Studies on Indium-Catalyzed Synthetic Reactions Using Hydrosilanes

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General Introduction

The importance of indium chemistry has been almost entirely due to the significance of indium semiconductors and other relevant materials. However indium has recently emerged as a metal of high potential in organic synthesis because of certain unique properties that it possesses. Indium metal is unaffected by air or oxygen at ambient temperatures and can be handled safely without any apparent toxicity. Indium chemistry directed towards organic synthesis closely parallels the chemistry of certain transition metals and other heavier main group elements such as zinc and tin, making possible a wide variety of organic useful transformations known for these metals.[1]

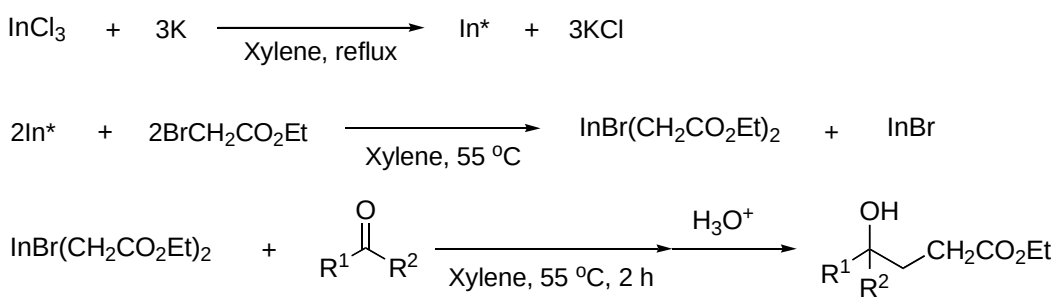
What are the 'appealing' properties of indium making it different from most other elements used as reagents in similar reactions like magnesium, zinc, tin, and others? The most appealing point is that, its first ionization potential is much lower than that of zinc or tin, and for that matter, even magnesium. In addition, the difference between the second and third ionization potential in indium is much smaller than that in zinc (Table 1). If the reactions of organic compounds with metals proceed through a single electron transfer (SET) mechanism, indium may well be effective in such reactions.[2]

Table 1. First to Fourth Ionization Potential of Some Metals

Metal	Ionization Potential (eV)			
	I	II	III	IV
Indium	5.785	18.86	28.03	54.4
Aluminum	5.984	18.82	28.44	119.96
Magnesium	7.646	15.035	80.143	109.29
Zinc	9.39	17.96	39.7	
Tin	7.34	14.63	30.49	40.72

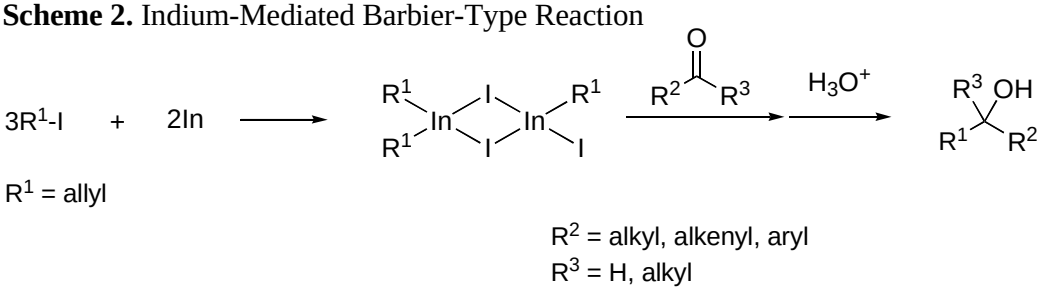
The first example of an indium-mediated reaction was published by Rieke and co-worker in 1975. To accomplish the reaction, they used especially activated indium metal prepared from indium chloride and potassium metal. This activated indium efficiently mediated the Reformatsky-type reaction of ethyl bromoacetate with carbonyl compounds (Scheme 1).[3]

Scheme 1. Indium-Mediated Reformatsky-Type Reaction

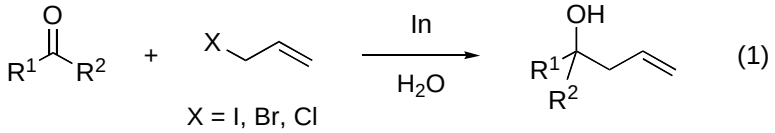


Since 1988 when Araki and Butsugan used indium for the Barbier-type addition of allyl bromide to carbonyl compounds, synthetic use of indium metal has attracted considerable attention from many research groups working on the development of new synthetic methods, and a number of indium-mediated reactions have been reported (Scheme 2).[4]

Scheme 2. Indium-Mediated Barbier-Type Reaction

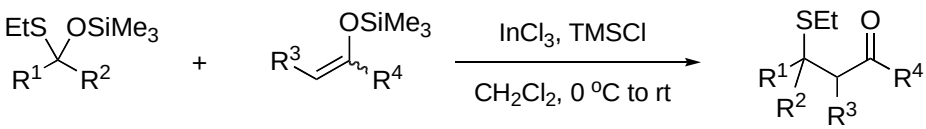


Although some indium-mediated reactions are unprecedented in organic synthesis and offer inherent advantages over other metals and organometallics, the reactivity and selectivity of indium species in organic solvents are, in many instances, comparable to those of zinc[5], tin[6] and other metal species.[7] At this stage of knowledge, one could consider organoindium compounds as reagents looking for a problem. The recent development of aqueous organometallic reactions, assisted by elemental metals and water-tolerant organometallics, has turned considerable attention to the use of indium species in view of its exceptional stability to air and water. In fact, synthetic reactions in aqueous media evidence the advantages of indium reagents. For example, indium metal effects the allylation of aldehydes and ketones with allyl halides in water at room temperature without inert atmosphere (Eq. 1).[2]



(1)

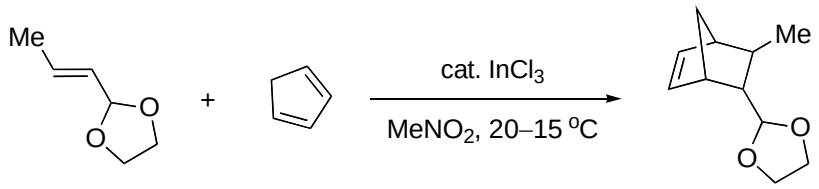
Lewis acids play a vital role in synthetic organic reactions since their use avoids the conventional, traditional and corrosive or harsh acid-catalyzed route. Lewis acids most habitually encountered in organic synthesis are $AlCl_3$, BF_3-Et_2O, $ZnCl_2$ and $SnCl_2$. Even though indium belongs to the same group in the periodic table as boron and aluminum, indium salts as Lewis acids for organic reactions had not been exploited unlike the other Lewis acids.[8] But recently, it has been proven that indium salts are mild, worthwhile Lewis acids. In 1990, Mukaiyama and Kobayashi reported that a chlorotrimethylsilane-indium (III) chloride complex is effective in promoting the carbon-carbon bond-forming reaction of *O*-trimethylsilyl monothioacetal with silylenolates (Eq. 2). Since this pioneering work, indium salts have frequently been used as Lewis acids for a wide variety of organic transformations.[9a]



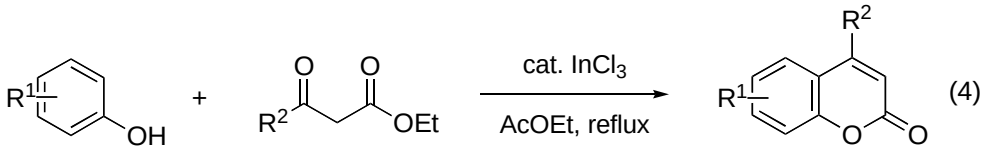
(2)

Indium salts such as indium halides are useful for the syntheses of aryl hydrazides,[9b] 2-haloamines,[9c] *cis*-aziridinecarboxylates,[9d] chiral furan diol,[9e] quinolines,[9f] and homoallyl acetates.[9g] They serve as efficient catalysts for various synthetic reactions: reductive Friedel-Crafts alkylations of aromatics with ketones and

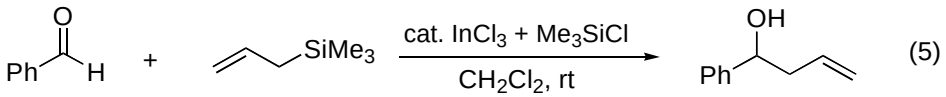
aldehydes,[9h-i] the allylation of acid chlorides with allylstannanes,[9j] the insertion of α-diazoketones,[9k] Biginelli reaction,[9l] conjugate addition of indoles to electron-deficient olefins,[9m] Diels–Alder reactions (Eq. 3),[9n-q] Pechmann reactions (Eq. 4),[9r] Hosomi–Sakurai reactions (Eq.5),[9s-t] and so on.[10]



(3)

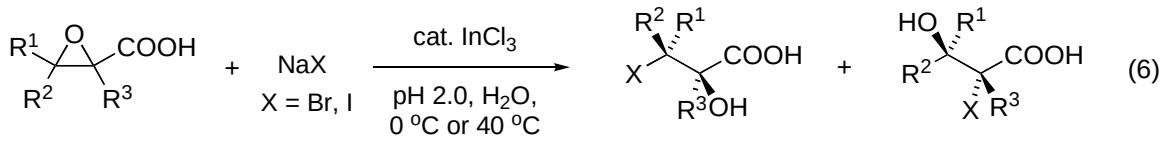


(4)



(5)

Indium(III) chloride ($InCl_3$) is relatively stable in aqueous media although it acts as a mild Lewis acid. For this reason, $InCl_3$ has been used as Lewis acid catalyst for synthetic reactions in H_2O such as ring-opening reactions of α,β-epoxycarboxylic acids (Eq. 6),[11a] Mukaiyama and direct aldol reactions (Eq. 7),[8c,11b] Diels–Alder reactions (Eq. 8),[8c,11e] and so on.[11f-h]



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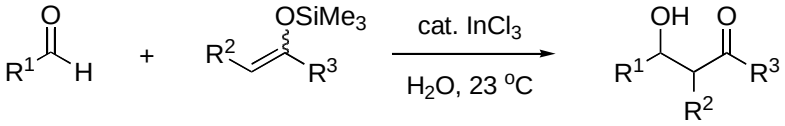
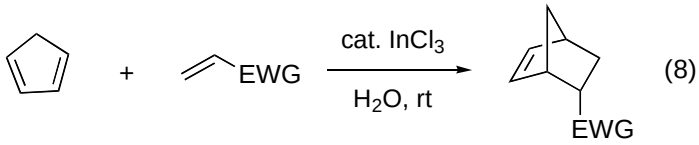
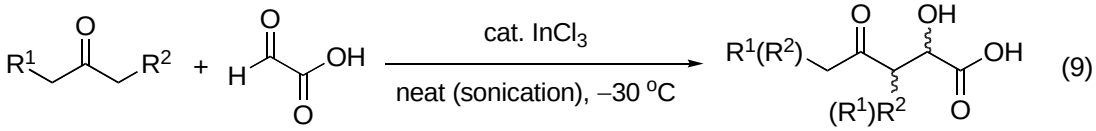


(7)



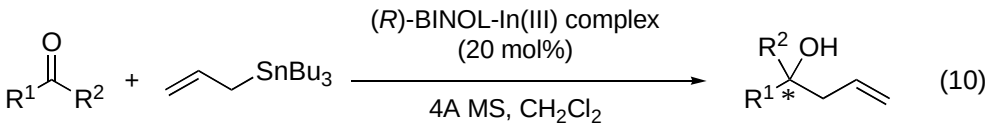
(8)

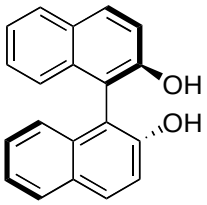
The mild Lewis acidity of $InCl_3$ allows, the direct aldol reactions of various ketones with glyoxylic acid and glyoxylates under solvent-free conditions (Eq. 9).[12]



(9)

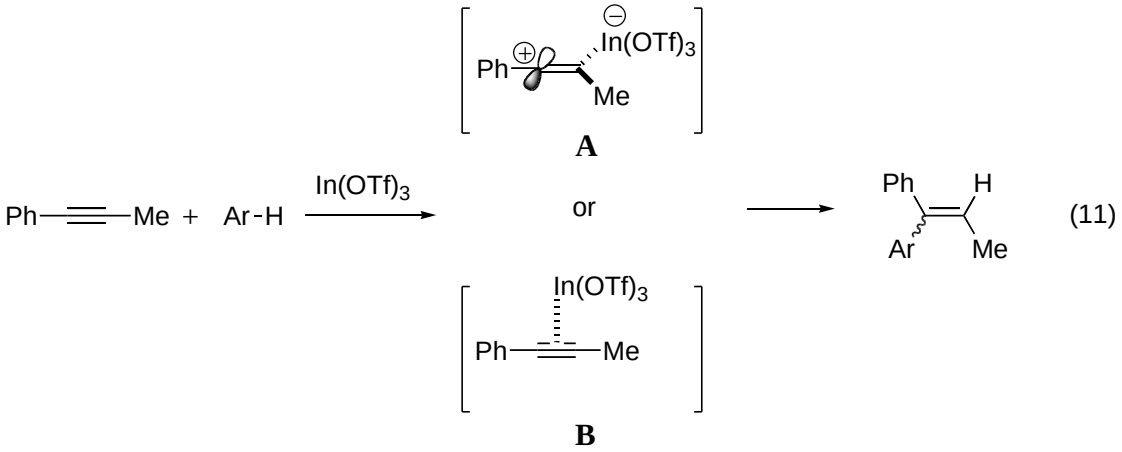
Chiral indium catalysts prepared from indium salts and homochiral ligands are valuable for catalytic, asymmetric carbon–carbon bond formation. Particularly, Loh and co-workers have reported highly enantioselective allylation of carbonyls using a chiral indium catalyst derived from BINOL (Eq. 10).[13]



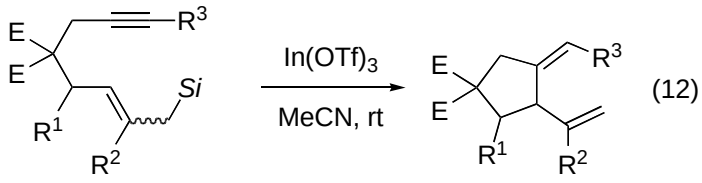


(*R*)-BINOL

Indium salts are effective not only in carbonyl activation but also in the activation of carbon–carbon triple bonds. The role as π-Lewis acid enhances the reactivity of alkynes to nucleophiles.[14] For example, Shirakawa and co-workers reported a Friedel–Crafts type alkenylation of arenes with 1-aryl-1-alkynes under catalysis by indium(III) triflate ($In(OTf)_3$).[14a] A plausible mechanism for this alkenylation involves zwitterionic species **A** or an indium-alkyne complex **B**, which causes electrophilic substitution of arenes to give 1,1-diaryl-1-alkenes (Eq. 11).

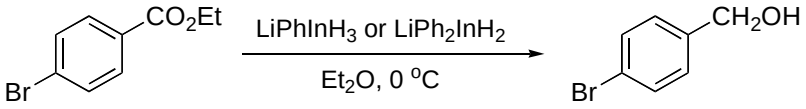


This research group has previously reported the $In(OTf)_3$-catalyzed intramolecular allylation of alkynes with allylsilanes (Eq. 12). Also in this reaction, $In(OTf)_3$ would act as π-Lewis acid to activate the triple bond.[14g]



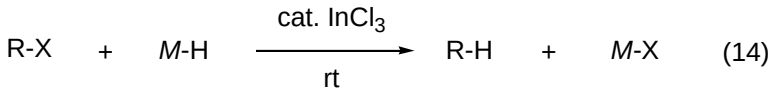
E = MeO_2C
Si = $SiMe_3$, $SiMe_2Ph$

Indium hydrides were not utilized for synthetic reactions, though they had been known since the old days.[15] It is probably because indium hydrides are unstable and less reactive to carbon electrophiles. In particular, indium trihydride (InH_3) is readily decomposed into indium metal and hydrogen.[16] Wiberg and Schmidt, who first prepared InH_3, disclosed its reducing ability: acetamide, acetonitrile, butanoic acid, and quinone were reduced with InH_3, whereas butanal, benzaldehyde, and 4-butanolide were inert.[17] Butsugan and Araki demonstrated that lithium phenylindium hydrides ($LiPhInH_3$ and $LiPh_2H_2$) are useful for selective reduction of various organic compounds. These reagents can reduce esters and epoxides at room temperature. $NaBH_4$ does not reduce these compounds under the same conditions. Unlike $LiAlH_4$, $LiPhInH_3$ and $LiPhInH_2$ are unreactive to nitriles. Therefore, these lithium phenyl indium hydrides are roughly intermediate between $LiAlH_4$ and $NaBH_4$ in reducing ability (Eq. 13).[18]



(13)

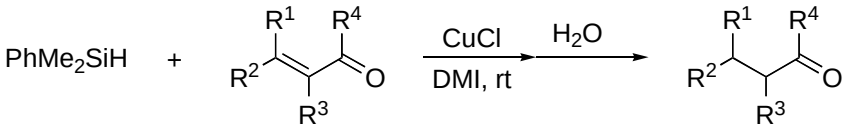
Baba and Shibata reported that $HInCl_2$, prepared from $InCl_3$ and Bu_3SnH,[20] mediated radical reductions of organic halides. Then they developed an $InCl_3$-catalyzed radical reduction using $NaBH_4$ as the stoichiometric reducing agent. In this reduction, $HInX_2$ (X= halogen) is regenerated in situ by the reaction of InX_3 with $NaBH_4$.[20] Carbon radicals generated from organic halides by this method are useful for intramolecular radical addition to alkenes. Similar catalytic systems have recently been achieved by using other hydride sources such as DIBAL-H,[21] Et_3SiH,[22] and so on.[23] Radical-initiated addition of $HInCl_2$ to alkynes provides a stereoselective route to vinylindiums. $HInCl_2$ is effective also in reduction of aldehydes and electron-deficient alkenes by a polar process.



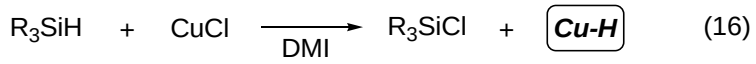
(14)

M-H = Bu_3SnH, $NaBH_4$, DIBAL-H, Et_3H

Continuous efforts to develop synthetic use of hydrosilanes have been made in this laboratory. In general, hydrosilanes are insensitive to carbon electrophiles. Activation of hydrosilanes with an additive is a solution for an efficient reduction of carbon electrophiles. This laboratory previously developed the CuCl-promoted 1,4-reduction of α-enones with hydrosilanes (Eq. 15). A proposed mechanism involves a copper hydride species as an active reducing agent, which is generated by transmetalation between hydrosilanes and CuCl (Eq. 16). The author therefore focused his interests on catalytic activation of hydrosilanes with other metal salts. As the results of many attempts, he found that indium(III) acetate ($In(OAc)_3$) effectively promoted the reduction of α-enones with phenylsilane ($PhSiH_3$). Thus the catalytic system using $In(OAc)_3$ and $PhSiH_3$ was applied to reduction and carbon–carbon bond formation of carbon electrophiles.



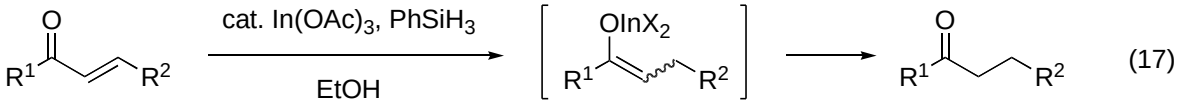
(15)



This thesis consists of the following three parts.

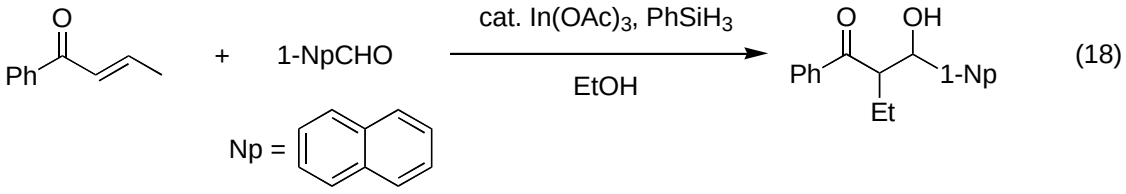
(1) Indium(III)-Catalyzed Reduction of Carbonyl Compounds with Phenylsilane and Its Application to Carbon-Carbon Bond Formation
(2) Indium(III)-Catalyzed Reduction of Organic Halides with Hydrosilanes via a Radical Chain Process
(3) Indium(III)-Catalyzed Intermolecular Radical Addition of Organic Halides to Electron-Deficient Alkenes

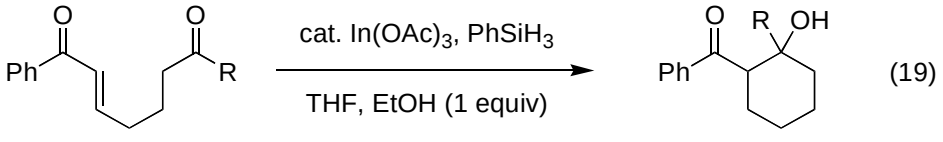
In Chapter 1, the author mainly described the $In(OAc)_3$-catalyzed reaction of α-enones with $PhSiH_3$. He found that $In(OAc)_3$ catalyzed the 1,4-reduction of α-enones with $PhSiH_3$ in EtOH at room temperature (Eq. 17). A plausible mechanism for this reduction involves the formation of an indium hydride species, its 1,4-reduction to α-enones, and solvolysis of the resultant indium enolate. This catalytic system is unable to reduce of aldehydes.



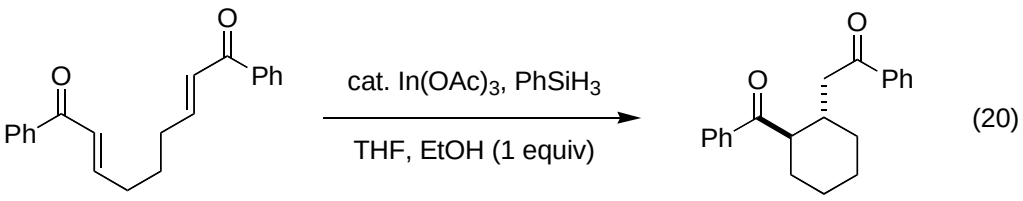
R^1 and R^2 = Ph, Me, *etc*.

The indium enolate intermediate was successfully utilized for inter- and intramolecular carbon–carbon bond formation. Thus the $In(OAc)_3$-catalyzed reaction of α-enones with $PhSiH_3$ and aldehydes gave aldols in moderate to good yield with *syn*-stereoselectivity (Eq. 18). In the intramolecular version, the enolate intermediate added smoothly to formyl and acetyl groups (Eq. 19) and an enone moiety (Eq. 20).



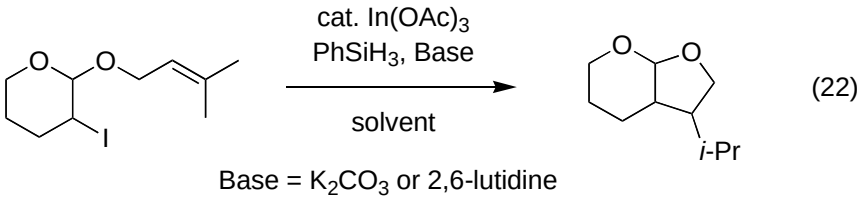


R = H, Me



Chapter 2 discloses the $In(OAc)_3$-catalyzed hydrodehalogenation of organic halides with $PhSiH_3$. The $In(OAc)_3$–$PhSiH_3$ system is effective also in highly chemoselective reduction of bromo- and iodoalkanes (Eq. 21). The reduction mechanism includes a radical chain process via carbon radicals, in which an indium hydride species acts as an active reducing agent and an chain carrier. The intermediary carbon radical is valuable for intramolecular carbon–carbon bond formation (Eq. 22).

$$\mathrm{RPX} + \mathrm{PhSiH_3} \xrightarrow[\text{THF or EtOH}]{\text{cat. } In(OAc)_3\text{, (additive)}} \mathrm{RPH} \qquad (21)$$



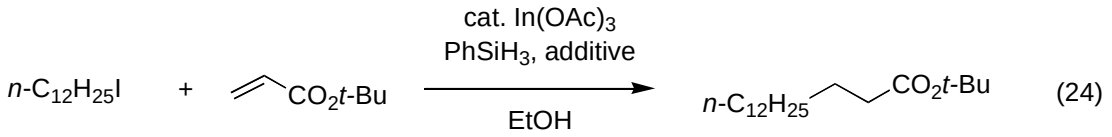
(22)

Base = K_2CO_3 or 2,6-lutidine

It was also found that the combination of gallium(III) chloride ($GaCl_3$) with poly(methylhydro-siloxane) (PMHS) serves for radical reduction of organic halides (Eq. 23). This reduction system, however, is not tolerant to polar functional groups.

$$\mathrm{RPX} + \mathrm{PMHS} \xrightarrow[\text{DME}]{\text{cat. } GaCl_3\text{, air}} \mathrm{RPH} \qquad (23)$$

Chapter 3 deals with the application of the $In(OAc)_3$–$PhSiH_3$ system to intermolecular radical addition of organic halides. In the presence of $In(OAc)_3$ and $PhSiH_3$, iodoalkanes added smoothly to electron-deficient alkenes. Use of 2,6-lutidine and air as additives improved the reaction efficiency (Eq. 24). Simple and functionalized iodoalkanes and iodoarenes are applicable to this intermolecular addition.



(24)

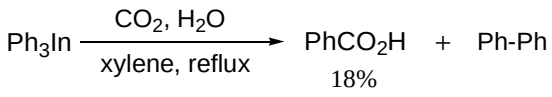
additive = air, 2,6-lutidine, H_2O

References

1. (a) Cintas, P. *Synlett* **1995**, 1087. (b) Ranu, B. C. *Eur. J. Org. Chem*. **2000**, 2347. (c) Podlech, J.; Maier, T. C. *Synthesis* **2003**, *5*, 633.
2. (a) Li, C. J.; Chan, T. H. *Tetrahedron Lett*. **1991**, *32*, 7017. (b) Loh, T. –P.; Chua, G. –L. *Chem. Commun.* **2006**, 2739.
3. Chao, L. –C.; Rieke, R. D. *J. Org. Chem*. **1975**, *40*, 2253.
4. Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem*. **1988**, *53*, 2253.
5. Wilson, S. R.; Guazzaroni, M. E. *J. Org. Chem*. **1989**, *54*, 3087.
6. Wu, S.; Huang, B.; Gao, X. *Syn. Commun.* **1990**, *20*, 1279.
7. Einhorn, C.; Einhorn, J.; Luche, J. –L. *Synthesis* **1989**, 787.
8. (a) Babu, S, A, *Synlett* **2002**, *3*, 531. (b) Ranu, B. C. *Eur. J. Org. Chem*. **2000**, 2347. (c) Chauhan, K. K.; Frost, C. G.. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015. (d) Yasuda, M. *Journal of Synthetic Organic Chemistry* **2007**, *65*, 99. (e) Onishi, Y.; Ito, T.; Yasuda, M.; Baba, A. *Tetrahedron* **2002**, *58*, 8227.
9. (a) Mukaiyama, T.; Ohno, T.; Nishimura, T.; Han, J. S.; Kobayashi, S. *Chem. Lett*. **1990**, 2239. (b) Yadav, J. S.; Reddy, B. V. S.; Kumar, G. M. Madan, C. *Synlett* **2001**, 1781. (c) Yadav, J. S.; Reddy, B. V. S.; Kumar, G. M. *Synlett* **2001**, 1417. (d) Sengupta, S.; Mondal, S. *Tetrahedron Lett*. **2000**, *41*, 6245. (e) Babu, B. S.; Balasubramanian, K. K. *J. Org. Chem*. **2000**, *65*, 4198. (f) Ranu, B. C.; Hajra, A.; Jana, U. *Tetrahedron Lett*. **2000**, *41*, 531. (g) Yadav, J. S.; Reddy, B. V. S.; Madhuri, C. H.; Sabitha, G.. *Chem Lett*. **2001**, 18. (h) Miyai, T.; Onishi, Y.; Baba, A. *Tetrahedron* **1999**, *55*, 1017. (i) Miyai, T.; Onishi, Y.; Baba, A. *Tetrahedron Lett.* **1998**, *39*, 6291. (j) Inoue, K.; Shimizu, Y.; Shibata, I.; Baba, A. *Synlett* **2001**, 1659. (k) Sengupta, S.; Mondal, S. *Tetrahedron Lett*. **1999**, *40*, 8685. (l) Ranu, B. C.; Hajra, A.; Jana, U. *J. Org. Chem*. **2000**, *65*, 6270. (m) Yadav, J. S.; Abraham, S.; Reddy, B. V. S.; Sabitha, G. *synthesis* **2001**, 2165. (n) T. Ali, K. K. Chauhan and C. G. Frost, *Tetrahedron Lett.* **1999**, *40*, 5621. (o) Reddy, B. G.; Kumareswaran, R.; Vankar, Y. D. *Tetrahedron Lett.* **2000**, *41*, 10333. (p) Prajapati, D.; Laskar, D. D.; Sandhu, J. S. *Tetrahedron Lett.* **2000**, *41*, 8639. (q) Ali, T.; Chauhan, K. K.; Frost, C. G. *Tetrahedron Lett.* **1999**, *40*, 5621. (r) Bose, D. S.; Rudradas, A. P.; Babu, M. H. *Tetrahedron Lett*. **2002**, *43*, 9195. (s) Lee, P. H.; Lee, K.; Sung, S. -Y.; Chang, S.; *J. Org. Chem*. **2001**, *66*, 8646. (t) Onishi. Y.; Ito, T.; Yasuda, M.; Baba, A. *Eur. J. Org. Chem.* **2002**, 1578.
10. (a) Muthusamy, S.; Babu, S. A.; Gunanathan, C. *Tetrahedron Lett.* **2001**, *42*, 359. (b) Babu, B. S.; Balasubramanian, K. K. *Tetrahedron Lett.* **2000**, *41*, 1271. (c) Ranu, B. C.; Jana, U. *J. Org. Chem*. **1998**, *63*, 8212. (d) Reddy, B. G.; Kumarewswaran, R.; Vankar, Y. D. *Tetrahedron Lett.* **2000**, *41*, 10333. (e) Inoue, K.; Yasuda, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 113. (f) Ranu, B. C.; Jana, U. *J. Org. Chem*. **1998**, *63*, 8212. (g) Onishi. Y.; Ito, T.; Yasuda, M.; Baba, A. *Tetrahedron* **2002**, *58*, 8227. (h) Nakamura, M.; Endo, K.; Nakamura, E. *J. Am. Chem. Soc.* **2003**, *125*, 13002. (i) Yasuda, M.; Yamasaki, S.; Onishi, Y.; Baba, A. *J. Am. Chem. Soc*. **2004**, *126*, 7186. (j) Anniyappan, M.; Muralidharan, D.; Perumala, P. T.; Vittal, J. J.; *Tetrahedron* **2004**, *60*, 2965. (k) Yasuda, M.; Yamasaki, S.; Onishi, Y.; Baba, A. *J. Am. Chem. Soc*. **2004**, *126*, 7186. (l) Liu, L. -L.; Tang, L.; Yu, L.; Cang, W. -X, Li, J. *Tetrahedron* **2005**, *61*, 10930. (m) Babu, S. A.; Yasuda, M.; Okabe, Y.; Shibata, I.; Baba, A. *Org. Lett*. **2006**, *8*, 3029. (n) Babu, S. A.; Yasuda, M.; Shibata, I.; Baba, A. *Org. Lett*. **2007**, *9*, 405. (o) Nishimoto, Y.; Yasuda, M.; Baba, A. *Org. Lett*. **2007**, *9*, 4931. (p) Yasuda, M.;

Onishi, Y.; Ito, T.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 2425. (r) Babu, G.; Perumal, P. T. *Tetrahedron* **1999**, *55*, 4793.

