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Indium-Catalyzed Radical Reductions of Organic Halides with Hydrosilanes

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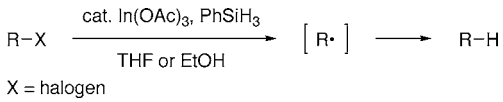

The $In(OAc)_3$-catalyzed reaction of bromo- and iodoalkanes with $PhSiH_3$ in THF at 70 °C gave dehalogenated alkanes in good to high yields. In the presence of Et_3B and air, the reduction proceeded smoothly at 30 °C. When 2,6-lutidine and air were used as additives, the $In(OAc)_3$-catalyzed system enabled an efficient reduction of simple and functionalized iodoalkanes in EtOH. Catalytic use of $GaCl_3$ was found to be effective in the reduction of haloalkanes with poly(methylhydrosiloxane) (PMHS). These catalytic reductions probably involve a radical chain mechanism in which indium or gallium hydride species work as the actual reductants.

Introduction

Hydrosilanes have widely been used as mild reducing agents for fine organic synthesis.[1] In general, they do not react spontaneously with carbon electrophiles; however, activation of themselves or the substrates induces the reaction. A proper choice of activator enables fine control of the reduction process. In the course of our study on the synthetic use of hydrosilanes,[2] we found that a copper salt can activate hydrosilanes by transmetalation and that the copper hydride species thus formed is valuable for the reduction of carbonyl compounds.[3] These observations prompted us to investigate catalytic activation of hydrosilanes with other metal salts and its application to an efficient reduction of carbon electrophiles. We then focused our interest on the use of indium and gallium salts as the catalytic activator.

Baba and Shibata had reported the $InCl_3$-catalyzed reduction of organic halides using Bu_3SnH and $NaBH_4$ as stoichiometric reducing agents before we started the present study.[4] A radical chain mechanism in which $HInCl_2$ works as radical mediator was proposed for this reduction. Oshima's group demonstrated that, in the presence of Et_3B (a radical initiator), organic halides were efficiently reduced with metal hydrides prepared from MCl_3 (M═Ga, In) and aluminum hydrides.[5] We expected that use of hydrosilanes as the hydride sources would enhance the synthetic utility of these radical reductions because hydrosilanes are less toxic and have moderate reactivity enabling high compatibility with polar functional groups. In this context, Baba and Shibata have recently introduced $InCl_3$-hydrosilane systems for radical reduction.[6,7] We herein report the details of our study on the indium- and gallium-catalyzed reductions of organic halides with hydrosilanes.

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Results and Discussion

Optimization of Reaction Conditions. Initially, the reaction of 1-bromo-3-phenylpropane (**1a**-Br) with $PhSiH_3$ was selected to examine catalytic activities of commercially available indium and gallium salts (eq 1). Among the salts tested, $InCl_3$, $In(OH)_3$, $In(OAc)_3$, and $GaCl_3$ effectively catalyzed the reduction of **1a**-Br to propylbenzene (**2a**) at 70 °C. Particularly, the $In(OAc)_3$-catalyzed reduction achieved the best yield of **2a**. Screening of hydrosilanes was then performed by using the $In(OAc)_3$-catalyzed system. As a result, $PhSiH_3$ was found to be much more effective than other hydrosilanes such as Et_3SiH, Ph_3SiH, $PhSiH_2Cl$, and poly(methylhydrosiloxane) (PMHS) (eq 2). Use of 0.5 equiv of $PhSiH_3$ reduced the yield of **2a** to 47%. Judging from the low reactivity of $PhSiH_2Cl$, this disappointing result is probably due to low reactivity of $PhSiH_2X$ (X═Br, OAc) generated from $PhSiH_3$.

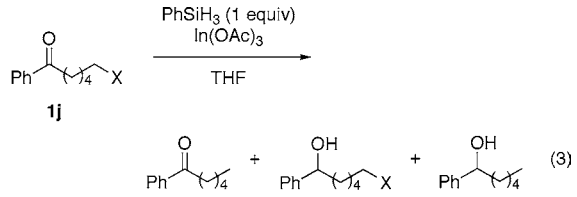
$$\underset{\textbf{1a}\text{-Br}}{Ph(CH_2)_3Br} + \underset{(1\ \text{equiv})}{PhSiH_3} \xrightarrow[\text{THF, 70 °C, 24 h}]{MX_3\ (10\ \text{mol\%})} \underset{\textbf{2a}}{Ph(CH_2)_2CH_3} \quad (1)$$

MX_3 (yield / %): none (0), $InCl_3$ (86), $In(acac)_3$ (52), $In(OH)_3$ (88), $In(OTf)_3$ (13), $In(OAc)_3$ (94), $GaCl_3$ (86), $Ga(acac)_3$ (72), $Ga(OH)_3$ (trace)

$$\underset{(1\ \text{equiv})}{\textbf{1a}\text{-Br} + \textit{Si}\text{–H}} \xrightarrow[\text{THF, 70 °C, 24 h}]{In(OAc)_3\ (10\ \text{mol\%})} \textbf{2a} \quad (2)$$

