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Characterization of the Nucleophilic Allylindium Species Generated from Allyl Bromide and Indium(0) in Aqueous Media

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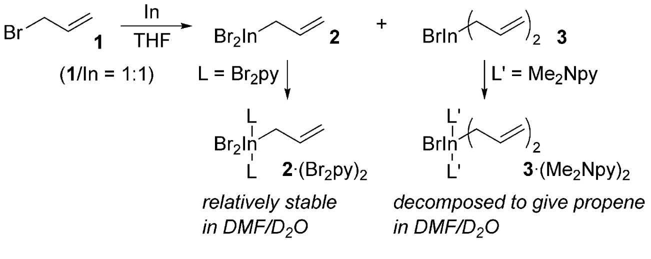
The reductive system of allyl bromide and indium(0) in water generated monoallylindium(III) dibromide and diallylindium(III) bromide. These compounds were characterized by X-ray analysis after complexation with 3,5-dibromopyridine or 4-(dimethylamino)pyridine, respectively. Both isolated complexes showed high nucleophilicity and reacted with benzaldehyde to give the allylation product. The diallylindium(III) bromide was less stable in water than the monoallylindium(III) dibromide. The reaction of the diallylindium(III) with benzhydrol gave a (μ-alkoxido)indium species that showed nucleophilicity. This result suggests that allyl(μ-hydroxido)indium also acted as a nucleophile in an aqueous Barbie-type reaction system.

Introduction

Allylindium compounds have been widely employed for effective carbon–carbon bond formation.[1,2] There are two methods by which allylindium compounds are generated: transmetalation[3,4] and reduction.[5,6] The structural determination of indium species, however, is rarely reported. Recently, we used X-ray crystallographic analysis to determine the structures of the allylindium(III) species generated in organic solvents both by tin/indium transmetalation[7] and by reduction methods.[8] X-ray analysis required stabilization of the indium species by use of appropriate substituents on the allylic carbon chain and ligands to the indium center.[9,10] Many practical synthetic protocols use a reductive method in aqueous media to synthesize allylindium compounds. These protocols were more stereoselective and effective than those that used organic media.[11] Generally, aqueous conditions are thought to generate allylindium(I) compounds based on the NMR spectroscopic data reported by Chan.[11g] The $\mathrm{In^I}$ species was confirmed by NMR spectroscopy by comparison with the species prepared from an organomercury compound. Recently, a structural analysis of an allylindium compound based on ESI-MS data, conductivity measurements, and ^{1}H NMR spectrosopy was reported.[12] However, unambiguous determination of the structure remains to be performed, and X-ray analysis is required. There is still a serious lack of research on unsubstituted allylindium compounds (namely allylindium itself) in aqueous media. In the present study, we used X-ray crystallographic analysis to characterize the unsubstituted allylindium compound generated in water, and based on these data we speculate on the active species involved in the reaction course.

Results and Discussion

Before investigating the aqueous system, we examined the structure of unsubstituted allylindium, which had never been isolated before, in an organic solvent. Mixing of allyl bromide (**1**) with indium(0) in THF gave two sets of allyl signals in the NMR spectrum. Two compounds were independently crystallized by mixing with different pyridine ligands: allylindium dibromide **2**·$(\mathrm{Br_2py})_2$ complexed with 3,5-dibromopyridine and diallylindium bromide **3**·$(\mathrm{Me_2Npy})_2$ complexed with DMAP (Scheme 1). The two allylindium compounds were analyzed by using X-ray crystallography.[13]



Scheme 1. Isolation of two types of generated allylindium species in THF and their stability in aqueous media.

