, 1991; Vol. 8, Chapter 1.1.

(2) (a) Cotton, F. A.; Wilkinson, G. In *Advanced Inorganic Chemistry*, 4th ed.; John Wiley & Sons: New York, 1980; Part 2, Chapter 7. (b) In *CRC Handbook of Chemistry and Physics*, 63rd ed.; Weast, R. C., Ed., Astle, M. J., Associate Ed.; CRC Press: Boca Raton, FL, 1982; Section D, p 109.

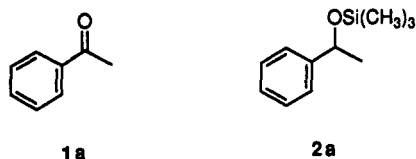
(3) Cotton, F. A.; Wilkinson, G. In *Advanced Inorganic Chemistry*, 2nd ed.; John Wiley & Sons: New York, 1966; Part 2, Chapter 8.

(4) Brown, C. A. *J. Org. Chem.* 1974, 39, 3913.

(5) Review: Brown, H. C.; Krishnamurthy, S. *Tetrahedron* 1979, 35, 567.

occurred when a 1:1 mixture of **1a** and solid  $(\text{LiH})_n$  was stirred at room temperature in an aprotic solvent such as dichloromethane, toluene, or THF. We then investigated the activation ability of a series of Lewis acids and related compounds with the expectation that the latent ability of the Lewis acid to form an ate complex with LiH would effect the reductive transformation.<sup>5,9</sup> However, the results were again disappointing. A catalytic amount of aluminum triisopropoxide, triethylaluminum,  $\text{BF}_3$ -diethyl ether complex, trimethyl borate, or triethylborane did not activate  $(\text{LiH})_n$  at all. Addition of an equimolar amount of 18-crown-6, dodecyltrimethylammonium chloride, LiCl,  $\text{LiBF}_4$ , methanesulfonyl chloride, tetraphenylphosphonium chloride, or trimethylsilyl trifluoromethanesulfonate did not promote the reduction either.

However, the effects of chlorotrimethylsilane were noteworthy. At 28 °C, the chlorosilane did not promote the reaction of **1a**, but 1-phenylethyl trimethylsilyl ether (**2a**) was obtained in 33% yield when a mixture of **1a**,  $(\text{LiH})_n$ , and chlorotrimethylsilane (1:1:1 molar ratio) in dichloromethane was heated at 100 °C for 60 h in a sealed tube. Furthermore, once a Zn salt, the third, catalytic component of the reagent system, was added, the reaction was dramatically accelerated even at 28 °C. Thus, when a mixture of ketone **1a**,  $(\text{LiH})_n$ , chlorotrimethylsilane (1:1:1 molar ratio), and 1 mol % of zinc methanesulfonate in dichloromethane was stirred at 28 °C for 30–40 h, hydrosilylated product **2a** was obtained in 81–93% yield. Only a few percent of unreacted **1a** was detected in the reaction mixture. When 1.5–2 equiv of  $(\text{LiH})_n$  and chlorotrimethylsilane relative to the substrate were used in the 30-g scale reaction, the yield of **2a** reached 95–98%.



The zinc methanesulfonate catalyst exhibited the highest activity in promoting the hydrosilylation. Decreasing the amount of the Zn catalyst to 0.1 mol % resulted in 56% conversion after a 58-h reaction period. Increasing the amount of the Zn catalyst to 20 mol % gave **2a** in 80% yield along with various side products. The optimum level of the Zn catalyst was 1–5 mol %. The powdered Zn catalyst, which was prepared by a reaction of diethylzinc and 2 equiv of methanesulfonic acid in dichloromethane and subsequent evaporation of solvent, kept its catalytic activity even after a 3-month storage period in an airtight apparatus. However, almost all soluble and insoluble zinc salts of type  $\text{ZnX}_2$  ( $\text{X} = \text{Cl}, \text{OC}_6\text{H}_5, \text{SC}_6\text{H}_5, \text{OCOCH}_3, \text{OSO}_2\text{CF}_3$ , etc.), which are either commercially available or prepared in situ, were generally usable. Large differences were not observed (see Experimental Section). Commercial Zn powder (1–2 mol %) was equally usable, and it is probably the most convenient catalyst. In contrast to the remarkable catalytic effects of Zn salts and Zn powder, other metal salts including  $\text{MgCl}_2$ ,  $\text{BaCl}_2$ ,  $\text{CeCl}_3$ ,  $\text{TiCl}_4$ ,  $\text{ZrCl}_4$ ,  $\text{WCl}_6$ ,  $\text{FeCl}_2$ ,  $\text{FeCl}_3$ ,  $\text{NiCl}_2$ ,  $\text{CuCl}$ ,  $\text{CdCl}_2$ ,  $\text{AlCl}_3$ ,  $\text{GaCl}_3$ ,  $\text{InCl}_3$ ,  $\text{SnCl}_2$ , and  $\text{SnCl}_4$  appeared not to catalyze the hydrosilylation.