Si–H (yield / %): $PhSiH_3$ (94), Et_3SiH (39), Ph_3SiH (3), $PhSiH_2Cl$ (21), PMHS (20)

Scope and Limitations. With the initial results in hand, we investigated the scope and limitations of the $In(OAc)_3$-catalyzed reduction with $PhSiH_3$ at 70 °C (Method A in Table 1). Nonfunctionalized bromo- and iodoalkanes were efficiently reduced to the corresponding alkanes (entries 1, 2, 4−7, 9, and 10). The reduction of chloroalkanes and 1-bromonaphthalene (**1e**-Br) resulted in low yields (entries 3, 8, 11, and 12). This reduction system was tolerant to ester and alkyl ether moieties (entries 14−17). However, the presence of hydroxy and siloxy groups complicated the $In(OAc)_3$-catalyzed reaction (entries 18−20). Bromoketone **1j**-Br underwent competitive reduction of C−Br and C═O bonds to give the desired product **2j** and carbonyl reduction products **3** and **4** (entry 22, eq 3).



	2j	3	4
Method A, X = Br:	12%	29%	32%
Method B, X = Br:	38%	<9%	27%
Method B, X = I:	20%	<12%	53%

Mechanistic Aspects. To gain mechanistic insight, the $In(OAc)_3$-catalyzed reaction of **1a**-Br with $PhSiH_3$ was quenched with D_2O. GC-MS analysis of the reaction mixture revealed no incorporation of deuterium in the dehalogenated product. On the other hand, use of $PhSiD_3$ instead of $PhSiH_3$ gave the deuterated product **2a-*d*** (78%*d*, eq 4). This result indicates that $PhSiH_3$ works as the main hydrogen source in the reduction of **1a**-Br.

$$\underset{\textbf{1a}\text{-Br}}{} + PhSiD_3 \xrightarrow[\text{THF, 70 °C, 24 h}]{In(OAc)_3\ (10\ \text{mol\%})} \underset{\textbf{2a-}\textit{d}\text{, 82\%, 78\%}\textit{d}}{Ph(CH_2)_2CH_2D} \quad (4)$$

The reaction of $In(OAc)_3$ with an excess amount of $PhSiH_3$ (10 equiv) gave indium foil in 93% yield with the evolution of H_2 (THF, 70 °C, 24 h). Identification of the product was based on measurement of the melting point (157 °C). Since InH_3 easily decomposes to indium metal and H_2,[8] this observation suggests the formation of InH_3 and other indium hydride species from $In(OAc)_3$ and $PhSiH_3$. In addition, the reduction of **1a**-Br was completely suppressed by galvinoxyl, a radical scavenger, while it was accelerated by Et_3B-air, a radical initiator (vide infra).[5,9] Accordingly, the reaction mechanism would involve transmetalation (hydride transfer) of the hydride source and subsequent

TABLE 1. $In(OAc)_3$-Catalyzed Reduction with $PhSiH_3$ in THF[a]

$$\underset{\textbf{1-X}}{R\text{–}X} + PhSiH_3 \xrightarrow[\text{THF, 24 h}]{\text{cat. } In(OAc)_3,\ (Et_3B)} \underset{\textbf{2}}{R\text{–}H}$$

			yield (%)[b]	
entry	R-X	compound name	method A[c]	method B[d]
1	$Ph(CH_2)_3$-Br	(**1a**-Br)	94	91 (61)[e]
2	$Ph(CH_2)_3$-I	(**1a**-I)	90	90 (91)[e]
3	$Ph(CH_2)_3$-Cl	(**1a**-Cl)	5	9
4	*n*-$C_{12}H_{25}$-Br	(**1b**-Br)	94	96
5	*n*-$C_{12}H_{25}$-I	(**1b**-I)	78	83 (91)[e]
6	*c*-$C_{12}H_{23}$-Br	(**1c**-Br)	91	86
7	*c*-$C_{12}H_{23}$-I	(**1c**-I)	96	90 (93)[e]
8	*c*-$C_{12}H_{23}$-Cl	(**1c**-Cl)	42	36
9	1-adamantyl-Br	(**1d**-Br)	94	96
10	1-adamantyl-I	(**1d**-I)	78	87
11	1-adamantyl-Cl	(**1d**-Cl)	19	35
12	1-naphthyl-Br	(**1e**-Br)	12	41
13	1-naphthyl-I	(**1e**-I)	19	61
14	$PhCO_2(CH_2)_3$-Br	(**1f**-Br)	75	82
15	$PhCO_2(CH_2)_3$-I	(**1f**-I)	75	93 (98)[e]
16	*n*-$C_8H_{17}O(CH_2)_3$-Br	(**1g**-Br)	82	97
17	*n*-$C_8H_{17}O(CH_2)_3$-I	(**1g**-I)	99	96 (94)[e]
18	$CH_3CH(OH)(CH_2)_{11}$-Br	(**1h**-Br)	33	84
19	$CH_3CH(OH)(CH_2)_{11}$-I	(**1h**-I)	trace	26 (24)[e]
20	$CH_3CH(OTBS)(CH_2)_{11}$-Br	(**1i**-Br)	40	93
21	$CH_3CH(OTBS)(CH_2)_{11}$-I	(**1i**-I)	80	81
22	$PhC(O)(CH_2)_5$-Br	(**1j**-Br)	12	38
23	$PhC(O)(CH_2)_5$-I	(**1j**-I)		20