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The ORTEP drawings of **2**·$(Br_2py)_2$ and **3**·$(Me_2Npy)_2$ are shown in Figure 1. In either case, the indium center has a trigonal-bipyramidal coordination sphere. These are the first reported examples of a crystallographic characterization of unsubstituted allylindium species as nucleophiles.[14]

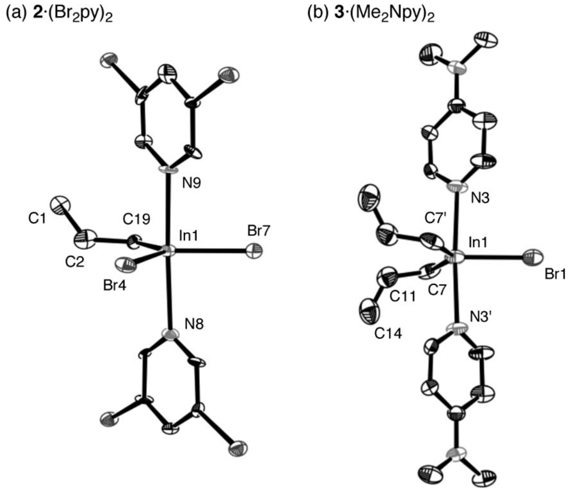
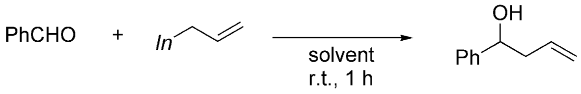


Figure 1. ORTEP drawing of (a) allyllindium dibromide **2**·$(Br_2py)_2$ and (b) diallylindium bromide **3**·$(Me_2Npy)_2$ (all hydrogen atoms are omitted for clarity).

The stability of isolated **2**·$(Br_2py)_2$ and **3**·$(Me_2Npy)_2$ was examined in aqueous media. When monoallylindium compound **2**·$(Br_2py)_2$ was dissolved in DMF/D_2O at room temp. for 30 min, almost no decomposition was observed by NMR spectroscopy.[15] By contrast, after 10 min, **3**·$(Me_2Npy)_2$ had decomposed, releasing propene. These results suggest that **3**·$(Me_2Npy)_2$ is much less stable in water than **2**·$(Br_2py)_2$ (Scheme 1). The addition of **2**·$(Br_2py)_2$ to a suspension of benzaldehyde in water with stirring at room temp. for 1 h gave the homoallyl alcohol in 77% yield [Equation (1)]. The reaction under the same conditions with **3**·$(Me_2Npy)_2$ resulted in a lower yield (51%). In homogeneous aqueous media, DMF/H_2O (3:1), similar results were observed with a 95% yield from **2**·$(Br_2py)_2$ and 88% from **3**·$(Me_2Npy)_2$. The lower yields from **3**·$(Me_2Npy)_2$ were caused by decomposition due to proton quenching of **3**·$(Me_2Npy)_2$. In fact, premixing of the allylindium species in DMF/H_2O for 2 min followed by loading of benzaldehyde gave significantly different results for **2**·$(Br_2py)_2$ and **3**·$(Me_2Npy)_2$ [Equation (2)]. Monoallylindium **2**·$(Br_2py)_2$ gave the product in 68% yield, whereas diallylindium **3**·$(Me_2Npy)_2$ resulted in recovery of the starting benzaldehyde unreacted.



allylindium	solvent	yield
2·$(Br_2py)_2$	H_2O	77%
3·$(Me_2Npy)_2$	H_2O	51%
2·$(Br_2py)_2$	DMF/H_2O (3:1)	95%
3·$(Me_2Npy)_2$	DMF/H_2O (3:1)	88%

(1)

As no NMR spectra of allylindium generated in water were previously reported in the literature,[11g] we performed an NMR study (Figure 2). Allyl bromide (**1**) was mixed with indium(0) in D_2O with stirring, and the resulting heterogeneous mixture was monitored by ^1H NMR (Figure 2a). The allyl signals (red) correspond with the allylindium(I) species assumed in the literature.[11g] However, we confirmed the monoallylindium(III) species in the following experiment. Loading of $[D_7]$DMF caused the hetero-