Chlorotrimethylsilane should be used as the silylating agent. *tert*-Butylchlorodimethylsilane, chlorotriphenylsilane, and chlorotriethylsilane in combination with zinc

methanesulfonate showed no activation ability toward  $(\text{LiH})_n$ . Dry hydrogen chloride in dichloromethane could not replace chlorotrimethylsilane either. These observations suggest that chlorotrimethylsilane acts not only as a silylating agent to stabilize the product but also as an activator of  $(\text{LiH})_n$ .

Dichloromethane and toluene were equally good solvents for the reaction, and the reaction occurred smoothly at 28 °C. The use of THF as solvent retarded the reaction to a considerable extent.

Since this reduction is heterogeneous throughout the reaction, vigorous stirring is necessary to obtain a reasonable reaction rate. The reaction goes to completion, and the results are reproducible. Silyl ether product **2a** of 99% purity was easily isolated without aqueous workup by direct filtration of the reaction mixture through Celite, concentration of the filtrate, and distillation. This type of workup eliminates any hydrolytic degradation. The free alcoholic product can also be obtained by desilylation of the crude product with methanolic hydrochloric acid followed by distillation.

It should be added that this method is not applicable to activation of commercial NaH and KH.<sup>8</sup> With NaH, for example, the reduction of **1a** only proceeded to 30–40% conversion.

**Scope and Limitation.** The remarkable activity of  $(\text{LiH})_n$  in the presence of chlorotrimethylsilane and a Zn catalyst in the reaction of **1a** prompted us to probe the scope and limitations of this reducing system. As exemplified in Table 1, other carbonyl compounds were also reductively silylated in high yield. The experiments were not batch dependent and showed reasonable reproducibility. The reaction of less reactive aliphatic ketones **1b** and **1c** required refluxing dichloromethane for 25–50 h to complete the consumption of the substrates. Cycloalkanones **1d** and **1e** were also reducible. The reductive silylation of 4-*tert*-butylcyclohexanone (**1e**) gave hydrosilylated product **2e** as a 2.6:1 mixture of the *cis* and *trans* isomers.<sup>10</sup> Likewise, benzaldehyde (**1f**) and pivalaldehyde (**1g**) were also reduced to give the corresponding trimethylsilyl ethers **2f** and **2g**. Enolizable aldehydes such as octanal and cyclohexanecarboxaldehyde gave complex mixtures containing aldol products. (*E*)-4-Phenyl-3-buten-2-one (**1h**) was converted to the silyl ether of the allylic alcohol, **2h**, in 50% yield together with some high-boiling byproducts. No conjugate reduction product was obtained.<sup>10</sup>

The reductive silylation occurs mostly with ketones and certain aldehydes. Benzonitrile, phthalic anhydride, nitrobenzene, 4-nitrobenzyl bromide, and 1-bromo-4-*tert*-butylbenzene were recovered unchanged. 4-Phenyl-1-butene and phenylacetylene were also inert to the reaction conditions. When methyl benzoate was subjected to the standard conditions, **2f** was obtained in 20–30% yield. Cyclohexene oxide and styrene oxide were converted mainly to the silyl ethers of the corresponding  $\beta$ -chlorohydrins.

**Advantages.** The present procedure has many attractive features. A major chemical advantage arises from the low basicity of the reaction system, resulting in ketone

(10) The reductive silylation of **1e** by the  $\text{NaHNaO}-t\text{-C}_6\text{H}_{11}\text{-ZnCl}_2$ -chlorotrimethylsilane (ZnCRASi) mixed system gave *cis*- and *trans*-**2e** in a 1:4 ratio. Reaction of **1h** gave **2h** in an excellent yield: Brunet, J.-J.; Besozzi, D.; Caubère, P. *Synthesis* 1982, 721. Recent review: Caubère, P. In *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; Ohno, A., Furukawa, N., Okuyama, T., Associate Eds.; MYU: Tokyo, 1991; Vol. 4, pp 78–139.