[a] All reactions were carried out with a haloalkane **1** (1.00 or 0.50 mmol), $PhSiH_3$ (1.0 equiv), and $In(OAc)_3$ (10 or 20 mol %) in THF (1.0 mL/1 mmol of **1**) for 24 h under N_2 (2 L balloon). [b] The yield was determined by GC analysis (entries 1−13, 16, and 17), by ^1H NMR analysis (entries 18 and 19), or by isolation (entries 14, 15, and 20−23). [c] Method A: $In(OAc)_3$ (10 mol %), 70 °C, 24 h. [d] Method B: $In(OAc)_3$ (20 mol %), Et_3B (1.0 M in hexane, 20 mol %), dry air (10 mL/1 mmol of **1**), 30 °C, 24 h. [e] The result without Et_3B-dry air is shown in parentheses.

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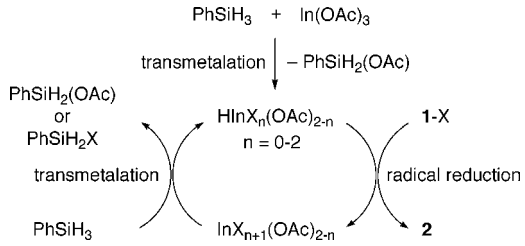
SCHEME 1



radical reduction with indium hydride species as proposed by Baba and Shibata (Scheme 1).[4,7] The initiation step is the formation of $HIn(OAc)_2$ from $In(OAc)_3$ and $PhSiH_3$. The indium hydride reacts with a haloalkane **1**-X by a radical chain mechanism to give the corresponding dehalogenated product **2** and $InX(OAc)_2$.[4,5] The indium salt undergoes hydride transfer from $PhSiH_3$ to regenerate the indium hydride species, $HIn(OAc)_2$ and HInX(OAc). After the first turnover, further reduction of the remaining haloalkane was carried out with $HInX_n(OAc)_{2-n}$ ($n = 0-2$).

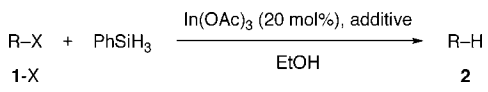
Reduction at 30 °C. Our efforts were next directed at developing an efficient catalytic reduction of haloalkanes under milder conditions. The reduction of **1a**-Br using $In(OAc)_3$ (10 mol %) and $PhSiH_3$ at room temperature for 24 h resulted in a low yield of **2a** (35%). Use of 20 mol % $In(OAc)_3$ at 30 °C improved the yield to 61%. Additionally, when Et_3B (0.2 equiv) and dry air were employed as radical initiators,[9] the reduction was completed within 24 h to give **2a** in 91% yield. The Et_3B-initiated reduction at 30 °C was applied to various haloalkanes (Method B in Table 1). The results with non-functionalized haloalkanes are similar to those of Method A (entries 1−11). In the reduction of 1-halonaphthalenes and functionalized haloalkanes, Method B was generally superior to Method A (entries 12−21). Unfortunately, Method B as well as Method A was not effective in selective reduction of haloketones **1j** (entries 22 and 23, eq 3).

Iodoalkanes were efficiently reduced even in the absence of Et_3B-dry air (entries 2, 5, 7, 15, and 17). In these cases, adventitious oxygen (air) might initiate the radical reduction. The initiation by oxygen might also affect the reduction by Method A. Indeed, as described next, it turned out that addition of only air accelerated the In-catalyzed reduction of organic halides.

Reduction in EtOH. We have recently reported the generation of indium hydride species from $In(OAc)_3$ and $PhSiH_3$ in EtOH and its application to catalytic 1,4-reduction of α-enones.[7b] Since EtOH is an environmentally benign organic solvent, we examined the $In(OAc)_3$-catalyzed reduction in EtOH. First, the Et_3B-initiated method used for Method B was applied to the reduction of bromo- and iodoalkanes (Method C in Table 2). However, except for the case of **1c**-I, the yields of **2** were moderate because of incomplete conversion of haloalkanes (ca. 70−80% conversion). The reduction of bromoalkanes was accompanied by the formation of indium metal.

