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Isolation and Crystallographic Characterization of Allylindium Species Generated from Allyl Halide and Indium(0)

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Keywords: Indium / Allylation / N ligands / X-ray analysis / Reactive intermediates

The reaction of cinnamyl bromide with indium(0) gave two allylindium species, cinnamylindium dibromide and dicinnamylindium bromide. Either species were isolated after complexation of appropriate pyridine-type Lewis bases. The use of 3,5-dibromopyridine (Br_2py) as a Lewis base gave cinnamylindium dibromide with two Br_2py ligands. Dicinnamylindium bromide was isolated with 4-(dimethylamino)pyridine (Me_2Npy) ligands. In both cases, the indium atom showed a trigonal-bipyramidal coordination sphere with the cinnamyl group(s) and bomine atom(s) in equatorial and the pyridine-type ligands in axial positions. The cinnamylindium bromide transformed to dicinnamylindium bromide with formation of $InBr_3$ in the presence of Me_2Npy. The dicinnamylindium bromide had a higher reactivity than the monoallyl compound for carbonyl addition.

Introduction

A multitude of research into indium-mediated carbon–carbon bond formation has recently been conducted in organic synthesis,[1] particularly for stereoselective reactions with allylindium species.[2] One of the most valuable uses is the in situ generation of indium species from allyl halide/indium(0) in a reductive manner, and its direct reaction with electrophiles.[3,4] The structure of the generated allylindium compounds has been discussed based mainly on NMR spectroscopy, in which two types of allylic species, allylindium sesquihalide[3a,3b] or a mixture of (allyl)dihalogenidoindium(III)/allylindium(I),[3e,3j] have been proposed. Surprisingly, the reductively generated allylindium species have not been isolated and crystallographically analyzed in spite of a great number of synthetic reports. In this context, an unambiguous determination of the structure would be very important for wider synthetic applications. We have recently determined the structure of a series of organoindium species by X-ray analysis: butenylindium,[5] allylindium,[6] and vinylindium species.[7] However, the analyzed allylindium species was limited to that generated by transmetalation between an allylstannane and $InBr_3$. Here, we report the actual structures of reductively generated allylindium species[10] commonly used for indium-mediated Barbier-type allylation in a practical synthetic method.[3]

Results and Discussion

Two sets of different ratios of cinnamyl bromide (**1**) and indium metal (**1**/In = 1:1 and 1.5:1) in THF were observed by ^1H NMR spectroscopy (Figure 1, Charts a and b).[8] It was found that two types of cinnamylindium species, **2** and **3**, were generated in situ, and that the formed ratio [integration ratio of **2**/**3** = 1:1.32 (a) or 1:0.48 (b)] depended considerably on the mixing ratio of **1**/In. This result indicates that these two species are independent of one another.[3e,3j,9] Species **2** showed a doublet for the methylene protons at δ = 2.23 ppm, and species **3** showed that doublet at δ = 1.97 ppm. To stabilize and isolate the species, pyridine was added to the mixture as a coordinative ligand (**1**/In = 1:1).[5,6,10] The ^1H NMR spectrum showed that both species **2** and **3** were complexed by the ligand (see Supporting Information), but a solid was not obtained after the usual treatment. Next, the addition of 3,5-dibromopyridine (Br_2py) gave complexed species of **2** and **3** at an integration ratio of 1:1.38 (= $\mathbf{2}\cdot L_n/\mathbf{3}\cdot L_n$) (Chart c). Recrystallization of the mixture containing both $\mathbf{2}\cdot L_n$ and $\mathbf{3}\cdot L_n$ gave suitable crystals for X-ray crystallography. The analysis clearly proved the structure to be cinnamylindium dibromide with two Br_2py units.[11] This species originated from **2** because its NMR signals are identical to those of an authentic monoallylindium compound generated by transmetallation between tributyl(cinnamyl)stannane and $InBr_3$ after complexation by Br_2py (Chart d).[6] To obtain species **3**, various