Table 1. Reductive Silylation of Carbonyl Compounds Promoted by a Zn Catalyst<sup>a</sup>

carbonyl substrate	reducing system, equiv			conditions		% yield of product 2 <sup>b</sup>	
	1/n (LiH) <sub>n</sub> + (CH <sub>3</sub> ) <sub>3</sub> SiCl	Zn catalyst	solvent	temp °C	time, h		
1a	1.5	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	28	50	98 <sup>c</sup> (92)
1a	1.5	ZnCl <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	28	40	98 (91)
1a	1.5	Zn	0.01	CH <sub>2</sub> Cl <sub>2</sub>	28	50	97 (90)
1a	1.5	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	toluene	28	50	98 (89)
1a	1.5	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	THF	28	70	49
1a	1.0	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	28	40	81
1b	2.0	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.011	CH <sub>2</sub> Cl <sub>2</sub>	40	38	99 (95)
1b	1.5	ZnCl <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	40	50	99 (92)
1c	1.5	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	40	36	99 (85)
1d	2.0	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	40	40	97 (91)
1d	2.0	Zn	0.012	CH <sub>2</sub> Cl <sub>2</sub>	40	40	97 (89)
1e	2.0	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.012	CH <sub>2</sub> Cl <sub>2</sub>	40	50	95 <sup>d</sup> (88)
1f	2.0	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.012	CH <sub>2</sub> Cl <sub>2</sub>	28	50	93 (84)
1g	1.5	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	40	32	96
1h	1.5	Zn(OSO <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub>	0.01	CH <sub>2</sub> Cl <sub>2</sub>	28	50	(50)

<sup>a</sup> Reaction conditions are given in the Experimental Section. <sup>b</sup> Determined by 400-MHz <sup>1</sup>H NMR and/or GC analysis. Values in parentheses are isolated yields. <sup>c</sup> A 30-g-scale reaction. <sup>d</sup> A 2.6:1 mixture of the cis and trans isomers.

hydrosilylation with high efficiency. Unlike less aggregated, reactive LiH prepared by hydrogenolysis of alkyl-lithiums aided by TMEDA,<sup>7b</sup> commercial (LiH)<sub>n</sub> produces only small amounts of lithium enolates from ketonic substrates. A NaH- or KH-chlorotrimethylsilane system without a Zn catalyst has been reported to convert cyclohexanones predominantly to enol trimethylsilyl ethers.<sup>11</sup>

The present reaction is operationally simple. Hydrosilylation of carbonyl compounds is conventionally achieved with a 4-fold excess of the ZnCRASi mixed system<sup>10,12</sup> and trialkylsilanes in trifluoroacetic acid<sup>13a</sup> or with transition-metal catalysts.<sup>13b</sup> However, the manageability of our system is much superior to existing methods because the latter require highly pyrophoric trialkylsilanes. Commercial solid (LiH)<sub>n</sub> is a very safe material. In our study, a 0.25-mol-scale reaction was the largest one carried out, but no technical problems are foreseen.

The reagent cost for this procedure is less than \$8/mol according to the 1992/1993 catalogue of Aldrich Chemical Co. (LiH, \$2.2/mol; chlorotrimethylsilane, \$5.4/mol; ZnCl<sub>2</sub>, \$4.6/mol; Zn powder, \$1.2/mol). This reagent is much cheaper than triethylsilane (\$88/mol) and diphenylsilane (\$376/mol), a safe silane agent. Overall, the present method has proved practical from both technical and economical points of view.

**Mechanistic Considerations.** It is premature to discuss the reaction mechanism of the reductive silylation in detail. However, the following observations may help the elucidation of the mechanism in the future.

(1) Trimethylsilane is not the active species. The filtrates obtained from an equimolar mixture of (LiH)<sub>n</sub>, chlorotrimethylsilane, and ZnX<sub>2</sub> (X = Cl or OSO<sub>2</sub>CH<sub>3</sub>) stirred for 30 h contained no detectable amount of

trimethylsilane, as judged by 400-MHz <sup>1</sup>H NMR analysis. Furthermore, attempted hydrosilylation of ketone 1a with triethylsilane in dichloromethane was not catalyzed at all by 1 mol % of zinc methanesulfonate. These results eliminate the possibility of the known hydrosilylation mechanism.