Effects of additives on the reduction of **1b**-I in ethanol were further investigated to improve the reaction system (Table 3). The reaction was accelerated by Et_3B-dry air; however, the addition of only dry air was also effective (entries 2 and 3). Molecular oxygen itself presumably serves as radical initiator in the latter case. Use of K_2CO_3 gave **2b** in good yield, although the reaction mixture included many unidentified byproducts (entry 4). Among the bases tested, 2,6-lutidine brought about a clean conversion of **1b**-I to **2b** (entry 7). The combined use of 2,6-lutidine and dry air realized a high yield of **2b** (entry 8).

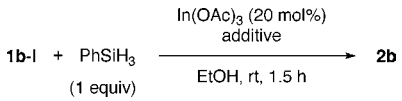
TABLE 2. $In(OAc)_3$-Catalyzed Reduction with $PhSiH_3$ in EtOH[a]



entry	R-X	compound name	yield (%)[b] method C[c]	yield (%)[b] method D[d]
1	$Ph(CH_2)_3$-Br	(**1a**-Br)	66	trace
2	*n*-$C_{12}H_{25}$-Br	(**1b**-Br)	56	trace
3	*n*-$C_{12}H_{25}$-I	(**1b**-I)	67 (45)[e]	87 (79)[f]
4	*c*-$C_{12}H_{23}$-Br	(**1c**-Br)	65	99
5	*c*-$C_{12}H_{23}$-I	(**1c**-I)	80 (43)[e]	97 (77)[f]
6	1-adamantyl-I	(**1d**-I)	55 (37)[e]	35 (3)[f]
7	1-naphthyl-I	(**1e**-I)	24 (5)[e]	69[g] (0)[f]
8	$PhCO_2(CH_2)_3$-I	(**1f**-I)	67 (37)[e]	100
9	*n*-$C_8H_{17}O(CH_2)_3$-I	(**1g**-I)		89
10	$CH_3CH(OH)(CH_2)_{11}$-I	(**1h**-I)		98
11	$CH_3CH(OTBS)(CH_2)_{11}$-I	(**1i**-I)		90[h]
12	$PhC(O)(CH_2)_5$-Br	(**1j**-Br)		0
13	$PhC(O)(CH_2)_5$-I	(**1j**-I)		87
14	$CH_3CH(O)(CH_2)_{11}$-I	(**1k**-I)		96

[a] All reactions were carried out with a haloalkane **1** (0.50 mmol), $PhSiH_3$ (0.50 mmol), and $In(OAc)_3$ (0.10 mmol) in ethanol (1.0 mL) under N_2 (2 L balloon). [b] GC yields in entries 1−7 and 9. Isolated yields in entries 8 and 10−14. [c] Method C: Et_3B (1.0 M in hexane, 0.10 mmol), dry air (5 mL), 30 °C, 24 h. [d] Method D: 2,6-lutidine (0.25 mmol), dry air (5 mL), rt, 1.5 h. [e] The result without Et_3B-dry air is shown in parentheses. [f] The result without dry air is shown in parentheses. [g] An increased amount of dry air (38 mL) was used. [h] The reaction time is 3 h.

TABLE 3. Effects of Additives on Reduction of 1b-I[a]



entry	additive	yield of **2b** (%)[b]	recovery of **1b**-I (%)[b]
1	None	44	42
2	dry air (5 mL)	62	27
3	Et_3B (0.2 equiv) and dry air (5 mL)	74	19
4	K_2CO_3 (0.5 equiv)	77	trace
5	Et_3N (0.5 equiv)	2	86
6	pyridine (0.5 equiv)	5	83
7	2,6-lutidine (0.5 equiv)	79	10
8	2,6-lutidine (0.5 equiv) and dry air (5 mL)	87	4

[a] See footnote a in Table 2. [b] Determined by GC analysis.

The reaction system using 2,6-lutidine and dry air (Method D) was applied to other haloalkanes. The results are shown in the last column of Table 2. Unfortunately, primary bromoalkanes were not reduced at all by Method D, and they remained unchanged (entries 1, 2, and 12 in Table 2). In these cases, the formation of indium metal was more rapid than that in the reaction by Method C. In sharp contrast to primary bromoalkanes, **1c**-Br and iodoalkanes except **1d**-I were efficiently reduced to the corresponding alkanes without deposition of indium metal (entries 3−5, 8−11, 13, and 14 in Table 2). Particularly, iodoketones **1j**-I and **1k**-I were converted into the dehalogenated ketones in high yield. They hardly underwent carbonyl reduction under these conditions. The reaction of **1d**-I gave a complex mixture of products, and the yield of **2d** was rather low (entry 6). 1-Iodonaphthalene (**1e**-I) was reduced to

naphthalene (**2e**) in moderate yield. This reduction did not occur at all in the absence of air (entry 7).