11. (a) Amantini, D.; Fringuelli, F.; Pizzo, F.; Vaccaro, L. *J. Org. Chem*. **2001**, *66*, 4463. (b) Loh, T. -P.; Pei, J.; Cao, G. -Q. *Chem. Commun.* **1996**, 1819. (c) Kobayashi, S.; Busujima, T.; Nagayama, S. *Tetrahedron Lett.* **1998**, *39*, 1579. (d) Kobayashi, S.; Nagayama, S.; Busujima, T. *J. Am. Chem. Soc.* **1998,** *120*, 8287. (e) Loh, T. -P.; Pei, J.; Lin, M. *Chem. Commun.*, **1996**, 2315. (f) Lu, W.; Chan, T. H. *J. Org. Chem*. **2000**, *65*, 8589. (g) Cho, Y. C.; Kim, H. Y.; Cha, J. H.; Pae, A. N.; Koh, H. Y.; Choi, J. H.; Chang, M. H. *Org. Lett.* **2002**, *4*, 2025. (h) Loh, T. –P.; Wei, L. -L. *Tetrahedron Lett.* **1998**, 39, 323.
12. Loh, T. -P.; Feng, L. -C.; Wei, L. -L. *Tetrahedron* **2001**, *57*, 4231.
13. (a) Loh, T. -P.; Lu, J.; Hong, M. L.; Ji, S. J.; Teo, Y. C. *Chem. Commun.* **2005**, 4217. (b) Loh, T. -P.; Teo, Y. C.; Goh, J. D. *Org. Lett.* **2005**, *7*, 2743. (c) Teo, Y. -C.; Tan, K. -T.; Loh, T. -P. *Chem. Commun.* **2005**, 1318. (d) Lu, J.; Ji, S. -J.; Loh, T. -P. *Chem. Commun.* **2005**, 2345. (e) Teo, Y. -C.; Tan, K. -T.; Loh, T. -P. *Org. Lett.* **2005**, *7*, 2539. (f) Zhang, X.; Chen, D.; Liu, X.; Feng, X. *J. Org. Chem.* **2007**, *72*, 5227. (g) Takita, R.; Yakura, K.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, 127, 13760.
14. (a) Tsuchimoto, T.; Maeda, T.; Shirakawa, E.; Kawakami, Y. *Chem. Commun.* **2000**, 1573. (b) Tsuchimoto, T.; Matsubayashi, H.; Kaneko, M.; Shirakawa, E.; Kawakami, Y. *Angew. Chem. Int. Ed*. **2005**, *44*, 1336. (c) Tsuchimoto, T.; Hatanaka, K.; Shirakawa, E.; Kawakami, Y. *Chem. Commun.* **2003**, 2454. (d) Harada, S.; Takita, R.; Ohshima, T.; Matsunaga, S.; Shibasaki, M. *Chem. Commun.* **2007**, 948. (e) Lin, M. -J.; Loh, T. -P. *J. Am. Chem. Soc.* **2003**, *125*, 13042. (f) Zhang, J.; Blazecka, P. G.; Angell, P.; Lovdahl, M.; Curran, T. T. *Tetrahedron* **2005**, *61*, 7807. (g) Miura, K.; Fujisawa, N.; Toyohara, S.; Hosomi, A. *Synlett* **2006**, 1883. (h) Tsuchimoto, T.; Matsubayashi, H.; Kaneko, M.; Shirakawa, E.; Kawakami, Y. *Angew. Chem. Int. Ed*. **2005**, *44*, 1336.
15. (a) Grundstroem, B. *Nature* **1938**, *141*, 555. (b) Dennis, L. M.; Work, R. W.; Rochow, E. G.; Chamot, E. M. *J. Am. Chem. Soc.* **1934**, *56*, 1047. (c) Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 2353. (One example of alkyl indium reaction is reported. This organic reaction may be the oldest among the reactions where the indium species was used.[15c])



16. Hibbs, D. E.; Jones, C.; Smithies, N. A. *Chem. Commum*. **1999**, 185.
17. Wiberg, E.; Schmidt, M. *Zeitschrft fuer Natuerforschung. Teil B, Chemie, Biochemie, Biophysik, Biologie und Verwandte Gebiete* **1957**, *12b*, 54.
18. (a) Yamada, M.; Tanaka, K.; Araki, S.; Butsugan, Y. *Tetrahedron Lett.* **1995**, *36*, 3169. (b) Yamada, M.; Horie, T.; Kawai, M; Yamamura, H.; Araki, S. *Tetrahedron* **1997**, *46*, 15685.
19. (a) Miyai, T.; Inoue, K.; Yasuda, M.; Shibata, I.; Baba, A. *Tetrahedron Lett*. **1998**, *39*, 1929. (b) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *Tetrahedron Lett*. **2001**, *42*, 4661. (c) Hayashi, N.; Honda, H.; Yasuda, M.; Shibata, I.; Baba, A. *Org. Lett.*, **2006,** *8*, 4553.
20. (a) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc*. **2002**, *124*, 906. (b) Ranu, B. C.; Samanta, S. *Tetrahedron Lett*. **2002**, *43*, 7405.
21. Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima.; K. *Tetrahedron* **2003**, *59*, 6627.
22. Hayashi, N.; Shibata, I.; Baba, A. *Org. Lett.*, **2004,** *6*, 4981.

23. Hayashi, N.; Shibata, I.; Baba, A. *Org. Lett*. **2005,** *7*, 3093.
24. Shibata, I.; Kato, H.; Shibata, I.; Yasuda, M.; Baba, A. *Angew. Chem. Int. Ed*. **2004**, *43*, 711.
25. (a) Ito, H.; Ishizuka, T.; Tateiwa, J.; Sonoda, M..; Hosomi, A. *J. Am. Chem. Soc.* **1998**, *120*, 11196. (b) Ito, H.; Sensui, H.; Arimoto, K.; Miura, K.; Hosomi, A. *Chem. Lett*. **1997**, 639. (c) Ito, H.; Arimoto, K.; Sensui, H.; Hosomi, A. *Tetrahedron Lett*. **1997**, *38*, 3977.
26. (a) Ito, H.; Ishizuka, T.; Arimoto, K.; Miura, K.; Hosomi, A. *Tetrahedron Lett*. **1997**, *38*, 8887. (b) Ito, H.; Yamanaka, H.; Ishizuka, T.; Tateiwa, J.; Hosomi, A. *Synlett* **2000**, 479.

General Method

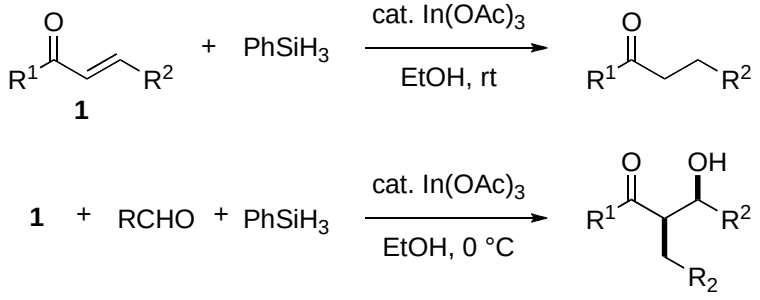
Unless otherwise noted, all reactions and distillation were carried out under N_2. Solvents were dried by distillation from sodium metal/benzophenone ketyl (THF, Et_2O), CaH_2 (MeCN, CH_2Cl_2, $CHCl_3$), and magnesium (MeOH, EtOH). Haloalkanes were distilled from pure copper wires and stored in the presence of copper splinter. $Me_3SiOS(O)_2CF_3$ (TMSOTf) were simply distilled and stored as a CH_2Cl_2 solution (1.0 M). Amines, H_2O, and $PhSiH_3$ were simply distilled. All other commercially obtained reagents were used as received. Gas chromatography was carried out with Shimadzu GC-8A (Shimadzu glass column 8G, 3.2 mm x 2.0 m; 15% of SE-30 on Chromosorb WAW-DMCS 60-80 mesh; 60 mL/min N_2) and GC-17A (Restec capillary column, 0.25 mm x 30 m; Crossbond® 100% dimethyl polysiloxane 0.25μm; 40 mL/min N_2). Boiling points were determined by measuring the temperature of steam at the inlet of condenser. Bath temperature was employed as boiling point in distillation using Kugelrohr apparatus. Infrared spectra were measured with a JASCO FT/IR-230 spectrophotometer. ^1H NMR spectra at 270 MHz and ^{13}C NMR spectra at 67.7 MHz were recorded on a JEOL JNM-EX270 instrument. The chemical shifts (δ) are reported with reference at 0.00 ppm (Me_4Si), 7.26 ppm ($CHCl_3$), 7.20 ppm (C_6D_6), or 127.95 ppm (centered on the signal of C_6D_6) for the carbon. Mass spectra were measured (by EI method) on a Shimadzu GCMS-QP5000 and QP5050 instruments. Elemental analysis was performed by the Analysis Center of University of Tsukuba.

Chapter 1

Indium(III)-Catalyzed Reduction of Carbonyl Compounds with Phenylsilane and Its Application to Carbon−Carbon Bond Formation

Abstract

A catalytic amount of indium(III) acetate smoothly promoted 1,4-reduction of certain α-enones with phenylsilane in ethanol at ambient temperature. Aldehydes were also reduced to alcohols under these conditions. The intermediary enolates in the reduction of α-enones could be used for inter- and intramolecular aldol reactions and intramolecular Michael addition.



1. Introduction

Catalytic 1,4-hydrometalation of α-enones provides a reliable and efficient method for regioselective formation of metal enolates.[1-4] Recently, much attention has been paid for the development of catalytic systems effecting both the enolate formation and the subsequent reaction with coexistent carbon electrophiles.[5-7] Some transition metal salts and complexes work as effective catalysts of this tandem process. All catalytic systems except those reported by Krische's group[5,7] were utilized only for reductive aldol reactions of α-enones with aldehydes.

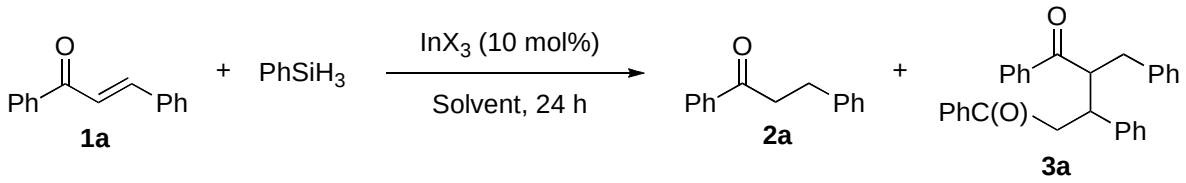
The author herein discloses that $In(OAc)_3$ efficiently catalyzes the reduction of certain α-enones, aldehydes, and the related compounds with $PhSiH_3$. The reduction of α-enones proceeds via a 1,4-hydrometalation. The intermediary enolates can be used for carbon–carbon bond-forming reactions with aldehydes, ketones, and α-enones. In this context, Ranu and co-workers have reported the $InCl_3$-catalyzed 1,4-reduction of electron-deficient alkenes with $NaBH_4$.[8] They proposed that $HInCl_2$ generated from $InCl_3$ and $NaBH_4$ should be the actual reducing agent. Quite recently, Baba and Shibata have reported a similar catalytic system for reductive aldol reaction, in which $InBr_3$ and Et_3SiH are used as catalyst and reducing agent, respectively.[9] In this chapter, the author describes an environmentally benign method for reductive aldol reaction, in which EtOH is used as solvent.

2. Results and Discussion

2.1. 1,4-Reduction of α-Enones

The author initially found that several indium salts catalyzed the 1,4-reduction of (*E*)-1,3-diphenyl-2-propen-1-one (chalcone, **1a**) with $PhSiH_3$ (Table 1). For instance, the $In(OAc)_3$-catalyzed reaction in THF at 70 °C gave ketone **2a** as the major product along with a significant amount of dimerization product **3a** (entry 3). $InCl_3$ catalyzed the reaction of **1a** with $PhSiH_3$ at room temperature; however, the use of $InCl_3$ resulted in an increased amount of **3a** (entry 1). $In(OH)_3$ and $In(acac)_3$ as well were not suitable for the 1,4-reduction of **1a** (entries 4 and 5).

Table 1. Indium(III)-Catalyzed 1,4-Reduction of α-Enone **1a** with $PhSiH_3$



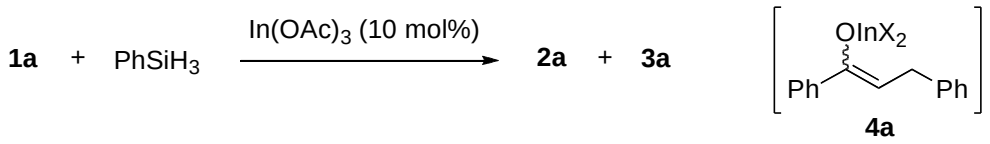
Entry	InX_3	Solvent	Temp / °C	Isolated Yield / %	
				2a	**3a**
1	$InCl_3$	Et_2O	rt	29	49
2	$In(OTf)_3$	Et_2O	rt	Complex mixture.	
3	$In(OAc)_3$	THF	70	56	26
4	$In(OH)_3$	THF	70	19	10
5	$In(acac)_3$	THF	70	34	65

[a] Unless otherwise noted, all reactions were carried out with **1a** (208 mg, 1.00 mmol), $PhSiH_3$ (108 mg, 1.00 mmol), and InX_3 (0.10 mmol) in solvent (2.0 mL) for 24 h.

The $In(OAc)_3$-catalyzed reaction was next optimized for selective 1,4-reduction of **1a**. The formation of **3a** is attributable to the Michael addition of indium enolate intermediate **4a** to **1a**. Therefore, proton sources such as water and EtOH were used to suppress this side reaction by protonation of **4a** (entries 2 and 3 in Table 2). As a result, the addition of EtOH was found to be effective not only in suppressing the formation of **3a** but also in accelerating the 1,4-reduction of **1a**. The use of EtOH as solvent further enhanced the reaction rate to allow the reduction to proceed at room temperature (entry 4). Thus the $In(OAc)_3$-catalyzed reduction of **1a** with $PhSiH_3$ in EtOH was completed in 1.5 h at room temperature to give **2a** in 90% yield.[10] Use of a half amount of $PhSiH_3$ lowered the yield to 62% (entry 5). Other hydrosilanes (Et_3SiH, $PhMe_2SiH$, and poly(methylhydrosiloxane)) did not cause the reduction of **1a** under the same conditions.

Indium metal was deposited under the reaction conditions of entry 4. Since indium trihydride is known to easily decompose to indium metal and H_2,[10] this observation is indicative of the formation of indium hydride species. Without $In(OAc)_3$, the reduction of **1a** did not proceed at all (entry 6). Accordingly, indium hydride species would act as the actual reductant.

Table 2. Optimization of Reaction Conditions for $In(OAc)_3$-Catalyzed 1,4-Reduction[a]



Entry	Solvent	Additive	Temp / °C	Time / h	Isolated Yield / %	
					2a	**3a**
1	THF	none	70	24	56	26
2	THF	H_2O[b]	70	24	67	trace
3	THF	EtOH[b]	70	3	76	trace
4	EtOH	none	rt	1.5	90	0
5[c]	EtOH	none	rt	1.5	62	0
6[d]	EtOH	none	rt	1.5	0	0

[a] Unless otherwise noted, all reactions were carried out with **1a** (208 mg, 1.00 mmol), $PhSiH_3$ (108 mg, 1.00 mmol), and $In(OAc)_3$ (30 mg, 0.10 mmol) in solvent (2.0 mL).

[b] One equivalent (1.00 mmol) of H_2O or EtOH was used.

[c] A half amount of $PhSiH_3$ (0.50 mmol) was used.

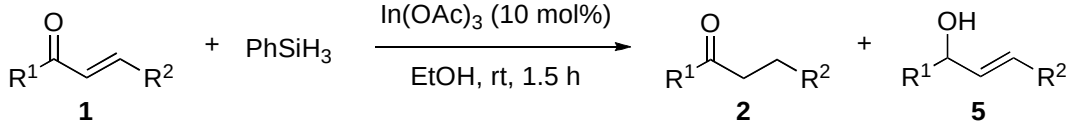
[d] Without $In(OAc)_3$.

The $In(OAc)_3$-catalyzed system using EtOH as solvent was applied to the reduction of some α,β-unsaturated carbonyl compounds (Table 3). Similar to **1a**, (*E*)-1-phenyl-2-buten-1-one (**1b**), 1-phenyl-2-propen-1-one (**1c**), and (*E*,*E*)-1,5-diphenyl-1,4-pentadien-3-one (**1d**) underwent 1,4-reduction to give the corresponding ketones **2** in good yields (entries 1-4). In the case of **1d**, a small amount of 1,5-diphenyl-3-pentanone was formed by double 1,4-reduction. The reduction of (*E*)-4-phenyl-3-buten-2-one (**1e**) gave 1,4- and 1,2-reduction products, **2e** and **5e**, in low yields, and **1e** was recovered in 75% yield (entry 5). Similarly, (*E*)-3-decen-2-one (**1f**) was less reactive than **1a**-**d**. Slow addition of $PhSiH_3$ slightly improved the

yield of **2f** (entry 6). 5-Phenyl-1-penten-3-one (**1g**), a vinyl ketone, showed high reactivity, but low chemoselectivity (entry 7). The reduction of **1g** gave allyl alcohol **5g** in 23% yield.

The present catalytic system was ineffective in the reduction of ethyl cinnamate (**1h**) (entry 8). In the case of cinnamaldehyde (**1i**), only the 1,2-reduction was observed (entry 9). The 1,4-reduction system was applicable to benzylidenemalononitrile (**6a**), a highly electron-deficient alkene; however, diethyl benzylidenemalonate (**6b**) was much less reactive than **6a** (Eq. 1). Methyl *trans*-cinnamate, *trans*-cinnamonitrile and ynones could not be reduced under the present conditions. The reduction of diethyl acetylenedicarboxylate proceeded smoothly to give a mixture of diethyl fumarate and maleate (Eq. 2).

Table 3. Reduction of α,β-Unsaturated Carbonyl Compounds with $PhSiH_3$[a]



Entry	Substrate			Isolated Yield / %	
	R^1	R^2		**2**	**5**
1	Ph	Ph	(**1a**)	90	0
2	Ph	Me	(**1b**)	84	0
3	Ph	H	(**1c**)	93	0
4	(*E*)-PhCH=CH	Ph	(**1d**)	72[b]	0
5	Me	Ph	(**1e**)	15[c]	8[c]
6	Me	*n*-Hex	(**1f**)	30[c,d] (54)[c,e]	0
7	$PhCH_2CH_2$	H	(**1g**)	63	23
8	EtO	Ph	(**1h**)	0	0
9	H	Ph	(**1i**)	0	80

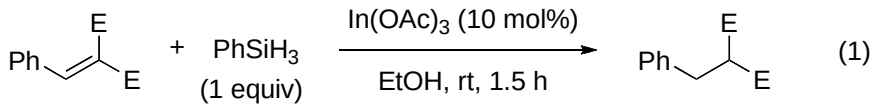
[a] Unless otherwise noted, all reactions were carried out with **1** (0.50 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), and $In(OAc)_3$ (15 mg, 0.05 mmol) in EtOH (1.0 mL) at room temperature for 1.5 h.

[b] 1,5-Diphenyl-3-pentanone also was obtained in 14% yield.

[c] The yield was determined by ^1H NMR analysis using benzyl acetate as the internal standard.

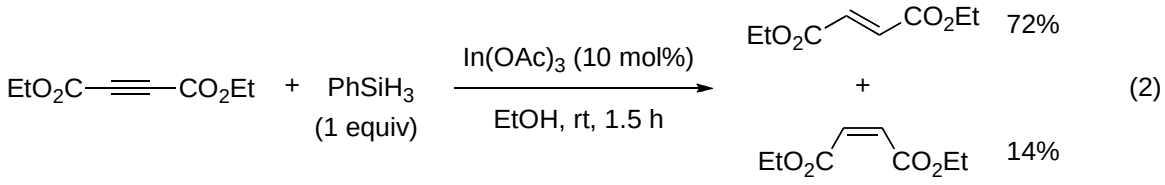
[d] The reaction was run for 24 h.

[e] The result in parentheses was obtained by the following method. $PhSiH_3$ was dropwise added to the mixture of **1f**, $In(OAc)_3$, and EtOH over 1 h. The resultant mixture was stirred for 24 h.



(1)

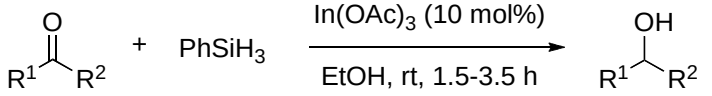
6a, E = CN: **7a**, 89%
6b, E = CO_2Et: **7b**, 14%



(2)

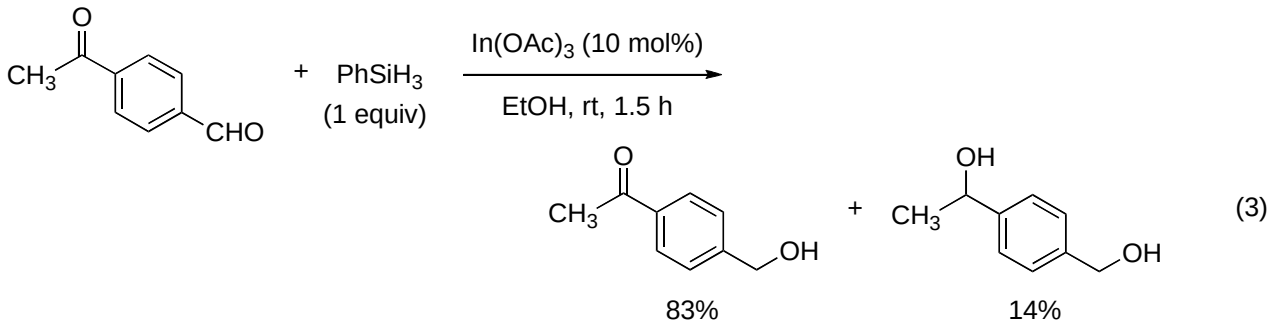
As described above, the $In(OAc)_3$-catalyzed reaction achieved an efficient 1,2-reduction of **1i**. This fact prompted the author to investigate the reactivities of aldehydes and ketones in the present reduction system. The results of the reduction of aldehydes and ketones are summarized in Table 4. Aliphatic and aromatic aldehydes were efficiently reduced to the corresponding alcohols, while ketones showed lower reactivity than aldehydes. Use of 4-formylacetophenone led to chemoselective reduction of the formyl group (Eq. 3).

Table 4. Reduction of Aldehydes and Ketones with $PhSiH_3$[a]



Entry	R^1	R^2	Isolated Yield / %
1	1-Naphthyl	H (**8a**)	82
2	*n*-$C_{11}H_{23}$	H	81
3	Ph	Ph	0
4	Ph	Bu	7
5	Bn	Me	18

[a] All reactions were carried out with an aldehyde or a ketone (0.50 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), and $In(OAc)_3$ (15 mg, 0.05 mmol) in EtOH (1.0 mL) at room temperature for 1.5 to 3.5 h.

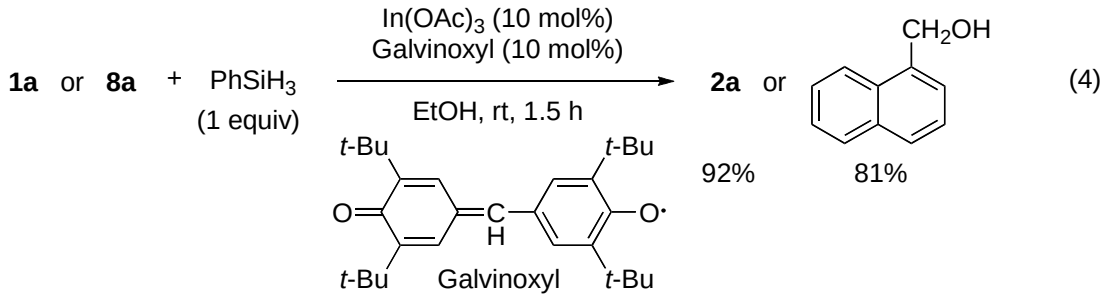


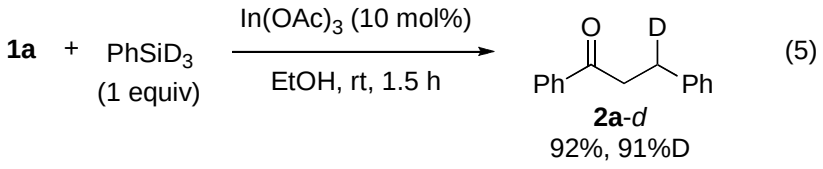
(3)

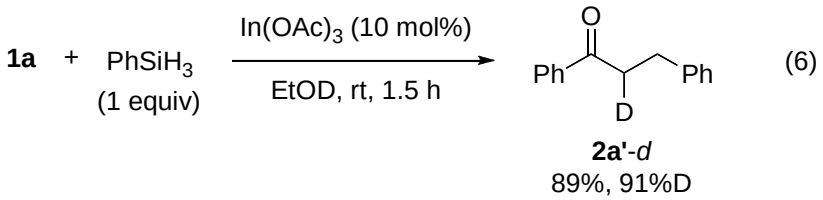
2.2. Reaction Mechanism for 1,4-Reduction

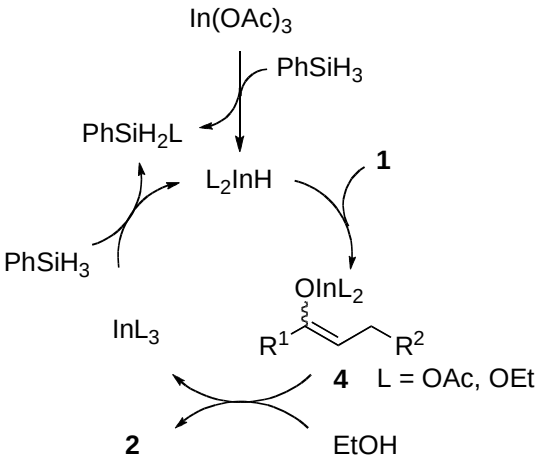
Dichloroindium hydride (Cl_2InH) has been reported to be valuable for radical reduction of alkyl halides.[11] The $In(OAc)_3$-catalyzed reduction of **1a** and 1-naphthaldehyde (**8a**) gave **2a** and 1-naphthalenemethanol efficiently even in the presence of galvinoxyl, a radical scavenger (Eq. 4). The present 1,4-reduction would therefore not involve a radical chain mechanism although the deposition of indium metal suggests the presence of indium hydride species. In the 1,4-reduction of **1a**, the use of $PhSiD_3$ instead of $PhSiH_3$ provided **2a-*d*** by β-deuteration (Eq. 5), while the use of EtOD as solvent resulted in α-deuteration (Eq. 6). Judging from these results, the present 1,4-reduction could proceed via the following

mechanism (Scheme 1): (1) transmetalation between $In(OAc)_3$ and $PhSiH_3$ in EtOH forms an indium hydride species ($HInL_2$, L = OAc, OEt), (2) 1,4-addition of the hydride to an α-enone **1** leads to the corresponding indium enolate **4**, (3) solvolysis of **4** gives the 1,4-reduction product **2** and InL_3, (4) transmetalation between InL_3 and $PhSiH_3$ regenerates $HInL_2$.









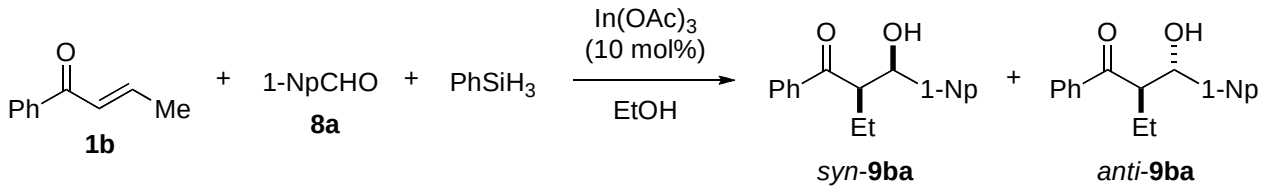
Scheme 1

2.3. Reductive Aldol Reaction of α-Enones

The mechanistic consideration induced the author to utilize the indium enolate intermediate **4** for carbon-carbon bond formation. He thus examined the $In(OAc)_3$-catalyzed reductive aldol reaction of α-enones and aldehydes with $PhSiH_3$. Initially, enone **1b** and 1-naphthaldehyde (**8a**) were selected as the substrates for optimization of the reaction conditions (Table 5). Expectedly, the reaction of **1b**, **8a**, and $PhSiH_3$ (molar ratio = 1:1:1) at room temperature gave the desired aldol **9ba** in 65% yield along with **2b**

(32%) and 1-naphthylmethanol (*ca.* 30%) (entry 1).[12] This result indicates that the $In(OAc)_3$-catalyzed reduction of **1b** is faster than that of **8a**.[13] The use of an excess amount of **8a** improved the yield of **9ba** (entry 2). Lowering the reaction temperature brought about high *syn* selectivity, although the reaction rate became much slower (entry 3). With a decreased amount of EtOH, **9ba** was obtained in high yield with high *syn* diastereoselectivity (entries 4 and 5).[14]

Table 5. Optimization of Reaction Conditions for $In(OAc)_3$-Catalyzed Reductive Aldol Reaction[a]

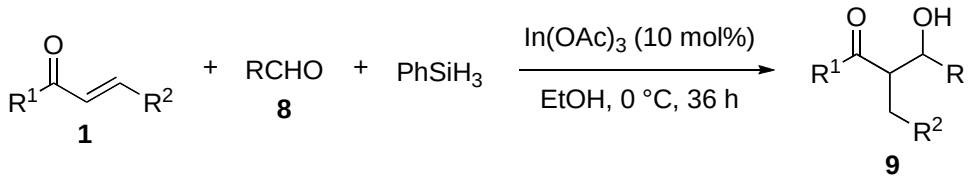


Entry	EtOH / mL	Temp. / °C	Time / h	Isolated Yield / %	*syn* : *anti*
1[b]	1.0	rt	24	65	74 : 26
2	1.0	rt	13	82	84 : 16
3	1.0	0	60	45	92 : 8
4	0.5	0	60	82	92 : 8
5	0.25	0	36	83	92 : 8

[a] Unless otherwise noted, all reactions were carried out with **1b** (73 mg, 0.50 mmol), **8a** (102 mg, 0.65 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), and $In(OAc)_3$ (15 mg, 0.05 mmol) in EtOH.

[b] With **8a** (0.50 mmol).

Table 6. Reductive Aldol Reaction of α-Enones **1**, Aldehydes **6**, and $PhSiH_3$[a]



Entry	Substrates				Yield / %[b]	*syn* : *anti*
	R^1	R^2		R		
1	Ph	Me	(**1b**)	1-Np	83	92 : 8
2[c]				Ph	84	92 : 8
3				*p*-$MeOC_6H_4$	96	96 : 4
4				*p*-NCC_6H_4	85	69 : 31
5[c]				*n*-C_7H_{15}	66	77 : 23
6				*c*-Hex	37	72 : 28
7	Ph	Ph	(**1a**)	1-Np	86	86 : 14
8[c]				Ph	94	87 : 13
9[c]				*n*-C_7H_{15}	71	70 : 30
10[c]				*c*-Hex	53	71 : 29
11	Ph	H	(**1c**)	1-Np	92	92 : 8

12[c]	Me	*n*-Hex	(**1f**)	1-Np	49	87 : 13
13	$Ph(CH_2)_2$	H	(**1g**)	1-Np	59	81 : 19
14	Me	H	(**1j**)	1-Np	47	88 : 12
15				Ph	60	85 : 15

[a] Unless otherwise noted, all reactions were carried out with **1** (0.50 mmol), **8** (0.65 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), and $In(OAc)_3$ (15 mg, 0.05 mmol) in EtOH (0.25 mL) at 0 °C for 36 h.

[b] Isolated yield.

[c] The reaction time is 72 h.

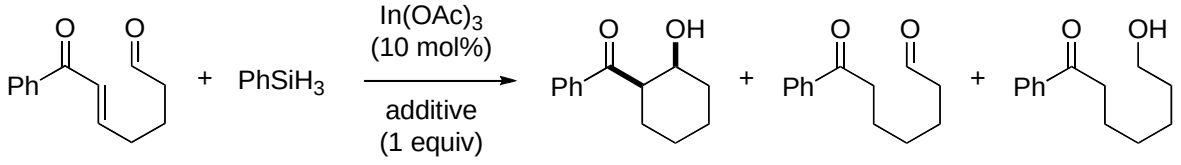
The optimized conditions were applied to other combinations of enones **1** and aldehydes **6** (Table 6).[15] The reductive aldol reaction of phenyl ketones **1a-c** with aromatic aldehydes proceeded in high yields with high *syn* diastereoselectivity except the case with *p*-cyanobenzaldehyde (entries 1-4, 7, 8, and 11). The use of aliphatic aldehydes lowered the reaction efficiency and the *syn* selectivity (entries 5, 6, 9, and 10).[16] Aliphatic α-enones also underwent the reductive coupling to give the corresponding aldol products in moderate yields (entries 12-14).