(2) The combined system consisting of solid (LiH)<sub>n</sub>, chlorotrimethylsilane, and a catalytic amount of a Zn compound was indispensable for the promotion of the reduction. The reductive silylation is believed to occur on the surface of insoluble aggregates. This view was supported by the observations discussed below. A 1:1:0.01 molar mixture of solid (LiH)<sub>n</sub>, chlorotrimethylsilane, and insoluble zinc methanesulfonate in dichloromethane was stirred at 28 °C for 18 h, and then the supernatant was removed by filtration. The resulting white solid had no reduction ability toward ketone 1a in dichloromethane. Notably, renewed addition of chlorotrimethylsilane to this suspension restored the reactivity toward 1a (path 1 in Scheme 1). In addition, the colorless filtrate had no reactivity either. The addition of (LiH)<sub>n</sub> did not restore the reactivity. The original reactivity was not restored until additional Zn salt (path 2 in Scheme 1) was added. Furthermore, a filtrate of a 1:1:1 molar mixture of the three components was also unreactive. These observations indicate that, in the presence or absence of Zn species, (LiH)<sub>n</sub> and chlorotrimethylsilane do not cause significant irreversible chemical reactions, but the two components cooperate in the Zn-catalyzed hydrosilylation of carbonyl compounds. The white solid obtained by path 1 was equivalent to a mixture of (LiH)<sub>n</sub> and the Zn salt, and the colorless solution obtained by path 2 contained only chlorotrimethylsilane. Thus, the combination of the three independent components, (LiH)<sub>n</sub>, chlorotrimethylsilane, and zinc methanesulfonate, is necessary for the reductive silylation, but the real active species barely dissolves in dichloromethane. However, at this moment, we should refrain from postulating any transition-state models.

(3) This reaction proceeds even in the presence of 5 mol % of *p*-dinitrobenzene, a fact which rules out mechanisms involving electron-transfer processes via anion radicals.<sup>14</sup>

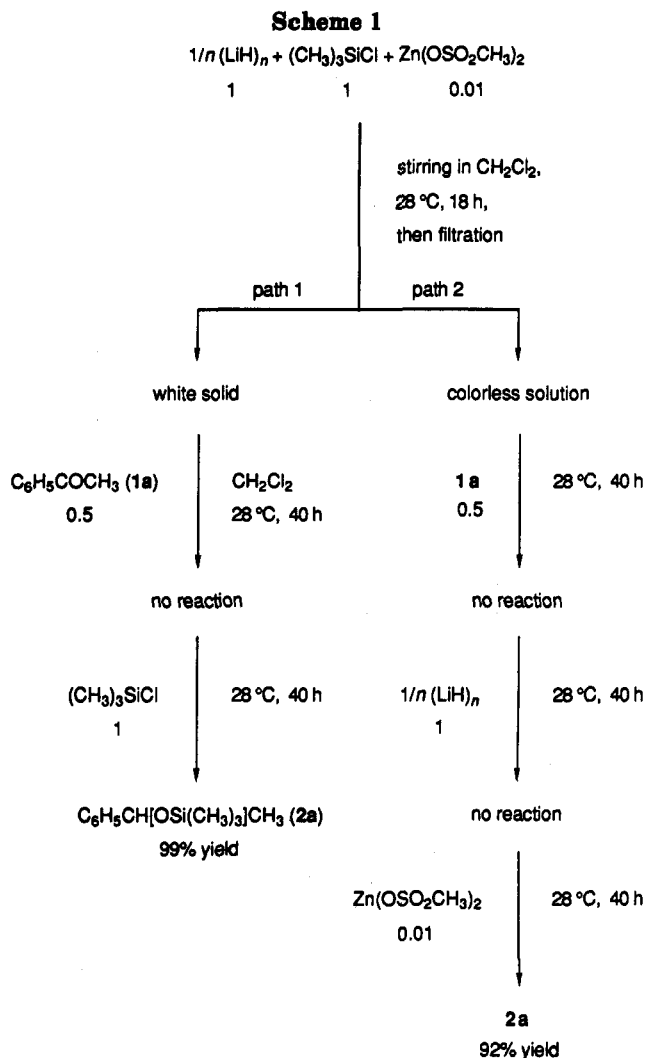
(4) A Zn(II) species seems to be the real catalyst of the hydrosilylation using the solid (LiH)<sub>n</sub>-chlorotrimethylsilane mixed system, in spite of the fact that Zn powder