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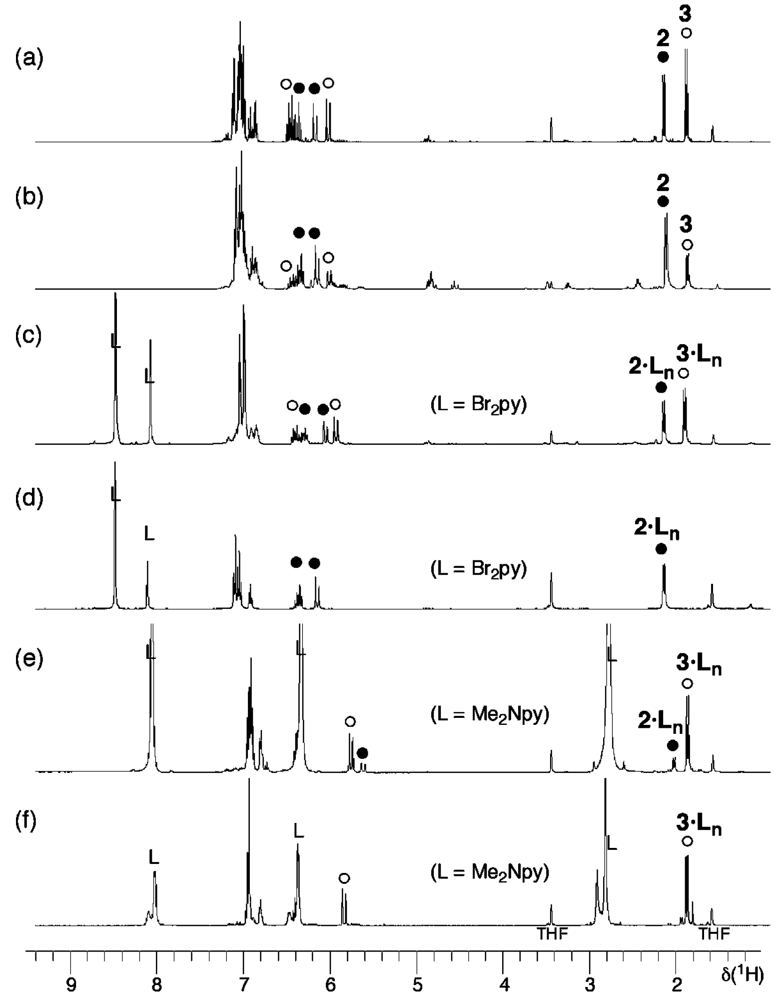
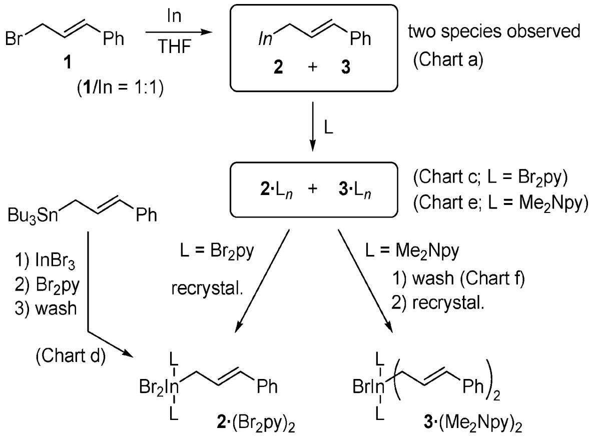


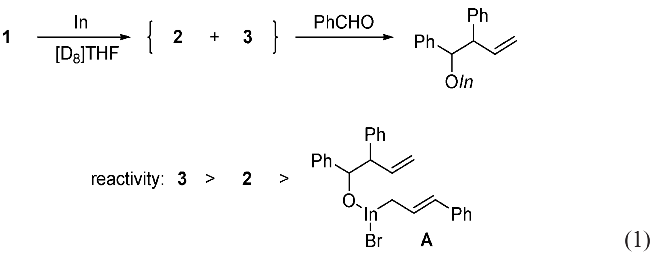
Figure 1. NMR spectra of allyindium compounds in solution ([D$_8$]THF): (a) 1:1 mixture of **1**/In. (b) 1.5:1 mixture of **1**/In. (c) Addition of 3,5-dibromopyridine to the mixture (a). (d) Isolated indium species **2**·L$_n$ from Sn/In transmetalation. (e) Addition of 4-(dimethylamino)-pyridine to the mixture (a). (f) Isolated indium species **3**·L$_n$.

mixing ratios of **1**/indium metal were tried, but **3** was not preferably formed, and the crystallized solids by complexation with Br$_2$py were always the species that corresponded to **2**. Gratifyingly, the addition of a stronger Lewis base, 4-(dimethylamino)pyridine (Me$_2$Npy) changed the formed integration ratio of **2**/**3** to 1:6 (Chart e), and the complex from **3** was selectively obtained after washing with hexane (Chart f). X-ray analysis of the complex proved the structure to be dicinnamylindium bromide with two Me$_2$Npy units. These results suggest that cinnamylindium dibromide (**2**) and dicinnamylindium bromide (**3**) were generated in situ by a Barbier-type method from cinnamyl bromide (**1**) with indium(0) (Scheme 1).

