

Indium-Catalyzed Reduction of Allyl Bromide with Gallium or Aluminum. Formation of Allylgallium and Allylaluminum Sesquibromides

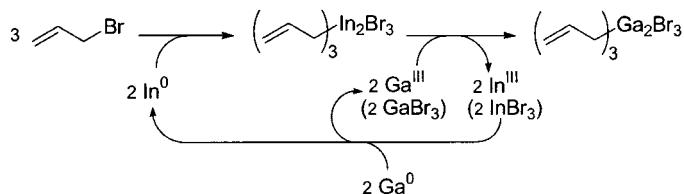
Kazuhiko Takai* and Yoshito Ikawa

Department of Applied Chemistry, Faculty of Engineering, Okayama University,
Tsushima, Okayama 700-8530, Japan

ktakai@cc.okayama-u.ac.jp

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ABSTRACT



Fast transmetalation of an allyl group from indium to gallium enables the assembly of a catalytic cycle of indium, which accelerates the formation of allylgallium sesquibromide. A solution of allylaluminum sesquibromide in THF is also prepared from allyl bromide and aluminum metal under indium catalysis.

Although there are many methods for preparing organometallic compounds, direct reduction of organic halides with low-valent metals has several advantages.¹ In particular, this approach allows many types of organometallic compounds to be made. A key issue when using a direct reduction is how to accelerate the electron transfer from the metal to the organic compound. For this purpose, several methods such as the Rieke's activation method^{1a} and the metal-graphite method^{1d} have been developed. Another method for the acceleration of electron transfer is to add a catalytic amount of a second metal element to the target metal.² This sometimes has the advantage of activating the target metal under mild conditions. We report here a novel activation

method for metallic gallium or aluminum using a catalytic amount of indium. The method is useful for the preparation of both allylgallium³ and allylaluminum sesquibromides⁴ in THF under mild conditions.

Despite its reducing power (E° : $\text{Ga}^{\text{III}}/\text{Ga}^0$, -0.549 V),⁵ gallium metal has not been used widely in organic synthesis.^{3b,6} In contrast to allylations involving indium metal, where the allylic indium species can be prepared allowing Grignard-

(3) (a) Araki, S.; Ito, H.; Butsugan, Y. *Appl. Organomet. Chem.* **1988**, 2, 475. (b) Han, Y.; Huang, Y.-Z. *Tetrahedron Lett.* **1994**, 35, 9433. (c) Yamaguchi, M.; Sotokawa, T.; Hirama, M. *Chem. Commun.* **1997**, 743. (d) Araki, S.; Horie, T.; Kato, M.; Hirashita, T.; Yamamura, H.; Kawai, M. *Tetrahedron Lett.* **1999**, 40, 2331. (e) Usugi, S.-i.; Yorimitsu, H.; Oshima, K. *Tetrahedron Lett.* **2001**, 42, 4535. (f) Takai, K.; Ikawa, Y.; Ishii, K.; Kumanda, M. *Chem. Lett.* **2002**, 172.

(4) Some selected examples of the Barbier-type reactions. (a) $\text{Al}-\text{PbBr}_2$: Tanaka, H.; Yamashita, S.; Hamatani, T.; Ikemoto, Y.; Torii, S. *Synth. Commun.* **1987**, 17, 789. (b) Tanaka, H.; Nakahata, S.; Watanabe, H.; Zhao, J.; Kuroboshi, M.; Torii, S. *Inorg. Chim. Acta* **1999**, 296, 204. (c) $\text{Al}-\text{InCl}_3$: Araki, S.; Jin, S.-J.; Idou, Y.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1992**, 65, 1736.

(5) Standard reduction potential (E°) of $\text{In}^{\text{III}}/\text{In}^0$ is -0.3382 V; see: *CRC Handbook of Chemistry and Physics*, 82nd ed.; CRC Press: Boca Raton, 2001; p 8–21.

(6) Zhang, X.-L.; Han, Y.; Tao, W.-T.; Huang, Y.-Z. *J. Chem. Soc., Perkin Trans. 1* **1995**, 189.