As shown in Table 2, EtOH was not an effective solvent in the $In(OAc)_3$-catalyzed reduction of primary bromoalkanes. Irrespective of the use of 2,6-lutidine, this reduction was accompanied with the formation of indium metal (In(0)); therefore, the poor result is probably due to deactivation of the In(III) catalyst by its conversion into In(0). Since In(0) is formed by the decomposition of InH_3 (vide supra), the formation of In(0) indicates that EtOH induces hydride transfer from $PhSiH_3$ to $In(OAc)_3$ (in other words, transmetalation of $PhSiH_3$) more effectively than THF. The rapid formation of In(0) in the reaction of primary bromoalkanes by Method D suggests that 2,6-lutidine should further accelerate the hydride transfer. The origin of the rate-accelerating effects of EtOH and 2,6-lutidine is not clear, but it may be the nucleophilic attack of EtOH to $PhSiH_3$ and its acceleration by deprotonation with 2,6-lutidine.

Unlike primary bromoalkanes, **1c**-Br (a secondary bromoalkane) and iodoalkanes were efficiently reduced with the aid of 2,6-lutidine. This remarkable difference is explainable by the difference in reactivity toward radical reduction. With primary bromoalkanes, less reactive substrates,[10] their slow reduction and the fast hydride transfer in EtOH containing 2,6-lutidine would cause further hydride transfer from $PhSiH_3$ to indium monohydride species, which ultimately forms unreactive In(0) to impede the catalytic cycle (Scheme 1). In contrast, **1c**-Br and iodoalkanes can eliminate the undesired pathway because they react much faster with indium hydride species. The rapid reduction of these substrates is likely due to a fast turnover of the catalytic cycle by acceleration of both hydride transfer and radical reduction.

As shown in Scheme 1, the reduction of haloalkanes would form Lewis acidic species such as $InX_{n+1}(OAc)_{2-n}$, and $PhSiH_2X$, which can lead to HX and its equivalents by the reaction with EtOH. The incomplete reduction of iodoalkanes by Method C is attributable to the acid-catalyzed solvolysis of $PhSiH_3$ with EtOH. To prove this hypothesis, the Me_3SiI (0.2 equiv)-catalyzed reaction of $PhSiH_3$ in EtOH (2 mL per 1 mmol of $PhSiH_3$) was performed and followed by GC analysis. The conversion of $PhSiH_3$ reached 54% at 40 min, and $PhSiH_3$ was mostly consumed in 3 h with the formation of $PhSiH(OEt)_2$ and $PhSi(OEt)_3$. Thus, $PhSiH_3$ easily underwent ethanolysis under the acidic conditions. The acid-catalyzed solvolysis of $PhSiH_3$ as well as the over-reduction of the In(III) catalyst is likely responsible for the incomplete reduction of bromoalkanes by Method C.

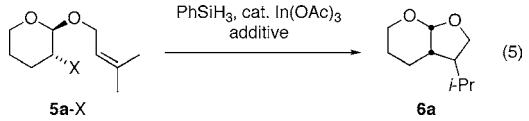
Expectedly, addition of 2,6-lutidine (0.5 equiv) effectively suppressed the Me_3SiI-catalyzed ethanolysis of $PhSiH_3$ (13% conversion at 2 h). This result indicates that, in the reduction by Method D, 2,6-lutidine serves not only for acceleration of hydride transfer from $PhSiH_3$ but also for neutralization of the reaction system to prevent the undesired reaction. The highly selective reduction of iodoketones **1j**-I and **1k**-I is explainable by the neutralization with 2,6-lutidine, which can suppress the acid-catalyzed reduction of the carbonyl group with $PhSiH_3$.

TABLE 4. $In(OAc)_3$-Catalyzed Cyclization of 5a-I with $PhSiH_3$[a]

entry	additive (equiv)	solvent	*T* (°C)	time (h)	yield (%)[b]
1	None	THF	70	24	CM[c]
2	AcOK (2)	THF	70	24	83
3	K_2CO_3 (1)	THF	70	24	95
4[d]	K_2CO_3 (1)	THF	30	24	42
5	None	EtOH	rt	6	46 (59)[e]
6	K_2CO_3 (1)	EtOH	rt	7[f]	65 (83)[e]
7	2,6-lutidine (0.5)	EtOH	rt	6	68 (87)[e]

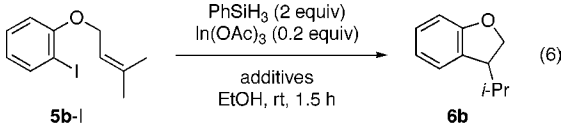
[a] Unless otherwise noted, all reactions were carried out with **5a**-I (0.50 mmol), $PhSiH_3$ (0.50 mmol), and $In(OAc)_3$ (0.05 mmol) in THF (0.5 mL) or EtOH (1.0 mL) under N_2 (2 L balloon). [b] Isolated yield. The diastereomeric ratio ranged from 64:36 to 76:24. [c] Complex mixture. [d] An increased amount of $In(OAc)_3$ (0.10 mmol) was used. [e] The result with increased amounts of $PhSiH_3$ (1.00 mmol) and $In(OAc)_3$ (0.10 mmol) is shown in parentheses. [f] When increased amounts of $PhSiH_3$ and $In(OAc)_3$ were used, the reaction was performed for 4.5 h.