The reaction of the in situ generated allylindium compounds with benzaldehyde was observed by NMR spectroscopy [Equation (1)], with benzaldehyde being added in several portions. Species **3** was first consumed with the formation of a new allylic species (δ =1.44 ppm for the methylene protons), suggested to be carbonyl adduct **A**.[12] The addition of the next portions successively decreased the amounts of **2** and **A**. These results clarified the reaction course of the Barbier-type indium-mediated allylation; electronegative substituents retarded the nucleophilicity of the allylindium compounds, and the three formed species showed a reactivity in the order of **3** > **2** > **A**.



Scheme 1. Isolation of the two types of generated allylindium species by complexation.



(1)

The ORTEP drawing of $\mathbf{2}\cdot(\mathrm{Br_2py})_2$ is shown in Figure 2. The indium atom has a trigonal-bipyramidal coordination sphere with two bromine atoms, an allyl group in an equatorial plane, and two ligands ($\mathrm{Br_2py}$) in the axial positions. The sum of the bond angles in the equatorial plane is 359.4° [Br(2)–In(1)–Br(4) 113.66(4), Br(4)–In(1)–C(13) 117.5(2), C(13)–In(1)–Br(2) 128.9(2)]. The pyridine ligands coordinate to the indium center at an angle of 174.5(3)° [N(8)–In(1)–N(9)]. The bond length of In(1)–C(13) is 2.181(11) Å and is close to the reported average indium–carbon bond length (2.184 Å). The ORTEP drawing of $\mathbf{3}\cdot(\mathrm{Me_2Npy})_2$ is shown in Figure 3. In this case, the indium atom has also a trigonal-bipyramidal coordination sphere. The C(6)–In(1)–C(6′) bond angle [146.40(13)°] is larger than that of the angles between equatorial atoms in $\mathbf{2}\cdot(\mathrm{Br_2py})_2$. The sum of the angles in the equatorial plane [Br(2)–In(1)–C(6) 106.80(9) and Br(2)–In(1)–C(6′) 106.80(9)] forms 360°. The ligand pyridine groups coordinate to the indium atom at an angle of 174.15(11)° [N(3)–In(1)–N(3′)] in the same manner as $\mathbf{2}\cdot(\mathrm{Br_2py})_2$. The bond length of In(1)–C(6) is 2.146(2) Å. The olefin moiety C(7)–C(9) has a larger bond length [1.350(5) Å] than that [1.284(19) Å] of the corresponding C(15)–C(19) bond in $\mathbf{2}\cdot(\mathrm{Br_2py})_2$. Both isolated allylindium species $\mathbf{2}\cdot(\mathrm{Br_2py})_2$ and $\mathbf{3}\cdot(\mathrm{Me_2Npy})_2$ reacted with benzaldehyde to give the homoallylic alcohol almost quantitatively (see Supporting Information). Therefore, the isolated species reflect the active species generated in conventional indium-mediated synthetic procedures by using a polar organic solvent that could coordinate with the indium center. In our previous study, the isolated and analyzed allylindium species resulting from transmetalation had bulky substituents on the reaction site and inadequate reactivity with aldehydes.[6] However, the indium species obtained in the present study, **2** and **3**, have a cinnamyl group and showed high reactivity. It should be noted that, in this study, the actual reactive species were directly isolated and analyzed. Most importantly, the reductive system generated two independent species, and thus their reactivity should be considered for investigating the reaction course.

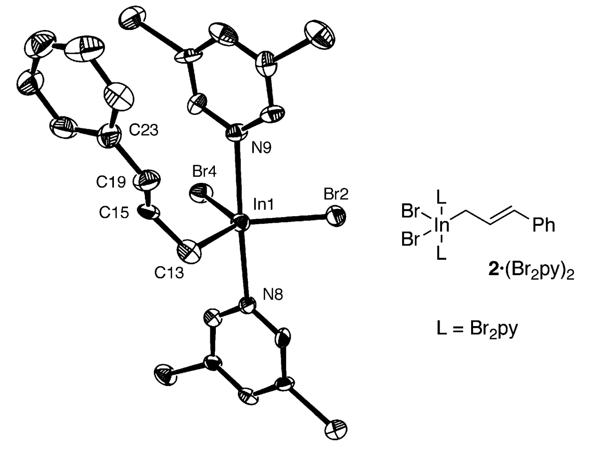


Figure 2. ORTEP drawing of cinnamylindium dibromide [$\mathbf{2}\cdot(\mathrm{Br_2py})_2$] (all hydrogen atoms are omitted for clarity). Selected bond lengths [Å]: In1–C13 2.181(11), C13–C15 1.504(16), C15–C19 1.284(19), C19–C23 1.442(18), In1–Br2 2.5249(13), In1–Br4 2.5346(14), In1–N9 2.474(11), In1–N8 2.444(11). Selected bond angles [°]: Br2–In1–Br4 113.66(4), Br4–In1–C13 117.5(2), C13–In1–Br2 128.9(2), N9–In1–N8 174.5(3).