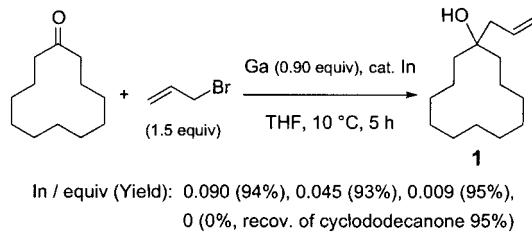
(1) For reviews of activated metals in organic synthesis, see: (a) Rieke, R. D. *Top. Curr. Chem.* **1975**, 59, 1. Rieke, R. D. *Aldrichimica Acta* **2000**, 33, 52. (b) Fürstner, A. *Angew. Chem., Int. Ed. Engl.* **1993**, 32, 164. (c) Cintas, P. *Activated Metals in Organic Synthesis*; CRC Press: Boca Raton, 1993. (d) Fürstner, A. *Active Metals: Preparation, Characterization, Application*; VCH: Weinheim, 1996.

(2) (a) Li–Na: Kamienski, C. W.; Esmay, D. L. *J. Org. Chem.* **1960**, 25, 1807. Smith, W. N., Jr. *J. Organomet. Chem.* **1974**, 82, 1. (b) Zn–Cu: Shank, R. S.; Shechter, H. *J. Org. Chem.* **1959**, 24, 1825. LeGoff, E. *J. Org. Chem.* **1964**, 29, 2048. (c) Mn–Pb: Takai, K.; Ueda, T.; Hayashi, T.; Moriwake, T. *Tetrahedron Lett.* **1996**, 37, 7049.

type allylations to be achieved,⁷ the reported gallium-mediated reactions are only conducted in Barbier-type procedures. Moreover, the gallium-mediated Barbier-type allylation in THF requires heating at reflux.^{3b,8} Therefore, we explored the formation of allylgallium species by addition of a catalytic amount of a second metal element.⁹

A Barbier-type addition of allylic bromide to cyclododecanone with gallium(0) was chosen as a probe for the activating effects. Because of the low melting point (29.8 °C) of the gallium metal, the allylation was examined at 10 °C in order to avoid the formation of spherical gallium liquid, which has the smallest surface area.¹⁰ Among the reactions examined, addition of an indium metal to gallium(0) was effective to promote the Barbier-type allylation. In addition, the amount of indium metal could be reduced to 1 mol % of gallium(0). For example, treatment of a mixture of cyclododecanone (1.0 mmol) and allyl bromide (1.5 mmol) in THF with gallium(0) (0.90 mmol) and indium(0) (0.009 mmol) at 10 °C for 5 h gave 1-allylcyclododecanol (**1**) in 95% yield (Scheme 1). This reaction only proceeded when

Scheme 1. Addition of Allylgallium Species to Cyclododecanone



the catalytic amount of indium was added. When indium(0) was not used, cyclododecanone was recovered in 95% yield. On the other hand, when gallium(0) was not used in the Barbier-type allylation, the reaction proceeded with only a stoichiometric amount of indium(0) (0.90 mmol), but the yield of **1** was 64% and the ketone was recovered in 29% yield.

The allylation of the ketone could also be conducted using the Grignard procedure. For example, when a catalytic amount of indium(0) (powder, 0.045 mmol)¹¹ was added to a mixture of allyl bromide (1.5 mmol) and gallium metal (powder, 0.90 mmol)¹¹ in THF (5 mL), all of the gallium powder dissolved after 2 h stirring at 10 °C.^{12–14} On treatment of a solution of cyclododecanone (1.0 mmol) in THF (5 mL)

(7) (a) Araki, S.; Shimizu, T.; Johar, P. S.; Jin, S.-J.; Butsugan, Y. *J. Org. Chem.* **1991**, *56*, 2538. (b) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831.

(8) Tertiary-amine accelerated allylgallation of terminal alkynes does not proceed in DMF.^{3f} Thus, a preparative method for a solution of allylgallium sesquibromide in THF is required.

(9) Activating effects by addition of PbCl₂ or KI–LiCl on gallium were not observed at 25 °C in our experiments.

(10) The melting point of gallium lowered to 15.3 °C when 21.4 wt % of indium was added.

(11) Gallium powder (99.9% purity, particle size ca. 0.85 mm diameter), shot (99.99%, ca. 1 g), and indium powder (99% purity, particle size ca. 75 µm diameter) were purchased from Kojundo Chemical Lab Co., Ltd.