The author tried the reductive aldol reactions of **1b** with formaldehyde and ketones (cyclohexanone and acetophenone) under the same conditions. However, no aldol adducts were obtained in both cases. The reaction with formaldehyde resulted in a low yield of **2b**. This result may be due to fast reduction of formaldehyde with the indium hydride species. In the case with ketones, **2b** was formed in good yield. Therefore, the unsuccessful result is attributable to low reactivity of ketones to the indium enolate intermediate **4b**. The slow aldol process would allow ethanolysis of **4b** leading to **2b**.

2.4. Intramolecular Reductive Aldol Reaction of α-Enones

Our attention was next focused on intramolecular reductive coupling by the $In(OAc)_3$–$PhSiH_3$ system. The $In(OAc)_3$-catalyzed reaction of α-enone **10**,[17] bearing a formyl group, with $PhSiH_3$ was performed under similar conditions as those used for the intermolecular reductive aldol reaction (entry 1 in Table 7). However, the desired cyclized product **11** was obtained only in a poor yield. The formation of reduction products **12** and **13** was favored over the intramolecular aldol reaction. Use of THF as solvent suppressed these side reactions, although the conversion of **10** became slow (entry 2). In the presence of EtOH (1 equiv), the cyclization of **10** in THF smoothly proceeded at reflux to give *cis*-**11** in 77% yield (entry 5).[18,19] The *trans* isomer of **11** was not obtained.

Table 7. Intramolecular Reductive Aldol Reaction of α-Enone **10**[a]



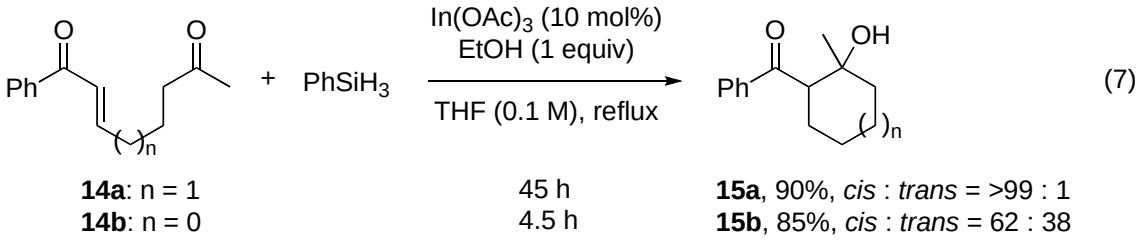
10 *cis*-**11** **12** **13**

Entry	Solvent	Additive	Temp.	Time / h	Isolated Yield / %			
					cis-**11**	**12**	**13**	**10**
1	EtOH	none	rt	4	11	15	26	-
2	THF	none	reflux	36	17	-	-	54

3	THF	EtOH	rt	24	23	-	-	65
4	THF	EtOH	reflux	4	23	-	-	59
5	THF	EtOH	reflux	8.5	77	-	-	0

[a] All reactions were carried out with **10** (101 mg, 0.50 mmol), $PhSiH_3$ (54 mg, 0.50 mmol), and $In(OAc)_3$ (15 mg, 0.05 mmol) in solvent (5 mL).

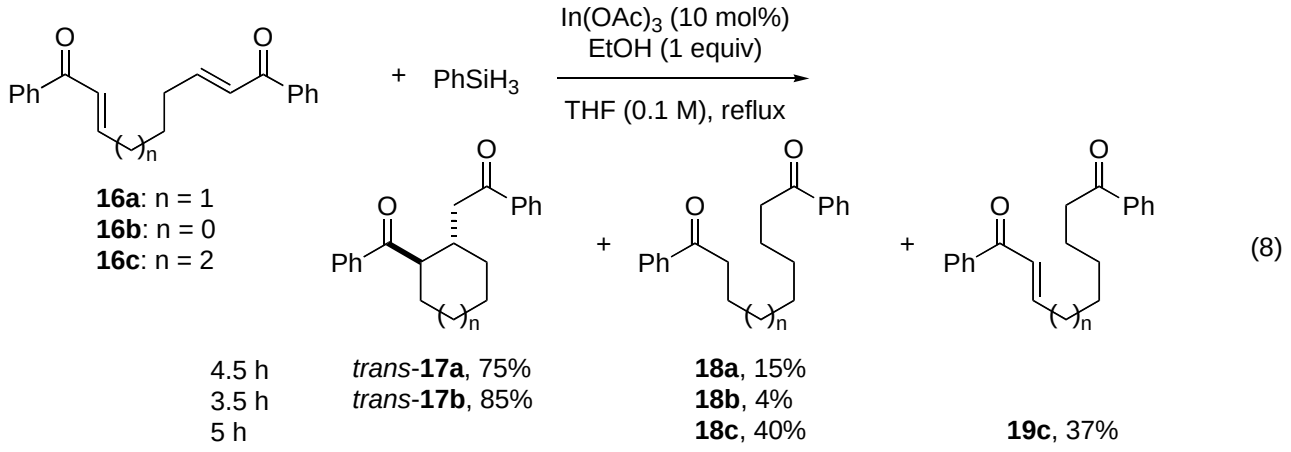
Under the reaction conditions of entry 5 in Table 7, enones **14a** and **14b** as well were efficiently cyclized to aldols **15a** and **15b**, respectively (Eq. 7).[17,18] The reaction of **14a** afforded *cis*-**15a** with complete stereocontrol.[19] Enone **14b** showed much higher reactivity than **14a**, but the cyclization resulted in low diastereoselectivity.



(7)

2.5. Intramolecular Reductive Michael Reaction of α-Enones

As shown in Table 1, the indium(III)-catalyzed reduction system using $PhSiH_3$ is usable for dimerization of **1a** by the Michael addition of indium enolate **4a** to **1a**. Therefore, the author tried an intramolecular version of this reductive Michael reaction. The reaction of bis-enone **16a** in THF without a proton donor resulted in low conversion of the substrate. Use of EtOH as additive brought about fast cyclization of **16a** to 1,5-diketone **17a** with complete *trans* selectivity (Eq. 8).[19] Diketone **18a** was also obtained as a byproduct. The cyclization of bis-enone **16b**, bearing an ethylene tether, proceeded smoothly under the same conditions. In contrast, the reaction of bis-enone **16c**, bearing a longer tether, afforded reduction products **18c** and **19c** without the desired product **17c**.



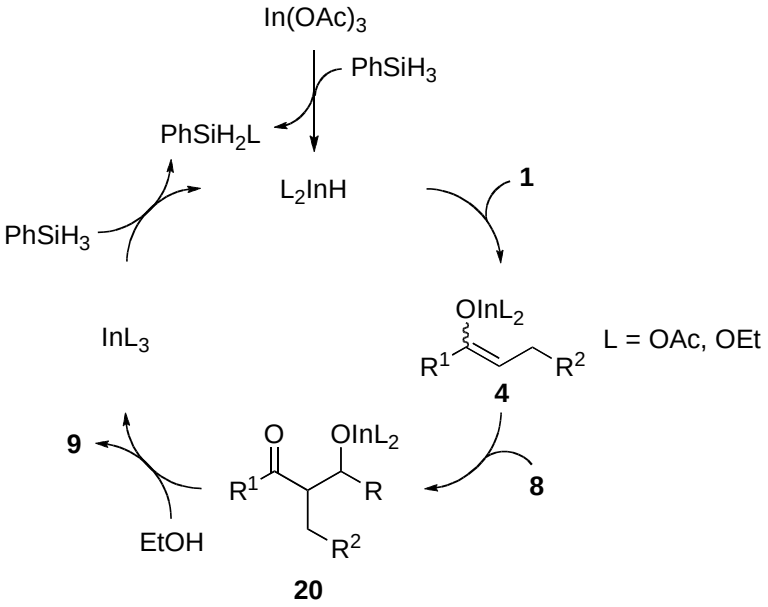
(8)

2.6. Reaction Mechanism for Reductive Aldol and Michael Reactions

A plausible mechanism for the $In(OAc)_3$-catalyzed reductive aldol reaction is shown in Scheme 2. Similar to the case of the $In(OAc)_3$-catalyzed 1,4-reduction, it involves the formation of an indium enolate intermediate **4** by 1,4-hydroindation of an α-enone with an indium hydride species. The aldol reaction of **4** with **8** gives an indium aldolate intermediate **20**. Then ethanolysis converts **20** into the corresponding aldol **9**

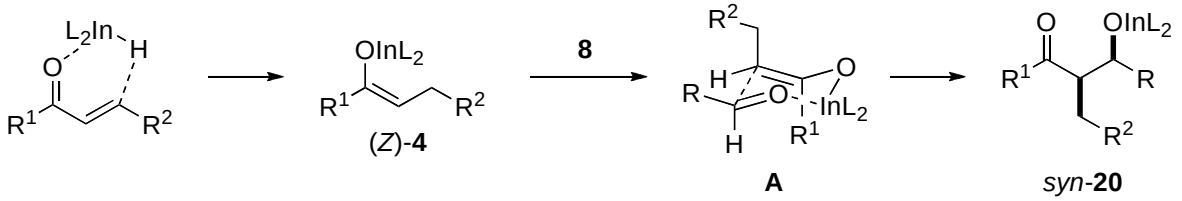
and an indium salt (InL_3). Transmetalation between InL_3 and $PhSiH_3$ regenerates an indium hydride species.

The successful reaction indicates that the aldol step is faster than ethanolysis of **4** to **2**. However, as shown in Table 5, the catalytic turnover of reductive aldol reaction is much slower than that of 1,4-reduction. Judging from the fast aldol step, the rate-determining step should be ethanolysis of the aldolate **20**. Intramolecular coordination of the carbonyl oxygen to the indium center may stabilize **20** to decelerate the ethanolysis step.



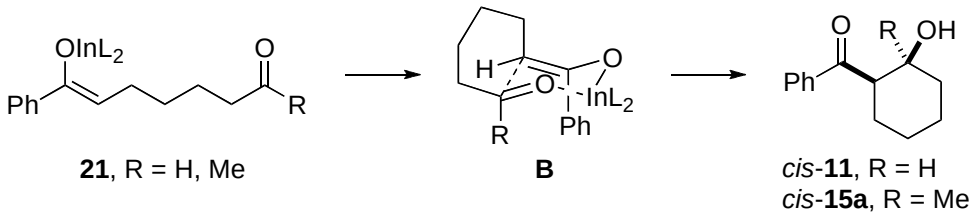
Scheme 2

As proposed by Baba and co-workers,[9] the *syn*-selectivity of the present reductive aldol reaction is attributable to the formation of (*Z*)-**4** by a concerted hydroindation of the s-*cis* form of α-enones and subsequent aldol addition via cyclic transition structure **A** (Scheme 3). Actually 2-cyclohenone, an s-*trans* α-enone, did not undergo 1,4-reduction under the present conditions. However, we have no direct evidence of the selective formation of (*Z*)-**4**.



Scheme 3

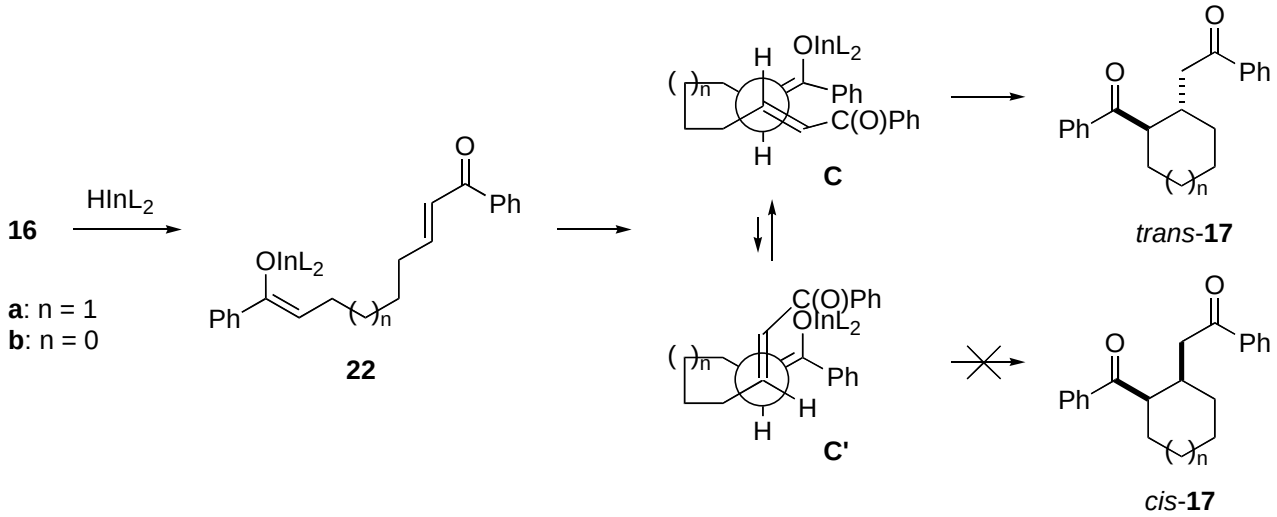
The *cis*-selectivity of the cyclization of **10** and **14a** can be rationalized by intramolecular aldol reaction of intermediary (*Z*)-enolates **21** (R = H, Me) via bicyclic transition structure **B** (Scheme 4). In the case with **14b**, a high strain energy originated from the five-membered ring formation may reduce energy difference between such a transition structure and other transition structures leading to *trans*-**15b**.



21, R = H, Me **B** *cis*-**11**, R = H
cis-**15a**, R = Me

Scheme 4

The reductive Michael reaction of **16** proceeds probably via indium enolate **22**. Concerning transition structures of the intramolecular reaction of **22**, conformation **C** is energetically favored over **C'** because **C** is sterically less hindered (Scheme 5). The observed *trans*-diastereoselectivity can be reasonably explained by the cyclization via **C**.



Scheme 5

3. Conclusion

The author has found that the combination of $In(OAc)_3$ and $PhSiH_3$ is quite useful for both 1,4-reduction of certain α-enones and their intermolecular reductive aldol reaction under mild conditions.[9] The $In(OAc)_3$-$PhSiH_3$ system is rather neutral (less Lewis acidic) and it works well in EtOH, a less harmful solvent, at room temperature or 0 °C. This catalytic system is applicable to intramolecular reductive aldol and Michael reactions with some modifications of the reaction conditions.

4. Experimental Section

4.1. General Method

See page 11.

4.2. Access to Catalysts, Reagents, and Substrates

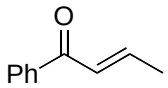
Indium salts, $PhSiH_3$, some enones (**1a** and **1d-f**), α,β-unsaturated esters (**1h**, **6b**, and diethyl acetylenedicarboxylate), nitrile **6a**, aldehydes, and ketones were purchased from chemical companies. Indium salts were used as received. Other commercially available compounds were used after purification by distillation or recrystallization. $PhSiD_3$ and some enones (**1b-c**, **1g**, **10**, **14a-b**, and **16a-c**) were prepared by the known methods as described below. CAS registry numbers are shown in the title lines.

Trideuteriophenylsilane [18164-03-9][20]

$PhSiD_3$

A solution of trichlorophenylsilane (6.7 g, 32.0 mmol) in Et_2O (60 mL) was dropwise added to a stirred suspension of lithium aluminum deuteride (1.9 g, 45 mmol) in Et_2O (30 mL) at 0 ℃ over 20 min. The mixture was heated to reflux stirred and for 11 h. The resultant mixture was treated with D_2O (5 mL) at 0 ℃ and poured into water. The extract with Et_2O (20 mL x 2) was dried over Na_2SO_4 and concentrated under atmospheric pressure. Purification of the crude product by distillation gave the title compound (1.54 g, 14.2 mmol, >99%*d*) in 43% yield. Trideuteriophenylsilane**:** ^{1}H NMR (270 Hz, $CDCl_3$) δ 7.32–7.62 (m, 3H), 7.58–7.62 (m, 2H).

1-Phenyl-2-buten-1-one (1b) [53931-59-2][21]



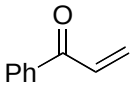
Butyllithium (1.64 M in hexane, 37 mL, 60 mmol) was dropwise added to a solution of diisopropylamine (8.4 mL, 60 mmol) in THF (150 mL) at 0 ℃ over 30 min. After being stirred for 30 min, the mixture was cooled to –78 ℃. Acetophenone (5.8 mL, 50 mmol) was dropwise added to the stirred mixture. After 30 min, acetaldehyde (>90%, 3.7 mL, 60 mmol) was dropwise added to the stirred mixture. After 30 min, the resultant mixture was treated with saturated aqueous $NaHCO_3$ (30 mL) at room temperature, and extracted with *t*-BuOMe (20 mL x 2). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane : AcOEt = 2 : 1) gave 3-hydroxy-1-phenyl-1-butanone in (5.5 g, 34 mmol) 67% yield. 3-Hydroxy-1-phenyl-1-butanone [13505-39-0]**:** ^{1}H NMR ($CDCl_3$) δ 1.31 (d, *J* = 6.3 Hz, 3H), 3.04 (dd, *J* = 17.8, 8.7 Hz, 1H), 3.19 (dd, *J* = 17.8, 3.6 Hz, 1H), 3.31 (d, *J* = 3.1 Hz, 1H), 4.35–4.48 (m, 1H), 7.45–7.63 (m, 3H), 7.94–7.97 (m, 2H).

Methanesulfonyl chloride (2.90 mL, 38.0 mmol) was dropwise added to a solution of 3-hydroxy-1-phenyl-1-butanone (5.52 g, 34.0 mmol) and triethylamine (7.10 mL, 51.0 mmol) in CH_2Cl_2 (50 mL) at 0 ℃ over 90 min. The reaction mixture was treated with saturated aqueous $NaHCO_3$ (30 mL) at room temperature and extracted with *t*-BuOMe (20 mL x 2). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane : AcOEt = 10 : 1). gave the title compound (2.50 g, 17.1 mmol) and 3-mesyloxy-1-phenyl-1-butanone (3.25 g, 13.4 mmol) were obtained in 50% and 39% yield, respectively. **1b**: ^{1}H NMR ($CDCl_3$) δ 2.01 (dd, *J* = 6.7, 1.5 Hz, 3H), 6.91 (dq, *J* = 15.3, 1.5 Hz, 1H), 7.01 (dd, *J* = 15.3, 6.7 Hz, 1H), 7.43–7.59 (m, 3H), 7.91–7.95 (m, 2H). 3-Mesyloxy-1-phenyl-1-butanone (byproduct): ^{1}H NMR ($CDCl_3$) δ 1.59 (d, *J* = 6.3 Hz, 3H), 3.06 (s, 3H),

3.09 (dd, *J* = 17.5, 4.6 Hz, 1H), 3.62 (dd, *J* = 17.5, 7.6 Hz, 1H), 5.32–5.44 (m, 1H), 7.47–7.52 (m, 2H), 7.58–7.64 (m, 1H), 7.93–7.97 (m, 2H).

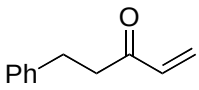
Triethylamine (2.80 mL, 20.0 mmol) was added to a stirred solution of 3-mesyloxy-1-phenyl-1-butanone (3.24 g, 13.4 mmol) in Et_2O (20 mL) at room temperature. After 90 min, the reaction mixture was poured into with H_2O (30 mL), and extracted with *t*-BuOMe (10 mL x 2). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane : AcOEt = 10 : 1) gave the title compound (1.54 g, 10.5 mmol) in 81% yield.

1-Phenyl-2-propen-1-one (1c) [768-03-6]



Triethylamine (10.0 mL, 70.0 mmol) was added to a stirred solution of 3-chloro-1-phenyl-1-propanone (5.0 g, 30 mmol) in $CHCl_3$ (70 mL) at room temperature. After 18 h, the reaction mixture was washed with aqueous HCl (1 M, 150 mL), H_2O (150 mL), and saturated aqueous $NaHCO_3$ (150 mL). The solution was dried over $MgSO_4$ and evaporated. Purification of the crude product by distillation gave the title compound (3.35 g, 25.3 mmol) in 86% yield. **1c**: bp 120 ºC (0.5 Torr). ^{1}H NMR ($CDCl_3$) δ 5.94 (dd, *J* = 10.6, 1.7 Hz, 1H), 6.44 (dd, *J* = 17.2, 1.7 Hz, 1H), 7.16 (dd, *J* = 17.2, 10.6 Hz, 1H), 7.45–7.62 (m, 3H), 7.93–7.98 (m, 2H).

5-Phenyl-1-penten-3-one (1g) [53931-59-2][22]

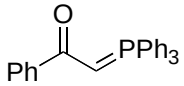


Concentrated H_2SO_4 (6.0 mL, 10.0 mmol) was dropwise added to a stirred solution of 3-phenylprpanoic acid (15.0 g, 100 mmol) in MeOH (50 mL). After being stirred for 2 h at reflux, the reaction mixture was cooled to room temperature and diluted with *t*-BuOMe (50 mL). The resultant mixture was washed with H_2O (150 mL), saturated aqueous $NaHCO_3$ (50 mL x 3), and saturated aqueous NaCl (50 mL). The solution was dried over $MgSO_4$ and evaporated. Methyl 3-phenylpropanoate (16.4 g, 100.0 mmol) was obtained in 100% yield. Methyl 3-phenylpropanoate [103-25-3]**:** ^{1}H NMR ($CDCl_3$) δ 2.64 (t, *J* = 7.8 Hz, 2H), 2.96 (t, *J* = 7.8 Hz, 2H), 3.67 (s, 3H), 7.18–7.32 (m, 5H).

Titanium(IV) isopropoxide (6.8 mL, 20 mmol) was added to a solution of methyl 3-phenylpropanoate (16.4 g, 100 mmol) in Et_2O (320 mL). Ethylmagnesium bromide (0.97 M in Et_2O, 240 mL, 240 mmol) was slowly added over 1 h. After being stirred for 10 min, the reaction mixture was poured into 10 % aqueous H_2SO_4 (500 mL) at 0 ℃ and extracted with *t*-BuOMe (100 mL x 3). The extract was washed with H_2O, dried over Na_2SO_4, and evaporated. Purification of the crude product by distillation gave 1-(2-phenyletheyl)cyclopropanol (14.5 g, 89.4 mmol) in 89% yield. 1-(2-Phenyletheyl)cyclopropanol [13068-05-8]: ^{1}H NMR ($CDCl_3$) δ 0.46 (dd, *J* = 6.7, 5.2 Hz, 2H), 0.76 (dd, *J* = 6.7, 5.2 Hz, 2H), 1.76 (s, 1H), 1.85–1.91 (m, 2H), 2.83–2.89 (m, 2H), 7.15–7.32 (m, 5H).

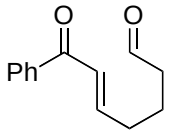
Palladium acetate (934 mg, 4.1 mmol) and triphenylphosphine (1.09 g, 4.1 mmol) were added to a solution of 1-(2-phenyletheyl)cyclopropanol (13.5 g, 83 mmol) in MeCN (400 mL). The mixture was stirred for 63 h at 50 ℃. The reaction mixture was filtered through florisil® and evaporated. Purification of the crude product by silica gel column chromatography (hexane : AcOEt = 15 : 1) gave the title compound (1.31 g, 8.2 mmol) in 10% yield. **1g**: ^{1}H NMR ($CDCl_3$) δ 2.90–300 (m, 4H), 5.82 (dd, *J* = 10.2, 1.5 Hz, 1H), 6.21 (dd, *J* = 17.7, 1.5 Hz, 1H), 6.36 (dd, *J* = 17.7, 10.2 Hz, 1H), 7.17–7.32 (m, 5H).

Triphenylphosphine Benzoylmethylene [859-65-4][23a]



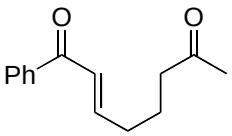
Phenacyl bromide (49.8 g, 250 mmol) was slowly added to a stirred solution of Ph_3P (65.6 g, 250 mmol) in $CHCl_3$ (375 mL) at 0 ℃. After 3 h, the reaction mixture was poured into *t*-BuOMe (1.5 L). The precipitate formed was taken out by filtration and washed with *t*-BuOMe. It was dissolved into water (1.5 L) and treated with Na_2CO_3 (150 g) for 19 h. The resultant mixture was filtered. The precipitate obtained was washed with Et_2O and dissolved into hot benzene (500 mL). The solution was poured into *t*-BuOMe (1.5 L). The crystal formed was taken out by filtration, washed with Et_2O, and dried under reduced pressure. The title compound (48.5 g, 127 mmol) was obtained in 51% yield. Triphenylphosphine benzoylmethylene: ^{1}H NMR ($CDCl_3$) δ 7.34–7.76 (m, 19H), 7.95–7.99 (m, 2H).

(*E*)-7-Oxo-7-phenyl-5-heptenal (10) [169892-12-0][23]



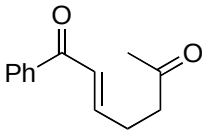
Ozone was introduced into a solution of cyclopentene (6.2 mL, 70 mmol) in CH_2Cl_2 (150 mL) at –78 ℃ until it turned blue. N_2 was introduced into the resultant mixture until the color disappeared. After addition of Ph_3P (18.4 g, 70 mmol), the reaction mixture was warmed to room temperature. After 2 h, a solution of triphenylphosphine benzoylmethylene (7.6 g, 20 mmol) in CH_2Cl_2 (30 mL) was slowly added to the reaction mixture. After 24 h, the resultant mixture was evaporated. Purification of the crude product by silica gel column chromatography (hexane : AcOEt = 4 : 1) gave the title compound (1.89 g, 9.3 mmol) in 47% yield. **10**: ^{1}H NMR ($CDCl_3$) δ 1.86 (quintet, *J* = 7.2 Hz, 2H), 2.36 (td, *J* = 7.2, 6.6 Hz, 2H), 2.51 (td, *J* = 7.2, 1.2 Hz, 2H), 6.90 (d, *J* = 15.6 Hz, 1H), 7.01 (dt, *J* = 15.6, 6.6 Hz, 1H), 7.40-7.60 (m, 3H), 7.90-7.95 (m, 2H), 9.78 (t, *J* = 1.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 20.4 (CH_2), 31.8 (CH_2), 43.0 (CH_2), 126.6 (CH), 128.5 (CH x 2), 128.6 (CH x 2), 132.8 (CH), 137.7 (CH), 148.1 (CH), 190.5 (C), 201.7 (CH).

(*E*)-1-Phenyl-2-Octene-1,7-dione (14a) [132559-69-4][23]



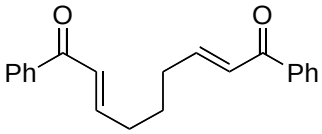
Ozone was introduced into a solution of methylcyclopentene (3.2 mL, 30 mmol) in CH_2Cl_2 (100 mL) at –78 ℃ until it turned blue. N_2 was introduced into the resultant mixture until the color disappeared. Ph_3P (7.9 g, 30 mmol) and triphenylphosphine benzoylmethylene (12.6 g, 33 mmol) were added to the reaction mixture. After being stirred for 1 h at –78 ℃, the reaction mixture was warmed to at room temperature. After 24 h, the resultant mixture was evaporated. Purification of the crude product by silica gel column chromatography (hexane : AcOEt = 4 : 1) gave the title compound (3.75 g, 17.3 mmol) in 58% yield. **14a**: ^{1}H NMR ($CDCl_3$) δ 1.82 (tt, *J* = 7.3, 7.1 Hz, 2H), 2.10 (s, 3H), 2.34 (td, *J* = 7.1, 6.5 Hz, 2H), 2.50 (t, *J* = 7.3 Hz, 2H), 6.89 (d, *J* = 15.4 Hz, 1H), 7.02 (dt, *J* = 15.4, 6.5 Hz, 1H), 7.44-7.64 (m, 3H), 7.91-7.94 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_2), 29.7 (CH_3), 31.6 (CH_2), 42.3 (CH_2), 126.0 (CH), 128.2 (CH x 2), 128.2 (CH x 2), 132.4 (CH), 137.4 (C), 148.3 (CH), 190.2 (C), 207.9 (C).

(*E*)-1-Phenyl-2-heptene-1,6-dione (14b) [147032-71-1][23]



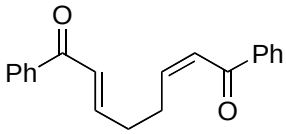
According to the method for the synthesis of **14a**, the title compound was prepared from 1,5-dimethyl-1,5-cyclooctadiene with 2.5 equiv of triphenylphosphine benzoylmethylene in 32% yield. **14b:** ^{1}H NMR ($CDCl_3$) δ 2.19 (s, 3H), 2.55–2.71 (m, 4H), 6.90 (d, *J* = 15.4 Hz, 1H), 7.01 (dt, *J* = 15.4, 6.0 Hz, 1H), 7.43–7.59 (m, 3H), 7.90–7.94 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 26.3 (CH_2), 29.8 (CH_3), 41.3 (CH_2), 126.3 (CH), 128.3 (CH x 2), 128.3 (CH x 2), 132.6 (CH), 137.5 (C), 147.5 (CH), 190.3 (C), 206.7 (C).

(2*E*,7*E*)-1,9-Diphenyl-2,7-nonadiene-1,9-dione (16a) [140137-94-6][23]



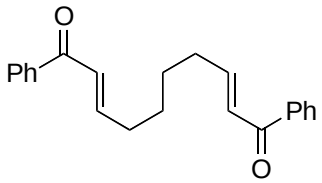
According to the method for the synthesis of **14a**, the title compound was prepared from cyclopentene with 2.2 equiv of triphenylphosphine benzoylmethylene in 65% yield. **16a**: ^{1}H NMR ($CDCl_3$) δ 1.79 (m, *J* = 7.4 Hz, 2H), 2.41 (td, *J* = 7.4, 6.7 Hz, 4H), 6.92 (d, *J* = 15.3 Hz, 2H), 7.07 (dt, *J* = 15.3, 6.7 Hz, 2H), 7.44–7.57 (m, 6H), 7.91–7.95 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 26.5 (CH_2), 32.0 (CH_2 x 2), 126.3 (CH x 2), 128.4 (CH x 4), 128.4 (CH x 4), 132.6 (CH x 2), 137.7 (C x 2), 148.4 (CH x 2), 190.4 (C x 2).

(2*E*,6*E*)-1,8-Diphenyl-2,6-octadiene-1,8-dione (16b) [182888-28-4][23]



According to the method for the synthesis of **14a**, the title compound was prepared from 1,5-cyclooctadiene with 4.4 equiv of triphenylphosphine benzoylmethylene in 28% yield. **16b**: ^{1}H NMR ($CDCl_3$) δ 2.57 (d, *J* = 5.9 Hz, 4H), 6.95 (d, *J* = 15.3 Hz, 2H), 7.07 (dt, *J* = 15.3, 5.9 Hz, 2H), 7.43–7.59 (m, 6H), 7.90–7.94 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 31.1 (CH_2 x 2), 126.6 (CH x 2), 128.4 (CH x 4), 128.4 (CH x 4), 132.7 (CH x 2), 137.5 (C x 2), 147.3 (CH x 2), 190.3 (C x 2).

(2*E*,8*E*)-1,10-Diphenyl-2,8-decadiene-1,10-dione (16c) [140137-93-5][23]



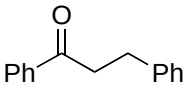
According to the method for the synthesis of **14a**, the title compound was prepared from cyclohexene with 2.2 equiv of triphenylphosphine benzoylmethylene in 39% yield. **16c:** ^{1}H NMR ($CDCl_3$) δ 1.58–1.63 (m, 4H), 2.36 (br d, *J* = 6.8 Hz, 4H), 6.90 (d, *J* = 15.4 Hz, 2H), 7.06 (dt, *J* = 15.4, 6.8 Hz, 2H), 7.44–7.59 (m, 6H), 7.91–7.94 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 27.7 (CH_2 x 2), 32.5 (CH_2 x 2), 126.0 (CH x 2), 128.4 (CH x 4), 128.4 (CH x 4), 132.6 (CH x 2), 137.8 (C x 2), 149.2 (CH x 2), 190.7 (C x 2).