Intramolecular Radical Addition. The reduction system using $In(OAc)_3$ and $PhSiH_3$ was also applied to radical cyclization of haloalkenes. Our attempts at an efficient cyclization of bromoalkene **5a**-Br were not successful (eq 5). We therefore directed our efforts to the cyclization of iodoalkene **5a**-I. The $In(OAc)_3$-catalyzed reaction of **5a**-I with $PhSiH_3$ in THF at 70 °C (Method A) gave a complex mixture of products (entry 1 in Table 4). However, the addition of K_2CO_3 or KOAc enabled high yields of **6a** (entries 2 and 3).[11] The cyclization in THF at 30 °C resulted in a low yield of **6a** (entry 4). In the presence of K_2CO_3 or 2,6-lutidine, an efficient cyclization in EtOH was achieved with increased amounts of $In(OAc)_3$ and $PhSiH_3$ (entries 6 and 7). Thus, the use of bases was effective in a smooth conversion of **5a**-I into **6a**. The bases would suppress destructive reactions of acetals **5a**-I and **6a** with acidic species generated in situ.



(5)

Next, the cyclization of iodoalkene **5b**-I was examined. Use of THF as a solvent gave discouraged results even in the presence of K_2CO_3. As the result of some reactions in EtOH, the combined use of dry air and K_2CO_3 or 2,6-lutidine as additives was found to achieve an efficient, rapid cyclization of **5b**-I (eq 6). Without these additives, the yield of **6b** was rather low.



(6)

no additive	23%
dry air	31%
2,6-lutidine (0.5 equiv)	5%
2,6-lutidine (0.5 equiv)-dry air[a]	87%, 96%[b]
K_2CO_3 (0.5 equiv)-dry air[a]	94%

[a] 10 mL of air per 0.5 mmol of **5b**-I. [b] The reaction time is 6 h.

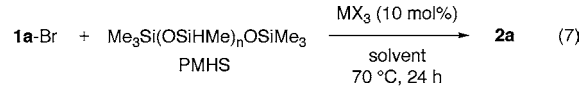
Use of PMHS. Poly(methylhydrosiloxane) (PMHS) has frequently been used as an inexpensive, stable reducing agent.[12]

(10) Bond dissociation enthalpies of carbon−halogen bonds suggest that primary bromoalkanes are less reactive toward homolytic substitution than iodoalkanes and secondary bromoalkanes. (a) Isaacs, N. S. *Physical Organic Chemistry*; Longman: Harlow, UK, 1987; p 36. Actually, halogen abstraction from iodoalkanes and secondary bromoalkanes with triorganostannyl radicals is faster than that from primary bromoalkanes. (b) Davies, A. G. *Organotin Chemistry*; Wiley-VCH: Weinheim, 2004; p 340. (c) Ito, O.; Hoteiya, K.; Watanabe, A.; Matsuda, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 962.

(11) Oshima et al. reported that the $GaCl_3$ (0.2 equiv)-catalyzed cyclization of **5a**-I using Red-Al (1.5 equiv) and Et_3B (0.2 equiv) gave **6a** in 79% yield. See ref 5.

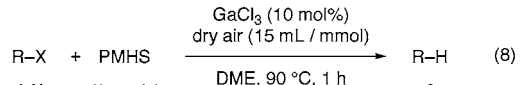
(12) Lawrence, N. J.; Drew, M. D.; Bushell, S. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3381.

Aiming at a more practical method for radical reduction of haloalkanes, PMHS was selected as a stoichiometric hydride source. In the reduction of **1a**-Br with PMHS at 70 °C, $GaCl_3$ showed higher activity than $InCl_3$ and $In(OAc)_3$ (eq 7). Use of 1,2-dimethoxyethane (DME) as solvent remarkably improved the reaction efficiency. The reaction at room temperature resulted in a poor yield of **2a** (DME, rt, 24 h, 10% yield). Raising the reaction temperature (90 °C) with an increased amount of PMHS (3 equiv) shortened the reaction time, and the introduction of dry air (15 mL per 1 mmol of **1a**-Br) also accelerated the reduction. Under the optimized conditions, the reduction of **1a**-Br was completed within 1 h to give **2a** in a quantitative yield (eq 8). Even with 5 mol % $GaCl_3$, the yield of **2a** reached 90%.