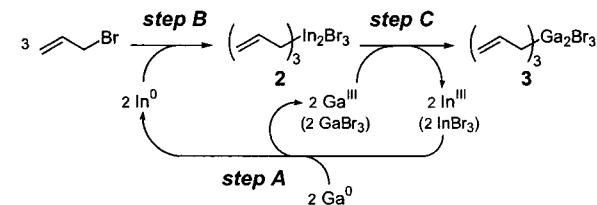
(12) When a shot of gallium(0) was used, the metal dissolved in 24 h.

with the THF solution of allylgallium at 10 °C for 5 h, **1** was obtained in 96% yield.¹⁵

The ¹H and ¹³C NMR spectra of the prepared allylgallium solution in THF-*d*₈ exhibited two sets of allyl peaks (see Supporting Information).¹⁶ The allylic methylene of the allylgallium appeared at δ 1.63 and 1.93 ppm in a 2:1 ratio, supporting the corresponding sesquibromide structure (allyl)₃Ga₂Br₃.¹⁷

A possible catalytic cycle for the formation of allylic gallium compounds by indium is shown in Scheme 2. The

Scheme 2. Possible Catalytic Cycle for the Formation of **3**



surface of commercially available indium metal is covered with oxidized indium(III). Because the reducing power of gallium is stronger than that of indium, the indium(III) is reduced with gallium(0) to generate indium(0) with no oxidized layer (step A).⁵ Indeed, a fine powder having a metal luster appeared when a catalytic amount of indium metal was added to a suspension of gallium(0) in THF at 10 °C. Allylic bromide is reduced with a catalytic amount of this indium(0) to produce the allylindium species **2** (step B).⁷ Reduction of allylic bromide with the indium(0) proceeds smoothly because it is freshly generated *in situ*. Then, transmetalation of the allylindium species **2** with gallium(III) proceeds to give the allylgallium species **3** and indium(III) (step C). As expected from the mechanism, the allylgallium species **3** could also be prepared by addition of a catalytic amount of InCl_3 instead of the indium metal.

(13) A standard solution of allylgallium in THF (ca. 1.0 M solution, allyl bromide excess) was prepared as follows. A catalytic amount of indium powder (0.90 mmol) was added to a mixture of allyl bromide (30 mmol) and gallium metal (shot, 18 mmol) in THF (28 mL), and the mixture was stirred at 10 °C for 24 h. When gallium powder was used, all of the gallium dissolved at 10 °C within 2 h. The solution of allylgallium in THF could be stored at 5 °C (in a refrigerator) for 1 month without decreasing the reactivity, but the reactivity decreased gradually at 25 °C. An allylgallium solution without contamination of allyl bromide could be prepared by using an excess amount of gallium metal; however, the reactivity of this solution decreased faster at 25 °C than that of the solution containing an excess amount of allyl bromide, and the solution became viscose.

(14) A solution of allyl gallium in DME or DMF could also be prepared in the same fashion.

(15) Addition of **3** to 3-phenylpropanal in THF occurred at 10 °C in 30 min; however, the yield of 1-phenyl-5-hexen-1-ol (**4**) was 74% as a result of the formation of the corresponding ketone derived by Oppenauer-type oxidation in 7% yield and the dialylation product in 5% yield. See ref 4b. Formation of these byproducts was suppressed by addition of DMF (1.0 equiv of the gallium metal) in the reaction mixture, and **4** was obtained in 93% yield.

(16) To consume all of the allyl bromide, an excess amount of gallium metal was used for the preparation of the allylgallium species in THF-*d*₈ solution. The supernatant solution was used for the NMR measurement.

(17) Araki reported the NMR data of the allylindium species. (Allyl)₃In₂I₃; ref 7b. AllylInI₂: Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. *J. Organomet. Chem.* **1989**, *369*, 291. Allylindium(I): Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228.

This is not a simple process of recycling indium with gallium(0) as a reductant but involves generating the allylgallium species. Therefore, the transmetalation (step C) should proceed quickly in order to construct the catalytic cycle with a reasonable turnover frequency.¹⁸ In step C, indium(III) is consumed by reduction with gallium(0), whereas the amount of the allylgallium species **2** is increased by reaction of the regenerated indium(0) and allyl bromide. In addition, indium has the largest difference of the bonding energies between $MtI-Br$ and $MtI-C$ in the metal elements of the 12–15 groups,¹⁹ and this provides an important driving force for the transmetalation. During the transmetalation step, the $In-C$ and $Ga-Br$ bonds rearrange to $Ga-C$ and $In-Br$ bonds. Because the sum of the bond energies on the right side ($Ga-C + In-Br$) of the arrows (step C) is larger than the left side ($In-C + Ga-Br$), formation of carbon–gallium bonds is more favorable and the transmetalation proceeds smoothly.