(11) Hudrlik, P. F.; Takacs, J. M. *J. Org. Chem.* 1978, 43, 3861. In our operations, treatment of 1a with a 2-fold excess of the NaH-chlorotrimethylsilane mixture in dichloromethane or toluene at 28 °C did not generate the enol silyl ether of 1a. The reactivity of this system as a base strongly depends on the substrate and conditions, including the solvent and the temperature.

(12) For the reducing ability of the NaH-ZnCl<sub>2</sub>-chlorotrimethylsilane mixed system, see: (a) Caubère, P.; Vanderesse, R.; Fort, Y. *Acta Chem. Scand.* 1991, 45, 742. (b) Nordahl, A.; Carlson, R. *Acta Chem. Scand.* 1990, 44, 274.

(13) Reviews: (a) Magnus, P. D.; Sarkar, T.; Djuric, S. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed., Stone, F. G. A., Deputy Ed., Abel, E. W., Executive Ed.; Pergamon Press: Oxford, 1982; Vol. 7, Chapter 48. (b) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: Chichester, 1989; Part 2, Chapter 25.

(14) Kerber, R. C.; Urry, G. W.; Kornblum, N. *J. Am. Chem. Soc.* 1965, 87, 4520.



also promotes the reaction. In the latter case, Zn(II) species are probably generated in situ. The reaction of 1a with more than 1 equiv of Zn powder gives only pinacol-type coupling products.

(5) The oxidation state of the Zn catalyst can be inferred by the XAES (X-ray induced Auger electron spectroscopy)<sup>15,16</sup> measurements of the insoluble portion of the reaction mixture. An analytical sample of the reaction mixture of ketone 1a,  $(\text{LiH})_n$ , and chlorotrimethylsilane catalyzed by either zinc methanesulfonate or commercial Zn powder at 60% or 80% conversion, respectively, was collected by filtration under argon. When the methanesulfonate was used as the catalyst, the Auger parameter of the Zn species deposited on the surface of the fine gray powder obtained by removal of the trace amount of oily material was 2011.4 eV. When compared to the literature values of 2010 to 2011 eV,<sup>16</sup> the Auger value showed that the metallic species was a Zn(II) salt with unidentified counter anions. The Zn(II) content of the surface area was higher than that of the  $100 \pm 5 \mu\text{m}$  inner area of the powder. No evidence was obtained for the presence of possible Zn(0) species on the surface. Even when Zn

powder was used as a catalyst, a Zn(II) salt was detected as the main species on the surface, with an Auger parameter of 2011.0 eV; Zn(0) was the main species of the inner area, with an Auger parameter of 2014.1 eV.<sup>16</sup> Zn(II) species have proved to be thermodynamically favored over Zn(0) under the reaction conditions and would probably act as the true catalysts on the surface of the  $(\text{LiH})_n$ . However, the XAES measurements cannot exclude the possibility of the participation of a kinetically active Zn(0) species as the catalyst.

## Conclusion

We have succeeded in giving a synthetic role to commercially available  $(\text{LiH})_n$ , which has previously remained virtually unutilized. The direct activation of solid  $(\text{LiH})_n$  with chlorotrimethylsilane and a catalytic amount of a Zn(II) salt or Zn powder provides a practical method for reductive silylation of carbonyl compounds. The extreme manageability and cost efficiency of this reduction system will be invaluable for practical use. Central to unraveling the mechanism of the Zn(II)-catalyzed reduction is ascertaining how chlorotrimethylsilane interacts with solid  $(\text{LiH})_n$  to result in the activation of  $\text{LiH}$  as a hydride source rather than as a base. However, the reaction is believed to occur on the surface of  $(\text{LiH})_n$ . Despite the ambiguity of the mechanism, the unprecedented use of  $(\text{LiH})_n$  as a hydride source encourages the further application of the system for organic reactions.