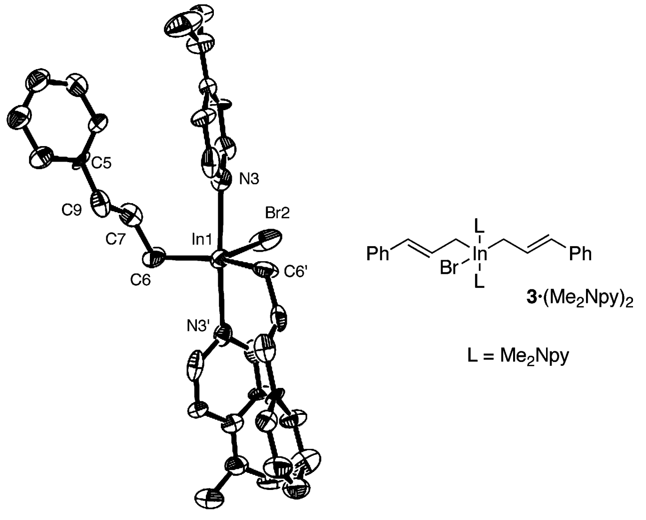
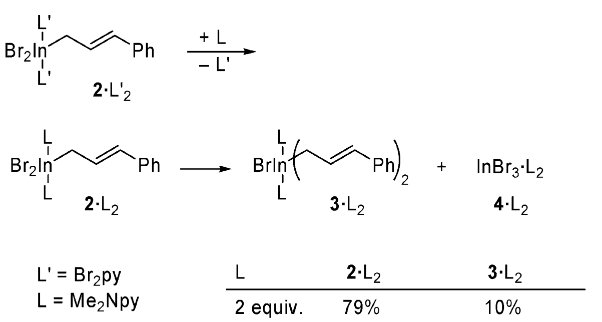


Figure 3. ORTEP drawing of dicinnamylindium bromide [$\mathbf{3}\cdot(\mathrm{Me_2Npy})_2$] (all hydrogen atoms are omitted for clarity). Selected bond lengths [Å]: In1–C6 2.146(2), C6–C7 1.511(4), C7–C9 1.350(5), C9–C5 1.443(5), In1–Br2 2.6212(12), In1–N3 2.483(2). Selected bond angles [°]: Br2–In1–C6 106.80(9), C6–In1–C6′ 146.40(13), C6′–In1–Br2 106.80(9), N3–In1–N3′ 174.15(11).

The effect of the added ligand on the ratio of generated species **2**/**3** was investigated [Equation (2)], because $\mathrm{Me_2Npy}$ largely changed the ratio as shown in Figure 1. To the isolated monoallylindium compound $\mathbf{2}\cdot(\mathrm{Br_2py})_2$ the aminopyridine $\mathrm{Me_2Npy}$ (2 equiv.) was added to give 10% of $\mathbf{3}\cdot(\mathrm{Me_2Npy})_2$ and $\mathbf{2}\cdot(\mathrm{Me_2Npy})_2$ (79%). Addition of 4 equiv. of $\mathrm{Me_2Npy}$ afforded a larger amount of



L' = Br₂py
L = Me₂Npy
CDCl₃, 30min (10 h)*

L	2·L₂	3·L₂
2 equiv.	79%	10%
4 equiv.	48% (30%)*	25% (34%)*

(2)

3·$(Me_2Npy)_2$ with a decreasing amount of **2**·$(Me_2Npy)_2$. In this system, $InBr_3$ was presumably formed, and its complexation by the ligand could be a driving force that affords **3** from **2**. An added ligand controlled the ratio of generated species **2**/**3**.

Conclusions

The structures of reductively generated allylindium species from a cinnamyl bromide/indium(0) system in THF were determined by X-ray crystallography, and were found to be mono- and diallylindium(III) species. This finding leads to new aspects of synthetic organic chemistry with allylindium compounds under reductive conditions when considering the reaction mechanism. The diallyl species had a higher reactivity than the monoallyl one for carbonyl addition. Ligands on the indium center controlled the ratio of generated species of monoallyl-/diallylindium species. Analysis of allylindium species generated in aqueous media[13] and other types of allylic species, including unsubstituted versions, are now under investigation.