To examine the transfer of the allyl group from indium to gallium in step C, the following NMR experiments were conducted. A solution of gallium(III) bromide (1 M solution) in $THF-d_8$ was added portionwise at 25 °C to a 1 M solution of allylgallium sesquibromide derived from indium metal (2 mmol) and allyl bromide (3 mmol) in $THF-d_8$. When 0.5 mmol of gallium(III) bromide was added to the solution, the allylic proton peak of the diallylgallium bromide at δ 1.74 ppm disappeared with the appearance of that of diallylgallium bromide at δ 1.63 ppm and increase of the allylgallium dibromide peak at δ 2.03 ppm. Allylic protons of diallylgallium dibromide at δ 1.90 ppm were not observed. On further addition of gallium(III) bromide, proton peaks of diallylgallium dibromide appeared and both peaks of allylgallium dibromide and diallylgallium bromide decreased. When 3 mmol of gallium(III) bromide was added to the solution, the peak of allylgallium dibromide was only observed in the allylic proton region.²⁰ These results suggest the fast transmetalation.

Further, we examined this concept by designing a new indium-catalyzed cycle for activation of a different metal. To clarify the effectiveness, a candidate metal should have a stronger reducing power than indium(0); however it should

(18) Gallium(III) tribromide is soluble in the ethereal solvents to some extent.

(19) The bond energies between metals and carbon were estimated from their trimethyl compounds. $In-C$, 160 kJ mol⁻¹; $Ga-C$, 247 kJ mol⁻¹; $Al-C$, 274 kJ mol⁻¹. See: O'Neill, M. E.; Wade, K. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 1, p 5. The bond energies between metals and bromine are as follows: $In-Br$, 414 ± 21 kJ mol⁻¹; $Ga-Br$, 444 ± 17 kJ mol⁻¹; $Al-Br$, 429 ± 6 kJ mol⁻¹. See: *CRC Handbook of Chemistry and Physics*, 82nd ed.; CRC Press: Boca Raton, 2001; p 9–51.

(20) A solution of allylgallium dibromide in $THF-d_8$ was also generated by addition of gallium(III) bromide to a solution of allylgallium sesquibromide in $THF-d_8$. Allylic protons appeared at δ 1.90 ppm.

not reduce allyl bromide directly (or at least the reducing rate should be quite slow). Also, for the fast transmetalation step, the metal should satisfy the following inequality for the bond energy: $(In-Br - In-C) > (MtI-Br - MtI-C)$. Following these guidelines, we selected aluminum metal.

Aluminum metal has been used as a source of electrons, e.g., as a reducing agent of allylic bromides to allylic aluminum species, with a catalytic amount of $PbCl_2$ or $InCl_3$.⁴ However, the reported additions of allylic aluminum species to carbonyl compounds were not conducted under the Grignard but the Barbier conditions. By using a catalytic amount of indium, allylic aluminum species could be prepared and used in Grignard-type additions. For example, allyl bromide (1.5 mmol) was added to a mixture of aluminum (cut foil, 2 mm × 2 mm, 1.0 mmol) and a catalytic amount of indium(0) (powder, 0.050 mmol) in THF (5 mL), and the mixture was stirred at 25 °C. All of the aluminum foils were dissolved in 30 min. Grignard-type addition of the allyl aluminum compound to cyclododecanone (1.0 mmol) proceeded at 10 °C within 30 min to give **1** in 98% yield. $InCl_3$ could be used instead of the indium(0) in this reaction.^{4c}

The 1H and ^{13}C NMR spectra of the prepared allylaluminum solution in $THF-d_8$ revealed two sets of allyl peaks, suggesting the allylaluminum sesquibromide ($allyl_3Al_2Br_3$). All of the proton signals of the allylaluminum shifted upfield compared to those of the allylgallium sesquibromide; the allylic methylene of the allylaluminum appeared at δ 1.19 and 1.32 ppm in a 2:1 ratio (Supporting Information).²¹

In conclusion, allylgallium and allylaluminum sesquibromides were prepared by direct reduction of allylic bromides using a catalytic amount of indium as a mediator.

Acknowledgment. Financial support from the Ministry of Education, Science, Culture, and Technology of Japan is gratefully acknowledged. We would also like to thank Professor Shuki Araki of Nagoya Institute of Technology for valuable information about the NMR of allyl indium species.

Supporting Information Available: Proton and carbon spectra for allylgallium and allylaluminum sesquibromides. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(21) Barbier-type allylation of carbonyl compounds with allyl bromide and indium(I) regenerated on an aluminum sacrificial anode in THF was reported quite recently. Although the authors think indium(I) plays an important role in the reaction, they do not eliminate the possibility of the aluminum species for the allylation. Hilt, G.; Smolko, K. *I. Angew. Chem., Int. Ed.* **2001**, *40*, 3399.