4.3. Reduction of Electron-deficient Alkenes

General procedure

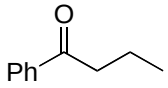
An electron-deficient alkene (0.50 mmol) and $PhSiH_3$ (54 mg, 0.50 mmol) were added to a suspension of $In(OAc)_3$ (15 mg, 0.05 mmol) in EtOH (1.0 mL). The mixture was stirred at room temperature for 1.5 h and quenched with saturated aqueous $NaHCO_3$. The extract with *t*-BuOMe was dried over Na_2SO_4 and evaporated. The residual oil was purified by silica gel column chromatography. When the products are known in the literature, their identity was determined by comparison in spectral data.

1,3-Diphenyl-1-propanone (2a) [1083-30-3]



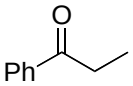
^{1}H NMR ($CDCl_3$) δ 3.07 (t, *J* = 7.2 Hz, 2H), 3.31 (t, *J* = 7.2 Hz, 2H), 7.17–7.59 (m, 6H), 7.64–7.98 (m, 4H).

1-Phenyl-1-butanone (2b) [495-40-9] (*commercially available*)



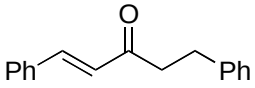
^{1}H NMR ($CDCl_3$) δ 1.01 (t, *J* = 7.4 Hz, 3H), 1.78 (qt, *J* = 7.4, 7.3 Hz, 2H), 2.95 (t, *J* = 7.3 Hz, 2H), 7.43–7.59 (m, 3H), 7.95–7.98 (m, 2H).

1-Phenyl-1-propanone (2c) [93-55-0] (*commercially available*)



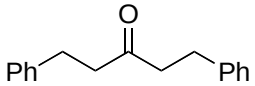
^{1}H NMR ($CDCl_3$) δ 1.23 (t, *J* = 7.3 Hz, 3H), 3.02 (q, *J* = 7.3 Hz, 2H), 7.44–7.56 (m, 3H), 7.95–7.99 (m, 2H).

(*E*)-1,5-Diphenyl-1-penten-3-one (2d) [39728-15-9]



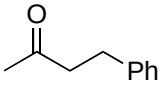
^{1}H NMR ($CDCl_3$) δ 3.01 (s, 4H), 6.73 (d, *J* = 16.2 Hz, 1H), 7.22–7.51 (m, 11H).

1,5-Diphenyl-3-pentanone [5396-91-8]



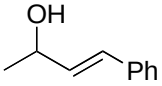
^{1}H NMR ($CDCl_3$) δ 2.70 (t, *J* = 7.4 Hz, 4H), 2.89 (t, *J* = 7.4 Hz, 4H), 7.13–7.31 (m, 10H).

4-Phenyl-2-butanone (2e) [2550-26-7] (*commercially available*)



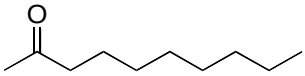
^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3H), 2.76 (t, *J* = 7.8 Hz, 2H), 2.90 (t, *J* = 7.8 Hz, 2H), 7.16–7.31 (m, 5H).

(*E*)-4-Phenyl-3-buten-2-ol (5e) [36004-04-3]



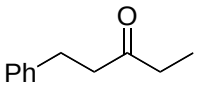
^{1}H NMR ($CDCl_3$) δ 1.23 (d, *J* = 6.3 Hz, 1H), 1.38 (d, *J* = 6.2 Hz, 3H), 4.45–4.54 (m, 1H), 6.26 (dd, *J* = 15.8, 6.4 Hz, 1H), 6.57 (d, *J* = 15.8 Hz, 1H), 7.21–7.40 (m, 5H).

2-Decanone (2f) [693-54-9] (*commercially available*)



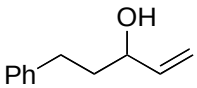
^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 6.7 Hz, 3H), 1.27 (br s, 10H), 1.55–1.61 (m, 2H), 2.13 (s, 3H), 2.42 (t, *J* = 7.4 Hz, 2H).

1-Phenyl-3-pentanone (2g) [20795-51-1]

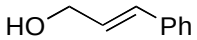


^{1}H NMR ($CDCl_3$) δ 1.04 (t, *J* = 7.3 Hz, 3H), 2.41 (q, *J* = 7.3 Hz, 2H), 2.73 (t, *J* = 7.9 Hz, 2H), 2.90 (t, J = 7.9 Hz, 2H), 7.16–7.30 (m, 5H).

5-Phenyl-1-penten-3-ol (5g) [37904-38-4][24]

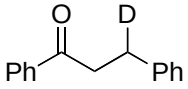


(*E*)-3-Phenyl-2-propen-1-ol (5i) [4407-36-7]

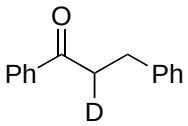


^{1}H NMR ($CDCl_3$) δ 1.44 (br s, 1H), 4.33 (br s, 2H), 6.37 (dt, *J* = 15.8, 5.6 Hz, 1H), 6.62 (br d, *J* = 15.8 Hz, 1H), 7.24–7.41 (m, 5H).

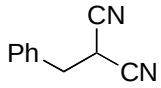
3-Deuterio-1,3-Diphenyl-1-propanone (2a-*d*) [93698-11-4][25]



2-Deuterio-1,3-Diphenyl-1-propanone (2a'-*d*) [93698-10-3][25]

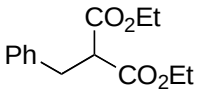


Benzylmalononitrile [1867-37-4]



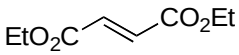
^{1}H NMR ($CDCl_3$) δ 3.30 (d, *J* = 6.8 Hz, 2H), 3.91 (t, *J* = 6.8 Hz, 1H), 7.31–7.42 (m, 5H).

Diethyl Benzylmalonate [607-81-8] (*commercially available*)



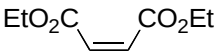
^{1}H NMR ($CDCl_3$) δ 1.20 (t, *J* = 7.2 Hz, 6H), 3.22 (d, *J* = 7.8 Hz, 2H), 3.64 (t, *J* = 7.8 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 4H), 7.19–7.31 (m, 5H).

Diethyl Fumarate [623-91-6] (*commercially available*)



^{1}H NMR ($CDCl_3$) δ 1.32 (t, *J* = 7.1 Hz, 6H), 4.26 (q, *J* = 7.1 Hz, 4H), 6.85 (s, 2H).

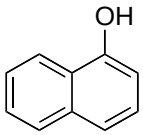
Diethyl Maleate [141-05-9] (*commercially available*)



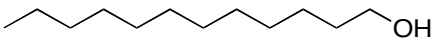
^{1}H NMR ($CDCl_3$) δ 1.31 (t, *J* = 7.1 Hz, 6H), 4.25 (q, *J* = 7.1 Hz, 4H), 6.23 (s, 2H).

4.4. Reduction of Aldehydes and Ketones

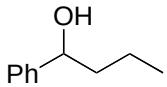
1-Naphthol [90-15-3] (*commercially available*)



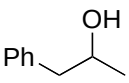
Dodecanol [112-53-8] (*commercially available*)



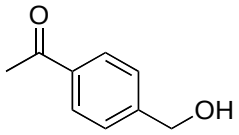
1-Phenyl-1-pentanol [583-03-9][26]



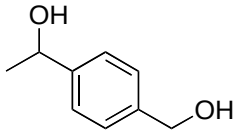
1-Phenyl-2-propanol [698-87-3] (*commercially available*)



4-(Hydroxymethyl)acetophenone [75633-63-5][27]



1-(4-(Hydroxymethyl)phenyl)ethanol [80463-22-5][28]

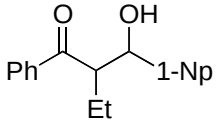


4.5. Reductive Aldol Reaction of α-Enones

General procedure

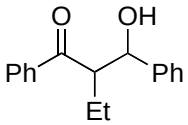
An α-enone **1** (0.5 mmol), an aldehyde (0.65 mmol), and $PhSiH_3$ (0.50 mmol) were added successively to a suspension of $In(OAc)_3$ (15 mg, 0.050mmol) in EtOH (0.25 mL) at 0 ℃. After being stirred for 36 or 72 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The extract with *t*-BuOMe was dried over Na_2SO_4 and evaporated. The residual oil was purified by silica gel column chromatography.

2-(Hydroxy(1-naphthyl)methyl)-1-phenyl-1-butanone (9ba, *syn* : *anti* = 92 : 8) [785798-49-4][10]



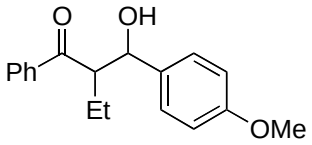
IR (neat) 3540 (br s, OH), 1680 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.69 (t, *J* = 7.6 Hz, 2.76H), 0.86 (t, *J* = 7.6 Hz, 0.24H), 1.63–1.79 (m, 1H), 1.89–2.08 (m, 1H), 3.52 (d, *J* = 5.9 Hz, 0.08H), 3.80 (d, *J* = 1.7 Hz, 0.92H), 3.96 (ddd, *J* = 9.1, 3.8, 3.6 Hz, 0.92H), 4.11 (ddd, *J* = 8.2, 6.2, 5.9 Hz, 0.08H), 5.82 (dd, *J* = 6.2, 5.9 Hz, 0.08H), 5.85 (br s, 0.92H), 7.31–7.96 (m, 12H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 12.3 (CH_3), 20.2 (CH_2), 51.6 (CH), 70.1 (CH), 122.5 (CH), 124.5 (CH), 125.3 (CH), 125.3 (CH), 126.0 (CH), 127.9 (CH), 128.4 (CH x 2), 128.8 (CH x 2), 129.1 (CH), 129.9 (C), 133.6 (CH), 133.7 (C), 136.7 (C), 137.2 (C) 206.4 (C). For the minor isomer (only well-resolved peaks) δ 11.9 (CH_3), 24.2 (CH_2), 53.1 (CH), 72.9 (CH), 123.0 (CH), 124.4 (CH), 125.4 (CH), 129.0 (CH), 130.5 (C) 133.2 (CH), 138.2 (C), 206.1 (C).

2-(Hydroxy(phenyl)methyl)-1-phenyl-1-butanone (9bb, *syn* : *anti* = 92 : 8) [84466-81-9][10,36]



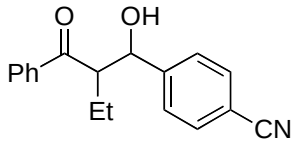
IR (neat) 3470 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.78 (t, *J* = 7.4 Hz, 2.76H), 0.82 (t, *J* = 7.4 Hz, 0.24H), 1.68–2.00 (m, 2H), 3.07 (d, *J* = 5.4 Hz, 0.08H), 3.20 (d, *J* = 2.0 Hz, 0.92H), 3.73 (ddd, *J* = 4.5, 4.4, 4.3 Hz, 0.92H), 3.78 (ddd, *J* = 7.0, 5.5, 5.4 Hz, 0.08H), 5.02 (dd, *J* = 7.0, 5.4 Hz, 0.08H), 5.09 (dd, *J* = 4.5, 2.0 Hz, 0.92H), 7.19–7.64 (m, 8H), 7.88–7.91 (m, 2H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 12.2 (CH_3), 20.4 (CH_2), 54.1 (CH), 73.7 (CH), 126.2 (CH x 2), 127.4 (CH), 128.2 (CH x 2), 128.3 (CH x 2), 128.6 (CH x 2), 133.4 (CH), 137.4 (C), 142.0 (C), 205.3 (C). For the minor isomer (only well-resolved peaks) δ 11.6 (CH_3), 23.7 (CH_2), 54.3 (CH), 75.7 (CH), 126.4 (CH), 127.8 (CH), 128.4 (CH x 2), 128.6 (CH x 2), 131.2 (CH). Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13%. Found: C, 79.97; H, 7.00%.

2-(Hydroxy(4-methoxyphenyl)methyl)-1-phenyl-1-butanone (9bc, *syn* : *anti* = 96 : 4) [475674-14-7][10.37]



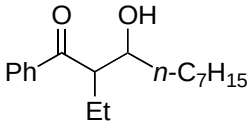
IR (neat) 3480 (br s, OH), 1680 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) for the major isomer δ 0.79 (t, *J* = 7.8 Hz, 3H), 1.66–2.21 (m, 2H), 3.77 (s, 3H), 3.79 (d, *J* = 1.7 Hz, 1H), 3.68–3.76 (m, 1H), 5.03 (br d, *J* = 5.1 Hz, 1H), 6.81–6.86 (m, 2H), 7.22–7.56 (m, 5H), 7.86–7.96 (m, 2H). For the minor isomer (only well-resolved peaks) δ 0.98 (t, *J* = 7.4 Hz, 3H), 3.79 (s, 3H), 4.25 (ddd, *J* = 6.8, 6.7, 3.1 Hz, 1H), 4.98 (br d, *J* = 6.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 12.1 (CH_3), 20.8 (CH_2), 55.5 (CH_3), 55.2 (CH), 73.5 (CH), 113.6 (CH), 127.4 (CH), 128.2 (CH x 3), 128.6 (CH x 2), 133.3 (CH), 134.2 (C), 137.5 (C), 158.8 (C), 205.1 (C). For the minor isomer (only well-resolved peaks) δ 11.6 (CH_3), 23.7 (CH_2), 54.3 (CH_3), 55.2 (CH), 75.4 (CH), 113.8 (CH), 127.6 (CH), 128.3 (CH), 128.5 (CH), 131.1 (CH). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09%. Found: C, 75.72; H, 7.05%.

2-(Hydroxy(4-cyanophenyl)methyl)-1-phenyl-1-butanone (9bd, *syn* : *anti* = 69 : 31) [785798-56-3][10]



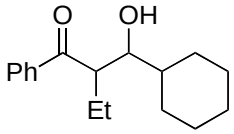
IR (neat) 3480 (br s, OH), 1600 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) for the major isomer δ 0.76 (t, *J* = 7.5 Hz, 3H), 1.61–1.95 (m, 2H), 3.58 (d, *J* = 1.7 Hz, 1H), 3.65–3.76 (m, 1H), 5.15 (dd, *J* = 3.9, 1.7 Hz, 1H), 7.04–7.64 (m, 7H), 7.86–7.96 (m, 2H). For the minor isomer (only well-resolved peaks) δ 0.98 (t, *J* = 7.4 Hz, 3H), 3.79 (s, 3H), 4.25 (ddd, *J* = 6.8, 6.7, 3.1 Hz, 1H), 4.98 (br d, *J* = 6.8 Hz, 1H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 12.1 (CH_3), 20.4 (CH_2), 53.4 (CH), 73.0 (CH), 111.1 (C), 127.0 (CH x 2), 128.3 (CH x 2), 128.8 (CH x 2), 132.0 (CH x 2), 133.8 (CH), 136.9 (C), 147.5 (C), 204.8 (C). For the minor isomer (only well-resolved peaks) δ 11.7 (CH_3), 23.7 (CH_2), 53.6 (CH), 74.5 (CH), 118.7 (C), 137.4 (C), 148.3 (C), 205.2 (C).

2-Ethyl-3-hydroxy-1-phenyl-1-decanone (9be, *syn* : *anti* = 70 : 30) [785798-58-5][10]



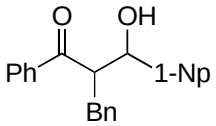
IR (neat) 3460 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) for the major isomer δ 0.88 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H), 1.25–1.63 (m, 12H), 1.76–1.95 (m, 2H), 2.58 (br s, 1H), 3.46 (ddd, *J* = 4.6, 4.5, 4.3 Hz, 1H), 3.87–3.92 (m, 1H), 7.46–7.64 (m, 3H), 7.94–7.99 (m, 2H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 12.3 (CH_3), 14.0 (CH_3), 22.6 (CH_2), 26.1 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 31.7 (CH_2), 34.0 (CH_2), 34.9 (CH_2), 52.2 (CH), 72.1 (CH), 128.3 (CH x 2), 128.7 (CH x 2), 133.3 (CH), 137.4 (C), 205.4 (C). For the minor isomer (only well-resolved peaks) δ 11.9 (CH_3), 20.6 (CH_3), 22.5 (CH_2), 25.9 (CH_2), 28.8 (CH_2), 29.0 (CH_2), 31.6 (CH_2), 35.7 (CH_2), 51.7 (CH), 72.5 (CH), 128.2 (CH), 133.4 (CH).

2-(Cyclohexyl(hydroxy)methyl)-1-phenyl-1-butanone (9bf, *syn* : *anti* = 71 : 29) [785798-60-9][10]



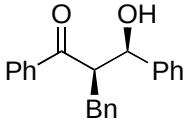
IR (neat) 3460 (br s, OH), 1680 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) for the major isomer δ 0.88 (t, *J* = 7.4 Hz, 3H), 0.93–2.02 (m, 13H), 2.66 (d, *J* = 2.7 Hz, 1H), 3.57 (ddd, *J* = 9.6, 3.9, 2.7 Hz, 1H), 3.67 (ddd, *J* = 9.6, 3.8, 3.6 Hz, 1H), 7.46–7.63 (m, 3H), 7.93–7.98 (m, 2H). For the minor isomer (only well-resolved peaks) δ 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 12.4 (CH_3), 19.6 (CH_2), 26.0 (CH_2), 26.1 (CH_2), 26.3 (CH_2), 29.0 (CH_2), 29.5 (CH_2), 40.7 (CH), 48.7 (CH), 75.9 (CH), 128.3 (CH x 2), 128.8 (CH x 2), 133.4 (CH), 137.4 (C), 205.6 (C). For the minor isomer (only well-resolved peaks) δ 12.1 (CH_3), 23.9 (CH_2), 25.8 (CH_2), 26.1 (CH_2), 28.6 (CH_2), 30.1 (CH_2), 42.0 (CH), 48.0 (CH), 77.1 (CH), 128.2 (CH), 133.4 (CH), 137.6 (C), 207.0 (C).

2-Benzyl-3-hydroxy-3-(1-naphthyl)-1-phenyl-1-propanone (9aa, *syn* : *anti* = 86 : 14) [785798-62-1][10]



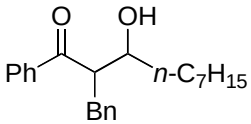
IR (neat) 3460 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.99–3.13 including 3.03 (dd, *J* = 13.5, 3,3 Hz, 1H), 3.21–3.31 including 3.25 (dd, *J* = 13.5, 10.6 Hz, 1H), 3.78 (d, *J* = 1.8 Hz, 0.86H), 3.89 (br s, 0.14H), 4.25 (ddd, *J* = 10.6, 3.3, 3.2 Hz, 0.86H), 4.34 (ddd, *J* = 7.6, 4.6, 4.5 Hz, 0.14H), 5.71–5.75 (m, 0.14H), 5.86 (br s, 0.86H), 6.78–8.02 (m, 17H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 33.4 (CH_2), 53.2 (CH), 70.4 (CH), 122.4 (CH), 124.8 (CH), 125.4 (CH), 126.0 (CH), 126.2 (CH), 128.2 (CH x 2), 128.2 (CH), 128.3 (CH), 128.3 (CH x 2), 128.4 (CH x 2), 128.9 (CH x 2), 129.2 (CH), 129.9 (CH), 133.3 (CH), 133.8 (C), 136.3 (C), 137.1 (C), 139.1 (C), 205.9 (C). For the minor isomer (only well-resolved peaks) δ 36.8 (CH_2), 53.0 (CH), 71.6 (CH).

***syn*-2-Benzyl-3-hydroxy-1,3-diphenyl-1-propanone (*syn*-9ab)** [135414-45-8][10,38]



Mp 85.2–86.8 °C (EtOH). IR (neat) 3460 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 3.05 (dd, *J* = 13.5, 3.6 Hz, 1H), 3.19 (dd, *J* = 13.5, 10.5 Hz, 1H), 4.03 (ddd, J = 10.5, 4.5, 3.6 Hz, 1H), 5.11 (br d, *J* = 4.3 Hz, 1H), 6.94–7.55 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 33.5 (CH_2), 55.6 (CH), 73.9 (CH), 126.1 (CH x 2), 126.2 (CH), 127.6 (CH), 128.2 (CH x 2), 128.2 (CH x 2), 128.3 (CH x 3), 128.3 (CH x 2), 128.9 (CH), 133.0 (CH), 137.3 (C), 139.3 (C), 141.6 (C), 204.8 (C). Anal. Calcd for $C_{22}H_{20}O_3$: C, 83.51; H, 6.37%. Found: C, 83.30; H, 6.40%.

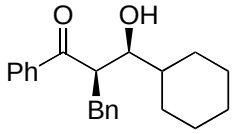
2-Benzyl-3-hydroxy-1-phenyl-1-decanone (9ae, *syn* : *anti* = 70 : 30) [785798-65-4][10]



IR (neat) 3460 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) for the major isomer δ 0.87 (t, *J* = 7.5 Hz, 3H), 1.18–1.56 (m, 12H), 2.67 (d, *J* = 3.2 Hz, 1H), 3.09 (dd, *J* = 13.2, 5.1 Hz, 1H), 3.16 (dd, *J* = 13.2, 9.1 Hz, 1H), 3.80 (ddd, *J* = 9.1, 5.1, 4.0 Hz, 1H), 3.90–3.94 (m, 1H), 7.07–8.00 (m, 10H). ^{13}C NMR ($CDCl_3$)

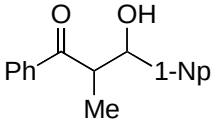
for the major isomer δ 13.9 (CH_3), 22.5 (CH_2), 25.9 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 31.6 (CH_2), 33.8 (CH_2), 34.9 (CH_2), 53.5 (CH), 72.2 (CH), 126.0 (CH), 128.2 (CH x 2), 128.2 (CH x 2), 128.3 (CH x 2), 128.8 (CH x 2), 132.9 (CH), 137.4 (C), 139.6 (C), 204.7 (C). For the minor isomer (only well-resolved peaks) δ 24.7 (CH_2), 26.0 (CH_2), 31.5 (CH_2), 35.9 (CH_2), 36.1 (CH_2), 52.2 (CH), 72.4 (CH), 133.2 (CH), 138.9 (C), 206.0 (C).

***syn*-2-Benzyl-3-cyclohexyl-3-hydroxy-1-phenyl-1-propanone (*syn*-9af)** [785798-67-6][10]



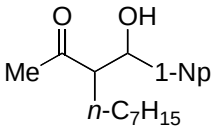
Mp 70.0–71.8 °C (EtOH). IR (neat) 3460 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.90–1.34 (m, 6H), 1.52–1.78 (m, 2H), 2.03 (br d, *J* = 12.7 Hz, 1H), 2.76 (d, *J* = 2.8 Hz, 1H), 3.03 (dd, *J* = 13.6, 3.6 Hz, 1H), 3.20 (dd, *J* = 13.6, 10.5 Hz, 1H), 3.59 (ddd, *J* = 7.8, 3.5, 2.8 Hz, 1H), 4.00 (ddd, *J* = 10.5, 3.6, 3.5 Hz, 1H), 7.05–7.51 (m, 10H), 7.65–7.67 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 26.3 (CH_2), 26.6 (CH_2), 26.8 (CH_2), 29.7 (CH_2), 29.9 (CH_2), 32.9 (CH_2), 41.1 (CH), 50.3 (CH), 76.5 (CH), 126.6 (CH), 128.7 (CH x 2), 128.9 (CH x 2), 129.0 (CH x 2), 129.4 (CH x 2), 133.6 (CH), 137.6 (C), 140.3 (C), 205.7 (C). Anal. Calcd for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13%. Found: C, 81.84; H, 8.28%.

3-Hydroxy-2-methyl-3-(1-naphthyl)-1-phenyl-1-propanone (9ca, *syn* : *anti* = 92 : 8) [187848-81-3][10,39]



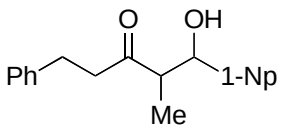
^1H NMR ($CDCl_3$) δ 1.11 (d, *J* = 7.3 Hz, 0.24H), 1.17 (d, *J* = 7.3 Hz, 2.76H), 3.30 (d, *J* = 4.9 Hz, 0.08H), 3.91 (qd, *J* = 7.3, 2.1 Hz, 0.92H), 4.03 (d, *J* = 2.0 Hz, 092H), 4.18–4.25 (m, 0.08H), 5.80 (dd, *J* = 7.8, 4.9, 0.08H), 6.05 (br s, 0.92H), 7.46–7.61 (m, 6H), 7.82–7.97 (m, 6H).

3-(Hydroxy(1-naphthyl)methyl)-2-decanone (9fa, *syn* : *anti* = 87 : 13) [none]



IR (neat) 3460 (br s, OH), 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) for the major isomer δ 0.90–1.34 (m, 6H), 1.52–1.78 (m, 2H), 2.13 (br s, 3H), 2.76 (d, *J* = 2.8 Hz, 1H), 3.03 (dd, *J* = 13.6, 3.6 Hz, 1H), 3.20 (dd, *J* = 13.6, 10.5 Hz, 1H), 3.59 (ddd, *J* = 7.8, 3.5, 2.8 Hz, 1H), 4.00 (ddd, *J* = 10.5, 3.6, 3.5 Hz, 1H), 7.05–7.51 (m, 10H), 7.65–7.67 (m, 2H). For the minor isomer (only well-resolved peaks) δ 2.02 (br s, 3H), 2.82 (d, *J* = 2.6 Hz, 1H). ^{13}C NMR ($CDCl_3$) for the major isomer δ 26.3 (CH_2), 26.6 (CH_2), 26.8 (CH_2), 29.7 (CH_2), 29.9 (CH_2), 32.9 (CH_2), 41.1 (CH), 50.3 (CH), 76.5 (CH), 126.6 (CH), 128.7 (CH x 2), 128.9 (CH x 2), 129.0 (CH x 2), 129.4 (CH x 2), 133.6 (CH), 137.6 (C), 140.3 (C), 205.7 (C).

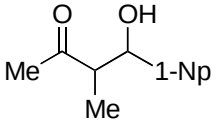
1-Hydroxy-2-methyl-1-(1-naphthyl)-5-phenyl-3-pentanone (9ga, *syn* : *anti* = 81 : 19) [none]



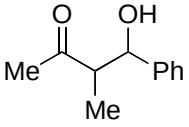
^1H NMR ($CDCl_3$) δ 0.95 (d, *J* = 7.3 Hz, 0.57H), 1.02 (d, *J* = 7.1 Hz, 2.43H), 2.78–3.00 (m, 5H), 3.21

(d, *J* = 2.5 Hz, 0.81H), 3.27–3.33 (m, 0.19H), 5.55 (dd, *J* = 7.8, 5.3, 0.19H), 5.89 (dd, *J* = 2.6, 2.5Hz, 0.81H), 7.16–7.30 (m, 3H), 7.46–7.52 (m, 4H), 7.69–7.89 (m, 5H).

4-Hydroxy-3-methyl-4-(1-naphthyl)-2-butanone (9ja, *syn* : *anti* = 88 : 12) [785798-72-3][29]

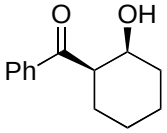


4-Hydroxy-3-methyl-4-phenyl-2-butanone (9jb, *syn* : *anti* = 85 : 15) [74676-21-4][30]



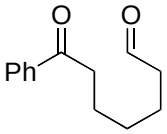
4.6. Reductive Cyclization

***cis*-2-Hydroxycyclohexyl Phenyl Ketone (*cis*-11)** [33830-24-9][40]

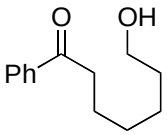


^{1}H NMR ($CDCl_3$) δ 1.36–1.56 (m, 4H), 1.72–2.01 (m, 4H), 3.37 (br d, J = 4.3 Hz, 1H), 3.95 (br s, 1H), 4.29 (br s, 1H), 7.45–7.64 (m, 3H), 7.92–7.94 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 19.5 (CH_2), 24.5 (CH_2), 25.5 (CH_2), 31.9 (CH_2), 48.0 (CH), 66.3 (CH), 128.3 (CH x 2), 128.7 (CH x 2), 133.4 (CH), 135.6 (C) 205.9 (C).

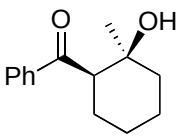
7-Oxo-7-phenylheptanal (12) [88773-76-6][31]



7-Hydroxy-1-phenyl-1-heptanone (13) [263565-77-1][32]

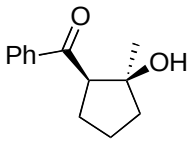


***cis*-2-Hydroxy-2-methylcyclohexyl Phenyl Ketone (*cis*-15a)** [489473-50-9][41]



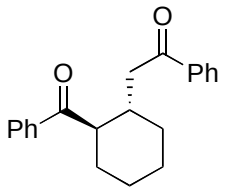
^{1}H NMR ($CDCl_3$) δ 1.19 (s, 3H), 1.26–1.41 (m, 2H), 1.52–1.55 (m, 2H), 1.69–1.91 (m, 4H), 3.31 (dd, J = 11.7, 3.5 Hz, 1H), 4.45 (d, J = 2.3 Hz, 1H), 7.46–7.63 (m, 3H), 7.94–7.97 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 21.1 (CH_2), 25.4 (CH_2), 26.9 (CH_2), 29.6 (CH_3), 38.9 (CH_2), 51.3 (CH), 70.0 (C), 128.2 (CH x 2), 128.7 (CH x 2), 133.6 (CH), 136.5 (C) 207.0 (C).

2-Hydroxy-2-methylcyclopentyl Phenyl Ketone (*cis* -15b) [489473-55-4][41]



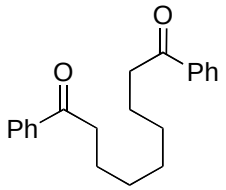
Mp 58.0–59.6 °C (EtOH–Hex). ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 3H), 1.53–2.22 (m, 6H), 3.91 (dd, *J* = 8.1, 7.9 Hz, 1H), 5.21 (br s, 1H), 7.45–7.57 (m, 3H), 8.04–8.08 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 22.1 (CH_2), 25.5 (CH_3), 30.3 (CH_2), 40.7 (CH_2), 54.0 (CH), 80.9 (C), 128.3 (CH x 2), 128.7 (CH x 2), 133.6 (CH), 137.2 (C) 205.6 (C).

***trans*-2-(2-Benzoylcyclohexyl)-1-phenylethanone (*trans*-17a)** [13471-32-0][42]

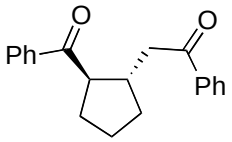


^{1}H NMR ($CDCl_3$) δ 1.31–1.40 (m, 4H), 1.73–2.00 (m, 4H), 2.44–2.62 (m, 2H), 3.14 (br d, *J* = 12.7 Hz, 1H), 3.32 (ddd, *J* = 12.7, 10.3, 3.5 Hz, 1H), 7.45–7.56 (m, 6H), 7.96–8.01 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 25.5 (CH_2), 25.9 (CH_2), 31.2 (CH_2), 31.4 (CH_2), 35.8 (CH), 44.2 (CH_2), 50.6 (CH), 128.2 (CH x 2), 128.4 (CH x 2), 128.5 (CH x 2), 128.7 (CH x 2), 132.9 (CH), 133.1 (CH), 136.7 (C), 136.8 (C), 199.8 (C), 203.7 (C).

1,9-Diphenyl-1,9-nonanedione (18a) [28861-21-4][33]

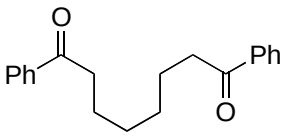


***trans*-2-(2-Benzoylcyclopentyl)-1-phenylethanone (*trans*-17b)** [137448-48-7][7a]

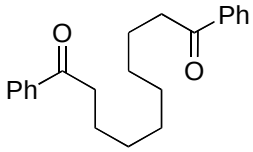


^{1}H NMR ($CDCl_3$) δ 1.39–1.56 (m, 1H), 1.66–1.85 (m, 3H), 2.04–2.17 (m, 2H), 2.86 (dd, *J* = 14.5, 8.4 Hz, 1H), 2.93–3.06 (m, 1H), 3.20 (dd, *J* = 14.5, 5.1, 1H), 3.47–3.56 (m, 1H), 7.41–7.56 (m, 6H), 7.93–7.99 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 24.6 (CH_2), 31.2 (CH_2), 32.3 (CH_2), 38.7 (CH), 43.7 (CH_2), 52.5 (CH), 128.2 (CH x 2), 128.4 (CH x 2), 128.5 (CH x 4), 132.8 (CH), 132.9 (CH), 136.7 (C), 137.0 (C), 199.7 (C), 202.2 (C).