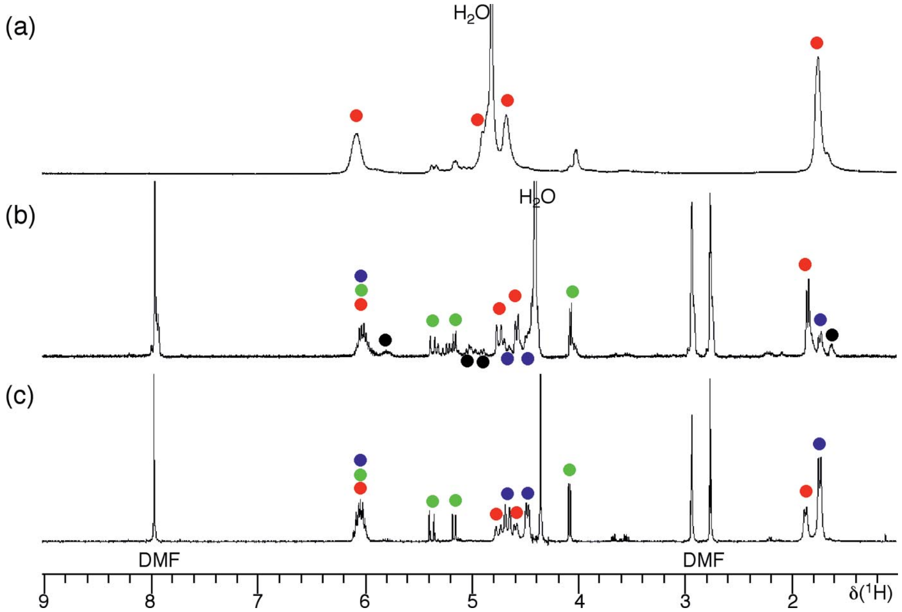
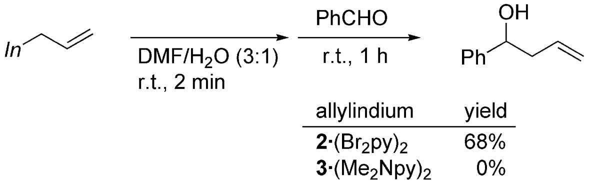
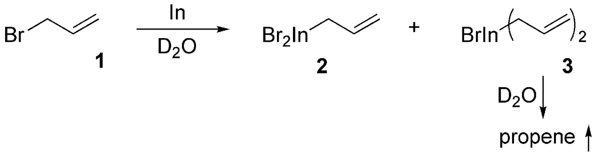


Figure 2. ^1H NMR spectra under various conditions (red, **2**; green, **3**; blue, **1**; black, propene). (a) Mixing of **1** with In^0 in D_2O at room temp. for 30 min. (b) Addition of $[D_7]$DMF to the mixture (a), giving a DMF/D_2O (3:1) solution. (c) Mixing of **1** with In^0 in DMF at room temp. for 30 min and addition of D_2O, giving a DMF/D_2O (3:1) solution.



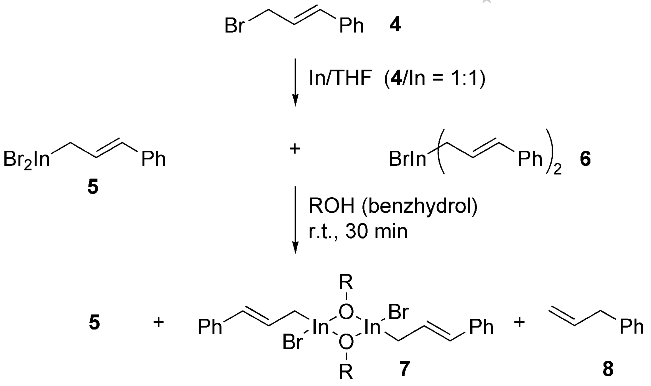
(2)

geneous sample to become homogeneous, giving the spectrum in (Figure 2b) (DMF/D_2O = 3:1) that indicates the presence of monoallylindium dibromide (**2**) (red), diallylindium bromide (**3**) (blue), allyl bromide (**1**) (green), and propene (black). These signals are consistent with Figure 2c, which shows authentic samples of **2** and **3** in DMF/D_2O (see Supporting Information). These results show that the reductive system that used **1** and In^0 in water gave monoallylindium(III) dibromide (**2**) and diallylindium bromide (**3**), similar to the results obtained with an organic solvent. Although a lower ratio of **3** was observed in the aqueous system owing to its faster decomposition in water,[16] **3** survived in the system [Equation (3)]. Therefore, diallylindium compound **3** should be considered in a Barbier-type reaction course in the coexistence of carbonyl compounds.