MX_3 (yield / %) (THF as solvent, PMHS (1 equiv)):
$In(OAc)_3$ (20), $InCl_3$ (3), $GaCl_3$ (45)

solvent (yield / %) ($GaCl_3$ as catalyst, PMHS (2 equiv)):
THF (65), MeCN (15), AcOEt (0),1,4-dioxane (80), DME (94)



1-X (yield / %): $Ph(CH_2)_3Br$ (99, 90*), $Ph(CH_2)_3I$ (99), $Ph(CH_2)_3Cl$ (6), *c*-$C_{12}H_{23}Br$ (92), *c*-$C_{12}H_{23}I$ (94), *c*-$C_{12}H_{23}Cl$ (<34), *n*-$C_8H_{17}O(CH_2)_3Br$ (69), $CH_3CH(OTBS)(CH_2)_{11}Br$ (74)
*With 5 mol% $GaCl_3$.

The $GaCl_3$-PMHS system was efficient in the reduction of non-functionalized bromo- and iodoalkanes but not in the reduction of chloroalkanes (eq 8). Bromoalkanes **1g**-Br and **1i**-Br, bearing an ether moiety, were reduced in good yield. In contrast, the reduction of **1h**-Br and **1j**-Br, bearing a hydroxy or carbonyl group, caused the destruction of these functionalities.

The $GaCl_3$-catalyzed reduction of **1a**-Br with PMHS did not occur in the presence of galvinoxyl. This observation and the rate-accelerating effect of air imply that the reduction proceeds via a radical chain process mediated by a gallium hydride species,[5,13] although the detailed mechanism is not clear.

Conclusion

We have demonstrated that indium and gallium salts can catalyze the dehalogenation of organic halides with hydrosilanes. The $In(OAc)_3$-$PhSiH_3$ reduction system is applicable to various bromo- and iodoalkanes. A plausible mechanism for this reduction involves radical reduction of haloalkanes with indium hydride species catalytically generated by transmetalation of $PhSiH_3$. Similar indium-catalyzed systems using $NaBH_4$, Bu_3SnH, hydrosilanes, and DIBAL-H as terminal reductants have been reported by other research groups.[4,5a] We have succeeded in catalytic radical reduction using $PhSiH_3$, a mild and less toxic reducing agent. The $In(OAc)_3$-$PhSiH_3$ system enables an efficient reduction of both simple and functionalized iodoalkanes in EtOH, a environmentally friendly solvent, with the aid of 2,6-lutidine and dry air. In addition, we have found that $GaCl_3$ is an effective catalyst of radical reduction with PMHS, an inexpensive hydrosilane. The present study has also disclosed that air plays an important role probably as radical initiator in these radical reductions using indium and gallium hydride species. In summary, we have developed new catalytic systems valuable for tin-free radical reactions.[14] Application of the $In(OAc)_3$-$PhSiH_3$ system to intermolecular radical addition of haloalkanes to electron-deficient alkenes is now under investigation, and the results will be reported in due course.

Experimental Section

General Procedure for $In(OAc)_3$-Catalyzed Reduction of Organic Halides with $PhSiH_3$ in THF (Method A, Entry 1 in Table 1). Under a nitrogen atmosphere (2 L balloon), 1-bromo-3-phenylpropane (**1a**-Br, 99 mg, 0.50 mmol) and $PhSiH_3$ (54 mg, 0.50 mmol) were added to a stirred suspension of $In(OAc)_3$ (15 mg, 0.050 mmol) in THF (0.5 mL). The mixture was warmed to 70 °C and stirred for 24 h. Saturated aqueous $NaHCO_3$ (0.5 mL) was added to the stirred reaction mixture at room temperature. The mixture was diluted with *t*-BuOMe and dried over Na_2SO_4. The dried solution was subjected to GC analysis using an internal standard (undecane) to determine the yield of the product, propylbenzene (**2a**, 94%); otherwise, it was evaporated and purified by silica gel column chromatography (hexane) to demonstrate the identity and purity of the product.

General Procedure for Et_3B-Initiated, $In(OAc)_3$-Catalyzed Reduction of Organic Halides with $PhSiH_3$ (Methods B and C, Entry 1 in Table 1). Under a nitrogen atmosphere (2 L balloon), 1-bromo-3-phenylpropane (**1a**-Br, 99 mg, 0.50 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), Et_3B (1.0 M in hexane, 0.10 mmol), and dry air (5 mL) were successively added to a stirred suspension of $In(OAc)_3$ (29 mg, 0.10 mmol) in THF (0.5 mL) at 30 °C (Method B). After being stirred for 24 h, the mixture was subjected to the same workup as performed in Method A. The yield of the product **2a** was determined by GC analysis (91%). In Method C, EtOH (1.0 mL) was used instead of THF.

General Procedure for $In(OAc)_3$-Catalyzed Reduction of Organic Halides with $PhSiH_3$ in EtOH Containing 2,6-Lutidine (Method D, Entry 3 in Table 2). Under a nitrogen atmosphere (2 L balloon), 1-iodododecane (148 mg, 0.50 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), dry air (5 mL), and 2,6-lutidine (27 mg, 0.25 mmol) were successively added to a stirred suspension of $In(OAc)_3$ (29 mg, 0.10 mmol) in ethanol (1.0 mL) at room temperature. After being stirred for 1.5 h, the mixture was subjected to the same workup as performed in Method A. The yield of the product, dodecane (**2b**), was determined by GC analysis (87%). Purification of the crude product by silica gel column chromatography (hexane) was performed to demonstrate the identity and purity of the product.