1,8-Diphenyl-1,8-octanedione (18b) [6268-58-2][34]



1,10-Diphenyl-1,10-decanedione (18c) [6268-61-7][35]



5. References

1. 1,4-Hydrosilylation: (a) Speier, J. L.; Webster, J. A.; Barnes, G. H. *J. Am. Chem. Soc.* **1957**, *79*, 974. (b) Bourhis, R.; Frainnet, E.; Moulines, F. *J. Organomet. Chem.* **1977**, *141*, 157. (c) Barlow, A. P.; Boag, N. M.; Stone, G. A. *J. Organomet. Chem.* **1980**, *191*, 39. (d) Kogure, T.; Ojima, I. *Organometallics* **1982**, *1*, 1390. (e) Mahoney, W. S.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 8818. (f) Hilty, T. K.; Revis, A. *J. Org. Chem.* **1990**, *55*, 2972. (g) Chan, T. H.; Zheng, G. Z. *Tetrahedron Lett.* **1993**, *34*, 3095. (h) Johnson, C. R.; Raheja, R. K. *J. Org. Chem.* **1994**, *59*, 2287. (i) Lipshutz, B. H.; Keith, J.; Papa, P.; Vivian, R. *Tetrahedron Lett.* **1998**, *39*, 4627. (j) Appella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9473. (k) Lipshutz, B. H.; Chrisman, W.; Noson, K.; Papa, P.; Sclafani, J. A.; Vivian, R. W.; Keith, J. M. *Tetrahedron* **2000**, *56*, 2779.
2. 1,4-Hydroboration: Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 5678.
3. 1,4-Hydroalumination: (a) Tsuda, T.; Hayashi, T.; Satomi, H.; Kawamoto, T.; Saegusa, T. *J. Org. Chem.* **1986**, *51*, 537. (b) Ikeno, T.; Kimura, T.; Ohtsuka, Y.; Yamada, T. *Synlett* **1999**, 96.
4. 1,4-Hydrostannylation: (a) Four, P.; Guibe, P. *Tetrahedron Lett.* **1982**, *23*, 1825. (b) Keinan, E.; Gleize, P. A. *Tetrahedron Lett.* **1982**, *23*, 477.
5. Huddleston, R. R.; Krische, M. J. *Synlett* **2003**, 12.
6. (a) Revis, A.; Hilty, T. K. *Tetrahedron Lett.* **1987**, *28*, 4809. (b) Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, 2005. (c) Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990**, *31*, 5331. (d) Kiyooka, S.; Shimizu, A.; Torii, S. *Tetrahedron Lett.* **1998**, *39*, 5237. (e) Taylor, S. J.; Morken, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 12202. (f) Ooi, T.; Doda, K.; Sakai, D.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 2133. (g) Taylor, S. J.; Duffey, M. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (h) Zhao, C.-X.; Duffey, M. O.; Taylor, S. J.; Morken, J. P. *Org. Lett.* **2001**, *3*, 1829.
7. (a) Baik, T.-G.; Luis, A. L.; Wang, L.-C.; Krische, M. J. *J. Am. Chem. Soc.* **2001**, *123*, 5112. (b) Wang, L.-C.; Jang, H.-Y.; Roh, Y.; Lynch, V.; Schultz, A. J.; Wang, X.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 9448. (c) Jang, H.-Y.; Huddleston, R. R.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 15156. (d) Huddleston, R. R.; Krische, M. J. *Org. Lett.* **2003**, *5*, 1143.
8. (a) Ranu, B. C.; Samanta, S. *Tetrahedron Lett.* **2002**, *43*, 7405. (b) Ranu, B. C.; Samanta, S. *J. Org. Chem.* **2003**, *68*, 7130.
9. Shibata, I.; Kato, H.; Ishida, T.; Yasuda, M.; Baba, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 711.
10. Abernethy, C. D.; Cole, M. L.; Jones, C. *Organometallics* **2000**, *19*, 4852.
11. (a) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 906. (b) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2001**, *42*, 4661. (c) Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627.
12. As shown here, the reductive aldol reaction is much slower than the 1,4-reduction. This observation is attributable to slow regeneration of the indium hydride species from the indium aldolate intermediate.
13. The $In(OAc)_3$-catalyzed reduction of **8a** with $PhSiH_3$ (rt, 1.5 h) gave 1-naphthylmethanol in 82% yield.
14. As proposed by Baba et al. (ref. 9), the *syn* selectivity can be attributed to the formation of (*Z*)-**4b** by a concerted hydroindation and the subsequent aldol addition via a cyclic transition state. However, the author has no evidence of the selective formation of (*Z*)-**4b**. See page 21.
15. Typical procedure for the $In(OAc)_3$-catalyzed reductive aldol reaction of α-enones with aldehydes: Under N_2, α-enone **1b** (73 mg, 0.50 mmol), **8a** (102 mg, 0.65 mmol), and $PhSiH_3$ (54 mg, 0.50

mmol) were added to a suspension of $In(OAc)_3$ (15 mg, 0.05 mmol) in EtOH (0.25 mL). The mixture was stirred at 0 °C for 36 h. The work-up and purification were performed by the procedure described in general procedure. See page 30.

16. The reaction of **1b** with octanal was carried out in THF containing an equimolar amount of EtOH at 70 °C. However, both the yield of **9** and the *syn* selectivity dropped to 52% and 56% *syn*, respectively.
17. According to the method reported by Montgomery *et al.*, **10** and **16a** were prepared by ozonolysis of cyclopentene and the subsequent Wittig olefination with $Ph_3PCHC(O)Ph$. This method was used also for the preparation of **14a**, **14b**, **16b,** and **16c** from 1-methylcyclopentene, 1,5-dimethyl-1,5-cyclo-octadiene, 1,5-cyclooctadiene, and cyclohexene respectively. See pages 25–26. (a) Montgomery, J.; Savchenko, A. V.; Zhao, Y. *J. Org. Chem.* **1995**, *60*, 5699. See also the following paper for the preparation of **14a** and **14b**. (b) Huddleston, R. R.; Cauble, D. F.; Krische, M. J. *J. Org. Chem.* **2003**, *68*, 11.
18. For the stereochemical assignment of **11**, **17a**, and **17b**, see ref 7a. The relative configurations of **15a** and **15b** were determined by their NMR data reported in ref 17b.
19. Krische *et al.* have reported *cis*-selective reductive aldol reactions of **10** and **14a**, and *trans*-selective reductive Michael reaction of **16**. See refs 7 and 17b.
20. Trevoy, L. W.; Brown, W. G.; *J. Am. Chem. Soc.* **1949**, *71*, 1675.
21. Oare, D. A.; Henderson, M. A.; Sanner, M. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 132.
22. (a) Kulinkoich, O. G.; Sviridov, S. V.; Vasilevski, D. A. *Synthesis* **1991**, 234. (b) Okumoto, H.; Takamitsu, J.; Shimizu, H.; Harada, Y.; Suzuki, A. *Synlett* **2000**, 629.
23. (a) Ramirez, F.; Dershowitz, S. *J. Org. Chem.* **1957**, *22*, 41. (b) Montgomery, J.; Savchenko, A. V.; Zhao, Y. *J. Org. Chem.* **1995**, *60*, 5699. (c) Huddleston, R. R.; Cauble, D. F.; Krische, M. J. *J. Org. Chem.* **2003**, *68*, 11.
24. Compound data for 5-Phenyl-1-penten-3-ol: Schmit, B. *J. Org. Chem*. **2004**, *69*, 7672.
25. Compound data for **2a-*d*** and **2a'-*d***: Wang, Z.; Zou, G.; Tang, J. *Chem. Commun.*, **2004**, 1192.
26. Compound data for 1-Phenyl-1-pentanol: Law, M. C.; Wong, K, -Y.; Chan, T. H. *J. Org. Chem.* **2005**, *70*, 10434.
27. Compound data for 4-(Hydroxymethyl)acetophenone: Wiles, C.; Watts, P.; Haswell, S. J. *Tetrahedron Let.* **2006**, *47*, 5261.
28. Compound data for 1-(4-(Hydroxymethyl)phenyl)ethanol: Matsumoto, H.; Ori, A.; Inokuchi, F.; Shinkai, S. *Chem. Lett*. **1996**, 301
29. Compound data for **9ja**: Luo, S.; Xu, H.; Li, J.; Zhang, L.; Cheng, J. -P. *J. Am. Chem. Soc*. **2007**, *129*, 3074.
30. Compound data for **9jb**: Mahrwald, R.; Schetter, B. *Org. Lett*. **2006**, *8*, 281.
31. Compound data for **12**: Jang, H. Y.; Huddleston, R. R.; Krische, M. J. *J. Am. Chem. Soc*. **2002**, *124*, 15156.
32. Compound data for **13**: Rahim, M. D.; Fujiwara, T.; Takeda, T. *Tetrahedron* **2000**, *56*, 763.
33. Compound data for **18a**: Kakino, R.; Narahashi, H.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.*,**2002**, *75*, 1333.
34. Compound data for **18b**: Blay, G.; FernaÂndez, I.; Formentin, P.; Monje, B.; Pedrop, J. R.; Ruiz. R. *Tetrahedron* **2001**, *57*, 1075.
35. Compound data for **18c**: Overberger, C. G.; Tashlick, I.; Bernstein, M.; Hiskey, R. G. *J. Am. Chem. Soc*. **1958**, *80*, 6556.
36. Fry, A. J.; Susla. M.; Weltz, M. *J. Org. Chem.* **1987**, *52*, 2496.

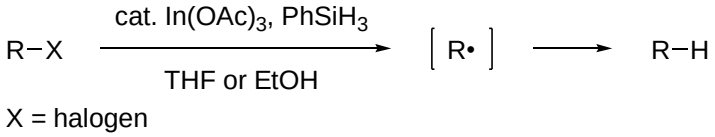
37. Inoue, K.; Ishida, T.; Shibata, I; Baba, A *Advanced Synthesis & Catalysis*, **2002**, *344*, 283.
38. Shibata, I.; Kato, H.; Ishida, T.; Yasuda, M.; Baba, A. *Angew. Chem., Int. Ed*. **2004**, *43*, 711.
39. Hamada, T.; Manabe, K.; Ishikawa, S.; Nagayama, S.; Shiro, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 2989.
40. Lee, H. -Y.; An, M. *Tetrahedron Lett.* **2003**, *44*, 2775.
41. Huddleston, R. R.; Cauble, D. F.; Krische, M. J. *J. Org. Chem*. **2003**, *68*, 11.
42. Wang, L. -C.; Jang, H. -Y.; Roh, Y.; Lynch, V.; Schultz, A. J.; Wang, X.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 9448.

Chapter 2

Indium(III)-Catalyzed Reduction of Organic Halides with Hydrosilanes via a Radical Chain Process

Abstract

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.



1. 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 studies on synthetic use of hydrosilanes,[2] this laboratory found that a copper salt can activate hydrosilanes by transmetalation, and that the copper hydride species thus formed is valuable for reduction of carbonyl compounds.[3] These observations prompted the author to investigate catalytic activation of hydrosilanes with other metal salts and its application to an efficient reduction of carbon electrophiles. He then focused his 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 he 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] The author 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] He herein report the details of his study on the indium and gallium-catalyzed reductions of organic halides with hydrosilanes.

2. Results and Discussion

2.1. 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 $PhSiH_3$ 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 $PhSiH_3$ during the reaction.

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

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)

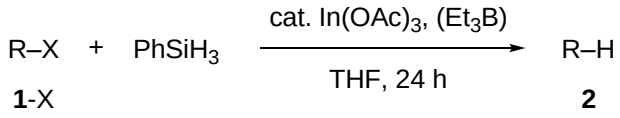
$$\underset{\textit{Si}\text{–H}}{\textbf{1a}\text{-Br}} + \underset{(1\ \text{equiv})}{\textit{Si}\text{–H}} \xrightarrow[\text{THF, 70 °C, 24 h}]{In(OAc)_3\ (10\ \text{mol\%})} \textbf{2a} \qquad (2)$$

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

2.2. Scope and Limitations

With the initial results in hand, the author investigated the scope and limitations of the $In(OAc)_3$-catalyzed reduction with $PhSiH_3$ at 70 °C (Method A in Table 1). Non-functionalized 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 yield (entries 3, 8, 11 and 12). This reduction system was tolerant to ester and alkyl ether moieties (entries 14-17).

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



entry	R-X		yield / %[b]	
			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).

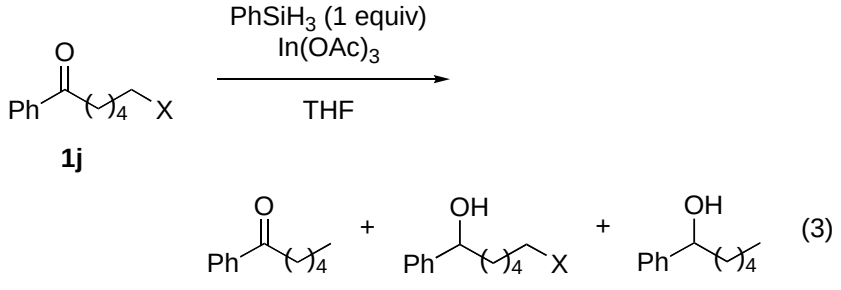
[b]The yield was determined by GC analysis (entries 1-13, 16 and 17), by ^1H NMR analysis (entries 18 and 19) or by isolation (entries 14, 15 and 20-23).

[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.

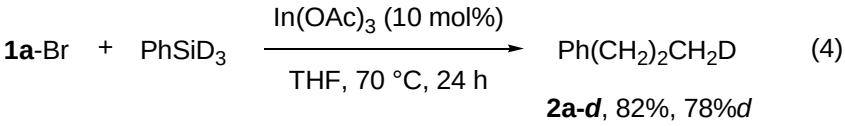
However, the presence of hydroxy and siloxy groups complicated the $In(OAc)_3$-catalyzed reaction (entries 18-20). Bromoketone **1j**-Br underwent competitive reduction of C-Br and C=O bonds to give the desired product **2j** and carbonyl reduction products **3** and **4** (entries 22 and 23, eq 3).



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

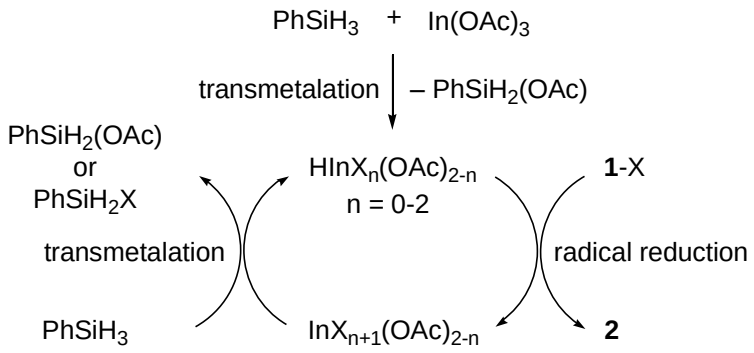
2.3. Mechanistic Aspects

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 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.



The reaction of $In(OAc)_3$ with an excess amount of $PhSiH_3$ (10 equiv) gave indium foil in 93% yield with 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 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 indium hydride species, $HIn(OAc)_2$ and HInX(OAc). After the first turnover, further reduction of

the remaining haloalkane is carried out with $HInX_n(OAc)_{2-n}$ (n = 0-2).



Scheme 1

2.4. Reduction at 30 °C

His effort was 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 initiator,[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 by 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 below, it turned out that addition of only air accelerated the In-catalyzed reduction of organic halides.

2.5. Reduction in EtOH

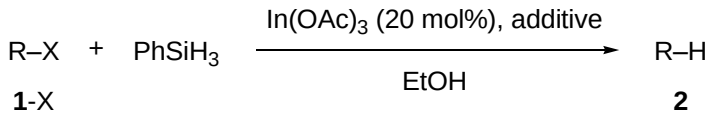
The author has reported the generation of indium hydride species from $In(OAc)_3$ and $PhSiH_3$ in EtOH and its application to catalytic 1,4-reduction of α-enones.[7b] Since EtOH is an environmentally benign organic solvent, he examined the $In(OAc)_3$-catalyzed reduction in EtOH. First, the Et_3B-initiated method used in Method B was applied to the reduction of bromo- and iodoalkanes (Method C in Table 2). However, except 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 with 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, 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 a lot of 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).

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 bromo-

alkanes, **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).

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



Entry	R-X		Yield / %[b]	
			Method C[c]	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.

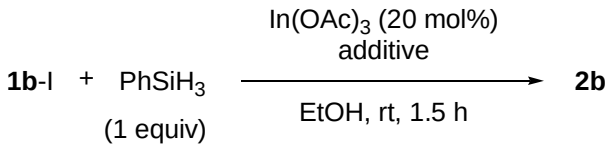
[e]The result without Et_3B-dry air is shown in parentheses.

[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.

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 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 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 fast turnover of the catalytic cycle by acceleration of both hydride transfer and radical reduction.

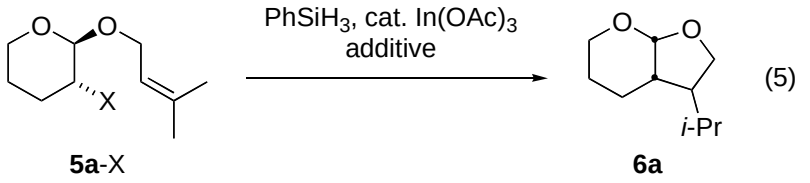
As shown in Scheme 1, the reduction of haloalkanes would form Lewis acidic species such as $InX_{n+1}(OAc)_{2-n}$ and $PhSiH_2X$, which can lead to HX and its equivalents by the reaction with EtOH. The incomplete reduction of iodoalkanes by Method C is attributable to the acid-catalyzed solvolysis of $PhSiH_3$ 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 overreduction 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% conv. 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 $PhSiH_3$.

2.6. Intramolecular Radical Addition.

The reduction system using $In(OAc)_3$ and $PhSiH_3$ was also applied to radical cyclization of haloalkenes. The cyclization of bromoalkene **5a**-Br gave disappointed results (eq 5). The author therefore directed his effort 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, 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.



5a-X **6a** (5)

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

Entry	Additive (/ equiv)	Solvent	Temp / °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.

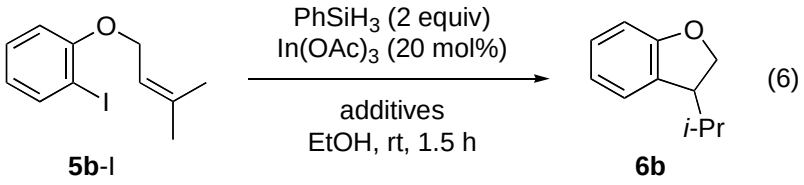
[c]Complex mixture.

[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.

Next, the cyclization of iodoalkene **5b**-I was examined. Use of THF as 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)

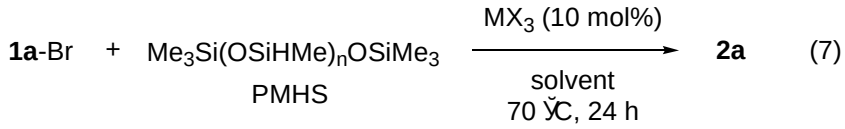
5b-I **6b**

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.

2.7. Use of Poly(methylhydrosiloxane)

Poly(methylhydrosiloxane) (PMHS) has frequently been used as an inexpensive, stable reducing agent.[12] Aiming at a more practical method for radical reduction of haloalkanes, PMHS was selected as 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.



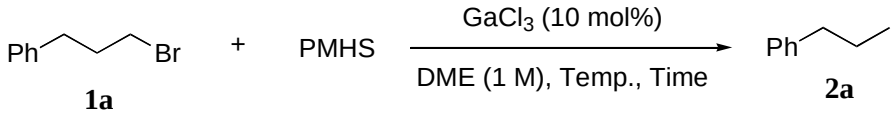
(7)

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)

The author optimized the amount of PMHS and the reaction time (entries 1-9 in Table 5). As the results of optimization, it was found that the reaction of **1a**-Br was completed with 3 equiv. PMHS in 12 h. The reactions at low temperatures (rt and 50 °C) resulted in low yields of **2a** (entries 10 and 11). An increase in reaction temperature was effective promoting the reduction. The reaction at 90 °C for 4 h achieved a quantitative yield of **2a** (entry 15). The gallium-catalyzed reduction may involve a radical chain mechanism; therefore, the author investigated the effects of light and oxygen on the **1a**-Br reaction rate. The reaction in the dark gave a result similar to that of the reaction conducted under a fluorescent lamp (entry 16). In contrast, introduction of a small amount of oxygen or air is quire effective in rate acceleration (entries 17-19). In the presence of oxygen or air, the reaction at 90 °C was completed in 1 h (entry 20). Under the optimized conditions, the reduction proceeded efficiently ever with 5 mol% $GaCl_3$ (entries 21-23).

Table 5. Optimization of Amount of PMHS



Entry	PMHS (equiv of *Si*-H))	O_2 or dry air (mL)	Temp. (°C)	Time / h	Yield / %[a]
1	3	0	70	1	26
2	3	0	70	3	73
3	3	0	70	6	90
4	3	0	70	12	>99
5	3	0	70	24	>99
6	4	0	70	1	17
7	4	0	70	3	73
8	4	0	70	6	99
9	4	0	70	24	>99
10	3	0	rt	3	0
11	3	0	50	3	15
12	3	0	80	3	90
13	3	0	90	1	56
14	3	0	90	2	75
15	3	0	90	4	99
16[b]	3	0	90	1	49
17	3	O_2 (1)	90	1	98
18	3	Under O_2	90	1	92
19	3	air (4.8)	90	1	89
20	3	air (30)	90	1	99
21[c]	3	air (30)	90	1	90
22[d]	3	air (30)	90	1	40
23[e]	3	air (30)	90	1	0

[a]Determined by GC analysis.

[b]In the dark.

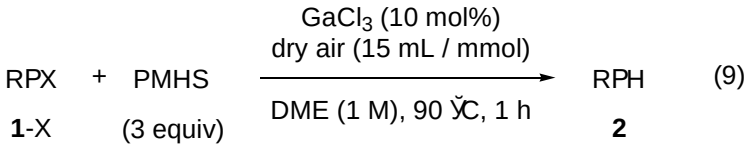
[c]An increased amount of $GaCl_3$ (5 mol%) was used.

[d]An increased amount of $GaCl_3$ (1 mol%) was used.

[e]$GaCl_3$ was not used.

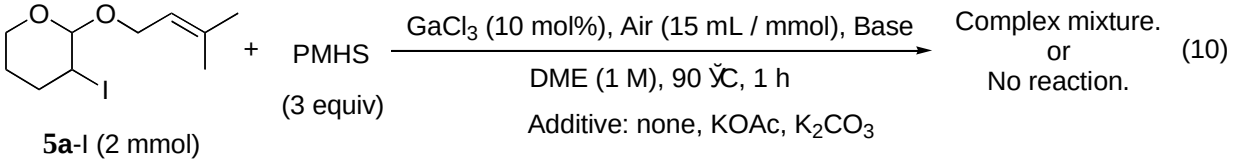
The $GaCl_3$-PMHS system is efficient in reduction of non-functionalized bromo- and iodoalkanes, but not in reduction of chloroalkanes (Eq 9). Bromoalkanes **1g**-Br and **1i**-Br, bearing an ether moiety, were reduced in good yield. In contrast, the reduction of **1h**-Br and **1j**-Br, bearing a hydroxy or carbonyl group,

caused the destruction of these functionalities. The $GaCl_3$-PMHS system was not suitable for the cyclization of iodoalkenes (Eqs. 10-11).

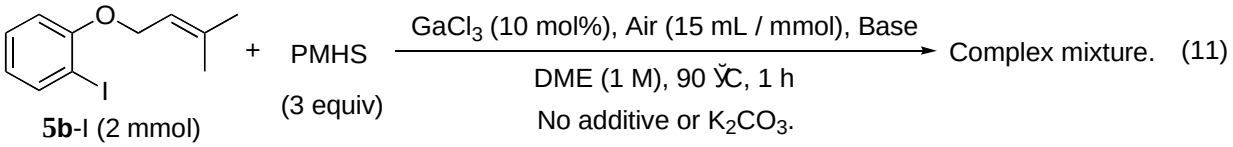


(9)

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), $PhC(O)O(CH_2)_3Br$ (<15), $CH_3CH(O)(CH_2)_{11}Br$ (0), $CH_3CH(OH)(CH_2)_{11}Br$ (CM)
*With 5 mol% $GaCl_3$.



(10)



(11)

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 gallium hydride species[5,13] although the detailed mechanism is not clear.

3. Conclusion

The author has demonstrated that indium and gallium salts can catalyze 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] The author has 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, an environmentally friendly solvent, with the aid of 2,6-lutidine and dry air. In addition, he has 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, he has developed new catalytic systems valuable for tin-free radical reactions.[14].

4. Experimental Section

4.1. General Method

See page 11.

4.2. Access to Substrates and Reagents

Simple organic halides **1a-e** and hydrosilanes except $PhSiH_2Cl$ were commercially available. Functionalized haloalkanes **1f-k** and haloalkenes **5** were obtained by the methods described below. $PhSiD_3$ (CAS 18164-03-9) was prepared from $PhSiCl_3$ by reduction with $LiAlD_4$.[15,16]

4.3. Preparation of Substrates

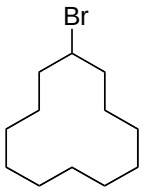
The substrates prepared were identified by comparison of their spectral data with those reported previously (**1c**-Cl, **1c**-Br, **1c**-I, **1f**-Br, **1f**-I, **1h**-Br, **1j**-Br, **1j**-I, **1k**-I, **5a**-Br, **5a**-I, and **5b**-I) or by full characterization (**1g**-Br, **1g**-I, **1h**-I, **1i**-Br, and **1i**-I). CAS registry numbers and reference numbers leading to the reported spectral data of the title compounds are shown in the title lines.

Chlorophenylsilane [4206-75-1][17]

$PhSiH_2Cl$

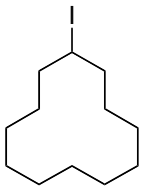
A solution of phenysilane (14.0 g, 130 mmol) in dry CCl_4 (55 mL) was dropwise added to a solution of phosphorus(V) chloride (21.6 g, 104 mmol) in dry CCl_4 (170 mL) over 30 min at room temperature. After being stirred for 24 h, the reaction mixture was concentrated. Purification of the crude product by distillation gave the title compound ($PhSiHCl_2$: $PhSiH_2Cl$ = 1: 9, 7.82 g, 54.8 mmol) in 42% yield. Chlorophenylsilane: ^{1}H NMR (C_6D_6) δ 5.10 (s, 2H), 7.03–7.26 (m, 3H), 7.38–7.55 (m, 2H).

Bromocyclododecane (1c-Br) [7795-35-9][18]



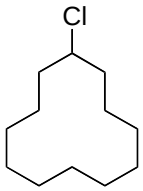
Tribromophosphine (2.3 g, 8.5 mmol) was added to a solution of cyclododecanol (3.1 g, 17 mmol) in Et_2O (34 mL) at 0 °C and stirred for 1.5 h. The reaction mixture was warmed to room temperature and stirred for 24 h. The resultant mixture was treated with aqueous $Na_2S_2O_3$ (4 M, 50 mL), and extracted with hexane (50 mL x 3). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by distillation gave the title compound (0.5 g, 2.0 mmol) in 12% yield. **1c**-Br: ^{1}H NMR ($CDCl_3$) δ 1.30–1.50 (m, 18H), 1.82–1.94 (m, 2H), 1.99–2.09 (m, 2H), 4.21–4.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 23.7 (CH_2 x 2), 23.4 (CH_2 x 4), 23.6 (CH_2 x 2), 23.7 (CH_2), 34.6 (CH_2 x 2), 54.0 (CH); MS *m*/*z* (relative intensity) 167 (M^+ – Br, 5), 111 (14), 55 (100).

Iodocyclododecane (1c-I) [61682-10-8][19]



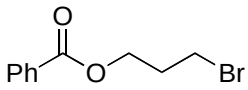
H_3PO_4 (85% solution in H_2O (100 mL)) was added to a mixture of cyclododecanol (18.4 g, 100 mmol) and potassium iodide (83 g, 500 mmol), and stirred for 3 h at 120 °C. The reaction mixture was treated with saturated aqueous $NaHCO_3$ (4 M, 300 mL), and extracted with *t*-BuOMe (100 mL x 3). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by distillation gave the title compound in 44% yield (12.8 g, 43.6 mmol). **1c**-I: ^{1}H NMR ($CDCl_3$) δ 1.30–1.50 (m, 18H), 1.88–2.12 (m, 4H), 4.35 (quint, *J* = 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.4 (CH_2 x 6), 23.5 (CH_2 x 7), 23.7 (CH_2), 24.1 (CH_2 x 6), 33.8 (CH), 36.5 (CH_2 x 2); MS *m*/*z* (relative intensity) 167 (M^+ – I, 5), 111 (14), 55 (100).

Chlorocyclododecane (1c-Cl) [34039-83-3][20]



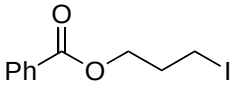
Triphenylphosphine (18.4 g, 70.0 mmol) was added to a solution of cyclododecanol (12.6 g, 69.0 mmol) in CCl_4 (25 mL) at room temperature and stirred for 96 h. The reaction mixture was treated with aqueous $Na_2S_2O_3$ (4 M, 80 mL), and extracted with hexane (50 mL x 3). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by distillation gave the title compound in 27 % yield (3.7 g, 18.7 mmol). **1c**-Cl: ^{1}H NMR ($CDCl_3$) δ 1.30–1.50 (m, 18H), 1.88–2.12 (m, 4H), 4.35 (quint, *J* = 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.4 (CH_2 x 2), 23.5 (CH_2 x 4), 23.7 (CH_2), 24.1 (CH_2 x 2), 33.8 (CH), 36.5 (CH_2 x 2); MS *m*/*z* (relative intensity) 167 (M^+ – Cl, 5), 111 (14), 55 (100).

3-Bromopropyl Benzoate (1f-Br) [6065-69-6][21]



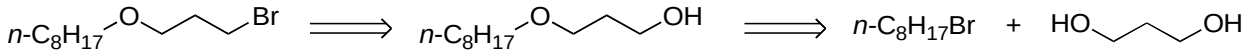
Benzoyl chloride (1.41 g, 10.0 mmol) was added to a stirred solution of 3-bromo-1-propanol (1.39 g, 10.0 mmol) and Et_3N (1.11 g, 11.0 mmol) in Et_2O (10 mL) at 0 °C. After being stirred mixture at 0 °C for 1 h, the mixture was warmed to room temperature. After 8.5 h, the reaction mixture was poured into water. The extract with *t*-BuOMe (50 mL) was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 10:1) gave the title compound (2.40 g, 9.90 mmol) in 99% yield.

3-Iodopropyl Benzoate (1f-I) [245758-34-3][21]



The title compound was prepared from benzoyl chloride and 3-iodo-1-propanol by a similar method as described above (85% isolated yield), in which pyridine was used instead of Et_3N.

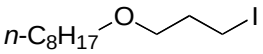
1-(3-Bromopropoxy)octane (1g-Br) [920518-03-2]



NaH (60% in mineral oil, 3.2 g, 80 mmol) was placed in a reaction flask. After the flask was filled with N_2, NaH was washed with dry hexane, and DMF (120 mL) was introduced. 1,3-Propanediol (6.1 g, 80 mmol) was added to the resultant suspension at 0 °C, and the mixture was stirred at 0 °C for 30 min and at room temperature for 1 h. 1-Bromooctane (15.5 g, 80 mmol) was added to the mixture at 0 °C. After being stirred at 0 °C for 30 min and at room temperature for 21 h, the reaction mixture was poured into water. The extract with *t*-BuOMe was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 3:1) gave 3-octoxy-1-propanol (8.5 g, 45 mmol) in 56% yield.[22] 3-Octoxy-1-propanol [60851-87-8]: IR (neat) 3384 (br, OH), 2927, 2856, 1117 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.7 Hz, 3H), 1.19–1.35 (m, 10H), 1.52–1.62 (m, 2H), 1.83 (tt, *J* = 5.7, 5.6 Hz, 2H), 2.55 (br s, 1H), 3.43 (t, *J* = 6.6 Hz, 2H), 3.62 (t, *J* = 5.7 Hz, 2H), 3.74–3.81 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 22.5 (CH_2), 26.0 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 31.7 (CH_2), 31.9 (CH_2), 61.8 (CH_2), 69.9 (CH_2), 71.3 (CH_2); MS *m/z* (relative intensity) 129 ($M^+ - C_3H_7O$, 0.9), 89 ($M^+ - C_7H_{15}$, 23), 57 (100).