## Experimental Section

**General.** Gas chromatographic (GC) analysis was conducted with a G-300 column (polyethylene glycol,  $df = 1.0 \mu\text{m}$ , 1.2 mm i.d.  $\times$  20 m, Chemicals Inspection & Testing Institute, Japan) using helium carrier gas ( $0.5 \text{ kg/cm}^2$ ). The GC data are described as follows unless otherwise specified: retention time ( $t_R$ ), column temperature, injection temperature. All experiments were performed under an argon atmosphere using standard Schlenk techniques in a water bath (28 °C) or oil bath (40 °C).

**Materials.** Dichloromethane ( $\text{CH}_2\text{Cl}_2$ ) was freshly distilled from calcium hydride under argon. Chlorotrimethylsilane ( $(\text{CH}_3)_3\text{SiCl}$ ) was distilled from calcium hydride under argon and stored in a Schlenk tube. Lithium hydride ( $(\text{LiH})_n$ , 30-mesh powder, 95% purity) was purchased from Aldrich Chemical Co. All substrates for reductive silylation were purchased from Tokyo Chemical Industry Co., purified by distillation from 4-Å molecular sieves, and kept in Schlenk tubes. Diethylzinc (1.0 M solution in hexane) was purchased from Aldrich Chemical Co.  $\text{ZnCl}_2$  (98% purity) and zinc powder (>90% purity) were purchased from Nacalai Tesque, Inc.  $\text{ZnBr}_2$  (99.9% purity) was purchased from Wako Pure Chemical Industries. Methanesulfonic acid (99% purity) was purchased from Tokyo Chemical Industry Co. These zinc compounds and methanesulfonic acid were used without further purification. Celite (65 gal/ft<sup>2</sup>/h) was purchased from Nacalai Tesque, Inc.

**Preparation of Zinc Methanesulfonate ( $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$ ).**<sup>17</sup> To a solution of methanesulfonic acid (1.92 g, 20.0 mmol) in  $\text{CH}_2\text{Cl}_2$  (30 mL) at 0 °C was added diethylzinc (1.0 M hexane solution, 10.0 mL, 10.0 mmol) dropwise. The pale yellow suspension was warmed to 28 °C and vigorously stirred for 2 h. The resulting white suspension (estimated to be 0.25 M) was used as the catalyst.

White solid  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (2.63 g, quantitative yield) was prepared by removing the solvent in vacuo and drying the residue under reduced pressure (0.5 mmHg) at 28 °C for 10 h.

The suspension and solid were stored in an airtight apparatus under argon.

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**Typical Procedure for the Reductive Silylation: 1-Phenylethyl Trimethylsilyl Ether (2a).**<sup>10</sup> To a stirred suspension of  $(\text{LiH})_n$  (3.13 g, 374 mmol) in  $\text{CH}_2\text{Cl}_2$  (100 mL) at 28 °C was added  $(\text{CH}_3)_3\text{SiCl}$  (40.7 g, 375 mmol), and the mixture was stirred for 30 min. To this mixture were added a solution of acetophenone (1a) (30.3 g, 252 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 mL) and a suspension of  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  in  $\text{CH}_2\text{Cl}_2$  (0.25 M, 10 mL, 2.5 mmol). The mixture was then vigorously stirred with a magnetic stirrer for 50 h. The insoluble part of the reaction mixture was removed by Celite (15 g) filtration. The filter cake including excess  $(\text{LiH})_n$  was added to a large amount of water for safe hydrolysis. Silyl ether 2a (44.9 g, 92% yield, 99% purity) was obtained by concentration of the filtrate followed by fractional distillation of the residue with a 20-cm Vigreux column (bp 85–86 °C/16 mmHg): GC, 4.4 min, 100 °C, 140 °C.

When  $\text{ZnCl}_2$  (68 mg, 0.50 mmol) was used instead of  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$ , 1a (6.01 g, 50.0 mmol) was converted to 2a (8.86 g, 91% yield, 99% purity). Zinc powder (33 mg, 0.50 mmol) catalyzed the reaction of 1a (6.08 g, 50.6 mmol) to give 2a (8.83 g, 90% yield, 99% purity).

Toluene could be used as the solvent to convert 1a (6.01 g, 50.0 mmol) to 2a (8.63 g, 89% yield, 98% purity).