General Procedure for $GaCl_3$-Catalyzed Reduction of Organic Halides with PMHS in DME (eq 8). In a glove box filled with argon, $GaCl_3$ (18 mg, 0.10 mmol) was introduced into a reaction flask, which was brought out from the box and connected with an argon balloon (2 L). DME (1.0 mL), 1-bromo-3-phenylpropane (**1a**-Br, 199 mg, 1.00 mmol), PMHS (180 mg, 3.00 mmol of Si−H), and dry air (15 mL) were added to the flask. The stirred mixture was warmed to 90 °C. After being stirred for 1 h, the resultant mixture was cooled to room temperature and subjected to the same workup as performed in Method A. The yield of the product **2a** was determined by GC analysis (99%). Purification of the crude product by silica gel column chromatography (hexane) was performed to demonstrate the identity and purity of the product.

(13) It is known that $HGaCl_2$ can be prepared from $GaCl_3$ and Me_3SiH by transmetalation. Ohshita, J.; Schmidbaur, H. *J. Organomet. Chem.* **1993**, *453*, 7.

(14) (a) *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001. (b) Baguley, P. A.; Walton, J. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3073.

Demonstration of Identity and Purity of Products. When the product was known and commercially available, its identity was demonstrated by comparison with the authentic sample in ^{1}H NMR and GC data. When the product was known, but not commercially available, its identity was demonstrated by comparison of the ^{1}H NMR data with the reported ones. For demonstration of purity of the known products, copies of the ^{1}H NMR spectra are presented in the Supporting Information. Identity and purity of products whose ^{1}H NMR data are not available were demonstrated by full characterization as described next.

1-Propoxyoctane (2g). Bp 95 °C (0.5 Torr, bath temp). IR (neat) 2958, 2927, 2856, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H), 1.25−1.36 (m, 10H), 1.52−1.66 (m, 4H), 3.36 (t, J = 6.8 Hz, 2H), 3.40 (t, J = 6.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 10.6 (CH_3), 14.1 (CH_3), 22.7 (CH_2), 22.9 (CH_2), 26.2 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 70.9 (CH_2), 72.6 (CH_2); MS *m*/*z* (relative intensity) 143 ($M^+ - C_2H_5$, 0.3), 129 ($M^+ - C_3H_7$, 0.3), 57 (100). Anal. Calcd for $C_{11}H_{24}O$: C, 76.68; H, 14.04%. Found: C, 76.29; H, 13.99%.

2-Tridecanol (2h). Bp 155 °C (0.5 Torr, bath temp). IR (neat) 3346 (br, OH), 2958, 2925, 2854 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3H), 1.19 (d, J = 6.3 Hz, 3H), 1.20−1.50 (m, 21H), 3.73−3.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.7 (CH_2), 23.4 (CH_3), 25.8 (CH_2), 29.3 (CH_2), 29.61 ($CH_2 \times 3$), 29.64 ($CH_2 \times 2$), 31.9 (CH_2), 39.3 (CH_2), 68.2 (CH); MS *m*/*z* (relative intensity) 185 ($M^+ - CH_3$, 0.5), 182 ($M^+ - H_2O$, 0.7), 45 (100). Anal. Calcd for $C_{13}H_{28}O$: C, 77.93; H, 14.09%. Found: C, 77.75; H, 14.24%.

2-(*t*-Butyldimethylsiloxy)tridecane (2i). Bp 190 °C (0.5 Torr, bath temp). IR (neat) 2927, 2856, 1254, 835, 773 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 6H), 0.85−0.90 (m, 12H) including 0.88 (s), 1.11 (d, J = 6.1 Hz, 3H), 1.19−1.45 (m, 20H), 3.71−3.82 (m, 1H); ^{13}C NMR ($CDCl_3$), δ −4.7 (CH_3), −4.4 (CH_3), 14.1 (CH_3), 18.2 (C), 22.7 (CH_2), 23.8 (CH_3), 25.8 (CH_2), 25.9 ($CH_3 \times 3$), 29.3 (CH_2), 29.7 ($CH_2 \times 5$), 31.9 (CH_2), 39.8 (CH_2), 68.7 (CH); MS *m*/*z* (relative intensity) 257 ($M^+ - C_4H_9$, 18), 159 (4.0), 75 (100). Anal. Calcd for $C_{19}H_{42}OSi$: C, 72.53; H, 13.46%. Found: C, 72.60; H, 13.12%.

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Supporting Information Available: Procedure for the synthesis of substrates, the cyclization of iodoalkenes **5**-I, and the experiments for mechanistic insights. Analytical and spectral characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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