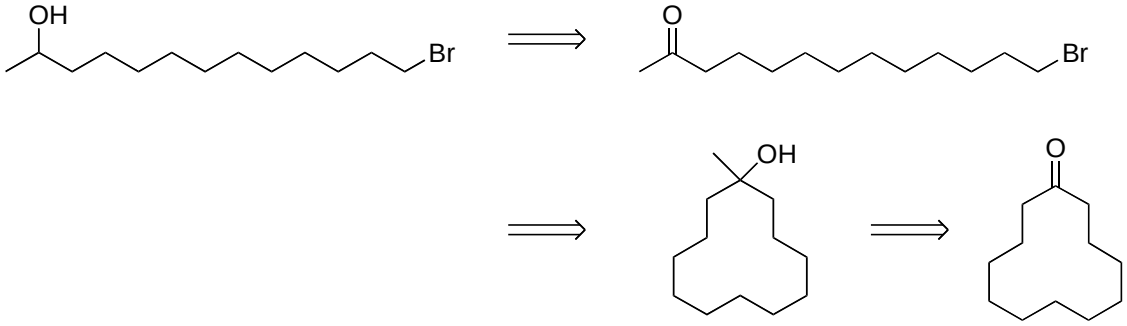
To a solution of 3-octoxy-1-propanol (7.5 g, 40 mmol) in Et_2O (20 mL) was dropwise added PBr_3 (5.4 g, 20 mmol) at 0 °C. After being stirred at 0 °C for 1.5 h and at room temperature for 1.5 h, the resultant mixture was poured into saturated aqueous $NaHCO_3$ (30 mL). The extract with *t*-BuOMe (30 mL x 3) was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 20:1) gave the title compound (4.3 g, 17 mmol) in 42% yield.[23] **1g**-Br: bp 110 °C (1 Torr, bath temp). IR (neat) 2927, 2856, 1466, 1115 cm^{-1}; ^1H NMR ($CDCl_3$), δ 0.88 (t, *J* = 6.7 Hz, 3H), 1.19–1.40 (m, 10H), 1.50–1.60 (m, 2H), 2.09 (tt, *J* = 6.6, 5.9 Hz, 2H), 3.42 (t, *J* = 6.6 Hz, 2H), 3.51 (t, *J* = 6.6 Hz, 2H), 3.53 (t, *J* = 5.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.6 (CH_2), 26.1 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.7 (CH_2), 30.8 (CH_2), 31.8 (CH_2), 32.9 (CH_2), 68.0 (CH_2), 71.2 (CH_2); MS *m/z* (relative intensity) 153 ($M^+ + 2 - C_7H_{15}$, 4.9), 151 ($M^+ - C_7H_{15}$, 5.1), 141 (10), 139 (12), 57 (100). Anal. Calcd for $C_{11}H_{23}BrO$: C, 52.59; H, 9.23%. Found: C, 52.48; H, 8.92%.

1-(3-Iodopropoxy)octane (1g-I) [926921-08-6][24]



Bromide **1g**-Br (0.510 g, 2.03 mmol) was added to a stirred mixture of NaI (3.0 g, 20 mmol) and acetone (2.0 mL). The mixture was heated to reflux and stirred for 2.5 h. After being cooled to room temperature, the reaction mixture was diluted with *t*-BuOMe, passed through a filter paper, washed with 10% aqueous $Na_2S_2O_3$ (4 M, 15 mL), and dried over Na_2SO_4. Evaporation and purification by silica gel column chromatography (hexane-AcOEt 20:1) gave the title compound (0.581 g, 1.95 mmol) in 96% yield. **1g**-I: bp 120 °C (0.5 Torr, bath temp). IR (neat) 2927, 2856, 1180, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.6 Hz, 3H), 1.22–1.35 (m, 10H), 1.50–1.61 (m, 2H), 2.04 (tt, *J* = 6.8, 5.8 Hz, 2H), 3.28 (t, *J* = 6.8 Hz, 2H), 3.41 (t, *J* = 6.6 Hz, 2H), 3.46 (t, *J* = 5.8 Hz, 2H); ^{13}C NMR (C_6D_6) δ 3.7 (CH_2), 14.4 (CH_3), 23.1 (CH_2), 26.7 (CH_2), 29.8 (CH_2), 29.9 (CH_2), 30.2 (CH_2), 32.3 (CH_2), 33.9 (CH_2), 70.0 (CH_2), 71.2 (CH_2); MS *m/z* (relative intensity) 298 (M^+, 1.6), 186 (11), 169 (9.2), 57 (100). Anal. Calcd for $C_{11}H_{23}IO$: C, 44.30; H, 7.77%. Found: C, 44.38; H, 7.81%.

13-Bromo-2-tridecanol (1h-Br) [81819-08-1][28,29]

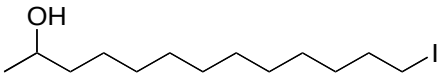


A solution of iodomethane (22.7 g, 160 mmol) was slowly added to a mixture of magnesium (3.9 g, 160 mmol) and Et_2O (35 mL) at 0 °C. The mixture was stirred for 21 h. The resultant solution of magnesium methyl iodide was slowly added to a solution of cyclododecanone (14.6 g, 80 mmol) in Et_2O (50 mL). After 1 h, the reaction mixture was treated with H_2O (200 mL), and extracted with AcOEt (50 mL x 3). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by recrystallization and silica gel column chromatography gave 1-methylcyclododecanol (13.2 g, 66.3 mmol) in 83% yield.[25] 1-Methylcyclododecanol [32400-09-2]**:** ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 3H), 1.24–1.60 (m, 23H); ^{13}C NMR ($CDCl_3$) δ 19.85 (CH_2 x 2), 21.98 (CH_2 x 2), 22.44 (CH_2 x 2), 25.94(CH_2), 26.35 (CH_2 x 2), 28.99 (CH_3), 36.08 (CH_2 x 2), 73.59 (C); MS *m*/*z* (relative intensity) 198 (M^+, 2), 180 (M^+ – OH, 6), 71 (100);

Potassium carbonate (49.8 g, 360 mmol) was portionwise added to a solution of 1-methylcyclododecanol (11.9 g, 60 mmol in $CHCl_3$ (200mL)). After 10 min, bromine (48.0 g, 300 mmol) was slowly added by five times and stirred for 4 h. The reaction mixture was treated with aqueous $Na_2S_2O_3$ (8 M, 150 mL), and extracted with hexane (50 mL x 3). The extract was dried over Na_2SO_4 and evaporated. Purification of the crude product by distillation gave the title compound (10.3 g, 37.3 mmol) in 62 % yield.[26] **1k-Br** [96562-67-3]: ^{1}H NMR ($CDCl_3$) δ 1.20–1.35 (m, 12H), 1.42 (quint, *J* = 7.1 Hz, 2H), 1.85 (quint, *J* = 7.6 Hz, 2H), 2.13 (s, 3H), 2.42 (t, *J* = 7.6 Hz, 2H), 3.41 (t, *J* = 7.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.6 (CH_2), 28.0 (CH_2), 28.6 (CH_2), 29.0 (CH_2), 29.2 (CH_2 x 3), 29.3 (CH_2), 30.0 (CH_3), 32.6 (CH_2), 33.8 (CH_2), 43.6 (CH_2), 209.0 (C); MS *m*/*z* (relative intensity) 276 (M^+, 1), 197 (M^+ – Br, 1), 58 (100).

$NaBH_4$ (0.83 g, 22 mmol) was portionwise added to a stirred solution of 13-bromo-2-tridecanone (5.5 g, 20 mmol) in MeOH (20 mL) at room temperature. After 1 h, the reaction mixture was poured into a mixture of AcOEt (30 mL) and water. After removal of the organic layer, the aqueous layer was extracted with AcOEt (20 mL). The combined organic layer was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 5:1) gave the title compound (5.3 g, 19 mmol) in 95% yield.[27] **1h**-Br: ^{1}H NMR ($CDCl_3$) δ 1.18–1.50 (m, 12H), 1.86 (tt, *J* = 7.6, 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 3.79 (tq, *J* = 6.3, 5.9 Hz, 1H).

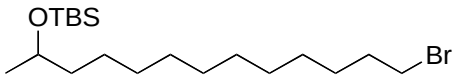
13-Iodo-2-tridecanol (1h-I) [81819-08-1][28]



The title compound was prepared from **1h**-Br by a similar method to that used for the synthesis of **1g**-I (81% yield). The reaction of **1h**-Br was performed with NaI (10 equiv) in acetone (2 mL per 1 mmol of **1h**-Br) at reflux for 3 h.[24] **1h**-I: mp 47–48 °C (hexane-AcOEt). IR (KBr) 3309 (br, OH), 2912, 2846, 1163, 1132 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.66 (br d, *J* = 4.1 Hz, 1H), 1.00 (d, *J* = 6.1 Hz, 3H), 1.01–1.52 (m, 20H), 2.72 (t, *J* = 7.0 Hz, 2H), 3.47–3.58 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 7.3 (CH_2), 23.4 (CH_3), 25.7 (CH_2), 28.5 (CH_2), 29.3 (CH_2), 29.47 (CH_2 x 2), 29.54 (CH_2), 29.6 (CH_2), 30.4 (CH_2), 33.5 (CH_2), 39.3 (CH_2), 68.1 (CH); MS *m/z* (relative intensity) 311 (M^+ – CH_3, 0.1), 266 (M^+ – H_2O – C_3H_6, 0.6), 199 (M^+ – I, 0.6), 45 (100). Anal.

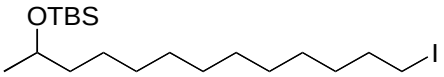
Calcd for $C_{13}H_{27}IO$: C, 47.86; H, 8.34%. Found: C, 48.09; H, 8.31%.

1-Bromo-12-(*t*-butyldimethylsiloxy)tridecane (1i-Br) [926921-10-0][30]



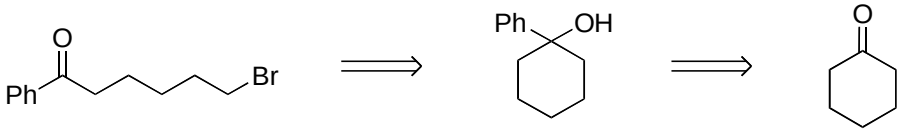
TBS-OTf (1.98 g, 7.50 mmol) was added to a stirred solution of **1h**-Br (1.40 g, 5.00 mmol) and 2,6-lutidine (1.07 g, 10.0 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After 20 min, the reaction mixture was poured into water. The extract with *t*-BuOMe (15 mL) was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 5:1) and distillation gave the title compound (1.86 g, 4.73 mmol) in 95% yield. **1i**-Br: bp 200 °C (0.5 Torr, bath temp). IR (neat) 2927, 2854, 1254, 835, 773 cm^{-1}; ^1H NMR (C_6D_6) δ 0.09 (s, 3H), 0.10 (s, 3H), 1.01 (s, 9H), 1.02–1.57 (m, 23H) including 1.13 (d, J = 6.1 Hz), 2.96 (t, J = 6.8 Hz, 2H), 3.68–3.79 (m, 1H); ^{13}C NMR (C_6D_6) δ −4.5 (CH_3), −4.2 (CH_3), 18.3 (C), 24.1 (CH_3), 26.1 (CH_3 x 3), 26.1 (CH_2), 28.4 (CH_2), 29.0 (CH_2), 29.8 (CH_2), 29.9 (CH_2), 30.0 (CH_2), 30.1 (CH_2), 30.2 (CH_2), 33.0 (CH_2), 33.7 (CH_2), 40.2 (CH_2), 68.8 (CH); MS *m/z* (relative intensity) 255 (M^+ – HBr – C_4H_9, 0.8), 159 (M^+ – $C_{11}H_{22}Br$, 12), 75 (100). Anal. Calcd for $C_{19}H_{41}BrOSi$: C, 57.99; H, 10.50%. Found: C, 57.89; H, 10.49%.

12-*t*-Butyldimethylsiloxy-1-iodotridecane (1i-I) [926921-11-1][30]



The title compound was prepared from **1h**-I by a similar method to that used for the synthesis of **1i**-Br (90% yield). The reaction of **1h**-I was performed with TBS-OTf (1.5 equiv) and 2,6-lutidine (2 equiv) in CH_2Cl_2 (1 mL per 1 mmol of **1h**-I) at 0 °C for 10 min. **1i**-I: bp 215 °C (0.5 Torr, bath temp). IR (neat) 2927, 2854, 1254, 835, 773 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04 (s, 6H), 0.86 (s, 9H), 1.11 (d, J = 6.1 Hz, 3H), 1.23–1.45 (m, 18H), 1.77–1.87 (m, 2H), 3.19 (t, J = 7.1 Hz, 2H), 3.71–3.82 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −4.7 (CH_3), −4.4 (CH_3), 7.2 (CH_2), 18.1 (C), 23.8 (CH_3), 25.8 (CH_2), 25.9 (CH_3 x 3), 28.5 (CH_2), 29.4 (CH_2), 29.51 (CH_2), 29.53 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 30.5 (CH_2), 33.6 (CH_2), 39.7 (CH_2), 68.6 (CH); MS *m/z* (relative intensity) 425 (M^+ – CH_3, 0.3), 383 (M^+ – C_4H_9, 3.4), 75 (100). Anal. Calcd for $C_{19}H_{41}IOSi$: C, 51.80; H, 9.38%. Found: C, 51.81; H, 9.48%.

6-Bromo-1-phenyl-1-hexanone (1j-Br) [82777-11-5][29]

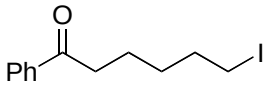


Bromobenzene (18.8 g, 120 mmol) was slowly added to a mixture of magnesium (3.2 g, 132 mmol) and Et_2O (100 mL) over 1 h. After 3 h, a solution of cyclohexanone (4.9 g, 50 mmol) in Et_2O (10 mL) was dropwise added to solution of phenylmagnesium bromide. After being stirred for 1 h. The resultant mixture was treated with dilute aqueous HCl (1 M, 150 mL). The extract with Et_2O (100 mL x 3) was dried Na_2SO_4 and evaporated. Purifications of the residual oil by silica gel column chromatography gave 1-phenyl-1-cyclohexanol (7.3g, 41.2 mmol) in 82%.[31] 1-Phenyl-1-cyclohexanol [1589-60-2]: ^1H NMR ($CDCl_3$) δ 1.24–1.34 (m, 1H), 1.37–1.91 (m, 10H), 7.21–7.38 (m, 3H), 7.48–7.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 22.04 (CH_2 x 2), 25.42 (CH_2), 38.65 (CH_2 x 2), 73.01 (C), 124.49 (CH x 2), 126.51 (CH), 128.04 (CH x 2), 149.35 (C); MS *m/z* (relative intensity) 176 (M^+, 26), 158 (M^+ – OH, 42), 55 (100).

Bromine (33.2 g, 240 mmol) was added to a mixture of 1-phenyl-1-cyclohexanol (7.1 g, 40 mmol),

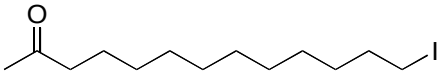
potassium carbonate (33.2 g, 240 mmol), and $CHCl_3$ (133 mL) at 0 °C. After being stirred for 4 h, the resultant mixture was treated with aqueous $Na_2S_2O_3$ (8 M, 150 mL), the extract with *t*-BuOMe (70 mL x 3) was dried over Na_2SO_4 and evaporated. Purification of the residual oil by silica gel column chromatography gave the title compound (9.9 g, 38.8 mmol) in 97% yield. **1j**-Br: ^{1}H NMR ($CDCl_3$) δ 1.48–1.60 (m, 2H), 1.78 (tt, *J* = 7.7, 7.4 Hz, 2H), 1.92 (tt, *J* = 7.7, 6.7 Hz, 2H), 3.00 (t, *J* = 7.2 Hz, 2H), 3.43 (t, *J* = 6.7 Hz, 2H), 7.43–7.59 (m, 3H); MS *m*/*z* (relative intensity) 254 (M^+, 1), 175 (M^+ – Br, 1), 105 (100).

6-Iodo-1-phenyl-1-hexanone (1j-I) [71919-91-0][32]



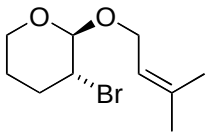
6-Bromo-1-phenyl-1-hexanone (0.51 g, 2.0 mmol) was slowly added to a suspension of sodium iodide (6.0 g, 40 mmol) in acetone (4 mL) at 0 °C. The mixture was heated to reflux. After being stirred for 2.5 h, the mixture was poured into aqueous $Na_2S_2O_3$ (4 M, 15 mL). The organic layer was removed, and the aqueous layer was extracted with hexane (50 mL x 3). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by the silica gel column chromatography gave the title compound (0.60 g, 1.97 mmol) in 98% yield.

13-Iodo-2-tridecanone (1k-I) [790686-37-2][33]



13-Bromo-2-tridecanone (2.77 g, 10 mmol) was slowly added to a suspension of sodium iodide (15 g, 100 mmol) in acetone (50 mL)at 0 °C. The mixture was heated to reflux. After being stirred for 2 h, the mixture was poured into aqueous $Na_2S_2O_3$ (4 M, 60 mL). The organic layer was removed, and the aqueous layer was extracted with hexane (50 mL x 3). The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by the silica gel column chromatography gave the title compound (3.4g, 10 mmol) quantitatively. **1k**-I: ^{1}H NMR ($CDCl_3$) δ 1.19–1.38 (m, 18H), 1.82 (quint, *J* = 7.0 Hz, 2H), 2.14 (s, 3H), 2.42 (t, *J* = 7.6 Hz, 2H), 3.19 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 7.3 (CH_2), 23.8 (CH_2), 28.4 (CH_2), 29.1 (CH_2), 29.3 (CH_2 x 3), 29.4 (CH_2), 29.8 (CH_3), 30.4 (CH_2), 33.5 (CH_2), 43.7 (CH_2), 209.3 (C); MS *m*/*z* (relative intensity) 197 (M^+ – I, 12), 179 (6), 58 (100).

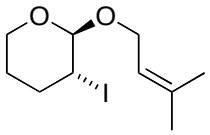
***trans*-3-Bromo-2-(3-methyl-2-butenyloxy)tetrahydropyran (5a-Br)** [121693-22-9][34,35]



3-Methyl-2-buten-1-ol (2.44 mL, 24.0 mmol) and 3,4-dihydro-2*H*-pyran (1.82 mL, 20.0 mmol) were successively added to a suspension of *N*-bromosuccinimide (3.56 g, 20.0 mmol) in CH_2Cl_2 (100 mL) at –30 °C.[11] After being stirred for 43 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (100 mL). After removal of the organic layer, the aqueous layer was extracted with *t*-BuOMe (70 mL x 3). The combined organic layer was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 10:1) gave the title compound (3.16 g, 12.7 mmol) in 64% yield. **5a**-Br: ^{1}H NMR ($CDCl_3$) δ 1.49–1.58 (m, 1H), 1.69 (s, 3H), 1.76 (s, 3H), 1.86–2.00 (m, 1H), 2.34–2.45 (m, 1H), 2.34–2.45 (m, 1H), 3.58 (ddd, *J* = 10.9, 4.5, 3.7 Hz, 1H), 3.89–4.11 (m, 4H), 4.63 (d, *J* = 4.3 Hz, 1H), 5.32–5.39 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 17.9 (CH_3), 23.2 (CH_2), 25.7 (CH_3), 30.0 (CH_2), 49.5 (CH), 62.4

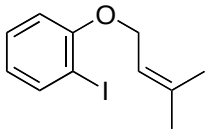
(CH_2), 64.2 (CH_2), 99.9 (CH), 120.0 (CH), 138.0 (C); MS *m*/*z* (relative intensity) 170 (M^+ – Br, 0.2), 69 (100).

***trans*-3-Iodo-2-(3-methyl-2-butenyloxy)tetrahydropyran (5a-I)** [260557-53-7][35,36]



The title compound was prepared from 3-methyl-2-buten-1-ol, 3,4-dihydro-2*H*-pyran, and *N*-iodosuccinimide by a similar method to that used for the synthesis of **5a**-Br (80% isolated yield). The reaction was performed at –30 °C for 2 h. **5a-I:** ^{1}H NMR ($CDCl_3$) δ 1.50–1.64 (m, 1H), 1.69 (s, 3H), 1.76 (s, 3H), 1.95–2.08 (m, 1H), 2.32–2.43 (m, 1H), 2.33–2.44 (m, 1H), 3.58 (ddd, *J* = 11.2, 7.6, 3.5 Hz, 1H), 3.96–4.13 (m, 3H), 4.19–4.26 (m, 1H), 4.66 (d, *J* = 5.5 Hz, 1H), 5.33–5.41 (m, 1H); MS *m*/*z* (relative intensity) 169 (M^+ – I, 1), 69 (100).

1-Iodo-2-(3-methyl-2-butenyloxy)benzene (5b-I) [120568-94-7][34,37]



NaH (60% in mineral oil, 0.48 g, 12 mmol) was placed in a reaction flask. After the flask was filled with N_2, NaH was washed with dry hexane, and DMF (5 mL) was introduced. To the resultant suspension was added a solution of 2-iodophenol (2.20 g, 10.0 mmol) in DMF (10 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min and at room temperature for 2 h. 1-Bromo-3-methyl-2-butene (2.24 g, 15.0 mmol) was added to the mixture at 0 °C. After being stirred at 0 °C for 30 min and at room temperature for 1.2 h, the reaction mixture was poured into water. The extract with Et_2O (20 mL x 4) was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 10:1) gave the title compound (2.7 g, 9.4 mmol) in 94% yield.

4.4. Reduction of Organic Halides

Hydrocarbons **2a**-**e**, propyl benzoate (**2f**), 1-phenyl-1-hexanone (**2j**) and 2-tridecanone (**2k**) were identified by comparison with the corresponding commercial compounds in gas chromatogram and ^{1}H NMR spectra. 1-Phenyl-1-hexanol (**4**, CAS 4471-05-0) was identified by comparison of its spectral data with those reported previously.[14] The structures of other reduction products were determined by full characterization.

GC data (retention time) for the products whose yields were determined by capillary GC analysis (40 to 270 °C, 10 °C/min) are as follows: **2a**, 5.35 min; **2b**, 9.41 min; **2c**, 11.44 min; **2d**, 7.66 min; **2e**, 8.95 min; **2g**, 9.17 min.

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 (2L 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 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 (2L 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.

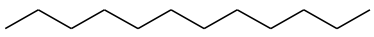
General Procedure for $In(OAc)_3$-Catalyzed Reduction of Organic Halides with $PhSiH_3$ in EtOH Containing 2,6-Lutidine (Method D, Entry 3 in Table 2)

Under a nitrogen atmosphere (2L 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 identity and purity of the product.

General Procedure for $GaCl_3$-Catalyzed Reduction of Organic Halides with PMHS in DME (Eq. 8)

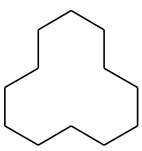
In a glove box filled with argon, $GaCl_3$ (18 mg, 0.10 mmol) was introduced into a reaction flask, which was brought out from the box and connected with an argon balloon (2 L). DME (1.0 mL), 1-bromo-3-phenylpropane (**1a**-Br, 199 mg, 1.00 mmol), PMHS (180 mg, 3.00 mmol of Si-H) and dry air (15 mL) 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 identity and purity of the product.

Dodecane (2b) [112-40-3] (*commercially available*)



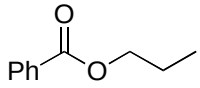
^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.2 Hz, 6H), 1.22−1.30 (m, 20H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3 x 2), 22.8 (CH_2 x 2), 29.5 (CH_2 x 2), 29.8 (CH_2 x 2), 32.1 (CH_2 x 2); MS *m*/*z* (relative intensity) 170 (M^+, 4), 141 (M^+ – Et, 1), 57 (100).

Cyclododecane (2c) [294-62-2] (*commercially available*)



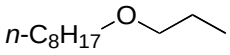
^{1}H NMR ($CDCl_3$) δ 1,34 (s, 24H); ^{13}C NMR ($CDCl_3$) δ 23.67 (CH_2 x 12); MS *m*/*z* (relative intensity) 168 (M^+, 10), 141 (M^+ – Et, 1), 55 (100).

Propylbenzoate (2f) [2315-68-6]



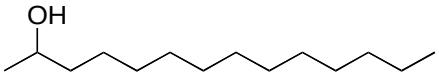
^{1}H NMR ($CDCl_3$) δ 1.03 (t, *J* = 7.4 Hz, 3H), 1.8 (qt, *J* = 7.4, 7.2 Hz, 2H), 4.29 (t, *J* = 6.8 Hz, 2H), 7.23–7.59 (m, 3H), 8.01–8.08 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.5 (CH_3), 22.1 (CH_2), 66.5 (CH_2), 128.5 (CH x 2), 129.5 (CH x 2), 130.5 (C), 132.8 (CH), 166.7 (C); MS *m/z* (relative intensity) 176 (M^+, 5), 120 (M^+ – C_4H_9, 33), 105 (100).

1-Propoxyoctane (2g) [29379-41-7]



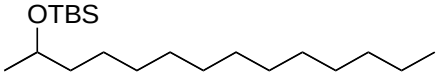
Bp 95 °C (0.5 Torr, bath temp). IR (neat) 2958, 2927, 2856, 1120cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 1.25–1.36 (m, 10H), 1.52–1.66 (m, 4H), 3.36 (t, *J* = 6.8 Hz, 2H), 3.40 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 10.6 (CH_3), 14.1 (CH_3), 22.7 (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) [1653-31-2]



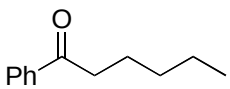
Bp 155 °C (0.5 Torr, bath temp). IR (neat) 3346 (br, OH), 2958, 2925, 2854 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.7 Hz, 3H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.20–1.50 (m, 21H), 3.73–3.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.7 (CH_2), 23.4 (CH_3), 25.8 (CH_2), 29.3 (CH_2), 29.61 (CH_2 x 3), 29.64 (CH_2 x 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) [926921-12-2]



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 x 3), 29.3 (CH_2), 29.7 (CH_2 x 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%.

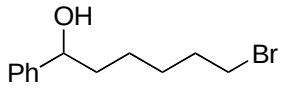
1-Phenyl-1-hexanone (2j) [942-92-7]



^{1}H NMR ($CDCl_3$) δ 0.91 (t, *J* = 6.9 Hz, 3H), 1.26–1.80 (m, 6H), 2.96 (t, *J* = 7.6 Hz, 2H), 7.42–7.58 (m, 3H), 7.94–7.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 22.5 (CH_2), 24.0 (CH_2), 38.6 (CH_2), 128.0 (CH x 2), 128.5 (CH x 2), 130.9 (C), 132.8 (CH), 200.6 (C); MS *m/z* (relative intensity) 164 (M^+, 2), 123 (M^+ –

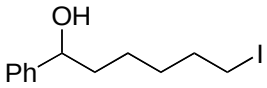
C_3H_7, 40), 105 (100).

6-Bromo-1-phenyl-1-hexanol (3-Br) [926921-13-3]



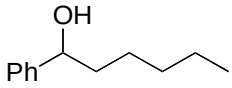
Bp 142 °C (1 Torr, bath temp). IR (neat) 3373 (br, OH), 2935, 2856, 1454, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23–1.53 (m, 4H), 1.67–1.90 (m, 5H), 3.39 (t, *J* = 6.8 Hz, 2H), 4.68 (dd, *J* = 7.4, 5.8 Hz, 1H), 7.25–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$), δ 24.7 (CH_2), 27.8 (CH_2), 32.5 (CH_2), 33.7 (CH_2), 38.6 (CH_2), 74.1 (CH), 125.7 (CH x 2), 127.3 (CH), 128.2 (CH x 2), 144.6 (C); MS *m/z* (relative intensity) 258 (M^+ + 2, 1.6), 256 (M^+, 1.4), 107 (100). Anal. Calcd for $C_{12}H_{17}BrO$: C, 56.04; H, 6.66%. Found: C, 55.71; H, 6.62%.

6-Iodo-1-phenyl-1-hexanol (3-I) [926921-14-4]



Bp 175 °C (0.5 Torr, bath temp). IR (neat) 3367 (br, OH), 2931, 700 cm^{-1}; ^1H NMR (C_6D_6) δ 0.94–1.25 (m, 5H), 1.29–1.64 (m, 4H), 2.64 (t, *J* = 7.0 Hz, 2H), 4.28 (ddd, *J* = 7.6, 5.4, 3.3 Hz, 1H), 7.07–7.21 (m, 5H); ^1H NMR ($CDCl_3$) δ 1.17–1.44 (m, 4H), 1.59–1.80 (m, 5H), 3.09 (t, *J* = 6.9 Hz, 2H), 4.59 (dd, *J* = 7.5, 5.8 Hz, 1H), 7.17–7.31 (m, 5H); ^{13}C NMR (C_6D_6) δ 6.7 (CH_2), 24.9 (CH_2), 30.5 (CH_2), 33.6 (CH_2), 39.3 (CH_2), 74.2 (CH), 125.8 (CH x 2), 127.6 (CH), 128.5 (CH x 2), 144.7 (C); ^{13}C NMR ($CDCl_3$) δ 7.0 (CH_2), 24.7 (CH_2), 30.3 (CH_2), 33.4 (CH_2), 38.8 (CH_2), 74.5 (CH), 126.1 (CH x 2), 128.5 (CH x 2), 128.7 (CH), 145.8 (C); MS *m/z* (relative intensity) 117 ($M^+ - H_2O - C_3H_6I$, 29), 107 ($M^+ - C_5H_{10}I$, 100). Anal. Calcd for $C_{12}H_{17}IO$: C, 47.38; H, 5.63%. Found: C, 47.44; H, 5.63%.

1-phenyl-1-hexanol (4) [4471-05-0][38]



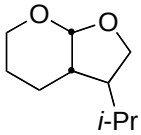
Diethoxyphenylsilane [17872-93-4][39] and **Triethoxyphenylsilane** [780-69-8][39]

$PhSiH(OEt)_2$ and $PhSi(OEt)_3$

4.5. Radical Cyclization

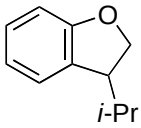
The $In(OAc)_3$-catalyzed cyclization of haloalkenes **5** with $PhSiH_3$ was performed by similar methods to those used for the reduction of haloalkanes. The cyclization products were identified by comparison of their spectral data with those reported previously. CAS registry numbers and reference numbers leading to the reported spectral data of the title compounds are shown in the title lines.