**Comparison of the Reactivity of Zinc Catalysts.** Many zinc catalysts, which were either prepared as described above or purchased, could be used for reductive silylations of 1a. Chemical yields (<sup>1</sup>H NMR and/or GC analysis) obtained by reactions of 1a,  $(\text{LiH})_n$ ,  $(\text{CH}_3)_3\text{SiCl}$ , and zinc catalyst (1:1:1:0.01 molar ratio) under standard conditions (28 °C, 40 h) were  $\text{ZnBr}_2$  64,  $\text{ZnCl}_2$  62,  $\text{Zn}(\text{OC}_2\text{H}_5)_2$  78,  $\text{Zn}(\text{O}-i\text{-C}_3\text{H}_7)_2$  67,  $\text{Zn}(\text{O}-t\text{-C}_4\text{H}_9)_2$  44,  $\text{Zn}(\text{OC}_6\text{H}_5)_2$  74,  $\text{Zn}(\text{OCH}(\text{CH}_3)\text{C}_6\text{H}_5)_2$  65,  $\text{Zn}(\text{OCH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{CH}_3)_2$  75,  $\text{Zn}(\text{ON}(\text{C}_6\text{H}_5)\text{CO}(\text{C}_6\text{H}_5))_2$  55,  $\text{Zn}(\text{N}(\text{C}_2\text{H}_5)_2)_2$  56,  $\text{Zn}(\text{SC}_6\text{H}_5)_2$  78,  $\text{Zn}(\text{OCOCH}_3)_2$  74,  $\text{Zn}(\text{OPO}(\text{OC}_6\text{H}_5)_2)_2$  65,  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  81,  $\text{Zn}(\text{OSO}_2\text{CF}_3)_2$  72, zinc powder 71.

**2-Octyl Trimethylsilyl Ether (2b).**<sup>18</sup>  $(\text{LiH})_n$  (835 mg, 99.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (10.9 g, 100 mmol), 2-octanone (1b) (6.41 g, 50.0 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (solid, 143 mg, 0.560 mmol), 40 °C, 38 h. 2b (9.59 g, 95% yield, 99% purity): bp 82–83 °C/16 mmHg; GC,  $t_R$  9.7 min, initial column temp 30 °C (15 min), final column temp 80 °C (20 min), progress rate 5 °C/min, injection temp 120 °C.

When  $\text{ZnCl}_2$  (68 mg, 0.50 mmol) was used as the catalyst, 1b (6.41 g, 50.0 mmol) was converted to 2a (9.34 g, 92% yield, 98% purity).

**3,3-Dimethyl-2-butyl Trimethylsilyl Ether (2c).**<sup>19</sup>  $(\text{LiH})_n$  (626 mg, 74.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (8.15 g, 75.0 mmol), pinacolone (1c) (5.01 g, 50.0 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (0.25 M suspension, 2.0 mL, 0.50 mmol), 40 °C, 36 h. 2c (7.46 g, 85% yield, 98% purity): bp 64–66 °C/62 mmHg; GC, 2.1 min, 30 °C, 70 °C.

**Cyclohexyl Trimethylsilyl Ether (2d).**<sup>10</sup>  $(\text{LiH})_n$  (835 mg, 99.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (10.9 g, 100 mmol), cyclohexanone (1d) (4.92 g, 50.1 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (solid, 130 mg, 0.509 mmol), 40 °C, 40 h. 2d (7.83 g, 91% yield, 98% purity): bp 68–69 °C/21 mmHg; GC,  $t_R$  4.7 min, initial column temp 30 °C (10 min), final column temp 80 °C (15 min), progress rate 5 °C/min, injection temp 120 °C.

The use of zinc powder (38 mg, 0.58 mmol) as the catalyst also gave 2d (7.65 g, 89% yield, 98% purity).

**4-tert-Butylcyclohexyl Trimethylsilyl Ether (2e).**<sup>10</sup>  $(\text{LiH})_n$  (835 mg, 99.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (10.9 g, 100 mmol), 4-tert-butylcyclohexanone (1e) (7.81 g, 50.6 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (powder, 148 mg, 0.579 mmol), 40 °C, 50 h. 2e (10.15

g, 88% yield, 98% purity) as a 2.6:1 mixture of the cis and trans isomers. The <sup>1</sup>H NMR spectrum of the cis isomer showed the C-1 methine proton signal at  $\delta$  3.95, whereas the corresponding signal of the trans isomer appeared at  $\delta$  3.50. The structure was established by comparison with commercial alcohol samples (Tokyo Chemical Industry Co.) after desilylation (vide infra): bp 102–105 °C/11 mmHg.