(3)

To further discuss the results of the NMR study shown in Figure 2, we were interested in the process by which the diallylindium species undergoes decomposition. A relatively stable allylindium compound [cinnamylindium prepared from cinnamyl bromide (**4**) and In^0] was investigated in alcohol instead of water as a model reaction of diallylindium decomposition in water. The allylic species generated from cinnamyl bromide with indium(0) in THF, i.e., monoallylindium compound **5** and diallylindium compound **6**,[8] were mixed with benzhydrol with stirring at room temperature for 30 min and analyzed by using NMR spectroscopy.[17] As expected, the monoallylindium compound **5** remained unchanged, and the diallylindium compound **6** was converted into the allylindium alkoxide **7** along with the generation of 3-phenylpropene (**8**) (Scheme 2).



Scheme 2. Reaction of an allylindium species with benzhydrol to give allyl(μ-oxido)indium compound **7**.

X-ray analysis demonstrated that **7** was a (μ-alkoxido)-indium complex (Figure 3). The indium atom has a tetrahedral geometry with bridging oxygen atom, bromide and allyl groups. The isolated allylindium compound **7** showed a considerable reactivity toward benzaldehyde to give the addition product in 47 % yield [Equation (4)]. This structure supports the generation of allyl(μ-hydroxido)indium species **9** in an aqueous **1**/In^0 system.

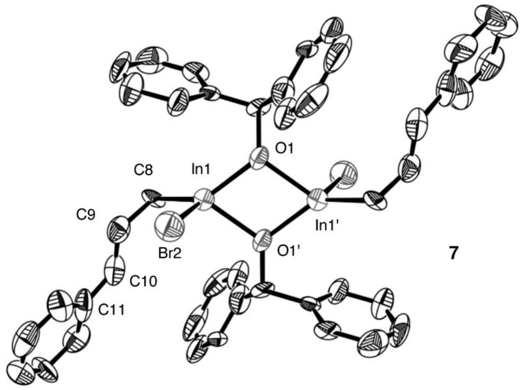
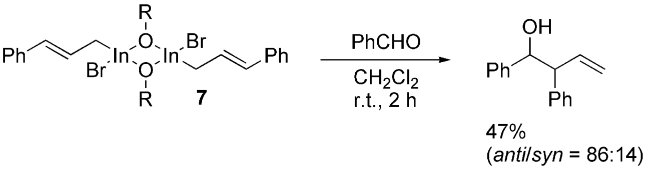


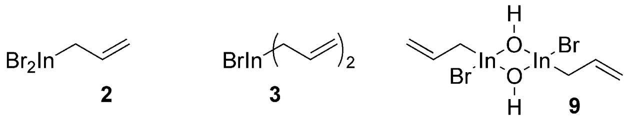
Figure 3. ORTEP drawing of (μ-alkoxido)allylindium compound **7** (all hydrogen atoms are omitted for clarity).



(4)

Conclusions

We identified the species generated in the system of allyl bromide with In^0 in water to be monoallylindium(III) compound **2**, diallylindium(III) compound **3**, and the μ-oxido form **9** (Scheme 3). The isolation of allyl(μ-hydroxido)-indium with stabilizing bulky substituents is currently under investigation.



Scheme 3. Allylindium species generated in water.