1,6-*Cis*-7-isopropyl-2,9-dioxabicyclo[4.3.0]nonane (6a) [223677-90-5][40]



The method for entry 3 in Table 4 is described. Iodoalkene **5a**-I (148 mg, 0.500 mmol) and $PhSiH_3$ (54 mg, 0.50 mmol) were added to a stirred suspension of $In(OAc)_3$ (15 mg, 0.050 mmol) and K_2CO_3 (69 mg, 0.50 mmol) in THF (0.50 mL). The mixture was heated 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 diluted with *t*-BuOMe was dried over Na_2SO_4 and evaporated. Purification of the crude product by silica gel column chromatography (hexane-AcOEt 10:1) gave the title compound (81.0 mg, 0.476 mmol) in 95% yield. **6a**: ^{1}H NMR ($CDCl_3$) for major isomer δ 0.78 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 1.27–1.43 (m, 1H), 1.50–1.74 (m, 4H), 1.85–1.95 (m, 2H), 3.64–4.79 (m, 3H), 3.92 (dd, *J* = 7.8, 7.8 Hz, 1H), 5.27 (d, *J* = 3.0 Hz, 1H); for minor isomer δ 0.85 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 1.29–1.39 (m, 1H), 1.58–1.75 (m, 2H), 1.75–1.92 (m, 3H), 2.08 (dddd, *J* = 8.7, 8.1, 8.1, 7.2 Hz, 1H), 3.41 (ddd, *J* = 11.4, 11.4, 2.4 Hz, 1H), 3.66 (dd, *J* = 8.4, 8.1 Hz, 1H), 3.86 (ddd, *J* = 11.4, 3.9, 3.3 Hz, 1H), 4.16 (dd, *J* = 8.7, 8.4 Hz, 1H), 4.97 (d, *J* = 3.6 Hz, 1H), ^{13}C NMR ($CDCl_3$) for major isomer δ .18.8 (CH_2), 21.0 (CH_3), 21.7 (CH_3), 23.3 (CH_2), 26.3 (CH), 35.7 (CH), 48.9 (CH), 60.7 (CH_2), 69.0 (CH_2), 102.0 (CH); for minor isomer δ 19.47 (CH_2), 20.7 (CH_3), 21.5 (CH_3), 23.5 (CH_2), 30.1 (CH), 41.3 (CH), 44.3 (CH), 64.3 (CH_2), 71.1 (CH_2), 102.5 (CH); MS *m*/*z* (relative intensity) for major isomer 170 (M^+, 12), 140 (M^+ – Pr, 9), 55 (100); for minor isomer 170 (M^+, 11), 140 (M^+ – Pr, 10), 69 (100).

2,3-Dihydro-3-(1-methylethyl)-benzofuran (6b) [3279-17-2][40]



The fourth method in eq 6 is described. Iodoalkene **5b**-I (144 mg, 0.500 mmol), $PhSiH_3$ (108 mg, 1.00 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 6 h, the reaction mixture was subjected to the same workup as described above. Purification by silica gel column chromatography (hexane-AcOEt 20:1) gave the title compound (78.0 mg, 0.480 mmol) in 96% yield.

4.6. Experiments for Mechanistic Insights

$In(OAc)_3$-Catalyzed Reduction of 1-Bromo-3-phenylpropane with $PhSiD_3$

The reaction was performed by Method A described in the text. The D-content of the product was estimated by ^{1}H NMR analysis, namely, integration of the methyl signal.

Reaction of $In(OAc)_3$ with Excess $PhSiH_3$

$PhSiH_3$ (540 mg, 5.00 mmol) was added to a stirred suspension of $In(OAc)_3$ (146 mg, 0.500 mmol) in THF (0.5 mL). The mixture was heated to 70 °C and stirred for 24 h. The foil formed was taken out of the reaction mixture by filtration and washed with *t*-BuOMe. After drying under reduced pressure, indium foil (53.4 mg, 0.465 mmol, mp 157 °C) with metallic luster was obtained in 93% yield.

With the gas evolved by this reaction, (*E*)-1-phenyl-1-propene was reduced to propylbenzene under

catalysis by Pd-C. This result indicates the evolution of H_2 from $PhSiH_3$.

Reaction of 1-Bromo-3-phenylpropane with $PhSiH_3$ in the Presence of Galvinoxyl

The $In(OAc)_3$-catalyzed reduction of 1-bromo-3-phenylpropane (**1a**-Br, 0.500 mmol) by Method A was completely suppressed by adding galvinoxyl (10.5 mg, 0.025 mmol).

Solvolysis of $PhSiH_3$ with EtOH

Me_3SiI (1.00 mmol) and $PhSiH_3$ (5.00 mmol) were successively added to a stirred mixture of EtOH (10 mL) and decane (1.00 mL, internal standard) at room temperature. The amount of $PhSiH_3$ was monitored by GC analysis. At each reaction time, 0.50 mL of the reaction mixture was diluted with Et_2O (5.0 mL) and subjected to GC analysis. The conversion of $PhSiH_3$ at each reaction time is as follows: 35% at 20 min, 54% at 40 min, 77% at 80 min, 86% at 120 min, and 94% at 180 min. As the consumption of $PhSiH_3$, $PhSiH(OEt)_2$ (CAS 17872-93-4)[15] and $PhSi(OEt)_3$ (CAS 780-69-8)[39] increased in amount. $PhSiH_2(OEt)$ (CAS 18246-20-3) was not detected. In the presence of 2,6-lutidine (2.50 mmol), the conversion of $PhSiH_3$ was effectively suppressed as follows: 7% at 20 min, 11% at 40 min, 10% at 80min, and 13% at 120 min. The solvolysis of $PhSiH_3$ hardly occurred in the absence of Me_3SiI (1% conversion of $PhSiH_3$ at 120 min).

5. References

1. (a) Pietruszka, J. In *Science of Synthesis*, Vol. 4; Bellus, D.; Ley, S. V.; Noyori, R.; Regitz, M.; Reider, P. J.; Schaumann, E.; Shinkai, I.; Thomas, E. J.; Trost, B. M., Eds., Thieme, Stuttgart, 2002, p 159. (b) Brook, M. A. *Silicon in Organic, Organometallic Polymer Chemistry*, Wiley, New York, 2000, p 171.
2. (a) Nishikori, H.; Yoshihara, R.; Hosomi, A. *Synlett* **2003**, 561. (b) Miura, K.; Ootsuka, K.; Suda, S.; Nishikori, H.; Hosomi, A. *Synlett* **2002**, 313. (c) Miura, K.; Ootsuka, K.; Suda, S.; Nishikori, H.; Hosomi, A. *Synlett* **2001**, 1617. (d) Miura, K.; Nakagawa, T.; Suda, S.; Hosomi, A. *Chem. Lett.* **2000**, 150. (e) Hojo, M.; Murakami, C.; Fujii, A.; Hosomi, A. *Tetrahedron Lett.* **1999**, *40*, 911.
3. (a) Ito, H.; Ishizuka, T.; Arimoto, K.; Miura, K.; Hosomi, A. *Tetrahedron Lett.* **1997**, *38*, 8887. (b) Ito, H.; Yamanaka, H.; Ishizuka, T.; Tateiwa, J.; Hosomi, A. *Synlett*, **2000**, 479.
4. (a) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2001**, *42*, 4661. (b) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 906. (c) Baba, A.; Shibata, I. *Chem. Record* **2005**, *5*, 323.
5. (a) Mikami, S.; Fujita, K.; Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, *3*, 1853. (b) Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627.
6. (a) Hayashi, N.; Shibata, I.; Baba, A. *Org. Lett.* **2004**, *6*, 4981. (b) Hayashi, N.; Shibata, I.; Baba, A. *Org. Lett.* **2005**, *7*, 3093.
7. Baba's group and the author have succeeded in catalytic generation of indium hydrides with hydrosilanes and its application of reductive aldol reaction of α-enones with aldehydes. (a) Shibata, I.; Kato, H.; Ishida, T.; Yasuda, M.; Baba, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 711. (b) Miura, K.; Yamada, Y.; Tomita, M.; Hosomi, A. *Synlett* **2004**, 1985.
8. (a) Hibbs, D. E.; Hursthouse, M. B.; Jones, C.; Smithies, N. A. *Chem. Commun.* **1998**, 869. (b) Hibbs, D. E.; Jones, C.; Smithies, N. A. *Chem. Commun.* **1999**, 185. (c) Abernethy, C. D.; Cole, M. L.; Jones, C. *Organometallics* **2000**, *19*, 4852.
9. For Et_3B-initiated radical reduction of haloalkanes with Bu_3SnH, see: Miura, K.; Ichinose, Y.; Nozaki, K.; Fugami, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 143.
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, 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.
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.
15. See page 23.
16. Synthetic procedure for $PhSiD_3$: (a) Nebergall, W. H. *J. Am. Chem. Soc.* **1950**, *72*, 4702. (b) Finholt, A. E.; Bond, A. C.; Wilzbach, K. E.; Schlesinger, H. I. *J. Am. Chem. Soc.* **1947**, *69*, 2692.

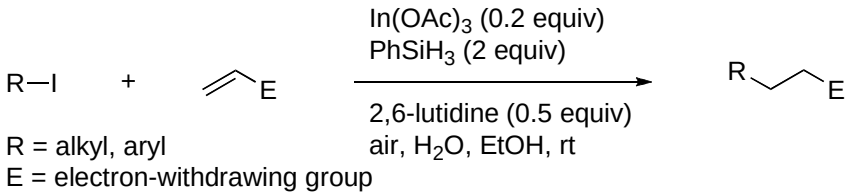
17. (a) Wyman, D. P.; Wang, J. Y. C.; Freeman, W. R. *J. Org. Chem.* **1963**, *28*, 3173. (b) Synthetic procedure and compound data for $PhSiH_2Cl$: Kunai, A.; Kawakami, T.; Toyoda, E.; Ishikawa, M. *Organometallics* **1992**, *11*, 2708.
18. Matsubara, S.; Matsuda, H.; Hamatani, T.; Schlosser, M. *Tetrahedron* **1988**, *44*, 2855.
19. Takai, K.; Nitta, K.; Fujimura, O.; Utimoto, K. *J. Org. Chem*. **1989**, *54*, 4732.
20. Yasuda, M.; Yamasaki, S.; Onishi, Y.; Baba, A. *J. Am. Chem. Soc*. **2004**, *126*, 7186.
21. (a) Mikami, S.; Fujita, K.; Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, *3*, 1853 (b) Synthetic procedure and compound data for **1f**-Br: Hoeger, S.; Rosselli, S.; Ramminger, A.-D.; Enkelmann, V. *Org. Lett.* **2002**, *4*, 4269. (c) Compound data for **1f**-I: Thompson, A. M.; Delaney, A. M.; Hamby, J. M.; Schroeder, M. C.; Spoon, T. A.; Crean, S. M.; Showalter, H. D. H.; Denny, W. A. *J. Med. Chem.* **2005**, *48*, 4628.
22. Ferguson, A. C.; Haines, A. H. *J. Chem. Soc., C*. **1969**, 2372.
23. Bartleson, J. D.; Burk, R. E.; Lankelma, H. P. *J. Am. Chem. Soc*. **1946**, *68*, 2513.
24. Pross, A.; Sternhell, S. *Aust. J. Chem. Soc.* **1949**, *71*, 1675.
25. Callen, J. E.; Dornfeld, C. A.; Cokman, G. H. *Org. Synth., III* **1995**, 26.
26. Zhang, W.-C.; Li, C.-J. *J. Org. Chem* **2000**, *65*, 5831
27. Ritchie, C. D.; Pratt, A. L. *J. Am. Chem. Soc*. **1964**, *86*, 1571.
28. Compound data for **1h**-Br: Wasserman, H. H.; Gambale, R. J.; Pulwer, M. J. *Tetrahedron* **1981**, *37*, 4059.
29. Synthetic procedure and compound data for **1j**-Br and **1k**-Br: Zhang, W.-C.; Li, C.-J. *J. Org. Chem* **2000**, *65*, 5831.
30. Synthetic procedure for TBDMS ethers **1i**-Br and **1i**-I: Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
31. Gregnrd, V. *Chem. Rev*. **1900**, *130*, 1322.
32. Compound data for **1j**-I: (a) Antunes, C. S. A.; Bietti, M.; Lanzalunga, O.; Salamone, M. *J. Org. Chem.* **2004**, *69*, 5281. (b) Wagner, P. J.; Lindstrom, M. J.; Sedon, J. H.; Ward, D. R. *J. Am. Chem. Soc*. **1981**, *103*, 3842.
33. Compound data for **1k**-I: Barluenga, J.; Gonzalez-Bobes, F.; Murguia, M. C.; Ananthoju, S. R.; Gonzalez, J. M. *Chem. Eur. J*. **2004**, *10*, 4206.
34. Compound data for **5a**-Br, **5b**-I, **6a**, and **6b**: Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627.
35. Synthetic procedure for **5a**-Br and **5a**-I: Ueno, Y.; Chino, K.; Watanabe, M.; Moriya, O.; Okawara, M. *J. Am. Chem. Soc*. **1982**, *104*, 5564.
36. Synthetic procedure and compound data for **5a**-I: Ollivier, C.; Renaud, P. *J. Am. Chem. Soc*. **2002**, *123*, 4717.
37. Synthetic procedure and compound data for **5b**-I: Curran, D. P.; Totleben, M. J. *J. Am. Chem. Soc*. **1992**, *114*, 6050.
38. Compound data for **4**: (a) Fujita, K.; Asai, C. Yamaguchi, T.; Hanasaka, F.; Yamaguchi, R. *Org. Lett.* **2005**, *7*, 4017. (b) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A.; Parker, D. *J. Org. Chem.* **1984**, *49*, 3928.
39. Compound data for $PhSiH(OEt)_2$ and $PhSi(OEt)_3$: Ohshita, J.; Taketsugu, R.; Nakahara, Y.; Kunai, A. *J. Organomet. Chem.* **2004**, *689*, 3258.
40. Compound data for **6a** and **6b**: Takemi, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627.

Chapter 3

Indium(III)-Catalyzed Intermolecular Radical Addition of Organic Halides to Electron-Deficient Alkenes

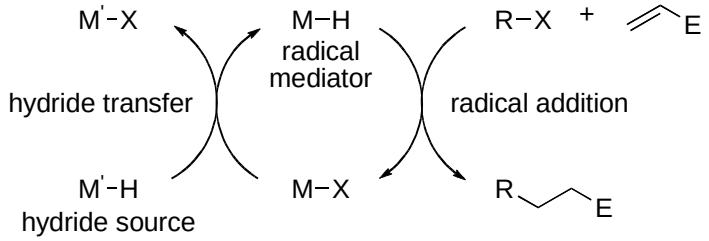
Abstract

In the presence of phenylsilane and a catalytic amount of indium(III) acetate, organic iodides added to electron-deficient alkenes in ethanol at room temperature. Both simple and functionalized organic iodides were applicable to this reaction. A plausible reaction mechanism involves the formation of indium hydride species via hydride transfer from silicon to indium and an indium hydride-mediated radical chain process.



1. Introduction

Synthetic radical reactions directed toward fine organic synthesis have rapidly been developed in the last three decades.[1] At present carbon radicals are recognized as reactive, but controllable carbon species valuable for highly selective, efficient bond formation. Triorganotin hydrides such as Bu_3SnH have frequently been used as efficient radical mediators, which serve for generation of carbon radicals and radical quenching by hydrogen donation.[1] Unfortunately, their use has two critical drawbacks, that is, the toxicity of organostannanes and the difficulty of product purification.[2,3] A number of hydride-based radical mediators have been developed as substitutes for triorganotin hydrides.[4-7] Additionally, the catalytic use of radical mediators in the presence of stoichiometric hydride sources has received much attention from the viewpoint of environmentally friendly and economical synthesis.[5c,6,8] Such catalytic reactions are very effective in radical reduction and intramolecular radical addition of organic halides and pseudohalides. However, intermolecular addition of these radical precursors (R-X) to alkenes (CH_2=CHE) using catalytic mediators (M-H) shows much room for improvement (Scheme 1).[6b,8b]



Scheme 1

The author has developed the $In(OAc)_3$-catalyzed radical reduction of organic halides with $PhSiH_3$. With the aid of 2,6-lutidine and dry air, the catalytic system enables an efficient reduction of various iodoalkanes in EtOH at room temperature.[9] He herein describes that the reaction system using $In(OAc)_3$, $PhSiH_3$, 2,6-lutidine, and dry air is valuable also for catalytic radical addition of organic iodides to electron-deficient alkenes (M = X_2In, M' = PhH_2Si in Scheme 1). In this context, Baba and Shibata have reported that similar reaction systems using In(III) catalysts and stoichiometric hydride sources are usable for intermolecular radical addition.[6a,b] However, the limited examples were not enough to demonstrate the applicability and synthetic utility of these systems. The reaction efficiency was not necessarily good even with a large excess (5−10 equiv) of alkenes. This chapter reveals that the $In(OAc)_3$-catalyzed system using $PhSiH_3$ as hydride source can be applied to a variety of organic iodides, and that it realizes moderate to good yield of desired adducts with 2−3 equiv of alkenes under mild, environmentally friendly conditions.

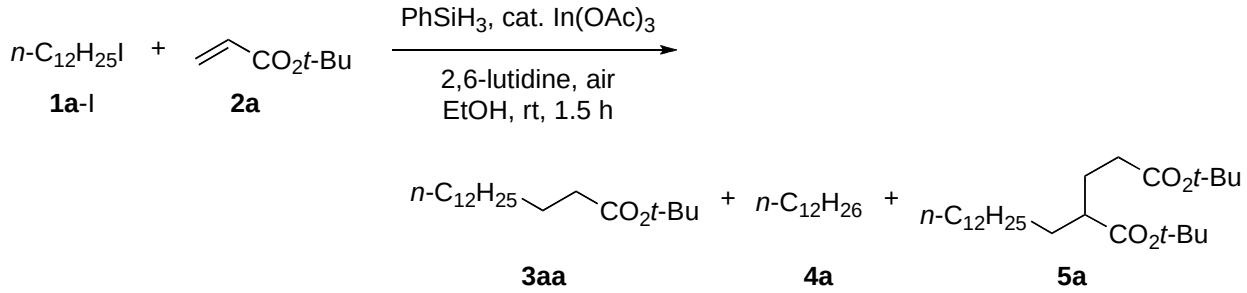
2. Results and Discussion

2.1. Optimization of Reaction Conditions

1-Iodododecane (**1a**-I) and *tert*-butyl acrylate (**2a**) were initially selected as substrates to optimize the reaction conditions. On the basis of the conditions used for the $In(OAc)_3$-catalyzed reduction of organic halides,[9] the reaction of **1a**-I (1 equiv) with **2a** (3 equiv) was carried out with $PhSiH_3$ (1 equiv), $In(OAc)_3$ (0.2 equiv), 2,6-lutidine (0.5 equiv), and dry air in EtOH at room temperature (entry 1 in Table 1). The reaction under these conditions gave the desired adduct **3aa** in 50% yield with a 10% recovery of **1a**-I. Dodecane (**4a**) and adduct **5a** were also formed as byproducts. The latter byproduct **5a** consists of one

molecule of **1a**-I and two molecules of **2a**. With an increased amount of $PhSiH_3$ (2 equiv), the yield of **3aa** was improved to 60-67% (entry 2). The control experiment without 2,6-lutidine resulted in a lower yield of **3aa** (entry 3). Reproducible results were not obtained in the absence of air. Addition of H_2O did not affect the yield of **3aa**; however, it decreased unidentified byproducts to facilitate the isolation of **3aa** by silica gel column chromatography (entry 4). Use of one or two equivalents of **2a** still led to a similar yield of **3aa** (entries 5-7). As expected, the equimolar reaction of **1a**-I with **2a** increased the amount of **4a** and suppressed the formation of **5a**.

Table 1. Addition of 1-Iodododecane to *tert*-Butyl Acrylate [a]



entry	**2a**	$PhSiH_3$	GC yield / %		
	/ equiv	/ equiv	**3aa**	**4a**	**5a**
1[b]	3	1	50	11	8
2	3	2	60-67[c]	7-10[c]	12
3[d]	3	2	53	9	-
4[e]	3	2	67 (64)[f]	14	-
5	2	2	64	6	12
6[e]	2	2	65 (56)[f]	11	10
7[e]	1	2	(63)[f]	22	5

[a] Unless otherwise noted, all reactions were carried out with **1a**-I (0.50 mmol), **2a** (0.50–1.00 mmol), $PhSiH_3$ (0.50–1.00 mmol), $In(OAc)_3$ (0.10 mmol), 2,6-lutidine (0.25 mmol), dry air (4.8 mL), and EtOH (1.0 mL) under N_2 (2 L balloon) at room temperature for 1.5 h.

[b] **1a**-I was recovered in 10% GC yield.

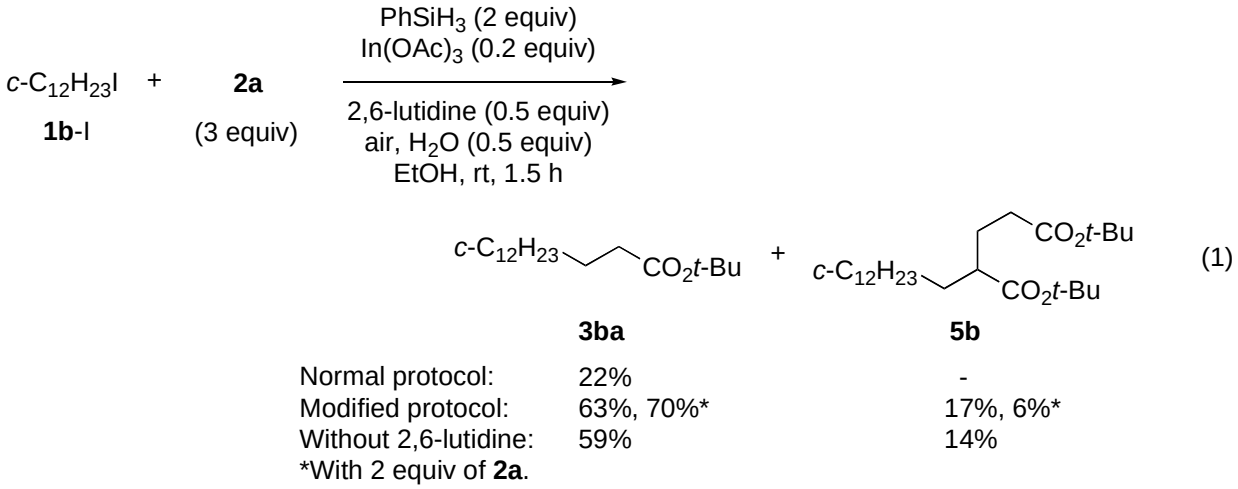
[c] The results of three runs.

[d] Without 2,6-lutidine.

[e] H_2O (0.25 mmol) was used as an additive.

[f] The isolated yield is shown in parentheses.

Under the conditions of entry 4 in Table 1, the reaction of iodocyclododecane (**1b**-I) with **2a** resulted in low yield of the desired adduct **3ba** and recovery of **1b**-I (Eq 1). In this protocol, 2,6-lutidine was introduced into the reaction flask last of all at a 20-30 second interval after the addition of $PhSiH_3$ (see the Experimental Section). The author found that the addition of 2,6-lutidine after an interval of 10 min was effective in the intermolecular reaction. With the modified protocol, the reaction using 2 equiv of **2a** afforded **3ba** in 70% isolated yield. In the absence of 2,6-lutidine, **3ba** was obtained in slightly lower yield.



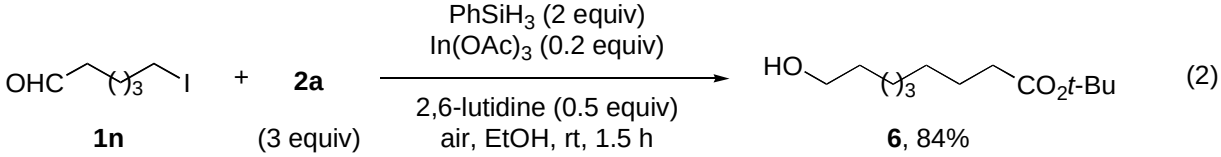
	3ba	**5b**
Normal protocol:	22%	-
Modified protocol:	63%, 70%*	17%, 6%*
Without 2,6-lutidine:	59%	14%

*With 2 equiv of **2a**.

2.2. Scope and Limitations

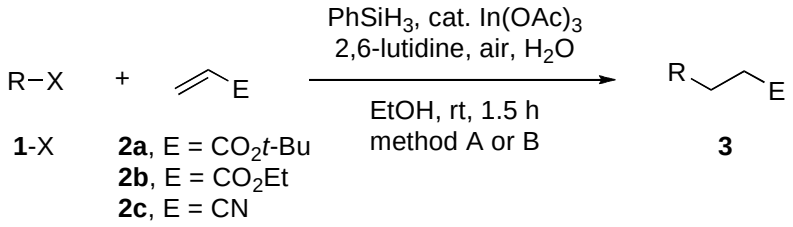
The scope and limitations of the $In(OAc)_3$-catalyzed intermolecular addition are summarized in Table 2. The addition of **1a**-I and **1b**-I to ethyl acrylate (**2b**) and acrylonitrile (**2c**) proceeded in moderate to good yields (entries 1–3 and 5). 1-Iodoadamantane (**1c**-I), a tertiary iodide, smoothly added to **2a** (entry 7). The reactions without 2,6-lutidine showed lower efficiency, proving its effectiveness in the present reaction system (entries 4, 6, and 8). 1-Bromododecane (**1a**-Br) was quite unreactive to **2a** irrespective of the presence of 2,6-lutidine (entries 9 and 10). In contrast, bromocyclododecane (**1b**-Br), a secondary bromide, was reactive enough for the addition to **2a**, and the corresponding adduct **3ba** was obtained in good yield (entry 11). Without 2,6-lutidine, the yield of **3ba** dropped remarkably (entry 12). The difference between **1a**-Br and **1b**-Br in reactivity is consistent with the previous results of the reduction of these bromides by a similar reaction system (entry 9). 1-Bromoadamantane (**1c**-Br) was not as reactive as **1b**-Br (entry 13).

The $In(OAc)_3$-catalyzed addition was applicable to functionalized iodoalkanes as well as simple iodoalkanes (entries 15–22). The mild reaction conditions bring about high compatibility with oxygen functional groups such as ester, ketone, ether, and alcohol. Particularly, iodoketone **1e** added to **2a** without carbonyl reduction (entry 16). The tolerance of the carbonyl group is attributable to the low reactivities of $PhSiH_3$ and indium hydride species as hydride nucleophiles.[9,10] The addition of iodo alcohols **1h** and **1i** proceeded efficiently without degradation of the hydroxy group (entries 19–22). Attempts at the reaction of 1-iodohexanal (**1n**) with **2a** were not successful. In this case, hydroxyester **6** was formed in high yield by reduction of the formyl group simultaneously with the carbon–carbon bond formation (Eq 2).[10]



Iodoarenes also underwent the $In(OAc)_3$-catalyzed intermolecular addition to electron-deficient alkenes (entries 23 and 26–30). Oxygen functional groups on the benzene ring remained intact under these conditions. 2,6-Lutidine and air played critical roles also in the reaction of iodoarenes. For example, the addition of iodobenzene (**1j**) to **2a** using both additives gave **3j** in 71% yield. In the absence of 2,6-lutidine or air, the yield dropped to 23% or <5%, respectively (entries 24 and 25). H_2O was not effective in acceleration of the reaction (entries 23 and 26), but helpful for reduction of byproducts as in the case of **1a**-I.

Table 2. Addition of Haloalkanes to Electron-Deficient Alkenes[a]



1-X **2a**, E = CO_2t-Bu; **2b**, E = CO_2Et; **2c**, E = CN — **3**

entry	R-X	**2**	method[b]	product	isolated yield / %
1	*n*-$C_{12}H_{25}$I (**1a**-I)	**2b**	A	**3ab**	61[c]
2	**1a**-I	**2c**	A	**3ac**	76[c]
3	*c*-$C_{12}H_{23}$I (**1b**-I)	**2b**	A[d]	**3bb**	65
4	**1b**-I	**2b**	B	**3bb**	59
5	**1b**-I	**2c**	A[d]	**3bc**	74
6	**1b**-I	**2c**	B	**3bc**	55
7	1-Ad-I (**1c**-I)	**2a**	A	**3c**	63
8	**1c**-I	**2a**	B	**3c**	55
9	*n*-$C_{12}H_{25}$Br (**1a**-Br)	**2a**	A	**3aa**	0
10	**1a**-Br	**2a**	B	**3aa**	0
11	*c*-$C_{12}H_{23}$Br (**1b**-Br)	**2a**	A	**3ba**	71
12	**1b**-Br	**2a**	B	**3ba**	35
13	1-Ad-Br (**1c**-Br)	**2a**	A	**3c**	30
14	**1c**-Br	**2a**	B	**3c**	<5
15	$PhCO_2(CH_2)_3$I (**1d**)	**2a**	A	**3d**	61, 56[c]
16	$MeC(O)(CH_2)_5$I (**1e**)	**2a**	A	**3e**	56
17	$TBSO(CH_2)_3$I (**1f**)	**2a**	A	**3f**	50
18	*n*-$C_8H_{17}O(CH_2)_3$I (**1g**)	**2a**	A	**3g**	55
19	$HO(CH_2)_3$I (**1h**)	**2a**	A[e]	**3d**	69
20	**1h**	**2c**	A	**3hc**	75
21	$MeCH(OH)(CH_2)_{11}$I (**1i**)	**2a**	A	**3ia**	63
22	**1i**	**2c**	A	**3ic**	83
23	PhI (**1j**)	**2a**	A[f]	**3j**	75, 71[g]
24	**1j**	**2a**	B[f]	**3j**	23[g]
25	**1j**	**2a**	A[h]	**3j**	<5[g]
26	4-MeC_6H_4I (**1k**)	**2a**	A[f]	**3k**	52, 55[g]
27	4-$MeOC_6H_4$I (**1l**)	**2a**	A[f]	**3l**	54
28	4-HOC_6H_4I (**1m**)	**2a**	A[f]	**3m**	65[g]

29	4-AcC_6H_4I (**1o**)	**2a**	A[f]	**3o**	37
30	4-ClC_6H_4I (**1p**)	**2a**	A[f]	**3p**	46[i]

[a] Unless otherwise noted, all reactions were carried out with **1** (0.50 mmol), **2** (1.50 mmol), $PhSiH_3$ (1.00 mmol), $In(OAc)_3$ (0.10 mmol), dry air (4.8 mL), H_2O (0.25 mmol), and EtOH (1.0 mL) under N_2 (2 L balloon) at room temperature for 1.5 h.

[b] In method A, 2,6-lutidine (0.25 mmol) was used as an additive. In method B, 2,6-lutidine (0.25 mmol) was not used.

[c] The result with 1.00 mmol of **2**.

[d] 2,6-Lutidine was added at an interval of 10 min after the addition of $PhSiH_3$.

[e] To ease the isolation of the product **3ha**, it was converted into **3d** by treatment with benzoyl chloride and pyridine.

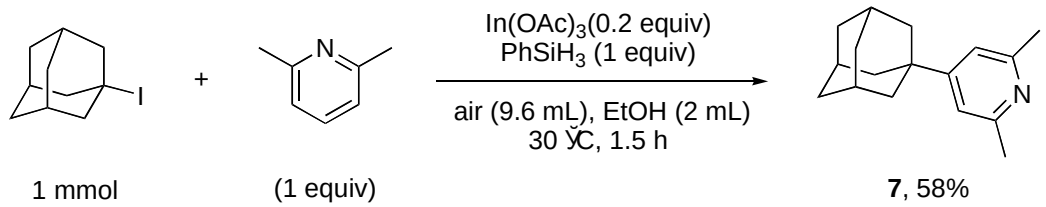
[f] An increased amount of dry air (9.6 mL) was used.

[g] The result *without water.

[h] Without dry air.

[i] The result with 1.00 mmol of **1**.

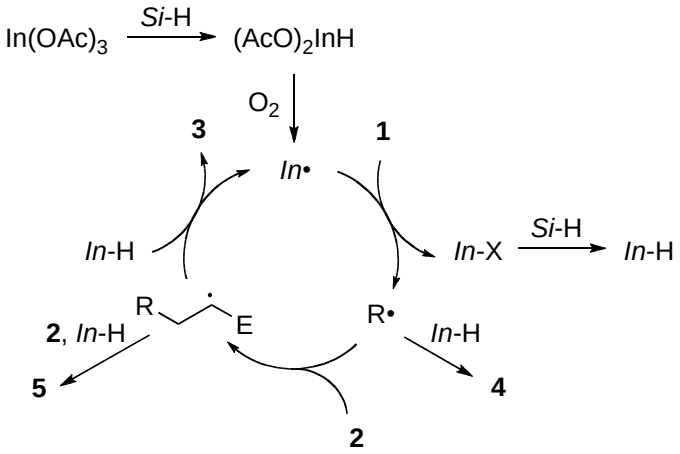
The formation of 4-(1-adamantyl)-2,6-dimethylpyridine (**7**) as a byproduct was observed in the reaction of **1c**-I (entries 7 and 8). Acrylate **2a** did not seem to participate in the formation of **7**. The author therefore attempted the reaction without **2a** under similar conditions. As expected, **7** was obtained in moderate yield. The reaction mechanism may involve the radical addition of a 1-adamantyl radical to 2,6-lutidine although it remains unclear.