Experimental Section

Generation and Isolation of Allyllindium Species 2·$(Br_2py)_2$: Cinnamyl bromide (**1**) (1.5 mmol, 0.297 g) was added to indium powder (1.0 mmol, 0.115 g) in THF (8 mL) at room temperature. After stirring for 30 min, 3,5-dibromopyridine (2.0 mmol, 0.474 g) was added to the mixture, which was stirred for 30 min. The solvent was evaporated to give a yellow solid. This solid was washed with hexane (5 × 10 mL) to give a pure product as a pale yellow solid (0.34 g, 40 %). A suitable crystal for X-ray analysis was obtained after recrystallization from dichloromethane solution. ^1H NMR (400 MHz, $[D_8]$THF): δ = 8.57 (s, 4 H), 8.20 (s, 2 H), 7.19 (d, J = 7.7 Hz, 2 H), 7.13 (dd, J = 7.7, 7.2 Hz, 2 H), 7.01 (d, J = 7.2 Hz, 1 H), 6.47 (t, J = 15.4, 8.7 Hz, 1 H), 6.26 (d, J = 15.4 Hz, 1 H), 2.23 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $[D_8]$THF): δ = 148.9, 141.2, 138.3, 129.7, 128.2, 126.3, 125.8, 125.1, 120.7, 26.1 ppm.

Generation and Isolation of Allyllindium Species 3·$(Me_2Npy)_2$: Cinnamyl bromide (**1**) (2 mmol, 0.396 g) was added to indium powder (2 mmol, 0.230 g) in THF (8 mL) at room temperature. After stirring for 30 min, 4-(dimethylamino)pyridine (4 mmol, 0.488 g) was added to the mixture, and the resulting precipitate was filtered off. The filtrate was concentrated to give a yellow solid, which was washed with hexane (3 × 10 mL) to give a pure product as a pale yellow solid (0.263 g, 0.396 mmol, 40 %). A suitable crystal for X-ray crystal-structure analysis was obtained after recrystallization from dichloromethane solution. ^1H NMR (400 MHz, $[D_8]$THF): δ = 8.08 (d, J = 6.5 Hz, 4 H), 7.05 (t, J = 8.0 Hz, 4 H), 7.00 (d, J = 8.0 Hz, 4 H), 6.91 (t, J = 7.0 Hz, 2 H), 6.49–6.41 (m, 6 H), 5.89 (d, J = 15.2 Hz, 2 H), 2.90 (s, 12 H), 1.98 (d, J = 9.0 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, $[D_8]$THF): δ = 154.6, 149.0, 139.5, 133.4, 127.9, 124.8, 124.7, 124.4, 122.8, 106.4, 38.1, 25.5 ppm.

X-ray Crystallography: CCDC-735713 [**2**·$(Br_2py)_2$] and -735712 [**3**·$(Me_2Npy)_2$] contain the supplementary crystallographic data for this paper, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Experimental procedures.

Acknowledgments

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[8] Some metallic indium had remained in one case of **1**/In = 1:1, and almost all indium was consumed in a case of of **1**/In = 1.5:1.

[9] When D_2O (THF/D_2O ≈ 2:1, v/v) was added to a solution of the in situ generated allylindium compounds (mixture of **2**/**3**), no decomposition was observed at room temp. after 1 h. After ca. 10 h, the amount of **3** had slightly decreased. Therefore, **2** and **3** are independent species, and the generated allylindium compounds are relatively stable in water.

[10] a) In a related system with allylindium, the structure of propargylindium generated under reductive conditions was reported based on X-ray analysis: B. Xu, M. S. Mashuta, G. B. Hammond, *Angew. Chem. Int. Ed.* **2006**, *45*, 7265–7267; b) B. Xu, G. B. Hammond, *Chem. Eur. J.* **2008**, *14*, 10029–10035.

[11] The NMR spectrum of pure isolated **2**·L_n after recrystallization was not obtained because of the small amount available. An

alternative method by transmetallation proved the formation of a monoallylindium species.

[12] ^{1}H NMR spectroscopic data for an oxygen-substituted allylsilane, whose methylene signals showed an upfield shift: a) N. L. Lewis, *J. Am. Chem. Soc.* **1990**, *112*, 5998–6004; b) W. Uhlig, *J. Organomet. Chem.* **1993**, *452*, 29–32.

[13] Because the solvent effect might be important for the generation of allylindium compounds, the reductive formation of allylindium compounds in aqueous media would be another interesting topic worthy of investigation.

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