Experimental Section

Allylindium Dibromide–3,5-Dibromopyridine Complex 2·$(Br_2py)_2$: Allyl bromide (3.1 mmol, 0.376 g) was added to indium powder

(3.1 mmol, 0.3514 g) in THF (10 mL) at room temperature. After stirring for 30 min, 3,5-dibromopyridine (6.0 mmol, 1.420 g) was added to the mixture, followed by stirring for 30 min. The solvent was evaporated to give a white solid. This solid was washed with hexane (5 × 10 mL) to give a pure product as a white solid (0.53 mmol, 0.42 g, 17%). A suitable crystal for X-ray analysis was obtained after recrystallization from THF solution. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 4 H), 8.20 (s, 2 H), 6.02–5.90 (m, 1 H), 4.86 (d, J = 17.9 Hz, 1 H), 4.78 (d, J = 9.6 Hz, 1 H), 2.31 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 143.4, 136.4, 121.4, 111.5, 26.9 ppm.

Diallylindium Bromide–4-(Dimethylamino)pyridine Complex 3·($Me_2Npy)_2$: Allyl bromide (3 mmol, 0.363 g) was added to indium powder (3 mmol, 0.344 g) in THF (8 mL) at room temperature. After stirring for 30 min, 4-(dimethylamino)pyridine (6 mmol, 0.733 g) was added to the mixture, followed by stirring for 16 h. The solvent was evaporated to give a white solid, which was washed with hexane (3 × 10 mL) to give a product (a slightly excess amount of DMAP remained) as a white solid (0.49 g, purity 81%, 0.76 mmol, 25%). A suitable crystal for X-ray analysis was obtained after recrystallization from THF solution. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, J = 6.3 Hz), 6.50 (d, J = 6.3 Hz), 6.10 (ddt, J = 17.9, 9.6, 8.7 Hz, 2 H), 4.73 (dd, J = 17.9, 0.9 Hz, 2 H), 4.54 (dd, J = 9.6, 0.9 Hz, 1 H), 3.02 (s, NMe_2), 1.94 (d, J = 8.7 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 148.9, 139.5, 107.6, 106.5, 38.9, 24.0 ppm.

(μ-Alkoxido)cinnamylindium Compound 7: Cinnamyl bromide (3.0 mmol, 0.59 g) was added to indium powder (3.0 mmol, 0.34 g) in THF (10 mL) at room temperature. After stirring for 30 min, benzhydrol (6.0 mmol, 1.10 g) was added to the mixture, followed by stirring for 30 min. The solvent was evaporated to give a mixture. It contained monocinnamylindium compound **5**, allylbenzene (**8**), and (μ-alkoxido)cinnamylindium compound **7** were observed in the ^{1}H NMR spectrum (CCl_3). This mixture was washed with hexane (5 × 10 mL) to give a pure product as a white solid (0.18 mmol, 0.18 g, 6%). A suitable crystal for X-ray analysis was obtained after recrystallization from dichloromethane solution. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, J = 6.8 Hz, 8 H), 7.37–7.16 (m, 22 H), 6.10 (s, 2 H), 5.86 (d, J = 15.5 Hz, 2 H), 5.70 (dt, J = 15.5, 8.7 Hz, 2 H), 1.40 (d, J = 8.7 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 137.6, 129.3, 128.6, 128.5, 128.4, 126.8, 126.5, 126.4, 125.7, 79.9, 24.7 ppm.

CCDC-781656 [**2**·(Br_2py)], -781655 [**3**·($Me_2Npy)_2$] and 781657 (**7**) contain the supplementary crystallographic data for this paper. 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 and spectroscopic data for allylic compounds.

Acknowledgments

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[13] The addition of 3,5-dibromopyridine effectively crystallized allylindium compound **2** from the mixture of **2** and **3**. The addition of aminopyridine shifted the equilibrium toward **3**. This situation has been reported in our previous paper.[8]

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[15] Very slow decomposition occurred, and only half the amount of **2**·(Br$_2$py)$_2$ was consumed after 1 d.

[16] The reactivity of **2** and **3** as electrophiles is of the same order (diallylindium bromide > allylindium dibromide) as discussed in our previous report.[8]

[17] The reaction of the allyl bromide/water system was too fast to be observed. Benzhydrol was used instead of water because water caused a too fast decomposition.

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