2.3. Mechanism

A plausible mechanism for the present reaction is shown in Scheme 2.[6a,b] The first step is the formation of $(AcO)_2InH$ by hydride transfer from $PhSiH_3$ to $In(OAc)_3$. The indium hydride undergo H-abstraction by O_2 in air to give $(AcO)_2In•$ (*i.e.*, $(AcO)_2In(II)$). The active species abstracts halogen from a halide **1** (R-X) to generate the corresponding carbon radical R• and $(AcO)_2InX$. The addition of R• to an alkene **2** followed by H-abstraction from indium hydrides (*In*-H) gives the corresponding adduct **3** with regeneration of indium radicals (*In*•). The indium salt formed, $(AcO)_2InX$, is converted into *In*-H by the reaction with $PhSiH_3$ in EtOH. The formation of **4** is the result of direct H-abstraction of R• from *In*-H. The successive addition of R• to two molecules of **2** forms the adduct **5**. The present system enables proper control of the concentration of *In*-H to avoid these side reactions.

The effect of 2,6-lutidine on reaction efficiency was remarkable in the reaction of less reactive substrates such as bromoalkanes and iodoarenes. As reported previously, 2,6-lutidine would serve for neutralization of the reaction system, which prevents the solvolysis of $PhSiH_3$ with EtOH. The diminished effectiveness of 2,6-lutidine in the reaction of iodoalkanes is attributable to their fast reaction prior to the solvolysis.



In = Y_2In (Y = AcO, EtO, halogen)
Si = PhH_2Si

Scheme 2

3. Conclusion

The author has developed a new method for tin-free radical addition of organic iodides to electron-deficient alkenes, which realizes high compatibility to functional groups as well as mild, environmentally sound reaction conditions. The present study has demonstrated that indium catalysis is valuable not only for radical reduction and radical cyclization but also for intermolecular radical addition. On the basis of the present indium catalysis, more cost-effective methods for radical reactions using inexpensive hydride sources and bases are now under investigation.

4. Experimental Section

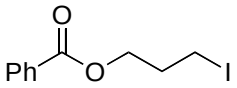
4.1. General Method

See page 11.

4.2. Access to Substrates and Reagents

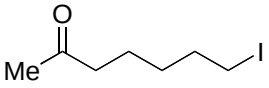
Bromo- and iodoalkanes **1a-c**, 3-iodo-1-propanol (**1h**), iodoarenes **1j-m** and **1o-p**, alkenes **2a-c**, $PhSiH_3$, and $In(OAc)_3$ were purchased from chemical companies. Functionalized iodoalkanes **1d-g**, **1i**, and **1n** were prepared by the known methods. CAS registry numbers are shown in the title lines.

3-Iodopropyl Benzoate (1d) [245758-34-3]



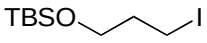
The title compound was prepared from benzoyl chloride and 3-iodo-1-propanol by the known method.[11] The identity of **1d** was confirmed by comparison of its spectral data (^1H and ^{13}C NMR) with the literature data.[12]

7-Iodo-2-heptanone (1e) [4305-27-5]



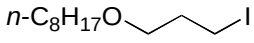
The title compound was prepared from 7-bromo-2-heptanone by the reaction with NaI (71% yield). For the replacement of bromine by iodine, see the synthetic procedure for **1g** in ref. 1. 7-Bromo-2-heptanone was prepared from cyclohexanone by the reported method.[13] The identity of **1e** was confirmed by comparison of its spectral data (IR, ^1H and ^{13}C NMR) with the literature data.[14]

1-*t*-Butyldimethylsiloxy-3-iodopropane (1f) [78878-05-4]



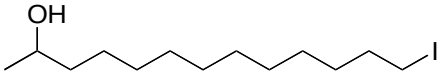
The title compound was prepared from 3-iodo-1-propanol (**1h**) by the reaction with TBS-OTf and 2,6-lutidine in CH_2Cl_2.[15] The identity of **1f** was confirmed by comparison of its spectral data (^1H and ^{13}C NMR) with the literature data.[16]

1-(3-Iodopropoxy)octane (1g) [926921-08-6]



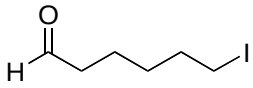
The title compound was prepared from 1,3-propanediol and 1-bromooctane by the known method. The identity of **1g** was confirmed by comparison of its spectral data (IR, ^1H and ^{13}C NMR) with the literature data.[17]

13-Iodo-2-tridecanol (1i) [926921-09-7]



The title compound was prepared from 13-bromo-2-tridecanone by the known method. The bromo-ketone was prepared from cyclododecanone by the reported method. The identity of **1i** was confirmed by comparison of its spectral data (IR, ^{1}H and ^{13}C NMR) with the literature data.[18]

6-Iodohexanal (1n) [91712-75-3]

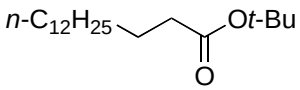


The title compound was prepared from 6-bromo-1-hexanol by the Swern oxidation using DMSO, $(COCl)_2$ and Et_3N,[19] and subsequent reaction with NaI.[17] The identity of **1n** was confirmed by comparison of its spectral data (IR, ^{1}H and ^{13}C NMR) with the literature data.[20]

4.3. Intermolecular Radical Addition

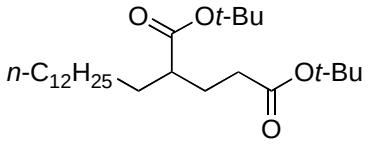
Adducts **3aa**, **3ac**, **3bc**, **3e**, **3f**, **3hc**, **3j**, **3m**, and **6** were identified by comparison of their spectral data with the literature data. Other adducts **3** and **5** were identified by full characterization. CAS registry numbers are shown in the title lines if available.

***t*-Butyl Pentadecanoate (3aa, Typical Procedure)** [882976-19-4]



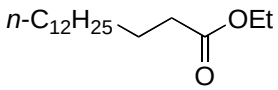
$In(OAc)_3$ (29 mg, 0.10 mmol) and a magnetic stirring bar were placed in a two-necked, round-bottomed flask (20 mL) fitted with a rubber septum and a three-way stopcock connected to a vacuum source and an N_2 balloon (2 L). The atmosphere in the flask was replaced with N_2. Dry air (4.8 mL) and EtOH (1.0 mL) were introduced into the flask with syringes. H_2O (4.5 mL, 0.25 mmol), 1-iododododecane (**1a**, 148 mg, 0.50 mmol), *t*-butyl acrylate (**2a**, 192 mg, 1.50 mmol), and $PhSiH_3$ (108 mg, 1.00 mmol) were successively added to the mixture under stirring at room temperature. After the addition of $PhSiH_3$, the mixture was stirred for 20-30 s, then 2,6-lutidine (54 mg, 0.50 mmol) was added to the mixture. After being stirred for 1.5 h, the resultant mixture and the washings with *t*-BuOMe (20 mL) were poured into a mixture of saturated aqueous $NaHCO_3$ (1 mL) and *t*-BuOMe (5 mL). The aqueous mixture was dried over Na_2SO_4 and filtered. The dried organic phase was subjected to GC analysis using undecane as an internal standard (67% GC yield). In the case of isolation, the organic phase was evaporated and subjected to silica gel column chromatography (hexane-Et_2O 10:1). The title compound was obtained in 64% isolated yield. The identity of **3aa** was confirmed by comparison of its spectral data (IR, ^{1}H and ^{13}C NMR) with the literature data.[21]

Di-*t*-butyl 2-Tridecylpentanedioate (5a)



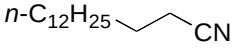
Bp 200 °C (bath temp, 1.0 Torr). IR (neat) 2925, 2854, 1730 (C=O), 1367, 1147 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.20–1.60 (m, 44H), 1.65–1.87 (m, 1H), 2.12–2.31 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.7 (CH_2), 27.2 (CH_2), 27.6 (CH_2), 28.12 (CH_3 x 3), 28.14 (CH_3 x 3), 29.37 (CH_2), 29.48 (CH_2), 29.53 (CH_2), 29.58 (CH_2), 29.66 (CH_2 x 2), 29.68 (CH_2 x 2), 31.9 (CH_2), 32.5 (CH_2), 33.3 (CH_2), 45.7 (CH), 80.1 (C), 80.2 (C), 172.6 (C), 175.3 (C). Anal. Calcd for $C_{26}H_{50}O_4$: C, 73.19; H, 11.81%. Found: C, 72.79; H, 11.73%.

Ethyl Pentadecanoate (3ab) [41114-00-5]



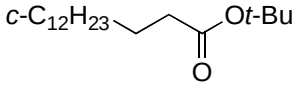
Bp 172 °C (bath temp, 1.0 Torr). IR (neat) 2929, 2854, 1739 (C=O), 1178 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.5 Hz, 3H), 1.20–1.35 (m, 25H), 1.56–1.66 (m, 2H), 2.29 (t, *J* = 7.6 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 14.2 (CH_3), 22.6 (CH_2), 24.9 (CH_2), 29.1 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.56 (CH_2), 29.61 (CH_2 x 2), 29.64 (CH_2 x 2), 31.9 (CH_2), 34.3 (CH_2), 60.1 (CH_2), 173.9 (C); EI-MS *m*/*z* (relative intensity) 270 (M^+, 9.8), 225 (M^+ – OEt, 6.8), 88 (100). Anal. Calcd for $C_{17}H_{34}O_2$: C, 75.50; H, 12.67%. Found: C, 75.23; H, 12.80%.

Pentadecanenitrile (3ac) [18300-91-9]



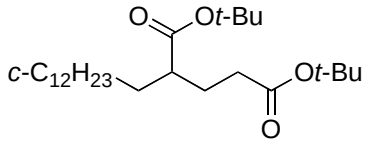
The identity of **3ac** was confirmed by comparison of its spectral data (IR, ^1H NMR) with the literature data.[22]

***t*-Butyl 3-Cyclododecylpropanoate (3ba)** [882976-20-7]



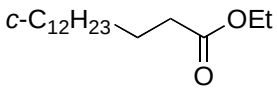
IR (neat) 2931, 1731 (C=O), 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19–1.60 (m, 34H), 2.22 (t, *J* = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_2 x 2), 23.3 (CH_2 x 2), 23.4 (CH_2 x 2), 24.0 (CH_2), 24.7 (CH_2 x 2), 28.1 (CH_3 x 3), 28.9 (CH_2 x 2), 30.2 (CH_2), 33.4 (CH), 33.7 (CH_2), 79.8 (C), 173.5 (C); EI-MS *m*/*z* (relative intensity) 241 (M^+ – C_4H_7, 12), 240 (M^+ – C_4H_8, 15), 57 (100). Anal. Calcd for $C_{19}H_{36}O_2$: C, 76.97; H, 12.24%. Found: C, 76.74; H, 12.27%.

Di-*t*-butyl 2-(Cyclododecylmethyl)pentanedioate (5b)



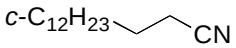
Bp 230 °C (decomposition, bath temp, 1.0 Torr). IR (neat) 2931, 1730 (C=O), 1147 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07–1.86 (m, 45H), 2.12–2.40 (m, 3H); ^{13}C NMR (C_6D_6) δ 21.8 (CH_2), 22.3 (CH_2), 23.19 (CH_2), 23.24 (CH_2), 24.2 (CH_2), 24.3 (CH_2), 24.4 (CH_2), 25.01 (CH_2), 25.05 (CH_2), 28.11 (CH_3 x 6), 28.9 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 32.2 (CH), 33.4 (CH_2), 38.5 (CH_2), 43.8 (CH), 79.6 (C x 2), 172.0 (C), 175.0 (C). Anal. Calcd for $C_{26}H_{48}O_4$: C, 73.54; H, 11.39%. Found: C, 73.81; H, 11.51%.

Ethyl 3-Cyclododecylpropanoate (3bb)



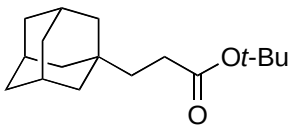
Bp 150 °C (1.0 Torr, bath temp). IR (neat) 2931, 2862, 1738 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17–1.45 (m, 26H), 1.51–1.59 (m, 2H), 2.30 (t, J = 7.7 Hz, 2H), 4.12 (q, J= 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 14.3 (CH_3), 21.6 (CH_2 x 2), 23.3 (CH_2 x 2), 23.4 (CH_2 x 2), 24.1 (CH_2), 24.7 (CH_2 x 2), 28.8 (CH_2 x 2), 30.0 (CH_2), 32.5 (CH_2), 33.6 (CH), 60.2 (CH_2), 174.2 (C); EI-MS *m/z* (relative intensity) 268 (M^+, 4.6), 239 ($M^+ – C_2H_5$, 2.9), 101 (100). Anal. Calcd for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02%. Found: C, 75.94, H 12.23%.

3-Cyclododecylpropanenitrile (3bc) [69300-14-7]



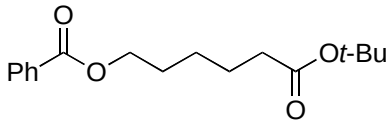
The identity of **3bc** was confirmed by comparison of its spectral data (IR, ^1H and ^{13}C NMR) with the literature data.[23]

***t*-Butyl 3-(1-Adamantyl)propanoate (3c)**



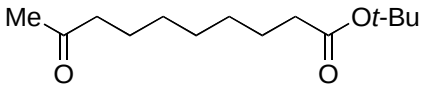
Mp 46–48 °C (hexane–AcOEt). IR (KBr) 1728 (C=O), 1146 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34–1.40 (m, 2H), 1.44–1.72 (m, 21H), 1.94 (br s, 3H), 2.14–2.21 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 28.1 (CH_3 x 3), 28.6 (CH x 3), 29.3 (CH_2), 31.9 (C), 37.1 (CH_2 x 3), 39.0 (CH_2), 42.1 (CH_2 x 3), 79.8 (C), 174.1 (C); EI-MS *m/z* (relative intensity) 264 (M^+, 0.03), 209 ($M^+ – C_4H_7$, 29), 208 ($M^+ – C_4H_8$, 23), 135 (100). Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67%. Found: C, 77.04, H 10.83%.

5-(*t*-Butoxycarbonyl)pentyl Benzoate (3d)



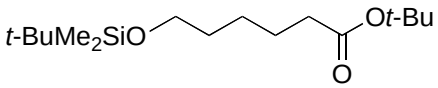
Bp 172 °C (bath temp, 1.6 Torr). IR (neat) 1722 (C=O), 1274, 1151, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34–1.50 (m, 11H) including 1.44 (s), 1.61–1.85 (m, 4H), 2.25 (t, J = 7.3 Hz, 2H), 4.32 (t, J = 6.6 Hz, 2H), 7.41–7.46 (m, 2H), 7.52–7.58 (m, 1H), 8.02–8.05 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 24.7 (CH_2), 25.5 (CH_2), 28.0 (CH_3 x 3), 28.4 (CH_2), 35.4 (CH_2), 64.7 (CH_2), 80.0 (C), 128.2 (CH x 2), 129.5 (CH x 2), 130.4 (C), 132.7 (CH), 166.5 (C), 172.9 (C); EI-MS *m/z* (relative intensity) 237 ($M^+ - C_4H_7$, 1.6), 236 ($M^+ - C_4H_8$, 3.6), 105 (100). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27%. Found: C, 69.54; H, 8.31%.

***t*-Butyl 9-Oxodecanoate (3e)** [77383-18-7]



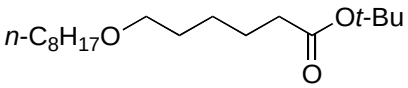
The identity of **3e** was confirmed by comparison of its spectral data (IR, ^1H NMR) with the literature data.[24]

***t*-Butyl 6-(*t*-Butyldimethylsiloxy)hexanoate (3f)** [874796-67-5]



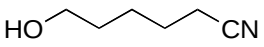
The identity of **3f** was confirmed by comparison of its spectral data (^1H and ^{13}C NMR) with the literature data.[25]

***t*-Butyl 6-Octoxyhexanoate (3g)**



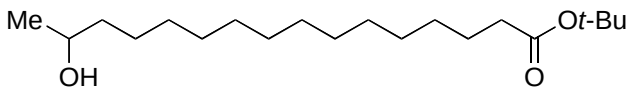
Bp 195 °C (bath temp, 1.2 Torr). IR (neat) 2929, 2856, 1734 (C=O), 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3H), 1.20–1.40 (m, 12H), 1.44 (s, 9H), 1.48–1.67 (m, 6H), 2.22 (t, J = 7.5 Hz, 2H), 3.39 (t, J = 6.8 Hz, 2H), 3.40 (t, J = 6.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.6 (CH_2), 24.9 (CH_2), 25.7 (CH_2), 26.2 (CH_2), 28.1 (CH_3 x 3), 29.3 (CH_2), 29.4 (CH_2 x 2), 29.7 (CH_2), 31.8 (CH_2), 35.5 (CH_2), 70.6 (CH_2), 71.0 (CH_2), 79.9 (C), 173.2 (C); EI-MS *m/z* (relative intensity) 243 ($M^+ - C_4H_9$, 1.9), 227 ($M^+ - C_4H_9O$, 1.6), 115 (78), 57 (100). Anal. Calcd for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08%. Found: C, 72.35, H 12.39%.

6-Hydroxyhexanenitrile (3hc) [2453-48-7]



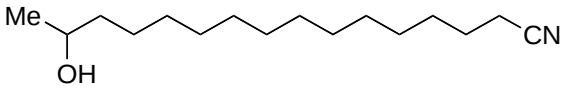
The identity of **3hc** was confirmed by comparison of its spectral data (IR, ^1H NMR) with the literature data.[26]

***t*-Butyl 15-Hydroxyhexadecanoate (3ia)**



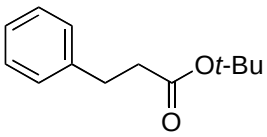
Bp 155 °C (bath temp, 0.7 Torr). IR (neat) 3386 (br s, OH), 2925, 2854, 1734 (C=O), 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, *J* = 6.3 Hz, 3H), 1.22–1.48 (m, 32H), 1.50–1.60 (m, 2H), 2.20 (t, *J* = 7.4 Hz, 2H), 3.70–3.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 23.4 (CH_3), 25.1 (CH_2), 25.7 (CH_2), 28.0 (CH_3 x 3), 29.0 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 29.5 (CH_2 x 2), 29.6 (CH_2 x 4), 35.6 (CH_2), 39.3 (CH_2), 68.0 (CH), 79.8 (C), 173.3 (C); EI-MS *m/z* (relative intensity) 255 ($M^+ - C_4H_9O$, 1.0), 57 (100). Anal. Calcd for $C_{20}H_{40}O_3$: C, 73.12; H, 12.27%. Found: C, 72.77, H 12.33%.

15-Hydroxyhexadecanenitrile (3ic)



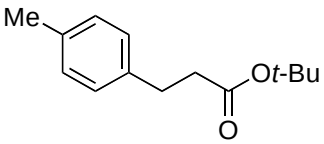
Mp 50.0–50.5 °C (Hexane-Et_2O). IR (KBr) 3411 (br s, OH), 2918, 2850, 2249 (CN), 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, *J* = 6.3 Hz, 3H), 1.20–1.56 (m, 23H), 1.60–1.71 (m, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 3.75–3.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 17.1 (CH_2), 23.5 (CH_3), 25.4 (CH_2), 25.8 (CH_2), 28.6 (CH_2), 28.7 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.56 (CH_2 x 2), 29.59 (CH_2 x 2), 29.63 (CH_2), 39.4 (CH_2), 68.2 (CH), 119.6 (C); EI-MS *m/z* (relative intensity) 235 ($M^+ - H_2O$, 0.7), 41 (100). Anal. Calcd for $C_{16}H_{31}NO$: C, 75.83; H, 12.33; N, 5.53%. Found: C, 75.68; H, 12.48; N, 5.41%.

***t*-Butyl 3-Phenylpropanoate (3j)** [16537-10-3]



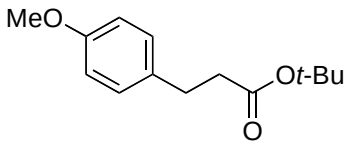
The identity of **3j** was confirmed by comparison of its spectral data (IR, ^1H and ^{13}C NMR) with the literature data.[27]

***t*-Butyl 3-(4-Methylphenyl)propanoate (3k)** [379218-64-1]



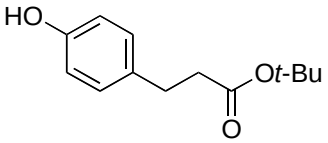
Bp 110 °C (bath temp, 1.0 Torr). IR (neat) 1734 (C=O), 1147 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (s, 9H), 2.31 (s, 3H), 2.51 (t, *J* = 7.8 Hz, 2H), 2.87 (t, *J* = 7.8 Hz, 2H), 7.09 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 20.9 (CH_3), 28.0 (CH_3 x 3), 30.6 (CH_2), 37.2 (CH_2), 80.2 (C), 128.1 (CH x 2), 129.0 (CH x 2), 135.5 (C), 137.7 (C), 172.3 (C); EI-MS *m/z* (relative intensity) 164 ($M^+ - C_4H_8$, 39), 147 ($M^+ - C_4H_9O$, 7.1), 105 (100). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15%. Found: C, 76.11, H 9.36%.

***t*-Butyl 3-(4-Methoxyphenyl)propanoate (3l)** [85277-69-6]



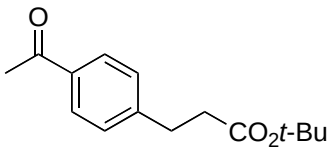
Bp 110 °C (bath temp. 1.0 Torr). IR (neat) 1720, 1512, 1365, 1244, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (s, 9H), 2.50 (t, *J*= 7.7 Hz, 2H), 2.85 (t, *J* = 7.7 Hz, 2H), 3.78 (s, 3H), 6.82 (d, *J* = 8.6 Hz, 2H), 7.11 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 28.0 (CH_3 x 3), 30.2 (CH_2), 37.3 (CH_2), 55.2 (CH_3), 80.2 (C), 113.7 (CH x 2), 129.2 (CH x 2), 132.8 (C), 157.9 (C), 172.3 (C); EI-MS *m/z* (relative intensity) 236 (M^+, 3.2), 180 (M^+ –C_4H_8, 23), 121 (100). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53%. Found: C, 70.94, H 8.71%.

***t*-Butyl 3-(4-Hydroxyphenyl)propanoate (3m)** [51458-31-2]



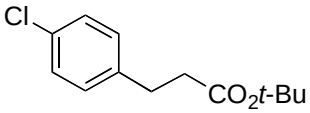
The identity of **3m** was confirmed by comparison of its spectral data (IR, ^1H and ^{13}C NMR) with the literature data.[28]

***t*-Butyl 3-(4-Acetylphenyl)propanoate (3o)** [780761-58-2]



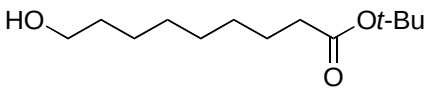
Bp 109 ℃ (bath temp. 2.1 Torr). IR (neat) 2177, 1728 (C=O), 1684 (C=O), 1269 (C–O), 1147 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.41 (s, 9H), 2.56 (t, *J* = 7.6 Hz, 2H), 2.59 (s, 3H), 2.97 (t, *J* = 7.7 Hz, 2H), 7.26–7.34 (m, 2H), 7.83–7.93 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 26.5 (CH_3), 27.9 (CH_3 x 3), 30.9 (CH_2 x 2), 36.3 (CH_2 x 1), 80.5 (C), 128.5 (CH x 4), 135.2 (C), 146.4 (C), 171.7 (C), 197.7 (C). M/S m/z (relative intensity) 56 (100), 147 (M^+ – $C_5H_9O_2$, 14), 175 (M^+ – C_4H_9O, 4).

***t*-Butyl 3-(4-Chlorophenyl)propanoate (3p)**



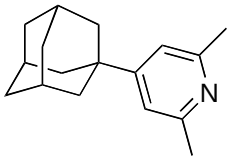
IR (neat) 3583, 2139, 1896, 1730 (C=O), 1298, 1255, 1149, 1093 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.41 (s, 9H), 2.51 (t, *J*= 7.8 Hz, 2H), 2.87 (t, *J*= 7.7, 2H), 7.11–7.29 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 28.0 (CH_3 x 3), 30.3 (CH_2), 36.8 (CH_2), 80.4 (C), 128.4 (CH x 2), 129.6 (CH x 2), 131.8 (C), 139.2 (C), 171.8 (C). M/S m/z (relative intensity) 57 (100), 167 (M^+ – C_4H_9O, 10). Anal. Calcd for $C_{13}H_{17}ClO_2$: C, 64.86; H, 7.12%. Found: C, 64.78, H 7.17%.

***t*-Butyl 9-Hydroxynonanoate (6)** [171926-99-1]



The identity of **6** was confirmed by comparison of its spectral data (IR, ^{1}H and ^{13}C NMR) with the literature data.[29]

4-(1-Adamantyl)-2,6-dimethylpyridine (7)



Mp 112 ℃. IR (KBr) 3365, 2904, 2178, 1799cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.58–1.99 (m, 12H), 2.04–2.19 (m, 3H), 2.50 (s, 6H), 6.91 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 24.6 (CH_3 x 2), 28.7 (CH x 3), 30.7 (C), 36.6 (CH_2 x 3), 42.4 (CH_2 x 3), 116.8 (CH x 2), 157.3 (C x 2), 160.5 (C). M/S m/z (relative intensity) 106 ($M^+ - C_{10}H_{15}$, 2), 135 ($M^+ - C_7H_8N$, 14), 241 (M^+, 100).

5. References

1. (a) Renaud, P.; Sibi, M. P. *Radicals in Organic Synthesis*; Wiley-VCH: Weinheim, 2001. (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, 1996. (c) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost B. M.; Fleming, I. Eds.; Pergamon Press: Oxford, 1991, Vol. 4, Chaps. 4.1-4.2, p 715. (d) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986.
2. Boyer, I. J. *Toxicology* **1989**, *55*, 253.
3. Baguley P. A.; Walton, J. C. *Angew. Chem. Int. Ed.* **1998**, *37*, 3073 and references therein.
4. Hydrosilanes and related compounds: (a) Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681. (b) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188. (c) Chatgilialoglu, C.; Guerra, M.; Guerrini, A.; Seconi, G. *J. Org. Chem.* **1992**, *57*, 2427. (d) Yamazaki, O.; Togo, H.; Matsubayashi, S.; Yokoyama, M. *Tetrahedron* **1999**, *55*, 3735. (e) Studer, A.; Amrein, S.; Schleth, F.; Schulte, T.; Walton, J. C. *J. Am. Chem. Soc.* **2003**, *125*, 5726.
5. Hydrogermanes: (a) Sakurai, H.; Mochida, K.; Hosomi, A.; Mita, F. *J. Organomet. Chem.* **1972**, *38*, 275. (b) Chatgilialoglu C.; Ballestri, M. *Organometallics* **1995**, *14*, 5017. (c) Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 747. (d) Miura, K.; Ootsuka, K.; Hosomi, A. *Synlett* **2005**, 3151.
6. Indium and gallium hydrides: (a) Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 906. (b) Hayashi, N.; Shibata, I.; Baba, A. *Org. Lett.* **2005**, *7*, 3093. (c) Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627 and references therein.
7. Dialkyl phosphites and hypophosphorous acid: Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. C. *J. Org. Chem.* **1993**, *58*, 6838 and references therein.
8. (a) Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1975**, *40*, 2554. (b) Giese, B.; González-Gómez, J. A.; Witzel, T. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 69. (c) Lopez, R. M.; Hays, D. S.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 6949.
9. Miura, K.; Tomita, M.; Yamada, Y.; Hosomi, A. *J. Org. Chem.* **2007**, *72*, 787.
10. The author has previously reported that the $In(OAc)_3$-catalyzed reaction of α-enones with $PhSiH_3$ in EtOH gives ketones by 1,4-reduction without overreduction leading to alcohols, and that the reduction system is effective in the conversion of aldehydes into alcohols. Miura, K.; Yamada, Y.; Tomita, M.; Hosomi, A. *Synlett* **2004**, 1985.
11. See page 52 and ref 9. (a) Mikami, S.; Fujita, K.; Nakamura, T.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, *3*, 1853 (b) Synthetic procedure and compound data for **1f**-Br: Hoeger, S.; Rosselli, S.; Ramminger, A.-D.; Enkelmann, V. *Org. Lett.* **2002**, *4*, 4269.
12. Compound data for **1d**: Thompson, A. M.; Delaney, A. M.; Hamby, J. M.; Schroeder, M. C.; Spoon, T. A.; Crean, S. M.; Showalter, H. D. H.; Denny, W. A. *J. Med. Chem.* **2005**, *48*, 4628.
13. See page 56. Synthetic procedure and compound data for 7-bromo-2-heptanone: Zhang, W.-C.; Li, C.-J. *J. Org. Chem.* **2000**, *65*, 5831.
14. Compound data for **1e** and **1n**: Barluenga, J.; Gonzalez-Bobes, F.; Murguia, M. C.; Ananthoju, S. R.; Gonzalez, J. M. *Chem. Eur. J.* **2004**, *10*, 4206.
15. Synthetic procedure for TBS ether **1f**: Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
16. Compound data for **1f**: Gu, X.; Sun, M.; Gugiu, B.; Hazen, S.; Crabb, J. W.; Salomon, R. G. *J. Org. Chem.* **2003**, *68*, 3749.

17. See page 54.
18. See page 55.
19. Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
20. Barluenga, J.; Gonzaelez-Bobes, F.; Murguia, M. C.; Ananthoju, S.; R.; Gonzaelez, J. M. *Chem. Eur. J.* **2004**, *10*, 4206.
21. Compound data for **3aa** (IR, EI-MS, ^{1}H and ^{13}C NMR): Miura, K.; Ootsuka, K.; Hosomi, A. *Synlett* **2005**, 3151.
22. Compound data (IR, EI-MS, ^{1}H NMR) for **3ac**: Bhattacharya, S.; Vemula, P. K. *J. Org. Chem.* **2005**, *70*, 9677.
23. Compound data (IR, ^{1}H NMR, ^{13}C NMR) for **3bc**: Ardarelli, A. M.; Fagnoni, M.; Mella, M.; Albini, A. *J. Org. Chem.* **2001**, *66*, 7320.
24. Compound data (Bp, IR, ^{1}H NMR) for **3e**: Tanaka, K.; Matsui, S.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3619.
25. Compound data (^{1}H NMR, ^{13}C NMR) for **3f** : Yeom, C.-E.; Kim, Y. J.; Lee, S. Y.; Shin, Y. J.; Kim, B. M. *Tetrahedron* **2005**, *61*, 12227.
26. Compound data (IR, ^{1}H NMR) for **3hc**: Neokosmidi, A.; Ragoussis, V.; Zikos, C.; Paravatou-Petsotas, M.; Livaniou, E.; Ragoussis, N.; Evangelatos, G. *J. Agric. Food Chem.* **2004**, *52*, 4368.
27. Compound data (IR, ^{1}H NMR, ^{13}C NMR) for **3j**: (a) Kissling, R. M.; Gagne, M. R. *Org. Lett.* **2000**, *2*, 4209. (b) Kunishima, M.; Kawachi, C.; Morita, J.; Terao, K.; Iwasaki, F.; Tani, S. *Tetrahedron* **1999**, *55*, 13159.
28. Compound data (IR, ^{1}H NMR, ^{13}C NMR, EI-MS) for **3m**: Clough, J. M.; Jones, R. V. H.; McCann, H.; Morris, D. J.; Wills, M. *Org. Biomol. Chem.* **2003**, *1*, 1486.
29. Compound data (IR, ^{1}H NMR, ^{13}C NMR, EA) for **6**: Reding, M. T.; Buchwald, S. L. *J. Org. Chem.* **1995**, *60*, 7884.

List of Publications

1. “Indium(III) Acetate-Catalyzed 1,4-Reduction and Reductive Aldol Reactions of α-Enones with Phenylsilane”

   Miura, K.; Yamada, Y.; Tomita, M.; Hosomi, A.

   Synlett **2004**, 1985–1989.

2. “Indium-Catalyzed Radical Reductions of Organic Halides with Hydrosilanes”

   Miura, K.; Tomita, M.; Yamada, Y.; Hosomi, A.

   J. Org. Chem. **2007**, *72*, 787–792.

3. “Indium(III) Acetate-Catalyzed Intermolecular Radical Addition of Organic Iodides to Electron-Deficient Alkenes”

   Miura, K.; Tomita, M.; Ichikawa, J.; Hosomi, A.

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