**Benzyl Trimethylsilyl Ether (2f).**<sup>10</sup>  $(\text{LiH})_n$  (835 mg, 99.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (10.9 g, 100 mmol), benzaldehyde (1f) (5.31 g, 50.0 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (solid, 147 mg, 0.575 mmol), 28 °C, 50 h. 2f (7.53 g, 84% yield, 99% purity): bp 97–100 °C/30 mmHg; GC,  $t_R$  7.2 min, initial column temp 80 °C (15 min), final column temp 130 °C (20 min), progress rate 10 °C/min, injection temp 170 °C.

**Neopentyl Trimethylsilyl Ether (2g).**<sup>20</sup>  $(\text{LiH})_n$  (626 mg, 74.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (8.15 g, 75.0 mmol), pivalaldehyde (1g) (4.31 g, 50.0 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (solid, 128 mg, 0.501 mmol), 40 °C, 32 h; 96% yield determined by GC after desilylation: column G-450 (50% trifluoropropyl methyl silicone,  $df = 1.0 \mu\text{m}$ , 1.2 mm i.d.  $\times$  40 m),  $t_R$  (neopentyl alcohol) 13.3 min, 40 °C, 80 °C.

**(E)-1-Phenyl-3-((trimethylsilyloxy)-1-butene (2h).**<sup>10</sup>  $(\text{LiH})_n$  (626 mg, 74.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (8.15 g, 75.0 mmol), (E)-4-phenyl-3-buten-2-one (1h) (7.41 g, 50.7 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (solid, 128 mg, 0.501 mmol), 28 °C, 50 h. 2h (5.56 g, 50% yield, 99% purity): bp 82–84 °C/1.1 mmHg; GC, column G-100 (methyl silicone,  $df = 1.0 \mu\text{m}$ , 1.2 mm i.d.  $\times$  40 m),  $t_R$  9.9 min, initial column temp 100 °C (3 min), final column temp 260 °C (30 min), progress rate 10 °C/min, injection temp 300 °C.

**1-Phenylethanol.** The reductive silylation was performed by means of the typical procedure.  $(\text{LiH})_n$  (626 mg, 74.8 mmol),  $\text{CH}_2\text{Cl}_2$  (30 mL),  $(\text{CH}_3)_3\text{SiCl}$  (8.15 g, 75.0 mmol), 1a (6.01 g, 50.0 mmol),  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$  (solid, 128 mg, 0.501 mmol), 28 °C, 50 h. The reaction mixture was filtered through Celite (5 g) in the open air. To the filtrate at 28 °C was added a solution of hydrochloric acid in methanol (0.05 M, 10.0 mL, 0.50 mmol), which was prepared by dilution of concd hydrochloric acid with methanol. The pale brown solution obtained was stirred for 30 min, and then the solvent was removed under reduced pressure. The title alcohol (5.39 g, 88% yield, 98% purity) was obtained by fractional distillation of the residue (bp 98–100 °C/22 mmHg). The addition of an excess of hydrochloric acid (2 M) to the reaction mixture and the usual workup including extraction gave product also. All physical data were identical with those of commercial alcohol samples (Tokyo Chemical Industry Co.): GC 36.3 min, 100 °C, 140 °C.

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**Registry numbers supplied by author:** 1a, 98-86-2; 1b, 111-13-7; 1c, 75-97-8; 1d, 108-94-1; 1e, 98-53-3; 1f, 100-52-7; 1g, 630-19-3; 1h, 1896-62-4; 2a, 14856-75-8; 2b, 18023-52-4; 2c, 31650-04-1; 2d, 13871-89-1; cis-2e, 32147-26-5; trans-2e, 32147-25-4; 2f, 14642-79-6; 2g, 18246-63-4; 2h, 76987-16-1; 1-phenylethanol, 98-85-1;  $\text{Zn}(\text{OSO}_2\text{CH}_3)_2$ , 33684-80-9; Zn, 7440-66-6;  $\text{ZnCl}_2$ , 7646-85-7; LiH, 7580-67-8;  $(\text{CH}_3)_3\text{SiCl}$ , 75-77-4; methanesulfonic acid, 75-75-2.

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